PHARMACOLOGY
AND
DENTAL THERAPEUTICS

PHARMACOLOGY AND DENTAL THERAPEUTICS

A Textbook for Students and Practitioners

BY

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NINTH EDITION, REWRITTEN AND REVISED

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Dedicated

to the memory of

HORACE WELLS

who one hundred years ago

discovered anesthesia

PREFACE TO THE NINTH EDITION

The ninth edition of *Pharmacology and Dental Therapeutics* has been brought up to date with the *United States Pharmacopoeia* XII, the *National Formulary* VII, *New and Nonofficial Remedies* (1944), and *Accepted Dental Remedies* (1944). The entire contents of the book have been rearranged, the drugs being grouped under their chief sites of action. This gives an organization of content which facilitates the study of drugs under their therapeutic uses and concomitantly articulates pharmacology with the other preclinical sub jects—anatomy, physiology, chemistry, etc. The text is now more readable, with a thread of continuity not only in each chapter but throughout the book.

The contents of this edition are divided into two sections: the first on general pharmacology and the second on dental therapeutics. Many new drugs have been included; some have only a limited usefulness in dental practice but are necessary for a comprehensive study of drugs. The section on dental therapeutics applies the science of pharmacology to the treatment of oral diseases and was especially designed to serve the practitioners of dentistry in keeping abreast with the current knowledge of drug usage. The chapter on prescription writing has been enlarged and simplified, making the writing of prescriptions an easier procedure. Many prescriptions and preparations useful in dental practice are included.

Several chapters, including those on the central nervous system, local and general anesthetics, vitamins, sulfonamides and penicillin, analgesics, dental therapeutics, etc., have been rewritten. The other chapters have been rearranged and brought up to date.

As the compilation of the material for the ninth edition was very extensive, it was necessary to draw freely from original papers and books. The reviser wishes to thank all of the authors from whose works he has drawn so freely and to acknowledge formally a few to whom he is particularly indebted, as Harry Archer, Floyd D. Ostrander, James Aiguier, J. R. Blayney, H. Youngken, W. Bastedo, Edmunds and Gunn, Goodman and Gilman, F. R. Davison, B. Harrow, and Jenkins and Hartung.

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PREFACE TO THE EIGHTH EDITION

The purpose of this book is to present the principles of pharmacology and to apply this information to the science of therapeutics. Every effort has been made to delete the obsolete drugs and theories, and to include both the more useful drugs and later conceptions of pharmacodynamics and therapeutics.

The title of this edition is changed from *Dental Materia Medica and Therapeutics* to *Pharmacology and Dental Therapeutics* to conform with the change in emphasis from materia medica to pharmacodynamics.

The drugs and preparations mentioned in this revision are chiefly those listed in the Eleventh Decennial Revision of the *United States Pharmacopoeia,* the sixth edition of the *National Formulary, New and Nonofficial Remedies* for 1940, and the sixth edition of *Accepted Dental Remedies.*

The reviser has followed closely these authentic texts, thus giving to this edition a standardization of names and dosages acceptable to both the American Dental Association and the American Medical Association.

New drugs were included whenever their importance warranted it. As the dental office is not the place for drug research the practitioner should wait for the Councils of the American Dental Association or the American Medical Association to approve the use of these remedies before incorporating them into daily practice.

The material pertaining to therapeutics follows more closely the expressed opinions of the Council on Dental Therapeutics and of the Council of Pharmacy and Chemistry than the evidence presented in individual research publications.

Many of the early references are omitted, and late ones substituted. This is not to belittle the importance of the former contributions but to give busy readers more available and current material.

The reviser wishes to give credit to the many excellent authorities from whom he has drawn freely, namely: Bard, Bastedo, Blayney, Clark, Cushny, Davison, Finlay, Goodman and Gilman, Harrow, McGehee, McGuigan, and countless others. He also wishes to thank publicly Dr. Frank J. Slama for his aid in proofreading, and Miss Dorothy Rice for her invaluable aid in typing and arranging this material.

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PREFACE TO THE FIRST EDITION

A systematic classification of drugs which shall answer all purposes has never been, and probably never will be, successfully arranged. Such a classification will, according to the standpoint from which the subject is treated, evince individual trend of thought. The chemist, for example, prefers a classification according to the chemical relationship of the drugs, the pharmacologist is principally interested in a classification according to the physiologic action of drugs, while the clinician groups the drugs according to their therapeutic effects. The author, guided by extensive classroom experience and clinical practice, has made an effort to point out how pharmacologic research and clinical observations may be advantageously combined in the rational use of remedial agents for the purpose of favorably influencing disease. The entire subject matter is, therefore, treated from the standpoint of the pharmacotherapeutist.

The practice of dentistry requires, in addition to specific pharmaceutic preparations, quite a large number of remedies which are seldom employed by the medical practitioner, unless used by him for totally different purposes. These remedies are generically termed dental remedies, and consequently their importance demands special discussion. To draw a definite line of demarcation between dental and general remedies not only is impossible but is distinctly undesirable. Frequently conditions arise where a knowledge of general remedies is absolutely necessary for the dental practitioner—as, for example, the treatment of certain phases of pericementitis requires the administration of uric acid solvents; specific infection calls for cathartics, antipyretics, etc.; and the mitigation of pain may necessitate general anodynes.

The progress of dental pharmacotherapeutics has not kept pace with the remarkable advances made in the technical branches of dentistry. The unsatisfactory classification of dental remedial agents is largely due to a gross disregard of the progress made in general pharmacology and pathology. The principal part of operative dentistry is surgery, but unfortunately the average practitioner applies the same mechanism to drug action and, expecting too much from a drug, is frequently disappointed.

The difficulties which presented themselves to the author in systematizing the subject were the many conflicting statements found in literature relative to the action of dental remedies. An effort has

been made to avoid vague information and to elucidate only clinical facts which have been established by pharmacologic research. Both factors are essential in determining the true value of the action of a drug. The pharmaceutic descriptions of chemicals and drugs, and their preparations and doses, are in conformity with those given in the latest editions of the Pharmacopoeias of the United States and Great Britain.

The author acknowledges his indebtedness to workers in both general and dental pharmacotherapeutics, and especially to the textbooks of A. Cushny, R. Kobert, R. Heinz, T. Sollmann, and many others which he has freely consulted. He desires to thank his friends, Professor Carl Jung, of Berlin, for the use of the photomicrographs of tooth powder preparations, and Doctors James A. Brown and L. Neuhoff for assistance in the preparation of most of the original illustrations. He also acknowledges his obligations to the S. S. White Dental Manufacturing Company, Ransom & Randolph Company, Lennox Chemical Company, Gebauer Chemical Company, Modern Medical Company, Consolidated Dental Manufacturing Company, Wm. Meyer Company, R. S. Squibb & Sons, Burroughs Wellcome & Co., and Parke, Davis & Co. for the use of various illustrations of dental appliances.

H. P.

Washington University Dental School,
St. Louis, September, 1909.

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PHARMACOLOGY AND DENTAL THERAPEUTICS

PART I

CHAPTER 1

INTRODUCTION TO PHARMACOLOGY AND DENTAL THERAPEUTICS

The practice of medicine is as old as the human race. However crude the efforts may have been, we are justified in believing that men have tried from the earliest times to render assistance to their fellowmen in case of illness. Very likely these first attempts were principally of a surgical nature, and only later internal diseases received attention. In due time the natural instinct inherent in both man and beast led to the utilization of the products of their immediate surroundings—primarily of herbs, roots, etc., and later of animal drugs. With the progress of civilization and the entering of religion into the routine duties of daily life, diseases were mostly regarded as punishments from the gods, and it was left to the priests to care for both the spiritual and the bodily welfare of their congregations. Among the less cultured, the treatment of diseases consisted of administering mysterious concoctions, accompanied by the claptrap of the conjuror, a remnant of which we find in the present practice of the medicine man of the aborigines. With the evolution of the races, the practice of selecting suitable remedies for certain diseases became a matter of empiric observation and study. Instinctive empiricism selected a number of remedies especially suited for its purposes—those which were used to remove certain dangerous symptoms, or to bring about and strengthen other symptoms which apparently had a beneficial influence upon the disease. Irritants and counterirritants applied externally and, to a limited extent, internally were probably the first therapeutic attempts at influencing diseased conditions. They were followed by those remedies which mitigate irritation and allay inflammation, and finally by those which alleviate pain. Empiric medicine is the foundation of the scientific therapeutics of all nations. Naturally, the remedial agents differ with each nation. Systematic search for new remedies was introduced much later as a result of close observation of the action of certain drugs.

The early history of dental medicine is so closely interwoven with that of medical therapeutics that it is impossible to distinguish it from its mother science. The Babylonians, Egyptians, Assyrians, Hebrews, Hindus, Greeks, and Romans were the early cultured inhabitants of whom historical records exist. The Egyptian medical history is principally recorded in the various papyri, especially those of Ebers, Brugsch, and Smith, which probably cover the period of 3700 to 1500 B.C. The Egyptian physicians were largely specialists, and it is very probable that some were selected to care for the teeth. Most of the dental remedies found in the papyri consist of pastes, powders, plasters, decoctions, etc. The treatment of abscesses, dental caries, and loose teeth seems to have been known. The Hindus were apparently very proud of their teeth. It is recorded that the use of tooth powders and washes, and especially the use of the tooth cleaner, "rinacarya," were necessities of their daily toilet. As a toothpick they employed a bitter tasting wood which when chewed produced a fibrous bundle used as a brush for the gingiva and the teeth. The aborigines of the western coast of Africa still use the wood of the sissako and the molungo tree for such purposes. In the writings of Hippocrates and Pliny, frequent allusion is made to drugs which were especially advocated for diseases of the teeth and the mouth. With the simpler remedies, as hyssop, licorice, dog's milk, goat's butter, etc., many disagreeable substances, especially of the animal kingdom, were recommended. In Pliny's writings we find, among other dental suggestions, that "if one wishes to be free from toothache, one should eat a whole mouse twice a month."

The freeborn Roman looked upon the practice of medicine as a handicraft, the pursuit of which was not compatible with the dignity of a "civis Romanus." The practice of medicine in Rome was carried on by "servus medicus" (slaves), or the "pater familias." Some of these latter representatives of lay medicine gathered together quite an extensive knowledge of the healing art, and their records furnish some of the most valuable data to the medical historians. Celsus, Pliny, and Cato are examples of Roman lay practitioners who were voluminous and fruitful littérateurs on this subject. To the cultured Romans, who were highly conscious of the blessings of personal hygiene, the service of some practitioner who would keep their masticating organs in condition was a matter of necessity.

Pedanius Dioscorides, or Dioskurides of Anazarbus (Asia Minor), lived during the second half of the first century. Nothing definite is known concerning his life. It seems, however, that at one time

he was engaged as an army surgeon, and during his sojourn with the Roman legions visited many countries. As he states of himself, from early youth he was passionately fond of nature study, and his love for botany is largely responsible for his minute and accurate description of the many hundred specimens of vegetable drugs, of which he gives a detailed account in his *Materia Medica.* Incidentally, with the creation of this work the term *materia medica* was introduced into general medicine. The volume is divided into five books and contains descriptions of nearly one thousand drugs, primarily of the vegetable kingdom, although many animal drugs and quite a few mineral compounds are included. Dioscorides has depicted the medicinal plants so accurately that with his aid, more than 1900 years later, botanists were able to locate the greater majority of these plants in the respective countries. For more than sixteen centuries this important work has formed the basis of all teachings in botany and pharmacognosy. It has been translated into most of the languages of the cultured nations, and innumerable editions have appeared. In the various libraries of Europe and the United States there are about twelve more or less complete codices (manuscripts) of this work of Dioscorides. During a careful perusal of this most interesting text, we have been able to locate more than one hundred passages referring to diseases of the teeth and their adnexa.

The patron saint of dentistry, St. Apollonia, was canonized in Rome about A.D. 300. Being a Christian, St. Apollonia was tortured by her persecutors by having her teeth extracted, one by one, and finally suffered death upon the pyre. Her martyrdom is commemorated on the ninth of February each year. Remains of her skeleton are preserved in the various churches of Rome, Naples, Cologne, Antwerp, Brussels, and Quebec, and excellent pictures of the saint by Guido Reni, Carlo Dolci, and others are found in Milan, Florence, and other cities. The name of St. Apollonia is frequently mentioned in the prayer books of the Middle Ages, in prayers intended for the relief of toothache.

Prior to 1840, comparatively few important publications on dental therapeutics had appeared. The foremost literature of that time was published in France and England, and a few books of importance appeared in Germany. The United States was at this period principally concerned with the practical development of this new branch of the healing art. Dental textbooks, if used at all, were imported from England, or translations of French works were utilized. It must be remembered that the individual practitioner of this period was extremely jealous of any special knowledge which

he happened to possess and usually guarded this acquired proficiency very carefully. *No specific current dental literature was in existence at that time, and comparatively few journals tried to disseminate* the progress of medical or dental knowledge. The few existing journals were seriously hindered by the very limited postal facilities.

No specific books on dental remedies were then in existence, and the meager knowledge concerning the action of drugs was scattered through the few dental works, or was closely guarded by its possessor. Since then quite an extensive literature on dental materia medica and therapeutics has appeared, which furnishes ample proof of the immense strides made in this particular phase of dental science. The drugs which were principally applied as dental remedies were usually such agents as were also employed, according to their therapeutic indications, for disturbances of a similar pathologic nature in other parts of the body. Prominent among these remedies were the commoner astringents—nutgalls, oak bark, myrrh, alum, etc. Of the caustics, silver nitrate and the mineral acids, especially nitric acid, were much in vogue. Arsenic trioxide, as a powerful caustic, was recommended by Shearjashub Spooner (1836) for the purpose of destroying the dental pulp. Creosote and, to a still greater extent, phenol were favorite remedies employed as caustics, obtundents, and antiseptics. The antiseptic era was inaugurated by Joseph Lister in 1867, when he published his epoch-making paper entitled: "On the Antiseptic Principle of the Practice of Surgery." Many of the essential oils—the oils of clove, cinnamon, peppermint, spearmint, turpentine, etc.—were employed for centuries as obtunding and flavoring agents for mouth preparations. Of the true analgesic drugs, opium and aconite are the most important representatives. Innumerable formulas for tooth powders are found in the older works pertaining to the treatment of the teeth. These formulas consist largely of a base made from prepared chalk, burnt oyster shells, charcoal, pumice stone, cuttlefish bone, magnesia, mixed with vegetable powders, especially spices, and coloring materials.

A record concerning the more important events of the development of dental pharmacology would be incomplete if the discovery of general anesthesia were not mentioned, even if only *en passant*. To the dental profession of the United States belongs the honor of having introduced into surgery the first practical method of obtaining complete surgical anesthesia. The discovery of anesthesia is the greatest boon ever bestowed on mankind for the relief of suffering. With the introduction of nitrous oxide as a general anesthetic in 1844 by Horace

Wells, and that of ether by Crawford W. Long and William T. G. *Morton (1842-1846), the stimulation for further researches was initiated, and the future development of anesthesia followed.*

The remarkable achievements made by the progress of organic chemistry have materially aided the rapid development of pharmacotherapeutics. The discovery of the active constituents of plants—the alkaloids, glucosides, etc.—and their preparation in a pure state have furnished the dentist with a great many very important medicinal agents, which are now used by him in preference to the crude drugs. The discovery of morphine, the chief alkaloid of opium, by Sertürner, in 1805, marked a new era in pharmaceutical chemistry. It was rapidly followed by the discovery of atropine in belladonna leaves, cocaine in coca leaves, strychnine in nux vomica, etc., and at present there are probably very few medicinal plants of which the active constituents have not been isolated. These alkaloids allow an accurate dosage, and, to increase the rapidity of their action, F. Rynd (1844) and Alexander Wood (1853) introduced an important change in their administration, namely, the hypodermic method. The analysis of the alkaloids has led the way to the discovery of a number of synthetic compounds which proved to be, in some instances at least, superior in action to the natural alkaloids in the treatment of disease. For instance, after the chemical constituents of cocaine had been positively worked out, various groupings of the original molecules, with certain additions and omissions, furnished the many synthetic cocaine substitutes which since have proved to be of even greater value than the original cocaine. This is also true of many antipyretics, antiseptics, diuretics, diaphoretics, and a host of similar synthetic substances.

The newer remedies, which have been introduced into materia medica within the last century, owe their discovery almost exclusively to the chemical laboratory. They were discovered, not by accident, but by definite, previously outlined experimental work. The introduction of chloral hydrate as a hypnotic by Liebreich, in 1869, was probably the first step in modern experimental pharmacology. Lauder Brunton, in 1867, introduced amyl nitrite for the purpose of lowering the blood pressure; in 1884 Filehne discovered antipyrine, which was soon followed by acetanilid, phenacetin, and numerous other antipyretics. Not only did plant alkaloids furnish their quota of remedial agents, but the various glands of animals supplied active constituents for the treatment of disease. In 1894 Oliver, Schäfer,

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and Moore discovered the blood-pressure-raising principle of the suprarenal medulla, and since then a number of similar organic preparations have found their way into modern therapy.

The Aim of Therapeutics

The object of therapeutics is to cure disease, to relieve suffering, and to maintain health. Aside from the various technical means employed in relieving the sick, there are at the service of the dentist hygienic and physical measures and a number of substances which, when applied to, or introduced into, the body, bring about decided changes. These substances are known as drugs. The rational administration of drugs depends on a clear conception of their pharmacologic action. It is supposed, however, that the dentist possesses a comprehensive knowledge of the causes of disease and that he utilizes this knowledge, together with that of the physiologic and therapeutic action of drugs, in combating disease.

The materials and substances used as medicines comprise the animal, vegetable, and mineral kingdoms; and the study of their names, sources, physical and chemical properties, their preparations, doses, etc., is referred to as *materia medica.* The term materia medica, as stated above, was introduced by Dioscorides in the first century A.D. He published the first descriptive compilation of drugs, which were mostly vegetable in character, while the first collection of prescriptions, a formulary, was edited by Scribonius Largus. Drugs, *pharmaca,* are remedies; the study of drugs—that is, the changes which are induced in the living organism by their administration—is known as *pharmacology. Remedies,* in the broadest sense, are anything which cures, palliates, or prevents disease, and, consequently, include the utilization of all means and methods employed for the purpose of relieving the sick and favorably influencing the evolution of disease. *Medicines* are the material substances obtained from the animal, vegetable, and mineral kingdoms and are employed as therapeutic agents to produce a cure. They are refined, chemical, animal, vegetable, or synthetic substances. "Crude drugs" is a commercial term designating the natural animal or vegetable drugs as they are brought to the market. In a restricted sense, pharmacology is defined as a study of the changes which are produced by the action of drugs on healthy or diseased tissues, while the drug action itself is designated as *pharmacodynamics.* At the present time pure pharmacology is considered a department of biology; all biologic sciences, however, serve in some form or another as aids to general medicine.

In the teaching, as well as in the clinical application, of pharmacology a number of questions arise, which indicate its close relationship

to physiology and pathology. Through the action of drugs on normal tissues we are led to understand their effects on the disturbed functions of these tissues. In the experimental study of antipyretics, for instance, their influence on normal temperature as well as on increased temperature, together with an understanding of the nature of fever, is essential for the full comprehension of their therapeutic action. In its broadest conception, then, pharmacology is defined as the science of the changes which occur in healthy and diseased tissues under the influence of chemical substances. The application of remedial substances in the treatment of diseased conditions is based on our knowledge of pharmacology, and it is at present referred to as *pharmacotherapy,* a term which was introduced by Kobert (1887). It constitutes the most important branch of therapeutics. Some substances when ingested into the living body possess little medicinal value, or may act as poisons by bringing about dangerous or even fatal results. The study of their effects on tissues and the methods of their detection is known as *toxicology.* It is difficult to draw a distinct line between a drug and a poison; frequently only the quantity given or the method of its administration will determine whether the substance acts as a food, a drug, or a poison. A *poison* may be any substance which, independent of any mechanical action, uniformly causes disease or death when applied to, introduced into, or developed within the body. Any drug given in excess may cause dangerous or fatal symptoms.

The description of the drugs—their habitats, their composition, and their recognition—is spoken of as *pharmacognosy. Pharmacy* may be defined as the art of preparing medicines for use and dispensing them on the order of the therapeutist. The application of remedial measures for the purpose of relieving the sick and favorably modifying disease is referred to as *therapeutics.* In the past the administration of remedies was largely based on empiric conceptions, while modern dental practice endeavors to employ rational methods for the treatment of disease. *Empiric therapeutics* is the treatment of the sick by the alleviation of symptoms only, knowing nothing of the causation of the disease, while *rational therapeutics* implies basing the treatment on a thorough knowledge of the causative factors. A few diseases, as malaria, syphilis, anemia, etc., are directly amenable to drug action, and the remedies employed for such definite purposes are known as *specifics.* The introduction of salvarsan by Ehrlich-Hata in 1910 as an etiotropic remedy for the treatment of syphilis marked a new era in experimental therapy. Unfortunately only a very few of these specifics are at our command, and most of them were discovered by empiric medication. Within recent years rational methods

were adopted in the treatment of certain infectious diseases, which resulted in the discovery of definite, specific products—*serums, vaccines, antitoxins,* etc. Antitoxins act against the disease-producing toxins very much in the same manner as an antidote acts against a poison.

It is not always possible to treat the diseased organ directly, that is, to remove the causative factors of the disease. Sometimes it may be found that a disease has progressed so far as to exclude direct medication. The therapeutist may, however, be able to relieve the painful symptoms, or at least mitigate them. Symptomatic treatment is frequently of great benefit to the patient, who is principally interested in obtaining relief. The dentist must be able to judge, from the diagnosis of the disease, what remedies are indicated for his patient. He must know the best method of their administration, their dosage, the length of time they should be given, etc. If a disease has altered or destroyed parts of certain tissues or their functions, it does not necessarily follow that a permanent injury will result. A kidney may become so affected that its removal is indicated. This does not necessarily mean that the patient has to succumb, for the other sound kidney may be sufficiently active to carry on the work which nature had intended for the two organs, and the patient may still enjoy fairly good health. When, however, an organ is altered by a disease and its work cannot be accomplished by another organ—for example, if the valves of the heart have become weakened—drugs may be administered which will beneficially influence the symptoms, but they cannot cure the ailment.

Etiologic and symptomatic therapeutics are usually applied simultaneously. It should not, however, be understood that the symptoms of disease, even if they cause more or less annoyance to the patient, should be treated at once by drug administration. These subjective disturbances are frequently reactive measures of the body, created for the purpose of destroying the disturbing elements. It is immaterial whether these disturbances are the cause of the disease or its product. Fever is generally considered a means of self-defense marshaled by nature against the disturbing agents which have gained access to the tissues. Nature may, however, in her efforts to battle infection, go too far, and the fever may rise above 104° F. (40° C.), and, as a consequence, endanger not only the disease producers but also the body tissues. It is now the duty of the dentist to regulate the activity of the body and keep it in physiologic range by the application of suitable remedies. Again, in inflammation, which is recognized as a reaction of the tissues against injury, the

preliminary hyperemia is one of the foremost means of self-defense that the body possesses. The application of antiphlogistics is usually contraindicated in the early stages; if the pain that accompanies it becomes unbearable, then it is the duty of the dentist to counteract the eager efforts of nature by applying carefully selected remedies.

While modern dentistry has profited extensively by its association with pharmaceutical chemistry, it should not be forgotten that the old and well-tried remedies still hold important places in the armamentarium of the conscientious dentist. It is an illusion that only the new is valuable and reliable and the old a relic of the past. On the other hand, it should be remembered that there still prevail many notions regarding the action of certain remedies which are not in harmony with the rational conception of drug action. Some of these "pharmacologic fetishisms" are so deeply implanted that some practitioners have become slaves to them. For instance, the administration of potassium chlorate with the intention of exerting a beneficial influence on all forms of diseases of the mouth by the liberation of nascent oxygen is wholly unfounded.

Quite frequently the question is asked, "Do drugs ever cure?" Before an attempt is made to answer this question, we must understand what constitutes a "cure" and, incidentally, what is meant by health and disease. Whenever the normal equilibrium of cell activity is disturbed by a morbific cause, the organism reacts against it, producing a series of phenomena which is known as disease. Nature possesses as an inherent quality the power of re-establishing normal conditions, *vis medicatrix naturae*, i.e., to heal the disease. To aid nature in the reconstruction of her disturbed functions, the dentist applies remedial agents. Expressed in the words of Celsus, these two processes are defined as *natura sanat, medicus curat.* In the layman's mind there is not the remotest doubt that a drug or a combination of drugs possesses the power of producing a cure. He takes a headache powder with the definite expectation that it will cure his headache. Even Galen complained bitterly about this, saying: "The people want prescriptions!" Since the publication of Virchow's *Cellular Pathology* in 1858, and the subsequent advances made in experimental pharmacology, it was shown that drugs had no direct influence on the disease itself. As soon as this became known it was fashionable to laugh at the curative effects of drugs. This drug skepticism frequently follows the misunderstanding of drugs or the improper use of them. Unfamiliarity with the fundamental principles of incompatibility is frequently another cause of drug nihilism. While we are aware that the *vis medicatrix naturae* is the basis of a cure, we are

also aware that the action of drugs is instrumental in coaxing nature to bring about a favorable change in the prevailing conditions.

A small number of drugs, meeting everyday indications, should be employed for a large part of the dentist's work. Constant acquaintance familiarizes him with their nature and their uses, and with these few remedies his best work is generally done. Therapeutic nihilism is just as erroneous as the polypharmaceutical shotgun prescription of our ancestors. Practitioners of large experience usually obtain the best results with a few of the simple remedies, while many of the younger disciples of Aesculapius seize after new compounds because they do not know how to employ the old. When called to guide a patient through an illness, the dentist should be a watchman, and a therapeutist only when necessity arises.

Recapitulation of Pharmacologic Terms

PHARMACOLOGY is the science of drugs, particularly their action and effect on normal and diseased tissues. This science is closely related to experimental physiology, which had its beginning about the middle of the nineteenth century largely through the efforts of the French physiologist, Claude Bernard (1813-1878). The first independent pharmacology laboratory was founded by Rudolf Bucheim at the University of Dorpat in 1856. At the close of the nineteenth century the first separate departments of pharmacology were established in this country: one at the University of Michigan, headed by Arthur Cushny (1866-1926), and the second at the Johns Hopkins University, headed by John J. Abel (1857-1938). William H. O. McGehee[1] is accredited with giving the first course in pharmacology in an American dental school, at the Medical College of Virginia in 1900.

The function of pharmacology is to apply the many new drugs to the practice of therapeutics and to study the older drugs in order that they may be more intelligently used in the treatment of disease. These important functions are carried out by animal experimentation; the seemingly useful and safe drugs are then tried in therapeutics. The nature of the work attempted in each laboratory depends upon the ability and training of the staff members, but the direction is always the same: to improve the older drugs and to discover new, safer, and more efficient ones.

MATERIA MEDICA is the science of crude drugs, especially their source, collection, preservation, constituents, uses, dosage, and prepa-

[1]McGehee, W. H. O.: Dental Pharmacology, Materia Dentica and Pharmaco-Therapeutics, Philadelphia, 1936, The Blakiston Company, page 10.

rations. It is an old term introduced by Dioscorides in the first century. The term "materia medica" has been falling into disuse since the advent of experimental pharmacology.

PHARMACOGNOSY is a branch of botany concerned with the study of the plants used in the treatment of disease. This is an important branch of pharmacy and emphasizes the cultivation, habitat, selection, identification, and adulteration of vegetable drugs.

PHARMACY is the science and art of preparing, compounding, and dispensing medicines. It is the oldest branch of medicine and is the father of chemistry. Too much cannot be written in praise of this great profession.

PHARMACEUTICAL CHEMISTRY is that branch of general chemistry particularly concerned with the study of chemical structure as related to drug activity, with the synthesis of new and better drugs, and the improvement of existing drugs. It is an outgrowth of iatrochemistry and is opening the way for a more intelligent approach to the treatment of disease.

THERAPEUTICS is the science and art of the treatment of disease. It is a study and application of drugs and agents to correct, alleviate, and cure disease. Therapeutics is based on pathology, biochemistry, physiology, medicine, surgery, psychiatry, bacteriology, etc., and is, therefore, a branch of medical science. EMPIRIC THERAPEUTICS is the older form of treatment of disease before the advent of chemistry, bacteriology, biochemistry, pathology, physiology, diagnosis, etc., and was directed toward the relief of symptoms. RATIONAL THERAPEUTICS is a newer practice in which treatment is withheld until an intelligent diagnosis is made and specific treatment indicated. It is concerned more with the correction and alleviation of the causes of disease and less with the control of symptoms.

DRUGS are various substances which produce an action or effect on organs and tissues. They may or may not be useful in therapeutics. Nicotine is a good example: it affects the autonomic nervous system but has limited therapeutic value. Drugs are obtained from the plant, animal, and mineral kingdoms or are synthesized in the chemical laboratories. OFFICIAL DRUGS are those drugs and preparations included in the current editions of the *United States Pharmacopoeia* and the *National Formulary*.

MEDICINES are drugs and agents used in the treatment and prevention of disease. They may be a chemical substance, such as bicarbonate of soda, or an agent, such as ultraviolet rays, which is used in the treatment of rickets.

REMEDIES are drugs and agents used in the correction and treatment of disease. Included under agents are surgery, exercise, massage, physiotherapy, fresh air, directed work (psychiatry), x-ray therapy, artificial and induced heat, applied cold, splints, etc.

TOXICOLOGY is the science of poisons and their treatment. This is an old science and is closely related to legal medicine. It is concerned with the symptoms, detection, pathology, antidotes, and the general treatment of toxicity. As many cases of poisoning are suicidal or homicidal the legal aspect must always be considered. Industrial and food poisoning are very common, thus relating toxicology to public health.

POISONS are chemical substances which in moderately small doses produce disease and death. Medicines in large doses may act as poisons, and normal dosage of drugs may have a poisonous reaction in susceptible individuals; aminopyrine is a good example.

HORMONES are chemical activators produced within the body to correlate tissue functions and metabolism. Epinephrine is a good example of a hormone. These chemical substances are incompletely understood at present, and their usage will increase with a better understanding of their properties.

Dentistry, A Public Health Specialty

Apparently there is still some misunderstanding as to whether a dentist has the legal right to administer drugs intended for systemic treatment. While there is no specific legislation on this particular question, the courts in the United States and Great Britain have uniformly held that the registered dental practitioner has the right to employ such therapeutic measures, including drugs, as may be needed for the relief of suffering, or to produce curative results, in dental disorders. The qualified dentist is fully entitled to prescribe drugs for local or general disorders which bear a direct relationship to the practice of dentistry, including the administration of anesthetics. Dentistry, in the broadest sense of the term, is "a special department of the science and art of healing, embracing a knowledge of the structures, physiology, and pathology, and the therapeutic, surgical, and mechanical treatment of the mouth and its contained organs; also a knowledge of the materials used and their manipulation in the restoration of the dental and oral structures" (Kirk).

The evolution of the medical specialist within the province of the general practitioner received its present impetus with the dawn of the nineteenth century through the introduction of specific research.

Even in the remotest periods of medical history, however, we meet with examples in which physicians confined their activity to the treatment of special diseases. Apparently there has always existed a desire on the part of the general practitioner to limit the field of his usefulness to the care of disturbances of single organs or to the treatment of specific ailments. Herodotus, for instance, makes a very positive assertion regarding the specialization among the Egyptian physicians. He states that "Medicine is practiced among them (the Egyptians) upon a plan of separation; each physician treats a single disease and no more. Thus the country swarms with medical practitioners, some undertake to cure diseases of the eye, others of the head, others again of the teeth, others of the intestines, and some others which are not local." Among the Greeks, medical specialists apparently were of common occurrence. Similar conditions prevailed among the Romans, since their leading physicians were either native Greeks or had received their medical education on Greek soil. The paralyzing influence of medievalism on scientific matters in general also retarded the development of medicine. The only bright star in this period of orthodox despotism is the appearance of Paracelsus, the Luther of medicine.

Fortunately, medicine has had its renaissance. With the reorganization of the Vienna Medical School by van Swieten in 1750, scientific research received new stimulation. Laryngology had its birth in 1855 with the introduction of the laryngoscope, more or less simultaneously, by Garcia, Czermak and Tuerck; although Liston had stated in 1837 that "the existence of the swelling of the laryngeal mucosa can often be ascertained by means of a speculum; by such a glass as is used by the dentists on a long stalk previously dipped in hot water," etc. The dental mirror, the most useful instrument of our whole armamentarium, was introduced about 1800 by Chevalier Bartholomeo Ruspini, a prominent Italian dentist then practicing in London. There seems to be sufficient evidence to assume, however, that the Roman surgeons at the beginning of the Christian era used such an instrument for the inspection of the oral cavity.

The diseases of the teeth and their adnexa can, by reason of special fitness, best be treated by the dentist. The oral cavity is his chosen field. At present dentistry is regarded as a distinct profession. In education and practice it is closely related to, but not identical with, medicine and surgery. A dentist is, therefore, not to be classified as a specialist of a branch of medicine. In other words, to be a medical specialist means to be primarily the possessor

of that knowledge, according to the conception of the law, which entitles one to practice medicine in all its branches by virtue of the state medical license. Most courts hold that dentistry is not a specialty of medicine. In the opinion of the Supreme Court of Minnesota, in the case of State vs. Taylor,[1] a person holding a state medical license cannot practice dentistry under the statutes of that state. The following is a synopsis of the decision in that case:

For reasons of public policy, with which the Court has no particular concern, the Legislature adopted the policy of dividing the field of medicine and surgery, and making a separate profession of a part thereof. It was thought that men who engaged in the treatment of diseases of the dental organs should receive special preparation and be specially licensed to practice that particular branch or department of medicine and surgery. A State Board of Dental Examiners was created and authorized to determine who should be licensed and entitled to practice dentistry in the state. A department of Dental Surgery was also established at the University (of Minnesota), with a course of study, the satisfactory completion of which would entitle the student to a special degree of Dental Surgery. An examination of this course shows that it includes a considerable part of the work required in the medical school, but it also includes studies which relate particularly to diseases of the dental organs and others designed to insure efficiency in the mechanical work connected with the treatment. From an examination of the statutes of other states relating to the practice of dentistry, the Court learns that many contain express exceptions in favor of physicians and surgeons. Probably the most of them permit physicians to extract teeth, or perform such other comparatively simple work. In the absence of any such exceptions, it must conclude that the Legislature intended to restrict the scope of the practice of the physician and surgeon, and require him, if he desires to practice dentistry, to obtain a license from the State Board of Dental Examiners in addition to his other certificate.

This case clearly demonstrates the protection offered to dentistry. The physician, surgeon, osteopath, chiropractor, etc., cannot practice dentistry lawfully.

Care and Selection of Drugs

To obtain the best results it is essential to procure and use the purest drugs and preparations obtainable. For many reasons it is good policy to order drugs in original containers from a reliable pharmacist. Drugs and chemicals from an open stock frequently deteriorate. For example, the essential oils may be thick, viscid, and discolored; oxygen compounds may have lost much of their oxygen from frequent exposures to moist air; zinc oxide may have changed to zinc carbonate by absorbing carbon dioxide from the air; formaldehyde solution may have lost most of its gaseous con-

[1] J. A. M. A., 1909, p. 122.

tents, etc. Inefficient drugs applied in the treatment of dental diseases are worse than dull instruments; both are the result of neglect and should be eliminated. It is gratifying to learn that the dental profession is showing an increasing interest in the pharmacologic action of drugs and in their rational application. The practitioner of today is discarding untrustworthy and feeble remedies and ready-made compounds and is depending more and more on those drugs whose efficiency has been clinically established. It is a safe practice to use only official drugs—those listed in the *United States Pharmacopoeia* and the *National Formulary*—or in the case of new drugs to wait for their inclusion in *New and Nonofficial Remedies* or *Accepted Dental Remedies,* before using them in daily practice.

Drugs, chemicals, pharmaceutical preparations, etc., must be carefully stored to preserve their potency. The original containers should be kept in a cool place, protected from light. The office preparation bottles are preferably selected from stock made of colored glass. For liquid preparations the dropping bottles are best adapted, while for semisolid and dry materials the glass-stoppered salt-mouth bottles are very serviceable. Office preparation bottles may now be procured with indestructible labels, which materially assist in keeping the containers neat in appearance.* In using drugs or chemicals, the necessary quantity is preferably placed on a glass slab or a watch crystal, and then applied, instead of dipping the instrument directly into the bottle. For applying the various solutions of active drugs, such as sulfuric acid, iodine, silver nitrate, etc., a looped iridoplatinum wire, which is readily sterilized in an open flame, inserted into a metal handle is advisable. By bending the wire in the desired direction, any tooth surface in the mouth may be reached. A number of these applicators of various sizes should be kept on hand.

Pharmacognosy

Pharmacognosy is the study of crude plant drugs. It includes the history, cultivation, collection, selection, identification, preservation, adulteration, and commerce of crude drugs.

Some plants do not have therapeutic properties, and others contain active therapeutic principles in amounts too small to be of commercial value.

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*__Label varnish.__ A suitable translucent label varnish may be prepared as follows:

Gum mastic	5 parts
Gum sandarac	20 parts
Alcohol	80 parts

Place in a clean bottle and allow to stand until dissolved.

The active principles are not distributed equally throughout the plant but are contained in greatest amounts in certain parts, i.e., the leaves, roots, etc. This is determined by assaying the different parts of the plant for the amount of active substance contained in each tissue.

Careful cultivation of medicinal plants has been found to increase the amounts of active principles in the tissues, and careful preservation insures the minimal loss of drug potency during storage and shipping.

A complete course in pharmacognosy includes a study of all vegetable drugs listed in the *United States Pharmacopoeia* and *National Formulary*. Each drug is studied under the following headings:

English name.	Assay.
Latin name.	Habitat.
Official abbrevation.	Macroscopic and microscopic anatomy.
Official synonyms.	Constituents.
Botanical source.	Uses.
Part used.	Dosage.
Impurities.	Adulterants.

The following parts of a plant may be official:[1]

BARK—a term applied to that portion of a plant outside of the cambium ring.

BUD—a short young shoot with leaves or rudimentary leaves compactly arranged in concentric layers.

BULB—a thickened underground stem consisting of concentric layers of fleshy scales.

CORM—a thickened, solid underground stem with buds on the superior part and rootlets on the inferior part.

EXUDATE—a liquid portion of a plant.

FLOWER—a shoot which has metamorphosed for a reproductive function.

FRUIT—a mature pistil which may include other parts than the ovary.

LEAF—a thin bladelike appendage of a plant.

LEAFLET—a blade of a compound leaf.

RHIZOME—a creeping underground stem.

ROOT—an underground stem.

SEED—a fertilized ovule containing an embryo.

STEM—the plant axis that grows above the ground and bears leaves.

TRICHOME—an epidermal outgrowth, as an epidermal hair.

[1] Youngken, H. W.: Pharmaceutical Botany, ed. 8, The Blakiston Co.

WOOD—that portion of the stem beneath the cambium ring.

PARASITIC GROWTH—a replacement of a part of a plant by a fungous growth.

EXCRESCENCE—a hyperplasia of a plant tissue caused by stimulation of a foreign agent, nutgall.

Constituents of Vegetable Drugs

Vegetable drugs are composed of medicinally active constituents and of medicinally inactive constituents.

The inert constituents of botanical drugs are principally cellulose, wood, starch, albumin, wax, fat, coloring matter, etc., which exhibit practically no pharmacologic action although they may modify the activity of the pharmacologic principle.

The active constituents are comprised of pharmacologically active principles which act on the animal tissues, and pharmaceutically active principles which may cause precipitation or otherwise chemically influence a mixture or compound. The physiologic action of a crude drug depends, either wholly or in part, upon its contained active principles.

The active constituents of organic drugs may be divided into:

ORGANIC ACIDS AND THEIR SALTS.—Tartaric acid of grapes, citric acid of lemon, tannic acid of oak bark, salicylic acid of sweet birch, etc., are representatives of this class. They exist in plants chiefly as potassium, sodium, and calcium salts. In the body they may be oxidized to carbon dioxide and water which are excreted, leaving behind the metal ion which gives them an alkaline effect.

ALKALOIDS.—They are natural organic bases containing principally carbon, hydrogen, and nitrogen and possess the power of neutralizing acids with the formation of salts without the elimination of hydrogen. With very few exceptions, the alkaloids are solids. All alkaloids have certain properties in common: they have a bitter taste, they are colorless, turn red litmus paper blue, have a profound physiologic action, and leave no postmortem changes. They are soluble in ether, chloroform, and oils, less so in alcohol, and are comparatively insoluble in water. Alkaloidal salts are soluble in water and alcohol, but are insoluble in ether or chloroform. They end in "ine," pronounced ēn.

Examples:

ALKALOIDS	SALTS
Morphine	**Morphine Sulfate**
Strychnine	**Strychnine Sulfate**
Pilocarpine	**Pilocarpine Hydrochloride**

GLUCOSIDES.—These are proximate principles existing in plants and in most instances are chemically neutral compounds. When treated with weak acids, alkalies, or ferments, they decompose and form glucose with one or more other substances. They do not follow rules in regard to taste or solubility. They do not form salts. They end in "in," pronounced in.

Examples:

Digitalin	Salicin
Glycyrrhizin	Strophanthin

SAPONINS.—They are substances found in many plants and possess the common property of foaming or making suds when agitated in aqueous solution; they also hold resinous and fatty substances in suspension in water. As a rule they are amorphous bodies, though a few are crystallizable, and possess the properties of glucosides; they are irritants when applied to the skin or mucous membranes, and given internally they cause nausea, vomiting, and diarrhea.

Examples of Saponin-containing Drugs:

Quillaja	Bittersweet
Sarsaparilla	Senega

NEUTRAL PRINCIPLES.—These are organic substances generically known as *neutral principles* which closely resemble glucosides. They are practically insoluble in water, have a more or less pronounced bitter taste, and contain no nitrogen.

TANNINS.—They are an ill-defined class of substances, derivatives of benzol, and distinguished by giving a bluish-green color with ferric salts. They are soluble in water and alcohol but readily form insoluble compounds with many substances, i.e., metallic salts, alkaloids, proteins, etc. This precipitation gives them an astringent action. Tannins may be physiologic or pathologic products of plants.

SUGARS, STARCHES, AND GUMS.—These compounds are known as carbohydrates; they possess only slight importance as remedies, being usually employed for their soothing action as demulcents, sweeteners, foods, and as vehicles and diluents. They constitute one of the most important classes of useful products of nature. The gums are water-soluble substances which are readily precipitated by alcohol. Examples: gum arabic and tragacanth.

ENZYMES.—They are substances capable of producing chemical changes without entering into the reaction or forming a part of the end product. Examples: pepsin, pancreatin, and papain.

RESINS.—They are alcohol-soluble constituents of vegetable drugs. Examples: podophyllin and jalapin.

OLEORESINS.—They are ether-soluble constituents of vegetable drugs containing oils and resins. Examples: copaiba, male fern, and capsicum.

BALSAMS.—They are mixtures of resins and oleoresins containing benzoic acid, cinnamic acid, etc. The chief balsams are those of Peru, tolu, and storax.

CAMPHORS.—They are organic compounds which are insoluble in water but soluble in alcohol, ether, etc. Examples: camphor, eucalyptol, menthol, etc.

GUM RESINS.—They are mixtures of gum with resins or oleoresins, and are soluble in diluted alcohol. Examples: asafetida, myrrh, and gamboge.

FIXED OILS.—They are compounds of fatty acids and glycerin. They are greasy and insoluble in water and in alcohol (except croton oil and castor oil). They combine with alkalies to form soap and glycerin. They cannot be distilled without decomposition and leave a stain on paper or cloth which will not disappear on warming. Examples: olive oil, linseed oil, castor oil, etc.

VOLATILE OILS.—They are odorous, volatile, nongreasy liquids which do not contain glycerin. They are soluble in alcohol and to a slight extent in water. They are usually obtained by distillation. Examples: oils of cassia, clove, eucalyptus, etc.

Pharmaceutical Methods

The following are methods of preparing drugs for pharmaceutical use:

COMMINUTION.—A process of dividing a crude drug into smaller parts by mechanical means, as grinding or rasping.

DECANTATION.—Drawing or pouring off a supernatant liquid into another vessel.

DECOCTIONS (decoctiones).—Aqueous preparations made by boiling the vegetable drug in water for fifteen minutes and then filtering. Decoctions represent about a 5 per cent solution of the drug (5 Gm. per 100 cc.).

DESICCATION, OR DRYING.—Driving off some volatile constituent from the solid, the fixed residue being the portion desired. Crude drugs are subjected to this method to reduce their bulb, to assist preservation, and to facilitate comminution. Drying may be accomplished by spreading the drugs in airy lofts or by heat in drying closets. Care must be taken not to injure the volatile ingredients of the drugs.

DISTILLATION.—Evaporation of a liquid and condensing the vapor into a liquid in a separate vessel. Fractional distillation is the

process of separating a mixture of liquids of different boiling points by distillation.

EVAPORATION.—Vaporizing a solvent from a solution so as to concentrate the dissolved substance.

EXPRESSION.—Separation of liquids from solids by pressure.

EXSICCATION, OR CALCINATION.—Depriving a solid of its moisture or volatile constituents by heat without fusion.

FILTRATION.—Separation of liquids from suspended solids by pouring them through a filter, as filter paper, charcoal, sand, etc.

FINENESS OF POWDERS.—Determined by the size of the meshes through which it passes:

Coarse powder	No. 20—20 meshes to a linear inch.
Moderately coarse powder	No. 40—40 meshes to a linear inch.
Fine powder	No. 60—60 meshes to a linear inch.
Very fine powder	No. 80—80 meshes to a linear inch.

MACERATION.—Dissolving soluble active constituents of drugs by suspending them in a menstruum for a sufficient length of time.

PRECIPITATION.—Separating solids from their solvents, which is usually accomplished by chemical or physical means.

PERCOLATION.—A process of exhausting a drug by a suitable menstruum. It consists in "subjecting a substance or mixture of substances in powder, contained in a vessel called a percolator, to the solvent action of successive portions of a certain menstruum in such a manner that the liquid, as it traverses the powder in its descent to a receiver, shall be charged with the soluble portion of it, and pass through the percolator free from insoluble matter" (U.S.P.).

PULVERIZATION.—A process of dividing a drug into a fine powder—grinding.

SOLUTIONS.—Drugs dissolved in a solvent to facilitate dispensing. Example: Dobell's Solution, N.F.

SUBLIMATION.—Separating a volatile from a nonvolatile solid by heat. A change from a solid to a gas without passing through a liquid state (camphor).

TRITURATION.—Rubbing a substance to a very fine powder in a mortar.

Definitions of Solid Preparations

AMPULS (AMPULLAE).—Hermetically sealed glass containers for medicinal substances containing a sterile solution for parenteral use. Example: Ampuls of Procaine Hydrochloride, N.F.

CAPSULES (CAPSULÆ).—Gelatin coverings of various sizes for dispensing drugs. (See Fig. 1.)

CERATES (CERATA).—Unctuous preparations similar to ointments, having for their bases the simple cerate, composed of 30 parts white wax, 20 parts petrolatum, 50 parts benzoinated lard. Example: Cantharides Cerate, N.F.

COLLODIONS (COLLODIA).—Liquid preparations having for their base a solution of guncotton (pyroxylin) in a mixture of ether and alcohol. Example: Flexible Collodion, U.S.P.

CONFECTIONS (CONFECTIONES).—Medicinal substances formed into a mass with sugar, honey, and water, as confection of rose.

DECOCTIONS (DECOCTA).—Vegetable substances boiled in water and strained, as decoction of sarsaparilla.

ELIXIRS (ELIXIRIA).—Sweetened, hydro-alcoholic preparations containing medicinal substances in small quantities. Example: Elixir of Barbital, N.F.

EMULSIONS (EMULSA).—Aqueous preparations in which oils, oleoresins, balsams, resins, or other substances which are insoluble in water are suspended by means of gum or other viscid excipients. Example: Emulsion of Cod Liver Oil, U.S.P.

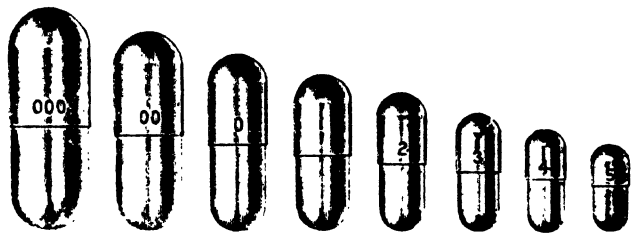


Fig. 1.—Empty gelatin capsules.

EXTRACTS (EXTRACTA).—Solid or semisolid substances of active principles of drugs obtained by percolation and desiccation. Extracts are generally four or five times as potent as the crude drug. Example: Extract of Opium. The pill extracts are pastes and the powder extracts are powders; Extract of Cascara Sagrada and Powdered Extract of Belladonna are examples.

KONSEALS (rice flour capsules) or Wafers (thin sheets of dried flour paste).—Sometimes used to enclose drug powders.

MASSES (MASSÆ).—Dough mixtures of pillular consistency for making pills. Example: Mass of Mercury, N. F.

OINTMENTS (UNGUENTA).—Soft, fatty mixtures melting by friction at body temperature. Example: Zinc Oxide Ointment, U.S.P.

OLEATES (OLEATA).—Solutions of metallic salts or alkaloids in oleic acid. Example: Oleate of Mercury, U.S.P.

OLEORESINS (OLEORESINÆ).—Natural, as copaiba and turpentine; or artificially prepared by extracting drugs with ether. Example: Oleoresin of Ginger, N.F.

PAPERS (CHARTÆ).—Paper impregnated with medicinal substances. Example: Mustard paper.

PILLS (PILULÆ).—Small spherical bodies, containing medicinal substances by aid of some vehicle and covered with various substances. Example: Blaud's Pills, U.S.P.

PLASTERS (EMPLASTRA).—Adhesive, fatty, or resinous compounds spread on textile fibers, leather, muslin, etc.; they are either dry or soft. Example: Belladonna Plaster, U.S.P.

POULTICES (CATAPLASMATA).—Means of applying heat and moisture to certain parts of the body. Example: Cataplasm of Kaolin, N.F.

POWDERS (PULVERES).—Drug mixtures in very fine state of division. Example: Dover's Powder, N.F.

RESINS (RESINÆ).—Natural exudations, as rosin; prepared extracts of drugs, as Resin of Jalap, N.F.

SUPPOSITORIES (SUPPOSITORIA).—Medicines mixed with cocoa butter and formed into cones intended for introduction into the rectum or vagina. Example: Suppositories of Glycerin, U.S.P. For urethral use they are called bougies.

TRITURATIONS (TRITURATIONES).—Mixtures containing active drugs in powdered form prepared by mixing the substance (10%) with lactose.

TROCHES (TROCHISCI) (LOZENGES).—Tablets intended to be dissolved in the mouth for their local effect on the mucous membrane of the mouth and the throat. Example: Troches of Elm, N.F.

Definitions of Liquid Preparations

AROMATIC WATERS (AQUAE AROMATICAE).—The official aromatic waters are saturated aqueous solutions (unless otherwise specified) of volatile substances, usually volatile oils. They are used as vehicles for the more active water-soluble drugs. Example: Peppermint Water, U.S.P.

FLUIDEXTRACTS (FLUIDEXTRACTA).—Active principles of drugs prepared by percolation. They are liquid, and one gram of the drug corresponds to one cubic centimeter of the finished product. Example: Fluidextract of Ergot, U.S.P.

GARGLES (GARGARISMA).—Mixtures or solutions for application to the pharynx and the mouth.

GLYCERITES (GLYCERITA).—Mixtures or solutions of medicinal substances with or in glycerin. Example: Glycerite of Tannic Acid, U.S.P.

INFUSIONS (INFUSA).—Fresh aqueous preparations made by pouring hot or cold water over drugs, allowing the mixture to stand for a definite period, and then straining.

INJECTIONS (INJECTIONES).—Liquid preparations for introduction into the cavities of the body by means of a syringe. They are sterile, nonirritating, and isotonic to the tissue cells. Example: Ampuls of Camphor, N.F.

JUICES (SUCCI).—Expressed juices of fresh drugs, as lemon juice.

LINIMENTS (LINIMENTA).—Liquid ointments to be applied with friction to the skin. Example: Soap Liniment, U.S.P.

LOTIONS (LOTIONES).—Mixtures or solutions of medicinal agents for external application. Example: Calamine Lotion, N.F.

MIXTURES (MIXTURÆ).—Solids suspended in aqueous liquids. Example: Brown Mixture, N.F.

MUCILAGES (MUCILAGINES).—Gums dissolved in water. Example: Mucilage of Acacia, U.S.P.

SOLUTIONS (LIQUORES).—Watery solutions of nonvolatile substances. Example: Solution of Magnesium Citrate, U.S.P.

SPIRITS (SPIRITUS).—Solution of volatile substances in alcohol. Example: Spirit of Peppermint, U.S.P.

SYRUPS (SYRUPI).—Syrups are aqueous solutions of medicinal substances rendered palatable by the addition of sugar. Example: Syrup of Senna, U.S.P.

TINCTURES (TINCTURÆ).—Tinctures with few exceptions are alcoholic or hydroalcoholic extractive preparations of animal or vegetable drugs. The pharmacopoeial tinctures of potent drugs (except tinctures of iodine) represent uniformly 10 Gm. of drug in 100 cc. of the preparation, while tinctures of less potent drugs vary in strength but represent usually 20 Gm. of drug in 100 cc. of the preparation. Simple tinctures contain only one drug; compound tinctures contain more than one drug.

VINEGARS (ACETA).—Solutions of active principles of drugs in dilute acetic acid. Example: Vinegar of Squill, N.F.

WATERS (AQUÆ).—Solutions of volatile substances in water. Example: Peppermint Water, U.S.P.

WINES (VINA).—Solutions of medicinal substances in wine. Example: wine of opium.

The Pharmacopoeia

In all civilized countries the governments have found it necessary to issue at certain intervals a standard guide for the regulation of medicinal preparations. This book is termed a Pharmacopoeia—from *pharmakon* (a drug) and *poiein* (to make). The United States gov-

ernment, however, does not issue the Pharmacopoeia, but it recognizes its authority as published by the National Committee of Revision, a body composed of members by appointment or elected by a convention of the various medical, dental, and pharmaceutical societies, schools, and United States Medical and Dental Corps. The book is revised every ten years, the present edition being the Twelfth Decennial Revision, published by authority of the United States Pharmaceutical Convention, held in Washington, D.C., in 1940. The Pharmacopoeia furnishes the official standard for the identification, purity, strength, and quality, with suitable directions for preparation, purification, and preservation, of drugs, chemicals, and medicinal preparations. The title of the drug is given in Latin, followed by the Latin abbreviation, English name, synonym, and, in the case of chemicals, by the formula and molecular weight. The preparations contained in the Pharmacopoeia are therefore termed "official," while all other medicinal substances usually kept in a drugstore are termed "nonofficial." Quite a number of drugs and preparations which are not contained in the *United States Pharmacopoeia* are standardized by listing in the *National Formulary*, a book published and revised at intervals under the direction of the American Pharmaceutical Association. Another very large class of remedies is those substances which are usually termed *the newer remedies*. These agents are either too new to have gained recognition by the Committee on Revision of the Pharmacopoeia, or they possess so little real merit that they have been purposely omitted, although they are prescribed. To clarify somewhat this chaos of grain and chaff, the American Medical Association in 1906 created a Council of Pharmacy and Chemistry, whose duty it is to select from the enormous mass of drugs and preparations, those which comply with the rulings of this body, and they are termed *New and Nonofficial Remedies*.

In 1927 the American Dental Association established a Bureau of Chemistry to analyze preparations sold in the name of dentistry. It was soon learned that many of these preparations were sold through misrepresentation and had practically no merit. In 1929 the Board of Trustees of the American Dental Association established the Council on Dental Therapeutics, a standing committee functioning like the Council of Pharmacy and Chemistry of the American Medical Association. This Council consists of individuals trained in related sciences, half of whom are not members of the dental profession. Since 1929 the Council on Dental Therapeutics has investigated thousands of drugs and proprietary preparations that are useful in dental practice. These products with description, dosage, pharma-

cologic action, and therapeutic use have been compiled in a volume known as "Accepted Dental Remedies" (A.D.R.). This volume is revised periodically and, with the *United States Pharmacopoeia* and the *National Formulary*, designates the official and accepted status of drugs.

The pharmacopoeias of different countries vary greatly not only with regard to the drugs they contain but also with regard to strength and composition of preparations with similar names. To overcome these difficulties a tentative attempt has been made to unify pharmacopoeial formulas of potent drugs. The then existent governments of Great Britain, Germany, Austria-Hungry, Belgium, Bulgaria, Denmark, Spain, the United States of America, France, Greece, Italy, the Grand Duchy of Luxembourg, Norway, the Netherlands, Portugal, Russia, Servia, Sweden, and Switzerland, having recognized the utility of concluding an agreement with the view to the unification of the pharmacopoeial formulas for potent drugs on the basis indicated in the Final Protocol signed on September 20, 1902, as a result of the conference held at Brussels, agreed upon the following stipulations: (a) No potent drug shall be directed to be prepared in the form of a medicinal wine. (b) Tinctures of potent drugs shall be directed to be prepared of the strength of 10 per cent and by percolation. (c) Fluidextracts of potent drugs shall be prepared of the strength of 100 per cent. (d) The Contracting Governments shall adopt a normal drop-measure, the external diameter of whose outlet tube shall be exactly 3 millimeters, that is to say, which, at a temperature of 15° C. and with distilled water, shall yield 20 drops to the gram. Later the League of Nations also considered certain aspects of the subject.

Besides the *United States Pharmacopoeia* and *National Formulary* there are books which contain descriptive matter of substances used in medicine, with various detailed information. These books are compilations and commentaries on the above works, and are termed *dispensatories*. Various books of this character are published in the United States—the *United States Dispensatory* and the *National Standard Dispensatory* being in general use.

CHAPTER II

INTRODUCTION TO THE STUDY OF DRUGS

Methods of Administering Medicines

Medicines may be administered to any of the accessible tissues or cavities of the body, and the mode of administration very often determines the effect of the remedy. In general, medicines may be applied locally (topically) or internally. By the former mode they are usually intended to produce local effects, while by the latter, through their absorption into the blood, they produce systemic actions. Relative to the general action of drugs, it should be remembered, as we have stated before, that a drug must be in solution or in vapor form to produce an action. The solution which brings the drug to interact with the protoplasm of the cells should be so constituted as to be readily miscible in the body fluids. In certain cases retarded absorption is important, and therefore colloidal substances, and sometimes fatty substances, are added to the solution. Retarded action generally goes hand in hand with prolonged effects.

In the administration of medicines usually one of the following methods is selected:

By inunction.
By the sublingual route.
By the alimentary canal
By rectum.
By hypodermic injection.
By inhalation.
By inoculation.

Local action of remedies is expected when they are applied to the skin, to the mucous membrane of the alimentary, respiratory, and genitourinary tracts, to the eye, and to the teeth. The *skin* is not an absorbing organ, and it is protected by the horny layer of the epidermis and by sebaceous secretions, which prevent the ready penetration of aqueous solutions. Oily or fatty substances mix readily with the sebaceous matter of the skin and are more readily absorbed than aqueous preparations. The animal fats are absorbed best, the vegetable fats next, and the mineral oils least. If friction is applied, the substances may penetrate through the outer layer and even into the deeper structures. Diffusible and volatile substances, such as

chloroform, ether, alcohol, essential oils, etc., penetrate comparatively quickly and may reach the blood stream. The application of remedies to the skin with the object of producing general action is largely discarded at present, although inunctions with mercury ointment are still in favor with some practitioners. Remedies applied to the skin to produce local effects are principally used to act on some local disturbance. Blisters, poultices, liniments, plasters, powders, lotions, collodions, etc., are examples of local medicaments. Occasionally absorption of the drug will occur, and a general action is produced. The *enepidermic method* endeavors to bring about the absorption of drugs through the skin by simple contact without rubbing; chloroform and solutions of drugs in oleic acid (oleates) are used for this purpose. In the *epidermic method,* or *inunction,* the remedy is usually employed in the form of an ointment, oil, etc., with rubbing to promote the passage of the drug through the epidermis.

The *mucous membranes* quickly absorb aqueous solutions of drugs, while fatty substances are absorbed to a lesser degree. If an ointment is applied, the moist surface should be previously dried. Drugs absorbed by the mucous membranes are quickly disseminated by the rich blood supply, and a systemic effect may result. In applying solutions to the sensitive mucous surfaces, it should be remembered that isotonic solutions produce the least irritation. If the drugs themselves do not produce an isotonic solution, the addition of sodium chloride readily accomplishes the purpose. The solution should be of the proper viscosity to permit prolonged therapeutic action. The application of remedies to the mucous membranes, with the exception of those of the stomach and the intestines, is principally intended for their local action. These drugs are administered as solutions, paints, powders, mixtures, solids, or in vapor form. Diseases of the mouth and throat are treated with mouthwashes, gargles, paints, lozenges, powders, and sometimes salves.

For the absorption of concentrated remedies directly into the circulation, Paulson regards the *sublingual* space as the most reliable absorbing surface in the whole body. The only preparation necessary is rinsing with water if the mouth is dry. A morphine or atropine tablet, powdered and dropped just behind the teeth and beneath the tongue, will be absorbed in a few minutes. An apomorphine tablet, administered in this way, will induce vomiting at once. Compared with hypodermic injection, Prinz considers the sublingual method quicker, easier, safer, and more reliable.

The *alimentary canal* is the commonest route for the absorption of remedies. The remedies which are given *orally* may act locally on the

stomach and intestines, or they may act after being absorbed into the blood. Most remedies are given in aqueous solution or in mixtures, emulsions, etc., for the purpose of increasing their absorption. Nauseous, ill-tasting medicines, or those prepared for special purposes or for convenience, are given in pills, powders, capsules, cachets, confections, troches, etc. Relatively speaking, medicines are slowly absorbed from the stomach. They are usually diluted with the gastric juice, unless they chemically react with it, and are gradually passed into the small intestine, where absorption takes place. In most cases oils and fats pass unaltered through the stomach, and are emulsified and hydrolyzed by the pancreatic juice. Drugs of a protein nature may be hydrolyzed by the digestive enzymes into inert compounds, and they should not be administered by the oral route. Epinephrine is a good example. To protect medicines against the action of the gastric juice, they may be administered in pill form and coated with some substance that is insoluble in the gastric fluids, as keratin, salol, etc.

Pathologic conditions may occur which contraindicate the oral route for drug administration, i.e., disturbances of esophageal, gastric, or intestinal function.

The mucous membrane of the *rectum* is sometimes selected as a site for the absorption of remedies and foods. Substances soluble in water, or those which may be transformed into soluble materials, are preferably employed for such purposes. An injection into the rectum (enema, clyster) varies in quantity, and depends on the specific purposes for which it is intended. A nutrient enema usually measures from four to six ounces, while simple injections intended for local action may measure from one-half to two pints. Glycerin enemas, which are strongly irritating when used in large quantities, are generally given in one- to two-dram doses. *Proctoclysis* is the slow injection of large quantities of a liquid into the rectum; it is also referred to as the *Murphy drip*. *Suppositories* are solid preparations which melt at body temperature. They are usually cone-shaped and intended for rectal application. Their effect is generally local, although the drug may be absorbed and produce a systemic effect.

The hypodermic method is usually used to introduce medicines in aqueous solutions into the subcutaneous tissues, from which the solution is quickly absorbed. A special syringe, carrying a sharp, hollow needle, is used for this purpose. Hypodermic injections were introduced by Rynd (1844) and Wood (1853). The syringes used at present are modifications of the one designed by the French surgeon, Pravaz. The least sensitive parts of the body, such as the back, the dorsum of the thigh or the arm, should be selected for the injection.

Care should be exercised not to inject air into the tissues. The injection into the oral tissues necessitates detailed description. (See Local Anesthesia.) The hypodermic method has an advantage, in that precise doses of powerful alkaloids can be quickly administered, avoiding possible reactions between the drugs and the digestive ferments. The solutions should always be made fresh from sterile water, or, still better, from an isotonic saline solution, which materially lessens the pain of the hypodermic injection. The skin at the place of injection should be cleansed, and aseptic care must be taken to avoid infection, as otherwise abscesses are sure to follow. The quantity of solution injected is usually limited to 15 to 30 drops (1 to 2 cc.), although antitoxic sera frequently require larger doses. The absorption takes place very rapidly along the lymph canals and into the capillaries, and usually a typical drug effect is obtained within fifteen minutes. The same dose of medicine administered in solution by mouth would require half an hour or more before the action could be demonstrated. *Subcutaneous* injections are made by depositing the solution in the connective tissue just beneath the skin. This is the most common injection procedure. *Intramuscular injection* is sometimes resorted to, and is usually restricted to oily or aqueous solutions of irritant drugs. *Intravenous injection* (transfusion, hypodermoclysis) is occasionally given; it consists in injecting directly into a vein. It is frequently employed for the transfusion of blood or for the injection of a large quantity of physiologic saline solution for the purpose of restoring the quantity of blood after severe hemorrhage, or securing excretions in certain intoxications, as in uremia, diabetic coma, etc. It is a hazardous route and should be used only by those who are accustomed to this method of drug administration.

Inhalations are employed in the administration of remedial substances into the upper air passages or into the lung by active inspiration. Substances in vapor form or in very fine division in the form of fumes or clouds are inhaled and thus brought into close contact with the diseased surfaces, or, by ready absorption in the lungs, they act on the general system, as in general anesthesia. In the latter case special apparatus (masks, etc.) is necessary, while in the former a spray (atomizer) conveys the medicine into the posterior part of the nasal pharynx.

Inoculation is employed for the purpose of introducing medicinal agents through the scraped or punctured skin (vaccination). The vaccines act as antigens, causing an active immunity to be established. The vaccines are attenuated microorganisms which cause specific antibodies to be formed in the tissues. These protective protein substances

immunize the patient against a subsequent infection from similar microorganisms. This acquired immunity is not fully established for several weeks, and its duration varies from one to seven or more years.

Nature and Site of Drug Action

Within the last fifty years the theories regarding the pharmacologic action of drugs have undergone remarkable changes. Empiricism in medicine had held sway ever since remedies were used for the purpose of alleviating diseases, and it was only through the introduction of experimental pharmacology in the early sixties of the last century that a slow but radical change in the administration of drugs took place. The science of modern pharmacology is based on Virchow's conception of cellular pathology, and with its introduction into general medicine, in 1858, the humoral pathology of Hippocrates received its death blow. In the conception of the great physician of Cos, Hippocrates, the knowledge of medicine was based on seven natural phenomena, *res naturales,* and he considered the body as being made up of the four elements, i.e., fire, earth, air, and water. These elements were supposed to invest the body with the proper temperaments *(complexiones),* heat, cold, dry, and wet, which when combined in different proportions in different individuals were productive of the four humors, i.e., blood *(sanguis),* phlegm *(phlegmon),* yellow bile *(choler),* and black bile *(melancholer).* It was further supposed that one or the other of these humors must always be present in a preponderance, so as to create the specific physical organization which is peculiar to the individual.

In the practice of medical art, including the specialty of dentistry, the remedies employed in treating diseases were in accordance with the predominating school. The remedies which are at the disposal of the dentist are countless; the drugs of real merit, however, may be gathered within a small compass. In the Ebers papyrus, for instance, which comprises the period from 3700 to 1500 B.C., about eight hundred remedies are enumerated, and Dioscorides describes about a thousand drugs. Again, in the *Pharmacopœia Medico-physica,* published by Schröder in 1664, the goodly number of six thousand remedies is recorded. We may probably gain a better understanding of the use of these many drugs when we remember that in that period polypharmacy had reached its zenith. In those days the combination of ten, twenty, or even more drugs in a single prescription was very much of a routine practice. An example of polypharmacy is Warburg's tincture, which originally contained some twenty-odd drugs.

The action of drugs on the organism is known only in a very few instances. After a drug is absorbed by the tissues, a chemical reaction between this substance and the protoplasm of the cell occurs, which is generically expressed as *irritation.* What constitutes this irritation and its subsequent reaction with the diseased organism is as yet unknown. Apparently all pharmacologic action is governed by the same basic biologic law, usually referred to as the Arndt-Schulz law, which controls many manifestations of the living cell, i.e.: minute irritation stimulates vital function, medium irritation increases it, strong irritants depress these functions, and the strongest irritation inhibits them completely, which invariably leads to death of the cell.

The basic law governing pharmacologic action may be expressed as follows: *Drugs taken into the body must be soluble in the tissue fluids in order to combine with the cell contents and thereby exercise their function.* This axiom, well known to the ancient medical chemists, was dogmatically expressed as: *Corpora non agunt nisi soluta seu solubilia.* In other words, pharmacodynamic action is the result of a chemical reaction between a solution of the drug and the living cells. The term "chemical" in this particular instance, however, must not be restricted too narrowly; the reaction between the drug and the cell contents, i.e., albumin, lecithin, salts, water, and other compounds usually is not of a pure chemical nature but, in most instances, a physicochemical process in which adsorption, diffusion, filtration, and osmotic pressure also play important parts. In tissue fluids the term "solubility" is of significance, and one's first conception must not be based on similar reactions observed outside of the body. Expressed in simple language, a test-tube experiment must not be interpreted as comparable to the reactions within the living organism. As a well-known example we may cite the pharmacologic action of calomel. The mild mercurous chloride is insoluble in ordinary fluids in the test tube; when administered internally, however, marked therapeutic effects are observed. The action of calomel is not to be explained on the mechanical basis of its mere presence, but as the result of its entering into solution through the agencies of the tissue fluids. Whether minute quantities of the readily soluble sublimate or intermediary products are formed is of little importance at this moment. The mere fact remains that the otherwise insoluble calomel *does* enter into solution when brought in contact with the living cells and hence by its physicochemical reaction is capable of bringing about profound therapeutic effects.

Certain drugs apparently react with all the cells, while others possess a selective action to specific cell groups. To produce pharmacologic action, an adequate amount of the drug, constituting its average

dose, is essential. Only an immeasurably small portion of the administered drug reacts with the specifically susceptible cells. After absorption, the blood and the lymph streams distribute the drug throughout the whole body and, depending on its special affinity, it is retained by various cells. Apparently, no direct relationship exists between the quantity of the absorbed drug and its elective pharmacologic action; as yet we have no more conception as to why a grain of strychnine will kill a sound, healthy man within a few minutes after absorption than why a spark falling into a barrel of gunpowder will cause its explosion. Two definite factors apparently play an important role in the therapeutic action of drugs—first, the potency possessed by the drug itself, and, second, the reactive power possessed by the organism. Experimental observations seem to point to the fact that pathologically altered tissues react quite differently to chemical substances than do normal tissues, and that the condition of the organism, within certain limits, determines whether the same pharmacologic action will produce good or bad results. The irritation produced by the absorbed drug manifests itself as *stimulation* or as *depression* of the functions of the organism. Some drugs, when ingested in small quantities, increase the bodily functions, while, when taken in large doses, decrease the same function. Again, certain drugs exercise specific influence on certain organs. All changes which occur within the tissues as a result of the action of a drug are of a physicochemical nature. At least three forms of reaction between the drug and the animal cell are recognized:

1. A superficial combination between the "cell wall" and the chemical substance occurs, which lasts as long as the cell is active and is not injured. The chemical substance does not enter into the protoplasm of the cell.

2. A combination of the chemical substance and the cell contents is produced as a result of the easy penetration of the substance through the "cell wall" into the protoplasm proper.

3. A combination is formed between the chemical substance and the cell enzymes, which affects the oxidation-reduction system and alters the physiology of the cell.

Nature will always resist drug action as long as it possesses vitality. Drug action on normal tissue may result in injury or death, while on diseased tissue it may restore normal function.

Excretion and Detoxication

All drugs which are ingested into the body are removed by the secretions and excretions. This process depends largely on the stability of the union which the drug has formed with the tissues.

Drugs are primarily excreted by the urine and the feces and through the lungs (volatile drugs). All the other secretory channels, i.e., saliva, sweat, etc., play only a minor part in their elimination. Saliva excretes to a limited extent the haloids (iodides), sulfocyanates, potassium, ammonia, mercury, lead, quinine, morphine, etc. The excretion may begin within twenty minutes after ingestion and may last for many hours.

Drugs may be eliminated from the body in a changed or an unchanged condition. The changes which may result are oxidation, reduction, decarboxilation, deaminization, conjugation, etc. The altered compound is generally less toxic and is more easily excreted than the original drug. All tissues take an active part in the detoxication of drugs, but the liver is the most important organ.

Selection of the Remedy

After the diagnosis of a disease is made, the proper remedy is selected. Depending on the nature of the disease, a psychic, a physical, a hygienic, a surgical, or a pharmacologic method is chosen for the treatment of the ailment. Usually a combination of two or more methods is employed. No sharp line of demarcation can be drawn between the various groups of remedial agents, and a division of the whole subject matter is therefore difficult. Dentistry is not an abstract science; it has its fashions and its schools. In the early days of medical practice the Greek and Roman schools were predominant, and the pharmacologic treatment consisted principally of the use of innumerable pharmaceutical compounds of vegetable drugs, which today are known as galenic preparations (after Galen). The Arabian physicians continued the same practice but added to the materia medica a number of new organic and inorganic compounds which were prepared by their chemists or were accidentally discovered by the alchemists. With the introduction of iatrochemistry by Paracelsus, the galenic preparations and the methods of treatment of the Greek and Arabian physicians received a severe setback. When on St. John's Day, in 1527, Paracelsus burned publicly on the market place of Basel the works of Celsus, Galen, Avicenna, and others, exclaiming, "I have burnt all these books so that all misery may be carried away with their smoke," a new era had dawned in scientific therapeutics. During the seventeenth and eighteenth centuries a complete change in the practice of therapeutics was inaugurated. This change started almost simultaneously in various parts of Europe. Sydenham, of London (1660); Boerhaave, of Leyden (1720); van Swieten, of Vienna (1745); Hoffmann, of Halle (1725), and Stahl, of Berlin (1730) were the most influential reformers, and their names are indelibly in-

scribed on pages describing the progress of modern therapeutics. The growing tendency of overdrugging received a severe check through the introduction of Hahnemann's (1810) method of treating diseases with very small doses, which, combined with other extreme changes in therapeutics, resulted in the foundation of the *homeopathic* school.

No definite knowledge regarding drug action was then available to the practicing physician, and, as a consequence, it became customary to ridicule those who regarded drugs necessary in the treatment of disease. Skoda and Dietl (1830 to 1870), of the Vienna school, expressed erratic views in regard to drug medication, and both extremists carried the idea of drug nihilism to such an extent as almost to eliminate materia medica from the curriculum of the medical schools.

Therapeutic methods may be conveniently divided into:

1. *Physical Therapeutics, Physiotherapy.*—They include the physical and hygienic means and methods employed as remedies, such as light, heat, cold, electricity, climate, exercise, and x-ray.

2. *Mechanical Therapeutics.*—They are represented by massage, exercise, orthodontics, and the instruments utilized in the performance of orthopedic surgery.

3. *Psychologic Therapeutics, Psychiatry.*—They are principally concerned with the psychologic influences exercised by the dentist and physician on the patient. Nervous patients are amenable to this method of treatment, although certain bodily functions may also be materially influenced by this method.

4. *Pharmacotherapeutics, Drug Therapy.*—They include diets, the many spas, and, finally, the great mass of drugs, natural and synthetic.

Synopsis of the National Narcotic (Harrison) Law as It Affects the Dental Practitioner

On March 1, 1915, the National Narcotic (Harrison Antinarcotic Bill, H. R. 6282) Law, went into effect. This law* has, in many respects, a direct bearing on the practice of dentistry, as the two basic drugs to which it refers—namely, opium and cocaine and their derivatives—are frequently employed by the dental practitioner. The following summary is a synopsis of the law as it affects the dentist:

(1) The law provides that on and after July, 1915, and annually thereafter, every person, firm, or corporation that imports, manufactures, compounds, deals

*In a decision rendered April, 1917, by the United States Circuit Court of Appeals for the Second Circuit confirming the decision of the United States District Court, it was held that procaine, anesthesine, orthoform, and holocaine do *not* come under the National Narcotic (Harrison) Law and, therefore, dentists prescribing or using these drugs may do so under the above ruling without registering or employing the Harrison narcotic blanks in ordering them.

in, disposes of, sells, distributes, or gives away opium, or coca leaves, or any compound, manufacture, salt, derivative, or preparation thereof, shall register with the Collector of Internal Revenue of the district in which he resides, his name or style and his place of business. Persons registered under this law will be held responsible for the acts of their employees in dispensing or distributing any of the drugs coming within the scope of this law. Where two or more dentists are in partnership, doing business under a firm name, it is necessary for the firm to be registered, the firm registry number to be indicated in ordering any of the drugs for use in the office practice of the members of the firm. Each individual dentist in such partnership should register and pay the annual tax under his own name, if also engaged in private practice. If maintaining an office in more than one internal revenue district each dentist must register in each district.

(2) Specified drugs for office use may be purchased only upon official order blanks issued by the Internal Revenue Department, at a cost of one cent each for each original order or duplicate thereof. Whenever the dentist orders any of the above-named drugs, he must fill out the official order blank, retaining the duplicate copy thereof for two years and in a manner open to inspection by the proper authorities.

RECORD OF NARCOTICS DISPENSED OR DISTRIBUTED

DATE	KIND OF DRUG	QUANTITY	PATIENT'S NAME	PATIENT'S ADDRESS

Fig. 2.—Sample page of record of narcotic drugs dispensed.

(3) The dispensing or distribution of any of the aforesaid drugs to a patient by a dentist duly registered under the act, in the course of his professional practice, is not interfered with by this law, nor does the law apply to the sale or disposal in any way of the said drugs by a pharmacist on the written prescription of a dentist. But such prescriptions must be dated as of the date on which they were signed and must bear the signature of the dentist who issued them. A duplicate copy thereof should be retained for two years by the prescriber. Further, it is held that a dentist who does not dispense narcotics in good faith, for the purposes of curing a sick person or curing a person of the narcotic habit, violates the law.

(4) The dentist may, without restriction, dispense to his patients the prescribed drugs when he personally attends his patient, in the course of his professional practice. If the dentist does not personally attend the patient and distributes or dispenses any of the prescribed drugs, he must keep a record of such drugs so dispensed or distributed, the amount dispensed or distributed in each instance, the date, and the name and address of the patient. It will be noted that this record is required *only* when the dentist does not personally attend the patient.

(5) The law exempts from its provisions all preparations and remedies which do not contain more than two grains of opium, or more than one-fourth grain of morphine, or more than one grain of codeine, or of any salt or derivative of

any of them, in one fluid ounce, or, if a solid or semisolid preparation, in one avoirdupois ounce. The exemptions as to the preparations above named apply only when they are sold, distributed, given away, dispensed, or otherwise disposed of as medicines and not for the purpose of evading the provisions of the act. Dentists using in office practice cocaine and similar drugs are permitted to make up stock solutions, recording only the date of preparation and the date of exhaustion.

The law, as construed by the Supreme Court, holds it to be a crime for any person, including practitioners, to furnish an addict with narcotics for the purpose of satisfying his cravings for the drug. It is also held that an order for a narcotic issued by a practitioner to an habitual user thereof but not in the course of professional treatment in an attempted cure of the habit, but for the purpose of providing the user with narcotic drugs sufficient to keep him comfortable by maintaining his customary use, is not a prescription under the law, and that the practitioner who issues an order under such circumstances, as well as the druggist who knowingly fills such an order, has committed an indictable offense.

(6) It is a crime under the act for any person who is not registered and has not paid the tax to have in his possession or under his control any of the aforesaid drugs, and such possession will be construed as presumptive evidence of a violation of the act. This provision, however, does not apply to any employee of a registered person, or to a nurse under the supervision of a dentist registered under the act, having such possession by virtue of his employment or occupation and not on his own account. This act in no way interferes with the operation of the laws of any State respecting the manufacture, sale, or use of narcotic drugs unless such laws are in direct conflict therewith.

The penalty for violating any of the requirements of the act is a fine of $2,000, or imprisonment for not more than five years, or both, in the discretion of the court.

From all appearances, all local anesthetic solutions, tablets, pellets, pastes, etc., containing cocaine or opium, or any of their derivatives, are amenable to this law. Liniments, ointments, or other preparations containing drugs not specifically exempt, used for oral, nasal, aural, ocular, rectal, urethral, or vaginal administration, are not in such cases used externally and are therefore not exempt from the provisions of this law.

Tropacocaine is a synthetic product of cocaine; consequently, its sale will be governed by the law, while chloretone, procaine, monocaine, and quinine and urea hydrochloride are not affected by it.

The practitioner who purchases ready-made solutions, tablets, or other pharmaceutic compounds should carefully read the attached labels so as to familiarize himself with the components of the respective preparations. Aside from the before-mentioned drugs there are a number of pharmaceutic preparations employed by the dental practitioner upon which the law has a direct bearing. The most important compounds are herewith enumerated: fluidextracts, tinc-

tures, and elixirs, powders, pills, tablets (compressed and hypodermic), and pastes containing opium, coca, or their derivatives.

Demerol (1944) was included under the supervision of this act.

Classification of Remedies

The first classification of drugs according to their pharmacologic action was introduced by Buchheim in 1856, but from a practical as well as a didactic point of view, it was a failure. In the earlier editions of this book Prinz classified drugs chiefly according to their action—pharmacotherapeutics. The present classification emphasizes the site of action of the drug, and the arrangement of the material in the text closely follows it. An overlapping of one group into another must be expected, as no absolute boundaries can be established. To facilitate a ready comprehension of the various classes, the site of action of the drugs listed precedes each group.

I. Systemic Drugs Which Act on Specific Tissues

Drugs Which Affect the Central Nervous System:

General Anesthetics
Intoxicants
Hypnotics
Analgesics
Antipyretics
Cerebral Stimulants and Depressants
Medullary Stimulants and Depressants
Spinal Cord Stimulants and Depressants

Drugs Which Affect the Peripheral Autonomic Nervous System and the Voluntary Motor Nerves:

Adrenergic
Cholinergic

Drugs Which Affect the Pain Fibers:

Local Anesthetics

Drugs Which Affect the Circulatory System:

Drugs Which Affect the Heart
Drugs Which Affect the Blood Vessels
Drugs Which Affect the Blood

Drugs Which Affect the Respiratory System:

Respiratory Stimulants and Depressants
Expectorants
Drugs Which Affect the Bronchi

Drugs Which Affect the Gastrointestinal System:

Drugs Which Affect the Glands
Drugs Which Affect the Smooth Muscles
Carminatives
Stomachics, Bitters, and Digestives
Emetics and Antiemetics
Gastric Antacids
Teniafuges and Anthelmintics
Intestinal Antiseptics
Cathartics

Drugs Which Affect the Genitourinary System:

Diuretics and Antiduretics
Urinary Antiseptics
Drugs Which Affect the Urinary pH

II. Drugs Which Are Applied Locally

Drugs Used on the Skin and Mucous Membranes:

Emollients and Demulcents
Protectives
Detergents
Antiseptics and Germicides
Astringents
Counterirritants and Irritants
Caustics

Drugs Used in the Oral Cavity:

Oral Antacids
Oral Antiseptics and Germicides
Oral Astringents
Oral Counterirritants
Oral Caustics
Oral Topical Anesthetics
Oral Deodorants
Oral Detergents
Oral Emollients and Protectives
Oral Styptics
Drugs Which Inhibit Gagging

Drugs Used on the Hard Tissues of the Teeth:

Dentifrices and Abrasives
Antacids
Obtundents

Protectives
Caustics
Antiseptics and Germicides
Bleaching Agents
Restorative Materials

Drugs Used on the Dental Pulp and in Root Canals:

Antiseptics and Germicides
Styptics
Protectives
Caustics
Obtundents
Detergents
Restorative Materials

III. Drugs and Agents Which Do Not Act on Specific Tissues

Chemotherapy and Specific Drugs:

Organotherapy:

Glandular Therapy
Antitoxins
Serums
Vaccines

Dietary Factors:

Foods
Inorganic Substances
Vitamins

Physiotherapy:

Heat
Cold
Light
X-ray
Cataphoresis

CHAPTER III

DRUGS WHICH DEPRESS THE CENTRAL NERVOUS SYSTEM

GENERAL ANESTHETICS

Anesthetics (without sensation), sometimes referred to as *narcotics* (loss of sensation and consciousness), are substances which, when absorbed by the blood, act on the central nervous system and cause deprivation of all sensation. The principal general anesthetics employed for dental purposes are nitrous oxide, ethyl chloride, ether, vinethene, and ethylene.

History of Anesthetics

The discovery and the application of anesthetics for surgical and other painful operative practices have played a most important part in the evolution of American dentistry. The blessings of anesthesia to suffering humanity cannot be overestimated, and what Liecky has written is certainly true: "It is probable that the American inventor of the first anesthetic has done more for the general happiness of mankind than all the moral philosophers." It is not our intention to present a detailed account of this most important occurrence, but we wish merely to refer to a few incidents which may facilitate a clearer comprehension of the matter. Since nitrous oxide was the first general anesthetic used, and since it still holds first place among the general anesthetics used in dentistry, it will be discussed in more detail.

Nitrous oxide was discovered in 1722 by Joseph Priestly, who gave it the name "dephlogisticated nitrous air."[1] In the succeeding years it aroused general interest, becoming an important subject for discussion in the learned societies. The big lecture hall of the Royal Institute of England was frequently the scene of public demonstrations of the physiologic effects of the "dephlogisticated nitrous air." It remained, however, for an American dentist to discover and demonstrate the application of anesthetics to surgery.

[1]Excellent accounts of the discovery of anesthesia are found in the following works: Nevius: Discovery of Modern Anesthesia, 1894. McManus: Notes on the History of Anesthesia and the Wells Memorial Celebration, 1896. Hewitt: Anesthetics and Their Administration, 1907. The many works on general anesthesia usually furnish more or less extended records on this subject.

The preparation of nitrous oxide from ammonium nitrate appears to have been first achieved by Laplace. Sir Humphry Davy conducted careful investigations of this substance, and soon became acquainted with its exhilarating influence. His experiments were published in 1800. It is interesting to observe that Davy made various allusions to the physiologic action of this gas. He recognized its possible use as an anesthetic, for he says that "it may probably be used to advantage during surgical operations in which no great effusion of blood takes place," a prophecy which required nearly half a century to become true. Not only was its anesthetic effect recognized by him, but he also pointed out its comparatively safe administration by saying, "Modifications of the powers of nitrous oxide by mixtures of gas with oxygen or common air will probably enable the most delicately sensible to respire it without danger, and even with pleasurable effects."

Demonstrations of the exhilarating effects of nitrous oxide were a source of public entertainment in England in the years following its discovery, and in due time found their way into the United States. It was at one of these demonstrations that the conception of its utilization for the purpose of producing insensibility to pain was conceived by a dentist. This conception and its successful application marked the discovery of anesthesia for surgical purposes. The incident is recorded as follows:[1]

On the evening of December 10, 1844, Dr. Horace Wells, a practicing dentist of Hartford, Conn., attended in that city a chemical lecture by Mr. G. Q. Colton, during or after which the lecturer administered to Mr. Samuel A. Cooley and others the nitrous oxide gas. Mr. Cooley, on being brought under its influence, became unusually excited, and, during his consequent activity, sustained severe bruises, of which fact he was unconscious until after recovery from the effects of the gas. His asseverations of want of knowledge of any pain while in the unconscious condition took strong hold on the mind of Dr. Wells, and he immediately expressed his belief that teeth could be painlessly extracted during the inhalation of this agent. So strongly was he thus impressed that the next day he requested Mr. Colton to provide some of the gas for him, which he took himself, holding the bag in his lap, and while under its influence underwent the extraction of a molar tooth at the hands of Dr. John M. Riggs, a fellow dentist of Hartford. Upon his recovery Wells exclaimed in high glee, "A new era in tooth pulling!" The exclamation was prophetic. So elated were Drs. Wells and Riggs at the success of their experiment that they immediately turned their attention to the extraction of teeth by the aid of this agent, and continued to devote themselves, in conjunction, to this subject for several weeks almost exclusively. Dr. Wells used the gas freely during the whole time of his dental practice, and Dr. Riggs employed it constantly "as people demanded it.

[1] A History of Dental and Oral Science in America, prepared under the direction of the American Academy of Dental Science, 1876.

which they ordinarily did," until 1847, when he began to employ chloroform in its stead. Wells, however, was not content to demonstrate the availability of nitrous oxide as an anesthetic in dentistry alone, but carried it into general surgery. The first recorded case of this character occurred on August 17, 1847, being the extirpation of a large scirrhous growth by E. E. Marcy, M.D., then of Hartford. The case is reported at length in the *Boston Medical and Surgical Journal*, September 1, 1847. The gas was administered by Dr. Wells, and its operation was entirely satisfactory. The second case was amputation of the thigh, occurring January 1, 1848; the operator, Dr. P. W. Ellsworth, and the gas given by Dr. Wells. This case is also reported in the above periodical, Vol. XXVII, p. 498. The last we shall mention was the removal of a fatty tumor from the shoulder at Hartford, January 4, 1848; S. B. Beresford, M.D., the operator, and the gas given as before, by Horace Wells. This was only twenty days before Wells' death. Almost immediately upon Wells' discovery the use of the gas became quite general with the Hartford dentists. John B. Terry (afterward Dr. Wells' associate in practice), John Braddock, and E. E. Crowfoot, all dentists of that city, used the agent between the time when Wells brought it to notice and September 30, 1846, a date which will be presently noticed in connection with the subject of ether. A short time after his discovery, Dr. Wells visited Boston in order to bring it before the medical men of that city. Calling on Professor Warren, of the Harvard Medical College, he communicated the facts to him, and was referred to the students for examination, before whom he administered the gas to a patient who desired a tooth drawn; but, probably because the bag containing the agent was withdrawn too soon, the patient made some noise during the operation, although he afterward asserted that he had not felt pain. From this unfortunate circumstance the majority present thought the experiment a failure, though many considered that complete anesthesia had been produced, and afterwards made oath or published statements to that effect. Of these may be mentioned Wm. M. Cornell, Mason M. Miles, and C. A. Taft. While in Boston at this time, and previous to his experiment at the Harvard school, Dr. Wells called on Dr. Charles T. Jackson and Dr. Wm. T. G. Morton, the latter an old pupil and partner of his, and communicated his discovery to them. This, it will be remembered, occurred in December, 1844. These gentlemen "expressed themselves in the disbelief that surgical operations could be performed without pain, both admitting that the *modus operandi* was entirely new to them." The fact of this visit, at the date and for the purpose alleged, is admitted by Morton in his subsequent memoir to the French Academy of Arts and Sciences on the subject of this discovery of the anesthetic effects of sulfuric ether. After the discovery was made, Wells had frequent interviews with Morton on the subject, and the latter requested instructions in the preparation of the gas, as he wished to try it in Boston. Probably aware of the danger, to a nonchemist, of preparing the nitric oxide in place of the nitrous oxide, Wells advised Morton to go to Dr. Jackson in Boston, who was a chemist and could prepare the gas properly. This fact is susceptible of abundant proof.

Ether was discovered in the middle of the sixteenth century by Cordus, but it remained for two American physicians and two American dentists to introduce it as a general anesthetic between 1842 and 1846. Crawford W. Long, M.D., Charles T. Jackson, M.D., and the dentists, Horace Wells and William T. G. Morton, are the four claimants for this honor. Long used ether as a general anesthetic as early as 1842, but, living in a small, obscure country place

in Georgia, and not having made public his experiences with this anesthetic, the discovery remained unknown to the world at large. The first publication by Long regarding the use of ether appeared in December, 1847.[1] Without knowledge of Long's discovery, Morton introduced ether in Boston in 1846 as letheon—ether mixed with essential oils to disguise its odor. The ether was prepared for him by Jackson. Wells, however, who had been experimenting with nitrous oxide and other anesthetic substances two years prior to Morton's discovery, administered ether as an anesthetic in 1845. Wells received the suggestion of using ether for such purposes from E. E. Marcy, M.D., of Hartford, Conn., in 1844. It is not our intention to prove the rights of priority regarding the introduction of ether as a general anesthetic; volumes have been written about the controversy between the various claimants. Let it suffice to say that the above-named gentlemen participated in this great discovery.

This year (1944) the American Dental Association is celebrating the centennial of anesthesia, and honoring Horace Wells as its discoverer.

Chloroform was discovered simultaneously (1831-1832) by Samuel Guthrie, of Sackett's Harbor, N. Y.; by Liebig, of Germany, and by Soubeiran, of France. It was introduced as a general anesthetic by Simpson, who in 1847 published a lengthy report concerning its superiority over ether as observed by him in the clinics of Edinburgh University. Chloroform soon replaced ether in popularity on both continents. Americans returned to the use of ether much earlier than the Europeans.

Ethyl chloride was discovered in 1759 by Bouelle. In 1848 it was introduced as a general anesthetic by Heyfelder. The high cost of ethyl chloride and the difficulty of obtaining a pure product prevented its ready adoption as an anesthetic. In 1867 Rottenstein called attention to the use of ethyl chloride as a refrigerant agent for local anesthetic purposes, and in 1889 Rhein suggested methyl chloride for the same purpose. In 1891 ethyl chloride was reintroduced as a refrigerant agent by Redard, and in 1895 Carlson observed two cases of general anesthesia resulting from inhaling its vapors when employed locally in the mouth. Thiesing, in 1896, once more investigated this agent for its general anesthetic properties, and in the same year Lotheisen, Ludwig, and Pischer, followed in short succession by Billeter, Ruegg, Respinger, Seitz, Brodtbeck, and others, introduced it again in general and dental surgery.

Ethylene, introduced by Luckhardt and Carter[2] and Brown,[3] is a general anesthetic providing all the advantages of nitrous oxide and devoid of many of the disadvantages of ether. It is very explosive when mixed with oxygen, and many serious accidents have occurred from its use.

Vinethene is a liquid anesthetic introduced by Leake and Chen[4] in 1930 and it is rapidly being introduced into dentistry as a general anesthetic. It has an advantage over nitrous oxide in not requiring complicated apparatus but has the disadvantage of being more toxic in the hands of untrained anesthetists.

[1]Long: An Account of the First Use of Sulphuric Ether by Inhalation as an Anesthetic in Surgical Operations, Southern M. & S. J., 1847.

[2]Luckhardt and Carter: J. A. M. A., March 17, 1923.

[3]Brown: Canad. M. A. J., March 7, 1923.

[4]Leake, C. D., and Chen, M. Y.: Proc. Soc. Exper. Biol. & Med. 28: 151, Nov., 1930.

The future will offer many new inhalation anesthetics, but the dentist must be cautious in accepting them until they have been tried and their value in dentistry established.

Recently some of the barbituric acid derivatives administered in large doses intravenously have been advocated for surgical anesthesia. At the present time this anesthetic measure is still in the experimental stage and is not recommended for the anesthetic needs of dental practice.

General Discussion of Anesthetics

Anesthesia is a depressed state of consciousness produced by a drug. The site of action is the central nervous system, beginning with the cerebral cortex and progressing to the basal ganglia, midbrain, spinal cord, and medulla. The drugs first stimulate and then depress the affected nerve tissue. *Anesthetics* are drugs which produce anesthesia. Chemically they are compounds of the methane series and substitutions thereof; nitrous oxide is an exception. Anesthetic agents are subdivided into *local anesthetics* and *general anesthetics.* Local anesthetics are drugs which produce an insensibility to pain in the area to which they are applied and do not produce a loss of consciousness. General anesthetics act systemically after absorption, circulating in the blood and producing loss of consciousness and total insensibility to external stimuli, as pain. *Analgesics* are drugs which inhibit or abolish sensations of pain by a central action without a loss of consciousness. This state is known as *analgesia,* and its use in dentistry is assuming greater importance. *Narcosis* is a state of depressed consciousness produced by a drug. The depressed state of consciousness may vary from sleep, where the patient is awakened easily, to *stupor,* where the patient is awakened with difficulty, to *coma,* where the patient cannot be awakened.

Preanesthetic medication is the administration of drugs to patients who are about to receive an anesthetic. Morphine and atropine are generally given about one-half hour before the anesthetic is administered. *Basal anesthesia* is the administration of a narcotic drug to a patient rendering him unconscious. The surgical state of anesthesia is then induced and maintained by the addition of a general anesthetic at the time of surgery.

Pharmacodynamics of Anesthetics

The anesthetic drug circulates in the blood stream in solution. This solution may be a gas-liquid phase (ether) or a solid-liquid phase (avertin). The lipids of the nerve cells concentrate the drug in the central nervous system, and an alteration of physiology pro-

duces the symptoms of narcosis. This altered physiologic response is brought about by at least two factors: (1) an anoxia resulting in a partial suffocation of the nerve cells and (2) a direct narcotic effect of the drug on the protoplasm.

The action of general anesthetics is on the cerebral cortex, midbrain, basal ganglia, cerebellum, spinal cord, and medullary centers, and in the order given. Usually the sensory areas are affected first and the motor areas next. The parts of the cell affected are the cell membrane, cell protoplasm, and the enzyme system. The drug affects the cell by a physicochemical combination: physically by adsorption, osmosis, and polarization; chemically by oxidation, reduction, and substitution. The responses that a living cell may make to a drug are limited to *stimulation* and *depression*. Some authorities believe that depression is always secondary and that stimulation is always primary, even though momentary. *Drugs do not change the functional habits of the cells; they only increase or decrease their normal functional behavior.*

According to our present limited knowledge regarding the composition of living matter, we are unable to explain the nature of these changes, but it is plausible to assume that this union between the drug and the cell protoplasm must be very labile, as no alterations occur in the cell contents. Furthermore, this union is easily broken up, as anesthesia passes off quickly after the drug is stopped, and the patient awakens without apparent serious disturbances. The interchanges which occur between the nerve cells and the anesthetic depend on certain chemicophysical properties of the anesthetic. It is important that the drug be administered in vapor form, and be mixed with the inspired air so as to bring it into intimate contact with the circulating blood in the alveoli of the lungs. The blood, which is saturated with the anesthetic vapor, carries it to all the tissues of the body, but the nerve cells possess special affinity for the anesthetic and quickly absorb these drugs from the blood. When the supply of anesthetic is stopped, the pressure of the narcotic vapor in the lung decreases, and the blood, which is now free from tension, reabsorbs the anesthetic from the nerve cells and carries it back to the lungs, to be exchanged for normal air. This process of removal is continued until all the anesthetic is exchanged for normal air.

A comparison of the boiling points of various anesthetics and their mixtures, if we based it on statistics of the death rate from their administration, would indicate that the lower the boiling point, ap-

parently the safer the anesthetic. Nitrous oxide has the lowest boiling point and is by far the safest of all general anesthetics. There is much room for further elucidation of this interesting subject.

Theories of Anesthesia

Meyer-Overton Theory (Overton-Meyer theory) states that the anesthetic drug circulates in the blood stream and is taken up by the cells of the central nervous system. As most anesthetics are fat solvents, the lipids of the nerve cells attract and hold the drug, and this combination alters the function of the brain tissue, producing anesthesia.

Moore and Roaf Theory accepts the Meyer-Overton premise of solubility of the drug in the lipids of the nerve cells, but they add that it is not this combination which alters the physiology of the cells. The drug produces its effect by combining loosely with the protoplasm, and the narcosis remains as long as the vapor pressure of the drug in the blood exceeds that of the cell.

Verworn Theory accepts the Meyer-Overton theory but believes that the effect is one of asphyxiation which is brought about by the drug. This theory is partly true but is not the whole theory.

Methods of Administering Anesthetics

1. *Open Method* of administering general anesthetics is by dropping the drug on a gauze mask, the patient being permitted to breathe air as well as vaporized drug. This is the safest method and the one most often used with the liquid anesthetics. It is a wasteful technique.

2. *The Semiopen Method* is similar to the open method except that a towel is wrapped about the mask to prevent a too rapid loss of anesthetic and to restrict the amount of air inspired by the patient.

3. *Closed Method* is accomplished by having the patient breathe and rebreathe into a closed circuit. The amounts of anesthetic, oxygen, and carbon dioxide are regulated and the patient is forced to breathe this mixture. The very volatile, explosive, and expensive anesthetics are administered in this manner.

Stages of General Anesthesia

The symptomatic description of general anesthesia begins with the first breath of the anesthetic and ends with the return of the patient to consciousness. For the sake of convenience, the description is divided and subdivided into stages, substages, and planes. While there is an anatomic and functional explanation for this classifica-

tion, it should be kept in mind that there is no definite line of demarcation between the stages, the one blending into the other.

General anesthesia, for convenience of description, is divided into three stages: (1) *induction,* which is the developing of the narcosis to the surgical anesthetic substage; (2) *maintenance,* which is the preservation of that substage throughout the operation; and (3) *recovery,* which is the discontinuance of the anesthetic and the return of the patient to consciousness.

The induction stage is subdivided into four substages for simplicity of description.

The first substage begins with the first inhalation of the anesthetic and is characterized by sensory stimulation followed by depression with analgesia. The symptoms are caused by a reflex from the irritating fumes of the anesthetic on the sensitive mucous membranes and from a direct effect of the drug on the cells of the cerebral cortex. There is no doubt that fear brings on a strong sympathetic stimulation in many patients. The respiration is deep and regular; the pulse is full and slightly rapid but regular; the blood pressure is normal or slightly elevated; the pupils of the eye are constricted, showing a parasympathetic stimulation; the reflexes are normal, the consciousness is not lost. At the end of this substage, a state of analgesia exists which is used to obtund pain in operative dentistry. This analgesia is brought about by a depression of the sensory cells of the cerebral cortex.

The second substage is characterized by muscular excitement, intoxication, and loss of consciousness. The symptoms are caused by a stimulation of the motor centers of the cerebral cortex and by a depression of the sensory centers which results in an intoxication and finally in a loss of consciousness. During this stage the respiration is irregular, interrupted by coughing, swallowing, and often vomiting. The pulse is rapid and irregular; the blood pressure is normal or raised; the pupils are normal or mildly dilated and react to light. The reflexes vary from normal to exaggerated, and the color of the skin may be flushed or cyanosed. The anoxemia is caused by the patient's holding his breath or by lack of sufficient oxygen in the anesthetic mixture. The patient is often uncooperative and is in a fighting spirit. He is aware of pain but generally does not recall it upon awakening—amnesia. The spinal cord is stimulated and a moderate amount of rigidity may be present. All reflexes are present and may be exaggerated.

The third substage of induction anesthesia is the state of surgical anesthesia. It is subdivided into three planes. The cerebral cortex has been depressed and all consciousness to external stimuli has been abolished. The midbrain is depressed, and the patient remains quiet as in a deep sleep—coma. The spinal cord is being depressed and a gradual relaxation of the voluntary muscles takes place, until all spinal reflexes disappear. Respiration becomes slow and regular, as in sleep. The pulse is slow and strong, the blood pressure may be normal for sleep or slightly elevated because of stimulation of the medullary centers. Later, as the drug depresses the vital medullary centers, the blood pressure falls. The pupillary and conjunctival reflexes disappear, showing that the autonomic nerves are being depressed. The pupils temporarily constrict from a parasympathetic stimulation, but as the anesthetic state progresses, the pupils dilate. At the end of the third substage is the toxic stage, and it is not resorted to except when complete muscular relaxation is necessary.

The three subdivisions under substage 3, the surgical anesthetic stage, are as follows: *Plane 1* is a light stage of surgical anesthesia. The patient is unconscious and does not feel pain, but as the voluntary muscles are not relaxed, surgical procedures requiring muscular relaxation cannot be performed. The involuntary reflexes are present but are less active than normally. *Plane 2* is the optimal surgical anesthetic plane and is characterized by a complete relaxation of the voluntary muscles. The involuntary muscles are still responsive but slightly depressed. The involuntary reflexes are feeble but present. This is the plane for general surgery. *Plane 3* is characterized by an absence of all reflexes. The vital processes may be temporarily stimulated but are soon depressed. This is a dangerous anesthetic plane and is not resorted to unless indicated by the operation and then only for a short time.

In the fourth substage, medullary paralysis, all of the higher centers have been depressed, and the drug begins its insidious poisoning of the vital centers of respiration, cardiac acceleration, and vasomotor control, with a general paralysis of the autonomic nervous system. Respiration becomes slow and weak, cyanosis is present, and the Cheyne-Stokes type of respiration prevails, showing that the respiratory center is losing its specificity to carbon dioxide. Death generally occurs from respiratory failure and anoxemia. The heart muscle is directly depressed, causing it to function less efficiently; the blood vessels dilate, causing the blood pressure to fall.

The pressure nerves of the heart do not correct the circulatory failure, and the anoxia becomes more profound until the poisoned heart muscle fails. The sphincter muscles dilate, and the eye pupils are in wide dilatation and do not respond to light.

The *maintenance stage* is a continuance of the stage of surgical anesthesia throughout the operation. The depth of the anesthesia depends upon the needs of the operation and the reactions of the patient. The lighter the anesthesia the safer the anesthesia.

Stages of Recovery From Anesthesia

The stage of recovery is the same as the stage of induction anesthesia, only reversed in order. There is usually less excitement. The patient may pass out of the anesthetic stage and sleep for hours, or may be awakened for short periods by nausea or vomiting. There may be periods of struggling and incoherent speech to be followed by quiet sleep. The patient is shocked by the anesthetic and surgery and will remain prostrated for one or more days. A liquid diet is usually given as soon as the patient will take it. The drinking of water should be encouraged to aid in the elimination of drug and toxins. A saline infusion is routine in many hospitals following all major operations. The patient must be kept warm and the pain relieved with analgesics. Good nursing care is essential.

Outline of the Stages of General Anesthesia

Stage I. Induction stage—beginning with the first breath of the anesthetic and ending with the patient's passing into the stage of surgical anesthesia.

Substage 1. Mental excitement and analgesia. Consciousness depressed but not lost. Caused by a stimulation followed by a depression of the sensory areas of the cerebral cortex.

Substage 2. Motor excitement and unconsciousness. Caused by a stimulation followed by a depression of the motor and sensory areas of the cerebral cortex.

Stage II. Surgical anesthesia—beginning with the end of Stage I and terminating with the stoppage of the anesthetic. The patient is *maintained* in this stage throughout the operation.

Substage 3. Surgical anesthesia characterized by a complete loss of consciousness, freedom from pain, and relaxation of the voluntary muscles. Caused by a depression of the sensory and motor ganglia of the midbrain and a stimulation and depression of the spinal cord from below upwards.

Light surgical plane—incomplete muscular relaxation since the spinal cord is only partially depressed.

Optimum surgical plane—complete muscular relaxation.

Deep surgical plane—slight depression of the vital centers.

SUBSTAGE 4. Toxic stage characterized by depression of the vital centers of respiration and circulation and loss of the involuntary reflexes.

Stage III. Recovery stage—begins when the anesthetic is stopped and continues until consciousness is regained. It resembles Stage I, only in reverse order.

TABLE OF ANESTHETIC CHANGES IN INHALATION ANESTHESIA*

STAGE	RESPIRATION	EYELID REFLEX	EYEBALL ACTIVITY	PUPILS		
				NO PREMEDICATION	MORPH. ¼ GR. AND SCOP. 1/150 GR.	MORPH. ¼ GR.
First	Normal	Normal	Normal	Normal or reflex dilation	Normal (usually)	Constriction
Second	Irregular	Normal	Active	Normal or reflex dilation	Normal (usually)	Constriction
Third Plane I	Regular rhythm; hyperpnea; depth of respiration increased	Absent	Active	Normal	Normal	Constriction
Plane II	Same as Plane I	Absent	Paralyzed	Dilation	Slight paralytic dilation	Constriction
Plane III	Onset of respiratory paralysis, gasping inspiration, decreased respiratory volume	Absent	Paralyzed	Dilation	Paralytic dilation	Dilation
Plane IV	Decreased respiratory volume, cessation of respiration	Absent	Paralyzed	Marked dilation	Complete paralytic dilation	Marked dilation
Fourth	Paralysis of respiration					

*From Davison: *Materia Medica, Toxicology and Pharmacology*, 1940.

Contraindications to General Anesthetics

Ether should be avoided in pulmonary disease.

Nitrous oxide should be avoided in arteriosclerosis and high blood pressure.

Chloroform is not indicated in cardiac or liver disease.

Preventive Measures in General Anesthesia

Use nitrous oxide for the first and second substages of induction anesthesia to allay the symptoms of excitement.

Preanesthetic narcotics such as morphine, ⅙ to ¼ grain.

Injection of $\frac{1}{120}$ grain of atropine sulfate twenty minutes before the anesthetic to allay excessive oral and bronchial secretion and cardiac depression.

Have the stomach, urinary bladder, and rectum empty.

Avoid preliminary starvation which increases the acidosis and liver degeneration.

Avoid hydragogues which deplete the body of fluid.

Selection of the Anesthetic

The choice of the anesthetic is determined largely by the type of operation and the condition of the patient. Complete and prolonged anesthesia requires previous examinations and preparations quite beyond the scope of the average dental office. Even partial anesthesia (analgesia), recently advocated with nitrous oxide for certain operative procedures, is not without danger and should be used with caution. Generally speaking, general anesthetics should be administered by trained anesthetists only in hospitals and in adequately equipped dental offices.

Nitrous oxide, ethyl chloride, and vinethene are anesthetics which are principally employed in the United States and England for short dental operations. In hospitals where adequate equipment is available, ethylene is gaining in popularity. The general condition of the patient will determine which anesthetic is indicated in his particular case; sex and age are of consequence in regard to choice. Young patients are good subjects for nitrous oxide or ethyl chloride. Patients suffering from bronchitis and pulmonary tuberculosis must be carefully watched to avoid undue cyanosis if nitrous oxide is given; a liberal supply of oxygen should always be administered with it.

The principal contraindications to chloroform are fatty degenerations of the heart, hepatitis, and patients in danger of acidosis. The contraindications to ether are acute respiratory and renal diseases, brain tumor, and hemorrhage. In advanced diabetes and in fatty degeneration of the heart, chloroform and ether are both contraindicated and ethylene is the anesthetic of choice.

For the average dental operation, nitrous oxide in combination with oxygen from experience has proved by far the safest of all

anesthetics. Because of the somewhat more elaborate apparatus required for nitrous oxide, many operators have preferred ethyl chloride or vinethene. However, the relative safety of nitrous oxide as compared with these compounds explains the trend in favor of the former. Chloroform and, to some extent, ether should not be employed as anesthetics for minor dental operations. The many deaths which have occurred from the use of chloroform in dental operations probably find an explanation in the dangerous upright position of the patient when seated in the operating chair and in incomplete anesthesia. Where adequate safety factors are employed, ethylene may be the anesthetic of choice.

Treatment of Accidents of General Anesthesia

The disturbances resulting from the administration of anesthetics may conveniently be classified as those affecting, first, the digestive apparatus; second, the circulation; third, the respiration; and fourth, the nervous system. Disturbances in the digestive apparatus usually manifest themselves in nausea or vomiting. This state is the direct result of reflex movement of the pharynx, esophagus, and stomach, and is most likely caused by the irritating vapor of the anesthetic or the direct effect of the drug on the emetic center. It is most frequently observed in the administration of chloroform, ether, and ethyl bromide, and rarely with ethylene, ethyl chloride, or nitrous oxide. Treatment is seldom called for, as nature usually helps herself. Vomiting is more frequently present in cases where a full meal is taken shortly before the anesthetic is administered. By vomiting, the stomach empties itself, and, except dieting for a short time, no further treatment is required. It is essential to clear the mouth and throat of all vomited matter as soon as possible to avoid obstruction of the air passages.

Disturbances of the circulation are dangerous. While they cannot be directly observed upon the organs of circulation or the blood, fortunately they manifest themselves externally by cyanosis or extreme pallor. Cyanosis is the expression of severe anoxia. The blue color appears primarily in the end organs of the body—the lips, cheeks, fingers, nose, etc. Cyanosis is always present in dyspnea and asphyxia. Syncope, or fainting, is a temporary inhibition of the functions of the brain, resulting from cerebral anemia, usually accompanied by more or less complete inhibition of all senses. If the heart should stop, general collapse results. Syncope, when occurring in the early stages of the administration, and when accompanied by a typical staring of enlarged or reduced pupils, indicates

idiosyncrasy to the anesthetic used. The treatment of the disturbances of circulation consists in applying mechanical and chemical means to bring about increased or renewed heart action. Artificial respiration and powerful rhythmic compression of the heart's region are essential. The compression of the heart is best accomplished by standing on the left side of the patient, and forcefully pressing with the right thumb into the region between the apex of the heart and the left wall of the sternum; the left hand should be placed over the right thoracic region of the patient to steady the body, and compression should be applied about a hundred times a minute. Slapping the face and chest of the patient with towels wrung out in cold water acts as an active reflex stimulant. Lowering the head, or complete inversion of the body, to promote rapid flow of blood to the anemic brain may prove helpful. Stimulation by chemical agents consists of applying strong, irritating substances to the nostrils. In the early stages of collapse, ammonia, in the form of smelling salts or in its various solutions, may be indicated. Aromatic spirit of ammonia, in half-teaspoonful doses, well diluted, and swallowed, is much lauded for resuscitation. Camphor, in the form of a 10 per cent sterile oil solution (in ampuls) injected hypodermically, has been advocated in collapse; it stimulates the pathologically altered heart and increases the frequency and activity of the heartbeat. Large (1 cc.) doses of epinephrine solution may be injected intravenously in very extreme cases. As a powerful dilator of the peripheral vessels, the vapors of amyl nitrite may at times be useful —three to five drops of this fluid may be placed on a napkin and held before the patient's nostrils for inhalation; flushing of the face and an increase in the frequency of the pulse follow almost instantly. Normal respiration is absolutely essential to aerate the blood in circulatory disturbances.

Disturbances of respiration are either mechanical or functional in nature. To avoid possible mechanical obstruction which may occlude the trachea during narcosis, careful inspection of the oral cavity should always be made before beginning to anesthetize. Artificial teeth, removable bridges, chewing gum, tobacco, and other things may be looked for in the mouth. In extracting teeth, extreme care should be exercised actually to deposit the tooth outside of the mouth. A tooth is liable to spring from the forceps, or, when forced from an alveolus by an elevator, may fall backward and enter the trachea. If the tooth cannot be caught with the finger or an instrument, an effort should be made, in extreme cases only, to force the tooth into the esophagus.

In the early stages of anesthesia, occasionally inhibition of respiration is produced by tonic spasms of the muscles of the tongue, thus forcing this organ against the soft palate and the posterior wall of the pharynx. This same phenomenon may occur during profound anesthesia in a patient assuming a recumbent position. To overcome stenosis of the larynx, the lower jaw should be thrown forward by pressing against the two rami posteriorly. A tongue forceps may be inserted and the tongue pulled forward, or even piercing the tongue with a needle threaded with stout silk and applying rhythmic traction has been resorted to.

The typical organic impairments of respiration are known as apnea, dyspnea, and asphyxia. The differentiation between these three forms of suffocation rests probably more with the severity of the disturbance than with the kind; they are primarily the result of a lesser or greater paresis of the respiratory centers. The supreme remedy is artificial respiration—an artificial means for the thorough ventilation of the blood and lungs, replacing the narcotic with air until normal function of the organs is established. Artificial respiration may be applied by any of the known methods that serve the purpose, provided the method employed is thoroughly understood.

Faradization of the diaphragm is sometimes useful; too much, however, should not be expected from the electric current in this connection. Dilating the anus with a suitable speculum is also recommended. A careful and quickly instituted artificial respiration is the first choice of all methods of resuscitation. The proper use of the first minute is of more real value in the preservation of the extinguishing life than all the hours thereafter. No precious moments should be lost by rubbing the patient, applying smelling salts, or other secondary means. Artificial respiration may often be profitably continued for an hour or longer until fairly normal lung activity is established.

Nervous disturbances during or following anesthesia usually manifest themselves in two definite forms: sensory and motor. Psychic excitement is a common occurrence in the preliminary stages of narcosis; hysterical patients and alcoholics furnish by far the largest contingent. In a patient with a history of hysteria or alcoholism, the administration of a barbital an hour before the anesthetic will materially lessen the preliminary excitement, and less anesthetic will be required. Occasionally a patient will awake from the anesthetic in an apparently normal physical condition, but without perfect control of the sensorium. The patient remains for some hours in a sort of lethargic sleep, which may at times reach a deep comatose state. Following this stupor the patient does not recall what has

happened (amnesia). Smelling salts held to the nostrils, cold water dashed in the face, and loud talking or shaking will arouse the patient. Disturbances of the motor centers result in more or less severe spasm. Singultus, the ordinary hiccough, is often seen in the early and late stages. Tremor of a single group of muscles or of the entire body is noticed more or less frequently after the taking of small quantities of the anesthetic; similar tremors are seen as a result of indulging in other stimulants, as tea, coffee, or tobacco, in those who are not addicts to these drugs. These muscle tremors are usually confined to the early stages of inhalation, and are not dangerous. If they should occur after the anesthetic passes off, the strong will power of the patient materially assists in overcoming these tremors. Convulsions, combined with clonic or tonic spasms, occur frequently under nitrous oxide anesthesia, but much less under the other anesthetics. Care should be exercised to prevent the patient from injuring himself. The removal of the anesthetic quickly relieves the condition. Tetany, the persistent contraction of voluntary muscles, is frequently seen in the early stages of anesthesia; less, however, when chloroform is used. Typical trismus, tonic spasms of the muscles especially those of mastication, is often very troublesome in dental anesthesia. As a precaution, a suitable mouth prop should always be put in place. Severe forms of tetanic convulsions, bending the head and feet backward, known as opisthotonos, are also seen under anesthesia in the early stages. These muscle disturbances rarely call for treatment. Carefully watching the patient to prevent injury is of first importance.

For the purpose of readily meeting unexpected side effects of anesthetics, every practitioner should place in an easily accessible compartment of his medicine chest a stock of emergency drugs consisting of:

Hypodermic tablets of morphine sulfate, 1/8 grain.
Sterile ampuls of epinephrine hydrochloride.
Sterile ampuls of camphor.
Ether.
Amyl nitrite, in 5-drop glass capsules.
Aromatic spirit of ammonia.
Hypodermic syringe in good working condition.

Preparation of the Patient

A patient who is to be anesthetized for an operation requires certain preparation.[1] This preparation varies with the nature of the operation. The anesthetization for a dental operation, which is

[1]Christiansen, G. W.: J. A. D. A. 23: 2232, December, 1936.

usually completed within a few minutes and which is conducted under nitrous oxide or ethyl chloride, requires a less elaborate preparation of the patient than a major operation under chloroform or ether. If possible, the patient should have the bowels emptied by a purgative, given the night before the operation. Very little food should be taken on the following morning—a cup of tea or coffee and a little toast are sufficient for breakfast. The best time to operate is the early forenoon—at nine o'clock—as the body is at its highest resistance at that hour.

Diagnosis and Treatment of Untoward Symptoms in General Anesthesia

Acidosis

The development of acidosis following general anesthesia, as shown by the appearance of acetone, acetoacetic acid, and hydroxybutyric acid in the urine, is a matter of considerable importance. Ewing and Becker found acetonuria in two-thirds of all ether anesthetized patients. Therefore, general anesthesia requires special consideration in diabetes, eclampsia, vomiting of pregnancy, general sepsis, and uremia. The acidosis is due to faulty metabolism.

Cyanosis

Cyanosis is characterized by a blueness of the skin and mucous membranes. It is due to a lack of oxygen in the blood. This may be brought about by excessive secretion in the throat, larynx, or bronchi; by prolapse of the tongue, closing off the larynx; by slow, shallow respiration, diseases of the lungs, slow, weak heart action, faulty administration of the anesthetic, etc. Extreme cyanosis is a dangerous symptom and should be corrected or the anesthetic stopped.

Apnea

Apnea is a temporary cessation of breathing, generally due to a hyperoxygenation of the blood. It may also be due to the irritating action of the anesthetic fumes on the throat and bronchi, causing the patient to hold his breath, or on the epiglottis, causing it to remain closed. It is not a dangerous symptom.

Nausea

Nausea and vomiting are common postoperative occurrences when the liquid anesthetics are used. They do not constitute a serious complication, even though they do occur in 70 per cent of all ether anesthetics (Cushny). A stimulation of the vomiting center is probably the cause.

Shock

Shock is due to a depression of the vital medullary centers. The symptoms develop rapidly and are characterized by a relaxation of the voluntary and involuntary muscles, resulting in a rapid weak pulse, low blood pressure, respiratory embarrassment, prostration, cold, clammy skin, subnormal body temperature, fear, restlessness, with consciousness, semiconsciousness, or unconsciousness. Shock is always serious, and prevention is better than treatment. Shock during an operation may be caused by: (1) an overdose of the anesthetic drug, too rapid administration, or when an idiosyncrasy exists; (2) an injury to the tissues which depresses the vital circulatory centers by sensory stimulation; (3) an injury to the tissues which causes the liberation of a toxic amine, such as histamine; and (4) a loss of blood, lymph, or tissue fluids which reduces the blood volume. One or all of these factors may contribute to the depressed state of the circulation known as shock.

Collapse is similar to shock, except that the symptoms come on more slowly.

Treatment of shock:

Rest and quiet.
Shock position—head lower than feet.
Keep warm with blankets and warm objects.
Give analgesics for pain.
Give stimulants when circulation and respiration are failing.
Give hypnotics to insure quietness and rest.
Give fluids to replace the lost blood volume.

Preanesthetic Medication

Drugs are given before the anesthesia to quiet the patient, prevent apprehension, lessen the amount of anesthetic necessary, and to inhibit oral and bronchial secretions.

Morphine sulfate, 1/8 to 1/4 gr., one hour before.
Atropine sulfate, 1/150 to 1/100 gr., one-half to one hour before.
Scopolamine hydrobromide, 1/150 to 1/110 gr.
Barbiturates, for office practice.
Tribromoethanol (avertin), basal anesthetic.

Nitrous Oxide

Nitrous Oxide; Oxidum Nitrosum (Oxid. Nitros.), N_2O. U.S.P. (Nitrogen Monoxide).

Nitrous oxide contains not less than 95 per cent by volume of N_2O. It probably was first prepared by Priestly, in 1722, by the action of

nitric acid on moist iron filings. Laplace and, later, Berthollet prepared the gas from ammonium nitrate; and Deiman and Troostweijk, in 1773, determined its composition. Davy, in 1800, observed its exhilarating effects and referred to its probable use as a general anesthetic. Nitrous oxide is usually prepared from pure ammonium nitrate by heat. At present a mixture of dried sodium or potassium nitrate and dried ammonium sulfate is also employed.

Nitrous oxide is a colorless, elastic gas, having a very slightly agreeable odor and a sweetish taste. It has a specific gravity of 1.6 (Dalton), and a gallon of it weighs approximately ¼ ounce (1 liter weighs about 2 Gm.). At 32° F. (0° C.) and under a pressure of 50 atmospheres it is liquefied into a stable, colorless, very mobile fluid; at −148° F. (−100° C.) it solidifies into colorless crystals. Liquefied nitrous oxide boils at about −126° F. (−88° C.). The gas is fairly soluble in water, alcohol, ether, and volatile and fixed oils. At present its preparation is not undertaken by the general practitioner in his office. It is now obtained from the dental depots in liquid form, stored in variable sized steel cylinders. These cylinders are painted blue to differentiate them from the cylinders containing compressed oxygen, which are painted green.

Physiologic Action.[1]—Nitrous oxide is not decomposed in the lungs; it enters the blood stream unchanged. It does not combine chemically with the contents of the blood but enters into solution. The degree of solubility is dependent upon the gas pressure (Henry's Law) in the lungs, the greater the pressure the greater the solubility. When the gas pressure is removed from the lungs, the concentration of nitrous oxide in the blood rapidly falls. When an animal is exposed to N_2O gas, the metabolism of the tissue cells is inhibited in exactly the same manner as by the presence of any other indifferent gas (nitrogen), and the animal dies of asphyxiation. Nitrous oxide also exercises a depressing influence on the central nervous system, beginning with the cerebrum, passing on to the cerebellum and midbrain and cord, and finally the medulla. The stages are the same as for ether, only they are passed through more quickly and more quietly.

Nitrous oxide depresses the respiratory center, and toxic doses usually kill by asphyxiation. The vasoconstrictor center is stimulated, producing a rise in blood pressure; therefore, this anesthetic is not indicated for patients having high blood pressure or arteriosclerosis. Anesthesia is produced in from one to three minutes; upon stopping the anesthetic, the return to consciousness is within two or

[1]Jacobs, M. H.: J. A. D. A. 23: 1729, September, 1936.

three minutes. There are usually no bad postanesthetic symptoms; the patient may return home on the same day. A mixture of 95 per cent nitrous oxide and 5 per cent oxygen has been used as an anesthetic with good results. The new gas anesthetic machines permit the using of N_2O, O_2, CO_2, and $(C_2H_5)_2O$, combined or alone, making nitrous oxide combinations the safest and most satisfactory general anesthetics for short operations. Nitrous oxide is routinely used for the first two stages of ether anesthesia, the third stage being attained and maintained with ether. Nitrous oxide anesthesia, like ether anesthesia, is quieter when preanesthetic medication of morphine, barbiturates, etc., is given. It does not produce complete relaxation of the voluntary muscles and is not satisfactory for abdominal surgery.

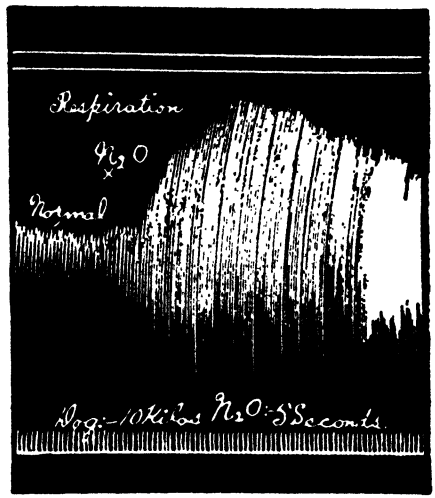


Fig. 3.—Effect of nitrous oxide on respiration. The respiration at once becomes deeper and more rapid. (From Jackson: *Experimental Pharmacology and Materia Medica.*)

SYMPTOMS.—During nitrous oxide administration the pulse is increased in rate and amplitude. Respiration is influenced by the amount of oxygen: large doses of oxygen will slow the respiration while small doses produce suffocation and increase respiration. The respiration may be stimulated by increasing the carbon dioxide intake. The pupils are normal or slightly dilated. During surgical anesthesia the conjunctival reflexes disappear, the pupil reacts slowly to light.

THERAPEUTICS.—When properly administered, nitrous oxide with oxygen is the safest of all general anesthetics. While the refined local

anesthetic techniques have lessened the need for general anesthesia in dentistry, nitrous oxide still holds a most important place in dental practice. The use of nitrous oxide analgesia in operative dentistry is a practice which is safe, and it is gaining in popularity. A special gas machine is desirable and the patient administers his own anesthetic.[1] Competent administration of nitrous oxide requires special training quite beyond the scope of this text. The operator should carefully select standard equipment and then receive instruction for its use from qualified anesthetists.

TOXICOLOGY.—Nitrous oxide, with the normal complement of oxygen (21 per cent), is the safest general anesthetic for the dental office. Unfortunately, with this concentration of oxygen the patient cannot be anesthetized deep enough to be free from pain. To overcome this deficiency, premedication may be used or a more potent anesthetic may be combined with the nitrous oxide. The restriction of the oxygen in the anesthetic mixture to the low level necessary for surgical anesthesia may damage the cells of the central nervous system, and must be condemned. Just how much damage is done by restricting the oxygen intake during general anesthesia cannot be determined readily, as manifestation of damage to the cerebral cortex is not readily detected. The safest anesthetic to mix with nitrous oxide for dental use is ether (Neff) or avertin.[2]

ETHER

ETHER; AETHER $(C_2H_5)_2O$, U. S. P. (Ethyl Ether, Diethyl Ether).

SOURCE AND CHARACTER.—Ether is a liquid, composed of from 96 to 98 per cent by weight of absolute ether (ethyl oxide) and about 2 to 4 per cent of alcohol, and a little water. It is a transparent, colorless, mobile liquid, having a characteristic odor and a burning and sweetish taste. It is soluble in about 12 times its volume of water and miscible in all proportions with alcohol, chloroform, and fixed and volatile oils. It boils at 96° F. (35.5° C.). Ether is very inflammable, and should be kept in tightly stoppered tin cans in a cool place.

PHARMACODYNAMICS.—Ether is a general protoplasm poison. When applied locally, it acts as an irritant which gives it antiseptic and counterirritant properties. When taken orally in a diluted solution, it acts as a carminative and, after absorption, as an intoxicant. When volatilized and administered by inhalation as a general anesthetic, it acts on the central nervous system, first as a stimulant and then as a

[1] Frank, M. S.: J. A. D. A. 26: 50, January, 1939.
[2] Archer, W. H.: J. A. D. A. 30: 1547, October, 1943.

depressant. The early symptoms of anesthesia are due to the effects of the drug on the cerebral cortex, midbrain, basal ganglia, and cerebellum; the later symptoms from the effects on the spinal cord and medulla. The spinal cord is depressed, generally, while the medullary centers are still stimulated. This fact permits muscular relaxation during surgical anesthesia without symptoms of ether toxicity, and gives a good margin of safety.

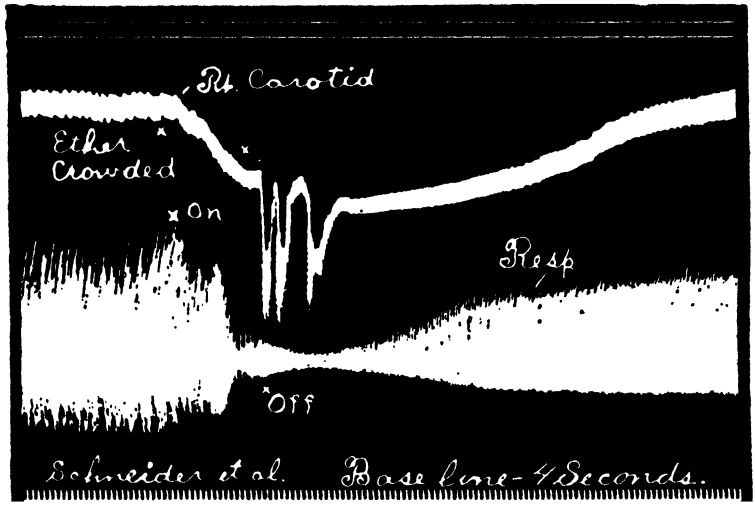


Fig. 4.—Blood pressure, respiration, base line, and time in four-second intervals showing action of concentrated ether vapor. (From Jackson: *Experimental Pharmacology and Materia Medica.*)

Fig. 5.—Different methods of dropping ether. The two illustrations on the left show the wick in the can as described; next is a pipe cleaner, and on the right is a safety pin passed through the cap. (From Archer, W. H.: General Anesthesia Under War Conditions, J. A. D. A., 1943.)

Normal doses of ether have little effect on respiration; the circulation is slightly stimulated, resulting in a rise in blood pressure which returns to normal or subnormal as time progresses. Toxic doses depress the respiratory center, resulting in anoxia and failure of respira-

tion. The heart continues to beat for a few minutes after respiration has stopped, which permits resuscitation measures.

THERAPEUTICS.—Ether is a solvent for many drugs. In 1 cc. doses, well diluted with water, it is a useful carminative. Applied locally as a spray, it acts as a refrigerant anesthetic, but it is inferior to ethyl chloride for this purpose. The chief use of ether is as a general anes-

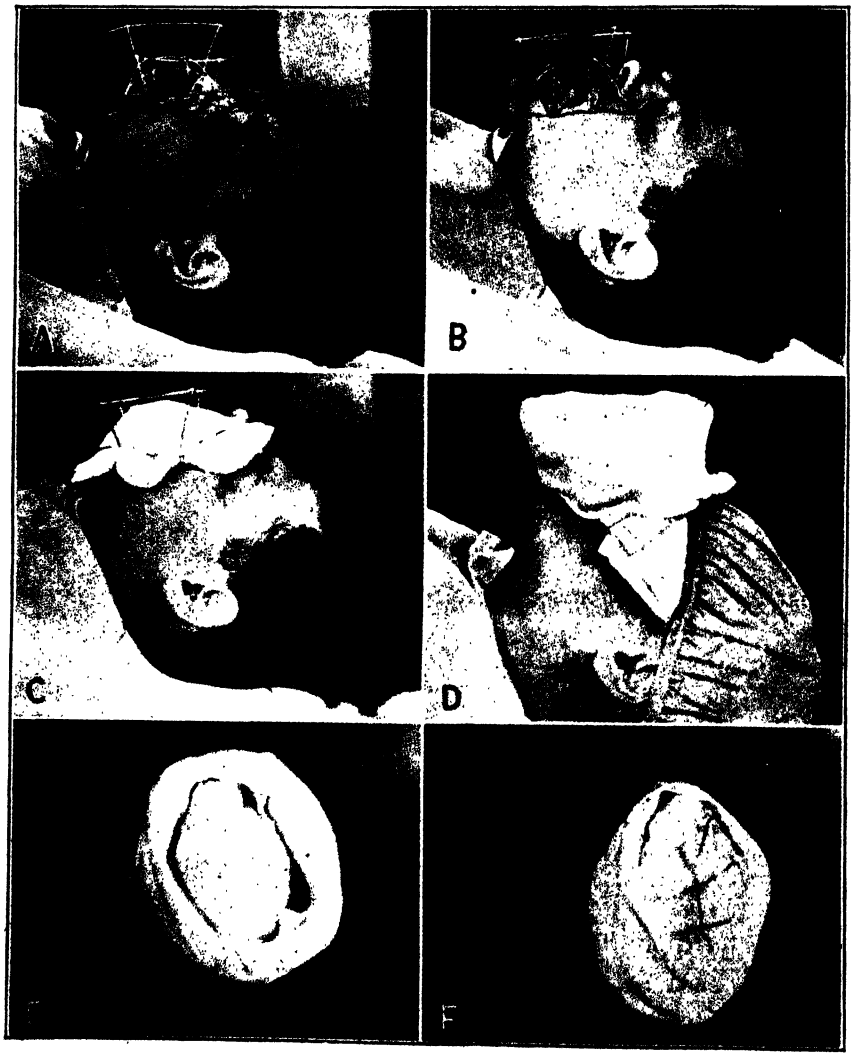


Fig. 6.—*A*, wire frame improperly adapted to patient's face. *B*, framework properly adapted. *C*, convex portion covered with six layers of surgical gauze. *D*, whole frame covered with Canton flannel hood. *E*, upper chamber; ether dropped on convex portion. *F*, lower chamber, fitting over patient's face. (From Archer, W. H.: J. A. D. A., 1948.)

thetic. Cushing gives the death rate from ether anesthesia as 1 in 10,000. About 70 per cent of the patients have postoperative nausea and vomiting. For dental office practice, it is not the anesthetic of choice.

Chloroform

Chloroform; Chloroformum (Chlorof.), $CHCl_3$, U.S.P.

Source and Character.—Chloroform is a liquid, consisting of 99 to 99.5 per cent by weight of absolute chloroform and 0.5 to 1 per cent of alcohol for preservative purposes. It should be kept in dark-colored bottles and in a cool, dark place. It is a heavy, clear, mobile,

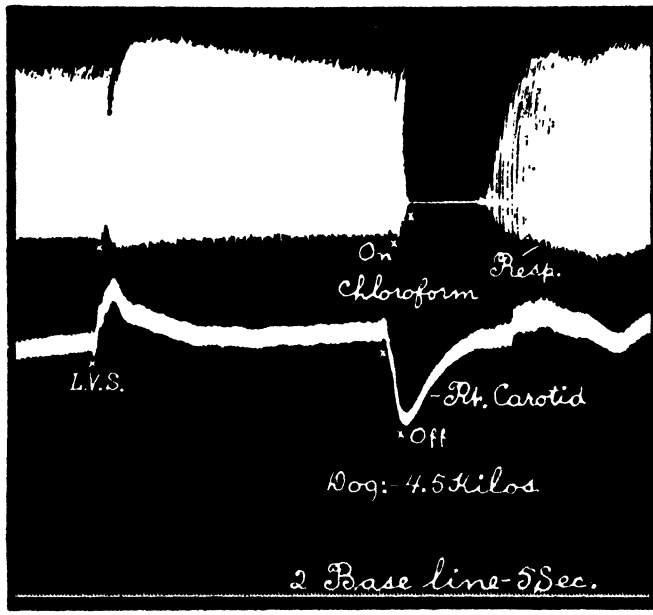


Fig. 7.—Effect of concentrated chloroform vapors on respiration (depression of the respiratory center) and on blood pressure (due mainly to depression of heart.) (From Jackson: *Experimental Pharmacology and Materia Medica.*)

and diffusible liquid, having a characteristic ethereal odor and a burning taste. It has a specific gravity of 1.478, and is soluble in all proportions in alcohol, ether, petroleum benzin, and in fixed and volatile oils. When agitated with water, it is soluble in about 210 parts of the latter. Chloroform is readily volatilized and boils at 141° F. (61° C.). It is not inflammable, but its vapors burn with a green flame. Chloroform deteriorates readily under the influence of heat, light, and air, forming carbonyl chloride and free chlorine, both of which are toxic.

MEDICAL PROPERTIES.—Chloroform is a general anesthetic, rubefacient, analgesic, carminative, antiemetic, antihysteric, and mild antiseptic.

PHARMACODYNAMICS.—Chloroform is a general protoplasm poison and, when applied locally, it has antiseptic and irritant action. When inhaled, chloroform irritates the respiratory mucous membranes, producing a reflex stimulation through the vagus centers. This results in

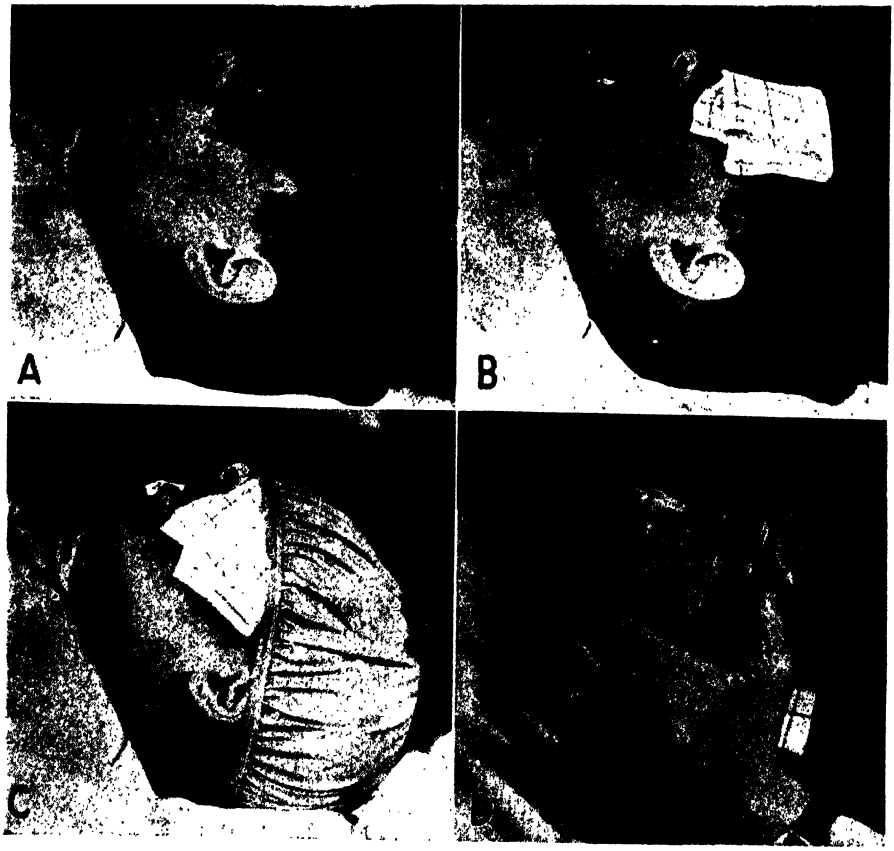


Fig. 8.—Measures to protect eyes. *A*, piece of notched rubber dam over eyes. *B*, rubber covered with towel. *C*, rubber cap covering head and holding towel and rubber dam in place. *D*, dam lifted and olive oil dropped in each eye. (From Archer, W. H.: J. A. D. A., 1943.)

a slowed heart rate, and in extreme cases the heart may stop and death result. The effects of chloroform on the nervous system resemble those of ether, except that the medullary centers are more readily depressed. The halogen substitutions on the carbon atom form a molecule with a direct toxic influence on the heart muscle. The vaso-

constrictor center is easily depressed, producing a slow shallow respiratory rate. The heart generally fails first and the respiration soon follows, thus making chloroform a dangerous general anesthetic agent. Cushing estimates the death rate from chloroform as 1 in 3,000, or about four times as toxic as ether.

