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MATERIA MEDICA
FOR
PHARMACY TECHNICIANS

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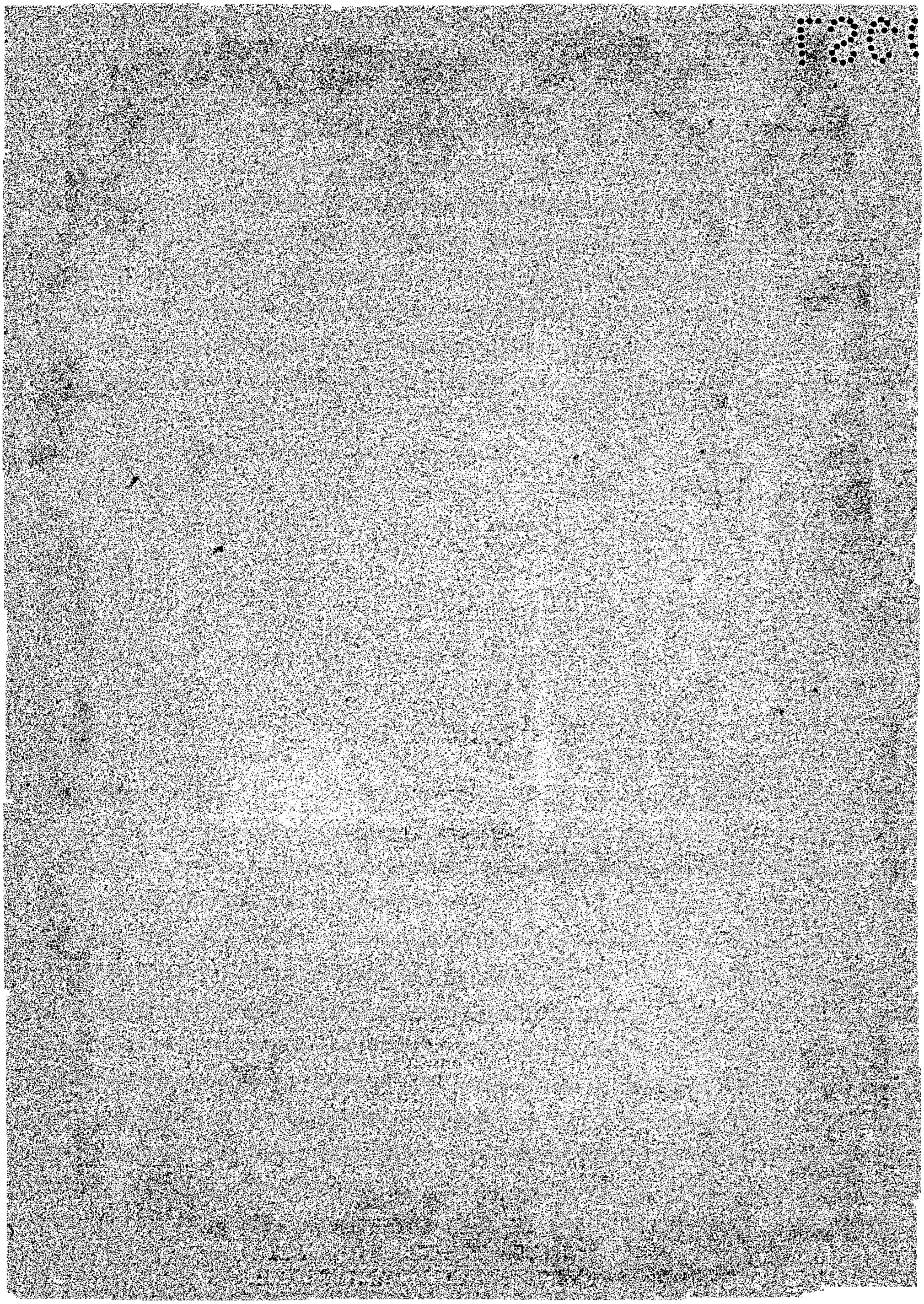

PHARMACY SECTION
File No. 148

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MATERIA MEDICA

For

PHARMACY TECHNICIANS

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MATERIA MEDICA FOR PHARMACY TECHNICIANS

Materia Medica is the science which treats with the origin, composition, and properties of medicinal agents. For the purpose of this course, we will extend the meaning of the term to include action and the doses of drugs or medicinal agents. Broadly then, we are really studying pharmacology, which is the science which treats of drugs, including their source, properties, both chemical and physical, therapeutic action, dosage, identification, and also includes materia medica, itself. In a more restricted sense, pharmacology treats with a study of the action of drugs on the animal organism to which it is administered. This is broken down into pharmaco-dynamics, which deals with the action of drugs on healthy organisms, and therapy-dynamics, which deals with the action of drugs on diseased organisms, or tissues. In this course, we will devote our time to the study of actions, uses, and doses of drugs, primarily.