THERAPEUTICS.—Locally chloroform is used as an irritant which gives it rubefacient and counterirritant properties, useful for the treatment of myalgic and neuralgic pain. It is a solvent for many drugs and resinous compounds. Rosin and gutta-percha in chloroform are extensively used in dentistry. Internally, in diluted solutions, it may have a carminative and antiemetic action. It is a dangerous anesthetic and has no place in civilian dental practice. As it has a higher boiling point than ether, it has been advocated as a general anesthetic in very warm climates.

ETHYL CHLORIDE

ETHYL CHLORIDE: AETHYLIS CHLORIDUM (AETHYL. CHLOR.), C_2H_5Cl, U.S.P.

SOURCE AND CHARACTER.—It is a haloid derivative, prepared by the action of hydrochloric acid gas on absolute ethyl alcohol. On account of its extreme volatility it is preserved in hermetically sealed glass or metal tubes. It is a colorless, mobile, very volatile fluid, having a characteristic ethereal odor and a burning taste. It boils at about 55° F. (12.8° C.), and burns with a smoky, green-edged flame. When liberated from its container it vaporizes at once, and the resultant gas is very inflammable.

MEDICAL PROPERTIES.—General and refrigerant anesthetic.

PHARMACODYNAMICS.—Locally, it is sprayed on the skin as a refrigerant anesthetic. It vaporizes with such rapidity that it removes heat from the exposed tissues, lowering the temperature and producing local anesthesia. It is extensively used in extraoral surgery as a refrigerant anesthetic, but it is not designed for intraoral anesthesia. For desensitizing the dentine it is not satisfactory, as the application of the drug is often more painful than the intended operation.

Systemically it is used to produce general anesthesia by inhalation, the patient being anesthetized in one or two minutes. Recovery from the anesthesia is generally complete in one to five minutes. It is a reliable anesthetic for short operations, with not over 2 cc. of the drug being used for children or 5 cc. for adults. It is not without danger, as the drug may depress the heart and later the respiration. For short operations on children in the dental office, it is very successful when properly administered.

THERAPEUTICS.—Locally, it is sprayed on the part until the tissues become blanched and ice forms. Surgery may then be done with very little pain to the patient. The anesthesia is superficial and the duration is short—about one minute. Pronounced tissue-freezing produces death of the superficial cells with subsequent sloughing.

To produce general anesthesia, ethyl chloride is sprayed on a gauze mask. This is known as the open method. Or the drug may be placed in a closed mask, and the patient made to breathe and rebreathe into a closed circuit. While this method conserves the anesthesia, it restricts the oxygen supply and increases the toxicity of the anesthetic. As a general anesthetic, ethyl chloride is not as safe as nitrous oxide, but it has the advantage of convenience, for no expensive or complicated apparatus is necessary for its administration.

A. *B.*

Fig. 9.—*A*, anesthetization with ethyl chloride or vinyl ether. *B*, position of hand, mask and can for drop ether anesthesia. (From Archer, W. H.: J. A. D. A., 1943.)

ETHYLENE

ETHYLENE; AETHYLENUM (AETHYLEN.), $CH_2 = CH_2$, U.S.P.

Ethylene has a sweetish disagreeable odor, is inflammable, and will not support life. With air, oxygen, or nitrous oxide it forms an explosive mixture; the ignition may occur from an electric spark, cigarette, cautery, sterilizer, etc. It is obtained from the manufacturers in metal cylinders.

PHYSIOLOGIC ACTION.—Ethylene is used with oxygen in a 90:10 per cent mixture which does not produce cyanosis or asphyxia. When inhaled, a state of surgical anesthesia is promptly induced. The action

seems to be intermediate between ether and nitrous oxide, resembling ether as to depth and muscular relaxation, and nitrous oxide as to rapidity of induction and recovery. The same stages are passed through in the induction as with ether but more quickly and more quietly. After a few inhalations, the patient loses consciousness and in from two to five minutes, as a rule, is completely anesthetized. With cessation of administration, recovery is prompt and relatively free from unpleasant after-effects. The respiration is slow and regular, and the pulse slowly falls to normal and remains there. The vasoconstrictor center is not affected to any extent. There is no irritation to the respiratory mucous membranes. Nausea and vomiting may result in 30 per cent of the patients.

Ethylene is a good anesthetic for short or long operations. The reason it is not more popular is that it forms a very explosive mixture with oxygen. It must not be used in the dental office unless special precautions are used to prevent discharges of static electricity.

Vinyl Ether

Vinethene (Merck), $CH_2 : CH\text{-}O\text{-}CH : CH_2$, N.N.R.

Vinyl ether occurs as a colorless, volatile, inflammable liquid which deteriorates upon exposure to light and air. It should not be used for anesthetic purposes after the container has been open for twenty-four hours (N.N.R.).

This narcotic drug[1, 2] is used as an inhalant anesthetic for short operations, as in dental surgery. Its danger lies in the ease of passage from the anesthesia stage into the toxic stage. The eye signs are unreliable and the anesthetist must determine the dosage from the respiratory signs, such as rate, depth, and regularity. Normal anesthetic dosage does not produce cyanosis. It is an irritant to the mucous membrane and stimulates secretion which may cause post-anesthetic complications.

Vinethene is used extensively in minor oral surgery on children. It is not as safe an anesthetic as nitrous oxide but has the advantage of needing less equipment. The open drop method of administration is generally used. The anesthetic is administered until the child loses consciousness and until the mouth may be opened; then the drug is stopped and the operation started. The induction period is from one to two minutes; the period of anesthesia is up to five minutes and recovery is from one to five minutes. Nausea and vomiting are infrequent occurrences.

[1] Zaus, E. A.: J. A. D. A. 30: 439, March 1, 1943.
[2] Rosamilia, P. A.: J. A. D. A. 25: 1465, September, 1938.

It may be combined with nitrous oxide to deepen the narcosis and to permit the normal complement of oxygen in the anesthetic mixture.

Cyclopropane

Cyclopropane; Cyclopropanum (Cycloprop.), U.S.P.

This compound was first described by von Freund in 1882. The first clinical reports were made by Waters and Schmidt in 1934. Cyclopropane became official in the 1939 Supplement of the U.S.P. XI.

Chemically it has three CH_2 groups arranged in a ring.

Physically it occurs as a colorless gas with a pungent but not too unpleasant odor. The gas is heavier than air, and forms an inflammable and explosive mixture with air or oxygen.

The margin of safety of this anesthetic was demonstrated by Waters and Schmidt (1934), who made an analysis of the anesthetic mixture during the various planes (not stages) of surgical anesthesia.

Plane I, 7.4 per cent cyclopropane
Plane II, 13.1 per cent cyclopropane
Plane III, 23.3 per cent cyclopropane
Plane IV, 42.9 per cent cyclopropane

These figures show a wide margin of safety between Planes III and IV. The narcotic effect of cyclopropane is great enough to permit a liberal amount of oxygen (20 per cent) in the anesthetic mixture without sacrificing the depth of the anesthesia. Induction is slower than with nitrous oxide (20 to 180 seconds) but quicker than with ether. The inhaled gas is not irritating to the respiratory tract and does not produce excessive salivation. The symptoms of surgical anesthesia are few and not as definite as with ether. The toxic stage is ushered in with apnea, bradycardia, and a falling blood pressure. The anesthetic gas is expensive, requiring the closed system for its administration.

Dosage.—See *Useful Drugs.*

Basal Anesthetics

This form of anesthesia cannot be used in the dental office; it is confined to the hospital where the patients are not necessarily ambulatory. The drug is administered in narcotic doses an hour or so before the general anesthetic is given. The patient in a comatose condition is wheeled to the operating room and prepared for the operation. A general anesthetic is administered throughout the operation.

This form of anesthetic (basal) prevents undue psychic shock to the patient and also lessens the amount of general anesthetic necessary for the anesthesia.

Tribromoethanol

Tribromoethanol; **Tribromoaethanol** (**Tribromoaeth.**), $Br_3C.CH_2OH$, U.S.P. (Tribromoethyl Alcohol).

Tribromoethanol occurs as a white crystalline solid, slightly soluble in water and freely soluble in amylene hydrate (U. S. P.), which is its accepted solvent. The molecule slowly decomposes at room temperature, and light increases the rate of decomposition.

Tribromoethyl alcohol was introduced as avertin by Willstaetter and Duisberg as a rectal anesthetic in 1926. Today it is chiefly employed as a basal anesthetic in selected cases.

Chemically, tribromoethanol is bromated ethyl alcohol. The molecule has a depressing (narcotic) action on the central nervous system. Since there is little or no dissociation of the molecule, the bromine ion as such is not a factor. The molecule acts as a whole.

Avertin has the characteristic narcotic action of the methane-derived drugs. The induction period of anesthesia is from five to fifteen minutes; the patient merely "falls asleep." The basal anesthetic state is reached in twenty to thirty minutes and is maintained at a peak for about one hour. In about two or three hours consciousness is reached. A period of postoperative sleep follows, with amnesia existing for several hours. With basal anesthetic doses only incomplete muscular relaxation occurs, but with the addition of ether a complete relaxation is obtained. The cardiac and vascular muscles and the vasoconstrictor centers are directly depressed, resulting in a fall in blood pressure. This reduction in blood pressure is small and temporary and cannot be classed as a dangerous symptom. Average doses seldom cause respiratory embarrassment, but with toxic doses or an idiosyncrasy the respiration fails before the circulation. The basal metabolic rate is depressed as in sleep, 10 to 15 per cent. Kidney function may be impaired by this drug, resulting in albuminuria and kidney failure. As avertin is excreted by the kidneys as a glucuronate, it is contraindicated in renal disease. The liver appears not to be affected by the drug.

Therapeutics.—Tribromoethanol is generally administered rectally and is rapidly absorbed. The narcotic action varies with the dosage: 50 to 60 mg. per Kg. of body weight acts as a hypnotic, 70 to 80 mg. as an analgesic and as a basal anesthetic.

PREPARATION.—

Solution of Tribromoethanol; Liquor Tribromoaethanolis (Liq. Tribromoaeth.), $C_2H_2Br_3OH$, U.S.P. (Solution of Tribromoethyl Alcohol).

DOSAGE.—*Rectal, 0.06 cc. for each kilogram of body weight and should not exceed 8 cc. for women and 10 cc. for men* (U.S.P.).

Intravenous Anesthesia in War Surgery

The following discussion and figures on intravenous anesthesia in war surgery were contributed by Dr. W. Harry Archer.[1]

"Technic for Intravenous Anesthesia.—

"It has been predicted that 'quick-acting barbiturates administered intravenously will be used more often than any other type of anesthetic agent' in war surgery.[2, 3, 4] Intravenous anesthesia with pentothal sodium is my first choice for exodontia and oral surgery in the hospital. This method of producing complete loss of consciousness seems to be particularly well adapted to war surgery. The equipment is simple, easily transported, and readily obtainable. The drug is easily transported. It is put up as powder in a sealed glass ampul. If the content of a 1 Gm. ampul is dissolved in the content of a 20 cc. ampul of sterile distilled water, we have a 5 per cent solution. If it is dissolved in 40 cc. of sterile distilled water, we have a 2.5 per cent solution. Administration of the drug is easy and relatively safe, with a rapid induction period without delirium or excitement. The drug is nonirritating and nonexplosive, which allows the use of the cautery. While some authorities stress the opinion that intravenous anesthesia should be used only for operative procedures lasting from ten to fifteen minutes, in our experience some patients have been under anesthesia for as long as two hours, the average case lasting about an hour, without untoward effects. Thomas,[5] in reporting 10,000 cases of pentothal sodium anesthesia, writes, 'The duration of anesthesia extended from three minutes to four and a quarter hours.' This series has now reached 16,000 cases, and Thomas[6] now reports that 'the operating time factor

[1]Archer, W. Harry: General Anesthesia Under War Conditions, J. A. D. A. 30: 1547, October, 1943.

[2]Pender, Joan W., and Lundy, J. S.: Anesthesia in War Surgery, War Med. 2: 193, March, 1942.

[3]Donaghy, G. E.: Modern Anesthesia for War Surgery, Mil. Surgeon 86: 577, June, 1940.

[4]Crane, R. M., and Sankey, B. B.: Recent Developments in Anesthesia of Significance to Military Surgeon, Cur. Res. Anes. & Anal. 20: 151, May-June, 1941.

[5]Thomas, G. J.: Report on 10,000 Pentothal Sodium Anesthetics, Pennsylvania M. J. 45: 467, February, 1942.

[6]Idem: Personal communication to author, April 1943.

is not an important item in considering the selection of pentothal sodium as the anesthetic agent.' Recovery is rapid and analgesia prolonged, with no postanesthetic complications such as nausea or vomiting, and no headache. Pentothal sodium anesthesia has a favorable psychic effect on anxious patients, and they do not fear future anesthesia with this method should additional operative procedures be required.

"Preparation of Patient.—

"The stomach, bladder, and rectum should be empty as possible. Morphine sulphate, one-sixth grain, and atropine, one one-hundred-fiftieth grain, is injected one-half hour before the operation. The operative field is prepared and draped. Everything is in readiness for the operation. A tourniquet is applied to the upper arm, and

A. *B.*

Fig. 10.—*A*, hand clenched, tourniquet applied and skin scrubbed over vein with 70 per cent alcohol. *B*, skin tensed with thumb, for venipuncture. (From Archer, W. H.: J. A. D. A., 1943.)

the patient is instructed to close his fist. The median basilic vein in the antecubital fossae or a dorsal metacarpal vein in the back of the hand is usually selected. In some cases, it may be necessary to use the saphenous vein in the ankle. The skin over the vein is prepared by scrubbing with a sponge saturated with 70 per cent alcohol. (Fig. 10*A*.)

"For making the injection, a 10 cc. syringe is used, to which a 1¼ inch 20-gauge needle is attached by means of rubber tubing. The skin is tensed and a venipuncture is made. (Fig. 10*B*.)

"The Technic of Venipuncture.—

"Step 1. The needle is inserted in the skin and the tissue overlying the vein moved to the side of the vein. The needle is then

thrust into the tissue at the side of the vein. The needle point is then returned to a position directly over the vein, and the puncture is made. (Fig. 11.)

"Step 2. In large veins the bevel of the needle is turned up. In small veins the bevel is turned down to avoid having the bevel lie partially in and partially outside the vein.

"The venipuncture having been made, a small quantity of blood is aspirated into the glass sight tube to make certain that the needle has entered the vein. (Fig. 12.) The patient is asked to count slowly and loudly. From 4 to 6 cc. of the 2.5 per cent solution is

Fig. 11.—Insertion of needle in skin over vein. The tissue overlying the vein is moved to the side of the vein. The needle is then thrust into the tissue at the side of the vein. The needle point is returned to a position directly over the vein and the puncture is made. (From Archer, W. H.: J. A. D. A., 1943.)

injected in about ten seconds. The effects are closely observed. If the patient loses consciousness at the end of this small dose, he is susceptible to the drug and requires only small amounts to maintain surgical anesthesia. The use of large amounts would cause marked respiratory depression. If no effect is noted, in other words if the patient continues to count beyond thirty seconds after the original injection, an additional 4 to 6 cc. is injected, with about ten seconds to inject this amount. As a rule, this additional amount is sufficient to produce unconsciousness, as indicated by the patient ceasing to count and subsequent relaxation of the jaw.

"In an oral operation, the lips are coated with petrolatum, the Molt prop is placed to separate the jaws, a piece of gauze is placed over the upper and lower surfaces of the tongue, and the tongue is grasped between the gauze surfaces by the fingers and drawn forward between the teeth. A double strand of 00 catgut, threaded in a tonsil needle, is passed through the midline of the tongue three-fourths inch from the tip. The suture material passed through the tongue should be long enough to permit four strands to extend at least four inches from the mouth. The needle is cut off, and the ends of the four strands are tied together in a knot. A hemostat is clamped on the knot. This is the most efficient method of controlling the tongue, keeping it forward and out of the pharynx so that it is not a source of mechanical respiratory embarrassment. The suture is not removed from the tongue until the patient responds to

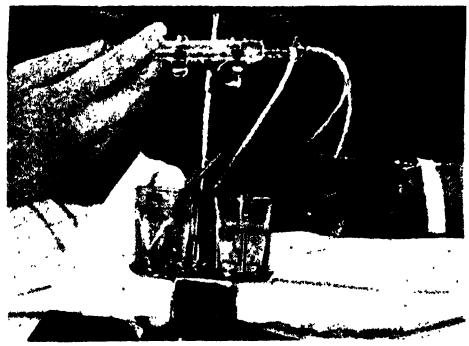


Fig. 12.—Needle held in vein by means of strip of adhesive tape over manifold and halfway around arm. Injection of from 4 to 6 cc. of 2.5 per cent solution should require ten seconds. (From Archer, W. H.: J. A. D. A., 1943.)

questions. The patient does not have any soreness in the tongue afterward. Under pentothal sodium anesthesia, metal or hard rubber airways extending into the pharynx should be avoided because their presence results in irritation, which frequently gives rise to the most distressing symptom seen under pentothal anesthesia, laryngospasm. When this is encountered, the anesthesia must be temporarily deepened, and oxygen under pressure must be administered intermittently if the spasm persists more than one-half minute.

"An assistant holds the tongue forward by keeping traction on the hemostat. Even for other surgical procedures under pentothal sodium anesthesia, a suture should be placed through the tongue to aid in maintaining an open airway. A gauze oral-pharyngeal partition is carefully placed so as to prevent the aspiration of blood and

yet not embarrass the respiration. A suction machine for constant use is essential during oral surgery.

"In surgical anesthesia, the respirations are shallow and quiet. A depressed head and chin block normal respirations. The head and chin must be held up at all times. So quiet and shallow is respiration that it is a good plan to use a respiration indicator made of a square of tissue paper suspended between the nose and chin. This, of course, cannot be used for oral operations. When possible, it is well to administer oxygen by means of a nasopharyngeal tube. The tube is lubricated with petrolatum, inserted through the nose into the pharynx and held in position by a strip of adhesive tape. The tube is connected with a wash bottle, which, in turn, is connected with a tank of oxygen. This adjunct not only improves muscular relaxation, but also helps prevent the tendency to lowered oxygenation of the blood, a natural result of the shallow depressed respiration present with this anesthetic.

"Anesthesia is maintained by the intermittent injection of small amounts of the solution, a fraction of 1 cc., when the patient shows some sign of feeling pain. Pain may be indicated by slight movements of the fingers or toes, tightening of the mandible, phonation, or increased respiration.

"Much of the difficulty that some anesthetists have with this form of anesthesia can be explained by the fact that they are injecting more solution and too frequently without a definite need for it. They do this to prevent the needle from being clogged by clotted blood or because they are afraid that the surgeon will object if the patient moves or phonates. Hence, they 'overdose' the patient, forgetting that the drug has a cumulative effect. To prevent needle clogging, the Thomas double syringe outfit (Fig. 13) is used, in which one syringe is connected with a reservoir of physiologic sodium chloride solution, which can be injected through the needle as often as desired. The surgeon will readily cooperate when it is explained that the greater the amount of anesthetic, the deeper the respiratory depression, the longer the recovery period, and the greater the danger of atelectasis. Furthermore, within a matter of seconds, the anesthesia plane can be deepened.

"The needle, of course, remains in the vein throughout the operation. It must be remembered that, the drug being administered intermittently, there may suddenly be a cumulative effect. Hence, it is highly important to pause between injections and observe the effects of that dose before making an additional injection. As the

operation progresses, increasingly smaller additional amounts of solution are needed to maintain a satisfactory surgical plane. The intravenous set that I personally prefer is shown in the illustration, consisting of two syringes connected with one needle by a manifold. (Fig. 13.) By means of small two-way valves, the Luer-Lok syringe can be filled independently of the two reservoirs and injected intravenously independently. Thus, in the one reservoir, we can have 2.5 pentothal sodium solution, and, in the other, we can have a physiologic solution of sodium chloride. Or we can place analeptics, cardiac and respiratory stimulants such as coramine, in the saline solution and inject it immediately. Some operators who start with a 4 per cent solution, dilute this to a 2 per cent as the operation proceeds. For prolonged operations, 50 per cent nitrous oxide and 50 per cent oxygen can be used. This method supplies adequate oxygen and reduces the amount of pentothal sodium needed to maintain anesthesia.

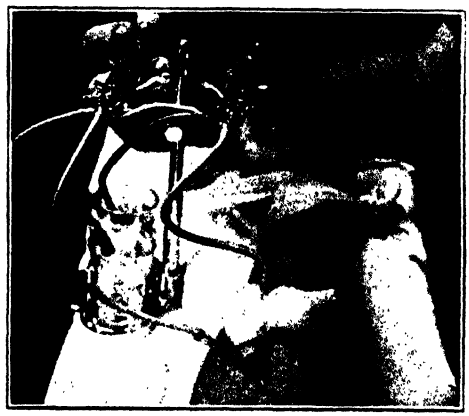


Fig. 13.—Thomas double syringe, intravenous outfit. (From Archer, W. H.: J. A. D. A., 1943.)

"Consciousness usually is regained in from ten to fifteen minutes after the administration of an average dose of pentothal sodium. Patient response can be elicited, but analgesia is present for several hours, as desired. This obviates postoperative medication for several hours. Nausea and vomiting or headaches are rarely seen. If respiratory failure occurs, artificial resuscitation is necessary until the effects of the drug have worn off. Use of a resuscitator is effective.

"A cardiac and respiratory stimulant such as coramine should also be injected intravenously. The patient should never be cyanotic.

Some untoward effects of pentothal sodium anesthesia are acute laryngeal spasm, which may occur if mucus or blood enters the larynx. Tremors, sneezing, or violent coughing may take place.

"During the operation, there may be signs of circulatory deficiency and shock. The skin is pale, cold and wet, and immediate treatment is needed.

"The treatment is as follows:

"1. The cause, if still active, is removed.

"2. An oxygen-rich atmosphere, up to 100 per cent, is provided, with artificial aid to respiratory exchange if indicated.

"3. A free airway is insured.

"4. The head is placed slightly lower than the heart.

"5. Fluids are injected intravenously.[1]

"Conclusion.—

"The dentist trained in anesthesia has a perfect legal, ethical, and moral right to administer any and all types of anesthesia for all surgical and obstetrical procedures. The subject of general anesthesia has been neglected to a great extent in the majority of dental schools in this country. Now there is a pressing need for trained men in this field, and it is imperative that dental schools not now having an adequate course in this subject immediately institute such a course."

[1]National Research Council, Subcommittee on Anesthesia; Fundamentals of Anesthesia, an Outline, Chicago, American Medical Association Press, 1942.

CHAPTER IV

DRUGS WHICH DEPRESS THE CENTRAL NERVOUS SYSTEM

HYPNOTICS

Hypnotics (sleep producers), sometimes referred to as *soporifics* or *somnifacients,* are drugs administered for the purpose of inducing sleep. Following the introduction of anesthetics in surgery, investigators turned their attention to other members of the methane series for narcotics less pronounced in action but of longer duration, that is, they produce the first effect of narcosis over a longer period of time. Anesthesia by inhalation is best adapted to short but complete narcosis. For the more lasting effects, the slower absorption from the bowels best serves the purpose. The early success with the chloral group led to the discovery of many other useful hypnotics. They may relieve pain by paralyzing certain parts of the cerebrum and midbrain, and consequently they are closely related to general anesthetics, narcotics, anodynes, and analgesics. From the viewpoint of the pharmacologist, hypnotics cannot be classified as a specific group of remedies, but for clinical purposes this grouping answers satisfactorily. Some of the hypnotics are soluble in water, others are not; all are, however, soluble in fatty oils. No final explanation has as yet been offered regarding the action of hypnotics.* Sleep and wakefulness are periodical functions of the central nervous system which occur at rhythmical intervals. These periodical functions are often disturbed by external and internal irritants. Physical and mental strain, nervous diseases, lessened resistance, and many somatic disturbances are frequent causes of insomnia. Sleep should not be artificially induced at once in every case in which the patient complains of insomnia; regulating the diet, proper exercise, eliminating the nervous disturbances; lukewarm baths, etc., are of prime importance in inducing natural sleep. Hypnotics should not be given for an extended time, as they are very prone to create habits. It is often advisable to change the remedy at short intervals if it must be given for a long period.

PHARMACODYNAMICS.—This class of drugs produces its effect by depressing the central nervous system. The ideal hypnotic should not

*For an additional discussion see Accepted Dental Remedies.

appreciably affect, in normal doses, the medullary centers of circulation or respiration. They act on the cerebral cortex and midbrain or possibly both.

Hypnotics are thought to produce their effect by retarding the oxidation of glucose in the brain by inhibition of the dehydrogenases. The inhibition occurs in vitro with the same concentration of drug which produces narcosis in vivo. It is suggestive that the dehydrogenases are highly sensitive to narcotic drugs, and the result is a retardation of oxidation by the brain tissue of glucose, lactate, and pyruvate.[1]

THERAPEUTICS.—Natural sleep is more desirable than sleep induced by drugs. Hypnotic drugs, therefore, should be used only when other methods of inducing sleep have failed. Their continued administration leads to habit formation, tolerance, and cumulative effect.

TOXICOLOGY.—Large doses of the hypnotic drugs or the cumulative effect of many small doses produce marked depression of the cerebral and medullary centers resulting in slow, weak heart action, low blood pressure, feeble respiration, cyanosis, coma, anoxemia, shock, and death, if untreated.

TREATMENT.—If the drug is thought to be in the stomach, it should be removed with a stomach pump or by emesis. A stimulant, such as an injection of caffeine with sodium benzoate (3 grains), should be given to stimulate the circulation and respiration. Oxygen and carbon dioxide are indicated in cyanosis and anoxemia. If respiration fails, artificial respiration is indicated.

Drugless Measures for Inducing Sleep:

Have the environment quiet and dark.
Prohibit exciting factors, such as visitors.
Prohibit stimulants, such as tea or coffee.
Prescribe hot baths, massage, warm food and drinks for nervousness.
Reassure nervous patients that they are getting well.
For fever prescribe an alcohol rub and liquids.
For anxiety have someone in the room.

Drug Measures for Inducing Sleep:

For nervousness give a cerebral sedative, such as sodium bromide (1 Gm.).
For pain give an analgesic, such as aspirin (0.3 Gm.).
For fever give an antipyretic, such as aspirin (0.3 Gm.).
For idiopathic insomnia or as a hypnotic for a short duration, the following drugs may be prescribed.

[1]Science 94: 421, Oct. 31, 1941.

Aliphatic Series

This group of drugs is not extensively used as hypnotics because of their general anesthetic-like action. They are less specific in action than the urea group hypnotics and are more toxic.

PARALDEHYDE; PARALDEHYDUM (PARALDEHYD.), U.S.P. (Paracetaldehyde).

Paraldehyde is a polymer of acetaldehyde $(CH_3CHO)_3$. It occurs as a colorless liquid, having a strong characteristic odor and an unpleasant taste. It is freely soluble in water (1 to 8) and miscible with alcohol. When taken internally it acts as an irritant, producing first a burning and then a cooling sensation in the mouth. After absorption it acts as a motor depressant, a nerve sedative, hypnotic, and a general anesthetic, depending upon the dosage. It may be administered rectally, dissolved in physiologic salt solution or in a bland oil.

THERAPEUTICS.—Paraldehyde is a safe and reliable hypnotic but its odor and taste are so disagreeable that it is not extensively used. Its use in obstetrics as an analgesic, amnesic, and basal anesthetic has been very satisfactory (Douglas).

DOSAGE.—4 cc. (60 minims) (U.S.P.). Best administered with cracked ice or ice-cold liquids.

Aliphatic Series: Sulfon Substitutions

SULFONETHYLMETHANE; SULFONETHYLMETHANUM (SULFONETHYLMETH.) N.F. (Trional).

Sulfonethylmethane occurs as colorless, lustrous, odorless, crystalline scales, having a bitter taste in aqueous solutions. It is slightly soluble in water (1 in 200) and soluble in alcohol.

THERAPEUTICS.—In official doses it is a mild, reliable, and safe hypnotic, producing no pronounced undesirable side action. It is absorbed slowly, slow acting, and slowly destroyed and excreted by the body. Cumulative symptoms may occur if the drug is ingested more rapidly than it is eliminated.

DOSAGE.—0.75 Gm. (12 grains) (N.F.), best administered in hot drinks just before retiring.

SULFONMETHANE; SULFONMETHANUM (SULFONMETH.), N.F. (Sulfonal).

Sulfonmethane occurs as colorless, odorless, and nearly tasteless crystals or powder, slightly soluble in water (1 in 365) and sparingly soluble in alcohol (1 in 60).

It is a hypnotic and sedative similar to sulfonethylmethane, N.F., but acts more slowly. It may be used in dental medicine as a pre- and postoperative sedative.

DOSAGE.—0.75 Gm. (12 grains) (N.F.).

Aliphatic Series: Halogen Substitutions

The action of these compounds is due to the undissociated molecule and not to its ions. The halogen radical is bound and therefore cannot give the characteristic action of the halogen ion, as in sodium bromide.

The molecule generally contains an ethyl alcohol nucleus with substitutions. The substitution of a halogen increases the solubility of the molecule in fats and increases the hypnotic action. The toxicity is also increased, the drug acting directly on the heart and circulatory muscle, and in this way they resemble chloroform. The substitution of a methyl group in the molecule increases the hypnotic action and generally the toxicity. A hydroxyl group appears to be essential for hypnotic action.

CHLORAL HYDRATE; CHLORALIS HYDRAS (CHLORAL. HYDR.), $CCl_3CH(OH)_2$, U.S.P. (Chloral, Chloralum Hydratum).

Chloral hydrate is a crystalline solid containing not less than 99.5 per cent $C_2H_3O_2Cl_3$, having an aromatic, penetrating, and slightly acrid odor and a bitter, caustic taste. It is freely soluble in water, alcohol, ether, chloroform, and fixed and volatile oils. It was discovered by Liebig in 1832 and was introduced as a hypnotic in 1869 by Liebrick. It is usually prescribed in diluted solutions, syrup, etc. Its irritant properties prohibit its use for hypodermic purposes.

DOSAGE.—0.6 Gm. (10 grains) (U.S.P.), repeated, if necessary, in one or two hours.

PHARMACODYNAMICS.—When chloral hydrate is taken internally, it irritates the gastric mucosa and may produce nausea and vomiting. After absorption it acts as a sedative to the cerebral cortex, quieting sensory and motor excitement and inducing sleep. It is not very analgesic. With normal doses the drug does not affect the heart rate, blood pressure, respiratory rate, or basal metabolism, more than occurs in normal sleep.

THERAPEUTICS.—Chloral hydrate, in official doses, is a reliable and efficient hypnotic. It must be used with care in cardiac and circulatory diseases. It is not a hypnotic of first choice.

EXCRETION.—The drug is excreted chiefly through the kidneys. The molecule is not destroyed but is conjugated with glucuronic acid and excreted as such.

TOXICOLOGY.—Large doses or repeated small doses of chloral may produce toxic symptoms. The blood pressure is lowered because of a depression of the muscles of the heart and blood vessels. The action is directly on the muscle tissue and not neurogenic. Death occurs from circulatory failure and has occurred from a single dose of 4 grams. Chloral hydrate must not be combined with ethyl alcohol, as it forms an alcoholate (knock-out drops) which is very toxic.

TREATMENT.—If the drug is still in the stomach, remove it by emesis or stomach pump. To overcome the depression symptoms, give stimulants, such as caffeine with sodium benzoate in 3 grain doses hypodermically and repeat when necessary. Atropine sulfate, $\frac{1}{120}$ grain, or strychnine sulfate, $\frac{1}{30}$ grain, may be given orally or hypodermically.

TRIBROMOETHANOL; TRIBROMOAETHANOL (TRIBROMOAETH.), $Br_3C.CH_2OH$, U.S.P. (Tribromoethyl Alcohol).

Tribromoethanol contains not less than 99 per cent of $C_2H_3Br_3O$. The drug occurs as a white crystalline powder with a slight aromatic odor and flavor. It is unstable in air or light, soluble in water (1 in 35), and very soluble in amylene hydrate.

Chemically and therapeutically it resembles chloral hydrate. For basal anesthesia, tribromoethanol is dissolved in amylene hydrate and administered rectally. (See General Anesthetics for discussion.)

DOSAGE.—Rectal (for each kilogram of body weight), 60 mg. (1 grain) (U.S.P.). *Caution.—The total amount administered should not exceed 8 Gm. for women or 10 Gm. for men, regardless of weight* (U.S.P.).

CHLOROBUTANOL; CHLOROBUTANOL (CHLOROBUT.) $Cl_3C.C(CH_3)_2OH$, U.S.P.

Chlorobutanol resembles chloral hydrate (see for detail) chemically and therapeutically and is as dangerous when taken internally. When applied to abraded areas or mucous membranes, it acts as a local anesthetic. For this reason it is taken orally to allay nausea and vomiting in seasickness, alcoholism, pregnancy, etc. Applied locally to oral lesions, it allays pain and destroys bacteria.

DOSAGE.—0.6 Gm. (10 grains) (U.S.P.).

BROMETONE, $CBr_3C(CH_3)_2OH$, A.D.R.

Brometone occurs as a white crystalline powder which possesses a camphoraceous odor and taste. It is slightly soluble in water, soluble in alcohol, and melts at about 177° C.

It is claimed to have the sedative effect of the bromides without the disadvantage of producing "bromism." It is mildly analgesic.

Brometone may be used in dental medicine wherever a mild hypnotic, sedative, or analgesic is indicated.

DOSAGE.—0.3 Gm. (5 grains). Dispensed in 5 grain tablets by Parke, Davis & Company. Not over three tablets should be taken in twenty-four hours.

BROMURAL $[CH_3.CH(CH_3)CHBr.CO]HN.CO.NH_2$, A.D.R.

Bromural occurs as white needlelike crystals sparingly soluble in cold water and freely soluble in alcohol. It is tasteless and melts at 147° to 149° C. (N.N.R.).

It is a monobrome derivative of isovaleric acid and urea. The substitution of a methyl and a bromine radical in the aliphatic chain, plus the urea group, gives a mild hypnotic molecule. Its hypnotic action lasts from two to five hours. It is not analgesic and in normal doses does not appreciably affect the respiratory or circulatory systems. The A.D.R. ninth edition, recommends bromural* as a nerve sedative for nervous and apprehensive patients and to relieve a postoperative nervous state.

DOSAGE.—5 grains.

CARBROMAL; CARBROMALUM (CARBROM.), $CBr(C_2H_5)_2CO.NH.CONH_2$, N.F. (Bromdiethylacetylurea).

Carbromal occurs as a white, crystalline, odorless powder, very slightly soluble in water (1 in 3,000) and soluble in alcohol (1 in 18).

It is a mild nerve sedative and hypnotic with a short duration of action. It has been employed in general medicine, chiefly in neurasthenia, hysteria, chorea, and mental diseases. It has not been extensively used in dental practice, but may be indicated as a preoperative and postoperative nerve sedative in dental surgery.

DOSAGE.—0.5 Gm. (8 grains) (N.F.).

Aliphatic Series: Urea Derivatives

The barbiturates are salts of barbituric acid. The salts are white, odorless powders, having a bitter taste. They are soluble in water and slightly soluble in alcohol.

PHARMACODYNAMICS.—The action is most pronounced on the midbrain or subcortical areas (thalamus and corpus striatum). The absorption of barbiturates from the intestines is rapid. The excretion is chiefly through the kidneys. Its action on smooth muscle is a temporary loss of tonus. In hypnotic doses there is no effect on the circulation other than that found during normal sleep. In anesthetic doses there may be either a rise or a fall in blood pressure,

*Manufactured by Bilhuber-Knoll Corp., Orange, N. J.

varying from 10 to 40 mm. of Hg. Normal doses of barbiturates do not appreciably affect the respiration; after toxic doses the respiration stops before the heart fails. Mild doses, given in the daytime, allay nervousness with little or no drowsiness; a similar dose given at bedtime usually produces a restful sleep. The drug is slowly excreted and often leaves the patient with a "hangover feeling." Hypnotic doses do not affect the rate of basal metabolism nor lower body temperature.

UNTOWARD ACTION.—Patients with an idiosyncrasy for this drug may develop a skin rash and prolonged mental depression. The drug is slightly habit-forming. In most states it is not purchasable without a doctor's prescription.

CHEMISTRY OF THE BARBITURATES.—Barbituric acid is reactive and by substitution a molecule with hypnotic action is produced. An alkyl substitution up to 5 or 6 carbons increases the hypnotic potency, above 6 carbons decreases the potency and water solubility. Alkyl (alcohol) substitutions form compounds which are stable within the body and have a longer duration of action. Aryl (cyclic) substitutions are unstable within the body and are shorter acting; their potency and toxicity are increased. Sulfur substitutions increase the potency of the molecule and shorten the duration of action. An unsaturation in the substituted part of the molecule increases the potency. Sodium substitutions increase their solubility in water.

TOXICOLOGY.—The barbiturates are drugs often used for suicidal purpose. The toxic symptoms are depression, sleep, coma, slow respiration, fall in blood pressure, and, if untreated, death. Treatment for poisoning is to lavage the stomach and colon, increase elimination, and administer strychnine sulfate hypodermically in $\frac{1}{20}$ grain doses. Picrotoxin in fractional doses is a very satisfactory analeptic for barbital toxicity when given in 2 mg. ($\frac{1}{30}$ grain) doses every 15 minutes until symptoms of poisoning are relieved.

THERAPEUTICS.—The barbiturates are used to allay nervousness in the daytime, to produce rest at night, as a mild analgesic for pain, and as a sedative before a local or general anesthetic. They are good preparations to allay nervousness before a dental operation, to allay pain and nervousness during the operation, and to insure quiet and rest after the operation. There seems to be a synergistic action between the barbiturates and the analgesic drugs. Not more than four U.S.P. doses should be given in twenty-four hours. They are useful for preventing and treating procaine toxicosis.

PREPARATIONS.—

BARBITAL; BARBITALUM (BARBITAL.), $CO(HNCO)_2C(C_2H_5)_2$, U.S.P. (Diethylbarbituric Acid, Diethylmalonylurea, Barbitone).

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.), in powder in hot milk half an hour before bedtime; or pills or tablets, which should be crushed and taken with water.

Elixir of Barbital; Elixir Barbitali (Elix. Barbital.), N.F.—Barbital (3.5%) in caramel, compound spirit of vanillin, alcohol, and glycerin. Absolute alcohol content about 30 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Tablets of Barbital; Tabellae Barbitali (Tab. Barbital.), U.S.P.

DOSAGE.—0.3 Gm. (5 grains) of barbital (U.S.P.).

BARBITAL SODIUM; BARBITALUM SODICUM (BARBITAL. SOD.), $OCNa.NCO.NHCO.C(C_2H_5)_2$, U.S.P. (Soluble Barbital).

USES.—The same as those of barbital; it is absorbed a little more rapidly.

Barbital sodium is a white, crystalline powder. It has a bitter alkaline taste and is much more soluble in water than in barbital. Soluble barbital acts more rapidly than barbital.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Barbital Sodium Tablets; Tabellae Barbitali Sodici (Tab. Barbital. Sod.), U.S.P. (Soluble Barbital Tablets).

DOSAGE.—0.3 Gm. (5 grains) of soluble barbital (U.S.P.).

PHENOBARBITAL; PHENOBARBITALUM (PHENOBARB.), $CO(NHCO)_2C(C_2H_5)(C_6H_5)$, U.S.P., Phenylethylmalonylurea, Phenobarbitone.

It differs from barbital in that one ethyl group (C_2H_5) is replaced by one phenyl group (C_6H_5).

Phenobarbital is a white, slightly bitter powder. It is slightly soluble in water (1 in 1,000). It is soluble in alkaline solutions as well as in alcohol (1 in 10), ether, and chloroform.

ACTION AND THERAPEUTIC USES.—The replacement of an ethyl group (C_2H_5) by a phenyl group (C_6H_5) increases both the sedative and the hypnotic action of phenobarbital, but unfortunately its toxicity is also increased. Its lower dosage requirements compensate for the difference so that phenobarbital may be used as a safe hypnotic and sedative in preoperative and postoperative medication.

DOSAGE.—30 mg. (½ grain) (U.S.P.).

Elixir of Phenobarbital, Elixir Phenobarbitali (Elix. Phenobarb.), U.S.P.—Phenobarbital (0.4%) in glycerin, alcohol, syrup, solution

BARBITURIC ACID DERIVATIVES*

NAME	CHEMICAL NAME	FORMULA
Barbital (Veronal)	Diethylbarbituric acid	$(C_4N_2H_2O_3) = (C_2H_5)_2$
Soluble Barbital (Soluble Veronal)	Sodium diethylbarbiturate	$(C_4N_2HNaO_3) = (C_2H_5)_2$
Phenobarbital (Luminal)	Phenylethylbarbituric acid	$(C_4N_2H_2O_3) <^{(C_2H_5)}_{(C_6H_5)}$
Soluble Phenobarbital (Soluble Luminal)	Sodium phenylethylbarbituric acid	$(C_4N_2HNaO_3) <^{(C_2H_5)}_{(C_6H_5)}$
Amytal	Isoamylethylbarbituric acid	$(C_4N_2H_2O_3) <^{(C_2H_5)}_{CH_2.CH <^{(C_2H_5)}_{(CH_3)}}$
Sodium Amytal	Sodium isoamylethylbarbiturate	$(C_4N_2HNaO_3) <^{(C_2H_5)}_{CH_2.CH <^{(C_2H_5)}_{(CH_3)}}$
Pentobarbital (Nembutal)	Sodium ethyl (*l*-methylbutyl) barbiturate	$(C_4N_2HNaO_3) <^{(C_2H_5)}_{CH <^{(CH_3)}_{(C_3H_7)}}$
Alurate	Allylisopropylbarbituric acid	$(C_4N_2H_2O_3) <^{(C_3H_5)}_{(C_3H_7)}$
Sodium Alurate	Sodium allylisopropyl barbiturate	$(C_4N_2HNaO_3) <^{(C_3H_5)}_{(C_3H_7)}$
Ipral Calcium	Calcium ethylisopropyl barbiturate	$\left((C_4N_2HO_3) <^{C_3H_7}_{C_2H_5}\right)_2 Ca.3H_2O$
Ipral Sodium	Sodium ethylisopropyl barbiturate	$(C_4N_2HNaO_3) <^{(C_3H_7)}_{(C_2H_5)}$
Neonal	N-Butylethylbarbituric acid	$(C_4N_2H_2O_3) <^{(C_4H_9)}_{(C_2H_5)}$
Nostal	Isopropyl bromallyl barbituric acid	$(C_4N_2H_2O_3) <^{(C_3H_7)}_{CH_2CBr:CH_2}$
Ortal Sodium	Sodium *n*-hexylethyl barbiturate	$(C_4N_2HNaO_3) <^{(C_2H_5)}_{CH_2CH_2CH_2CH_2CH_2.CH_3}$
Pernoston	Butyl β-bromallyl barbituric acid	$(C_4N_2H_2O_3) <^{CH(CH_3)CH_2CH_3}_{CH_2CBr:CH_2}$
Phanodorn	Cyclohexenyl ethyl barbituric acid	$(C_4N_2H_2O_3) <^{C:CHCH_2CH_2CH_2CH_2}_{(C_2H_5)}$ (ring closed from C to terminal CH_2)
Sandoptal	Isobutylallyl barbituric acid	$(C_4N_2H_2O_3) <^{(C_4H_9)}_{(C_3H_5)}$

*From Davison: *Materia Medica, Toxicology and Pharmacology*, 1940.

of amaranth, and distilled water, and flavored with tincture of sweet orange peel. Absolute alcohol content about 14 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (U.S.P.).

Tablets of Phenobarbital, Tabellae Phenobarbitali (Tab. Phenobarb.), U.S.P.

DOSAGE.—30 mg. (½ grain) of phenobarbital (U.S.P.)

THERAPEUTICS OF THE BARBITALS.—There are many barbituric acid derivatives, but only those most extensively used have been presented here.[1]

During recent years many dentists have been interested in the use of the barbitals and because of the extensive study made of their uses by the Council on Dental Therapeutics, those interested are referred to accepted Dental Remedies, tenth edition, for additional information.

Prescriptions for Hypnotics

℞ Tablets of Barbital 0.3 Gm.
No. XII
Sig.: One tablet before retiring, repeat if necessary.

℞ Elixir of Barbital 120.0 cc.
Sig.: 4 cc. in water before retiring, repeat if necessary.

℞ Pentobarbital Sodium Capsules 0.1 Gm.
No. VI
Sig.: Take one capsule one-half hour before visiting the dentist.

℞ Barbital Sodium 3.0 Gm.
M. et ft. cap. No. X
Sig.: One capsule before retiring, repeat if necessary.

[1] Uses and Abuses of Barbitals, J. A. D. A. 18: 152-155, Jan., 1931.

CHAPTER V

DRUGS WHICH DEPRESS THE CENTRAL NERVOUS SYSTEM

ANALGESICS

Analgesics, sometimes referred to as *anodynes,* and as *narcotics* (to stupefy), are remedies employed for the purpose of relieving pain. By pain we understand the conscious manifestation of morbid changes within the nerve centers caused by some form of irritation which is usually manifested at the periphery. Analgesics are administered internally and act by inhibiting the sensory functions of the central nervous system. They do not form a specific pharmacologic group of remedies but are closely related in their general action to the general anesthetics. The action of the latter group inhibits not only the sensory functions but also the motor functions and consciousness. When analgesics are locally applied, they are often referred to as local anesthetics. General anesthetics are rarely employed for the purpose of relieving pain and are principally used to prevent pain. The foremost drugs which are employed to relieve pain are opium and its alkaloids and certain compounds of the aromatic series. The latter are, however, also used to reduce the body temperature and to act as antipyretics. The most important analgesic is morphine; it is the sovereign remedy in all cases where severe pain is to be controlled.

The painful nature of operations involving the teeth has provided the stimulus and opportunity for dentistry to make its contribution in the relief and control of pain in surgical and medical practice.

Opium and Opium Derivatives

OPIUM; OPIUM, U.S.P. (Gum Opium).

Opium has been used in medicine for many centuries, and none of the substitutes has succeeded in replacing it. It is the dried milky exudation obtained by incising the unripe capsules of the opium plant, *Papaver somniferum.* The dried powder yields not less than 9.5 per cent or more than 10.5 per cent of crystallized morphine. Opium contains numerous alkaloids of which about twenty have been isolated. The principal opium alkaloids are: morphine, 10 per cent; codeine, 0.3 per cent; thebaine, 0.4 per cent; narcotine, 5 per cent; narceine,

and papaverine. Pantopone and narcophine, artificial mixtures, are claimed to represent the total alkaloids of opium in the form of soluble hydrochloride salts and free from inert vegetable matter.

PHYSICAL PROPERTIES.—A light brown powder, bitter in taste.

DOSAGE.—0.06 Gm. (1 grain).

PREPARATIONS.—

Granulated Opium; Opium Granulatum (Opium Gran.), U.S.P.—Yields about 10.25 per cent of anhydrous morphine.

DOSAGE.—0.06 Gm. (1 grain) (U.S.P.).

Powdered Opium; Opium Pulveratum (Opium Pulv.), U.S.P. (Opii pulvis, P. I.).—Contains about 10.25 per cent of anhydrous morphine.

DOSAGE.—0.06 Gm. (1 grain) (U.S.P.).

Powder of Ipecac and Opium; Pulvis Ipecacuanhae et Opii (Pulv. Ipecac. et Opii), U.S.P. (Compound Powder of Ipecac, Dover's Powder, Pulvis opii et ipecacuanhae compositus P.I.).—Powered opium and ipecac (each 10%) with lactose.

USES.—Especially as a diaphoretic in incipient colds.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Syrup of Ipecac and Opium; Syrupus Ipecacuanhae et Opii (Syr. Ipecac. et Opii), N.F. (Syrup of Dover's Powder).—Tincture of ipecac and opium (8.5%) with spirit of cinnamon in syrup. Absolute alcohol content about 1.5 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Tincture of Ipecac and Opium; Tinctura Ipecacuanhae et Opii (Tr. Ipecac. et Opii), N.F. (Tincture of Dover's Powder).—This preparation represents tincture of opium (100%) and fluidextract of ipecac (10%) in diluted alcohol. Absolute alcohol content about 20 per cent.

DOSAGE.—0.5 cc. (8 minims) (N.F.).

Tincture of Opium; Tinctura Opii (Tr. Opii), U.S.P. (Laudanum, Tincture of Deodorized Opium, Tinctura opii P.I.).—Granulated opium (10%) in alcohol and water; a purified or deodorized aqueous extract yielding about 1 per cent anhydrous morphine.

DOSAGE.—0.6 cc. (10 minims) (U.S.P.).

Camphorated Tincture of Opium; Tinctura Opii Camphorata (Tr. Opii Camph.), U.S.P. (Paregoric, Tinctura opii benzoica P.I.).—Tincture of opium (4%), camphor (0.4%), benzoic acid and oil of anise in diluted alcohol. Absolute alcohol content about 45 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (U.S.P.).

Compound Mixture of Opium and Glycyrrhiza; Mistura Opii et Glycyrrhizae Composita (Mist. Opii et Glycyrrh. Comp.), N.F.

(Brown Mixture).—Camphorated tincture of opium (12%), antimony and potassium tartrate (0.024%), with fluidextract of glycyrrhiza, glycerin, and spirit of ethyl nitrite in distilled water. Absolute alcohol content about 10 per cent.

USES.—A popular expectorant; effective mainly through its opium and antimony content.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Alkaloids of Opium

MORPHINE HYDROCHLORIDE; MORPHINAE HYDROCHLORIDUM (MORPH. HYDROCHLOR.), N.F.

Morphine hydrochloride occurs as white, silky, glistening needles, or in small crystalline cubes; it is odorless and has a bitter taste. It is soluble in about 17 parts of water and in 52 parts of alcohol.

DOSAGE.—8 mg. (⅛ grain) (N.F.).

MORPHINE SULFATE; MORPHINAE SULFAS (MORPH. SULF.), U.S.P.

Morphine sulfate occurs as white, feathery crystals or cubical masses; it is odorless and has a bitter taste. It is soluble in about 16 parts of water and about 570 parts of alcohol.

DOSAGE.—10 mg. (⅙ grain) (U.S.P.).

Tablets of Morphine Sulfate; Tabellae Morphinae Sulfatis (Tab. Morph. Sulf.), U.S.P.—These tablets contain 93 to 107 per cent of the stated amount of morphine sulfate.

DOSAGE.—10 mg. (⅙ grain) of morphine sulfate (U.S.P.)

CODEINE; CODEINA (CODEIN.), U.S.P. (Methylmorphine).

An alkaloid obtained from opium, or prepared from morphine by methylation.

DOSAGE.—30 mg. (½ grain) (U.S.P.).

CODEINE PHOSPHATE; CODEINAE PHOSPHAS (CODEIN. PHOS.), U.S.P.

Codeine phosphate occurs in fine white, needle-shaped crystals, or as a crystalline powder; it is odorless and has a very bitter taste. It is soluble in about 2.5 parts of water and 325 parts of alcohol.

ACTION AND USES.—Same as those of codeine; preferred for hypodermic use because of greater solubility.

DOSAGE.—30 mg. (½ grain) (U.S.P.).

Tablets of Codeine Phosphate; Tabellae Codeinae Phosphatis (Tab. Codein. Phos.), U.S.P.—Yield codeine equal to 93 to 107 per cent of the stated amount of codeine phosphate.

DOSAGE.—30 mg. (½ grain) of codeine phosphate (U.S.P.).

CODEINE SULFATE; CODEINAE SULFAS (CODEIN. SULF.), U.S.P.

ACTION AND USES.—Same as those of codeine. Preferred for hypodermic injections because of greater solubility.

DOSAGE.—30 mg. (½ grain) (U.S.P.).

Tablets of Codeine Sulfate; Tabellae Codeinae Sulfatis (Tab. Codein. Sulf.), U.S.P.—These tablets contain 93 to 107 per cent of the stated amount of codeine sulfate.

DOSAGE.—30 mg. (½ grain) of codeine sulfate (U.S.P.).

THERAPEUTICS.—Morphine, when given in average doses, inhibits the entire function of the cerebrum and thereby abolishes sensibility to pain and produces sleep. It reduces the irritability of the centers of respiration, and almost invariably contracts the pupils, but these latter actions are not utilized therapeutically. The circulation is not affected by morphine. The peristaltic movement of the bowels is usually lessened.

Morphine is a powerful poison and kills by paralyzing the centers of respiration. Man is by far the most sensitive to the action of morphine. The lower the organization of the animal, the less reaction is produced by this poison, i.e., bacteria are not influenced by its solution. Small children are very sensitive to opium and morphine; even very small doses may produce dangerous symptoms.

Morphine is readily absorbed, especially when injected hypodermically, and manifests its action within a few minutes. In most people it produces at first very slight excitement, which is immediately followed by psychic rest and a feeling of contentment, with more or less inhibition of volition. A state of general analgesia results without interfering markedly with the cerebral functions. Morphine does not produce general or, when applied externally, local anesthesia. In due time drowsiness results, which soon passes into sleep; the latter lasts from eight to twelve hours. On awakening, a slight dizziness, loss of appetite, and constipation are often experienced. Large doses of morphine produce a comatose condition; all reflexes are abolished, the face appears sallow and cyanosed, the eyeballs are turned upward, and the pupils are contracted. The respiration becomes shallow and is interrupted by Cheyne-Stokes breathing. Respiration ceases entirely before the heartbeat stops. In poisoning with morphine, even when given hypodermically, morphine is often found in the stomach. The stomach should always be thoroughly washed, and the patient must be kept awake and in motion if at all possible. Artificial respiration, even after life seems to be extinct, should be persistently applied. The injection of full doses of strychnine is indicated.

The continuous use of morphine readily leads to an addiction to the drug. Extreme care should be exercised in prescribing quantities of morphine for prolonged use, and under no conditions should the patient be allowed to administer a hypodermic injection to himself. Sufferers from persistent facial neuralgia frequently become addicted to this poison.

Morphine is the supreme analgesic and will reduce the most persistent and apparently unbearable pain. It should not, however, be used indiscriminately because of the possibility of inducing morphinism. Morphine should always be substituted by some other analgesic if possible, such as the barbiturates, the salicylates, or the phenetidins. It should be used only in cases of absolute necessity. Pain arising from certain forms of acute alveolar abscesses, difficult eruption of a lower third molar, etc., may in extreme cases call for its administration. Morphine is very beneficial in diseases of the respiratory apparatus.

For dental office use, codeine is better than morphine, as it is not so depressing for ambulatory patients. In half grain doses it will allay most of the severe dental pain and yet allow the patient to continue with his daily duties.

THE AROMATIC COMPOUNDS

These compounds are obtained from coal tar by synthesis. They have the benzene ring as a nucleus. The aniline derivatives are oxidized in the body to para-aminophenol, which is the compound that gives them their therapeutic properties. They are efficient analgesics for pain arising on the periphery of the body but to a lesser extent on pain arising from smooth muscle and viscera. Their site of action is chiefly the midbrain, probably the thalamus. They are rapidly excreted by the kidneys as a conjugation product with glucuronic acid or sulfuric acid. These compounds are not readily injurious to the normal heart but are to the organically diseased heart muscle. Cyanosis is an early sign of poisoning; the blueness is due to the formation of methemoglobin. This condition, complicated with heart failure, produces respiratory embarrassment. These drugs are habit-forming. Chronic poisoning is treated by withholding the drug. Acute poisoning is treated by emesis, catharsis, increased fluid intake, oxygen, and supportive treatment.

Salicylates

The salicylates as a group are analgesic, antirheumatic, antipyretic, and caustic. For an analgesic and antipyretic action, aspirin is prob-

ably the preparation of choice; for an antirheumatic action, sodium salicylate is more often used; as a keratolytic, salicylic acid is the one of choice.

ACETYLSALICYLIC ACID; ACIDUM ACETYLSALICYLICUM (ACID. ACETYLSAL.), $C_6H_4OCOCH_3.COOH$, 1:2, U.S.P. (Aspirin).

Acetylsalicylic acid occurs as a colorless, odorless, crystalline powder, slightly soluble in water (1 in 300) and freely soluble in alcohol (1 in 5). It is incompatable with many substances and is safer when prescribed alone.

THERAPEUTICS.—Locally it acts as an obtundent and irritant and internally as an analgesic, antipyretic, and antirheumatic. The site of action is the optic thalamus, where pain sensations are depressed and kept from reaching the centers of perception. Aspirin allays pain from the cutaneous areas of the body and to a lesser extent from the viscera. It is excreted chiefly through the kidney; the drug may be detected fifteen minutes after the administration, and the excretion continues for two or three days.

Normal doses of aspirin have little or no effect on the normal heart, making it one of the safest analgesics.

In the stomach this ester of salicylic acid is not readily decomposed into salicylic acid and does not produce gastric irritation to the same extent as the salts. As with all drugs some few patients are hypersensitive to it and may have gastritis, urticaria, and edema.

The maximal dose for analgesic efficiency is about five grains, and the analgesic maximum is reached in two hours; therefore the best signatura is 0.3 Gm. taken every two hours.

TOXICOLOGY.—The symptoms of salicylism are a feeling of muscular weakness, heartburn due to gastric irritation, angioneurotic edema of the face and throat, urticaria of the skin and mucous membrane, depression of the heart muscle, cyanosis, and circulatory collapse.

TREATMENT.—Stop the drug. Remove the drug from the stomach by inducing vomiting and from the intestines by catharsis. Keep patient warm and quiet. Give plenty of water to aid in elimination. Give stimulant, such as caffeine, when necessary.

In dentistry, aspirin is useful alone or combined with stronger analgesic drugs for the control of oral pain.

DOSAGE.—0.3 Gm. (5 grains) administered every two or three hours. The drug should be stopped when symptoms of salicylism occur.

PREPARATIONS.—

Tablets of Acetysalicylic Acid; Tabellae Acidi Acetylsalicylici (Tab. Acid. Acetylsal), **U.S.P. (Aspirin Tablets).**

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Compound Paste of Acetylsalicylic Acid; Pasta Acidi Acetysalicylici Composita (Past. Acid. Acetylsal. Comp.), N.F. (Dental Anodyne Paste).

THERAPEUTICS.—Used locally as an anodyne paste in dental surgery.

SODIUM SALICYLATE; SODII SALICYLAS (SOD. SALICYL.), $C_6H_4.OH.COONa$, U.S.P.

Sodium salicylate occurs as a powder or scales, which are very soluble in water (1 in 1) and freely soluble in alcohol (1 in 10). It is without odor, but has a sweet, saline taste. Being incompatible with acids and acid salts, it forms salicylic acid which is very irritating to the tissues.

THERAPEUTICS.—The sodium salt of salicylic acid is employed to give the constitutional effect of salicylic acid. Its chief use is to allay pain in acute rheumatic fever, but its action is not curative, and the prognosis is not changed by its administration.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

PREPARATIONS.—

Tablets of Sodium Salicylate; Tabellae Sodii Salicylatis (Tab. Sod. Salicyl.), U.S.P.

DOSAGE.—0.6 Gm. (10 grains) (U.S.P.).

Ampuls of Sodium Salicylate; Ampullae Sodii Salicylatis (Ampul. Sod. Salicyl.), N.F. Each 1 cc. of the sterile aqueous solution contains 0.2 Gm. of the drug.

DOSAGE.—1 Gm. (15 grains) (N.F.).

Elixir of Sodium Salicylate; Elixir Sodii Salicylatis (Elix. Sod. Salicyl), N. F.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

AMINOPYRINE

AMINOPYRINE; AMINOPYRINA (AMINOPYRIN.), U.S.P. (Amidopyrine).

Aminopyrine occurs as a white crystalline solid, odorless, and almost tasteless. It is soluble in water (1 in 18) and freely soluble in alcohol (1 in 1.5).

THERAPEUTICS.—It is an analgesic with a slower but stronger action than aspirin, often lasting from twelve to twenty-four hours. Because of its toxic action, *Useful Drugs* no longer lists it. It must be used cautiously in infectious fever, as occasional cases of granulocytopenia following its use have been reported.* Under Federal Law the sale

*Agranulocytosis: A Critical Review of Causes and Treatment, J. A. D. A. 22: 487, 1935. A Council on Dental Therapeutics Report.

of aminopyrine and its preparations is restricted to a prescription order.

PREPARATIONS.—

Elixir of Aminopyrine; Elixir Aminopyrinae (Elix. Aminopyrin), N.F. (Elixir of Amidopyrine).

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Tablets of Aminopyrine; Tabellae Aminopyrinae (Tab. Aminopyrin.), N.F. (Amidopyrine Tablets).

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

ACETANILID

ACETANILID; ACETANILIDUM (ACETANIL.), $C_6H_5NHCOCH_3$, U.S.P.

Acetanilid occurs as a white crystalline powder with a slight burning taste and no odor. In water it is slightly soluble (1 in 190) and in alcohol, freely soluble (1 in 3.5). It liquefies when mixed with chloral hydrate or antipyrine.

THERAPEUTICS.—Acetanilid is a reliable analgesic for the relief of headaches and neuralgic pain, but it is not as efficient for pain due to inflammation. It is not a drug of first choice for the relief of pain due to pulpitis, as its vasodilating action increases the pulpal congestion. It is a cardiac depressant because of the para-aminophenol, a decomposition product formed from acetanilid in the body. The hemoglobin is inactivated by this substance and becomes less efficient as an oxygen carrier.

In toxic doses acetanilid and related compounds produce circulatory failure, and in individuals with an allergy, similar symptoms result from normal doses. It is contraindicated in debilitated patients, especially those with cardiac disease. Its indiscriminate use in headache powders is dangerous. (See *Useful Drugs,* pp. 9-10, thirteenth edition.)

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.) in powders which may be placed in capsules, or tablets which should be crushed before swallowing. It is well to begin with 0.1 Gm. or about 1½ grains, and, if necessary, to repeat cautiously.

PREPARATIONS.—

Compound Powder of Acetanilid; Pulvis Acetanilidi Compositus (Pulv. Acetanil. Comp.), N.F.—This powder contains acetanilid (70%), caffeine (10%), and sodium bicarbonate (20%).

THERAPEUTICS.—An irrational mixture which has no use in dental therapeutics.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

Tablets of Acetanilid; Tabellae Acetanilidi (Tab. Acetanil.), N.F.

DOSAGE.—0.2 Gm. (3 grains) (N.F.).

ACETOPHENETIDIN

ACETOPHENETIDIN; ACETOPHENTIDINUM (ACETPHEN.), $C_6H_4OC_2H_5NHCH_3CO$, U.S.P. (Acetphenetidin, Phenacetin).

Acetophenetidin occurs as a white crystalline powder, slightly soluble in water (1 in 1,300) and freely soluble in alcohol (1 in 15). It has an acid taste and is odorless. Its list of incompatibilities is great, suggesting it should be prescribed alone.

THERAPEUTICS.—Acetophenetidin is similar in chemical structure, pharmacodynamics, therapeutics, and toxicology to acetanilid (see). The maximal analgesic effect is obtained with the official dose, and larger doses generally have no additional effect other than toxicity.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

PREPARATION.—

Acetophenetidin Tablets; Tabellae Acetophenetidini (Tab. Acetphen.), U.S.P. (Phenacetin Tablets).

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Aliphatic Compounds

TRICHLOROETHYLENE, TRICHLOROAETHYLENUM, $CHCl = CCl_2$, U.S.P.

Trichloroethylene acts as a volatile analgesic and has been used with varying success in trigeminal neuralgia. In patients with low blood pressure it may produce symptoms of fainting. Its use as an analgesia for operative dentistry has not been satisfactory. It has limited therapeutic value.

DOSAGE.—1 cc. (15 minims) (U.S.P.), by inhalation. Larger doses or repeated doses do not give summated effects.

CHAPTER VI

DRUGS WHICH DEPRESS THE CENTRAL NERVOUS SYSTEM

SEDATIVES

Sedatives (from *sedare,* to quiet) are drugs employed to reduce the irritability of the central nervous system. They affect both motor and sensory centers. In their principal action, sedatives are related to general anesthetics. When administered in therapeutic doses, they do not produce effects other than mild sedation. Whenever the central nervous system becomes intensely irritated through external sources, or from factors which originate within the body, general excitement results, which is designated by the general term nervousness. Sedatives are indicated for these disturbances, and they usually subdue the state of excitement within a reasonably short time, while on the healthy individual they apparently have no effect. The most important representative of this therapeutic group is bromine in the form of its alkali salts. It has been experimentally shown that the bromine salts will reduce irritability of the centers of the cerebrum without inducing other effects. Aside from bromine compounds, the analgesics, hypnotics, and antipyretics are often prescribed in mild nervousness. A few vegetable and animal drugs which are characterized by their specific, intense, and frequently disagreeable odor—valerian, asafetida, castoreum, etc.—were in great favor as nerve sedatives with the older practitioners. So far no definite pharmacologic action has been attributed to these latter compounds.

Sedatives frequently render valuable service in preparing a hypersensitive patient for a dental operation. It has been clinically demonstrated that the hypersensitiveness of the teeth, which in many cases is merely an expression of a general nervous irritation, may be materially reduced by a sedative administered shortly before the operation begins. The strain of a lengthy or painful dental operation may also be lessened by the administration of a sedative.

Salts of Bromine

Potassium Bromide; Potassii Bromidum (Pot. Bromid.), KBr, U.S.P.

Potassium bromide forms colorless or white crystals, or a granular powder, having a strongly saline taste. It is soluble in 1.5 parts of water and in 250 parts of alcohol.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Elixir of Potassium Bromide; Elixir Potassii Bromidi (Elix. Pot. Bromid.), N.F.—Potassium bromide (17.5%) in syrup, water, and aromatic elixir. Absolute alcohol content about 6 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Compound Effervescent Salt of Potassium Bromide; Sal Potassii Bromidi Effervescens Compositum (Sal Pot. Bromid. Eff. Comp.), N.F. (Effervescent Potassium Bromide with Caffeine).—In 115 Gm. of the salt there are caffeine (0.8 Gm.), potassium bromide (8.3 Gm.), sodium bicarbonate (58.7 Gm.), lithium carbonate (4.2 Gm.), tartaric acid (18 Gm.), and citric acid (25 Gm.), yielding citrates and tartrates of lithium and sodium.

USES.—"Headache" mixture; generally undesirable and complex.

DOSAGE.—6 Gm. (90 grains) (N.F.).

SODIUM BROMIDE; SODII BROMIDUM (SOD. BROMID.), NaBr, U.S.P.

Sodium bromide forms colorless or white crystals, or a granular powder, having a saline, slightly bitter taste. It is soluble in about 1.2 parts of water and 16 parts of alcohol.

USES.—Sodium bromide is used as a nerve sedative and cerebral depressant. Symptoms of bromism should be watched for.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Elixir of Five Bromides; Elixir Bromidorum Quinque (Elix. Bromid. Quinq.), N. F.—One hundred cc. of the elixir contain the equivalent of 18.5 to 20 grams of bromine in the form of the bromides of sodium, potassium, calcium, lithium, and ammonium in flavored aromatic elixir and water. Absolute alcohol content about 5 per cent.

USES.—There is no evidence that this preparation is in any way superior to sodium bromide or potassium bromide.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Elixir of Three Bromides; Elixir Bromidorum Trium (Elix. Bromid. Tri.), N.F.

Bromides of ammonium, potassium, and sodium (each 8%) in solution of amaranth and compound elixir of benzaldehyde. Absolute alcohol content about 4 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Elixir of Sodium Bromide; Elixir Sodii Bromidi (Elex. Sod. Bromid.), N.F.—Sodium bromide (1.75%) in syrup, water, and aromatic elixir. Absolute alcohol content about 6 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Syrup of the Bromides; Syrupus Bromidorum (Syr. Bromid.), N.F. —Potassium bromide and sodium bromide (each 8%), ammonium

bromide (5%), calcium bromide (2.5%), lithium bromide (0.8%), flavored with tincture of vanilla and colored with compound tincture of cudbear in compound syrup of sarsaparilla, sucrose, and water.

USES.—This complex mixture has no advantage over a single bromide.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Tablets of Three Bromides; Tabellae Bromidorum Trium (Tab. Bromid. Tri.), N.F. (Triple Bromide Tablets).—Bromides of ammonium, potassium, and sodium in equal proportions having total bromine content of 75 per cent of the stated amount of total bromides.

DOSAGE.—0.3 Gm. (5 grains) each of ammonium bromide, potassium bromide, and sodium bromide (N.F.). One tablet.

Tablets of Sodium Bromide; Tabellae Sodii Bromidi (Tab. Sod. Bromid.), N.F.

DOSAGE.—1 Gm. (15 grains) of sodium bromide (N.F.).

AMMONIUM BROMIDE; AMMONII BROMIDUM (AMMON. BROMID.), NH_4Br, N.F.

Ammonium bromide forms colorless, prismatic crystals or a white crystalline powder, is odorless, and has a pungent, saline taste. It is soluble in about 1.3 parts of water and 12 parts of alcohol.

DOSAGE.—1 Gm. (15 grains) (N.F.), in solution.

Other bromides—the salts of lithium, calcium, and strontium, hydrobromic acid, etc.—are used in therapeutics; their action depends principally on their bromine content. Bromine salts are best prescribed in solution and should be taken well diluted with water. The irritation resulting from the injection of bromine salts into the tissues prohibits their application for such purposes. The bromides act by depressing the sensory and motor areas of the cerebral cortex and the cordal synapses between the anterior motor and the posterior horn cells of the spinal cord.

Questionable Sedatives

VALERIAN; VALERIANA (VALER.), N.F.

Valerian and its many galenic preparations (from dried rhizome and roots of *Valeriana officinalis*) have a wide reputation as nerve sedatives. Nervous and hysteric women are especially partial to these preparations. Their effect is attributed to the psychologic impression resulting from the disagreeable odor and taste of the drug.

INTOXICANTS

Intoxicants are drugs which have a depressing action on the higher cerebral areas, inhibiting pain, reason, judgment, equilibrium, and terminating in stupor.

Alcohol as a cerebral depressant is principally employed in the form of fermented liquors and wines containing from 3 to 50 per cent of pure ethyl alcohol. Alcohol in concentration of 65 per cent or more precipitates albumin and acts as an irritant. The mucous membranes of the mouth and throat of those who are accustomed to strong alcoholic drinks are not affected by liquors containing 40 to 50 per cent of pure alcohol, while in the unaccustomed there is a feeling of burning and coughing after their use. Opinions regarding the use of fermented liquors as a cerebral depressant differ widely. The general consensus is that alcohol administered to the patient in rational doses seemingly reduces the excitability caused by external or internal irritation. In certain infectious diseases—septicemia, pyemia, etc.—the administration of alcohol was once believed to be useful, but this has been questioned by more recent observers. Again, alcohol in the form of whisky is lauded as a stimulant of the circulation, especially the heart; its usefulness under these conditions is referred to under Circulatory Stimulants. Whether alcohol is a nutrient in the true sense of the word is as yet not fully proved; it is certain, however, that it inhibits the rapid disintegration of the albuminous contents of the cells, especially in lasting febrile diseases, and thereby acts as an indirect means of saving valuable bodily strength. Incidentally, it is often employed as a vehicle for the administration of nutritious substances—yolk of egg in the well-known form of eggnog. The habitual use of liquors containing more than 30 per cent of alcohol, especially when taken into the empty stomach, causes a chronic form of gastritis.

ALCOHOL; ALCOHOL, U.S.P. (Ethyl Alcohol, Ethanol).

Alcohol is a colorless volatile liquid obtained by distillation from fermented carbohydrates. It is extensively used in pharmacy as a preservative and vehicle.

PHARMACODYNAMICS.—When applied locally it acts as an antiseptic, irritant, astringent, refrigerant, and on the mucous membrane as a caustic. Its local action is due to precipitation of the tissue protein by dehydration and by changing the dispersion medium of the tissue colloids.

SYSTEMICALLY.—The drug is rapidly absorbed from the empty stomach and from the intestines. Food in the stomach delays

absorption. After absorption, it acts by depressing the cells of the cerebral cortex. There is a short period of stimulation, probably due to the depressing action of the alcohol on the higher centers of reason and judgment. Later the entire cerebrum is depressed, producing analgesia, hypnosis, and narcosis. Larger doses act as an anesthetic, depressing the cerebrum, midbrain, spinal cord, and, last, the vital medullary centers. Normal doses of alcohol stimulate the respiratory center directly and indirectly by a reflex from the throat and stomach, thereby increasing the rate and depth of respiration. The direct action on the respiration may be due to the increased carbon dioxide in the blood, caused by the specific dynamic action of the oxidizing alcohol, and to the muscular excitability of the patient. There is a local vasodilation in the head and neck regions with a vasocontraction in the splanchnic regions, a rise in systolic blood pressure, and a possible lowering of the diastolic blood pressure. The normal heart is not appreciably affected, but the weakened heart may be improved by the rise in systolic pressure. The cutaneous vasodilation results in sweating and a lowering of the body temperature in fever. Dilute solutions of alcohol, as in beer and wines, may increase gastric peristalsis and stimulate the flow of gastric juice, acting as an appetizer and digestant. Large doses of concentrated alcohol, as in whisky, gin, and brandy, inhibit gastric secretion, destroying the digestive enzymes and decreasing the appetite.

Alcohol is oxidized chiefly in the liver to carbon dioxide and water, giving off 7 calories for each gram. Large doses, quickly absorbed, act as an irritant and are excreted through the kidneys. It cannot be classed as a food, as it does not furnish energy for muscle contraction. It does not form a true habit. It is taken for the pleasant mental stimulation it produces. Continued use in the mentally and morally weak produces degeneracy. Children of drunkards are not as physically, mentally, or morally alert as are children of more normal parents. Alcoholism is a disease that needs medical treatment. The prognosis is not favorable.

The kidneys excrete from 2 to 4 per cent, the lungs eliminate 6 to 8 per cent by expiration, and from 90 to 98 per cent is oxidized in the body. The rate of oxidation is constant when the body is at rest but increases with exercise. Normally about 10 to 15 cc. of absolute alcohol are burned per hour. Insulin appears to be necessary for the rapid oxidation of alcohol. Injections of glucose and insulin hasten the burning of alcohol in the body and may be used as antidotes (Luckhardt).

THERAPEUTICS.—

1. Vehicle and preservative.
2. Local refrigerant in a 70 per cent solution.
3. Local antiseptic in a 70 per cent solution.
4. Local astringent, skin 70 per cent, mucous membrane, 10 to 50 per cent.
5. Cutaneous vasodilator, relieving congestion in deeper areas of the respiratory system (colds).
6. Local antidote for phenol poisoning.

PREPARATIONS.—

Alcohol; Alcohol, U.S.P. (Ethanol).—Alcohol contains not less than 92.3 per cent of C_2H_5OH by weight or about 95 per cent by volume.

Diluted Alcohol; Alcohol Dilutum (Alcohol Dil.), U.S.P.—Diluted alcohol contains about 41.5 per cent of C_2H_5OH by weight.

Dehydrated Alcohol; Alcohol Dehydratum (Alcohol Dehyd.), U.S.P. —Absolute Alcohol contains not less than 99 per cent of C_2H_5OH by weight.

BEVERAGES.—

Whisky; Spiritus Frumenti (Sp. Frum.), U.S.P.—Whisky contains about 50 per cent of ethyl alcohol.

DOSAGE.—Not given in U.S.P. (15 to 45 cc.).

Brandy; Spiritus Vini Vitis (Sp. Vin. Vit.), U.S.P.

Brandy contains about 50 per cent C_2H_5OH.

DOSAGE.—Not given in U.S.P. (15 to 45 cc.).

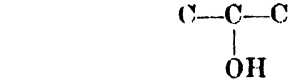
Methyl Alcohol, Methanol, is not official. It is prepared by the destructive distillation of wood. It has no use in therapeutics but is of importance because of its toxicity. It is often taken by mistake for ethyl alcohol or may be inhaled in large quantities as an occupational hazard.

PHARMACODYNAMICS and TOXICOLOGY.—Methyl alcohol is an intoxicant when taken internally. It is oxidized in the body to formaldehyde and formic acid, both of which act as violent poisons which result in degeneration of the optic nerve and blindness, depression of the heart muscle, cardiac failure, and frequently death.

TREATMENT.—Lavage the stomach. Give alkali to relieve the acidosis and give plenty of water to aid elimination through the kidneys.

ISOPROPYL ALCOHOL

Isopropyl alcohol is a secondary alcohol with the following structure:



Commercially it is used as a solvent and medicinally as a substitute for ethyl alcohol. Because of the need of ethyl alcohol in the essential war effort, it has become practically unobtainable for civilian use. For local application isopropyl alcohol is a good substitute for ethanol, which it resembles physically. Tainter has shown that its greatest antiseptic action is produced in a 50 per cent solution. Internally, isopropyl alcohol is slightly more toxic than ethyl alcohol, with no toxic symptoms appearing from its use in industry. In the body it is oxidized at about the same rate as ethanol and is apparently oxidized to carbon dioxide and water, with no symptoms of toxicity.

Isopropyl alcohol is a good substitute for ethyl alcohol for dental needs.

CHAPTER VII

DRUGS WHICH ACT ON THE CENTRAL NERVOUS SYSTEM

ANTIPYRETICS

Antipyretics or *antifebriles* (against fever) are remedies employed for the purpose of reducing body temperature in fever. They incidentally act as sedatives and analgesics and are frequently employed in dentistry for the relief of pain. Therapeutic doses of antipyretics do not materially change the normal body temperature.

The normal temperature of man is comparatively constant, that is, the changes vary within a very narrow limit. Normally, the body temperature ranges between 98° and 99.5° F. (36.7° and 37.4° C.). The external air has very little influence on the temperature of the human body. It is immaterial whether we are exposed to the broiling sun of the equator (120° F., 49° C.) or to the icy cold of Spitzbergen (–40° F., –40° C.); our inner temperature of 99° F. (37.3° C.) remains unaltered. The regulation of the body temperature is controlled by specific nerves, although we are able by suitable protection —heavy or light clothing, warm rooms or shady, airy, open spaces— materially to influence the radiation of body heat. The regulation of heat-producing foodstuffs is of prime importance; cold climates require easily combustible fats and carbohydrates, while in the tropics we instinctively avoid a steaming dish of heavy food. A rise of temperature of the surroundings causes dilatation of the peripheral vessels, which forces the warm blood to the surface to be cooled off, and the ready evaporation of perspiration from the stimulated sweat glands cools the body surface. The combined process of heat production and regulation is based on physiologic, chemical, and physical laws. An increased heat produced by physical exertion and unfavorable external conditions—high heat, humid atmosphere, etc.—may lead to overheating of the body; 104° F. and even as high as 113° F. (40° to 45° C.) have been observed in cases of sunstroke.

A rise in the body temperature is, in the majority of cases, the symptom of fever, provided this higher temperature is of a fairly constant nature. Fever is not a disease, but a symptom. In most

cases fever is the result of infection, although traumatic disturbances—fractures—may cause a so-called aseptic fever. There are various theories as to the causes of hyperpyrexia; the present consensus seems to point to the fact that fever indicates that the centers of heat regulation are gauged to a higher level than is normally present in the body. Accepting this hypothesis, we may explain fever as follows: certain pyrogens (fever producers) act on the centers of heat regulation, resulting in a shift of these centers to a higher plane and a higher constant body temperature. The true antipyretics act on the higher gauged centers, and their influence causes a return of normal function. The heat center by a reflex, as stated by Barber, acts by changing the blood concentration and the cutaneous blood flow, affecting the dissipation of heat. External influence on heat production and regulation does not interfere with the action of the true antipyretics. Quinine, salicylic acid, etc., sometimes called indirect antipyretics, influence the heat centers partially, but they act principally on heat production and heat radiation.

At one time it was thought that fever was a dangerous disease and had to be cured, and again it was looked upon as an expression of *vis medicatrix naturae*, a view which is at present favored by leading clinicians. Consequently, fever should not be "treated" immediately. If, however, the organism, in its effort to combat an infection, produces a dangerously high temperature, it is the duty of the practitioner to administer suitable antipyretics—to coax nature to return to her normal functions. Fever may damage the organism in various ways. Abnormally high temperature is dangerous to the heart, and furthermore a high temperature causes increased metabolism and loss of strength, as the destroyed albumin molecule cannot be replaced with sufficient rapidity. The increased temperature is accompanied by a disturbed psyche; the patient is fidgety, and sleeplessness and restlessness cause a loss of much needed resistance.

Aromatic Antipyretics

The aromatic antipyretics reduce the body temperature in fever but have no influence on the normal temperature. They act by producing (1) a cutaneous vasodilation which increases the amount of blood passing through the peripheral circulation, (2) a stimulation of sweat production which by evaporation removes body heat, (3) a decrease in the viscosity of blood which increases the peripheral circulation, and (4) restoration of the heat-regulating center to normal.

QUININE; QUININA (QUIN.), N.F.

Quinine is an alkaloid obtained from cinchona bark.

THERAPEUTICS.—Bitter tonic, analgesic, and antipyretic; specific against malaria.

DOSAGE.—1 Gm. (15 grains) (N.F.).

QUININE SULFATE; QUININAE SULFAS (QUIN. SULF.), U.S.P.

SOURCE AND CHARACTER.—It is the sulfate of the alkaloid quinine, obtained from the various species of *Cinchona*. It appears in white, silky, light, flexible crystals, or hard prismatic needles, colorless, and having a persistent bitter taste. It absorbs moisture from the air. It is soluble in 810 parts of water, 120 parts of alcohol. It is *incompatible* with ammonia, alkalies, limewater, tannin, potassium iodide, etc.

DOSAGE.—0.6 Gm. (10 grains) (U.S.P.).

THERAPEUTICS.—Quinine is one of the earliest drugs used to reduce fevers, but it has been largely replaced by other antipyretics. Quinine is the sovereign remedy in malaria; here its action is quite specific. It is a protoplasm poison; administered in therapeutic doses, it destroys the causative factors of malaria, the *Plasmodia malariae*, without materially altering the protoplasm of the cells of the host. Quinine should be administered three to four hours before the typical malarial attack is manifested, so as to allow sufficient time for its absorption. It is a prompt prophylactic against the symptoms of this disease. Its action as an antiseptic on bacteria or their spores is limited. It inhibits the migration of leucocytes, and for this reason Binz and Helmholz recommended it at one time as an antiphlogistic.

Quinine acts on the central nervous system as an analgesic; it reduces the irritability of the sensory nerves, and has been used as an antineuralgic. In influenza and in septicemia it has been recommended but without results. Quinine is best administered in loose-filled capsules, in pills, or suspended in syrup of yerba santa. Injected locally in the readily soluble form of quinine and urea hydrochloride, it acts as a local anesthetic (see Local Anesthetics).

ACETYLSALICYLIC ACID; ACIDUM ACETYLSALICYLICUM (ACID. ACETYLSAL.), $C_6H_4.OCOCH_3.COOH$ 1:2, U.S.P. (Aspirin).

PROPERTIES.—Acetylsalicylic acid is soluble in alcohol (1 in 5) and slightly soluble in water (1 in 300). It occurs as a white, crystalline powder which has an acidulous taste.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

MEDICAL PROPERTIES.—Analgesic, antipyretic, and antirheumatic.

THERAPEUTIC USES.—Acetylsalicylic acid is extensively used by the laity in the treatment of coryza and for the relief of headache. It is frequently prescribed for preoperative and postoperative dental treatment. The injudicious use of acetylsalicylic acid may lead to untoward effects in susceptible individuals. Its promiscuous use by the laity should be discouraged. Salicylic acid and its many salts and synthetic substitutes have been referred to under Analgesics.

Acetylsalicylic Acid Tablets; Tabellae Acidi Acetylsalicylici (Tab. Acid. Acetylsal.), U.S.P. (Aspirin Tablets).

DOSAGE.—0.3 Gm. (5 grains) of acetylsalicylic acid (U.S.P.).

ANTIPYRINE; ANTIPYRINA (ANTIPYRIN.), $C_{11}H_{12}ON_2$, U.S.P. (Phenazone).

Antipyrine is a derivative of pyrazolon, and forms a colorless, almost odorless, crystalline powder, having a slightly bitter taste. It is soluble in less than 1 part of water, and 1.3 parts of alcohol. It is *incompatible* with acids, alkalies, tannin, salicylates, etc.

USES.—Antipyretic and analgesic, similar to acetanilid.

THERAPEUTICS.—Antipyrine is a general antipyretic and anodyne. It acts on the central nervous system, and reduces the higher gauged centers of heat regulation to their normal function. It is an effective remedy in neuralgia, migraine, lumbago, and sciatica. Some patients show a distinct idiosyncrasy to this drug which is often accompanied by skin eruptions.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.), in solution, given with even greater caution than acetanilid.

ACETANILID; ACETANILIDUM (ACETANIL.), $C_6H_5NH.CH_3CO$, U.S.P.

Acetanilid is the monacetyl derivative of anilin. It is a colorless, crystalline powder, odorless, and has a slightly burning taste. It is soluble in 190 parts of water, 3.5 parts of alcohol, 4 parts of chloroform, and 17 parts of ether. It is *incompatible* with nitrous ether, bromides, iodides, phenol, resorcinol, and thymol.

THERAPEUTICS.—Acetanilid acts on the central nervous system as a strong analgesic. In large doses it acts as a blood poison by forming methemoglobin, which manifests itself in pronounced cyanosis. Acetanilid forms the base of many headache powders and of many proprietary preparations generically known as coal tar derivatives. Many cases of poisoning resulting from the indiscriminate use of these compounds are on record.[1, 2] Acetanilid is a prompt antipyretic; it is

[1]Accepted Dental Remedies, 1939, pages 180-181.

[2]Hanzlik, Paul J.: J. A. D. A. 27: 1505-1512 (September), 1672-1678 (October), 1833-1838 (November), 1940.

best administered in powder (capsules, tablets, or cachetes), in alcoholic solutions, or as the compound powder of acetanilid.

It is well to begin with 0.1 Gm. or about 1½ grains, and, if necessary, to repeat cautiously.

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.).

Compound Powder of Acetanilid; Pulvis Acetanilidi Compositus (Pulv. Acetanil. Comp.), N.F.—Acetanilid (70%), caffeine (10%), and sodium bicarbonate (20%).

USES.—An irrational acetanilid preparation.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

Tablets of Acetanilid; Tabellae Acetanilidi (Tab. Acetanil.), N.F.

DOSAGE.—0.2 Gm. (3 grains) of acetanilid (N.F.).

ACETOPHENETIDIN; ACETOPHENETIDINUM (ACETPHEN.), $C_6H_4.OC_2H_5.NH.CH_3CO$, U.S.P. (Acetphenetidin, Phenacetin).

Acetophenetidin is a derivative of aniline and is closely related to acetanilid, but it is less poisonous than the latter. It is a white crystalline powder with no odor but a slightly bitter taste. It is soluble in 1,300 parts of water and in 15 parts of alcohol. It is best administered in powder form. It is a prompt antipyretic and anodyne, and its toxic side action, as compared with acetanilid, is decidedly less.

ACTION AND USES.—Analgesic, antipyretic, and, in excessive doses, a cardiac depressant.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Acetophenetidin Tablets; Tabellae Acetophenetidini (Tab. Acetphen.), U.S.P. (Phenacetin Tablets).

DOSAGE.—0.3 Gm. (5 grains) of acetophenetidin (U.S.P.).

Tablets of Acetophenetidin and Phenyl Salicylate; Tabellae Acetophenetidini et Phenylis Salicylatis (Tab. Acetphen. et Phenyl. Salicyl.), N.F. (Phenacetin and Salol Tablets).

DOSAGE.—0.15 Gm. (2½ grains) each of acetophenetidin and phenyl salicylate (N.F.).

AMINOPYRINE; AMINOPYRINA (AMINOPYRIN.), U.S.P. (Amidopyrine).

Aminopyrine occurs as nearly tasteless, white crystals or crystalline powder. It is soluble in alcohol (1 in 1.5) and slightly soluble in water (1 in 18).

MEDICAL PROPERTIES.—Antipyretic and anodyne.

THERAPEUTICS.—Aminopyrine acts similarly to antipyrine except that it is more potent, requiring about one-half the dosage. Its action is slower but more prolonged. Aminopyrine is suspected of being a causative factor in the production of agranulocytic angina.

There is considerable clinical evidence in support of this view, but experimental confirmation is lacking. For a more complete analysis of the evidence, the student is referred to a report of the Council on Dental Therapeutics.[1]

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

PREPARATIONS.—

Elixir of Aminopyrine; Elixir Aminopyrinae (Elix. Aminopyrin.), N.F. (Elixir of Amidopyrine).—Aminopyrine (4%), in compound spirit of orange, glycerin, syrup, alcohol, compound tincture of cudbear, and distilled water. Absolute alcohol content about 19 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Tablets of Aminopyrine; Tabellae Aminopyrinae (Tab. Aminopyrin.), N.F. (Amidopyrine Tablets).

DOSAGE.—0.3 Gm. (5 grains) of aminopyrine (N.F.).

[1] Agranulocytosis: A Critical Review of Causes and Treatment, J. A. D. A. 22: 487, 1935.

CHAPTER VIII

DRUGS WHICH ACT ON THE CENTRAL NERVOUS SYSTEM

CEREBRAL STIMULANTS

Cerebral stimulants are drugs which physiologically excite the cells of the cerebral cortex. They are also known as *excitants* or as *analeptics* (from *analeplikos,* to restore). In the excitement caused by drug stimulation, other centers, as the respiration, the heart, the vasomotor centers, etc., are also involved. It may be observed, however, that general excitement, which manifests itself in an increased physical activity, garrulity, etc., is not always the result of cerebral stimulation; often the reverse is the case—that is, a paralysis of the higher inhibiting centers.

Caffeine is the most useful representative of the cerebral stimulants; it causes physical excitement without being followed by depression. Cocaine (see Local Anesthetics), in its pure form or as the coca leaf, is freely used as a cerebral stimulant by the Indians of Bolivia and Peru. On account of its poisonous nature it is not employed medicinally for this purpose. Certain substances, as strychnine, increase the irritability of the centers of reflex stimulation to a marked degree, while other alkaloids have a special predilection for the tetanic centers in the brain and in the spinal cord. Alcohol, in its many modifications and administered in small doses, is a cerebral stimulant of importance; although many pharmacologists deny this characteristic effect, claiming that alcohol is a narcotic. In the hands of the clinician, however, alcohol in small doses proves to be a valuable stimulant.

Strong infusions of coffee and tea are well-known cerebral stimulants. For a short time they may increase mental and physical activity and depress the feeling of hunger, which, however, is often followed by a slightly increased appetite. In some respects large doses of caffeine (coffee or tea) act antagonistically to those of alcohol; strong coffee and tea increase the mental faculties and are often productive of insomnia, especially in nervous individuals, while large doses of alcohol stupefy and consequently invite sleep.

Caffeine

Caffeine is a feebly basic alkaloid obtained from coffee, tea, guarana, kola, maté, etc. It occurs as white needle-shaped crystals, with a

bitter taste and no odor. It is sparingly soluble in water (1 in 50) and in alcohol (1 to 70).

PHARMACODYNAMICS.—Caffeine has no local action when applied to the skin, mucous membranes, or abraded areas. After absorption its chief site of action is the cerebral cortex, motor and sensory, increasing its irritability, stimulating the intellect and perception,

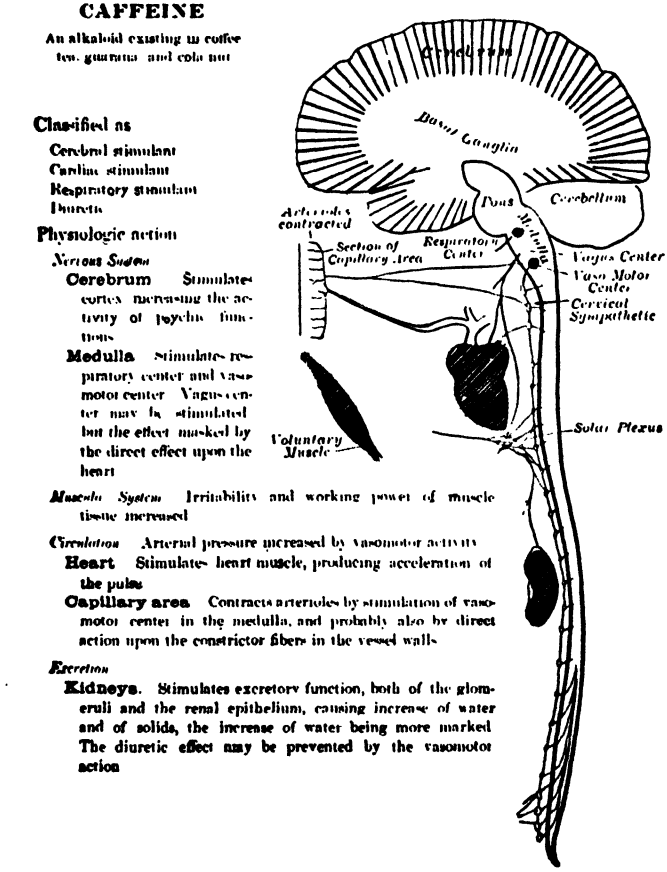


Fig. 14.—Caffeine. The areas shaded by solid lines represent regions stimulated by caffeine. (Redrawn from McGuigan: *Experimental Pharmacology*. Lea & Febiger.)

and increasing muscular efficiency. Larger doses stimulate the spinal cord and medulla, increasing muscular tonus and stimulating the vital centers, respiration, vagus, and vasoconstriction. The results of this medullary stimulation are uncertain. Generally the respiration is increased and the ventilation of the lungs improved. While the heart is depressed by the central vagus stimulation, the drug

has a direct stimulating action on the myocardium which normalizes the efficiency of the heart. A central vasoconstriction tends to increase the blood pressure by narrowing the splanchnic vessels. The direct action of the caffeine on the blood vessels is one of relaxation, and the resultant action on blood pressure is often nil. The coronary circulation is also relaxed, but not enough to make this drug of value in angina pectoris, but it also does not contraindicate its use in patients with coronary artery disease. The smooth muscles throughout the body are generally relaxed.

Caffeine is a good diuretic, increasing kidney function generally but decreasing the output of nitrogen compounds, thus contraindicating the use of caffeine beverages in patients with gout. The increase in urine production is brought about by an increased permeability of the glomerular capillaries, increased blood flow through the glomeruli, and by an increase in the number of glomeruli functioning.

THERAPEUTICS.—Caffeine and caffeine preparations are often contained in beverages, such as tea, coffee, kola, etc., and act as mild central nervous system stimulants. Such mild doses (one cup of strong tea or coffee contains from 2 to 3 grains of caffeine) are not harmful to the average adult. Young, old, and nervously unstable individuals are overstimulated by this drug and should not use it for beverage purposes. As a medullary stimulant it acts only in large doses, acting better on centers which have been previously depressed by drugs, such as in morphine poisoning. It is most efficient as a respiratory center stimulant in failure due to drugs or poisons. It is a good diuretic.

TOXICOLOGY.—The excessive drinking of tea, coffee, coca-cola, etc., often results in extreme irritability of the nervous system, characterized by nervousness and muscular twitching. The symptoms are relieved by stopping the ingestion of caffeine and prescribing a bromide to relieve the excitement temporarily. About 80 per cent of ingested caffeine is oxidized to urea, the remaining 20 per cent is excreted in the urine unchanged.

CAFFEINE; CAFFEINA (CAFF.), U.S.P. (Trimethylxanthine).

Caffeine is a feebly basic substance obtained from the dried seed of coffee, *Coffea arabica*, or the dried leaves of tea, *Thea sinensis*, etc. It occurs in long white, silky crystals, which are odorless and have a bitter taste. It is soluble in about 50 parts of water, 70 parts of alcohol, and readily soluble in boiling water.

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.), in capsules.

MEDICAL PROPERTIES.—Cerebral stimulant and diuretic.

THERAPEUTICS.—Caffeine has been found useful as a stimulant in nervous exhaustion, and as a respiratory stimulant in collapse and in narcotic poisoning involving respiration.

CITRATED CAFFEINE; CAFFEINA CITRATA (CAFF. CIT.), U.S.P.

Citrated caffeine is a white powder, consisting of a weak chemical combination of citric acid with caffeine, equal parts. It is soluble in about 4 parts of water.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.), in solution or capsules. Its acidity renders it unsuitable for hypodermic administration.

Tablets of Citrated Caffeine; Tabellae Caffeinae Citratae (Tab. Caff. Cit.), N.F.—These tablets yield anhydrous caffeine equal to 43 to 53 per cent of the stated amount of citrated caffeine.

DOSAGE.—0.3 Gm. (5 grains) of citrated caffeine (N.F.).

CAFFEINE AND SODIUM BENZOATE; CAFFEINA ET SODII BENZOAS (CAFF. ET SOD. BENZ.), U.S.P.

Caffeine and sodium benzoate about equal parts.

USES.—This is the form of caffeine usually employed for hypodermic administration, since it is freely soluble.

DOSAGE.—Oral or hypodermic, 0.5 Gm. (7½ grains) (U.S.P.).

Caffeine and Sodium Benzoate Injection; Injectio Caffeinae et Sodii Benzoatis (Inj. Caff. et Sod. Benz.), U.S.P. (Caffeine and Sodium Benzoate Ampuls).—This is a sterile solution of caffeine and sodium benzoate in water for injections.

DOSAGE.—Intramuscular, 0.5 Gm. (7½ grains) of Caffeine and Sodium Benzoate (U.S.P.).

Tablets of Caffeine with Sodium Benzoate; Tabellae Caffeinae cum Sodii Benzoate (Tab. Caff. c. Sod. Benz.), N.F.

DOSAGE.—0.3 Gm. (5 grains) of caffeine with sodium benzoate (N.F.).

CAFFEINE WITH SODIUM SALICYLATE; CAFFEINA CUM SODII SALICYLATE (CAFF. C. SOD. SALICYL.), N.F.

Caffeine with sodium salicylate, in equal parts, occurs as a white, odorless powder. It is freely soluble in water (1 in 2).

DOSAGE.—0.2 Gm. (3 grains) (N.F.).

ALCOHOLIC BEVERAGES

WHISKY; SPIRITUS FRUMENTI (SP. FRUM), U.S.P.

An alcoholic liquid obtained by the distillation of the mash of fermented grain. It is an amber-colored fluid, having a distinctive

odor and taste, and should contain from 47 to 53 per cent by volume of absolute alcohol. (See Intoxicants.)

USES.—Its action depends upon the alcohol that it contains.

BRANDY; SPIRITUS VINI VITIS (SP. VIN. VIT.), U.S.P.

Absolute alcohol content about 51 per cent.

USES.—Its action depends upon the alcohol that it contains.

WHITE WINE; VINUM ALBUM.

It is the fermented juice of fresh grapes and should contain from 8 to 15 per cent by volume of absolute alcohol.

RED WINE; VINUM RUBRUM.

It is the fermented juice of fresh red-colored grapes and should contain from 8 to 15 per cent by volume of absolute alcohol.

EPHEDRINE

Ephedrine is an alkaloid obtained from *Ephedra equisetina* and other species of Ephedra. (See chapter on Sympathetic Stimulants for a more complete description.)

THERAPEUTICS.—Ephedrine and its salts have a pronounced and lasting stimulating action on the cells of the cerebral cortex. It is not a drug of first choice for such purposes, as other tissues are equally affected, giving undesirable side actions.

Ephedrine is more stable than epinephrine and may be given orally to obtain a systemic effect.

PREPARATIONS.—(See Sympathomimetic Amines.)

EPHEDRINE SULFATE; EPHEDRINAE SULFAS (EPHEDRIN. SULF.), U.S.P.

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

BENZEDRINE

AMPHETAMINE SULFATE; BENZEDRINE SULFATE, N.N.R.

PHARMACODYNAMICS.—The mode of action of benzedrine is uncertain. It is not similar in action to epinephrine, as repeated doses give a decreasing response; ergot does not cause a vasomotor reversal action, and cocaine does not potentiate its action. Therefore its action is similar to ephedrine (see); it inhibits the amine esterase from destroying the liberated epinephrine which is allowed to accumulate in the tissues and give an exaggerated response. The action of this drug is the same as obtained by sympathetic stimulation, only more prolonged.

THERAPEUTICS.—Orally benzedrine sulfate is administered as an analeptic and as a narcoleptic. Its use by the laity as a "pick-me-up" should be discouraged, as habituation may result. Drugs should not be used to take the place of sleep or to allay fatigue, as collapse may result. Benzedrine inhalers may be used as directed for relief of nasal congestion. A 1 per cent solution in light liquid petrolatum may be dropped in the nose for the same purpose. Benzedrine sulfate is contraindicated in patients with cardiovascular disease or those who are hypersensitive to the sympathomimetic amines.

MEDULLARY CENTER STIMULANTS

COCCULUS

COCCULUS; COCCULUS (COCCUL.) N.F. (Coceulus Indicus).

Cocculus occurs as the dried ripe fruit of the *Anamirta Cocculus*, family *Menispermaceae*.

PICROTOXIN

Picrotoxin is a glycocide obtained from *Cocculus Indicus* berries which grow in the East Indies. It is a white crystalline powder slightly soluble in water (1 in 350) and freely soluble in boiling alcohol (1-3).

PHARMACODYNAMICS.—Picrotoxin is a powerful stimulant to the central nervous system, having its strongest action on the brain with a lesser action on the spinal cord. The midbrain and medulla are chiefly affected, the cerebral cortex next. It is not used in therapeutics to any extent because no appreciable effect is seen until a convulsive dose is administered. The cerebral cortex is rapidly stimulated and quickly depressed. All of the medullary centers are stimulated.

THERAPEUTICS.—In 1931 the drug was suggested as an antidote for barbiturate poisoning for which it is most effective. Koppanyi (1936) suggested it as an antidote for morphine poisoning.

TOXICOLOGY.—It is destroyed rapidly in the tissues.

PREPARATIONS.—

Picrotoxin; Picrotoxinum (Picrotox.), U.S.P. (Cocculin).

DOSAGE.—2 mg. (1/30 grain) or more, depending on the severity of the barbiturate poisoning (U.S.P.).

Picrotoxin Injection; Injectio Picrotoxini (Inj. Picrotox.), U.S.P.

DOSAGE.—2 mg. (1/30 grain) or more (U.S.P.).

METRAZOL

METRAZOL, N.N.R.

It is a synthetic alkaloid which acts as a strong central nervous system stimulant.

PHARMACODYNAMICS.—Metrazol acts as a powerful stimulant of the spinal cord, resulting in tonic convulsions as the dosage is increased. Its stimulating action on the cerebral cortex, the midbrain, and the medulla is antagonistic to the barbiturates. The centers of respiration and vasoconstriction are stimulated, this action being due to central stimulation with no peripheral action. This drug is a good central nervous system stimulant and will be useful in therapeutics when it is better understood.

DOSAGE.—0.1 to 0.3 Gm.

CORAMINE

Coramine (Nikethamide).

It is a pyridine derivative with the following formula: $C_5NH_4.CON(C_2H_5)_2$. It occurs as an oily substance, water soluble, and of synthetic composition.

PHARMACODYNAMICS.—Average doses of coramine act as a respiratory stimulant with little effect on other medullary centers. Its site of action is probably on the carotid body, resulting in a reflex stimulation of the respiratory center. Like most drugs, its action is more pronounced when the center is depressed, as in anesthetic or morphine poisoning. It is less efficient than picrotoxin in treating barbituric acid poisoning. Coramine has only a slight effect on the circulatory system. The margin of safety is good; in animals the toxic dose is ten times the effective therapeutic dose. Coramine is a drug which should be useful in therapeutics when its action is better understood.

CAMPHOR

Camphor is a crystalline stearopten obtained from the *Cinnamomum Camphora*, family *Lauraceae*, or produced synthetically.

PHARMACODYNAMICS.—When applied locally, camphor preparations act as antiseptics, obtundents, rubefacients, and impart a feeling of coolness. The temperature of the part is not altered; the action is probably a stimulation of the cold receptors.

Internally the drug is readily absorbed from the tissues. Parenteral injections cause pain which may account for a primary stimulating action. The literature is not in agreement on the usefulness of this drug. Studies on animals reveal that it is not a reliable respiratory or circulatory stimulant.

TOXICOLOGY.—The drug is eliminated in a conjugated form in the urine. Large doses produce convulsions which are probably due to a stimulation of the cerebral motor areas.

DOSAGE.—By mouth or hypodermic injection, 0.2 Gm. (3 grains) (U.S.P.).

PREPARATION.—

Ampuls of Camphor; Ampullae Camphorae (Ampul. Camphor.), N.F. (Ampuls of Camphor in Oil).

DOSAGE.—0.2 Gm. (3 grains) (N.F.).

CAFFEINE AND CAFFEINE PREPARATIONS

Caffeine and its preparations are used in therapeutics as medullary stimulants. In normal doses, they act only as cerebral stimulants with little or no medullary action. In larger than normal doses, they do act as mild medullary stimulants. Their action is greater when the centers have been previously depressed by drug action. Caffeine and its preparations are often used to overcome the depression of narcotic, hypnotic, and anesthetic drugs. They are not reliable circulatory or respiratory stimulants for all purposes.

PREPARATION.—(See Cerebral Stimulants.)

Caffeine and Sodium Benzoate Injection; Injectio Caffeinae et Sodii Benzoatis (Inj. Caff. et Sod. Benz.), U.S.P. (Caffeine and Sodium Benzoate Ampuls).

A sterile solution in water for parenteral use.

DOSAGE.—Intramuscularly, 0.5 Gm. (7½ grains) of caffeine and sodium benzoate (U.S.P.).

MEDULLARY CENTER DEPRESSANTS

This group of drugs is not used in therapeutics because of their toxic action. Normal doses of drugs do not produce a general medullary depression, but very large doses give toxic reactions. Practically all substances in large enough quantities will depress the medullary centers; the general anesthetics, hypnotics, and narcotics are particularly prone to do so.

SPINAL CORD STIMULANTS

NUX VOMICA

Nux Vomica is the dried, ripe seed obtained from *Strychnos Nux-vomica,* family *Loganiaceae,* a tree grown in India. Its active principle is an alkaloid, strychnine.

PHARMACODYNAMICS.—Because of a bitter taste, nux vomica and its alkaloid, strychnine, act as stimulants to the salivary and gastric glands, aiding digestion. After absorption, its chief site of action is the neuron synapses interpolated between the posterior sensory root cells and the anterior motor root cells of the spinal cord. It does not originate nerve impulses but exaggerates them when once formed. Average doses increase the tonus of the voluntary muscles, while larger doses produce a violent muscular spasm which becomes incoordinated. Gastric and intestinal peristalsis is increased by a stimulation of the nerve plexus of Auerbach. There is a slight stimulation of the motor and sensory areas of the cerebral cortex. Normal doses do not affect the heart. The vasomotor center may be stimulated slightly, producing a vasoconstriction in the splanchnic area with a rise in blood pressure. The respiratory center is but slightly stimulated. Strychnine stimulates the subcortical areas and is antagonistic to the barbiturates in this area.

The mode of action of strychnine is to inhibit the cholinesterase and thereby intensify the action of the liberated acetylcholine (Nachmansohn, 1938). Further study is necessary for a more comprehensive understanding of this very interesting drug.

USES.—Tonic, appetizer, and stimulant.

TOXICOLOGY.—Strychnine is detoxified in the liver (80 per cent), excreted by the kidneys (20 per cent), and is completely eliminated in 10 hours. The symptoms of poisoning are chiefly of central nervous system stimulation. The respiration often fails to resume activity following a convulsive attack.

TREATMENT.—Give tannic acid to form an insoluble precipitate, and remove the gastric contents by lavage. To relieve the convulsions give barbiturates (hypodermic) or inhalations of chloroform. Give artificial respiration if breathing ceases.

PREPARATIONS.—

Strychnine Nitrate; Strychninae Nitras (Strych. Nitras), N.F.

USES.—Same as those of strychnine.

DOSAGE.—2 mg. (1/30 grains) (N.F.).

Tablets of Strychnine Nitrate; Tabellae Strychninae Nitratis (Tab. Strych. Nitrat.), N.F.—Contain 88 to 112 per cent (in tablets of less than 0.0012 Gm.) or 91 to 109 per cent (in tablets of less than 0.02 Gm. and not less than 0.0012 Gm.) or 92.5 to 107.5 per cent (in tablets of 0.02 Gm. or more) of the stated amount of strychnine nitrate.

DOSAGE.—2 mg. (1/30 grain) of strychnine nitrate (N.F.).

STRYCHNINE PHOSPHATE; STRYCHNINAE PHOSPHAS (STRYCH. PHOS.), N.F.

USES.—The same as those of strychnine.

DOSAGE.—2 mg. (1/30 grain) (N.F.).

STRYCHNINE SULFATE; STRYCHNINAE SULFAS (STRYCH. SULF.), U.S.P.

Colorless or white crystals or white powder, odorless; efflorescent in dry air. Sparingly soluble in water (1 in 35) and in alcohol (1 in 85).

USES.—Same as those of strychnine.

DOSAGE.—2 mg. (1/30 grain) (U.S.P.).

Tablets of Strychnine Sulfate; Tabellae Strychninae Sulfatis (Tab. Strych. Sulf.), U.S.P.—Contain 93 to 107 per cent (in tablets of less than 0.02 Gm. and not less than 0.0012 Gm.) or 90 to 110 per cent (in tablets of 0.02 Gm. or more) of the stated amount of strychnine sulfate.

DOSAGE.—2 mg. (1/30 grain) of strychnine sulfate (U.S.P.).

CAFFEINE

Caffeine and caffeine salts stimulate the cerebrum, medulla, and spinal cord. Normal doses affect only the cerebrum. Larger than normal doses affect the medullary centers and still larger doses affect the spinal cord. Therefore, caffeine is not a drug of first choice as a cordal stimulant. (See Cerebral Stimulants.)

SPINAL CORD SEDATIVES

This group of drugs is not extensively used in therapeutics. They are used as antidotes in strychnine poisoning and as sedatives for the sexual glands.

PREPARATION.—

Chloroform; Chloroformum (Chlorof.), $CHCl_3$, U.S.P.

USES.—As an antidote for strychnine convulsions by inhalation.

Sodium Bromide; Sodii Bromidum (Sod. Bromid.), U.S.P.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

CHAPTER IX

DRUGS WHICH ACT ON THE AUTONOMIC NERVOUS SYSTEM

THE AUTONOMIC NERVOUS SYSTEM

History.—The adrenal glands were first described in 1563 by Eustachius who showed that the gland has two distinct portions: a medulla and a cortex. In 1855, Addison demonstrated that the symptom complex of Addison's disease was due to changes in the suprarenal glands. Brown-Séquard, 1856, found that a complete removal of the glands caused death in animals within twenty-four to forty-eight hours. Abel and Crawford, in 1897, isolated an active principle of the suprarenal medulla in the form of a benzoyl compound. Takamine and Aldrich, working independently, obtained the hormone in a crystalline form and named it adrenalin, 1901. Stalz and Flächer, 1904 to 1908, were the first to produce epinephrine synthetically.

The first reference to the "chemical mediation of nerve impulses" was probably made by Dubois-Raymond, in 1877. F. R. Eliot, in 1904, postulated that epinephrine (sympathin) was liberated by the sympathetic nerve endings and that it acts as a mediator of nerve impulses. In 1906, Dixon associated muscarine action with parasympathetic stimulation. During the same year Reid Hunt announced his studies of acetylcholine as a mediator of parasympathetic stimulation. The liberated acetylcholine is hydrolyzed by the choline-esterase in an exceedingly short time. During the refractory period of the muscle, the acetylcholine is broken down to choline and acetic acid. Epinephrine is not hydrolyzed as quickly as acetylcholine, and no exclusive enzyme is known which produces its decomposition.

Anatomy.—The autonomic nervous system has two main divisions: the sympathetics and the parasympathetics. They are involuntary in action and regulate the vital life functions. Whenever the two systems of nerves are distributed to the same tissues, their action is generally antagonistic. They distribute their impulses through ganglion cells. The sympathetic ganglia are near the central nervous system and away from the tissues they innervate, while the parasympathetic ganglia are further away from the central nervous system and closer to the tissues they innervate. The preganglionic fibers are medullated, and the postganglionic fibers are nonmedullated.

The sympathetic nerves exit from the thoracicolumbar regions of the spinal cord, from the seventh cervical to the third lumbar segments, from the lateral horn cells.

A few of the functions of the sympathetic nerves are: (1) vasoconstriction, (2) cardiac acceleration, (3) inhibitor action to the intestinal muscles, (4) constrictor nerves to the many sphincter muscles, (5) production of glycogenolysis in the liver, (6) stimulation of the medulla of the suprarenal glands, and so forth. (See Table I.)

TABLE I

EFFECT OF STIMULATION OF SYMPATHETICS AND PARASYMPATHETICS*

ORGAN	SYMPATHETICS	PARASYMPATHETICS
Pilomotor muscles.	Stimulate.	No effect.
Musculature of sweat glands.	Contract muscle, and force sweat from glands.	No effect.
Sweat glands.	Stimulate.	Possibly stimulate.
Vasomotor system.	Contract throughout.	Dilate in structures of head and genital organs.
	Dilate in trunk and limbs.	No effect in trunk and limbs.
Heart.	Increase rapidity.	Slow.
Eye.	Dilate pupil.	Contract pupil.
	Contract Müllerian muscle.	No effect.
	No effect.	Contract and relax muscles of accommodation.
Lacrimal glands.	Decrease secretion.	Increase secretion.
Mucous membrane of nose and throat.	Decrease secretion.	Increase secretion.
Salivary glands.	Decrease of watery component of secretion.	Stimulate watery component of secretion.
Respiratory tract.	Relax musculature and decrease secretion.	Contract musculature and increase secretion.
Stomach.	Decrease motility and secretion including hydrochloric acid.	Increase motility and secretion, including hydrochloric acid.
	Control blood vessels.	
Intestinal tract.	Relax musculature, decrease secretion, and control blood vessels.	Stimulate musculature and increase secretion.
Sphincters.	Contract.	Relax.
Ureter.	Contract.	No effect.
Uterus.	Contract.	No effect.
Bladder.	Contract muscles of trigone and sphincter, relax musculature of body.	Relax musculature of trigone and sphincter, stimulate musculature of body.

*Synopsis of Materia Medica, Toxicology and Pharmacology by F. R. Davison. 1940, p. 306.

The parasympathetic nerves originate from the midbrain, the medulla, and the sacral portion of the spinal cord. The cranial nerves are the oculomotor (3rd), the facial (7th), the glossopharyngeal (9th), the vagus (10th), and the spinal accessory (11th). The

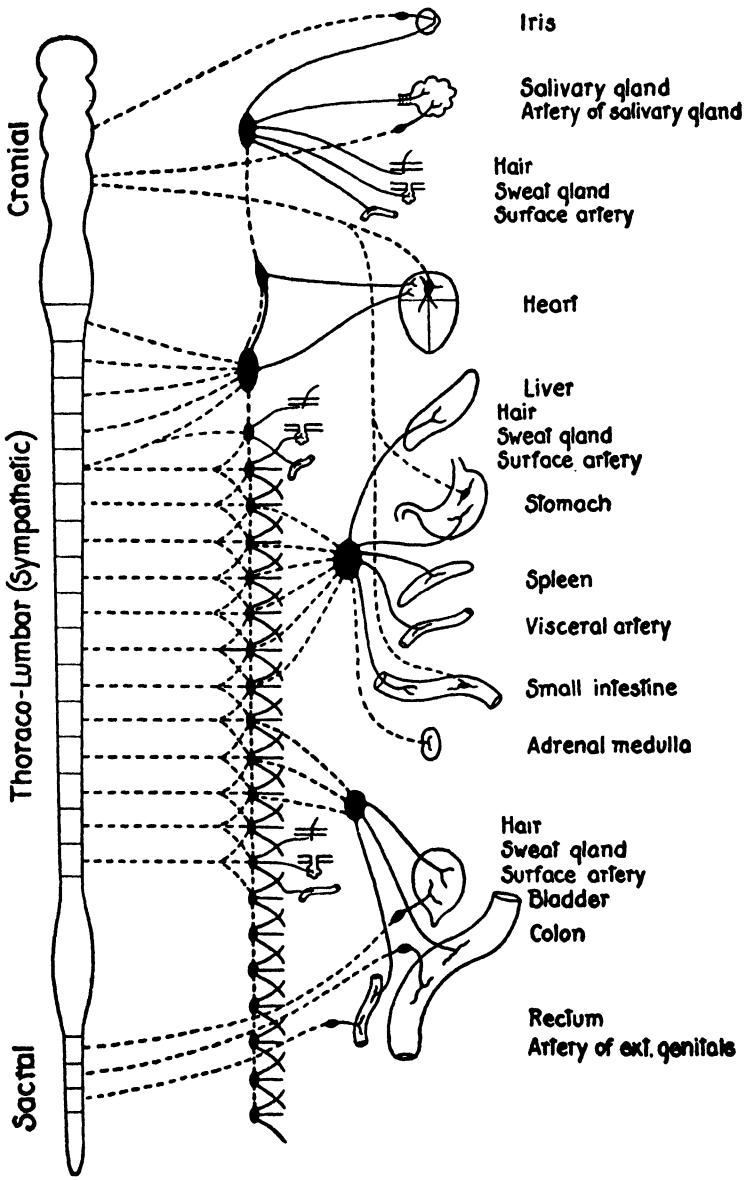


Fig. 15.—Diagram of the general arrangement of the autonomic nervous system. The brain and spinal cord are represented at left. The nerves of the somatic system are not shown. The preganglionic fibers are in broken lines, the postganglionic in solid lines. For further description see text. (From Bard after Cannon: *The Foundations of Experimental Psychology.* Clark Univ. Press.)

cordal portions of the parasympathetic nerves make their exit from the sacral portion of the cord and distribute their fibers to the urinary bladder, rectum, and genital organs.

A few of the functions of the parasympathetic nervous system are: cardiac inhibition, secretory for practically all glands, constrictor nerve to the pupils of the eye, constrictor nerve to the intestines, inhibitor nerves to the many sphincter muscles, etc.

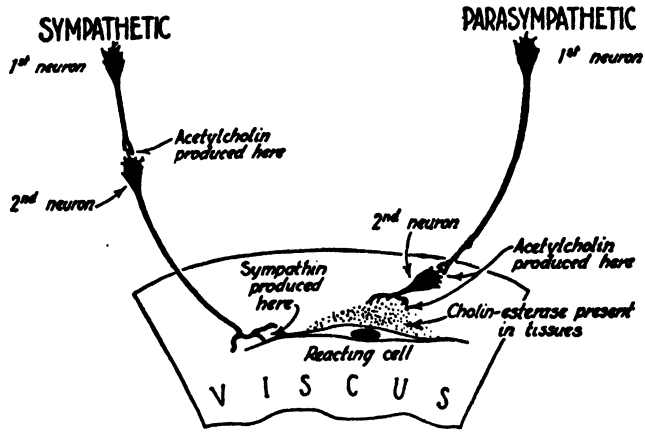


Fig. 16.—Balance between sympathetic and parasympathetic nerves and esterase. (Myerson: J. A. M. A., 1938.)

Adrenergic Drugs

EPINEPHRINE; EPINEPHRINA (EPINEPH.), $C_9H_{13}O_3N$, U.S.P.

DOSAGE.—Hypodermic, 0.5 mg. ($\frac{1}{120}$ grain) (U.S.P.).

Epinephrine is an active principle of the suprarenal medulla. It is a light yellow-brown amorphous powder, having a slight characteristic odor, and is partially soluble in water. The powdered glands and the extracts are rarely used at present; their isolated, active principle and synthetic products have superseded the cruder preparations. The alkaloid is extensively employed in dentistry in a 1:1000 solution. The solutions are preserved with small quantities of chloretone, thymol, sodium bisulfite, etc. Epinephrine solutions do not keep well; exposure to air or minute quantities of alkali quickly destroys them; this process is hastened by diluting the solution. Artificial substitutes have been prepared which, if levorotary, are as active as the natural product. Synthetic epinephrines, optically inactive, are only about one-half as active as the products obtained from the adrenal glands. Substitutes, chemically related, have been tried, but in dentistry epinephrine is most used.

Pharmacodynamics.—Epinephrine[1] and related synthetic compounds act on the "effector cell," whether it is upon the receptor substance or on the contractile or secretory part of the cell has not been determined. It acts after nerve degeneration and on the smooth muscles of the placenta which probably do not have nerve innervation. The drug, epinephrine, has a dual principle, that is, some tissues may be stimulated while other tissues are being depressed. The same tissue, such as the smooth muscles of the blood vessels, is often first depressed, then stimulated, and finally depressed. This epinephrine reversal was shown by Dale, who administered epinephrine after the sympathetic system was inhibited by ergot and recorded only the depressing action of the drug on the blood vessels, which was demonstrated by a fall in blood pressure. This phenomenon is of particular interest to the dentist because with small subcutaneous doses, as are often administered hypodermically in procaine-epinephrine solutions, the reversal action is the only demonstrable systemic effect, and this causes the toxic symptoms so often encountered with this drug.

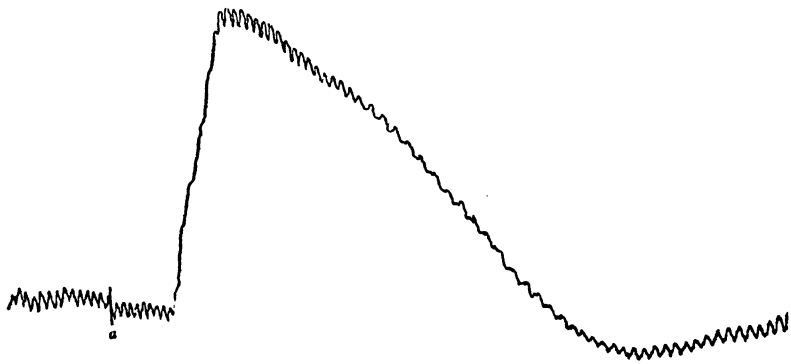


Fig. 17.—Tracing the blood pressure under synthetic epinephrine. One milligram of the hydrochloride solution, 1:1,000, was injected at *a* into the carotid artery of a dog. (Abderhalden-Müller.)

The heart is stimulated by epinephrine due to a direct sympathetic stimulation and a direct action on the myocardium. This increases the output of blood and the arterial pressure. The vagus center is reflexly stimulated by the rise in blood pressure through the carotico-aortic inhibitor centers. This vagal inhibition may be removed with atropine. Official subcutaneous doses are often so slowly absorbed from the tissues that a vasodilation rather than a vasoconstriction is generally produced in man.

[1]Cori, C. F., and Welch, A.: The Adrenal Medulla, J. A. M. A. 116: 2590, June 7, 1941.

The rate and amplitude of respiration are not greatly affected by epinephrine. The bronchioles are dilated and the capillary exudation checked, which make it a drug of choice in asthma.

The general metabolic rate may be increased due to a stimulation of the thyroid gland. The glycogen in the liver is broken down to glucose which increases the blood sugar.

THERAPEUTICS.—

1. Applied in a 1:1,000 solution to produce ischemia of inflamed mucous membranes.
2. Applied in a 1:1,000 solution as a styptic.
3. Combined in local anesthetic solutions as a pressor drug in a 1:25,000 to 1:60,000 solution.
4. To raise blood pressure in shock, 0.5 mg. hypodermically.
5. To relax bronchial spasms in asthma, 0.5 mg. hypodermically.
6. To inhibit capillary permeability in urticaria and angioneurotic edema, 0.5 mg. hypodermically.

The action of epinephrine is of short duration and repeated doses are necessary to maintain the therapeutic effect.

PREPARATIONS.—

Epinephrine Hydrochloride Injection; Injectio Epinephrinae Hydrochloridi (Inj. Epineph. Hydrochlor.), U.S.P.—A measured quantity of sterile solution of epinephrine hydrochloride, U.S.P., unless otherwise stated.

DOSAGE.—1 cc., containing about 1 mg. of epinephrine hydrochloride.

Solution of Epinephrine Hydrochloride; Liquor Epinephrinae Hydrochloridi (Liq. Epineph. Hydrochlor.), U.S.P.—It contains in 1 cc. about 1 mg. of epinephrine hydrochloride. It is standardized by comparing its effects on systolic blood pressure with that of a standard (U.S.P.) solution of epinephrine hydrochloride.

DOSAGE.—By parenteral injection, 0.5 cc. (8 minims). Dosage not given in U.S.P. XII.

SUPRARENIN (BITARTRATE).—Synthetic epinephrine in the form of the bitartrate; 0.091 Gm. bitartrate is equivalent to 0.05 Gm. of epinephrine (base). Synthetic epinephrine obtained by the method of Stolz and Fläcker (Ztschr. f. physiol. Chem. vol. 58, p. 189). (A.D.R.)

RELATED SYNTHETIC COMPOUNDS.—

COBEFRIN HYDROCHLORIDE.—Racemic 3, 4-dihydroxy-phenyl-propanol-amine-hydrochloride. — Racemic amino-propanol-catecholhydrochloride. — Racemic alphahydroxy-betamethyl-beta-amino-ethyl-

meta, para-dihydroxy-benzene-hydrochloride—$(OH)_2$ C_6H_3CHO-$HCHNH_2CH_3HCl$.—The hydrochloride of an alkaloid prepared synthetically by the reduction of the corresponding ketone. (A.D.R.)

CHEMISTRY.—Cobefrin hydrochloride is an isomer of epinephrine, the methyl group is attached to the alpha-carbon instead of the nitrogen.

PROPERTIES.—It is a white crystalline solid, soluble in water (1 Gm. in 1.5 cc.) and in alcohol (1 Gm. in 15 cc.). It is optically inactive and has a melting point of 178°-179° C.

PHARMACODYNAMICS.—Its site of action is the same as that of epinephrine. It is about one-fifth as strong as epinephrine and about four times less toxic, making its toxicity in local anesthetic solutions about equal to that of epinephrine. A 1:10,000 solution is equal in pressor effect to a 1:50,000 epinephrine solution.

THERAPEUTICS.—It is supposed to have two advantages over epinephrine: it does not stimulate the cerebral cortex as much, and it does not produce a vasomotor reversal (vasodilation) when absorbed in small amounts into the general circulation. It is used with 2 per cent procaine solutions in a 1:10,000 solution, and many find this combination as good a local anesthetic mixture as the 2 per cent procaine with 1:50,000 epinephrine hydrochloride solution.[1]

NEOSYNEPHRIN HYDROCHLORIDE, A.D.R., N.N.R.—Laevo-α-hydroxy-β-methylamino-3-hydroxy ethylbenzene hydrochloride.

The hydrochloride of the laevo isomer of a synthetically prepared derivative of phenylethylamine having the formula $C_6H_4OH.CHOH.CH_2NHCH_3.HCl$. (A.D.R.)

Neosynephrin hydrochloride[1] is a synthetic alkaloid related in its action to epinephrine. It has a monohydroxy substitution in the benzene ring in the meta position. This position of the hydroxyl group gives greater activity than the para, and for that reason neosynephrin replaced synephrin (para). It is a racemic compound, and this lowers its activity. The monohydroxyl compounds are more stable than the dihydroxyl (epinephrine) and are less liable to decompose in prepared solutions. It gives a systemic effect when taken orally.

PHARMACODYNAMICS.—(See Epinephrine.) It is less toxic than epinephrine (1/45) but only about one-sixth as active, making it about one-eighth as toxic as compared with the equivalent pressor activity of epinephrine (A.D.R.). After an intravenous injection the pressor action lasts for about fifteen minutes; when injected intramuscularly or subcutaneously, its pressor activity lasts for two or three hours. It

[1]Tainter, M. L., and Stockton, A. B.: Am. J. M. Sc. 185: 832, June, 1933.

does not produce a strong central nervous center stimulation or cause a fall in blood pressure and therefore produces less undesirable symptoms when used in local anesthetic solutions.

DENTAL THERAPEUTICS.—

1. Used as a pressor drug in local anesthetics in a 1:2500 to 1:3500 solution.

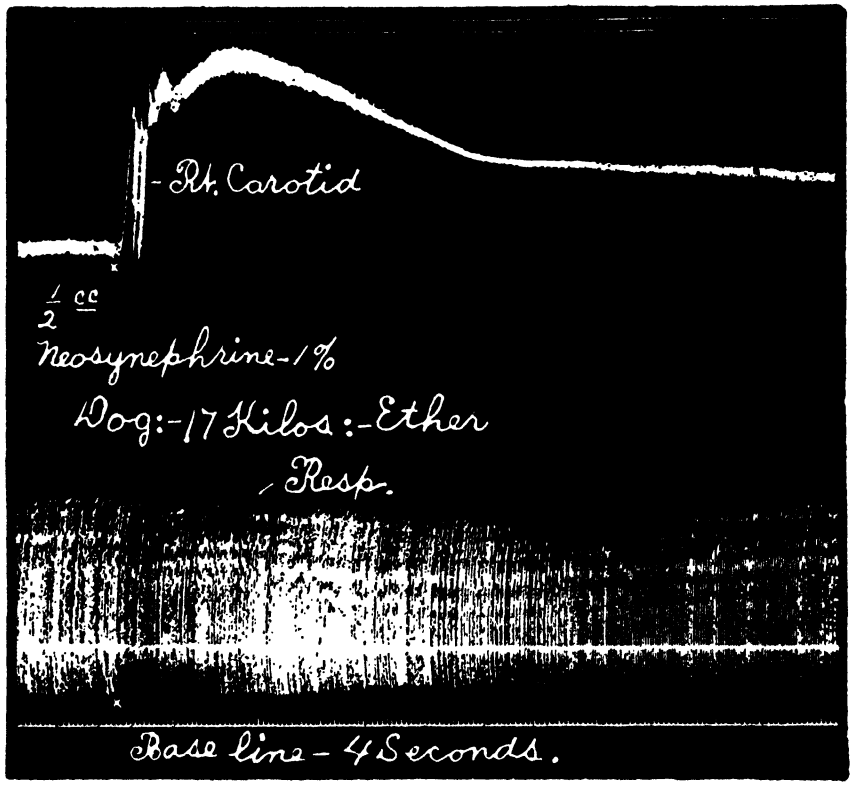


Fig. 18.—Blood pressure and respiration following administration of neosynephrin. Note the drop in blood pressure which occurs from reflex cardiac inhibition shortly after the initial abrupt rise. (From Jackson: *Experimental Pharmacology and Materia Medica.*)

Ephedrine and Related Drugs

These compounds are similar chemically and pharmacodynamically to epinephrine, but they differ in their site and mode of action.

EPHEDRINE, EPHEDRINA (EPHEDRIN.), $C_{16}H_{15}ON$, U.S.P.

Ephedrine is a white crystalline solid soluble in both water and alcohol. It has no odor but a very bitter taste. With acids, it

forms salts by an addition reaction. The salts are white crystalline solids, odorless, and with a bitter taste. They are freely soluble in water and soluble in alcohol. The alkaloid is obtained from the *Ephedra equisetina* and *Ephedra sinica,* plants known to Chinese medicine for 5,000 years. Chen and Schmidt investigated this drug in 1923 and noted its ephedrine-like action. It was immediately introduced into therapeutics as a sympathomimetic amine.

The alkaloid and its salts are stable and can be administered orally. It will stand sterilization by boiling and exposure to air and sunlight without a rapid molecular decomposition.

PHARMACODYNAMICS.—Ephedrine is a sympathomimetic drug resembling epinephrine in its effect on the sympathetic nervous system, only less intense and of longer duration. Ergot does not produce a reversal action nor does cocaine potentiate it, and it is inactive after nerve degeneration. It is a stable molecule due to the absence of two hydroxyl groups in the ring and can therefore produce a systemic effect when given orally.

Its site of action is in the "effector cell" probably preventing the liberated epinephrine from being destroyed by the amine esterases, thereby intensifying and prolonging the sympathetic stimulation. It does not originate stimuli and will not act in the absence of epinephrine. It has only a vasoconstricting action on the blood vessels.

THERAPEUTICS.—In dentistry the use of ephedrine has been limited. It is most commonly used in the treatment of congestion of the nasopharynx.

1. Applied locally in a 1-5 per cent solution to produce ischemia of inflamed mucous membranes.
2. Applied locally as a styptic in a 5 per cent solution.
3. To relax bronchial spasms, orally in 3/8 grain doses.
4. To check capillary permeability in urticaria and angioneurotic edema, orally in 3/8 grain doses.
5. To raise blood pressure in shock, orally in 3/8 grain doses.

PREPARATIONS.—

EPHEDRINE HYDROCHLORIDE; EPHEDRINAE HYDROCHLORIDUM (EPHEDRIN. HYDROCHLOR.), $C_{10}H_{15}ON.HCl$, U.S.P.

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Tablets of Ephedrine Hydrochloride; Tabellae Ephedrinae Hydrochloridi (Tab. Ephed. Hydrochlor.), N.F.

The tablets contain 91 to 109 per cent of the stated amount of ephedrine hydrochloride.

DOSAGE.—15 mg. (1/4 grain) of ephedrine hydrochloride (N.F.).

EPHEDRINE SULFATE; EPHEDRINAE SULFAS (EPHEDRIN. SULF.), $(C_{10}H_{15}ON)_2H_2SO_4$, U.S.P.

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Ampuls of Ephedrine Sulfate; Ampullae Ephedrinae Sulfatis (Ampul. Ephed. Sulf.), N.F.

There is approximately 50 mg. of ephedrine sulfate in 1 cc. of sterile aqueous solution.

DOSAGE.—50 mg. of ephedrine sulfate (N.F.).

The differences in action of ephedrine and epinephrine may be summarized as follows:

Less potent sympathetic stimulant.
Longer duration of action.
Action not potentiated by cocaine.
Has no vasodilator action.
Does not show a vasomotor reversal with ergot.
Gives a systemic effect when administered orally.
Acts by inhibiting the amine esterase in the effector cells.

Synthetic Related Compounds

BENZEDRINE

AMPHETAMINE; BENZEDRINE.—Alpha-methyl-phenethylamine.—Racemic desoxy-nor-ephedrine.—A synthetically prepared racemic mixture of bases having the formula $C_6H_5CH_2CHNH_2CH_3$, N.N.R.

Benzedrine has a marked stimulating action on the cerebral cortex.

AMPHETAMINE SULFATE; BENZEDRINE SULFATE.—Alpha methylphenethylamine sulfate—Racemic desoxy-norephedrine sulfate.—Racemic benzyl-methyl carbinamine sulfate.—$[C_6H_5.CH_2CH(NH_2).CH_3]_2.H_2SO_4$. (N.N.R.)

Benzedrine sulfate is a synthetic sympathomimetic amine. It has a marked stimulating effect on the central nervous system, particularly the cerebral cortex. Like ephedrine it is effective after oral administration. In therapeutics the sulfate salt is chiefly used.

PHARMACODYNAMICS.—It probably acts like ephedrine by inhibiting the amine esterase, prolonging and intensifying the action of the liberated epinephrine on the effector cells. (See Ephedrine.)

USES.—Inhaled to produce a vasoconstriction in the nasal mucosa. It may be taken orally to produce a stimulation of the cerebral cortex and the vital medullary centers.

DOSAGE.—Initial doses should be small, ranging from 2.5 to 10 mg., and increased gradually until a definite effect manifests itself. The use of small test doses is particularly important in the treatment of

depressive states. Effective dosage varies considerably, depending on the condition being treated. In certain cases it may be necessary to repeat the use of the drug three times daily, but it is recommended that such a dosage not exceed 10 to 20 mg. It is preferable, if possible, to administer the effective quantity of this drug during the morning, to avoid interference with sleep. (N.N.R.)

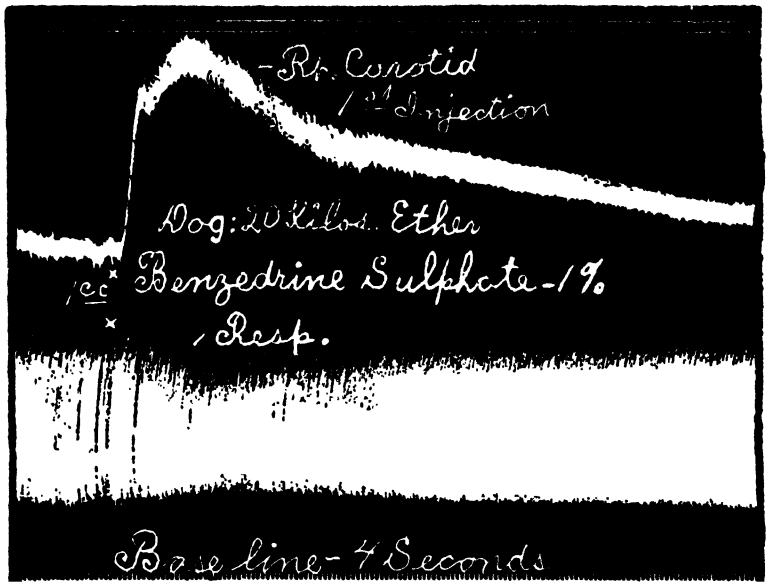


Fig. 19.—Effect of amphetamine (benzedrine) on blood pressure and respiration. (From Jackson: *Experimental Pharmacology and Materia Medica.*)

PROPADRINE

PROPADRINE HYDROCHLORIDE.—dl-1-phenyl-2-aminopropanol-1-hydrochloride. — α-hydroxy-β-amino-propyl-benzene hydrochloride.— $C_6H_5.CHOH.CHNH_2.CH_3.HCl$. Propadrine hydrochloride is the monohydrochloride of a base resembling ephedrine (*lacvo*-α-hydroxy-β-methyl-amino-propyl-benzene) but differs in that the methyl group on the amino group is replaced by a hydrogen atom. (N.N.R.)

PHARMACODYNAMICS.—Propadrine hydrochloride is used chiefly for local action to reduce congested mucous membranes in a 1 per cent aqueous solution or in a 0.65 per cent solution in jelly. Its duration of action is said to be longer than that of ephedrine. Its action on the cerebral cortex is thought to be less than that of ephedrine with less tendency to produce anxiety symptoms.

DOSAGE.—As a spray or instillation, 1 per cent aqueous solution, or application of 0.66 per cent jelly locally; orally, as three-eighths grain capsule every two to four hours as indicated. Although no toxic effects have been noted, continued overdosage should be avoided as with other vasoconstrictors. (N.N.R.)

Sympathetic Depressant Drugs

ERGOT

ERGOT; ERGOTA, U.S.P. (Ergot of Rye).

Ergot is a fungus growth which replaces the grain of rye. At least three alkaloids of ergot are recognized: ergotoxine and ergotamine, which are different chemically but identical therapeutically, and ergotinine, which is innert physiologically. Ergot and ergot preparations deteriorate rapidly and are not therapeutically reliable. (Thompson, M. J.) Ergot was first used by "midwives" and was mentioned in the literature by Lonicer in 1565. It was introduced into American medicine by Stearns in 1807.

PHARMACODYNAMICS.—Ergot and ergot alkaloids act on the effector cells and receptor substance, destroying their reactiveness to epinephrine. This drug does not prevent the formation of epinephrine.

THERAPEUTICS.—Ergot in normal doses in man produces only a slight sympathetic blocking effect, and the vasomotor reversal of Dale is not demonstrated. The blood pressure may rise because of the direct action of the drug on the smooth muscle of the blood vessels. Ergot appears to inhibit the glycogenolysis induced by epinephrine on the liver. Ergot acts as a powerful stimulant to the uterine muscles, particularly at parturition. The action of the drug is directly on the smooth muscles and not on the nerve tissue. Oxytocic drugs should never be used during the first or second stage of labor but only during the third stage when the cervix is dilated. It is accepted practice to administer posterior pituitary extract at the onset of the third stage of labor and to give ergot preparations after the placenta has been expelled to prevent excessive postpartum hemorrhage.

TOXICOLOGY.—Ergot is contraindicated for therapeutic abortions. During the first few months of pregnancy the uterus is very resistant to drugs. Large doses often cause only uterine hemorrhage which may endanger the patient's life, often necessitating surgical intervention to prevent infection. Toxic doses often cause vasomotor spasms in the extremities of the body, resulting in local circulatory failure with a saprophytic infection (gas gangrene). Ergot is a drug which must be used only when the patient is carefully supervised.

PREPARATIONS.—

Fluidextract of Ergot; Fluidextractum Ergotae (Fldext. Ergot.), U.S.P.

DOSAGE.—2 cc. (U.S.P.).

Ergotamine Tartrate; Ergotaminae Tartras (Ergotam. Tart.), U.S.P.

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain).

Cholinergic Drugs

The action of these drugs on the tissues is similar to that produced by parasympathetic stimulation.

ACETYLCHOLINE

Acetylcholine is a cholinergic substance liberated by all autonomic ganglia, by postganglionic fibers of the parasympathetic nerves at the myoneural and adenoneural junctions, by the terminals of the somatic motor nerves in voluntary muscles, and by the sympathetic nerves terminating in the sweat glands. The acetylcholine acts as a mediator of nerve impulses from the nerves into the tissues they activate. The action of acetylcholine is very short, the molecule being instantly broken up into inert substances, choline and acetic acid.

CHEMISTRY.—$CH_3COOCH_2N(CH_3)_3Cl$.

The duration of action of acetylcholine is so short that it has no therapeutic action. For that reason acetyl-β-methylcholine is used in its stead $CH_3COO(CH_2)_2N(CH_3)_3Cl$.

PILOCARPINE

Pilocarpus Jaborandi is a shrub which grows wild in the forests of Brazil or is cultivated for the drug market. The leaflets are the parts used in therapeutics. Its chief alkaloid is pilocarpine which acts as a parasympathetic stimulant.

Pilocarpine is a white crystalline alkaloid which is official as the hydrochloride and nitrate salts.

PHARMACODYNAMICS.—Pilocarpine acts as a parasympathetic stimulant but is selective in its action. The site of action is the effector cell, acting on the receptor substance, e.g., the contractile substance of muscle cells or the secretory substance of gland cells. It acts, also, on the sweat glands as a stimulant of secretion. These glands are activated by the cholinergic sympathetic nerves. Pilocarpine does not affect the transmission of impulses through the autonomic ganglia and is therefore not antagonistic to nicotine. On the smooth muscles and glands which are stimulated by the parasympathetic nervous system, pilocarpine acts as a stimulant and is antagonistic to atropine on these tissues.

THERAPEUTICS.—Used as a diaphoretic and sialogogue.

PREPARATIONS.—

Pilocarpine Hydrochloride; Pilocarpinae Hydrochloridum (Pilocarpin. Hydrochlor.), N.F.

DOSAGE.—5 mg. (1/12 grain) (N.F.).

Pilocarpine Nitrate; Pilocarpinae Nitras (Pilocarpin. Nitras), U.S.P.

DOSAGE.—5 mg. (1/12 grain) (U.S.P.).

PHYSOSTIGMINE

Physostigmine is an alkaloid usually obtained from the dried ripe seed of the *Physostigma venenosum* (calabar bean), family *Leguminosae*. The official salt is Physostigmine Salicylate which occurs as white or faintly yellow, odorless crystals. It is sparingly soluble in water (1 in 75) and soluble in alcohol (1 in 16).

PHARMACODYNAMICS.—Physostigmine acts on the effector cell, inhibiting the cholinesterase which permits the accumulation of acetylcholine in the tissues and gives a parasympathetic stimulation effect. The action of physostigmine is demonstrated only in tissues activated by acetylcholine, such as smooth muscles, cardiac muscle, skeletal muscles, autonomic ganglia, and glands. It is therefore antagonistic to atropine in the smooth and cardiac muscles and in glands, antagonistic to nicotine in the autonomic ganglia, and antagonistic to curare in the skeletal muscles. Physostigmine does not act after cholinergic nerve degeneration

THERAPEUTICS.—Because physostigmine affects so many tissues, its physiologic action upon a tissue is not always predictable. The characteristic action on the eye is pupillary constriction and a loss of accommodation due to muscular spasms. The gastrointestinal tract is stimulated in general, the smooth muscles contracting and peristalsis increasing; the sphincter muscles dilate, and the glands are stimulated. The skeletal muscles are stimulated, increasing the tonus; larger doses produce twitching. The circulatory system is generally depressed, resulting in a fall in blood pressure.

TOXICOLOGY.—The symptoms of physostigmine poisoning are of parasympathetic stimulation.

TREATMENT.—Give a parasympathetic depressant drug, such as atropine sulfate.

PREPARATIONS.—

PHYSOSTIGMINE SALICYLATE, PHYSOSTIGMINAE SALICYLAS (PHYSOSTIG. SALICYL.), U.S.P. (Eserine Salicylate).

DOSAGE.—2 mg. (1/30 grain).

Prostigmine

Prostigmine is a synthetic alkaloid resembling physostigmine therapeutically. It is a newer drug, having been introduced into therapy in 1931. It occurs as a white crystalline solid without odor, bitter, and freely soluble in water. Prostigmine is not official, but the salts Prostigmine Bromide and Prostigmine Methylsulfate are listed in *New and Nonofficial Remedies.*

Pharmacodynamics.—Prostigmine and its salts have the same action as physostigmine, a parasympathetic stimulating effect. It has no advantages over physostigmine (which see) except a more stable molecule.

Preparations.—

Prostigmine Bromide, N.N.R.

Dosage.—15 mg. (¼ grain) three times per day.

Prostigmine Methylsulfate, N.N.R.

Dosage.—1 mg. (1/60 grain) hypodermically, three times per day.

Muscarine

Muscarine is an alkaloid obtained from poisonous mushrooms. It was isolated and described by Schmiedberg and Koppe in 1869.

Pharmacodynamics.—Its action is similar to a stimulation of the parasympathetic nervous system. The action on any tissue is nearly the same as that of acetylcholine, which compound it resembles chemically. On the autonomic ganglia its action is weak but noticeable.

Therapeutics.—None.

Toxicology.—Muscarine-containing mushrooms may be eaten by mistake with symptoms of poisoning following. The symptoms are characteristic of parasympathetic stimulation, death occurs from respiratory failure, during a convulsive attack. Many forms of mushrooms are poisonous, and it is reasonable to expect that the toxic substance in all cases is not the same.

Treatment.—Repeated injections of atropine sulfate. Remove the contents of the gastrointestinal tract and give supportive treatment.

Drugs Which Depress the Parasympathetic Nervous System

This group of drugs includes belladonna, stramonium, and hyoscyamus. They belong to the *Solanaceae* (potato) family and are very toxic.

Belladonna is a plant which is cultivated in the United States, Yugoslavia, England, India, etc., for the drug markets. Its botanical origin is the *Atropa belladonna* (Linné); the leaves, tops, and the

roots are the official parts used. The purity rubric requirements are not less than 0.3 per cent of belladonna alkaloids, the chief ones being atropine, hyoscyamine, and scopolamine. The action of the belladonna preparation is due to the action of the alkaloids which it contains.

PREPARATIONS.—

BELLADONNA LEAF; BELLADONNAE FOLIUM (BELLAD. FOL.), U.S.P. (Deadly Nightshade Leaf.)

DOSAGE.—60 mg. (1 grain).

Belladonna Plaster; Emplastrum Belladonnae (Emp. Bellad.), U.S.P.

It contains about 0.27 per cent of the alkaloids.

Extract of Belladonna; Extractum Belladonnae (Ext. Bellad.), U.S.P.

It contains about 1.25 per cent of the belladonna alkaloids.

DOSAGE.—15 mg. (¼ grain).

Fluidextract of Belladonna Leaf; Fluidextractum Belladonnae Folii (Fldext. Bellad. Fol.), N.F.

It contains 100 per cent of the belladonna leaf and about 0.3 per cent of the alkaloids.

DOSAGE.—0.06 cc. (1 minim) (N.F.).

Tincture of Belladonna; Tinctura Belladonnae (Tr. Bellad.), U.S.P. (Tincture of Belladonna Leaf).

DOSAGE.—0.6 cc. (10 minims).

Belladonna Ointment; Unguentum Belladonnae (Ung. Bellad.), U.S.P.

It yields 0.12 per cent of the belladonna alkaloids.

BELLADONNA ROOT; BELLADONNAE RADIX (BELLAD. RAD.), U.S.P. (Deadly Nightshade Root).

DOSAGE.—45 mg. (¾ grain).

Fluidextract of Belladonna Root; Fluidextractum Belladonnae Radicis (Fldext. Bellad. Rad.), N.F.

It contains 100 per cent belladonna root, yielding about 0.45 per cent of the alkaloids in about 68 per cent alcohol.

DOSAGE.—0.05 cc. (¾ minim).

Belladonna Liniment; Linimentum Belladonnae (Lin. Bellad.), N.F.

It contains fluidextract of belladonna root 95 per cent, camphor 5 per cent, and absolute alcohol about 68 per cent.

USES.—A mildly analgesic liniment.

Alkaloids of Belladonna.—

SCOPOLAMINE HYDROBROMIDE; SCOPOLAMINAE HYDROBROMIDUM (SCOPOL. HYDROBROM.), U.S.P. (Hyoscine Hydrobromide).

Scopolamine is an odorless, crystalline alkaloid obtained chiefly from belladonna. The official salt is levorotatory scopolamine hydrobromide, which is freely soluble in water (1 in 1.5) and soluble in alcohol (1 in 20).

PHARMACODYNAMICS.—Scopolamine resembles atropine in its action except that it depresses the cerebral cortex, while atropine stimulates. The hypnotic action occurs soon after the administration and lasts for several hours. Euphoria may be present with small doses, and violent hallucinations occur as the dosage is increased. Large doses produce amnesia. The respiration and circulation are not appreciably affected by therapeutic doses. The vagus center is mildly depressed, and the heart rate may increase slightly.

Scopolamine and morphine are synergistic in action, producing, in normal doses, a deep narcotic state. This combination is known in obstetrics as "twilight sleep." The mother is in a comatose state, awakening only when labor pains occur, and can therefore assist in the delivery. The drugs depress the respiratory center of the offspring, resulting in "blue babies" and possibly stillborns.

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain).

PREPARATION.—

Tablets of Scopolamine Hydrobromide; Tabellae Scopolaminae Hydrobromidi (Tab. Scopol. Hydrobrom.), N.F. (Hyoscine Hydrobromide Tablets).

DOSAGE.—0.6 mg. ($\frac{1}{100}$ grain) of scopolamine hydrobromide per tablet.

ATROPINE; ATROPINA (ATROP.), U.S.P.

Atropine is an alkaloid obtained chiefly from belladonna. It occurs as a white crystalline solid, slightly soluble in water (1 in 460) and soluble in alcohol (1 in 2). Atropine is generally prescribed as the sulfate salt which is also official in the *United States Pharmacopoeia.*

PHARMACODYNAMICS.—Atropine depresses the myoneural and adenoneural junctions of the parasympathetic nerves in the smooth muscles and glands innervated by the craniosacral outflow of autonomic nerves. It will act after nerve degeneration, demonstrating that its site of action is not on the nervous tissue but on the chemoreceptor substance of the effector cell. The mode of action is to inhibit the receptor substance so that it will no longer respond to acetylcholine.

Atropine also acts on the cholinergic fibers of the sympathetic nervous system, such as the sweat glands. It does not act on the autonomic ganglia and is therefore not antagonistic to nicotine on this tissue; nor does it act on the voluntary muscles innervated by the cholinergic somatic motor nerves and is therefore not antagonistic to curare on this tissue.

THERAPEUTICS.—Locally it is applied to the skin as a liniment or plaster and acts as an obtundent and counterirritant. Its absorption through the skin is questionable.

Systemically it arrests secretion of all glands innervated by cholinergic fibers. This includes the sweat, salivary, lacrimal, mucous, gastric, and pancreatic glands. It inhibits the activity of the gastrointestinal tract, retarding peristalsis in the stomachic and intestines and increasing the tonus of the sphincter muscles. It produces relaxation of the bile duct, urethra, and uterus. The bronchioles are dilated and their secretions checked. The respiration is slightly stimulated by normal doses; larger doses depress the respiration, and toxic doses check respiration, and death ensues from anoxemia. The heart rate may be depressed by a direct stimulating effect of the drug on the vagus center. A single official dose has little or no cardiac effect; larger doses or repeated official doses will inhibit the vagus influence on the heart muscle, allowing the sympathetic influence to increase the heart rate. Atropine acts as a mydriatic on the eye, making the iris muscles insensitive to light, and also paralyzes the accommodation of the lens, adjusting it to far vision only. This mydriasis must be considered when atropine is administered before a general anesthetic when the depth of anesthesia is determined by the eye symptoms.

TOXICOLOGY.—Many patients are hypersusceptible to this drug, and normal doses produce untoward responses. The toxic symptoms are dryness of mouth and throat, dilated pupils, slow respiration, cyanosis, and a rapid heart; death rarely follows.

TREATMENT.—Give stimulants such as pilocarpine hydrochloride, 10 mg.; or caffeine and sodium benzoate, 0.8 Gm., injected; oxygen and carbon dioxide by inhalation, and artificial respiration if necessary.

DOSAGE.—0.4 mg. ($\frac{1}{150}$ grain).

PREPARATIONS.—

Atropine Sulfate; Atropinae Sulfas (Atrop. Sulf.), U.S.P.

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain).

Homatropine Hydrobromide; Homatropinae Hydrobromidum (Homotrop. Hydrobrom.), U.S.P.

It is a synthetic alkaloid, related chemically to atropine and used in ophthalmology to relax the intrinsic muscles of the eye. Five drops of a 0.2 per cent solution are generally sufficient.

SALIENT POINTS ON ATROPINE.—

Acts on the myoneural and adenoneural junctions of the parasympathetic nervous system and the cholinergic fibers of the sympathetic nerves.

Does not act on the other cholinergic areas, such as the autonomic ganglia and myoneural junction of the somatic motor nerves in the skeletal muscles.

Acts on the affector cells, desensitizing the chemoreceptor substance to acetylcholine, both the stimulation and the inhibition.

STRAMONIUM

STRAMONIUM; STRAMONIUM (STRAMON.), U.S.P. (Jamestown Weed, Jimson Weed).

Stramonium consists of the dried leaf and flowering top of the *Datura stramonium*, family *Solanaceae*. It should yield not less than 0.25 per cent of alkaloids, the most important being hyoscyamine, atropine, apoatropine, belladonnine, and scopolamine. Daturine is a mixture of hyoscine and atropine.[1] The U.S.P. assay is chemical, the same as hyoscyamus.

PHARMACOLOGY AND THERAPEUTICS.—Similar to belladonna over which it has no advantages.

DOSAGE.—Not given in U.S.P.; 75 mg. (1¼ grains).

PREPARATIONS.—

Extract of Stramonium; Extractum Stramonii (Ext. Stramon.), U.S.P.

Two forms are official: Pilular Extract of Stramonium and Powdered Extract of Stramonium. One gram of the extract represents about 4 grams of stramonium and yields about 1 per cent of alkaloids.

DOSAGE.—20 mg. (⅓ grain).

Tincture of Stramonium; Tinctura Stramonii (Tr. Stramon.), U.S.P.

Stramonium (10%), yielding about 0.025 per cent of alkaloids, absolute alcohol content about 67 per cent.

DOSAGE.—0.75 cc. (12 minims) (U.S.P.).

[1] Youngken, Heber W.: Text-Book of Pharmacognosy, ed. 5, Philadelphia, 1943, The Blakiston Co., p. 767.

Hyoscyamus

Hyoscyamus; Hyoscyamus (Hyosc.), U.S.P. (Henbane).

Hyoscyamus is the dried leaf, with or without the tops, of the *Hyoscyamus niger,* family *Solanaceae.* It yields not less than 0.04 per cent of alkaloids. The natural habitat of the plant is Europe and Asia. Its constituents are hyoscyamine, a crystalline alkaloid; scopolamine (hyoscine) an amorphous alkaloid; hyoscypicrin, a glucoside; volatile oil; etc. (Youngken).

Pharmacodynamics.—The mode and site of action of hyoscyamus are similar to those of belladonna but hyocyamus is less active. (See Belladonna.)

Dosage.—0.2 Gm. (3 grains) (U.S.P.).

Official Preparations.—

Extract of Hyoscyamus; Extractum Hyoscyami (Ext. Hyosc.), U.S.P. (Extract of Henbane, Extractum Hyoscyami P.I.).

It yields about 0.15 per cent of alkaloids.

Dosage.—50 mg. (¾ grain) (U.S.P.).

Tincture of Hyoscyamus; Tinctura Hyoscyami (Tr. Hyosc.), U.S.P. (Tincture of Henbane, Tinctura Hyoscyami P.I.).

Tincture of Hyoscyamus contains about 10 per cent hyoscyamus which should yield not less than 0.0034 per cent of alkaloids. The absolute alcohol content is about 67 per cent.

Dosage.—2 cc. (30 minims) (U.S.P.).

Alkaloids of Hyoscyamus.—

Hyoscyamine (nonofficial) is an optical isomer of atropine and is not found in the pure form. It racemizes readily, and there is but little doubt that it is this molecular configuration which occurs naturally and that during isolation it changes into atropine.[1]

Its physical properties are similar to those of atropine.

Pharmacodynamics.—Levorotatory hyoscyamine has about twice as potent a peripheral action as the d-form, atropine. Its site of action is the adenoneural and myoneural junctions of the cholinergic nerves and the central nervous system where it exerts only a stimulating action. (See Atropine.)

Therapeutics.—Hyoscyamine has a cholinergic action. (See Atropine for a detailed description.)

[1]Jenkins, G. L., and Hartung, W. H.: The Chemistry of Organic Medicinal Products 1: 386, 1941.

Drugs Which Affect the Autonomic Ganglia

Nicotine

Nicotine is an alkaloid obtained from the leaves of tobacco and isolated by Posselt and Reiman in 1828. Langley, about sixty years later, studied the action of this drug on the autonomic ganglia. Nicotine occurs as a colorless volatile liquid which turns brown upon standing. It is strongly alkaline and forms water-soluble salts with acids. The alkaloid is readily soluble in water and alcohol.

Chemistry.—The alkaloid is a combination of pyridine and pyrollidine rings.

Pharmacodynamics.—Nicotine acts on the central nervous system, autonomic ganglia, carotid body, and skeletal muscles first as a stimulant and then as a depressant. The smoking of tobacco acts only as a stimulant, while in large oral doses or when applied directly to the tissues nicotine acts as a stimulant and then as a depressant. In toxicology, the characteristic action is one of depression; in tobacco poisoning the action is one of stimulation. The site of action is the effector cell on the chemoreceptor substance, making it more responsive and then less responsive to the influence of acetylcholine. The alkaloid therefore does not act after nerve degeneration, nor does it affect the liberation of acetylcholine. The cerebral cortex is stimulated by the drug, the medullary centers of respiration, vasomotor, and emetic centers are first stimulated and then depressed. The respiration may be reflexly stimulated by a direct action of the drug on the chemoreceptor substance in the carotid body. The general action of the drug on the skeletal muscles is stimulation; local application of the drug directly to the tissue results in a depressant action. The gastrointestinal motor activity is increased, nausea and vomiting result from stimulation of the emetic center. The effects of nicotine on the circulation are varied. The heart rate is first slowed by vagus center stimulation. The rate may later increase because of sympathetic stimulation resulting from the action of the drug on the autonomic ganglia and medullary portion of the suprarenals. The blood pressure is generally increased from sympathetic stimulation, therefore the use of tobacco in hypertension is contraindicated. The glands of internal secretion are not generally affected by nicotine, except in large doses when it acts as a stimulant.

Therapeutics.—Nicotine is not used therapeutically.

Toxicology.—There is more than enough nicotine in a cigar to kill an adult. The alkaloid is volatilized by the heat of the burning tobacco and inhaled into the respiratory tract where a part of it is absorbed. The acute symptoms are well known to most smokers and

result from stimulation of the gastrointestinal tract and the emetic center. As the alkaloid is rapidly destroyed in the liver, the symptoms are of short duration. Death may occur from the accidental ingestion of the drug as in insect sprays but not from tobacco smoking and is caused by depression of the respiratory center.

TREATMENT.—As the drug is rapidly destroyed in the liver, time is the important factor. Supportive treatment, medullary stimulants, oxygen and carbon dioxide inhalation, and at times artificial respiration are necessary to maintain the patient until the drug is destroyed or eliminated by the body. The presence of the alkaloid in the gastrointestinal tract necessitates its removal by emesis and catharsis.

LOBELIA

Lobelia; Lobelia (Lobel.), N.F. (Indian tobacco).

Lobelia (Indian tobacco) is the dried leaves and flowering tops of the *Lobelia inflata,* an herb which grows wild throughout the United States. Its chief alkaloid was first crystallized by Wieland (1915) and named alpha-lobeline. Like nicotine it contains the pyridine ring as the nucleus. The alkaloid is not official.

USES.—Expectorant, nauseant, and emetic, resembling tobacco.

PHARMACODYNAMICS.—The drug has a similar action on the cerebral cortex, medullary centers, autonomic ganglia, and skeletal muscles to nicotine, acting first as a stimulant and in larger doses as a depressant. It is interesting to note that the two drugs used for smoking have alkaloids with similar actions.

THERAPEUTICS.—The drug alpha-lobeline has been advocated as a respiratory stimulant for respiratory failure during general anesthetics in 5 mg. doses. Its value is questionable.

DOSAGE.—0.1 Gm. (1½ grains) (N.F.).

PREPARATIONS.—

Fluidextract of Lobelia; Fluidextractum Lobeliae (Fldext. Lobel.), N.F.

The fluidextract of lobelia contains lobelia 100 per cent in water and alcohol (39%).

DOSAGE.—0.1 cc. (1½ minims) (N.F.).

Tincture of Lobelia; Tinctura Lobeliae (Tr. Lobel.), N.F.

It contains lobelia 10 per cent, absolute alcohol about 46 per cent, and acetic acid.

DOSAGE.—1 cc. (15 minims) (N.F.).

CHAPTER X

LOCAL ANESTHETICS

Local anesthetics (without pain) are agents which are employed for the purpose of producing insensibility to pain in a circumscribed area of tissue. They are known to act in two ways. Primary, or true, local anesthetics are those which act at once on the nerve endings; and secondary, or painful, anesthetics are those which are preceded in their anesthetic action by a period of intense irritation. The latter group is principally represented by alcohol, which is used in the treatment of trifacial neuralgia. Certain essential oils also act as painful anesthetics and possess valuable obtunding properties; they are frequently employed for such purposes in dentistry. Specific forms of local anesthesia may also be produced by paralyzing the sensory ganglia and the spinal cord; these methods have, however, no bearing on the subject under consideration.

From an historical viewpoint, comparatively few important methods for the purpose of locally obtunding pain are to be recorded prior to the introduction of cocaine (1884). The compression of nerve trunks for the abolition of pain seems to be old and of an unknown origin. It was revived by Guy du Chauliac and Ambroise Paré, and finally found a place in surgery as the Esmarch elastic bandage. Physically reducing the temperature of a part of the body by the application of cold was instituted much later. Bartholin and Severino introduced this method in the middle of the sixteenth century. It became a lost art, however, until John Hunter, of London, again called attention to its benefits by demonstrating its use upon animals; yet the idea never seems to have occurred to him that the same agent might be useful in abolishing human suffering. Larrey, the chief surgeon of Napoleon's army, employed it for amputating purposes (1807). James Arnott, in 1848, utilized a freezing mixture, consisting of ice and salt, as a means of producing local anesthesia. Through the efforts of Sir B. W. Richardson, in 1866, it was placed on a rational basis by the introduction of the ether spray and later ethyl chloride. The various narcotics which were employed for internal purposes were also made use of as local applications. Mandragora, henbane, aconite, the juice of the poppy head, and many other analgesic drugs enjoyed a wide reputation.

The empiric search for new local anesthetic methods pressed the mysticism of the electric current into service, opening a prolific field

to the charlatan, which even to this day has not lost its charm. Richardson's voltaic narcotism for a time attracted the attention of the medical and dental profession. Its inventor claimed "that by the action of a galvanic current, passing through a narcotic solution, held in contact with the part to be operated upon, some of the narcotic substance passed much more rapidly into the tissue, and that in many instances local anesthesia was produced . . ." Francis, in 1858, recommended the attachment of the electric current to the well-insulated handles of the forceps for the painless extraction of the teeth. In 1880 Bonwill suggested his method of "rapid breathing as a pain obtunder," which he claimed "produces a similar effect to that of ether, chloroform, and nitrous oxide gas in their primary stages." In the early days of modern dentistry many feeble efforts were made to alleviate pain during trying operations. In 1844, F. Rynd, an Irish surgeon, introduced a method of general medication by means of hypodermic injections, which, in 1853, was much improved by Alexander Wood, of Edinburgh, and a few years later the French surgeon Pravaz modified the old style syringe for this special purpose. At once it was suggested to apply such drugs as morphine or tincture of opium for the purpose of producing local anesthesia. The results were not encouraging, however, until cocaine was advocated. Cocaine was discovered by Niemann in 1859, but it required twenty-five years to make known the remarkable anesthetic properties of this alkaloid. It was on September 15, 1884, that Carl Koller,[1] of Vienna, had presented his epoch-making communication at the Ophthalmologic Congress at Heidelberg, in which he demonstrated the effects of cocaine as a local anesthetic. With the introduction of this drug into therapeutics, local anesthesia achieved results which were beyond expectations, and its final adoption created a new era in local anesthesia.

Local anesthetics produce insensibility to pain. By pain we understand the conscious manifestation of morbid changes within the body.

The local inhibition of pain is incompletely accomplished as the sensations of touch and of temperature are only partially abolished. The sensation of pressure may be inhibited in its entirety. Motion is usually not interfered with.

Local anesthetics must be absorbed to produce their typical effect; the oral mucous membranes are not easily penetrated by topically applied anesthetic solutions, and superficial anesthesia is not readily produced. The horny layer of the skin does not allow penetration; endodermic or hypodermic injections are necessary to bring the anesthetic solution into close contact with the nerve endings. To prevent

[1]Koller, Carl: 16th Ophthalmologenkongress, Heidelberg, 1884.

a too rapid absorption by the blood and by the lymph stream, blocking of the circulation within the injected area is essential. The application of a suitable bandage applied near the seat of the anesthetic field or the injection of powerful vasoconstrictor drugs incorporated in the anesthetic solution are both effective. To prevent unnecessary damage to the cells, the solution must correspond to the isotonic index of the tissue fluids.

Local anesthesia, according to Preyer's conception, is produced as follows: The anesthetic agent possesses a distinct affinity for the living protoplasm of the nerve fiber, forming a labile union and thus producing local anesthesia, which lasts until this temporary union is broken, releasing the drug—not as the original anesthetic, however, but as inert compounds of simpler structures. The products resulting from the decomposition of the anesthetic are removed from the living tissues by the routine channels of elimination. In dead tissues the injected anesthetic will not undergo any change.

Local anesthesia is indicated in all minor and in relatively many major operations on the mucous surfaces, the skin, and the teeth. Certain reflex disturbances—vomiting from an irritated stomach or hyperesthesia of the mucous membrane of the mouth during taking of an impression, and many forms of neuralgia—are frequently benefited by the application of local anesthetics. Observations made by Spiess, Rosenbach, Fischer, and Kirchner have fully demonstrated the therapeutic value of local anesthetics in the abortive treatment of inflammation. Inflammation in its early stages, according to Spiess, may be completely aborted if it is possible to prevent the occurrence of pain. Spiess applies local anesthetics at the seat of inflammation, while Rosenbach advocates general analgesics, such as morphine, for this purpose. The advantages of local therapeutic applications in dental surgery for the above purposes are apparent, and Fischer and Kirchner have frequently made use of Spiess' suggestion. The beneficial influence of local anesthetics on inflammatory processes is explained by Spiess as follows: When the exposed nerve fibers are brought in direct contact with the anesthetic, they become at once insensible, but the anesthetic must not interfere with the blood vessels—they must not act as vasoconstrictors. The important factor in this treatment seems to be to bring and to hold the local anesthetic in close contact with the wound surface until all subjective pain is more or less abolished, and to keep the wound surface in this analgesic state.

Local anesthesia is not a substitute for general anesthesia; its usefulness is materially increased by familiarizing one's self with modern methods and with a perfect mastering of the technique. The

danger of poisoning has been practically eliminated by using isotonic solutions containing a relatively small percentage of the anesthetic in combination with the alkaloid of the suprarenal medulla. Even if the danger of general anesthesia is small under the most favorable conditions, the danger from local anesthesia is always less. The majority of all dental operations can be safely carried out under local anesthesia, provided the operator has acquired a complete working knowledge of the various components which, as a whole, constitute this important branch of dental therapeutics.

For the sake of convenience, local anesthetics are divided into:

1. Soluble local anesthetics.
2. Insoluble local anesthetics.
3. Refrigerant local anesthetics.

Properties of a Good Local Anesthetic

A good injection anesthetic should be soluble in water and nonirritating to the tissues. It should be relatively nontoxic in dosages adequate for complete local anesthesia. If the anesthetic is a vasodilator, it should be such that it will combine with a vasoconstrictor to overcome this undesirable effect. A local anesthetic must be sterilizable and therefore must be able to stand boiling without molecular decomposition. Local anesthetics are often marketed in prepared solutions, and the factor of molecular stability is very important. As local anesthetics are repeatedly injected, they should not act as an antigen producing antibodies which would make the drug less potent for further use or sensitize the tissues, which would result in an anaphylactic shock upon subsequent use. The anesthetic must be decomposed in the nerve tissues, giving anesthesia adequate for a normal operation but not so prolonged as to destroy function for a long period of time. The tissues should be able to destroy, detoxify, or eliminate the drug as fast as it passes into the blood and lymph stream, preventing a toxic concentration in the vital medullary centers.

Properties of a Good Local Anesthetic Drug.—

Soluble in water.
Does not decompose upon standing—ampuls.
May be sterilized by heat without decomposition.
Nonirritating to tissues when made isotonic.
Nontoxic in amounts used for local anesthetic purposes.
Should not act as an antigen—anaphylaxis.
Must be slowly destroyed in the nerve tissue.

Must be rapidly destroyed in the blood stream.

A vasoconstrictor; if a vasodilator, it should be able to combine with a vasoconstrictor drug.

Economical and available in large quantities.

PHARMACODYNAMICS OF THE LOCAL ANESTHETIC

Little is known regarding the pharmacodynamics of the local anesthetics. The drug appears to have a selected affinity for sensory nerve fibers and a lesser affinity for voluntary motor nerves, proprioceptor, cold and hot, and pressure nerves, etc. The drug apparently passes through the neurilemma and into the axon where it combines with the nerve fiber chemically, altering its function of conductivity. The anesthetic will also affect the synaptic transmission of nerve impulses as demonstrated by Harvey (1939). The local anesthetics are fat-soluble and to a certain extent obey the law of Myer-Overton. To make the alkaloids water-soluble they are dispensed as acid salts. Their anesthetic efficiency and the rate of anesthetic induction is inversely proportional to their water solubility. Therefore, the addition of alkali decreases their water solubility and increases their potency.[1, 2] Too much alkali will produce flocculation of the drug and a loss of potency.

The local anesthetics of the procaine group are vasodilators and are combined with epinephrine hydrochloride in a 1:25,000 to 1:60,000 solution to overcome this undesirable property.

This group of anesthetics is rapidly destroyed in the liver, and by the nerves and other body tissues to a lesser extent. Liver disease contraindicates the use of this group of drugs. Procaine is not a narcotic drug and is not subject to the regulations of the National Narcotic Act.

TOXICOLOGY.—It is of interest to note that all of the local anesthetic drugs produce similar toxic symptoms but in varying degrees. The symptoms are first of central nervous system stimulation followed by depression with a failure of respiration. The early symptoms are of excitement, nervousness, tremors, fear, perspiration, weak rapid pulse, fall in blood pressure; weak, irregular respiratory movements which may cease altogether.

Hypnotic drugs are best for the prevention and treatment of these symptoms. The barbiturates are the most valuable. These untoward reactions must be classified as an idiosyncrasy and are not necessarily dependent upon size of the dose.

[1]Talnter, M. L., Throndson, A. H., and Moose, S. M.: J. A. D. A. 26: 920, June, 1939.

[2]Miller, H. C.: J. A. D. A. and Dent. Cos. 25: 391, March, 1938.

Soluble Local Anesthetic Drugs

Cocaine

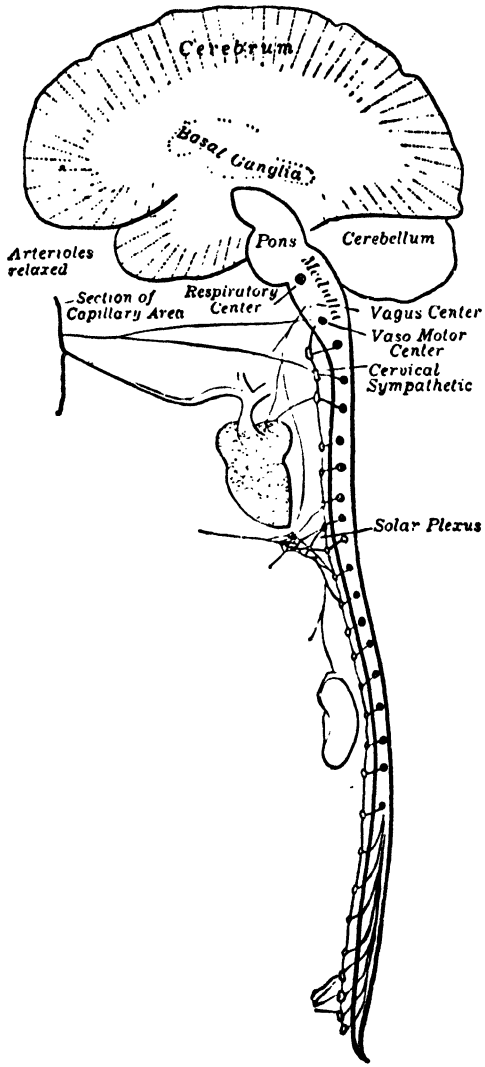
History.—The coca plant, *Erythroxylon coca,* is found principally in Peru and Bolivia, where it has been cultivated from time immemorial. It has played an important mission in the religious and political life of the aborigines. The coca plant is regarded by the Indians of South America as a divine gift, which "satisfies the hungry, strengthens the weak, and supplies new vitality to the exhausted, while the unhappy are made to forget their troubles." The Incas restricted to the royal families the right to cultivate and use the coca leaves. With the conquest of Peru by Pizarro (1532) the Spanish first monopolized and later levied a heavy tax on coca leaves, which became a rich source of income to the Spanish crown. The aborigines of South America chew the coca leaves mixed with alkalies, usually wood ashes, to facilitate the ready solution of the alkaloids. The stimulating action of the cocaine, which makes them endure greater physical labor and elude temporarily the necessity of sleep, is well known to the South American Indians; they are also acquainted with the dangers of its too free indulgence. The small green or greenish-brown leaves of the coca plant are plucked from the shrub, dried in the sun, and immediately packed for shipment. Niemann and Lossen, working in Wöhler's laboratory in Göttingen, were the first to isolate cocaine. Later on it was synthetically prepared by Merck, Liebermann, and Giesel. The first records of the anesthetic properties of cocaine were published by Scherzer, followed by Niemann (1860) and others. Von Anrep, in 1878, published the first detailed report of its definite local anesthetic properties on the eye and other tissues. It remained for Koller, however, to introduce it permanently into surgery through his communication addressed to the Ophthalmologic Congress held in Heidelberg in 1884. Cocaine was now readily accepted by the profession at large, and very soon it became the most important drug for the purpose of producing local anesthesia.

As dental surgery has to deal so much with pain, it is not at all surprising that cocaine was so quickly admitted to this special field of surgery. Hillischer published his experiments in 1884, which were soon followed by those of Hughes, Audina, David, Barker, and others. The most complete essays on the use of cocaine in dentistry, which materially assisted in making the drug widely known in dental circles, were published in 1886. Adolph Witzel, of Essen, presented a valuable contribution in German, which was followed a few months later by a similar essay by George Viau, of Paris. Witzel advocated a 20 per cent solution, using one grain of cocaine of a questionable purity for one injection. It is surprising that more serious intoxications from such enormous quantities did not occur.

Cocaine; Cocaina (Cocain.), U.S.P.

Cocaine is an alkaloid obtained from the leaves of the *Erythroxylon coca,* a shrub which grows in South America. The hydrochloride salt is also official and is generally used because of its greater solubility in water. Cocaine is a very efficient surface and injection anesthetic but is very toxic. It is habit-forming and is included in the list of drugs regulated by the National Narcotic Act. Chemically, cocaine is not closely related to procaine. The alkaloid occurs as a white, odor-

less powder, slightly soluble in water (1 in 600), freely soluble in alcohol (1 in 7), and very soluble in ether (1 in 3.5), and olive oil (1 in 12).



COCAINE

The poisonous effects of Coca, or the secondary effects of a large dose, are depressant, following quite definitely the lines of previous stimulation.

Nervous System.

Brain. Cerebral functions are first stimulated, then depressed, frequently with production of narcosis or convulsions.

Medulla. Depresses respiratory center and probably vasomotor center.

Spinal Cord. Depresses reflex center.

Circulation. Arterial pressure is lessened.

Heart. Depressed by direct action of the drug.

Capillary Area. Arterioles relaxed, probably through paralysis of vasomotor center.

Eye is dilated. Acts as a nerve block.

Respiration. Depresses the respiratory functions by lessening the irritability of the center in the medulla.

In general, the depressant action is that of a general protoplasmic poison, the commonest evidence of which is its paralyzant influence upon nerve tissue when locally applied. The sensory nerves are more susceptible.

Fig. 20.—The dotted areas indicate the depressant effects of a toxic dose of cocaine. (Redrawn from McGuigan: *Experimental Pharmacology.* Lea & Febiger.)

PHARMACODYNAMICS.—Cocaine does not pass through the unbroken skin but does pass through the mucous membranes, producing paralysis of the pain nerves and to a lesser extent the other nerves. It acts

as a vasoconstrictor drug by sensitizing the smooth muscles of the blood vessels to sympathetic stimulation (sympathomimetic) and it also may have a direct epinephrine-like action. It stimulates the cerebral cortex and then depresses it, followed by the midbrain, cord, and medulla. The stimulation of the central nervous system produces a feeling of well-being, increases circulation and respiration, and motor irritability. The inhibition produces depression, coma and circulatory and respiratory failure.

THERAPEUTICS.—Cocaine was the first local anesthetic to be used; it was isolated by Niemann in 1860, introduced as a surface anesthetic by Carl Koller in 1884, and as an injection anesthetic in dentistry by Hall and Halsted in 1885 and 1886. It is an efficient local anesthetic but is too toxic for dental use. For topical anesthesia in a 1 to 4 per cent solution it is efficient and moderately safe. For an injection anesthesia a 0.25 per cent solution is efficient and has been used for years without many untoward reactions (Henneberger). It is very habit-forming, and this alone would contraindicate its universal use in dentistry. As a pulp anesthetic, the regular procaine-epinephrine tablets will take the place of cocaine. The purchasing, keeping, or prescribing of cocaine or its salts requires a narcotic license.

DOSAGE.—Not given in U.S.P.; 15 mg. (¼ grain).

TOXICOLOGY.—The toxic symptoms of cocaine poisoning are due to its cerebral and medullary action. The first symptoms are of sensory stimulation followed by depression, then cerebral motor stimulation followed by depression. The vital medullary centers are then stimulated and finally depressed, resulting in respiratory failure and circulatory depression. The symptoms are of excitement, anxiety, fear, pallor, perspiration, fainting, muscular spasms, weak pulse, slow irregular respiration which may fail, death occurring from anoxemia. Treatment should be immediately administered.

PREPARATION.—

Cocaine Hydrochloride, Cocainae hydrochloridum (Cocain. Hydrochlor.), U.S.P. (Cocaini Hydrochloridum P.I.)

Cocaine hydrochloride occurs as colorless crystals, without odor, and with a bitter taste. It is very soluble in water (1 in 0.5), freely soluble in alcohol (1 in 3.5), and incompatible with borax, alkalies, phenol, and tannic acid.

The salt is used in preference to the alkaloid becauses of its greater solubility in water.

DOSAGE.—Not given in U.S.P.; 15 mg. (¼ grain).

COCAINISM.—The repeated administration of cocaine may readily establish an addiction to this drug, known as cocainism or cocaine habit. The exhilarating effect of cocaine on the nervous system, *euphoria,* is largely responsible for the craving for the drug. Cocaine addicts are very insistent upon the mode of administration of the poison. Whether they take the drug by insufflation or by injection, or even by the rectum, they will always strenuously insist upon the particular method they originally adopted. Usually the hypodermic injection is preferred by the white race, while the Negro prefers to snuff his cocaine. The continuous puncturing with the needle in injecting cocaine into the tissues produces an injurious effect on the skin in the cocaine addict; abscesses form, and the resulting scars frequently cover all available spaces of the body, especially the arms and the legs. Cocainism usually manifests itself in disturbed digestion, salivation, and emaciation, the most important changes occurring in the nervous system. Sleeplessness and tremors, and occasionally convulsions, hallucinations, insanity, and delirium have been noted after long abuse, along with indefinite disturbances of sensation and motion.

While the addiction to cocaine is very appalling, cocainism apparently yields readily to treatment. Sanitarium treatment, with the proper medical care, is the most efficient method for the eradication of the habit.

TOPICAL ANESTHETIC, A.D.R.

(1% Solution)

℞	Cocaine Hydrochloride	0.15 Gm.	gr. iiss
	Distilled water, to make	15.00 cc.	ʒ ss
	Mix.		
	Sig.: Apply.		

PROCAINE

PROCAINE HYDROCHLORIDE; PROCAINAE HYDROCHLORIDUM (PROCAIN. HYDROCHLOR.), U.S.P. (Novocain, Procaine); P-amino-benzoyldiethylaminoethanol Hydrochloride; $C_6H_4.NH_2.CO_2.C_2H_4.N(C_2H_5)_2.HCl$.

SOURCE AND CHARACTER.—Procaine is the monohydrochloride of a synthetically prepared alkaloid. It is a white crystalline powder, or colorless needle-shaped crystals, melting at about 311° F. (155° C.). It may be heated to 200° F. (93° C.) without decomposition. It is soluble in 1 cc. of water, the solution having an acid character; in cold alcohol it dissolves in the proportion of 1 to 30. Caustic alkalies

and alkaline carbonates precipitate the free base from the aqueous solution in the form of a colorless oil, which soon solidifies. It is *incompatible* with the alkalies and alkaline carbonates, with picric acid, iodides, borates, and tannic acid.

Abbott Laboratories suggest the following purity test for procaine hydrochloride: Procaine crystals or tablets are dissolved in warm alcohol. If decomposed, the solution on standing takes on a yellowish tint within a few minutes.

DOSAGE.—The total dose varies widely with the purpose for which it is used. For details of use see *Useful Drugs*.

HISTORY.—Procaine was synthesized by Einhorn in 1905 and introduced as novocaine. This drug immediately replaced cocaine as an injection local anesthetic, and after 39 years it is still the most important drug in this field. The alkaloid is sparingly soluble in water, and for that reason the hydrochloride salt, which is soluble in water, was made official in the U.S.P.

CHEMISTRY.—The aromatic primary amine is weakly basic and does not react readily with acids. The tertiary aliphatic amine is more basic and reacts with acids to form salts, by direct addition. The para-amino-benzoyl nucleus gives the compound its anesthetic properties and is the nucleus for many of the related local anesthetic compounds of this group. The ester portion (—C—C—) increases the anesthetic properties and decreases the solubility in water. Longer chains or alkyl substitutions in this part of the molecule (ester) increase the anesthetic potency and increase the toxicity. An increase in the length of the carbon chain of the tertiary amine, increases the anesthetic potency and increases the toxicity.

PHARMACODYNAMICS.[1, 2]—When a solution of procaine hydrochloride is injected into the tissue, it is generally acid in reaction and hydrophilic in nature. The tissue fluids raise the pH of the anesthetic solution from about 4 to 7. It is then hydrophobic and lipophilic and diffuses readily into the nerve fibers, disturbing their function of conduction. Pain impulses arising in the periphery are interrupted in their transmission and do not reach the sensory centers in the cerebral cortex. The nature of this reaction is not well understood.

The arterioles are dilated by procaine by a direct action on the smooth muscles of the blood vessels. This is an undesirable property, as it decreases the efficacy of the anesthetic, decreases the duration of anesthesia, and increases the toxicity. This occurs from

[1]Tainter, M. L.: Anesthesiology, 2: 489, September, 1941.
[2]Higgins, J. A.: J. A. D. A. 27: 10, January, 1940.

the increased amount of blood in the part which washes the drug rapidly into the general blood and lymph circulation.

Procaine solutions are nonirritating up to 3 per cent; higher concentrations are not only irritating but are caustic.[1] The keeping or using of procaine or related drugs is not supervised by the National Narcotic Act. These compounds are not habit-forming and may be used over long periods of time.

TOXICOLOGY AND TREATMENT.[2-5]—Generally speaking, procaine hydrochloride is a safe drug for local anesthesia. Like all drugs, some few patients are allergic to it and respond unfavorably to even very small doses. This allergic reaction, while often severe, is seldom fatal. The exact mechanism of this reaction is not well understood but may be associated with a toxic reaction on the heart muscles, producing symptoms of shock and sudden heart failure. Treatment must be immediate.

Procaine is detoxified by the liver cells and excreted through the kidneys. Kidney or liver disease contraindicates the use of local anesthetics.

When a solution of procaine hydrochloride with epinephrine hydrochloride is injected into the subcutaneous tissues, vasoconstriction localizes the drugs and prevents a rapid systemic absorption. The small amount of drugs which passes into the general circulation is generally removed by the liver and kidneys, preventing a concentration in the tissues of such amounts as will produce toxic symptoms. Subcutaneous injections of procaine-epinephrine solutions are about one-seventh as toxic as cocaine. When the anesthetic solution is injected directly into an artery or vein, the concentration of the drug in the blood is too great for immediate removal, and toxicity results. The early symptoms are of central nervous system origin. Local anesthetics first stimulate and then depress; the cerebral centers are first affected and last the medullary centers. The stimulation and depression may be orderly or may be mixed. When the sensory area of the cerebral cortex is stimulated, the patient shows signs of excitement, such as nervousness, anxiety, and talkativeness.[6] The motor area of the cerebral cortex may next be stimulated, resulting in restlessness, trembling, and at times convulsive movements. The vital medullary centers may next be stimulated, increas-

[1]Council Report, J. A. D. A. 31: 278, February, 1944.
[2]Miller, H. C.: J. A. D. A. and Dent. Cos. 24: 515, April, 1937.
[3]Wallace, D. A., and Hansen, H. L.: J. A. D. A. 28: 1000, June, 1941.
[4]Schamp, J. R., Jr.: Dent. Res. 20: 425, October, 1941.
[5]Gwinn, C. D., and Ferber, E. W.: J. A. D. A. 23: 1298, July, 1936.
[6]Tainter, M. L., and Throndson, A. H.: J. A. D. A. and Dent. Cos. 25: 966, June, 1938.

ing the rate and amplitude of respiration. The vagus center may be stimulated, resulting in a temporary slowing of the heart. The cardiac accelerator center may be stimulated, which will increase the rate and strength of the heartbeat. The vomiting center may be stimulated, resulting in emesis. The vasoconstrictor center may be stimulated, producing a cutaneous vasoconstriction with an increase in blood pressure. These symptoms may be annoying to the patient and doctor, but they are not serious. Death occurs from depression of the medullary centers. The respiratory center may fail to respond to the normal carbon dioxide concentrations in the blood, and respiration may stop. Artificial respiration plus respiratory stimulants are generally successful as a restorative measure. The vasoconstrictor center may be depressed, resulting in a fall in blood pressure and symptoms of vasomotor collapse. Hypodermic injections of 0.5 mg. of epinephrine hydrochloride are useful to raise the lowering blood pressure. The cardiac accelerator center may be depressed, resulting in a slow weak heart action which further lowers the blood pressure. The heart may fail from a direct toxic action of procaine on the heart muscle. Epinephrine injections are also useful as cardiac stimulants.

Fortunately the symptoms of medullary depression are very infrequent. The dentist is more concerned with the less severe symptoms associated with central nervous system stimulation. The salts of barbituric acid are very useful in preventing and correcting these toxic manifestations of local anesthetic poisoning. Premedication with barbital in 0.3 gram doses, giving one to three tablets the day prior to the operation and the same number following the operation will often induce a "successful" operation. When these toxic symptoms occur, hypodermic administration of a soluble barbiturate is considered the treatment of choice.

THERAPEUTICS.—Acid solutions of procaine hydrochloride have but slight topical anesthetic potency when applied to the oral mucous membrane. A 20 per cent aqueous solution made alkaline with sodium bicarbonate to a pH about 8, gives a profound surface anesthesia. The addition of a vasoconstrictor drug does not increase its anesthetic power.

For local injection anesthesia a 2 per cent solution of procaine hydrochloride is generally used in dental surgery; higher concentrations are irritating and more toxic. Epinephrine hydrochloride in a 1:25,000 to 1:60,000 solution is used as a pressor drug. The isotonicity is maintained by adding 0.5 to 0.6 per cent of sodium

chloride. Sodium bisulfite is often added to the prepared solutions to prevent oxidation of the epinephrine and procaine. Potassium sulfate.[1, 2] may be added to increase the anesthetic potency of the solution. Its value is questioned.

The pH of the prepared solution made from tablets is between 4 and 5. Alkaline procaine solutions are more efficient than acid in producing a rapid and profound anesthesia. Such solutions deteriorate very rapidly and for that reason have not been very popular or satisfactory.

Freshly prepared solutions of procaine-epinephrine are probably the most satisfactory for general dentistry. The concentration of drugs may be regulated to the patient and to the needs. These solutions may be boiled without fear of molecular decomposition. The following alkaline saline solution has been used for years in the Oral Surgery Department of the University of Maryland Dental School:

℞	Sodium Chloride (U.S.P.)		5.00 Gm.
	Sodium Carbonate (U.S.P.)		0.35 Gm.
	Distilled water	q.s. ad	1000.00 cc.

Sig.: To be used with procaine-epinephrine tablets.

PREPARATIONS.—

Ampuls of Procaine Hydrochloride; Ampullae Procainae Hydrochloridi (Ampul. Procain. Hydrochlor.), N.F. (Ampuls of Procaine). —A measured quantity of sterile solution of procaine hydrochloride, unless otherwise stated. Approximately 0.02 Gm. of procaine hydrochloride in 1 cc.

DOSAGE.—1 cc. containing about 0.02 Gm. of procaine hydrochloride which gives a 2 per cent solution.

Solution of Procaine Hydrochloride; Liquor Procainae Hydrochloridi (Liq. Procain. Hydrochlor.), N.F.—Procaine hydrochloride (2%) in sterile physiologic sodium chloride solution. Solution of epinephrine hydrochloride 0.01 cc. should be added to each cubic centimeter of solution of procaine hydrochloride just before it is injected hypodermically.

DOSAGE.—Average parenteral dose: 1 cc. (N.F.).

Tablets of Procaine Hydrochloride; Tabellae Procainae Hydrochloridi (Tab. Procain. Hydrochlor.), N.F.—Contain 92.5 to 107.5 per cent of the stated amount of procaine hydrochloride. One tablet dissolved in 2.5 cc. of saline solution will give a 2 per cent solution. Solution of epinephrine hydrochloride, 0.01 cc. per cc. of prepared solution, should be added before injecting hypodermically.

[1] Schamp, H. M.: Endocrinology 29: 459, September, 1941.
[2] Tainter, M. L., and Throndson, A. H.: J. A. D. A. 27: 71, January, 1940.

DOSAGE.—50 mg. (¾ grain) of procaine hydrochloride (N.F.).

METHOD OF PREPARING PROCAINE SOLUTION FOR DENTAL PURPOSES.—A standard isotonic solvent for procaine is prepared according to the following formula:

Sodium chloride, U.S.P.	4 Gm.
Potassium sulfate, C.P.	2 Gm.
Distilled water	1000 cc.

When needed, 100 cc. of this standard solvent and 2 Gm. of procaine hydrochloride are slowly boiled in an Erlenmeyer flask, stoppered with cotton, for from four to five minutes. When cool, the solution is filtered through paper (using a freshly flamed glass funnel) into a sterile glass-stoppered bottle.

When needed, mix in a sterile glass dish, 2 cc. anesthetic solution and 1 drop epinephrine solution. If larger quantities are desired, prepare according to this table:

3- 5 cc. anesthetic solution + 2 drops epinephrine solution
6- 8 cc. anesthetic solution + 3 drops epinephrine solution
9-10 cc. anesthetic solution + 4 drops epinephrine solution.

No matter how much procaine solution is used at one time, never employ more than five drops of epinephrine as the maximum quantity. The epinephrine stock solution (only 1 oz. bottles should be procured) should be kept in a dark, cool place. Of the numerous epinephrine solutions on the market, we prefer the synthetic suprarenin (Winthrop) or the adrenalin (Parke, Davis & Co.).

STOCK ALKALINE SALINE SOLUTIONS TO BE USED WITH PROCAINE-EPINEPHRINE TABLETS

℞	Sod. Chlorid., U.S.P.		5.00 Gm.
	Sod. Carb. Monohyd., U.S.P.		0.35 Gm.
	Aq. Dest. Bull.	q.s. ad	1000.00 cc.
	M. et ft. Sol.		
	Sig.: For office use.		

℞	Sod. Carb. Monohyd., U.S.P.		0.35 Gm.
	Sod. Chlorid., U.S.P.		5.00 Gm.
	Pot. Chlorid., U.S.P.		0.20 Gm.
	Aq. Dest. Bull.	q.s. ad	1000.00 cc.
	M. et ft. Sol.		
	Sig.: For office use.		

When these solutions are used with procaine-epinephrine tablets, a safe alkaline anesthetic solution for hypodermic administration is obtained. The solution to be injected should be boiled just prior to use.

All glassware used in preparing and storing the standard solvent, the procaine solution, and the epinephrine solution must be alkali-free. Alkali-free glassware for this purpose is readily prepared by immersing the bottles, etc., for twenty-four hours in a weak (about 5 per cent) solution of hydrochloric acid. Thorough washing in running water after removal from the acid is essential. Alkali-free glassware is necessary to prevent the ready decomposition of epinephrine. (Pyrex or Jena glassware is alkali-free.)

ANESTHETICS, TOPICAL, FOR ORAL USE

℞[1] Procain. Hydrochlor.		5.0 Gm.
Ephedrin. Sulf.		0.6 Gm.
Sod. Bicarb.		1.2 Gm.
Alcohol		3.0 cc.
Aq. Dest.	q.s. ad	30.0 cc.

M. et ft. Sol.

Sig.: Apply to the oral mucous membrane for 5 minutes on a pellet of cotton.

PROCAINE BORATE

PROCAINE BORATE (A.D.R.) occurs as white, odorless crystals, with a bitter taste, freely soluble in water (1 in 4), soluble in alcohol, and insoluble in ether. The crystals melt at 163° to 166° C., and the solutions are alkaline to litmus. Chemically it is $NH_2(C_6H_4CO)OC_2H_4N(C_2H_5)_2.5HBO_2$.

THERAPEUTICS.[2]—Procaine borate closely resembles procaine hydrochloride in its actions and uses. Its potency and toxicity are closely proportional to its content of procaine base. A 20 per cent solution applied topically to the oral mucous membrane for 5 minutes produces a mild surface anesthesia; the addition of alkali did not increase its surface anesthetic potency. It is marketed for injection anesthesia in a 2 per cent solution combined with epinephrine. Its alkalinity is supposed to give it an advantage over the acid hydrochloride salt, but this has not been confirmed by usage. The toxicology and treatment are the same as for procaine hydrochloride.

PROCAINE BUTYRATE

PROCAINE BUTYRATE, A.D.R. A white crystalline powder having a slight aromatic odor. It is very soluble in water and alcohol and some-

[1] Dobbs, E. C.: Procaine Hydrochloride as a Surface Anesthetic, Dent. Cosmos 78: 812, 1936.

[2] Tainter, M. L., Throndson, A. H., and Moose, S. M.: J. A. D. A. and Dent. Cos. 24: 276, March, 1937.

what less in vegetable oils. Solutions may be sterilized by short boiling. It is recommended as a substitute for procaine hydrochloride, over which it has no advantage.

Procaine Nitrate

Procaine Nitrate, Procainae Nitras (N.N.R.), occurs as a white crystalline solid, soluble in water and alcohol, acid to litmus, and melts at 100° to 102° C.

Therapeutics.—Same as those for procaine hydrochloride, U.S.P., over which it has no advantages.

Monocaine

Monocaine Hydrochloride (A.D.R.) occurs as a white crystalline solid, soluble in water. It has a bitter taste and can be sterilized by heat. Monocaine was introduced by Samuel D. Goldberg and Willet F. Whitmore before the American Chemical Society in April, 1937.

Pharmacodynamics.[1]—Monocaine hydrochloride is a local anesthetic of the procaine group. When locally applied it is a more active surface anesthetic than procaine. When injected in solution, it is twice as potent as procaine but is also about 1.6 times as toxic. It is a vasoconstrictor drug and therefore may be used with or without epinephrine. Because of its vasoconstrictor principle, it is said not to cause a fall in blood pressure, and therefore fainting and weakness are less frequently produced than with procaine. These advantages in dental surgery have not been confirmed by clinical study.

Chemistry.—Monocaine hydrochloride is the mono-iso-butyl amino ethyl para amino benzoate and is closely related to procaine, $p\text{-}NH_2.C_6H_4.COO.(CH_2)_2.NH.OOCCH_3.HCl$.

It melts at 192° to 194° C., and in solution has a pH of 3.75 to 3.9.

Therapeutics.—Monocaine hydrochloride is used as an injection anesthetic in a 1 to 1.5 per cent solution with 1:75,000 epinephrine. While monocaine is more toxic than procaine, the prepared solution contains less of the drug and is said to be no more toxic. Tainter and Throndson found that monocaine gave more undesirable postoperative complications than procaine. As one would expect from the chemistry of monocaine, it is not appreciably different from procaine and probably has no advantages over it.

Eucaine Hydrochloride; Eucainae Hydrochloridum (Eucain. Hydrochlor.), U.S.P. (Betaeucaine Hydrochloride).

Betaeucaine hydrochloride is a white crystalline powder, soluble in 30 parts of water. Its solutions may be boiled without decomposition;

[1]Tainter, M. L., and Throndson, A. H.: J. A. D. A. 28: 1604, October, 1941.

they are slightly antiseptic. It is about three and a half times less poisonous than cocaine, but also less active. When combined with epinephrine, it partially destroys the vasoconstrictor power of the latter.

ACTION AND USES.—Local topical anesthetic, in a 2 or 3 per cent solution for the eye or 5 to 10 per cent solution for the mouth.

CHLOROBUTANOL

CHLOROBUTANOL; CHLOROBUTANOL (CHLOROBUT.), U.S.P.

Chlorobutanol occurs as white crystals, having an unpleasant odor and taste; it is slightly soluble in water (1 in 125), freely soluble in alcohol (1 in 1), ether, and volatile oils.

PHARMACODYNAMICS.—Chlorobutanol does not have a similar chemical structure to procaine, yet its action on sensory nerves is similar. Chemically, it is related to chloral hydrate, having a formula of $CCl_3.C(CH_3)_2OH$, and has similar systemic actions. It is irritating because of the liberation of chlorine, and it is fat soluble, which may explain its local anesthetic and obtundent properties. Because of its odor and taste, it is a disagreeable drug to take orally. After absorption it depresses the central nervous system, producing sedation, analgesia, and hypnosis. Large doses depress the medullary centers, causing circulatory and respiratory failure; death occurs from anoxemia. The heart muscle is directly depressed, causing circulatory embarrassment and failure. Like chloral, it is a dangerous drug for internal use.

THERAPEUTICS.—When chlorobutanol is applied to the mucous membranes or abraded areas, it is readily absorbed and acts as a topical anesthetic. When taken internally, it allays gastric irritation, preventing nausea and vomiting, and it is useful in pregnancy and seasickness. It is about 15 times as antiseptic as boric acid and is used as a bacteriostatic agent. As an analgesic, sedative, local anesthetic, and hypnotic it is not a drug of choice.

DOSAGE.—0.6 Gm. (10 grains) (U.S.P.).

PREPARATION.—

Toothache Drops, Odontalgicum, N.F.—Toothache drops, N.F., contain chlorobutanol, 25 per cent in olive oil. This is a good preparation as a topical anesthetic and an obtundent for odontalgia.

CHLOROBUTANOL, 10% IN 45% ALCOHOL, A.D.R.

℞	Chlorobutanol		3.00 Gm.	gr. xlv
	Alcohol, 45%	To make	30.00 cc.	ʒ i

Mix.

Sig.: Topical anesthetic.

METYCAINE

METYCAINE HYDROCHLORIDE (N.N.R.) occurs as a white, crystalline, odorless powder. It is stable in air, freely soluble in water (1 in 1), soluble in alcohol and chloroform, and insoluble in oil. Metaycaine melts at 172° to 175° C., and in solution it is faintly acid to litmus.

CHEMISTRY.—The nucleus of metycaine differs from that of procaine by not having an amine radical attached to the benzene ring, by having a propyl group in place of an ethyl as the ester radical, and by not having a free amine group attached to the ester group. It is an asymmetrical compound, but is optically inactive and is therefore a racemic mixture ($C_6H_5COO[CH_2]_3.NC_6H_{12}.HCl$).

PHARMACODYNAMICS.—Metycaine is a satisfactory injection or topical anesthetic. It is about three times as toxic as procaine and is at least twice as potent as an infiltration anesthetic. It is a vasodilator drug and must be combined with a vasoconstrictor before using.

THERAPEUTICS.—It is marketed in ampuls in a 2 per cent solution with epinephrine hydrochloride, 1:25,000 and 1:50,000.

PHENACAINE

PHENACAINE HYDROCHLORIDE; PHENANCAINAE HYDROCHLORIDUM (PHENACAIN, HYDROCHLOR.), U.S.P.

Phenacaine hydrochloride occurs as colorless, odorless, crystals, with a faintly bitter taste. Chemically, it is the hydrochloride of ethenyl-p-diethoxydiphenyl-amidine and is sparingly soluble in water (1 in 50) and freely soluble in alcohol.

THERAPEUTICS.—Phenacaine hydrochloride is a quick-acting local anesthetic used chiefly in the eye in a 1 per cent solution. It is about 10 times as toxic as procaine hydrochloride and is not a surface anesthetic of first choice in dentistry.

BUTACAINE

BUTACAINE SULFATE; BUTACAINAE SULFAS (BUTACAIN. SULF.), U.S.P.

Butacaine sulfate occurs as a white, odorless, crystalline powder which is slowly but very soluble in water (1 to 1), very soluble in alcohol, and insoluble in ether. It melts at 100° to 103° C. Chemically, it resembles procaine except that the ethyl ester is replaced by a propyl, and the diethylamine is replaced by a normal dibutyl.

THERAPEUTICS.—Butacaine sulfate is a more potent surface anesthetic than cocaine and is about four times as potent an injection anesthetic as procaine. Its toxicity is equal to or greater than that

of cocaine which contraindicates its use in injection anesthesia. For surface anesthesia in dentistry it is applied in a 10 per cent solution for five minutes on a gauze sponge, the drug being held in close contact with the mucous membrane. The anesthetic potency may be increased by making the solution alkaline with sodium bicarbonate. For injection anesthesia it has been used in a 0.5 to 0.75 per cent solution, not over 8 cc. to be injected at one time. An alkaline 10 per cent solution of butacaine sulfate (Butyn) is the best topical anesthetic solution investigated by the author.

BUTYN (5%), A.D.R.

℞	Butyn		1.50 Gm.	gr. xxiii
	Distilled water	to make	30.00 cc.	ʒ i
	Mix.			
	Sig.: Apply.			

AMYLCAINE

AMYLCAINE HYDROCHLORIDE (N.N.R.) is mono-*n*-amyl-aminoethyl-*p*-aminobenzoate hydrochloride. It occurs as a white odorless powder with a bitter taste. It is soluble in water, sparingly soluble in alcohol, and insoluble in ether. In aqueous solutions it is acid to litmus.

THERAPEUTICS.—Amylcaine hydrochloride is used as a topical anesthetic in a 2 per cent solution. It has no use in dental therapeutics.

TETRACAINE

TETRACAINE HYDROCHLORIDE; TETRACAINAE HYDROCHLORIDUM (TETRACAIN. HYDROCHLOR.), U.S.P. (Pontocaine).

It occurs as a white, crystalline, odorless powder, with a slightly bitter taste. It melts at 147° to 150° C. and is stable in air at ordinary temperatures; it is very soluble in water, soluble in alcohol, and insoluble in ether. Chemically, it is p-butylaminobenzoyl-dimethylaminoethanol hydrochloride, differing from procaine by having a butane substitution on the ring amino group and two methyl substitutions instead of a diethyl on the aliphatic amino group ($C_4H_9NH.C_6H_4.COOC_2H_4N[CH_3]_2.HCl$).

THERAPEUTICS.—Pontocaine hydrochloride is a local anesthetic similar to procaine, and is used chiefly as a surface anesthetic for which it is less potent than cocaine but more potent than procaine. It is applied in a 2 per cent solution. Pontocaine hydrochloride is not a local anesthetic of first choice in dentistry. It has recently been introduced as a prepared solution containing procaine (2%) with pontocaine (0.15%) and is now being marketed to the profession. This preparation is comparable in potency and toxicity to a 3 per cent procaine solution.

Diothane

Diothane Hydrochloride (N.N.R.) is piperidinopropanediol-*di*-phenylurethane hydrochloride. It occurs as a white crystalline, odorless powder with a bitter taste. It is freely soluble in water, soluble in alcohol, and insoluble in ether. (For tests and standards see N.N.R.) It is a vasodilator, and epinephrine hydrochloride may be added to the anesthetic solution. Sterilization by boiling is possible without molecular decomposition.

Therapeutics.—Topically in a 5 to 10 per cent solution, injection in a 0.5 to 2 per cent solution. It is not a local anesthetic of first choice in dentistry.

Tutocaine

Tutocaine Hydrochloride (N.N.R.) occurs as an ivory colored crystalline powder, with a faintly bitter taste. It is stable in air, soluble in water (1 in 4), difficulty soluble in alcohol (1 in 50), acid to litmus paper, and melts at 81° C.

Therapeutics.—Tutocaine hydrochloride is a potent surface and injection local anesthetic. The duration of anesthesia is longer than with procaine, but the onset is slower but equally as profound. Its toxicity, as reported by the Council on Pharmacy and Chemistry, is four times as great as that of procaine; a fatality has resulted from an injection of 8 cc. of a 2 per cent solution into the urethra. It is not a local anesthetic drug of first choice in dentistry.

Saligenin

Saligenin, Saliginum (A.D.R.).—Salicylalcohol occurs as white rhombohedral plates or as a powder, which is stable in air, has an aromatic odor and a burning taste. It is soluble in water and chloroform, freely soluble in alcohol, ether, and the fixed and volatile oils. Chemically it resembles benzyl alcohol with a hydroxyl group in the para position, $C_6H_4.OH.CH_2OH$.

Therapeutics.—Saligenin is a local anesthetic similar to procaine in its action but less toxic. A 10 to 20 per cent solution applied topically acts as a surface anesthetic. For infiltration anesthesia it is injected in a 2 per cent solution; epinephrine is not necessary, as the drug has a prolonged effect without its addition.

Saligenin in Alcohol, 10%, A.D.R.

℞	Saligenin		3.00 Gm.	gr. xlv
	Alcohol	To make	30.00 cc.	ʒ i
	Mix.			
	Sig.: Apply			

Benzyl Alcohol

Benzyl Alcohol; Alcohol Benzylicum, $C_6H_5CH_2OH$, A.D.R., N.N.R.

Pharmacodynamics.—Benzyl alcohol, in concentrated solutions, resembles liquefied phenol, only it is less caustic and antiseptic. In a 1 to 4 per cent solution, made isotonic with sodium chloride, it is non-irritating and may be used as an injection anesthetic. When applied to the mucous membranes, it is readily absorbed, producing profound anesthesia in the area. It is used as an obtundent for sensitive dentine, as in odontalgia, and may be used as a substitute for eugenol.

Toxicology.—Locally it acts as a caustic similar to phenol. Internally it is about one-sixth as toxic as procaine.

Therapeutics.—It has limited usefulness in oral medicine, serving best as an obtundent.

Nupercaine

Nupercaine Hydrochloride (N.N.R.) is β-diethyl-aminoethylamide of 2-butoxycinchoninic acid hydrochloride. It occurs as a white, crystalline, odorless powder with a bitter taste; very soluble in water (2 in 1) and freely soluble in alcohol. In aqueous solution it is acid to litmus.

Therapeutics.—Nupercaine hydrochloride is a local anesthetic many times more potent than procaine and at least thirty-five times as toxic. It is used for producing infiltration anesthesia in a 1:1,000 to 1:2,000 solution. It should be prepared with distilled water in alkaline-free glassware, as it is readily precipitated by free alkali. It is not an injection anesthetic of first choice, but is used in a 2 to 5 per cent solution as a topical anesthetic in dentistry. Its use is always potentially dangerous.

Apothesine

Apothesine Hydrochloride (N.N.R.) occurs as a white crystalline solid, practically odorless, with a faintly bitter taste. It is very soluble in water, readily soluble in alcohol, and slightly soluble in acetone and ether. The aqueous solution is neutral to litmus and may be sterilized by boiling.

Chemistry.—Apothesine hydrochloride is gamma-diethyl-aminopropyl cinnamate. (See N.N.R. for tests and standards.)

Pharmacodynamics.—Locally applied, apothesine is a weak topical anesthetic. When injected in a 0.5 to 2.0 per cent solution, it is a slow-acting anesthetic with no more potency than procaine but with

greater toxicity. When used as an injection anesthetic, it may be combined with epinephrine. Its absolute toxicity is about twice that of procaine; therefore it is not extensively used as a local anesthetic.

Alypin

Alypin Hydrochloride (N.N.R.) is 2-benzoxy-2 dimethylamino-methyl-l-dimethylaminobutane. It occurs as a white crystalline solid, hygroscopic, without odor, and with a bitter taste. It is very soluble in water, freely soluble in alcohol, and insoluble in ether. Aqueous solutions are neutral to litmus, may be sterilized by boiling, and in a 2 per cent solution alypin is quite stable. (For tests and standards, see N.N.R.)

Therapeutics.—In dentistry it is used in a 2 per cent solution with epinephrine hydrochloride added as a vasoconstrictor. It is not a local anesthetic of first choice for dental use.

Larocaine

Larocaine Hydrochloride (N.N.R.) belongs to the series of local anesthetics obtained by esterification of an amino-alcohol with p-amino-benzoic acid. Larocaine hydrochloride is a white crystalline powder, easily soluble in water (1:3) and less soluble in cold alcohol. Its aqueous solution may be boiled for ten minutes without decomposition. It is primarily employed in dentistry as a topical anesthetic in 5 per cent aqueous solution.

Quinine and Urea Hydrochloride; Quininae et Ureae Hydrochloridum (Quin. et Urea Hydrochlor.), U.S.P.

At ordinary temperature the salt dissolves in its own weight of water with a marked lowering of temperature; its solution is strongly acid. A concentrated solution is straw-colored. The salt is not hygroscopic and is unalterable in the air. It fuses at about 167° F. (75° C.) into a yellow liquid, which congeals on cooling into a yellow mass, with about 10 per cent loss of water of crystallization. It is also readily soluble in alcohol but only sparingly in chloroform. Solutions of quinine and urea hydrochloride can be boiled without alteration, but they readily decompose on standing. They are slightly antiseptic and are tolerant to the addition of ordinary doses of epinephrine. For hypodermic injections, it is usually employed in a 2 per cent solution, using a physiologic saline solution as a vehicle.

When brought in contact with the human blood the poisonous nature of the quinine completely arrests the amoeboid movements of the leucocytes, which assume a darker color, and finally break up into

granular debris. Quinine is a protoplasm poison which in due time kills the tissue cell. The prolonged analgesia, which remains for hours or even days, finds an explanation in the coagulation of the protoplasm. More or less persistent induration follows the injection; it may be traced to an exudate of fibrinous material into the infiltrated tissues, resulting to an edema which may last for weeks. Urea hydrochloride, which is added to quinine hydrochloride in the preparation of this compound, has apparently no physiologic effect on the tissues in the comparatively small doses in which it is employed; its sole purpose is to render the rather sparingly soluble quinine hydrochloride (about 1:34) more soluble. Urethane, antipyrine, and other bodies exercise a similar action on the salt.

Quinine and urea hydrochloride, when employed as a local anesthetic possesses no advantage but many disadvantages as compared to procaine.

DOSAGE.—Not given in U.S.P. (Hypodermic, one dose daily, 1 Gm. [15 grains]. Used chiefly in the treatment of malaria.)

Ampuls of Quinine and Urea Hydrochloride; Ampullae Quininae et Ureae Hydrochloridi (Ampul. Quin. et Urea Hydrochlor.), N.F.—Approximately 0.5 Gm. quinine and urea hydrochloride in 1 cc. of sterile aqueous solution.

DOSAGE.—1 cc. containing about 0.5 Gm. of quinine and urea hydrochloride (N.F.).

Insoluble Local Anesthetic Drugs

The water-insoluble anesthetic drugs cannot be used for injection purposes and are therefore used topically. They may be applied in solution in an organic solvent, such as alcohol, in a suspension in oils or fats, in a paste, or as a dry powder. Their use in solution is restricted by the causticity of the solvents on the mucous membranes. The insoluble powder has little or no topical anesthetic potency. On abraded areas the reaction is different, as all states of the drug produce anesthesia. Their use is confined to allaying pain from abraded areas, for which they are very efficient, analgesia being produced for a considerable period of time. They are relatively nontoxic when used in small quantities.

ETHYL AMINOBENZOATE

ETHYL AMINOBENZOATE; AETHYL AMINOBENZOAS (AETHYL. AMINOBENZ.), U.S.P. (Benzocaine).

Benzocaine occurs as a white crystalline powder, odorless, tasteless, almost insoluble in cold water, soluble in dilute acids, alcohol (1 in 5)

ether, and fatty oils. Chemically it contains the procaine base para-amino benzoic acid esterized with ethyl alcohol, 1-4 $NH_2.C_6H_4.COO.C_2H_5$.

THERAPEUTICS.—Ethyl aminobenzoate is not used as an injection anesthetic drug because of its insolubility in water. It is not an efficient topical anesthetic for the mucous membranes because of the causticity of most of its solvents. In solution in oils, or in suspension in fats it is applied to abraded areas as an obtundent for which it is efficient and long acting. For the control of postoperative pain following tooth extraction A.D.R. gives the following preparation:

℞	Benzocaine		1.5 Gm.
	Chlorobutanol		1.5 Gm.
	Methyl Salicylate		0.3 cc.
	Petrolatum or Lanolin	q.s. ad	30.0 Gm.

PREPARATION.—

Ethyl Aminobenzoate Ointment; Unguentum Aethylis Aminobenzoatis (Ung. Aethyl Aminobenz.), U.S.P.

This ointment is a 5 per cent solution of the drug in white ointment, U.S.P.

BUTYL AMINOBENZOATE

BUTYL AMINOBENZOATE, BUTYLIS AMINOBENZOAS (BUTYL. AMINOBENZ.), U.S.P. (Butesin).

Butyl aminobenzoate occurs as a white, crystalline powder. It is odorless and tasteless, very sparingly soluble in water (1 in 7,000), soluble in dilute acids, alcohol, ether, and in fatty oils. It melts between 57° and 59° C. Chemically it is similar to ethyl aminobenzoate with the ethyl replaced by a butyl group ($C_6H_4NH_2.COOC_4H_9$).

THERAPEUTICS.—The uses of butyl aminobenzoate are similar to those of ethyl aminobenzoate.

ORTHOFORM

ORTHOFORM, A.D.R. Orthoform-New is methyl *m*-amino-*p*-hydroxybenzoate, $C_6H_3.NH_2.OH.CO.O.CH_3$,3:4:1. It occurs as a white crystalline, odorless and tasteless powder, neutral in reaction and melting at 141° to 143° C. It is almost insoluble in water, freely soluble in alcohol and ether, decomposed by boiling, and incompatible with alkalies.

THERAPEUTICS.—Orthoform is beneficial for the relief of pain when placed on excoriated surfaces—as ulcers, burns, etc.—and deserves to be mentioned for the treatment of afterpains arising from the extraction of teeth. As orthoform is irritating to the soft tissues, occasionally sloughing is observed after its too free use as a dusting powder.

Anesthetic Mixtures

			METRIC	APOTH.
℞	Aethyl. Aminobenz.		3 Gm.	gr. xlv
	Glycerin		4 cc.	f3 i
	Alcohol	q.s. ad	30 cc.	f℥ i

M. et ft. Sol.

Sig.: Apply to areas to prevent gagging and to allay pain during prophylaxis.

℞	Benzocaine		3 Gm.	gr. xlv
	Alcohol	To make	30 cc.	℥ i

Mix.

Sig.: Apply (A.D.R.).

℞	Orthoformii			
	Amyli	āā	4 Gm.	3 j

M.

Sig.: Dusting powder.

℞	Benzocaine			
	Chlorobutanol	āā	2 Gm.	3 ss
	Lanolini		30 Gm.	℥ j

M. f. unguentum.

Sig.: Apply.

REFRIGERANT ANESTHETICS

Nerve conduction is most efficient when the temperature of the nerve fiber approximates that of the rest of the body. When the temperature of the nerve is lowered, the conductivity decreases until at 0° C. it is nil. The application of cold was used for years to obtund the sense of pain in inflammation and in minor surgery.

Applications of ice and salt were used with varied results when conditions permitted. It is an emergency measure and has no place in modern surgery.

PREPARATION.—

ETHYL CHLORIDE; AETHYLIS CHLORIDUM (AETHYL. CHLOR.), C_2H_5Cl, U.S.P.

Ethyl chloride is a colorless volatile liquid with an agreeable odor. It boils at 12° C., and must be stored in a solid container. For local refrigerant anesthesia, it is dispensed in a glass tube with a spray nozzle. The drug is applied as a liquid which rapidly evaporates, removing heat from the tissues. The anesthesia is not complete and lasts for about one minute. This is not a satisfactory procedure for intraoral surgery. Care must be practiced to prevent

destruction of tissue or anesthesia of the patient by inhalation of the gas. The vapor is very inflammable.

METHYL CHLORIDE; METHYLIS CHLORIDUM, CH_3Cl.

A colorless, mobile, and very volatile fluid having a rather agreeable odor. It boils at −12° F. (−24.5° C.) and must be kept in strong metallic cylinders. The methyl chloride spray produces a very quick and intense freezing of the tissues, frequently resulting in necrosis; for this reason it is seldom applied in its pure state.

Local anesthesia by means of refrigerant agents is much less employed at present than in former years. The general applicability and comparative safety of local anesthesia by procaine or its substitutes have almost completely superseded the freezing method.

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CHAPTER XI

DRUGS WHICH ACT ON THE RESPIRATORY SYSTEM

Respiration is divided into external and internal respiration. External respiration is carried on by the lungs; it consists of the absorption of oxygen and the giving off of carbon dioxide by the blood as it passes through the lungs. Internal respiration is concerned with the interchanges of oxygen and carbon dioxide by the capillaries and the tissue cells. By the prolonged absence of oxygen and the increase of carbon dioxide the centers of respiration become paralyzed. The normal rhythmic movements of the latter are regulated by certain ganglia. Most of the inhaled oxygen is chemically bound to the hemoglobin, and only a small part is physically dissolved in the blood. Carbon dioxide is always present in the air in small quantities (0.04 per cent); when this amount is materially increased, the air becomes "foul." The exhaled air of man or animal is not poisonous, provided it does not contain too large quantities of carbon dioxide. Pure carbon dioxide is a poisonous gas and produces asphyxia.

Respiration, aside from the changes occurring in the composition of the air, may be materially influenced by injuries of the muscles of the thorax or diaphragm; by contraction of the larger and smaller bronchi and alveoli, which may interfere with the ready passage of the air; by interference with the ready flow of blood through the capillaries preventing close contact with the oxygen; by an inability of the blood to absorb oxygen—when the blood is already chemically saturated with some other gas, as in carbon monoxide poisoning, etc.; or by an inability of the tissue cells to take up oxygen, as in poisoning with cyanides. The usual result of these many disturbances is dyspnea—that is, a difficult or labored breathing. Dyspnea, forcible respiration, is the usual method employed by nature to give relief.

The artificial provision of oxygen, including air, under slight pressure is usually of marked benefit, and incidentally quickly replaces the accumulated carbon dioxide. Drugs which are intended to relieve the various causes of disturbances of respiration depend on the nature of the latter. Hypersecretion of the mucous membranes is checked by mild doses of atropine sulfate, while an increased elimina-

tion is usually obtained by the administration of expectorants. Ipecac, potassium iodide, and ammonium chloride, together with many drugs containing sugar and mucilaginous substances are used to liquefy the dried-up secretions. While not always advisable, the irritation of a cough is best allayed by opium or codeine. Irritability of the centers of respiration is usually readily reduced by opium and related products. True asthma—tonic spasms of the smooth muscle fibers of the bronchial alveoli—is relieved by carefully adjusted doses of atropine sulfate, amyl nitrite, or epinephrine. The centers of respiration may be directly stimulated by hypodermic injections of caffeine. Artificial respiration is of prime importance in cases of complete cessation of respiration.

Respiratory Stimulants

Carbon Dioxide

Carbon Dioxide; Carbonei Dioxidum (Carbon. Dioxid.), U.S.P. (Carbonic Acid Gas).

Carbon dioxide occurs as a heavy, odorless, tasteless, and colorless gas which is freely soluble in water. At high pressures it is converted into a colorless fluid and may be stored in this state.

Pharmacodynamics.—Carbon dioxide is a potent respiratory stimulant when its concentration in the inspired air is above 1 per cent. Excessive amounts, 25 to 30 per cent, cause a depression of respiration and circulation, resulting eventually in death. Haldane and Priestly and Peabody found that a carbon dioxide concentration in the inspired airs of 1.7 per cent increased the minute volume of air over 40 per cent; of 5 per cent CO_2, over 190 per cent; and that 15 to 20 per cent for an hour was not harmful to animals.

Therapeutics.—Carbon dioxide is used by inhalation as a respiratory stimulant. It may be combined with an anesthetic drug for that purpose. As a resuscitation stimulant it is combined with oxygen in a 5 to 7 per cent mixture, and the prostrated patient is forced to inhale it. Carbon dioxide as liberated from carbonated drinks stimulates the stomach, acting as a carminative. It may also be absorbed, acting as a mild respiratory and circulatory stimulant.

Oxygen

Oxygen; Oxygenium (Oxygen), O_2, U.S.P.

Oxygen occurs as a colorless, odorless, tasteless gas, which supports combustion and life. The gas dissolves in water (1 in 32) and in alcohol (1 in 7) at normal pressure and 20° C. It is stored in metal cylinders for therapeutic use.

PHARMACODYNAMICS.—Oxygen is a gas necessary for metabolism in plants and animals. Excessive amounts of oxygen in the inspired air cause a temporary cessation of breathing (apnea); an insufficient amount will cause labored breathing (dyspnea), cyanosis, coma, and death from anoxia. The content of oxygen in the air is about 21 per cent, and the tidal air is about 500 cc., making the volume of oxygen per inspiration about 100 cc. As the expired air contains about 15 per cent oxygen, the amount of this gas removed with each cycle is only about 25 cc. or less. While this supply of oxygen is enough in health, the demands may be greatly increased in disease. Physiologically this is cared for by an increase in the rate and amplitude of respiration; therapeutically the oxygen in the inspired air may be increased until the respiration is normalized.

THERAPEUTICS.—Oxygen is often administered with an anesthetic drug to prevent anoxia. With nitrous oxide, about 5 per cent is added and with ethylene about 10 per cent is added to the anesthetic mixture. For resuscitation a gas mixture of oxygen (5 to 7 per cent) and carbon dioxide (93 to 95 per cent) is used. Oxygen may be administered from a mask, an oxygen tent, or a specially built oxygen chamber.

PICROTOXIN

PICROTOXIN; PICROTOXINUM (PICROTOX.), U.S.P. (Cocculin).

PHARMACODYNAMICS.—Picrotoxin shows only toxic symptoms on normal subjects, large doses producing convulsions. When the respiratory center is depressed by a drug, picrotoxin acts as an analeptic, increasing the rate and amplitude of respiration. (See Medullary Stimulants.)

THERAPEUTICS.—Picrotoxin is an analeptic of first choice in the treatment of poisoning from derivatives of barbituric acid.

DOSAGE.—2 mg. ($\frac{1}{30}$ grain) (U.S.P.).

CAFFEINE

CAFFEINE; CAFFEINA (CAFF.), U.S.P. (Trimethylxanthine).

Caffeine is an alkaloid obtained from coffee, tea, guarana, maté, etc. (See Cerebral Stimulants.)

PHARMACODYNAMICS.—The site of action of caffeine is the medullary center. Normal doses taken orally have little or no stimulating action while similar doses administered parenterally will act as a mild respiratory stimulant. A more pronounced action is observed when the

centers have been depressed, as by drugs, or when greater than average doses of caffeine are given.

THERAPEUTICS.—Caffeine preparations are useful in the treatment of respiratory collapse from drug poisoning.

PREPARATIONS.—

CAFFEINE AND SODIUM BENZOATE INJECTION; INJECTIO CAFFEINAE ET SODII BENZOATIS (INJ. CAFF. ET SOD. BENZ.), U.S.P. (Caffeine and Sodium Benzoate Ampuls).

A sterile solution of a soluble caffeine preparation for hypodermic use.

DOSAGE.—Intramuscular, 0.5 Gm. (7½ grains) (U.S.P.).

Tablets of Caffeine with Sodium Benzoate; Tabellae Caffeinae cum Sodii Benzoate (Tab. Caff. c. Sod. Benz.), N.F.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

STRYCHNINE

Strychnine is an alkaloid obtained from Nux vomica. (See Spinal Cord Stimulants.)

PHARMACODYNAMICS.—The action of strychnine on respiration is probably of central origin. The drug sensitizes the medullary centers exaggerating their actions. Such large doses are necessary for medullary "stimulation" that the cord reflexes are also exaggerated which makes the drug of questionable value. Strychnine is antagonistic to the action of the hypnotics on the medullary centers.

THERAPEUTICS.—Strychnine preparations are of questionable value as respiratory stimulants. They are probably more effective when the centers have been depressed as by a drug, than on the normal centers.

PREPARATIONS.—See Spinal Cord Stimulants.

STRYCHNINE SULFATE TABLETS; TABELLAE STRYCHNINAE SULFATIS (TAB. STRYCH. SULF.), U.S.P.

DOSAGE.—2 mg. (1/30 grain) (U.S.P.).

CAMPHOR

CAMPHOR, CAMPHORA (CAMPH.), U.S.P.

Camphor occurs as a white mass having a characteristic aromatic odor and mildly burning taste. In water it is slightly soluble (1 in 800) and freely soluble in alcohol (1 in 1), chloroform (1 in 0.5), ether (1 in 1), and in fixed and volatile oils.

Camphor is a ketone obtained from the *Cinnamomum camphora*, family *Lauraceae*, or prepared synthetically.

Its molecular weight is 152.23, specific gravity about 0.990 at 25° C., melting point between 175° and 179° C., and it forms eutectic mixtures with chloral hydrate, menthol, thymol, paramonochlorphenol, etc.

PHARMACODYNAMICS.—Systemically, after absorption, its chief site of action is on the medullary centers. Average doses probably have a slight stimulating effect on the circulation and respiration. The cutaneous vessels are slightly dilated with a slight fall in blood pressure. Its action on depressed centers is probably greater than on normal centers, and this conclusion may justify its use in therapeutics.

THERAPEUTICS.—Camphor is a dangerous and unreliable medullary stimulant. It may have some value in treating circulatory and respiratory collapse during the administration of a general anesthetic.

DOSAGE.—Oral or intramuscular, 0.2 Gm. (3 grains) (U.S.P.).

PREPARATION.—

Ampuls of Camphor, Ampullae Camphorae (Ampul. Camphor.), N.F. (Ampuls of Camphor in Oil).

DOSAGE.—Intramuscular, 0.2 Gm. (3 grains) (N.F.).

CORAMINE

Coramine (Nikethamide) is a pyridine derivative with the following formula $C_6H_5CON(C_2H_5)_2$.

It has an oily consistency, is water soluble, and is of synthetic composition.

PHARMACODYNAMICS.—Average doses of coramine act as a respiratory stimulant with little effect on other medullary centers. Its site of action is probably on the carotid body, resulting in a reflex stimulation of the respiratory center. Like most drugs, its action is more pronounced when the center is depressed as in anesthetic or morphine depression. It is less efficient than picrotoxin in treating barbituric acid poisoning. Coramine has only a slight effect on the circulatory system. The margin of safety is good; in animals the toxic dose is ten times the effective therapeutic dose. Coramine is a drug which should be useful in therapeutics when its action is better understood.

Drugs Which Increase Bronchial Secretion

This group of drugs act as parasympathetic stimulants. Their use in therapeutics is very limited. They act on the chemoreceptor substance of the secretory cell, sensitizing it to the action of acetylcholine.

PILOCARPINE NITRATE; PILOCARPINAE NITRAS (PILOCARPIN. NITRAS), U.S.P.

DOSAGE.—5 mg. (1/12 grain) (U.S.P.).

Drugs Which Decrease Bronchial Secretion

The secretory nerves to the glands of the respiratory tract are from the vagus. Therefore, parasympathetic depressant drugs are used to diminish bronchial secretion. Their site of action is on the chemoreceptor substance of the secretory cells, inhibiting the stimulating action of the liberated acetylcholine.

TINCTURE OF BELLADONNA; TINCTURA BELLADONNAE (TR. BELLAD.), U.S.P. (Tincture of Belladonna Leaf).

It contains belladonna leaf (10%), alcohol (68%), and water, and is made by percolation; it yields about 0.03 per cent of alkaloids.

DOSAGE.—0.6 cc. (10 minims) (U.S.P.).

ATROPINE SULFATE; ATROPINAE SULFAS (ATROP. SULF.), U.S.P.

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain) (U.S.P.).

Drugs Which Constrict the Bronchi

The use of bronchial constrictors in therapeutics is very limited. In the aged, the muscles lose tonus, and this condition may be partially corrected by drugs which increase the reactiveness of the spinal cord.

STRYCHNINE SULFATE; STRYCHNINAE SULFAS (STRYCH. SULF.), U.S.P.

DOSAGE.—2 mg. ($\frac{1}{30}$ grain) (U.S.P.).

Drugs Which Dilate the Bronchi

The motor nerves to the smooth muscles of the bronchi are from the vagus; therefore, parasympathetic inhibitor drugs or, better, sympathetic stimulator drugs will relax bronchial spasms in allergic attacks, such as asthma.

ATROPINE SULFATE; ATROPINAE SULFAS (ATROP. SULFAS), U.S.P.

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain) (U.S.P.).

EPINEPHRINE HYDROCHLORIDE INJECTION; INJECTIO EPINEPHRINAE HYDROCHLORIDI (INJ. EPINEPH. HYDROCHLOR.), U.S.P.

A sterile solution of epinephrine hydrochloride in water for injections.

DOSAGE.—1 mg. ($\frac{1}{60}$ grain) (U.S.P.).

EPHEDRINE SULFATE; EPHEDRINAE SULFAS (EPHEDRIN. SULF.), U.S.P.

DOSAGE.—25 mg. ($\frac{3}{8}$ grain) (U.S.P.).

AMYL NITRITE; AMYLIS NITRIS (AMYL. NITRIS), U.S.P.

It acts directly on the smooth muscle, relaxing the spasm.

DOSAGE.—0.2 cc. (3 minims) by inhalation. The amyl nitrite pearl is a very convenient preparation.

AMPHETAMINE SULFATE (BENZEDRINE SULFATE), N.N.R.

It is a volatile sympathomimetic amine which may be administered orally or by inhalation.

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain).

Drugs Which Depress the Cough Centers

The cough center is located in the medulla. The center acts reflexly, and any drug which depresses this center tends to inhibit coughing.

TINCTURE OF OPIUM; TINCTURA OPII (TR. OPII), U.S.P. (Laudanum).

Tincture of opium contains 10 per cent of granulated opium in water and alcohol.

DOSAGE.—0.6 cc. (10 minims) (U.S.P.).

COMPOUND MIXTURE OF OPIUM AND GLYCYRRHIZA; MISTURA OPII ET GLYCYRRHIZAE COMPOSITA (MIST. OPII ET GLYCYRRH. COMP.), N.F. (Brown Mixture).

This mixture contains camphorated tincture of opium 12%, antimony and potassium tartrate 0.024%, with fluid extract of glycyrrhiza, glycerin, and spirit of nitrous ether. Absolute alcohol about 10%.

USES.—Popular cough remedy and expectorant.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

CODEINE, CODEINA, U.S.P.

Codeine acts by directly depressing the cough center.

DOSAGE.—30 mg. ($\frac{1}{2}$ grain) (U.S.P.).

Expectorants

Expectorants are remedies which facilitate the expulsion of mucus from the respiratory tract. They act by decreasing the viscosity of the mucus or by hastening the rate of elimination by activation of the cilia. Expectorants are used to rid the respiratory tract of mucus which acts by obstructing the interchange of gases in external respiration. Their chief uses are in colds, coughs, bronchitis, and pneumonia.

IPECAC

IPECAC; IPECACUANHA (IPECAC.), U.S.P. (Ipecacuanhae radix P.I.)

The root and rhizome of the *Cephaëlis ipecacuanha* and *Cephaëlis acuminata* (family *Rubiaceae*) which grows in the forests of Brazil and Colombia. It must yield not less than 2 per cent of ether-soluble alkaloid, of which emetine is the most important.

THERAPEUTICS.—Ipecac and emetine act as irritants to the stomach, producing nausea, vomiting, and indirectly an expectorant action. They are also indicated in the treatment of amebic dysentery.

DOSAGE.—Emetic, 0.5 Gm. (7½ grains) (U.S.P.). Expectorant dosage 0.1 gm. (1½ grains).

PREPARATIONS.—

Fluidextract of Ipecac, Fluidextractum Ipecacuanhae (Fldext. Ipecac.), U.S.P.

It contains ipecac (100%) in alcohol (30%) and water.

DOSAGE.—Emetic, 0.5 cc. (8 minims) (U.S.P.). Expectorant dosage 0.1 cc. (1½ minims).

Syrup of Ipecac; Syrupus Ipecacuanhae (Syr. Ipecac.), U.S.P.

It contains fluidextract of ipecac (7%) in glycerin and syrup.

DOSAGE.—Emetic, 8 cc. (2 fluidrachms) (U.S.P.).

Tincture of Ipecac; Tinctura Ipecacuanhae (Tr. Ipecac.), N.F.

It contains fluidextract of ipecac (10%), alcohol (21%), and water.

DOSAGE.—0.6 cc. (10 minims) (N.F.).

AMMONIUM SALTS

AMMONIUM CHLORIDE; AMMONII CHLORIDUM (AMMON. CHLORID.), U.S.P.

Ammonium chloride occurs as a white powder, with an ammoniacal odor and a strong saline taste, freely soluble in water (1 in 2.6), sparingly soluble in alcohol (1 in 100), and hygroscopic when exposed to air.

THERAPEUTICS.—Ammonium chloride acts as an expectorant by being secreted with the bronchial mucus, lowering its viscosity which aids in its elimination. It may also excite the bronchial cilia. It is a mild diuretic, increasing the acidity of the urine. Because of its irritating action it is generally prescribed in capsules or added to cough remedies, i.e., Brown Mixture.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

PREPARATION.—

Ammonium Chloride Capsules; Capsulae Ammonii Chloridi (Cap. Ammon. Chlorid.), U.S.P.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

TERPIN HYDRATE

TERPIN HYDRATE; TERPINI HYDRAS (TERPIN. HYD.), U.S.P.

Terpin hydrate is prepared from oil of turpentine and occurs as a colorless crystalline substance sparingly soluble in water (1 in 200)

and freely soluble in alcohol (1 in 13). It is secreted into the bronchi, and by virtue of irritation, it facilitates the removal of mucus by stimulation of the cilia.

PREPARATIONS.—

Elixir of Terpin Hydrate; Elixir Terpini Hydratis (Elix. Terpin. Hyd.), N.F.

It contains terpin hydrate (1.7%), alcohol (40%), glycerin (40%), and water, pleasantly flavored with orange and benzaldehyde and sweetened with syrup (10%).

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Elixir of Terpin Hydrate and Codeine; Elixir Terpini Hydratis et Codeinae (Elix. Terpin. Hyd. et Codein), N.F.

This elixir contains 0.2% of codeine dissolved in the elixir of terpin hydrate. Each spoonful contains 7 mg. (1/8 grain) of codeine. This preparation is not restricted by the National Narcotic Act.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

IODIDES

POTASSIUM IODIDE; POTASSII IODIDUM (POT. IODID.), KI, U.S.P.

Potassium iodide occurs as a white granular powder, without odor, with a pungent saline taste, very soluble in water (1 in 0.7), and soluble in alcohol (1 in 22).

THERAPEUTICS.—Potassium iodide is a saline expectorant being secreted into the bronchi and increasing ciliary activity by irritation. It is also a diuretic, antirheumatic, and nonspecific for syphilis.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

GLYCYRRHIZA (LICORICE)

Licorice is a demulcent which relieves throat irritation and allays coughs. It occurs as a brown powder insoluble in water and alcohol.

PREPARATION.—

Compound Mixture of Opium and Glycyrrhiza; Mistura Opii et Glycyrrhizae Composita (Mist. Opii et Glycyrrh. Comp.), N.F. (Brown Mixture).

This compound contains fluidextract of glycyrrhiza as a demulcent, camphorated tincture of opium (12%) as a cough center depressant, antimony and potassium tartrate as an expectorant, spirit of ethyl nitrite as a bronchial dilator, alcohol (10%), and water.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Benzoin

Compound Tincture of Benzoin; Tinctura Benzoini Composita (Tr. Benz. Co.), U.S.P.

Compound tincture of benzoin contains benzoin (10%), aloe (2%), storax (8%), tolu balsam (4%), in alcohol (77%), and water.

It is used as a local protective for the skin and mucous membranes and as a local stimulant. By inhalation from hot water for the relief of bronchial irritation, use 4 cc. per pint of water.

CHAPTER XII

DRUGS WHICH ACT ON THE CIRCULATORY SYSTEM

CIRCULATORY STIMULANTS AND DEPRESSANTS

Drugs which are employed for the purpose of stimulating the circulation are known as *circulatory stimulants,* and they are referred to as *vasoconstrictors;* while drugs which depress the circulation are spoken of as *circulatory depressants* or *vasodilators.* Those drugs which exercise a tonic influence on the heart are known as *cardiac stimulants.*

Every organ of the body requires for its undisturbed function an uninterrupted rich supply of continuously renewed blood. The blood is inclosed in a system of elastic tubes—the arteries and veins—and the heart. The latter exercises the double function of a muscular suction and pressure pump, and by rhythmic contraction and relaxation produces circulation.

When the normal functions of the circulation are disturbed and the heart has to perform an increased amount of labor, nature has fortunately provided for this emergency by increasing the diameter of the fibers of the heart muscle, and thereby hypertrophy of the heart is established. The heart muscle may carry on this increased work for years, provided the patient avoids any undue exertion, without materially interfering with his welfare; it compensates the weak heart. To relieve or mitigate this compensation, digitalis is the supreme remedy. It performs two functions—it slows the heartbeat and increases the arterial pressure.

Occasionally it is necessary to overcome an acute weakness of the heart—"heart failure." A direct stimulation is best accomplished with caffeine and sodium benzoate, camphor, or epinephrine; to insure their prompt action, they should be injected hypodermically.

For the purpose of increasing the activity of the vasomotor centers, which results in an increase of the blood pressure, stimulants are administered. They act by direct or by reflex action. The principal drugs employed for such purposes are caffeine and, to some extent, atropine. Caffeine acts principally on the vasomotor centers of the medulla oblongata; it increases the blood pressure and the heartbeat becomes slower. To insure quick action caffeine is

preferably administered by hypodermic injection. Atropine in small doses increases the pulse rate as a result of its inhibitory influence on the vagi nerves; it apparently antagonizes the action of morphine, and is much lauded as an antidote in morphine poisoning.

Paralysis, or diminished activity of the vasomotor centers, is accomplished by the administration of the nitrites. The nitrites dilate the peripheral vessels, especially those of the face and in the brain, and they reflexly increase the heartbeat. Amyl nitrite and nitroglycerin are the principal representatives of this group. The vessel wall may be directly influenced by certain drugs, which are applied locally, or by internal administration through the blood. The dilation or contraction of the vessel wall is the result of the action of the drug on the muscle fibers or nerve centers. Dilation of vessels is quickly obtained by externally applied irritants (see Irritants and Counterirritants), while contraction of the vessel is the direct result of the application of certain astringents (see Astringents.) Other drugs exhibit specific action as vasoconstrictors without possessing all the functions of an astringent. The two typical representatives of locally applied vasoconstrictors are cocaine and an extract of the suprarenal gland. The suprarenal gland extract, on account of the ready decomposition of its solution, is not used therapeutically. The hydrochloric salt of its alkaloid, epinephrine, and its synthetic substitutes are the principal pharmaceutic preparations employed for such purposes.

For convenience of study this large group of drugs is subdivided. The pharmacodynamics cannot be understood without a knowledge of the physiology and the gross and microscopic anatomy of the tissues concerned.

Drugs Which Affect the Heart

Drugs may affect the heart action directly or indirectly. Directly they may act on the heart muscle, affecting its irritability and tonus and/or by acting on the conducting tissue, affecting the passage of motor impulses over the heart. The heart may be affected indirectly by changing the peripheral circulation, increasing or decreasing the resistance of the blood in the vessels, or by a nervous reflex from the caroticoaortic system, acting through the autonomic nervous system. Adrenergic and cholinergic drugs act directly on the myoneural junction of the autonomic nerves in the cardiac tissue. The drugs may act as stimulants or as depressants and at times both, resulting in an unreliable response. A stimulation of the heart resulting in a rapid heart rate is not an indication of improved cardiac

function; in fact, it should be construed as a decrease in functional efficiency. The efficient heart is one which is maintaining the optimal blood pressure with the minimal effort. This is generally accomplished with a normal heart rate which allows time for the heart to fill, to empty completely, and to have adequate rest and nutrition. Therefore, most so-called cardiac stimulants normalize the heart rate and increase the minute volume of blood put out by the heart. An overdistention of the cardiac muscle in clinical heart failure probably represents an adaptive mechanism and not a cause of the condition. The overdistention of the cardiac muscle will generally correct itself when the efficiency of the heart is increased. Likewise an increase in venous pressure is a symptom and not a causative agent and will correct itself when the cardiac output is increased. The improved cardiac function observed from digitalis and similar agents in cardiac failure is due chiefly to its action on the heart muscle directly, increasing the tension which the muscle can develop during systole.[1]

Digitalis

DIGITALIS; DIGITALIS (DIGIT.), U.S.P. (Foxglove, Digitalis folium P. I.).

Digitalis is the dried leaves of the second year's growth of the *Digitalis purpurea,* family *Scrophulariaceae.* The potency of digitalis shall be such that, when assayed as directed, 0.1 Gm. shall be equivalent to not less than 1.0 U.S.P. Digitalis Unit. It shall contain less than 6 per cent of moisture and yield less than 5 per cent of acid-insoluble ash. The active principles are glucosides which have a tendency to deteriorate with age. The more important glucosides are digitalin, digitoxin, and digitonin. Digitalis is preferably administered in the form of a powder, tincture, or infusion.

PHARMACODYNAMICS.—The effects of digitalis are seen chiefly on the heart and blood vessels. They are brought about by the action of the drug on four separate structures: (1) heart muscle, (2) conducting tissue in the heart, (3) smooth muscles of the blood vessels, and (4) the autonomic nervous system, affecting the medullary centers, ganglia, and/or myoneural junctions.

Digitalis acts as a cardiac stimulant chiefly by strengthening the heart muscle directly, increasing the tension which the muscle can develop during systole, which results in a stronger contraction and a less complete relaxation. The heart is emptied more completely

[1] Gold, H., and Cattell, M.: Arch. Int. Med. 65: 263, February, 1940.

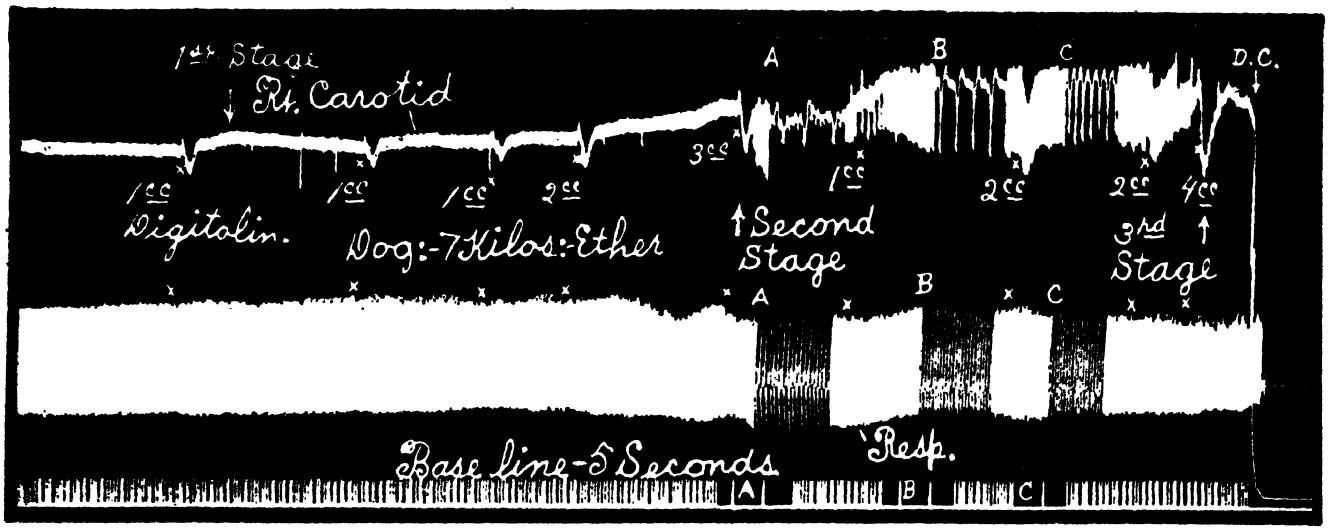

Fig. 21.—Blood pressure and respiration showing the action of digitalin. The three stages are shown and also the fatal delirium cordis, *D.C.* (ventricular fibrillation). Note that the pressure falls to zero at once when the ventricles start to fibrillate. At three places the drum was run at great speed to show the irregularities of the blood pressure (*A, B, C*). The first is the therapeutic stage. (From Jackson: *Experimental Pharmacology and Materia Medica.*)

and the blood ejected with a greater force, which increases the cardiac output and normalizes the blood pressure. The secondary influence of digitalis on the heart may be due, in part, to the primary action of the drug and also to the drug action on other structures. The vagus center is stimulated, resulting in a decrease in the heart rate. This slowing allows time for the auricles to fill more completely and also gives time for rest and for a more normal coronary circulation which results in a more favorable state of muscle nutrition. This vagus influence may be due to a reflex from the sensitized caroticoaortic centers, or to a direct action of the drug on the vagus center. Digitalis retards the transmission of nerve impulses through the auriculoventricular bundle of His, inhibiting auricular fibrillation and permitting the ventricles to contract slowly and to empty completely, thereby increasing the cardiac output. Digitalis produces a stimulation of the vasoconstrictor center, thereby increasing the blood pressure which aids a failing heart in maintaining a normal circulation and prevents further cardiac damage from overwork.

THERAPEUTICS.—Digitalis produces its effect in cardiac failure by increasing the output of the heart, which in turn normalizes the blood pressure, relieves the venous congestion, dyspnea, and dropsy, and increases the kidney output.

Toxic doses are generally manifested by nausea and vomiting resulting from a stimulation of the emetic center.

PREPARATIONS.—

Powdered Digitalis; Digitalis Pulverata (Digit. Pulverat.), U.S.P. Potency.—0.1 Gm. equivalent to 1 U.S.P. Digitalis Unit.

DOSAGE.—0.1 Gm. (1½ grains) (U.S.P.). Overdosage causes nausea and vomiting.

Digitalis Capsules; Capsulae Digitalis (Cap. Digit.), U.S.P.—Digitalis capsules contain an amount of powdered digitalis corresponding to 100 per cent of the labeled amount of powdered digitalis.

DOSAGE.—0.1 Gm. (1½ grains) of digitalis (U.S.P.).

Extract of Digitalis; Extractum Digitalis (Ext. Digit.), N.F. (Powdered Extract of Digitalis).—0.1 Gm. has the potency of 2.75 to 3.25 U.S.P. Digitalis Units.

DOSAGE.—0.03 Gm. (½ grain) (N.F.).

Infusion of Digitalis; Infusum Digitalis (Inf. Digit.), N.F.—Powdered Digitalis (1.5%), alcohol (10%), spirit of cinnamon, and distilled water; freshly prepared. This is an effective form of digitalis, but has no advantage over the tincture.

DOSAGE.—6 cc. (1½ fluidrachms) (N.F.).

Digitalis Injection; Injectio Digitalis (Inj. Digit.), U.S.P.—Digitalis Ampuls). A sterile solution of digitalis alkaloids in water for injection purposes.

DOSAGE.—Intravenous, 1 U.S.P. unit of digitalis (U.S.P.).

Digitalis Tablets; Tabellae Digitalis (Tab. Digit.), U.S.P.

DOSAGE.—0.1 Gm. (1½ grains) of powdered digitalis, U.S.P.

Tincture of Digitalis; Tinctura Digitalis (Tr. Digit.), U.S.P. (Tinctura Digitalis P. I.).—Digitalis (10%) in alcohol and water. Potency: 1 cc. of the tincture is equivalent to 1 U.S.P. Digitalis Unit. Absolute alcohol content about 70 per cent.

DOSAGE.—1 cc. (15 minims) (U.S.P.).

STROPHANTHUS

STROPHANTHUS; STROPHANTHUS (STROPHANTH.), N.F. (Strophanthus seed).

Strophanthus is the dried, ripe seed of the *Strophanthus Kombé* or the *Strophanthus hispidus,* family *Apocynaceae.* When assayed by the prescribed method it possesses a potency per gram equivalent to not less than 55.0 mg. of standard ouabain.

Powdered strophanthus is yellow to light olive in color, odorless, and has a bitter taste.

PHARMACODYNAMICS.—Strophanthus and its glucoside, strophanthin, have an action on the heart and blood vessels similar to that of digitalis, over which it has no advantage. Its action is less predictable than that of digitalis, and often diarrhea is an undesirable side action. Absorption from the alimentary tract is so variable that oral administration is inadvisable.

DOSAGE.—60 mg. (1 grain) (N.F.).

PREPARATION.—

Tincture of Strophanthus; Tinctura Strophanthi (Tr. Strophanth.), N.F. (Tinctura Strophanthi P.I.).—The tincture contains a 10 per cent extract of Strophanthus in benzin and alcohol (90%). One cc. has a potency equivalent to about 5.5 mg. of U.S.P. XII reference ouabain.

DOSAGE.—0.5 cc. (8 minims) (N.F.).

STROPHANTHIN; STROPHANTHINUM (STROPHANTHIN.), U.S.P.

Strophanthin occurs as a glucoside or mixture of glucosides obtained from *Strophanthus Kombé.* The white or yellowish powder is souble in water and diluted alcohol and is nearly insoluble in ether and chloroform.

THERAPEUTICS.—Its action is similar to that of digitalis over which it has no advantage and many disadvantages. In the intestines its absorption is uncertain, making its administration by mouth inadvisable. Strophanthin is extremely poisonous.

DOSAGE.—Daily intravenous, 0.5 mg. ($\frac{1}{120}$ grain) (U.S.P.). Caution should be used in patients who have been taking digitalis.

PREPARATION.—

Strophanthin Injection; Injectio Strophanthini (Inj. Strophanthin.), U.S.P. (Strophanthin Ampuls).

A sterile solution of strophanthin in water for injection purposes.

DOSAGE.—Intravenous, 0.5 mg. ($\frac{1}{120}$ grain) of strophanthin (U.S.P.). Caution should be exercised in using nonofficial strophanthin preparations which have not been carefully standardized (U.D.).

SQUILL

SQUILL, SCILLA (SCILL.), N.F. (Scillae bulbus P.I.).

Squill consists of the cut and dried inner scales of the bulb of the white variety of *Urginea maritima*, known in commerce as white or Mediterraneum squill or of *Urginea indica*, known in commerce as Indian squill, family *Liliaceae*. Powdered squill is yellowish white to pale brown, has slight odor, bitter taste, and it cakes in moist atmosphere.

THERAPEUTICS.—Squill and squill preparations have an action on the heart and circulation similar to digitalis over which it has no advantage.

PREPARATIONS.—

Vinegar of Squill; Acetum Scillae (Acet. Scill.), N.F.—It contains 10 per cent of squill in diluted acetic acid.

DOSAGE.—1 cc. (15 minims) (N.F.).

Syrup of Squill; Syrupus Scillae (Syr. Scill.), N.F.—It contains Vinegar of Squill 45 per cent in sucrose and water.

DOSAGE.—2 cc. (30 minims) (N.F.).

Tincture of Squill, Tinctura Scillae (Tr. Scill.), N.F.—It contains 10 per cent of Squill in alcohol (65%) and water.

DOSAGE.—1 cc. (15 minims) (N.F.).

Fluidextract of Squill, Fluidextractum Scillae (Fldext. Scill.), N.F. —Squill (100%). Absolute alcohol content about 49 per cent.

DOSAGE.—0.1 cc. (1½ minims) (N.F.).

Quinidine

Quinidine is an alkaloid obtained from cinchona bark. It is used in the treatment of malaria and heart disease. Its effects on the heart are produced by (1) decreasing the excitability of the cardiac muscle, preventing premature systoles; (2) increasing the refractory period of the heart muscle as much as 100 per cent, slowing the heart rate and inhibiting fibrillations; (3) depressing the sinoauricular node, producing bradycardia; and (4) inhibiting the conduction of impulses over the heart, resulting in a slower heartbeat and greater cardiac efficiency. This may be caused by a decrease in the excitability of the auriculoventricular node which allows more time between the contraction of the auricles and ventricles.

Quinidine Sulfate; Quinidinae Sulfas (Quinidin. Sulf.), U.S.P.

Quinidine sulfate occurs as white, needle-shaped crystals which darken on exposure to light; it is odorless, has a bitter taste, is sparingly soluble in water (1 in 100), and soluble in alcohol (1 in 10).

Therapeutics.—Quinidine sulfate is a protoplasm poison and destroys protozoa more actively than bacteria. In malaria it is prescribed when quinine is not tolerated. It decreases the conductivity and irritability of the muscles of the auricles and is used to restore normal rhythm of the heart in auricular fibrillations.

Dosage.—(Caution) 0.2 Gm. (3 grains), four times a day (U.S.P.).

Preparation.—

Quinidine Sulfate Tablets; Tabellae Quinidinae Sulfatis (Tab. Quinidin. Sulf.), U.S.P.—The tablets contain 100 per cent of the labelled amount of quinidine sulfate.

Dosage.—0.2 Gm. (3 grains) (U.S.P.).

Epinephrine and Related Drugs

Epinephrine and related drugs act as sympathomimetic substances, i.e., they produce a response in the animal body similar to a sympathetic stimulation. The site of action is the chemoreceptor substance in the effector cells of the heart. These drugs act as a direct stimulant on the chemoreceptor substance or inhibit the action of the esterases which break up the liberated epinephrine. Epinephrine-like substances act as cardiac stimulants (1) by a direct stimulation of the heart muscle, increasing its rate and amplitude, (2) by improving the coronary circulation by a vasodilatation, (3) by a direct stimulation of the peripheral capillaries, and (4) by a reflex stimulation of the vagus center which may normalize the other effects.

PREPARATIONS.—(See Drugs Which Affect the Autonomic Nervous System.)

Solution of Epinephrine Hydrochloride, Liquor Epinephrinae Hydrochloridi (Liq. Epineph. Hydrochlor.), U.S.P.—A sterile solution of epinephrine hydrochloride in water, each 1 cc. contains about 1 mg. of drug.

DOSAGE.—By parenteral injection, 0.5 cc. (8 minims), U.S.P.

RELATED PREPARATIONS:

EPHEDRINE SULFATE; EPHEDRINAE SULFAS (EPHEDRIN. SULF.), U.S.P.

DOSAGE.—25 mg. (3/8 grain) (U.S.P.) Oral.

CAFFEINE AND CAFFEINE PREPARATIONS

CAFFEINE; CAFFEINA (CAFF.), U.S.P. (Trimethylxanthine).

Caffeine is an alkaloid obtained chiefly from coffee. (For complete description, see Cerebral Stimulants.) Caffeine and related xanthine compounds have a stimulating action on the heart; the rate, amplitude, and cardiac output are increased. This effect is brought about by a direct action of the drug on the cardiac muscle. The vagus center is also stimulated, making the cardiac response uncertain. The coronary vessels are probably relaxed, increasing the blood supply to the heart muscle. The blood pressure response is variable. Toxic doses overexcite the heart, often resulting in arrhythmias. Caffeine is a marked cerebral stimulant, often making the patient show signs of mental and motor excitement. It is not a drug of first choice as a cardiac stimulant.

DOSAGE.—0.2 Gm. (3 grains) in capsules (U.S.P.).

PREPARATIONS.—(See Cerebral Stimulants.)

CITRATED CAFFEINE; CAFFEINA CITRATA (CAFF. CIT.), U.S.P.

It is not a new compound but a mixture of caffeine and citric acid, equal parts.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

CAFFEINE AND SODIUM BENZOATE; CAFFEINA ET SODII BENZOATE (CAFF. ET SOD. BENZ.), U.S.P. (Caffeine Sodio-Benzoate).

It is not a new compound but a mixture of caffeine and sodium benzoate, about equal parts. This form of caffeine is freely soluble and employed for hypodermic administration.

DOSAGE.—Oral or intramuscular, 0.5 Gm. (7½ grains) (U.S.P.).

STRYCHNINE

STRYCHNINE; STRYCHNINA (STRYCH.), N.F. (For complete description, see Spinal Cord Stimulants.)

Strychnine and its salts in normal doses have little or no effect on the circulatory system. Larger than normal doses may sensitize the vital medullary centers which exaggerate any stimuli which are received by the circulatory centers.

DOSAGE.—1.5 mg. (1/40 grain) (N.F.).

PREPARATIONS.—

STRYCHNINE NITRATE; STRYCHNINAE NITRAS (STRYCH. NITRAS), N.F.
DOSAGE.—2 mg. (1/30 grain) (N.F.).

STRYCHNINE PHOSPHATE; STRYCHNINAE PHOSPHAS (STRYCH. PHOS.), N.F.
DOSAGE.—2 mg. (1/30 grain) (N.F.).

BELLADONNA AND RELATED DRUGS

Belladonna, hyoscyamus, and stramonium contain alkaloids with a similar action, i.e., blocking the passage of vagus impulses to the heart and thereby removing vagal inhibition. This tends to increase the rate and amplitude of the heartbeat by allowing the sympathetic nervous influence to dominate. The site of action of these drugs is the chemoreceptor substance in the effector cells of the heart, which is depressed and no longer responds to the liberated acetylcholine.

PREPARATIONS.—(See Drugs Which Affect the Autonomic Nervous System.)

Drugs Which Depress the Heart Action

This group of drugs is not used in therapeutics for their effect on the heart. Their importance is from a toxic standpoint; therefore only those drugs used in dental medicine will be mentioned.

PILOCARPINE

Pilocarpine and its salts will depress the rate and amplitude of the heartbeat because of its cholinergic action. The site of action is the chemoreceptor substance in the effector cells of the heart muscle, the drug sensitizing this tissue to the action of acetylcholine. This allows the parasympathetic nervous system to dominate, inhibiting the heart rate. (For a complete description, see Drugs Which Depress the Parasympathetic Nervous System.)

ACONITE

ACONITE; ACONITUM (ACONIT.), N.F. (Monkshood, Aconite Root, Aconiti Tuber. P.I.).

The source is from the dried tuberous root of the *Aconitum Napellus*, family *Ranunculaceae*. Powdered aconite is pale brown to yel-

lowish orange in color with a very slight odor and sweetish taste, which becomes acrid upon standing.

PHARMACODYNAMICS.—Its active principle is the alkaloid aconitine which is insoluble in water and readily soluble in alcohol. The alkaloidal content of the tubers will vary greatly, and for this reason the crude drug is not used as such. The liquid preparations deteriorate on standing, therefore only freshly prepared solutions should be used. Aconite is a powerful poison which slows the heart rate and weakens the heart muscle. This is accomplished by a stimulation of the vagus center and by a direct action on the heart muscle. It also depresses the respiratory center. As it reduces the body temperature in fever, it was used as an antipyretic. Locally applied, aconite preparations anesthetize the terminations of the sensory nerves of the skin and mucous membranes, hence its use in dentistry as a local obtundent for pain of infectious or neuralgic origin.

THERAPEUTICS.—Becauses of it toxicity the use of aconite-containing preparations is contraindicated for application to the skin and mucous membranes.

TOXICOLOGY.—If a large dose of tincture of aconite is absorbed, a peculiar feeling of warmth in the mouth and the throat is manifested. It is followed by a pricking and tingling sensation, and accompanied by a profuse flow of saliva and frequent vomiting. Death results from paralysis of the respiratory centers. Emetics, strong coffee, and tea are indicated, together with general stimulants.

PREPARATIONS.—

Compound Dental Liniment of Aconite and Iodine; Dentilinimentum Aconiti et Iodi Compositum (Dentilin. Aconit. et Iodi Comp.), N. F.—Iodine (2%) and chloroform (30%), in fluidextract of aconite (25%), alcohol and distilled water. Absolute alcohol content about 53 per cent.

Fluidextract of Aconite; Fluidextractum Aconiti (Fldext. Aconit.), N.F.—One cubic centimeter is equivalent to 1.5 mg. of Reference Aconitine, U.S.P. Absolute alcohol content 65 per cent.

DOSAGE.—0.06 cc. (1 minim) (N.F.). Better to use the tincture.

Liniment of Aconite and Chloroform; Linimentum Aconiti et Chloroformi (Lin. Aconit. et Chlorof.), N.F.—Fluidextract of aconite (4.5%), in alcohol, chloroform, and camphor and soap liniment.

Tincture of Aconite; Tinctura Aconiti (Tr. Aconit.), N.F. (Tinctura Aconiti P.I.).—Aconite (10%) in alcohol and distilled water. Assayed biologically (see under Aconitum). Absolute alcohol content about 65 per cent.

DOSAGE.—0.6 cc. (10 minims) (N.F.).

Drugs Which Affect the Caliber of the Blood Vessels

The changes in the caliber of the blood vessels may be local, affecting the blood supply in a small area or in one organ; or it may be general, affecting the blood supply of all tissues and affecting the general blood pressure. The vasomotor nerves are of two sets, the vasoconstrictor nerves which are from the sympathetic outflow (thoracicolumbar) and the vasodilator nerves which are from the parasympathetic outflow (craniosacral). This is only a general rule, as there are variations. The veins are scarcely, if at all, influenced by the vasomotor nerves. The capillaries have no muscular coat and dilate or contract as the blood pressure varies. The importance of maintaining a normal blood pressure is to insure an adequate circulation of blood to the vital organs.

Vasoconstrictor Drugs

For epinephrine and related drugs, see Adrenergic Drugs, p. 138.

Ammonia Compounds

Ammonia is obtained as a by-product in the manufacture of coal gas. It occurs as a colorless gas, having an irritating odor; it is soluble in water, hydrolyzing to form ammonium hydroxide.

Pharmacodynamics.—Locally, ammonia and ammonium compounds are irritants, rubefacients, vesicants, and caustics, depending on the concentration and the time of exposure. It is an irritant to the stomach, producing a carminative action.

Following the inhalation of the gas or the swallowing of an ammonia preparation, the irritated mucous membranes produce a reflex stimulation of the vasoconstrictor and respiratory centers; thereby increasing the blood pressure, decreasing the amount of blood in the large vessels, increasing the amount of blood in the brain, and increasing the rate and amplitude of respiration.

After the drug is absorbed, it is rapidly changed to urea in the liver, chiefly, often before any central action can be produced. This demonstrates that the action of ammonia is chiefly local.

Therapeutics.—Ammonia-liberating compounds act as reflex stimulants to the heart and blood vessels, increasing the blood pressure. The vasoconstriction removes the blood stasis in the large vessels, normalizing the distribution of blood throughout the body. This makes ammonium compounds useful in the prevention and treatment of fainting. Normal respiration is not appreciably affected but a depressed respiratory rate may be temporarily stimulated. Ammonia preparations are also effective as expectorants, carminatives, and antacids.

PREPARATIONS.—

Ammonia Liniment; Linimentum Ammoniae (Lin. Ammon.), N.F. (Hartshorn Liniment).

Ammonia liniment is a 25 per cent solution of ammonia water in oleic acid and sesame oil.

THERAPEUTICS.—It is used locally as a counterirritant.

Diluted Solution of Ammonia; Liquor Ammoniae Dilutus (Liq. Ammon. Dil.), U.S.P. (Ammonia Water).—It is a 10 per cent solution of ammonia gas in distilled water.

THERAPEUTICS.—Used locally as a counterirritant and antacid. It is too strong for inhalation use.

Strong Solution of Ammonia; Liquor Ammoniae Fortis (Liq. Ammon. Fort.), U.S.P. (Stronger Ammonia Water).—It is a 28 per cent solution of ammonia gas in water.

THERAPEUTICS.—It has no therapeutic use.

DOSAGE.—*Caution:* the solution and gas are very caustic.

Anisated Spirit of Ammonia; Spiritus Ammoniae Anisatus (Sp. Ammon. Anis.), N.F.—It contains ammonia water (20%), anethol, alcohol (73%), and water.

THERAPEUTICS.—It is an aromatic carminative.

DOSAGE.—1 cc. (15 minims) (N.F.).

AMMONIUM SALTS.—

Solution of Ammonium Acetate; Liquor Ammonii Acetatis (Liq. Ammon. Acet.), N.F.

Solution of ammonium acetate contains $CH_3COO.NH_4$ (7%) and should be freshly prepared, as it deteriorates readily.

THERAPEUTICS.—It is a diaphoretic and diuretic of questionable value.

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

AMMONIUM CARBONATE; AMMONII CARBONAS (AMMON. CARB.), U.S.P.

Ammonium carbonate is an impure mixture of ammonium hydrogen carbonate and ammonium carbamate which yields about 31 per cent of ammonia. It occurs as a white crystalline solid, with the odor of ammonia and a sharp ammoniacal taste; it is very soluble in water (1 in 4), and incompletely soluble in alcohol.

THERAPEUTICS.—It is used in preparations as expectorants, cough preparations, and smelling salts.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Expectorant Mixture, Mistura Pectoralis (Mist. Pect.), N.F. **(Stoke's Expectorant).**

Expectorant mixture contains ammonium carbonate (1.8%), fluidextract of senega and squill (each 3.5%), camphorated tincture of opium (17.5%), syrup of tolu balsam, alcohol (11%) and water.

THERAPEUTIC.—Expectorant of questionable value.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Aromatic Spirit of Ammonia, Spiritus Ammoniae Aromaticus (Sp. Ammon. Arom.), U.S.P.—It contains ammonium carbonate (3.4%), ammonia water (9%), and oils of lemon, lavender, and myristica in alcohol (65%), and water.

THERAPEUTICS.—Aromatic spirit of ammonia is used orally and by inhalation for the prevention and treatment of fainting. The fainting patient should be placed in the shock position to return the blood to the brain. The unconscious patient should be given inhalations of the spirit, 2 cc. on a gauze sponge held before the nostrils; conscious patients may be given either inhalations or a diluted solution of the spirit orally. An unconscious patient should never be given fluid to drink as it may be aspirated into the lungs. It is useful as a gastric antidote in acid poisoning.

DOSAGE.—2 cc. (30 minims) by inhalation or well diluted in water.

AMMONIUM CHLORIDE; AMMONII CHLORIDUM (AMMON. CHLORID.), NH_4Cl, U.S.P.

Ammonium chloride occurs as a white crystalline solid, without odor and with a saline taste; it is freely soluble in water (1 in 2.6), and sparingly soluble in alcohol (1 in 100).

THERAPEUTICS.—It is an expectorant and often added to cough preparations. It has diuretic properties and renders the urine alkaline.

DOSAGE.—Expectorant, single dose, 0.3 Gm. (5 grains). Diuretic, daily dose 3 to 6 Gm. (45 to 90 grains).

Vasodilator Drugs

THE NITRITES

This group of nitrogen compounds is composed of nitrites, nitrous ethers, and compounds which by analysis liberate the above-mentioned compounds. The stable inorganic nitrates are slowly broken down by the intestinal flora and when taken in large amounts may give rise to nitrite poisoning. Less stable nitrates are readily reduced to liberate the active nitrite ion. The nitrites were introduced into therapeutics by Guthrie in 1859.

PHARMACODYNAMICS.—The nitrites produce a vasodilation without apparently depressing the vasoconstrictor center or stimulating the vasodilator center. The site of action is directly on the blood vessels, acting antagonistic to epinephrine. The effect of this vasodilation is a

fall in the blood pressure. The cutaneous vessels are affected first, then the visceral. The vasoconstrictor center is indirectly affected by the cerebral anemia which tends to overcome the peripheral vasodilation. The nitrites act on all smooth muscles after denervation, suggesting a depression action on the contractile substance. There is no direct effect on the heart; indirectly the heart rate is accelerated by a reflex stimulation through the caroticoaortic centers by the falling blood pressure. The respiratory center is stimulated by the cerebral anemia which increases the rate and amplitude of the breathing. The bronchioles are dilated, relieving motor spasms from asthma and anaphylaxis.

THERAPEUTICS.—The nitrites are used for the prevention and treatment of angina pectoris. They dilate the coronary artery, relieving the muscle spasms and normalizing the circulation of blood to the cardiac muscle. They lower the blood pressure and may be used for the temporary relief of hypertension. Continued use induces the formation of methemoglobin with all of its symptoms. This factor contraindicates the continued administration of these drugs. Fainting in patients with a normal heart may be revived with the nitrites. The falling blood pressure reflexly stimulates the heart and corrects the vasodilation. Care must be used in its administration in circulatory collapse, as it may exaggerate the symptoms. The blood supply to the kidneys may be increased, producing diuresis. Their duration of action is from five minutes to five hours, varying with each drug.

TOXICOLOGY.—The nitrites produce a rapid tolerance and continually larger doses must be administered to get a sustained action. The duration of action varies with the drug; amyl nitrite acts for only seven minutes, while erythrol nitrate lasts for five hours. The early symptoms of toxicity are headache, restlessness, dyspnea, and fainting. Methemoglobin may result with cyanosis and asphyxia. The cerebral cortex is stimulated, resulting in sensory and motor excitement.

TREATMENT.—The patient should be placed in the shock position to promote the circulation of blood to the brain. Vasoconstrictor drugs (epinephrine) may be given to normalize the blood pressure. Artificial respiration, or inhalations of oxygen and carbon dioxide are indicated in anoxia.

PREPARATIONS.—

Amyl Nitrite; Amylis Nitris (Amyl. Nitris), U.S.P.

The official preparation of amyl nitrite must contain not less than 90 per cent of iso-amyl nitrite ($C_5H_{11}ONO$). It occurs as a yellowish, volatile liquid, having a fruity odor and pungent taste. It is almost insoluble in water and miscible with alcohol.

THERAPEUTICS.—Amyl nitrite is a prompt acting vasodilator, used especially in vasospasms of angina pectoris, asthma, and in general convulsions. Its duration of action is short, generally lowering the blood pressure for five to seven minutes. The drug may be purchased in "pearls" which contain one official dose. These are broken and the contents inhaled.

DOSAGE.—0.2 cc. (3 minims) by inhalation (U.S.P.).

Spirit of Ethyl Nitrite; Spiritus Aethylis Nitritis (Sp. Aeth. Nitrit.), N.F. (Spirit of Nitrous Ether, Sweet Spirit of Nitre).—This preparation contains about 4 per cent ethyl nitrite in 90 per cent alcohol and water to make 100 per cent.

THERAPEUTICS.—It is very unstable and therefore unreliable in its action. Its chief use is as a weak diuretic and diaphoretic, having the characteristic action of a weak nitrite.

DOSAGE.—2 cc. (30 minims) (N.F.).

GLYCERYL TRINITRATE; GLYCERYLIS TRINITRAS ($C_3H_5(NO_3)_3$ (Nitroglycerin, trinitrin, Glonoin).

ACTION AND USES.—Vasodilator, acting more slowly than amyl nitrite.

Spirit of Glyceryl Trinitrate; Spiritus Glycerylis Trinitratis (Sp. Glyceryl. Trinitrat.), U.S.P. (Solutio nitroglycerini spirituosa P.I., Spirit of Nitroglycerin).

Spirit of glyceryl trinitrate consists of glyceryl trinitrate (1%) in alcohol.

It is a clear, colorless liquid, having the odor and taste of alcohol; even small doses produce violent headache. Glyceryl trinitrate is also marketed in tablet form; the tablets readily deteriorate.

Caution—Great care must be exercised in dispensing, handling, packing, transporting, and storing this Spirit, as a dangerous explosion may result if any considerable quantity of it is spilled, and the alcohol wholly or partially lost by evaporation. If, through accident, it is spilled, a solution of potassium or sodium hydroxide must be poured over it at once to decompose the glyceryl trinitrate. (U.S.P.)

DOSAGE.—0.06 cc. (1 minim) (U.S.P.), dropped on the tongue, or taken after diluting with water.

Tablets of Glyceryl Trinitrate; Tabellae Glycerylis Trinitratis (Tab. Glyceryl. Trinitrat.), U.S.P. (Nitroglycerin Tablets).

DOSAGE.—0.4 mg. ($\frac{1}{150}$ grain) of glyceryl trinitrate (U.S.P.).

SODIUM NITRITE; SODII NITRIS (SOD. NITRIS), $NaNO_2$, U.S.P.

Sodium nitrite occurs as colorless, odorless crystals, having a mild saline taste. It is freely soluble in water (1 in 1.5), but only spar-

ingly soluble in alcohol. It is deliquescent and decomposes when exposed to moisture or air.

THERAPEUTICS.—Sodium nitrite is a vasodilator drug similar in action to nitroglycerin, although the action is slower and more prolonged.

DOSAGE.—60 mg. (1 grain) (U.S.P.).

Tablets of Sodium Nitrite; Tabellae Sodii Nitritis (Tab. Sod. Nitrit.), U.S.P.

DOSAGE.—60 mg. (1 grain) of sodium nitrite (U.S.P.).

HISTAMINE

Histamine is obtained from the amino acid histadine by decarboxylation. It is liberated by the mucosa of the stomach, circulated by the blood, and acts as a hormone to stimulate gastric secretion (secretin). It is formed in damaged and diseased tissue and may be a symptom-producer in shock. The intestinal bacteria will form histamine by putrefaction, but its absorption and circulation in the blood, per se, is doubted. Its action varies with species. In man the site of action is the muscle cell; the arterioles and capillaries dilate. The permeability of the capillaries is decreased, and edema results. The uterus, bronchi, and gall gladder are stimulated by a direct action on the muscles.

THERAPEUTICS.—As a drug, it is applied to the skin where it is absorbed, producing vasodilation and acting as a counterirritant. It is ineffective when taken orally. Subcutaneous doses will produce a vasodilation by a direct action on the smooth vessels, resulting in a fall in blood pressure. It may also be used for testing the ability of the stomach to secrete hydrochloric acid. The toxic manifestations of histamine are varied and frequent, making it a doubtful drug for therapeutic use.

PREPARATIONS.—

Histamine Phosphate; Histaminae Phosphas (Histamin. Phos.), U.S.P.—Histamine phosphate occurs as colorless and odorless crystals and is soluble in water (1 in 4).

DOSAGE.—Subcutaneous, 0.3 mg. (1/200 grain) (U.S.P.)

Histamine Phosphate Injection; Injectio Histaminae Phosphatis (Inj. Histamin. Phos.), U.S.P.

DOSAGE.—Intramuscular, 0.3 mg. (1/200 grain) (U.S.P.).

CHAPTER XIII

DRUGS WHICH AFFECT THE BLOOD

ANTIANEMIC FACTORS

The successful treatment of anemia began about 1926 as a result of the researches of Whipple, and Minot and Murphy. Anemia may be classified as pernicious anemia and simple anemia.

Pernicious anemia is a symptom-complex arising from a long continued deficiency of a specific substance found chiefly in the liver. The exact nature of this substance is unknown, and it has been termed "antianemia principle." Pernicious anemia is a fatal disease unless controlled by proper medication. The known factors which control the formation of normal red blood cells are: (1) a dietary factor normally present in foods, (2) a substance secreted by the stomach during digestion, (3) a possible combination factor of 1 and 2 absorbed by the intestines, (4) storage of this antianemic substance by the liver, and (5) utilization of this antianemic substance by the hemopoietic tissues.

Simple anemia is not a fatal disease nor of complicated etiology. The causes may be (1) a dietary deficiency of adequate proteins, of vitamins, and of minerals, such as iron and copper, (2) hemorrhage, (3) corpuscular poisons as potassium chlorate, (4) infection, (5) red cell destroying agents such as snake venom, etc. The treatment is simple; rest, adequate diet, freedom from poisons, control of infections, fresh air, and exercise. Recovery is the rule but recurrences are frequent.

Biological Preparations

EXTRACT OF LIVER; EXTRACTUM HEPATIS (EXT. HEPAT.), U.S.P. (Dry Liver Extract).

Extract of liver is a dry brownish powder containing the soluble thermostable fraction of mammalian liver. It is used to increase the number of erythrocytes in the blood in both simple and pernicious anemia.

DOSAGE.—One U.S.P. unit.

Solution of Liver; Liquor Hepatis (Liq. Hepat.), U.S.P. (Liquid Extract of Liver).

USES.—Same as the extract.

DOSAGE.—One U.S.P. unit.

Liver Injection; Injectio Hepatis (Inj. Hepat.), U.S.P.

USES.—Same as the extract, except prepared for injection purposes.

POWDERED STOMACH; STOMACHUS PULVERATUS (STOMACH, PULV.), U.S.P. (Stomachus U.S.P. XI, Dried Stomach).

Powdered stomach is the dried, powdered, defatted wall of the hog stomach.

USES.—In the treatment of pernicious anemia.

AVERAGE DOSE.—One U.S.P. unit daily.