Toxicology is the science of poisons, and includes their effects and methods of counteracting these effects. A poison may be defined as any substance which, when introduced into a living body, causes harmful effects. In Army Regulations, AR-40-590, paragraph 18, poison is defined as "any substance, which, when taken into the body, is destructive to tissue or endangers life, in quantities of 4 grams." This is the definition given to the term by a number of the state statutes. However, unless some restriction is placed on the definition given first, it is obvious that any substance, even water, when taken in sufficient quantities, will cause harmful effects. In this course, we will accept the definition for poison as that given in Army Regulations, the number and paragraph indicated above.

Our study of toxicology, in connection with materia medica, will be limited to antidotes and related treatment. This is an important phase, as the pharmacist is often called upon in emergency to treat cases of poisoning. As time is a very important factor in these cases, he is not only justified, but morally obligated, to trespass upon what may be, technically, the physician's field. However, the pharmacist must bear in mind that his emergency treatment must not extend beyond this field and that, as soon as practicable, a physician should be summoned and the case turned over to him. Prompt and proper action by a pharmacist in administering the proper antidotes and first aid treatment in cases of poisoning, will oftentimes save a life, and it must be remembered that promptness of action is perhaps the most important of all virtues in treating cases of poisoning. In a very large proportion of instances, the fate of the patient depends upon what is done in the first fifteen minutes after the injection, or administration of the drug or poison.

Before attempting to study any scientific, or other subject, it is necessary that the student have a knowledge of the meaning of the various terms which will be encountered in the study. Administration, in connection with drugs, is the application of that drug to the organism. If there is any alteration or action on the tissue at the site of application, aside from that for which the drug is intended, this is known as a local side reaction. If the drug is administered to produce the effect at the site of application, this is known as a local action. This may take place on the skin, in the mouth, in the stomach, or in any point which can be reached by direct contact. If the

effect takes place after the medicinal agent, or drug, has been absorbed into the blood stream, we speak of this as a general, or systemic action, and any effect which is brought about within the body, by contact with a certain structure after such entrance, is termed a direct action. If the tissue, or organ, which is affected by the direct action, influences other tissues or organs in such a way that another result is obtained at some more distant point, the result is spoken of as an indirect or remote action. Side actions, as mentioned previously, are usually undesirable, but also, at the same time, unavoidable. Of course, if the side action is too severe, some other means of treatment, or some other means of medication must be found to replace that which causes the bad side action. The effect by which the actions are discerned are called symptoms. From a study of the symptoms, the cause, or the agent causing the condition, is determined and this is known as the diagnosis. The dose of a medicine is the amount to be given at any one time. It is impossible, however, to say that a particular drug has one definite dose, for the reason that the amount to be administered varies with varying circumstances. The age and condition of the patient, the severity of the disease, the idiosyncrasy, and tolerance for medicine, all become factors in determining the dose. For these reasons, an average dose is used in order to furnish a guide to pharmacists and physicians. The following quotation is from the General Notices in the Pharmacopoeia: "The insertion of doses has been continued in the 11th revision. The recommendation of the Pharmacopoeial Convention stated, 'It is to be understood that neither this convention, nor the committee of revision, created by it, intends to have these doses regarded as obligatory on the physician, or as forbidding him to exceed the doses given, whenever, in his judgment, this may seem advisable.'" The Pharmacopoeia further states: "The doses are given in both the metric and the apothecary systems. Figures are not interchangeable, nor are they to be considered as exact equivalents. Rounded figures are used in order to assist the memorizing of doses by the physicians and pharmacists.

"Average Dose. Under this term are stated the doses which may be expected ordinarily to produce the therapeutic effect for which the preparation is most commonly employed. The doses, when administered orally, are those for human adults, unless otherwise indicated."

There are numerous factors which influence the action of drugs, the most important of which are as follows:

1. The nature of the substance.
2. The susceptibility of body tissues and structures.
3. The quantity administered.
4. The amount reaching the organ to be affected.

That the character of the drug itself is an important factor is quite obvious. For example, the results obtained by administering a spirit and a tincture of the same preparation may be quite different, due to the fact, of course, that they contain different parts, or extractives, of the drug from which the preparation is made.