Copper Salts

Copper has been classed as a nutritional essential since 1921. This element apparently acts as a catalyst in the process of hemoglobin formation. Its chemistry of action is not understood. The daily requirement of copper has not been established but may be about 0.1 mg. per Kg. of body weight. Since the average mixed diet contains from 0.4 to 0.8 mg. per day; there is little likelihood of a dietary deficiency of this element in the adult diet. Infants on a milk diet may be deficient in both iron and copper which may predispose anemia. Copper in a soluble form is absorbed from the intestines. In the fluid and fixed tissues it probably exists as a copper proteinate, the exact nature of which is unknown. All tissues appear to store this element, particularly the erythrocytes, liver, and spleen. The action of copper in hemoglobin formation appears to be concerned with the metabolism of iron, producing a hemoglobin response in anemia. Its therapeutic indication in the treatment of anemias in adults on a normal dietary regime is questionable. For infants on a milk diet, a daily dose of 1 to 3 mg. dissolved in milk may be administered. The adult daily dosage is from 10 to 30 mg. taken in capsules to prevent nausea.

CUPRIC SULFATE; CUPRI SULFAS (CUPR. SULF.), $Cu\,SO_4.5\,H_2O$, U.S.P. (Copper Sulfate).

No official dosage.

COPPER CITRATE, CUPRUM CITRATUM, N.N.R.

Uses similar to those of copper sulfate but it ionizes less.

No official dosage.

Iron Preparations

The normal adult body contains about 3 grams of iron or enough to make a two-inch nail. The average amount of iron in the blood of an adult is about 52 mg. per 100 cc. Sherman found the average American diet to be deficient in this element, the adult requirements being about 12 to 18 mg. per day. Ingested iron, inorganic or organic, is absorbed chiefly in the duodenum and upper jejunum and to a

lesser extent in the lower intestine. The normal gastric acidity favors absorption by forming the more soluble chloride salt. The blood and red cells account for about 70 per cent of the total iron; the other 30 per cent is found as muscle hemoglobin, and in the liver, spleen, and bone marrow. The excretion of iron through the urine is negligible. The large intestine acts as the important organ for its elimination, the fecal content of iron being from 10 to 25 mg. per day.

The therapeutic indication for iron preparations is in hypochromic anemias. In uncomplicated cases the color index should show an immediate improvement after the administration of iron. Iron by the oral route may cause constipation or to a lesser extent, diarrhea. The ferric salts are more prone to offend than the ferrous salts. One salt seems to be about as efficacious as another. The number of erythrocytes will generally increase with iron treatment; the size and shape will approach normal. The reticulocyte count may also increase. (See *Useful Drugs.*)

PREPARATIONS.—The prescribing of iron preparations may be simplified by using only the U.S.P. listed preparations.

PILLS OF FERROUS CARBONATE; PILLULAE FERRI CARBONATIS (PIL. FERR. CARB.), U.S.P. (Blaud's Pills).

Each pill contains 1 grain of Fe CO_3.

DOSAGE.—5 pills (U.S.P.). This is suitable for small doses, but not for administration of the recommended daily dose, which is equivalent to 1 Gm. (15 grains) of metallic iron, and would require about 33 pills.

TINCTURE OF FERRIC CHLORIDE; TINCTURA FERRI CHLORIDI (TR. FERR. CHLOR.), N.F. (Tincture of Iron).

Tincture of ferric chloride contains not less than 4.5 per cent of iron in alcohol 61 per cent.

THERAPEUTICS.—Local astringent and relatively irritant hematinic.

DOSAGE.—0.6 cc. (10 minims) (N.F.).

IRON AND AMMONIUM CITRATES; FERRI ET AMMONII CITRATES (FERR. ET AMMON. CIT.), U.S.P.

Iron citrate is rendered more readily soluble by the addition of ammonium citrate. Iron and ammonium citrates contains about 17 per cent of iron.

THERAPEUTICS.—Practically nonirritating hematinic.

DOSAGE.—1 Gm. (15 grains). U.S.P.

Iron and Ammonium Citrates Capsules; Capsulae Ferri et Ammonii Citratum (Cap. Ferr. et Ammon. Cit.), U.S.P.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Green Iron and Ammonium Citrates; Ferri et Ammonii Citrate Virides (Ferr. et Ammon. Cit. Virid.), U.S.P.

Green iron and ammonium citrates contains about 15 per cent of iron.

THERAPEUTICS.—Hematinic.

DOSAGE.—By parenteral injection, 0.06 Gm. (1 grain), U.S.P.

Ampuls of Green Iron and Ammonium Citrates; Ampullae Ferri et Ammonii Citratum Viridum (Ampul. Ferr. et Ammon. Cit. Virid.), N.F.

THERAPEUTICS.—Hematinic.

DOSAGE.—0.1 Gm. (1½ grains) (N.F.).

AGRANULOCYTOSIS (LEUCOPENIA)

Agranulocytosis is a disease of the blood cells characterized by a marked fall in the leucocyte count. The cause of this blood dyscrasia is not well understood, but it has been associated with the ingestion of certain drugs, such as aminopyrine. As only a few patients respond to the drug in this manner, the basic cause appears to be an allergy. The symptoms of the disease are fever, ulcerative lesions of the mucous membranes, hypertrophic gingivitis, ulcerative gingivitis, gingival hemorrhage, general malaise, prostration, and death. The blood picture shows a marked fall in the number of granulocytes, the erythrocytes and platelets remaining unchanged. The site of the disease is the bone marrow, which becomes congested with immature granulocytes which fail to develop until proper medication is instituted.

Pentnucleotide, N.N.R., is a clear, pale yellow solution, having a mild saline taste.

DOSAGE.—Content of one vial (10 cc.) undiluted, injected into the gluteal muscle twice a day until the white cell count approaches normal and then once a day until the blood count is normal for at least three days. Repeat treatment if necessary. (N.N.R.)

HEMOSTATICS AND STYPTICS

Hemostatics and styptics are drugs and agents which arrest the flow of blood. Their action is local, applied to the bleeding area. Before attempting surgery it is wise to question the patient to ascertain whether or not he is a bleeder. In cases of doubt, a test of the bleeding time or the clotting time should be made. There are two types of dangerous hemorrhage: (1) a rapid loss of large amounts of blood and (2) a continuted hemorrhage that lasts for hours or days.

Both types result in shock and possibly death. Drugs are useful in controlling hemorrhage, but drugs plus a gauze sponge held in place with pressure is the procedure of choice in dental surgery.

The seat and the nature of the hemorrhage control the methods of treatment. Hemorrhage from large vessels is controlled preferably by mechanical means—as ligatures, torsion, tamponing, or by the actual cautery—while small external bleedings are often readily checked by the direct application of drugs which act as true hemostatics. Complete immobilization of the part and complete rest of the patient, with abstinence from liquid food, especially alcohol, are of marked benefit.

In accordance with the nature of their action, hemostatics are closely related to astringents, protectives, and caustics. For the sake of convenience, they may be divided as follows:

1. *Absorbents.* Purified cotton, styptic cotton, styptic collodion, and many indifferent powders—starch, talc, charcoal, etc. These materials form a protective matrix over the broken vessel wall.

2. *Caustics and astringents.* (a) Metallic salts—zinc chloride, silver nitrate, potassium permanganate, iron chloride, iron subsulfate, alum, etc., and all acids sufficiently diluted so as not to cauterize may be classified under this heading. (b) Tannic acid, or its various modifications.

3. *Agents which act after being absorbed into the circulation.* Gelatin solution, calcium chloride, calcium lactate, whole blood, etc.

4. *Agents which act on the vessels, but not on the blood.* The alkaloid of the suprarenal medulla, ephedrine, neosynephrine, cobefrin, styptol, etc. These drugs act as vasoconstrictors. The smooth muscular coat of the blood vessels is constricted by the direct action of drugs in two ways—either by their external application or by their absorption through the blood stream.

5. Vitamin K deficiency is associated with a hypoprothrombinemia which retards the time required for blood clotting. Its usefulness in dental therapeutics has not been established.[1, 2]

METHODS.—

1. Heat, theoretically, should hasten coagulation, but it also produces a vasodilation which may increase the bleeding time.

2. Cold produces a temporary vasoconstriction which may reduce the blood flow, but it also may increase the clotting time.

3. Application of foreign substances, such as sterile cotton or gauze, applied to the bleeding area and held firmly in place until the danger

[1] Snell, A. M., and Butt, H. R.: J. A. M. A. 113: 2056, Dec. 2, 1939.
[2] Report of the Council, J. A. D. A., Vol. 27, Dec. 1940, pages 1986-1988.

of hemorrhage is passed is the method of choice for dental surgery. This foreign substance acts as a matrix for the blood clot.

4. Tourniquet is a mechanical appliance for exerting pressure on an artery or vein to stop hemorrhage. For arterial bleeding it should be placed proximal to the hemorrhage; for venous bleeding it is placed distal to the hemorrhage.

5. Pressure at the site of hemorrhage, using a sterile pack and exerting pressure with the hand or by bandaging.

6. Suturing, closing an open wound with ligatures. A sterile procedure is necessary.

7. Ligation (tying off) an artery or vein. A sterile procedure is necessary.

8. Hemostatic forceps used for clamping blood vessels.

9. Rest of a part or of the entire body is always desirable.

10. Position of the part; elevation to lower the blood pressure in the bleeding area.

Absorbents

PURIFIED COTTON; GOSSYPIUM PURIFICATUM (GOSSYP. PURIF.), U.S.P. (Absorbent Cotton).

The hairs of the seed of the cotton plant freed from adhering impurities and deprived of fatty matter.

THERAPEUTICS.—Used as an absorbent surgical dressing and as a filtering agent.

CAUTION.—*Purified cotton must not be used for dressings without resterilization if the unopened container displays any evidence of damage or if the container has been opened previously.* (U.S.P.)

STYPTIC COTTON; GOSSYPIUM STYPTICUM.

Absorbent cotton saturated with various styptic solutions—solution of salts of iron, alum, stypticin, styptol, etc.

GAUZE BANDAGE; LIGAMENTUM CARBASI ABSORBENS (LIG. CARBAS. (ABSORB.), U.S.P. (Roller Gauze Bandage).

USES.—A sterile protective bandage.

Styptics

This group of compounds precipitates proteins from solution, contracts muscular tissue, and causes a condensation of other tissues. Their hemostatic action is accomplished by a coagulation of the blood and a contraction of the tissues at the site of hemorrhage which tends to obstruct the escape of blood from the ruptured vessel walls. The

best results are obtained with the application of the drug on gauze firmly held at the site of hemorrhage with pressure until the bleeding is checked.

Iron Salts

Solution of Ferric Chloride; Liquor Ferri Chloridi (Liq. Ferr. Chlor.), N.F. (Solution of Iron Perchloride).—$FeCl_3$ (about 10.5%). It is a reddish-brown liquid, having a faint odor of hydrochloric acid and a strongly styptic taste.

Dosage.—0.1 cc. (1½ minims) (N.F.).

Tincture of Ferric Chloride; Tinctura Ferri Chloridi (Tr. Ferr. Chlor.), N.F. (Tincture of Iron).—Ferric chloride (about 13%) corresponding to not less than 4.5 per cent of iron. Made by diluting a solution of ferric chloride (35%) with alcohol. Absolute alcoholic content about 61 per cent.

Action and Uses.—Astringent, hematinic but relatively irritant.

Dosage.—0.6 cc. (10 minims) (N.F.).

Ferric Subsulfate; Ferri Subsulfas (Iron Subsulfate, Monsel's Powder or Salt).

A yellowish hygroscopic powder, readily soluble in water and of an astringent, styptic taste. It should be kept in well-stoppered bottles.

Solution of Ferric Subsulfate; Liquor Ferri Subsulfatis (Liq. Ferr. Subsulf.), N.F. (Monsel's Solution, Solution of Basic Ferric Sulfate). Monsel's solution is an aqueous solution of basic ferric sulfate. It is a dark reddish-brown liquid, odorless or nearly so, strongly styptic taste and an acid reaction.

Uses.—Local styptic and astringent, undiluted.

Dosage.—0.2 cc. (3 minims) (N.F.).

The above-mentioned iron preparations form a dirty, black coagulum with the blood and the lacerated tissues.

Aluminum Salts

Alum; Alumen (Alum.), $AlNH_4(SO_4)_2.12H_2O$ or $AlK(SO_4)_2.12H_2O$, U.S.P.

Large colorless crystals, without odor, and having a sweetish and strongly astringent taste. Soluble in 5.2 parts of water at ordinary temperature or in 0.3 part of boiling water. Freely soluble in warm glycerin, but insoluble in alcohol.

Exsiccated Alum; Alumen Exsiccatum (Alum. Exsic.), **U.S.P. (Dried Alum, Burnt Alum).—Anhydrous $AlNH_4(SO_4)_2$ or anhydrous $AlK(SO_4)_2$. (The salt desired may be indicated.)**

Dried or burned alum. A white granular powder, without odor, having a sweetish, astringent taste. It is soluble in about 20 parts of water at ordinary temperature and 1½ parts of boiling water. It readily absorbs moisture from the air.

TANNIC ACID; ACIDUM TANNICUM (ACID. TAN.), U.S.P.

Tannic acid, which is the active constituent of all vegetable astringents, will quickly coagulate the blood if applied in substance or in concentrated solution. For smaller hemorrhages the glycerite of tannic acid is useful. Since the introduction of stypticin and styptol, tannic acid has lost much of its repute as a hemostatic.[1, 2]

LEMON JUICE AND ORDINARY VINEGAR are frequently employed by the laity as styptics.

THROMBOPLASTIC AGENTS

The value of a thromboplastic agent to check hemorrhage depends on its ability to supply to the blood (1) an ingredient that is necessary for coagulation and is deficient in the blood or (2) a substance that will render inert an anticoagulating substance in the blood. For example, in cirrhosis of the liver the fibrinogen content of the blood is low, and in hemophilia an excess of antiprothrombin is present.

A diagnosis of the factor or factors that promote the excessive bleeding should be made and the correct treatment instituted.

AGENTS.—

1. *Normal (whole) blood given by transfusion.* This replaces the blood lost and furnishes any substances which may be lacking in the patient's blood. This is a good procedure and is safe when the bloods are properly grouped.

2. *Human blood serum* is not as good as whole blood, as it does not contain all of the essential factors needed for coagulation and replacement.

3. *Blood plasma* is a substitute for whole blood, but it does not contain all of the essentials needed for coagulation and replacement.

4. *Citrated Normal Human Plasma; Plasma Humanum Normale Citratum (Plas. Human. Nor. Citr.),* U.S.P. (Normal Human Plasma).—Prepared from the liquid portion of citrated whole blood from human beings in accordance with the requirements of the National Institute of Health.

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[1] Winter, Leo, and Darlington, C. G.: The Control of Bleeding in Minor Oral Surgery Operations, J. D. Res. 6: 13, March 26, 1924.

[2] Tainter, M. L., and Throndson, A. H.: Hemostatic Effects of Administration of Calcium, Viosterol, Styptysate, and Cleanothyn by Mouth, J. A. D. A. 25: 633, 1938.

Citrated Normal Human Plasma may be dispensed as liquid plasma, as frozen plasma, or as dried plasma. It must be free from harmful substances detectable by animal inoculation and must not contain an excessive amount of preservative. (U.S.P.)

ACTION AND USES.—It is used in the treatment of surgical and traumatic shock and is a temporary substitute for whole blood in the treatment of hemorrhage. It is also used to combat hypoproteinemia in the treatment of burns.

DOSAGE.—Intravenous, 500 cc. (U.S.P.)

5. *Hemostatic Globulin* (Clotting Globulin) (Lederle). It is a globulin fraction derived from blood plasma and used locally for the control of capillary hemorrhage.

6. *Thromboplastin* (Squibb) is a solution of tissue extracts from ox brain. Two forms of thromboplastin are marketed; one for local application and one for hypodermic administration. This is an efficient preparation. A sensitivity test should be made before using it.

DOSAGE.—Hypodermically 15 to 20 cc. Locally injecting 4 cc. at the site of hemorrhage or applying the drug on a gauze pack.

7. *Fibrogen Local,* A.D.R. (Merrell). It is a suspension of tissue fibrinogen and cephalin obtained from beef lungs and is marketed in 7 cc. vials.

DOSAGE.—Apply.

8. *Kephalin,* N.N.R.—It is a dried ethereal extract of the brain of the ox or other mammal. A concentrated freshly prepared solution of kephalin in ether is applied to bleeding surfaces.

9. *Hemostatic Serum (Hemoplastin).*—It is a sterile serum concentrate composed principally of the prothrombin and anti-prothrombin of the blood in physiologically balanced solution. It is a clear, light-amber-colored liquid.

The average dose is 1 cc. to 2 cc. given intravenously or subcutaneously. The injection should be repeated at intervals of four to six hours until the bleeding is under control. The small dosage makes serum sickness less frequent.

Though intended for hypodermic administration principally, hemostatic serum is effective also on local application. Saturate a small piece of sterile gauze with the liquid and press it upon the source of the hemorrhage (Parke, Davis).

10. *Vitamin K.* Increases the content of prothrombin in the blood.

11. *Ovary; Ovarium,* N.F. May be used in cases of true hemophilia.

DOSAGE.—0.3 Gm. (5 grains) hypodermically.

12. *Calcium Salts.* The following paragraphs reflect the opinion of the Council on Dental Therapeutics of the American Dental Association on the value of calcium salts on the coagulation of blood.

"Calcium is necessary for the coagulation of the blood. Calcium salts have therefore been administered in hemorrhagic conditions such as hemophilia and purpura; but since these conditions are not due to a deficiency of calcium, the added calcium has no effect. The internal administration of calcium for hemorrhages in the oral cavity appears irrational for the same reason, although exodontists and other surgeons prescribe calcium lactate or some other form of calcium prior to extraction in those suspected of slow coagulation time. The coagulation time of the blood in normal human subjects is not significantly decreased by administration of either calcium gluconate or calcium gluconate with viosterol (Tainter and Throndson, *J. A. D. A.* 25: 638, 1938). The addition of calcium to hemophilic blood in vitro delays rather than hastens coagulation."

"Calcium salts have been administered as the chloride, lactate, and gluconate. Calcium salts of mineral acids such as the chloride when administered by mouth tend to produce acidosis because the chloride part of the molecule is absorbed, but the calcium for the most part is unabsorbed. Water insoluble calcium salts are converted by the gastric juice into the chloride before absorption or excretion. Recent experiments indicate that the gluconate is less irritating than any of the other forms. It is, as far as experimental evidence goes, the only salt of calcium which can be injected subcutaneously or intramuscularly without causing necrosis. Milk as a source of calcium (and of phosphorus) should not be overlooked.[1]"

CALCIUM GLUCONATE; CALCII GLUCONAS (CALC. GLUCON.), $C_{12}H_{22}O_{14}$-$Ca.H_2O$, U.S.P.

A white, odorless, tasteless, crystalline powder. Slowly soluble in water (1 in 30), and insoluble in alcohol.

THERAPEUTICS.—Restores normal calcium content of the blood in calcium deficiency; has the advantage over the chloride of causing less pain when injected intramuscularly.[2, 3]

DOSAGE.—Oral 5 Gm. (75 grains). Intravenous, 1 Gm. (15 grains), U.S.P.

Calcium Gluconate Injection; Injectio Calcii Gluconatis (Inj. Calc. Glucon.), U.S.P.—Calcium gluconate in physiologic solution of sodium chloride or other suitable solvent.

DOSAGE.—Hypodermic 1 Gm. (15 grains) of calcium gluconate.

CALCIUM LACTATE; CALCII LACTAS (CALC. LACT.), $Ca(C_3H_5O_3)_2.5H_2O$, U.S.P.

White, odorless, practically tasteless masses or powder. Soluble in water (1 in 20) and almost insoluble in alcohol.

[1] Accepted Dental Remedies, A. D. A., 1938, pp. 96-97.
[2] Useful Drugs, A. M. A., ed. 11, 1938, p. 59.
[3] Accepted Dental Remedies, A. D. A., 1939, p. 94.

THERAPEUTICS.—Used for the characteristic action of calcium; less irritating and therefore better adapted to hypodermic administration, than calcium chloride.

DOSAGE.—1 Gm. (15 grains), U.S.P., in solution.

Tablets of Calcium Lactate; Tabellae Calcii Lactatis (Tab. Calc. Lact.), N.F.

DOSAGE.—0.3 Gm. (5 grains) of calcium lactate (N.F.).

The injection or internal administration of soluble calcium salts, especially in hemophilia, has been tried without results. The local application of calcium salts with the hope of styptic action is a failure. In severe dental hemorrhage the following combination may be tried:

℞			
	Calcii Lact.	6 Gm.	3 jss
	Syrup. Aromatic.	30 cc.	fℨ j
	Aquæ Destill.	90 cc.	fℨ iij

Sig.: Tablespoonful every two hours in a glass of milk. The whole quantity should be taken within twenty-four hours.

Agents Which Act on the Vessels, But Not on the Blood

Solution of Epinephrine Hydrochloride; Liquor Epinephrinae Hydrochloridi (Liq. Epineph. Hydrochlor.), U.S.P.

This solution is used undiluted for external application, or by means of intraparenchymatous injections, 1:10,000 or 1:12,000. As a hemostatic for dental purposes it is of questionable value, but as an addition to local anesthetics on account of its vasoconstrictor action it is very important.

Miscellaneous

VIPER VENOM. The venom of the tiger-snake or Russell viper has been found to be most effective in checking dental hemorrhage. Burroughs Wellcome & Co. have prepared the venom of the Russell viper in suitable form for an extemporaneous solution when needed. This preparation is known as stypven. It is marketed in a dry state in rubber-stoppered bottles, accompanied by hermetically sealed ampuls of a solvent consisting of sterile distilled water containing 0.5 per cent phenol. A solution of the venom of the necessary concentration is thus readily prepared by adding, with a syringe, the solvent to the dry venom in the rubber-stoppered bottle provided.

The venom is applied *locally* only (not by injection) on a pledget of cotton with slight pressure directly upon the bleeding surface. The solution should be freshly prepared when needed.

Procedure for Testing Sensitivity to a Drug or Agent

A history of a previous injection or application of a similar preparation is helpful. Anaphylaxis depends on a preceding inoculation of the foreign substance into the body with the endothelial system producing an antibody which causes a violent reaction when that same substance is again present in or on the body. The symptoms of anaphylaxis are a rapid fall in blood pressure, spasms of the bronchial muscles, edema, and a dermitis. The treatment is injections of a Solution of Ephinephrine Hydrochloride, 0.5 cc., until blood pressure and other symptoms approach normal.

A satisfactory procedure for determining sensitivity is as follows: Make an intradermal injection of 0.1 cc. of the foreign substance. The presence of a red ring at the site of injection within a few minutes indicates a susceptible patient and contraindicates the use of the drug.

CHAPTER XIV

DRUGS WHICH ACT ON THE GASTROINTESTINAL SYSTEM

DRUGS WHICH AFFECT THE SALIVARY GLANDS

Sialogogues are drugs which stimulate the flow of saliva without necessarily affecting the ptyalin content; *antisialogogues* are drugs which give the opposite response. *Ptyalogogues* are drugs which increase the ptyalin content of the saliva without necessarily affecting the volume. Human saliva represents the mixed secretion from the three pairs of large salivary glands and the minute mucous glands distributed over the oral cavity. The flow of saliva is regulated by the autonomic nervous system, the daily volume being approximately 1 to 1.5 liters.

The composition and flow of saliva varies with the type of stimulation, such as diet, thought of food, odor of food, time of day, drugs, etc. The salivary pH varies with the individual, diet, time of day, drugs, and disease; the average is between 6.8 and 7.4. Generally, the greater the flow the more closely it approximates the pH of the blood. The water content of the saliva is about 99.3 per cent, the other 0.7 per cent is composed of solid matter of which 0.5 per cent is organic and 0.2 per cent inorganic matter. Of the organic matter, about 0.4 per cent is mucin, the rest being albumin, globulin, urea, uric acid, and ptyalin. The inorganic matter consists of carbonates, phosphates, and cyanates of calcium, sodium, potassium, and ammonia. The specific gravity is about 1.007. There is no definite correlation between the constituents of the saliva and dental caries or periclasia, but there is between pH and inorganic content and dental calculus.

Sialogogues

Sialogogues are indicated in an abnormal dryness of the mouth. Diminished secretion of saliva results from the injections of certain drugs—belladonna (atropine), henbane, opium, scopolamine, stramonium, etc.—or from so-called ptomaine poisoning, which may result from eating decaying meat, cheese, fish, etc. Many febrile diseases also diminish the flow of saliva or cause a drying up of the normal moisture of the oral mucous linings. Dry mouth (xerostomia) results from an impaired secretion of saliva, which may be caused by physical

or psychic disturbances of the nervous system, diseases of the digestive tract, atrophy of the salivary glands, and other unknown factors.

The supreme sialogogue is pilocarpus (jaborandi). It is best prescribed as the hydrochloric salt of the alkaloid, pilocarpine. Pilocarpine acts at the terminations of the secretory nerves. The secretory fibers to the salivary glands are the parasympathetics acting through the submaxillary and otic ganglia. A stimulation of these fibers increases the minute volume of saliva formed but decreases the solid content. It is principally indicated in the treatment of dry mouth

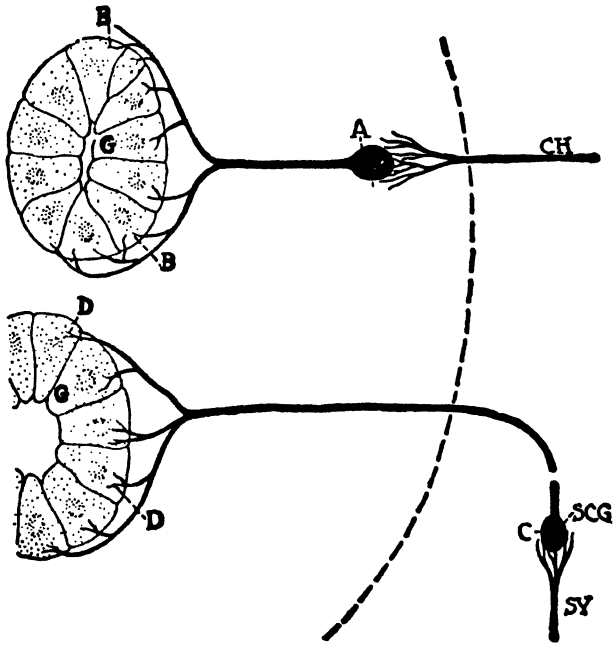

Fig. 22.—Diagram showing the different points of action of drugs on the submaxillary gland. Reflex effects are not shown. *G* = gland-cell; *SY* = sympathetic nerve; *SCG* = superior cervical ganglion; *D* = nerve-endings in the gland; *CH* = chorda tympani; *A* = nerve-cells and *B* = nerve-endings in the gland. The dotted line represents the periphery of the gland. (After Dixon.)

A and *C*	*B*	*D*	*G*
Nicotine + –	Pilocarpine +	Epinephrine +	Certain metals,
Coniine + –	Physostigmine +	Cocaine +	particularly
Lobeline + –	Muscarine +		Mercury +
Codeine –	Atropine –		
Curare –	Hyoscyamine –		
Sparteine –	Hyoscine –		

(+ represents stimulation and – depression)
From McGuigan-Krug: *Materia Medica and Pharmacology*, The C. V. Mosby Co.

(xerostomia). If this disease results from nervous disturbances, electrical stimulation is of some value. While recovery from true xerostomia is very problematic, the patient may be made comfortable by the use of pilocarpine.

PILOCARPINE HYDROCHLORIDE; PILOCARPINAE HYDROCHLORIDUM (PILOCARPIN. HYDROCHLOR.), N.F.

It is the hydrochloride of an alkaloid obtained from jaborandi leaves. It occurs as small white crystals, which are odorless but have a slightly bitter taste. It is very soluble in both water and alcohol. It acts by potentiating the action of acetylcholine on the chemoreceptor substance of the secretory cells.

DOSAGE.—5 mg. ($\frac{1}{12}$ grain), U.S.P. [See Parasympathetic Stimulants (Cholenergic) for a detailed description.]

PILOCARPINE NITRATE; PILOCARPINAE NITRAS (PILOCARPIN. NITRAS), U.S.P.

It forms a white crystalline powder, which is soluble in about 4 parts of cold water and in about 21 parts of alcohol.

DOSAGE.—0.005 Gm. ($\frac{1}{12}$ grain), U.S.P.

FOR DRY MOUTH

℞ Pilocarpin. Hydrochlor. 0.3 Gm.
Aq. Dest. 15.0 cc.
M.
Sig.: 5 drops three times daily. Slowly increase the dose by 1 drop until from 8 to 10 drops per dose are taken.

Ptyalogogues

Ptyalogogues are drugs which increase the secretion of ptyalin from the salivary glands. The sympathetic nerves act as a stimulant to the secretory cells, causing them to increase the amount of ptyalin secreted and to diminish the minute volume of saliva. Drugs of this group are sympathetic stimulants; ephedrine sulfate is an example. (See Sympathetic Stimulants for a description of this group of drugs.)

Antisialogogues

Antisialogogues are drugs which decrease the flow of saliva by inhibiting parasympathetic stimulation or by stimulating the sympathetic inhibition. The drugs generally used are those which inhibit the excitation of acetylcholine on the chemoreceptor substance of the secretory cells. The excessive flow of saliva during a dental operation is due to a nervous reflex from the manipulation in the oral cavity and is generally present in children and nervous adults. Excessive salivation is also caused by heavy metal poisoning, such as mercury, or from drugs, such as bromides or pilocarpine. These poisons may have been administered by mouth, hypodermically, or

they may have been absorbed from wound surfaces. The supreme remedy to check the flow of saliva is atropine; it paralyzes the parasympathetic nerve endings in the salivary glands. Small doses of atropine are often given advantageously to patients afflicted with an abnormal flow of saliva prior to dental operations in which the rubber dam cannot be applied.

ATROPINE SULFATE; ATROPINAE SULFAS (ATROP. SULF.), U.S.P.

Atropine sulfate is a white crystalline powder, prepared from the alkaloid atropine derived from belladonna leaves. It has a very bitter taste, and is freely soluble in water and alcohol.

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain) (U.S.P.).

Caution: Atropine sulfate is extremely poisonous (U.S.P.).

℞ Pil. Atropine Sulfate gr. $\frac{1}{150}$ (0.4 mg.)
No. ij
Sig.: One pill one hour before the dental operation.

BELLADONNA LEAF; BELLADONNAE FOLIUM (BELLAD. FOL.), U.S.P.

Tincture of Belladonna; Tinctura Belladonnae (Tr. Bellad.), U.S.P. (Tinctura Belladonnae Foliorum, Tinctura Belladonnae P.I.).—Belladonna leaf (10%) yielding about 0.03 per cent of alkaloids, in alcohol. Absolute alcohol content about 68 per cent.

DOSAGE.—0.6 cc. (10 minims) (U.S.P.).

℞ Tincture of Belladonna 15 cc.
Sig.: Ten drops in water two hours before the dental operation. Repeat if necessary.

Oral Antacids

Oral antacids are alkaline substances which are used locally to reduce oral acidity and to dissolve mucin films from the teeth. The soluble antacids have a pronounced action for a short time while the insoluble antacids are less active but act for a longer time. Both compounds will alkalinize the oral cavity only temporarily, and they must be repeated if a prolonged effect is desired. Oral acidity is generally caused by the end products of bacterial fermentation and not by the saliva. A clean mouth, free from carbohydrate debris, is the first requisite in the control of oral acidity.

The control of dental caries with alkaline washes and dentifrices has not met with success clinically. In case of gingival irritation of the soft and hard tissues, the application of antacids may give temporary relief. Permanent relief occurs only when the cause is removed. The antacids are constituents of solid and paste dentifrices; precipitated calcium carbonate is very satisfactory and will not

injure the teeth. Larger crystals, as of sodium chloride or sodium bicarbonate, may act as abrasives and cut the hard and soft tissues; they should be dissolved in water before using.

It is impossible to change the pH of the saliva by the internal administration of alkalies without also changing the alkaline reserve of the body, which makes it an undesirable procedure.

Sodium Salts

Sodium Bicarbonate; Sodii Bicarbonas (Sod. Bicarb.), $NaHCO_3$, U.S.P. (Baking soda).

It is used as a mouthwash and liquid dentifrice in a 2 to 5 per cent solution. A very fine powder may be used as a powder dentifrice, but coarse powders are abrasive for such purposes.

Sodium Perborate; Sodii Perboras (Sod. Perbor.), $NaBO_3.4H_2O$, U.S.P.

Sodium perborate contains not less than 9 per cent of available oxygen.

It is used as an alkaline antiseptic mouthwash in a 2 per cent solution. As a powder dentifrice the crystals should be very fine to prevent abrasion of the teeth. The boron salts are mildly toxic, and care must be exercised to prevent the swallowing of too large amounts of the drug.

Aromatic Sodium Perborate; Sodii Perboras Aromaticus (Sod. Perbor. Arom.), N.F. (N.F. Aromatic Sodium Perborate). Sodium perborate with oil of peppermint and soluble saccharin.

The uses are the same as those of sodium perborate.

Sodium Borate; Sodii Boras (Sod. Bor.), $Na_2B_4O_7.10\ H_2O$, U.S.P. (Borax).

It occurs as a white, odorless, alkaline-tasting powder; soluble in water (1 in 16) and insoluble in alcohol.

In therapeutics it is used the same as sodium bicarbonate, only it is more antiseptic. It should not be used internally.

Preparations.—

Compound Solution of Sodium Borate; Liquor Sodii Boratis Compositus (Liq. Sod. Bor. Comp.), N.F. (Dobell's Solution).—it contains sodium borate and sodium bicarbonate (each 1.5%), liquefied phenol (0.3%), in glycerin and water.

Therapeutics.—A mild antiseptic and alkaline mouthwash used diluted with equal parts of warm water, or as a liquid for the spray bottles. It may be colored and flavored if so desired.

Honey of Rose and Sodium Borate; Mel Rosae et Sodii Boratis (Mel Ros. et Sod. Bor.), N.F. (Honey of Rose and Borax).—It contains sodium borate and fluidextract of rose (each 10%) in glycerin and honey.

THERAPEUTICS.—It is an alkaline demulcent used in the treatment of thrush infections, applied undiluted.

CALCIUM SALTS

PRECIPITATED CALCIUM CARBONATE; CALCII CARBONAS PRAECIPITATUS (CALC. CARB. PRAEC.), $CaCO_3$, U.S.P. (Precipitated Chalk.)

THERAPEUTICS.—It is an insoluble antacid used in powder and paste dentifrices. It may be used as a mouthwash in 2 to 5 per cent suspension in warm water. The precipitated calcium carbonate is free from grit and is nonabrasive to the teeth.

N.F. Dentifrice; Dentifricium N.F. (Dentif. N.F.) (N.F. Tooth Powder).—It contains hard soap and precipitated chalk, sweetened with soluble saccharin and flavored with volatile oils.

It is used as a tooth powder.

CALCIUM HYDROXIDE; CALCII HYDROXIDUM.

Solution of Calcium Hydroxide; Liquor Calcii Hydroxidi (Liq. Calc. Hydrox.), Ca $(OH)_2$, U.S.P. (Liquor Calcis, Limewater).—It contains about 0.15 per cent of calcium hydroxide in water. This is a saturated solution, colorless, with a sweet alkaline taste.

Used undiluted as a mouthwash.

MAGNESIUM SALTS

MAGNESIUM OXIDE; MAGNESII OXIDUM (MAG. OXID.), U.S.P.

Used as an alkaline abrasive in tooth powders and pastes.

MAGNESIUM HYDROXIDE; MAGNESII HYDROXIDUM.

Magnesia Magma; Magma Magnesiae (Magma Mag.), U.S.P. (Milk of Magnesia).—A suspension of magnesium hydroxide, $Mg.(OH)_2$ (about 7.5%) in water, forming a thick white liquid.

It is used in dentifrices as an alkalizing agent. Applied night and morning to the gingiva, it is useful in alleviating sensitiveness about the necks of teeth. It is used as an alkaline mouthwash in 2 to 5 per cent solution.

DRUGS WHICH INHIBIT GAGGING

Drug preparations containing local anesthetics are employed by the dentist to check gagging during dental procedures. They may be applied as a mouthwash, gargle, topical, or lozenge. A 10 per cent

solution of butyn may be applied, a mouthwash or gargle of 0.5 per cent phenol, or a lozenge containing ethyl aminobenzoate, 2 to 3 per cent, will give good results. The ninth edition of A.D.R. gives the following prescription for a lozenge.

℞	Benzocaine	0.75 Gm.
	Vanillin	0.03 Gm.
	Sucrose	8.12 Gm.
	Powdered Tragacanth	0.25 Gm.
	Carmine	0.01 Gm.
	Distilled Water	
	M. et ft. loz. No. XII	

STOMACHICS AND DIGESTIVES

Stomachics (from *stomachum,* stomach) and *digestives* (from *digere,* to digest) form one of the many groups in pharmacotherapeutics which cannot be precisely defined. The remedies of this group are employed in the treatment of certain gastric and intestinal disorders. The stomach has to fulfill a motor function—that is, its rhythmic peristaltic movements mix the ingested foodstuffs with its own secretions and then pass the liquefied material through the pylorus into the small intestines. The stomach secretes the gastric juice, consisting of pepsin, rennin, hydrochloric acid, inorganic salts, and water. The hydrochloric acid disintegrates the albumins and muscle fibers, and prepares them for the action of the pepsin. The latter dissolves the albumin and changes the albuminates into proteoses and peptones. The rennin precipitates casein from the milk which has been taken into the stomach; the casein is dissolved by the proteolytic action of the pepsin. The stomach wall absorbs only very few dissolved substances. Water or aqueous solutions, even if they contain easily diffusible substances, are not absorbed, while alcohol, alcoholic solutions, and volatile substances are more readily absorbed. The hydrochloric acid component (0.2 per cent) of the gastric juice performs another important function; it acts as a sterilizing medium of the contents of the stomach. Many of the swallowed bacteria, especially the pathogens, are promptly destroyed by this acid. The mucous membrane of the stomach may become anatomically altered, and many diseases—catarrh, ulcer, hemorrhage, etc.—may result, which incidentally lessen or inhibit its function.

Antiseptics are occasionally administered to inhibit abnormal fermentation. Diluted hydrochloric acid, benzoic acid, or resorcinol in 1 per cent solution is used. Belching, which is caused by the irrita-

tion of organic acids as a result of abnormal fermentation, may be greatly relieved by mild antacids. Astringents are indicated to protect inflamed mucous surfaces, especially in ulcers of the stomach. Bismuth subnitrate alone or in combination with magnesia (milk of magnesia) is serviceable for such purposes. Pronounced astringent action is readily obtained with lavage of tannic acid solution, 1:1,000. Overproduction of hydrochloric acid in the stomach can be correctly determined only by a chemical analysis of a test meal. It calls for mild antacids—sodium bicarbonate, calcium carbonate, or milk of magnesia. The latter preparation is preferbly employed, as it does not form carbonic acid, which distends the stomach. If there is an insufficiency of hydrochloric acid, it is readily supplied by administering the well-diluted acid through a glass tube to prevent injury to the teeth. The latter is preferably given either before meals to increase the appetite or after meals to promote digestion. By reflex action the secretion of hydrochloric acid may be artificially increased; the simple bitters—as gentian, columbo, dandelion, etc.—are administered for such purposes. The ferments present in the gastric juice—pepsin and rennin—may also be artificially substituted in case of need. Pepsin, preferably in the form of its many solutions, or its vegetable substitute, papain, is indicated for the purpose. The various combined functions of the stomach may be increased in their total action by reflex stimulation. The simple bitters known as stomachics, digestives, aromatics, and by other titles, diluted alcohol in the form of wine or beer, and carbonated table waters are valuable reflex stimulants.

GENTIAN; GENTIANA (GENTIAN.), U.S.P. (Gentian Root).

The official parts are the rhizome and roots of *Gentiana lutea;* it contains several glucosides, a trace of tannic acid, and other bodies of less importance. In the form of an extract, fluidextract, or tincture it is widely used as a bitter tonic.

THERAPEUTICS.—Probably the most widely used of the simple bitters.

Elixir of Gentian; Elixir Gentianae (Elix. Gentian.), N.F.—Fluidextract of gentian (3.5%), compound spirit of cardamom, sodium citrate, glycerin, syrup, alcohol and distilled water. Absolute alcohol content about 16 per cent.

USES.—An agreeable aromatic bitter stomachic.

Compound Tincture of Gentian; Tinctura Gentianae Composita (Tr. Gentian. Co.), U.S.P.—Gentian (10%), bitter orange peel and

cardamom seed in glycerin, alcohol and distilled water. Absolute alcohol content about 45 per cent.

USES.—Aromatic bitter.

DOSAGE.—4 cc. (1 fluidrachm) (U.S.P.).

TARAXACUM; TARAXACUM (TARAX.), N.F. (Dandelion Root).

It is the dried rhizome and root of the dandelion *Taraxacum officinale,* family *Compositae,* and contains taroxin as a bitter substance. It is principally employed in the form of an extract, fluidextract, tincture, or the expressed juice. It is used as a bitter tonic and stomachic.

DOSAGE.—4 Gm. (1 drachm) (N.F.).

QUASSIA; QUASSIA (QUASS.), N.F. (Bitter Wood).

It is the heart wood of *Picrasma excelsa* or of *Quassia amara,* family *Simarubaceae,* and contains several bitter substances which resemble each other closely and are known as quassins. In the form of an extract, tincture, or infusion it is used as a bitter tonic and febrifuge.

DOSAGE.—0.5 Gm. (8 grains) (N.F.).

Fluidextract of Quassia; Fluidextractum Quassiae (Fldext. Quass.), N.F.—Quassia (100%); absolute alcohol content about 24 per cent.

DOSAGE.—0.5 cc. (8 minims) (N.F.).

Tincture of Quassia; Tinctura Quassiae (Tr. Quass.), N.F.—Quassia (20%) in alcohol and water. Absolute alcohol content about 30 per cent.

DOSAGE.—2 cc. (30 minims) (N.F.).

SERPENTARIA; SERPENTARIA (SERPENT.), N.F.

It is the rhizome and root of *Aristolochia Serpentaria* or *Aristolochia reticulata,* and contains a volatile oil (borneol), a bitter principle (aristolochin) and an alkaloid, aristolochine. It is usually employed in the form of a fluidextract, tincture, or infusion.

THERAPEUTICS.—Bitter with no advantage over gentian.

DOSAGE.—1 Gm. (15 grains) (N.F.).

Fluidextract of Serpentaria; Fluidextractum Serpentariae (Fldext. Serpent.), N.F.—Serpentaria (100%); absolute alcohol content about 65 per cent.

DOSAGE.—1 cc. (15 minims) (N.F.).

Tincture of Serpentaria; Tinctura Serpentariae (Tr. Serpent.), (N.F.) (Tincture of Virginia Snakeroot).—Serpentaria (20%) in alcohol and water. Absolute alcohol content about 72 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

HUMULUS; HUMULUS (HUMUL.), N.F. (HOPS).

They are the dried strobiles of *Humulus Lupulus,* family *Moraceae,* and contain a volatile oil, a bitter, neutral substance, lupuline, and resins. Hops are employed in the form of a fluidextract, oleo-resin, tincture, or infusion, and are used as a tonic, carminative, or diuretic.

AVERAGE DOSE.—2 Gm. (30 grains) (N.F.).

PEPSIN; PEPSINUM (PEPSIN.), N.F.

It is a proteolytic ferment obtained from the glandular layers of the fresh stomach of the healthy hog, *Sus scrofa,* family *Suidae,* and capable of digesting not more than 3,500 times its own weight of freshly coagulated egg albumin. It is a white or cream-colored amorphous powder, or thin, yellowish, translucent scales, free from any offensive odor, and having a slightly acid or saline taste. It is freely soluble in water, and its solubility is increased if the water is slightly acidulated with hydrochloric acid. Pepsin is usually administered during or after meals.

THERAPEUTICS.—Used to assist in the gastric digestion of proteins. Usually superfluous, since gastric juice generally contains sufficient pepsin. The alcohol of the elixirs may be distinctly harmful in gastric disorders.

DOSAGE.—0.5 Gm. (8 grains) (N.F.).

Elixir of Pepsin; Elixir Pepsini (Elix. Pepsin.), N.F.—Pepsin (3.5%) equivalent to 1.75 Gm. of Reference Pepsin, citric acid (1.2%), exsiccated sodium phosphate (1.3%), glycerin (20%), aromatic elixir, and distilled water. Absolute alcohol content about 14 per cent.

DOSAGE.—8 cc. (2 fluidrachms) (N.F.).

Elixir of Pepsin and Rennin; Elixir Pepsini et Rennini (Elix. Pepsin. et Rennin.), N.F. (Essence of Pepsin).—Pepsin (4.5%) equivalent to 2.25 Gm. of Reference Pepsin, rennin (1.8%), tincture of sweet orange peel, glycerin, alcohol, oil of myristica, and distilled water. Absolute alcohol content about 19 per cent.

DOSAGE.—8 cc. (2 fluidrachms) (N.F.).

PANCREATIN; PANCREATINUM (PANCREAT.), U.S.P.

It is a mixture of enzymes which exist in the pancreas of warm-blooded animals, and is usually obtained from the fresh pancreas of the hog, *Sus scrofa,* family *Suidae,* or of the ox, *Bos taurus,* family *Bovidae.* It forms a yellowish or grayish-white amorphous powder, having a faint odor and a meatlike taste. It is slowly soluble in water, but insoluble in alcohol. It is given in powder or in very weak acid or alkaline solution; it should never be given in combination with

pepsin. Pancreatin digests proteins and converts starch into maltose and dextrose and converts 25 times its weight of each.

DOSAGE.—0.5 Gm. (8 grains) (U.S.P.).

Compound Powder of Pancreatin; Pulvis Pancreatini Compositus (Pulv. Pancreat. Comp.), N.F. (Peptonizing Powder).—Pancreatin (20%) and sodium bicarbonate.

USES.—Predigestion of milk.

EMETICS

Emetics (to vomit) are remedies which cause forcible expulsion of the contents of the stomach through the esophagus. They were more frequently employed in former years than at present. Vomiting is a localized process; it is artificially, sometimes spontaneously, produced to relieve an overfilled stomach or to remove poison. The use of the stomach tube has greatly lessened the systematic administration of emetics, and the tube should be employed whenever possible. Vomiting is partially a physiologic process; it occurs very frequently and without further disturbances in infants and young children. The older we get, the less often we vomit, and the more we suffer from the accompanying disagreeable side effects. The physiologic act of vomiting is produced by an irritation of the vomiting centers in the medulla. The irritation is carried to these centers from the periphery, the mucous coat of the stomach, and other organs of the abdominal cavity. The act of vomiting consists of a series of definite processes; a strong, positive pressure is brought on the abdomen, which contracts the abdominal muscles, and causes a negative pressure in the thoracic cavity. Incidentally the cardiac end of the stomach is opened, and its contents are suddenly forced into the esophagus. The muscles of respiration will also contract, and the resulting positive pressure forces the food from the esophagus into the mouth. During the process of vomiting large quantities of saliva and mucus are secreted by the glands of the mouth, pharynx, and esophagus. Vomiting always depresses the circulation. The preliminary psychic stage of vomiting is accompanied in man by an intensely disagreeable, sickening feeling known as nausea. Emetics act by reflex action or by direct stimulation. By reflex action—irritation of the pharynx, the stomach, the intestines, the uterus, etc.—vomiting is easily produced. The direct stimulation of the centers of vomiting may result from anemia of the brain, pressure on the brain, and from chemical substances. The metallic salts and ipecac produce only reflex action; they have to be ingested into the stomach to create vomiting, and will not act when injected

hypodermically or subcutaneously. Apomorphine acts by direct stimulation of the vomiting centers, and produces prompt results when injected hypodermically.

Emetics are indicated to remove foreign bodies from the esophagus or the stomach. If a foreign body has lodged in the trachea and is not removed by a coughing spell, pressure produced by spasmodic vomiting may occasionally be helpful in its dislodgment. This procedure may be of some service in case a tooth has fallen into the upper trachea during its extraction. Poisons which have entered the stomach should be removed as quickly as possible to prevent absorption. While lavage of the stomach with the stomach tube is the correct procedure for such treatment, emetics are often of great assistance. Occasionally an overloaded stomach needs the quick removal of its contents. Emetics are also of some service in aiding the therapeutic action of expectorants. The false membranes of croup may be forcibly removed by inducing vomiting which incidentally produces an increased secretion of the mucous membrane of the pharynx and larynx, and probably of the upper bronchi. Emetics are contraindicated in aneurysms, arteriosclerosis, pulmonary tuberculosis, hernia, in the senile, and in the last stages of pregnancy.

ANTIMONY AND POTASSIUM TARTRATE; ANTIMONII ET POTASSII TARTRAS (ANTIMON. ET POT. TART.), U.S.P. (Antimonyl Potassium Tartrate, Tartar Emetic).

It forms colorless, transparent crystals, or a white granular powder, without odor, and having a sweetish and afterward disagreeable metallic taste. It is soluble in 12 parts of cold water and insoluble in alcohol.

THERAPEUTICS.—Nauseant expectorant and emetic. Intravenously against certain protozoan infections, especially schistosomiasis, kala-azar, and granuloma inguinale.

DOSAGE.—3 mg. (1/20 grain) U.S.P., in solution. It is best to begin with small doses, 1 mg. (1/60 grain), which may be repeated hourly, care being taken to avoid too great depression. Intravenously the initial dose is 0.04 Gm. (2/3 grain) in 100 parts of physiologic solution of sodium chloride.

CUPRIC SULFATE; CUPRI SULFAS (CUPR. SULF.), $CuSO_4.5H_2O$, U.S.P. (Copper Sulfate).

As an emetic it is given in 2 to 4 grain (0.13 to 0.25 Gm.) doses, dissolved in a glass of water and repeated if necessary.

ZINC SULFATE; ZINCI SULFAS (ZINC. SULF.), $ZnSO_4.7H_2O$, U.S.P.

As an emetic it is given in 1 Gm. (15 grains) doses, dissolved in a glass of water and repeated if necessary.

APOMORPHINE HYDROCHLORIDE; APOMORPHINAE HYDROCHLORIDUM (APOMORPH. HYDROCHLOR.), U.S.P.

It is the grayish-white crystalline hydrochloric salt of an artificially prepared alkaloid from morphine, odorless, and having a slightly bitter taste. It is soluble in water (1 in 50), turning green or even black when kept in solution.

Caution.—Apomorphine hydrochloride must be rejected if it at once imparts an emerald green color to 100 parts of distilled water when shaken with it in a test tube (U.S.P.).

THERAPEUTICS.—Prompt centrally acting emetic, especially adapted for hypodermic administration.

DOSAGE.—Emetic, by hypodermic injection, 5 mg. (1/12 grain) (U.S.P.). This may be repeated at ten-minute intervals until effective.

IPECAC; IPECACUANHA (IPECAC.), U.S.P. (Ipecacuanhae radix P.I.).

Rhizome and root, yielding not less than 2 per cent of ether-soluble alkaloids.

It is dried rhizome and root of *Cephaëlis ipecacuanha* or of *Cephaëlis acuminata,* family *Rubiaceae.* The powdered root, stirred in water, is used as an emetic.

DOSAGE.—Emetic, 0.5 Gm. (7½ grains) (U.S.P.).

Fluidextract of Ipecac; Fluidextractum Ipecacuanhae (Fldext. Ipecac.), U.S.P.—Ipecac (100%), yielding about 2 per cent of ether-soluble alkaloids. Absolute alcohol content about 30 per cent.

DOSAGE.—Emetic, 0.5 cc. (8 minims) (U.S.P.).

Syrup of Ipecac; Syrupus Ipecacuanhae (Syr. Ipecac.), U.S.P.—Fluidextract of ipecac (7%) in glycerin and syrup.

DOSAGE.—Emetic, 8 cc. (2 fluidrachms) (U.S.P.).

Tincture of Ipecac; Tinctura Ipecacuanhae (Tr. Ipecac.), N.F. (Tinctura Ipecacuanhae P.I.).—Fluidextract of ipecac (10%, yielding about 0.2% ipecac alkaloids) in diluted hydrochloric acid, alcohol and water. Absolute alcohol content about 21 per cent.

DOSAGE.—0.6 cc. (10 minims) (N.F.).

The chief alkaloids of ipecac are emetine, cephaeline, and psychotrine. Emetine acts similarly to ipecac, but it is relatively less emetic, while cephaeline is more emetic and less nauseous.

In cases of emergency a tablespoonful of powdered mustard stirred in a cupful of warm water, a teaspoonful of table salt dissolved in a

glass of hot water, a few grains of alum dissolved in a glass of water, or hot water alone may be tried. They all irritate, more or less, the mucous lining of the stomach (except the hot water, which produces nausea) and act as emetics.

CARMINATIVES

Carminatives are drugs or preparations which relieve gastrointestinal flatulence. This group of drugs acts (1) as mild irritants facilitating the expulsion of flatus, (2) as mild analgesics relieving the symptoms of distention, and (3) antiferments which inhibit fermentation and gas production.

Spirit of Peppermint; Spiritus Menthae Piperitae (Sp. Menth. Pip.), U.S.P. (Essence of Peppermint).—It is a 10 per cent solution of oil of peppermint, in alcohol (82%) and water. Carminative dose 5 minims in a glassful of warm water, sodium bicarbonate (2 Gm.) may be added as an antacid.

DOSAGE.—1 cc. (15 minims). Well diluted to taste.

Peppermint Water; Aqua Menthae Piperitae (Aq. Menth. Pip), U.S.P.—A saturated (0.2%) solution of the oil in water.

DOSAGE.—15 cc. (4 fluidrachms) undiluted.

Chloroform Water; Aqua Chloroformi (Aq. Chlorof.), U.S.P.—A saturated solution of chloroform in distilled water.

DOSAGE.—15 cc. (4 fluidrachms) well diluted with water.

Spirit of Ether, Spiritus Aetheris (Sp. Aeth.), N.F. (Hoffmann's Drops).—It contains ether (32.5%) and alcohol (63%).

DOSAGE.—4 cc. (1 fluidrachm) well diluted with water.

Gastric Antacids

Antacids are drugs which by their alkaline properties neutralize acids. They are basic chemical compounds which combine with the acid to form a salt which upon hydrolysis is less acid than the original compound. Gastric antacids are used in therapeutics for the relief of gastric hyperacidity. After absorption they act as a systemic alkalizer which raises the alkaline reserve of the body and decreases the urinary acidity. The treatment is symptomatic and not curative. Antacids may be classified as soluble and insoluble antacids. The insoluble compounds have a restricted local action and are less prone to produce a systemic effect. The continued use of the alkalies must be discouraged and curative treatment instituted.

Gastric hyperacidity is a symptom and not a disease. It may indicate a gastric ulcer, cancer, nervousness, etc. Acidosis is a decrease

in the alkaline reserve of the body. It is a symptom and not a disease and very often is pathognomonic of diabetes mellitus. The urine should not be alkalinized over long periods of time, as renal calculi may result.

Sodium Salts

Sodium Bicarbonate; Sodii Bicarbonas (Sod. Bicarb.), $NaHCO_3$, U.S.P. (Baking Soda).

It occurs as a white, odorless powder, freely soluble in water (1 in 10), and sparingly soluble in alcohol. It is decomposed by boiling or by acids.

Pharmacodynamics.—It is a soluble antacid which combines with acids to form alkaline or neutral salts. It is nonirritating to the mucous membranes and forms nonirritating salts. It is not curative and may upset the acid-base equilibrium of the body.

Therapeutics.—Sodium bicarbonate is too frequently used by the general public in the treatment of so-called "acid stomach." The salt is readily absorbed, altering the alkaline reserve and the urinary acidity.

Dosage.—2 Gm. (30 grains) (U.S.P.). For intravenous injection a 6 per cent solution sterilized by boiling and thus partly converted into the normal carbonate has been recommended. One thousand cubic centimeters of such a solution, which has been cooled and through which carbon dioxide has been passed, may be injected, but great care must be taken that none of the liquid gets outside the veins lest necrosis of the tissues occur. (U.S.P.).

Preparations.—

Solution of Soda and Mint; Liquor Sodae et Menthae (Liq. Sod. et Menth.), N.F.—It contains sodium bicarbonate (5%), aromatic spirit of ammonia (2%), and spearmint water.

Therapeutics.—Antacid and carminative.

Dosage.—8 cc. (2 fluidrachms) (N.F.).

Tablets of Sodium Bicarbonate; Tabellae Sodii Bicarbonatis (Tab. Sod. Bicarb.), N.F.

Dosage.—1 Gm. (15 grains).

Calcium Salts

Precipitated Calcium Carbonate; Calcii Carbonas Praecipitatus (Calc. Carb. Praec.), $CaCO_3$, U.S.P. (Precipitated Chalk).

It occurs as a white, odorless, tasteless powder; practically insoluble in water and insoluble in alcohol. It is decomposed by acids, liberating carbon dioxide gas.

THERAPEUTICS.—It is an insoluble antacid, useful in the treatment of gastric hyperacidity. The carbonate, per se, is not absorbed from the intestines. After reacting with the hydrochloric acid of the stomach, an irritating salt ($CaCl_2$) is formed, which may be absorbed. Calcium carbonate is extensively used as a basis for tooth powders.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Tablets of Calcium Carbonate; Tabellae Calcii Carbonatis (Tab. Calc. Carb.), N.F.

DOSAGE.—1 Gm. (15 grains) (N.F.).

SOLUTION OF CALCIUM HYDROXIDE; LIQUOR CALCII HYDROXIDI (LIQ. CALC. HYDROX.), $Ca(OH)_2$, U.S.P. (Liquor Calcis, Limewater).

It contains about 0.15 per cent of calcium hydroxide in water.

DOSAGE.—15 cc. (4 fluidrachms) (U.S.P.). Used chiefly as an antacid in children.

MAGNESIUM SALTS

MAGNESIUM CARBONATE; MAGNESII CARBONAS (MAG. CARB.), U.S.P. (Carbonate of Magnesia).

It is hydrated magnesium carbonate, equivalent to about 41 per cent MgO.

It occurs as a white, bulky powder, odorless and tasteless, and practically insoluble in water and alcohol.

DOSAGE.—Antacid, 0.6 Gm. (10 grains); laxative, 8 Gm. (2 drachms) (U.S.P.).

MAGNESIA MAGMA, MAGMA MAGNESIAE (MAGMA MAG.), U.S.P. (Milk of Magnesia).

It occurs as a suspension of magnesium hydroxide ($Mg[OH]_2$) (7.5%) in water, forming a thick white liquid.

DOSAGE.—Antacid, 4 cc. (1 fluidrachm); laxative, 15 cc. (4 fluidrachms) (U.S.P.).

MAGNESIUM OXIDE; MAGNESII OXIDUM (MAG. OXID.), U.S.P. (Magnesia, Light Magnesia).

It contains about 96 per cent of MgO.

DOSAGE.—Antacid, 0.25 Gm. (4 grains); laxative, 4 Gm. (60 grains) (U.S.P.).

MAGNESIUM TRISILICATE; MAGNESH TRISILICAS (MAG. TRISIL.), ($2\,MgO \cdot 3\,SiO_2 \cdot nH_2O$), U.S.P.

THERAPEUTICS.—It is used for the relief of gastric hyperacidity and for pain associated with gastric and duodenal ulcers.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Magnesium Trisilicate Tablets; Tabellae Magnesii Trisilicatis (Tab. Mag. Trisil), U.S.P.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

CATHARTICS

Cathartics, commonly known as *physics,* are remedies used for the purpose of evacuating the contents of the intestines *per anum*—defecation. They were used more freely in olden times; in fact, to take medicine internally was at one time almost synonymous with taking a physic. The term physic has been used, and is, to some extent, employed at present, to indicate the art of therapeutics.

Fig. 23.—The effect of excitation of both splanchnic nerves on the intestinal contractions. (From Starling.)

With the progress of therapeutic knowledge, a number of specific terms have been created to designate the many subdivisions of this large group. The Greeks spoke of *cathartics* and the Romans of *purgatives,* both meaning to clean up, when they referred to drugs which were employed to free the body of accumulated feces. The term *evacuant,* to remove the feces, is used, while *aperient* indicates to open the bowels. A *drastic,* to force through, is a strong cathartic, while a *laxative* is a drug which softens the fecal matter. *Carminatives* are employed to remove gases from the stomach. The flow of bile is increased by a *cholagogue,* and to produce watery evacuations *hydragogues* are administered. The term *saline* indicates a cathartic consisting of neutral salts of the metals of the alkalies or alkaline earths.

The formation of the feces is the result of the accumulation of nonabsorbable remnants of the mixed foodstuffs—cellulose, animal fibrous tissue, cartilage, etc.

The mechanical factor influencing the propulsion of digesting material through the intestines is the peristaltic wave. It involves a contraction above the stimulating bolus of material and a relaxation below. The stimulation for peristalsis originates in the intestine from the fecal contents and is dependent upon the integrity of Auerbach's plexuses. The muscular contractions will continue after the intestine is removed from the body, demonstrating its automatism, although its activity may be influenced by central nervous stimuli through the autonomic nervous system—vagus stimulators and splanchnic inhibitors. Therefore our mental conduct may influence our digestion and elimination. The feces in the large intestine are retarded under ordinary circumstances which allows time for the absorption of water, concentrating the feces. The inhibition of normal peristalsis produces acute and chronic constipation. The cause and site of the constipation should be determined before treatment is given. As cathartic drugs do not affect all parts of the intestinal tract equally, it is necessary to select the drug carefully. Constipation may result from causes other than muscular sluggishness, such as cancer or tuberculosis.

Regular use of drugs or agents to correct chronic constipation must be discouraged, as such agents have a tendency to upset the normal function of the intestines and aggravate the disorder. In acute constipation, or in acute poisoning, cathartic measures are indicated. Cathartics are contraindicated in peritonitis, appendicitis, after intestinal surgery, and sometimes during pregnancy.

Intestinal cramps following the ingestion of cathartic drugs are usually due to muscular spasms produced by irritation from the drug. Belladonna or its alkaloids will mitigate this effect.

Cathartics may be employed: (1) in cases of constipation, (2) for the removal of harmful material from the intestines (poison), (3) to correct some forms of diarrhea, (4) to remove fluid from the body as in dropsy and cerebral congestion.

The normal number of stools per day is one or two. Many people remain in apparent health, though they habitually depart from this rule. Hard dry feces are usually a sign of constipation.

The action of cathartics depends on the nature of the remedy employed. Direct irritation of the smooth muscular coat of the intestines is generally produced by the bulk of cathartics. Others act by an indirect irritation of the motor ganglia of the intestines, which results in an increased peristalsis. The quick propulsion of the feces by cathartics prevents their formation into a solid mass

and the resultant stool is usually of a fluid nature. The various alkali salts, as the sulfates, phosphates, and tartrates of the alkaline metals—magnesium, sodium and potassium, act by osmosis and as mild irritants. The salines retain in the bowel the water of their own solution; by osmosis they abstract fluid from the surrounding blood and lymph tissues until they become isotonic with the body fluids, and the bulk and fluidity, increase peristalsis and produce copious stools. The readily diffusible salts—sodium chloride, etc.—do not retain the water of their solution, and are easily absorbed. Certain mild cathartics act by indirect stimulation of the motor ganglia, caused by their bulky mass—flaxseed, agar-agar, etc. Dangerous irritation, followed by severe inflammation and annoying tenesmus, is often caused by the drastic cathartics, such as croton oil, jalap, colocynth. They are rarely employed at present.

The Vegetable Cathartics

The drugs of this group owe their cathartic properties to glucosides and resins which act as irritants, reflexly stimulating peristalsis. They all contain tannic acid or related compounds, which tend to constipate the patient. Some will produce spasms of the intestines and are not satisfactory for patients with irritable intestines. Their site of action is chiefly the colon, although the small intestine may be affected to a lesser extent. Normal doses produce no action other than catharsis; larger doses may produce symptoms of collapse. They are not absorbed to any extent and when absorbed do not irritate the kidneys.[1]

Senna; Senna (Senn.), U.S.P. (Senna Leaves).

The dried leaflets of *Cassia acutifolia*, or of *Cassia angustifolia*, family *Leguminosae*. Senna is principally administered in powder form.

Therapeutics.—These preparations are efficient cathartics and are the most efficacious of the anthraquinone group. They act chiefly on the large intestine and are used in the treatment of chronic constipation. Their use is not followed by secondary constipation.

Dosage.—2 Gm. (30 grains) (U.S.P.).

Preparations.—

Fluidextract of Senna; Fluidextractum Sennae (Fldext. Senn.), U.S.P.—Senna (100%). Absolute alcohol content about 25 per cent.

Dosage.—2 cc. (30 minims) (U.S.P.).

[1]Bastedo, Walter A.: Materia Medica Pharmacology Therapeutics and Prescription Writing, 1937, Philadelphia, Pa., W. B. Saunders Co.

Compound Powder of Senna; Pulvis Sennae Compositus (Pulv. Sen. Comp.), N.F. (Compound Licorice Powder).—Senna (18%), washed sulfur (8%) with glycyrrhiza (24%), oil of fennel (0.4%), and sucrose (50%).

DOSAGE.—4 Gm. (1 drachm) (U.S.P.).

Syrup of Senna; Syrupus Sennae (Syr. Senn.), U.S.P.—Fluidextract of senna (25%) and oil of coriander in sucrose and water. Absolute alcohol content about 6 per cent.

DOSAGE.—8 cc. (2 fluidrachms) (U.S.P.).

CASTOR OIL; OLEUM RICINI (OL. RICIN.), U.S.P.

It is the fixed oil expressed from the seeds of *Ricinus communis,* family *Euphorbiaceae.* It is one of the earliest known cathartics.

THERAPEUTICS.—The oil is an active cathartic but it produces constipation and is therefore not indicated in the treatment of chronic constipation. It acts on both the small and large intestines by virtue of its irritation and has value as an initial purge in acute diarrheas.

DOSAGE.—15 cc. (4 fluidrachms) (U.S.P.).

Aromatic Castor Oil; Oleum Ricini Aromaticum (Ol. Ricin. Arom.), N.F.—Castor oil flavored with saccharin, oil of cinnamon, oil of clove, vanillin, coumarin, and alcohol.

USES.—Less disagreeable taste than castor oil.

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

CROTON OIL; OLEUM TIGLII (OL. TIGLII), N.F.

It is a fixed oil, expressed from the seeds of *Croton tiglium,* family *Euphorbiaceae.*

USES.—This is a dangerous cathartic of doubtful therapeutic value.

DOSAGE.—0.06 cc. (1 minim) (N.F.).

COLOCYNTH; COLOCYNTHIS (COLOCYNTH.), N.F. (Colocynth Pulp, Bitter Apple).

It is the peeled dried fruit or pulp of *Citrullus colocynthis,* family *Cucurbitaceae.* It is best administered as an extract in pill form.

USES.—These preparations act as irritant hydragogue cathartics and have a limited range of usefulness. They are not suited for daily use.

DOSAGE.—0.125 Gm. (2 grains) (N.F.).

PREPARATIONS.—

Extract of Colocynth; Extractum Colocynthidis (Ext. Colocynth.), N.F. (Powdered Extract of Colocynth, Extract of Bitter Apple).—One Gm. of extract represents 4 Gm. of colocynth.

DOSAGE.—30 mg. (½ grain) (N.F.).

Compound Extract of Colocynth; Extractum Colocynthidis Compositum (Ext. Colocynth. Comp.), N.F. (Powdered Extract of Colocynth Compound).—Extract of colocynth (16%), aloe (65%), resin of ipomea (14%), and cardamom seed.

DOSAGE.—0.25 Gm. (4 grains) (N.F.).

Compound Pills of Colocynth and Jalap; Pilulae Colocynthidis et Jalapae Compositae (Pil. Colocynth. et Jalap. Comp.), N.F. (Vegetable Cathartic Pills).—Each pill contains compound extract of colocynth, 0.06 Gm. (1 grain), extract of hyoscyamus, 0.03 Gm. (½ grain), resin of jalap, 0.02 Gm. (⅓ grain), extract of leptandra and resin of podophyllum, each 0.015 Gm. (¼ grain) with oil of peppermint and diluted alcohol.

DOSAGE.—1 pill (N.F.).

JALAP; JALAPA (JALAP.), N.F. (Jalap Root).

It is the dried tuberous root of *Exogonium purga,* family *Convolvulaceae.* It yields not less than 9 per cent of resins. It is principally employed as a powder, extract, or tincture.

USES.—Drastic hydragogue cathartic.

DOSAGE.—1 Gm. (15 grains) (N.F.).

PREPARATIONS.—

Fluidextract of Jalap; Fluidextractum Jalapae (Fldext. Jalap.), N.F.—Jalap (100%). Absolute alcohol content about 71 per cent.

DOSAGE.—1 cc. (15 minims) (N.F.).

Compound Powder of Jalap; Pulvis Jalapae Compositus (Pulv. Jalap. Comp.), N.F.—Jalap (35%) and potassium bitartrate (65%).

DOSAGE.—2 Gm. (30 grains) (N.F.).

Resin of Jalap; Resina Jalapae (Res. Jalap.), N.F.—The resin from jalap.

DOSAGE.—0.125 Gm. (2 grains) (N.F.).

Tincture of Jalap; Tinctura Jalapae (Tr. Jalap.) N.F.—Jalap (20%), in alcohol and water. Absolute alcohol content about 79 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

PODOPHYLLUM; PODOPHYLLUM (PODOPH.), N.F. (Mandrake, May Apple).

It is the dried rhizome and roots of *Podophyllum peltatum,* family *Berberidaceae.* It yields not less than 5 per cent of resin. It is principally administered as an extract or resin in pill form.

Resin of Podophyllum; Resina Podophylli (Res. Podoph.), N.F. (Podophyllin).—The resin from podophyllum.

USES.—Slow and effective but irritant cathartic.

DOSAGE.—10 mg. (⅙ grain) (N.F.).

CASCARA SAGRADA; CASCARA SAGRADA (CASC. SAGR.), U.S.P. (Rhamnus Purshiana).

It is the dried bark of *Rhamnus purshiana,* family *Rhamnaceae.* It is principally administered as a fluidextract or as the extract.

THERAPEUTICS.—The preparations of cascara sagrada are laxative, acting on the colon. They have little tendency to constipate and may be used frequently without withdrawal symptoms and are extensively used in the treatment of chronic constipation.

PREPARATIONS.—

Elixir of Cascara Sagrada; Elixir Cascarae Sagradae (Elix. Casc. Sagr.), N.F.—Aromatic fluidextract of cascara sagrada (50%) and syrup of glycyrrhiza. Absolute alcohol content about 12 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Extract of Cascara Sagrada; Extractum Cascarae Sagradae (Ext. Casc. Sagr.), U.S.P. (Extract of Rhamnus Purshiana, Powdered Extract of Cascara Sagrada).—One Gm. of the extract represents 3 Gm. cascara sagrada.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Fluidextract of Cascara Sagrada; Fluidextractum Cascarae Sagradae (Fldext. Casc. Sagr.), U.S.P. (Fluidextract of Rhamnus Purshiana).—Cascara Sagrada (100%). Absolute alcohol content about 18 per cent.

DOSAGE.—1 cc. (15 minims) (U.S.P.).

Aromatic Fluidextract of Cascara Sagrada; Fluidextractum Cascarae Sagradae Aromaticum (Fldext. Casc. Sagr. Arom.), U.S.P. (Aromatic Fluidextract of Rhamnus Purshiana).—The fluidextract, sweetened and flavored to lessen its bitter taste; its effectiveness is also lessened. Absolute alcohol content about 18 per cent.

DOSAGE.—2 cc. (30 minims) (U.S.P.).

Compound Pills of Cascara; Pilulae Cascarae Compositae (Pil. Casc. Comp.), N.F. (Hinkle's Pills).—Each pill contains extract of cascara sagrada, 0.016 Gm. (¼ grain), aloin, 0.016 Gm. (¼ grain), resin of podophyllum, 0.01 Gm. (⅙ grain), extract of belladonna, 0.008 Gm. (⅛ grain), oleoresin of ginger, 0.004 Gm. (1/16 grain), and glycyrrhiza 0.01 Gm. (⅙ grain) with glucose.

DOSAGE.—1 pill (N.F.).

FRANGULA; FRANGULA (FRANG.), N.F. (Buckthorn Bark).

It is the dried bark of *Rhamnus frangula,* family *Rhamnaceae.* It is principally administered as a fluidextract.

USES.—Similar to those of cascara sagrada.

DOSAGE.—1 Gm. (15 grains) (N.F.).

Fluidextract of Frangula; Fluidextractum Frangulae (Fldext. Frang.), N.F. (Fluidextract of Buckthorn Bark).—Frangula (100%). Absolute alcohol content about 23 per cent.

DOSAGE.—1 cc. (15 minims) (N.F.).

RHUBARB; RHEUM, U.S.P.

It is the dried rhizome and roots of *Rheum officinale,* or of *Rheum palmatum* and other species of the family *Polygonaceae.* It is principally administered as an extract, fluidextract, or tincture.

THERAPEUTICS.—Used as a bitter tonic, stomachic, and cathartic. It acts chiefly on the colon, and because of its astringent property its cathartic action is followed by constipation.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

PREPARATIONS.—

Alkaline Elixir of Rhubarb; Elixir Rhei Alkalinum (Elix. Rhei Alk.), N.F. (Neutralizing Cordial).—Fluidextract of rhubarb (1.6%), fluidextract of hydrastis (0.8%), and potassium carbonate (1.6%) with tincture of cinnamon, spirit of peppermint in syrup and diluted alcohol. Absolute alcohol content about 36 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Extract of Rhubarb; Extractum Rhei (Ext. Rhei), U.S.P. (Powdered Extract of Rhubarb).—One Gm. of extract represents 2 Gm. of rhubarb.

DOSAGE.—0.5 Gm. (7½ grains) (U.S.P.).

Fluidextract of Rhubarb; Fluidextractum Rhei (Fldext. Rhei), N.F.—Rhubarb (100%). Absolute alcohol content about 59 per cent.

DOSAGE.—1 cc. (15 minims) (N.F.).

ALOE; ALOE, U.S.P. (Aloes).

It is the inspissated juice of the leaves of *Aloe Perryi* or of *Aloe ferox* and other species of the *Liliaceae* family. It is principally administered in its purified form as an extract, tincture, or wine.

THERAPEUTICS.—An irritating cathartic acting chiefly on the large intestine. Large doses may produce griping pains. Advocated for the treatment of chronic constipation.

DOSAGE.—0.25 Gm. (4 grains) (U.S.P.), as pills.

PREPARATIONS.—

Extract of Aloe; Extractum Aloes (Ext. Aloe.), N.F. (Powdered Extract of Aloe).

DOSAGE.—0.125 Gm. (2 grains) (N.F.).

Pills of Aloe; Pilulae Aloes (Pil. Aloe.), N.F.—Each pill contains aloe, 0.13 Gm. (2 grains), with soap.

DOSAGE.—2 pills (N.F.).

Pills of Aloe and Mastic; Pilulae Aloes et Mastiches (Pil. Aloe. et Mastic.), N.F. (Lady Webster Dinner Pill).—Each pill contains aloe, 0.13 Gm. (2 grains) and mastic, 0.04 Gm. (⅔ grain), with rose.

DOSAGE.—2 pills (N.F.).

Pills of Aloe and Myrrh; Pilulae Aloes et Myrrhae (Pil. Aloe. et Myrrh.), N.F.—Each pill contains aloe, 0.13 Gm. (2 grains), and myrrh, 0.06 Gm. (1 grain), with aromatic powder and glucose.

DOSAGE.—2 pills (NF.).

Tincture of Aloe; Tinctura Aloes (Tr. Aloe.), N.F.—Aloe (10%) and glycyrrhiza in diluted alcohol. Absolute alcohol content about 46 per cent. It is a disagreeable cathartic.

DOSAGE.—2 cc. (30 minims) (N.F.).

Tincture of Aloe and Myrrh; Tinctura Aloes et Myrrhae (Tr. Aloe. et Myrrh.), N.F.—Aloe and myrrh (each 10%) and glycyrrhiza in alcohol and water. Absolute alcohol content about 62 per cent.

DOSAGE.—2 cc. (30 minims) (N.F.).

Saline Cathartics

The saline cathartics act as hydragogues by virtue of their osmotic influence which extracts fluids from the tissues increasing the bulk in the intestines and stimulating peristalsis. These salts are not readily absorbed and have little or no direct effect on the kidneys. They act on both the large and small intestines. Their continued use cannot be considered harmless.

SODIUM PHOSPHATE; SODII PHOSPHAS (SOD. PHOS.), $Na_2HPO_4.7H_2O$, U.S.P.

Sodium phosphate, representing about 46 per cent of the anhydrous salt, appears in large, colorless crystals, odorless, and having a saline, cooling taste. It is soluble in about 4 parts of water and almost insoluble in alcohol. Sodium phosphate is best administered as the effervescent sodium phosphate, U.S.P.

USES.—It has a more pleasant taste and is less active than magnesium sulfate.

DOSAGE.—4 Gm. (1 drachm) (U.S.P.).

PREPARATIONS.—

Solution of Sodium Phosphate; Liquor Sodii Phosphatis (Liq. Sod. Phos.), N.F.—Exsiccated sodium phosphate (40%) and citric acid in glycerin and distilled water.

DOSAGE.—8 cc. (2 fluidrachms) (N.F.).

Effervescent Sodium Phosphate; Sodii Phosphas Effervescens (Sod. Phos. Eff.), U.S.P.—109 Gm. of the salt contain exsiccated sodium phosphate (20 Gm.) in a mixture of sodium bicarbonate (47.7 Gm.), tartaric acid (25.2 Gm.), and citric acid (16.2 Gm.), the last three yielding sodium citrate and sodium tartrate.

DOSAGE.—10 Gm. (2½ drachms) (U.S.P.).

Exsiccated Sodium Phosphate; Sodii Phosphas Exsiccatus (Sod. Phos. Exsic.), Na_2HPO_4, U.S.P. (Dried Sodium Phosphate).

It occurs as a white powder which absorbs moisture readily, and is freely soluble in water (1 in 8), but insoluble in alcohol.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

SODIUM SULFATE; SODII SULFAS (SOD. SULF.), $Na_2SO_4.10H_2O$, U.S.P. (Glauber's Salt).

It appears in large, colorless crystals, is odorless, and has a saline taste. It is soluble in about 1.5 parts of water and almost insoluble in alcohol.

DOSAGE.—15 Gm. (4 drachms) (U.S.P.).

MAGNESIUM SULFATE; MAGNESII SULFAS (MAG. SULF.), $MgSO_4.7H_2O$, U.S.P. (Epsom Salt).

It appears in small, colorless needles, without odor, and has a cooling, saline, and bitter taste. It is soluble in 1 part of water and practically insoluble in alcohol. It is best administered as the effervescent magnesium sulfate.

THERAPEUTICS.—These preparations are active hydragogue cathartics and are not absorbed to any extent from the intestines. When injected intramuscularly they act as an anticonvulsant. It is a dangerous drug for parenteral use, as it may arrest respiration. Its antidote is physostigmine salicylate, U.S.P. (1 to 2 mg. given hypodermically).

DOSAGE.—15 Gm. (4 drachms) (U.S.P.), in solution.

PREPARATIONS.—

Ampuls of Magnesium Sulfate; Ampullae Magnesii Sulfatis (Ampul. Mag. Sulf.), N.F.—It contains a sterile solution of magnesium sulfate in ampul water, and yields anhydrous magnesium sulfate, $MgSO_4$, equal to 46 to 54 per cent of the labeled amount of magnesium sulfate.

DOSAGE.—1 Gm. of magnesium sulfate (N.F.).

Effervescent Salt of Magnesium Sulfate; Sal Magnesii Sulfatis Effervescens (Sal Mag. Sulf. Eff.), N.F.—1000 Gm. of the salt contain magnesium sulfate (50 Gm.), sodium bicarbonate (40.3 Gm.), tartaric acid (21.1 Gm.), and citric acid (13.6 Gm.) yielding sodium tartrate and sodium citrate.

DOSAGE.—16 Gm. (4 drachms) (N.F.).

MAGNESIUM CITRATE; MAGNESII CITRAS.

Solution of Magnesium Citrate; Liquor Magnesii Citratis (Liq. Mag. Cit.), U.S.P.—Magnesium citrate corresponding to about 1.8 per cent of magnesium oxide.

USES.—Efficacious and pleasant mild saline laxative.

DOSAGE.—200 cc. (7 fluidounces) (U.S.P.).

POTASSIUM BITARTRATE; POTASSII BITARTRAS (POT. BITART.), $KHC_4H_4O_6$, U.S.P. (Cream of Tartar, Acid Potassium Tartrate).

It is a white, gritty powder, odorless, and has a pleasant, acidulous taste. It is soluble in about 165 parts of water and almost insoluble in alcohol (1 in 8,820).

USES.—Diuretic and aperient.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

POTASSIUM CITRATE; POTASSII CITRAS (POT. CIT.), $C_3H_4OH.(COOK)_3.H_2O$, U.S.P.

It is a white, granular powder, odorless, and having a cooling, saline taste. It is soluble in about 1 part of water and almost insoluble in alcohol. It is best administered as effervescent potassium citrate, U.S.P.

USES.—Sytemic alkali and diuretic, like potassium acetate, but more laxative.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Effervescent Potassium Citrate; Potassii Citras Effervescens (Pot. Cit. Eff.), U.S.P.—An effervescent mixture representing approximately potassium citrate (20%), and sodium bicarbonate (47.7%), tartaric acid (25.2%), and citric acid (16.2%) yielding sodium citrate and tartrate.

DOSAGE.—4 Gm. (1 drachm) (U.S.P.).

POTASSIUM AND SODIUM TARTRATE; POTASSII ET SODII TARTRAS (POT. ET SOD. TART.), U.S.P. (Rochelle Salt).

It is a white powder, odorless, and having a cooling, saline taste. It is soluble in about 1 part of water and almost insoluble in alcohol.

USES.—One of the less objectionable tasting saline cathartics.

DOSAGE.—10 Gm. (2½ drachms) (U.S.P.) in water.

Compound Effervescent Powders; Pulveres Effervescentes Compositi (Pulv. Eff. Co.), U.S.P. (Seidlitz Powder).—The blue paper contains sodium bicarbonate (2.5 Gm.) and potassium and sodium tartrate (7.5 Gm.). The white paper contains tartaric acid (2.2 Gm.).

DOSAGE.—The contents of a white and of a blue paper, dissolved separately in about one fluidounce of water, and the solutions mixed (U.S.P.).

When the powders are dissolved separately in water and the solutions are mixed, the tartaric acid acts on the sodium bicarbonate and releases carbonic acid, with effervescence.

Miscellaneous Cathartics

SULFUR

WASHED SULFUR; SULFUR LOTUM (SULFUR LOT.), U.S.P.

It is prepared by washing sublimed sulfur with water and ammonia. It is a fine, yellow powder, insoluble in water and slightly soluble in alcohol.

THERAPEUTICS.—Used locally in parasitic diseases of the skin and as a mild cathartic, especially in hemorrhoids.

DOSAGE.—4 Gm. (1 drachm) (U.S.P.).

PRECIPITATED SULFUR; SULFUR PRAECIPITATUM (SULFUR PRAEC.), U.S.P.

Made by precipitating a solution of calcium sulfide with hydrochloric acid.

DOSAGE.—4 Gm. (1 drachm) (U.S.P.).

SUBLIMED SULFUR; SULFUR SUBLIMATUM (SULFUR SUBLIM.), U.S.P. (Flowers of Sulfur).

THERAPEUTICS.—Same as those of washed sulfur.

MERCUROUS PREPARATIONS

MILD MERCUROUS CHLORIDE; HYDRARGYRI CHLORIDUM MITE (HYDRARG. CHLORID. MIT.), HgCl, U.S.P. (Mercurous Chloride, Calomel, Subchloride of Mercury).

It is a white, heavy powder, odorless and tasteless; insoluble in alcohol, water, and ether. It is *incompatible* with bromides, iodides, sulfates, sulfides, carbonates, limewater, alkalies, ammonia, cocaine, etc. It is best administered in powder form.

THERAPEUTICS.—Calomel is a slowly acting but efficient cathartic. It should be followed (8 hours) by a saline laxative and should not be used regularly, as mercurialism may result.

DOSAGE.—Laxative, 0.12 Gm. (2 grains) (U.S.P.). From 0.005 to 0.02 Gm. (1/12 to 1/3 grain) may be given every half hour or hour until from 0.1 to 0.2 Gm. (1½ to 3 grains) have been given. In the treatment of syphilis 0.1 Gm. (1½ grains) in oily suspension is injected about once a week.

PREPARATIONS.—

Compound Pills of Mild Mercurous Chloride; Pilulae Hydrargyri Chloridi Mitis Compositae (Pil. Hydrarg. Chlorid. Mit. Comp.), N.F. (Compound Cathartic Pills).—Each pill contains compound extract of colocynth, 0.08 Gm. (1⅓ grains), mild mercurous chloride, 0.06 Gm. (1 grain), resin of jalap, 0.02 Gm. (⅓ grain), and gamboge, 0.015 Gm. (¼ grain).

DOSAGE.—2 pills (N.F.).

Tablets of Mild Mercurous Chloride; Tabellae Hydrargyri Chloridi Mitis (Tab. Hydrarg. Chlorid. Mit.), N.F. (Calomel Tablets).—Contain 92.5 to 107.5 per cent of the stated amounts of mild mercurous chloride.

DOSAGE.—60 mg. (1 grain) of mild mercurous chloride (in tablets usually containing an aliquot portion of the average dose) (N.F.).

Tablets of Mild Mercurous Chloride and Sodium Bicarbonate; Tabellae Hydrargyri Chloridi Mitis et Sodii Bicarbonatis (Tab. Hydrarg. Chlorid. Mit. et Sod. Bicarb.), N.F. (Calomel and Soda Tablets).—Contain about 100 per cent of the stated amount of mild mercurous chloride.

DOSAGE.—60 mg. (1 grain) of mild mercurous chloride (in tablets usually containing an aliquot portion of the average dose) (N.F.).

PHENOLPHTHALEIN; PHENOLPHTHALEINUM (PHENOLPHTHAL.), C_6H_4-$CO_2.CO.(C_6H_4OH)_2$, U.S.P.

Phenolphthalein is a white, odorless, tasteless, crystalline powder. It is insoluble in water but soluble in 15 parts of alcohol. It has supplied the base for many proprietary cathartic exploitations. In moderate doses it acts as a mild cathartic, but in large doses as a hydragogue. It acts on the large intestine as an irritant, increasing peristalsis. When absorbed it may act as a kidney irritant, and in allergic individuals it may cause a persistent skin rash.

DOSAGE.—60 mg. (1 grain) (U.S.P.).

Tablets of Phenolphthalein; Tabellae Phenolphthaleini (Tab. Phenolphthal.), N.F.—Contain 92.5 to 107.5 per cent of the stated amount of phenolphthalein.

DOSAGE.—60 mg. (1 grain) of phenolphthalein (N.F.).

LIQUID PETROLATUM; PETROLATUM LIQUIDUM (PETROLAT. LIQ.), *U.S.P.* (Liquid Paraffin, White Mineral Oil).

A mixture of liquid hydrocarbons. Official as Heavy Liquid Petrolatum and Light Liquid Petrolatum. It may be obtained as such or sold under various proprietary names; it is used extensively as a laxative. When administered internally it is not absorbed from the intestinal canal but acts purely mechanically as a lubricant of the tract. It may be given in doses of one or two tablespoonfuls at bedtime, the amount to be increased or reduced according to the need.

DOSAGE.—15 cc. (4 fluidrachms) (U.S.P.).

PREPARATIONS.—

Emulsion of Liquid Petrolatum; Emulsum Petrolati Liquidi (Emuls. Petrolat. Liq.), U.S.P. (Mineral Oil Emulsion).—Liquid petrolatum (50%), acacia, syrup, vanillin, alcohol, and distilled water.

USES.—Intestinal lubricant and vehicle.

DOSAGE.—30 cc. (1 fluidounce) (U.S.P.).

Emulsion of Liquid Petrolatum with Phenolphthalein; Emulsum Petrolati Liquidi cum Phenolphthalcino (Emuls. Petrolat. Liq. c. Phenolphthal.), N.F.—Heavy liquid petrolatum (50%), phenolphthalein (0.4%), agar, acacia, alcohol, vanillin, saccharin, and distilled water.

USES.—It combines the laxative action of phenolphthalein with the lubricating action of emulsion of liquid petrolatum.

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

Cholagogue Cathartics

Cholagogues are drugs which promote the flow of bile. They may act as stimulants to the liver function, thereby increasing the formation of bile, or they may cause the gall bladder to empty. Bile is necessary for normal digestion and absorption and for the elimination of metabolites. Bile salts are the most efficient liver stimulants, and the presence of fats in the upper intestines causes the gall bladder to empty.

BILE

OX BILE; FEL BOVIS, U.S.P. (Oxgall).

It occurs as a brownish green viscid liquid with a peculiar odor and a disagreeable, bitter taste.

THERAPEUTICS.—Oxgall is used in the form of the extract as a cholagogue and laxative. It contains bile salts of which the two most important are the sodium salts of glycocholic and taurocholic acids. They are absorbed from the intestines and, by a hormonal action, stimulate bile formation in the liver. The bile salts aid in the absorption of fats, sterols, and fat-soluble substances.

PREPARATIONS.—

Extract of Ox Bile; Extractum Fellis Bovis (Ext. Fel. Bov.), U.S.P. (Powdered Extract of Oxgall).

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Extract of Ox Bile Tablets; Tabellae Extracti Fellis Bovis (Tab. Ext. Fel. Bov.), U.S.P.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

OLIVE OIL

OLIVE OIL; OLEUM OLIVAE (OL. OLIV.), U.S.P. (Sweet Oil).

It is a fixed oil obtained from the ripe fruit of the *Olea europoea,* family *Oleaceae.*

THERAPEUTICS.—The oil is digested in the intestines to fatty acids and glycerin which are absorbed. Its presence in the upper intestinal tract causes the gall bladder to empty, giving it a cholagogue action. Part of the oil escapes digestion and acts as a lubricant cathartic. The part which is absorbed acts as a food.

DOSAGE.—30 cc. (1 fluidounce) (U.S.P.).

MAGNESIUM SULFATE

MAGNESIUM SULFATE; MAGNESII SULFAS (MAG. SULF.), U.S.P. (Epsom Salt).

USES.—An active saline cathartic that may also act as a gall bladder emptier.

DOSAGE.—15 Gm. (4 drachms) (U.S.P.), in solution.

PREPARATION.—

Effervescent Salt of Magnesium Sulfate; Sal Magnesii Sulfatis Effervescens (Sal Mag. Sulf. Eff.), N.F.

In 1000 Gm. of the salt there are magnesium sulfate (50 Gm.), sodium bicarbonate (40.3 Gm.), tartaric acid (21.1 Gm.), and citric acid (13.6 Gm.) yielding sodium tartrate and sodium citrate.

DOSAGE.—16 Gm. (4 drachms) (N.F.).

Softening Agents

Softening agents are drugs which prevent the formation of hard feces and thereby allay intestinal irritation. Hard feces are de-

hydrated by prolonged stasis in the intestines. This may be prevented by hastening the expulsion of fecal matter from the large intestine by adding to the diet a nondigestible substance which holds moisture (agar), or by using a nonabsorbable substance which keeps the stools soft (petrolatum).

Petrolatum

Liquid Petrolatum; Petrolatum Liquidum (Petrolat. Liq.), U.S.P. (Liquid Paraffin, White Mineral Oil, Heavy Liquid Petrolatum).

It is a mixture of liquid hydrocarbons which occurs as a colorless, transparent, oily, nearly odorless and tasteless liquid; insoluble in water and alcohol.

Therapeutics.—Liquid petrolatum is not digested or absorbed in the intestines and is not a food. It passes through unchanged, acting mechanically as a softening agent for the feces. The daily use of this drug cannot be considered harmless, as it may act as an irritant to the intestinal mucosa.

Dosage.—15 cc. (4 fluidrachms) (U.S.P.).

Preparations.—

Emulsion of Liquid Petrolatum; Emulsum Petrolati Liquidi (Emuls. Petrolat. Liq.), U.S.P. (Mineral Oil Emulsion).

It contains liquid petrolatum (50%), acacia, syrup, vanillin, alcohol, and distilled water.

Uses.—Lubricant cathartic.

Dosage.—30 cc. (1 fluidounce) (U.S.P.).

Emulsion of Liquid Petrolatum With Phenolphthalein; Emulsum Petrolati Liquidi cum Phenolphthaleino (Emuls. Petrolat. Liq. c. Phenolphthal.), N.F.

It contains liquid petrolatum (50%), phenolphthalein (0.4%), agar, acacia, alcohol, vanillin, saccharin, and distilled water.

Uses.—It combines the cathartic action of phenolphthalein with the softening effect of liquid petrolatum.

Dosage.—15 cc. (4 fluidrachms) (N.F.).

See "Bulk Producers" for other softening agents.

Bulk-Producing Cathartics

The bulk-producing cathartics are dietary substances which are not digested or absorbed in the intestines. Their presence increases the bulk of the feces and results in a stimulation of peristalsis, giving a cathartic action.

AGAR

AGAR; AGAR, U.S.P. (Agar-Agar).

It is a mucilaginous substance extracted from certain seaweeds, the *Gelidium corneum,* and other species of *Gelidium,* family *Gelidiaceae.*

Agar occurs as colorless, tasteless, odorless, transparent strips. It is insoluble in cold water and slowly soluble in hot water.

THERAPEUTICS.—It is not digested or absorbed in the intestines. Its presence in the feces gives bulk, and it also has a demulcent and lubricant action. In chronic constipation with intestinal atony, it renders the feces soft and bulky and promotes peristalsis.

DOSAGE.—4 Gm. (1 drachm) (U.S.P.).

FLAXSEED

LINSEED; LINUM, U.S.P. (Flaxseed).

It occurs as the dried ripe seeds of the *Linum usitatissimum,* family *Linaceae.*

The seeds should be cooked and eaten as a cereal food. They are not well digested and increase the bulk of the feces.

TONICS AND ALTERATIVES

In the previous editions of this book, certain drugs have been classified as tonics and alteratives. The basis for their uses as such was determined largely by clinical experience. With the increasing knowledge of the pharmacologic action of drugs and with the better understanding of the primary causes of malnutrition, the number of drugs so classified has decreased to the extent that many of them may now be discussed more appropriately in other groupings. In view of this tendency and the uncertainty of the modus operandi, a less detailed discussion of these drugs will be given.

Tonics

Tonics are medicines intended to give increased vigor and "tone" to the system. Tonics, like alteratives, do not belong to a definite pharmacologic group; they are not prescribed to act on specific organs, but are believed to act on the organism as a whole. Tonics have been more or less empirically administered for the purpose of increasing the general metabolism, in consequence of which the patient is believed to have greater resistance to external deleterious influences. Compounds of iodine, iron, arsenic, phosphorus, and calcium represent the principal types of drugs that have been administered as tonics.

Iodine is essential for the normal activity of the thyroid gland. Iron exercises specific influence on the blood, and consequently it is sometimes used as a *hematinic.* Arsenic apparently causes a definite stimulation of cellular activity in general, and phosphorus furnishes a necessary component of the soft tissues as well as of the bones. Calcium is the essential component of bone structure and is present in the blood. Strychnine preparations were used to increase the tonus of muscles. Many vegetables, bitters, and some substances rich in essential food principles, such as cod liver oil, have been classified as tonics.

Alteratives

Alteratives (to change) are drugs which in the past have been extensively prescribed for the purpose of favorably modifying nutrition and thereby overcoming morbid processes; they aim to stimulate metabolism. Modern pharmacologists have discarded the term alteratives because the drugs belonging to this group do not act on specific organs, but on the organism as a whole. The drugs which are usually referred to as alteratives do not produce distinct symptoms when taken in ordinary doses; apparently no direct stimulation or depression can be observed, but nevertheless their therapeutic influence on the system as a whole has considerable support from clinical experience.

The iodides and some of the mercurials form the most important group of those drugs which have been designated as alteratives. Of the iodides, potassium and sodium iodide are the most favored representatives. The readily soluble salts of the bichloride and the biniodide of mercury are employed as the mercurial alteratives. Since the administration of these drugs, if used as alteratives, more appropriately belongs in the field of internal medicine, the interested student is referred to more comprehensive texts for their description and dosage.

ANTISPASMOTICS

The motor nerves to the gastrointestinal tract are from the parasympathetic nervous system. Any drug which inhibits the activity of this system will relax muscular spasms and relieve the symptoms of intestinal colic. (See Parasympathetic Depressant Drugs.)

TINCTURE OF BELLADONNA; TINCTURA BELLADONNAE (TR. BELLAD.), U.S.P.

DOSAGE.—0.6 cc. (10 minims) (U.S.P.).

ATROPINE SULFATE; ATROPINAE SULFATIS (ATROP. SULF.), U.S.P.
DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain) (U.S.P.).

INTESTINAL ANTISEPTICS

The intestinal tract normally contains bacteria. These microorganisms are physiologic, and no attempt should be made to decrease their number or destroy them. At times pathologic organisms are introduced, grow in the intestines, and produce disease. These infections may be treated by oral administration of drugs acting locally and/or systemically. It must be kept in mind that the infecting organisms are in the tissues where the antiseptic drug has difficulty in reaching them. As these drugs are absorbed in the intestines, the possibility of toxic reactions is always present and necessitates careful supervision of the patient.

PHENYL SALICYLATE; PHENYLIS SALICYLAS (PHENYL. SALICYL.), U.S.P. (Salol).

It occurs as a white powder with an aromatic odor and a characteristic taste. Very slightly soluble in water (1 in 6700); freely soluble in alcohol (1 in 6), and very soluble in fixed or volatile oils.

THERAPEUTICS.—It was introduced as an intestinal antiseptic but does not exert any action in the large intestine, and has only a brief, restricted action in the small intestines. The antiseptic action is due to the liberation of phenol and salicylic acid. It is used for coating enteric pills.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

Tablets of Phenyl Salicylate; Tabellae Phenylis Salicylatis (Tab. Phenyl Salicyl.), N.F. (Salol Tablets).

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

SULFAGUANIDINE, N.N.R. Sulfanilylguanidine monohydrate ($C_7H_{10}O_2N_4S.H_2O$).

It occurs as a white, odorless, crystalline powder and is soluble in hot alcohol and water (10% at 100° C.).

THERAPEUTICS.—It is administered by mouth and is soluble in the gastric and intestinal fluids but is poorly absorbed from the gastrointestinal tract. Its chief use is to exert a bacteriocidal or a bacteriostatic effect on the intestinal flora. Sulfaguanidine is the least toxic of the sulfonamides, chiefly because of its low rate of absorption. The blood concentration rarely exceeds 5 mg. per cent. In cases of drug poisoning the drug should be stopped and the contents of the stomach and intestines evacuated.

DOSAGE.—In bacillary dysentery the dosage is 0.05 gram per kilogram of body weight every four hours, day and night, until the number of daily stools is five or less, then reduce the number of doses to one every eight hours for at least three days. (See N.N.R.)

Teniafuges and Anthelmintics

Teniafuges are drugs which expel tapeworms, while *teniacides* destroy them. *Anthelmintics* are agents which act as poisons to many forms of intestinal worms. *Vermifuges* are substances which expel intestinal parasites but do not necessarily kill them. All of these drugs are toxic and should be used only after a careful diagnosis and under the care of a competent physician.

OIL OF CHENOPODIUM; OLEUM CHENOPODII (OL. CHENOPOD.), U.S.P. (Oil of American Wormseed).

It is a volatile oil, freely soluble (1 in 8) in alcohol.

THERAPEUTICS.—Anthelmintic, especially for roundworms and hookworms.

DOSAGE.—1 cc. (15 minims) U.S.P. The technique employed in administering oil of chenopodium in the treatment for hookworm is described in *Useful Drugs*, thirteenth edition. Even small doses may become toxic when repeated at intervals of several days.

SANTONIN; SANTONINUM (SANTONIN.), N.F.

An anhydride of santoninic acid.

THERAPEUTICS.—Used for its poisonous action on intestinal parasites, especially ascaris. When a poisonous dose is absorbed, it produces yellow vision and epileptiform convulsions. Finely powdered santonin should not be used, because it is absorbed readily.

DOSAGE.—0.06 Gm. (1 grain) (U.S.P.), in powder or capsules.

ASPIDIUM; ASPIDIUM, U.S.P. (Male Fern).

It consists of the rhizome and stipes of *Dryopteris Filix-mas*, or of the *Dryopteris marginalis*, family *Polypodiaceae*. It must yield not less than 1.5 per cent of crude filicin.

THERAPEUTICS.—Used as a teniacide in the form of an oleoresin.

Oleoresin of Aspidium; Oleoresina Aspidii (Oleores. Aspid.), U.S.P. (Oleoresin of Male Fern).

DOSAGE.—*Caution:* Single dose, once a day 4 Gm. (1 drachm) (U.S.P.), in capsules or in emulsion. Smaller doses are used for anemic or debilitated patients. The patient should be prepared by a light diet or fasting for twenty-four hours. The drug should be given early in the morning, preceded by a saline cathartic, and followed in

three hours by a saline laxative. Castor oil and other fixed oils should not be used in connection with oleoresin of aspidium, as they favor the absorption of the active principle.

ARECA; ARECA, N.F. (Areca Nut, Betel Nut).—Dried ripe seed.

THERAPEUTICS.—Used against intestinal parasites, principally in veterinary medicine.

Arecoline Hydrobromide; Arecolinae Hydrobromidum (Arecol. Hydrobrom.), N.F.

THERAPEUTICS.—Same as Areca.

CARBON TETRACHLORIDE, CARBONEI TETRACHLORIDUM (CARB. TETRACHLOR.) U.S.P.—CCl_4.

A clear, noninflammable, colorless liquid, having a characteristic ethereal odor resembling that of chloroform. It is very slightly soluble in water (1 in 2000); miscible with alcohol and with alcohol and other various solvents.

THERAPEUTICS.—It is used widely in the treatment of hookworm disease, but it is less useful against other intestinal parasites. Like the other powerful anthelmintics, it occasionally gives rise to toxic effects and should be used with caution, especially in those addicted to alcohol, those suffering from calcium deficiency in the blood, and patients heavily infested with ascarides. Headache is sometimes induced. A mild laxative is given to constipated patients on the day previous to treatment. Oils and fats should be avoided.

DOSAGE.—*Caution!* As anthelmintic for adults, single dose, 1 cc. (15 minims) (U.S.P.). Not to be repeated within three weeks.

Intestinal Amebicides

These drugs have a specificity of action on amebae, destroying them. They are especially useful in the treatment of amebic dysentery. Amebae may be isolated from periclasia pockets, but their pathogenicity has not been demonstrated.

IPECAC; IPECACUANHA, U.S.P. (Ipecacuanhae radix P.I.).—(For a detailed description see emetics.)

THERAPEUTICS.—Formerly used for amebic dysentery, but it has been displaced by emetine.

DOSAGE.—No dosage given as an amebicide.

Emetine Hydrochloride; Emetinae Hydrochloridum (Emet. Hydrochlor.), U.S.P.—An alkaloid of ipecac. (See Emetics.)

THERAPEUTICS.—It is given hypodermically for relief and prevention of amebic hepatitis and for the control of symptoms of acute

amebic dysentery. Its continued use causes neuritis, cardiac disturbances, and depression.

DOSAGE.—Daily, by intramuscular injection, 60 mg. (1 grain) (U.S.P.). Some authorities prefer daily doses of one-half grain. *Caution:* Under no circumstances should the total dosage of a course of treatment exceed 9 to 12 grains. The course should be interrupted at once if untoward symptoms occur.

Emetine Hydrochloride Injection; Injectio Emetinae Hydrochloridi (Inj. Emet. Hydrochlor.), U.S.P. (Emetine Hydrochloride Ampuls). —A sterile solution of emetine hydrochloride in water for injection.

DOSAGE.—Intramuscular, 60 mg. (1 grain) of emetine hydrochloride (U.S.P.).

CHINIOFON; CHINIOFONUM (CHINIOFON.), U.S.P. (Pulvis Chiniofoni, Chiniofon Powder U.S.P. XI).

Iodine content about 27 per cent.

THERAPEUTICS.—It is valuable in the treatment of amebic dysentery, but its use requires careful attention to the technique of administration. See *Useful Drugs,* thirteenth edition.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

CHAPTER XV

DRUGS WHICH AFFECT THE GENITOURINARY SYSTEM

DIURETICS

Diuretics (to increase the secretion of urine) are remedies employed for the purpose of promoting the secretion of urine. The organ which secretes the urine is the kidney. Under normal conditions the kidney performs three functions—it maintains the osmotic equilibrium of the blood, it removes the end products of metabolism, and it eliminates foreign substances from the body.

The urine is formed in the kidneys by filtration and secretion. The filtration occurs through the walls of the glomerular capillaries, forming the water and dialyzable contents of the urine. These capillaries are formed from the renal artery. The efferent capillaries are smaller than the afferent, therefore the blood pressure within the glomerular capillaries is higher than in the other capillaries of the body. The filtrate is collected within Bowman's capsule and passes through the tubular system. The tubular cells absorb much of the water and dialyzable substances, and return them to the blood. By a process of secretion in the tubules the nondialyzable substances are formed and passed out with the dialyzable ones to form the urine.

The urine may be acid, alkaline, or neutral in reaction. Occasionally it is desirable to produce an increased flow of urine which should react acid, alkaline, or neutral. From a physiologic point of view it is also of interest to know that with the urine certain drugs are excreted.

Diuretics are administered for the purpose of removing pathologic collections of exudates from the body tissues, as in diseases of the heart, nephritis, cellulitis, etc. They are also given to remove poisons which have entered the body or which are formed in the body. Flushing of the entire urinary tract includes the kidney, ureter, and bladder, and it is often employed for the purpose of preventing the formation of concrements in these tissues.

A number of drugs when administered internally will give various colors to the urine. For instance, analgesin changes the color of the urine to blood red, becoming yellow as it is rendered alkaline; aminopyrine changes it to cherry red; sulfonal to red brown; naphthalene

to black or grayish brown; salol to dark green or black after long usage; phenol to reddish brown; bromoform to dark green; naphthol to olive green or orange when strong doses are administered; santonin to yellow, turning to red on the addition of an alkali; cascara, senna, or rhubarb, to yellow or light red brown, turning red on the addition of an alkali, etc.

The function of the kidneys is dependent upon (1) the blood pressure within the glomeruli, (2) the number of glomeruli functioning (50 to 75% function normally), (3) the amount of blood passing through the glomeruli, (4) the condition of the glomerular capillaries and renal tubules, (5) the osmotic pressure of the body fluids, (6) the amount of water in the body, and (7) substances which inhibit the tubular function of absorption.

Diuretics Which Act by Stimulating the Kidneys

Xanthine Diuretics

The caffeine group contains caffeine, theobromine, and theophylline. They (1) produce an increase in the permeability of the tissue cells, causing them to give up water; (2) produce an increase in the permeability of the glomerular capillaries, thereby increasing the amount of glomerular filtrate; (3) stimulate the heart and circulation, causing more blood to pass through the kidney and increasing the blood pressure in the glomerular capillaries, and (4) increase the number of glomeruli functioning. All of these factors increase the amount of urine excreted.

Caffeine; Caffeina (Caff.), U.S.P.

Trimethylxanthine, an alkaloid obtained from coffee, chiefly.

Uses.—Diuretic. (See Cerebral Stimulants.)

Dosage.—0.2 Gm. (3 grains) (U.S.P.), in capsules.

Theobromine and Sodium Acetate; Theobromina et Sodii Acetas (Theobrom. et Sod. Acet.), U.S.P.

A hydrated mixture of sodium theobromine ($C_7H_7N_4O_2Na$) and sodium acetate ($NaC_2H_3O_2$) in approximately molecular proportions. It yields about 60 per cent of theobromine ($C_7H_8N_4O_2$).

It is a white crystalline powder, which is practically odorless, with a bitter taste. It is moderately hygroscopic, and on exposure to air it gradually absorbs carbon dioxide with the liberation of free theobromine. Soluble in water (1 in 1.5); slightly soluble in alcohol. Even weak acids precipitate the theobromine from the aqueous solution.

THERAPEUTICS.—It is used as a diuretic. It has the advantage over theobromine of greater solubility and toleration by the stomach. It is less effective but more sustained than theophylline.

DOSAGE.—0.5 Gm. (7½ grains) (U.S.P.).

Theobromine and Sodium Acetate Capsules; Capsulae Theobrominae et Sodii Acetatis (Cap. Theobrom. et Sod. Acet.), U.S.P.

They contain an amount of theobromine ($C_7H_8N_4O_2$) equivalent to about 60 per cent of the labelled amount of theobromine and sodium acetate, including all tolerances.

DOSAGE.—0.2 Gm. (3 grains) of theobromine and sodium acetate (U.S.P.).

THEOBROMINE WITH SODIUM SALICYLATE; THEOBROMINA CUM SODII SALICYLATE (THEOBROM. C. SOD. SALICYL.), N.F. (Theobrominae Sodio-Salicylas, Diuretin).

It is a white powder, which is odorless, but has a saline taste. It is soluble in water, but is decomposed in the presence of carbon dioxide. It should be given in well-diluted solutions.

THERAPEUTICS.—Mainly used as a diuretic.

DOSAGE.—1 Gm. (15 grains) (N.F.).

THEOPHYLLINE; THEOPHYLLINA (THEOPHYLL.), U.S.P. (Dimethylxanthine).

This is an isomer of theobromine.

THERAPEUTICS.—Theophylline has a diuretic action similar to that of theobromine but said to be not so lasting.

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.).

THEOPHYLLINE AND SODIUM ACETATE TABLETS; TABELLAE THEOPHYLLINAE ET SODII ACETATIS (TAB. THEOPHYLL. ET SOD. ACET.), U.S.P.

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.).

THEOPHYLLINE ETHYLENEDIAMINE; THEOPHYLLINA AETHYLENEDIAMINICA (THEOPHYLL. AETHYLENDIAM.), U.S.P. (Aminophylline).

It contains from 75 to 82 per cent anhydrous theophylline and not less than 12.3 per cent and not more than 13.8 per cent of ethylenediamine.

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.).

Theophylline Ethylenediamine Injection; Injectio Theophyllinae Aethylenediaminicae (Inj. Theophyll. Aethylenediam), U.S.P. (Theophylline Ethylenediamine Ampuls, Aminophylline Ampuls).

DOSAGE.—Intramuscular or intravenous, 0.1 Gm. (1½ grains) of theophylline ethylenediamine (U.S.P.).

Theophylline Ethylenediamine Tablets; Tabellae Theophyllinae Aethylenediaminicae (Tab. Theophyll. Aethylenediam.), U.S.P. (Aminophylline Tablets).—They contain anhydrous theophylline.

DOSAGE.—0.2 Gm. (3 grains) of ethylenediamine (U.S.P.).

THEOPHYLLINE AND SODIUM ACETATE; THEOPHYLLINA ET SODII ACETATE (THEOPHYLL. ET SOD. ACET.), U.S.P. (Theophyllina cum Sodii Acetas, U.S.P. XI).

USES.—The same as those of theophylline, but it has the advantage of being readily soluble.

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.).

Theophylline and Sodium Acetate Tablets; Tabellae Theophyllinae et Sodii Acetatis (Tab. Theophyll. et Sod. Acet.), U.S.P.

DOSAGE.—0.2 Gm. (3 grains) of theophylline and sodium acetate (U.S.P.).

Diuretics Which Act by Increasing the Blood Pressure in the Glomerular Capillaries

DIGITALIS

POWDERED DIGITALIS; DIGITALIS PULVERATA (DIGIT. PULVERAT.), U.S.P.—(For a general discussion of Digitalis see Cardiac Stimulants.)

THERAPEUTICS.—Digitalis preparations act as a direct cardiac stimulant, increasing the amount of blood and the blood pressure in the glomerular capillaries. It has therapeutic usefulness as a diuretic only when the circulation is impaired. An overdose causes nausea and vomiting.

DOSAGE.—0.1 Gm. (1½ grains) U.S.P.

PREPARATIONS.—(See Cardiac Stimulants.)

Drugs and Agents Which Act by Increasing the Amount of Blood Passing Through the Glomeruli

These drugs act by dilating the renal vessels, thereby increasing the amount of blood passing through the kidneys.

AGENTS.—Hot baths produce a dilatation of the cutaneous blood vessels and a concomitant vasodilation in the kidneys. The increase in diaphoresis has but little effect in increasing the elimination of waste products.

DRUGS.—The nitrites are a group of compounds which dilate the blood vessels by a direct action on the muscle walls. This action on the muscle walls is not dependent upon the innervation.

PREPARATIONS.—(See Drugs Which Affect the Blood Vessels for a complete description of the nitrites.)

Tablets of Sodium Nitrite; Tabellae Sodii Nitritis (Tab. Sod. Nitrit.), U.S.P.

DOSAGE.—60 mg. (1 grain) U.S.P.

Spirit of Ethyl Nitrite; Spiritus Aethylis Nitritis (Sp. Aeth. Nitrit.), N.F. (Sweet Spirit of Nitre).—It contains ethyl nitrite (4%) in about 90% alcohol.

THERAPEUTICS.—It is a weak and unreliable diuretic often prescribed as a diuretic for children.

DOSAGE.—2 cc. (30 minims) N.F.

Drugs Which Act by Irritating the Kidneys and Producing Vasodilation of the Glomerular Vessels

JUNIPER

OIL OF JUNIPER; OLEUM JUNIPERI (OL. JUNIP.), U.S.P. (Juniper Oil).

It occurs as a volatile oil distilled with steam, from the dried ripe fruit of the *Juniperus communis*, family *Pinaceae*. The oil is colorless to faintly green to yellow and has a characteristic odor and taste. It is insoluble in water and soluble in alcohol (1 to 4) and has a specific gravity about 0.85 at 25° C.

DOSAGE.—Not given as such.

Diuretics Which Act by Increasing the Osmotic Pressure of the Blood

These salts are dialyzed through the glomerular capillaries into Bowman's capsule and, by virtue of the osmotic pressure they exert, prevent the absorption of liquid in the renal tubules. The potassium salts are more efficient diuretics than the sodium salts because the body does not store the potassium to any extent, as it does the sodium. The excess salts are therefore rapidly eliminated through the kidneys, carrying with them the water of solution.

POTASSIUM DIURETICS

POTASSIUM ACETATE; POTASSII ACETAS (POT. ACET.), CH_3COOK, U.S.P.

It occurs as a white, odorless, crystalline powder or mass, with a saline taste. It is very soluble in water (1 in 5) and freely soluble in alcohol (1 in 5).

THERAPEUTICS.—A systemic alkali and diuretic often administered in milk or water.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

POTASSIUM CITRATE; POTASSII CITRAS (POT. CIT.), $C_3H_4OH.(COOK)_3.H_2O$, U.S.P.

It occurs as transparent crystals or a white powder; it is odorless and has a saline taste. It is freely soluble in water (1 in 1) and almost insoluble in alcohol.

THERAPEUTICS.—It acts as a systemic alkali and diuretic with a mild cathartic action.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

PREPARATIONS.—

Effervescent Potassium Citrate; Potassii Citras Effervescens (Pot. Cit. Eff.), U.S.P.—An effervescent mixture representing potassium citrate (20%), sodium bicarbonate (47.7%), tartaric acid (25.2%), and citric acid (16.2%). It yields sodium citrate and tartrate.

DOSAGE.—4 Gm. (60 grains) (U.S.P.).

Solution of Potassium Citrate; Liquor Potassii Citratis (Liq. Pot. Cit.), N.F.—It contains potassium citrate (8%), citric acid (6%) in water.

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

SODIUM DIURETICS

SODIUM BICARBONATE; SODII BICARBONAS (SOD. BICAR.), $NaHCO_3$, U.S.P. (Baking Soda).

(See Antacids for a detailed description.)

THERAPEUTICS.—Gastric antacid and systemic alkalyzer, with mild diuretic and cathartic action.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

MERCURIAL DIURETICS

The mercurial diuretics increase the flow of urine by a toxic inhibition of tubular function.[1] These compounds may be toxic when given in overdoses or to patients already suffering from kidney damage. They are not diuretics of first choice.

PREPARATION.—

Mercurophylline Injection; Injectio Mercurophyllinae (Inj. Mercurophyll.), U.S.P.—A sterile solution in water for injection of the sodium salt of β-methoxy-γ-hydroxymercuri propylamide of trimethyl

[1]Roby, Charles: J. Pharmacol. 69: 200, 1940.

cyclopentane dicarboxylic acid ($C_{14}H_{26}NO_5HgNa$), containing mercury equivalent to about 40 per cent.

THERAPEUTICS.—A potent diuretic used to remove fluid in edema of congestive heart failure, nephrosis, and cirrhosis of the liver with ascities.

DOSAGE.—Intramuscularly, 0.1 Gm. (1½ grains) (U.S.P.).

Diuretics Which Act by Increasing the Permeability of the Glomerular Capillaries

(See the Xanthine Group of Diuretics.)

URIC ACID SOLVENTS

Uric acid solvents, also referred to as *lithontriptics* or *antilithics* (stone destroyers) and as *antiarthritics* (gout remedies), are drugs employed for the purpose of dissolving uric acid and increasing its excretion.

Regarding the process of uric acid formation, excretion, destruction, retention, deposition, and solution in health and disease, very few absolute facts are known, and consequently the therapeutic measures, as far as remedies are concerned, are very limited. Only three important drugs used in general medicine in the treatment of gout and arthritic conditions will be presented here.

COLCHICUM CORM; COLCHICI CORMUS (COLCH. CORM.), N.F. (Colchicum Root).

It yields not less than 0.35 per cent of anhydrous colchicine.

THERAPEUTICS.—Antineuralgic and analgesic; frequently used in the treatment of acute gouty attacks. It may act as a cathartic.

DOSAGE.—0.25 Gm. (4 grains) (N.F.), in pills; or preferably as the tincture.

PREPARATIONS.—

Fluidextract of Colchicum Corm; Fluidextractum Colchici Cormi (Fldext. Colch. Corm.), N.F.—Colchicum corm (100%), yielding about 0.35 per cent of colchicine. Absolute alcohol content about 55 per cent.

DOSAGE.—0.25 cc. (4 minims) (N.F.).

Strong Tincture of Colchicum Corm; Tinctura Colchici Cormi Fortis (Tr. Colch. Corm. Fort.), N.F.—Fluidextract of colchicum corm (40%) yielding about 0.14 per cent of colchicine, in alcohol and water. Absolute alcohol content about 26 per cent.

DOSAGE.—0.6 cc. (10 minims) (N.F.).

COLCHICINE, COLCHICINA, U.S.P.

An alkaloid obtained from *Colchicum autumnale,* family ***Liliaceae.*** ***Caution.—Colchicine is extremely poisonous.*** (U.S.P.)

DOSAGE.—0.5 mg. ($\frac{1}{120}$ grain) (U.S.P.).

CINCHOPHEN; CINCHOPHENUM (CINCHOPHEN.), $C_6H_5C_9H_5N.COOH$, N.F. (Phenylcinchoninic Acid, Phenyl-quinoline-carboxylic Acid).

THERAPEUTICS.—Analgesic and antipyretic, used especially in arthritis to increase the excretion of uric acid.

DOSAGE.—0.5 Gm. (8 grains) (N.F.), in tablets or powder.

Tablets of Cinchophen; Tabellae Cinchopheni (Tab. Cinchophen.), N.F.—Contain 92.5 to 107.5 per cent of the stated amount of cinchophen.

DOSAGE.—0.5 Gm. (8 grains) of cinchophen (N.F.).

CHAPTER XVI

DRUGS WHICH ACT ON THE SKIN AND MUCOUS MEMBRANES

PROTECTIVES, DEMULCENTS, AND EMOLLIENTS

Protectives

Protectives are agents which are employed for the purpose of mechanically covering sensitive, wounded, diseased, or otherwise defective body surfaces, including the mouth, against external insults.

PYROXYLIN; PROXYLINUM (PYROXYLIN.), U.S.P. (Soluble Guncotton).—Chiefly cellulose tetranitrate.

USES.—As a base for collodions. It is very inflammable.

PREPARATIONS.—

Collodion; Collodium (Collod.), U.S.P.—It is a mixture of pyroxylin (4%) in ethyl oxide and alcohol.

USES.—Protective. May be used in operative dentistry as a covering for synthetic porcelain restorations until they have thoroughly set.

Flexible Collodion: Collodium Flexile (Collod. Flex.), U.S.P.—It is a mixture of collodion (95%) with camphor (2%) and castor oil (3%).

USES.—Same as for collodion. It does not contract as much as collodion in drying.

BALSAMS AND RESINS

These are organic compounds of obscure composition, insoluble in water and soluble in alcohol. They are aromatic in nature and have properties similar to those of resins.

BALSAM OF PERU; BALSAMUM PERUVIANUM (BALSAM. PERUV.), U.S.P. (Balsam of Peru, Peru Balsam).

It occurs as a dark brown, viscid liquid with a vanilla-like odor and bitter taste, insoluble in water and soluble in alcohol and chloroform.

USES.—Externally as a stimulating protective for abraded areas and indolent wounds. May be used for "capping" exposed dental pulps.

TOLU BALSAM; BALSAMUM TOLUTANUM (BALSAM. TOLU.), U.S.P. (Tolu, Balsam of Tolu).

It occurs as a yellowish-brown solid with a pleasant aroma of vanilla, and pleasant taste. It is insoluble in water and soluble in alcohol.

USES.—The tincture may be used as a protective.

Tincture of Tolu Balsam; Tinctura Balsami Tolutani (Tr. Balsam. Tolu.), U.S.P. (Tolu Tincture).—It contains tolu balsam (20%) in alcohol.

DOSAGE.—2 cc. (30 minims) (U.S.P.).

BENZOIN; BENZOINUM (BENZOIN), U.S.P.

A balsamic resin in the form of a liquid, insoluble in water and soluble in alcohol.

USES.—Applied locally as a stimulant protective for indolent wounds as the tincture.

Tincture of Benzoin; Tinctura Benzoini (Tr. Benzoin.), U.S.P.—It contains benzoin (20%) in alcohol (79%).

USES.—Protective and local stimulant.

Compound Tincture of Benzoin; Tinctura Benzoini Composita (Tr. Benz. Co.), U.S.P.—It consists of benzoin (10%), aloe (2%), storax (8%), tolu balsam (4%), in alcohol (77%).

USES.—Protective and local stimulant.

TURPENTINE; TEREBINTHINA (TERBINTH.), N.F. (Gum Thus, Gum Turpentine).

A solid oleoresin obtained from pine.

ROSIN; RESINA, U.S.P. (Colophony).

The residue left after distilling the volatile oil from turpentine.

USES.—Used in solution as a protective for the teeth.

Emollients

Emollients, sometimes referred to as protectives, are bland, oily substances which are employed externally to protect the skin, the surfaces of a wound, or the otherwise denuded epidermis from irritation by the air or other mechanical disturbances. Their action is purely local; they render the skin soft and more pliable. A drug, when applied to the skin, is more quickly absorbed when dissolved in an emollient, as it readily mixes with the sebaceous matter which covers the external epithelium. Animal, vegetable, and, more recently, mineral fats and oils are used for such purposes. Simple mechanical protectives, which have no medicinal action, are also classified as emollients.

LARD; ADEPS, U.S.P.

It is the purified fat from the abdomen of the hog.

USES.—Lard is used as an emollient and as a basis for ointments, particularly when absorption is desired.

Benzoinated Lard; Adeps Benzoinatus (Adeps Benz.), U.S.P.—It is lard containing benzoin which acts as a preservative, deodorant, and antiseptic.

USES.—Benzoinated lard is used as an antiseptic emollient and as a basis for ointments.

WOOL FAT; ADEPS LANAE (ADEPS LAN.), U.S.P. (Anhydrous Lanolin, Refined Wool Fat).

It is purified wool fat, freed from water.

USES.—Wool fat is used as an emollient and basis for ointment, but because of its tenacious consistency it should be mixed with some thinning agent.

Hydrous Wool Fat; Adeps Lanae Hydrosus (Adeps Lan. Hyd.), U.S.P. (Lanolin).—It is wool fat with about 27 per cent water.

USES.—Used as an emollient and base for ointments.

YELLOW WAX; CERA FLAVA (CERA ALB.), U.S.P. (Beeswax).

It is the yellow wax obtained from honey combs.

USES.—Beeswax is used in making ointments and plasters and in prosthetic dentistry. It does not melt at body temperature.

White Wax; Cera Alba (Cera Alb.), U.S.P. (Bleached Beeswax).—It is the yellow beeswax bleached.

USES.—Bleached beeswax is used as a basis for ointment, particularly to raise the melting point of the mixture.

CERATE, CERATUM (CERAT.), U.S.P. (Simple Cerate).

It contains white wax 30 per cent and benzoinated lard.

USES.—As an ointment base.

OLIVE OIL; OLEUM OLIVAE (OL. OLIV.), U.S.P. (Sweet Oil).

A fixed oil obtained from the ripe fruits of *Olea europoea,* family *Oleaceae.*

USES.—Emollient.

EXPRESSED OIL OF ALMOND; OLEUM AMYGDALAE EXPRESSUM (OL. AMYGD. EXP.), U.S.P. (Oil of Sweet Almond).

USES.—Emollient.

COTTONSEED OIL; OLEUM GOSSYPII SEMINIS (OL. GOSSYP. SEM.), U.S.P. (Cotton Seed Oil).

USES.—Emollient. (More economical than olive oil.)

CASTOR OIL, OLEUM RICINI (OL. RICIN.), U.S.P.

USES.—Locally as an emollient, particularly for the scalp.

SESAME OIL; OLEUM SESAMI (OL. SESAM.), N.F. (Teel Oil, Benne Oil).

USES.—As a substitute for olive oil.

THEOBROMA OIL; OLEUM THEOBROMATIS (OL. THEOBROM.), U.S.P. (Cacao Butter, Oil of Theobroma, Cocoa Butter).

USES.—Cocoa butter is principally used in suppositories, as a "nutrient" emollient, and in operative dentistry. It melts at body temperature.

PARAFFIN; PARAFFINUM (PARAFF.), N.F.

A purified mixture of solid hydrocarbons obtained from petroleum.

USES.—Used for increasing the melting point of ointments. It should not be injected into the tissues, for its acts as a foreign body, often resulting in a "paraffinoma."

PETROLATUM; PETROLATUM (PETROLAT.), U.S.P. (Petroleum Jelly).

A purified semisolid mixture of hydrocarbons obtained from petroleum.

USES.—Applied to the skin as a protective and emollient and used as the basis for ointments. It melts at body temperature.

Liquid Petrolatum; Petrolatum Liquidum (Petrolat. Liq.), U.S.P. (White Mineral Oil, Heavy Liquid Petrolatum).—A mixture of liquid hydrocarbons.

USES.—A vehicle for liquid preparation intended for local use and as a protective and emollient.

YELLOW OINTMENT; UNGUENTUM FLAVUM (UNG. FLAV.), U.S.P.

It contains wool fat (5%), yellow wax (5%), in petrolatum (90%).

USE.—As an ointment base. It melts at body temperature.

GLYCERIN; GLYCERINUM (GLYCERIN.), $C_3H_5(OH)_3$, U.S.P. (Glycerol).

A colorless, syrupy, odorless, sweet liquid; misicible with water and alcohol.

USES.—Used as a solvent, vehicle, demulcent, and emollient. It is drying to the skin.

LINIMENTS

Liniments are oily or hydroalcoholic liquid preparations intended for application to the skin. They are composed of irritating ingredients which produce a superficial hyperemia which relieves a deeper congestion—counterirritation. They do not penetrate the intact skin but act by superficial stimulation only. The relief of symptoms is the result of a redistribution of blood in the affected area, removing

the discomfort due to congestion. Liniments may be applied with or without rubbing, depending on the degree of irritation desired.

Camphor Liniment; Linimentum Camphorae (Lin. Camph.), U.S.P. (Camphorated Oil).—The liniment contains camphor (20%) dissolved in cottonseed oil.

USES.—Apply to skin.

Camphor and Soap Liniment; Linimentum Camphorae et Saponis (Lin. Camph. et Sapon.) U.S.P. (Soap Liniment).—It contains hard soap (6%), camphor (4.5%), Oil of Rosemary (1%), alcohol (64%) and water.

USES.—Apply.

Chloroform Liniment; Linimentum Chloroformi (Lin. Chlorof.), U.S.P.—It contains chloroform (30%) in camphor and soap liniment.

USES.—Apply.

Liniment of Aconite and Chloroform; Linimentum Aconiti et Chloroformi (Lin. Aconit. et Chlorof.), N.F.—The liniment contains fluidextract of aconite (4.5%), alcohol (8%), chloroform (12.5%), and camphor and soap liniment (75%).

USES.—The presence of aconite in local preparations makes them potentially toxic.

Ammonia Liniment; Linimentum Ammoniae (Lin. Ammon.), N.F. (Volatile Liniment, Hartshorn Liniment).—It contains diluted solution of ammonia (25%), oleic acid (1%), and sesame oil (74%).

USES.—Apply.

Belladonna Liniment; Linimentum Belladonnae (Lin. Bellad.), N.F.—It contains camphor (5%) in fluidextract of belladonna root.

USES.—The presence of belladonna in a local preparation makes it potentially toxic.

Turpentine Liniment; Linimentum Terebinthinae (Lin. Terebinth.), N.F. (Kentish Ointment).—It contains rosin cerate (65%) in oil of turpentine.

USES.—Apply.

Acetic Liniment of Turpentine; Linimentum Terebinthinae Aceticum (Lin. Terebinth. Acet.), N.F. (Linimentum Album, N.F., St. John Long's Liniment, Stoke's Liniment).—It contains oil of turpentine (40%), oil of lemon (1.6%), acetic acid (8%), egg, in water.

USES.—Apply.

Demulcents

Demulcents, sometimes referred to as vehicles, are usually colloidal, oily, or albuminous substances, which are employed for the purpose of mechanically covering sensitive, wounded, diseased, or otherwise

defective mucous surfaces against further injury. They are closely related to protectives and emollients. Demulcents are often given internally to envelop nauseous, ill-tasting medicines, or to give body to watery solutions of drugs; they retard the absorption of drugs. Oleo-resins, balsams, oils, and other substances insoluble in water are usually administered in aqueous mixtures in which the minute droplets are held in suspension in the form of an emulsion.

PREPARATIONS.—(See Protectives and Emollients.)

Diaphoretics

Diaphoretics and *sudorifics* are drugs which induce sweating while *diaphoresis* is the act of sweating.

Sweating is an important means of dissipating the body heat. The evaporation of sweat generally keeps pace with the production, but during warm weather or during physical exertion the sweat may collect and become visible. The amount of invisible sweat excreted per day is about 1,000 cc., while the amount of visible sweat may reach 3,000 cc. in 24 hours. Apparently the production of sweat diminishes with the age of the individual.

Perspiration is principally controlled by specific nerves. The center is probably located in the hypothalamus, the impulse mediating through the cholinergic sympathetic system.[1] A direct irritation of the sweat glands or a cutaneous vasodilation may also produce diaphoresis. Psychic influence—fear, excitement, etc.—may produce perspiration by a reflex action.

Sweat contains ammonia, lactates, glucose, fatty acids, nonprotein nitrogen, carbonates, and inorganic salts, as chlorides, sulfates, and phosphates of sodium and potassium chiefly, with about 98 per cent water. The normal fresh perspiration of man is acid in reaction, but the stagnated sweat is generally alkaline.

In infectious diseases the sweat may eliminate waste products of microbic origin; in diabetes it may contain glucose and fatty acid salts; in uric acid diathesis (gout) it may contain uric acid salts; and in nephrosis it may contain nitrogenous waste products. While diaphoresis may raise the excretion of toxic substances to a significant point, the method is only temporary and cannot take the place of kidney function. Absorbed drugs, as salicylic and benzoic acids, halogens, mercury, lead, quinine, essential oils, etc., may be excreted in the sweat.

[1]Bard, Philip: Macleod's Physiology in Modern Medicine, ed. 9, St. Louis, 1941, The C. V. Mosby Co., p. 181.

The effects of diaphoresis on the body are (1) to increase the basal metabolic rate which aids the body in destroying foreign substances; (2) to stimulate the blood flow, relieving blood and lymph congestion and aiding the body in elimination of toxic substances; (3) to produce a cutaneous vasodilation which results in a redistribution of blood, a better circulation in the diseased tissues, and a better flow of blood through the kidneys; and (5) to quiet the nervous system promoting rest and sleep.

Sweating is a therapeutic procedure which is not extensively practiced at present, except in certain chronic diseases and in respiratory infections generally termed "colds." Diaphoresis should not be overdone, as the patient may be weakened.

The simplest means of producing diaphoresis is by the ingestion of hot fluids and by diminishing heat radiation by wrapping the patient in heavy covers. Hot toddies in the form of coffee, tea, cocoa, or mild alcoholic fruit drinks are especially productive of free perspiration. Pilocarpine is the most effective of all diaphoretics and may be administered as its hydrochloride or nitrate salt. Dover's powder alone or combined with aspirin or a solution of ammonium acetate is frequently used. Turkish baths, hot rooms, hot baths, etc., are good diaphoretic measures, particularly if accompanied with the drinking of copious amounts of hot water.

Pilocarpine

Pilocarpine Nitrate; Pilocarpinae Nitras (Pilocarpin. Nitras), U.S.P.

Therapeutics.—Pilocarpine and its salts act as parasympathetic nervous system stimulants and as stimulants to the cholinergic fibers of the sympathetic nervous system. The result is a stimulation of all of the glands of the body, i.e., diaphoresis. It is toxic to a weakened heart.

Dosage.—5 mg. ($\frac{1}{12}$ grain) (U.S.P.).

Opium

Powder of Ipecac and Opium; Pulvis Ipecacuanhae et Opii (Pulv. Ipecac. et Opii), N.F. (Dover's Powder, Pulvis Opii et Ipecacuanhae Compositus P.I.).—It contains opium and ipecac (each 10%) with lactose.

Uses.—Diaphoretic, especially in mild respiratory infections.

Dosage.—0.3 Gm. (5 grains) (N.F.).

Syrup of Ipecac and Opium; Syrupus Ipecacuanhae et Opii (Syr. Ipecac. et Opii), N.F. (Syrup of Dover's Powder).—It contains tincture of ipecac and opium (8.5%), with spirit of cinnamon in syrup.

USES.—Diaphoretic.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Tincture of Ipecac and Opium; Tinctura Ipecacuanhae et Opii (Tr. Ipecac. et Opii), N.F. (Tincture of Dover's Powder).—It represents tincture of opium (100%) and fluidextract of ipecac (10%) in diluted alcohol.

DOSAGE.—0.5 cc. (8 minims) (N.F.).

AMMONIUM ACETATE

Solution of Ammonium Acetate; Liquor Ammonii Acetatis (Liq. Ammon. Acet.), N.F.—It contains about 7 per cent of ammonium acetate ($CH_3COO.NH_4$).

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

SALICYLATES

Acetylsalicylic Acid Tablets, Tabellae Acidi Acetylsalicylici (Tab. Acid. Acetylsal.), U.S.P. (Aspirin Tablets).

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

ACETOPHENETIDIN

Acetophenetidin Tablets; Tabellae Acetophenetidini (Tab. Acetophen.), $C_{10}H_{13}NO_2$, U.S.P. (Phenacetin Tablets).

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.). It has a toxic effect on the heart and must be used with care and supervision.

ALCOHOL

Hot toddies containing fruit juices with or without alcoholic beverages.

Diaphoretic Measures

1. Hot drinks.
2. Hot baths.
3. Warm environment.
4. Exercise.
5. Steam rooms.
6. Hot dry rooms.

CHAPTER XVII

CHEMOTHERAPY

The science of chemotherapy was introduced into medicine by Paul Ehrlich in 1910 when arsphenamine was suggested as the "magic bullet" for the cure of syphilis.

In 1936 Long and Bliss introduced sulfanilamide into therapeutics in this country, and since that time many related compounds have been synthesized and found to have marked therapeutic properties.

About the time of the outbreak of World War II, Professor H. W. Florey in England and others in this country had confirmed by clinical studies the effectiveness of penicillin in combating infectious diseases.

The advance in this field is so rapid that the material written at this time (1944) on penicillin will be incomplete when the book reaches the reader. For this reason, the "doctor" should read the current reports of the "Councils" of the American Dental Association and of the American Medical Association before using these drugs in practice.

These compounds have been introduced into therapeutics as specific chemical substances with a selectivity for certain groups of organisms. They are toxic drugs and should be used only when indicated by the symptoms and bacteriologic studies. It is well for the novice to get consultation before the drug is prescribed or else have the patient hospitalized for observation and regular blood studies.

PREPARATIONS USED IN THE TREATMENT OF SPIROCHETAL INFECTIONS

Syphilis was definitely diagnosed in Europe in 1495; at that time it was in epidemic proportions. It has been said that syphilis was brought to Europe from America by the expeditions of Columbus. It is very possible that the disease was present in Europe before 1495 but was not diagnosed.

Mercury and Mercury Preparations

MERCURY; HYDRARGYRUM (HYDRARG.), U.S.P. (Quicksilver).

It occurs as a shining, silvery, liquid metal, insoluble in the ordinary solvents.

PHARMACODYNAMICS.—Metallic mercury in large globules is not absorbed from the skin or mucous membranes, but when it is finely divided it is absorbed from the intestines and skin. Its absorption from the skin is aided by rubbing. The theory of its action as a spirocheticide is not well understood. The concentration of the mercury in the body tissues is too small to have any direct effect on the infecting organisms.

THERAPEUTICS.—Mercury was one of the earliest substances to be used in the treatment of syphilis. The finely divided metal particles are applied as an ointment and rubbed into the skin. Six applications are made on consecutive nights, different areas of the body being used for each application. A rest period of three or more months is allowed before a subsequent treatment.

Mercury and mercury salts are contraindicated in the treatment of Vincent's stomatitis.

TOXICOLOGY.—Symptoms of mercury poisoning are often seen from industrial, therapeutic, and suicidal causes. The acute symptoms are of gastrointestinal and genitourinary irritation, followed by collapse, nephritis, and death. The chronic symptoms are of especial interest to the dentist, as they are often manifested in the oral cavity, as salivation, gingivitis, blue gum line, alveoclasia, and exfoliation of the teeth.

TREATMENT.—When the drug is in the stomach, demulcent substances, as egg white, milk, starch paste, may be given and the stomach emptied by emesis or a stomach tube. Stimulants are given for collapse. Kidney function is maintained whenever possible. Hospitalization is essential. Formaldehyde sulfoxylate is accredited as a specific antidote for mercury ions.

PREPARATIONS.—

Strong Mercurial Ointment; Unguentum Hydrargyri Forte (Ung. Hydrarg. Fort.), U.S.P. (Mercurial Ointment).—It contains about 50 per cent of metallic mercury, 2 per cent of oleate of mercury in a fat base.

USES.—To secure the systemic effect of mercury by inunction. (See *Useful Drugs*).

MERCURY SALTS

MERCURY BICHLORIDE; HYDRARGYRI BICHLORIDUM (HYDRARG. BICHLORID.), $HgCl_2$, U.S.P. (Mercuric Chloride).

It occurs as heavy, colorless crystals, slowly soluble in water (1 in 13.5) and freely soluble in alcohol (1 in 3.8).

USES.—Antisyphilitic and germicidal.

DOSAGE.—4 mg. (1/15 grain), in solution or pills (U.S.P.). *Caution:* Mercury bichloride is extremely poisonous.

MERCURIC SALICYLATE; HYDRARGYI SALICYLAS (HYDRARG. SALICYL.), U.S.P.

It occurs as a white, odorless powder, nearly insoluble in water and alcohol.

USES.—Antisyphilitic, especially by intramuscular injection of an oily solution.

DOSAGE.—Intramuscular, 60 mg. (1 grain) (U.S.P.) twice a week (or less). It may be dissolved (10%) in oil.

MERCURIC SALICYLATE INJECTION; INJECTIO HYDRARGYRI SALICYLATIS (INJ. HYDRARG. SALICYL.), U.S.P. (Mercuric Salicylate Ampuls).

DOSAGE.—Intramuscular 0.1 Gm. (1½ grains) (U.S.P.).

ARSENIC SALTS

Arsenic salts may be inorganic as in arsenic trioxide (As_2O_3) or organic as in arsphenamine. They may be trivalent or pentavalent. The unsaturated molecule is more active and is of greater importance in therapeutics. The trivalent organic salts are used in the treatment of spirochetal infections, such as syphilis. Their mode of action is not well understood. It is known that the concentration of arsenic in the tissues is not sufficient to destroy the organisms by direct action. It is considered likely that the trivalent arsenic is oxidized at the expense of the tissues, and the spirochetes, being on borderline oxygen consumption, are destroyed.[1]

ARSPHENAMINE; ARSPHENAMINA (ARSPHEN.), U.S.P.

Contains not less than 31 per cent arsenic.

THERAPEUTICS.—The arsphenamines are used with success in a variety of spirochetal infections. In syphilis they have proved a specific. The spirochetes disappear in two or three days from the primary and secondary lesions, promptly removing the danger of infecting others. A single dose is not curative, however, as Ehrlich had hoped. A course of six treatments is given, one each week, followed by injections of bismuth for one year, with the entire treatment repeated during the second year. The disease is probably curable when properly treated. In the tertiary stage all the syphilitic symptoms regress at once, except those of an anatomic basis. The Wassermann and like serologic tests become negative in about five days.

[1]Sollmann, Torald: A Manual of Pharmacology, ed. 6, Philadelphia, 1942, W. B. Saunders Co.

The arrest of symptoms does not mean that the disease is cured, and the patient should be examined periodically.

Its use in Vincent's stomatitis is advocated in *Useful Drugs* (1942) both systemically and applied locally in a 2.5 per cent solution in glycerin. *Accepted Dental Remedies* (1940) questions the use of this drug for the systemic treatment of Vincent's stomatitis. This cautious stand by the Council of Dental Therapeutics is very wise considering the mild character of this oral infection in the majority of cases and the toxicity of this drug when administered by the intravenous route. Carr[1] recommends its systemic use in oral lesions when the symptoms suggest a metastatic infection. This is, no doubt, sound therapy, and drastic measures are justifiable.

TOXICOLOGY.—Toxic symptoms are not uncommon with arsenic therapy, due to the toxic metal and to the dangerous intravenous method of administration. When injected subcutaneously, irritation and ulceration follow. It is too irritating to be given orally, and the drug may be affected by digestion. Weeks and months after treatment neuritis of the eye, ear, and face may occur. The dentist should keep this in mind when treating patients with such symptoms. It is excreted chiefly through the liver—about 10 times as much arsenic is recovered in the feces as in the urine. Post-mortem findings include degeneration of the liver and kidney cells. The death rate for injections of 0.6 Gm. or less of arsphenamine is 1 in 163,000 patients.

NOTE.—All arsphenamine labels must bear an expiration date beyond which the arsphenamine must not be used. This date must not be more than five years from the date of manufacture. (U.S.P.)

DOSAGE.—*Caution:* Intravenous 0.3 Gm. (5 grains) dissolved in warm water without shaking. Prior to injection the solution must be alkalinized with 0.85 cc. of normal sodium hydroxide for each 0.1 Gm. of arsphenamine. (U.S.P.) The technique of the preparation and administration of the solution is described in *Useful Drugs*. Its use by any one who has not mastered the technique is dangerous.

NEOARSPHENAMINE; NEOARSPHENAMINA (NEOARSPHEN.), U.S.P.

It contains about 20 per cent of trivalent arsenic combined in an organic molecule. It is a sodium salt and is more soluble in water than is arsphenamine.

THERAPEUTICS.—It is used similarly to arsphenamine to which it is closely related chemically. It is irritating and must be injected intravenously. *Caution:* Solutions of neoarsphenamine must be freshly

[1]Carr, M. W.: J. Dental Research 16: No. 1, p. 1.

prepared when required for use. The solution should not be shaken during its preparation. (U.S.P.)

NOTE: The expiration date (the date beyond which the contents cannot be expected beyond reasonable doubt to retain their stability) shall not be more than 3 years from the date of release of that lot by the National Institute of Health. (U.S.P.)

SULFARSPHENAMINE; SULFARSPHENAMINA (SULFARSPHEN.), U.S.P.

It differs from neoarsphenamine by having two side chains instead of one, and the sulfur has a valence of six instead of two. It contains about 19 per cent of arsenic in the trivalent form.

It is more stable than arsphenamine, is less irritating, and may be given intramuscularly, which is a distinct advantage for dental use.

USES.—The same as for neoarsphenamine.

DOSAGE.—Intramuscular, 0.45 Gm. (7 grains) (U.S.P.).

PRESCRIPTIONS FOR LOCAL APPLICATION IN VINCENT'S STOMATITIS

℞[1]	Arsphenamine		0.3 Gm.
	Glycerin	qs. ad.	4.0 cc.
	M. et ft. sol.		
	Sig.: Apply sparingly to ulcerated areas.		

℞	Arsphenamine		0.2 Gm.
	Dextrose		1.0 Gm.
	Dist. Water	qs. ad.	4.0 cc.
	M. et ft. sol.		
	Sig.: Apply sparingly to ulcerated areas.		

Antimalarials

CINCHONA AND CINCHONA ALKALOIDS

CINCHONA; CINCHONA (CINCH.), N.F. (Cinchona Bark, Peruvian Bark).

It occurs as the dried bark of the stem or root of the *Cinchona succirubra*, or of the *Cinchona Ledgeriana* or hybrids of these with other species of Cinchona, family *Rubiaceae*. It must yield not less than 5 per cent of the Cinchona alkaloids of which there are about nineteen. The most important are quinine, quinidine, cinchonine, and cinchonidine. They all have similar therapeutic properties but differ in intensity of action.

PHARMACODYNAMICS.[2]—The cinchona alkaloids are specific in the treatment of malaria. They are protoplasm poisons, affecting pro-

[1] Reikford and Baker: J. A. M. A. 75: 1620, 1920.

[2] Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, 1941, The Macmillan Co.

tozoa more than bacteria. In malaria the asexual forms of the *Plasmodium vivax,* which are the symptom producers, are destroyed without materially altering the cells of the host. It is a prompt prophylactic against the symptoms of this disease but should be administered three or four hours before the typical malarial attack is manifested so as to allow time for absorption. The exact site or mode of action in malaria is not understood. Quinine is one of the earliest drugs used to reduce fever, but it has been largely replaced by other antipyretics. Because of its bitter taste it is recommended as a bitter tonic, but the systemic effect probably nullifies this local action. Normal doses slow the heart and dilate the arterioles, producing a slight fall in blood pressure. The alkaloids act directly on the heart muscle, reducing its irritability and conductivity. The central nervous system is depressed, giving a sedative and analgesic effect. Larger than normal doses stimulate the pregnant uterus and produce strong contractions resulting in an abortifacient action. Normal doses of quinine reduce the number of polymorphonuclear blood cells as much as 50 per cent. Quinine also inhibits the migration of leucocytes and for this reason was recommended at one time by Helmholz as an antiphlogistic. Continued doses may depress the metabolism.

TOXICOLOGY.—Many patients show an anaphylactic reaction to these alkaloids, and care must be used to single out these patients. The alkaloids are irritating to the stomach and intestines, often producing nausea and vomiting. After absorption symptoms of middle ear congestion, as ringing in the ears, is a frequent occurrence. Toxic doses produce depression of the heart and respiration, terminating in collapse. Complete amblyopia and a permanent loss of sight may follow overdosage.

DOSAGE.—1 Gm. (15 grains) (N.F.).

CINCHONIDINE SULFATE; CINCHONIDINAE SULFAS (CINCHONID. SULF.), N.F.

An alkaloid obtained from Cinchona bark.

USES.—A cheap substitute for quinine, but it is less efficient and more convulsive.

DOSAGE.—0.15 Gm. (2½ grains) (N.F.).

CINCHONINE SULFATE; CINCHONINAE SULFAS (CINCHONIN. SULF.), N.F.

An alkaloid obtained from Cinchona bark.

USES.—Similar to Cinchonidine Sulfate.

DOSAGE.—0.15 Gm. (2½ grains) (N.F.).

QUINIDINE SULFATE; QUINIDINAE SULFAS (QUINIDIN. SULF.), U.S.P.

It occurs as white, needle-like crystals, sparingly soluble in water (1 in 100) and soluble in alcohol (1 in 10).

USES.—It is used in malaria when quinine is not tolerated. It has a depressing effect on the irritability and conductivity of the heart.

DOSAGE.—*Caution!* 0.2 Gm. (3 grains), four times per day (U.S.P.).

Quinidine Sulfate Tablets; Tabellae Quinidinae Sulfatis (Tab. Quinidin. Sulf.), U.S.P.

DOSAGE.—0.2 Gm. (3 grains) (U.S.P.).

QUININE SULFATE; QUININAE SULFAS (QUIN. SULF.), U.S.P.

It occurs as white, odorless, bitter, efflorescent crystals, slightly soluble in water (1 in 810) and in alcohol (1 in 120). It is incompatible with ammonia, alkalies, limewater, tannin, potassium iodide, etc.

USES.—The most commonly used quinine salt but probably inferior to the dihydrochloride which has greater solubility.

DOSAGE.—0.6 Gm. (10 grains) (U.S.P.).

Tablets of Quinine Sulfate; Tabellae Quininae Sulfatis (Tab. Quin. Sulf.), U.S.P.

DOSAGE.—0.6 Gm. (10 grains) (U.S.P.).

QUININE DIHYDROCHLORIDE; QUININAE DIHYDROCHLORIDUM (QUIN. DIHYDROCHLOR.), U.S.P.

A white odorless, bitter powder, very soluble in water (1 in 0.6) and soluble in alcohol (1 in 12).

USES.—Similar in action but with greater solubility than the sulfate salt.

DOSAGE.—(Oral) 1 Gm. (15 grains) (U.S.P.).

Ampuls of Quinine Dihydrochloride; Ampullae Quininae Dihydrochloridi (Ampul. Quin. Dihydrocholor.). N.F.—Each 1 cc. contains 0.5 Gm. of quinine dihydrocholoride in a sterile aqueous solution.

DOSAGE.—0.5 Gm. (7½ grains) for parenteral use.

Quinine and Urea Hydrochloride, U.S.P. (See local anesthetics.)

Other Antimalarial Drugs

Quinacrine Hydrochloride; Quinacrinae Hydrochloridum (Quinacrin. Hydrochlor.), U.S.P. (Mepacrine Hydrochloride).—A bright yellow, crystalline powder, soluble in water (1 in 35) and in alcohol.

USES.—It acts like quinine in malaria by destroying the asexual forms of the parasite and checking the symptoms of the disease. It is

not as efficient as quinine for the malignant subtertian form, but it has less undesirable side actions. The urine may be colored yellow.

DOSAGE.—0.1 Gm. (1½ grains) (U.S.P.).

Quinacrine Hydrochloride Tablets; Tabellae Quinacrinae Hydrochloridi (Tab. Quinacrin. Hydrochlor.), U.S.P.

DOSAGE.—0.1 Gm. (1½ grains) (U.S.P.).

ATABRINE

ATABRINE DI-HYDROCHLORIDE, N.N.R. (A brand of quinacrine).

PHARMACODYNAMICS.—Atabrine, like quinine, destroys the asexual form (trophozoites) of the causative organisms in all types of malaria and thus checks the symptoms and progress of the disease. It affects to a lesser degree the sexual forms (gametocytes) of the organisms and may lessen the chance of spreading the infection through mosquito transmission.

THERAPEUTICS.—Atabrine is probably as efficient as quinine in treating the benign tertian and the quartan types but probably inferior for the malignant subtertian. As a prophylactic it is satisfactory and will reduce the incidence of clinical malaria. It does not produce as many undesirable side actions as quinine.

DOSAGE.—(See N.N.R.) Oral. Adult: 0.1 Gm. (1½ grains) three times a day for 5 days. Children under 8 years require smaller doses.

PROPHYLACTIC DOSE.—Adults, 0.2 Gm. (3 grains) twice weekly. Children: 0.05 Gm. (¾ grain) every other day. (N.N.R.)

PLASMOCHIN

Plasmochin was introduced into therapeutics as an antimalarial by Mühlins in 1926. It occurs as a white, tasteless powder. Chemically it is a quinoline derivative with alkaloidal properties.

PHARMACODYNAMICS.—Plasmochin differs from the cinchona alkaloids in its mode of action. Its specific toxicity is on the gametocytes and to a lesser extent on the asexual forms. By destroying the sexual forms of plasmodia there is less chance of the patient's causing infection in others.

TOXICITY.—Plasmochin produces fewer undesirable side actions than quinine. It is destroyed by the tissues and excreted by the kidneys.

THERAPEUTICS.—Plasmochin is not a substitute for quinine but is generally used in conjunction with it, the doses of each being reduced. The quinine destroys the asexual forms which are the symptom producers. While the plasmochin destroys the sexual forms of the plas-

modia and prevents infection of others, it fails to affect the parasites causing the symptoms of malignant tertian malaria.

DOSAGE.—20 mg. given three times a day for not over 14 days. When given with quinine, the dosage is reduced one-half. See, *The Pharmacological Basis of Therapeutics,* by Goodman and Gilman, The Macmillan Co.)

DRUGS USED IN THE TREATMENT OF LEPROSY

CHAULMOOGRA OIL; OLEUM CHAULMOOGRAE (OL. CHAULMOOG.), U.S.P. (Hydnocarpus Oil).

It is a fixed oil expressed from the ripe seed of *Taraktogenos Kurzii* (King) family *Flacourtiaceae.* This oil is a triglyceride of unsaturated fatty acids, chiefly chaulmoogric and hydnocarpic.

PHARMACODYNAMICS.—In vitro, chaulmoogra oil has a specific toxicity for certain acid-fast bacilli, but there is no satisfactory evidence that such an action exists in the body.

THERAPEUTICS.—It is without specific curative action in leprosy.

DOSAGE.—1 cc. (15 minims) in capsules three times a day, increasing the dosage to the limit of tolerance. (See *Useful Drugs.*)

ETHYL CHAULMOOGRATE; AETHYLIS CHAULMOOGRAS (AETHYL. CHAULMOOG.), U.S.P.

It occurs as a clear yellow liquid.

USES.—It is similar to the oil but less irritating.

DOSAGE.—Oral or intramuscular, 2 cc. (30 minims) (U.S.P.).

ANTIBIOTICS

PENICILLIN

Penicillin[1] is a product of the common mold found on old cheese and damp bread. It is not the result of an overnight discovery, the mold being isolated and studied in 1824 by the German botanist, Link, who named it *Penicillin notatum.* Professor Alexander Fleming, at St. Mary's Hospital, London, while examining culture plates was first to notice the bacteriostatic influence of mold growth on microorganisms. In the June, 1929 issue of the *British Journal of Experimental Pathology,* Fleming published his results. About the time of the outbreak of World War II, Professor H. W. Florey in England and others in this country of the Rockefeller Foundation had confirmed by clinical studies the effectiveness of this agent in combating infec-

[1]Smith, Austin E.: The Present Status of Penicillin, J. A. D. A. 31: 790, June 1, 1944.

tious diseases. There is good evidence to support the belief that it is equal to the sulfonamides as an internal antiseptic, and for the treatment of *Staphylococcus aureus* and *albus* and the *Streptococcus viridans* infections, it is apparently superior. Like the sulfonamides the bacteria may develop a resistance to penicillin, and this is maintained even after repeated (30) passages through mice. The resistance to one drug fortunately does not impart resistance to the other, therefore sulfa-fast organisms do respond to penicillin therapy.

The mold grows well on nutrient broth at a pH of 4.5. The pH of the media not only aids in the growth of the organisms but also in the persistence of the extracellular bacteriostatic substance. It is supplied to the market as the sodium salt; with an empiric formula of $C_{24}H_{34}O_{11}NSrNa$. It occurs as an orange colored powder; it is very soluble in water and slowly decomposes on standing. When thoroughly dried and sealed in ampuls it is reasonably stable at ordinary temperatures and keeps best in a refrigerator. Penicillin (Merck) is packaged in sterile ampuls, and need not be sterilized before administration. The rate of absorption of penicillin varies with the site of administration; the oral route is extremely poor, as is the rectal route, the subcutaneous route gives a delayed action, the intravenous route seems best at this time. An intravenous dose of 5,000 units produces a bacteriostatic effect for about thirty to forty minutes, whereas a dose in excess of 20,000 units lasts for three or four hours.

The indications for its use are in bacterial infections associated with the following microorganisms; *Staphylococcus aureus* and *albus*, *Streptococcus viridans*, pneumococcus, gonococcus, meningococcus, probably hemolytic streptococci, and others.

The toxicity of penicillin is remarkably low. It is excreted in part by the kidneys and to a lesser extent by the liver. The symptoms of toxicity are chills, sometimes fever, and at times urticaria.

The dosage has not been worked out. Merck Company gives the following instructions (Nov., 1943); a constant intravenous injection of a penicillin solution adjusted to deliver 5,000 to 10,000 units per hour. This dosage is varied as the conditions warrant. After the temperature has returned to normal, the dosage is cut in half and maintained for at least seven days. For local application in dentistry a concentration of 250 to 500 units per cc. are employed and held to the infected area for hours.[1]

Tyrothricin, tyrocidine, and gramicidin are not extensively used at present. They are of a fungus origin and are similar in origin to

[1]Fechtner, J. L.: Fungi and Bacteria Antibiotics, J. A. D. A. 31: 1217, Sept., 1944.

penicillin. Their toxicity is such as to prevent their intravenous use but they may be applied locally to control localized infections.

SULFONAMIDES

HISTORY.—The sudden introduction of the sulfonamides into therapeutics and their immediate acceptance by the dental and medical professions suggest that their discovery was of an "overnight" nature. Like so many other great scientific contributions, the sulfonamides were the result of years of effort by many research workers.

The synthesis of para-aminobenzene sulfonamide was accomplished by a German dye chemist in 1908. This molecule was intended as a dye and not as a medicine.

In 1919, two Americans working in the Rockefeller Institute in New York (M. Heidelberger and W. A. Jacobs) found that this compound would kill microorganisms in vitro.

The scene reverts to Germany with the synthesis of a red dye called "prontosil" by Mietsch and Klaren (1932). Domagh observed in the same year that injections of this dye protected mice against a fatal dose of hemolytic streptococci. Bovet, in France, after a prolonged study of prontosil, suggested that the bacteriostatic effect was not due to the intact molecule but to a decomposition product, sulfanilamide (1935).

In this country Long, Bliss, Marshall, et al., at Johns Hopkins University (1936), confirmed the results of the European workers and introduced these drugs into American therapeutics.

PHARMACODYNAMICS.—The mode of action of the sulfonamides as bacteriocidal and bacteriostatic agents has not been completely worked out. Long,[1] in 1941, suggested the following hypothesis: that the sulfanilamide is oxidized in the presence of hydrogen peroxide and an essential catalyst(s) to an active compound. This compound of sulfanilamide continues to accumulate until the reducing systems within the bacterial cell are inhibited, resulting in a bacteriostasis or a bacteriocidal action (Shaffer).

The second hypothesis deals with the observations of Locke, Main, Mellon, and Shinn, who found that the living bacterial cell has the power of converting sulfanilamide by oxidation into derivatives which act as active anticatalases. This reaction permits an accumulation of hydrogen peroxide to a toxic level. The result is a bacteriostatic or bacteriocidal action on sensitive organisms.

[1]Long, Perrin H.: Sigma, XI Quart. 29: 149, October, 1941.

These two theories are based on the premise that the molecule of sulfanilamide is changed by oxidation into an active compound. In the studies of Long et al., it was ascertained that sulfanilamide and sulfapyridine were active on hemolytic streptococci and pneumococci under various conditions of anaerobiosis which discredited the concept that these drugs were activated by molecular oxygen.

The third theory is based on the concept that the sulfanilamides act on the bacteria to prevent their utilization of the substrate, or upon the substrate to prevent its utilization by the bacteria. These observations pointed to the fact that they acted directly by inhibiting the metabolism of susceptible bacteria by affecting the co-enzyme system. D. D. Woods, in April, 1940, reported the effect of para-aminobenzoic acid as an inactivator of the sulfonamides. This compound, or a related molecule, combines with a protein to form a co-enzyme essential for growth and multiplication of certain bacterial cells. The sulfonamides compete for this position to form an inert molecule which restricts the growth, development, and possibly the life of the susceptible bacterial cell.

The sulfonamides may also affect the endotoxins of certain organisms, i.e., gonococcus, meningococcus, etc., while others are unaffected. These activities have not been wholly confirmed at this time (1944).

Therapeutics.—General: The sulfonamides check the growth and development of certain organisms in the fluid and fixed tissues of the body.[1] The mechanism of action (see Pharmacodynamics) is to change the enzyme systems within the bacterial cell so that the normal functions of growth, reproduction, and life are inhibited or destroyed. The bacteriostatic effect takes place slowly in the tissues, and time is required for its action (48 hours). The drug must be given for days or weeks (2) after the symptoms have ameliorated to prevent relapse. The best results are obtained with an optimal concentration of the drug in the tissues; the blood levels will vary with each drug. The dosage of the drug is determined by blood analysis[2] which requires the aid of a laboratory, private or hospital. (See Tables II and III.)

The sulfonamide drugs have a specificity of action[3] affecting only certain groups of bacteria. A bacteriologic study to determine the type of infecting organism(s) should be made before the drug is

[1]Sollman, T.: A Manual of Pharmacology, Philadelphia, 1942, W. B. Saunders Company.

[2]Bratton, A. C., and Marshall, E. K.: J. Biol. Chem. 128: 537, May, 1939.

[3]Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics. New York, 1940, The Macmillan Company.

selected. The accompanying chart was taken from *Useful Drugs*, thirteenth edition, page 220, 1942, and is an aid in the selection of the drug.

TABLE II

CHOICE OF SULFONAMIDES

ORDER OF CHOICE	1	2	3
Lancefield's Group A Hemolytic Streptococcus Infections	Sulfadiazine	Sulfanilamide	Sulfapyridine
Pneumococcic Infections	Sulfadiazine	Sulfathiazole	Sulfapyridine
Gonococcic Infections	Sulfathiazole	Sulfapyridine	Sulfadiazine
Meningococcic Infections	Sulfadiazine	Sulfathiazole	Sulfanilamide
Friedländer Bacillus Infections	Sulfadiazine	Sulfapyridine	Sulfathiazole
Staphylococcic Infections	Sulfadiazine	Sulfathiazole	
Acute Bacillary Dysentery	Sulfaguanidine	Sulfathiazole	
Actinomycosis	Sulfanilamide	Sulfapyridine	
Chancroid	Sulfanilamide		

Before the dentist uses these drugs internally, he should read the current revisions of *Useful Drugs* and *Accepted Dental Remedies.*

"Since the dosages suggested below are based on body weight in the metric system, the following table of approximations may be convenient for translating pounds into kilograms:"

11 pounds = 5 kilograms	110 pounds = 50 kilograms
22 pounds = 10 kilograms	132 pounds = 60 kilograms
33 pounds = 15 kilograms	154 pounds = 70 kilograms
44 pounds = 20 kilograms	176 pounds = 80 kilograms
55 pounds = 25 kilograms	198 pounds = 90 kilograms
66 pounds = 30 kilograms	220 pounds = 100 kilograms
88 pounds = 40 kilograms	242 pounds = 110 kilograms

(*Useful Drugs*, 1942.)

The dosage of the sulfonamides is discussed under the drug headings.

The fate of the sulfonamides in the body varies with the drug. They are excreted through the kidneys, chiefly, unchanged or conjugated (acetylated). The rate of excretion varies with the drug used and with the patient, changing with the condition of the kidneys. A careful check on the urine output is generally sufficient to assure a normal excretion, 1000 cc. or over per day being essential.

Local: The use of the sulfonamide drugs for topical medication is now a common dental practice.[1] The drug is absorbed in the abraded area, and the local concentration in the immediate tissues is many times greater than can be obtained by systemic medication.[2] As the amount of drug used is necessarily small and generally of short duration, the danger of systemic reactions is practically nil.

[1] Dobbs, E. C.: J. A. D. A. 31: 832, June 1, 1944.

[2] Meacham, P. L., and Osgood, E. C.: J. A. D. A. 28: 1640, October, 1941.

The form in which the drug is applied is of some importance. The tablets may disintegrate very slowly or may contain insoluble substances which will give a foreign body reaction. Pastes vary with the base; a water-soluble binder is better than an oil binder, generally. A finely divided powder which has been sterilized is best for local use.

Adams[1] has the following to say on the selection of a sulfonamide for local use. Neoprontosil has no local action. Sulfapyridine and sulfadiazine are both very insoluble in water and may persist in the tissues long enough to act as foreign body irritants. Sulfaguanidine has not been shown to have any value when applied locally. The sodium salts of both sulfathiazole and sulfanilamide are strongly alkaline, pH 10 to 11, and are irritants. Sulfathiazole and sulfanilamide are bacteriostatic, are soluble enough to be absorbed by the tissues, and are less prone to act as foreign body irritants. Adams continues by saying that it is doubtful whether any sulfonamide possesses an advantage for local use over sulfanilamide, with the possible exception of sulfathiazole which is more effective against staphylococcus. The army is still using sulfanilamide for local application. Hawkins[2] and Ostrander[3] consider sulfathiazole superior to sulfanilamide for dental use. On this point the literature does not agree, but both may be used with safety and efficiency.

The healing process is generally not retarded by the local application of the sulfonamides.[4, 5] Brick[6] concludes that these drugs slightly inhibit fibroblastic proliferation and that unless infection is suspected their use is contraindicated. On this point the majority of workers are in agreement.

Levy[7] suggests the following procedure for applying the sulfonamides to alveoli. The area is cleaned of blood clots and other debris. The sterile powder is applied to the abraded area and covered with a sterile sponge saturated with mineral oil. Pressure is applied by having the patient bite on the pack, which forces the drug into the tissues. The sponge is held in place for at least half an hour and the drug not disturbed for four or more hours.

A saturated solution of sulfonamides is advocated for irrigating infected tissue in and about the mouth. It is nonirritating and

[1]Adams, F. R.: J. A. D. A. 30: 58, January, 1943.
[2]Hawkins, F.: Lancet 1: 786, June 21, 1941.
[3]Ostrander, F. D.: J. A. D. A. 30: 1829, Dec. 1, 1943.
[4]Sinclair, J. A.: Bull. N. Carolina Dent. Soc. 23: 16, January, 1940.
[5]Sinclair, J. A., and Barker, O. C.: New York Jour. Dent. 11: 280, July-August, 1941.
[6]Brick, E. M.: J. A. M. A. 118: 511, Feb. 14, 1942.
[7]Levy, A. F.: J. A. D. A. 30: 1045, July, 1943.

causes no pain. If a viscid solution is desired, a 5 per cent solution in glycerin or glycerin and water is satisfactory. The bacteriocidal action of these solutions is greatly increased by slight increases in temperature.[1] Adams[2] also suggests the use of these solutions in root canal therapy, and those interested are referred to his article for the procedure.

TOXICOLOGY.—The toxic symptoms from average doses of the sulfonamides are mild and incidental to the treatment. About 10 per cent of the patients cannot tolerate these drugs; this group should be discovered early and other forms of treatment instituted.

The early and milder symptoms associated with sulfonamide medication are of central nervous system origin. The patient acts as if intoxicated with alcohol; patients under therapy should be observed and restricted in their activities when necessary. The symptoms of dizziness, middle-ear congestion, headache, malaise, anorexia, nausea, vomiting, diarrhea, rash, cyanosis, and stomatitis are generally not of a serious nature, and these symptoms regress when the administration is lessened or stopped.

The gastrointestinal symptoms may complicate the absorption of the drug and the normal intake of food and fluid. The fluid intake must be maintained, orally or otherwise. The circulatory symptoms are of cyanosis, purpura, anemia, acute granulocytopenia, and leucopenia. Cyanosis is a very common early symptom and may or may not be due to the formation of methemoglobin. Wendel (1937) suggested the injection of methylene blue to correct the symptoms of anoxia. The other symptoms of blood dyscrasias are of a more serious nature and must be looked for by repeated blood studies.

The symptoms of kidney damage are of hematuria, anuria, and albuminuria. Repeated examinations of the urine are also necessary.

The liver is sometimes damaged by these drugs with symptoms of liver failure—jaundice.

The skin symptoms are of drug rash, jaundice, purpura, etc.

Unfortunately this group of drugs may act as antigens in the body, producing symptoms of anaphylaxis at a later date. Many patients who have taken the sulfonamides for a mild infection find that they are not tolerated later when needed as a life-saving aid. The dentist must always consider this possibility when tempted to prescribe sulfanilamide and related compounds to dental patients.

[1]Adams, F. R.: J. A. D. A. 30: 58, Jan., 1943.
[2]Adams, F. R.: Dent. Items of Int. 62: 315, April, 1940.

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SULFANILAMIDE; SULFANILAMIDUM (SULFANILAMID.), $NH_2.C_6H_4.SO_2NH_2$, U.S.P.

It occurs as a white, odorless, crystalline powder, soluble in 125 parts of water and 37 parts of alcohol.

THERAPEUTICS.—It renders the body fluids unfavorable for the growth of certain bacteria. It is of accepted value in the treatment of infections with the beta hemolytic streptococci of the Lancefield's Group A, meningococci, *Clostridium welchii*, and *Actinomyces bovis*. It may be taken internally (oral) or applied locally. (See *Useful Drugs*.)

It has been shown that para-aminobenzoic acid and related compounds (local anesthetics) may inhibit the bacteriostatic action of this drug. The combination of these two incompatible substances into one preparation is therefore irrational. The injection of the usual amounts of procaine hydrochloride into patients receiving sulfonamide medication should give the dentist no concern. Any effect will be of a very temporary nature.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

The dosage varies with the type and severity of the infection. *Useful Drugs* has the following to say on dosage: "In cases of serious infection an initial peroral dose of 0.1 Gm. per kilogram (45 mg. per pound) of body weight should be given followed by one-sixth of this amount administered at four-hour intervals until the temperature has been normal for seventy-two hours, at which time the dose is gradually decreased until complete convalescence is established so that relapses do not occur. It should be remembered that the concentration in the blood or other tissue fluids is the main index of adequate dosage. If the drug cannot be taken by mouth it may be given by subcutaneous injections of a 1 per cent solution of sulfanilamide, preferably in one-sixth molar sodium racemic lactate solutions. It may be administered at from six- to eight-hour intervals in the same dosage proportions."

For local use, only sterile preparations should be used.

Sulfanilamide Tablets, Tabellae Sulfanilamidi (Tab. Sulfanilamid.), U.S.P.—Contain not less than 95 per cent and not more than 105 per cent of the labeled amount of sulfanilamide ($C_6H_8N_2O_2S$), including all tolerances.

DOSAGE.—2 Gm. (30 grains).

SULFAPYRIDINE; SULFAPYRIDINUM (SULFAPYRIDIN.), U.S.P.

It occurs as pale yellow, odorless, crystals, granules, or powder. It is stable in air but decomposes in sunlight. One gram dissolves in

about 3500 cc. of water, 440 cc. of alcohol, and is freely soluble in diluted acids and hydroxides.

THERAPEUTICS.—Sulfapyridine is effective in the treatment of pneumococcus infections regardless of typings and also in infections caused by the Friedländer bacillus. To a lesser extent it is effective against the influenza bacillus, gonococcus, meningococcus, and *Streptococcus viridans,* chiefly.

It is equally as toxic as sulfanilamide and probably more prone to produce renal irritation (Long).

DOSAGE.—2 Gm. (30 grains). "In adults suffering from lobar pneumonia large initial doses such as 4 Gm. of the drug are administered in a single dose followed by 1 Gm. every four hours by mouth until the temperature has been normal for seventy-two hours. Concentrations of 4 to 6 mg. of free sulfapyridine for each hundred cubic centimeters of blood seem to be the desired therapeutic level. In infants and children the initial dose is 0.06 Gm. per pound up to 40 pounds (18 Kg.) of body weight; larger children require slightly less in proportion to their weight, 40 grains (2.6 Gm.) being sufficient for a child weighing not more than 50 pounds (23 Kg.)." (*Useful Drugs,* thirteenth edition, 1942.)

Sulfapyridine Tablets; Tabellae Sulfapyridini (Tab. Sulfapyridin.), U.S.P.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

Sterile Sulfapyridine Sodium; Sulfapyridinum Sodicum Sterile (Sulfapyridin. Sod. Steril.), U.S.P.—It occurs as an odorless, crystalline, white powder; freely soluble in water (1 in 5), in alcohol (1 in 10), and decomposes in light.

USES.—The monohydrate sodium salt of sulfapyridine has the same therapeutic activities and properties as sulfapyridine. At the present time it has been proved effective in severe pneumococcic, meningococcic, hemolytic streptococcus and severe gonococcic infections.

DOSAGE.—2 Gm. (30 grains). "The intravenous injection of 0.01 Gm. per kilogram of body weight of the sodium salt of sulfapyridine will produce within an hour a concentration of approximately 1 mg. of sulfapyridine per hundred cubic centimeters of blood. The usual initial dose of the drug for patients severely ill with pneumonia is based on 0.06 Gm. per kilogram of body weight. The drug is weighed out and is then dissolved in sufficient sterile distilled water to make a 5 per cent solution. This solution will have a pH of about 10.8. It should not be sterilized by boiling or autoclaving, because the sodium salt is unstable under such conditions." (*Useful Drugs,* thirteenth edition, 1942.)

SUCCINYLSULFATHIAZOLE; SUCCINYLSULFATHIAZOLUM (SUCCINYLSULFATHIAZOL.), $C_4H_5O_3.NH.C_6H_4.SO_2.NH.CSC_2H_2N$, U.S.P.

It occurs as a yellowish white crystalline powder, odorless, stable in air, and darkening on exposure to light. One gram dissolves in 4800 cc. of water and is sparingly soluble in alcohol.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

Succinylsulfathiazole Tablets; Tabellae Succinylsulfathiazolum (Tab. Succinylsulfathiazol.), U.S.P.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

SULFADIAZINE; SULFADIAZINUM (SULFADIAZIN.), $NH_2C_6H_4.SO_2.NH.C_4N_2H_3$, U.S.P.

It occurs as a slightly yellow powder, odorless, stable in air, and slowly darkening on exposure to light. One gram dissolves in about 13,000 cc. of water and is sparingly soluble in alcohol.

THERAPEUTICS.—Sulfadiazine is useful in a variety of infections such as those caused by hemolytic streptococci, pneumococci, Friedländer bacilli, meningococci, influenza bacilli, gonococci, and in scarlet fever. It is effective to a lesser extent with *Clostridium welchii*, ray fungi, colon bacilli, *Staphylococcus aureus*, and Ducrey bacilli.

It is relatively free from toxicity.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

"In adults suffering from pneumococcic pneumonia, severe hemolytic streptococcus infections, severe staphylococcic infections or meningococcic meningitis, the initial dose should be based on 0.10 Gm. per kilogram of body weight. In pneumococcic pneumonia subsequent doses of 1 Gm. should be given every four hours day and night until the temperature has been normal for seventy-two hours. The drug may then be stopped. In severe streptococcic, staphylococcic and meningococcic infections subsequent doses of 1.0 to 1.5 Gm. should be administered every four hours day and night until the temperature has been normal for from five to seven days. In children suffering from pneumonia the initial oral dose should be based on 0.10 to 0.15 Gm. per kilogram of body weight, and subsequent doses should be one-fourth of the initial dose given at intervals of six hours until the temperature has been normal for at least forty-eight hours. In severe streptococcic, staphylococcic or meningococcic infections in children the drug should be continued until five to seven days of normal temperature have elapsed.

"In mild or moderate hemolytic streptococcus infections, an initial oral dose of 0.05 Gm. per kilogram of body weight, followed by a

total daily dose based on 0.10 Gm. per kilogram of body weight, this to be divided into six doses and given every four hours day and night by mouth until the temperature has been normal for three to five days, has been suggested as a satisfactory dosage schedule. In mild or moderately severe streptococcic infections, concentrations of the drug in the blood of 5 to 10 mg. per hundred cubic centimeters are usually satisfactory." (*Useful Drugs*, 1942.)

Sulfadiazine Tablets; Tabellae Sulfadiazini (Tab. Sulfadiazin.), U.S.P.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

SULFADIAZINE SODIUM; SULFADIAZINUM SODICUM (SULFADIAZIN. SOD.), U.S.P.

It occurs as a white powder, freely soluble in water (1 in 2) and slightly soluble in alcohol.

USES.—Similar to sulfadiazine (see) only more soluble in water and alkaline in reaction. It is too alkaline for topical use.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

Sterile Sulfadiazine Sodium; Sulfadiazinum Sodicum Sterile (Sulfadiazin. Sod. Steril.), U.S.P. (Sterile Sodium Sulfadiazine).—A clear, aqueous, sterile solution of sodium sulfadiazine in sealed ampuls.

USES.—For parenteral use.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

SULFAGUANIDINE; SULFAGUANIDINUM (SULFAGUANIDIN.), $NH_2.C_6H_4.SO_2.NHCNH_2NH.H_2O$, U.S.P.

It occurs as a white, needle-like, crystalline powder, odorless, stable in air, and darkening on exposure to sunlight. One gram dissolves in about 1000 cc. of water at 25° C., and about 10 cc. at 100° C. It is sparingly soluble in alcohol.

THERAPEUTICS.—Sulfaguanidine is not readily absorbed from the digestive tract, and for that reason it is less toxic than the more soluble sulfonamides. The concentration of drug in the gastrointestinal tract is easily maintained, and it is a good preparation for controlling infection in this region. It is moderately effective in bacillary dysentery and ulcerative colitis. Its use in dentistry has not been demonstrated.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

Sulfaguanidine Tablets; Tabellae Sulfaguanidini (Tab. Sulfaguanidin.), U.S.P.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

TABLE III

COMPARATIVE CLINICAL VALUE OF SULFONAMIDES

TYPE OF INFECTION	CAUSATIVE ORGANISM	SULFONAMIDE DRUG					
		SULFANILAMIDE	SULFAPYRIDINE	SULFATHIAZOLE	SULFADIAZINE	SULFAGUANIDINE	SUCCINYLSULFATHIAZOLE
Local sepsis; infections of ear, nose and throat; osteomyelitis	Hemolytic streptococcus	+++	++	+	++++		
	Staphylococcus aureus	+	++	++++	+++		
Pneumonia	Pneumococcus	+	++	+++	++++		
	Hemolytic streptococcus	+++	++	+	++++		
	Staphylococcus aureus	+	++	++++	+++		
	Friedländer bacillus	+	++++?	+++	++++		
Bacterial meningitis	Meningococcus	+	++	+++	++++		
	Pneumococcus	+	+++	++	++++		
	Hemolytic streptococcus	++++?	++	0	++++		
	Influenza bacillus	++	+++		++++?		
	Staphylococcus aureus	+	++	++++	+++		
Urinary tract infections	All organisms except enterococcus	++	+	++++	+++		
Gastrointestinal infections	Bacillary dysentery			++	++?	++	+++
	Ulcerative colitis				+	+	++?
Venereal infections	Gonorrhea	+	+++	++++	+++?		
	Gonococcic arthritis	+	+++	++++	+++		
	Lymphogranuloma venereum	++	+++?	++++	+++		
	Chancroid (Ducrey bacillus)	++++	++	++++?	+++		

++++, most effective.

Bacteremia	Hemolytic streptococcus	+++	++	++	++++		
	Staphylococcus aureus	+	++	++++	+++		
	Pneumococcus	+	+++	+++	++++		
	Gonococcus	+++	+++	++++	++++		
	Meningococcus	+++	+++	+++	++++		
	Streptococcus viridans	+	+++	++	++		
	Colon bacillus	++	++	+++	+++		
	Friedländer's bacillus	0	+	+	++		
Peritonitis	Most organisms	+++	++	+	++++		
	Hemolytic streptococcus	+++	++	+	++++		
	Pneumococcus	+	++++	+++	++++?		
Puerperal infections	Hemolytic streptococcus	+++	++	+	++++		
	Mixed infections	++	+	+++	++++		
Miscellaneous infections	Trachoma	++	+++				
	Brucellosis (undulant fever)	+++?	++	+++	++		
	Actinomycosis	+++	++	++	+++?		
	Clostridium welchii	+	+	++	+++		
	Erysipelas	+++	++	+	++++		
	Scarlet fever	+++	+	++	++++		
	Malaria	0	0	+	++		
	Tularemia	+	?	++	?		
	Plague	?	?	++	?		
	Subacute bacterial endocarditis	+	++	++	+		

SULFATHIAZOLE; SULFATHIAZOLUM (SULFATHIAZOL.), $NH_2.C_6H_4.SO_2.NHCSC_2H_2N$, U.S.P.

It occurs as pale, yellowish white crystals, granules, or powder; soluble in water and insoluble in alcohol.

THERAPEUTICS.—Sulfathiazole is principally used in pneumococcus and *Staphylococcus aureus* infections and to a lesser extent in *Eberthella coli* and gonococcus infections. It is apparently less toxic externally and internally than sulfapyridine. Skin reactions are quite common.

In dental practice it is extensively used in treating mixed infections by oral administration or local application. Sulfathiazole, like sulfanilamide, does not give a foreign body reaction, nor does it retard to any extent the healing of tissue.

DOSAGE.—2 Gm. (30 grains) U.S.P. "In the treatment of pneumococcic pneumonia in adults the initial dose of sulfathiazole should be 4 Gm., to be followed by 1 Gm. every four hours day and night until the patient's temperature has been normal for seventy-two hours. The drug should then be discontinued. In children ill with pneumococcic pneumonia the initial dose should be based on 0.15 Gm. per kilogram (up to 25 Kg. of body weight), and the total daily dose is calculated on the same basis. The total daily dose should be divided into four equal parts and administered at six-hour intervals until the temperature has been normal for thirty-six hours. The drug should then be stopped. From 4 to 6 mg. per 100 cc. of blood is the desirable concentration, although in acute infections concentrations of 7 to 10 mg. per 100 cc. may be sought." (*Useful Drugs*, thirteenth edition, 1942).

Sulfathiazole Tablets; Tabellae Sulfathiazoli (Tab. Sulfathiazol.), U.S.P.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

SULFATHIAZOLE SODIUM; SULFATHIAZOLUM SODICUM (SULFATHIAZOL. SOD.), U.S.P.

It occurs as a pale yellowish white powder. One grain dissolves in about 2.5 c.c. of water and in about 15 cc. of alcohol.

USES.—Same as sulfathiazole, but it has greater solubility in water, It is too alkaline to use for topical medication.

Sterile Sulfathiazole Sodium; Sulfathiazolum Sodicum Sterile (Sulfathiazol. Sod. Steril.), U.S.P. (Sterile Sodium Sulfathiazole).

It occurs as a colorless sterile solution contained in ampuls for parenteral use.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

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CHAPTER XVIII

GLANDULAR, TOXIN, ANTITOXIN, AND VACCINE THERAPY

ORGANOTHERAPY

While the study of the effects of these agencies belongs more appropriately in the fields of bacteriology and biological chemistry, their practical application belongs to the domain of therapeutics. Since many of these preparations now have pharmacopeial recognition, a brief account of their uses will be given here.

The immense strides which have been made within the last few decades in general therapeutics have occasioned the utilization of animal tissues or their products for medicinal purposes.

History.—The use of animal drugs for medicinal purposes is probably as old as the history of the human race; organic secretions, parts of the animal, and, in some instances, the whole animal have played a more or less important role in the treatment of diseases. The use of testicles against impotence, the gall of snakes, birds, fishes, etc., in diseases of the brain, and the bile of a snake or scorpion have been accredited with high curative power. The tendency to apply organic preparations seems to center in the natural desire to cure a diseased organ by an extraction, decoction, tincture, or other preparation of the same organ or its secretion obtained from some animal. The empiric evolution of therapeutic applications was apparently based on the supposition that like things cured like, a doctrine which later was adopted as *similia similibus curantur* by the homeopathic school. Modern organotherapy received its scientific incentive from the work of Brown-Séquard by the presentation of his essay relative to the use of the extract of testicles before the French Academy of Science in 1869. He based his conception on "internal secretions," which, as he claims, continuously supply the blood and lymph stream with materials which perform important functions in the cycle of living processes. Claude Bernard called attention to the secretion of the ductless glands, as well as to certain other glands, which produce specific substances. These substances are absolutely essential for the maintenance of bodily functions.

Glandular Therapy

The thyroid gland is a typical ductless gland. The administration of the dried, powdered gland or its extract in diseases which are connected in one way or another with this gland—myxedema, goiter, cretinism—has produced remarkable results. Its administration must be continued for a long period, often throughout life, to prevent relapses. The thyroid gland contains in its cells a peculiar globulin known as thyroglobulin. The active constituent of this substance seems to be an organic form of iodine—thyroxin. Its greatest influence is manifested by its action on metabolism.

The extract of the testicles is recommended in cases where diminished sexual powers call for a stimulation of their activity. The extract of bone marrow and that of the spleen have been, and now of liver is, recommended in pernicious anemia to increase the formation of erythroblasts. The thymus gland or its extract has been advised in exophthalmic goiter. An extract of the pituitary body has been advocated in diseases associated with the hypophysis. Fresh and purified ox gall has been employed as a cholagogue, purgative, and intestinal antiseptic. The extract of the suprarenal gland or its alkaloid, epinephrine, has been suggested in Addison's disease.

EPINEPHRINE; EPINEPHRINA (EPINEPH.), $C_9H_{13}O_3N$, U.S.P. (Adrenalin).

DOSAGE.—Hypodermic, 0.5 mg. ($\frac{1}{120}$ grain).

Epinephrine Hydrochloride Injection; Injectio Epinephrinae Hydrochloridi (Inj. Epineph. Hydrochlor.), U.S.P. (Epinephrine Hydrochloride Ampuls).—A sterile solution of epinephrine hydrochloride in water for injection.

DOSAGE.—Subcutaneous or intramuscular, 1 mg. ($\frac{1}{60}$ grain) of epinephrine hydrochloride (U.S.P.).

Solution of Epinephrine Hydrochloride; Liquor Epinephrinae Hydrochloridi (Liq. Epineph. Hydrochlor.), U.S.P.—It contains in 1 cc. about 1 mg. of epinephrine hydrochloride. It is standardized by comparing its effects on systolic blood pressure with that of a standard (U.S.P.) solution of epinephrine hydrochloride.

DOSAGE.—By parenteral injection, 0.5 cc. (8 minims) (U.S.P.).

INSULIN; INSULIN, N.N.R.

Insulin[1] occurs as an aqueous solution obtained from the pancreatic islands. When injected into animals, it lowers the blood sugar by

[1]New and Nonofficial Remedies, 1940, pp. 278-288.

mobilizing the blood glucose into glycogen which is stored by the liver and muscles. The oxidation of fatty acids is enhanced, and the acetone bodies are removed from the blood and urine. The exact mode of action is not well understood at the present time.[2]

Insulin Injection; Injectio Insulini (Inj. Insulin.), U.S.P. (Insulin, Insulin Hydrochloride).—An acidified aqueous solution of the active principle of the pancreatic gland.

Insulin injection is so standardized that each cubic centimeter contains either 20, 40, 80 or 100 U.S.P. Insulin Units.

It occurs as a colorless or almost colorless liquid, free from turbidity and from insoluble matter.

DOSAGE.—Administered by injection usually into the loose subcutaneous tissue. At times it is administered intravenously. The dose of insulin is to be determined by the physician in accordance with the needs of the patient.

PROTAMINE ZINC INSULIN, N.N.R.

A preparation of insulin modified with protamine and a zinc salt. It has a longer duration of action than insulin.

OVARY; OVARIUM (OVAR.), N.F. (Ovarium Siccum. Desiccated Ovarian Substance).

A dried undefatted, powdered ovary of cattle, sheep, or hogs. One part represents approximately 6 parts by weight of fresh glands. It contains no diluent or preservative. It occurs as a yellow or brown powder with a characteristic odor and is partially soluble in water.

THERAPEUTICS.—Not well defined; probably useless when administered orally.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

Ovarian Residue; Residuum Ovarii (Resid. Ovar.), N.F. (Desiccated Ovarian Residue).—Dried, undefatted, powdered ovary without the corpus luteum from cattle, sheep, or hogs. One part represents approximately 6 parts by weight of fresh ovary without the corpus luteum. It contains no diluent or preservative.

USES.—Not well defined; probably useless when administered orally.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

These ovarian preparations are used in the treatment of ovarian dysfunctions. The natural and synthetic ovarian hormones are more generally used.

[2]Bard, Philip: Macleod's Physiology in Modern Medicine, ed. 9, St. Louis, 1940 The C. V. Mosby Co., pp. 759-766.

Ox Bile, Fel Bovis, U.S.P. (Oxgall).

Uses.—Used in the form of the extract as cholagogue and laxative.

Extract of Ox Bile; Extractum Fellis Bovis (Ext. Fel. Bov.), U.S.P. (Powdered Extract of Oxgall).—One gram of extract represents 8 Gm. of ox bile.

Dosage.—0.3 Gm. (5 grains) (U.S.P.).

Pancreatin; Pancreatinum (Pancreat.), U.S.P.

Contains enzymes from the pancreas of the hog or ox, principally amylopsin, trypsin, and steapsin. Converts not less than 25 times its own weight of starch into soluble carbohydrates, and 25 times its weight of casein into proteoses.

Therapeutics.—It contains protein and starch-splitting enzymes and is used in pancreatic hypofunction, administered orally as enteric pills.

Dosage.—0.5 Gm. (7½ grains) (U.S.P.).

Compound Powder of Pancreatin; Pulvis Pancreatini Compositus (Pulv. Pancreat. Co.), N.F. (Peptonizing Powder).—Pancreatin (20%) and sodium bicarbonate.

Uses.—Predigestion of milk.

Pepsin; Pepsinum (Pepsin.), N.F.

Contains a proteolytic enzyme from the stomach of the hog.

Therapeutics.—Used to assist in the gastric digestion of proteins. (See Digestants.)

Dosage.—0.5 Gm. (8 grains) (N.F.).

Parathyroid; Parathyroideum.

Parathyroid Injection; Injectio Parathyroidei (Inj. Parathyroid.), U.S.P.—The water-soluble principle or principles of the parathyroid glands.

Therapeutics.—Abolishes the effects of parathyroid deficiency; used in tetany and in calcium deficiency of the blood. (See *Useful Drugs.*)

Dosage.—Intramuscular, 25 U.S.P. units (U.S.P.).

Anterior Pituitary; Pituitarium Anterius (Pituitar. Anter.), N.F. (Pituitary Anterior Lobe, Pituitary Body Anterior Lobe, Desiccated Pituitary Anterior Lobe).

The dried, partially defatted, powdered anterior lobe of the pituitary gland of cattle, sheep or hogs. One part represents approximately 5 parts by weight of fresh anterior lobe. It contains no diluent or preservative.

THERAPEUTICS.—The gland elaborates a number of important hormones, but there is no satisfactory evidence that the oral administration produces any therapeutic effects.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

POSTERIOR PITUITARY; PITUITARIUM POSTERIUS (PITUITAR. POST.), U.S.P. (Hypophysis Sicca, Pituitary).

The posterior lobe obtained from the pituitary body of cattle.

THERAPEUTICS.—The solution is administered hypodermically to strengthen the uterine contraction after the first stage of labor or in post-partum hemorrhage. It acts as an antidiuretic in diabetes insipidus and stimulates the smooth muscles of the blood vessels, increasing the blood pressure.

Posterior Pituitary Injection; Injectio Pituitarii Posterioris (Inj. Pituitar. Post.), U.S.P.—It contains the water-soluble principles from the fresh posterior lobe of the pituitary body of domesticated animals used for food by man. *The potency of Posterior Pituitary Injection shall be such that 0.1 cc. of the Injection shall possess an activity equivalent to 1 U.S.P. Posterior Pituitary Unit. (U.S.P.)*

DOSAGE.—By hypodermic injection, 1 cc. (15 minims) (U.S.P.).

THYROID; THYROIDEUM (THYROID.), U.S.P.

The thyroid glands of domesticated animals which are used for food by man, free from connective tissue and fat, dried and powdered. Contains about 0.2 per cent of iodine.

THERAPEUTICS.—Used in the thyroid-deficiency diseases.

DOSAGE.—0.06 Gm. (1 grain) (U.S.P.).

Thyroid Tablets; Tabellae Thyroidei (Tab. Thyroid.), U.S.P.

DOSAGE.—60 mg. (1 grain) of thyroid (U.S.P.).

THYROXIN; THYROXINUM (THYROX.), U.S.P.

The active principle obtained from the thyroid gland or prepared synthetically; it contains not less than 64 per cent of iodine.

THERAPEUTICS.—It is used in the treatment of cretinism and myxedema. The basal metabolism is increased slowly, the maximum being reached in about ten days. Its use in obesity is not without danger.

DOSAGE.—0.5 ($\frac{1}{120}$ grain) (U.S.P.).

SUPRARENAL; SUPRARENALUM (SUPRAREN.), N.F. (Desiccated Suprarenal. Dried Adrenal Substance. Suprarenalum Siccum. Suprarenal Gland).—Dried, partially defatted, powdered suprarenal gland of cattle, sheep or hogs. One part represents approximately 6 parts by weight of the fresh gland. It contains no diluent or preservative.

THERAPEUTICS.—The usefulness of this preparation is obscure.

DOSAGE.—0.25 Gm. (4 grains) (N.F.).

Biologic Products

Biologic products are employed to induce immunity to bacterial disease. Immunity to infectious diseases depends on the presence of antibodies in the body fluids. In *active immunity* the human organism is stimulated to produce its own *antibodies* by the injection of various substances known as *antigens* or by having the disease. The antigen may be a suspension of living microorganisms (viruses), as the smallpox virus; or a suspension of dead microorganisms (vaccines), as typhoid vaccine; or an extract of bacteria, as tuberculin; or a soluble toxin elaborated by bacteria, as diphtheria toxin.

In *passive immunity* the blood serum of an animal which has had the disease and which contains antibodies is injected. The injected antibodies confer a passive immunity to the patient. This form of immunity is produced more promptly than is the active immunity, but it is of shorter duration. Antimicrobic serum contains antibodies which attack the bacteria directly, as antibodies or antitoxins which neutralize the soluble toxins produced by the bacteria. It is the bacterial toxins which produce the characteristic symptoms of the disease. Some serums are both antitoxic and antimicrobic.

Since biologic products are changed by digestion; they are administered subcutaneously or intravenously.

If hypersusceptibility to a serum is suspected, a test is made by injecting subcutaneously 0.1 cc. repeated every 15 minutes for 5 doses. If no symptoms of serum sickness appear, the required dose may be given. (See *Useful Drugs.*)

The application of serum therapy in dentistry is as yet in its infancy; the results obtained with biologic therapeutics in general medicine should encourage investigations for the application of the same principle in diseases of the oral tissues.

Since organotherapy in its present stage of development is largely of concern to the general practice of medicine, the student is referred to more comprehensive works on the subject.

The preparations listed below are official and are recorded as found in the *Epitome of the United States Pharmacopoeia* and *National Formulary,* a publication of the American Medical Association.

Antitoxins

DIPHTHERIA ANTITOXIN; ANTITOXINUM DIPHTHERICUM (ANTITOX. DIPH.), U.S.P. (Purified Antidiphtheric Serum, Concentrated Diphtheria Antitoxin, Refined Diphtheria Antitoxin, Antidiphtheric Globulins).

Certain antitoxic substances from the blood serum or plasma of a healthy animal immunized against diphtheria toxin and dissolved in physiologic solution of sodium chloride to which a preservative is added (not more than 0.5% of phenol or 0.4% of cresol). It has a potency of not less than 500 antitoxic units in each cubic centimeter.

THERAPEUTICS.—Curative and prophylactic agent in diphtheria.

DOSAGE.—By parenteral injection: therapeutic, 20,000 units; prophylactic, 1,000 units (U.S.P.). In urgent cases diphtheria antitoxin is often given intravenously.

SCARLET FEVER STREPTOCOCCUS ANTITOXIN; ANTITOXINUM SCARLATINEA STREPTOCOCCICUM (ANTITOX. SCARLAT. STREPTOCOC.), U.S.P. (Scarlet Fever Streptococcus Antitoxin, Refined Scarlet Fever Antitoxin, Concentrated Scarlet Fever Antitoxin, Anti-Scarlet Fever Globulins).

Antitoxic substances obtained from the blood serum or plasma of a healthy animal immunized against scarlet fever toxin, in solution with sodium chloride and some preservative: potency of not less than 400 antitoxic units per cubic centimeter.

THERAPEUTICS.—Used to distinguish the rash of scarlet fever from other rashes, by the local reaction; probably induces temporary immunity to scarlet fever, and may influence the course of the disease favorably.

DOSAGE.—By parenteral injection: therapeutic, 6,000 units; prophylactic, 2,000 units (U.S.P.).

TETANUS ANTITOXIN; ANTITOXINUM TETANICUM (ANTITOX. TET.), U.S.P. (Purified Antitetanic Serum, Concentrated Tetanus Antitoxin, Refined Tetanus Antitoxin, Antitetanic Globulins).

Certain antitoxic substances from the blood serum or plasma of a healthy animal immunized against tetanus toxin and dissolved in physiologic solution of sodium chloride to which a preservative is added (not more than 0.5% of phenol or 0.4% of cresol). It has a potency of not less than 400 antitoxic units in each cubic centimeter.

THERAPEUTICS.—Prophylactic agent in tetanus; also used for curative purposes.

DOSAGE.—By parenteral injection: therapeutic, 20,000 units; prophylactic, 1,500 units (U.S.P.).

Serum Therapy

The introduction of bacteriology into general therapeutics exercised a great influence on the biologic conception of infectious diseases.

The discovery of specific organisms as the causative factors of specific infectious diseases notably changed the therapeutic application of remedial measures by treatment known as *serum therapy* or as *biologic therapeutics.*

The bacteria of certain infectious diseases invade the body only in definite places—as diphtheria in the throat, but nevertheless the reaction of the entire body to this disease indicates that specific products of this organism must have reached the circulation. True infection is accompanied by intoxication; the latter is the result of absorbed toxins. The isolation of these poisons (toxins of bacterial origin, especially from putrefying protein substances) led to the discovery of ptomaines—cadaverine, putrescine, etc. These compounds are very powerful poisons, and the smallest quantity will produce toxic symptoms which are not equalled in their intensity by any other known substance. The toxins differ from other poisons insofar as they require a certain period of time before they develop and they are not necessarily equally poisonous to all animals.

Serums

ANTIMENINGOCOCCIC SERUM; SERUM ANTIMENINGOCOCCICUM (SERUM ANTIMENINGOCOC.), U.S.P. (Antimeningococcus Serum, Meningococcus Serum, Meningitis Serum).

Obtained from the blood of an animal immunized with cultures of several types of meningococci.

THERAPEUTICS.—Used in the treatment of meningitis.

DOSAGE.—Therapeutic by parenteral injection, 20 cc. (U.S.P.).

ANTIPNEUMOCOCCIC SERUM—TYPE SPECIFIC; SERUM ANTIPNEUMOCOCCICUM (SERUM ANTIPNEUMOCOC.), U.S.P. (Antipneumococcus Serum, Pneumonia Serum).

Obtained from the blood of an animal immunized with cultures of a pneumococcus *(Diplococcus pneumoniae).*

THERAPEUTICS.—Used early in the treatment of lobar pneumonia. A typing of the organisms determines which type of serum is to be administered.

DOSAGE.—Therapeutic, by parenteral injection, 20,000 to 100,000 units (U.S.P.).

NORMAL HUMAN SERUM; SERUM HUMANUM NORMALE (SER. HUMAN. NOR.), U.S.P. (Human Serum).

The sterile serum obtained by pooling approximately equal amounts of the liquid portion of coagulated whole blood from eight or more humans *(Homo sapiens).*

THERAPEUTICS.—It is used in the treatment of shock from surgery, trauma, burns, or hemorrhage, and as a temporary substitute for whole blood.

DOSAGE.—Intravenous, 500 cc. (U.S.P.).

HUMAN MEASLES IMMUNE SERUM; SERUM IMMUNE MORBILLOSI HUMANUM (SER. IMMUN. MORBILL. HUMAN.), U.S.P. (Measles Convalescent Serum).

A sterile serum obtained from the blood of healthy persons who have survived an attack of measles.

THERAPEUTICS.—It is administered during the incubation period to prevent or modify an expected attack of measles. Its value as a specific treatment is not established.

DOSAGE.—Parenteral, therapeutic, 20 cc.; prophylactic, 10 cc. (U.S.P.).

HUMAN SCARLET FEVER IMMUNE SERUM; SERUM IMMUNE SCARLATINAE HUMANUM (SER. IMMUN. SCARLET. HUMAN.) U.S.P. (Scarlet Fever Convalescent Serum).

THERAPEUTICS.—It is of value in transferring passive immunity to patients exposed to scarlet fever. Its curative value is not established.

DOSAGE.—Parenteral, therapeutic 20 cc.; prophylactic, 10 cc. (U.S.P.).

Vaccines

OLD TUBERCULIN; TUBERCULINUM PRISTINUM (TUBERCULIN. PRIST.), U.S.P. (Tuberculin-Koch, Concentrated Tuberculin, Crude Tuberculin).

A sterile solution of the soluble products of growth of the tubercle bacillus. It contains about 50 per cent of glycerin.

THERAPEUTICS.—Used for the diagnosis of tuberculosis. For discussion of its use see *Useful Drugs.*

DOSAGE.—Diagnostic, intracutaneous—0.00001 cc. to 0.001 cc.; therapeutic, subcutaneous—0.00000001 cc. to 0.000001 cc. (U.S.P.).

RABIES VACCINE; VACCINUM RABIES (VAC. RABIES), U.S.P. (Antirabic Vaccine, Antirabic Virus, Pasteur Treatment, Pasteur Prophylactic).

A sterile suspension of the attenuated, diluted, dried or dead, fixed virus of rabies. U.S.P.

THERAPEUTICS.—For establishing immunity to rabies in one who has been bitten by a rabid animal.

DOSAGE.—The contents of one container (hypodermically), to be repeated at proper intervals (U.S.P.). The treatment consists of a series of doses continued for from 14 to 21 days, dependent upon the location and severity of the injury.

BACTERIAL VACCINE MADE FROM THE TYPHOID BACILLUS; VACCINUM TYPHOSUM (VAC. TYPHOS.), U.S.P. (Typhoid Prophylactic, Enteric Vaccine, Typhoid Vaccine).

A sterile suspension of killed typhoid bacilli in an isotonic solution of sodium chloride or other suitable diluent and must contain at least 1,000,000,000 typhoid organisms in each cubic centimeter of the vaccine.

THERAPEUTICS.—Used for establishing immunity to typhoid fever.

DOSAGE.—Prophylactic, by hypodermic injection, 0.5 cc. and 1 cc., the latter dose to be repeated once making a total of three injections.

BACTERIAL VACCINE MADE FROM THE TYPHOID BACILLUS AND THE PARATYPHOID "A" AND "B" BACILLI; VACCINUM TYPHO-PARATYPHOSUM (VAC. TYPHO-PARATYPHOS.), U.S.P. (Typhoid Combined Vaccine, Typhoid-Paratyphoid Combined Vaccine, Typhoid Mixed Vaccine Prophylactic, Typhoid-Paratyphoid Prophylactic, Mixed Enteric Vaccine).

A suspension in physiologic solution of sodium chloride of killed typhoid bacilli, and killed paratyphoid bacilli "A," and "B." At least 1,000,000,000 typhoid organisms and at least 250,000,000 of each of the paratyphoid organisms in each cubic centimeter of the vaccine.

THERAPEUTICS.—Used for establishing immunity to typhoid and paratyphoid fevers. This preparation is used a great deal for foreign protein therapy.

DOSAGE.—Prophylactic, by hypodermic injection, 0.5 cc. and 1 cc., the latter dose to be repeated once (U.S.P.). For foreign protein therapy one usually starts with a dose of 5 to 10 million organisms (1/400 to 1/200 cc.) intravenously. This dose is usually obtained by accurate dilution of the official vaccine, in order that this number of organisms will be present in a measurable amount of solution. Injections may be given every 3 to 5 days. The common practice is to double the dose up to doses of as much as 500,000,000 to 1,000,000,000.

SMALLPOX VACCINE; VACCINUM VARIOLAE (VAC. VAR.), U.S.P. (Virus Vaccinicum, Glycerinated Vaccine Virus, Jennerian Vaccine, Antismallpox Vaccine).

It consists of a glycerinated suspension of the vesicles of vaccinia or cowpox which have been obtained from healthy vaccinated cattle.

The product must comply with the requirements established by the United States Public Health Service.

It must be kept at a very low temperature, preferably below 0° C., and never above 5° C., as it loses potency rapidly at higher, even moderate temperatures. (U.S.P.)

USES.—Prophylactic vaccination against smallpox.

Toxoids

DIPHTHERIA TOXOID; TOXOIDUM DIPHTHERICUM (TOXOID. DIPHTHERIC.), U.S.P.

A sterile aqueous solution of the products of the diphtheria bacillus which are nontoxic but retain antigenic property.

THERAPEUTICS.—For inducing an active immunity to diphtheria.

DOSAGE.—Hypodermic, for active immunization, 1 cc. to be repeated at proper intervals until a negative Schick test is obtained. (U.S.P.)

TETANUS TOXOID; TOXOIDUM TETANICUM (TOX. TET.), U.S.P.

A sterile solution of the products of the growth of the tetanus bacillus which are nontoxic but retain antigenic property.

THERAPEUTICS AND DOSAGE.—It is used to produce an active immunity to tetanus in three doses of 1 cc. each, preferably subcutaneously at weekly intervals. An additional 1 cc. may be injected at time of exposure or at intervals of one year to confer continuous immunity.

CHAPTER XIX

PHYSICAL THERAPEUTICS

ARTIFICIAL HYPEREMIA

In the treatment of disease a variety of methods and measures are employed as remedial agents which cannot be properly classified as drugs if we restrict the term to organized substances which, when introduced into the living body, counteract disease. A *remedy,* in the broadest sense of the term, is anything which cures, palliates, or prevents disease, and, consequently, therapeutics comprises the utilization of all means and methods which are employed for the purpose of relieving the sick and favorably modifying the evolution of disease—i.e., the art of healing. In addition to the use of drugs and surgical procedures, a number of mechanical and physical forces are employed, which, for the want of a better term, are classified as physical therapeutics, and they include artificial hyperemic treatment, massage, heat, cold, light, electricity, etc.

At present it is generally conceded that inflammation is not a disease, but a local reaction of the tissues against injury, manifesting itself by more or less pronounced symptoms—as redness, heat, swelling, pain, and impaired function. The most important changes occur in the blood vessels, which are distended by an increased influx of blood. The white corpuscles congregate near the vessel wall, especially in the veins and capillaries, while the red blood corpuscles keep more to the center of the blood stream. The leucocytes and lymphocytes pass between the endothelial cells through the vessel walls of the veins and the capillaries, but not of the arteries. This wandering of the white corpuscles—diapedesis—is accompanied by the transudation of blood serum, which fills the surrounding tissues, causing an edematous swelling. Later on the red blood corpuscles follow, but they migrate in much smaller numbers. Another important, but as yet less recognized, symptom of inflammation is the increased osmotic pressure within the infiltrated area. Under normal conditions the osmotic pressure is promptly regulated by the organism; probably, according to Massart, through specific nerves—that is, the normal equilibrium of the isotonic index of the blood and tissue fluids remains stationary. In pathologically altered tissues the composition is continually interfered with and usually results in a marked increase of

the osmotic pressure—hypertonicity. Increased osmotic pressure produces pronounced morphologic changes in the cells and is largely responsible for the pain, followed by inflammation, within the affected area. According to Ritter the various changes in tissues, if a simple abscess is taken as an example, may be described as follows: In the center of the pus cavity the osmotic pressure may reach a density of 0.6° to 1.4° C. (0.56° being normal), but in the surrounding hyperemic zone the pressure is less, gradually diminishing, becoming less and less toward the periphery until normal pressure is reached. Aside from these quantitative changes within the inflamed area, qualitative changes of the constituents of the exudates undoubtedly have some important significance. The nature of these latter changes is at present too obscure to allow any definite statements to be made.

Fig. 24.—Inflamed mesentery of frog: *a*, margination of leucocytes in the dilated capillaries; *b*, migration of leucocytes; *c*, escape of red corpuscles; *d*, accumulation of leucocytes outside the capillaries. (After Ribbert.) (From Prinz: *Diseases of the Soft Structures of the Teeth*, Lea & Febiger)

Whenever living tissue is injured—whether by mechanical, thermal, or chemical means—the system at once tries to protect itself by an increased rush of blood into the injured area, resulting either in complete resolution or in necrosis.

Local hyperemia, which is the forerunner of acute inflammation, results from an increase in the quantity of blood in the injured part. If it is due to an increase in the flow of blood, it is referred to as arterial or active hyperemia, while, if resulting from an obstruction

which retards its outflow, it is known as venous or passive hyperemia. In active hyperemia the involved area is bright red in color, the temperature is slightly elevated, and there is usually marked swelling. Passive hyperemia manifests itself by a bluish-red color (cyanosis) of the involved area with a somewhat lessened temperature. The veins are distended, and an edematous swelling is soon observed, resulting from the transudation of the various constituents of the blood. At present it is generally accepted that the therapeutic benefits derived from hyperemia find an explanation in the bactericidal action of the blood serum and the increase in temperature. Let it suffice to say that nature utilizes, so far as we know, three important principles of self-protection against local infection—preparation for transudation of the serum, positive chemotaxis, and increased cell proliferation. Quite a number of theories have been pro-

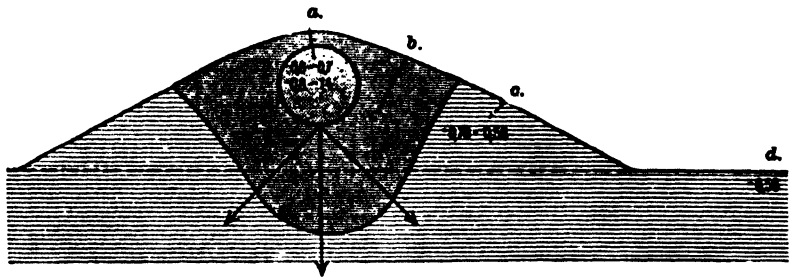

Fig. 25.—Schematic drawing of an abscess. The abscess and the surrounding infiltrated area show the various degrees of osmotic pressure: *a*, abscess; *b*, hyperemic zone; *c*, manifest edema; *d*, latent edema.

mulgated to explain the nature of the defensive properties of hyperemia. Buchner attributes these defensive properties to the increase of the leucocytes and the accompanying alexins. Hamburger believes that the increased amount of carbonic acid in the blood as a result of the congestive hyperemia is responsible. The same views are shared by Chantemesse and Lubarsch. Nötzel favors this view, provided it is restricted to recent exudations, while Metchnikoff, supported by Leyden, Lazarus, and others, believes that the phagocytotic action of the leucocytes is the predominating factor. Be that as it may, the facts remain that hyperemia is the essential factor which nature provides to combat local infection, and that we owe it to Bier to have utilized therapeutically this very same principle artificially to assist nature in warding off disease by producing inflammation. It seems paradoxical to speak of warding off disease by providing inflammation. From the earliest times heat, in the form of a poultice or fomentation, has been applied by means of heated water, stones, china, etc.,

and has always ruled supreme in the treatment of local infections. Tincture of iodine paint, the hot-water bottle or the ice bag, the modern alcohol liniments or the Priessnitz bandage, the therapeutic lamp or the electric heat bath, and massage accomplish in reality one and the same purpose—they produce certain forms of artificial hyperemia. Many of these remedies act only by counterirritation, producing a secondary inflammation in order to relieve the primary irritation.

The bactericidal function of congestive hyperemia has been fairly well established by carefully conducted experiments. Nötzel has shown that an injection of virulent cultures of streptococci into the extremities of animals subjected to congestive hyperemia would do little harm, while the same injection into control animals invariably produced death. It is furthermore sufficiently proved by experimental work, as well as by clinical experience, that active hyperemia as produced by direct heat materially increases the absorption of watery and water-soluble materials by the capillaries, all solid and non-water-soluble liquids being absorbed solely by the lymphatics.

Local hyperemia exerts a definite solvent or softening power upon exudates which may have collected about joints or in the tissues—as blood clots, joint stiffness, phlegmonous infiltration, etc. It favorably influences nutrition, and it seems to be a well-established fact that the formation of callus, especially the amount of calcium salts, in the repair of broken bone is materially increased.

Therapeutic Applications

Acute and particularly chronic inflammations and their sequelae —adhesions, infiltrations, and exudations—are readily amenable to active hyperemic treatment. Of the specific diseases, neuralgia and myalgia in their various forms are especially favorably influenced by heat. The affected part is brushed over with the therapeutic lamp for about ten minutes, and immediately after, or even during, the heat application the area is massaged. Acute infections are treated during their early stages with cold, i.e., ice bags, while heat (hot water) is generally used during the later stages.

Massage

Massage (kneading or rubbing) is a therapeutic measure employed for the purpose of treating diseases by mechanical movements. In medicine it is known by various terms—kinesitherapy (motion treatment), mechanotherapy, massotherapy, and more re-

cently osteopathy. Its systematic employment has been equally lauded in bygone days by the physicians of Babylon, Alexandria, Athens, and Rome; and, while Europe enjoys a revival of massage under the name of Swedish movement, the United States had its apostle of the art in the person of Dr. Still, the founder of the osteopathic cult.

By massage we understand a series of mechanical movements best executed by the hands of the operator, affecting the skin as well as the deeper structures of the body. To employ it on a scientific basis, a fair knowledge of regional anatomy and physiology must be possessed by the operator. It is somewhat difficult to describe minutely the various movements employed in the art of massaging, and they are best acquired by personal instructions by a skilled operator. The object of massage is to bring about increased cell activity in the parts. Massage increases the flow of body fluids (blood, lymph, chyle, etc.), increases secretion and excretion, and excites muscular activity. In general, its physiologic effects and therapeutic advantages are nearly identical with those obtained from any other source which is capable of producing artificial hyperemia.

The technique of massage may be divided into the following methods of application: stroking, friction, kneading, percussion and vibration, active and passive movements, or medical gymnastics. The movement of the hands in applying massage depends on the method employed. In stroking, the whole palm or the radial border of the hand, or the tips of the fingers are used, the pressure being light in the beginning and gradually increasing to as much force as the case demands. The direction of the strokes in most cases is venous—centripetal, or toward the heart. Upon the head the movements are directed from the vertex downward. Friction is best applied by forcible, circular rubbing of the surface, starting at the border of the altered tissues and working toward the center from all directions. In kneading, squeezing, rolling, etc., the movements of pressure and relaxation are alternately and rhythmically employed to simulate natural muscular action, the object being to act upon the circulation of the deeper seated structures. The veins, capillaries, lymph vessels, and lymph spaces are emptied by pressure, the valves in the vessels preventing a return of the expelled fluids, but making room for a fresh influx. Percussion and vibration consist of a series of tapping, pounding, or beating movements very rapidly and rhythmically performed with the fingers, with the radial border of the hands, or by means of mechanical contrivances worked by the hand, a spring, or electricity, which causes muscular con-

traction. In the active, or Swedish, movement the patient concentrates on the muscle under treatment, causing it to act, while the operator tries to resist the movement with slightly less force. After the muscle has fully contracted, the operator employs force, while the patient diminishes his resistance, until the muscle is brought back to its original position. In passive massage all the movements of the muscles and joints are executed by the operator without resistance or assistance on the part of the patient.

Medical gymnastics are principally employed for the purpose of exercising all those muscles which are seldom used, or which, for some special reason, require strengthening.

From the viewpoint of the dental therapeutist, massage is a serviceable adjunct to his armamentarium. It is indicated in all those conditions where a sluggish circulation in the soft tissues exists, and consequently all those diseases in which chronic inflammation is an etiologic factor—gingivitis, pyorrhea alveolaris, etc.—are directly amenable to this treatment. As a prophylactic measure, massage, in combination with the daily routine toilet of the mouth, deserves to be highly recommended. In the mouth proper the finger (bare or covered with a coarse linen finger cot or stall), the toothbrush (made of soft or coarse bristles, rubber, or woody fibers), or even some specially devised mechanical appliances are used. Existing conditions and the individuality of the patient govern the methods and their application. The operator has to decide which grade and what kind of a toothbrush is best for the case in hand. Rotary movement and moderate pressure applied by a fairly coarse brush apparently produce better results than a too soft or a too coarse brush used with heavy friction. The time required for oral massage is also dependent on conditions. On the average about five minutes three times daily are sufficient. For external facial massage, the finger tips or the electric vibrator is indicated. This also depends on conditions, the operator selecting the method best suited to his purpose.

Light Therapy

Within recent years, light, in the form of sunlight or artificial light, has been freely discussed as a therapeutic agent of some importance. A comprehensive knowledge of light rays from the physicist's point of view is essential to a clear understanding of their therapeutic action. The solar spectrum furnishes a band of colors consisting of violet, indigo, blue, green, yellow, orange, and red shades which overlap each other. Beyond either end of the spectrum there are found a number of rays, the more important ones being known as the infrared and the ultraviolet rays. Certain

rays possess specific functions. The infrared rays are heat producers and are spoken of as thermic or caloric rays; the yellow and green rays are predominant in the production of light and are referred to as luminous rays, while the blue and violet rays, especially the ultraviolet rays, exercise a marked chemical influence on organic and inorganic matter and are known as chemical or actinic rays. Concerning the therapeutic value of the various rays, it is known that the thermic rays produce active hyperemia, the actinic rays exercise a definite chemical influence on cell structure, and the luminous rays possess an analgesic effect. By specially constructed apparatus certain rays may be concentrated, others may be eliminated, and combinations of the rays in varying degrees may be produced at will. The various sources of light employed for therapeutic purposes are direct sunlight, the Finsen light, and the incandescent bulb. For dental purposes, direct sunlight is probably rarely used. The Finsen light, on account of its expense, is largely confined to special sanatoriums; while the incandescent bulb, on account of its simplicity, deserves to be recommended.

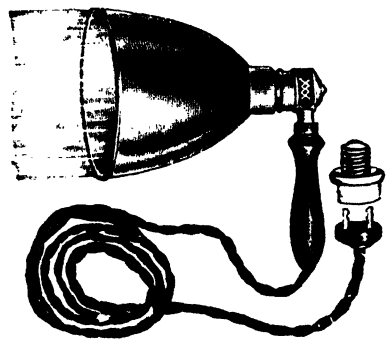

Fig. 26.—Dental electric therapeutic lamp.

The Finsen lamp produces an intense, cold light; it is especially rich in ultraviolet rays, while the thermic rays have been largely excluded. The chemical influence of the Finsen light manifests itself principally in the destruction of the pus-producing elements, without, however, unfavorably influencing cell proliferation. Its essentially preservative action results in the formation of white, smooth scars without contraction of the tissues. The Finsen light is much lauded for the treatment of lupus and similar diseases of the skin and mucous membranes. As stated above, the therapeutic action of the mixed light rays is destructive to micro-organisms; the rays act as analgesics, and they produce intense active hyperemia with all its sequences.

The electric light best suited for dental purposes is a one-hundred candle-power incandescent bulb having a hard carbon filament and inclosed in a suitable projector. Much confusion exists regarding the relative therapeutic value of lamps of different candle power. It should be borne in mind that a one-hundred candle-power lamp is just as efficient, therapeutically speaking, as a five-hundred candle-power light. The patient can bear only a certain amount of heat, and any more heat produced by the lamp is wasted. A one-hundred candle-power lamp furnishes sufficient caloric rays to burn tissue readily. The projector should be of the parabolic type—that is, so constructed as to furnish parallel rays only. It is claimed that the metal best suited for a reflector is an alloy of aluminum and manganese. To modify or intensify the various rays of this lamp, yellow, blue, or amber colored glass screens may be clamped to the projector.

In the practice of dentistry the mixed rays of light obtained from what is technically known as a one-hundred candle-power therapeutic lamp are generally employed. The lamp is held in front of the affected part, the distance depending on the degree of heat desired. The light is used with a brushing motion, and should not be focused too persistently on any one point. A thin coat of petroleum jelly spread over the surface to be treated relieves undue tension. To receive the full benefit of the light treatment, the part to be treated should be continuously exposed twice at one sitting for about fifteen minutes each time, with an interval of half an hour, and preferably immediately followed by massage.

Radioactive Substances

In 1896 Roentgen made the discovery that certain rays obtained from a Crookes' tube would penetrate substances which, under ordinary conditions, are known to be opaque. In the same year the French physicist, Henry Becquerel, observed that a photographic plate protected by a tight-fitting cover of black paper becomes exposed when brought into contact with uranium salts. Certain substances are known to possess the power of emitting light rays; i.e., fluorescence or phosphorescence. It should be borne in mind, however, that these latter substances have to be exposed to sunlight or artificial light for some time before they re-emit some of this stored energy in the form of light rays. On the other hand, minerals which contain uranium will bring about the same phenomenon without being previously exposed to light rays.

Light is a form of energy which cannot be completely destroyed nor can it be created out of nothing. Since uranium salts produce light rays apparently indefinitely, it was supposed that they must contain certain specific substances which possess, as an inherent property, the power of light emanation. The isolation of these substances was finally accomplished, and their discovery is primarily to be credited to the late Professor Pierre Curie and to his wife, Mme. Curie, of Paris. Both experimenters worked with crude uranium minerals and from it they isolated radium—the radiant—and polonium, so termed in honor of Mme. Curie's native country, Poland. Shortly after the discovery of these two elements, Debierne of Paris isolated a third radio-active element from the crude uranium, which he named actinium.

Radioactive Substances.—These substances may be classified in three distinct groups: actinium, thorium, and uranium. Each primary element, by transmutation, transforms itself into a number of other substances. According to Rutherford and Soddy, all radioactive substances are continuously undergoing transformation. During the transformation of a radioactive element, another element is created whose atoms possess less power of emanation than is possessed by the one from which it is created.

Radium is an element closely related to barium in its chemical behavior. It is a white metal, melting at about 1,316° F. (700° C.), and energetically decomposing water. Aside from the ordinary properties possessed by the barium group, it is endowed with three remarkable additional functions: it emits heat continuously at a constant rate, it is the source of radiation, and it generates a gas which is radioactive.

Radiation Energy.—The transformation of one radioactive element into another is accompanied by the liberation of various rays, which are known as the alpha, beta, and gamma rays. Alpha and beta rays are not true rays; the alpha rays are positively charged ions of helium given off by the element, while the beta rays are negatively charged ions. The gamma rays are true rays; they do not contain free ions and are very similar to the roentgen rays. The gamma rays are not distorted in a magnetized field, while the other two rays are turned to the right or left, respectively. The power of penetration of these various rays differs markedly; the alpha rays are least active, the beta rays are slightly more so, while the gamma rays pass through a sheet of lead one centimeter thick, the human body, the walls of a house, etc.

Biologic and Physiologic Action of Radioactive Substances.—Every living cell, when subjected to radium emanation, is influenced by it; however, the reaction of the cell depends upon its specific nature and upon the kind of rays employed. In consequence, certain tissues are more easily amenable to the rays than others. Nervous tissue reacts most energetically, while intestinal and serous tissues are far less strongly influenced. Muscle tissue is the least reactive. Connective tissue, when subjected to the rays, is readily stimulated to proliferation. Histologic examination indicates that the typical phenomena of inflammation, with their many changes, i.e., from an early hyperemia to the final necrosis, may be produced at will. The internal organs react in various ways; readily influenced are lymphoid tissues, especially the spleen, less so the kidneys, and still less the salivary glands and mucous membrane. No living tissue will stand the prolonged exposure to the rays without showing some definite change, and it is immaterial whether the tissue is of animal or of vegetable origin. Ferments, on an average, are slightly activated. Low-type organisms, i.e., bacteria, protozoa, etc., are very slightly influenced by radiation. Upon pathologic tissues the effect of the rays is much more pronounced than upon normal structure, hence the great significance of the rays in the treatment of disease. The physiologic effect, as Von Norden expresses it, results in an internal electric ionization of the tissues. So far, no danger from the application of small doses of emanation has been observed; large doses are productive of destructive results. From a therapeutic point of view, innumerable diseases have been subjected to the effects of radium emanation. In due time it was found that specific results were obtained in certain forms of skin diseases, neoplasms, glandular hypertrophy, disturbances of metabolism, and painful alterations of the nervous system, i.e., neuralgia, etc.

Heat and Cold

Heat and cold are frequently referred to as distinct entities, but in reality they are merely relative terms expressing the variations above and below normal temperature. By that term the temperature of the human body—about 98.6° F. (36.9° C.)—is meant and is taken as the average caloric indicator.

Heat is applied in two forms—dry heat and moist heat. The physiologic effect of both is the same, and they produce a pronounced active hyperemia with all its phenomena. Dry heat can be borne by the body at a very much higher degree than moist heat. In a "hot room" temperatures as high as 140° to 150° F. (60°

to 66° C.) are frequently reached, while moist heat in the form of a poultice should be limited to 105° to 110° F. (40° to 43° C.). Above this temperature moist heat is injurious to the soft tissues. The body protects itself against great heat by the evaporation of profuse perspiration and the powerfully accelerated blood stream within the heated area. Dry heat is conveyed to the tissues through the air, and, as air is a very poor conductor, much of the heat is lost, while moist heat is kept in intimate contact with the tissues and is held there for a definite period. The continuous application of heat in pathologically altered tissues produces definite changes in the structures. The resulting increased osmotic pressure exerts a powerful influence on the centrifugal flow of the lymph, and the products of the early stages of inflammation are carried away from the center toward the periphery to be poured into the circulating blood stream or otherwise disposed of. If pus is about to form, the heat will materially assist in the ready breaking down of the affected structures and will help to localize the abscess.

The general effects of cold on the tissues manifest themselves in lowering the temperature, diminishing the sensibility, and contracting tissues and vessels, thereby reducing the volume of the part. Cold continuously applied benumbs the part and produces in due time a definite local anesthesia. Cold, when locally and continuously applied in the form of an ice pack, cold water bottle, towels wrung out in iced water, etc., causes a temporary inhibition of inflammation in its very early stages. Its antiphlogistic action is manifested by retarding circulation and inhibiting the emigration of the leucocytes. As soon as the cold application is removed, the inflammatory process may again start with renewed activity.

Therapeutic Applications

Apparently there exists quite a diversity of opinion relative to the use of moist heat, dry heat, and cold. Both forms of heat, locally applied, are productive of the same results. They induce intense active hyperemia, and apparently it makes little difference which form of heat is employed. The choice between heat and cold is largely governed by the condition of the patient. If we are dealing with a pericemental inflammation and the formation of an abscess, the requirement of heat and cold can be more definitely outlined. Clinical experience has taught that in the early stages of inflammation ice chips held in the mouth or cold applied externally is useful in retarding the process of inflammation and mitigating the pain. If the infiltration of the tissues has proceeded to such an extent as to indicate possible pus formation, a hot poultice placed

directly over the offending area and covering the entire inflamed area is extremely serviceable.

Poultices are soft, moist applications, usually employed hot, but sometimes cold; occasionally they may contain drugs intended to exert some specific action. Poultices furnish more or less constant heat and moisture, and thereby relax the skin, thus favoring swelling and lessening tension in the tissues. Whenever a hot poultice is employed, it should always cover the field of inflammation in its entirety, and should never be so small as to cover the center of inflammation only, as then the pain is certain to increase. A hot poultice has no place on an opened or a septic wound, as it would practically seal up the infected focus, and the pent-up infection would rapidly involve the surrounding tissues.

For the application of dry heat on external body surfaces many forms of heat carriers are employed. The heated brick, hot-water bottle, heated salt bags, and many other means are utilized to retain heat for a limited time. A permanent source of heat is obtained with an electric heating pad which seems to serve its purpose well.

IONIC MEDICATION

Ionic Medication is the local application of drugs to tissues by means of an electric current. The drug must be dispersed in an ionic solution, and the electric current furnishes the energy which propels the charged particles into the tissues. It is used for the introduction of drugs through the body surfaces into the superficial tissue. The rationale of ionization depends upon the interaction of two definite processes: (1) the dissociation of a suitable chemical compound (electrolyte) in a solvent into ions, and (2) the migration of these ions in the direction of specific poles within the tissues, brought about by the passage of a weak galvanic current.

When a solid, liquid, or gas enters into solution and is capable of conducting an electric current, according to Arrhenius, the solution undergoes certain changes which are grouped under the generic term *electrolysis*. This latter term with the following nomenclature was introduced by the English physicist Faraday (1791-1867) and is still universally employed. The solution itself is known as the *dielectric* (D), while the dissociated products are referred to as *ions* (E and F). The terminals at which the electric current enters or leaves the solution are called *electrodes* (A and B). An ion (ion = *going*) may be referred to as being the dissociated product of a chemical decomposition which is capable of conducting an electric charge and which travels in the direction of an oppositely charged pole. Those ions which are charged negatively migrate to the anode, i.e., the positive

pole, and are known as *anions,* while the positively charged ions migrate to the negative pole, the cathode, and are known as *cations.* Relatively speaking, all metals, alkaloids and hydrogen, are positive ions, i.e., cations; while all acid radicals, halogens, hydroxyl radicals, and oxygen are negative ions, i.e., anions. As Ostwald has suggested, the cation may be designated by the positive sign + and the anion by the negative sign –.

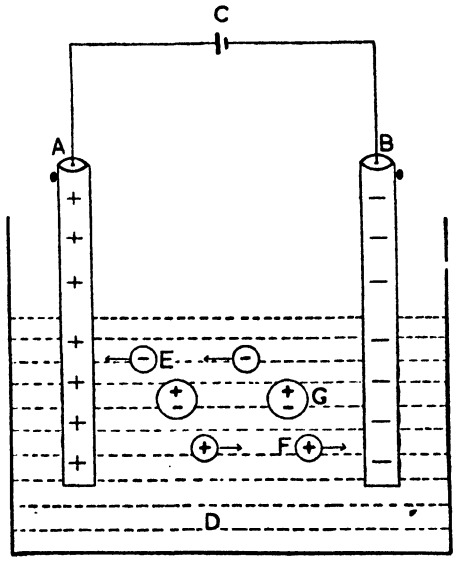

Fig. 27.—Scheme showing the movement of ions.

A simple solution of salt in water dissociates the salt into electromolecules, the ions, which exist independently of the action of a galvanic current. The number of positively and negatively charged ions is equimolecular. The ions themselves are suspended in the solution in a chaotic mixture. The passing of the galvanic current by its electromotive force causes a definite movement of the ions in an orderly direction to their specific centers of attraction, i.e., respectively to the positive or the negative poles.

The only current suitable for ionization is the direct current. The alternating current as such cannot be used unless it is changed by a transformer. The source of the current may be obtained from the main line, from an accumulator or a storage battery, or from a series of cells. If the street current is used, it must be reduced by a rheostat to about 30 to 40 volts. If cells are employed about 18-24 ordinary dry cells (Columbia No. 6) are the most useful.

The two electrodes are terminals attached for the purpose of conveying the current to the patient and consist of a negative electrode

which is to be placed on the patient's skin surface, and a positive electrode, generally, to be introduced into or about a tooth. The negative electrode may be a piece of metallic tubing held firmly in the patient's hand or a sponge electrode fastened to the wrist, or one of various modifications thereof. The size of the negative hand electrode is important; it should present at least five square inches surface area, which are to be brought into contact with the patient. A large surface of the negative electrode reduces the resistance, and consequently the tingling sensation or even blistering caused by the heat of a small electrode is avoided. We prefer the plain tube hand electrode, as it avoids the cumbersome wetting with salt water, loss of time in adjustment, etc. It is immaterial in which hand the electrode is held. Rings, bracelets, wrist watches, etc., must be removed; otherwise blistering of the patient's skin by mere contact may occur. Placing the negative electrode upon the patient's cheek, lip, gum surface, or tooth, by means of a clamp or spring, as recommended by some operators, is to be avoided, for the reason that severe burns may result. It has been stated that this blistering results from the formation of caustic hydroxides near the negative pole. The blistering is the result of imperfect contact between the skin and the metal electrode, thereby increasing the resistance of a small area to such an extent as to produce high heat or an electric burn. The positive electrode to be introduced into the tooth consists of a piece of iridoplatinum wire, No. 20 gauge, about one inch long and tapered to a delicate point. The iridoplatinum alloy possesses the necessary flexibility, which is lacking in pure platinum. The point itself is ground blunt so as to avoid being caught when introduced into tortuous canals. Various sizes of these points may be kept on hand. No other metal should be employed for such purposes. Substitution of the iridoplatinum point by zinc, copper, or any other metal, with the view of aiding its therapeutic effects, not only is useless, but markedly interferes with the action of electrolysis in the relatively small area of a root canal; also the resultant ions may discolor the tooth. A long-handled electrode holder, insulated with hard rubber, is essential to unite the electrode suitably with the conductive cord. The holders may be of various types, so as to give ready access to all parts of the oral cavity.

Cataphoresis is similar in principle to ionic medication, with the exception of the size of the drug particles. In ionic medication the particles exist as ions and in cataphoresis the particles exist as charged molecules or molecular aggregates. The required apparatus is the same in both instances, as is the procedure.

PART II

DENTAL THERAPEUTICS

CHAPTER XX

PRESCRIPTION WRITING

INTRODUCTION

A prescription, from the Latin *prae* (before) and *scribo* (I write), may be defined as a written order for medicines sent by a qualified medical, dental, or veterinary practitioner to a pharmacist. Prescriptions are termed *simple* if containing but one ingredient, and *compound* if containing more than one. Aside from vehicles which are used to give the requisite consistency to medicines, such as solvents, diluents, and excipients, drugs may be combined in prescriptions for the following reasons: (1) to obtain the conjoint effect of two or more active substances; (2) to diminish or annul undesirable effects produced by one or more of the active ingredients; (3) to increase the solubility or aid in the dispensing of the active substances; and (4) occasionally, to produce a new compound. The writing of a prescription involves a series of difficult problems, and, when first attempted, imposes a great task on the student. To become an expert prescription writer is largely a matter of practice. There are, however, a few simple, fundamental rules which, when once fixed in the mind, will materially assist in overcoming these difficuties.

Latin is the language of choice in prescription writing. The reasons for the preference are: (1) It is the language of science and is understood to a greater or lesser extent throughout the civilized world. (2) It is a dead language and therefore not subject to the changes that are common to all living forms of speech. (3) The Latin names for medicines are distinctive and very nearly the same in all countries. (4) It is frequently necessary, and always advisable, to withhold from the patient the names and properties of the medicinal agents prescribed. (Remington.)

At present there is a tendency among medical and dental practitioners in favor of English prescription writing; and the various arguments advanced by these advocates deserve consideration.

The often discussed question of the ownership of the prescription has given rise to much unnecessary complexity. As a matter of fact, it is not a question of ownership, but a question of possession. Ownership implies an intrinsic value in the thing owned, while possession denotes to have or to hold as a property.

A prescription does not exhibit the same character or purpose at all periods of its existence, and therefore the right to possess it does not always lie with the same individual. As long as it remains in the hands of the dentist, it represents the embodiment of that therapeutic skill which the prescriber has decided that his patient stands in need of, in the form of an order upon a licensed druggist to carry out the material details of the treatment. Up to this point it belongs to the dentist. As soon as it is given to the patient, the nature of its purpose changes. It now becomes the embodiment of advice which the patient has received from the doctor and to which he unquestionably has the right of possession and disposition. He may avail himself of the skill which it represents by having it filled; or he may reject it. Whatever disposition he may make of it, it is certain that until the prescription is turned over to the druggist for filling, the right to possess it lies with the patient or his assigns. The instant it is given to a druggist to be filled, the character of its purpose undergoes a further change. Having received the treatment, in the shape of medicine, for which the prescription calls, the transaction between the dentist and the patient is completed, and so far as the relations between these two are concerned, the prescription might just as well be destroyed. The druggist, on the other hand, has every reason for possessing it, and therefore every right to its possession at this time. It has ceased to be an embodiment of medical advice, given or received, and has taken on the character of a voucher. The law, enacted for the protection of both doctor and patient, prohibits the druggist from dispensing those drugs unless specifically ordered to do so by the prescriber. The law may at any moment require the druggist to show cause for dispensing the drugs in question, and unless he possesses the prescription, he is a criminal. In fact, the laws of some states, and in case of dispensing opium or cocaine, etc., of the United States, require the druggist to preserve all prescriptions on file for several years and to produce them for inspection to properly constituted authorities.

If a copy of a prescription is demanded of the druggist, it must be a true copy of the original, it must be written distinctly, and it must bear the name and address of the pharmacy or pharmacist who compounded the prescription and who gave the copy.

Parts of an Ideal Prescription

A modern prescription may be divided into the following parts:

1. *Date.* Required by the National Narcotic Law for all prescriptions containing drugs included in the National Narcotic Act.

2. *Name* and *Address* of the patient. (The age of children is often included so that the pharmacist may check the dosage.)

3. *Superscription.* ℞—recipe (take). The final stroke on the ℞ is probably derived from the old symbol 2ℓ which represented a prayer to Jupiter.

4. *Inscription.* Contains the names of the drugs ordered and the amount of each drug desired. The names may be written in Latin or English, as the doctor desires. Compound prescriptions are divided into the following parts:

A. *Basis* or principal drug.
B. *Adjuvants* or drugs which aid the action of the principal drug.
C. *Correctives* or drugs which modify some undesirable action of the basis and adjuvant.
D. *Vehicles* or substances which facilitate the dispensing or the administering of the other ingredients. It is the solvent for the liquid preparations and the base for the ointments. The drugs are usually arranged in the prescription as listed here; basis, adjuvants, corrective, and vehicle. All compound prescriptions need not contain these four parts in the inscription; it is entirely dependent on the doctor's wishes.

5. *Subscription.* The directions to the pharmacist. It is usually written in Latin and abbreviated. Good English is always acceptable and is better than incorrect Latin.

6. *Signa* (Sig) or (S). The directions to the patient. It may be written in Latin or in English, abbreviations are acceptable. It is not good form to write "as directed"; the patient may not understand English well or may be nervous and not remember the directions given verbally by the doctor.

7. The name of the doctor and the degree which gives him the authority to prescribe medicines. It is well to write the name in full. The Federal Narcotic Law requires for all prescriptions containing narcotics: name of the doctor in full, the location of his office, date on which the prescription was signed, the registry number of the prescriber, and the name and address of the patient. The prescription must be written in ink.

Each ingredient and its quantity should occupy only one line, and the ingredients should follow each other in the order of their importance. "These four parts of a formula," says Pereira, "are intended to accomplish the object of Asclepiades: *Curare cito, tuto et jucunde,* or, in other words, to enable the basis to cure quickly, safely and pleasantly." Many prescriptions contain but one or two ingredients —there being no special use for a corrective, vehicle, or diluent—the

tendency of modern therapy being against polypharmacy and in the direction of simple remedies. There are, however, many advantages to be derived from the combination of ingredients even when they have similar medicinal action.

The following is an example of how a prescription should be written:

Name of Patient— Mr. Charles Jones,
Address— 3603 Hicks Avenue
Superscription— ℞

Inscription	Basis—	Acid. Benz.		4 Gm.
	Adjuvant—	Acid. Tan.		6 Gm.
	Corrective—	Ol. Menth. Pip.		1 cc.
	Vehicle—	Alcohol	q.s. ad	120 cc.

Subscription— M.
Signatura— Sig.: Half a teaspoonful in a glass of water as a mouthwash.

James King, D.D.S.
June 1, 1944

The present mode of having prescription blanks printed with the full name and address of the prescriber, etc., is greatly to be encouraged.

The following examples are of methods for writing a prescription (inscription). Only official drugs and official names may be used.

1. Using English in full.

℞
Sodium Borate
Distilled Water

2. Using English synonym:

℞
Borax
Distilled Water

3. Using Latin in full:

℞
Sodii Boratis
Aquae Destillatae

4. Using Latin as the official abbrevations:

℞
Sod. Bor.
Aq. Dest.

Only one system should be used in a prescription, as uniformity is essential for safety.

Pharmaceutical Latin

Most Latin names of drugs are merely Latinized English. These changes in names are made according to certain rules. The learning of these rules simplifies the writing and reading of prescriptions.

The genitive case is used in prescription writing. The nominative case is used in the textbooks and in the *United States Pharmacopoeia* and the *National Formulary*. The following is a list of nominative and genitive case endings, with examples of each.

NOM.	GEN.	EXAMPLE	
		1st declension	
a	ae	aqua	aquae
		2nd declension	
us	i	phosphorus	phosphori
um	i	acidum	acidi
		3rd declension	
l	lis	alcohol	alcoholis
is	itis	nitris	nitritis
as	atis	nitras	nitratis
r	ris	liquor	liquoris
on	onis	limon	limonis
ens	entis	potens	potentis
x	cis	borax	boracis
		4th declension	
us	us	spiritus	spiritus

Latin Grammar Rules

1. A noun limiting another noun is put in the genitive case. Ex: Capsula Caffeinae—here caffeine takes the genitive form because it limits the Latin noun "capsule."

2. A Latin adjective must agree with the gender of the noun it modifies.

Tinctura	Composita	*Feminine*
Syrupus	Compositus	*Masculine*
Extractum	Compositum	*Neuter*

Latin Pronunciation

The pronunciation of Latin words may be by the English or by the Roman method. The English method is approved by the Pharmaceutical Syllabus, although either is acceptable. We shall use the English method.

The Latin name of most drugs is the same as the English name, except for the last letter or letters. The following are examples:

ENGLISH	NOMINATIVE	GENITIVE
1. Alkaloids:		
ine (caffeine)	ina	inae
2. Glucosides, resinoids:		
in (digitalin)	inum	ini
3. Acids:		
acid	acidum	acidi
4. Metals:		
ium (sodium)	sodium	sodii
5. Salts:		
ate (chlorate)	chloras	chloratis
ite (chlorite)	chloris	chloritis
ide (chloride)	chloridum	chloridi

6. When English names end in *a, us, um,* the nominative is not changed; the genitive is formed by changing *a* to *ae; us* and *um* to *i.*

Latin Abbreviations Used in Prescription Writing

ABBREVIATION	LATIN	ENGLISH
a.	ante	before
aa.	ana	of each
a.c.	ante cibos	before meals
ad	ad	to, up to
add.	adde, addantur	add, let them be added
ad lib.	ad libitum	at pleasure
aeq.	aequalis	equal
agit.	agita	shake
aq.	aqua	water
b.	bis	twice
bene	bene	well
b.i.d.	bis in die	twice a day
c. or c̄.	cum	with
cap.	capiat	let the patient take
caps.	capsula	a capsule
coch. mag.	cochleare magnum	a tablespoonful
coch. med.	cochleare medium	a dessertspoonful
coch. parv.	cochleare parvum	a teaspoonful
d.	dies	a day
da	da	give
d.t.d.	dentur tales doses	give such doses
dieb. alt.	diebus alternis	every other day
disp.	dispensa, dispensetur	dispense
div.	divide	divide
dos.	dosis	a dose
et	et	and
ex	ex	out of
ex aq.	ex aqua	with water
e.m.p.	ex modo prescripto	after the manner prescribed, as directed
f., ft.	fiat, fiant	make
gtt.	gutta, guttae	a drop, drops
hor.	hora	an hour
hor. som. or h. s.	hora somni	at bedtime
m.	mane	morning
m. dict.	more dictu	as directed
mit. tal.	mitte tales	send of such
no.	numero	in number
non	non	not

ABBREVIATION	LATIN	ENGLISH
non rept. or n. r.	non repetatur	do not repeat
O.	Octarius	a pint
p.c.	post cibos	after meals
per	per	by means of
p.p.a.	phiala prius agitata	having first shaken the bottle
p.r.n.	pro re nata	as needed
q.s.	quantum sufficat	a sufficient quantity
℞	recipe	take thou
S., Sig.	signa, signatur	label, let it be labeled
s.o.s.	si opus sit	if needed
ss.	semis	half
S.V.R.	spiritus vini rectificatum	alcohol
t.i.d.	ter in die	three times a day
ung.	unguentum	ointment
ut dict.	ut dictum	as directed
v.	vel	or

Reference Abbreviations

U.S.P.--United States Pharmacopoeia.
B.P.----------British Pharmacopoeia.
P.G.----------German Pharmacopoeia.
N.F.----------National Formulary
A.D.R.-----Accepted Dental Remedies.
N.N.R.--New and Nonofficial Remedies.
U.D.----------Useful Drugs.

The following are examples of English, Latin nominative, and Latin genitive cases of drugs and preparations commonly prescribed:

ENGLISH	LATIN NOMINATIVE	LATIN GENITIVE
Sodium Borate	Sodii Boras	Sodii Boratis
Ammonium Bromide	Ammonii Bromidum	Ammonii Bromidi
Zinc Acetate	Zinci Acetas	Zinci Acetatis
Aluminum Sulfate	Alumini Sulfas	Alumini Sulfatis
Mercuric Salicylate	Hydrargyri Salicylas	Hydrargyri Salicylatis
Potassium Chloride	Potassii Chloridum	Potassii Chloridi
Potassium Chlorate	Potassii Chloras	Potassii Chloratis
Silver Nitrate	Argenti Nitras	Argenti Nitratis
Ethyl Nitrite	Aethylis Nitris	Aethylis Nitritis
Alcohol	Alcohol	Alcoholis
Aconite	Aconitum	Aconiti
Codeine	Codeina	Codeinae
Borax	Borax	Boracis
Sulfuric Acid	Acidum Sulfuricum	Acidi Sulfurici
Boric Acid	Acidum Boricum	Acidi Borici
Acetone	Acetonum	Acetoni
Acetophenetidin	Acetophenetidinum	Acetophenetidini
Antipyrine	Antipyrina	Antipyrinae
Water	Aqua	Aquae
Barbital	Barbitalum	Barbitali
Peruvian Balsam	Balsamum Peruvianum	Balsami Peruviani
Belladonna Root	Belladonnae Radix	Belladonnae Radicis
Ampuls of Procaine Hydrochloride	Ampullae Procainae Hydrochloridi	Ampullarum Procainae Hydrochloridi
Solution of Potassium Iodide	Liquor Potassii Iodidi	Liquoris Potassii Iodidi
Tablets of Aminopyrine	Tabellae Aminopyrinae	Tabellarum Aminopyrinae
Ammonia Water	Aqua Ammoniae	Aquae Ammoniae
Ammonia Liniment	Linimentum Ammoniae	Linimentum Ammoniae
Tincture of Iodine	Tinctura Iodi	Tincturae Iodi

Estimation of Quantities

The estimation of the quantity of each ingredient entering into a compound prescription is usually ascertained after the various drugs have been written in their order. The amount of the whole mixture, liquid, powder, etc., is written after the last ingredient, which is usually the vehicle, and the *quantity of each drug is then ascertained by multiplying the single dose by the number of doses represented in the whole prescription.* The following may serve as an example:

It is desired to write a prescription for a four-ounce mixture, using the apothecaries system, with a drachm (a teaspoonful) as the dose, each dose to represent two grains of quinine sulfate, one-eighth of a grain of codeine phosphate, half a drachm of syrup of licorice, and water enough to make a teaspoonful. As 4 ounces are 32 drachms, the prescription will read as follows:

℞				
	Quinine Sulfate	2 gr.	× 32 =	3 j
	Codeine Phosphate	⅛ gr.	× 32 =	gr. iv
	Syrup of Licorice	½ drachm	× 32 =	ʒ ij
	Water	enough to make		ʒ iv

M.

Sig.: One teaspoonful every two hours.

To assist the pharmacist in filling the prescription, it is customary to express the total amounts of the drugs, when they closely approximate, in round numbers. In the above case, to be exact, 64 grains of quinine sulfate are called for, but, following the rule, one drachm is written.

If the metric system of weight and measure is to be used, and it should be used whenever possible, a similar procedure is followed. The above dosage expressed in the metric system would be quinine sulfate 0.12 Gm., codeine phosphate 0.008 Gm., syrup of licorice 2 cc., and water to make one teaspoonful. The prescription will now read as follows:

℞				
	Quinine Sulfate	0.12 Gm.	× 32 =	4.0 Gm.
	Codeine Phosphate	0.008 Gm.	× 32 =	0.25 Gm.
	Syrup of Licorice	2 cc.	× 32 =	64.0 cc.
	Water	q.s. ad.	=	120.0 cc.

M. et sol.

Sig.: One teaspoonful every two hours.

For the novice the official dosage of the drug or preparation should be used in prescription writing. This dosage prescribed three or four times a day is generally often enough. The amount of each drug to be prescribed must be figured out, taking into consideration (1) the single dosage for each drug and (2) the number of doses which will probably be needed.

When *only* one drug is prescribed.

Examples:

1. ℞

	METRIC	APOTHECARIES
Magnesium Sulfate	120 Gm.	ʒ iv

Sig.: One tablespoonful dissolved in water before breakfast.

2. ℞

Acetylsalicylic Acid	4 Gm.	3 i

M. et ft. Cap. No. XII
Sig.: One cap. q. 4 h.

3. ℞

Acetylsalicylic Acid	0.3 Gm.	gr. v

M. et ft. Cap. No. I, d.t.d. No. XII
Sig.: One cap. q. 4 h.

4. ℞

Tab. of Acetylsalicylic Acid No. XII	0.3 Gm.	gr. v

Sig.: One tab. q. 4 h.

Prescriptions containing *more than one* drug.—When more than one drug is combined into a prescription, generally less than the official dosage of each drug is prescribed; one-half the official dosage is usually safe.

Examples:

1. ℞

	METRIC	APOTHECARIES
Magnesium Sulfate	60 Gm.	ʒ ij
Sodium Sulfate	60 Gm.	ʒ ij

M.
Sig.: One tablespoonful in a half glass of water before breakfast.

2. ℞

Acetylsalicylic Acid	2.5 Gm.	gr. xxxviij
Acetanilid	1.2 Gm.	gr. xviij
Caffeine	0.4 Gm.	gr. vi

M. et ft. Cap. No. XII
Sig.: One cap. q. 4 h.

3. ℞

Acetylsalicylic Acid	0.2 Gm.	gr. iij
Acetanilid	0.1 Gm.	gr. iss
Caffeine	0.03 Gm.	gr. ss

M. et ft. Cap. No. I, d.t.d. No. XII
Sig.: One cap. q. 4 h.

4. ℞

Tablets of Three Bromides	1 Gm.	gr. xv

Sig.: One tab. q. 4 h.
(This tablet contains 0.3 Gm. each of sodium, potassium and ammonium bromide)

Compound Prescription for Mouthwashes

1. ℞

Sodium Borate	7.5 Gm.	gr. cxij
Sodium Bicarbonate	7.5 Gm.	gr. cxij
Liquefied Phenol	1.5 cc.	m xxiv
Distilled Water q.s.ad.	500.0 cc.	fl℥ xvj

M. et sol.

Sig.: Use undil. as a mouthwash, m. et n.

2. ℞

Dobell's Solution	500 cc.	fl℥ xvi

Sig.: Use undil. as a mouthwash, m. et n.

CONTAINERS FOR DRUGS

The bottles used in the United States and the British Empire have a capacity of one, two, and four fluidrachms, and one, two, three, four, six, eight, twelve, sixteen, and thirty-two fluidounces, or their relative metric equivalents expressed in cubic centimeters. It is good practice, in prescription writing, to conform the quantity of the mixture to the above sizes of bottles. The quantity of medicine ordered should last from two to three days, except in the treatment of chronic diseases. Mouthwashes may be ordered in four- to sixteen-ounce quantities. In measuring out the medicine at home, a graduated medicine glass is preferable to the household measures, as the latter vary considerably. The domestic teaspoonful varies greatly in size, and Wilbert therefore suggests that a teaspoonful should be represented by 1¼ drachms, or 5 cubic centimeters instead of 4. Drops should always be measured with a medicine dropper or dispensed in a special drop bottle. The size of the individual drops and the number present in a given amount of fluid vary greatly; depending largely on the specific gravity, consistency, surface tension, temperature of the liquid, and on the lip of the bottle from which they are dropped, etc. Dr. Seaman recommended to the Committee on Revision of the United States Pharmacopoeia the following method of accurate drop measure: "An official medicine dropper has its delivery end three millimeters in external diameter, and is adapted to deliver 20 drops of distilled water to a gram at 15° C."

Powders are usually prescribed to weigh from three to ten grains; if they contain nauseating drugs, they should be dispensed in capsules. Pills usually weigh from one to five grains, and those that weigh less than a grain are known as granules. Salves are prescribed in one-half to two-ounce quantities. Oils, vitamins, oleo-

resins, and similar liquids, if prepared in drop doses, are best dispensed in soft or hard gelatin capsules. Solid and semi-solid dentifrices—such as powders and soaps—are usually dispensed in specially prepared containers with sprinkler tops.

The following are containers used by the pharmacist for the dispensing of drugs. The doctor should know the sizes of the containers and should prescribe enough of the drug to fill them. A 90 cc. bottle with only 50 cc. of preparation suggests to the patient that the full amount was not delivered.

Ampuls (ampullae) are glass containers for dispensing liquid preparations. Ampuls for parenteral use must be prepared in a sterile manner (see (N.F. VII, pp. 35 to 38).

Bottles are glass containers designed for dispensing liquid preparations. They are manufactured in the following sizes:

METRIC	APOTHECARIES
8 cc.	0.25 fluidounce
15 cc.	0.50 fluidounce
30 cc.	1.00 fluidounce
60 cc.	2.00 fluidounces
90 cc.	3.00 fluidounces
120 cc.	4.00 fluidounces
180 cc.	6.00 fluidounces
240 cc.	8.00 fluidounces
360 cc.	12.00 fluidounces
380 cc.	16.00 fluidounces
960 cc.	32.00 fluidounces

Dark bottles should be prescribed for preparations which are decomposed by light.

Capsules (capsulae) are gelatin containers for powdered drugs and intended for oral use. Enteric capsules are so treated that they do not dissolve until they get into the intestines. Capsules vary in size from No. 5, which holds 1 grain or less, to No. 000 which holds 1 gram or less.

Jars are glass containers for semi-solid preparations (salves). They vary in size from 8 grams (0.25 ounce) to 240 grams (4 ounces).

Pearls are soft gelatinous capsules intended for liquid preparations. Because of their consistency they are easily swallowed.

Plasters (emplastra) are cloth or leather strips with drug attached. They are used as adhesives or for the application of drugs to the body surfaces for counterirritation.

Prescriptions (Examples)

℞ Sol. Acidi Borici sat. 30 cc.
Sig.: Use as an eye wash m. et n.

℞ Linimenti Chloroformi 90 cc.
Sig.: Rub well on shoulder every four hours.

℞ Capsulae Quininae Sulphatis 0.3 Gm.
No. xii
Sig.: One cap. t.i.d.p.c.

℞ Quininae Sulphatis 4 Gm.
M. et Cap. No. xii.
Sig.: One cap. t.i.d.p.c.

℞ Quininae Sulphatis 0.3 Gm.
M. et Cap. D.t.d. No. xii.
Sig.: One cap. t.i.d.p.c.

℞ Acetphenetidini 1.6 Gm.
Acetanilide 0.8 Gm.
Strychninae Sulphatis 0.2 Gm.
M. et Cap. No. xii.
Sig.: One cap. t.i.d.p.c.

℞ Phenolis 1 Gm.
Sodii Boratis 20 Gm.
Aquae q.s. ad 500 cc.
M. et sol.
Sig.: Dilute with equal parts of water as a mouthwash t.i.d.

℞ Sodium Perborate 90 Gm.
Sig.: 4 cc. in half glassful of water as a mouthwash q. 3 h.

℞ Tinctura Belladonnae 30 cc.
Sig.: 10 gtts. in water before visiting the dentist.

℞ Elixir Bromidorum Trium 120 cc.
Sig.: 4 cc. t.i.d. the day before the visit to the office and one dose the day of the visit to the office.

℞ Potassii Permanganatis 2.4 Gm.
Aquae q.s. ad 120.0 cc.
M. et sol.
Sig.: 4 cc. in glassful of warm water as a mouthwash t.i.d.

℞ Sodium Bromide 24 Gm.
Water 90 cc.
M. et sol.
Sig.: 4 cc. in water t i.d.p.c.

INCOMPATIBILITIES

Incompatibilities may be defined as conditions produced by bringing substances together which result in chemical decomposition, pharmaceutical dissociation, or therapeutic opposition (Remington).

In writing a prescription which contains more than one drug, one or all of the above possibilities may be the result of the mixture, unless the prescriber exercises extreme care in considering the physical, chemical, and physiologic properties of the ingredients entering into the compound. Never prescribe more than one drug at a time, if the one ingredient will serve the purpose for which the prescription is intended.

1. CHEMICAL INCOMPATIBILITY.—It may result in (a) *explosion*—in mixing chlorates or permanganates with readily oxidizable substances; (b) *precipitation*—the salts of heavy metals precipitate organic substances; (c) *production of a substance with undesirable properties*—tannic acid with a solution of iron. As a rule, a chemical is incompatible with the reagent used as a test for its presence.

2. PHARMACEUTICAL INCOMPATIBILITY.—(a) Alcohol should not be added to solutions of acacia, gelatin, and proteins, or to emulsions and strong salt solutions; (b) water should not be added to alcoholic liquids in general (tinctures, spirits, fluidextracts); (c) certain chemicals, like camphor or antipyrin, when mixed with phenol, thymol, cocaine, salol, resorcinol, etc., produce oily liquids; (d) alkaloids and alkalies form an insoluble precipitate.

3. THERAPEUTIC INCOMPATIBILITY.—As a rule, a drug is incompatible with its antidotes—as pilocarpine and atropine; cocaine and morphine; strychnine and bromides.

As it is impossible to consider in detail all the incompatibilities, only a few of the more important ones will be enumerated:

An acid should not be combined with an alkali.

Most of the acids precipitate albumin.

Phenol forms a phenolsulfonate when added to a soluble sulfate.

Salicylic acid is incompatible with salts of iron.

Alkalies should not be combined with alkaloids, as a precipitate is formed.

Alkaloids and metallic salts are incompatible with tannic acid or substances containing tannin, and with alkalies or their salts.

Alcoholic fluidextracts are precipitated by water or aqueous liquids.

Iodine or iodides should not be mixed with alkalies.

Oils, volatile and fixed, resins, oleoresins, resinoids, and balsams are precipitated by water.

Sugar forms an explosive with sulfuric acid.

Corrosive sublimate, silver nitrate, potassium iodide, and the salts of lead should preferably be prescribed alone. Substances containing loosely combined oxygen—as chromic acid, concentrated nitric acid, permanganates, etc.—should not be combined with easily oxidizable substances as tannic acid, sulfur, sulfides, sulfites, iodine, iodides, phosphorus, phosphites, and reduced iron, as they form highly explosive compounds.

Vegetable astringents containing tannic acid should not be mixed with iron, as they form a tannate of iron (ink).

Alcohol and alcoholic liquids are incompatible with mucilages.

Examples of Incompatibility.

℞ Procaine Hydrochloride gr. xv
Sodium Chloride gr. vi
Sodium Bicarbonate gr. iv
Distilled Water, ad ℥ ij
M.
Sig.: To be used as a local anesthetic.

The procaine salt will be precipitated by the sodium bicarbonate.

℞ Pot. Permang. 3 j
Liq. Hydrog. Perox. 3 ij
Aquae, ad ℥ viij
M.
Sig.: Antiseptic solution.

The potassium permanganate is decomposed by the solution of hydrogen peroxide.

℞ Phenol
Camphor āā 3 ij
M. f. plv. No. j.
Sig.: Dissolve in a quart of water.

Phenol and camphor liquefy when triturated together, and very little of the camphor will dissolve in the water.

℞ Mag. Oxid. ʒ ij
Aq. Menth. Pip. ℥ iij
M. Shake the bottle.
Sig.: Tablespoonful three times daily.

The magnesia settles, forming a solid mass, which cannot be readily disintegrated by shaking.

℞ Sod. Bor. gr. iij
Zinc. Sulf. gr. iv
Aq. Destil. fl℥ j
M.
Sig.: Drop into the eye.

An insoluble zinc borate is formed.

℞ Argenti nitratis 3 ij
Aq. Rosæ fl℥ j
M.
Sig.: Concentrated silver nitrate solution for dental purposes.

Most of the silver nitrate is precipitated as a black powder by the oil of rose and the impurities of the rose water. Only distilled water should be used in making silver nitrate solutions.

℞ Pot. Chloras. 3 j
Acid. Tan. 3 ss
Amylum, ad ℥ ij
M. f. plv.
Sig.: Use as a dusting powder.

An explosive compound results.

POSOLOGY

The Twelfth Decennial Revision (1942) of the *Pharmacopoeia of the United States* has again admitted average approximate doses of medicines for adults to be used internally or hypodermically. These doses are not, however, obligatory to the dentist, and they may be increased or reduced according to circumstances. It is a matter of clinical experience with each practitioner to adjust the dosage safely for the case in hand. In using a powerful remedy, it is best to start with a small dose and increase cautiously. Various circumstances which modify the dosage and demand attention are:

Age
Weight
Sex
Route of administration
Frequency and time of administration
Rate of detoxication and excretion
Idiosyncrasy, tolerance and allergy
Cumulative effect and synergy
Habits
Condition of patient.

Dosage for Adults

Adults are classed in posology as men or women from 18 to 60 or 70 years of age. The average weight for an adult male is 150 pounds; for a female 128 pounds. The aged require a smaller dose of some drugs, while of other drugs, as cathartics, they may require a larger dose. Children generally require less than the official dosage.

Fractional Dosage for Children

Age.—Children require smaller doses than the adult. The following rule of Dr. Young for calculating the child's dose is now almost universally adopted. Divide the age of the child in years by the age plus twelve to obtain the fraction of the adult dose:

$$\frac{\text{age}}{\text{age} + 12} = \text{fraction of adult dosage.}$$

Example: Age of patient—4

$$\frac{4}{4 + 12} = \frac{4}{16} = \frac{1}{4} \text{ of adult dosage.}$$

Cowling's Rule of Dosage for Children.—The age of the child at his next birthday is divided by 24 and equals the fraction of the adult dosage.

$$\frac{\text{Age of child at next birthday}}{24} = \text{fraction of adult dosage.}$$

Example: Age of patient—4

$$\frac{5}{24} = \frac{1}{5} \text{ of adult dosage.}$$

Weight.—Children and underweight adults require smaller doses of drugs. Very toxic drugs are given in doses which vary with the body weight, e.g., so many milligrams of the drug per kilogram of body weight.

Clark's Rule of Dosage.—This rule assumes that the average weight of an adult is 150 pounds. The weight of the patient divided by 150, gives the fraction of the adult dose, or $\frac{\text{Official Dosage}}{150} \times$ weight of the child in pounds.

Example.—Weight of patient is 100 pounds, dosage of drug is 15 grains

$$\frac{15 \text{ gr.}}{150} \times 100 = 10 \text{ grains.}$$

Sex and Temperament.—Females and persons of sanguine temperament require somewhat smaller doses than males and the phlegmatic.

Route of Administration.—The official dosage given in the *United States Pharmacopoeia* and the *National Formulary* are for oral administration unless otherwise noted. It is a safe rule, regardless of the route of administration, to give only the official dosage and to repeat as often as is necessary.

Frequency and Time of Administration.—The therapeutic action of any drug determines the frequency and the time at which it should be administered. Saline purgatives are usually taken in a single dose in the morning; emetics are taken once, and repeated only in case vomiting is not induced; drugs which induce sleep are naturally given at bedtime; stomachics and tonics are taken before meals, three times a day continuously. The interval between the doses should be calculated and the second dose administered before the effect produced by the first has passed off. The *daily* dose is *three times* as large as the *single* dose. In estimating the maximum daily dose, the day is to be counted as 24 hours.

Rate of Detoxication and Excretion.—To get a sustained effect from drug administration, the dosage should be repeated before the concentration of the drug in the tissues is depleted by detoxication and excretion. The time varies with each drug; i.e., aspirin, every two hours and barbital, every eight hours.

Idiosyncrasy, Tolerance, and Allergy.—Certain persons exhibit peculiar pronounced reactions toward ordinary doses of drugs. This characteristic state of individuality is referred to as *idiosyncrasy*. As yet no satisfactory explanation of this peculiarity has been brought forward. It is well known that apparently normal individuals will quickly react to extremely small doses of calomel, opium, antipyretics, etc. Occasionally it is observed that an individual apparently does not react to the ordinary dose of a medicine, i.e., *tolerance* to the drug is recognized. The prolonged use of a drug, i.e., morphine, arsenic, or cocaine, may establish an acquired tolerance known as drug habit. The most familiar examples of acquired tolerance are those of tobacco, alcohol, coffee, and tea. Some drugs—as calomel, chloral hydrate, and arsenic—are peculiarly well borne by children, being taken by them in relatively large doses. On the other hand, children are peculiarly susceptible to the influence of opium. Again, many drugs—as ipecacuanha, tartar emetic, alcohol, etc.—have different action in different doses. Occasionally it will be observed that the ingestion of drugs and, to some extent articles of food, is followed by a peculiar form of skin eruption, known as *drug rash* (dermatitis medicamentosa). This

disturbance may be the result of ingesting an excessive amount of the drug or to an allergy of the individual. The commonest drug dermatoses are those following the ingestion of bromides and iodides; although quinine, salicylic acid, belladonna or atropine, arsenic, antipyrine, and other drugs and articles of food, as strawberries, buckwheat, and shellfish are known to produce this disease. The prolonged use of mouth preparations (washes, powders, and pastes) containing appreciable quantities of such skin irritants as salicylic acid, salol, menthol, and essential oils is occasionally productive of morbiliform eruptions about the corners of the mouth or the lower lip in susceptible patients. These eruptions are generically known as mouthwash eczema. Formalin is prone to cause a most persistent and painful eczematous eruption about the hands of the dentist.

Cumulative Effect and Synergy.—Drugs may be given at longer or shorter intervals, depending on the circumstances. Custom, habit, and tolerance play the most important parts. Occasionally in the administration of drugs, it will be observed after a number of doses have been taken that sudden symptoms arise which are much more pronounced than those manifested after the first dose. This effect is referred to as *cumulative action of drugs.* Absorption may be more rapid than elimination, and each new dose thus adds to the total quantity present in the blood and in the organs of the body. A classic example is digitalis, although strychnine, atropine, arsenic, iodides, etc., are known to induce this state of cumulative action. The metallic salts, especially those of mercury, lead, copper and silver, are productive of chronic poisoning by these cumulative effects. In most cases, except in those of the metallic salts, the retention will last only a few days, rarely weeks, while arsenic, mercury, lead, etc., may remain for months; silver, under suitable conditions, may be retained for years or even permanently in the tissues. Frequently mixtures of drugs, of which each individual substance is known to produce the same effect in the body, are administered to induce increased action—a cooperation of the actions known as *synergy.* The synergistic effect of mixtures of purgatives offers a striking example; the mixture acts usually distinctly more efficiently than any one drug of the same mixture given in a quantity equal to all of them. Of great practical importance is the synergism of the narcotics, i.e., the combined effects of scopolamine and morphine or morphine and ether, etc.

Habits.—The habits of the patient may affect his response to a drug. Patients who habitually take drugs as aspirin, morphine, arsenic, etc., must be given larger than the official dosage to obtain a normal drug action.

Condition of Patient.—Drugs may have a different action in health and in disease. Antipyretics will reduce the body temperature in hyperpyrexia but will not affect the normal temperature. Patients with cardiac disease should be given only small doses of cardiac depressing drugs, such as acetanilid, chloral hydrate, etc. Pregnant women should not be given large doses of aspirin, castor oil, quinine, etc. Debilitated patients are generally more susceptible to drugs than the normal adult. All of these factors will vary the dosage of a drug. It, therefore, necessitates that the dentist study his patient and write a prescription which is personally adapted to him.

Definition of Terms

Official dosage is the dosage listed in the U.S.P. or N.F. If the drug is not official, use the dosage listed in A.D.R., N.N.R., or U.D.

Minimum dosage is the smallest quantity of a drug which when administered to an adult will give the characteristic action and effect of the drug.

Maximum dosage is the largest quantity of a drug which may be given with safety. Never prescribe more than three times the official dosage within 24 hours.

Toxic dosage is that dosage of a drug which will produce symptoms of poisoning.

Minimum Lethal Dosage (M.L.D.) is ascertained experimentally on animals and represents the amount of drug which is fatal to 50 per cent of the animals.

Therapeutic dosage is the amount of drug which should be administered in a single dose for an individual patient. This dosage will vary, depending on the age, size, weight, sex, and condition of the patient. For the novice the official dosage should be the therapeutic dosage for adult patients.

Fractional dosage is a fraction of the official dosage and is used when two or more similar drugs are combined into one prescription. One-half the official dosage is safe and generally adequate. Fractional dosage also may be used to define a smaller than normal dose which is given at shorter intervals.

METROLOGY

Metrology is the science of weight and measure. There are two accepted systems of recording weight and measure in prescription writing in the United States, the *apothecaries'* and the *metric* system. The apothecaries' system is the older; it was accepted in this country in 1836, and is extensively used by the older dentists. The

metric system was legalized in this country by an Act of Congress in 1866 which made its use manditory in the Army, Navy, and Marine Hospitals. The metric system is the system of choice and should be used in prescription writing in preference to the apothecaries', although both systems must be memorized.

Signs and Numerals Used in Metrology

℔	libra	a pound.
ʒ	uncia	an ounce.
ʒ	drachma	a drachm.
℈	scrupulus	a scruple.
gr.	granum	a grain.
C	congius	a gallon.
O	octarius	a pint.
fl ʒ	fluiduncia	a fluidounce.
fl ʒ	fluidrachma	a fluidrachm
♏	minim	a minim.
gtt	gutta	a drop.
ss	semis	half.

Roman Numerals

All Roman numbers are expressed by one, or a combination of two or more, of the following letters: I, V, X, L, C, D, and M. I means 1; V, 5; X, 10; L, 50; C, 100; D, 500; and M, 1000. These should be written together as capital letters, but in prescriptions we find them usually written as small letters, or in print as "lower case" letters, and it is customary to write a single "i," or the final "i" when several numeral letters are used together, as a small "j." The letters are combined thus:

I	1	XX	20
II	2	XL	40
III	3	L	50
IV	4	LX	60
V	5	XC	90
VI	6	C	100
VII	7	CC	200
VIII	8	D	500
IX	9	DC	600
X	10	M	1000
XI	11	MCMXLIV	1944

Tables of Weight and Measure

Apothecaries' Weight	*Approximate*
1 grain (gr.)	
20 grains (gr.)	1 Scruple (℈) (obsolete)
60 grains	1 drachm or dram (ʒ)
480 grains; 8 drachms	1 ounce (ʒ)
5760 grains; 12 ounces	1 pound (lb.)

Apothecaries' Measure

1 minim (♏)	
60 minims (♏)	1 fluidrachm (fl. ʒ)
480 minims	1 fluidounce (fl. ℥)
7680 minims	1 pint (O)

Apothecaries' Approximate Equivalents

Weight	*Measure*
1 grain	1 minim (♏)
1 drachm (ʒ)	1 fluidrachm (fl. ʒ)
1 ounce (℥)	1 fluidounce (fl. ℥)

The Roman numerals are used with the apothecaries' system of weights and measures. Less than one is expressed as a fraction The numerals follow the symbol (abbreviations).

The Metric System

The metric or decimal system of weights and measures originated with Prince de Talleyrand, bishop of Autun, in 1790. Its almost universal adoption by civilized nations, its legality (though not compulsion) in England and the United States, and its adoption by the *United States Pharmacopoeia* of 1890 demand that it should be understood by the practicing dentist. Except in the English-speaking world, it is the only system of weights and measures used for governmental, statistical, and scientific purposes. It is based upon the decimal system—that is, the denominations increase by tens and decrease by tenths. The starting point is the unit of linear measure, the *meter,* which represents one-ten-millionth part of the polar quadrant of the earth—that is, the distance from the equator to the poles —and is equivalent to 39.37 English inches. The *gram* (Gm.) is the unit of weight; the *liter,* of capacity. The denominations representing the subdivisions of any unit are expressed by prefixing the Latin numerals *deci, centi,* and *milli* to the unit—meaning respectively one-tenth, one-hundredth, and one-thousandth; the multiples are expressed by prefixing the Greek numerals *deka, hecto, kilo,* and *myria*—meaning ten, hundred, thousand, and ten thousand.

The gram is derived as follows: The meter is divided into one hundred equal parts, called *centimeters.* On one centimeter as a base a cube is erected, having for its three dimensions one centimeter (cm.) each. The contents of this cube will be one cubic centimeter (cc.), measuring one milliliter. This quantity of distilled water at its maximum density (39.2° F., 4° C.) and 30 inches barometric pressure weighs one gram, or 15.432 grains.

The liter is derived as follows: The meter is divided into ten equal parts, called *decimeters*. On one decimeter as a base a cube is erected, having for its three dimensions one decimeter (dm.) each. The contents of this cube will be one cubic decimeter ($dm.^3$), the capacity of which is one liter, equivalent to 1,000 cubic centimeters, or 33.81 fluidounces, or 2.113 pints. One liter of distilled water at 4° C. and 30 inches barometric pressure weighs 1,000 grams, or 1 kilogram, or 2.2 pounds avoirdupois, or 15,432 grains. The U. S. Bureau of Standards has declared that there is a slight difference betwen the thousandth part of a liter and the cubic centimeter; i.e., one liter was determined to be equivalent to 1.000027 cubic decimeters.

Metric System

Weight	
1 gram (Gm.)	
1000 grams (Gm.)	1 kilogram (Kg.)
0.001 gram (Gm.)	1 milligram (mg.)
Measure	
1 cubic centimeter (cc.)	1 milliliter (ml.)
1000 cubic centimeters (cc.)	1 liter (L.)

Metric Approximate Equivalents

Weight	*Measure*
1 gram (Gm.)	1 cubic centimeter (cc.)
1 kilogram (Kg.)	1 liter (L.)

Approximate Equivalents

Apothecaries' Weight and Metric Weight:

1 grain	0.06 gram or 60 milligrams (mg.)
15 grains	1.0 gram (Gm.)
60 grains or 1 drachm	4.0 gram (Gm.)
8 drachms or 1 ounce	30.0 grams
12 ounces or 1 pound (lb.)	384.0 grams

Apothecaries' Measure and Metric Measure:

1 minim	0.06 cubic centimeters (cc.)
15 minims	1.0 " "
1 fluidrachm	4.0 " "
8 fluidrachms or 1 ounce	30.0 " "
16 fluidounces or 1 pint	480.0 or 500 cubic centimeters

The *Arabic* numerals are used with the metric system of weights and measures. Less than one is expressed as a decimal (0.5). The numerals precede the abbreviations.

Apothecaries' Measure and Metric Equivalents

1	minim	=	0.06 cc.
2	minims	=	0.12 "
3	"	=	0.20 "
4	"	=	0.25 "
5	"	=	0.30 "
6	"	=	0.35 "
7	"	=	0.42 "
8	"	=	0.50 "
9	"	=	0.55 "
10	"	=	0.60 "
15	"	=	0.92 "
20	"	=	1.25 "
25	"	=	1.54 "
30	"	=	1.90 "
40	"	=	2.50 "
45	"	=	2.80 "
50	"	=	3.10 "

60	minims (1 fluidrachm)	=	4.00 cc.
1¼	fluidrachms	=	5.00 "
1½	"	=	6.00 "
1¾	"	=	7.00 "
2	"	=	8.00 "
3	"	=	12.00 "
4	"	=	15.00 "
8	" (1 fl. oz.)	=	30.00 "
	(more exactly)	=	29.57 "
2	fluidounces	=	60.00 "
3	"	=	90.00 "
4	"	=	120.00 "
8	"	=	250.00 "
16	" (1 pint)	=	500.00 "
32	"	=	1000.00 "
128	" (1 gallon)	=	3785.43 "

Table of Approximate Measure

HOME	APOTHECARIES'	METRIC
1 drop (gtt.)	1 minim	0.06 cc.
1 teaspoonful	1 fluidrachm	4.0 cc.
1 dessertspoonful	2 fluidrachms	8.0 cc.
1 tablespoonful	4 fluidrachms	15.0 cc.
1 wineglassful	2 fluidounces	60.0 cc.
1 cupful	4 fluidounces	120.0 cc.
1 glassful	8 fluidounces	240.0 cc.

A graduated medicine glass is the most satisfactory home device for measuring liquid preparations.

Apothecaries' Weight and Metric Equivalents

1/150	grain	=	0.0004 grams
1/120	"	=	0.0005 "
1/100	"	=	0.0006 "
1/60	"	=	0.001 "
1/50	"	=	0.0013 "
1/40	"	=	0.0015 "
1/30	"	=	0.002 "
1/20	"	=	0.003 "
1/15	"	=	0.004 "
1/12	"	=	0.005 "
1/10	"	=	0.006 "
1/8	"	=	0.008 "
1/6	"	=	0.010 "
1/5	"	=	0.012 "
1/4	"	=	0.015 "
1/3	"	=	0.020 "
1/2	"	=	0.030 "
3/4	"	=	0.045 "
1	grain	=	0.060 "
2	grains	=	0.12 "
3	"	=	0.2 "
4	"	=	0.25 "
5	"	=	0.30 "
6	"	=	0.40 "
8	"	=	0.50 "
10	"	=	0.65 "
12	"	=	0.75 "

15	grains	=	1.0 grams
20	"	=	1.3 "
24	"	=	1.50 "
30	"	=	2.0 "
40	"	=	2.6 "
45	"	=	3.0 "
50	"	=	3.3 "
60	" (1 drachm)	=	4.0 "
1½	drachms	=	6.0 "
1¾	"	=	7.0 "
2	"	=	8.0 "
2½	"	=	10.0 "
3	"	=	12.0 "
4	"	=	16.0 "
5	"	=	20.0 "
6	"	=	24.0 "
1	ounce (480 gr.)	=	30.0 "
2	ounces	=	60.0 "
3	"	=	90.0 "
4	"	=	125.0 "
6	"	=	185.0 "
8	"	=	250.0 "
10	"	=	300.0 "
12	"	=	375.0 "
16	" (1 pound)	=	480.0 "

Troy Weight

POUND		TROY OUNCES		PENNYWEIGHTS		TROY GRAINS
℔ 1	=	12	=	240	=	5760
		℥ 1	=	20	=	480
				dwt. 1	=	gr. 24

Wine Measure (United States)

GALLON		PINTS		FLUID-OUNCES		FLUID-DRACHMS		MINIMS		CUBIC INCHES
Cong. 1	=	8	=	128	=	1024	=	61440	=	231.0
		O 1	=	16	=	128	=	7680	=	28.875
				fl℥ 1	=	8	=	480	=	1.8047
						fl℥ 1	=	♏ 60	=	0.2256

Liquid Measure

1 gallon	=	4 quarts.	1 pint	=	4 gills.
1 quart	=	2 pints.	1 gill	=	4 fluidounces.

Imperial Measure (British Pharmacopoeia)

GALLON		PINTS		FLUID-OUNCES		FLUID-DRACHMS		MINIMS
1	=	8	=	160	=	1280	=	76800
		1	=	20	=	160	=	9600
				1	=	8	=	480
						1	=	60

Conversion Equivalents (Approximate)

To convert grains to grams divide by 15 (or multiply by 0.06). *Problem:* 45 gr. are how many Gm.?

To convert grams to grains multiply by 15 (or divide by 0.06). *Problem:* 10 grams are how many grains?

To convert minims to cubic centimeters divide by 15 (or multiply by 0.06). *Problem:* 30 minims are how many cc.?

To convert cubic centimeters to minims multiply by 15 (or divide by 0.06). *Problem:* 3 cc. are how many minims?