Each drug has a selective affinity for a certain tissue and does not affect the other part at all, or, if it does affect them, to a lesser extent. An ideal condition, indeed, would prevail, if it were possible to find drugs which would affect only the diseased portions of the body. This condition

does exist in some cases, but ordinarily, there is some side action associated with the desired action. Digitalis is a very valuable and important drug, used in the treatment of heart conditions, but at the same time may prove quite irritating to the gastro-intestinal tract. Similarily, sulfapyridine has proven an excellent treatment for certain types of pneumonia, but it usually, at the same time, causes nausea and stomach upset. The quantity to be administered is perhaps the most important factor concerned with the disease treatment. The reason is obvious and needs no further comment.

The amount of drug reaching the organ to be affected is very much related to the other three factors.

There are many different modes of administration for drugs, and the six most important are listed in this text. The method chosen, of course, is dependent upon the conditions surrounding the case and the nature of the drug itself.

Perhaps the most used method of administration is by mouth. This naturally is the most logical, since all food is ordinarily taken by this route and absorption is great in the alimentary tract. There are a number of cases in which this method cannot be followed. Sometimes the nature of the drug is such that it will cause great irritation of the gastro-intestinal tract; sometimes the action by this method is not sufficiently rapid to produce the results when needed; in still other cases, the action of the digestive fluids on the drug destroy therapeutic value. A very good example of this is found in the use of insulin in the treatment of diabetes. If this particular drug, insulin, is given by mouth, the digestive juices and ferments destroy it, so it is absolutely of no value for the treatment of the disease for which it is intended, however, when given by hypodermic injection it is of immeasurable value. In cases such as these, some other means of administration must be chosen. Another factor which must be considered when giving medicine by mouth, is that the absorption varies with the presence or absence of food in the digestive tract.

Some medicinal agents are administered through the unbroken skin. In such cases, the medicine is applied or rubbed into the skin and absorbed into the blood stream. This method of administration is called <u>inunction</u>. Since the skin is composed of more or less fatty tissue, which is impervious to water, the medicament to be administered in this manner, must be in an oily or fatty medium. The big disadvantage of this method is the fact that so much time is required to obtain any action. It is seldom used now.

Drugs are administered rectally when it is advisable and advantageous over the oral method. In some cases, absorption by this method is quite rapid, although usually it is not the rule. For the most part, the rectal dose of a drug is larger than the oral, but in some few instances it is smaller. The form of medication most commonly employed by rectal administration is the suppository.

The conjunctiva, urethra, and bladder, are also utilized for the purpose of administering drugs. Although absorption is rapid in all of these, with the exception of the bladder, there is really not much reason for employing this method in preference to oral administration and the sites are used usually for local application only.

Hypodermic administration has become very popular in recent years and today it is very widely used. Hypodermic injection means that the medication is administered by a syringe and a hypodermic needle and may be injected between the outer and inner skin, called intracutaneous injection; under the skin, called subcutaneous injection; deep into the muscular tissue, intramuscular injection, and directly into the veins, which is called intravenous injection. For intravenous and subcutaneous administration, the arm is usually used. For intramuscular administration, the hip or shoulder, where there is a lot of muscle, is usually chosen as the site of injection. For intravenous administration, the inside of the arm at the elbow joint, where the veins are prominent, is chosen. The latter method produces the most rapid results and is chosen only when the other methods are not suitable. Of all the other methods of administration, hypodermic injection is the most rapid means of getting results.

The respiratory tract is chosen as a means of administration of drugs frequently. Absorption from this method is very rapid and it is usually used for administering volatile liquids. Aromatic spirits of ammonia, or smolling salts, present good examples of drugs which are administered by inhalation.

A phenomenon quite frequently encountered in connection with the administering of drugs to patients, is idiosyncrasy. By this is meant that certain individuals may possess or exhibit peculiar, untoward reactions toward one or more drugs. This is often caused by hypersensitiveness of the individual for these drugs which produce the untoward reaction. Much the same conditions are found when certain people eat some foods. Strawberries are a very common offender, and one often hears that strawberries give a certain person hives, or itch, etc. The patient's physical condition at the time of administration of a drug has considerable to do with the allergic manifestations which result.

It is not at all uncommon to find certain individuals who develop a tolerance for some drug. By this we mean that he can take seemingly large or excessive doses of a particular drug and not receive much or any benefit or harm from this dose. On the other hand, we have what is termed increased susceptibility, which means that relatively small doses of certain drugs will produce toxic symptoms in some individuals. Sometimes people of one race are more susceptible, or more tolerant, as the case may be, to a certain class of drugs than are people of another race.

Some drugs, when administered, are eliminated very slowly and as a result exhibit what is called a cumulative action. This means that as more is given it increases the amount retained in the system until toxic symptoms may follow. Lead, digitalis, and mercury, are examples of this type of drug.

The mental state of a patient at the time of administration of a drug has much to do with the results obtained. It is a well-known fact that the will to get well or remain sick has a big bearing on the course the disease will follow. Patients who want to get well quickly oftentimes require less medication than do those who are obstinate and want to remain sick, or even have the idea they want to die.

There are some drugs which, when given together, will produce better results than either one alone, even though both serve the same purpose when given separately, only to a lesser degree. Drugs which exhibit this phenomenon are called synergists. A good example of this is aspirin and phenacetin. The combination of these two drugs produces a much better analgesic effect than does either one alone, even though the separate drugs are given in larger amounts. On the other hand, drugs which are opposite in action, when combinod may have little or no effect, due to the fact that one neutralizes the effect of the other. These substances are spoken of as antagonists. A good example of this antagonism is atropine, which paralyzes the nerves, and pilocarbine, which stimulates them, so when given together, one prevents the action of the other. The antagonistic action may be evidenced by the effect on different organs of the body.

Before beginning the study of drugs contained hercin, it seems a good idea to say just a little about toxicology and antidotes, so that the student may apply the knowledge to the different drugs studied as he progresses.

Any method of treatment for poisoning may be divided into five steps. The first is to discontinue administration of the poison. This is not so important since the majority of cases of poisoning are not due to a continual ingestion of the poison, but more frequently, to a single large dose, taken either by mistake, or with the intent to commit suicide.

The second step calls for administration of an antidote which will counteract the action of the poison, either mechanically, physiologically, or chemically. There is much misunderstanding and consequent misuse of antidotes. First, a distinction is to be made between antidotes and antagonists; an antidote, properly speaking, is a substance which chemically lessens or destroys the activity of a poison; agents which are used to combat the harmful effects of poison should be called antagonists.

In a great many cases, the action of the antidote is only to lessen, not to abolish, the toxic properties of the poison. For instance, precipitates formed by either tannic acid or iodine, with the alkaloids, are by no means inert; they are simply relatively insoluble and the antidote therefore delays absorption of the poison until the stomach and intestines can be emptied. In most instances, one should not trust to the antidote alone, but should use it in connection with methods for evacuation of the alimentary canal. The dream of the ancients of finding some drug or combination of drugs which would counteract the injurious effect of all poisons is about as likely of realization as the hope of Ponce de Leon of finding the 'Fountain of Perpetual Youth'. Nevertheless, there have been devised, mixtures which have more or less antidotal effects, to so many substances that the high-sounding title of 'Universal Antidote' is not altogether ridiculous. The most important of these are powders which depend for their value on their absorptive properties. There are some colloidal powders which have the property of mechanically, or at least without causing any alteration of the chemical structures, removing certain undissolved substances from their solution. Among these should be mentioned in particular certain clays, as, Fuller's Earth, Lloyd's reagent, and charcoals, especially activated charcoal.

Of these, charcoal, while not the most efficient, is usually the one most quickly obtainable, and therefore to be recommended; it may be given in tablespoonful doses; it is not necessary to stop to measure it accurately for it is quite incapable of harm, only be sure to give enough. Many writers recommend that with the charcoal be combined magnesium oxide. The latter will neutralize any acid, lessen the irritating effect of many heavy metals (such as copper sulfate, alum, etc.), tend to delay the absorption of alkaloids, and perhaps have some effect against arsenic. In view of the frequency of arsenical poisoning, it is commonly advised to add ferric hydroxide to the universal antidote, but unless the ingredients for its preparation be readily at hand, time should not be wasted trying to make it. In a case of poisoning by an unknown agent, emetics stand first in importance, but it may be well to follow them with a mixture containing about one tablespoonful of magnesium and two tablespoonfuls of activated charcoal.

Where several antidotes are named, choose the one that can be obtained most quickly. Do not mix antidotes, either in the patient's stomach, or outside. Generally speaking, they are more likely to neutralize each other, rather than the poison. Tannic acid, iodine, potassium permanganate, are antidotals to the alkaloids, but all are mutually incompatible.