To convert drachms to grams multiply by 4. *Problem:* 12 drachms are how many grams?

To convert grams to drachms divide by 4. *Problem:* 36 Gm. are how many drachms?

To convert cubic centimeters to ounces divide by 30. *Problem:* 60 cc. are how many ounces?

To convert ounces to cubic centimeters multiply by 30. *Problem:* 2 ounces are how many cubic centimeters?

To convert cubic centimeters to fluidrachms divide by 4. *Problem:* 40 cc. are how many fluidrachms?

To convert fluidrachms to cubic centimeters multiply by 4. *Problem:* 10 fluidrachms are how many cubic centimeters?

To convert grams to ounces, divide by 30. *Problem:* 60 Gm. are how many ounces?

To convert ounces to grams multiply by 30. *Problem:* 2 ounces are how many Gm.?

Metrology Problems

1. How many grams of sodium chloride are necessary to make 200 cc. of a 5 per cent solution?

   $200 \times .05 = 10.0$ Gm.

2. How many grains of procaine hydrochloride are necessary to make one fluid-ounce of a 2 per cent solution?

   480 gr. $\times$ 0.02 = 9.60 grains.

3. How many grains of crystal phenol are necessary to make one pint of a 1:500 aqueous solution?

   500 cc. $\times$ 0.002 = 1.0 Gm. $\times$ 15.0 = 15 gr.

4. Make one liter of 0.9 per cent salt solution from a 10 per cent stock solution.

   $\frac{0.009}{.10} \times 1000 = 90$ cc. and dilute to 1000 cc.

5. How many grains of procaine hydrochloride are used when 4 cc. of a 2 per cent solution are injected?

   $4 \times 15.0 = 60.0 \times 0.02 = 1.20$ gr.
   or
   $4 \times 0.02 = 0.08 \times 15.0 = 1.20$ gr.

6. How much sodium perborate is necessary to make ½ glassful (4 oz.) of a 5 per cent solution?

   30 cc. $\times$ 4 oz. = 120 cc.
   120 cc. $\times$ 0.05 = 6.00 Gm.

7. How many grams of codeine sulfate should be prescribed to make 18 capsules, when each capsule contains 0.3 gram?

   $18 \times 0.03 = 0.54$ Gm.

8. How many grams of potassium permanganate should be dissolved in 4 ounces of water, so that one teaspoonful of this solution in a glassful of water will make a 1:3000 solution?

   30 cc. $\times$ 8 oz. = 240 cc. in a glass of water.
   240 cc. $\times$ 0.0003 = 0.0720 Gm.
   0.0720 $\times$ 32 = 2.0 Gm. in the 4 oz.

9. How many grains of sodium bromide are contained in one teaspoonful of a solution, when 4 ounces of the solution contain 480 gr. of the drug?

   480 + 32 = 15 gr. in one teaspoonful.

10. How much tannic acid should be dissolved in one liter of 3 per cent boric acid solution to make a 1:800 solution of tannic acid?

    1000 cc. + 800 = 1.25 Gm.

Percentage Solution Table (Apothecaries')

WATER	GRAINS OR MINIMS OF DRUG TO MAKE A SOLUTION CONTAINING													
Fluid ounces	1 in 5000	1 in 2000	1 in 1000	1 in 500	½%	1%	2%	3%	4%	5%	10%	20%	25%	50%
½	0.046	0.114	0.228	0.456	1.14	2.3	4.6	6.8	9.1	11.4	22.8	45.6	57.0	114.0
1	0.091	0.228	0.456	0.912	2.28	4.6	9.1	13.7	18.2	22.8	45.6	91.2	114.0	228.0
2	0.182	0.456	0.912	1.820	4.56	9.2	18.2	27.3	36.5	45.6	91.2	182.4	228.0	456.0
3	0.273	0.684	1.370	2.730	6.84	13.7	27.4	41.0	54.7	68.4	136.8	273.6	342.0	684.0
4	0.365	0.912	1.820	3.640	9.12	18.2	36.5	54.7	73.0	91.2	182.4	364.8	456.0	912.0
6	0.546	1.370	2.740	5.470	13.68	27.4	54.7	82.0	109.5	136.8	273.6	547.0	684.0	1368.0
8	0.729	1.820	3.650	7.300	18.24	36.5	73.0	119.4	146.0	182.4	364.8	729.0	912.0	1824.0
12	1.094	2.740	5.470	10.940	27.40	55.0	109.5	164.4	218.9	273.6	547.2	1094.0	1368.0	2736.0
16	1.460	3.650	7.300	14.600	36.50	73.0	146.0	218.9	291.8	364.8	729.6	1459.0	1824.0	3648.0

Percentage Solution Table (Metric)

WATER	GRAMS OR CC. OF DRUG TO MAKE A SOLUTION CONTAINING													
Fluid ounces	1 in 5000	1 in 2000	1 in 1000	1 in 500	0.5%	1%	2%	3%	4%	5%	10%	20%	25%	50%
½	0.003	0.007	0.015	0.03	0.07	0.15	0.30	0.45	0.60	0.75	1.50	3.0	3.75	7.0
1	0.006	0.015	0.030	0.06	0.15	0.30	0.60	0.90	1.20	1.50	3.00	6.0	7.50	15.0
2	0.012	0.030	0.060	0.12	0.30	0.60	1.20	1.80	2.40	3.00	6.00	12.0	15.00	30.0
3	0.018	0.045	0.090	0.18	0.45	0.90	1.80	2.70	3.60	4.50	9.00	18.0	22.50	45.0
4	0.025	0.062	0.125	0.25	0.62	1.25	2.50	3.75	5.00	6.25	12.50	25.0	31.25	62.5
6	0.035	0.090	0.180	0.35	0.90	1.80	3.50	5.40	7.00	9.00	18.00	36.0	45.00	90.0
8	0.050	0.125	0.250	0.50	1.25	2.50	5.00	7.50	10.00	12.50	25.00	50.0	62.00	124.0
10	0.060	0.150	0.300	0.60	1.50	3.00	6.00	9.00	12.00	15.00	30.00	60.0	75.00	150.0
12	0.075	0.180	0.360	0.72	1.80	3.60	7.20	10.80	14.40	18.00	36.00	72.0	90.00	180.0
16	0.100	0.250	0.500	1.00	2.50	5.00	10.00	15.00	20.00	25.00	50.00	100.0	125.00	250.0

CHAPTER XXI

COLORING, FLAVORING, AND SWEETENING AGENTS

COLORING AND FLAVORING AGENTS

These coloring and flavoring agents are intended for liquid preparations which are to be used for internal medication. They are used to disguise the taste of the drug(s) and to facilitate solution. They generally contain water, alcohol, sugar, and flavor. The selection depends upon the taste or odor of the drug, the color of the original solution, and the likes of the patient. The alcohol or water content depends upon the solubility of the drug and the need of a preservative. By usage, many flavors are associated with definite colors, as cinnamon with a red and peppermint with a green color. The novice should use only one coloring and flavoring agent if it will serve the purpose. A haphazard blending does not give pleasing results. The preparations in general use for coloring and flavoring agents are waters, syrups, elixirs, solutions, spirits, and tinctures. For convenience each group will be considered separately.

Aromatic Waters (Aquae Aromaticae)

The official aromatic waters are aqueous solutions of volatile oils, generally a 0.2 per cent solution. They are nonirritating and nontoxic and may be used undiluted (q.s. ad) in prescriptions.

PREPARATIONS.—

Anise Water; Aqua Anisi (Aq. Anisi), U.S.P.

DOSAGE.—None.

Cinnamon Water; Aqua Cinnamomi (Aq. Cinnam.), U.S.P.

DOSAGE.—None.

Fennel Water; Aqua Foeniculi (Aq. Foenic.), U.S.P.

DOSAGE.—None.

Peppermint Water; Aqua Menthae Piperitae (Aq. Menth. Pip.), U.S.P.

DOSAGE.—None.

Spearmint Water; Aqua Menthae Viridis (Aq. Menth. Vir.), U.S.P.

DOSAGE.—None.

Wintergreen Water; Aqua Gaultheriae (Aq. Gaul.), N.F.

DOSAGE.—None.

Waters (Aquae)

Water; Aqua, H_2O, U.S.P.

This is a good grade of tap water and is used in any amounts for facilitating solution of drugs. It should not be used parenterally.

Distilled Water; Aqua Distillata (Aq. Dest.), H_2O, U.S.P.

Tap water which is purified by distillation and is used chiefly for preparations intended for internal use or for mixing active drugs such as silver nitrate. It should not be used parenterally.

Redistilled Water; Aqua Redistillata (Aq. Redest.), N.F. (Redistilled Water).

It contains a negligible amount of oxidizable matter, nonvolatile matter, and gases. It is not advocated for parenteral purposes.

Sterilized Distilled Water; Aqua Destillata Sterilisata (Aq. Dest.), U.S.P. (Sterilized Distilled Water).

It should not be used parenterally in large amounts, as it contains pyrogenic substances.

Water for Injection; Aqua pro Injectione (Aq. pro Inject.), U.S.P.

This is sterile distilled water stored in a sealed or other suitable sterile container so that it is free and remains free from pyrogens. This preparation conforms to the sterility test for liquids as recorded in the U.S.P. XII.

Syrups (Syrupi)

The syrups are hydroalcoholic solutions pleasantly colored and flavored. The syrups may be used in liquid preparations up to 50 per cent as a vehicle.

Preparations.—

Syrup; Syrupus, U.S.P. (Simple Syrup).—It is a colorless solution of sucrose (85%) in water.

Dosage.—None.

Syrup of Acacia; Syrupus Acaciae (Syr. Acac.), N.F.—It contains acacia, flavored with vanilla, and sweetened.

Dosage.—None.

Syrup of Cacao; Syrupus Cacao (Syr. Cacao), N.F. (Cocoa Syrup, Chocolate-flavored Syrup).—This is a pleasant syrup particularly designed for children.

Dosage.—None.

Syrup of Cherry; Syrupus Cerasi (Syr. Ceras.), N.F.—It has a pleasant cherry flavor and red color.

DOSAGE.—None.

Syrup of Cinnamon; Syrupus Cinnamomi (Syr. Cinnam.), N.F.—It contains oil of cinnamon and sugar, and has a pink color.

DOSAGE.—None.

Syrup of Citric Acid; Syrupus Acidi Citrici (Syr. Acid. Cit.), U.S.P.—It is acid in reaction, lemon in flavor and odor, and yellow in color. It is used with salty drugs, such as bromides.

DOSAGE.—None.

Syrup of Glycyrrhiza; Syrupus Glycyrrhizae (Syr. Glycyrrh.), U.S.P. (Syrup of Licorice).—It has a licorice flavor and brown color. It acts as a demulcent and is extensively used in cough preparations.

DOSAGE.—None.

Syrup of Orange; Syrupus Aurantii (Syr. Aurant.), U.S.P.—It has an orange color and flavor.

DOSAGE.—None.

Syrup of Pine Tar; Syrupus Picis Pini (Syr. Pic. Pin.), U.S.P. (Syrup of Tar).—This syrup is used chiefly in cough preparations.

DOSAGE.—10 cc. (2½ fluidrachms) (U.S.P.).

Syrup of Raspberry; Syrupus Rubi Idaei (Syr. Rub. Id.), N.F.—It has a raspberry flavor and red color.

DOSAGE.—None.

Syrup of Tolu Balsam; Syrupus Balsami Tolutani (Syr. Balsam. Tolu.), U.S.P.—It has an amber color and aromatic taste.

DOSAGE.—None.

Syrup of Wild Cherry; Syrupus Pruni Virginianae (Syr. Prun. Virg.), U.S.P.—It has a red color with a slightly unpleasant taste. It is used chiefly in cough preparations and for acid drugs.

DOSAGE.—None.

Compound Syrup of Sarsaparilla, Syrupus Sarsaparillae Compositus (Syr. Sarsap. Co.), U.S.P.—It has a licorice flavor and red-brown color. Alcohol content about 10 per cent.

DOSAGE.—None.

Compound Syrup of White Pine; Syrupus Pini Albae Compositus (Syr. Pin. Alb. Comp.), N.F.—It has a pine odor and taste and a brown color, and its chief use is as a vehicle for cough preparations.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Syrup of Ginger; Syrupus Zingiberis (Syr. Zingib.), N.F.—It has a brown color and ginger flavor to be used in a 10 to 20 per cent solution.

DOSAGE.—10 cc. (2½ fluidrachms) (N.F.).

Elixirs (Elixira)

Elixirs are hydroalcoholic solutions containing sweetening, flavoring, and coloring agents, generally. They may or may not contain drugs. For coloring and flavoring preparations for internal medication, they may be used in concentrations up to 30 per cent.

PREPARATIONS.—

Aromatic Elixir; Elixir Aromaticum (Elix. Arom.), U.S.P. (Simple Elixir).—It has an orange flavor and a pale orange color and may be used in 25 to 30 per cent concentrations as a flavoring agent. Alcohol content is about 23 per cent.

DOSAGE.—None.

Compound Elixir of Benzaldehyde; Elixir Benzaldehydi Compositum (Elix. Benzald. Comp.), N.F.—It is pleasantly flavored of vanilla and has a pale yellow color.

DOSAGE.—None.

Elixir of Bitter Orange; Elixir Aurantii Amari (Elix. Aurant. Amar.), N.F. (Elixir Curassao).—It has an orange color and flavor.

DOSAGE.—None.

Elixir of Glycyrrhiza; Elixir Glycyrrhizae (Elix. Glycyrrh.), N.F. (Elixir of Licorice).—It has a licorice flavor and a brown color.

DOSAGE.—None.

Iso-Alcoholic Elixir, Elixir Iso-Alcoholicum (Elix. Iso-Alc.), N.F. (Iso-Elixir).—It contains two preparations of different alcoholic strengths. The low-alcoholic elixir containing 8 to 10 per cent of ethyl alcohol and the high-alcoholic elixir containing 73 to 78 per cent of ethyl alcohol. The two may be combined in any preparation to give the desired alcohol content indicated for that preparation. The prescriber writes Iso-Alcoholic Elixir and the amount desired (q.s. ad); the pharmacist compounds the preparation with the minimal alcohol requirement. This saves alcohol and the patient's money.

DOSAGE.—None.

Solutions (Liquores)

The official "solutions" are generally nonvolatile drugs dissolved in water; a few of them are used as coloring and flavoring agents. They may be used as coloring agents for internal preparations in 2 to 5 per cent solution.

Solution of Amaranth; Liquor Amaranthi (Liq. Amaranth), U.S.P.—Amaranth is a red dye, a 1 per cent solution in water.

DOSAGE.—None.

Solution of Carmine; Liquor Carmini (Liq. Carmin.), N.F.—Carmine is a red dye (6.5%), in ammonia water, glycerin, and water.

DOSAGE.—None.

Solution of Cochineal; Liquor Cocci (Liq. Cocci), N.F.—Cochineal is a red dye dissolved in water.

DOSAGE.—None.

Spirits (Spiritus)

Spirits are hydroalcoholic solutions of essential oils. They are used chiefly as flavoring agents, but are very concentrated, and 10 to 12 per cent is generally enough for flavoring an internal preparation.

PREPARATIONS.—

Spirit of Anise; Spiritus Anisi (Sp. Anisi), U.S.P.—Alcohol content about 84 per cent.

DOSAGE.—1 cc. (15 minims) (U.S.P.).

Spirit of Benzaldehyde; Spiritus Benzaldehydi (Sp. Benzald.) N.F.—It has an aromatic odor and taste and contains about 75 per cent alcohol.

DOSAGE.—0.5 cc. (8 minims) (N.F.).

Spirit of Cinnamon; Spiritus Cinnamomi (Sp. Cinnam.), U.S.P.—It has a cinnamon odor and flavor and pale red color, with about 83 per cent alcohol.

DOSAGE.—1 cc. (15 minims) (U.S.P.).

Spirit of Lavender, Spiritus Lavandulae (Sp. Lavand.) U.S.P.—It has a lavender odor and flavor and no color; alcohol content about 88 per cent.

DOSAGE.—2 cc. (30 minims) (U.S.P.).

Spirit of Peppermint; Spiritus Menthae Piperitae (Sp. Menth. Pip.), U.S.P. (Essence of Peppermint).—It is a 10 per cent solution of oil of peppermint in alcohol (83%) and water.

DOSAGE.—1 cc. (15 minims) (U.S.P.).

Spirit of Spearmint; Spiritus Menthae Viridis (Sp. Menth. Vir.), U.S.P.—It contains 10 per cent of oil of spearmint, alcohol (83%) and water.

DOSAGE.—1 cc. (15 minims) (U.S.P.).

Compound Spirits of Cardamon; Spiritus Cardamomi Compositus (Sp. Cardam. Comp.), N.F.—It has an orangelike odor and reddish-yellow color with alcohol about 71 per cent.

DOSAGE.—None.

Compound Spirit of Orange; Spiritus Aurantii Compositus (Sp. Aurant. Co), U.S.P.—It has a pleasant orangelike color, odor, and flavor. Alcohol content about 68 per cent.

DOSAGE.—None.

Compound Spirit of Vanillin; Spiritus Vanillini Compositus (Sp. Vanillin, Comp.), N.F.—It has a vanilla-like odor and taste and contains about 68 per cent of alcohol.

DOSAGE.—None .

Tinctures (Tincturae)

Tinctures are hydroalcoholic extracts of crude drugs obtained by percolations. Their alcoholic content is high, and they should not be used in too concentrated amounts, generally a 10 to 15 per cent solution is enough to flavor a prescription. They may or may not have color.

PREPARATIONS.—

Tincture of Bitter Orange Peel; Tinctura Aurantii Amari (Tr. Aurant. Amar.), U.S.P.—It has an orange color, flavor, and odor; alcohol content about 60 per cent.

DOSAGE.—None.

Tincture of Cinnamon; Tinctura Cinnamomi (Tr. Cinnam.), N.F.—It has a cinnamon odor and flavor and a pale red color. The alcohol content is about 64 per cent.

DOSAGE.—1 cc. (15 minims) (N.F.).

Tincture of Cudbear; Tinctura Persionis (Tr. Persion.), N.F.—It is a red dye dissolved in alcohol (64%) and water. One cubic centimeter for a four-ounce prescription is generally adequate.

DOSAGE.—None.

Tincture of Lemon; Tinctura Limonis (Tr. Limon.), U.S.P. (Tinctura Limonis Corticis).—It has a lemon odor and flavor with a pale yellow color. Alcohol content 73 per cent.

DOSAGE.—None.

Sweet Tincture of Rhubarb; Tinctura Rhei Dulcis (Tr. Rhei Dulcis), N.F.—It has a rhubarb-like odor and flavor and a brown color. It is mildly cathartic and must be used only when that action is desired. Alcohol content is about 43 per cent.

DOSAGE.—4 cc. (1 fluidrachm) (N.F.).

Tincture of Sweet Orange Peel; Tinctura Aurantii Dulcis (Tr. Aurant. Dulc.), U.S.P.—It is orange in color, odor, and taste.

DOSAGE.—None.

Tincture of Vanilla; Tinctura Vanillae (Tr. Vanill.), N.F.—It has a vanilla odor and taste and a brown color with an alcohol content of about 40 per cent.

DOSAGE.—None.

Compound Tincture of Cudbear; Tinctura Persionis Composita (Tr. Persion. Comp.), N.F.—It is a reddish-brown dye in alcohol (22%) and water.

DOSAGE.—None.

Compound Tincture of Lavender; Tinctura Lavandulae Composita (Tr. Lavand. Co.), U.S.P. (Compound Spirit of Lavender).—It has a lavender odor and taste and a pink color. Alcohol content about 70 per cent.

DOSAGE.—None.

SWEETENING AGENTS

The best sweetening agent for preparations intended for internal use is sucrose. In concentrated solutions it acts as a protective and demulcent to the throat and for that reason is used in cough preparations up to 25 per cent; for other preparations a 10 to 20 per cent solution is adequate. Because sucrose and similar carbohydrates are contraindicated in diabetes mellitus, saccharin is used in its stead.

PREPARATIONS.—

Sucrose; Sucrosum (Sucros.), U.S.P. (Sugar).—It is obtained from sugar cane and sugar beets and is used as a sweetening agent.

DOSAGE.—None.

Syrup; Syrupus, U.S.P. (Simple Syrup).—It is an 85 per cent solution of sucrose in water.

DOSAGE.—None.

Saccharin, Saccharinum (Saccharin.), $C_6H_4COSO_2NH$, U.S.P.—It occurs as a white crystalline powder, nearly odorless and about 400 times as sweet as sugar, slightly soluble in water (1 in 290), and sparingly soluble in alcohol (1 in 31). As it is not metabolized in the body, it may be used as a sweetening agent in preparations for patients with diabetes mellitus.

DOSAGE.—½ grain tablet is equivalent in sweetness to a lump of table sugar. One to two grains for 8 ounces of solution is generally adequate as a sweetening agent for prescriptions.

Saccharin Sodium; Saccharinum Sodicum (Saccharin. Sod.), $C_6H_4COSO_2NaN$, U.S.P.—It is more soluble in water (1 in 1.5) and less soluble in alcohol (1 in 50) than saccharin, but is otherwise similar.

Saccharin Sodium Tablets; Tabellae Saccharini Sodici (Tab. Saccharin. Sod.), U.S.P.

DOSAGE.—30 mg. (½ grain) (U.S.P.) One tablet is equal to a lump of sugar.

FLAVORING AGENTS FOR ORAL PREPARATIONS

Flavoring agents in oral preparations (dentifrices and washes) mask the tastes of the drugs, disguise the mouth odors, and make a more pleasing preparation. The essential oils and their preparations and derivatives are extensively used as flavoring agents. The novice should use only one preparation if it will serve the purpose intended. A haphazard blending of flavors does not necessarily result in a pleasant preparation. The essential oils are only sparingly soluble in water and should not be used in aqueous preparations in over a 0.2 per cent solution. For convenience of prescribing, the aromatic waters are best and may be used without fear of irritation or insolubility and are used undiluted (q.s. ad).

Anise Water; Aqua Anisi (Aq. Anisi), U.S.P.—It has an anise odor and flavor and no color. Use undiluted.

Camphor Water; Aqua Camphorae (Aq. Camph.), U.S.P.—It has a camphor odor and flavor and no color. Use undiluted.

Cinnamon Water, Aqua Cinnamomi (Aq. Cinnam.), U.S.P.—It has a cinnamon odor and taste and no color. Use undiluted.

Peppermint Water; Aqua Menthae Piperitae (Aq. Menth. Pip.), U.S.P.—It has a peppermint odor and flavor, followed by a cool sensation which occurs without a change in the local temperature. It has a pale green color. Use undiluted.

Menthol; Menthol, U.S.P.—It is obtained from the oil of peppermint and other mint oils, or prepared synthetically. It occurs as colorless crystals with a peppermint odor and aromatic taste. It is slightly soluble in water and soluble in alcohol. When applied locally it acts as a counterirritant. As a flavoring agent for mouthwashes it may be used in a 0.2 to 0.4 per cent solution.

Wintergreen Water, Aqua Gaultheriae (Aq. Gaul.), N.F.—It has a wintergreen odor and flavor and no color.

Eucalyptol; Eucalyptol, U.S.P. (Cineol).—It is obtained from the volatile oil of eucalyptus and occurs as a colorless liquid with an aromatic odor and pungent cool taste. It is very sparingly soluble in water and soluble in alcohol. Used in oral washes in a 0.1 to 0.2 per cent solution.

Thymol; Thymol, U.S.P.—It occurs as colorless crystals, has a thyme-like odor and burning taste, and is slightly soluble in water (1 in 1000) and soluble in alcohol (1 in 1). It is used as an antiseptic and flavoring agent in oral washes in a 0.5 per cent solution.

SWEETENING AGENTS FOR DENTAL PREPARATIONS

The use of fermentable carbohydrates as sweetening agents in oral preparations is contraindicated. While the role of carbohydrates in dental caries is not clearly defined, it seems justified at this time to discourage their use in all oral preparations. The war has made glycerin unobtainable in large amounts and many of the dentifrices have turned to syrups as a substitute. To discourage this practice the Council on Dental Therapeutics of the American Dental Association has gone on record (1943) as not favoring the use of fermentable saccharides in oral preparations. As a sweetening agent for dental preparations saccharin is a substitute.

PREPARATIONS.—

Saccharin, Saccharinum (Saccharin.), U.S.P.—Saccharin, which occurs as a white powder, is about 400 times as sweet as sucrose. It is slightly soluble in water (1 in 290) and sparingly soluble in alcohol (1 in 31). Used for sweetening mouthwashes in 1 grain for 8 ounces of solution.

Saccharin Sodium, Saccharinum Sodicum (Saccharin. Sod.), U.S.P. —it is freely soluble in water (1 in 1.5) and soluble in alcohol (1 in 50). Uses the same as for saccharin.

COLORING AGENTS FOR MOUTHWASHES

Colored mouthwashes are more pleasing to use than uncolored preparations. There is a psychic advantage in using a colored preparation for some patients. It is advisable for the prescriber to know the original color of the preparation before prescribing a dye to change it, i.e., a red or brown color will blend better with a dark solution than will a pale yellow or green.

The following dyes may be used for coloring oral preparations in 2 to 4 cc. per 500 cc. of mouthwash.

Caramel; Caramel (Caram.), N.F.—Caramel is a dark brown syrupy fluid with a somewhat bitter taste. It is freely soluble in water and soluble in alcohol. It is obtained by browning sucrose and dissolving it in water. Used as a brown coloring agent.

Carmine; Carminum (Carmin.), N.F.—It is a red dye obtained from cochineal.

Solution of Carmine; Liquor Carmini (Liq. Carmin.), N.F.—It is a 6.5 per cent solution of carmine in water.

Cudbear; Persio, N.F.—A purplish-red powder obtained from lichens and used as a coloring agent.

Tincture of Cudbear; Tinctura Persionis (Tr. Persion.), N.F.—It is a solution of cudbear in alcohol (64%) and water.

Compound Tincture of Cudbear; Tinctura Persionis Composita (Tr. Persion. Comp.), N.F.—It contains tincture of cudbear and caramel in alcohol (22%) and water and has a reddish-brown color.

Solution of Amaranth; Liquor Amaranthi (Liq. Amaranth.), U.S.P. —It is a red dye (1%) dissolved in water.

Solution of Cochineal; Liquor Cocci (Liq. Cocci), N.F.—It is a red dye dissolved in water.

Compound Tincture of Lavender; Tinctura Lavandulae Composita (Tr. Lavand. Co.), U.S.P. (Compound Spirit of Lavender).—It contains essential oils, red saunders, alcohol (70%), and water. It has a lavender-like odor and flavor and a red color.

CHAPTER XXII

ANTISEPTICS

At present it is generally recognized that the breaking down of organic compounds, when subjected to certain causative conditions, is brought about by the activity of minute vegetable organisms—the bacteria. This process is called putrefaction, or, under certain conditions, fermentation. These terms are applied to strictly analogous processes, with this differentiation—putrefaction refers to the decomposition of animal proteins, while fermentation is restricted to the cleavage action of bacterial ferments on vegetable material. The presence of certain bacteria within the body is instrumental in the production of severe physiologic changes, resulting in the various vital phenomena known as infectious diseases. As soon as this fact became recognized, investigators directed their attention to the discovery of agents capable of inhibiting or destroying the action of these microorganisms and their products.[1-3]

By the term *sepsis,* we understand the existence of a condition in which bacterial infection and its sequelae—fermentation or putrefaction—are brought about by the presence of bacteria or their products, while *asepsis* implies an entire freedom from such infection—that is, an aseptic condition. If a primarily septic condition is changed by some method or means that inhibits the growth of putrefactive organisms, *antisepsis* is secured. Consequently *antiseptics* are chemical agents that merely inhibit the action and growth of bacteria, while *germicides* destroy the vitality of the infective organisms. *Disinfectants* also kill the bacteria and chemically change their poisonous products to inert compounds. *Disinfectants* must, therefore, be *germicides.* Thus it will be seen that an antiseptic is not necessarily a germicide or a disinfectant—that is, glycerin will inhibit the growth of certain bacteria, and is therefore antiseptic, but it has very little or no power to destroy the microorganisms or their spores, and consequently possesses no germicidal or disinfectant properties. On the other hand, formaldehyde solution is an effective germicide, possesses also powerful disinfectant properties, and is successfully employed for both purposes.

[1]Incident in Development of Antisepsis, Bull. Soc. M. Hist. Chicago 5: 105, 1937.

[2]Bacteriostasis, J. Inf. Dis. 61: 42, 1937.

[3]Modern Views on Infection and Disinfection, Lancet 1: 102, 1937.

Quite frequently putrefactive processes are accompanied by the production of malodorous gases arising from the formation of new compounds. Drugs are employed to destroy these offensive odors, and such agents are termed *deodorants*. The true deodorants may have little or no antiseptic action. If an agent is employed solely for its cleansing power, either mechanically or chemically—as soap—it is termed a *detergent*, while all those chemicals that possess the power to inhibit the action of ferments are called *antizymotics*.

The action of antiseptics depends on their chemical relationship to the albumin of the cell; they act as *protoplasm poisons*, and are therefore closely related to caustics and astringents. The ideal antiseptic would be one that inhibits or destroys the bacteria and their products without seriously injuring the cell of the host. According to our present conception of biologic laws, the search for such a material is apparently fruitless.

Antiseptics are usually divided into those used for external or local application and those employed internally. External antiseptics include all those agents that are used on the skin, the external mucous surfaces, including the oral cavity, wounds, and ulcers, the intestinal tract, the bronchi and lungs, and, in a roundabout way, the urinary tract; while the destruction of infectious material on instruments, clothing, rooms, food, etc., is accomplished by disinfectants. The destruction of all forms of bacteria and their products, and their removal from objects, are referred to as *sterilization*, and are usually performed by means of heat.

The administration of internal antiseptics is based on the supposition that the blood and the body fluids become saturated with the drug to such an extent as to kill or neutralize the microorganisms and their waste products without harming the tissues themselves. As yet little is known about the action of antiseptics when administered in the above manner. Clinical observations show, however, that certain infectious diseases—as malaria, syphilis, amebiasis, pneumonia and others—are positively influenced by such treatment, and that the use of antiseptics is therefore justified.

When we speak about the potency of any given antiseptic, it should be remembered that this potency is only relatively expressed. We have as yet no accepted standards of antiseptic strength.[1] Various efforts have been made in this respect; for instance, Rideal and Walker introduced the *phenol coefficient*. There are also other

[1]Knighton, Holmes T.: Significance of Tests for the Evaluation of Antiseptics and Germicides, J. A. D. A. 26: 2047 (December), 1939.

methods, such as the Lancet method and the Allen method. None has proved universally satisfactory.[2-6]

Briefly stated, the phenol coefficient in the Rideal-Walker method is arrived at by dividing the figure indicating the degree of dilution of the disinfectant that kills an organism in a given time by that expressing the degree of dilution of the phenol that kills the same organism in the same time under exactly similar conditions. Leaving out details, the determination of the Rideal-Walker coefficient is substantially as follows:[7]

Certain standard conditions are considered essential to the proper performance of the test. Phenol solutions of known strength are used; cultures are grown in a standard medium, transplants being made every 24 hours; the loops used for all inoculations are of a standard size (about 4 mm. in diameter). Usually four dilutions of suitable strengths of the disinfectant to be used are made. Phenol controls of a suitable strength are also prepared. Five cc. of each of these dilutions are placed in sterile test tubes, to which are added at intervals of one-half minute a 24-hour broth culture of *E. typhosa* in the proportion of 1 drop of culture to each cubic centimeter of disinfectant used (according to Partridge, 1 drop of culture equals about 0.1 cc.). At the end of two and a half minutes a loopful of each of the mixtures is inoculated into a test tube containing 5 cc. of standard broth, an interval of half a minute being thus allowed between taking the samples from the different dilutions. This is repeated at 5, 7½, 10, 12½, and 15 minutes. The broth tubes, after being incubated at 37° C. for 48 hours, are examined for growth. The results of the examination are then noted, and if suitable comparative strengths of the disinfectant and phenol have been selected, the phenol coefficient is determined as above stated.

The accompanying table illustrates the manner of determining the phenol coefficient of a disinfectant according to the Rideal-Walker method:

Name, "A."

Temperature of medication, 20° C.

Culture used, *E. typhosa*, 24-hour, extract broth, filtered.

Proportion of culture and disinfectant, 0.1 cc.—5 cc.

SAMPLE	DILUTION	TIME CULTURE EXPOSED TO ACTION OF DISINFECTANT IN MINUTES						PHENOL COEFFICIENT
		2½	5	7½	10	12½	15	
Phenol								100)550
	1.900	−	−	−	−			
	1.100	+	+	+	−	−	−	5.5
Disinfectant "A"	1.500	+	+	−	−	−	−	coefficient
	1.550	+	+	+	−	−	−	
	1.600	+	+	+	+	−	−	

[2]An Experimental Critique of the Allen Method of Evaluating the Bactericidal Action of Antiseptics, Am. J. Pub. Health 25: 1125, 1935.

[3]Kitchin: J. A. D. A. 20: 263, 1933.

[4]Phenol Coefficient as Measure of Practical Value of Disinfectants, J. Bact. 32: 215, 1936.

[5]Antiseptics: Comparative Study of Laboratory and Practical Tests, J. Am. Pharm. A. 25: 1117, 1936.

[6]Comparative Studies of Most Common Disinfectants. München. med. Wchnschr. 83: 299, 1936.

[7]Anderson and McClintic: Hygienic Laboratory Bulletin No. 82, Washington, 1912.

All those chemicals which are generically termed "antiseptics" may, for the sake of convenience, be grouped under the following headings:

1. *Salts of the heavy metals, their oxides, and their organic compounds.*
2. *Acids.*
3. *Alkalies.*
4. *Halogens and their derivatives.*
5. *Solutions which evolve nascent oxygen.*
6. *Antiseptics of the aromatic series.*
7. *Antiseptics of the aliphatic series.*
8. *Essential oils, their derivatives, and their synthetic substitutes.*

HEAVY METAL SALTS, THEIR OXIDES, AND THEIR ORGANIC COMPOUNDS

The salts of the heavy metals form an important group of therapeutic agents which are collectively termed *antiseptics.* Metals, in their pure state, do not usually induce any serious symptoms in the living organisms unless their salts or oxides are formed. Mercury, copper, silver, etc., may pass unaltered through the body without causing poisonous effects. The silver salts may be absorbed and deposited in a reduced form in the connective tissues, causing a grayish discoloration of the skin (argyria). Lead, bismuth, and mercury salts are readily absorbed and consequently, when administered in continuous doses, produce typical chronic intoxications—lead colic, blue gum line, and mercurialism. When administered in sufficiently large doses, the absorbable salts of the heavy metals cause collapse and death; in small doses they produce necrosis of specific tissues, affecting primarily the liver and the kidneys. Certain metals—as mercury, bismuth, iron, etc. —are readily excreted by the lower bowel; some metals, as mercury, arsenic, and bismuth, show a predilection for diseased mucous membranes. Various types of stomatitis are caused by the absorption of particles of metals in the form of dust, vapor, or solution which are deposited as sulfides within the mucous membrane about the teeth. Some few metals, in their pure state, possess antiseptic action. According to Miller, gold, silver, and mercury—and, to a lesser extent, copper, nickel, and zinc—inhibit the growth of certain forms of pathogenic microorganisms, while iron, tin, and lead show practically no action. This antiseptic action is the result, according to Behring, of a reaction of the bacteria with those metals which are capable of forming small quantities of soluble salts.

The salts of the heavy metals are principally protoplasm poisons, but differ widely in their toxic action. In concentrated solutions they may act as severe caustics, while, when well diluted, only astringent effects are obtained. The soluble metallic salts possess an astringent and nauseating, sweetish taste. If swallowed in more or less concentrated solutions, they induce vomiting, which is so very effective with certain metallic salts that they are frequently employed as reliable *emetics*—as copper sulfate and zinc sulfate. The insoluble salts of the heavy metals do not, of course, possess any germicidal action, or even produce physiologic effects—as, for instance, the insoluble mercury sulfide. It should be remembered, however, that insolubility in water does not necessarily mean insolubility in the body fluids. While

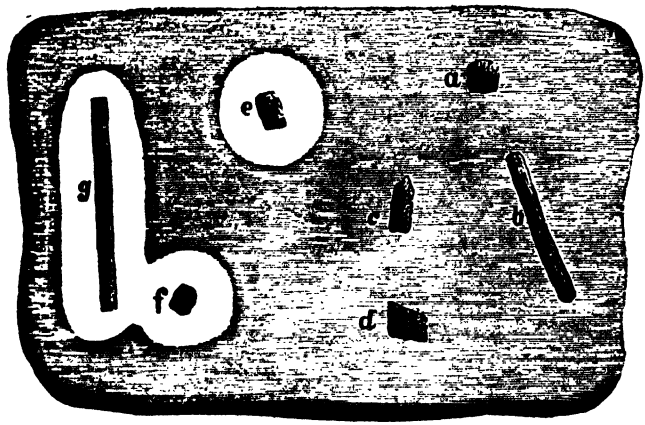

Fig. 28.—Culture plate with Pack's cylinders and Abbey's noncohesive foil: *a, b, c, d,* annealed; *e, f, g,* not annealed. The latter did not allow any growth to appear within close proximity. (Miller.)

the latter are largely aqueous in their nature, they contain sodium chloride, fatty acids, albumin, enzymes, etc., which are prone to produce soluble salts. On this supposition we are able to explain why the otherwise insoluble calomel or bismuth subnitrate produces definite action when brought in contact with the surface of a wound or of the intestines.

The local action of the metallic salts does not depend upon the action of their molecules as a whole, but on the dissociated ions in solution.

To comprehend more readily the effect of a solution—the dissociation of a solid, liquid, or gas in a liquid—on tissue, it is necessary to understand the physical laws governing this process—that is, the theory of electrolytic dissociation of Arrhenius.

A simple solution of salt in water dissociates the salt into electromolecules, the ions, which exist independently of the action of a galvanic current. The number of positively and negatively charged ions is equimolecular; i.e., the solution is electrically neutral. The ions themselves are suspended in the solution in a chaotic mixture. Furthermore, the ion concentration depends, with limits, on the degree of dilution of the solution; a certain definite dilution dissociates completely all molecules, and further dilution merely separates the ions farther from each other. In the case of mercury bichloride, $HgCl_2$, the cation is Hg and the anions are the Cl. The charge of the Cl ion is one negative unit, and that of the Hg ion is two positive units. Water has, so far as known, the greatest dissociating power. Formic acid, methyl alcohol, ethyl alcohol, ammonia,

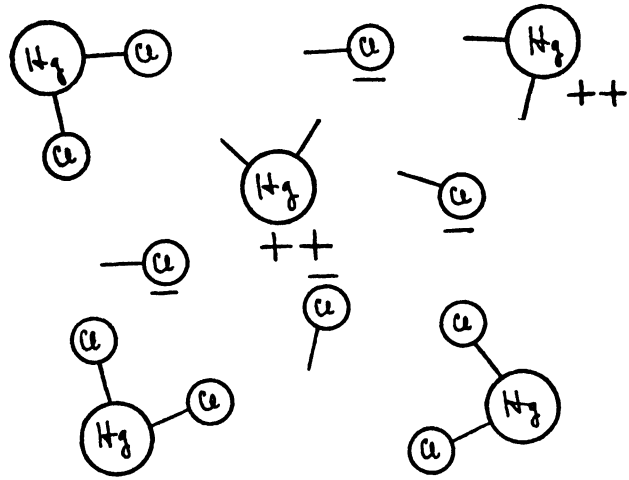

Fig. 29.—Imaginary diagram of a solution of mercuric chloride in water. The atoms of mercury are represented by the large circles marked Hg, the chlorine atoms by the smaller circles marked Cl. Some of the mercury atoms are depicted joined on the two chlorine atoms to form the salt. Some are depicted as dissociated "ions" swimming about in the free state. The signs + and — attached to these indicate positive (cations) and negative (anions) electric charges. (Andrews.)

and others are, however, known to possess this property to a greater or lesser degree. The organic compounds are much less dissociated than the inorganic salts, and their ions are more complex and are not so well understood.

The practical application of the above theories of physical chemistry in relation to the action of the metallic salts on bacteria is very significant. Now, if we remember that an electrolyte in solution is dissociated into its ions only in part when the solution is not infinitely diluted, then the effect of this solution must be attributed

to the combined actions of the ions and the undissociated molecules present in it. Paul and Krönig investigated, first of all, the role played by the ions of the undissociated molecules in the disinfectant solutions. For this purpose the germicidal power of several mercury compounds, which are dissociated to different degrees in aqueous solutions, was examined. The following are the names of a few of these compounds, arranged in the order of their decreasing degree of dissociation:

1. Mercuric chloride, $HgCl_2$.
2. Mercuric bromide, $HgBr_2$.
3. Mercuric cyanide, $Hg(CN)_2$.

If the germicidal action of the halogen ions and the undissociated molecules is slight as compared with that of the Hg ions, then the bacteriostatic action of these solutions will be dependent in the main on the concentration of the Hg ions. We may conclude from these experiments that the greater the dissociation of the mercury compounds —that is, the greater the number of mercury ions present per unit volume of the given solution—the greater is its antiseptic action. Furthermore, it is not so much the molecular concentration of the solution, as the specific action of the metallic ion that influences its activity as a disinfectant. Similar results were obtained by Paul and Krönig with silver, gold, and copper salts.

The antiseptic properties of the more important metals may be arranged according to the following scale, beginning with the mildest one: iron, aluminum, lead, copper, zinc, silver, and mercury. The organic metallic compounds form weak precipitates with albumin and are less irritating.

In general, the metallic salts have an acid reaction and precipitate albumin by virtue of their acid components. These precipitates differ very markedly in regard to their density, and depend largely on the various metallic salts employed. Silver nitrate, for instance, produces a hard, compact, and dry precipitate, which is definitely localized and which prohibits the further penetration of the salt, while zinc chloride produces a loose, flocculent mass resembling the precipitate of alkalies, and this sponge-like precipitate does not prohibit the further penetration of the salt in depth and width. Hence metallic salts or other antiseptics which precipitate albumin or combine with organic matter are less effective as disinfectants—as bichloride of mercury for sterilizing blood stained instruments.

For some time, chemists have endeavored to remedy the irritating properties of the inorganic metallic salts by preparing synthetically

organic metallic compounds. Quite a number of these compounds have appeared on the market, especially organic salts of silver and mercury. Some of these compounds are very satisfactory, and it seems safe to prognosticate a good future for their general use.

The antiseptic action of the metallic salts depends largely on the formation of metallic precipitates when brought in contact with the protein molecule. Usually these newly formed proteinates are insoluble in water; some, however, are soluble in an excess of proteins—as mercury—and some will dissolve in solutions of neutral salts (sodium chloride) or organic acids (tartaric or citric acid).

When a solution of a metallic salt is applied to a mucous membrane or to the surfaces of a wound, the protein is at once precipitated, and the acid with which the metal is combined is set free. Thus a more or less dense and continuous film is formed over the surface, which acts as a mechanical protective to the parts involved, lessening, or even completely checking, the further penetration of the drug into the deeper structures. The free acid acts as an irritant, which stimulates the circulation of the involved part, thereby increasing cell activity and effusion of exudates. The germs that are present, being largely protein in nature, are acted on in the same manner as the superficial cells; they become coagulated and the surrounding medium is changed simultaneously to an unfavorable pabulum for the continued growth of microorganisms. The tissue exudates, being freed of their protein, become more diffusible and are more easily absorbed, while the blood vessels slightly contract and become less permeable.

Through the investigations of Bredig, solutions of very pure metals in water have been introduced for antiseptic purposes. These solutions are termed colloidal solutions. It seems paradoxical to speak of a water-soluble gold, silver, mercury, etc. It must be borne in mind, however, that such solutions are merely mechanical suspensions of extremely fine particles of metal—metals in their amorphous state in water. Silver, mercury, copper, iron, gold, and numerous other metals are produced at present in this form and are used in therapeutics and the industries. Their action is physical (adsorption) rather than chemical.

The question of the oligodynamic action of metals has been freely discussed in the literature. The term *oligodynamie*, which was coined by the Swiss botanist Naegeli in 1893, designates the bactericidal action of certain metals, especially silver, mercury, copper, etc., and their salts when present in extremely diluted concentration. These solutions

are so very weak that it is difficult to determine the presence of the metal by the ordinary chemical reaction. At present, the opinion regarding the oligodynamic action of metals is not settled. One fact, however, seems to be certain; i.e., a part of the metal or its salt or oxide has to go in solution, otherwise no action is obtained. Pure silver or its alloys have little bactericidal action; on the other hand, silver oxide is relatively effective. When a piece of pure silver wire, free from formed oxide on its surface, is placed in infected agar, very little action is observed. When this same wire is oxidized by placing it in hydrogen dioxide solution (3 per cent) for twenty-four hours and thereby assumes a grayish-black coating on its surface, it becomes active as an antiseptic agent. This bactericidal property is lost after repeated platings but may be "reactivated" again and again by merely immersing it in the above solution.

The following is a recapitulation of the action of metallic salts on the proteins of bacteria and tissues:

1. Produces a precipitation of the cell colloids by forming a metallic proteinate, a chemical reaction.

2. Produces a precipitation of the cell colloids by dehydration, which is an osmotic effect.

3. Produces a precipitation of the cell colloids by adsorption, which is a physical phenomenon.

4. Produces a precipitation of the cell colloids by approaching the isoelectric point of the colloid.

Mercury and Mercury Compounds

MERCURY; HYDRARGYRUM (HYDRARG.), U.S.P.; Quicksilver; Hg.

PROPERTIES.—The element mercury is a silvery-white liquid metal with a specific gravity of 13.5 and a boiling point of 357° C. Because of its low position in the electromotive series it is relatively inactive chemically. It does not form oxides in air but is affected by sulfur fumes. Plato, in the fourth century B.C., described this liquid metal and named it quicksilver. Later the Romans gave it the official name of "hydrargyrum" from which the symbol Hg was derived. The most important source of the metal is cinnabar (mercuric sulfide) by reduction and distillation.

$$HgS + O_2 = Hg + SO_2$$

Mercury which has been contaminated by air-borne impurities may be recovered by filtering through chamois. Mercury forms alloys with practically all of the common metals except iron and platinum. These

alloys are called amalgams, and those containing silver, copper, tin, zinc, and gold are used extensively as a restorative metal[1] in operative dentistry.

PHARMACODYNAMICS.—Metallic mercury in large globules is not readily absorbed from the intestines, but when it is dispersed in fine particles it is absorbed and produces its characteristic symptoms. This metal, combined with a fat base, is applied to the skin as an inunction and is absorbed. While the skin is not an absorbing organ, this drug does gain entrance to the general circulation, producing a therapeutic effect. The finely divided particles of metal may gain entrance through sweat and sebaceous glands and are absorbed from there by the blood and lymph.

The action of mercury as an antispirochetal agent is not well understood. There is a possibility that the metallic mercury after absorption is ionized by the tissue fluids and the ions combine chemically or physically with the treponema, producing an antiseptic action.

THERAPEUTICS.—Antisyphilitic and diuretic. Mercury is probably contraindicated in the treatment of Vincent's stomatitis. The Council on Dental Therapeutics has specifications for mercury (J. A. D. A. 19: 57, Jan., 1932). The U.S.P. mercury is satisfactory for all dental needs.

TOXICOLOGY.—Metallic mercury as an inunction is generally administered to the point of toxicity, and the treatment is then discontinued. In industry the fumes of mercury are absorbed through the lungs into the blood, resulting in chronic and acute mercury poisonings. The dental practitioner is in a strategic position to diagnose this toxemia because of the characteristic oral symptoms and salivation. Nephritis, retention, nephrosis, coma, and death may follow the ingestion of large amounts of this metal. Some few individuals are sensitive to mercury or mercury preparations and will develop contact lesions on the skin and mucous membrane.[2-4]

The systemic treatment is to stop the ingestion of the poison; cathartics, and copious water drinking to increase the elimination, and sodium formaldehyde sulfoxylate may be useful as a systemic antidote. Mercury is eliminated chiefly through the kidneys and to a lesser ex-

[1]Taylor, J. A.: History of Dentistry, Philadelphia, 1922, Lea & Febiger, page 127, "In 1837, J. L. Murphy of London, England, published a work which described amalgam."

[2]Ellis, F. A., and Robinson, H. M., Jr.: Cutaneous Sensitivity to Merthiolate and Other Mercurial Compounds, Arch. Dermat. & Syph. 46: 425-430, Sept., 1942.

[3]Belote, G. H., and Marshall, D.: Metaphen Dermatitis, J. Michigan M. Soc. 34: 172, Mar., 1935.

[4]Lawrence, J., and Strauss, M. J.: Dermatitis Due to Potassium Mercuric Iodide, Arch. Dermat. & Syph. 29: 76, July, 1934.

tent through the feces, bile, sweat, and saliva. No cases of mercury poisoning from amalgam restorations have been recorded, regardless of the large amount of discussion on this subject.[1-6]

Strong Mercurial Ointment; Unguentum Hydrargyri Forte (Ung. Hydrarg. Fort.), U.S.P. (Unguentum Hydrargyri, Mercurial Ointment).—Metallic mercury (about 50%) and oleate of mercury (2%) with wool fat, white wax, and white petrolatum.

USES.—To secure the systemic effect of mercury by inunction.

Mild Mercurial Ointment; Unguentum Hydrargyri Mite (Ung. Hydrarg. Mit.), U.S.P. (Unguentum Hydrargyri P.I., Diluted Mercurial Ointment, Blue Ointment).—Ointment made by diluting strong mercurial ointment with 20 per cent of a mixture of petrolatum and white wax. Mercurial content about 10 per cent.

USES.—Especially in pediculosis.

MERCURY BICHLORIDE; HYDRARGYRI BICHLORIDUM (HYDRARG. BICHLORID.), U.S.P. (Corrosive Sublimate, Mercuric Chloride, Corrosive Mercuric Chloride).—$HgCl_2$.

ETYMOLOGY.—From the Greek *hydrargyros* (liquid silver).

SOURCE AND CHARACTER.—Mercuric chloride is obtained by subliming a mixture of mercuric sulfate, sodium chloride, and some black oxide of manganese. The latter is added to prevent the formation of calomel.

$$HgSO_4 + 2NaCl + MnO_2 = HgCl_2 + Na_2SO_4 + MnO_2.$$

It occurs in heavy, colorless rhomboid crystals or masses, odorless, and has an acrid and persistent metallic taste; permanent in the air. When in fine powder it is soluble at 60° F. (16° C.) in 13½ parts of water, in 3.8 parts of alcohol, in 25 parts of ether, in 2 parts of boiling water, and in about 12 parts of glycerin. It is *incompatible* with alkalies, and their carbonates, potassium iodide, limewater, tartar emetic, silver nitrate, albumin, soaps, and tannic acid. It attacks steel and nickel-plated instruments.*

AVERAGE DOSE.—4 mg. (1/15 grain).

[1]Storazzi, D. C., and Elkins, H. B.: Mercury Absorption From Mercury-Bearing Dental Fillings and Antiseptics, J. Indus. Hyg. & Tox. 23: 459-465, Dec., 1941.

[2]Hayes, L. V.: Clinical Diagnosis of Diseases of Mouth, New York, 1936, Dental Items of Interest Publishing Co., p. 34.

[3]Prinz, Hermann, and Greenbaum, S. S.: Diseases of Mouth and Their Treatment, Philadelphia, 1939, Lea & Febiger, pp. 218-220.

[4]Souder, Wilmer, and Sweeney, W. T.: Is Mercury Poisonous in Dental Amalgam Restorations? Dental Cosmos 73: 1158, Dec., 1931.

[5]Idem: p. 1150.

[6]Traub, E. F., and Homes, R. H.: Dermatitis and Stomatitis From Mercury of Amalgam Fillings, Arch. Dermat. & Syph. 38: 349, Sept., 1938.

*Regarding the action of corrosive sublimate on metallic objects, it should be remembered that not only does it cause a precipitate of metallic mercury on them, but the disinfectant solution is also reduced in proportion as the mercury is precipitated.

PREPARATIONS.—

Large Poison Tablets of Mercury Bichloride; Toxitabellae Hydrargyri Bichloridi Magnae (Toxitabel. Hydrarg. Bichlor. Mag.), U.S.P. (Large Corrosive Sublimate Tablets, Large Bichloride Tablets).

Tablets of an angular shape of a distinctive color, not white, and in an angular container having a red printed label bearing the word "POISON." Each tablet contains about 0.5 Gm. (8 grains) of mercury bichloride.

Small Poison Tablets of Mercury Bichloride; Toxitabellae Hydrargyri Bichloridi Parvae (Toxitabel. Hydrarg. Bichlor. Par.), U.S.P. (Small Corrosive Sublimate Tablets, Small Bichloride Tablets).—Tablets of an angular shape, of a distinctive color, not white, in a container of angular shape, having a red printed label bearing the word "POISON" and a statement of the amount of mercury bichloride in each tablet. Each tablet contains about 0.125 Gm. (2 grains) of mercury bichloride.

MEDICAL PROPERTIES.—Antiseptic, disinfectant, caustic, and antispirochetal.

LOCAL ACTION.—Applied on the unbroken skin, mercury bichloride produces little irritation unless kept there for some time. On wounds and mucous surfaces, weak solutions are antiseptic and disinfectant; if concentrated, they are caustic. Solutions are readily absorbed, and they may produce poisonous effects. Mercury bichloride coagulates albumin and combines with the protoplasm of the cells. This precipitated albuminate of mercury is, however, soluble in an excess of albumin or in sodium chloride solutions. For the sake of convenience, corrosive sublimate tablets are now prepared, having tartaric acid, citric acid, ammonium chloride, etc., as a component to render the mercury more soluble and to prevent its precipitation as an insoluble compound. The large bichloride tablets are a convenient form for making extemporaneous solutions. Each tablet contains 8 grains of mercury bichloride. One tablet dissolved in 1,000 cc. of water gives a 1:2,000 solution. These tablets are frequently colored blue with small quantities of aniline dyes.

THERAPEUTICS.—Mercury bichloride is still used in antiseptic surgery. For disinfectant purposes a solution of 1:1,000 to 1:5,000 is employed as a general antiseptic. In dentistry its application as a mouthwash, although efficient, is not to be recommended; the superficial epithelial cells of the mucous lining of the mouth are readily de-

stroyed by its prolonged use. As a disinfectant for putrescent root canals and for abscesses and fistulas, a slightly acid solution of 1 part in 1,000 parts of a solution of hydrogen peroxide is one of the most effective agents at our command. It is also recommended for the disinfection of periclasia pockets (a glass syringe with a platinum point should be used).

℞ Hydrarg. Bichlorid. 0.1 Gm. gr. iss
Liq. Hydrog. Perox. q.s. 240.0 cc. f℥ viii
M. et ft. sol.
Sig.: Apply.

Administered internally, corrosive sublimate, like all other mercurials, enters the blood very rapidly, but seems to have no direct action on it. It quickly leaves the blood and enters the tissues, where it may remain indefinitely; here it manifests its specific influence on syphilis. As it is very slowly excreted, the secretions of all the glands (saliva, milk, sweat, urine, and bile) are stimulated. It is a powerful sialogogue, causing an increased flow of saliva which contains mercury. The saliva has a metallic taste, and acts as an irritant on the mucous membrane of the mouth, which may result in a typical ulceration, known as mercurial stomatitis.

Toxicology.—At present it is assumed that when 4 milligrams (1/16 grain) of mercury bichloride per kilogram (about 2¼ pounds) of body weight has entered the body, death regularly occurs, and that we have no adequate grounds for believing that death is preventable by any known form of treatment. If swallowed in poisonous doses, intense pain in the throat, stomach, and bowels is produced, accompanied by nausea, retching, bloody vomiting, diarrhea, cold sweats, and difficult respiration followed by convulsions and death. The treatment should be primarily directed to relieve the gastroenteritis; white of eggs beaten up with water, or milk, to form insoluble albumin compounds, should be freely given, or wheat flour may be substituted. The stomach should be washed out before the acid contents render the albumin compounds soluble. Practical therapeutic efforts should be directed toward the accomplishment of two things: (1) mechanical removal of the poison from the lumen of the alimentary tract; (2) antidoting the poison after it reaches the general circulation. The after effects should be treated with opiates, counterirritants, and demulcent drinks. Two grains have been known to kill a man in half an hour, and an infant died from the constitutional effects of corrosive sublimate sprinkled on an excoriated sur-

face. The best systemic treatment is gastric lavage with a 5 per cent solution of sodium formaldehyde sulfoxylate.

MERCURIC CYANIDE; HYDRARGYRI CYANIDUM: $Hg(CN)_2$.

It forms colorless crystals, without odor and with a bitter, metallic taste. It is soluble in about 12 parts of water, in 15 parts of alcohol, and in 3 parts of boiling water. Mercuric cyanide resembles corrosive sublimate closely in its action, but it is less active and much less irritating. It does not attack steel instruments very readily.

YELLOW MERCURIC OXIDE; HYDRARGYRI OXIDUM FLAVUM (HYDRARG. OXID. FLAV.), HgO, U.S.P. (Yellow Precipitate).

USES.—Antiseptic and stimulant.

PREPARATIONS.—

Yellow Lotion; Lotio Flava (Lot. Flav.), N.F. (Yellow Wash, Aqua Phagedaenica Flava).—A suspension of mercuric oxide produced by the action of limewater on mercury bichloride.

USES.—Mercurial antiseptic for local application.

Black Lotion; Lotio Nigra (Lot. Nig.), N.F. (Black Wash, Aqua Phagedaenica Nigra).—A suspension of mercur*ous* oxide, Hg_2O, produced by the action of limewater on mild mercurous chloride.

USES.—Mercurial antiseptic for local application.

Yellow Mercuric Oxide Ointment; Unguentum Hydrargyri Oxidi Flavi (Ung. Hydrarg. Oxid. Flav.), U.S.P.—Yellow mercuric oxide (1%) in wool fat, liquid petrolatum, yellow wax, and petrolatum.

USES.—Mercurial antiseptic for the eye.

AMMONIATED MERCURY OINTMENT; UNGUENTUM HYDRARGYRI AMMONIATI (UNG. HYDRARG. AMMON.), U.S.P. (White Precipitate Ointment).

Ammoniated mercury (5%) in white petrolatum, white wax, and hydrous wool fat.

USES.—Mercurial antiseptic for local application.

Organic Mercury Preparations

MERCUROCHROME

Mercurochrome-220, Soluble.—It is the disodium salt of dibromoxymercury-fluorescein. It occurs as iridescent green scales or as granules readily soluble in water, with the formation of a deep cherry-red solution. This compound contains about 25 per cent of mercury in organic combination with the dye molecule. In this form, the

mercury, while retaining most of its germicidal value, does not show the chemical reactions of the true mercury salts, that is, it is not precipitated by alkali or by ammonium sulfide, nor does it precipitate protein; and because of this fact, relatively concentrated solutions of the drug may be used on the mucous membrane without irritation. It is not suited for root canal purposes, as it will stain the tooth more or less permanently a deep pink hue.

As a preoperative skin disinfectant, mercurochrome may be employed as a substitute for tincture of iodine. A 2 per cent solution for this purpose may be prepared as follows: Dissolve 2 grams mercurochrome in 35 cc. distilled water, add 55 cc. of 95 per cent alcohol and 10 cc. acetone. (Scott's Solution.)

OFFICIAL PREPARATION.—

MERBROMIN; MERBROMINUM, N.F.

It contains about 25 per cent of mercury and about 20 per cent bromine. It occurs as iridescent, green scales or granules, freely soluble in water and practically insoluble in alcohol.

THERAPEUTICS.—A moderately active antiseptic.

Solution of Merbromin; Liquor Merbromini (Liq. Merbrom.), N.F. —A two per cent solution of merbromin in distilled water.

THERAPEUTICS.—Topical antiseptic.

Surgical Solution of Merbromin, Liquor Merbromini Chirurgicalis (Liq. Merbrom. Chir.), N.F.

A 2 per cent solution of merbromin in water (35%), in acetone (10%), and alcohol (55%).

THERAPEUTICS.—A topical antiseptic for use on the skin and abraded areas.

METAPHEN

METAPHEN, N.N.R.—$C_6H_2.CH_3.O.NO_2.Hg$.

It is a mercuri-ortho cresol compound of a yellowish color, odorless and tasteless. It is soluble in dilute aqueous sodium hydroxide solution and in ammonium hydroxide solution.

Metaphen in the form of a tincture or as germicidal solution is claimed to be more powerful than mercuric chloride and many of the newer organic mercury compounds. It is stated to be relatively nontoxic and nonirritating to mucous membrane or the skin. It will not attack metallic instruments and rubber. It is employed as a mouthwash in a 1:5,000 solution and in the treatment of ulceromembranous gingivitis, etc., in a 1:1,000 solution applied.

PREPARATIONS.—

Solution Metaphen, 1:500; N.N.R.—Metaphen, 1 part, dissolved in water by means of sodium hydroxide to form the sodium salt of metaphen.

Solution Metaphen, 1:2,500; N.N.R.—Metaphen, 1 part, dissolved in 2,500 parts of water containing 0.33 per cent each of sodium bicarbonate and sodium carbonate to form the sodium salt of metaphen.

Tincture of Metaphen, 1:200; N.N.R.—It contains metaphen 0.5 Gm. dissolved in a mixture of acetone, 10 cc., water, 40 cc. and alcohol, 50 cc.

MERTHIOLATE

MERTHIOLATE, N.N.R.—$C_2H_5Hg.S.C_6H_4COONa$.

It contains about 49 per cent of mercury in an organic combination.

USES.—Merthiolate is a reliable germicide for many nonsporulating bacteria and fungi. Like the other mercurial antiseptics, its action on sporulating organisms is questionable.

DOSAGE.—Used in dentistry as a local antiseptic on the skin and mucous membrane in a 1:1,000 solution.

PREPARATIONS.—

Merthiolate Ointment, N.N.R.—It contains merthiolate 0.05 per cent in a petrolatum base.

Merthiolate Solution, N.N.R.—One gram of merthiolate and 1 Gm. of monoethanolamine in 1,000 cc. of water, buffered with 1.4 Gm. of sodium borate in 1,000 cc. and containing sodium chloride to make the solution approximately isotonic.

Tincture of Merthiolate, N.N.R.—Contains merthiolate, 0.1 Gm., and monoethanolamine, 0.1 Gm., dissolved in alcohol, 50 cc.; acetone, 10 cc., and water, sufficient to make 100 cc.

MERPHENYL NITRATE

MERPHENYL NITRATE (BASIC), N.N.R.

A molecular compound of phenylmercuric nitrate and phenylmercuric hydroxide—$C_6H_5HgNO_3.C_6H_5HgOH$.

USES.—Antiseptic for the skin and mucous membranes, applied as the solution. A good fungistatic agent for drugs in solution in a 1:10,000 concentration.

PREPARATION.—

Merphenyl Nitrate (Basic) Solution, 1:1,500; N.N.R.—An aqueous solution of basic phenylmercuric nitrate 0.067 per cent (1:1,500), with boric acid 0.1 per cent.

Organic Silver Compounds

A number of compounds of silver with organic acids, which for a short time were inclined to be considered equal in their action to silver nitrate, have appeared on the market. Prominently among these salts are silver citrate, and silver lactate. Both salts were introduced by Credé. Silver citrate is a white powder, soluble in 3,000 parts of water; it is nonirritating, and has been employed as a dusting powder on wound surfaces. Silver lactate, a white powder, is soluble in 15 parts of water; it is caustic even in diluted solutions. Both silver salts and their solutions must be protected from light; they stain the tissues black. Silver acetate, another compound of this group, has never been employed therapeutically. to any extent. Credé further recommended a form of colloidal silver known as *collargol*—metallic silver in an extremely fine state of division, which is soluble in water and albuminoid fluids.

Silver Citrate; Argenti Citras; $Ag_3C_6H_5O_7$, A.D.R.—The normal silver salt of citric acid.

DOSAGE.—Solutions of from 1:4,000 to 1:10,000 used locally.

Silver Lactate; Argenti Lactas; $Ag_3C_3H_5O_3.H_2O$, N.N.R.—The normal silver salt of lactic acid.

DOSAGE.—From 1:100 to 1:2,000 applied locally.

STRONG PROTEIN SILVER; ARGENTUM PROTEINICUM FORTE (ARG. PROT. FORT.), U.S.P. (Argento-Proteinum Forte, U.S.P. X, Strong Silver Protein, Strong Protargin).

A colloidal compound of silver oxide and protein containing about 8 per cent of silver. Strong silver protein usually occurs as a brown powder, freely but slowly soluble in water (about 1:2), forming colloidal solutions. It is also soluble in glycerin, but insoluble in alcohol and oils. Solutions are dark in color; they are best prepared by sprinkling the substance on distilled water and allowing solution to take place spontaneously. It is used on mucous membranes in solution varying in concentration from 1:10 to 1:1,000.

MILD PROTEIN SILVER; ARGENTUM PROTEINICUM MITE (ARG. PROT. MIT.), U.S.P. (Mild Silver Protein, Mild Protargin).

Contains from 19 to 23 per cent of silver. Mild silver protein occurs in dark brown or almost black lustrous scales or granules freely soluble in water, forming deeply colored colloidal solutions. It is also soluble in glycerin, but insoluble in alcohol and oils. It is used on mucous membranes in solution varying in concentration from 1 to 20 per cent. *Caution*—Solutions of Mild Protein Silver should be freshly prepared and should be dispensed in amber-colored bottles (U.S.P.).

The percentage of silver present in the more important silver compounds is:

	PERCENTAGE OF SILVER
Silver nitrate	63.6
Silver citrate	60.8
Silver lactate	51.5
Mild Protein Silver, U.S.P.	19.0 to 23.0
Neosilvol	18.0 to 22.0
Strong Protein Silver, U.S.P.	7.5 to 8.5

Of all the previously named organic silver compounds, the mild and the strong silver proteins are by far the most favored ones. They deserve to be recommended as general antiseptics. For irrigation of the maxillary sinus, weak solutions of from 0.5 to 1 per cent are employed, while for alveolar abscesses from 10 to 20 per cent solutions should be used. The solutions should always be freshly prepared with cold water and kept in a colored bottle; heat and light cause rapid oxidation of the solutions, which are then strongly irritating to the tissues.

Bismuth Preparations

BISMUTH SUBNITRATE; BISMUTH SUBNITRAS (BISM. SUBNIT.), U.S.P. (Basic Bismuth Nitrate).

A basic bismuth nitrate of varying composition, yielding at least 79 per cent of Bi_2O_3.

SOURCE AND CHARACTER.—It is a white heavy powder, consisting of a mixture of bismuth oxide, nitrate, and hydrate, and containing about 80 per cent of pure bismuth oxide. It is odorless and almost tasteless, insoluble in water or alcohol, but soluble in nitric and hydrochloric acid. It is *incompatible* with potassium iodide, calomel, salicylic acid, tannic acid, and sulfur.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

MEDICAL PROPERTIES.—Astringent, mild antiseptic, and protective.

THERAPEUTICS.—Bismuth subnitrate is principally used as an internal astringent in diseases of the gastrointestinal canal and as a dusting powder on wound surfaces. For the latter purpose it is useful, as it readily diminishes the secretions of the wound. A number of fatal poisonings have been recorded in which bismuth subnitrate was used in large quantities as dusting powder or in the form of Beck's bone paste. Bismuth poisoning manifests itself in the mouth by a distinct bluish-black line about the gingival margin, salivation, and swelling of the gingiva and tongue.

Bismuth subnitrate is used in the form of an unctuous injection (bismuth subnitrate, 10 parts; oil of cotton seed or oil of sesame, 15

parts; spermaceti, 30 parts) in radioscopy. The liquefied material is injected into the cavity, and the x-ray picture shows a deep black shadow which distinctly outlines the normal or pathologic cavity, fistula, etc. Occasionally, general poisoning is observed with this bismuth suspension; i.e., the insoluble bismuth subnitrate is changed by the tissue fluids into a soluble nitrite which gives it the toxicity.

During the first world war bismuth paste, as introduced by Morison, was lauded as a useful antiseptic. It is made by mixing bismuth subnitrate (1 part) and iodoform (2 parts) with sufficient liquid paraffin oil to make a thick paste of such consistency that it may be readily spread in a thin layer with the help of a spatula or spoon. This mixture, which is commonly known as "B.I.P.," was first recommended for the treatment of infected war wounds in which suppuration was already established. Later it was used to a considerable extent for the treatment of fresh wounds, partly owing to its ease of application and the fact that frequent redressing was usually unnecessary, although adequate provision had to be made for free drainage. In most cases treated with this paste a heavy black line of bismuth sulfide was observed along the gingival margin and, at times, more or less severe types of bismuth stomatitis were observed. Bismuth salts have a very limited usefulness in dentistry.

BISMUTH SUBCARBONATE; BISMUTH SUBCARBONAS (BISM. SUBCARB.), U.S.P. (Basic Bismuth Carbonate).

A basic bismuth carbonate yielding not less than 90 per cent of Bi_2O_3. White or nearly white, odorless, tasteless powder. Insoluble in water or alcohol.

USES.—Similar to those of other insoluble salts of bismuth as a protective and healing agent for wounds, diarrheas, etc., and in x-ray work. It is to be preferred to the subnitrate.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

BISMUTH SUBGALLATE; BISMUTHI SUBGALLAS (BISM. SUBGAL.), N.F. (Basic Bismuth Gallate, Dermatol).

A basic bismuth gallate yielding when dried for three hours at 100° C. between 52 and 57 per cent of Bi_2O_3. A bright yellow, odorless, tasteless powder which is insoluble in water or alcohol.

USES.—Similar to those of bismuth subcarbonate, over which it has no advantage.

DOSAGE.—1 Gm. (15 grains) (N.F.).

THE ACIDS

All inorganic and most organic acids possess more or less antiseptic action. Many of the acids also act as astringents when applied in weak solutions, and as caustics when used in a pure state. All inorganic acids, with the exception of phosphoric acid, the chlorine substituting fatty acids, and many of the aromatic acids, provided they are readily soluble in water, act as precipitants of albumin. The inorganic acids, with the exception of boric acid, cannot be used as antiseptics in the oral cavity, as they attack the tooth structure.

Hydrochloric acid is frequently administered in diluted form in disturbances of gastric secretion. It should never be taken through a glass tube as so frequently recommended by the physician. When taken through a tube, a part of the acid flows over the tongue against the palatal surfaces of the upper incisors, and it is retained in this region for some time. Thereby the enamel of these teeth is often destroyed. If mineral acids are to be taken orally, they should be diluted and swallowed quickly. Immediately thereafter, the mouth should be thoroughly rinsed twice or three times with a solution of sodium bicarbonate.

The investigation of the germicidal action of acids and bases has brought to light many interesting facts. A few of the general conclusions drawn are as follows:

The germicidal action of solutions of acids runs parallel to their degree of dissociation—that is, parallel to the number of hydrogen ions contained in the unit volume of solution. The anions, and also the undissociated radicals as hydrofluoric, nitric, and trichloracetic acid, may also have a toxic effect on bacteria. This toxicity, when compared with the germicidal effects of the hydrogen ions, becomes insignificant with progressive dilution.

The same metals attached to different acid radicals have different effects: antiseptic, astringent, to caustic. The chlorides and the nitrates form the most corrosive acids, the sulfates are milder, while the iodides and bromides are still less irritating. The mildest salts are those formed from the organic acids.

Many of the organic acids are classified as aromatic compounds and others as caustics, and consequently they are discussed under their respective headings. (See Antiseptics of the Aromatic Series, and Caustics.)

Inorganic Acids

Boric Acid; Acidum Boricum (Acid. Boric.), U.S.P. (Boracic Acid); H_3BO_3.

SOURCE AND CHARACTER.—It is usually prepared from native borax (sodium borate). It is a light, white, very fine powder, unctuous to the touch, or translucent, colorless scales, odorless, and having a faintly bitter taste. It is soluble in 18 parts of water, 18 parts of alcohol, 4 parts of glycerin, and readily soluble in boiling water.

DOSAGE.—A watery solution, ranging from 2 per cent to a saturated solution (4%). Externally used as dusting powder.

MEDICAL PROPERTIES.—Antiseptic and astringent.

PHARMACODYNAMICS.—Its antiseptic action is due to (1) the liberated H-ions and (2) the action of the boron ion which acts as a colloid precipitant.

THERAPEUTICS.—Boric acid is a mild, nonirritating antiseptic and astringent to mucous membranes; it is the only mineral acid which does not affect tooth structure. In the form of a dusting powder, as a glycerite or an ointment, and in saturated aqueous solutions, it is widely used as an external antiseptic. It is apparently more active on molds and fission fungi than on pathogenic bacteria. In the form of a saturated solution, it is of service in washing out the antrum or other body cavities. Because of its very mild acidity it is largely used as the principal component of many proprietary mouthwashes in a 2 to 4 per cent solution. As a dusting powder on large wound surfaces, boric acid must be used with caution, to prevent too rapid absorption. A few cases of poisoning, of which two have ended fatally, have resulted from the too liberal use of this antiseptic. Boric acid is sometimes added to foods as a preservative, which has given rise to heated discussions in regard to its deleterious effects on the health of the consumer. Its use for such purposes is prohibited in the United States.

PREPARATIONS.—

Glycerite of Boroglycerin; Glyceritum Boroglycerini (Glycer. Boroglyc.), U.S.P.—It is a compound formed by heating boric acid in glycerin, which is then dissolved in glycerin. It contains 31 per cent of boric acid.

Boric Acid Ointment; Unguentum Acidi Borici (Ung. Acid. Bor.), U.S.P.—Boric acid (10%) in wool fat, white wax and white petrolatum.

N.F. Antiseptic Solution; Liquor Antisepticus N.F. (Liq. Antisep. N.F.), N.F.

It contains 2.5 per cent boric acid, 0.05 per cent chlorothymol, 0.05 per cent thymol, and is flavored with eucalyptol, menthol, methyl salicylate, and thyme. This solution is apparently intended to replace

the many proprietary compounds of a similar nature. If this is true, it is a poor substitute. Its taste is most disagreeable, and its combination is not in accordance with modern conceptions of an antiseptic solution. Strictly speaking, *Liquor Antisepticus* is a toilet preparation of limited therapeutic value. It is used as a mouthwash diluted with equal parts of warm water.

THE ALKALIES

The antiseptic action of the alkalies depends principally on their power of disorganizing albumin by dissolution. They are, therefore, closely related to the caustics. The alkali salts which liberate oxygen or halogens during their dissociation—zinc peroxide, sodium hypochlorite, etc.—act principally through their negative ions. The hydrates of the alkalies are the strongest and the carbonates are the weakest antiseptics of this group. The soaps (alkaline oleates) are weak antiseptics; they act principally as detergents by virtue of their solvent power on fats, etc. Soaps are often combined with specific antiseptics (sulfathiazole, phenol, tar, etc.), and then they become important antiseptic agents. Liquid soap, containing alcohol with the addition of an active antiseptic, is a valuable hand disinfectant; it is to be preferred for the operating room over the ordinary cake soap. Lime, in the form of freshly slaked lime, or milk of lime, is a powerful disinfectant for excreta, provided it is used in at least 20 per cent solutions. Its action is decidedly more powerful when combined with chlorine (chlorinated lime). Bicarbonates of sodium and potassium cannot be classed as antiseptics; sodium chloride, in a 0.9 per cent solution (physiologic salt solution), heated to body temperature, may be used as a temporary mouthwash when an absolute, neutral, mild lotion is required. Ammonia is a weak antiseptic; its powerful irritating properties (see Irritants and Counterirritants) prohibit its use for antiseptic purposes. The hydroxides of potassium and sodium are powerful caustics and must be used with extreme care.

The disinfectant action of bases—as calcium, sodium, lithium, and ammonium hydroxide—runs parallel to the number of free hydroxyl ions contained in the unit volume of the solution.

SODIUM BORATE; SODII BORAS (SOD. BOR.), $Na_2B_4O_7.10H_2O$, U.S.P. (Borax, Sodium Tetraborate).

SOURCE AND CHARACTER.—It forms colorless crystals or a white powder, odorless, and having a sweetish, alkaline taste. It is soluble in 16 parts of water, very soluble in glycerin, but insoluble in alcohol.

USES.—Antiseptic, detergent, and alkaline. It should not be used internally because of its toxicity.

THERAPEUTICS.—Sodium borate is a mild antiseptic, and is freely employed in diseases of the mucous membranes. It is an important component of the widely used Dobell's solution. In a saturated solution in water or alcohol it prevents rusting and when combined with solutions of formaldehyde, it is found to be very serviceable for the sterilization of metallic instruments.

DOBELL'S SOLUTION (N.F.)

℞	Sodium Borate	15 Gm.
	Sodium Bicarbonate	15 Gm.
	Liquefied Phenol	3 cc.
	Glycerin	30 cc.
	Water, ad	1000 cc.

STERILIZING FLUID FOR INSTRUMENTS

℞	Solution of Formaldehyde	20 cc.
	Sodium Borate	18 Gm.
	Liquefied Phenol	4 cc.
	Water, q.s. ad	100 cc.

HARD SOAP; SAPO DURUS (SAPO DUR.), U.S.P. (Sapo, U.S.P. X, Soap, Castile Soap); Soda Soap.

A white or whitish solid or powder, having a faint, peculiar odor and an alkaline taste. Soluble in water and alcohol.

USES.—Used chiefly as a detergent and in solution as a vehicle for liniments.

MEDICINAL SOFT SOAP; SAPO MOLLIS MEDICINALIS (SAPO MOLL.), U.S.P. (Green Soap).

Prepared from vegetable oils and potassium hydroxide. A soft, unctuous, yellowish-white to brownish-yellow mass, having a slight, characteristic odor and an alkaline taste.

USES.—Dissolved in diluted alcohol, it is employed in the preparation of various liniments, and is a detergent.

Liniment of Soft Soap; Linimentum Saponis Mollis (Lin. Sapon. Moll.), U.S.P. (Tincture of Green Soap).—Soft soap (65%) and oil of lavender in alcohol. Absolute alcohol content about 30 per cent.

Compound Liniment of Soft Soap; Linimentum Saponis Mollis Compositum (Lin. Sapon. Moll. Comp.), N.F. (Compound Tincture of Green Soap).—Soft soap (15%), juniper tar (2%) and alcohol. Absolute alcohol content about 77 per cent.

THE HALOGENS AND THEIR DERIVATIVES

The antiseptic value of the halogens—bromine, chlorine, fluorine, and iodine—depends on the chemical reaction which ensues when they are brought in contact with the cell proteins; they substitute their own atoms for the hydrogen atoms of the albumin molecule and thereby destroy the latter. The halogen acids which are formed on hydrolysis act as precipitants of albumin. The halogens are rarely used as antiseptics or disinfectants in solid form or as gases. In aqueous solution they are powerful disinfectants, and are used as such, especially chlorine. Bromine and fluorine or their compounds are not employed as antiseptics. Sodium fluoride possesses powerful antiseptic properties; its use has been suggested as an addition to tooth preparations for the control of dental caries, and it is largely employed in the industries for checking fermentation in manufacturing yeast, in distilleries, breweries, etc. Head introduced ammonium bifluoride as a "tartar solvent." Chlorine in the form of chlorinated lime has found a wide field of application as a disinfectant for dejecta, bedding, etc., and incidentally as a bleaching agent. Iodine in compound aqueous solutions and as thymol iodide possesses powerful antiseptic properties; at one time the latter compound was recommended as an antiseptic for root canal treatment, but it has never come into general use. Tincture of iodine applied as an antiseptic is extensively used on the mucous membranes. Surgeons utilize the powerful antiseptic properties of iodine in alcoholic solution with marked success as a means of asepticizing the skin prior to an incision. The technique is very simple. The field of operation is cleansed in the ordinary way with hot water and soap, and the tincture of iodine is painted over the surface within the region of the incision in the form of a broad band. The iodine solution keeps the bacteria and their debris fixed to the surface during the operation. To stimulate rapid cell proliferation, the slightly irritating property of tincture of iodine is useful. The action of its alcoholic component is responsible for the light form of hyperemia which, together with the iodine, favorably influences the healing of the wound; and usually a clean, small scar results. Iodine achieved its greatest triumph through its many aromatic compounds, of which iodoform is the typical representative. The various solutions of iodine are principally employed as irritants (see Irritants and Counterirritants), while its salts are largely used as specifics in the third stage of syphilis and to influence metabolism favorably. (See Alteratives.)

Iodine-Liberating Compounds

IODOFORM; IODOFORMUM (IODOF.), CHI_3, N.F. (Triiodomethane).

SOURCE AND CHARACTER.—It is usually obtained by the action of iodine on alcohol in the presence of an alkali or alkali carbonate. It is a fine lemon-yellow powder or small crystals, possessing a very persistent and penetrating odor and a disagreeable taste. It is practically insoluble in water, but soluble in about 60 parts of alcohol, 8 parts of ether and fixed and volatile oils. It is *incompatible* with calomel, mercuric oxide, silver nitrate, tannin, and balsam of Peru.

MEDICAL PROPERTIES.—Antiseptic, irritant, and obtundent.

THERAPEUTICS.—Iodoform is the wound antiseptic par excellence. It has objections which materially limit its use in surgery. Iodoform, per se, does not possess antiseptic properties, in spite of its high iodine component (96 per cent); ordinarily it is not even sterile. Its very penetrating and persistent odor, which invades everything with which it comes in contact, makes its use disagreeable to patient and practitioner alike. Iodoform is easily decomposed; when it is dissolved in alcohol, ether, or fatty oils, it readily liberates free iodine. The secretions of a purulent wound contain large quantities of fatty substances which dissolve and decompose iodoform. Iodine *in statu nascenti* acts as a powerful antiseptic. The products of bacterial activity are oxidized by iodoform, and hence it acts as a deodorant. Its slightly irritating properties stimulate cell proliferation and reduce the migrating power of the leucocytes. On sensitive skin it may cause various exanthematous eruptions. When large quantities of iodoform are quickly absorbed, a toxic reaction results; as the iodoform action is better understood, intoxications are rare at present.

Iodoform is a sovereign remedy to keep clean, fresh wounds aseptic and to check wound secretions. In abscess cavities and on ulcerating surfaces, or in regions which are easily infected from their surroundings—the mouth—it acts as an extremely serviceable bacteriostatic. It quickly cleans and deodorizes a foul wound; it is obtundent and by irritation favors granulation.

The opinions regarding the use of iodoform in dentistry are divided. Some practitioners have lauded it very highly, especially as an excellent antiseptic in root canal therapy, while others condemn it absolutely. In the form of iodoform gauze it is superior to any other known iodine preparation for the dressing of foul ulcers, deep-seated periclasia pockets, purulent alveoli, certain disturbances arising from the difficult eruption of a lower third molar, etc. For the treatment of the purulent stages of pyorrhea, iodoform as a paste or an emulsion

is still employed by many practitioners. As a component of a permanent root canal filling it is favored by many, although it is difficult to understand what purpose it should serve in this connection.

Whenever the odor of iodoform is removed, its composition is chemically altered and its therapeutic action is largely destroyed. To overcome the many drawbacks of iodoform, chemists have endeavored to create iodine compounds which are free from these objections. So far no perfect substitute has been produced, although a few of the more recent compounds answer the purpose fairly well. Aristol—thymol iodide—has been widely employed for some time; it is very readily decomposed, but its iodine component is materially less than that of iodoform.

THYMOL IODIDE; THYMOLIS IODIDUM (THYMOL. IOD.), U.S.P. (Aristol.).

It is a light reddish-yellow bulky powder, with a slight aromatic odor, containing 43 per cent of iodine. It is insoluble in water and glycerin, but readily soluble in alcohol, chloroform, ether, and volatile and fatty oils. It is supplanting iodoform in dental practice.

Chlorine-Liberating Compounds

CHLORINATED LIME; CALX CHLORINATA (Bleaching Powder).

Chlorinated lime is often improperly called chloride of lime. It is a mixture of calcium hypochlorite, calcium chloride, lime, and water, and it should contain not less than 30 per cent of available chlorine. It is a white or grayish-white powder, with the odor of chlorine, and giving off chlorine gas in the air, especially in the presence of an acid. It is only partially soluble in water. It should be preserved in air-tight containers, in a cool and dry place. Chlorinated lime is used in the preparation of the various chlorinated solutions, as a bleaching agent, and as a disinfectant on a large scale. For the latter purposes it is best employed in the form of milk of lime, with an excess of acid; it must be used liberally if complete success should be insured. As a deodorizer of the oral cavity in the form of a tooth powder it should not be used.

PREPARATIONS.—

Solution of Sodium Hypochlorite; Liquor Sodii Hypochloritis (Liq. Sod. Hypochlor.), U.S.P.—About 5 per cent NaOCl.

USES.—This preparation should be diluted with ten parts of water before using in the Carrel technique. It is a germicide and deodorant.

Diluted Solution of Sodium Hypochlorite; Liquor Sodii Hypochloritis Dilutus (Liq. Sod. Hypochlor. Dil.), N.F. (Liquor Sodae

Chlorinatae Chirurgicalis, U.S.P. X, Modified Dakin's Solution).—NaOCl (about 0.48%).

USES.—This solution is an active germicide and deodorant for infected wounds for irrigation by the Carrel method or with a syringe. It does not precipitate proteins, but because of its alkalinity it dissolves necrotic tissue and removes foul odors by oxidation. It is used undiluted for irrigation, diluted with 3 to 5 parts of water as a mouthwash or spray, and a dilution of 10 to 20 parts for continuous irrigation.

CHLORAMINE-T; CHLORAMINA-T (CHLORAM.-T), $C_6H_4.CH_3.SO_2NNaCl.3H_2O$, U.S.P.

It is a white, crystalline powder, having a slight chlorous odor. It is freely soluble in water, a saturated solution at room temperature containing about 12 per cent of the salt. One part of chloramine dissolves in two parts of boiling water. It is insoluble in benzene, ether, and chloroform.

Chloramine is an active germicide much like the hypochlorites; it is, however, less irritating. It has the advantage over mercuric chloride, zinc chloride, etc., that it does not coagulate or precipitate proteins, such as blood serum, and it is practically nontoxic. It is used in a 1 to 2 per cent solution for irrigating infected wounds.

DICHLORAMINE-T; DICHLORAMINA-T (DICHLORAM.-T), $C_6H_4.CH_3.SO_2NCl_2$, N.F. (Dichloramina). Paratoluensulfondichloramide.

It is a yellowish-white crystalline powder, having a sweetish, rather pungent chlorous odor and containing a little more than 29 per cent of active chlorine. It melts at about 80° C. (176° F.). In the solid state, when kept in the dark it is stable. It is practically insoluble in water, but is readily soluble in most organic solvents, i.e., chloroform, benzene, eucalyptol, etc. It quickly reacts, undergoing decomposition with evolution of nascent chlorine when brought into contact with most organic substances, such as acids, alcohol, and the amines, with hydrogen dioxide, water, etc., and certain metals. It should be stored in small amber-colored glass-stoppered bottles and protected from heat.

The most satisfactory solvent for dichloramine-T is an oily compound known as "chlorcosane." It is a bland, heavy, viscid oil, having a slight yellowish color, and is prepared from hard paraffin melting at about 50° C. (122° F.) by replacing a part of its hydrogen by chlorine. Chlorcosane does not contain any "free" chlorine, although it absorbs from 45 to 55 per cent of its own weight. The chlorine combines with the carbon of the paraffin somewhat in the

same manner as chlorine and sodium combine to form the ordinary inert sodium chloride. Chlorcosane, by the application of moderate heat, will readily dissolve 8 per cent of dichloramine-T, which is more than amply sufficient for dental purposes. Chloramine-T is more suited for dental purposes.

CHLORINATED PARAFFIN; PARAFFINUM CHLORINATUM (PARAFF. CHLORINAT.), N.F. (Chlorocosane).

A light yellow, or light amber, clear, thick, oily liquid; odorless and stable in air; insoluble in water; slightly soluble in alcohol; miscible with fat solvents.

USES.—Used as a solvent for dichloramine-T, which it dissolves to form an 8 per cent solution.

AZOCHLORAMID, A.D.R.—A product containing approximately 96 per cent of N, N-Dichlorazodicarbonamidine; $H_2N.ClN.CN.NC.NCl.NH_2$—An N-chloro derivative of azodicarbonamidine.

PROPERTIES.—Azochloramid occurs in bright yellow needles or plates. It possesses an odor suggestive of chlorine and has a burning taste. When pure it is odorless and practically tasteless. It is very slightly soluble in water, slightly soluble in glycerin and ether; soluble in alcohol; soluble (incompletely) in glacial acetic acid, acetone and ethyl acetate; very slightly soluble in chloroform; and nearly insoluble in carbon tetrachloride and liquid petrolatum.

USES.—Azochloramid liberates available chlorine more slowly than some other chlorine liberating compounds. It appears to be an effective germicide in the presence of pus, serum, or other organic matter. It has recently gained quite a reputation in root canal sterilization. It is used for this purpose on paper points dipped in triacetin 1:100. For other dressings and wound packing a triacetin solution 1:500 is used (A.D.R.). It has no superiority over chloramine-T.

SOLUTIONS WHICH EVOLVE NASCENT OXYGEN

Molecular oxygen, in its pure state or mixed with nitrogen and other gases in the form of air, does not manifest an inhibitory or destructive action on bacteria. For years chemists have been familiar with the powerful affinity of oxygen in its nascent state for other substances, which process is known as oxidation. Robin has experimentally shown that the therapeutic effect of a substance is greatly intensified if it is set free from its compound in a nascent state. This is especially true of many of the oxygen compounds.

Nascent oxygen may be furnished by two kinds of auto-oxidizers—one direct source is its allotropic form known as ozone, and the other

is represented by the many dioxides, chiefly hydrogen dioxide, and those of the alkali and alkaline earth metals. The nascent oxygen obtained from both sources is based on the same principle of formation:

Ozone = O—O—O, or O_3, is split up in $O_2 + O$ (nascent state).

A dioxide,* X—O—O, or XO_2, is split up in $XO + O$ (nascent state).

According to Nernst, the formation and the dissociation of ozone are illustrated by the following equation:

$$O_3 \rightleftarrows O_2 + O \text{ (Atomic)}$$
$$O_2 \rightleftarrows O^{--} + O^{--} \text{ (Ionic)}$$

Only one atom of the three atoms of the ozone molecule enters into active or atomic oxygen, the other two forming molecular or inactive oxygen. This very fact is true of the oxygen molecule of a dioxide—one atom is set free, while the other one remains combined with the metal in the form of an oxide. The ozone molecule and the dioxide molecule play the role of a single atom of oxygen in the reaction of oxidation. The amount of available oxygen in a dioxide depends on the degree of superoxidation of the original oxide. Ozone and the dioxides are endothermic compounds—that is, they require energy in the form of heat or electricity for their formation. They are easily decomposed, liberating again the same amount of energy in the form of heat which was absorbed in their formation. Ozone has, so far, been produced only as a gas, while the dioxides, with the exception of hydrogen dioxide, are solids. Ozone obtained from oxygen is usually produced by electric energy at the place of its consumption; it is an unstable gas which, for practical purposes, cannot be stored. The dioxides are usually fairly stable compounds which furnish nascent oxygen when so desired.

Atomic oxygen—oxygen in its nascent state—has a free valency; it cannot remain in that state, but energetically seeks to combine chemically. This powerful affinity for every oxidizable substance, including albumin, is known as oxidation, or, when accompanied by heat and light, as combustion. The antiseptic action of the oxygen-carrying metals depends on this fact. The nascent oxygen which is set free during ionization of the metallic dioxides is only slightly irritating to the soft tissue, while certain of the metallic derivatives act as caustics; this factor may prohibit the use of the latter compounds as wound antiseptics—sodium dioxide which forms sodium hydroxide.

*X represents any metal combined with two atoms of oxygen into a dioxide.

Of the many dioxides, hydrogen, calcium, magnesium, and zinc, and the perborate of sodium and, indirectly, ozone, are medicinally employed. Aside from its action as an antiseptic and sterilizing agent, nascent oxygen is employed as a bleacher of discolored teeth, and as an oxidizing or reducing agent in certain metallurgical processes in the dental laboratory. General medicine has made use of pure oxygen in the treatment of pulmonary diseases and as a restorative agent in accidents from general anesthesia or in poisoning with other gases.

HYDROGEN PEROXIDE; HYDROGENII PEROXIDUM (HYDROGEN DIOXIDE), H_2O_2.

Absolute hydrogen dioxide (about 99 per cent pure) is a thick, oily, colorless liquid, specific gravity 1.45, which does not congeal at - 22° F. (-30° C.). When brought in contact with certain metals or when exposed to sunlight or heat, it readily decomposes, often with explosive violence.

Besides the official 3 and 6 per cent solutions of hydrogen dioxide, higher concentrated solutions are found on the market. A 25 per cent solution of hydrogen dioxide in ether is known as *pyrozone*, and a 30 per cent solution in water is known as *perhydrol*. Pyrozone is put up in glass tubes containing a few cubic centimeters, while perhydrol is marketed in paraffin-lined bottles of various sizes. In opening a pyrozone tube great care should be exercised to prevent explosion by placing the tube in cold water and wrapping it in a wet towel before the end is broken off. Its contents must be transferred at once to a glass-stoppered bottle, provided with a ground cap, to prevent evaporation of the ether. Perhydrol solution is to be greatly preferred whenever a highly concentrated solution of hydrogen dioxide is desired. It is a chemically pure solution of H_2O_2 in distilled water, furnishing about 30 per cent by weight or 100 per cent by volume of available oxygen. It is absolutely free from acid, and may be diluted with water or alcohol to any desired strength. Solutions should preferably be made fresh when needed. If carefully preserved in the original container and stored in a cool place, perhydrol will retain its oxygen for some time.

Strong hydrogen peroxide solutions possess distinct styptic properties; they should not be used for such purposes in root canals, as their action on the hemoglobin of the blood may cause a discoloration of the tooth structure. Strong solutions of H_2O_2 (pyrozone, perhydrol) are powerful caustics, and they are used as such for the destruction of gum tissue, in fistulous tracts, in pockets of pyorrheal teeth, and as

styptics in severe hemorrhage. Andresen advocated perhydrol as the sovereign remedy in the treatment of hypersensitive dentin, especially in cervical cavities. The caustic solution requires careful handling, and the soft tissues have to be well protected by suitable napkins, a coating of petroleum jelly, etc. Burns from caustic H_2O_2 solutions are relieved by immediate washings with water and covering the burned surfaces with a mild ointment.

Solution of Hydrogen Peroxide; Liquor Hydrogenii Peroxidi (Liq. Hydrog. Perox.), U.S.P. (Liquor Hydrogenii Dioxidi, U.S.P. X, Solution of Hydrogen Dioxide).—H_2O_2 (about 3 per cent).

SOURCE AND CHARACTER.—Hydrogen dioxide was discovered by Thénardin in 1818, and was then known as oxygenated water. It was not used to any extent until Richardson, in 1860, introduced it into medicine. It is often found in small quantities in the atmosphere after heavy storms, or by any other process in which ozone is formed in the presence of water. Whenever solutions of certain dioxides—sodium dioxide or barium dioxide—are treated with diluted acids, it is readily formed according to the following equation:

$$BaO_2 + H_2SO_4 = H_2O_2 + BaSO_4.$$

For manufacturing purposes, usually barium dioxide is decomposed in the presence of sulfuric or phosphoric acid; the acids form an insoluble compound with the barium. For dental purposes an alkaline solution of hydrogen dioxide of various strengths may be extemporaneously prepared by dissolving sodium perborate in water. The official preparations are slightly acidulous aqueous solutions of hydrogen dioxide, containing, when freshly prepared, about 3 per cent by weight of the pure H_2O_2, which corresponds to about 10 per cent by volume of available oxygen. It has a specific gravity of 1.01 at 25° C. Its solutions are preferably stored in amber-colored bottles, away from light and sudden changes of temperature. It will gradually diminish in strength, and age, heat, and protracted agitation decompose it prematurely into water and oxygen. To preserve hydrogen dioxide solution, tannic acid and acetanilid in small quantities have been suggested. Of the former, about 1:6,000 and of the latter about 1:2,000 are necessary. Almost all the present commercial hydrogen dioxide solutions contain small quantities of acetanilid as a preservative.

It is *incompatible* with alkalies, albumin, ammonia, arsenous salts, phenol, chlorides, ferric salts, iodides, limewater, mercurous salts, nitrates, permanganates, sulfates, tartrates, and with most tinctures.

THERAPEUTICS.—The ideal external antiseptic for the body—the skin, external mucous membranes, and wound surfaces—is a substance

which destroys the bacteria and their products, but which will not harm the tissues of the host. Hydrogen dioxide approaches this ideal more closely than any other known antiseptic. When brought in contact with bacteria and their products, it acts as a powerful antiseptic and deodorant; it is not absorbed by the tissues, but by its reaction with the living cell it is split up into oxygen and water. This decomposition of hydrogen dioxide into molecular oxygen and water depends primarily upon the presence of the ferment catalase. This ferment is present everywhere in living animal tissues, especially in the blood and in all secretions and excretions, including the saliva. More or less all fungi and bacteria contain appreciable quantities of catalase. According to Heinz[1-2] its action on *Staphylococcus pyogenes aureus* and *Bacillus pyocyaneus* is recorded as follows:

SOLUTION OF HYDROGEN DIOXIDE

CONCENTRATION	STAPHYLOCOCCUS PYOGENES AUREUS			BACILLUS PYOCYANEUS		
	AFTER 24 HOURS	AFTER 48 HOURS	AFTER 72 HOURS	AFTER 24 HOURS	AFTER 48 HOURS	AFTER 72 HOURS
1.00 per cent	–	–	–	–	–	–
0.75 per cent	–	–	–	–	–	–
0.50 per cent	–	–	–	–	–	–
0.25 per cent	–	–	–	+	+	+
0.10 per cent	+	+	+	+	+	+

Much confusion seems to exist in the minds of some practitioners relative to the nature of acidity of hydrogen dioxide solutions. It should be remembered that normally the official solution of hydrogen dioxide is " a slightly acid, aqueous solution," the acidity corresponding to 10 cc. of a tenth-normal sulfuric acid for 100 cc. of the dioxide solution. Unfortunately, many of the commercial preparations contain much higher percentages of acid; as much as 26.6 cc. of a tenth-normal sulfuric acid has been found. While some of this acid content may be of an organic nature as a result of the decomposition of the preservative acetanilid added to the dioxide solution; nevertheless too high percentages of inorganic acids are frequently observed. Distinct marks of decalcification of tooth structure in the mouths of persons who use such acid compounds as a daily mouthwash have been observed, hence the importance of rendering the dioxide solution alkaline by the addition of small quantities of borax at the time of its use. An absolute neutral preparation may be obtained by the proper dilution of perhydrol with distilled water.

[1]Heinz: Handbuch der Experimentallen Pathologie und Pharmakologie, 1904.
[2]Harrow, B.: Textbook of Biochemistry, ed. 2, Philadelphia, 1940, W. B. Saunders Co., Chap. 6.

When hydrogen dioxide is brought in contact with blood, pus, serum, wound exudates, etc., it produces a heavy froth as a result of the catalytic action of the enzyme perioxidase, incidentally destroying the bacteria chemically and cleansing the wound surfaces mechanically. It acts as a strong deodorant by oxidizing the odorous gases arising from putrefactive processes. It should not be injected into pus cavities unless free drainage is established, as otherwise the free liberation of oxygen will force the infection into deeper structures. The same principle holds good in treating disturbances of the sinuses. To remove any obstructions, it should always be preceded in such cases by copious injections of physiologic saline solution heated to body temperature. On fresh granulating surfaces it should not be employed, as it tends to break down this new delicate tissue growth. In the various forms of stomatitis, and as a prophylactic in mercurial administration in syphilis, it deserves to be highly recommended, and rendered slightly alkaline as, for instance, by the addition of small quantities of borax.

Antiseptic Solutions

℞ Hydrarg. Bichlor. 0.06 Gm. gr. j
Liq. Hydrog. Perox. 60.00 cc. fℨ ij
M.

Sig.: Inject with a platinum-pointed syringe into the periclasia pockets.

Mouthwash for Vincent's Stomatitis

℞ Hydrarg. Bichlor. 0.09 Gm. gr. jss
Liq. Hydrog. Perox. 240.00 cc. fℨ viii
M.

Sig.: Dilute with equal parts of warm water as a mouthwash t.i.d.

Alkaline Oxidizing Mouthwash

℞ Sodii Boratis 8 Gm. ʒ ii
Liq. Hydrog. Perox. q.s. ad 240 cc. fℨ viii
M.

Sig.: Dilute with two parts of warm water as a mouthwash m. et n.

Acid Oxidizing Mouthwash

℞ Liq. Hydrog. Perox., U.S.P. 120 cc. fℨ iv

Sig.: Dilute with equal parts of warm water and use as a mouthwash.

CALCIUM DIOXIDE; CALCII DIOXIDUM, $CaCO_2$, CALCIUM PEROXIDE.

It is a light-yellow powder, odorless and tasteless, and containing about 13 per cent available oxygen. It is almost insoluble in water, but decomposes in the presence of moist organic matter. Weak acids readily decompose it into active oxygen and, usually, into insoluble calcium salts. Calcium dioxide has been advocated as a component of tooth powders for the purpose of liberating free oxygen in the mouth. It is not as well suited for this purpose as some of the other oxygen compounds. (See Preparations for the Mouth and Teeth.) As an internal remedy it is much lauded in acid dyspepsia and in summer diarrhea of children in 3- to 10-grain (0.2 to 0.6 Gm.) doses. Calcium dioxide is also largely used in the industries as a harmless preservative of foods, for aging beverages, as a preventive of seed diseases, etc.

MAGNESIUM DIOXIDE; MAGNESII DIOXIDUM, MgO_2; MAGNESIUM PEROXIDE, MAGNESIUM PERHYDROL.

It is a compound of magnesium dihydroxide and magnesium hydroxide, containing from 20 to 30 per cent of pure magnesium dioxide and averaging about 7 to 8 per cent available oxygen. It is a tasteless, white, amorphous powder, almost insoluble in water, but readily soluble in the presence of acid media. On account of its very mild alkalinity it is much lauded as a component of tooth powders (see Preparations for the Mouth and Teeth). Magnesium dioxide can be safely employed as a harmless disinfectant for the sterilization of drinking water.

STRONTIUM DIOXIDE; STRONTII DIOXIDUM, SrO_2; STRONTIUM PEROXIDE.

It contains about 80 per cent of pure strontium dioxide and furnishes about 12 per cent available oxygen. It is a voluminous white powder, almost insoluble in water, but parts with its oxygen in the presence of acids. In its general behavior it resembles closely calcium dioxide, and is used more or less for the same purposes.

SODIUM PEROXIDE; SODII PEROXIDUM, Na_2O_2.

It contains at least 90 per cent of sodium peroxide, equivalent to 18.4 per cent of available oxygen (A.D.R.). Sodium peroxide is a yellowish powder, which is readily soluble in water, developing great heat with the formation of caustic soda and the evolution of hydrogen dioxide. It is a very hygroscopic salt, and must be kept in tightly closed tin cans or glass bottles. To ascertain its efficiency, the following simple test may be employed: In a clean, dry test tube place

about 15 grains (1 Gm.) of the powder and add to it 15 to 30 minims (1 to 2 cc.) of water. If the specimen is of a good quality, enough oxygen should be generated to kindle a glowing splinter held at the mouth of the tube. Sodium dioxide is an exceedingly active oxidizer. It was introduced into dentistry in 1893 by Kirk for the purpose of bleaching teeth and for the treatment of putrescent root canals. For such purpose it is used as a dry powder. When sodium dioxide is fused, a solid mass is obtained, which is marketed as "oxone."

ZINC DIOXIDE; ZINCI DIOXIDUM, ZnO_2; ZINC PEROXIDE, ZINC PERHYDROL.

It is a superoxidized zinc oxide, containing about 45 per cent of pure zinc dioxide, and averaging about 8 per cent available oxygen. It is a yellowish-white powder, insoluble in water, but readily soluble in an acid medium. In the presence of moisture from a wound, moist skin surfaces, etc., it will slowly and continuously liberate active oxygen; the remaining zinc oxide is a nonirritating astringent. Hence its greatest field of therapeutic application lies in the domain of the dermatologist. It is widely used in skin diseases as a dusting powder or in the form of ointments, and it is much lauded for the treatment of burns. When applied in the form of an ointment it should never be mixed with an animal fat, as it will decompose the latter, forming rancid (fatty acid) compounds with the ointment base, which would, of course, irritate the skin or wound surfaces. Either liquid or solid petrolatum should be used for such purposes.

SODIUM PERBORATE; SODII PERBORAS (SOD. PERBOR.), $NaBO_3.4H_2O$, U.S.P.

It should furnish not less than 9 per cent of available oxygen. It is a white crystalline powder, readily soluble in about 40 parts of water, forming a colorless alkaline solution of hydrogen dioxide.

$$NaBO_3 + H_2O \rightarrow H_2O_2 + NaBO_2$$

With a rise of temperature and the addition of small quantities of acids, the solubility of sodium perborate is increased and solutions of various strengths may be readily obtained.

On account of their mild alkalinity, these freshly made solutions of hydrogen peroxide are especially useful in those diseases of the mucous membrane where the acidity of the ordinary hydrogen dioxide is an objection. As an addition to tooth powders, dusting powders, dry dressings, etc., sodium perborate is a valuable means of furnishing nascent oxygen in the presence of moisture. There are, however, idiosyncrasies to sodium perborate; it has proved extremely irritating

and toxic to certain patients. There is no objection to its use when the dentist is supervising the treatment and prescribing sodium perborate preparation for temporary use. It has no place, however, for general use as a dentifrice. Sodium perborate is used in a 2 to 4 per cent solution as a mouthwash in the treatment of Vincent's stomatitis, three times a day for mild cases to every hour for acute cases. The use of sodium perborate pastes in the oral cavity requires care to prevent chemical burns.[1]

℞ Sodium Perborate 90 Gm. ʒ iii
Sig.: One teaspoonful in a half glass of warm water as a mouthwash.

℞ Sod. Perbor. 120.0 Gm. ʒ iv
Ol. Menth. Vir. 0.3 cc. *m* v
M.
Sig.: 3 ss to half glass of warm water and use as a mouthwash every 3 hours.

NOTE: The above directions are suggested for acute cases. The following directions are suggested for chronic cases—Sig.: 3 ss to half glass of warm water as a mouthwash t.i.d.

As the improper use of Sod. Perbor. may give rise to "chemical burns" of the oral mucosa (Hirschfeld, Jour. A.D.A. 21: 776, May, 1934), its use should be confined to the supervision of the dentist or physician.

To recapitulate, the action of sodium perborate is due to (1) the liberated nascent oxygen, (2) the alkalinity, and (3) the metallic action of the boron radical.

N.F. Aromatic Sodium Perborate; Sodii Perboras Aromaticus N.F. (Sod. Perbor. Arom. N.F.); Sodium perborate with oil of peppermint and soluble saccharin.

This is a flavored sodium perborate preparation designed for dental purposes.

℞ Sod. Perbor. Arom., N.F. 120 Gm. ʒ iv
Sig.: The dentist should write directions to meet the needs of the patient.

POTASSIUM PERMANGANATE; POTASSII PERMANGANAS (POT. PERMANG.), $KMnO_4$, U.S.P.

SOURCE AND CHARACTER.—It appears in dark-purple or deep violet-red slender crystals, which have a bluish, metallic luster. It is odorless and has an astringent taste. It is readily soluble in 15 parts of water at ordinary temperature, very soluble in boiling water, while when brought in contact with alcohol it is decomposed. Its aqueous solutions, which react neutral to litmus paper, have a deep violet color when concentrated and a rich rose color when much diluted.

[1] Report to the Council, J. A. D. A. 22: 1761, Oct., 1935.

Readily oxidizable substances—as glycerin, citric acid, acetic acid, tartaric acid, sugar, gum, tannin, etc.—are quickly oxidized when brought in contact with potassium permanganate solutions. When mixed with glycerin, syrup, and other organic liquids, or when triturated in a mortar with sulfur or other inflammable bodies, the mixture readily explodes.

THERAPEUTICS.—Potassium permanganate has beeen much lauded as an oral antiseptic and deodorant. Only very dilute solutions are of service for such purposes, but, on account of the persistent discoloration of the teeth resulting from the precipitation of manganese oxide and of the deleterious action on tooth substances, it should not be used as a mouthwash for any length of time. In weak solutions (1:3,000) it is of some service in washing out abscess cavities, and as a mouthwash in the treatment of Vincent's stomatitis. It may be administered orally in a 0.1 per cent solution as an alkaloidal antidote. The contents of the stomach should be removed immediately.

PHARMACODYNAMICS.—Potassium permanganate produces its antiseptic and deodorant action by the liberation of nascent oxygen and by the precipitation of cell colloids by a metallic action of the manganese radical. The manganese is reduced and the cell protoplasm oxidized.

$$2\ KMnO_4 \rightarrow K_2MnO_4 + MnO_2 + 2\ (O)$$

MOUTHWASH FOR VINCENT'S STOMATITIS

℞	Potassium Permanganate		2 Gm.
	Distilled Water	q.s. ad	120 cc.
	M.		

Sig.: One teaspoonful in a glassful of warm water as a mouthwash.

Tablets of Potassium Permanganate, Tabellae Potassii Permanganatis (Tab. Pot. Permang.), N.F.

USES.—For making solutions.

DOSAGE.—60 mg. (1 grain) of Potassium Permanganate (N.F.).

POTASSIUM CHLORATE; POTASSII CHLORAS (POT. CHLORAS), $KClO_3$, N.F.

SOURCE AND CHARACTER.—It appears in colorless, shining plates or crystals; it is odorless, and has a soothing saline tase and a neutral reaction. When heated to about 634° F. (334° C.) it melts, and at a slightly higher temperature gives up free oxygen. Potassium

chlorate is soluble in about 16 parts of water at ordinary temperature, very soluble in hot water, and soluble in about 130 parts of alcohol. When brought in contact with organic matter—cork, tannic acid and its many modifications, sugar, etc.—or with easily oxidizable substances—sulfur, phosphorus, antimony sulfide—or if the mixture is subjected to heat, trituration, or concussion, violent explosions are liable to occur. Special care should be exercised in prescribing the salt as a component of tooth powders.

AVERAGE DOSE.—No official dose.

THERAPEUTICS.—Potassium chlorate has a very limited range of usefulness. At one time it was believed that this salt possessed specific properties which made it invaluable for the treatment of infectious disturbances of the oral cavity. This belief is still entertained by many practitioners. Kobert, Cushny, Heinz, and others have called attention to the easy manner in which this salt is readily absorbed by the tissues when used as a gargle. After it has entered the blood it produces severe changes, resulting in the destruction of the red blood corpuscles, with the production of hemoglobinuria, a condition which is known as "potassium chlorate poisoning." Cases are on record where the simple gargling with potassium chlorate solution has resulted in death. About 90 per cent of the absorbed potassium chlorate is excreted by the urine, and the balance leaves the body through the salivary and other glands. Its antiseptic action is about equal to that of sodium chloride. Potassium chlorate in the form of a paste, powder, or as a gargle in diseases of the mouth, or as a toilet requisite for daily use, should be emphatically prohibited.

Potassium chlorate is not reduced in the body or when applied to the skin or mucous membranes, and is therefore not an oxygen former. Its limited antiseptic action is due to its molecule and ions and not to a decomposition product.

TOXICOLOGY.—Pain in gastric region; nausea, vomiting. Dyspnea, cyanosis. Skin may be jaundiced. General excitation, delirium, collapse, coma. Methemoglobinemia, disintegration of corpuscles. Later, scanty urine or complete anuria, albuminuria, hematuria, methemoglobinuria and nephritis.

TREATMENT.—Gastric lavage; mucilaginous drinks. External heat. Carbon dioxide-oxygen inhalation. Caffeine hypodermically, if necessary. Blood transfusion in severe cases. Treat as for potential nephritis.

CHROMIUM TRIOXIDE; CHROMII TRIOXIDUM (CHROM. TRIOX.), CrO_3, U.S.P. (Chromic Anhydride).

Dark purplish-red, odorless, deliquescent crystals. Very soluble in water (1 in 0.6). Incompatible with most organic substances. *Caution:* Chromium trioxide should not be brought into intimate contact with organic substances (such as alcohol and glycerin) as serious explosions are likely to result. (U.S.P.)

Chromium trioxide is the acid anhydride of chromic acid.

$$CrO_3 + H_2O \rightarrow H_2CrO_4$$

PHARMACODYNAMICS.—Chromic acid acts as an antiseptic, astringent, and caustic by virtue of its liberated nascent oxygen, its precipitating action on cell colloids by the metallic ion, and also by the acidity. The chromium is reduced, oxidizing the cell contents.

$$2\ H_2CrO_4 \rightarrow Cr_2O_3 + 2\ H_2O + 3\ (O)$$

INCOMPATIBILITIES.—Because of its powerful oxidizing properties, chromium trioxide should not be brought in contact with alcohol, glycerin or other oxidizable substances lest an explosion result.

USES.—In dentistry chromium trioxide is used only as a caustic in the solid form or in solutions over 10 per cent. Because of its escharotic character, it should be used with extreme care; and the hard tissues should be protected by suitable means. Its use in mouthwash form is contraindicated since it dissolves the enamel. For Vincent's infection[1] it is applied in conjunction with a 1 per cent solution of hydrogen peroxide which is used as a mouthwash.

Chromic acid[2] has been used therapeutically as a germicide, astringent, and caustic. It destroys tissue cells and bacteria with which it comes in contact. Its therapeutic property is due to its oxidizing action, its acidity and its precipitating action on proteins. Chromic acid has been used in dentistry in a 3 to 10 per cent solution for treating oral ulcers and Vincent's stomatitis. The drug is applied by the dentist to the infected part. The acid action of chromic acid can decalcify the hard tissues of the teeth. This decalcification may produce sensitiveness about the necks of the teeth. The teeth should be protected from the corrosive action of chromic acid with a coating of petrolatum.

[1]For a review of the drugs used in treating Vincent's infection, see Musberger, L. E.: Dent. Cosmos 70: 1029 [Oct.], 1928; Lyons, H.: Dental Science and Dental Art, A. M. Gordon, Ed., 1938, p. 439, and Report of the Council, J. A. D. A. 25: 2026, 1938.

[2]Dobbs, E. C., Chromic Acid, Dental Cosmos. 77: 92, 1935.

SOLUTIONS FOR VINCENT'S STOMATITIS, ORAL ULCERS

℞	Chromium Trioxide		1.5 Gm.	gr. xxiii
	Distilled Water	q.s. ad	30.0 cc.	f℥ i
	M. et ft. sol.			
	Sig.: Apply with caution.			

ANTISEPTICS OF THE AROMATIC SERIES

According to the earliest historical records, the balsams, the spices and wood tar and many of its derivatives have been utilized to check the effects of decay and to heal wounds. With the introduction of phenol into surgery by Lister in 1868 the aromatics became important factors in the treatment of wounds. A very large number of chemicals belonging to the aromatic series have been discovered within the last fifty years; some have become important constituents of materia medica, while others, after a very brief sojourn, have been discarded.

Of the hydroxyl compounds, phenol, C_6H_5OH, is the most important member; it is the oldest important representative and is still largely used. By substituting chlorine for hydrogen in the benzol ring, monochlorphenol, C_6H_4ClOH, is formed. By oxidation three hydroxybenzols are obtained, of which resorcinol stands out prominently. The latter is a good oral antiseptic. Closely related to the phenols are the cresols; the latter are largely used at present in the form of cresol, $C_6H_4CH_3.OH$—that is, a mixture of the three isomeric cresols, or in the form of any of the many modifications of which the compound solution of cresol is the best representative. The addition of the methyl group (CH_3) to the phenol radical increases the germicidal properties and decreases the causticity. Thymol, $C_{10}H_{14}O$, and its isomer carvacrol are prepared from oil of thyme. The former is much lauded in dentistry. Of the naphthols the betanaphthol, $C_{10}H_7OH$, has found many admirers. Creosote, a mixture of phenol and phenol derivatives, prepared from beechwood tar, has been used widely in dentistry, even long before the inauguration of the antiseptic era. Its chief constituent, guaiacol, $C_6H_4.OH.OCH_3$, was much praised, either alone or in any of its many modifications. Through the introduction of the carboxyl group, COOH, into the aromatic series many important compounds are formed which are much less poisonous than the original phenol. Some of the important representatives of this group are benzoic acid and salicylic acid, and their many derivatives. A very large group of aromatic antiseptics is represented by the essential oils and their

derivatives, and their importance in dentistry necessitates detailed description in a special section.

The antiseptics of the aromatic series play a very important role in the practice of conservative dentistry and oral hygiene, and are principally applied locally. When the aromatic poisons are brought in contact with living protoplasm, they kill the cell without visible changes, and consequently they are referred to as protoplasm poisons. The strongest antiseptic action is obtained from those substances which are readily soluble in a fluid which is also soluble in the protoplasm of the cell. Quite a few of the antiseptics of the aromatic series act as caustics by precipitating albumin. It should be borne in mind, however, that the newly formed precipitate is of a loose, flocculent nature, which does not check the further penetration of the antiseptic. The precipitation of the cell colloids is brought about by a solution of the drug in the dispersion medium affecting the stability of the colloidal state and flocculation occurs. The aromatic drugs destroy the cells of the host as well as the bacterial cells and must be used with care to prevent irritation and necrosis. It should be observed that the action of these organic compounds is from the undissociated molecule and not from its ions.

Phenol and Phenol Preparations

PHENOL; PHENOL, C_6H_5OH, U.S.P. (Carbolic Acid).

SOURCE AND CHARACTER.—Phenol was discovered in 1834 in coal tar by Runge. It is obtained from coal tar by fractional distillation or made synthetically. It appears in colorless, needle-shaped crystals or white masses, and melts at about 104° F. (40° C.), having a peculiar odor and a sweetish, burning taste. It is deliquescent in moist air. With age the liquid phenol usually acquires a slightly pinkish tint; this is not, however, an indication of any impurity, as it develops most rapidly in the pure acid and does not in any way affect its medicinal action. Phenol is soluble in about 15 parts of pure water at ordinary temperature; it is very soluble in alcohol, ether, chloroform, and glycerin, and in fixed and volatile oils. It reacts faintly acid to blue litmus paper.

It is stated in some textbooks that phenol will coagulate albumin, while creosote will not. This certainly is a mistake, as both behave in exactly the same manner toward albumin.

DOSAGE.—60 mg. (1 grain).

MEDICAL PROPERTIES.—Antiseptic, antipyretic, caustic, and obtundent.

General and Local Action.—Phenol, when administered internally in very diluted form, is promptly absorbed and exercises a definite influence on the central nervous system. It acts as a depressing and stupefying agent, and rarely produces convulsions in man. The respiration and the heart's action are accelerated and the temperature is slightly decreased, while the secretions are increased. The urine becomes brownish-black; it should be understood that this discoloration is not due to the presence of blood, but is due to phenol compounds. Locally applied, phenol acts as a general protoplasm poison. Phenol solutions are only weakly ionized; their action does not depend so much on the ion, C_6H_5O, as on the whole molecule, C_6H_5OH, and this is partially the reason why the phenol salts, which are much more readily dissociated in solution, are much less active antiseptically. Phenol pricipitates albumins and other proteins, but the resultant precipitate is quite different from that formed by tannic acid or the metallic salts. The phenol precipitate of albumin is of a loose, flocculent nature; it does not prevent the further penetration of the phenol, and the latter may be readily washed out from the precipitate. The question of phenol coagulation at one time gave rise to heated discussions in dental circles until York, in 1899, proved the soundness of the above-mentioned facts. On bacteria the action of phenol varies greatly with the species of the microorganisms. The ordinary pyogenic bacteria are usually readily destroyed by a 3 to 5 per cent solution, while spores are very resistant even to concentrated solutions. When applied to the skin in concentrated solution, phenol produces a white opaque eschar, which falls off in a few days, leaving a light, reddish-brown stain, which may remain for several days, or even weeks. Even in weak solution (5 per cent), when applied for some time and prevented from evaporating, it may produce necrosis of the parts. Numbness of the covered area, or even almost complete anesthesia, may accompany the phenol application. If phenol is applied to mucous membranes in concentrated solution, it produces sloughing, and acute inflammation may follow. Sometimes general effects are observed from the absorption of large quantities of the solution when applied locally. Phenol is a rather poor deodorant. It should be remembered, however, that deodorization does not mean antiseptic action.

Therapeutics.—The antiseptic value of phenol in solution depends largely on the solvents used. If a chemical is to penetrate into the structure of an organism (bacterium), it must be as soluble in the

cell fluids as in the fluids in which it is applied. Koch pointed out long ago that phenol and other antiseptics dissolved in alcohol and especially in oil are practically valueless when applied as antiseptics. It is interesting to observe that, on the other hand, the addition of small quantities of sodium chloride to an aqueous phenol solution increases its antiseptic action very markedly. Temperature also has a decided influence on the antiseptic action of phenol solution. Raising the temperature to 120 to 140° F. (50 to 60° C.) increases its germicidal action very materially. Phenol solutions are rarely used at present for surgical purposes. Its irritating action and the possibility of producing necrosis are probably the chief causes for its lessened usage. As a mouthwash, 0.2 to 1 per cent solutions are employed. Carbolated oil or petroleum jelly (5 to 10 per cent) is recommended as a disinfecting lubricant for surgical instruments. Liquid phenol is quite freely used as a caustic for small tumors, gum tissue, fistulous tracts, abscess cavities, etc. Its application should be immediately followed by alcohol to limit its action.

Toxicology.—Phenol is frequently taken with suicidal intent. It is a mostly deadly poison; the lethal dose is about 0.25 cc. of the official liquid phenol per pound of body weight and usually it produces its effects very quickly. The presence of food in the stomach greatly increases the chances of recovery, even though a large quantity of the poison has been taken. The odor of phenol and the caustic action on the mucous membranes of the mouth and the lips are in most cases readily recognizable symptoms of phenol poisoning. The treatment consists of the removal of the poison with the stomach tube and the administration of demulcent drinks, as white of egg, or lime suspended in sugared water. According to Macht,[1] lavage of the stomach is the prime requisite in treating phenol poisoning. From experimental study of the subject, he reaches the following conclusions:

1. The efficiency of lavage in phenol poisoning depends on the quantity of poison taken, on the time after poisoning that the lavage is begun, and on the solution used for washing the stomach.

2. A strong solution of sodium sulfate appears to be the most useful for the purpose; next in efficiency comes plain water.

3. The influence of alcohol in phenol poisoning depends on the time of its administration. An animal that is previously intoxicated with alcohol can withstand better the effects of phenol taken after-

[1]Macht, D. I.: The Johns Hopkins Hospital Bulletin 26: April, 1915.

ward. On the other hand, alcohol administered to an animal after poisoning with phenol, will aggravate the symptoms and hasten death.

4. The use of alcohol in phenol poisoning should therefore be strongly discouraged except for local use.

Heat applied to the body surfaces and the judicious use of general stimulants are useful adjuncts. As stated above, the internal administration of alcohol in the belief of forming definite chemical inert compounds with phenol is a mistake, as there is no evidence of chemical antagonism between the two substances. The local caustic effects of phenol may be quickly mitigated by thoroughly washing the parts with alcohol, which dissolves out the phenol, then covering the cauterized surfaces with a bland ointment.

Quite a large number of phenol compounds have been favorites with dental practitioners. Some of the better known compounds, including their approximate composition, are given:

SOLUTION OF SODIUM PHENOLATE (PHENOL SODIQUE)

℞			
	Phenol Crystals	30 Gm.	ʒ j
	Sodium Hydroxide	2 Gm.	ʒ ss
	Water	30 cc.	fʒ j

Dissolve the sodium hydroxide in the water, add the phenol, and warm gently.

PREPARATIONS.—

Phenolated Water; Aqua Phenolata (Aq. Phenol.), N.F. (Solutio Phenoli, P.I., Carbolic Acid Water).—Phenol (2.2%) in distilled water.

USES.—Dilute with 4 parts of water as a mouthwash.

Glycerite of Phenol; Glyceritum Phenolis (Glycer. Phenol.), N.F. (Glycerite of Carbolic Acid).—Liquefied phenol (20%) with sodium citrate in glycerin.

DOSAGE.—0.3 cc. (5 minims) (N.F.).

Phenolated Oil; Oleum Phenolatum (Ol. Phenol.), N.F. (Oleum Carbolatum, Carbolized Oil).—Phenol (5%) in olive oil.

USES.—A mild local stimulant and anesthetic but only feebly antiseptic.

Camphorated Phenol; Phenol Camphoratum (Phenol Camph.), N.F. (Camphor-Phenol).—Phenol (30%) and camphor (60%) in liquid petrolatum.

USES.—This preparation is designed for the treatment of infected root canals. It is probably less germicidal than phenol but it is also less caustic.

Liquefied Phenol; Phenol Liquefactum (Phenol Liq.), U.S.P. (Liquefied Carbolic Acid). Phenol liquefied by about 10 per cent of water.

USES.—This is the preparation of choice for application to the hard tissues of the teeth; use undiluted.

Dental Therapeutics:

1. For obtunding sensitive dentin.
2. For sterilizing prepared cavities.
3. For sterilizing infected dentin.
4. For sterilizing root canals.
5. As a caustic for soft tissues.

Phenol Ointment; Unguentum Phenolis (Ung. Phenol.), U.S.P. (Ointment of Carbolic Acid).—Phenol (2%), petrolatum (93%), and yellow wax (5%).

USES.—This ointment may be used about the lips whenever a protective, obtundent or antiseptic dressing is indicated.

Aromatic Solution of Phenol (Black's Mixture).—Oil of cinnamon, 1 volume, phenol, 2 volumes, and oil of wintergreen, 3 volumes (commonly referred to as Black's 1, 2, 3). (A.D.R.)

USES.—This preparation was designed for the treatment of non-infected root canals. It is of doubtful value in dental surgery and has no advantages over the official phenol preparations.

Zinc Phenolsulfonate; Zinci Phenolsulfonas (Zinc. Phenolsulf.), $Zn(C_6H_4OH.SO_3)_2.8H_2O$, N.F. *(Zinc Sulfocarbolate).*

It forms colorless, transparent crystals, odorless, and has an astringent, metallic taste. It is soluble in 1.6 parts of water or alcohol (1 in 1.8).

USES.—This preparation is supposed to have the advantage of being astringent as well as antiseptic. It is rapidly becoming obsolete.

CARBOLATED CAMPHOR; CAMPHOPHENIQUE.

A solution of camphor and phenol in liquid petrolatum. It is a simple solution of the two components and not, as it has been claimed, a new chemical compound. It is much less caustic than liquid phenol; the camphor and the liquid petrolatum act as solvents and diluents of the phenol and prevent its ready action on the tissues.

℞			
	Phenol	8 Gm.	ʒ ij
	Camphor	16 Gm.	ʒ iv
	Liquid Petrolatum	16 cc.	fl ʒ iv

Place the components in a dry bottle, and within a few hours they will form a homogeneous liquid.

A more effective and widely used substitute has the following composition:

℞			
	Phenol	30 Gm.	ʒ j
	Camphor	60 Gm.	ʒ ij
	Alcohol	10 cc.	fl3 iiss

Prepare as directed above.

PHENOLATED THYMOL; THYMOL-CAMPHENE.

A solution of phenol, thymol, and camphor. It was much lauded in the treatment of putrescent root canals.

℞			
	Phenol	8 Gm.	3 ij
	Thymol	8 Gm.	3 ij
	Camphor	4 Gm.	3 j

Place the components in a dry bottle, and within a few hours they will form a homogeneous liquid.

MONOCHLORPHENOL; PARA-MONO-CHLORO-PHENOL, $C_6H_4Cl.OH$.

It is a product of chlorine substitution, replacing one hydrogen atom of phenol. It is prepared by passing dry chlorine through melted phenol to the point of saturation. It appears in colorless crystals, is very soluble in ether and alkalies, and less soluble in water. In many respects it acts like phenol, but it is much more poisonous to microorganisms. It possesses very strong disinfecting properties, and has a great power of penetration. Ordinary thermal or actinic changes do not affect its stability or potency. By trituration it combines readily with gum camphor to form a transparent, oily, light amber-colored liquid, i.e., camphorated chlorphenol. This solution is stable; it should be preserved in a dark bottle away from heat.

Monochlorphenol, as introduced into dentistry by Walkhoff in 1891, is one of the most serviceable therapeutic agents for the treatment of infected root canals. It should preferably be applied for this purpose in a 30 per cent solution in camphor. This solution does not cauterize the soft tissues. The pronounced antiseptic action of this compound rests primarily upon the slow liberation of nascent chlorine, leaving active phenol; the camphor merely serves the purpose of an oily vehicle.

Camphorated chlorphenol may be prepared according to the following formula:

Monochlorphenol (Crystals)	30 Gm.
Gum Camphor	70 Gm.

Place the two components in a dry bottle; within twenty-four hours they will form a permanent homogeneous liquid which does not deteriorate with age. To facilitate the ready solution of the compounds slight heat may be applied.

Creosote

CREOSOTE; CREOSOTUM (CREOSOT.), N.F. (Creosote, Wood Creosote).

SOURCE AND CHARACTER.—Creosote is a mixture of phenols and phenol derivatives, chiefly guaiacol and creosol, obtained from wood tar, preferably from beech tar. It is an almost colorless, yellowish oily liquid, with a smoky odor and a burning, acrid taste. It is soluble in about 140 parts of water at ordinary temperature, readily soluble in alcohol, ether, chloroform, and fixed or essential oils.

DOSAGE.—0.25 cc. (4 minims) (N.F.), in capsules.

THERAPEUTICS.—Creosote was introduced into dentistry soon after its discovery by Reichenbach (1830), and it at one time occupied a very prominent place in dentistry, being the most important antiseptic used for the treatment of diseases of the pulp. It is a useful antiseptic in noninfected root canal therapy, being two to three times as antiseptic as phenol and less caustic.

Guaiacol

GUAIACOL; GUAIACOL, $C_6H_4.OH.OCH_3$, N.F.

It is one of the principal products of wood creosote, or prepared synthetically. It is a colorless crystalline solid, melting at about 85° F. (30° C.), or a colorless refractive liquid, having an agreeable aromatic odor. It is soluble in about 60 to 70 parts of water, and in alcohol, ether, and glycerin.

THERAPEUTICS.—Similar to creosote.

DOSAGE.—0.5 cc. (8 minims) (N.F.).

Cresol

CRESOL; CRESOL, $C_6H_4.CH_3.OH$, U.S.P.

SOURCE AND CHARACTER.—Cresol presents a mixture of three isomeric cresols obtained from coal tar, freed from phenol, hydrocarbons, and water. Commercially the mixture is known as tricresol. It is a straw-colored reactive liquid, having a phenol-like odor and turning brown on prolonged exposure to light. Cresol is soluble in 50 parts of water at ordinary temperature, and it is miscible with alcohol, ether, glycerin, and alkali hydroxide solution. By fractional distillation the following constituents are obtained:

Orthocresol, at about 371° F. (188° C.), colorless crytals. (35 per cent.)

Paracresol, at about 389° F. (198° C.), crystalline masses. (25 per cent.)

Metacresol, at about 394° F. (201° C.), light-yellowish liquid. (40 per cent.)

THERAPEUTICS.—Cresol is a strong antiseptic, resembling closely phenol in its local action. It is said to be about three to four times as active as phenol, but less caustic. Metacresol is by far the most active of the cresols. The cresols are principally used as external antiseptics and as germicides. Like all phenols, they act as local obtundents. The cresols are soluble in solutions of certain organic substances—in soap solution and other alkaline solutions. The most important representative of this group is:

Saponated Solution of Cresol; Liquor Cresolis Saponatus (Liq. Cresol. Sap.), U.S.P. (Liquor Cresolis Compositus, U.S.P. X, Compound Solution of Cresol).—Cresol (50%) with vegetable oil, potassium hydroxide, and distilled water.

Resorcinol

RESORCINOL; RESORCINOL (RESORCIN.), U.S.P. (Resorcin).

SOURCE AND CHARACTER.—A neutral or slightly acid diatomic phenol obtained from benzol by various processes. It is found in galbanum, asafetida, ammoniac, and other gum resins. It occurs in colorless or slightly pinkish crystals, having a faint odor and a sweetish, disagreeable taste. It is soluble in 0.5 parts of water or alcohol, readily soluble in ether and glycerin and melts at about 248° F. (120° C.). It is *incompatible* with ferric salts and bromine water.

MEDICAL PROPERTIES.—Antiseptic and disinfectant.

THERAPEUTICS.—Resorcinol is much lauded as an antiseptic for the oral cavity. A 2 per cent aqueous solution, flavored with an essential oil, may be used with impunity as a mouthwash. While resorcinol seems to be as antiseptic as, or even more strongly antiseptic than, phenol, it is at present seldom employed as a substitute for the latter. In the form of an ointment (5 to 10 per cent) it is much used in skin diseases.

PREPARATIONS.—

Strong Paste of Resorcinol; Pasta Resorcinolis Fortis (Past. Resorcin. Fort.), N.F. (Lassar's Stronger Resorcinol Paste).—Resorcinol (20%), zinc oxide (20%), starch and light liquid petrolatum.

USES.—Strong antiseptic ointment.

Mild Paste of Resorcinol; Pasta Resorcinolis Mitis (Past. Resorcin. Mit.), N.F. (Lassar's Mild Resorcinol Paste).—Resorcinol (10%), zinc oxide (25%), starch and light liquid petrolatum.

USES.—Mild antiseptic ointment.

Compound Ointment of Resorcinol; Unguentum Resorcinolis Compositum (Ung. Resorcin. Comp.), N.F.—Resorcinol, zinc oxide, bis-

muth subnitrate and rectified oil of birch tar (each 6%), in yellow wax, petrolatum, wool fat and glycerin.

USES.—Complex antiseptic ointment.

Benzoic Acid and Its Salts

BENZOIC ACID; ACIDUM BENZOICUM (ACID. BENZ.), $C_6H_5.COOH$, U.S.P.

SOURCE AND CHARACTER.—An organic acid obtained from benzoin by sublimation, or prepared artificially, usually from toluol. It may be prepared also from hippuric acid and other organic compounds. It appears in light, feathery needles, having a slightly aromatic odor and a warm, acid taste. It is soluble in about 275 parts of water and 20 parts of boiling water, readily soluble in alcohol (1 in 3), ether, and in fixed or volatile oils. Its solubility in water is much increased by the addition of borax or other alkalies. It is *incompatible* with ferric chloride and other metallic salts. Benzoic acid should be preserved in amber-colored bottles.

DOSAGE.—1 Gm. (15 grains), best given in the form of soluble benzoates (see under Sodii Benzoas).

MEDICAL PROPERTIES.—Antiseptic, fungicide and antipyretic.

THERAPEUTICS.—A 1 per cent solution of benzoic acid will temporarily sterilize the oral cavity in about half a minute. (Miller.) It is preferable in many respects to thymol, phenol, and similar preparations as an effective constituent of mouthwashes. It is almost nonpoisonous, and has no irritating effect on the mucous membrane, but it does have a disagreeable taste. Tooth structure is apparently not affected by benzoic acid. Internally, benzoic acid and its salts are administered to increase the amount of expectoration.

PREPARATION.—

Ointment of Benzoic and Salicylic Acid; Unguentum Acidi Benzoici et Salicylici (Ung. Acid. Benz. et Salicyl.), N.F. (Whitfield's Ointment).—Benzoic acid (12%) and salicylic acid (6%) in wool fat and white petrolatum.

USES.—Antiseptic ointment for use in the treatment of fungous infections, i.e., ringworm, athlete's foot.

Sodium Benzoate; Sodii Benzoas (Sod. Benz.), C_6H_5COONa, U.S.P. It occurs as a white, odorless, sweet powder; freely soluble in water (1 in 2), and sparingly soluble in alcohol (1 in 50). It is incompatible with mineral acids and iron salts.

THERAPEUTICS.—It is a mild, practically nontoxic antiseptic and fungicide.

DOSAGE.—1 Gm. (15 grains).

Myrrh

MYRRH; MYRRHA (MYRRH.), U.S.P. (Gum Myrrh).

A gum-resin obtained from the *Commiphora abyssinica* and from other species of Commiphora (Fam. *Burseraceae*).

USES.—Protective and local stimulant to mucous membranes. Internally, carminative.

Tincture of Myrrh; Tinctura Myrrhae (Tr. Myrrh.), U.S.P.—Myrrh (20%) in alcohol. Absolute alcohol content about 85 per cent.

DOSAGE.—2 cc. (30 minims) (U.S.P.).

USES.—A liquid preparation of myrrh.

Salicylic Acid

SALICYLIC ACID; ACIDUM SALICYLICUM (ACID. SALICYL.), $C_6H_4.OH.COOH$, U.S.P. (Orthohydroxybenzoic Acid).

SOURCE AND CHARACTER.—Salicylic acid has been known since 1834 to exist in the form of an aldehyde (salicin) in many plants, especially in the oils of wintergreen, sweet birch, willow bark, etc. At present it is usually prepared synthetically. Salicylic acid appears in light, fine white needles; it is odorless, having a sweetish, afterward acrid, taste. It is soluble in about 460 parts of cold and in 15 parts of boiling water, in 3 parts of alcohol, in glycerin, ether, and chloroform. It is *incompatible* with ferric salts, quinine, and spirit of nitrous ether.

MEDICAL PROPERTIES.—Antipyretic, antiseptic, antirheumatic, germicide, and keratolytic.

DERIVATIVES.—

PHENYL SALICYLATE; PHENYLIS SALICYLAS (PHENYL. SALICYL.), $C_6H_4.OH.COOC_6H_5$, U.S.P. (Salol).

Salol is prepared by the interaction of a sodium salt of salicylic acid and phenol with phosphoryl chloride. It appears as a white crystalline powder, with a faintly aromatic odor and little taste. It is freely soluble in ether and alcohol, almost insoluble in water. It decomposes in the intestines to phenol and salicylic acid, giving it antiseptic properties.

THERAPEUTICS.—Salol is the constituent of proprietary mouthwashes; it is broken up by the saliva into its components—salicylic acid and phenol—and is as detrimental to the oral tissues as salicylic

acid alone. The prolonged use of a salol solution as a mouthwash is prone to produce morbilliform eruptions about the lips, especially about the corners of the mouth, which are known as "mouthwash eczema."

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.), best in powder; may be inclosed dry in capsules or cachets.

Tablets of Phenyl Salicylate; Tabellae Phenylis Salicylatis (Tab. Phenyl. Salicyl.), N.F. (Salol Tablets).—Contain 91 to 109 per cent of the stated amount of phenyl salicylate.

DOSAGE.—0.3 Gm. (5 grains) of phenyl salicylate (N.F.).

SODIUM SALICYLATE; SODII SALICYLAS (SOD. SALICYL.), $C_6H_4.OH.COONa$, U.S.P.

Sodium salicylate is a white odorless powder, with a sweetish, saline taste; it is very soluble in water (1 in 1) and freely soluble in alcohol (1 in 10).

USES.—The salt is usually employed to secure the constitutional action of salicylic acid; used extensively for the relief of pain in acute rheumatic fever.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

ACETYLSALICYLIC ACID; ACIDUM ACETYLSALICYLICUM (ACID ACETYLSAL.), $C_6H_4.OCOCH_3.COOH$ 1:2, U.S.P. (Aspirin).

It is a white powder, slightly soluble in water, but readily soluble in alcohol. It has a very slightly acid taste. It has a well-earned reputation as an analgesic.

DOSAGE.—0.3 Gm. (5 grains) (U.S.P.).

THERAPEUTICS.—As acetylsalicylic acid is only sparingly soluble in water, it is seldom employed as an antiseptic, although it is almost equal in strength to phenol. It is extensively used as a surgical dressing in the form of cotton impregnated with the acid. Salicylic acid acts deleteriously on tooth structure, and will decalcify the enamel. It is used as a specific for acute rheumatism; it reduces the temperature and the pain, and removes the local symptoms of this disease. Aspirin and similar preparations have largely supplanted the use of salicylic acid and sodium salicylate for internal medication.

PREPARATION.—

Compound Paste of Acetylsalicylic Acid; Pasta Acidi Acetylsalicylici Composita (Past. Acid. Acetylsal. Comp.), N.F. (Dental Anodyne Paste.—Aspirin 25 per cent.

THERAPEUTICS.—Used chiefly by dentists as an antiseptic and anodyne paste following tooth extraction.

Betanaphthol

BETANAPHTHOL; BETANAPHTHOL (BETANAPH.), U.S.P., (Naphthol; Betahydroxynaphthalene).

SOURCE AND CHARACTER.—A monatomic phenol occurring in coal tar, but usually prepared from naphthalene. It appears as a pale buff colored, shiny crystalline powder, having a faint phenol-like odor and a sharp, pungent taste. It is soluble in about 1,000 parts of water, very soluble in alcohol and ether.

DOSAGE.—Internally, 0.125 Gm. (2 grains) (U.S.P.). Externally as a 1 to 10 per cent ointment.

MEDICAL PROPERTIES.—Antiseptic and anthelmintic.

THERAPEUTICS.—Alcoholic solutions of betanaphthol in various concentrations are recommended as mouthwashes. It is more antiseptic than phenol and less caustic.

BETANAPHTHOL MOUTHWASH

℞	Betanaphthol	1 Gm.	gr. xv
	Alcohol		
	Glycerin		
	Water	āā 30 cc.	fl℥ j
	M.		

Sig.: Half teaspoonful in a small glass of warm water as a mouthwash, to be used twice a day.

ANTISEPTIC CAVITY VARNISH

℞	Select Gum Copal	8 Gm.	ʒ ij
	Ether	45 cc.	fl℥ jss
	Betanaphthol	4 Gm.	ʒ j

Filter through a well-covered filter, and add enough ether to make the whole measure 2 ounces (60 cc.). Keep in well-stoppered bottles.

Balsams

PERUVIAN BALSAM; BALSAMUM PERUVIANUM (BALSAM. PERUV.), U.S.P. (Balsam of Peru, Peru Balsam).

SOURCE AND CHARACTER.—Balsam of Peru is obtained from *Toluifera Pereiræ*, Baillon (Fam. *Leguminosæ*), a tree growing in El Salvador. It is a thick, viscid liquid, having a brown color and an agreeable vanilla-like odor. Its taste is of a bitter, acrid nature and very persistent. It is completely soluble in absolute alcohol, chloroform, and glacial acetic acid, partially soluble in ether, soluble in 5 parts of alcohol and nearly insoluble in water. Water, when agitated with the balsam, shows an acid reaction to blue litmus paper.

THERAPEUTICS.—Balsam of Peru has given good results in the treatment of skin diseases. When combined with a local anesthetic, i.e., about 10 per cent of procaine (novocain) and used as a packing upon iodoform gauze, it is used in the treatment of painful and infected alveoli after extraction and on lacerated surfaces. It has also been used internally as a stimulant and antiseptic expectorant in certain forms of bronchitis.

TOLU BALSAM; BALSAMUM TOLUTANUM (BALSAM. TOLU.), U.S.P. (Tolu, U.S.P. X, Balsam of Tolu).

Brown or yellowish-brown, plastic solid, transparent in thin layers and brittle when old, dried, or exposed to cold. It has a pleasant, aromatic odor resembling that of vanilla, and a mild, aromatic taste. It is soluble in alcohol and insoluble in water.

Tincture of Tolu Balsam, Tinctura Balsami Tolutani (Tr. Balsam. Tolu.), U.S.P. (Tinctura Tolu, U.S.P. X, Tolu Tincture).—Tolu balsam (20%) in alcohol. Used as a protective, antiseptic, and vehicle.

DOSAGE.—2 cc. (30 minims) (U.S.P.).

Trinitrophenol

TRINITROPHENOL; TRINITROPHENOL (TRINITROPHEN.), U.S.P. (Picric Acid); $C_6H_2(NO_2)_3OH$.

It occurs in yellow, lustrous crystals, odorless, and having an intense bitter taste. It is soluble in 12 parts of alcohol, 65 parts of ether, and 80 parts of water. It is readily oxidized, and forms dangerous compounds when mixed with sulfur, phosphorus, etc. It should never be applied in substance. It is claimed that a hydroalcoholic solution of picric acid is extremely useful in all forms of burns. Poisoning has occurred from application to large areas of the skin.

SOLUTION FOR BURNS

℞	Trinitrophenol	6 Gm.	ʒ iss
	Alcohol	60 cc.	fl ʒ ij
	Aq. Destillat.	ad 1000 cc.	fl ʒ xxxij

M.

Sig.: Strips of lint are soaked in this solution, placed over the burned surface and kept moist with it.

Dyes

The dyes are a group of organic compounds obtained chiefly by synthesis. They are cyclic in structure and as their name suggests, they possess color which is a distinct disadvantage in dental medicine.

Physically they may be classified as crystalloids, methylene blue being an example; or as colloids,[1] acriflavine being an example for this group. Chemically they are classified in New and Nonofficial Remedies according to structure: (1) the azo dyes which contain the .N:N. linkage, with scarlet red as an example; (2) the acridine dyes which contain the flavine nucleus, with acriflavine as an example; (3) the fluorescein dyes which contain the pyronine nucleus with mercurochrome as an example; (4) the phenolphthalein dyes which contain the quinoid nucleus with phenolsulfonphthalein as an example; (5) the triphenylmethane group which contains the triphenyl nucleus with gentian violet as an example, and (6) miscellaneous dyes, such as methylene blue. The physical and chemical classifications as given have but little informative value from a therapeutic perspective. Since the dyes have a specificity for certain types of organisms, a therapeutic classification would have greater clinical importance.

Taken as a group, the dyes are antiseptic, bacteriostatic, mild irritants, and internal antiseptics. They are not strong germicides but they exert an action over a period of time; they do not precipitate tissue proteins and therefore diffuse deeply into the tissues; they irritate the tissue cells with which they come in contact, thus imparting healing properties to indolent wounds; they are nonpoisonous and may be used locally without fear of systemic poisoning, and they stain dentin and cementum and nonmetallic dental restorations.

ACCEPTED DENTAL REMEDIES expresses the Council's opinion on the therapeutic importance of the dyes in dentistry by saying, "Much remains to be learned concerning the actions and uses of dyestuffs as dental medicinal agents. Conclusions concerning their therapeutic usefulness should be accepted with reserve, until such conclusions have been confirmed by independent workers."

USEFUL DRUGS does not give space to the dyes in the thirteenth edition, which reflects the opinion of the Council on Pharmacy and Chemistry of the American Medical Association on the importance of this group of therapeutic agents.

Because of the above statements and the staining properties of the dyes, they may be considered as drugs of limited value in dental medicine. References are given for the convenience of readers who desire a more complete study of this group of compounds.[2, 3]

[1] Hanzlik, P. J.: Proc. Soc. Exper. Biol. Med. 29: 369 and 728, 1932.

[2] McGuigan, H. A.: Applied Pharmacology, St. Louis, 1940, The C. V. Mosby Co., pp. 147-158.

[3] Edmunds and Gunn: Cushny's Pharmacology and Therapeutics, ed. 11, Philadelphia, 1936, Lea and Febiger, pp. 759, 760.

PREPARATIONS.—

METHYLTHIONINE CHLORIDE; METHYLTHIONINAE CHLORIDUM (METHYLTHIONIN. CHLOR.), U.S.P. (Methylene Blue).

It is obtained by the action of hydrogen sulfide upon an oxidation product of para-amino-dimethyl-aniline. It is a dark green, crystalline powder, readily soluble in water, somewhat less soluble in alcohol, the solution having a deep blue color.

Methylene violet, known as pyoktanin, and methylene yellow, known as auramin, are modifications of methylene blue. They are soluble in about 75 parts of water, in alcohol, etc. These various dyes have been lauded in the treatment of the ulcerative forms of stomatitis, especially the tuberculous types, Vincent's angina and similar disturbances of the oral cavity.

USES.—It is of doubtful value as a local or urinary antiseptic.

DOSAGE.—0.15 Gm. (2½ grains) (U.S.P.).

SCARLET RED; RUBRUM SCARLATINUM (RUB. SCAR.), N.F. (Scarlet Red Medicinal, Biebrich Scarlet Red—An azo dye; $CH_3C_6H_4N:NC_6H_3CH_3N:N.C_{10}H_6OH$.

It is a diazotized amino-azo-ortho-toluol with betanaphthol. It is a dark reddish-brown powder, insoluble in water, soluble in alcohol, ether, chloroform, fats, and fatty oils. An almost colorless modification of scarlet red, possessing the same characteristics, is known as *dimazon* or, in continental Europe, as *pellidol*. Scarlet red exercises a most beneficial influence on the new formations of epithelium over denuded surfaces when applied in the form of a 5 to 8 per cent ointment. Schmieden introduced this "scarlet salve" for the purpose of inducing fresh granulation and the results obtained are most gratifying. The ointment is spreaed thinly on the dressing material and covered by cotton or lint to prevent staining of the linen. If a less highly colored preparation is desired, dimazon ointment may be substituted.

USES.—Antiseptic and local stimulant for chronic ulcers. It is of doubtful value.

Ointment of Scarlet Red; Unguentum Rubri Scarlatini (Ung. Rub. Scar.), N.F.—Scarlet red (5%) in olive oil, wool fat, and petrolatum.

USES.—Should be alternated with a bland ointment to avoid irritation (N.F.).

Scarlet Red Sulfonate, the sodium salt of azobenzenedisulfonic acid, azobetanaphthol; $C_6H_4.SO_3Na.N:N.C_6H_3SO_3Na.N:N.C_{10}H_6OH$ is a dark, brownish red powder; odorless. It is soluble in water; slightly

soluble in ether, alcohol and acetone; almost insoluble in chloroform, benzene, fixed oils, fats, and petrolatum.

USES.—Same as scarlet red.

METHYLROSANILINE CHLORIDE; METHYLROSANILINAE CHLORIDUM (METHYLROSANIL. CHLORID.), U.S.P. (Gentian Violet, Methyl Violet, Crystal Violet).

Dark green powder or pieces having a metallic luster. Soluble in water (1 in 35) and freely soluble in alcohol (1 in 10).

Solution of Methylrosaniline Chloride; Liquor Methylrosanilini Chloridi (Liq. Methylrosanil. Chlorid.), N.F. (Solution of Gentian Violet, Solution of Methyl Violet, Solution of Crystal Violet).—Methylrosaniline Chloride (1%) in alcohol and water. Absolute alcohol content 10 per cent.

USES.—Used as an antiseptic and local stimulant in a 1-3 per cent solution. It has a specificity for gram-positive organisms.

CRYSTAL VIOLET, A.D.R.; Pararosaniline violet. The hydrochloride of the base hexamethylpararosaniline $(CH_3)_2N:C_6H_4:C:[C_6H_4N(CH_3)_2]_2$.

USES.—Used as an antiseptic and local stimulant in a 0.2 to 0.5 per cent solution. It is of doubtful value in dental medicine.

BRILLIANT GREEN. Malachite green-G; ethyl green. The sulfate of the base tetra-ethyl-diamino-triphenylmethane $(C_2H_5)_2N:C_6H_4:C.C_6H_5.[C_6H_4N(C_2H_5)_2]$.

These dyes, in general, possess great penetrating power, and they are often used with advantage in the treatment of fungous infections, as in thrush, etc. They are employed in aqueous solution containing ½ per cent of the dye; the solution should be made fresh when needed.

ACRIFLAVINE; ACRIFLAVINA (ACRIFLAV.), N.F. (Acriflavine Base, Neutral Acriflavine).

Neutral acriflavine, also known as proflavine or flavine, prepared from yellow acridine dyes, appears as brown crystals or as a brownish powder. It contains about 14.5 per cent chlorine. It is easily soluble in water, imparting to the latter in very dilute solution a bright yellow color with a greenish fluorescence. Solutions may be boiled without change, however they are very sensitive to light and are preferably made fresh when needed.

Acriflavine is a very strong antiseptic which does not injure the tissues. It readily diffuses, possesses little general toxicity, and is odorless. It may be applied in the strength of 0.1 to 5 per cent dissolved in a physiologic saline solution as an antiseptic in oral surgery

or in the treatment of stomatitis, etc. In the form of a 5 per cent gauze it is an admirable, odorless substitute for the ill-smelling iodoform gauze. Caution should be exercised in its use in the treatment of root canals, tooth cavities, etc., as it produces a penetrating yellow stain in dentin.

Acriflavine Hydrochloride; Acriflavinae Hydrochloridum (Acriflav. Hydrochlor.), N.F.—Chlorine (about 23.75 per cent). An orange-red or brownish-red, odorless powder. Freely soluble in water (1 in 3), and soluble in alcohol.

USES.—Similar to those of acriflavine.

PYRIDIUM—PHENYLAZO-2-6-DIAMINO-PYRIDINE MONOHYDROCHLORIDE.

It is the monohydrochloride of an azo dye of the pyridine series. Pyridium occurs as a red, odorless, microcrystalline powder, possessing a slightly bitter taste; slightly soluble in cold water (about 0.3 part in 100 parts), and about 5 parts in 100 parts boiling water; slightly soluble in alcohol; insoluble in acetone, benzene, chloroform, ether and toluene. These solvents, if not entirely free from water, may become yellow on the addition of pyridium. The aqueous solution (1:500) is red and is distinctly acid in reaction. It is primarily used in the treatment (oral and local) of genitourinary diseases.

ANTISEPTICS OF THE ALIPHATIC SERIES

Marsh gas (methane, CH_4) furnishes the basic radical of a very large group of organic compounds that have been used with remarkable success in therapeutics. The vast majority of these compounds are characterized by a depressing action on the nervous system. The hydroxyl compounds of certain derivatives of methane are known as alcohols. The simplest form is methyl alcohol, CH_3OH, a product of oxidation of methane. Methyl alcohol is rarely used as an antiseptic, and when further oxidized it produces a gaseous aldehyde, CH_2O, known as formaldehyde, according to the following equation:

$$CH_3OH + O = CH_2O + H_2O.$$

This latter compound is one of the most powerful disinfectants at our command. By substituting one H-atom of methane by the radical CH_3, a second member of the marsh gas series is produced, known as ethane, C_2H_6. If one H-atom of ethane is replaced by the hydroxyl group, OH, ethyl alcohol, C_2H_5OH, is obtained. By further increased substitutions, a number of higher alcohols—such as the propyl, butyl, and amyl alcohols—are obtained. Their therapeutic application is very limited.

Formaldehyde, Formaldehydum

SOLUTION OF FORMALDEHYDE; LIQUOR FORMALDEHYDI (LIQ. FORMALDEHYD.), U.S.P.

SOURCE AND CHARACTER.—An aqueous solution of not less than 37 per cent of absolute formaldehyde (H.CO.H.). It is an oxidation product of methyl alcohol. Water will take up about 52 per cent of formaldehyde gas, but it will not retain more than 35 to 40 per cent at ordinary temperature. On standing, slight separation of paraformaldehyde takes place. It is a clear, colorless liquid, having a pungent odor and a caustic taste. Its vapors are very irritating to the mucous membrane. It is readily miscible with water and alcohol, and its fresh solutions react neutral or faintly acid to litmus paper. It is *incompatible* with ammonia, alkalies, tannic acid, gelatin, iron preparations, and the salts of copper, iron and silver.

GENERAL AND LOCAL ACTION.—The vapors of formaldehyde are intensely irritating to the mucous membrane, the eyes, etc. Taken internally, it produces severe gastroenteritis, followed by collapse and death in a very short time. Two ounces of commercial formaldehyde solution are known to have killed a man.

Locally applied in diluted solutions, it roughens the skin, and concentrated solutions tan the skin to such an extent that the superficial layers, which have changed to a horny material, may be removed in shreds. If the ear of a living rabbit is thoroughly painted with a formaldehyde solution for some time, it becomes mummified and may be readily broken off. Its use as a preservative of milk is prohibited. For the preservation of physiologic and pathologic specimens it is serviceable, as it does not change the normal color of the tissues. On the mucous membrane formaldehyde, even when applied in very diluted solutions, acts as an irritant, and in concentrated solution it acts as a powerful caustic. Consequently formaldehyde should not be used as a component of mouthwashes, and the many proprietary preparations that contain it should not be continuously employed, as they tan the oral linings and thus lessen their resistance.

Formaldehyde is a very powerful germicide. According to Loew its bactericidal action on microorganisms and their products is believed to be due to its affinity for certain amino groups in the proteins. When formaldehyde is added to a solution of albumin or serum, a peculiar chemical compound, known as protagen, which is a denatured protein results. Applied in vapor form, it is one of the most certain means of disinfecting rooms and their contents.

Buckley lauded dry formaldehyde (trioxymethylene) in the form of a paste as: "A new, safe and reliable remedy for hypersensitive dentin."

The dental literature contains many references relative to the use of formaldehyde as a desensitizing agent. All agree that unless it is intelligently used, it may injure and, in some instances, kill the pulp.

Formalin Dermatitis. Since the introduction of formaldehyde in medicine and dentistry, a number of cases of formalin dermatitis have been reported in current literature, occurring especially among dental practitioners and workers in medical laboratories. Obstinacy to treatment has given rise to much discomfort to the patients. The disease probably results from a lessened resistance of the patient to the continuous exposure to the drug and not so much from a general predisposition. As a consequence the irritating action of the formalin soon manifests itself in a persistent and most painful itching of the finger tips, cracking of the skin, and bulbous eruptions within the affected areas, which frequently involve the nail folds. If once acquired, there is always a predisposition established. The disease may disable the dentist completely in the pursuance of his practice. The treatment consists primarily in avoiding contact with formalin. Rubber finger stalls should be worn.

Disinfection of Rooms. The room to be disinfected should have a temperature of 65° F. (18° C.) or more, and the air present must contain at least 75 per cent of moisture. This humidity can be produced by placing pans of steaming hot water about the room. Drawers, closet doors, etc., should be opened, and the furniture moved from the walls. Set on the floor in the middle of the room a large tin pail, in which is placed a tin can of suitable capacity. Put into the can six ounces of potassium permanganate crystals, and pour over them one pint of commercial formaldehyde solution.* These quantities are sufficient for every thousand cubic feet of air space. The operator should leave the room at once, as large quantities of formaldehyde gas are immediately evolved. The room must be closed air tight, and not opened for at least six hours. Furniture, draperies, carpets, pictures, etc., are not damaged by this method of disinfection. After the disinfection is completed, the formaldehyde gas can be neutralized by ammonia, so as to render the room fit for occupation. This may be readily accomplished by placing in a suitable vessel two pounds of freshly burnt lime, seven pints of boiling water, and three pints of strong ammonia water. After one hour's exposure to the ammonia vapors the room should be well aired.

*Sodium dichromate, 10 ounces (300 Gm.), and sulfuric acid, commercial, 1½ fluidounces (45 cc.), have been substituted with equally good results for potassium permanganate, 6 ounces (180 Gm.).

THERAPEUTICS.—Formaldehyde is much restricted in its therapeutic application by its powerful irritating property, its pungent odor, and by the rapid volatilization of the gas. To remove or neutralize these properties, a number of compounds have been produced by utilizing the peculiar affinity which formaldehyde has on starch, gelatin, and albumin solutions. It is also known that formaldehyde is readily liberated from certain organic compounds in the genitourinary tract when taken internally. Since this fact became known, innumerable compounds have been forced on the market, among which hexamethylenamine is the most prominent member. Torald Sollmann has shown that "of all the products examined for antiseptic value, hexamethylenamine is the only one which offers undoubted advantages over the other antiseptics."

As an antiseptic, formaldehyde has gained an enviable reputation in conservative dentistry. It is somewhat difficult to state at present who introduced this chemical into our profession. While we find some references relative to its dental use as early as 1894, the earliest important communications are those made by Marion (1895), Lepkowski (1895), Schröder (1896), Witzel (1898), Bönnecken (1898), Prinz (1898), etc. They are now followed in rapid succession by many writers here and abroad. On account of its strong irritating action, formaldehyde is diluted or combined with many other agents—alcohol, oil of geranium, cresol, phenol, etc.—and has been principally employed ever since in mixtures of this nature. In 1899 Gysi introduced a mixture of cresol and formalin for the treatment of infected root canals, but it remained for Buckley to bring this combination prominently before the Fourth International Dental Congress in 1904. It has also been used for relieving pain due to hypersensitive dentin (Treatment of Hypersensitive Dentin, Report of the Council, *J. A. D. A.* 21: 2050, 1934).

Cresolated Formaldehyde, N.F.V.; *Formaldehydum Cresolatum (Formal. Cresol.).*—Consists of orthocresol (40 per cent) and solution of formaldehyde (60 per cent).

The substitution of part of the formaldehyde solution by glycerin yields a clearer solution (A.D.R.).

The content of absolute formaldehyde in cresolated formaldehyde is about 22 per cent.

FORMOCRESOL

Cresol			
Sol. of Formaldehyde	aā	4 cc.	3 i
M. f. sol.			

Root Canal Filling Material

POWDER

Thymol	5 parts.
Exsiccated alum	10 parts.
Kaolin	25 parts.

LIQUID

Solution of formaldehyde	1 part.
Cresol	2 parts.
Alcohol	3 parts.

Pulp Mummifying Paste

Paraform	1 part.
Thymol	1 part.
Zinc oxide	2 parts.
Glycerin	enough to make a stiff paste.

Scheuer's Root Filling Paste

Zinc oxide	8 parts.
Zinc sulfate, dehydrated	2 parts.
Cresol	3 parts.
Formaldehyde solution	1 part.
Eugenol	1 part.
Glycerin	enough to make a stiff paste.

Creosote-Formaldehyde Solution

℞	Creosote	21 cc.
	Sol. of Formaldehyde	9 cc.
	M.	

Derivatives.—

Paraformaldehyde; Paraformaldehydum.

It is prepared by polymerizing formic aldehyde by heat. It is a white crystalline powder, very slowly soluble in water, alcohol, or ether, and melting at 340° F. (171° C.). At ordinary temperature it gives up formaldehyde vapors, which are readily increased by heat. Paraformaldehyde is largely used for disinfecting purposes, and forms an important component of the many mummifying pastes that are employed for the preservation of pulp stumps left in root canals.

Methenamine; Methenamina (Methenam.), U.S.P. (Hexamethylenamine, Hexamethylenetetramine). Also marketed as urotropine, aminoform, formamin, formin, cystamin, cystogen, urisol and urtone; $(CH_2)_6N_4$.

A condensation product of ammonia and formaldehyde. Colorless crystals or white powder, odorless and with a sweetish taste. Freely

soluble in water (1 in 1.5) and soluble in alcohol (1 in 12.5). Incompatible with acids, with ammonium salts, with tannin and with mercuric chloride.

USES.—Useful urinary antiseptic, through liberation of formaldehyde in the presence of acids.

DOSAGE.—0.5 Gm. (7½ grains) (U.S.P.).

Ampuls of Methenamine; Ampullae Methenaminae (Ampul. Methenam.), N.F. (Ampuls of Hexamethylenamine).—Approximately 0.4 Gm. of methenamine in 1 cc. of sterile aqueous solution.

DOSAGE.—5 cc. containing about 2 Gm. of Methenamine.

Methenamine Tablets; Tabellae Methenamine (Tab. Methenam.), U.S.P. (Hexamethylenamine Tablets).—Contain 100 per cent of the stated amount of methenamine.

DOSAGE.—0.5 Gm. (7½ grains) of Methenamine (U.S.P.).

Alcohol

ALCOHOL; ALCOHOL, U.S.P. (Ethanol, Ethyl Alcohol, Spiritus Vini Rectificatus).—Not less than 92.3 per cent by weight or 94.9 per cent by volume of C_2H_5OH.

It is a transparent, colorless, mobile, and volatile fluid, having an agreeable odor and taste. An absolute alcohol containing not more than 1 per cent by weight of water and the diluted alcohol containing 41 per cent by weight of ethyl alcohol are also official.

Ethyl alcohol possesses limited antiseptic power and precipitates albumin when applied to solutions containing at least 65 per cent or more of pure alcohol. It possesses great affinity for water, and absorbs it freely from the living tissue cell, thereby acting as an irritant. The mucous linings of the mouth and stomach of man, being more or less continuously abused, have acquired a higher resistance to the action of alcohol, and are apparently not much damaged by alcoholic solutions as high as 70 per cent. As an abortive treatment, alcohol indirectly possesses a counterirritant influence in the early stages of abscess formation. When applied in the form of an alcohol pack or bandage, it irritates the deeper structures, thereby producing congestive hyperemia, which causes an increased bacteriolytic action in the tissues.

The antiseptic action of alcohol is most pronounced when applied in dilutions of 70 per cent. Absolute alcohol possesses only slight antiseptic power, which is probably due to the rapid coagulation of albumin of the cell wall, which prevents the penetration of alcohol through this dense coagulated layer. It is also of importance to remember that water-soluble antiseptics lose much of their power when dissolved in or mixed with alcohol, while certain other antiseptics—

as phenol, lysol, and thymol—act more powerfully when dissolved in 50 per cent alcohol than when an equal quantity is dissolved only in water. Solutions of phenol in concentrated alcohol or in fatty oils are comparatively worthless. The bactericidal action of alcohol is always materially increased when applied to moist surfaces. A 70 per cent alcohol solution in water will be about equivalent in its efficiency to a 3 per cent phenol solution in water. Absolute alcohol in connection with the warm air blast is effectively employed as a dehydrating agent for dentin.

PREPARATIONS.—

Dehydrated Alcohol; Alcohol Dehydratum (Alcohol Dehyd.), U.S.P. ("Absolute Alcohol," Dehydrated Ethanol).—Not less than 99 per cent by weight of C_2H_5OH. A liquid with the color, odor and taste of alcohol.

Diluted Alcohol; Alcohol Dilutum (Alcohol Dil.), U.S.P. (Diluted Ethanol).—About 41.5 per cent by weight or 49 per cent by volume of C_2H_5OH.

THERAPEUTICS.—

1. Used as a preservative for pharmaceutical preparations in a 10 to 25 per cent solution.
2. Used as a vehicle in pharmaceutical preparations and in prescriptions.
3. Used as an antiseptic in a 70 per cent solution.
4. Used as an astringent in a 50 to 70 per cent solution.
5. Used as a detergent in cavity toilet in operative dentistry in a 70 per cent solution.
6. Used as a detergent and antiseptic in root canal therapy in a 70 per cent solution.

METHYL ALCOHOL; CH_3OH. Wood alcohol, wood spirit. A product of destructive distillation of wood. It is a colorless, clear liquid, having a characteristic odor and taste. It is miscible in all proportions with water, alcohol, ether, etc., and boils at 150° F. (65° C.). Wood alcohol is rarely employed for medicinal purposes, and its use as a substitute for grain alcohol is prohibited. Taken internally, or even inhaling its vapors, causes poisonous disturbances, frequently resulting in blindness.

ESSENTIAL OILS, THEIR DERIVATIVES, AND THEIR SYNTHETIC SUBSTITUTES

Essential, ethereal, volatile, or distilled oils, as they are variously termed, are usually derived by distillation, sometimes by pressure, or by maceration, from plants. The odor of the plants is primarily

due to the presence of these oils. The oils are obtained from the fruit, the flowering part, the bark, or from the entire plant. Occasionally a plant may produce two different oils, like the juniper tree, or even three different oils, like the orange tree, in its various parts. The cryptogamic plants rarely produce essential oils, the great bulk being obtained from the phanerogams of which the following families are typical representatives: birch, ginger, laurel, lily, myrtle, mustard, orange, parsley, pine, rue, sunflower, etc. The amount of oil obtained from the various plants differs widely, and may range from 0.1 to 20 per cent, but most plants produce only small quantities.

The oils are usually clear, colorless, sparkling fluids, which, by exposure, age, or the presence of some foreign matter, change to yellow, brown, red or green. Some few oils possess a distinctive color—as, the oil of wormwood is dark brown (becoming green or bluish-green with age), and the oil of chamomile exhibits a pale blue color. The stills or original metallic containers may impart a distinctive color to the oils—as, the green color of the oil of cajuput may be traced to the copper stills, or the copper canisters in which the oil is shipped.

Essential oils are soluble in alcohol, ether, chloroform, fatty oils, etc. They are easily vaporized without decomposition, but readily decompose with age and by absorbing oxygen; they become darker in color, and thick and viscid, depositing resinous precipitates. Agitated with water, they form a milky mixture, from which the oils soon separate, imparting their odor and taste to the water. Essential oils possess a strong odor and taste, and are used to a large extent in perfumery and in medicine as flavoring agents. According to their medicinal properties, they are classed as diuretics, expectorants, stomachics, and purgatives; while dentistry chiefly relies on their antiseptic, obtunding, and stimulating qualities.[1]

The volatile oils do not belong to a definite chemical group, and are consequently extremely difficult to classify. Most of the oils are composed of hydrocarbons, represented by various modifications of the general formula known as terpenes $(C_5H_8)_n$, or composed of oxygenated aromatic bodies, as alcohols of the fatty series, aldehydes, acids, ketones, phenols, esters, etc.; or they may represent a mixture of the terpenes with one or more of the other bodies. The terpenes do not necessarily carry the odorous principle of the oils, as was formerly supposed; by fractional distillation the terpenes may be removed entirely, and the oils are thus very highly concentrated. Organic chemistry has succeeded in producing by

[1] The Essential Oils in the Treatment and Sterilization of Live Dentin, D. Rec. 48: 250, 1928.

synthesis quite a number of these odoriferous principles—as methyl salicylate, geraniol, artificial oil of rose, heliotropin, cumarin, etc. Halogen derivatives have thus far not been isolated from essential oils. Certain oils deposit on standing, or when exposed to lower temperature, a solid crystalline substance known as stearopten or camphene, while the remaining fluid is termed eleopten. A few oils contain nitrogenous bodies in the form of cyanogen compounds (oil of bitter almonds) and of sulfur compounds (volatile oil of mustard). Volatile oils differ from fixed or fatty oils in so far as they do not form glycerites (soap) when treated with alkalies; they do not decompose by heat, and are not digestible.

The essential oils differ very widely in their antiseptic power. The latter depends largely on their volatility, which, according to Cushny, "enables them to penetrate readily into protoplasm, and lessens its vitality by acting as foreign bodies (molecular irritants); in addition, they are related to the benzol series, the members of which are all antiseptics and protoplasm poisons." They also possess obtundent properties. When applied to the skin or mucous membrane, the volatile oils act as strong irritants. This irritating property of the oils results most likely from the presence of the terpenes, which, like other volatile substances, are more or less prone to produce redness and itching. It has, however, been repeatedly shown that this irritating property of the oils on the higher tissue cells is much more pronounced than on the lower forms of life, as they penetrate the cell walls of the higher organisms much more rapidly than those of the bacterial cells. Administered internally in well-diluted form, they produce a feeling of warmth, and may give rise to an increased appetite. Aside from their physical properties, the oils may act also by virtue of their chemical nature. The explanation of this pharmacologic phenomenon is, in most instances, unknown—that is, we do not know why certain oils (volatile oil of mustard) produce such violent irritation, etc. As has been experimentally shown by Fischer, certain essential oils—oil of clove, peppermint, eucalyptus, cassia, etc.—produce severe irritation, and, if the application is continued, cause atrophy of the pulp. It is apparently immaterial whether the oils are applied directly to the pulp or indirectly on the dentin. The obtundent properties of certain essential oils which Liebreich has classified as *painful anesthetics*, manifest themselves at first by severe irritation, which is followed by pronounced anesthesia. This primary severe irritation of the delicate pulp tissue is frequently the cause of its final death, a factor which should be remembered in the conservative treatment of this tissue.

Some of the essential oils of the family *Myrtaceae*—as oil of eucalyptus, oil of cajuput, oil of myrtle, etc.—possess the additional property of dissolving gutta-percha. This property is attributed to cineol, the active constituent of these oils.

At present the medicinal value of the essential oils is graded according to the amount of active constituents which they contain—as, oil of cinnamon should contain at least 75 per cent of cinnamic aldehyde, etc. Essential oils have been and are still quite frequently adulterated with cheaper synthetic substitutes.

Volatile oils should be kept in well-stoppered amber-colored bottles in a dark, cool, and dry place, as the effect of heat and sunlight may spoil the best oils within a few weeks.

The value of essential oils as dental antiseptics is largely overestimated, as has been repeatedly shown by careful experiments made by Miller, Cook, MaWhinney, and others. Miller especially expressed himself very definitely on this particular point as follows:

"According to my own views it would be a misfortune for dentistry in its entirety if the endeavor to replace carbolic acid by the essential oils should succeed. Personally, I am convinced of the eminent antiseptic power of oil of cassia especially. In the last few years I have made experiments with this particular oil in treating diseased teeth. Lately I have again abandoned it, as in many cases where I formerly obtained good results with carbolic acid I did not succeed with oil of cassia. Also in many other cases, especially in pronounced apical root irritation as a result of gangrene, where the treatment with oil of cassia was a failure I have occasionally obtained a cure in a short time with carbolic acid. I feel certain that I have used the oil of cassia conscientiously, and in the beginning I had even a special liking for this medicament."

In the present routine practice of conservative dentistry very few essential oils are utilized, but these oils should be of the best quality. Better results are obtained from the application of their active chemical constituents—eugenol instead of oil of clove, cinnamic aldehyde instead of oil of cassia, eucalyptol instead of oil of eucalyptus, methyl salicylate instead of oil of wintergreen, etc. We particularly emphasize what we have already stated in regard to dental drug purchases—they should be the product of a reliable manufacturer and purchased only in original packages.

MaWhinney[1] recorded a series of experiments relative to the antiseptic value of the essential oils and other drugs.

[1]MaWhinney: Transactions Illinois State Dental Society, 1900, p. 125.

From the various tables accompanying MaWhinney's articles the following have been selected on account of their completeness:

DETERMINATION OF THE STRENGTH OF THE ANTISEPTICS

MEDICAMENT USED	AMOUNT OF MEDICAMENT USED	CONDITION IN 24 HOURS	CONDITION IN 96 HOURS
Oil cassia	1¼ minims	Growth	[1]Marked growth
Oil cinnamon	1¼ "	"	1 " "
Oil peppermint	1¼ "	Slight growth	[2]Growth
Oil cloves	1¼ "	" "	1 "
Oil cajuput	1¼ "	" "	[3]Marked growth
Black's 1-2-3	1¼ "	" "	[3]Growth
Oil wintergreen	1¼ "	Growth	1 "
Oil eucalyptus	1¼ "	"	3 "
Oil cedar	1¼ "	Slight growth	[3]Slight growth
Oil cade	1¼ "	" "	3 " "
Oil birch tar	1¼ "	" "	3 " "
Phenol, melted crystals	1¼ "	" "	[3]Growth
Creosote, pure beechwood	1¼ "	" "	3 "
Camphophenique	1¼ "	" "	[3]Good growth
Control tube	----------	Growth	[3]Very marked growth
Creolin	1 minim	No growth	[3]No growth
Tricresol	1 "	" "	3 " "
Chinosol, 10 per cent sol.	2 minims	" "	3 " "

[1]Oil in bottom of tube.
[2]Oil on top of broth.
[3]Soluble still.

To determine the strength of an antiseptic in the manner previously mentioned is by no means sufficient to establish the fact that it is either weak or strong. Painstaking tests and laborious records in regard to the time of the exposure of the bacteria, number, culture media, temperature, etc., are essential factors to obtain a fair amount of tangible material for comparison. The obtained results are, it should be remembered, only laboratory experiments, and the deductions drawn should not be transferred at once to active practice, for here we meet with many conditions which may lead to totally erroneous conclusions in regard to the real value of the employed antiseptic if these new surroundings are not carefully taken into consideration. For this very reason it is not surprising that so many contradictory statements are made as to the merit of any particular antiseptics.

In the following table "the germicidal power of the medicaments is determined by the *time* necessary to expose bacteria to it, and, as will be seen, a great difference appears. It will be noticed that some agents were used in full strength and others in varying concentrations, according as they could be used in practice. The bacteria used were mixed pus cultures."

DETERMINATION OF THE TIME REQUIRED FOR ANTISEPTIC ACTION

AGENT	PER CENT SOLUTION	TIME REQUIRED, MINUTES
Oil cassia	Full strength	40
Oil cinnamon	" "	40
Oil cloves	" "	40
Oil cajuput	" "	45
Oil eucalyptus	" "	40
Oil wintergreen	" "	60
Oil peppermint	" "	50
Oil cade	" "	25
Oil birch tar	" "	20
Oil pennyroyal	" "	45
Phenol	" "	30
Creosote, beechwood	" "	30
Camphophenique	" "	40
Mercury bichloride	1:1,000	25
Creolin	Full strength	5
Tricresol	" "	5
Sublamin	1:250	3
Kresamin	Full strength	5
Formalin	" "	2
Chinosol	10 per cent	.1
Phenol-sulfonic acid	Full strength	5
Tribromophenol	Saturated alcoholic solution	10
Trichlorphenol	" " "	8

Essential Oils

RECTIFIED OIL OF BIRCH TAR; OLEUM BETULAE EMPYREUMATICUM RECTIFICATUM (OL. BET. EMPYR. RECT.), N.F. (Oleum Rusci).

A volatile oil obtained from the bark and wood of the birch, *Betula pendula* Roth, and related species of *Betula* (Fam. *Betulaceæ*). It is a limpid, dark brown liquid, having a characteristic, strongly aromatic odor and taste, closely resembling that of Russia leather.

OIL OF CAJUPUT, OLEUM CAJUPUTI, OIL OF WHITE WOOD, ESSENCE DE CAJEPUT, F.; CAJEPUTÖL, G.

A volatile oil distilled from the leaves and twigs of several varieties of *Melaleuca leucadendron* Linné (Fam. *Myrtaceæ*). The oil of cajuput is very fluid and transparent. Usually it has a fine green color, and an agreeable, distinctly camphoraceous odor. Its active constituent is cineol (cajuputol), a chemical body of which it should contain at least 55 per cent, and which is identical with eucalyptol. Oil of cajuput is used as a carminative, stimulant, diaphoretic, and counterirritant.

AVERAGE DOSE.—8 minims (0.5 cc.).

OIL OF CARAWAY; OLEUM CARI (OL. CARI), N.F. (Caraway Oil).

A volatile oil distilled from caraway fruit, *Carum carvi* Linné (Fam. *Umbelliferæ*). The oil of caraway is somewhat viscid, of a

pale, yellowish color, becoming brownish by age, and with an odor of the fruit caraway. Its active constituent is carvone of which a good oil should contain not less than 50 per cent; it is identical with carvol, the active constituent of the oil of dill. It resembles the oil of clove in its antiseptic and anodyne action, and is also largely used as a carminative.

DOSAGE.—0.1 cc. (1½ minims) (N.F.).

OIL OF CINNAMON; OLEUM CINNAMOMI (OL. CINNAM.), U.S.P. (Oil of Cassia).

A volatile oil distilled from the leaves and twigs of *Cinnamomum Cassia* (cassia-cinnamon) which is from one or more undetermined species of cinnamon grown in China (Fam. *Lauraceae*). Two oils of cinnamon are found in commerce—one procured from the Ceylon cinnamon, the other from the Chinese cinnamon. The latter is often distinguished by the name of oil of cassia. There is no essential difference between the two oils. The Chinese oil is much cheaper and more abundant, although not so fine in flavor as the Ceylon product. It is a yellowish or brownish liquid, becoming darker and thicker with age and exposure to the air, having the characteristic odor of cinnamon, and a sweetish, spicy, and burning taste. The medicinal properties of cinnamon oil depend solely on the amount of cinnamic aldehyde present. A good oil should contain at least 80 per cent of cinnamic aldehyde. Quite a number of other chemical bodies—as eugenol, pinen, etc.—have been isolated from this oil. They are, however, present only in very small quantities. Cinnamon oil is used principally as a flavoring agent. It possesses carminative and stimulating qualities. Oil of cinnamon, like most of the essential oils, penetrates the tooth structure very readily, usually discoloring the tooth to a yellowish-brown hue, resulting from the deposition of a resinous substance, furfurol, in its tubules. Harlan claimed that ozonized oil of turpentine will remove such stains from the teeth; however, any of the oxygen-liberating compounds are suited for such purposes. (See Bleaching Agents.)

DOSAGE.—0.1 cc. (1½ minims) (U.S.P.).

OIL OF CORIANDER; OLEUM CORIANDRI (OL. CORIAND.), U.S.P. (Coriander Oil).

The oil is distilled from the dried ripe fruit of *Coriandrum sativum*, family *Umbelliferae*. It is freely soluble in alcohol (1 in 3) and sparingly soluble in water.

USE.—Carminative.

DOSAGE.—0.1 cc. (1½ minims).

OIL OF CLOVE; OLEUM CARYOPHYLLI (OL. CARYOPH.), U.S.P. (Oil of Cloves).

A volatile oil distilled from cloves, *Eugenia caryophyllata* (Fam. *Myrtaceæ*). Oil of clove, when recently distilled, is very fluid, clear, and colorless, but becomes yellowish, and finally reddish-brown and thick with age. Its medicinal properties depend on the presence of eugenol, a monatomic phenol, of which a good oil should contain at least 82 per cent. The value of a number of other oils also depends chiefly on the presence of eugenol—as cinnamon leaf oil, oil of bay, oil of pimenta, etc. Oil of clove enjoys an old and well-earned reputation of being a valuable obtunding remedy in the treatment of toothache arising from an irritated pulp. It also possesses stimulating properties and is as antiseptic as liquefied phenol.

OIL OF EUCALYPTUS; OLEUM EUCALYPTI (OL. EUCALYPT.), U.S.P. (Eucalyptus Oil).

A volatile oil distilled from the fresh leaves of the *Eucalyptus globulus* (Fam. *Myrtaceæ*). Oil of eucalyptus is a colorless or pale yellow liquid, with a characteristic, aromatic, and somewhat camphoraceous odor, and a pungent, spicy, and cooling taste. The value of this oil depends on the amount of eucalyptol (cineol) present, of which it should contain at least 70 per cent. As an antiseptic, oil of eucalyptus is practically valueless. It is a solvent for gutta percha.

DOSAGE.—0.5 cc. (8 minims) (U.S.P.).

OIL OF GAULTHERIA (OLEUM GAULTHERIAE), OIL OF WINTERGREEN; OIL OF TEABERRY; OIL OF PARTRIDGE BERRY; WINTERGRUENÖL, G.

A volatile oil distilled from the leaves of *Gaultheria procumbens* Linné (Fam. *Ericaceae*) or from the bark of *Betula pendula* Roth (Fam. *Betulaceae*) or produced synthetically. It consists almost entirely of methyl salicylate (see), and is nearly identical with the rectified oil of birch tar (sweet birch).

DOSAGE.—0.75 cc. (12 minims).

OIL OF JUNIPER; OLEUM JUNIPERI (OL. JUNIP.), U.S.P. (Juniper Oil). A volatile oil obtained from the *Juniperus communis*. Freely soluble in alcohol (1 in 4).

USE.—Irritant diuretic and flavoring agent.

DOSAGE.—0.1 cc. (1½ minims).

OIL OF LAVENDER; OLEUM LAVANDULAE (OL. LAVAND.), U.S.P. (Oil of Lavender Flowers).

A volatile oil distilled with steam from the fresh flowering tops of the *Lavandula officinalis*, family *Labiatae*. Freely soluble in alcohol (1 in 4).

USES.—Aromatic and flavoring agent.

OIL OF LEMON; OLEUM LIMONIS (OL. LIMON.), U.S.P. (Lemon Oil).

A volatile oil obtained by expression, without the aid of heat, from the fresh peel of the fruit of *Citrus Medica,* family *Rutaceae.* It is freely soluble in alcohol (1 in 3). *Note—Oil of Lemon which has a terebinthinate odor must not be used or dispensed.* (U.S.P.)

USE.—Flavoring agent.

OIL OF PEPPERMINT; OLEUM MENTHAE PIPERITAE (OL. MENTH. PIP.), U.S.P. (Peppermint Oil).

A volatile oil distilled from peppermint, *Mentha piperita* (Fam. *Labiatae*). The oil of peppermint is colorless, or of a light greenish-yellow color, which becomes reddish with age. Its odor is strong and aromatic. Its taste is warm, camphoraceous, and very pungent, but when air is admitted into the mouth, it gives a sense of coolness. The medicinal properties of this oil depend on the menthol present, of which it should yield 50 per cent. Oil of peppermint is stimulating and carminative, and is largely used as an external remedy in facial and other neuralgic pain. On account of its odor it is rarely employed as an antiseptic, but is much used as a flavoring agent for oral specialties.

OIL OF MYRISTICA; OLEUM MYRISTICAE (OL. MYRIST.), U.S.P. (Myristica Oil, Oil of Nutmeg).

A volatile oil distilled with steam from the dried kernels of the ripe seed of *Myristica fragrans,* family *Myristicaceae.* Freely soluble in alcohol (1 in 3).

USES.—Aromatic flavor and carminative.

OIL OF MYRCIA; OLEUM MYRCIAE (OL. MYRC.), N.F. (Oil of Bay).

A volatile oil distilled from *Pimenta acris* (Fam. *Myrtaceae*). This oil resembles very closely the oil of pimenta and the oil of clove. Its medicinal value depends on the amount of eugenol present. On account of its fragrance it is largely used as a perfume and as an ingredient in the preparation of bay rum.

ALLYL ISOTHIOCYANATE; ALLYLIS ISOTHIOCYANAS (ALLYL. ISOTHIOCYAN.), U.S.P. (Volatile Oil of Mustard, U.S.P. XI, Mustard Oil).

A volatile oil obtained from the seed of *Brassica nigra* or of *Brassica juncea* (Fam. *Cruciferae*) by maceration with water and subsequent distillation.

USES.—It is a very powerful irritant, and its use is limited to external application in alcoholic solutions. It is the active agent of the mustard plaster.

OIL OF TURPENTINE; OLEUM TEREBINTHINAE (OL. TEREB.), U.S.P. (Turpentine Oil, "Spirits of Turpentine").

A volatile oil obtained from the oleoresin of pine wood, *Pinus palustris*, family *Pinaceae*. Freely soluble in alcohol.

USES.—Applied externally as rubefacient and counterirritant.

THEOBROMA OIL; OLEUM THEOBROMATIS (OL. THEOBROM.), U.S.P. Cocoa Butter, Oil of Theobroma, Cacao Butter).

A solid fixed oil which melts at body temperature. It is used in general medicine as a protective, emollient, and diluent for solid preparations (suppositories). In dental medicine it is used as a lubricant and protective in operative dentistry.

OIL OF THYME; OLEUM THYMI (OL. THYMI), N.F. (Thyme Oil).

A volatile oil distilled from the leaves and flowering tops of *Thymus vulgaris* (Fam. *Labiatae*). Druggists list two varieties of this oil, the colorless and the red, the colorless oil being a purified product of the crude red oil. The medicinal properties of oil of thyme depend on the thymol present, of which it should yield not less than 20 per cent. The oil is used as an antiseptic and irritant in external applications.

DOSAGE.—0.1 cc. (1½ minims) (N.F.).

OIL OF YLANG-YLANG (OLEUM CANANGA).

Oil of Ylang-Ylang is distilled in Manila from the flowers of *Cananga odorata* (Fam. *Anonaceae*). This oil is especially noted for its delicious perfume. It seems to be a complex mixture, and the following bodies have been found in the oil: the esters of benzoic and salicylic acids, eugenol, iso-eugenol, geraniol, pinen, small quantities of paracresol, etc. Oil of cananga is a less fragrant oil of ylang-ylang, prepared from the same plant in Java.

Derivatives and Synthetic Substitutes of Essential Oils

BORNEOL, $C_{10}H_{18}O$. ARTIFICIAL BLUMEA CAMPHOR OF THE CHINESE; BORNEO CAMPHOR; BORNEOL, F.; BORNEOL, G.

A colorless, crystalline substance, having an odor somewhat different from that of ordinary camphor, resembling the odor of patchouly or ambergris. It is readily soluble in alcohol, chloroform, etc., but insoluble in water. It possesses antiseptic properties.

CAMPHOR; CAMPHORA (CAMPH.), $C_{10}H_{16}O$, U.S.P.

Camphor is a ketone obtained from the camphor tree, *Cinnamomum Camphora* or produced synthetically. It forms white translucent, crystalline masses, which are almost insoluble in water, but dissolve readily in alcohol, ether, chloroform, and in fixed and volatile oils. It

is *incompatible* with phenol, thymol, hydrated chloral, menthol, resorcinol, etc., in dry triturations, as it liquefies these substances to form a eutectic mixture.

DOSAGE.—By hypodermic injection, 0.2 Gm. (3 grains) (U.S.P.).—A 10 per cent solution in oil is used for hypodermic administration. Pear[1] suggests a liquid made of equal parts of camphor and monochlorphenol as a root canal antiseptic.

THERAPEUTICS.—On the skin and mucous membrane camphor acts as a mild irritant. It produces redness and a feeling of warmth when rubbed into the skin, and is principally applied externally in the form of alcoholic solutions or as a liniment (camphorated oil). It possesses slight antiseptic action, and is frequently used to modify the caustic action of phenol, thymol, resorcinol, etc. Internally it is used as a stimulant of the central nervous system, and is especially indicated in collapse arising from the action of general anesthetics, or from depression and weakness. It is usually injected hypodermically in sterilized solutions of olive oil.

℞	Camphor	30 Gm.
	Paramonochlorphenol	30 Gm.
	M. et allow to liquefy.	
	Sig.: Root canal antiseptic.	

ARKÖVY'S MIXTURE

℞	Oil of Cassia	8 Gm.
	Camphor	4 Gm.
	Oil of Eucalyptus	4 cc.

CARVOL, $C_{10}H_{14}O$. CARVONE, F.; CARVON, G.

A ketone forming the essential constituent of the oil of caraway seed and oil of dill. It is a pale yellow liquid, having the fine odor of caraway seed. It is used as a substitute for the oil of caraway and oil of dill. It is isomeric with thymol.

CINNAMIC ALDEHYDE; CINNALDEHYDUM, $C_6H_5CH:CHCHO$. ALDEHYDE CINNAMIQUE, F.; ZIMMTALDEHYD, G.

An aldehyde obtained from oil of cinnamon, or prepared synthetically. The oil should contain at least 80 per cent of cinnamic aldehyde. It is a colorless liquid, having a cinnamon-like odor and a burning, aromatic taste. It is sparingly soluble in water, soluble in all proportions in alcohol, ether, and fixed and volatile oils. It has been used as a substitute for the various oils of cinnamon in the treatment of putrescent root canals. Cinnamic aldehyde will not discolor tooth substance, which is frequently observed when oil of cinnamon is used.

[1]Pear, John R.: Bacteriocidal Effects of Some Drugs Used in Pulp Canal Therapy, J. A. D. A. 29: 244, February, 1942.

EUCALYPTOL; EUCALYPTOL, $C_{10}H_{18}O$, U.S.P. (CINEOL.).

A neutral body obtained from the volatile oil of *Eucalyptus globulus* and from various other sources. It is a colorless liquid, congeals below 32° F. (0° C.), having a camphor-like odor and a pungent, spicy, and cooling taste. It is identical with cajuputol and cineol. It is soluble in alcohol, ether, chloroform, etc., but insoluble in water. It is very mildly antiseptic, antispasmodic, expectorant, and antiperiodic; in combination with menthol and other bodies of a similar nature it is much in favor as an inhalant or as a spray diluted with a bland oil in bronchitis, asthma, pneumonia, rhinitis. It does not possess anesthetic properties.

THERAPEUTICS.—Eucalyptol is only slightly irritating to the soft tissues. It is a serviceable agent for the temporary treatment of root canals which require observation. As a lubricant for gutta-percha cones for the filling of root canals it is to be recommended. Eucalyptol will dissolve gutta-percha. If a perfect solution is desired, the gutta-percha should be first dissolved in chloroform, and then an equal amount of eucalyptol added, the bottle being left open until the chloroform is evaporated. This solution is superior to the so-called chloro-percha—a solution of gutta-percha in chloroform. (See Protectives, Demulcents, and Emollients.)

MODIFIED EUCALYPTOL

℞	Menthol	0.12 Gm.	gr. ij
	Thymol	0.18 Gm.	gr. iij
	Eucalyptol	4.00 cc.	3 j
	M.		
	Sig.: To be used in infected root canals (Buckley).		

EUGENOL; EUGENOL, $C_{10}H_{12}O_2$, U.S.P.

An unsaturated, aromatic phenol, obtained from oil of cloves and other essential oils. A colorless or pale yellow liquid, highly refractive, becoming brown on exposure to air, and having a strong aromatic odor of cloves and a pungent, spicy taste. It is soluble in alcohol, ether, chloroform, and diluted solutions of caustic soda; insoluble in water. It possesses antiseptic, stimulating, and local anesthetic properties. It is largely used as a substitute for oil of cloves.

THERAPEUTICS.—Eugenol is equally as strong an antiseptic as phenol, possessing decidedly less cauterant properties. It is an excellent obtundent for the treatment of pain arising from an irritated or diseased pulp, either alone or in combination with other suitable remedies. In the form of a paste it is recommended as a means of capping the exposed pulp or as a temporary filling in hypersensitive

cavities. In preparing such temporary cements, rather large quantities of eugenol must be incorporated into the powder. Combined with formaldehyde solution, it is recommended for the treatment of putrescent root canals. To isolate the strong anesthetic properties from eugenol, as the latter still acts as a mild cauterant, a number of compounds have been prepared synthetically, among which *p*-aminobenzoic acid has been found to be of the utmost importance. If this acid is combined with certain esters, it furnishes the basis on which some of the most important local anesthetics have been constructed. In the form of a temporary cement, it is employed as a temporary filling in painful conditions of the pulp arising from dental caries, and as a root filling material.

PULP CAPPING PASTE

℞	Aristol	4 Gm.	3 j
	Calcium Phosphate	40 Gm.	3 x
	Eugenol	enough to make a creamy paste.	

MENTHOL; MENTHOL, $C_{10}H_{20}O$, U.S.P.

A stearopten (camphene), having the character of a saturated secondary alcohol obtained from the official or from the Chinese or Japanese oil of peppermint. Japanese menthol appears in colorless crystals or in fused crystalline masses, having a strong odor of peppermint and a warm, aromatic taste, followed by a sensation of cold when air is drawn into the mouth. It melts at about 110° F. (42° C.). It is slightly soluble in water, but freely soluble in alcohol, ether, chloroform, etc. It possesses very weak, antiseptic, anesthetic, and analgesic properties. Menthol in the shape of compressed cones or combined in an ointment is largely employed for the relief of neuralgic pains. When applied to the skin, it produces at first slight pain, with a sensation of cold and benumbing of the skin. It is largely used as a substitute for oil of peppermint.

Camphorated Menthol; Menthol Camphoratum (Menthal Camph.), N.F. (Camphor-Menthol).—Equal parts of camphor and menthol.

USES.—Applied locally in the treatment of odontalgia.

METHYL SALICYLATE; METHYLIS SALICYLAS (METHYL. SALICYL.), U.S.P. (Oil of Gaultheria, Oil of Wintergreen, Oil of Betula, Oil of Sweet Birch).

Artificial or synthetic oil of wintergreen is a colorless or slightly yellowish liquid, having a characteristic, strong aromatic odor and a sweetish, warm taste. It is at present almost universally used as a substitute for the natural oil.

MYRTOL.—

A compound prepared by the fractional distillation of oil of myrtle, consisting largely of cineol, and therefore almost identical with eucalyptol and cajuputol. It is used as a substitute for oil of myrtle.

THYMOL; THYMOL, $C_{10}H_{14}O$, U.S.P.

Thymol is a phenol of the benzol series, occurring in the volatile oil of *Thymus vulgaris* and other volatile oils. It appears in colorless, crystalline masses, having an aromatic, pungent, and slightly caustic taste, and is of nearly neutral reaction. It is practically nontoxic. It melts at about 122° F. (50° C.), is slightly soluble in water (1:1,000), but very readily soluble in alcohol (1 in 1), ether, essential and fatty oils, chloroform, glacial acetic acid, etc. When treated with camphor, menthol, chloral, etc., it liquefies. In its local action it closely resembles phenol and salicylic acid. It is not so caustic as phenol, but more destructive to putrefactive substances.

THERAPEUTICS.—Thymol received its first attention by M. Bouillon, a French pharmacist, and soon it was introduced into general medicine (1876). Thymol has been highly recommended by dental practitioners, and its valuable antiseptic properties have been sustained.[1] In combination with other similar remedies, it is to be recommended on account of its persistent action. The following solution, known as thymocamphene, has proved quite satisfactory for the treatment of putrescent root canals:

℞	Thymol	4 Gm.	3 j
	Phenol	4 Gm.	3 j
	Camphor	2 Gm.	3 ss

Place the drugs in a dry amber-colored bottle. They will soon liquefy and remain liquid.

Köhler recommends the following combination for the same purpose:

℞	Thymol	4 Gm.	3 j
	Mono-chlorophenol	12 Gm.	3 iij
	Potassium Hydroxide	4 Gm.	3 j

Dissolve the thymol in the liquefied mono-chlorophenol and add to the solution the potassium hydroxide. Carefully heat over a low Bunsen flame until a perfect solution is produced. Immediately transfer to small, perfectly dry bottles, which should be protected by paraffined stoppers.

[1] Day, H. W.: Thymol in Cavity Sterilization, J. A. D. A. 31: 605, May 1, 1944.

HARTMAN'S DESENSITIZER*

Thymol	1½ parts
Ethyl alcohol	1 part
Sulfuric ether	2 parts

Parts are by weight.

It should be tightly corked and stored in a brown glass bottle, using cork or tin-lined stoppers only.

Hartman's solution is used as a dentin desensitizer in cavity preparation by topical application only; it is applied on a pellet of cotton directly to the dentin. The gingiva is protected with a rubber dam. If cotton rolls are used, varnish gums surrounding the tooth and change cotton rolls immediately after application. Allow the pellet to remain in contact with the tooth for one minute for children, one and one-half minutes for adults. Remove pellet and apply blast of warm air to area of application. Repeat the procedure as often as is necessary until cavity is prepared.

*Dobbs, E. C.: Dent. Cos. 78: 543, May, 1936.

CHAPTER XXIII

ASTRINGENTS

Astringents (from *stringere,* to bind) are substances which, when brought in contact with a wound or a mucous surface, cause the formation of a thin, skinlike protective film. The film results from:

1. The drying by and combining of the secretions with the astringent.
2. The coagulation of fibrogenous substances.
3. The precipitation of albuminous substances.
4. The chemical change of the tissue known as "tanning."

The term *astringent* is generally interpreted as drawing together. All astringents possess in a more or less marked degree this property so easily recognizable by the taste, and, if applied in concentrated solution, by the naked eye. It should be remembered that this is only a symptom of the astringent action as a whole. If astringents are applied in concentrated solutions, they precipitate proteins. The precipitated albumins form a protective layer over the wound or the mucous surfaces, while the deeper structures are contracted, thus causing a shrinkage of the entire tissue mass, which gives to the smooth, succulent surface a dry, dense character. This favorable influence of astringents is especially noticeable on inflamed soft tissues that have become morbidly relaxed. The wound or the inflamed mucous surfaces are tanned, a chemical process which is analogous to tanning hide into lather. Formaldehyde produces a similar action; the resultant chemical change differs from the true tanning, however, in so far as in genuine leather the tannic acid may be recovered, while from the formaldehyde-albumin combination the former cannot be removed.

The astringent action of drugs manifests itself in a combination of four definite ways:

1. By contracting the muscular coat of the arterioles.
2. By condensing the connective tissue.
3. By diminishing the secretion and exudation.
4. By checking the migration of leucocytes—the formation of pus.

The simple constriction of vessels is by no means identical with astringent action; for example, cocaine and, especially, epinephrine are very powerful vasoconstrictors without producing a true astringent effect. The diminished secretion and exudation and the checking of the migration of the leucocytes result from the tanning of the

intercellular cement substance between the endothelial cells, producing dense fibers of precipitated albumin which block the passage of fluids or semisolid materials. On unbroken skin, astringents act very slowly and in a milder degree.

If an astringent is dissolved in a surplus of blood, serum, or other tissue fluid, its typical action is destroyed. Absorbed astringents produce no effect through the circulation, and their internal administration for the purpose of acting through the blood is irrational.

Astringent action is primarily manifested by the salts of the heavy metals, by tannic acid and its many modifications, and by some very dilute organic and inorganic acids. Those metallic salts which are readily soluble in water and which are weak protoplasm poisons are frequently employed as astringents. A few insoluble or less readily soluble metallic salts, like the salts of bismuth and zinc, are also employed as astringents, and are frequently used as drying agents. The vegetable astringents are represented by tannic acid and its innumerable ill-defined modifications; they also precipitate proteins, gelatin, alkaloids, and glucosides. The acids are rarely employed as astringents, with the possible exception of diluted acetic acid (vinegar), citric acid (lemon juice), and weak solutions of boric acid. Diluted alcohol and glycerin are sometimes employed for astringent purposes; they act by virtue of their great affinity for water. In the following table Schuetz has recorded the weakest concentration of astringents employed for inhibiting tissue exudation.

Tannic acid	0.05 per cent	Silver nitrate	0.25 per cent
Alum	0.06 per cent	Ferric chloride	0.50 per cent
Mercuric bichloride	0.10 per cent	Copper sulfate	0.60 per cent
Lead acetate	0.22 per cent	Zinc sulfate	0.6 per cent

Astringents are closely related to caustics, styptics, antiseptics, and protectives; the difference in their action is largely a matter of time of exposure and concentration of solutions.

Astringents are employed to protect wounded or inflamed mucous surfaces, to check hypersecretion, to contract superficial blood vessels, and to reduce swollen mucous surfaces. All astringents coagulate normal blood rapidly when brought in intimate contact with it, and consequently they are used as styptics. Internally they are employed for the treatment of diarrhea.

Metallic Astringents

CUPRIC SULFATE; CUPRI SULFAS (CUPR. SULF.), $CuSO_4.5H_2O$, U.S.P. (Copper Sulfate).

ETYMOLOGY.—After Pliny, "*æs cuprium*, an ore primarily found in Cyprus."

SYNONYMS.—Cupric sulfate, blue vitriol, blue stone; sulfate de cuivre, F.; Kupfersulfat, blauer Galitzenstein, G.

SOURCE AND CHARACTER.—Copper sulfate is obtained by the interaction of water, sulfuric acid, and copper or copper oxide. It has a rich blue color, a strong disagreeable metallic taste, and appears in large crystals which slowly effloresce in dry air. It is odorless, soluble in about 3 parts of water, 3 parts of glycerin, very soluble in boiling water, and almost insoluble in alcohol (1 in 500). It is *incompatible* with alkalies and their carbonates, limewater, iodides, mineral salts (except sulfates), and most vegetable astringents. It corrodes steel instruments.

DOSAGE.—0.3 Gm. (5 grains), as an emetic.

MEDICAL PROPERTIES.—Astringent, stimulant, antiseptic, caustic, emetic, and hematinic.

THERAPEUTICS.—Copper sulfate, like all other metallic salts, precipitates albumin, producing a superficial film of copper albuminate. On exposed mucous membranes it acts as a caustic and strong astringent. It is milder in its action than silver nitrate or zinc chloride. Administered internally, by its irritating effect on the mucous membrane of the stomach and its nauseant taste, it acts as a rapid direct emetic and is well suited for that purpose when the stomach is to be surely and promptly emptied of a poison, like opium, etc. It is an antidote in acute phosphorus poisoning; it does not act merely as an emetic, but it partially oxidizes the phosphorus and partly covers it with metallic copper as a result of the reduction produced by the phosphorus. When it is administered for a longer period, it may cause greenish discoloration of the teeth, but not of the gingivae.

Copper sulfate is used in 0.5 to 2 per cent solutions as a stimulating astringent for indolent ulcers, the antrum, etc. It has a nauseating taste and is not used to any extent in the oral cavity. Copper sulfate enjoys a wide reputation as a means of destroying lower forms of life in polluted water. The cry of "poisoning with copper" is wholly unfounded, as the quantity necessary to purify water (1:1,500,000) is too small to cause any serious effects.

Aluminum Salts

ALUM; ALUMEN (ALUM.), $AlNH_4(SO_4)_2.12H_2O$ or $AlK(SO_4)_2.12H_2O$, U.S.P.

Colorless crystals or white powder, odorless and possessing a strongly astringent taste. Ammonium alum is somewhat more soluble (1 in 7) than potassium alum; both are insoluble in alcohol.

USES.—Astringent, styptic, and hemostatic. Seldom administered internally.

DOSAGE.—As a mouth wash, in from 1 to 2 per cent solution. It is acid and somewhat injurious to the teeth. It is used as a lotion in skin diseases, in 1 per cent solution.

Exsiccated Alum; Alumen Exsiccatum (Alum. Exsic.), U.S.P. (Dried Alum, Burnt Alum).—Anhydrous $AlNH_4(SO_4)_2$ or anhydrous $AlK(SO_4)_2$. (The salt desired may be indicated.)

White, odorless powder, with an astringent taste. Very slowly soluble in water (1 in 20); insoluble in alcohol.

USES.—Externally like alum, being more escharotic. *Alum* and *burnt alum* are useful astringents on wound surfaces, etc.

ALUMINUM ACETATE; ALUMINI ACETAS.

Solution of Aluminum Acetate; Liquor Alumini Acetatis (Liq. Alumin. Acet.), N.F. (Burow's Solution).—Contains neutral aluminum acetate [$Al(C_2H_3O_2)_3$] (about 5%). *Caution:* This solution should not be confused with a stronger preparation, now recognized under the name of Liquor Alumini Subacetatis (N.F.).

USES.—Popular astringent wash. Usually diluted with 10 parts of water (N.F.).

A solution of aluminum acetate, containing about 5 per cent of aluminum acetate, is much lauded as a mouthwash (a tablespoonful in a glassful of water) in all conditions where a mild, yet positive, astringent is indicated.

ALUMINUM CHLORIDE; ALUMINI CHLORIDUM (ALUMIN. CHLORID.), $AlCl_3.6H_2O$, N.F.

A nearly white deliquescent powder, with a sweet, astringent taste. Very soluble in water (1 in 0.5) and freely soluble in alcohol (about 1 in 4).

USES.—Antiseptic and astringent, without advantage over alum.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

Solution of Aluminum Chloride; Liquor Alumini Chloridi (Liq. Alumin. Chlorid.), N.F.—Aluminum chloride (25%) in water.

USES.—Used undiluted on unbroken skin.

ALUMINUM SUBACETATE; ALUMINI SUBACETAS, Basic aluminum acetate, $Al(C_2H_3O_2)_2OH$.

Solution of Aluminum Subacetate; Liquor Alumini Subacetatis (Liq. Alumin. Subacet.), N.F.—Contains basic aluminum acetate, $Al(C_2H_3O_2)_2OH$ (about 8%).

USES.—Astringent wash, usually diluted with 9 parts of water (N.F.). Some authorities prefer a dilution with 19 parts of water.

ALUMINUM SULFATE; ALUMINI SULFAS (ALUM. SULF.), $Al_2(SO_4)_3.18H_2O$, N.F.

A white, odorless powder, with an astringent taste. Freely soluble in water (1 in 1), but insoluble in alcohol.

USES.—Similar to, and without advantage over, alum.

Lead Salts

LEAD ACETATE; PLUMBI ACETAS (PLUMB. ACET.), $Pb(CH_3COO)_2.3H_2O$, U.S.P. (Sugar of Lead).

It forms colorless shining crystals, having a sweetish, astringent, afterward metallic taste. It is soluble in 1.6 parts of water and 30 parts of alcohol. Exposed to the air, it effloresces and absorbs carbon dioxide. It is *incompatible* with acids, sulfates, chlorides, tannin, phenol, and vegetable infusions and tinctures. Lead acetate is poisonous.

LEAD SUBACETATE; PLUMBI SUBACETAS.

USES.—Astringent; used externally in the form of the following preparations:

Solution of Lead Subacetate, Liquor Plumbi Subacetatis (Liq. Plumb. Subacet.), N.F. (Goulard's Extract).—Contains lead subacetate corresponding to about 22 per cent of lead.

USES.—For external use, dilute with 4 volumes of freshly boiled distilled water. (N. F.)

Diluted Solution of Lead Subacetate, Liquor Plumbi Subacetatis Dilutus (Liq. Plumb. Subacet. Dil.), N.F. (Lead Water).—Solution of lead subacetate (3.5%), corresponding to about 0.75 per cent of lead (Pb), with distilled water.

USES.—For external use, undiluted. Lead water is frequently employed as an external cooling sedative astringent in local inflammation, sprains, bruises, etc.; it is applied pure, or, following an old custom, in combination with laudanum in the proportions of 1 ounce of tincture of opium to ½ pint of lead water. The opium in this combination does not exercise any function whatsoever.

Zinc Salts

ZINC ACETATE; ZINCI ACETAS (ZINC. ACET.), $Zn(C_2H_3O_2)_2.2H_2O$, U.S.P.

Laminar crystals, having a faint vinegar-like odor and, in dilute solutions, an astringent metallic taste. Freely soluble in water (1 in 2.5), and soluble in alcohol (1 in 30).

USES.—Used locally, like zinc sulfate, being somewhat less astringent.

ZINC CHLORIDE; ZINCI CHLORIDUM (ZINC. CHLORID.), $ZnCl_2$, U.S.P.

ETYMOLOGY.—Zinc is first spoken of in the writings of Basilius Valentinus and Paracelsus in the fifteenth century, without mentioning where it was obtained. The later medical chemists usually spoke of zinc ores in general as "zinc."

SOURCE AND CHARACTER.—It is the product of the interaction between hydrochloric acid and zinc. It occurs as a white, granular powder or porcelain-like masses, or molded into pencils; odorless, and of such intensely caustic properties as to make tasting dangerous unless the salt be dissolved in much water. It has a strong metallic, astringent taste, is very deliquescent, and should be kept in glass-stoppered bottles. It is soluble in 0.5 part of water and very soluble in alcohol, glycerin, and ether, and its solutions have an acid reaction. It fuses at 240° F. (115° C.) to a clear liquid. It is *incompatible* with alkalies and their carbonates, with lead acetate, silver nitrate, the tannates, and limewater.

MEDICAL PROPERTIES.—Caustic, disinfectant, and astringent.

THERAPEUTICS.—In its local action, zinc chloride resembles closely the salts of lead, silver, and copper, forming albuminates by its chemical union with the contents of the mucous membranes and the tissue fluids. The precipitated albumin is of a loose, flocculent nature. Applied in substance, it quickly penetrates into and liquefies the soft tissues, which is usually accompanied by severe pain. It acts as a powerful and penetrating caustic. As a stimulating astringent, it is employed in aqueous solutions, either alone or in combination with antiseptics. As a component of mouthwashes which are to be used continuously, it should be limited to 1:3,000 solution. An 8 per cent aqueous solution of zinc chloride forms a suitable caustic for the local treatment of various types of stomatitis, aphthae, ulcers, etc. In the form of a paste, known as Canquoin's paste, consisting of equal parts of wheat flour and zinc chloride, with very little water, it was directly applied to carcinomatous growths, lupus, etc. It is seldom given internally.

Zinc chloride enjoys quite a reputation as a very efficient topical remedy for the treatment of hypersensitive dentin. It is applied to the isolated and partially dried tooth in substance or in a concentrated solution. At first usually severe pain is experienced, which soon ceases, leaving a superficially anesthetized surface. It does not

penetrate the dentine very deeply unless applied in excess or for a long period. Too close proximity to the pulp forbids its use for the above purpose, as it endangers the life of this organ. Technically, it is used in various dental cements and as a soldering flux in the laboratory.

TOXICOLOGY.—Internally, zinc chloride acts as a corrosive poison, somewhat similar to mercury bichloride. The treatment consists in emesis, which is usually produced by the salt itself, and in demulcent drinks (white of egg, alkalies, or milk), and stimulants.

CAUSTIC ZINC CHLORIDE SOLUTION

℞ Zinci Chloridi		2.6 Gm.	gr. xl
Aquæ	ad	30.0 cc.	fℨ j

M.

Sig.: Apply to the ulcerated surface.

ZINC IODIDE; ZINCI IODIDUM (ZINC. IODID.), ZnI_2, N.F.

It is a white granular powder, odorless, and has a sharp saline and metallic taste. It is readily soluble in water, alcohol, ether, and glycerin. The salt is liable to spontaneous decomposition, and, as it is also very deliquescent, it should be kept in glass-stoppered bottles. It is strongly astringent, and because of its iodine component promotes granulation. Talbot praised the value of zinc iodide in the form of a glycerinated solution for the treatment of inflammatory conditions of the gingiva accompanying pyorrheal disturbances. As all iodine preparations ruin ordinary metallic instruments, they are best applied on an iridoplatinum applicator or on a toothpick wound with cotton.

ZINC OXIDE; ZINCI OXIDUM (ZINC. OXID.), ZnO, U.S.P.

SOURCE AND CHARACTER.—Zinc oxide is made by exposing zinc carbonate to a dull red heat, or from metallic zinc by combustion. It is an amorphous white powder, without odor and taste. It is insoluble in water and alcohol; it gradually absorbs carbon dioxide from the air.

MEDICAL PROPERTIES.—Antiseptic, astringent, and basis for ointments and dental cements.

THERAPEUTICS.—Zinc oxide is employed as an exsiccant on excoriated surfaces by sprinkling it on the affected part, or in the form of an ointment (zinc oxide, 1 part; benzoinated lard, 4 parts, U.S.P.). It is used as a cosmetic in the form of face powder.

TECHNICAL USES.—Zinc oxide forms the base of the various zinc cements employed in dentistry. At present the oxychloride, the oxyphosphate, and the oxysulfate cements are utilized. In 1856 Sorel, of

Paris, introduced a method for preparing stucco work, "consisting of a coating of zinc oxide overlaid with a coating of zinc chloride." The inventor suggests its employment "to stop hollow teeth, for which its plasticity and subsequent impenetrability to the moisture of the mouth rendered it particularly applicable." Sorel's cement consists of a powder (calcined zinc oxide) and a liquid, which is a concentrated aqueous solution of zinc chloride. The addition of small quantities of borax lessens the rapid setting of the cement. The oxychloride cement is not used at present as a permanent filling material, but it is still used as a root canal filling, either alone or in combination with gutta-percha cones. If the cement is placed in too close proximity to the pulp, it may produce persistent irritation, or even death of this organ, as free HCl is liberated.

The Rostaings, father and son, dentists in Dresden, prepared in 1878 a filling material known as Dentinagen, consisting essentially of a mixture of phosphoric acid with zinc oxide. The combination is known at present as oxyphosphate of zinc cement. The various zinc oxyphosphate cements play an important role in operative dentistry. These cements consist principally of a powder (calcined zinc oxide) and a syrupy solution of orthophosphoric acid (H_3PO_4).

A zinc oxysulfate cement has proved itself to be a valuable agent for temporary filling purposes. It is essentially a mixture of calcined zinc oxide, calcined zinc sulfate, gum mastic, and a fluid consisting of a thin gum arabic solution. The mixture attains about the hardness of hydrated plaster of Paris. This cement is largely used for the retention of medicinal application in teeth, and, combined with formaldehyde, is sold under various names.

Oxysulfate of Zinc Cement

	POWDER		
℞	Powdered Mastic	30 Gm.	3 vijss
	Calcined Zinc Oxide	400 Gm.	3 C
	Calcined Zinc Sulfate	48 Gm.	3 xij
	LIQUID		
℞	Acacia	100 Gm.	3 xxv
	Water	260 cc.	fl3 lxv
	Alcohol	40 cc.	fl3 x
	Liquefied Phenol	1 cc.	℥ xv

Preparations.—

Paste of Zinc Oxide; Pasta Zinci Oxidi (Past. Zinc. Oxid.), N.F. (**Lassar's Plain Zinc Paste**).—Zinc Oxide (25%), starch, and petrolatum.

Paste of Zinc Oxide with Salicylic Acid; Pasta Zinci Oxidi cum Acido Salicylico (Past. Zinc. Oxid. c. Acid. Salicyl.), N.F. (Lassar's Zinc Paste with Salicylic Acid).—Salicylic acid (2%) in paste of zinc oxide.

Hard Paste of Zinc Oxide, Pasta Zinci Oxidi Dura (Past. Zinc. Oxid. Dur.), N.F. (Unna's Hard Zinc Paste).—Zinc oxide (25%) and purified siliceous earth in benzoinated lard.

Soft Paste of Zinc Oxide; Pasta Zinci Oxidi Mollis (Past. Zinc. Oxid. Moll.), N.F. (Unna's Soft Zinc Paste).—Zinc oxide (25%), precipitated calcium carbonate, linseed oil, oleic acid, and solution of calcium hydroxide.

Zinc Oxide Ointment; Unguentum Zinci Oxidi (Ung. Zinc. Oxid.), U.S.P. (Zinc Ointment).—Zinc Oxide (20%) in liquid petrolatum, wool fat, white wax, and white petrolatum.

ZINC PHENOLSULFONATE; ZINCI PHENOSULFONAS (ZINC. PHENOLSULF.), N.F. (Zinc Sulfocarbolate).

The hydrated salt appears in colorless, transparent crystals, and is soluble in about twice its weight of alcohol or water. It is an antiseptic, stimulant, and astringent. Its solutions have been employed for purposes similar to those of zinc sulfate and in about the same strength. Whether zinc phenolsulfonate possesses greater advantages than the other metallic astringents and antiseptics is questionable.

DOSAGE.—0.125 Gm. (2 grains) (N.F.).

ZINC STEARATE; ZINCI STEARAS (ZINC. STEAR.), U.S.P.

Zinc stearate with varying amounts of zinc palmitate corresponding to about 14 per cent of ZnO. Fine, bulky, white, tasteless powder, having a faint characteristic odor. Insoluble in water or alcohol.

USES.—Similar to zinc oxide.

Ointment of Zinc Stearate; Unguentum Zinci Stearatis (Ung. Zinc. Stear.), N.F.—Zinc stearate (35%) in liquid petrolatum and white petrolatum.

USES.—Similar to those of zinc oxide ointment.

ZINC SULFATE; ZINCI SULFAS (ZINC. SULF.), $ZnSO_4.7H_2O$, U.S.P.

SOURCE AND CHARACTER.—It is formed by the interaction of zinc and diluted sulfuric acid. It appears in colorless, transparent crystals, without odor, and has an astringent, metallic taste. It is soluble in 0.6 part of water, 2.5 parts of glycerin, and is insoluble in alcohol.

DOSAGE.—1 Gm. (15 grains), dissolved and well diluted with water, as an emetic.

MEDICAL PROPERTIES.—Astringent, antiseptic, and emetic.

THERAPEUTICS.—Zinc sulfate was used as local astringent in a 5 per cent solution in ulcerated conditions of the mouth. It is much weaker in its action than zinc chloride. By its irritating effect on the mucous membrane of the stomach, it acts as a direct and prompt emetic. Its use in dental therapeutics is limited because of its nauseant taste.

Bismuth Salts

BISMUTH SUBGALLATE; BISMUTHI SUBGALLAS (BISM. SUBGAL.), N.F. (Basic Bismuth Gallate, Dermatol).

An amorphous saffron-yellow powder, without odor and taste, yielding about 54 per cent of bismuth oxide. It is insoluble in water, alcohol, and ether, but soluble in diluted alkalies and acids. It is used as an intestinal astringent and antiseptic, and externally as a dusting powder on wound surfaces, etc.

DOSAGE.—1 Gm. (15 grains) (N.F.).

Tablets of Bismuth Subgallate, Tabellae Bismuthi Subgallatis (Tab. Bism. Subgall.), N.F.—Yield bismuth oxide equal to 48 to 61 per cent of the stated amount of Bismuth Subgallate.

DOSAGE.—1 Gm. (15 grains) of Bismuth Subgallate (N.F.).

BISMUTH AND POTASSIUM TARTRATE; BISMUTHI ET POTASSII TARTRAS (BISM. ET POT. TART.), U.S.P. (Potassium Bismuth Tartrate, Potassium Bismuthyl Tartrate).

Equivalent to about 62 per cent of bismuth.

USES.—Injected intramuscularly it is antisyphilitic and diuretic. (See article Bismuth Compounds in *Useful Drugs.*)

DOSAGE.—By parenteral injection, 0.15 Gm. (2½ grains) (U.S.P.). The technique of intramuscular administration is described in *Useful Drugs.*

BISMUTH SUBNITRATE; BISMUTHI SUBNITRAS (BISM. SUBNIT.), U.S.P. (Basic Bismuth Nitrate).

A basic bismuth nitrate of varying composition, yielding at least 79 per cent of bismuth oxide, Bi_2O_3.

The insoluble bismuth salts act as absorbents on wound secretions, thus rendering the surface less suitable for the growth of bacteria. Bismuth is not a harmless remedy when applied for a prolonged period, and several cases of poisoning have been recorded from its local use.

USES.—Somewhat more astringent than the subcarbonate, because of the liberation of nitric acid.

DOSAGE.—1 Gm. (15 grains) (U.S.P.). Preferably administered as a powder or in cachets.

Paste of Bismuth; Pasta Bismuthi (Past. Bism.), N.F. (Beck's Bismuth Paste).—Bismuth subnitrate (30%) in white wax, paraffin, and white petrolatum.

USES.—Used in wound cavities; should be used cautiously, as it may give rise to poisoning.

Tablets of Bismuth Subnitrate; Tabellae Bismuthi Subnitratis (Tab. Bism. Subnit.), N.F.—Yield bismuth oxide equal to 73 to 85 per cent of the stated amount of Bismuth Subnitrate.

DOSAGE.—1 Gm. (15 grains) of Bismuth Subnitrate (N.F.).

BISMUTH SUBSALICYLATE; BISMUTHI SUBSALICYLAS (BISM. SUBSALICYL.), U.S.P. (Basic Bismuth Salicylate).

A basic bismuth salicylate of varying composition, yielding 62 to 66 per cent of Bi_2O_3.

A white or nearly white amorphous or microcrystalline powder. It is odorless and stable in air. Practically insoluble in cold water or alcohol.

USES.—Injected intramuscularly as an antisyphilitic.

DOSAGE.—Gastrointestinal, 1 Gm. (15 grains).

VEGETABLE ASTRINGENTS

TANNIC ACID; ACIDUM TANNICUM (ACID. TAN.), U.S.P. (Gallotannic Acid, Tannin).

SOURCE AND CHARACTER.—Tannic acid is an organic acid obtained from nutgall. Nutgall is an excrescence on the oak tree, *Quercus infectoria (Quercus lusitanica),* caused by the puncture of and deposited ova of an insect, *Cynips tinctoria.* It is a light-yellow, amorphous bulky powder or spongy mass, with a slight odor and a strongly astringent taste. When exposed to the air and light, it gradually turns dark. It is soluble in 1 part water or glycerin, 0.6 part alcohol, very soluble in hot water and hot alcohol. With albumin and other tissue substances it forms definite compounds, which are insoluble in water, but partially soluble in alkalies and certain acids. Its astringent action is manifested even in very weak solutions (0.05 per cent). It is *incompatible* with the metallic salts, with the iodine compounds, and with easily oxidizable substances—as the permanganates, chlorates, etc.; with ferric salts it forms a black compound

(ink). It should be preserved in amber-colored bottles, well stoppered. Solutions of tannic acid should be made fresh, as they deteriorate with age.

DOSAGE.—As antidote, 1 Gm. (15 grains).

MEDICAL PROPERTIES.—Astringent, styptic, and antiseptic.

PREPARATIONS.—

Styptic Collodion; Collodium Stypticum (Collod. Stypt.), N.F.—Tannic acid (16%) and flexible collodion. There is no advantage in applying tannin in collodion.

Glycerite of Tannic Acid; Glyceritum Acidi Tannici (Glycer. Acid. Tan.), U.S.P. (Glycerite of Tannin).—Tannic acid (20%), sodium citrate (1%), in glycerin.

Tannic Acid Ointment; Unguentum Acidi Tannici (Ung. Acid. Tan.), U.S.P.—Tannic acid (20%), in glycerin and ointment. (*Caution:* During its manufacture and storage this ointment must not come in contact with iron utensils or containers. U.S.P.)

THERAPEUTICS.—Tannic acid acts as a powerful astringent, exercising its function on vessels and tissue fibers; it coagulates blood. When placed on the oral mucous membrane, a coagulation of the superficial layers results, which causes a feeling of constriction, dryness, and roughness in the mouth. By its combination with the secretions of a wound it forms a protective film over the denuded surfaces. If applied in concentrated solution, it irritates and may act even as a caustic. Tannic acid is used as an astringent gargle in catarrhal conditions of the pharynx (0.5 to 2 per cent solutions), and internally in disturbances of the stomach and the intestines. As an internal astringent in diarrhea and dysentery it is of doubtful value. It is much used as an external astringent and styptic in powder form or in concentrated solution, preferably as the glycerite of tannic acid. Care should be exercised in the use of tannic acid in the treatment of teeth as it may cause bluish-black discoloration resulting from a freshly formed iron tannate. The pure acid and its many modifications—rhatany, witch hazel, oak bark, etc.—are largely used as components of mouthwashes. (See Preparations for the Mouth and Teeth.)

Tannic acid is frequently employed as an antidote for alkaloids when these poisons are taken into the stomach. It readily precipitates the alkaloids, forming tannates, which should be removed from the stomach with emetics or the stomach pump. Tea or coffee is usually available for such purposes; they contain more or less sufficient tannin to render them important adjuncts in emergency treatment.

USES.—Somewhat more astringent than the subcarbonate, because of the liberation of nitric acid.

DOSAGE.—1 Gm. (15 grains) (U.S.P.). Preferably administered as a powder or in cachets.

Paste of Bismuth; Pasta Bismuthi (Past. Bism.), N.F. (Beck's Bismuth Paste).—Bismuth subnitrate (30%) in white wax, paraffin, and white petrolatum.

USES.—Used in wound cavities; should be used cautiously, as it may give rise to poisoning.

Tablets of Bismuth Subnitrate; Tabellae Bismuthi Subnitratis (Tab. Bism. Subnit.), N.F.—Yield bismuth oxide equal to 73 to 85 per cent of the stated amount of Bismuth Subnitrate.

DOSAGE.—1 Gm. (15 grains) of Bismuth Subnitrate (N.F.).

BISMUTH SUBSALICYLATE; BISMUTHI SUBSALICYLAS (BISM. SUBSALICYL.), U.S.P. (Basic Bismuth Salicylate).

A basic bismuth salicylate of varying composition, yielding 62 to 66 per cent of Bi_2O_3.

A white or nearly white amorphous or microcrystalline powder. It is odorless and stable in air. Practically insoluble in cold water or alcohol.

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(ink). It should be preserved in amber-colored bottles, well stoppered. Solutions of tannic acid should be made fresh, as they deteriorate with age.

DOSAGE.—As antidote, 1 Gm. (15 grains).

MEDICAL PROPERTIES.—Astringent, styptic, and antiseptic.

PREPARATIONS.—

Styptic Collodion; Collodium Stypticum (Collod. Stypt.), N.F.—Tannic acid (16%) and flexible collodion. There is no advantage in applying tannin in collodion.

Glycerite of Tannic Acid; Glyceritum Acidi Tannici (Glycer. Acid. Tan.), U.S.P. (Glycerite of Tannin).—Tannic acid (20%), sodium citrate (1%), in glycerin.

Tannic Acid Ointment; Unguentum Acidi Tannici (Ung. Acid. Tan.), U.S.P.—Tannic acid (20%), in glycerin and ointment. (*Caution:* During its manufacture and storage this ointment must not come in contact with iron utensils or containers. U.S.P.)

THERAPEUTICS.—Tannic acid acts as a powerful astringent, exercising its function on vessels and tissue fibers; it coagulates blood. When placed on the oral mucous membrane, a coagulation of the superficial layers results, which causes a feeling of constriction, dryness, and roughness in the mouth. By its combination with the secretions of a wound it forms a protective film over the denuded surfaces. If applied in concentrated solution, it irritates and may act even as a caustic. Tannic acid is used as an astringent gargle in catarrhal conditions of the pharynx (0.5 to 2 per cent solutions), and internally in disturbances of the stomach and the intestines. As an internal astringent in diarrhea and dysentery it is of doubtful value. It is much used as an external astringent and styptic in powder form or in concentrated solution, preferably as the glycerite of tannic acid. Care should be exercised in the use of tannic acid in the treatment of teeth as it may cause bluish-black discoloration resulting from a freshly formed iron tannate. The pure acid and its many modifications—rhatany, witch hazel, oak bark, etc.—are largely used as components of mouthwashes. (See Preparations for the Mouth and Teeth.)

Tannic acid is frequently employed as an antidote for alkaloids when these poisons are taken into the stomach. It readily precipitates the alkaloids, forming tannates, which should be removed from the stomach with emetics or the stomach pump. Tea or coffee is usually available for such purposes; they contain more or less sufficient tannin to render them important adjuncts in emergency treatment.

ASTRINGENT MOUTHWASH

℞ Tannic Acid 1 Gm.
Peppermint Water q.s. ad 500 cc.
M. et sol.
Sig.: Dilute with equal parts of warm water as a mouthwash.

℞ Glycerite of Tannic Acid 30 cc.
Distilled Water q.s. ad 120 cc.
M.
Sig.: 4 cc. in a glassful of warm water as a mouthwash.

STYPTIC DUSTING POWDER

℞ Alum.
Acid. Tannic. āā 4 Gm. 3 j
M.
Sig.: Styptic dusting powder.

THERAPEUTICS.—

1. As an astringent mouthwash in a 0.1 per cent solution.
2. As a topical astringent in a 2 per cent solution.
3. As a styptic, as a powder, or as the glycerite of tannic acid applied to the bleeding area.

GALLIC ACID; ACIDUM GALLICUM (ACID. GALLIC.), $C_6H_2.COOH.(OH)_3.H_2O$, N.F.

An organic acid, usually prepared from tannic acid. It has no astringent effect, and possesses very little medicinal value.

A large number of synthetically prepared tannic acid compounds have been introduced into therapeutics, especially for internal administration. The principal object of these preparations has been to overcome the disagreeable taste and irritating action of tannic acid, and to reach the upper intestines without being decomposed by the gastric juice.

DOSAGE.—1 Gm. (15 grains) (N.F.).

HAMAMELIS LEAF; HAMAMELIDIS FOLIUM (HAMAMEL. FOL.), N.F. (Witch-hazel Leaves).

USES.—Astringent, without advantage over other tannin-bearing drugs.

DOSAGE.—2 Gm. (30 grains) (N.F.).

Fluidextract of Hamamelis Leaf; Fluidextractum Hamamelidis Folii (Fldext. Hamamel. Fol.), N.F. (Fluidextract of Witch-hazel Leaves).—Hamamelis leaves (100%). Absolute alcohol content about 74 per cent.

DOSAGE.—2 cc. (30 minims) (N.F.).

Hamamelis Water; Aqua Hamamelidis (Aq. Hamam.) (Witch-hazel Water, Distilled Extract of Witch Hazel).—Witch-hazel twigs, distilled with water and preserved with about 14.5 per cent of alcohol.

USES.—Employed externally, for contusions.

KRAMERIA; KRAMERIA (KRAMER.), N.F. (Rhatany).

The dried roots of a variety of rhatany plants. Rhatany contains on an average from 7 to 8 per cent of kramero-tannic acid and some red coloring matter. It is especially to be recommended as a topical oral astringent in the form of a diluted tincture (*Krameria*, 1 part; diluted alcohol, 5 parts).

USES.—Actively astringent.

DOSAGE.—1 Gm. (15 grains) (N.F.).

Fluidextract of Krameria; Fluidextractum Krameriae (Fldext. Kramer.), N.F. (Fluidextract of Rhatany).—Krameria (100%). Absolute alcohol content about 63 per cent.

DOSAGE.—1 cc. (15 minims) (N.F.).

Krameria has no advantage over tannic acid as an oral astringent.

CHAPTER XXIV

IRRITANTS AND COUNTERIRRITANTS

The local application of *irritants* and *counterirritants* plays an important part in the clinical practice of dentistry. Depending on their intensity of action, irritants may be classed as rubefacients, vesicants, and pustulants. *Rubefacients* (reddening the skin) produce only mild symptoms of irritation in the form of congestion and redness, while *vesicants* (forming blisters) and *pustulants* (forming pustules) are very powerful in their action. In many instances irritants are applied to the healthy tissue somewhat distant from the primary seat of disturbance, with the intention of diverting the deep-seated congestion. Medicaments applied for this purpose are known as counter-irritants. If strong irritants are applied to a circumscribed area of tissue, an exudation of small globules of serum occurs; the latter soon coalesce and raise the epidermis of the true skin, thereby forming a blister. If the drugs applied as irritants cannot pass through the horny epidermis, they produce small exanthematous blisters, which may coalesce and form a large ulcer. This heroic form of medication is rarely employed at present; it was quite common with the practitioners of bygone days.

At present it is generally recognized that the milder irritants produce the preliminary stages of inflammation—hyperemia. An increased influx and a retarded efflux of blood in the irritated tissue are the consequence of the irritation. Depending on the nature of the irritant, the congestion may be superficial or deep. Tissues which are richly supplied with blood possess a very pronounced restorative power, and there is no doubt that artificial hyperemia exercises a distinct beneficial influence on infections and on the reparative processes. This is partially the reason why wounds in the oral cavity heal so much quicker than those in other parts of the body. Pain in deep-seated structures is often mitigated by applying an irritant. By counterirritation of a sensory surface located somewhat distant from the primary seat of irritation, we may be able to divert the congestion and pain to this newly excited focus. Such applications may be employed in the treatment of many forms of ill-defined pericemental disturbances. Some of the substances employed as irritants act by reflex action—that is, they produce a nervous reflex which has a beneficial influence on pathologic disturbances.

It should be remembered that the same irritant produces different effects on tissues of different resistance. The more delicate mucous membrane of the mouth requires naturally less severe irritation to produce definite results than the thick and horny layers of the skin.

Iodine in aqueous or in alcoholic solution occupies an important place among the irritants. It possesses a powerful and penetrating action. Alcohol, chloroform, the essential oils, and mustard are also favorite irritants, while cantharides is a typical representative of a blistering agent. Ammonia, well diluted, in the form of a liniment constitutes an important irritant in popular medication.

IODINE; IODUM (IOD.), U.S.P.

SOURCE AND CHARACTER.—Iodine (from the Greek *ioeides*, violet colored) was discovered by Courtois in 1811, and named iodine by Gay-Lussac on account of its violet-colored vapors. Iodine is prepared from crude iodine, which is obtained from kelp, but principally from the mother liquors of Chile saltpeter of South America. It forms heavy, bluish-black, friable crystals, having a characteristic odor and a sharp and acrid taste. It is soluble in 2,950 parts of water, 13 parts of alcohol, freely soluble in ether, chloroform, and in the solution of the iodides of the alkalies. Its alcoholic solution has a reddish-brown color, while, when dissolved in chloroform or carbon disulfide, it exhibits a violet tint. It volatilizes at ordinary temperature and fuses at about 239° F. (115° C.). It is *incompatible* with starch, tannin, vegetable colors, etc.

MEDICAL PROPERTIES.—Antiseptic, counterirritant, caustic, and alterative.

THERAPEUTICS.—Iodine, in concentrated solution, acts as a caustic; in diluted solution, applied locally, it produces only irritant effects. Iodine has a peculiar action on the vessel walls, as it increases their permeability. It produces typical fibrinous inflammation of the serous membranes. After the destruction of their epithelial coat, these serous membranes show a pronounced tendency to stick together and to heal by first intention. For this reason iodine is successfully employed in the treatment of fistulous tracts, etc. Painted on the skin, iodine quickly penetrates into the structures, and produces sensible irritation, thereby relieving pain which may be present in the deep-seated tissues. Incidentally it enlarges the walls of the various vessels, promotes absorption, and by reflex action produces venous hyperemia, which involves all the tissues within the affected area. Iodine is very freely employed in alcoholic solutions (tinctures of iodine), and as the milder acting Lugol's solution. In using the tinc-

ture of iodine the alcoholic component of the latter must be accredited with a certain share of its action.

To promote the more ready absorption of iodine, various solutions have been recently introduced.

Iodine, per se or in solution, is very destructive to metallic instruments. The top of the ground-glass cover office bottle containing the iodine solution should be coated with a thin lining of petroleum jelly as an additional protection.

PREPARATIONS.—

Tincture of Iodine; Tinctura Iodi (Tr. Iodi), U.S.P.—Iodine (7%), potassium iodide (5%), alcohol, and distilled water. Absolute alcohol content about 85 per cent.

USES.—Chiefly for external use as an antiseptic and counterirritant.

Mild Tincture of Iodine; Tinctura Iodi Mitis (Tr. Iodi Mit.), U.S.P.—An alcoholic solution of iodine (about 2%) and sodium iodide (about 2.3%). Alcohol content about 47 per cent.

USES.—Externally as an antiseptic and counterirritant. This preparation was designed for oral use.

Stronger Tincture of Iodine; Tinctura Iodi Fortior (Tr. Iodi Fort.), N.F. (Churchill's Tincture of Iodine).—Iodine (16.5%) and potassium iodide (3.5%) in water and alcohol. Absolute alcohol content about 62.5 per cent.

Strong Solution of Iodine; Liquor Iodi Fortis (Liq. Iodi Fort.), U.S.P. (Liquor Iodi Compositus, Compound Solution of Iodine U.S.P. XI, Lugol's solution).—Iodine (5%) and potassium iodide (10%) in distilled water.

DOSAGE.—0.3 cc. (5 minims) (U.S.P.).

Solution of Iodine; Liquor Iodi (Liq. Iodi), U.S.P.—It contains in each 100 cc., about 2 Gm. of iodine, and 2.4 Gm. of NaI.

USES.—A mild antiseptic and counterirritant for external use.

Glycerite of Iodine and Zinc Iodide; Glyceritum Iodi et Zinci Iodidi (Glycer. Iodi et Zinc. Iodid.), N.F. (Diluted Talbot's Solution).—Zinc iodide (8%), iodine (10%), glycerin, and water.

USES.—For external use as a counterirritant and caustic.

Ampuls of Iodine; Ampullae Iodi (Ampul. Iodi), N. F. (Iodine Swabs).—Contain a sterile solution of iodine (about 3.5%) and sodium iodide (2.5%) in about 60 per cent alcohol.

USES.—These ampuls are convenient for the application of iodine solution to the skin with cotton swabs.

THERAPEUTICS.—Tincture of iodine is universally employed as a counterirritant in pericemental disturbances. Its beneficial influence is based on three principal functions of iodine—to act as a derivant by sensory irritation, to produce artificial hyperemia, and to promote absorption. Its antiseptic properties are of less importance in this connection. If a definite iodine action is desired in the mouth, the ordinary tincture is not well suited for this purpose. Its alcoholic component causes superficial coagulation of the delicate mucous membrane, and in reality very little iodine is absorbed from this weak solution. If the tincture is repeatedly applied at short intervals, the caustic effect of the alcohol destroys the mucous lining, and a painful excoriated surface is the result. The irritating effect of the alcohol is probably as much responsible for the apparent results attributed to the tincture as its iodine component. Liquid iodine preparations for dental purposes should be aqueous solutions, preferably in the form of solution of iodine, U.S.P. A colorless tincture of iodine is occasionally demanded; ammonia water added to the tincture will quickly destroy its color and also its action. If higher concentrated iodine solutions are wanted, Churchill's solution of iodine is serviceable, but this compound should not be used indiscriminately on the mucous surfaces of the mouth as it is a caustic.

Tincture of iodine applied to the mucous membranes of the mouth is not as harmless a remedy as is presumed by some practitioners. The routine advice to patients to "paint with iodine" in cases of pericemental trouble is wholly unwarranted. From the ready absorption of iodine applied to the mucous membrane of the mouth for a certain length of time, edema of the glottis and, on rare occasions, iodism, have resulted.

TALBOT'S MODIFIED IODOGLYCEROL

Zinc Iodide	20 Gm.
Water	160 cc.
Iodine	20 Gm.
Glycerin	240 cc.

Dissolve the zinc iodide in the water, add the iodine and when completely dissolved, add the glycerin.

SKINNER'S DISCLOSING SOLUTION

Iodine	50 parts
Potassium Iodide	15 parts
Zinc Iodide	15 parts
Distilled Water	240 parts
Glycerin	240 parts

BLACK MUSTARD; SINAPIS NIGRA (SINAP. NIG.), U.S.P. (Brown Mustard).

DOSAGE.—Emetic, 10 Gm. (2½ drachms) (U.S.P.).

Mustard is represented in the pharmacopoeia by the dried ripe seeds of the black mustard. The seeds contain a glucoside, sinigrin, which is found only in the black seeds. When powdered mustard seed is mixed with water, decomposition of its glucoside takes place, which results in the formation of the volatile oil of mustard. (See allyl isothiocyanate, U.S.P.) This oil is intensely irritating to the skin, and when left long enough in contact therewith causes blistering. Ground mustard seed is principally employed in the form of a plaster and as a poultice to produce external irritation. When the plaster is dipped in warm water for a minute and placed on the body surface, the volatile oil is produced by slow decomposition of the glucoside. The poultice is prepared by mixing the ground seed with warm water; it is folded in a napkin and then placed on the body surface. Mustard, in combination with powdered capsicum, in the form of bags, as suggested by Flagg, or, still better, as small dental plasters, is a means of producing counterirritation over the roots of teeth. These plasters should not be adhesive; they are merely placed on the moist gingiva over the seat of irritation, and held in position by a pledget of cotton and the natural pressure of the cheek.

Mustard Plaster; Emplastrum Sinapis (Emp. Sinap.), U.S.P. (Mustard Paper).—A mixture of black mustard, deprived of its fixed oil, and a solution of rubber, spread on paper, cotton cloth or other fabric.

USES.—Counterirritant. *Note*—Before applying Mustard Plaster it should be thoroughly moistened with tepid water. (U.S.P.)

CAPSICUM; CAPSICUM (CAPSIC.), N.F. (Cayenne Pepper, African Chillies).

The dried ripe fruit of *Capsicum frutescens.* Capsicum contains some ill-defined, nonvolatile bodies which act as powerful irritants. It is principally employed externally in the form of a liniment or plaster, and internally as a stomachic.

USES.—Carminative and rubefacient.

DOSAGE.—60 mg. (1 grain) (U.S.P.).

Tincture of Capsicum; Tinctura Capsici (Tr. Capsic.), N.F.—Capsicum (10%) in alcohol and distilled water. Absolute alcohol content about 83 per cent.

DOSAGE.—0.5 cc. (8 minims) (N.F.).

Ointment of Capsicum; Unguentum Capsici (Ung. Capsic.), N.F.—Oleoresin of capsicum (5%) in a mixture of paraffin and petrolatum.

CANTHARIDES; CANTHARIS (CANTHAR.), N.F. (Spanish Flies, Russian Flies, Pulvis Cantharidis P.I.).

It is the dried beetle, *Cantharis vesicatoria,* yielding not less than 0.6 per cent cantharidin. The beetles contain cantharidin, a derivative of benzol, which is a powerful vesicant. In the form of a cerate, plaster, or collodion, it is largely used as a blistering agent, but there is rarely any need for the use of this powerful remedy in dentistry.

USES.—Externally, rubefacient and vesicant. Internally, genito-urinary irritant, often producing serious nephritis. Its internal use is never justified.

Cantharides Cerate; Ceratum Cantharidis (Cerat. Canthar.), N.F. (Blistering Cerate).—Cantharides (35%) with oil of turpentine, glacial acetic acid, yellow wax, rosin and benzoinated lard.

Plaster of Cantharides; Emplastrum Cantharidis (Emp. Canthar.), N.F.—Cantharides cerate spread on adhesive plaster. Each square centimeter of spread plaster contains 0.1 Gm. of cantharides cerate.

USES.—Convenient form for applying cantharides as a vesicant.

Tincture of Cantharides; Tinctura Cantharidis (Tr. Canthar.), N.F.—(Tinctura cantharidis P.I.).—Cantharides (10%), in glacial acetic acid (10%) and alcohol. Absolute alcohol content about 81 per cent.

DOSAGE.—0.1 cc. (1½ minims) (N.F.). Its internal use is not desirable.

AMMONIA; AMMONIA (NH_3).

Diluted Solution of Ammonia; Liquor Ammoniae Dilutis (Liq. Ammon. Dil.), U.S.P. (Aqua Ammoniae, Ammonia Water, U.S.P. XI).—It is an aqueous solution of ammonia (NH_3), containing 10 per cent by weight of gaseous ammonia.

USES.—Local irritant and antacid, preferably as a liniment. Volatile indirect circulatory and respiratory stimulant.

DOSAGE.—1 cc. (15 minims). This should be diluted with water. The aromatic spirit of ammonia is preferable for internal administration.

Strong Solution of Ammonia; Liquor Ammoniae Fortis (Liq. Ammon. Fort.), U.S.P.—NH_3 (about 28%) in water.

Ammonia Liniment; Linimentum Ammoniae (Lin. Ammon.), N.F. (Volatile Liniment, Hartshorn Liniment).—Ammonia water (25%) in oleic acid and sesame oil.

USES.—Popularly used as a counterirritant.

The various ammonia solutions are principally employed in diluted form as liniments in popular medicines; they act as rubefacients, and are used in sprains, bruises, etc. As skin irritants and vesicants they are rarely employed at present. In the form of smelling salts, ammonia is used by inhaling its gas as a reflex stimulant in fainting, etc.

ACONITE; ACONITUM (ACONIT.), N.F. (Monkshood, Aconite Root, Aconiti tuber P.I.).

SOURCE AND CHARACTER.—It is the dried tuberous root of *Aconitum Napellus*. Its principal constituent is the alkaloid aconitine. The latter is insoluble in water, but readily soluble in alcohol. Its potency is such that 0.1 Gm. is equivalent to not less than 0.150 mg. of Reference Aconitine, U.S.P.

DOSAGE.—0.06 Gm. (1 grain) (U.S.P.); not used as such.

THERAPEUTICS.—Aconite is principally employed in the form of the tincture. The alkaloidal content of the tuber differs greatly with the soil on which it is grown, and on account of its very poisonous nature, the alkaloid is rarely employed internally. The active principles of aconite, as presented in the liquid preparations, readily decompose on standing; hence, in prescribing, fresh preparations should be insisted upon. Aconite is a powerful poison; it slows and weakens the heart and circulation and quickly paralyzes the respiratory centers. As it reduces the temperature, it has been used as an antipyretic and also as a sedative, especially in children's diseases. Locally applied, tincture of aconite partially anesthetizes the terminations of the sensory nerves of the skin and the mucous membranes; hence its use in dentistry as a local anodyne and as a remedy for facial neuralgia. A mixture of equal parts of tincture of aconite and tincture of iodine, which is very largely used in dentistry as an anodyne or a counterirritant, is of little practical value; the official tincture merely dilutes the iodine solution. The aconite represented in this mixture is entirely too small to be of benefit, and, if a concentrated tincture (fluidextract) is used, the possibility of its quick absorption and subsequent untoward effects courts danger. Aconite and aconite preparations have no use in dental therapeutics.

CHAPTER XXV

CAUSTICS

Caustics (burn), sometimes called *escharotics* (a slough or burn), are substances which destroy living tissue by virtue of their coarse chemical or physical action. The older medical lexicographers restricted the term escharotic to substances which produce a dry, more or less insoluble, protective slough. They further differentiated between the *actual* cautery, i.e., the red hot iron, and the *chemical* cautery, i.e., an agent, like silver nitrate, which forms an eschar without the agency of actual fire.

Pure chemical drug action on living cell structure which endangers, or even kills, the cell without visible changes is referred to as *protoplasm poisoning,* while a drug which produces severe visible tissue changes, but without cell destruction, is spoken of as an *irritant.*

It has been stated that a protoplasm poison is a substance which, without producing directly evident alterations, harms or kills all *living* protoplasmic structures. Mercuric bichloride, quinine, arsenic trioxide, etc., are such poisons; whereas sulfuric acid, bromine, and similar substances that destroy life through their strong chemical action are not included in this category and are referred to as caustics. The protoplasmic poisons presumably act by combining with one or more of the constituents of cell protoplasm; i.e., mercuric bichloride probably combines with the proteins; chloroform with the cell lipids, etc.

Caustic action means destruction of protoplasm and the life of the cell. It may be produced:

1. *By abstracting water from the cell contents.* The normal quantity of water present in the living cell amounts to 75 to 90 per cent. If this water is removed, the cell will die. The active salts, alkalies, acids, etc., are chemicals which produce such an effect. Substances which act by virtue of their affinity for water alone are not employed as caustics but as astringents.

2. *By dissolution of the cell contents.* Alkalies are albumin solvents. The alkaline salts—potassium or sodium carbonate—are mild caustics, while potassium and sodium hydroxide, which contain free hydroxyl groups, are more powerful in their action. The caustic alkalies are not self-limiting; they penetrate deeply into the tissues, and destroy the mucous surfaces, the horny tissues, and the external skin. The lower fatty acids may also act as solvents of albumin.

3. *By precipitation of the cell contents.* Agents acting as albumin precipitants are: (a) *Acids*—all inorganic acids, except boric acid; the chlorine substitute fatty acids—trichloracetic acid, and those aromatic acids which are readily soluble in water to such an extent as to produce the desired acidity—salicylic acid. (b) *Solutions of metallic oxides and salts*—may act as precipitants of albumin through their acid as well as through their basic components; the precipitate produced by the metallic salts differs widely in regard to density—silver nitrate, for instance, produces a dry, dense scab, while zinc chloride combines with the albumin to form a loose, flocculent clot. (c) *Certain organic compounds*—as phenol, trinitrophenol (picric acid), and alcohol; the latter precipitates albumin only when applied in solutions containing at least 65 per cent or more of pure alcohol.

4. *By oxidation or reduction.* The strong reducing agents like nitrous acid and oxidizing agents like chromic acid disintegrate the cell contents.

5. *By substitution.* Iodine, bromine, and chlorine act on the albumin molecule by substitution—that is, atoms of hydrogen are replaced by halogen atoms. This destroys the life of the cell and at the same time halogen acids are formed which act as precipitants of albumin.

In general, caustics are more or less related qualitatively but not quantitatively to antiseptics, astringents, styptics, and irritants.

Caustics are indicated:

1. *To destroy specific poisons.* For the treatment of fresh infections on external surfaces resultant from the bite of a poisonous snake or a scorpion, or all such accidents which inoculate the wound with a nonbacterial or specific poison, potassium permanganate in concentrated solution is highly recommended.

2. *To destroy bacterial infection.* Local infection resultant from the bite of a vicious dog (hydrophobia) is destroyed by the application of caustics.

3. *To destroy tumors, neoplasms, and normal or abnormal tissue.* Polypi, epulides, small aneurysms, hypertrophied mucous membrane or gingival tissue, and intense granulation in a wound (proud flesh) are destroyed or checked by the application of caustics, as trichloroacetic acid.

4. *To inhibit the progress of dental caries.* Silver nitrate, applied in substance or in concentrated solution and reduced to a jet black, will inhibit the progress of dental caries.

5. *To keep fistulas open or to destroy their epithelial lining* by measures other than surgery. Liquefied phenol, followed by alcohol, deserves to be recommended.

6. *To obtund sensitive dentin.* Exposed dentin at the cervices of of teeth may be obtunded by caustic drugs; silver nitrate, liquefied phenol, solution of formaldehyde, and sodium fluoride are recommended.

The application of caustics is usually accompanied by severe pain, which, to some extent, may be mitigated by the previous application of local anesthetics. The destruction of a large area of tissue is usually followed by the formation of a more or less extensive cicatrix, and extreme care should therefore be exercised in the use of caustics.

Liquid Caustics

LACTIC ACID; ACIDUM LACTICUM (ACID. LACT.), U.S.P.

Equivalent to about 87 per cent lactic acid, $CH_3.CHOH.COOH$. It is freely miscible with water, alcohol, and ether, but insoluble in chloroform. It has a pronounced sour taste. In its pure form it is used as a caustic swab on the patches of leucoplakia and in pyorrhea pockets but is seldom used internally.

LIQUEFIED PHENOL; PHENOL LIQUEFACTUM (PHENOL. LIQ.), U.S.P. (Liquefied Carbolic Acid).

Phenol liquefied by about 10 per cent of water.

Liquefied phenol is frequently used as a caustic in dentistry. It is soluble in alcohol, and its action on the tissues is limited by following the application with a swab of 70 per cent alcohol.

HYDROCHLORIC ACID; ACIDUM HYDROCHLORICUM (ACID. HYDROCHLOR.), U.S.P. HCl about 36%.

It is a colorless, fuming liquid of a pungent odor and an intensely acid taste, and should be kept in glass-stoppered bottles. It is used in prosthetic dentistry for cleaning gold castings; it should be diluted with equal parts of water.

Diluted Hydrochloric Acid; Acidum Hydrochloricum Dilutum (Acid. Hydrochlor. Dil.), U.S.P.—HCl about 10 per cent. A colorless, odorless, strongly acid solution.

DOSAGE.—4 cc. (1 fluidrachm) (U.S.P.) of diluted hydrochloric acid after meals, diluted in one-half to one glass of water taken through a glass tube to protect the teeth.

NITRIC ACID; ACIDUM NITRICUM (ACID. NITRIC.), HNO_3, U.S.P.

It is a colorless, fuming liquid, of a very corrosive and caustic nature, having a suffocating odor. It stains the skin and the tissues a

bright yellow, and is used as a very powerful caustic by placing a drop of the acid with a glass rod on the tissue to be destroyed. It contains 68 per cent by weight of absolute nitric acid. It should be kept in glass-stoppered bottles. It is very caustic and corrosive, staining woolen fabrics and animal tissues a bright yellow—xanthroprotein. It should be handled with great care.

Nitric Acid Diluted; Acidum Nitricum Dilutum.

It contains 10 per cent by weight of absolute nitric acid.

SULFURIC ACID; ACIDUM SULFURICUM (ACID. SULFURIC.), U.S.P.

It is a colorless, oily liquid, containing 96 per cent by weight of absolute sulfuric acid. It is very caustic and corrosive, often causing charring of the tissues and leaving a black slough. It should be kept in well-stoppered bottles. Sulfuric acid in 50 per cent solution has been recommended by Callahan[1] as a means of opening and enlarging obstructed root canals. The acid may be carried to the root canal with a platinum probe or on a few fibers of asbestos wrapped about the probe. It is well to remember that in diluting pure sulfuric acid the acid must be added in a thin stream to the water with constant stirring, to avoid spluttering and overheating of the mixture.

Diluted Sulfuric Acid; Acidum Sulfuricum Dilutum (Acid. Sulfuric. Dil.), U.S.P.

It contains 10 per cent of absolute sulfuric acid.

Aromatic Sulfuric Acid; Acidum Sulfuricum Aromaticum (Acid. Sulfuric. Arom.).—It is an alcoholic solution, flavored with ginger and cinnamon, containing 20 per cent of absolute sulfuric acid, partly in the form of ethylsulfuric acid. It is employed as a caustic, styptic, and antiseptic.

SULFUROUS ACID; ACIDUM SULFUROSUM.

An aqueous solution containing not less than 6 per cent of sulfur dioxide, SO_2. It is a colorless, acid liquid, having a suffocating odor which when inhaled in the concentrated state proves fatal. It is miscible in all proportions with water. At present it is rarely employed in medicine. Technically, it is very largely used as a bleaching agent, as a preservative, in the manufacture of paper, etc.

PHENOLSULFONIC ACID; ACIDUM PHENOLSULFONICUM, $C_6H_4.OH.SO_3H$.

SOURCE AND CHARACTER.—When phenol is treated with sulfuric acid, the sulfate radical is substituted for an H in the C_6H_5OH of the phenol, and a salt is formed which is known as phenolsulfonic or

[1]Callahan: Proceedings Ohio State Dental Society, 1894.

sulfocarbolic acid. Depending upon the mode of procedure, three types of phenolsulfonic acid may be obtained—the ortho, the meta, and the para. The various acids thus obtained always contain a variable small amount of free sulfuric acid. Phenolsulfonic acid (the ortho or the para acid) is a syrupy, yellowish liquid, becoming darker with age and having a pronounced acid reaction. It is readily soluble in water, alcohol, and glycerin, but insoluble in ether, chloroform, and some oils. It is practically odorless, or only feebly so, resembling phenol. It should be kept in glass-stoppered bottles, protected from light.

MEDICAL PROPERTIES.—Antiseptic and caustic.

THERAPEUTICS.—Phenolsulfonic acid was introduced into chemistry by Laplace and Kékulé, and Annesen, Fraenkel, Vigier, Serrant, Hueppe, Schneider, and others worked out its therapeutic value. It was soon found, however, that it possessed no demonstrable advantage over sulfuric acid; hence it was quickly discarded by the medical profession. Dentistry owes its reintroduction principally to Buckley, Cook and MaWhinney. When phenolsulfonic acid is applied in weak aqueous solutions, it acts primarily as an antiseptic; in concentrated form it is a caustic. It has no therapeutic value in modern dental therapy.

PHOSPHORIC ACID; ACIDUM PHOSPHORICUM (ACID. PHOSPH.), U.S.P.

A colorless liquid, of syrupy consistency, containing 86.5 per cent by weight of absolute orthophosphoric acid. It has a strongly acid taste. It should be kept in glass-stoppered bottles.

In commerce three kinds of phosphoric acid are known:

Orthophosphoric acid, H_3PO_4.

Metaphosphoric acid, HPO_3 (glacial phosphoric acid).

Pyrophosphoric acid, $H_4P_2O_7$ (white, hygroscopic, glassy masses).

Metaphosphoric acid is used as a component of the so-called oxyphosphate of zinc dental cements. A satisfactory acid for dental cement powders may be prepared as follows: 1 ounce (30 Gm.) pure zinc phosphate, 20 ounces (600 Gm.) glacial phosphoric acid in sticks, and 10 ounces (300 Gm.) distilled water, all quantities by weight, are placed in a glass-stoppered bottle, and set aside in a moderately warm place and occasionally shaken until the solution is completed. The acid is then filtered through a cone of glass wool placed tightly into the neck of a glass funnel. The first portions of the filtrate are returned to the funnel until the solution runs off perfectly clear. The acid is immediately transferred to small dry glass bottles and tightly

corked. If the cement, when mixed with this acid, hardens too quickly, the latter may be slightly concentrated on a sand bath; if the cement sets too slowly, a very small quantity of distilled water should be added to the acid. Occasionally it will be found that the last part of the acid gives poor results in mixing the cement; it is then best to discard the fluid.

Diluted Phosphoric Acid; Acidum Phosphoricum Dilutum (Acid. Phosph. Dil.), U.S.P.—H_3PO_4 about 10%.

PICRIC ACID; ACIDUM PICRICUM.—See Trinitrophenol.

Dry Caustics

TRICHLOROACETIC ACID; ACIDUM TRICHLOROACETICUM (ACID. TRICHLOROACET.), $CCl_3.COOH$, U.S.P.

It forms colorless deliquescent crystals, having a pungent, characteristic odor. It is readily soluble in water, alcohol, and ether. It is a powerful caustic and astringent. In 50 per cent solution it is used to destroy polypi, epulitic growths, gingival tissue, etc. In 5 to 10 per cent solution as a local hemostatic and for removing epithelium in periclasia pockets.

POTASSIUM HYDROXIDE; POTASSII HYDROXIDUM (POT. HYDROX.), U.S.P. Caustic Potash).

Great caution is necessary in handling potassium hydroxide, as it rapidly destroys organic tissues. (U.S.P.) KOH not less than 85 per cent.

Dry white, fused masses, or in pencils, having a faint odor of lye and a very acrid caustic taste. It readily absorbs moisture and deliquesces. It is soluble in 1 part of water and in 3 parts of alcohol. Externally, it acts as a strong caustic, but it is difficult to control the area of action.

Solution of Potassium Hydroxide; Liquor Potassii Hydroxidi (Liq. Pot. Hydrox.), N.F.—KOH (approximately 6 per cent). An aqueous solution of potassium hydroxide.

SODIUM HYDROXIDE; SODII HYDROXIDUM (SOD. HYDROX.), U.S.P. (Caustic Soda).

Contains not less than 92 per cent NaOH. White, translucent crystals, which are deliquescent in the air. Very soluble in water (1 in 1) and freely soluble in alcohol.

USES.—Caustic.

Robinson's Remedy

℞ Phenolis
Potassii Hydroxidi āā 4 Gm. 3 j
Mix by triturating in a heated mortar until a crystalline paste is formed. (The addition of a few drops of glycerin improves the mixture.)
Sig.: Apply as a caustic.

Schreier's Alloy of Potassium and Sodium.

An alloy of metallic potassium and sodium kept in a bottle tightly sealed with a thick layer of paraffin. To remove the preparation, a barbed broach is pushed through the paraffin stopper. Handle with care! Formerly used as a pulp canal cleanser.

Osmium Tetroxide; Acidum Osmium; OsO_4; Osmic Acid.

Yellowish crystals, having a very pungent odor; readily soluble in water, alcohol, and ether. It is a very powerful caustic, and its vapors are exceedingly irritating to the air passages and the eyes. Osmic acid has a special affinity for fatty and nerve substance.

Chromium Trioxide; Chromii Trioxidum (Chrom. Triox.), CrO_3, U.S.P. (Chromic Anhydride).

It forms small crystals of a purplish-red color and a metallic luster; is odorless, and destructive to animal and vegetable tissues. It is deliquescent in moist air and very soluble in water. When brought in contact with organic substances—as cork, tannic acid, sugar, alcohol, collodion, glycerin, etc.—decomposition takes place, sometimes with explosive violence.

Solutions for Vincent's Stomatitis and Oral Ulcers

℞ Chromium Trioxide (3%) 1.0 Gm. gr. xv
Distilled Water q.s. ad 30.0 cc. f℥ i
M. et ft. sol.
Sig.: Apply with caution.

℞ Chromium Trioxide (8%) 2.4 Gm. gr. xxxvi
Distilled Water q.s. ad 30.0 cc. f℥ i
M. et ft. sol.
Sig.: Apply with caution.

Action and Uses.[1-4]—In dentistry, chromium trioxide is used only as a caustic in the solid form or in solution up to 10 per cent. Because of its escharotic character, it should be used with extreme care,

[1] Musbe:ger, L. E.: Dental Cosmos 70: 1029, Oct., 1928.
[2] Lyons, H.: Dental Science and Dental Art, 1938, S. M. Gordon, Ed., p. 439.
[3] Reports of the Council, J. A. D. A. 25: 2026, 1938; 29: 461, Mar., 1942.
[4] Dobbs, E. C.: Chromic Acid, Den. Cosmos. 77: 92, 1935

and the hard tissues should be protected by suitable means. Its use in mouthwash form is contraindicated since it dissolves the enamel.

Chromic acid has been used therapeutically as a germicide, astringent, and caustic. It destroys tissue cells and bacteria with which it comes in contact. Its therapeutic property is due to its oxidizing action, its acidity, and its precipitating action on proteins. Chromic acid has been used in dentistry in a 3 to 10 per cent solution for treating oral ulcers and Vincent's stomatitis. The drug is applied by the dentist to the infected part. The acid action of chromic acid can decalcify the hard tissues of the teeth. This decalcification may produce sensitiveness about the necks of the teeth and may predispose the teeth to dental caries. The teeth should be protected from the corrosive action of chromic acid.

SILVER NITRATE; ARGENTI NITRAS (ARG. NITRAS), $AgNO_3$, U.S.P.

ETYMOLOGY.—The word silver is derived from the Anglo-Saxon *seolfor*. The Latin *argentum* and the Greek *argyros* are derived from the same root, *argos*, meaning white. The alchemists termed silver *luna* or *diana*. Geber, the celebrated Arabian alchemist of the eighth century, was the first writer who referred to a formula for making crystalline silver nitrate, and Augustus Sala, at the end of the seventeenth century, called the attention of the medical chemists to this salt, which he named *crystalli dianae* or *magisterium argenti*, from which, by melting, he obtained the *lapis infernalis*.

SOURCE AND CHARACTER.—Silver nitrate is usually prepared by dissolving pure silver in diluted nitric acid and setting it aside for crystallization. It is a colorless and transparent tubular, rhombic crystalline salt, becoming gray or grayish-black on exposure to light in the presence of organic matter. It is odorless, having a bitter, caustic, and strongly metallic taste, and shows an acid reaction to litmus. It is soluble at 77° F. (25° C.) in 0.4 parts of water and 30 parts of alcohol, and in 0.1 part of boiling water and 6.5 parts of boiling alcohol. When heated to about 392° F. (200° C.) the salt melts, forming a faintly yellow liquid which, on cooling, congeals to a pure white crystalline mass. At a higher temperature it is gradually decomposed with the evolution of nitrous vapors. It should be kept in dark-colored vials, protected from light.

In the presence of reducing agents the solution stains the skin an indelible black. The solution also stains linen and cotton fibers and exposure to sunlight hastens this process. To remove the stains, a solution of sodium hyposulfite, potassium cyanide, or ammonium chloride may be employed. It is *incompatible* with ordinary water

because of the sodium chloride which it contains, with soluble chlorides in general, with the mineral acids, with alkalies and their carbonates, with limewater, and with tannic acid.

PREPARATION.—

Toughened Silver Nitrate; Argenti Nitras Induratus (Arg. Nitras Indur.), U.S.P. (Fused Silver Nitrate, Molded Silver Nitrate, Lunar Caustic).—$AgNO_3$ toughened by the addition of a small proportion of silver chloride. (U.S.P.)

MEDICAL PROPERTIES.—Antiseptic, astringent, caustic, and hemostatic.

LOCAL AND GENERAL ACTION.—When solid silver nitrate is brought in contact with living tissue, a deep staining of the superficial layer is produced. This is followed by acute pain and partial inflammation of the deeper structures, resulting in destruction of the upper layers, which finally separate as a slough. The corroded surfaces heal quickly. On the mucous membranes or the broken skin it acts much like zinc salts, but is more powerful. It is less active than the mercury salts. It readily precipitates albumins and chlorides from the plasma or the serumal discharge; in weak solutions it actively contracts arteries and veins. The formation of a protective layer of coagulated albumin and silver chloride limits its penetration into the deeper structures and reduces its action. The precipitation of albumin is fairly recognizable in 0.25 per cent solution; a 10 per cent solution produces a firm coagulum. In solid form it is employed as a hemostatic. Silver nitrate is the most powerful caustic and astringent of all the metallic salts which can be applied with safety. Locally it does not produce toxic effects or dangerous inflammatory disturbances, as its action is distinctly *self-limiting.* Given internally or even from the prolonged use of silver solution by external application on mucous surfaces or denuded skin, the silver is often absorbed by the system and permanently stains the body surfaces, thus giving the skin and mucous membrane an unsightly gray appearance, known as *argyria.* The pigmentation was commoner in earlier years than at present, owing to its restricted internal use.

ARSENIC TRIOXIDE; ARSENI TRIOXIDUM (ARSEN. TRIOXID.) As_2O_3, U.S.P. (Arsenous Acid, Arsenous Oxide).

ETYMOLOGY.—From the Greek *arsenikon.*

SOURCE AND CHARACTER.—Arsenic trioxide is an acid anhydride obtained by roasting arsenical ores. In Bohemia and Saxony it is largely produced from smelting crude cobalt ores, and in England

from arsenopyrite, known as *mispickel,* or arsenical iron. It appears in transparent, porcelain-like masses which change slowly to an opaque milk-white color or to a fine white powder. It has no taste or odor, and at 356° F. (180° C.) it is entirely volatilized by heat. When thrown on ignited charcoal, it emits a garliclike odor. It is slowly soluble in from 30 to 100 parts of water at ordinary temperature, depending on the variety employed. It is completely soluble in 15 parts of boiling water and in about 5 parts of glycerin, and sparingly soluble in alcohol. It is *incompatible* with the salts of iron and magnesium, with limewater, and astringent vegetable drugs. *Caution:* Arsenic Trioxide is extremely poisonous (U.S.P.).

DOSAGE.—2 mg. ($\frac{1}{30}$ grain) (U.S.P.).

ARSENIC TRIIODIDE; ARSENI TRIIODIDUM (ARSEN. TRIIOD.), AsI_3, N.F. (Arsenous Iodide).

USES.—Similar to those of arsenic trioxide, over which it has no advantage.

DOSAGE.—5 mg. ($\frac{1}{12}$ grain) (U.S.P.).

Caution: Arsenic Triiodide is extremely poisonous (U.S.P.).

LOCAL AND GENERAL ACTION.—If arsenic is applied to the unbroken skin, no change is produced unless it is allowed to remain in close contact for some time. On denuded surfaces and mucous membranes it acts as a slow, but very persistent, protoplasm poison by powerful oxidation; it does not form new compounds with the albuminous or protein materials of the cells. Arsenic trioxide does not, therefore, act as a true caustic, nor is it self-limiting in its action. Taken internally, arsenic acts as a powerful irritant, resulting in vomiting, pain, and inflammation. It does not combine with the albuminous contents of the stomach or intestines, but remains unchanged. Thus it stimulates the nerves and vessels, and causes a sense of hunger by increasing the gastric functions. It is readily absorbed and quickly enters the blood. In overdoses, arsenic is extremely poisonous. It manifests itself in a feeling of constriction in the throat, difficulty of swallowing, and violent pain, "rice water" stools, or bloody diarrhea accompanied by diminished urine, cold, damp skin, together with giddiness. Feeble pulse and respiration follow, soon ending in collapse. Chronic poisoning usually follows the prolonged absorption of small quantities, either from its therapeutic use or from the presence of arsenic in the rooms in the form of dyes on wallpaper, clothes, or in mines and factories. If arsenic is taken habitually in small quantities, a tolerance to the drug may be established, as with the arsenic eaters of Syria and the

Tyrol. As much as seven grains have been taken without ill effects at a single dose by a person accustomed to its use.

Specific Action of Arsenic Trioxide on the Tooth Pulp. Arsenic has had a most extensive use in dentistry for pulp devitalization, but with the advances made in the technique of administering local anesthetics arsenic as a pulp devitalizing agent has become obsolete.

Magma of Ferric Hydroxide; Magma Ferri Hydroxidi (Magma Ferr. Hydrox.).—A dilute solution of ferric sulfate and a mixture of magnesium oxide with distilled water, kept in separate bottles. When mixed, they yield ferric hydroxide.

USES.—Used as antidote for arsenic, but its value is problematic.

DOSAGE.—120 cc. (4 fluidounces).

CHAPTER XXVI

DIETARY FACTORS

The normal human diet should contain proteins, fats, carbohydrates, inorganic salts, vitamins, and water in adequate amounts. An exact balance is not necessary for normal growth, health, reproduction, etc. The physiologic range for these substances is wide, the body excreting those substances not used or storing and conserving those that are restricted. The *proteins* are essential for growth, health, and life. They contain amino acids which are building stones for the body tissues, i.e., necessary for growth and repair. Some of the amino acids are either not necessary or can be synthesized by the body and are therefore named nonessential amino acids. Other amino acids cannot be synthesized by the body, are essential, and must be included in the diet; they are called essential amino acids. There are about ten of them: methionine, lysine, tryptophane, threonine, leucine, isoleucine, phenylalanine, histidine, valine, and arginine. The best proteins are those containing large amounts of the essential amino acids, such as eggs, milk, kidneys, and livers; fish, poultry, and muscle tissue are next, with cereals, root vegetables, nuts, and legumes last. The dietary requirements of protein per day are 95 grams of which about 50 grams should be from animals—meat and milk. This makes up about 10 per cent of the calorie intake.

The *fats* are made up of long-chained aliphatic acids combined with glycerin to form the so-called neutral fats. The fatty acids may be saturated or unsaturated and can be synthesized in the body. There are exceptions, such as certain unsaturated fatty acids. The normal daily requirement for fats is about 85 grams which makes up about 25 per cent of the caloric intake.

The *carbohydrates* are organic compounds of carbon, hydrogen, and oxygen. They are found extensively in the plant kingdom. They are burned in the body, forming heat and energy. Since they act as a source of fuel, larger amounts of carbohydrates are necessary than of either of the other two; about 465 grams per day are adequate for a 3,000 calorie diet. They make up about 65 per cent of the caloric intake.

The *minerals* are not used as a source of heat and energy but are integral parts of the tissue cells. Most of the minerals are present

DAILY REQUIREMENT FOR AN ADULT

NAME	AMOUNTS PER DAY
Protein	95 Gm.
Fats	85 Gm.
Carbohydrates	460 Gm.
Sodium Chloride	10-15 Gm.
Calcium	0.80-1.50 Gm.
Phosphorus	1.50 Gm.
Iodine	0.15-0.30 mg.
Iron	12-15 mg.
Potassium	3 Gm.
Vitamin A	5,000 U.S.P. Units
B_1	2 mg. Thiamine HCl.
B_2	2.7 mg. Riboflavin
P.-P. factor	2 mg. Nicotinic Acid
C	75 mg. Ascorbic Acid
D	500 U.S.P. Units
Calories	3,000

in adequate amounts in an average diet. Those inorganic elements which are essential for normal nutrition are: calcium, phosphorus, iron, copper, iodine, sodium, potassium, chlorine, etc.

Vitamins are organic compounds which act in the body as catalysts. They are necessary for the normal metabolism of tissues. Their absence will produce deficiency diseases. Those vitamins which are accepted as necessary in general therapeutics are: vitamins A, B_1, B_2, P.-P. factor, C, D, and K.

INORGANIC SALTS

The tissues and fluids of the body contain large amounts of inorganic material, which may be recovered as ash upon incineration. About 4.4 per cent of the body weight is inorganic salts. They maintain the normal composition and the osmotic pressure in the fluids and tissues of the body and regulate the acid-base equilibrium. The salts are bound up in the structure of the living molecule and are necessary for its normal reactions and vitality. The special importance of calcium is noted in the coagulation of the blood and curdling of milk; potassium and sodium salts are responsible for the rhythmical contractions of the heart muscle, the irritability of muscular and nervous tissues, and the permeability of the capillary walls and other membranes. Dogs fed on ash-free diets died within a few weeks. They probably would have lived longer if no food had been given, as the ash-free diet helped to increase the loss of the salts from the body. Dietary studies have proved that in order to have a well-balanced diet attention must be paid to the composition of inorganic salts as well as the proportions of fats, carbohydrates, and proteins.

Sodium Chloride.—This is the only inorganic salt which is not found in sufficient amount to meet the body needs and must be added to the diet. From 10 to 20 grams are needed per day. This desire for salt is also observed in many animals, and for that reason the farmer provides his animals with salt-licks. It is apparent that the desire for salt is almost absent when animals are fed a meat diet, but on a vegetable diet there is always a craving for salt. One explanation for this is that most vegetables contain a large amount of potassium salts, and in the blood these react with the NaCl, forming KCl and Na_3PO_4, both of which are removed from the blood as foreign matter by the kidneys, thus depleting the sodium supply. No doubt more salt is eaten than is needed and if carried to excess, an edematous condition of the tissues may result, because of an osmotic influence. In cases of edema, reduction of salt will aid in the return of the tissues to a normal state of water balance.

Calcium Salts.—Calcium is found in the body chiefly as carbonate and phosphate salts. About 99 per cent of the calcium salts are stored in the hard body tissues, bones, and teeth. The blood serum contains about 9 to 11.5 mg. of calcium, children having more than adults. About 60 per cent of the blood calcium is in a diffusible form, and the other 40 per cent is nondiffusable. A blood calcium below 7 mg. per cent increases the irritability of the central nervous system and of the peripheral nerves, resulting in muscular spasms called tetany. The amount of ionic calcium in the blood is dependent on parathyroid secretion; a hypofunction produces a low calcium content and a hyperfunction produces high calcium content. Therefore, it is apparent that calcium retention is dependent on the parathyroid glands. The form of calcium ingested is not important as it is changed to calcium chloride in the stomach and is probably absorbed as such. The site of absorption is chiefly the small intestine which is slightly acid in reaction. Vitamin "D" increases the acidity of the intestines, thereby favoring calcium absorption. Calcium is excreted chiefly in the large intestine (70%) and in the urine (30%). Sherman suggests 0.7 to 1 Gm. of calcium per day as the normal daily requirement.

The structure of the calcium compound in bone and teeth is not known, perhaps it is $CaCO_3nCa_3P_2O_8$ where "n" is not less than 2 or more than 3.

The administration of calcium compound to increase the clotting properties of the blood has not produced satisfactory results.

PREPARATIONS.—

CALCIUM LACTATE; CALCII LACTAS (CALC. LACT.), U.S.P.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Tablets of Calcium Lactate; Tabellae Calcii Lactatis (Tab. Calc. Lact.), N.F.

DOSAGE.—0.3 Gm. (5 grains) (N.F.).

CALCIUM HYPOPHOSPHITE; CALCII HYPOPHOSPHIS (CALC. HYPOPHOS.), $Ca(PO_2H_2)_2$, N.F.

DOSAGE.—0.5 Gm. (8 grains) (N.F.).

Syrup of Hypophosphites; Syrupus Hypophosphitum (Syr. Hypophos.), N.F.

DOSAGE.—8 cc. (2 fluidrachms) (N.F.).

CALCIUM GLUCONATE; CALCII GLUCONAS (CALC. GLUCON.), U.S.P.

This salt is comparatively nonirritating and may be injected intravenously in 1 Gm. doses.

DOSAGE.—Oral 5 Gm. (75 grains) (U.S.P.).

PRECIPITATED CALCIUM CARBONATE; CALCII CARBONAS PRAECIPITATUS (CALC. CARB. PRAEC.), $CaCO_3$, U.S.P.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Iron Salts.—The iron salts are necessary for the production of new hemoglobin, and are found in the foods in an organic combination. Foods contain iron in varying amounts, spinach and egg yolks being the richest. In cases of simple anemias, the diet should be so regulated as to include foods which are rich in this element, rather than prescribe medicinal preparations. Not much is known about the metabolism of iron. No doubt, it takes place in the red bone marrow. The daily dietary need of iron is from 10 to 15 mg.

Phosphates.—It is estimated that there are some 700 grams of phosphorus in the adult body of which about 500 grams (70 per cent) are in the bones and teeth. The remainder is distributed in the soft tissues as phospholipids, nucleic acid, phosphoprotein, hexosephosphate, phosphocreatin, etc. These salts are necessary for tooth and bone formation, for normal absorption, synthesis, metabolism, and excretion of carbohydrates, fats, and possibly proteins. They are also necessary for maintenance of the normal acid-base balance of the tissues. Sherman found that for an adult about 0.9 gram was necessary per day and for children about 1.5 grams. It is better to have too much than too little. Too high a ratio of Ca to P in the diet retards the absorp-

tion of phosphorus. The most favorable Ca:P ratio is between 1 and 2. During pregnancy and lactation the intake must be higher to overcome the drain on the mother. Blood serum contains from 3 to 4 mg. per 100 c.c.; it is higher in children than in adults. A low serum phosphorus prevents normal bone and teeth formation, resulting in rickets. The relationship between phosphorus metabolism and dental caries and periodontoclasia has not been established. Phosphorus is excreted chiefly through the urine as acid phosphates. The daily requirement of dietary phosphorus is from 1.3 to 2.0 grams. The phosphorus salts are often administered to patients who are not ingesting adequate amounts of this element from the diet.

PREPARATIONS.—

SYRUP OF CALCIUM LACTOPHOSPHATE; SYRUPUS CALCII LACTOPHOSPHATIS, N.F.

DOSAGE.—10 cc. (2½ fluidrachms), N.F.

TRIBASIC CALCIUM PHOSPHATE; CALCII PHOSPHAS TRIBASICUS (CALC. PHOS. TRIBAS.), U.S.P. (Precipitated Calcium Phosphate.)

DOSAGE.—1 Gm. (15 grains), U.S.P.

Magnesium.—According to McCollum, this element is necessary for growth and development of animals. The average diet contains an adequate amount.