The third step involves the emptying of the stomach. This is accomplished by either an emetic or the stomach tube, or stomach pump. In a very large number of forms of poisoning, the emptying of the stomach is of more practical utility than the administration of the antidote. Emetics are contra-indicated in poisoning by mineral acids, by toxic alkalies, or by strychnine. The reason for this is that it is assumed, and sometimes is a fact, that the wall of the stomach has been so weakened by the action of the mineral acids or toxic alkalies, that the administration of an antidote, which causes a straining on the muscle tissue, would rupture, and more harm than good would result. The most thorough means of evacuating the stomach is by means of a stomach tube, or pump. This, however, requires familiarity with its use. In the hands of the unskilled, it is capable of very serious damage. Practically, the pharmacist will rely on emetic drugs. The frequent recommendation to provoke vomiting by tickling the back of the throat is so likely to fail and the need of quickness is so urgent that one should not waste the time trying it. If someone else is obtaining the emetic drug, or if none is at hand, tickling the throat, which can best be done with a feather, may be practiced temporarily.

Among the emetics for general use, first place should be given to zinc sulfate. Twenty grains, in two or three ounces of tepid water, may be given at a dose and if emesis has not occured, repeat in five minutes. Apomorphine hydrochloride is perhaps the most certain, and one of the quickest of the emetics, but requires that it be given hypodermically. The dose should not exceed 1/10 of a grain. A useful emergency emetic is mustard. It is very efficient and prompt for that purpose. Give a half a tablespoonful stirred up in a wineglassful of water. A lukewarm solution of ordinary salt, two tablespoonfuls to a glass of water, will sometimes provoke vomiting, especially if combined with throat tickling. Copper sulfate, 5 grains, may also be used.

The fourth step is taking action to eliminate the absorbed poison by such substances as cathartics, diuretics, diaphoretics, etc.

The fifth, and final, step, consists of relieving, or neutralizing the harmful effect already caused, by therapeutic measures. These involve relieving of pain, stimulation of weakened organs, soothing abrasions, etc.

The following list comprises the common antidotes and their uses:

ACIDS - mineral; including hydrochloric, sulfuric, nitric, and phospheric acids.

DO NOT GIVE EMETIC because the stomach may be so weakened by the caustic effect of the chemical that it will rupture during the vomiting; give an alkali; the one which can be used most quickly is the best.

Where there is an opportunity for choice, preference should be given to milk of magnesia, 2 tablespoonfuls, or magnesium oxide, 1 teaspoonful, because they do not liberate carbon dioxide gas which may distend and overstrain the weakened walls of the stomach. This danger is, however, generally over-estimated, and should not lead to the withholding of carbonates when other alkalies are not available. Calcium carbonate is a form of chalk. Two teaspoonfuls of chalk mixture, has more neutralizing effect, for the same amount of carbon dioxide gas, than sodium bicarbonate, in a dose of 1 teaspoonful. In the absence of other alkali, soap, or well-diluted solutions of the hydroxides may be used. Limewater is often recommended, but it should be remembered that it requires about 2 quarts of limewater to neutralize the same amount of acid as 2 fluid drams of milk of magnesia. White of an egg may be used if no alkali is available.

ACIDS - Oxalic, and the oxalates (salt of sorrel, ink-eradicator, etc.)

The best antidote is some form of lime: calcium chloride, 20 grains; chalk, a teaspoonful; most tooth powders contain chalk and may be used as an antidote. In the absence of lime, magnesium may be used as an antidote, either in the form of magnesium sulfate (epsom salts), 1 tablespoonful, or milk of magnesia, 2 tablespoonfuls.

ACONITE

A rapid and exceptionally dangerous poison. Give emetic; zinc sulfate, 20 grains, or ground mustard, 2 teaspoonfuls. Lugol's solution in a 20-drop dose, is probably the best chemical antidote, although none are of much value. Keep the patient in a horizontal position; do not allow him to sit up, even to vomit, turn the head to one side when vomiting; keep the patient warm.

ALKALIES - including sodium hydroxide, potassium hydroxide, calcium oxide, and ammonia.

DO NOT GIVE EMETIC! The chemical antidote is any dilute acid, the best is vinegar, 1 or 2 tablespoonfuls, diluted with an equal amount of water. Diluted hydrochloric acid may be used, one-half to 1 teaspoonful, well-diluted according to the amount of alkali which has been taken. Lemon juice, or orange juice, 2 or 3 tablespoonfuls diluted, are also useful. Olive oil, or any bland fixed oil, 2 or 3 tablespoonfuls, are of service, partly because of neutralizing effect, but mainly for the soothing action.

AMMONIA WATER - (See Alkalies)

ANTIMONY or TARTAR EMETIC

Give tannic acid, 20 grains, or glycerite of tannin, 1 teaspoonful. Other tannin-containing drugs as fluidextract of geranium, 2 teaspoonfuls, or tincture of kino, or of gambir, 2 or 3 teaspoonfuls, may be substituted. KEEP THE PATIENT IN A HORIZONTAL POSITION.

ARSENIC, or FOWLER'S SOLUTION - (Rough-on-Rats, and some other rat poisons contain arsenic)

Emetics are the most important. Zinc-sulfate, 20 grains, or ground mustard, 2 teaspoonfuls. The best chemical antidote is the official arsenic antidote, ferri hydroxidum cum magnesii oxido, one-half tumblerful. It may be prepared by adding either a solution of sodium carbonate or milk of magnesia to tincture of ferric chloride and straining the precipitate through cheese cloth. Give one or two tablespoonfuls of the precipitate. Milk of magnesia has some antidotal effects but is less valuable than the iron.

ATROPINE - (See Belladonna)

DARIUM SULFATE or other SALTS OF BARIUM

Give any soluble non-toxic sulfate, such as epsom salts or Glauber's salts. Dose should be at least equal to the quantity of barium salts. If this is unknown, give 3 tablespoonfuls. Sulfuric acid may be used in an emergency, but it is less valuable because a large quantity of acid may irritate the stomach (the dose of aromatic sulfuric acid to be given should be about 1 tablespoonful, well-diluted). Follow the antidote by an emetic such as zinc sulfate in a dose of 20 grains.

BELLADONNA, ATROPINE, STRAMONIUM, HYOSCYAMUS, AND ALLIED DRUGS

Give emetic; zinc sulfate, 20 grains; or mustard, 2 teaspoonfuls; the best chemical antidote is Lugol's solution, 10 minums; tannic acid, 20 grains, is less valuable; charcoal, or preferably activated charcoal, 2 teaspoonfuls, is also of some value. Whatever antidote is given, the stomach should be emptied, as the compounds formed are not entirely harmless. Poisoning by the solanaceous drugs, although very alarming, is not usually fatal.

BICHLORIDE OF MERCURY - (See Mercury)

CANNABIS

No antidote known. Give emetic. Very rarely does this cause dangerous poisoning.

CALABAR BEAN - (See Physostigma)

CANTHARIDES

Give emetic, zinc sulfate, 20 grains; or mustard, 3 teaspoonfuls. There is no chemical antidote, but charcoal, preferable activated charcoal, 2 teaspoonfuls, may be useful for its absorbent effect. After emptying the stomach,

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CYANIDES - (See Hydrocyanic Acid)

DIGITALIS

If the patient has not already vomited, give an emetic. There is no chemical antidote known; treatment, aside from evacuation, in general is of little avail.

DRASTICS

The drastic cathartics include colocynth, gamboge, croton oil, elaterin, scammony, jelap, etc. If vomiting has not already occured, give an emetic, or demulcents, mucilage of accacia, 2 tablespoonfuls, or white of egg.

ERGOT

Give emetic, zinc sulfate, 20 grains, or mustard, 2 teaspoonfuls. No satisfactory antidote.

ESERINE - (See Physostigma)

ETHER - (See Chloroform)

FISH BERRIES - (See Picrotoxin)

FORMALDEHYDE

Ammonia (aromatic spirits, 1 teaspoonful); ammonia water, U.S.P., 30 drops; ammonium carbonate, 10 grains, well-diluted; if the patient has not vomited, give emetic.

FOWLER'S SOLUTION - (See Arsenic)

GAS, ILLUMINATING - (See Carbon Monoxide)

GELSEMIUM - (Treat as Conium)

HYDROCYANIC ACID

Treatment must be prompt as this is one of the most quickly acting of poisons Indeed, it is so quick that few remedies have time to act. Every hospital should have the necessary materials ready in special case for the treatment of this poison, as seconds count in applying the antidote. The treatment consists of injecting intravenously, a solution of 3/10 gram of sodium nitrite and 10 cc. of water, which makes 3 percent solution. Follow by the intravenous injection of 25 grams of sodium thio-sulfate in 50 cc. of distilled water. One-half of the thio-sulfate solution is frequently sufficient In relapse, use half the dose of the antidote. Amyl nitrite may also be inhaled to expedite the treatment. Artificial respiration and oxygen inhalation are also of service.

HYOSCYAMUS - (Treatment same as Atropine)

IGNATIA - (See Strychnine)

INDIAN HEMP - (See Cannabis)

ILLUMINATING GAS - (See Carbon Monoxide)

IODINE - Starch, or flour, 2 tablespoonfuls, stirred up in water to make a paste. If the patient has not vomited, give emetic.

LARKSPUR - (Treat as under Aconite)

LEAD ACETATE or other LEAD SALTS

Magnesium sulfate, epsom salts, or sodium sulfate, 2 tablespoonfuls. As emetic, preference is for zinc-sulfate.