Copper.—According to Hess, copper is necessary for hemoglobin formation and is an essential part of the diet. The average diet contains an adequate amount of this element. It is sometimes administered to patients suffering from anemia.

Zinc.—According to Hart, zinc is necessary for normal growth and development. It may be necessary for normal hormonal action. The average diet contains adequate amounts of this element.

Iodine.—This element is a necessary constituent of the thyroid hormone, thyroxin, with possibly other unknown functions. It is found chiefly in foodstuffs obtained from salt water, such as fish. A low intake produces an enlargement of the thyroid gland, particularly at puberty, pregnancy, lactation, and menopause. Iodine is necessary for normal growth, development, and metabolism.

Aluminum may or may not be necessary for normal body functions. Aluminum containers for cooking foods are classed as harmless.

Manganese, according to Hart, is necessary for normal reproduction in male and females. Its actions are related to the sex hormones.

Fluorine may or may not be necessary for normal body functions. The diet always contains enough of this element. Too much fluorine in the diet interferes with normal tooth and bone formation. The

teeth are affected by opaque areas in the enamel. The enamel rod formation may be normal, but the interprismatic substance is improperly formed. This condition of *mottled enamel* occurs in endemic areas in this country in which the fluorine content of the drinking water is found to contain 1.0 to 10 mg. per liter of fluorine as compared to the normal of 0 to 0.9 mg. per liter. The teeth are affected only during their developing periods and not after their formation. Schour states that the dystrophies are produced by a direct toxic effect on the enamel-forming ameloblasts and that the dentin is not affected. A small amount of fluorine in the drinking water has been shown to protect the teeth from dental caries.

VITAMINS

Hopkins in 1906 demonstrated the presence of another dietary factor necessary for the growth and development of laboratory animals, and called these substances "accessory food factors." In 1910, Casimir Funk obtained certain definite facts from experimental work on animals indicating that these unknown substances were amino acids. He then coined the name "vitamines." About 1910, Drummond concluded that the vitamines were not all amines and suggested that the final "e" be dropped, and the word vitamin was coined and accepted. E. V. McCollum suggested naming the separate vitamins alphabetically (A, B, C) until their chemical composition and structure were known, and then to use the chemical name, omiting both the word vitamin and the letter.

The vitamins are "accessory food substances" necessary for life, health, growth, maintenance, and reproduction. They are often called "exogenous hormones." For many years it was known that a diet adequate in carbohydrates, fats, proteins, inorganic salts, and water failed to meet the full nutritional requirements of man. Avitaminosis results in various types of metabolic disturbances designated as deficiency diseases, such as scurvy, beriberi, rickets, pellagra, etc. Therefore, vitamins have come to play an important role in dietetics and in clinical dentistry.

Vitamins are organic food substances which are necessary in minute amounts for the normal functioning of tissues. They are definite chemical compounds which act as tissue catalysts. Their exact number is still unknown. The known vitamins of accepted value in human nutrition are A, B_1, B_2, P.-P. factor, C, D, E, and K. One vitamin cannot replace another. When there is a known deficiency of one vitamin, there is probably a general avitaminosis in the patient. It is difficult to have a diet deficient in one vitamin and ade-

quate in all of the others. The human body has the capacity of synthesizing some of the vitamins from precursors or provitamins, such as carotene which forms vitamin A on hydrolysis.

The direct action of the vitamins in the animal body is not thoroughly understood. They probably act as enzymes, enhancing cellular oxidation in the tissues. The enzyme is apparently inactive until combined with a protein molecule, the protein acting as a coenzyme and the vitamin as the prosthetic group. The vitamin proper gives to the molecule the general type of action, and the protein gives the specificity of action.

The vitamins are recognized biologically by their absence, rather than by their presence, as the characteristic symptoms of each vitamin deficiency must be produced before the positive effect of the vitamin in question can be demonstrated. The condition produced by an absence of the vitamins in the diet is known as avitaminosis, and an excess of the vitamins produces vitaminosis, which does not occur in persons on a natural diet. The plant and animal foods vary in the quality and the quantity of vitamins, depending on climate, season, soil, etc.

One vitamin cannot replace the activity of another; all vitamins must be present in adequate quantities for normal metabolism. The latter can occur at an optimum only when all vitamins are present in suitably balanced ratios. Vitamins are exceedingly delicate chemical compounds; such factors as temperature, exposure to air, length of storage, method of processing, etc., have definite effects upon the vitamin potency present in the foodstuff.

The Council on Dental Therapeutics has the following to say regarding the value of vitamin therapy in dental medicine.[1]

"It is significant that dental abnormalities and disturbances related to vitamin deficiencies are accompanied by other manifestations of inadequate intake or assimilation of these essentials. This suggests the necessity of cooperation between dentists and physicians in the treatment of these conditions. The importance of a diet containing adequate quantities of the known dietary essentials is well recognized. But the addition of vitamins to such a diet has not been shown to be of value in the treatment or prevention of dental diseases." This last sentence is not true for oral diseases.

Vitamin A

Vitamin A is a term which is applied to one or several substances occurring alone or in combination. It was discovered almost simul-

[1]Accepted Dental Remedies, 1943, ed. 9, pp. 199-210.

taneously by McCollum and Davis and by Osborne and Mendel in 1913. This vitamin is found in the plant kingdom as chemical compounds known as carotenes; the alpha, beta, and gamma forms are of chief importance. They exist in an inactive state, pro-vitamin or precursor, which are hydrolyzed in the liver to the active form. Animals cannot apparently synthesize this vitamin, but they can convert it from the precursor to the active form and store it for later use. Vitamin A is fat-soluble but not a fat or sterol. It is destroyed by prolonged heating (28 hours) and was separated from vitamin D by heating cod liver oil for 12 hours (McCollum, 1921). Vitamin A_1 is obtained from the livers of salt water fish, while vitamin A_2 is obtained from the livers of fresh water fish.

SOURCE.—The carotenes[1] are abundant in the yellow vegetables and leafy greens, i.e., carrots, sweet potatoes, apricots, tomatoes, asparagus, etc. Active vitamin A is found chiefly in butter, milk, cheese, eggs, and liver.

STANDARDIZATION.—The *United States Pharmacopoeia* (U.S.P.) and the International Unit (I.U.) for vitamin A are the same. One unit is equal in growth promoting and antiophthalmic action, in rats, to the biological activity of 0.0006 mg. of pure crystalline B-carotene.

PHARMACODYNAMICS.—Vitamin A has a specific effect on the epithelium which covers the mucous surfaces of the body. The change is a displacement of the normal epithelium by squamous epithelium which lowers the resistance of the tissue to infections. This is brought about by (1) the displacement of active epithelial cells by less active cells, (2) the decrease in the secretion of mucus and (3) a loss of cilial tissue which in the normal state keeps the mucous surfaces clean. This vitamin is not anti-infectious but does tend to decrease the number of infections, make them less severe when they do occur, and make the duration and convalescence shorter.

Vitamin A substances are necessary for the synthesis of visual purple in the rods of the retina. In the normal eye the visual purple, which is destroyed by light, is rapidly resynthesized and prevents night blindness from occurring.

The positive effects of vitamin A substances are active up to a point where no excess will promote beneficial changes. This vitamin is essential for the vitality of epithelial cells, accelerates growth, resists infections, regenerates visual purple, is essential for a normal pregnancy and lactation, and aids glandular functions.

[1]Bessey, O. A., and Wolbach, S. B.: J. A. M. A. 110: 2073, June 18, 1938.

When the diet is deficient in vitamin A substances and the body becomes depleted of its stored vitamins and precursors, deficiency symptoms result, such as xerophthalmia, keratomalacia, infection, weakness, loss of weight, atrophy of glands, decrease in amount of secretion, nerve degeneration, night blindness, poor tooth formation, alveolar atrophy, and gingival disease.

THERAPEUTICS.—A vitamin A deficiency in animals is associated with dystrophies of the enamel.[1] Hypoplasia of the human enamel occurs in individuals on a vitamin A deficient diet, occurring only in the teeth which are in the process of formation when the diet is deficient in this vitamin.[2] No changes have been demonstrated in formed teeth regardless of the degree of vitamin deficiency. There is no accepted relationship between vitamin A deficiency and dental caries in human beings. The reason that the enamel organ is chiefly affected by an "A" deficiency is that this tissue is of epithelial origin.

The allowable claims for vitamin A in the 1942 issue of *New and Nonofficial Remedies* are:

1. Evidence for the existence of vitamin A and its role in human nutrition is based on the fact that a characteristic eye disease, usually called xerophthalmia, results from a deficiency of this vitamin.
2. It is generally agreed that the first symptom or at least one of the first clinical symptoms of vitamin A deficiency is night blindness, or nyctalopia. For this type of night blindness vitamin A is a specific. Cases of nyctalopia exist which do not respond to treatment with vitamin A. These may be due to congenital defects or to other diseases than avitaminosis "A."
3. Vitamin A is reported to be effective in the treatment of certain types of hyperkeratosis of the skin of persons suffering from severe deficiency of vitamin A.
4. Vitamin A in excess of normal requirements has not been shown to be of value in the prevention of colds, influenza, and such infections.
5. There is at the present time inadequate evidence to warrant the claim that the ingestion of insufficient vitamin A will prevent the formation of renal calculi in man or that it is useful in the treatment of hyperthyroidism, anemia, degenerative conditions of the nervous system, sunburn, or ulcerative conditions of the skin.

DOSAGE.—Adults, 5,000 U.S.P. units. Children, from 1,500 to 5,000 U.S.P. units, varying with the age from birth to 12 years; over 12 years takes the adult dosage. Pregnant and lactating women, 6,000 to 8,000 U.S.P. units.

[1] Mellanby, May: Physiol. Rev. 8: 545, 1928.
[2] Boyle, P. E.: J. Dent. Res. 13: 39, 1933.

OFFICIAL PREPARATIONS.—

OLEOVITAMIN A; OLEOVITAMINA A (OLEOVITAMIN. A), U.S.P. (Natural Vitamin A in Oil).

Either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of vitamin A concentrate in fish liver oil or in an edible vegetable oil. The vitamin A shall be obtained from natural (animal) sources. Oleovitamin A contains in each Gm. not less than 50,000 and not more than 65,000 U.S.P. units of vitamin D.

THERAPEUTICS.—Used for its vitamin A content.

DOSAGE.—Prophylactic, 0.1 cc. (1½ minims), U.S.P.

Oleovitamin A Capsules; Capsulae Oleovitaminae A (Cap. Oleovitam. A), U.S.P.—These capsules are labeled to contain either 5,000 or 25,000 U.S.P. units of vitamin A.

THERAPEUTICS.—Used for its vitamin A content.

DOSAGE.—One capsule containing 5,000 U.S.P. vitamin A units.

VITAMIN A IN VARIOUS FOODS

ANIMAL PRODUCTS	UNITS IN 1 OUNCE	PLANT PRODUCTS	UNITS IN 1 OUNCE
Halibut liver oil	900,000 to 1,500,000	Escarole	6,000
		Spinach	1,500
Cod-liver oil	15,000	Turnip greens	1,419
Liver, beef	2,800	Carrots	1,300
Egg yolk	1,700	Prunes, dried	300
Cheese, cream	1,400	Peppers, green	284
Butter	950	Sweet potatoes	200
Cream, thick	447	Peas, fresh	175
Milk, whole	65		

CONTRIBUTIONS OF AVERAGE SERVINGS OF CERTAIN FOODS TO VITAMIN A REQUIREMENT

FOOD	AMOUNT
Cod-liver oil	1 teaspoonful
Milk	1 pint
Carrots	2 tablespoonfuls
Egg yolk	1 tablespoonful
Butter	1 teaspoonful

Vitamin B Complex

In the early days of vitamin history, it was assumed that vitamin B was a single substance. It is now known to be a complex mixture of at least twelve substances and termed "vitamin B complex." *Useful Drugs* (1942) accepts only three of these substances as being established as useful in human nutrition; thiamine, riboflavin, and nicotinic acid.[1] This complex includes all of the water-soluble fractions occurring in yeast.

[1]Council Report, J. A. D. A. 28: 213, Feb., 1941.

Vitamin B_1

THIAMINE HYDROCHLORIDE; THIAMINAE HYDROCHLORIDUM (THIAMIN. HYDROCHLOR.), U.S.P. (Thiamin Chloride, Vitamin B_1 Hydrochloride, Vitamin B_1).

It occurs as a colorless, crystalline powder; yeastlike odor and taste; soluble in water (1 in 1), sparingly soluble in alcohol (1 in 100), and insoluble in oils and fats.

The source of thiamine is yeast, or it may be prepared synthetically. It is comparatively stable toward dry heat but is readily destroyed by autoclaving and partly destroyed by pasteurization.

PHARMACODYNAMICS.—The pathologic condition associated with thiamine deficiency is thought to be due to a faulty carbohydrate metabolism in the nerve tissues, particularly the incomplete oxidation of pyruvic acid, which permits it to accumulate and act as a toxin.

THERAPEUTICS.—Thiamine hydrochloride is of value in the prevention and correction of beriberi in man and polyneuritis in animals. It is also recommended in cases of anorexia of dietary origin, and is a growth-producing factor. Thiamine deficiency may be present in patients with the following conditions: the pernicious vomiting of pregnancy, chronic alcoholism, hyperthyroidism, and in individuals doing vigorous muscular activity. Evidence is lacking that this vitamin is useful in cardiovascular disease other than a beriberi heart.

The body stores vitamin B_1 in amounts adequate for only a relatively short time, therefore a daily requirement in the diet is essential.

A few foods rich in this vitamin are: bran, enriched bread, wheat germ, dried legumes, nuts, soy beans, lean pork, milk, yeast, potatoes, etc.

The United States Pharmacopoeial standard unit for "B_1," and the International Unit are the same, 1 unit is equivalent to the biologic activity of 3 micrograms of crystalline thiamine hydrochloride.

The allowable claims for thiamine hydrochloride made by *New and Nonofficial Remedies* (1942) are as follows: (1) useful in the prevention and treatment of beriberi, (2) useful in the prevention and treatment of loss of appetite of dietary origin, (3) excess of the daily requirement may be useful in patients with conditions which interfere with the proper assimilation of vitamins, (4) useful in the prevention and treatment of neuritis of dietary origin, such as in pregnancy, alcholism, and jejunal fistula, (5) thiamine deficiency in animals, (6) increased requirements are necessary in augmented metabolism, fever, hyperthyroidism, or vigorous muscular activity.

There are oral but no dental indications for the use of thiamine hydrochloride.

DOSAGE.—5 mg. (1/12 grain) (U.S.P.).

PREPARATION.—

Thiamine Hydrochloride Tablets; Tabellae Thiaminae Hydrochloridi (Tab. Thiamin. Hydrochlor.), U.S.P. (Thiamin Chloride Tablets, Vitamin B_1 Tablets).

DOSAGE.—5 mg. (1/12 grain) (U.S.P.).

VITAMIN B_2

RIBOFLAVIN; RIBOFLAVINUM (RIBOFLAV.), U.S.P. (Lactoflavin, Vitamin B_2, Vitamin G).

It occurs as an orange yellow, crystalline powder which fluoresces in aqueous solution. It is practically insoluble in water (1 in 10,000) and alcohol and slightly more soluble in saline solution and dilute alkalies.

This vitamin contains the flavine nucleus with a pentose chain, and that obtained from milk is named lactoflavin; from egg, ovoflavin; and from liver, hepatoflavin. The difference in these compounds may be in the pentose side chain which permits eight isomers. The general name given to these compounds is riboflavin.

Riboflavin occurs in yeast, eggs, cream, bran, lean meats, cheese, prunes, fish, kidneys, liver, milk, whole grains, and greens.

PHARMACODYNAMICS.—Riboflavin is a necessary component of Warburg's respiratory enzyme and other oxidation enzymes with different specificities of action. This vitamin, like the others, probably combines in the body with a protein molecule to form a tissue enzyme. With riboflavin the vitamin is attached to the protein by phosphoric acid to form a compound of importance in cell respiration.

THERAPEUTICS.—Ariboflavinosis is characterized by a wide variety of pathologic changes involving growth, cheilosis, glossitis, seborrheic dermatitis, keratitis, etc. Many of these lesions are about the mouth, and the dentist may be the first to observe them.

STANDARD UNIT.—One unit of vitamin B_2 is that amount which when fed a vitamin B_2 depleted rat will permit a gain in weight of 3 grams per week during the test period.

No therapeutic claims are advanced in N.N.R. for the use of riboflavin.

DOSAGE.—5 mg. (1/12 grain) (U.S.P.).

PREPARATION.—

Riboflavin Tablets; Tabellae Riboflavini (Tab. Riboflav.), U.S.P.

DOSAGE.—5 mg. (1/12 grain) (U.S.P.).

SOURCES OF VITAMIN B_2

	UNITS IN 1 OUNCE		UNITS IN 1 OUNCE
Yeast, brewer's	210-425	Milk	17
Yeast, moist	75	Turnip tops	86
Liver, beef	257	Peas, dried	32
Kidney, veal	224	Spinach	29
Egg yolk	66	Water cress	29
Veal, lean	43	Cabbage, raw	21
Beef, lean	29	Lettuce	19

P.-P. FACTOR

This vitamin is the pellagra preventive factor and was demonstrated to be protective and curative in human pellagra by Goldberger. It is water-soluble and more thermostable than vitamin B_1, and more stable in alkaline media than in acid.

CHEMISTRY.—Elvehjem synthesized this factor in 1937 and called it nicotinic acid. Chemically it contains a pyridine nucleus with a carboxyl or a carboxylamide substitution.

SOURCE.—It is found abundantly distributed in nature in both plants and animals, and a normal diet should furnish the required amounts of this substance.

PHARMACODYNAMICS.—Nicotinic acid and amide are synthesized in the animal body into an active tissue enzyme intimately concerned with carbohydrate metabolism.

THERAPEUTICS.—An avitaminosis of the P.-P. factor is characterized by the following symptoms: diarrhea, dermatitis, and dementia. The mild deficiency symptoms are erythema, glossitis, indigestion, constipation, anorexia, loss of weight, tachycardia, etc.

OFFICIAL PREPARATIONS.—

NICOTINIC ACID; ACIDUM NICOTINICUM (ACID. NICOTIN.), U.S.P.

It occurs as a white crystalline powder. It is odorless, has a sour taste, and is sparingly soluble in water and freely soluble in alcohol.

THERAPEUTICS.—Used for the prevention and treatment of acute pellagra.[1] Its administration causes the disappearance of all alimentary, mental, and dermal symptoms. As with the other avitaminosis diseases in man, the deficiency is generally of more than one vitamin,

[1]Council Report: J. A. D. A. 28: 316, February, 1941.

therefore a well-balanced diet should accompany the drug administration. (See N.N.R., A.D.R., and Useful Drugs.)

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Nicotinic Acid Tablets; Tabellae Acidi Nicotinici (Tab. Acid. Nicotin.), U.S.P. (Niacin Tablets).

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

NICOTINAMIDE; NICOTINAMIDUM (NICOTINAMID.), U.S.P. (Nicotinic Acid Amide; Niacinamide).

It occurs as a white crystalline compound, nearly odorless, bitter taste. It is soluble in water (1 in 1) and in alcohol (1 in 5).

THERAPEUTICS.—Same as nicotinic acid (see).

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Nicotinamide Tablets; Tabellae Nicotinamidi (Tab. Nicotinamid.), U.S.P. (Niacinamide Tablets).

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Vitamin C

Theobald Smith in 1895 noted that guinea pigs kept upon a diet of oats developed a hemorrhagic disease. Holst and Tioloch, 1907, fed guinea pigs polished rice, and instead of beriberi developing as demonstrated in fowl, scurvy developed. The symptoms were loss of weight, joint soreness, hemorrhage, soreness and hyperemia of the gingiva, loosening of teeth, pulp changes, and separation of epiphyses in the long bones. Foods containing vitamin C rapidly lose their protective substances when kept at room temperature or in an icebox. There is smaller loss in an acid medium than in neutral or alkaline media. Heating for one-half hour at 110° C. in an alkaline medium destroyed much of its protective property, while heating for the same time and at the same temperature in an acid solution had but little effect. Drying has but slight destructive influence. Milk which is pasteurized at 165° F., for twenty minutes or 145° F. for thirty minutes has most of the vitamin C destroyed.

Rats have been found to synthesize this vitamin or not need it, while guinea pigs are supersensitive to a lack of "C." Later investigation shows that rats can exist on little or no "C," but are not normal and do need some vitamin C for health. A child weighing 8 or 10 kilograms needs about 15 cc. of orange juice daily. The vitamin can be stored in the body, but the supply is sufficient for only a short time. In 1921 it was observed that there is a rapid loss of calcium from bodies of scorbutic animals. Findlay associated a change in the blood vessels, particularly the capillary endothelium re-

PREPARATION.—

Riboflavin Tablets; Tabellae Riboflavini (Tab. Riboflav.), U.S.P.

DOSAGE.—5 mg. (1/12 grain) (U.S.P.).

SOURCES OF VITAMIN B_2

	UNITS IN 1 OUNCE		UNITS IN 1 OUNCE
Yeast, brewer's	210-425	Milk	17
Yeast, moist	75	Turnip tops	86
Liver, beef	257	Peas, dried	32
Kidney, veal	224	Spinach	29
Egg yolk	66	Water cress	29
Veal, lean	43	Cabbage, raw	21
Beef, lean	29	Lettuce	19

P.-P. FACTOR

This vitamin is the pellagra preventive factor and was demonstrated to be protective and curative in human pellagra by Goldberger. It is water-soluble and more thermostable than vitamin B_1, and more stable in alkaline media than in acid.

CHEMISTRY.—Elvehjem synthesized this factor in 1937 and called it nicotinic acid. Chemically it contains a pyridine nucleus with a carboxyl or a carboxylamide substitution.

SOURCE.—It is found abundantly distributed in nature in both plants and animals, and a normal diet should furnish the required amounts of this substance.

PHARMACODYNAMICS.—Nicotinic acid and amide are synthesized in the animal body into an active tissue enzyme intimately concerned with carbohydrate metabolism.

THERAPEUTICS.—An avitaminosis of the P.-P. factor is characterized by the following symptoms: diarrhea, dermatitis, and dementia. The mild deficiency symptoms are erythema, glossitis, indigestion, constipation, anorexia, loss of weight, tachycardia, etc.

OFFICIAL PREPARATIONS.—

NICOTINIC ACID; ACIDUM NICOTINICUM (ACID. NICOTIN.), U.S.P.

It occurs as a white crystalline powder. It is odorless, has a sour taste, and is sparingly soluble in water and freely soluble in alcohol.

THERAPEUTICS.—Used for the prevention and treatment of acute pellagra.[1] Its administration causes the disappearance of all alimentary, mental, and dermal symptoms. As with the other avitaminosis diseases in man, the deficiency is generally of more than one vitamin,

[1]Council Report: J. A. D. A. 28: 316, February, 1941.

therefore a well-balanced diet should accompany the drug administration. (See N.N.R., A.D.R., and Useful Drugs.)

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Nicotinic Acid Tablets; Tabellae Acidi Nicotinici (Tab. Acid. Nicotin.), U.S.P. (Niacin Tablets).

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

NICOTINAMIDE; NICOTINAMIDUM (NICOTINAMID.), U.S.P. (Nicotinic Acid Amide; Niacinamide).

It occurs as a white crystalline compound, nearly odorless, bitter taste. It is soluble in water (1 in 1) and in alcohol (1 in 5).

THERAPEUTICS.—Same as nicotinic acid (see).

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Nicotinamide Tablets; Tabellae Nicotinamidi (Tab. Nicotinamid.), U.S.P. (Niacinamide Tablets).

DOSAGE.—25 mg. (3/8 grain) (U.S.P.).

Vitamin C

Theobald Smith in 1895 noted that guinea pigs kept upon a diet of oats developed a hemorrhagic disease. Holst and Tioloch, 1907, fed guinea pigs polished rice, and instead of beriberi developing as demonstrated in fowl, scurvy developed. The symptoms were loss of weight, joint soreness, hemorrhage, soreness and hyperemia of the gingiva, loosening of teeth, pulp changes, and separation of epiphyses in the long bones. Foods containing vitamin C rapidly lose their protective substances when kept at room temperature or in an icebox. There is smaller loss in an acid medium than in neutral or alkaline media. Heating for one-half hour at 110° C. in an alkaline medium destroyed much of its protective property, while heating for the same time and at the same temperature in an acid solution had but little effect. Drying has but slight destructive influence. Milk which is pasteurized at 165° F., for twenty minutes or 145° F. for thirty minutes has most of the vitamin C destroyed.

Rats have been found to synthesize this vitamin or not need it, while guinea pigs are supersensitive to a lack of "C." Later investigation shows that rats can exist on little or no "C," but are not normal and do need some vitamin C for health. A child weighing 8 or 10 kilograms needs about 15 cc. of orange juice daily. The vitamin can be stored in the body, but the supply is sufficient for only a short time. In 1921 it was observed that there is a rapid loss of calcium from bodies of scorbutic animals. Findlay associated a change in the blood vessels, particularly the capillary endothelium re-

sulting in hemorrhage, with scurvy. The bone marrow shows degenerative changes; Hojer noted that in the teeth the odontoblasts were changed to osteoblasts. Bone formed during scurvy is of inferior quality. The increase of infections in scurvy is probably due to disturbances in the lymphoid tissue.

The work of Hojer has become of interest in that it offers an opportunity for determining vitamin C deficiency in laboratory animals. The most striking of these changes is described as a separation of the layer of the odontoblasts from the dentin, the space then becomes filled in with fluid. The odontoblasts themselves underwent changes in size, arrangement, and staining reaction. The bone changes were a cessation of bone formation with an accumulation of osteoblasts, particularly under the periosteum. An improvement of the tooth tissues was noted in forty-eight hours when vitamin C was restored to the diet. The scorbutic state may be characterized as one affecting the supporting tissues. The cells are unable to produce and maintain intracellular substance; it is most marked in intracellular substance of bone, cartilage, and connective tissue. Vitamin C can be synthesized in seeds by soaking them in water for ninety-six hours. For the synthesis chlorophyll does not seem to be needed but oxygen is required. Germination of the seeds must take place or no "C" is produced. An increase in C has been demonstrated six hours after germination began.

Avitaminosis C produces in man a nutritional deficiency disease known as scurvy. This disease was very prevalent and often fatal to crews at sea, soldiers in the armies, and to civilian populations living on a very meager diet. The etiology of this malady was unknown until 1912 when Holst and Fröhlich suggested that diet might be a factor. In 1917 Chick and Hume identified the preventive substance and by synthesis showed its chemical structure.

CHEMISTRY.—Vitamin C is synthesized in the plant from mannose or some related substance. The l-ascorbic acid is the active form, the d-acid being inactive. The molecule may exist in a saturated or unsaturated form with a gain or loss of hydrogen atoms.

PHARMACODYNAMICS.—Vitamin C is primarily concerned with the formation of the so-called "intracellular cement substances" of connective tissue. It is an active substance concerned with tissue oxidation and reduction, acting as a hydrogen acceptor or giver in plants and animals.

THERAPEUTICS.—True scurvy is not often seen today, but a subacute form is often seen by the observing dentist. The dental symptoms of this chronic disease are: hypertrophic gingivitis with a tend-

ency to hemorrhage, periclasia-like symptoms, alveoclasia with slight mobility of the teeth, hypoplastic dentin, pulpal hemorrhage, poor bone formation, and osteoporosis in adults. The general symptoms are of anorexia, malaise, loss of weight and in children of growth, pain in the joints, petechiae in the skin, etc.

STANDARDIZATION OF VITAMIN C: One International Unit (I.U.) or U.S.P. unit is equivalent in vitamin C efficiency to 50 micrograms of pure crystalline l-ascorbic acid. This amount has the same biologic activity as 0.1 cc. of lemon juice.

The allowable claims for vitamin C made by *New and Nonofficial Remedies* (1942) are:

1. Useful in the prevention and treatment of scurvy.
2. "Dental caries, pyorrhea, certain gum infections, anorexia, anemia, undernutrition, and infection are not in themselves sufficient indications of ascorbic acid deficiency but according to experimental and clinical investigation may be concomitant signs of ascorbic acid deficiency. Therefore, it is permissible to accept the claim for the therapeutic value of ascorbic acid in these symptomatic conditions *only when* it is definitely stated that they are the consequences of a deficiency or suboptimal amount of ascorbic acid or when there is a pathologic interference with assimilation of the amount necessary for the preservation of health."
3. Necessary for the health of all ages and should be obtained from foods whenever possible.

Accepted Dental Remedies, ninth edition, states, "Evidence is lacking, however, to indicate that periodontal disease or gingivitis in general, originates from this cause" (avitaminosis C).

The indication for vitamin C in dental therapeutics is very limited.[1, 2]

OFFICIAL PREPARATIONS.—

ASCORBIC ACID; ACIDUM ASCORBICUM (ACID. ASCORB.), U.S.P. (Vitamin C).

It occurs as a white crystalline powder, odorless, and with an acid taste. It is very soluble in water (1 in 3) and soluble in alcohol (1 in 30). In the dry state it is reasonably stable in air, but when moist it rapidly disintegrates in air.

THERAPEUTICS.—It is useful in the prevention and treatment of scurvy. Vitamin C is an essential constituent of the diet and should be obtained from that source whenever possible. Its use in the pre-

[1] King, C. G.: Physiol. Rev. 16: 238, 1936.
[2] Boyle, P. E., Bessey, O. A., and Wolbach, S. B.: J. A. D. A. 24: 1768, 1937.

vention and treatment of dental caries, gingivitis, periodontoclasia, and to hasten the healing process of soft tissue or bone is not established.

DOSAGE.—50 mg. (¾ grain) (U.S.P.).

Ascorbic Acid Tablets, Tabellae Acidi Ascorbici (Tab. Acid. Ascorb.), U.S.P. (Vitamin C Tablets).

DOSAGE.—50 mg. (¾ grain) (U.S.P.).

Vitamin D

Vitamin D represents three or more substances. The vitamin is fat-soluble, and not a fat but a sterol. Vitamins D and A are often found together in fish oils but may be separated by heating at 100° C., for twenty-eight hours which destroys the "A" fraction (McCollum, 1921).

SOURCE.—Vitamin D is present in fish or fish oils, milk and milk products, chocolate, egg yolk, meat, and irradiated foods. The body also obtains this vitamin from exposure to ultraviolet light, natural (sunshine) or artificial (lamp). Hess found that rays with a wave length shorter than 310 are effective, above 335 have no effect, and 290 are the most effective in antirachitic potency. The effective rays activate the skin, ergosterol converting it into active vitamin D.

PHARMACODYNAMICS.—The function of vitamin D is to aid the body in the absorption, retention, and metabolism of calcium and phosphorus. An avitaminosis D produces blood and bone changes. The blood calcium generally falls below the normal of say 10.5 mg. per cent to 6 mg. or less, where tetany results. The blood phosphorus may increase slightly. The bone development in children is retarded, the epiphyses of the growing bones fail to calcify normally, and the body weight often produces deformities such as bowlegs and knock-knees, and the muscle pull may produce pigeon chest, narrow pelvis, rachitic rosary, scoliosis, etc. The teeth are often improperly formed and spaced in rachitic children, and they may be predisposed to dental caries. In adults avitaminosis D may produce osteomalacia by removing calcium salts from the bones. Its mode of action is not well understood, but it may act by increasing the acidity of the intestinal tract, which aids the absorption of calcium, and by stimulating the parathyroid glands whose hormone aids the body in the retention and metabolism of calcium and phosphorus.

THERAPEUTICS.—Avitaminosis D produces in man a nutritional deficiency disease known as rickets. This condition is still prevalent in this country, particularly among the underprivileged children.

Rickets is a disease primarily of childhood and adolescence in which the metabolism of calcium and phosphorus is disturbed in such a way that normal calcification of the growing bones does not take place (Hess). This failure in calcification is not due to a bone fault but to the blood serum. The serum phosphatase is increased, and there is a disturbance in the Ca:P ratio, which singly or combined may be the etiologic factor.

Teeth being formed during a rachitic period are hypoplastic and often not in normal alignment. The eruption period is generally later than normal. These teeth are prone to develop a higher index of dental caries than normal teeth (Mellanby). The use of vitamin D in the prevention of dental caries is still in an experimental stage.

STANDARDIZATION.—The International Unit (1935) is the vitamin D activity of 1 mg. of the international standard solution of irradiated ergosterol. This unit is adopted by the Committee of Revision of the *United States Pharmacopoeia* and is referred to as the U.S.P. vitamin D unit.

The allowable claims for vitamin D made by *New and Nonofficial Remedies* in 1940 are:

1. Prevention and treatment of infantile rickets, tetany, osteomalacia, and abnormal calcium and phosphorus metabolism.
2. May play an important role in tooth formation and maintenance of tooth structure.
3. Insufficient evidence to support the conclusion that an adequate vitamin D intake will prevent dental caries.
4. Promotes a more economical utilization of dietary calcium and phosphorus.
5. Requirements are higher during infancy, growth, pregnancy, and lactation.
6. Insufficient evidence to support the claim that massive doses will be beneficial in chronic arthritis, allergy disorders, or in psoriasis.

Remarks from *American Dental Record,* 1940:

1. Vitamin D favors normal calcification of the teeth.
2. Avitaminosis D may predispose the dental enamel to hypoplasia.
3. Dental caries is not more prevalent in rachitic children.
4. Vitamin D is not the controlling factor in dental caries.

COD LIVER OIL; OLEUM MORRHUAE (OL. MORRH.), U.S.P.

It contains in each gram at least 850 U.S.P. units of vitamin A and 85 U.S.P. units of vitamin D with not more than 1 per cent of any official flavoring substance(s).

USES.—It is employed for prevention and cure of rickets. It contains both vitamins A and D which are necessary for normal bone and tooth formation. Their role in the prevention and treatment of

dental caries is not established. The researches of many investigators suggest the possibility that these vitamins when included in the diet in adequate amounts may prevent the incidence of dental caries. The dentist must be conservative and wait for more definite proof before subjecting his patients to vitamin therapy.

DOSAGE.—Infants and adults, 8 cc. (2 fluidrachms) (U.S.P.).

PREPARATIONS.—

Emulsion of Cod Liver Oil; Emulsum Olei Morrhuae (Emuls. Ol. Morrh.), U.S.P.—Cod liver oil (50%) with acacia, syrup, methyl salicylate and distilled water. Other flavors may be substituted for the methyl salicylate.

DOSAGE.—Infants and adults: 15 cc. (4 fluidrachms) (U.S.P.).

Emulsion of Cod Liver Oil with Hypophosphites; Emulsum Olei Morrhuae cum Hypophosphitibus (Emuls. Ol. Morrh. c. Hypophos.), N.F.—Cod liver oil (50%), calcium hypophosphite (1%), potassium hypophosphite and sodium hypophosphite (each 0.5%), acacia, saccharin, tincture of sweet orange peel, and distilled water. Absolute alcohol content about 8 per cent.

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

Emulsion of Cod Liver Oil with Malt; Emulsum Olei Morrhuae cum Malto (Emuls. Ol. Morrh. c. Malt.), N.F. (Malt and Cod Liver Oil).—Cod liver oil (30%), extract of malt (about 55%), tragacanth and distilled water.

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

Emulsion of Cod Liver Oil with Egg; Emulsum Olei Morrhuae cum Ovo (Emuls. Ol. Morrh. c. Ovo.), N.F.—Cod liver oil (50%), fresh egg yolk, syrup, tincture of sweet orange peel, and water. Absolute alcohol content about 9 per cent.

DOSAGE.—15 cc. (4 fluidrachms) (N.F.).

Note—Cod Liver Oil containing more than the minimum U.S.P. requirements for both vitamin A and vitamin D may be administered in proportionately lower doses (U.S.P.).

OLEOVITAMIN A AND D; OLEOVITAMINA A ET D (OLEOVITAM. A ET D), U.S.P.

It occurs as either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of vitamin A and D concentrates in fish liver oil or in an edible vegetable oil. The vitamin A shall be obtained from natural (animal) sources and the vitamin D may be obtained from natural (animal) sources or may be synthetic oleovitamin D. Oleovitamin A and D contains in each gram not less than

850 and not more than 1,100 U.S.P. units of vitamin A and not less than 85 and not more than 110 U.S.P. units of vitamin D.

A thin, oily liquid, which may have a fishy, but not rancid, odor and taste. Slightly soluble in alcohol, but is miscible in all proportions with ether and with chloroform.

USES.—Same as cod liver oil.

DOSAGE.—Infants and adults, 8 cc. (2 fluidrachms) (U.S.P.).

Concentrated Oleovitamin A and D; Oleovitamina A et D Concentrata (Oleovitam. A et D Conc.), U.S.P.—It occurs as either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of vitamin A and D concentrates in fish liver oil or in an edible vegetable oil. The vitamin A shall be obtained from natural (animal) sources and the vitamin D may be obtained from natural (animal) sources or may be synthetic oleovitamin D. Concentrated oleovitamin A and D contains in each Gm. not less than 50,000 and not more than 65,000 U.S.P. units of vitamin A, and not less than 10,000 and not more than 13,000 U.S.P. units of vitamin D.

A thin, oily liquid, which may have a fishy, but not rancid, odor and taste.

USES.—Same as cod liver oil.

DOSAGE.—Prophylactic, infants and adults, 0.1 cc. (1½ minims) (U.S.P.).

Concentrated Oleovitamin A and D Capsules; Capsulae Oleovitaminae A et D Concentratae (Cap. Oleovitam. A et D Conc.), U.S.P. (Concentrated Vitamin A and D Capsules).—It occurs as a concentrated oleovitamin A and D capsules contain about 100 per cent of the labeled amount of concentrated oleovitamin A and D, including all tolerances. Concentrated oleovitamin A and D capsules shall be labeled to contain 5,000 U.S.P. units of vitamin A and 1,000 U.S.P. units of vitamin D per capsule.

USES.—Same as cod liver oil.

DOSAGE.—One capsule (U.S.P.).

Synthetic Oleovitamin D; Oleovitamina D Synthetica (Oleovitam. D Synth.), U.S.P.—A solution of activated ergosterol, or activated 7-dehydro-cholesterol, in an edible vegetable oil. Synthetic oleovitamin D contains in each Gm. not less than 10,000 U.S.P. units of vitamin D. Synthetic oleovitamin D must be labeled to indicate whether it contains activated ergosterol *(Vitamin D_2 or Viosterol)* or whether it contains activated 7-dehydro-cholesterol (Vitamin D_3).

A clear, colorless to light yellow, oily liquid. It is almost odorless and has a bland taste. Slightly soluble in alcohol, but is miscible with ether and with chloroform.

USES.—Used for the cure and prevention of rickets in human infants.

DOSAGE.—Prophylactic, 0.1 cc. (1½ minims) (U.S.P.).

Vitamin K

At least two forms of natural vitamin K have been isolated; K_1 from alfalfa and K_2 from fish meal. Both of these are derivatives of naphthoquinone. They are fat-soluble but are not fats.

PHARMACODYNAMICS.—Vitamin K is absorbed from the upper portion of the jejunum by the lacteals chiefly and enters the general circulation via the thoracic duct into the vena cava. In the liver it is converted into prothrombin and is therefore concerned with the clotting of blood. The average American diet contains adequate amounts of the vitamin, but in liver disease, occlusion of the bile duct, or abnormal functioning of the intestinal mucosa with faulty absorption, symptoms of avitaminosis K may occur.

THERAPEUTICS.—As vitamin K is not stored to any extent in the body, a daily dietary supply is essential. When, for reasons of diet or a faulty absorption of this vitamin, a prothrombinemia occurs, the blood clotting time is increased. An avitaminosis K does not initiate spontaneous hemorrhage, but when hemorrhage occurs, it prevents the normal coagulation of the blood.

Its usefulness in dental therapeutics is limited to the prevention and control of hemorrhage from surgery and trauma. As this avitaminosis is caused by diseases in parts of the body other than the oral cavity, consultation with a physician is always advisable.

STANDARDIZATION.—A unit is defined as the antihemorrhagic activity of 1 microgram of the U.S.P. XII reference standard.

DOSAGE.—The exact daily requirements of vitamin K have not been determined. (See preparations.)

PREPARATIONS.—

MENADIONE; MENADIONUM (MENADION.), U.S.P.

It occurs as a bright yellow crystalline powder, nearly odorless and practically insoluble in water, soluble in alcohol (1 in 60), and soluble in vegetable oils.

THERAPEUTICS.—It acts as a specific in avitaminosis K by raising the prothrombin content of the blood.

DOSAGE.—1 mg. (1/60 grain) (U.S.P.).

Caution: Menadione powder and preparations are irritants to the mucous membranes and skin.

Menadione Tablets; Tabellae Menadioni (Tab. meniadion.), U.S.P.

DOSAGE.—1 mg. (1/60 grain) (U.S.P.).

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CHAPTER XXVII

DENTAL THERAPEUTICS

Therapeutics is the science of the treatment of disease. Its aim is to aid the patient in returning to health. We must consider health as abstract, varying with each patient and with the same patient under varied conditions. Whenever possible the cause of the disease should be ascertained and removed; if that is not possible, the symptoms must be ameliorated to permit the patient to pursue his occupation and enjoy life as best he can. There is no fundamental difference in the practice of general therapeutics and dental therapeutics. Dental practice by virtue of its type of specialization generally consists of patients in good health, but the dentist must always be alert to the possibility of more serious diseases which are manifested by symptoms in or about the oral cavity. It is only by such service that dentistry can reach its full professional stature.

Oral Hygiene

Oral hygiene—the science of oral health—treats of the preservation of the normal equilibrium of the oral cavity and its contents. The remedies intended for the maintenance of the health of the soft structures of the mouth and the teeth may be conveniently divided into those prescribed for specific diseased conditions and those employed as hygienic measures for daily use. Only those employed for hygienic purposes are claiming our interest at present.

In the mouths of most civilized races, the mucous membrane, because of the present methods of preparing and selecting foodstuffs and other extrinsic causes, is found more or less in a state of mild chronic inflammation, while the teeth are subjected to a process of molecular destruction, known as dental caries. While certain preliminary intrinsic causes, i.e., anomalies of position, and structure, etc., may profoundly alter the predisposition of the tooth to carious destruction as a whole or in part, dental caries will always occur if a tooth is subjected to the influences of a suitable environment. Miller formulated an explanation of the nature of the carious process, which, at present, is generally accepted and which defines this phenomenon as: a chemicoparasitic process consisting of two definite states, i.e., the decalcification of the tissues, and the dissolution of the remaining organic matrix. In caries of the enamel, the latter phenomenon is not observed because of the minute quantities of organic matter contained

therein. The accumulation of carbohydrate food debris on and about the teeth is considered the incipient factor in the production of the decalcifying agents, the direct factor is the splitting of these carbohydrates by bacteria into acids, i.e., principally lactic acid.

The hygienic care of the mouth is primarily to keep the mucous membrane and the teeth in a state of healthy equilibrium by overcoming the above-enumerated morbific processes. Nature has instituted protective measures of her own to accomplish the desired end. The normal mouth is fairly well protected against the continual onslaughts of bacteria through an unusually rich blood supply, a high resistance of the epithelial lining, and a free flow of saliva. The vigorous use of the organs of mastication during the chewing of properly selected food will bring about an active circulation and stimulation of the parts involved.

Human saliva represents the mixed secretions from the three pairs of salivary glands and the minute mucous glands distributed over the oral cavity. Saliva is a weak solution of alkalies. It contains, furthermore, several organic substances, among which are mucin and the other ferments which accelerate the hydrolysis of starches into maltose. The ferments of human saliva are principally represented by the carbohydrate-splitting type, i.e., amylase (ptyalin) and maltase, although oxidase and catalase are always present. The physiologic function of mucin consists in mechanically assisting the food bolus in an easy passage into the stomach and to protect the oral tissues against irritating substances.

The biologic laws governing the secretion of saliva are directly responsible for its composition, its quantity, and its influence on the digestion and, incidentally, on dental caries. Only the most fundamental facts concerning these biologic aspects can be touched upon at this moment. The secretion of saliva depends upon nervous impulses. The quantity of saliva secreted, i.e., the rapidity of its flow, depends upon the physical nature of the stimulant (foodstuffs). Psychic stimulation is of less importance in this connection. Incidentally, the composition of saliva depends very largely upon the rapidity of flow, i.e., its organic and inorganic contents are primarily influenced by the nature of the stimulant. Apparently, as has been shown experimentally by Pavlov and his pupils, saliva is a glandular secretion capable of adaptation. The fundamental basis of the secretion of saliva, however, rests with the process of mastication; i.e., the degree and manner of mastication increase or diminish very materially the amount of saliva. The much-discussed alkalinity of saliva depends directly on its inorganic content. With an increase of flow

an increase of alkalinity is always observed. The reaction of saliva collected during periods of physiologic rest of the salivary glands is so very weakly alkaline that its influence as a neutralizing agent is practically nil.

Rickert was not able to show experimentally in the human mouth any relationship between the amylase (ptyalin) content of saliva and dental caries.

The much-discussed bactericidal action of the saliva is still unsolved. In the normal mouth pathogenic microorganisms are usually less virulent, and they are less in number than of the saprophytic types. Flügge has shown that the pathogenic bacteria will become extremely active if the individual is afflicted with a slight local disturbance—as a simple cattarrh of the throat. It appears that the saliva of man and of some animals exercises an inhibitory function on certain microorganisms—the staphylococci and the streptococci.

Immunity *as referred to tooth structure* is, in the strict sense of the word, a misnomer, as it is *not* bound up with vital phenomena. In a biologic sense, immunity indicates a state in which the "living" body resists disease. In a pulpless tooth we are dealing with inert structure as far as the enamel is concerned, and it is this latter tissue only that concerns us in the elucidation of the question: Why do teeth decay? In a tooth with a vital pulp the enamel is capable of carrying on metabolic processes to a limited degree. The surface of so-called living enamel is practically an inert structure which offers no vital resistance to the physicochemical process of decay. The omnipresent surface colloids and the colloidal fluids present in the enamel in teeth with living pulps may modify the process of decay. Teeth which are imperfectly calcified have a lowered resistance and will sooner or later decay. If, however, the flow of saliva is impaired or completely checked, all teeth will be destroyed by caries unless some other means for the removal of food debris is established. The rapidity of destruction is dependent upon the severity of the impairment. Normally, the flow of saliva is regulated by the intensity of the stimulus as evinced during mastication. The stimulation by acids is of a temporary nature only, and of less importance. Therefore, vigorous mastication of correctly selected foodstuffs forms the basis for the natural prevention of dental decay. Subjecting wild tribes of the human race to the influences of civilized diet will always be followed by a marked increase in dental caries. Immigrants from countries where hard-baked black bread forms a large part of their diet when in the United States are frequently subject to intense ravages of dental decay. For instance, newly arrived Scandinavians,

accustomed to chewing "knäckebröd," forget to masticate our soft wheat bread, and, as they are often forgetful of the blessings of the toothbrush, rampant decay is frequently manifest within a few months after their arrival. Dental caries is rarely observed in the teeth of habitual tobacco chewers. Miller and others have demonstrated that tobacco juice possesses no antiseptic action. Its prophylactic effect, as far as the teeth are concerned, rests with the pharmacologic and physical action of tobacco, i.e., its alkaloid nicotine is a powerful salivary stimulant, and the mechanical action of chewing.

Several additional contributions to the subject have been made more recently which should be considered by the student. The Michigan group, and others who have devoted much time and study to the question of dental caries, have confirmed W. D. Miller's chemicobacterial (acidogenic organisms) theory as related to dental caries. This group of research workers with others has produced convincing experimental evidence that the amount of sugar and fermentable carbohydrates of the diet directly affects the activity of dental caries.[1-13]

The quantity and, to a less extent, the quality of saliva, because of our present methods of preparing and selecting foodstuffs and the consequent insufficient mastication, are frequently inadequate to bring about a proper physiologic cleansing of the oral cavity. To assist nature, suitable mechanical and chemical means may be employed to overcome this deficiency. The mechanical cleansing of the mouth and teeth by means of the brush, powder, paste, toothpick, floss silk, etc., constitutes the absolute fundamental principle of artificial oral hygiene. Food remnants and slimy adhesions between and upon the teeth, together with a large number of the adherent bacteria, are removed by mechanical cleansing. The mechanical cleansing of the

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[12]Breese, F.: Diet and the Teeth, Brit. D. J. 56: 120, February, 1934.

[13]Roos. Dental Caries in Switzerland, translated by Kronfeld, Chicago Dent. Bull. January, 1938.

oral cavity by these means may, however, be materially assisted by the judicious use of suitable mild astringent and indifferent antiseptic solutions. Powders, pastes, and washes containing drugs are employed for the avowed purposes of assisting nature in accomplishing the desired end; i.e., to favor the recovery of an inflamed mucous membrane, and mechanically to remove accumulated food debris.

A good oral preparation should possess the following properties:

1. It must be absolutely indifferent in regard to:
   (a) the mucous membrane—*noncaustic;*
   (b) the teeth—*nondecalcifying* (mechanical or chemical);
   (c) the organism as a whole—*nonpoisonous.*
2. It must not interfere with the normal physiologic cleansing of the oral cavity, i.e.:
   (a) it must not inhibit the secretion of saliva;
   (b) it must not perceptibly alter the reaction of saliva;
   (c) it must not destroy the ferments of saliva.
3. It must possess sufficient cleansing action, combined with:
4. Good taste and odor.

These various properties are rarely found in combination in a single oral preparation, and yet each one is of the utmost importance.

Hygienic measures as applied to the oral cavity are practiced in proportion to the pleasant sensation which they call forth; hence a mouth preparation which has a disgusting taste is ineffective because it will not be employed for any length of time by the laity. The great mass of the public will never be induced to practice oral hygiene that involves ill-tasting preparations. As stated above, mouth preparations must be absolutely free from danger as far as the mucous membrane, the teeth, and the body as a whole are concerned. Hence Roese's dictum should be indelibly fixed in the mind of every dental practitioner: The importance of oral hygiene is not so great that we are justified in assuming the slightest risk. This statement cannot be emphasized too strongly in view of the fact that numerous mouthwashes and tooth preparations of questionable value are continually forced on the market. Unless the composition of a ready-made mouth or tooth preparation is known, it should not be recommended.

The majority of the so-called dental preparations which are employed by the laity for daily use belong to a group of medicinal compounds generically known as proprietary preparations. As these compounds are not used for the avowed purpose of curing a specific disease but rather as hygienic measures, no objection is raised from an ethical point of view, provided that they are prepared from ap-

proved formulas and that they conform to the properties as outlined above. The best service that a conscientious practitioner can render to his clientele is to discourage the use of mouth preparations unacceptable to the Council on Dental Therapeutics. The acceptable dentifrices carry a seal of acceptance and are listed in Accepted Dental Remedies.

The search for so-called tartar solvents—substances which prevent or dissolve calcareous deposits about the teeth—as an addition to tooth preparations has occupied the minds of the dental hygienists for some time past. The chemical nature of the oral calculus indicates that its disintegration may be accomplished logically in two ways: first, by dissolving in an acid or an acid salt and, second, by disintegration with an alkali which removes its organic matrix and thereby renders the remaining inorganic base an easy prey to mechanical abrasives. Human oral calculus contains approximately 25 per cent of organic substances and water. For self-evident reasons, acids and acid salts cannot be employed for such purposes in the oral cavity. On the other hand, mild alkalies prevent the ready formation of calculus, and they help to remove fresh deposits. Just how much of this destruction or removal should be attributed to the mechanical scrubbing with the brush, and how much to the solvent action by the ingredients of the tooth powder or paste is very difficult to determine.

Innumerable experiments have been made to determine the so-called antiseptic strength of oral preparations. As a standard, the Rideal-Walker phenol coefficient or some other laboratory standard is usually employed. If these experiments are carried out in test tubes with cultures of isolated organisms, comparative deductions drawn from such tests are wholly unwarranted as they do not portray actual conditions existing in the oral cavity.[1] On the other hand, if these preparations are tested directly in the mouths of normal individuals, it is invariably found that only 50 per cent of the oral bacterial flora is inhibited. Authorities agree that it is impossible to render the oral cavity sterile, even for a short time, with any of the so far known antiseptic solutions in the strength in which these solutions can be employed with safety. The dilution of these preparations and the short time allowed for their action in the cavity as actually employed by the user necessarily minimize their antiseptic effect to such an extent as to render them practically valueless.

It has been repeatedly shown that a physiologic saline solution (approximately one drachm of sodium chloride to a pint of boiled water

[1] Crowley, M., and Rickert, U. G.: Effect of Certain Mouth Washes on the Number of Oral Bacteria, J. Bact. 30: 4, 1935.

and heated to body temperature) reduces the oral flora by 50 per cent and, incidentally, it is absolutely safe. E. Kells, Jr., Kirk, and many other observers have called attention to the remarkably good results obtained from the use of limewater. Its therapeutic effect depends on its solvent power of the mucin deposits on and about the teeth.

Rickert made innumerable tests with various dental preparations found on the market and verified what has been stated above, namely:

1. Sterilization of the oral cavity with any of the commercial dental preparations or any antiseptic in the strength in which it can be employed with safety, cannot be accomplished.

2. The cleansing of the oral cavity with an antiseptic solution alone or combined with the mechanical effects of the toothbrush, powder, or paste, reduces the number of oral bacteria approximately about 50 per cent. The claims made for the antiseptic strength of certain commercial preparations are, by actual tests, wholly unwarranted.

3. A physiologic saline solution of body temperature in conjunction with the toothbrush and precipitated calcium carbonate in the form of a suitable powder or a paste are the safest and most effective of all so far known artificial oral hygienic measures.

Preparations intended for the mouth and the teeth exercise their beneficial influence on the soft and hard tissues of the oral cavity, primarily, by their mechanical cleansing power and, secondarily, by inhibiting to a limited degree the activity of the extremely rich saprophytic flora which is always present. The rate of increase of bacteria in the oral cavity is enormous, as the conditions which favorably influence their growth are ideal. The mere preservation of the teeth and their adnexa is not the only function of those agents, as many other organs which are directly or indirectly connected with the oral cavity proper are frequently subjected to serious pathologic alterations by contamination. Oral sepsis, by way of continuity, may involve the tonsils, the pharynx, the glands of the jaws and the mouth, the stomach, lungs, etc. According to Hunter septic gastritis and toxic neuritis, and their many sequelae, may be caused by oral sepsis.

Preparations which are intended to exercise definite functions on the teeth and gingivae, the oral mucous membrane, the tongue, the salivary glands, and the tonsils, and to some extent on the breath, are known as *oralia*. This term has, however, never been universally recognized; the physical nature of the preparation has created specific names for definite classes—solid or semisolid tooth preparations are known as *dentifrices*, liquid tooth preparations are spoken of as

collutories, while liquids intended for the pharyngeal regions are referred to as *gargles.* According to their therapeutic indications, the drugs used in the mouth are grouped under *abrasives, antacids, antiseptics, astringents, stimulants, detergents,* etc.

With the establishment of the Council on Dental Therapeutics in 1929, some of the most despicable conditions of oral proprietary preparations have been improved. Before that time some of these preparations contained toxic substances. There were those of unreasonable abrasive action, while others produced allergic reactions to the patient; and the majority of them, as has been pointed out, made therapeutic claims that went far beyond the truth. The merchandising of these products has been much improved, and it is believed that through the influence of the council these despicable merchandising methods will come to an end.

The preparations used for the mouth and teeth are conveniently divided into mouthwashes, tooth powders, tooth pastes, and tooth soaps. Oral lozenges, trochisci, and chewing gums are also used by the laity; they are intended to flavor the breath, and possess slight medicinal value.

Drugs Used in Preparations for the Mouth and Teeth

In constructing a prescription for a mouth or tooth preparation the following substances must be avoided:

1. Strong precipitants of albumin (concentrated solutions of alcohol, mineral acids, with the exception of boric acid, metallic salts, phenol, and salicylic acid and many of their derivatives, etc.).
2. Liquefying caustics (potassium and sodium hydroxide).
3. Strong astringents (zinc chloride, etc.).
4. Abrasive and gritty substances (pumice stone, charcoal, crude chalk, etc.).
5. Fermentable substances (sugars, starches, vegetable powders).
6. Staining substances (organic and inorganic dyestuffs, iron salts, manganese salts, etc.).
7. Poisonous substances (potassium chlorate, etc.).

Dental Caries

Dental caries is a disease which affects the hard and soft tissues of the teeth. The infection begins in the enamel and may extend to the dentin and dental pulp. In the beginning the infection is local but when the pulp is involved it is potentially systemic. The localization of the lesion in the hard tissues is in the pits and fissures

and on the smooth surfaces which are not normally cleansed by the excursion of food. Children and adolescents are more susceptible than adults.[1] The initial lesion is probably a localized area of fermenting carbohydrate foods protected from the neutralizing influence of the saliva. The decomposition of the carbohydrates[2, 3, 4, 5] by bacteria liberates organic acids[6] which change the highly insoluble calcium phosphate of the tooth to a soluble calcium salt which is removed by solution and fracture. In the dentin proteolytic enzymes digest the organic matter while the acids decalcify the inorganic matter. By extension the pulp eventually becomes infected, and the bacteria and their toxins are free to enter the lymph and blood circulation and infect the body proper.

The organisms associated with dental caries are varied, suggesting a nonspecific infection.[7, 8]

A general oral acidity does not result in dental caries but in a general dissolution of the tooth tissue known as odontolysis. It is not advisable to administer alkalies to change the saliva pH, as other body fluids are likewise changed, resulting in an upset of the alkaline balance of the body.

THERAPEUTIC METHODS:

1. Seeing a dentist every three to six months for prophylaxis and treatment.
2. Thorough brushing of the teeth after meals and before retiring.
3. Use of dental floss for cleaning the interproximal surfaces of the teeth.
4. Use of detergent and alkaline mouthwashes after meals.
5. Normal diet,[9] low in carbohydrates has been suggested.[10]
6. Prophylactic odontotomy has been suggested by Hyatt.
7. Restore all carious teeth with copper or silver amalgan.

THERAPEUTIC AGENTS:

SILVER NITRATE.—Black and Miller lauded the use of silver nitrate as a method for controlling dental caries. The treatment stains the

[1]Slowman, E.: J. A. D. A. 28: 441, March, 1941.
[2]Fosdick, L. S.: J. A. D. A. 25: 415, March, 1939.
[3]Fosdick, L. S., and Wessenger, G. D.: J. A. D. A. 27: 203, February, 1940.
[4]Fosdick, L. S., and Starke, A. C.: J. A. D. A. 28: 234, February, 1941.
[5]Fosdick, L. S., Hansen, H. L., and Wessinger, G. D.: J. A. D. A. and D. Cos. 24: 1445, September, 1937.
[6]Fosdick, L. S.: J. A. D. A. 29: 2132, December, 1942.
[7]Bibby, Basil G., and Hine, M. K.: J. A. D. A. and D. Cos. 25: 1934, December, 1938.
[8]Bibby, B. G., Volker, J. F., and Van Kesteren, M.: J. Dent. Res. 21: 61, February, 1942.
[9]Robinson, H. B. G.: J. A. D. A. 30: 357, March, 1943.
[10]Boyd, Julian D.: J. A. D. A. 30: 1344, September, 1943.

tissues black, and for that reason it is used chiefly on deciduous teeth. For beginning caries the silver is precipitated in the decalcifying tissue and repeated every six months. When or if the caries are more extensive, the lost tissue should be restored. Adult patients with beginning class V cavities have been treated in this manner, thereby preventing a rapid destruction of tooth tissue.

If the applied silver nitrate is not reduced to the black form, no lasting effects are obtained. The reduced silver probably acts as a bacteriostatic agent and also as an antienzyme which prevents the break down of the foodstuffs into acids.

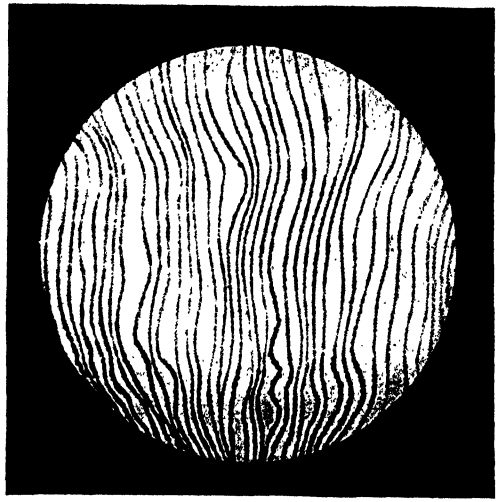

Fig. 30.—Action of silver nitrate on dentinal fibrils. (After Szabo.)

Brooks found that precipitated silver nitrate on areas of tooth erosion would prevent the continued destruction of the tooth tissue. These results have not been confirmed to my knowledge.

Method.—The area to be treated is cleaned of all debris and decalcified tissue. A careful diagnosis should be made to determine the extent of the infection; teeth with infected pulps should not be treated in this manner. The area is dried with warm air and the silver preparation applied until the area is saturated. Reduction of the silver is brought about by applying eugenol or formaldehyde solution (10%). This process is repeated until the area is stained. The penetration of the silver into the dentin is limited to about $\frac{1}{50}$ of an inch, a deeper penetration is not produced by applying a stronger solution or by repeated applications. The treatments are repeated every three, six, or twelve months as the case indicates.

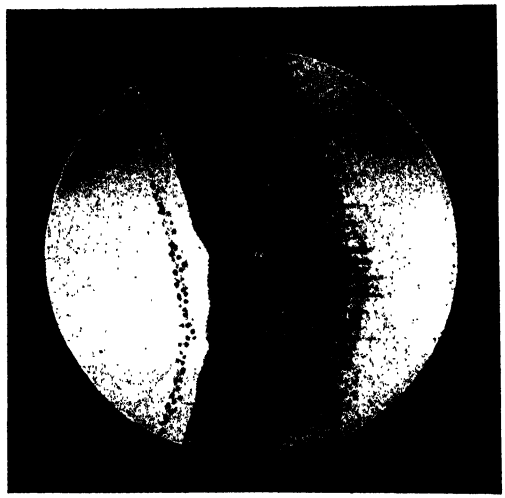

Fig. 31.—Action of silver nitrate on living dentine. Cervical cavity. (After Szabo.)

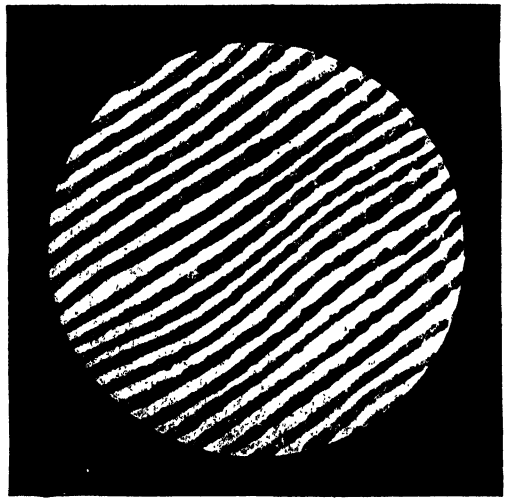

Fig. 32.—Silver nitrate applied to carious dentine. High power. (After Szabo.)

PREPARATIONS.—

1. Silver nitrate crystals are applied to the area to be treated and a drop of distilled water is added. Reduction is brought about with eugenol or formaldehyde solution (10%).

2. A strong solution of silver nitrate (25% to 40%) in distilled water is applied and reduced. Freshly prepared solutions of silver salts are always superior to old solutions.

3. *Ammoniacal Solution of Silver Nitrate; Liquor Argenti Nitratis Ammoniacalis (Liq. Arg. Nitrat. Ammon.),* N.F. (Ammoniacal Silver Nitrate, Howe).

The N.F. preparation is made as follows:

Silver Nitrate	70.4 Gm.
Distilled Water	24.5 cc.
Strong Solution of Ammonia, about	68.0 cc.

Dissolve the silver nitrate in the distilled water, warming if necessary. Cool to room temperature and add the Strong Solution of Ammonia, U.S.P., from a burette until all but a trace of the black precipitate is dissolved. Filter clear.

The silver ammonium complex ($Ag[NH_4]_2NO_3$) is very reactive and care must be used to prevent decomposition. Discolored solutions are not as effective as freshly prepared solutions.

Ammoniacal Silver Nitrate (A.D.R.).—A solution containing approximately 30 per cent silver as silver diammino nitrate. Solution of silver diammino nitrate—approximately 57 per cent. $Ag(NH_3)_2NO_3$.

PREPARATION.—"Put three grams of silver nitrate crystals into a test tube and add one cubic centimeter of water. Heat this mixture over a flame to dissolve, being careful not to let it boil. Let it cool until you can hold it in the palm of your hand. Now add strong ammonia water (28%) slowly. At first a black precipitate will be formed. Keep adding ammonia and shaking the mixture until the black is almost all dissolved. Do not let it all dissolve or you will have too much ammonia which is undesirable. The remaining black precipitate is removed by filtering through filter paper. The filtered solution should be kept in a brown bottle to protect it from light to which it is sensitive." (Forsyth Interne's Manual.)

Ampuls Ammoniacal Silver Nitrate—P. N. Condit: Solution of ammoniacal silver nitrate. Each ampul contains about 2 cc. of ammoniacal silver nitrate prepared according to the directions of Percy R. Howe (*D. Cosmos,* 59: 481, 1917). These ampuls are accompanied by ampuls containing 2 cc. of a solution of formaldehyde, approximately 10 per cent. (A.D.R.)

TOXICOLOGY AND TREATMENT.—Locally, silver nitrate is a self-limiting caustic. Its degree of penetration is limited by the chlorides and albumins, which form insoluble salts, neutralizing its action.

Sodium chloride is a good antidote for silver nitrate poison. The stains may be partially removed with hydrochloric acid (1%) or mild tincture of iodine, the halogen ions forming a colorless compound with the silver.

FLUORIDE PREPARATIONS.—The application of fluoride salts to the teeth for the prevention of dental caries is a comparatively new procedure. Bibby et al.,[1] working on children in the environs of Boston, applied a 0.1 per cent solution of sodium fluoride to the teeth three times per year and noted a lower incidence of dental caries in the treated group than in the controls. The teeth were cleaned with pumice, solution of hydrogen peroxide, and a motor-driven brush. They were dried with alcohol and air and isolated with cotton rolls. The solution of sodium fluoride (0.1%) was applied to the dental enamel by means of a cotton pellet held in dental tweezers. After the application the mouth was rinsed well with water to remove the uncombined fluoride. Its use as a mouthwash has been suggested by Atkins[2] and may be as satisfactory as the procedure suggested by Bibby.

The addition of fluorides to the drinking water as suggested by Cox and Levin[3] for controlling dental caries cannot be considered safe at this time. While much work has been done and much has been published on dental fluorosis, there is little information in the literature to show the chronic effects of this element on the other tissues. There is a possibility that fluoride may be incorporated in mouthwashes, dentifrices, lozenges and chewing gum, if this is not prohibited by law.

Mottled Enamel

Mottled enamel is a developmental defect of the enamel of the teeth. The dentin is affected to a lesser degree. Permanent teeth are more often affected than the deciduous teeth, the reason being the time of formation. The area chiefly affected is the labial surface of the incisor teeth although all surfaces and teeth may be affected.

Mottled enamel is an endemic condition occurring in many parts of the world. Race, color, or sex is not a factor. In the United States over 85 per cent of the cases are located west of the Mississippi River. The states which are the chief offenders are Texas, Colorado, South Dakota, and Arizona, and to a lesser extent Illinois, Idaho, West Virginia, Virginia, and the Carolinas.

Microscopically, the areas of mottled enamel show a poor calcification of the enamel rods with little or no interprismatic substance. Grossly, the affected areas are flat white and appear to have a roughened surface. Later pigments pass into the dystrophied enamel which gives the brown discoloration, so often seen in these teeth.

[1] Bibby, B. G.: Tuft's Dent. Outlook 15: 4, May, 1942.
[2] Atkins, A. P.: J. A. D. A. 31: 353, March 1, 1944.
[3] Cox, G. J., and Levin, M. M.: A. A. A. S. Publ. 19: 732, 1942.

The cause of mottled enamel is the fluorine content of the drinking water. Plants grown in soil which contains fluorine also contain fluorine but this source is not as important as the water. Measurements of the fluorine content of drinking water in the endemic areas show a concentration of 2 to 14 parts per 1,000,000.

The site of action of the fluoride ion in mottled enamel formation is the ameloblast. The mode of action is not clear. Fluorine ions are protoplasm poisons. They prevent enzyme action and inhibit the normal cellular metabolism. The ions are also antiseptic and antizymotic and thus prevent fermentation. This may be a reason for the lower incidence of dental caries in the endemic areas. Investigations are now being carried on to study this phase of caries control.

Mottled enamel cannot be cured. Restorations will correct the esthetic deformity. Prevention is possible by removing the child from the endemic area or by using water which does not contain appreciable amounts of fluorine.

ANTACIDS

Antacids are agents which neutralize acids by their alkaline or basic properties; their action is always of a chemical nature. In general medicine, antacids are usually employed to reduce the acidity of the secretions of the stomach and, sometimes, of the urine, and to increase the reduced alkalinity of the blood. In dentistry they are used locally to neutralize hyperacidity of the mouth. Before prescribing an antacid the acidity of the oral secretions should be positively established. To test the secretions, the mouth must be rinsed with a warm physiologic salt solution, and the saliva collected by letting it drip from the open mouth, head bent forward, into a suitable vessel. To determine the reaction of saliva in the oral cavity with test papers (litmus, etc.) is absolutely unreliable.

The action of the chemicals used in the mouth for the purpose of neutralizing the oral secretions is only of a temporary character. The insoluble carbonates of calcium and magnesium and the hydrate of the latter are preferred for such purposes. The readily soluble sodium bicarbonate is of only temporary assistance. Caustic alkalies must be carefully avoided in the mouth.

If antacids are indicated, the best time for their application is in the evening before retiring. After the mouth is thoroughly rinsed the teeth should be evenly coated with milk of magnesia, or a thin paste of precipitated calcium carbonate and water, and left in place over night. All traces of the coating should be removed by thorough rinsing the following morning.

Calcium Salts

TRIBASIC CALCIUM PHOSPHATE; CALCII PHOSPHAS TRIBASICUS (CALC. PHOS. TRIBAS.), $Ca_3(PO_4)_2$, U.S.P. (Precipitated Calcium Phosphate).

It is a white, odorless, tasteless powder, almost insoluble in water and alcohol.

USES.—As a basis for dentifrices.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

PRECIPITATED CALCIUM CARBONATE; CALCII CARBONAS PRAECIPITATUS (CALC. CARB. PRAEC.), $CaCO_3$, U.S.P. (Precipitated Chalk).

It is a fine white, impalpable powder, without odor and taste, and permanent in the air. It is almost insoluble in water and insoluble in alcohol. In diluted acetic, hydrochloric, or nitric acid it is completely soluble, with effervescence, forming an acid salt.

USES.—Oral antacid is extensively used as a basis for tooth powder.

DOSAGE.—1 Gm. (15 grains) (U.S.P.), as powder or as a suspension in liquid.

Tablets of Calcium Carbonate; Tabellae Calci Carbonatis (Tab. Calc. Carb.), N.F.

DOSAGE.—1 Gm. (15 grains) of calcium carbonate (N.F.).

N.F. Dentifrice; Dentifricium, N.F. (Dentif., N.F.), N.F. (N.F. Tooth Powder).—Hard soap and precipitated chalk, sweetened with soluble saccharin and flavored with volatile oils.

USES.—As a tooth powder.

PREPARED CHALK; CRETA PRAEPARATA (CRET. PRAEP.), U.S.P.

It is a native calcium carbonate, freed from most of its impurities by elutriation. It is a white or grayish fine powder or in the form of conical drops; odorless and tasteless, and permanent in the air. Chemically it behaves likes the precipitated calcium carbonate. Because of its content of foreign substances the natural calcium carbonate is too abrasive on the teeth to be used in dentifrices. The precipitated form is acceptable.

USES.—Used as a mild alkali, an antacid.

DOSAGE.—1 Gm. (15 grains) (U.S.P.), as a powder or in suspension.

Chalk Mixture; Mistura Cretae (Mist. Cret.), U.S.P.—Prepared chalk (6%), cinnamon water (40%) and distilled water. *Caution.*—This preparation must not be dispensed unless it has been recently prepared. (U.S.P.)

DOSAGE.—15 cc. (4 fluidrachms) (U.S.P.).

CALCIUM HYDROXIDE; CALCII HYDROXIDUM (CALC. HYDROX.), $Ca(OH)_2$, U.S.P. (Slaked Lime, Calcium Hydrate).

A soft, white, crystalline powder, with an alkaline, slightly bitter taste. Slightly soluble in water (1 in 630) but insoluble in alcohol.

USES.—Antacid; used chiefly in the form of the solution undiluted as a mouth rinse.

Solution of Calcium Hydroxide; Liquor Calcii Hydroxidi (Liq. Calc. Hydrox.), $Ca(OH)_2$, U.S.P. (Liquor Calcis, Limewater),—It is a saturated solution of slaked lime in water, containing about 0.15 per cent of calcium hydroxide. It is a clear, colorless liquid, without odor and having an alkaline, feebly caustic taste.

DOSAGE.—15 cc. (4 fluidrachms) (U.S.P.).

Magnesium Salts

MAGNESIUM OXIDE; MAGNESII OXIDUM (MAG. OXID.), U.S.P. (Magnesia, Light Magnesia).

MgO (not less than 96%). The magnesium compounds form white masses or amorphous powders, with an earthy, but not saline, taste. They are practically insoluble in water and alcohol, but readily soluble in acids, with effervescence.

USES.—Useful as an antacid.

DOSAGE.—Antacid, 0.25 Gm. (4 grains). Laxative, 4 Gm. (60 grains).

Heavy Magnesium Oxide; Magnesii Oxidum Ponderosum (Mag. Oxid. Pond.), U.S.P. (Heavy Magnesia); MgO (96%).

USES.—Similar to those of magnesium oxide.

DOSAGE.—Antacid, 0.25 Gm. (4 grains). Laxative, 4 Gm. (60 grains).

MAGNESIUM CARBONATE; MAGNESII CARBONAS (MAG. CARB.), U.S.P. (Carbonate of Magnesium).

Hydrated magnesium carbonate, equivalent to about 41 per cent MgO.

DOSAGE.—Antacid, 0.6 Gm. (10 grains). Laxative, 8 Gm. (2 drachms) (U.S.P.).

MAGNESIUM HYDROXIDE; MAGNESII HYDROXIDUM.

Magnesia Magma; Magma Magnesiae (Magma Mag.), U.S.P. (Milk of Magnesia).—A suspension of magnesium hydroxide, $Mg(OH)_2$, about 7.5% in water, forming a thick, white liquid.

USES.—Mild alkaline tooth wash.

DOSAGE.—Antacid, 4 cc. (1 fluidrachm). Laxative, 15 cc. (4 fluidrachms).

It is a hydrate of magnesia, and forms a semigelatinous liquid, containing freshly precipitated magnesium hydroxide prepared by the interaction of magnesium sulfate and ammonia water; the precipitate is collected and washed with distilled water until the washing ceases to give a reaction for sulfates.

Sodium Salts

SODIUM BICARBONATE; SODII BICARBONAS (SOD. BICARB.), $NaHCO_3$, U.S.P. (Baking Soda).

It is a white, odorless powder, having a cooling, mildly alkaline taste. It is soluble in about 10 parts of water at ordinary temperature; hot water gradually decomposes its solution. It is insoluble in alcohol. With acids its solutions effervesce strongly.

DOSAGE.—2 Gm. (30 grains) (U.S.P.).

℞ Sodium Bicarbonate 120 Gm.
Sig.: One level teaspoonful in a glassful of warm water as a mouthwash t.i.d.

SODIUM BORATE; SODII BORAS (SOD. BOR.), $Na_2B_4O_7.10H_2O$, U.S.P. (Borax, Sodium Tetraborate).

USES.—Antiseptic, detergent and alkaline. Used in solution as a wash for the skin and mucous membranes in a 2 per cent solution.

Compound Solution of sodium Borate; Liquor Sodii Boratis Compositus (Liq. Sod. Bor. Co.), N.F. (Dobell's Solution).—Sodium borate and sodium bicarbonate (each 1.5%) and liquefied phenol (0.3%) in glycerin and water.

USES.—Mild antiseptic. For use on mucous membranes: undiluted; or, for the dental spray bottle, dilute with 5 volumes of water (N.F.).

Honey of Rose and Sodium Borate; Mel Rosae et Sodii Boratis (Mel. Ros. et Sod. Bor.), N.F. (Honey of Rose and Borax).—Sodium borate and fluidextract of rose (each 10%) in glycerin and honey.

USES.—Alkaline demulcent.

Potassium Salts

POTASSIUM BICARBONATE; POTASSII BICARBONAS (POT. BICARB.), $KHCO_3$, U.S.P.

DOSAGE.—1 Gm. (15 grains) (U.S.P.).

Alkaline Aromatic Solution; Liquor Aromaticus Alkalinus (Liq. Arom. Alk.), N.F.—Potassium bicarbonate (2%), and sodium borate (2%), with thymol, eucalyptol, methyl salicylate and cudbear in alcohol, glycerin and water.

USES.—Of slight value as antiseptic, but a pleasant, cleansing, alkaline, mouthwash.

DOSAGE.—"For oral use; undiluted, or, for use in the dental spray bottle, dilute with 5 volumes of water" (N.F.).

DENTAL ABRASIVES

Tooth powders, pastes and soaps are principally employed for mechanically cleansing the accessible surfaces of the teeth. Their

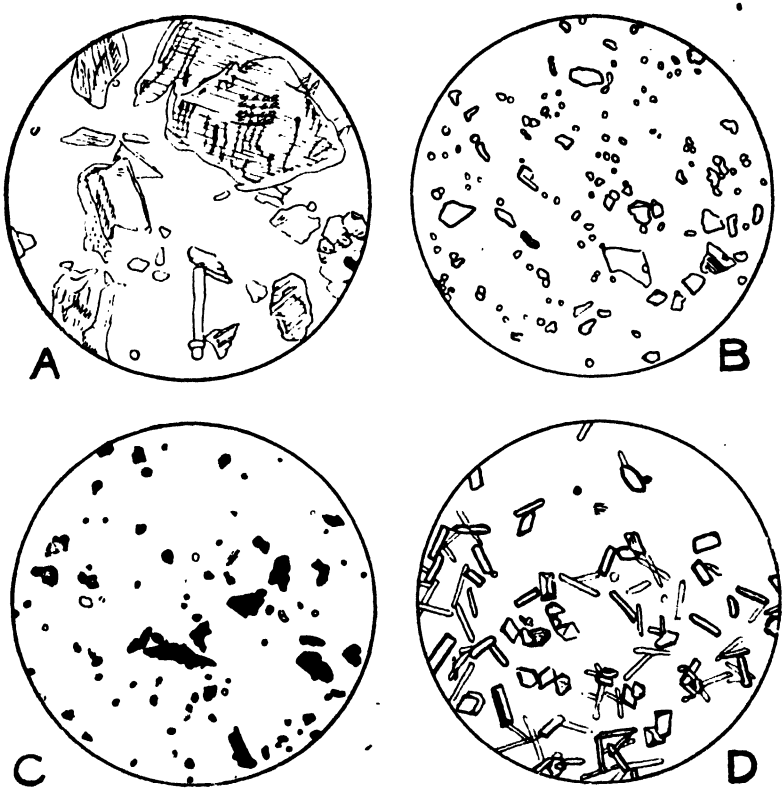

Fig. 33.—Magnified specimens of tooth powder substances. Magnification, 350×. *A*, Powdered pumice stone; *B*, powdered cuttlefish bone; *C*, powdered charcoal; *D*, powdered potassium bitartrate.

antiseptic effect on oral bacteria is of questionable value. Tooth powders or pastes should not contain gritty or fermentable substances or corrosive chemicals, which act deleteriously on tooth structure. The wasting away of tooth tissues, usually referred to as erosion or abrasion, is largely the result of the continuous use of powders, pastes, etc., which contain more or less abrasive substances.

The materials which are principally employed in the manufacture of commercial tooth powders, pastes, and soaps are prepared chalk, precipitated calcium carbonate, magnesium carbonate, soap, cuttlefish bone, orris root, and many other substances—as vegetable powders of various kinds, borax, boric acid, potassium bitartrate, alum, charcoal, tin oxide, etc. Some of these substances possess a pronounced abrasive character, while others are polishing agents consisting of various

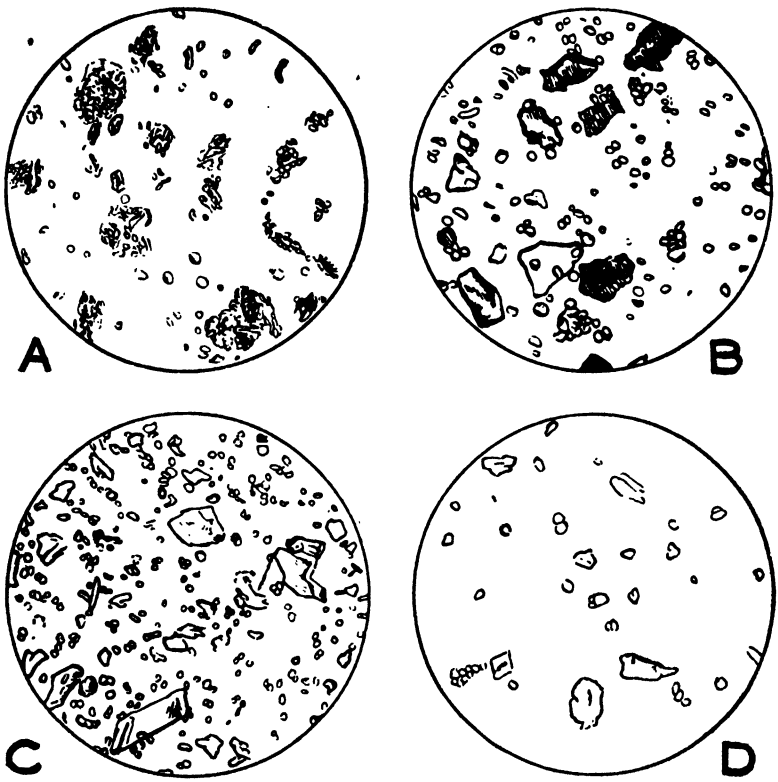

Fig. 34.—Magnified specimens of tooth powder substances. Magnification, 350×. *A*, Powdered magnesium carbonate; *B*, powdered prepared chalk; *C*, precipitated calcium carbonate, heavy; *D*, precipitated calcium carbonate, washed.

degrees of grit. The vegetable powders are principally used as adjuvants and diluents; their use in tooth powders is not to be encouraged, as they may lodge between the teeth, and the starch, which is present in most of these powders in variable quantities, may be the cause of acid fermentation.

An acquaintance with the physical nature of the ingredients entering into the makeup of tooth preparations in regard to their abrasive

qualities is essential for the dental practitioner. A microscopic examination of the more important powdered substances, together with a comparative knowledge of their physical and chemical composition, furnishes excellent information regarding their usefulness as components of dentifrices.

PREPARED CHALK; CRETA PRAEPARATA (CRET. PRAEP.), U.S.P.

Crude calcium carbonate is a white amorphous powder purified by mechanical means. Prepared chalk is *not* precipitated chalk but a

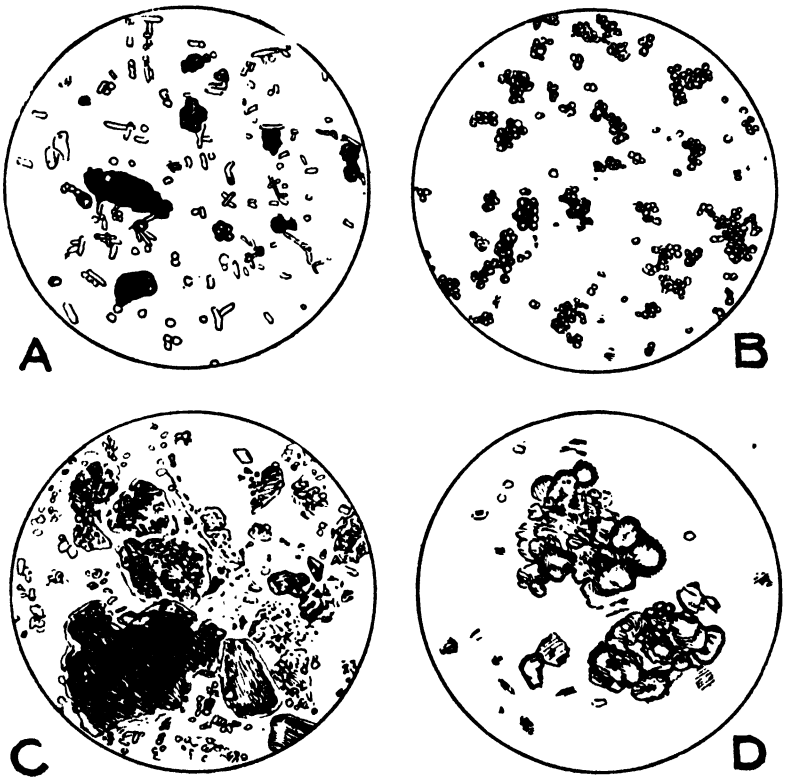

Fig. 35.—Magnified specimens of tooth powder substances. Magnification, 350×. *A*, Precipitated calcium carbonate (precipitated by heat); *B*, precipitated calcium carbonate (Schering's); *C*, powdered orris root; *D*, borax tooth powder.

native calcium carbonate. Prepared chalk contains in addition silica, alumina, and other impurities, and consists principally of the microscopic shells of many forms of infusora. The minute particles of prepared chalk are sufficiently hard and sharp to remove tooth substance when used in a dentifrice, and should therefore never be employed for such purposes.

PRECIPITATED CALCIUM CARBONATE; CALCII CARBONAS PRAECIPITATUS (CALC. CARB. PRAEC.), $CaCO_3$, U.S.P. (Precipitated Chalk).

A fine white, amorphous powder, prepared by chemical means. Depending on the process of manufacture, various grades of fineness, weight, and color are obtained. For the purpose of preparing tooth powders, pastes, etc., only the very finest bolted precipitated calcium carbonate is permissible.

DICALCIUM PHOSPHATE, secondary calcium phosphate; $CaHPO_4 2H_2O$.

Dicalcium phosphate contains approximately 97 per cent of the pure chemical.

Dicalcium phosphate is at present freely used in dentifrices of paste and powder form. Its use for this purpose is held to be advantageous because of the fineness of the particles and relative freedom from abrasiveness and scratching. It requires less glycerin when made into a paste than those containing calcium carbonate. It possesses excellent qualities as a polishing agent. It lends itself particularly to incorporation in soap-free dentifrices.

TRIBASIC CALCIUM PHOSPHATE; CALCII PHOSPHAS TRIBASICUS (CALC. PHOS. TRIBAS.), $Ca_3(PO_4)_2$, U.S.P.

Tricalcium phosphate contains approximately 90 per cent of the pure chemical. It is a mixture of tricalcium phosphate and basic dicalcium phosphate.

Tricalcium phosphate is at present largely used as a base in dentifrices, either as paste or as powder. Its use for this purpose offers certain advantages because of the fineness of the particles and the relative freedom from abrasiveness and scratching. Its glycerin absorptive capacity is relatively high. Typical tooth paste formulas made with tricalcium phosphate contain smaller amounts of the "polishing agent" than are present in dicalcium phosphate dentifrices. It may be employed with satisfaction in soap or soap-free dentifrices.

PUMICE; PUMEX, N.F.

A light, porous stone of volcanic origin, consisting chiefly of silica, with potassium and sodium. As may be expected from its composition, it is a powerful abrasive, and it should never enter into a tooth preparation intended for daily use. It forms the basis of most dentifrices used by the dentist for oral prophylaxis.

MAGNESIUM CARBONATE; MAGNESII CARBONAS (MAG. CARB.), U.S.P.

Two forms of magnesium carbonate are known—the light and the heavy. The light preparation is usually employed for tooth powder. It has no abrasive or polishing action on tooth structure. As it is a

voluminous powder, it is principally used to give bulk to tooth powders. Burnt magnesia, *Magnesium Oxide; Magnesii Oxidum (Mag. Oxid.),* U.S.P., is prepared from magnesium carbonate by calcination. It possesses no advantage over magnesium carbonate, and is used at present as a component of dentifrices because of its alkaline properties.

Cuttlefish bone, os sepia, is a calcareous substance found under the skin of the back of the cuttlefish, *Sepia officinalis.* It is composed of calcium carbonate, calcium phosphate, sodium chloride, gluten, and other substances which are readily recognized by their peculiar putrid odor. The external hard skin and the internal soft deposits of the cuttlefish bone are ground together, forming a powder, which is used as an abrasive.

ACTIVATED CHARCOAL; CARBO ACTIVATUS (CARBO ACTIVAT.), U.S.P.—Charcoal treated to increase its adsorptive power.

Charcoal is a very fine black powder prepared from soft wood (linden wood).* It is odorless and tasteless, and, when freshly prepared, readily absorbs offensive odors. Even the finest charcoal powder presents a mass of sharp crystalline cylinders under the microscope, which possess marked abrasive power. When used as a component in a tooth powder, the sharp particles imbed themselves in the gum tissue, producing a distinct bluish line near the margin. The gingiva becomes tattooed by the charcoal, and nothing can remove this pigmentation but a surgical operation. Charcoal should not be used as or in a tooth preparation.

Dentifrices

Soaps.—Soaps must be used very sparingly in oral cosmetics. A good tooth preparation should not contain more than 2 to 3 per cent of the best quality of castile soap. Many of the commercial preparations, especially tooth pastes and, naturally, tooth soaps, contain by far too large quantities of soap. Soaps are either potassium or sodium oleates; they are strong astringents and, in concentrated solutions, irritants. If used in concentrated form, they have a tendency to lower the resistance of the mucous linings of the oral cavity by irritation. Soaps are employed in tooth preparations for the purpose of emulsifying food debris, precipitated mucin, freshly deposited tartar, etc., adhering to the tooth surfaces. The churning of the abrasive, usually precipitated chalk, plus the foam produced by the soap, brush and water, mechanically removes these adhesions. When used in conjunction with warm water, soap acts as a mild antiseptic.

*Because of the possibility of permanent discoloration of the gingiva in occasional cases, the Council on Dental Therapeutics has discouraged the use of charcoal in dentifrices.

Powdered vegetable drugs—as the roots of calamus, rhatany, licorice, and orris, cinchona bark, sandal wood, myrrh, benzoin, etc.—have no place in tooth powders. As stated above, they are added to give flavor to the powder or to increase its bulk. The odor and taste of these vegetable substances are readily substituted by their respective essential oils or alcoholic extracts. The short time in which a tooth powder remains in the mouth is not long enough to allow the active constituents of these substances to enter into solution. Their abrasive action is of no value, but, as these vegetable powders may be forced between the teeth and remain there for some time, their starch constituent may give rise to acid fermentation.

Tooth powders are preferably dispensed in glass bottles or tin cans with suitable sprinkler tops.

Bodies for Colored Tooth Powders

RED

Carmine No. 40	20 parts
Ammonia Water	50 parts
Water	20 parts
Alcohol	30 parts
Calcium Carbonate, precipitated	1,000 parts

Dissolve the carmine in the ammonia water, add the water and alcohol, and mix thoroughly with the calcium carbonate. Spread on paper and dry at room temperature; rub through a No. 100 brass wire sieve.

PINK

Prepare same as red body, using only one-half of the carmine, 10 parts.

Philadelphia Dental Dispensary Tooth Powder*

Calcium Carbonate, precipitated	95 parts
Castile Soap	3 parts
Saccharin	⅛ part
Oil of Birch	1 part
Oil of Peppermint	½ part

Oxidizing Tooth Powder*

Calcium Carbonate, precipitated	75 parts
Magnesium Carbonate	10 parts
Sodium Perborate	10 parts
Castile Soap	3 parts
Oil of Peppermint	1 part

*N. B.—Parts as used in these prescriptions mean quantities by weight.

N.F. DENTIFRICE; DENTIFRICIUM, N.F. (DENTIF., N.F.), (N.F. TOOTH POWDER).

Hard Soap, in fine powder	50 Gm.
Precipitated Calcium Carbonate	935 Gm.
Soluble Saccharin	2 Gm.
Oil of Peppermint	4 cc.
Oil of Cinnamon	2 cc.
Methyl Salicylate	8 cc.
To make about	1,000 Gm.

A perfect tooth paste cannot be produced satisfactorily without the use of some "binding" agent. The most serviceable excipient is powdered tragacanth. Pastes which are massed with pure glycerin only are disappointing; the latter oozes from the tube, discoloring the label and forming an unsightly package. Glycerin is necessary, but it should not be employed alone. Syrup should never be used as a massing fluid, as it will easily ferment. The consistency of the excipient or massing fluid determines the character of the paste.

MASSING FLUIDS*

Powdered Gum Tragacanth	2 parts
Glycerin	50 parts
Water	50 parts

Dissolve the gum tragacanth in the water-glycerin mixture.

Another massing fluid is made by mixing:

Glycerin	2 parts
Mucilage of Acacia	2 parts

Tooth pastes may be prepared according to this general formula:*

Tooth powder body	10 parts
Massing fluid	7 to 10 parts

Tooth pastes are best dispensed in collapsible tubes of pure tin.

Mouthwashes

A mouthwash is usually prescribed as a rinse, to be used in conjunction with the toothbrush. The components of the wash should be so adjusted that one teaspoonful mixed with half a tumblerful of warm water (approximately 1 to 30) furnishes the correct proportions of its active ingredients intended for daily use. Powerful ex-

*N. B.—Parts as used in these prescriptions mean quantities by weight.

ercise of the muscles of the pharynx, the cheeks, and the lips is a material adjunct in forcing the fluid back and forth between the teeth. For rinsing the mouth one-half to one minute is the average time required for each mouthful, corresponding approximately to 15 or 30 cc.

Antiseptics

(W. D. MILLER)

DRUGS	DILUTION IN WHICH THEY CAN BE EMPLOYED IN THE MOUTH	TIME IN WHICH THE MOUTH BECOMES STERILIZED
Acid, Benzoic	1: 100	¼ minute
Acid, Boric	1: 50	above 11 minutes
Acid, Salicylic	1: 300	¾ to 1 minute
Eugenol	1: 750	above 10 minutes
Iodine Trichloride	1:2,000	above 1½ minutes
Lysol	1: 200	above 5 minutes
Mercuric Chloride, corrosive	1:2,500	½ to ¾ minute
Oil of Cinnamon	1: 400	above 8 minutes
Oil of Clove	1: 550	above 11 minutes
Oil of Eucalyptus	1: 625	above 8 minutes
Oil of Peppermint	1: 600	above 11 minutes
Oil of Wintergreen	1: 350	above 12 minutes
Phenol	1: 100	above 5 minutes
Potassium Permanganate	1:4,000	above 15 minutes
Solution Aluminum Acetate	1: 20	above 5 minutes
Solution Hydrogen Dioxide	2: 100	above 6 minutes
Thymol	1:2,000	above 5½ minutes

Astringents

Zinc Chloride	0.05 to 0.1 per cent
Tannic Acid	0.10 to 0.5 per cent
Benzoin	5.0 per cent

Spraying the oral cavity with a fluid antiseptic is readily accomplished by using an atomizer. This method of applying an antiseptic is especially of service before and after the removal of tartar and other operations about the mouth.

The proprietary mouthwashes which are now being marketed and advertised have no therapeutic value. Their use in oral medicine is only as a placebo, or at most as a detergent and deodorant.

Mouthwashes containing drugs are contraindicated for daily use and should not be used unless prescribed by the dentist. Patients should be so informed, and instructed to see an oral specialist whenever any changes from the normal are noticed in the mouth.

There is no drug or combination of drugs which will prevent or cure dental caries, periclasia pockets, alveoclasia, calculus, loosening of the teeth, toxic gingivitis, etc.

Mouthwashes for daily use:

1. Warm water.
2. Sodium Chloride, level teaspoonful in a glassful of water after meals.
3. Sodium Bicarbonate, as above.
4. Milk of Magnesia, as above.
5. Limewater, undiluted.

Antiseptic mouthwashes:

1. Boric acid (2%), undiluted.
2. Sodium Borate (2%), undiluted.
3. Phenol (0.2%), undiluted.
4. Resorcinol (2%), undiluted.
5. Sodium Perborate (2%), undiluted.
6. Solution of Hydrogen Peroxide, diluted with two parts of water.
7. Chloramine-T (2%), undiluted.
8. Solution of Sodium Hypochlorite (0.1%), undiluted.
9. Dobell's Solution, diluted with equal parts of warm water.
10. Boulton's solution, as above.
11. Alkaline Aromatic Solution, as above.

Prescription for a mouthwash *(Example):*

℞ Liquefied Phenol 1 cc.
Soluble Saccharin 60 mg.
Peppermint Water q.s. ad 250 cc.
M. et sol.
Sig.: Dilute with equal parts of warm water as a mouthwash after meals.

REFERENCE

Kronfeld, Rudolf: Histopathology of the Teeth and Their Surrounding Structures, ed. 2, Philadelphia, 1939, Lea and Febiger.

CHAPTER XXVIII

MISCELLANEOUS DENTAL PREPARATIONS

Dental Protectives

These preparations are employed in dental practice for the purpose of covering sensitive, wounded, or diseased body surfaces against further external insults. In operative dentistry they are used to protect the dental pulp, as in a direct exposure or in a deep-seated cavity preparation. They are also employed for covering newly placed synthetic porcelain fillings until they have set.

Rubber

Rubber; Elastica; Caoutchouc; India Rubber.

It is the prepared milk juice of several species of the family *Euphorbiaceæ,* and is commercially known as Pará rubber. Rubber forms the base of many important preparations. When mixed with sulfur and subjected to a high heat under pressure, it is known as vulcanized rubber or vulcanite. Vulcanite is largely used in the arts, in medicine, and in dentistry in the form of bandages, gloves, drainage tubes, catheters, bags, artificial dentures, etc. It is an important adjunct to surgical practice, while dentistry employs vulcanite chiefly as a cheap and reliable base for artificial dentures and in the form of rubber dam as a means of excluding moisture from the teeth during operations. Pará rubber is also largely used for the preparation of adhesive and other plasters.

Gutta-Percha

Gutta-Percha; Gutta-Percha.

It is the concrete milk juice of *Palaquium* and *Payena* trees. The purified gutta-percha is a white, odorless, and tasteless inert mass, which readily softens by the application of heat and rehardens on cooling. It is soluble in chloroform, xylol, liquid petrolatum, and those essential oils which contain cineol, i.e., eucalyptus oil, myrtle oil, cajuput oil, etc. It forms the base of many important preparations—tooth filling materials, surgical splints, and other appliances of a similar nature. A 10 per cent solution of purified gutta-percha in chloroform is known as *chloropercha,* and is used as a substitute for

collodion; it forms an excellent protective seal over small wounds in the mouth. In the form of chloropercha it is used as a root canal filling.

Chloropercha

Gutta-percha, base plate	8 Gm.	ʒ ij
Chloroform, a sufficient quantity to make a paste.		

Collodion

Collodion; Collodium (Collod.), U.S.P.

It is a solution of pyroxylin (4%) (colloxylin, guncotton) in a mixture of ether and alcohol. Collodion should be kept in a well-corked bottle, protected from light and fire.

Flexible Collodion; Collodium Flexile (Collod. Flex.), U.S.P.—A mixture of collodion (95%) with camphor (2%) and castor oil (3%).

Uses.—More pliable than collodion and does not contract as much in drying.

Benzoin

Tincture of Benzoin; Tinctura Benzoini (Tr. Benz.), U.S.P.

Benzoin (20%) in alcohol. Absolute alcohol content about 79 per cent.

Compound Tincture of Benzoin; Tinctura Benzoini Composita (Tr. Benz. Co.), U.S.P.—Benzoin (10%), aloe (2%), storax (8%), Tolu balsam (4%), in alcohol. Absolute alcohol content about 77 per cent.

Uses.—Protective and local stimulant, especially by steam inhalation in respiratory congestion.

Dentist's Hand Cream

Tincture of Benzoin	2 cc.	ʒ ss
Borax	4 Gm.	ʒ i
Lanolin	15 Gm.	ʒ ss
Glycerin	30 cc.	ʒ i
Petrolatum	45 Gm.	ʒ iss

Glycerin

Glycerin; Glycerinum (Glycerin.), $C_3H_5(OH)_3$, U.S.P. (Glycerol).

A liquid obtained by the decomposition of vegetable and animal fats, or fixed oils, and containing not less than 95 per cent of absolute glycerin, a triatomic alcohol. It is a clear, colorless liquid, of a thick, syrupy consistency, oily to the touch, with a sweet taste and no odor. It is soluble in all proportions in water and alcohol. It is principally employed as a solvent for other drugs, the preparations being known as glycerites (U.S.P.) and glycerins (B.P.).

Paraffin

Paraffin; Paraffinum (Paraff.), N.F.

A mixture of solid hydrocarbons, without odor and taste. It is soluble in ether, volatile oils, etc., but insoluble in water and alcohol. It melts at 125° to 135° F. (50° to 57° C.).

Uses.—As a base for ointments.

Petrolatum

Petrolatum; Petrolatum (Petrolat.), U.S.P. (Petroleum Jelly).—A purified semisolid mixture of hydrocarbons from petroleum.

Uses.—Protective, demulcent, emollient, and vehicle.

White Petrolatum; Petrolatum Album (Petrolat. Alb.), U.S.P. (White Petroleum Jelly).

Petrolatum decolorized or nearly so.

Uses.—Same as those of petrolatum.

White Ointment; Unguentum Album (Ung. Alb.), U.S.P. (Simple Ointment).—White petrolatum 90 per cent, wool fat 5 per cent, white wax 5 per cent.

These soft petrolates are yellow or white in color, tasteless, and readily liquefy a few degrees above body temperature. They are principally used as ointment bases.

Liquid Petrolatum; Petrolatum Liquidum (Petrolat. Liq.), U.S.P. (Liquid Paraffin, White Mineral Oil).

Gums

Acacia

Acacia; Acacia (Acac.), U.S.P. (Gum Arabic).

Gum arabic is a gummy exudate obtained from *Acacia Senegal* and other species of *Acacia,* and consists of the potassium, magnesium, and calcium salts of a weakly acid substance known as arabin, or arabimic acid. It appears in whitish, translucent, roundish tears; it is insoluble in alcohol, but slowly soluble in equal parts of water, and is used largely as a vehicle for other drugs.

Mucilage of Acacia; Mucilago Acaciae (Mucil. Acac.), U.S.P. (Mucilage of Gum Arabic).—Acacia (35%) with benzoic acid (0.2%) in distilled water. *Caution.*—Mucilage of Acacia must not be dispensed if it has become sour or moldy. (U.S.P.)

Syrup of Acacia; Syrupus Acaciae (Syr. Acac.), N.F.—Acacia (10%) with sodium benzoate, tincture of vanilla, sucrose, and distilled water.

USES.—Demulcent; mainly as a vehicle.

TRAGACANTH

TRAGACANTH; TRAGACANTHA (TRAG.), U.S.P. (Gum Tragacanth).

A gummy exudation from the *Astragalus gummifer* and various species of *Astragalus.* It appears in ribbon-shaped bands or in irregular pieces of a whitish color, somewhat translucent. Tragacanth, when treated with 50 parts of water, swells and gradually forms a cloudy, gelatinous jelly. It is chiefly used as a binding agent in pills, troches, etc. Powdered tragacanth is usually the principal component of the many powders which are advocated for the purpose of retaining artificial dentures.

Glycerite of Tragacanth; Glyceritum Tragacanthae (Glycer. Trag.), N.F.—Tragacanth (12.5%) in glycerin and distilled water.

Mucilage of Tragacanth; Mucilago Tragacanthae (Mucil. Trag.), U.S.P.—Tragacanth (6%), glycerin (18%), benzoic acid (0.2%), and distilled water.

KARAYA

KARAYA; KADAYA GUM.

It is a gum obtained from the *Cochlospermum religiosum,* family *Bixaceae,* grown in India and adjacent countries. Karaya occurs as round or vermiform tears with a rough surface and glassy fracture (Youngken).

USES.—It is used in dentistry in denture adhesive preparations.

GUM GHATTI

GUMMI INDICUM; GHATTI GUM (INDIAN GUM).

It is an exudate obtained from the stems of the *Anogeissus latifolia,* family *Combretaceae,* a tree grown in India and Ceylon (Youngken). It occurs in round or vermiform, transparent tears of many colors.

Plaster

EXSICCATED CALCIUM SULFATE; CALCII SULFAS EXSICCATUS; PLASTER OF PARIS.

A fine white powder, without odor and taste. When mixed with half its own weight of water, it forms a smooth, cohesive paste, which rapidly hardens. It should be kept in well-closed vessels and carefully

protected from moisture. A pinch of potassium sulfate, sodium chloride, or alum dissolved in the water before the plaster of Paris is added hastens the setting, and, to some extent, prevents expansion. The setting of plaster of Paris is much retarded by adding 2 to 4 per cent of powdered marshmallow root. A cold, saturated solution of sodium hyposulfite or concentrated sugar solutions will disintegrate "set" plaster of Paris.

Rosins

ROSIN; RESINA, U.S.P. (Colophony).

The crystalline residue left after the distillation of the volatile oil from turpentine.

USE.—Used in dentistry as a varnish.

CARBOLIZED ROSIN

Phenol	8 Gm.	ʒ ij
Rosin	8 Gm.	ʒ ij
Chloroform	6 cc.	fl3 jss

CAVITY VARNISH, A.D.R.

Rosin	2.0 Gm.
Sodium Carbonate Monohydrate	0.5 Gm.
Acetone	30.0 Gm.

Mix; do not filter.

SHELLAC

Shellac is made from decolorized lac, strained when liquid and stretched into thin sheets. Most of the lac is produced in India. The unbleached shellac is orange colored, while the bleached is a light tan.

USES.—In dentistry it is dissolved in a volatile solvent and used as a varnish.

SHELLAC VARNISH

Shellac	8 Gm.	ʒ ij
Alcohol	24 cc.	fl3 vi

STERESOL (ANTISEPTIC WOUND VARNISH)

Shellac	270 Gm.	℥ ix
Gum Benzoin	10 Gm.	ʒ ijss
Balsam of Tolu	10 Gm.	ʒ ijss
Phenol	100 Gm.	℥ iij ℈
Oil of Cinnamon	6 cc.	ʒ iss
Saccharin	6 Gm.	ʒ iss
Alcohol, enough to make	1,000 cc.	fl℥ xxxij

Mastic

MASTIC; MASTICHE (MASTIC.), N.F. (Mastich).

A concrete resinous exudate obtained from the mastic tree, *Pistacia Lentiscus*, family *Anacardiaceae*, grown in the Mediterranean Basin and islands.

It occurs as varied shaped tears, which are very soluble in ether, alcohol, and chloroform.

USES.—In dentistry it is used as a varnish.

Simplified Wound Varnish (Masticol)

Gum Mastic	20 Gm.	3 v
Acetone	50 cc.	3 xijss
Linseed Oil	1.3 cc.	♏. xx

Cavity Varnish, A.D.R.

Mastic	9 Gm.
Balsam Peru	9 cc.
Chloroform, to make	30 cc.

Dissolve the mastic and Peru Balsam in about 15 cc. chloroform and add sufficient chloroform to make 30 cc. or one ounce.

Sandarac

Sandarac is a resin obtained from various species of the *Pistacia*.

USE.—In operative dentistry it is used as a varnish.

Sandarac Varnish

Sandarac	4 Gm.	3 j
Rosin, light colored	4 Gm.	3 j
Alcohol	16 cc.	fl3 iv

Cavity Varnishes

1. Pulp Capping Varnish, N.F.V.	
Mastic	**9.00 Gm.**
Balsam Peru	**9.00 cc.**
Chloroform, to make	**30.00 cc.**
2. Resin	**2.00 Gm.**
Chloroform, to make	**30.00 cc.**
Mix and filter.	
3. Resin	**4.00 Gm.**
Thymol	**0.50 Gm.**
Menthol	**0.13 Gm.**
Chloroform, to make	**30.00 cc.**
4. Flexible Collodion	**30.00 cc.**
5. Tincture of Benzoin	**30.00 cc.**

Pulp-Capping Preparations

1. Gold foil, covered with dental cement.

2. Zinc Oxide and Eugenol, paste.

3. Tincture of Benzoin, apply.

4. Resin 4.0 Gm.
   Chloroform, to make 30.0 cc.
   Apply.

5. Zinc Oxide 20.0 Gm.
   Thymol 10.0 Gm.
   Mix and fuse with heat.
   Sig.: Melt and apply.[1]

6. Guaiacol 24.0 cc.
   Glycerin 24.0 cc.
   Balsam of Peru 45.0 Gm.
   Yellow Wax 8.0 Gm.
   (Paste)

7. Ethyl Aminobenzoate 6.0 Gm.
   Thymol Iodide 2.0 Gm.
   Lanolin q.s. ad 60.0 Gm.

8. Resorcinol 1.0 Gm.
   Chlorobutanol 3.0 Gm.
   Ethyl Aminobenzoate 6.0 Gm.
   Oil of Cinnamon 0.5 cc.
   Liquid Petrolatum 30.0 cc.
   White Petrolatum q.s. ad 60.0 Gm.
   M. et ft. ung.
   (Thin paste)

9. Resorcinol 1.0 Gm.
   Chlorobutanol 3.0 Gm.
   Ethyl Aminobenzoate 6.0 Gm.
   Oil of Cinnamon 0.5 Gm.
   Yellow Wax 3.0 Gm.
   White Petrolatum q.s. ad 60.0 Gm.
   (Thick paste)

Adherent Powders for Dentures

These preparations contain powdered gums such as karaya,[2] acacia, or tragacanth, pleasantly colored and flavored. When the powder is moistened, it absorbs water, forming a gel which increases the retention of the plate temporarily. Adherent powders are useful during the first weeks of denture-wearing before the patient has developed

[1] Alguier, J. E.: Dent. Cos. 70: 329, March, 1928.
[2] Figley, K. D.: J. A. M. A. 114: 747, March 2, 1940.

the habit of retaining the denture naturally. They are also helpful in "immediate denture work" to ease the pressure of the plate on the abraded tissue and to tide the patient over until a better fitting denture can be constructed. They should not be prescribed for retaining ill-fitting dentures.

Medicated adherent powders should not be prescribed because the medication may produce a local irritation or be absorbed, producing a systemic toxic reaction. Alkaline preparations containing sodium borate are now on the market. The continued use of these boron preparations must be discouraged, as a toxicity may result. (See *Accepted Dental Remedies.*)

The following preparation may be used:

℞	Tragacanth, finely powdered	22.0 Gm.
	Karaya Gum, finely powdered	7.5 Gm.
	Oil of Cinnamon	0.5 cc.

M.

Sig.: Sprinkle evenly on roof of denture and moisten with water.

Denture Cleaners

Denture cleaners are absolutely necessary for the hygienic care of dental appliances. Unclean dentures and removable bridges may produce halitosis, mouth irritation, anorexia, and possibly gastric and intestinal disturbances.

A good denture brush designed for cleaning the appliance is essential. Soap with or without an abrasive may be used with the brush. Use warm but never hot water on a denture, as heat may warp the material. Dentures may be soaked in detergent preparations, such as peroxide, sodium perborate, hypochlorite solutions, etc.

There are so many denture materials now in use that the correct cleaning agent should be prescribed by the dentist so as to avoid injury to the denture materials.

Denture cleansing agents, to be used with a brush and warm water.

Toilet soap.

Dentifrices.

Sodium Chloride (table salt).

Sodium Bicarbonate (baking soda).

Sodium Borate (borax).

Calcium Carbonate.

Calcium Phosphate.

The salts may be colored and flavored to please the patient.

Example:

℞	Calcium Carbonate	120.0 Gm.
	Oil of Cinnamon	0.4 cc.
	Solution of Amaranth	2.0 cc.
	Mix.	

The denture may be kept in the following solutions when not in the mouth:

Water.
Aromatic waters.
Sodium Chloride Solution, tip of a spoonful to a glassful of water.
Sodium Bicarbonate, as above.
Sodium Perborate, as above.
Solution of Hydrogen Peroxide, teaspoonful to a glassful of water.
Diluted Solution of Sodium Hypochlorite, as above.

Topical Anesthetics

Topical anesthesia[1] has not been as successful in dentistry as in the medical specialties, such as nose and throat surgery. The oral mucous membranes, with their layers of stratified squamous epithelium and covering of thick viscid saliva, are evidently not designed for easy penetration by drugs.[2] As practically all of the synthetic local anesthetic drugs are vasodilators, they have a tendency to be diluted in the tissues and to be removed by the blood and lymph before profound anesthesia develops. When aqueous solutions are used, the mucous membranes should be wiped dry before application of the drug. Because of these retarding influences, the drug must be applied in a concentrated solution, from 10 to 20 per cent. As time is necessary for an injected anesthetic to produce anesthesia, time is likewise necessary for a surface anesthetic to take effect. The time necessary with the following procedure is from four to five minutes: The area is dried with a gauze sponge, and a cotton pellet saturated with the anesthetic solution is applied to the tissues and held firmly in place from four to five minutes. The pH of the anesthetic solution is important in many instances.[3] This is particularly true of procaine hydrochloride, which, when made alkaline with sodium bicarbonate, gives profound surface anesthesia in a 20 per cent solution. The optimum pH for procaine hydrochloride is about 8. The concentration of anesthetic drug is important from a toxicologic standpoint, as administration of many of the anesthetic drugs can cause

[1]Dobbs, E. C.: Topical Medication, J. A. D. A. 31: 832, June 1, 1944.
[2]Tainter, M. L., and Moose, S. M.: J. A. D. A. 23: 309, February, 1936.
[3]Gwinn, C. D., and Ferber, E. W.: J. A. D. A. 24: 1298, July, 1936.

poisoning if they are not used cautiously. This is true for butyn, cocaine and tutocaine. Therefore, for the sake of safety, procaine in a 20 per cent solution and when used as an alkaline solution is probably the drug of choice for topical anesthesia, although butyn (10 per cent) is more extensively used.[1]

The concentration of alcohol in an anesthestic solution should not be greater than 10 per cent if it is to be applied as previously directed. Dentistry is in need of a safe and efficient topical anesthetic. To date, I know of no drug or preparation that meets all the requirements. Perhaps in the future a new drug or a new solvent for an old drug will afford a preparation that will serve the many useful purposes to which a topical anesthetic for the oral mucous membranes can be put.

The following formula has been used, but it may be irritating to the oral mucous membranes because of its alcohol content:

Benzocaine		10 Gm.
Alcohol		70 cc.
Water	q.s. ad	100 cc.

Topical anesthetics for the dentin, while desirable, are not very efficient. While dentin conducts pain impulses to the dental pulp and thus to the centers of consciousness, the exact mode of excitation and transmission has not been determined. The local anesthetic drugs are not very satisfactory dentin anesthetics. They have been applied topically, ionically and with pressure, with none too gratifying results. The caustic preparations, such as silver nitrate, are apparently best. Hartman's solution is the best preparation for topical use that I have studied. It is efficient in less than 40 per cent of the cases, working best in children's teeth and in Class V cavities. The preparation must be fresh, correctly made, and applied according to directions. While Hartman's solution is not the ideal topical anesthetic agent for the dentin, it is an adjunct for "painless dentistry" and may be employed in selected cases until a better preparation is suggested. (See sodium fluoride.)

Topical anesthesia of the pulp is sometimes resorted to. Application of a procaine hydrochloride pellet (hypodermic) plus a drop of water to the exposed pulp and pressure to force the anesthetic solution into the pulp tissue is a procedure that gives good results. This method for pulp anesthesia cannot take the place of injection anesthesia, which is by far the superior method.

[1] Tainter, M. L., Throndson, A. H., and Moose, S. M.: J. A. D. A. 24: 1480, September, 1937.

Root Canal Therapy

The status of root canal therapy is still disputable. Many practitioners of dentistry treat only the anterior single-rooted teeth, considering that the esthetic advantages will offset the possibility of a systemic infection or a general toxemia. The age and general health of the patient are factors which should also be considered.

An outline of a simple root canal technique is as follows:

1. Anesthesia of the tooth is obtained by injections of Procaine Hydrochloride.
2. The tooth is isolated by a rubber dam, preferably.
3. The tooth and immediate area are sterilized with Mild Tincture of Iodine.
4. Access to the dental pulp is attained by instrumentation.
5. The dental pulp is extirpated with burs and broaches.
6. The root canal is straightened and opened with files.
7. Sterility is maintained or produced with drugs.
8. The root canal and pulp chamber are filled.
9. The tooth is restored to its normal color, shape, and function.

Root Canal Antiseptics

Oil of Clove, undiluted.
Eugenol, undiluted.
Aromatic Solution of Phenol (A.D.R.), undiluted.
Alcohol (70%), undiluted.
Liquefied Phenol, undiluted.
Creosote, undiluted.
Cresol, undiluted.
Solution of Hydrogen Peroxide, undiluted.
Solution of Sodium Hypochlorite, undiluted.
Iodoform, paste.
Thymol Iodide, paste.
Chloramine-T, paste or solution.
Solution of Formaldehyde, diluted or undiluted.
Camphorated Phenol (N.F.), undiluted.

Root Canal Styptics

1. Solution of Epinephrine Hydrochloride, undiluted.
2. Alcohol, undiluted.
3. Zinc Chloride (10%), undiluted.
4. Alum (10%), undiluted.

Root Canal Filling Materials

1. Gutta-percha points.
2. Chloropercha, 10 per cent gutta-percha in chloroform.
3. Eucopercha, 10 per cent gutta percha in eucalyptol.
4. Silver amalgam.
5. Dental cements.
6. Silver points.

Sealing Dentinal Tubuli

℞[1] Rosin	2.0 Gm.
Sodium Bicarbonate	0.5 Gm.
Acetone	30.0 cc.

M.
Sig.: Apply.

Dentin Desensitizers

These drugs obtund sensitive dentin by destroying the odontoblastic fibrils thereby preventing sensory impulses from originating or from reaching the dental pulp tissue. Care must be exercised to prevent these caustic drugs from injuring the adjacent soft tissue.

Before treatment is started, a diagnosis of the condition should be made. Hypersensitive dentin must not be confused with pulpitis; at times both will be present, complicating the diagnosis.

Good results may be obtained by following these directions. The teeth should be isolated with a rubber dam or cottom rolls. The area to be treated is cleaned and polished with a motor-driven brush and pumice. A cotton pellet saturated with alcohol, ether, or chloroform is used to clean and dry the surface. The drug is applied and rubbed into the area with a wooden burnisher. More than one application may be made when necessary. Before the rubber dam or cotton rolls are removed, the area is painted with a varnish.

Preparations.—

Solution of Formaldehyde.—The solution (10% to 40%) is applied as directed above. It is satisfactory for anterior teeth where silver nitrate would produce a stain. It is a penetrating caustic and must not be used too close to the dental pulp, as it may cause injury or death. The local antidote for formaldehyde burns is solution of ammonium acetate, applied.

Silver Nitrate.—It is used as a 10 to 35 per cent solution as directed above. Lasting effects are produced only when the metal is reduced. This may be accomplished by precipitating the solution in

[1] Alguier, J. E.: Dent. Cos. 70: 329, March, 1928.

the tooth tissue by applications of eugenol, formaldehyde solutions, light, etc. Silver nitrate and its preparations are contraindicated for treating anterior teeth because of the black discolorations (See dental caries).

AMMONIACAL SOLUTION OF SILVER NITRATE (N.F.).—The silver nitrate exists as an ammonium complex ($Ag[NH_4]_2NO_3$) and is more readily reduced than other silver preparations.

ZINC CHLORIDE in a 10 per cent solution is used for anterior teeth. It is an efficient and nonstaining desensitizer.

SODIUM FLUORIDE.—Bibby suggested the use of a fluoride paste (sodium fluoride [33%], clay [33%], and glycerin [33%]) as a dentin abtundent for areas of abrasion and for the control of pain in cavity preparation. He suggests the application of a saturated aqueous solution of sodium fluoride, first, followed by the paste. The preparation is rubbed into the dentin until the sensitiveness disappears. While this method is still in an experimental stage, the early reports are quite hopeful.

SODIUM POTASSIUM CARBONATE.[1]—The preparation is made as follows:

Triturate in a mortar 1 part of potassium carbonate with 4 parts of sodium carbonate until a paste is formed; the water is absorbed from the air. To the paste add a few drops of glycerin and store in a stoppered bottle. To give the best results it must be well burnished into the dentin.

CREOSOTE.—Dr. C. Edmund Kells suggests the sealing in of creosote into sensitive cavities until the next appointment when operative procedures may be carried out with less pain.

LIQUEFIED PHENOL.—Use is similar to that of creosote.

BENZYL ALCOHOL.—Use is similar to that of creosote.

EUGENOL.—Use is similar to that of creosote. A 10 per cent solution of chlorobutanol in eugenol may also be used.

Obtundents for Painful Alveoli Following Tooth Extractions

The extreme pain following the extraction of teeth is caused by a number of conditions. A diagnosis should be made before treatment is planned. The so-called "dry socket" is of an infectious nature. The predisposing factors may be trauma, necrosis following the use of a vasoconstrictor drug, or introduced or auto-infection. The operator should keep in mind that he is dealing with an osteitis or an osteomyelitis and give the patient careful supervision and treatment.

[1]Council Report, Treatment of Hypersensitive Dentin, J. A. D. A. 21: 2050, 1934.

Pain may be controlled by the oral administration of analgesic drugs, fortified by local applications of obtundent drugs. The preparation is applied directly to the tissue or on a gauze sponge which is inserted loosely into the alveolus and changed every twenty-four hours.

PREPARATION.—

1. *Compound Paste of Acetylsalicylic Acid; Pasta Acidi Acetylsalicylici Composita* (Past. Acid. Acetylsal. Comp.), N.F. (Dental Anodyn Paste).

It contains eugenol (2%), balsam of Peru, acetylsalicylic acid (25%), white wax and wool fat.

2. Chlorobutanol		5 Gm.
Eugenol	q.s. ad	30 cc.
M. et ft. sol.		
3. Chlorobutanol		5 Gm.
Olive Oil		30 cc.
4. Guaiacol		15 cc.
Oil of Clove		15 cc.
5. Guaiacol		24 cc.
Glycerin		24 cc.
Balsam of Peru		45 Gm.
Yellow Wax		4 Gm.
(Liquid)		

Traumatic Ulcers

Traumatic ulcers, as the name suggests, are due to an injury of the mucous membranes which permits an infection to occur. These ulcers generally occur singly, are very painful, heal spontaneously in four to twelve days, and may produce a local adenitis. They are covered with a grayish-white membrane with a margin of reddened tissue.

TREATMENT.—*Dental office:*

1. Apply concentrated Hydrochloric Acid[1] to the ulcer for 20 to 30 seconds, followed immediately with a saturated solution of Sodium Bicarbonate.
2. Chromic Acid (3%), apply.
3. Ammoniacal Silver Nitrate, apply.
4. Silver Nitrate (10%), apply.
5. Zinc Chloride (8%), apply.[2]
6. Spirit of Camphor, apply.

[1]Dobbs, E. C.; J. A. D. A. 23: 260, February, 1936.
[2]Alguter, J. H.; Dent. Cos. 70: 329, March, 1928.

Home:

1. Dobell's Solution. Use diluted with equal parts of warm water as a mouthwash.
2. Copper Sulfate (2%), apply morning and night.

Herpes Labialis

The etiology of "cold sores" is not known. They may be of an infectious or neurotropic origin. These lesions are generally associated with respiratory infections, and there is a possibility that the cause of both is the same. Because of the mobility of the lips, the ulcer often becomes fissured and heals slowly, or at times the ulcer may become chronic.

TREATMENT.—*Acute herpes labialis:*

1. Spirit of Camphor, apply morning and night.
2. Tincture of Benzoin, apply.
3. Copper Sulfate (5%), apply.
4. Zinc Chloride (5%), apply.
5. Chromium Trioxide (3%), apply.
6. Boric Acid Ointment, apply.
7. Phenol Ointment, apply.

Chronic herpes labialis:

The ulcer should be cleaned with alcohol (70%) and immobilized with flexible collodion, adhesive tape, or sutures. Chronic herpes may be precancerous.

Vincent's Stomatitis

Vincent's stomatitis is an acute or chronic infectious disease associated with Vincent's spirilli and fusiform bacilli. These two organisms are found in symbiosis; pleomorphism is suggested but not confirmed. These organisms are generally not highly virulent but are opportunists and become infectious whenever the local resistance of the tissues is lowered. Any individual from childhood to senescence is susceptible. It is seldom seen in edentulous mouths.

The oral lesion may occur as a localized lesion or as a generalized stomatitis. The symptoms are those of inflammation followed by a grayish-white membrane. The sloughing may continue until large areas of tissue are destroyed, often resulting in the exfoliation of the teeth in severe cases.

The disease may be localized or diffuse with extension of the infection into the respiratory tract, resulting in pneumonia. As lowered resistance is a factor, the disease is often complicated with avitamino-

sis, drug poisoning, allergic reactions, anemia, leucemia, tuberculosis, diabetes, malignancy, etc. A careful medical study in all cases is therefore necessary.

Vincent's stomatitis resembles other oral infections and diseases, such as oral tuberculosis, syphilis, chicken pox (varicella), erythema multiforme, pregnancy, gingivitis, calculus irritation, canker sores, etc. A diagnosis is made by exclusion and by a smear which is positive only when the field is dominated by the spirilli and fusiform organisms. A characteristic foul odor is also indicative of this infection.

The treatment of this form of stomatitis is chiefly local.[1] The acute symptoms are first reduced with drugs, and then the oral hygiene is cared for, first by the dentist and then by the patient. In severe cases a liquid diet should be prescribed, laxatives should be prescribed if needed, ample intake of fluids is required, and rest and freedom from pain must be insured, using drugs if necessary. If complications are suspected, the consultation of a physician is desirable. The disease is infectious, and others should be protected from direct contact with the patient and infected materials.

LOCAL THERAPY *(Dental office):*

Chromium Trioxide solution (3%), apply.
Mild Tincture of Iodine, apply.
Potassium Permanganate solution (0.5%), apply.
Silver Nitrate solution (1%), apply.
Solution of Merbromin, apply.
Solution of Potassium Arsenite, apply.
Solution of Hydrogen Peroxide, dilute with equal parts of warm water, apply or spray.
Mercury Bichloride solution (0.1%), apply.
Diluted Solution of Sodium Hypochlorite, apply.
Arsphenamine solution (5%), apply.
Sodium Perborate solution (2%), apply.
Copper Sulfate solution (5%), apply.

SYSTEMIC TREATMENT.—The systemic use of arsenic, mercury, or bismuth is not indicated in the treatment of Vincent's stomatitis, unless metastasis occurs or is suspected. (See Spirocheticides.) Hospitalization is advisable for all patients who are seriously ill.

HOME TREATMENT.—

Solution of Hydrogen Peroxide, dilute with equal parts of warm water as a mouthwash.

[1]Brooks, F. R., and Wilson, W. A.: J. A. D. A. 31: 640, May 1, 1944.

Sodium Perborate, one level teaspoonful in a half glassful of warm water as a mouthwash.

Dobell's Solution, diluted with equal parts of warm water as a mouthwash.

Boulton's Solution, as above.

Medicated Mouthwashes

These preparations will temporarily reduce the number of bacteria in the oral cavity. They are of questionable value when the oral flora is normal for that individual, but when pathogenic organisms are present their use is often indicated. After a diagnosis of the causative organism has been made, a specific drug is selected and an outline of treatment formulated.

Mouthwashes are for home treatment and are intended as an adjunct to office treatment.

PREPARATIONS.—*Antiseptic:*

1. Resorcinol (2%).
2. Phenol (0.2%).
3. Boulton's Solution, dilute with equal parts of warm water.

Acid:

1. Boric acid (2%).
2. Benzoic acid (0.1%).
3. Solution of Hydrogen Peroxide, dilute with 2 to 3 parts of warm water.
4. Tannic acid (0.1%).

Alkaline:

1. Sodium Bicarbonate (2%).
2. Sodium Borate (2%).
3. Sodium Perborate (2%).
4. Aromatic Sodium Perborate (2%).
5. Dobell's Solution, dilute with equal parts of warm water.
6. Alkaline Aromatic Solution, N.F., used the same as Dobell's solution.

Antiseptic and Astringent:

1. **Zinc Sulfate** 5.0 Gm.
   Boric Acid 10.0 Gm.
   Peppermint Water q.s. ad 250.0 cc.
   M.
   Sig.: Use diluted with equal parts of warm water as a mouthwash.

2. Zinc Chloride 0.5 Gm.
Benzoic Acid 0.5 Gm.
Cinnamon Water q.s. ad 250.0 cc.
M.
Sig.: Use diluted with equal parts of warm water as a mouthwash.

3. Tannic Acid 0.5 Gm.
Spearmint Water q.s. ad 250.0 cc.
M.
Sig.: Use diluted with equal parts of warm water as a mouthwash.

Detergent Mouthwashes:

1. Boric Acid, crystals 90.0 Gm.
Sodium Perborate 90.0 Gm.
M.
Sig.: Level teaspoonful in half glassful of warm water as a mouthwash.

2. Sodium Borate 8.0 Gm.
Solution of Hydrogen Peroxide q.s. ad 250.0 cc.
M.
Sig.: Dilute with equal parts of warm water as a mouthwash. Coloring and sweeting agents may be added.

Bleaching Agents

Dental bleaching agents are chemicals used for the purpose of removing pigmentations from tooth structure. By bleaching we understand the changing of a pigment compound into a colorless material, which is produced by a chemical reaction between the bleaching agent and the color compound.

Discoloration of a tooth is usually the result of the death of its pulp, although metallic stains and pigmentations from medicines or other materials used in the tooth may also be causative factors. Superficial stains of the enamel or dentin, which are removed by simple mechanical means, are not classed as discolorations.

Causes of Discoloration

Substances which cause discoloration of a tooth may be classified as endogenous pigments, viz., color compounds formed within the tooth and exogenous pigments, viz., staining substances acquired from outside the tooth. In the majority of cases, endogenous pigments are the causes of permanent tooth discoloration, and these compounds are obtained primarily from the blood. Temporary discoloration from endogenous blood pigments is occasionally observed as a sequence of general disease. These stains occur only in teeth

having living pulps, and they usually disappear with the termination of the underlying disease.

A peculiar permanent brownish discoloration of the teeth is caused by fluorine when present in abnormal quantities in drinking water. This condition is known as "mottled enamel." It is usually characterized by dull paper-white patches scattered irregularly over the surfaces of the teeth. In some cases the entire surface of the crown has this unglazed appearance. The enamel may be badly pitted, and the tooth may or may not become stained at a later time. The teeth erupt in the mottled condition, and the brown stain does not make its appearance until a considerable time afterward, and then it accumulates gradually. Any water supply that contains fluorine to the extent of 1 part per 1,000,000 must be considered potentially disfiguring. Fluorine dystrophies are permanent; they cannot be removed by bleaching, but the staining material may be removed in some instances.[1] If the patient requests treatment of the mottled enamel, the latter should be cut out and replaced by a filling or a jacket crown.

Exogenous pigmentations usually result from the application of drugs to the teeth, from restorative materials, from medicines, from foodstuffs, or from chewing habits, such as tobacco, betel nuts, etc.

Hemolysis of the blood as a sequence of death of the dental pulp is the principal source of permanent discoloration. While this does not necessarily discolor the tooth structures, yet when the condition does exist the general cause is as stated. Progressive interstitial staining of the entire dentin structure is the usual result from death of the dental pulp.

Technique of Bleaching Teeth

Nonvital Teeth:

1. Clean the teeth to be bleached with an abrasive and brush.
2. Isolate the tooth with a rubber dam.
3. Gain access to the pulp chamber.
4. See that the root canal filling is properly placed and sealed.
5. Prepare cavity for the reception of a restoration, removing as much of the stained dentin as is advisable.
6. Determine the nature of the stain.
7. Select the correct bleaching agent.
8. Bleach the tooth to a shade lighter than the adjacent teeth.
9. Repeat bleaching as often as is necessary.
10. Insert a permanent restoration.

[1] Ames, J. W.: J. A. D. A. 24: 1674, Oct., 1937.

PREPARATIONS FOR BLEACHING TEETH.—

HYDROGEN PEROXIDE

Solution of Hydrogen Peroxide; Liquor Hydrogenii Peroxidi (Liq. Hydrog. Perox.), U.S.P. (Solution of Hydrogen Dioxide).—H_2O_2.

This solution contains about 3 per cent of hydrogen peroxide gas in water and is acidified for stabilization.

THERAPEUTICS.—It is a mild and safe bleaching agent for the teeth.

Stronger Solution of Hydrogen Peroxide; Liquor Hydrogenii Peroxidi Fortior (Liq. Hydrog. Perox. Fort.), U.S.P. (Stronger Solution of Hydrogen Dioxide).

This is an aqueous solution containing in each 100 cc. about 8 Gm. of hydrogen peroxide. It may be stabilized by the addition of one or more harmless substances.

THERAPEUTICS.—This preparation, because of its increased content of hydrogen peroxide, is well suited for bleaching teeth.

Superoxol (Merck) is an aqueous solution of hydrogen peroxide, 30 per cent by weight, which liberates about one hundred volumes of oxygen. It is explosive and must be handled with care.

USES.—A concentrated preparation of hydrogen peroxide. It is irritating to the soft tissues and must be used cautiously (Wessinger).

Pyrozone is a 25 per cent solution of hydrogen peroxide in ether. The ether acts as a fat solvent and gives greater penetration.

USES.—Similar to those of Superoxol (See).

CHLORINE LIBERATING COMPOUND

Solution of Sodium Hypochlorite; Liquor Sodii Hypochloritis (Liq. Sod. Hypochlor.), U.S.P.

It contains about 5 per cent solution of NaOCl.

USES.—This is a good indirect oxidizing agent for bleaching teeth.

MISCELLANEOUS BLEACHING AGENTS

Oxalic Acid.—It occurs as colorless crystals which are soluble in water.

USES.—A saturated solution is sealed in the tooth and left there overnight. This procedure is repeated until the tooth is the desired shade.

Diluted Hydrochloric Acid; Acidum Hydrochloricum Dilutum (Acid. Hydrochlor. Dil.), U.S.P.—HCl about 10 per cent.

USES.—Because of its destructive action on tooth tissue it may be used to remove pigment such as silver stains. Caution must be used to prevent destruction of sound tooth tissue.

Chemical Sterilization of Instruments

The sterilization of dental instruments by boiling or at higher temperatures in an autoclave, while efficient, is destructive to the temper and to the length of usefulness of the instrument. In these days of "emergency rationing" the procurement of new equipment is difficult and expensive.

The problem of sterilization of instruments is still in an experimental state. There is no doubt that heat is the most effective agent, and for instruments used in surgery it is still the method of choice. For instruments used in operative (not root canal) and prosthetic dentistry chemical sterilization may be permissible. The instruments must be carefully washed with a brush, soap, and warm water. All blood and other debris must be removed so that the disinfecting solution may come in direct contact with the metallic surface. Time is also necessary to allow the drug to destroy the microorganisms. Bacteria react differently to different agents[1] and to the same agent under varying conditions, i.e., spores may be only slightly affected. This method of sterilization is not adequate when used in patients with a definite oral infection or a communicable disease.

The term cold sterilization is used to contrast this method with heat sterilization, but it is nevertheless confusing. The disinfecting solution need not be cold; it will act more efficiently when at room temperature or even higher.

The composition of the solvent is important also. Water increases the oxidation of the metal and produces corrosion—rusting of steel. Alcohol, because of its water content, added or absorbed from the air, will corrode metal, but to a lesser extent than water alone. Acid solutions will form salts with metals, causing a pitting and a loss of edge. Alkalies will corrode only certain metals, such as aluminum. In addition, instruments of different metals suspended in an electrolytic solution will be corroded by a transfer of ions by electromotive force (Tainter, et al.). As a vehicle they (Tainter, et al.) suggest isopropyl alcohol in a 50 per cent solution. At this time (June, 1944) it is not being rationed and is obtainable at drugstores.

To avoid the corroding action of water or water and alcohol solutions many anti-oxidants have been suggested. Our work (Andrews and Dobbs) demonstrated the efficacy of a saturated solution of sodium borate. Tainter et al. in their excellent paper suggested the use of sodium nitrate (0.2%) and found it superior to the borate.

[1]Brewer, J. H.: J. A. D. A. 27: 276, Feb., 1940.

PREPARATIONS.—

(ANDREWS AND DOBBS)

I

Solution of Formaldehyde		100 cc.
Sodium Borate		20 Gm.
Methanol	q.s. ad	1,000 cc.

Mix and filter.

II

Solution of Formaldehyde		150 cc.
Sodium Borate		65 Gm.
Distilled Water	q.s. ad	1,000 cc.

Mix and filter.

(BLASS[1])

Solution of Formaldehyde	50 cc.
Sodium Borate	Sat. Sol.
Rubbing Alcohol (70%)	450 cc.

Mix.

(TAINTER ET AL.[2])

Solution of Formaldehyde (U.S.P.)	160 cc.
Monoethanolamine	60 cc.
Sodium Nitrite	4 Gm.
Oil of Rose Geranium	2 cc.
Oil of Cinnamon	4 cc.
Distilled Water	780 cc.
Isopropyl Alcohol	1,000 cc.

Mix.

Solvents for Dental Preparations

The use of solvents in dental preparations is complicated by priorities and the war demands. The use of glycerin in tooth pastes as a moistening agent and binder is a good example. Now that glycerin cannot always be obtained in large quantities, some manufacturers are forced to use substitutes. Syrups of certain monosaccharides and disaccharides are being used, but this procedure is frowned upon by the Council on Dental Therapeutics for obvious reasons. Ethylene glycol has been condemned because of its toxicity, and propylene glycol has not always been available in sufficient quantity to fill all dentifrice requirements. Sorbitol has been suggested and may prove to be a good substitute for glycerin in dentifrices. The pharmacists can obtain amounts of glycerin which will be adequate for prescription

[1]Blass, J. L., and Stryron, N. C.: J. A. D. A. 28: 2047, Dec., 1941.

[2]Tainter, M. L., Throndson, A. H., Beard, R. R., and Wheatlake, R. J.: J. A. D. A. 31: 479, Apr. 1, 1944.

needs. Glycerin is mildly irritating to the mucous membranes, but is not caustic and may be used, when obtainable, wherever a solvent, moistening agent or binder is needed.

The use of alcohol as a vehicle and solvent for oral preparations is common. Many of the tinctures and fluidextracts used on the oral tissues contain alcohol up to 87 per cent. Besides those mentioned, the uses of alcohol in oral preparations are as an antiseptic, astringent, counterirritant and caustic. The type of action obtained depends on the type of tissue, the concentration of the alcohol and the time of exposure. As a vehicle for local anesthetics, which are held on the tissues for five minutes, a 10 per cent solution is the maximum concentration. Not over a 20 per cent solution should be used in a mouthwash, and, for a topical application, 50 per cent or less is best. While the use of alcohol for medical purposes has been restricted, there is still enough for prescription purposes. The ethyl alcohol substitution product that is generally used is isopropyl alcohol. This is a good substitute, having similar physical, chemical, and pharmacodynamic properties. It is oxidized in the body at about the same rate and is probably no more toxic. It cannot be advocated for systemic use, but may be used locally with impunity. The dentist needing alcohol 70 per cent for office use may purchase isopropyl alcohol as "rubbing alcohol" at a nominal price in any drugstore. According to Tainter et al., the maximal antiseptic efficiency of isopropyl alcohol is obtained with a 50 per cent concentration.

Chloroform is sometimes used as a solvent for dental preparations. On the mucous membrane, it acts as an irritant and is therapeutically applied as a counterirritant. It must be used cautiously to prevent injury of the sensitive tissues. As a solvent in preparations for the hard tissues of the teeth, it is safe in any concentration, causing pain by its refrigerant action only.

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