LYE - (See Alkalies)

MERCURY BICHLORIDE or other SALTS OF MERCURY

Give emetic; zinc sulfate, 20 grains; or mustard, 2 teaspoonfuls. The commonly recommended white of an egg is of no value. The only antidote for mercury bichloride poisoning known to be absolutely safe and effective is sodium formaldehyde sulf-oxalate. It is administered as follows: wash the stomach with a 5% solution, allowing 200 cc. to remain. Inject intravenously 10 grams dissolved in 100 to 200 cc. of distilled water, taking 20 to 30 minutes for the injection. Repeat in 4 to 6 hours if necessary, using 5 to 10 grams of salt. This salt is marketed in convenient ampules and should be stocked by every drug store as an emergency item. Other antidotes which have been used are as follows: Fantus antidote; sodium hypophosphite, 5 grams; solution of hydrogen peroxide, 25 cc.; water, 5 cc. (this is the amount to neutralize one of the large bichloride tablets). If more has been taken, the dose must be correspondingly increased; the stomach should be washed out afterward. Carter's antidote consists of sodium phosphite, not hypophosphite, or phosphate, and sodium acetate. It is efficient, but as the first ingredient is not ordinarily found in drug stores, is of small praetical value. Calcium sulphide is also efficient but is poisonous of itself. It may be used when other remedies are not at hand, in doses of not over 5 grains.

METHANOL (Methyl alcohol, wood alcohol, etc.)

Empty the stomach with an emetic. Follow by sodium bicarbonate, 2 teaspoonfuls in water. This should be repeated as it tends to neutralize decomposition products of the poison in the system.

MORPHINE - (See Opium)

NUX VOMICA - (See Strychnine)

OIL OF BITTER ALMOND - (See Hydrocyanic Acid)

OILS, VOLATILE, including TANSY, RUE, CLOVE, PENNYROYAL, etc.

Poison by their local irritant effect. Empty the stomach if the patient has not already vomited. Afterward give demulcents as mucilage of acacia, 2 tablespoonfuls, or white of an egg.

OPIUM, MORPHINE, OR CODEINE

If seen early, give emetic. Zinc sulfate, 20 grains. After narcosis has set in, emetics fail to act. The best antidote is potassium permanganate, 5 grains, in a tumblerful of water. Tannic acid, 20 grains, or Lugol's solution, 10 minums, may be used when permanganate is not available. Keep the patient awake by shouting. Do not use commonly applied method of walking him; the best way of preventing sleep available is the electric brush. If breathing becomes very low, practice artificial respiration.

PARIS GREEN - (See Arsenic)

PHENOL

Give emetic, preferably zinc sulfate, 20 grains. Follow with magnesium sulfate, 2 tablespoonfuls; then with mucilage of acacia, 2 tablespoonfuls. AVOID THE USE OF OILS OR OF ALCOHOL. External burns by phenol should be washed with alcohol.

PHOSPHOROUS

As an emetic, preference should be given to copper sulfate, 5 grains, but if not at hand, other emetics may be used. The chemical antidotes are copper sulfate, or potassium permanganate, 5 grains, in a tumblerful of water. AVOID ALL OILS OR FATS.

PHYSOSTIGMA

Give emetic, zinc sulfate, 20 grains; or mustard, 2 teaspoonfuls. Chemical antidotes are potassium permanganate, 5 grains, or tannic acid, 20 grains. ARTIFICIAL RESPIRATION MAY BECOME NECESSARY.

PHYTOLACCA

If the patient has not already vomited, give an emetic. Zinc sulfate, 20 grains, or mustard, 2 teaspoonfuls. There is no chemical antidote known.

PICROTOXIN

Give emetic. Zinc sulfate, 20 grains; or mustard, 2 teaspoonfuls. There is no known antidote. Chloroform may be used cautiously to control convulsions.

POTASSIUM CYANIDE - (See Hydrocyanic Acid)

POTASSIUM HYDROXIDE - (See Alkalies)

PRUSSIC ACID - (See Hydrocyanic Acid)

PILOCARPINE

If taken by mouth, give emetic. As an antidote, use Lugol's solution, 10 minums, or tannic acid, 20 grains. Atropine is so valuable as a physiological antagonist that the pharmacist is justified in giving 1/100 of a grain without waiting for a physician.

SILVER NITRATE

Give sodium chloride, 2 teaspoonfuls in a glass of water. Follow by white of an egg.

SQUILL - (Treat as under Digitalis)

STAPHISAGRIA

Give Lugol's solution, 10 minums. KEEP THE PATIENT IN A HORIZONTAL POSITION. The drug acts much like aconite but is not so dangerous.

STRAMONIUM - (See Belladonna)

STROPHANTHUS - (Treat the same as Digitalis poisoning)

STRYCHNINE and its SALTS

Amyl nitrite by inhalation or hypodermically; tannic acid in warm water to wash the stomach; follow with potassium bromide by mouth or rectum; or give chloral hydrate; emetic; chloroform er ether to control convulsions.

TARTAR EMETIC - (See Antimony)

VERATRUM VIRIDE

Give Lugol's solution, 10 minums, or tannic acid, 20 grains. KEEP THE PATIENT IN A HORIZONTAL POSITION; do not allow him to arise to vomit; keep him warm. Artificial respiration may be necessary.

WOOD ALCOHOL - (See Methanol)

ZINC SULFATE or other ZINC SALTS

Chemical antidote is alkali; sodium bicarbonate, 1 teaspoonful, or sodium carbonate, 15 grains, well-diluted; or the corresponding salts of potassium. After administering these, follow with white of egg or mucilage of acacia.

DRUGS WHICH ACT LOCALLY

A. IRRITANT

Drugs, or substances, which, when applied to tissue, produce irritation of any sort, are called irritants. There are many different classifications of irritants, depending upon the severity or mildness of action, which, of course, is governed by the concentration, chemical properties, length of exposure, and volatility of the drug.

When any drug of this type is applied to the skin, the first effect is a reddening of the epidermis at the point of contact. The reddening is accompanied by itching, burning, and at times, by severe pain. The longer the drug remains on the part, the larger becomes the irritated area. If at this stage the substance is removed or if it is a type which will produce no further action the site will heal rapidly with little further discomfort to the individual. The agent used for this purpose is called rubefacient, and the process rubefaction.

If, however, the drug is left on for a longer period of time, small watery blisters appear under the outer layer of the skin. These then run together, or coalesce, and produce a large blister which is filled with serum. If the drug is removed at this point the action is stopped and healing takes place quite rapidly and leaves no scar. Agents which cause this action are called epispastics, vesicants, or blisters, and the process called vesication.

Some drugs bring about destruction of tissues without formation of blisters, although rubefaction is a preliminary action. Drugs such as mineral acids and alkalies are examples. A scar is formed by this action and the drugs which are used to destroy tissue in this manner are called escharotics.

Substances which coagulate albumen of protoplasm, and thus cause a constriction of tissue are called astringents.

Application of irritants under proper conditions, and with due selection, to open abrasions will, because of the stimulating effect, induce healing.

To sum up what we have said then, irritant drugs are used:

1. To cause astringency.
2. To produce rubefaction.
3. To destroy abnormal tissue.
4. To promote healing.

1. Scarlet Red

Scarlet red is a dye which has a marked power in stimulating the growth of epithelial cells. Opinions are divided as to the clinical value, but the dyes are used to promote the growth of epithelium in the treatment of burns, wounds, chronic ulcers, etc.

In chronic ulcers, however, it is requisite that the local circulation be good, in order to obtain a permanent result. Scarlet red preparations are most commonly used in the form of an ointment.

2. Balsam of Peru (Peruvian Balsam) - dose, 1 gram.

Balsam of Peru is mildly antiseptic and irritant and is used chiefly externally to promote the growth of epithelial cells and in skin diseases. It is also used as a preservative for fats, ointments, etc. Internally, it is employed occasionally as an antiseptic and stimulating expectorant, but is not of great value for such purposes.

3. Camphor - dose, 0.2 grams

   a. Camphor Water - dose, 10 cc.
   b. Spirit of Camphor - dose, 1 cc.
   c. Camphor Liniment (Camphorated Oil)

Camphor is used internally in hysteria and neuralgic headaches. Hypodermically, it is employed and is of considerable value as a heart stimulant. Locally, it is employed in nose and throat diseases and in liniment.

4. Turpentine

   a. Oil of Turpentine (Spirits of Turpentine)
   b. Rectified Oil of Turpentine - dose, 0.3 cc.

When applied to the skin, oil of turpentine causes reddening and burning and if left in contact with the skin for some time, produces blisters which heal very slowly. This action is more severe on mucous membrane and since absorption takes place very quickly, the kidneys are stimulated. Paint store turpentine, or turps, frequently consists of a mixture of turpentine of a petroleum distillate. Wood turpentine, made by distilling old stumps, pine, sawdust, or finely ground resinous wastewood, etc., with steam, also constitutes much of the cheap turpentine on the market. This variety, although closely resembling genuine oil of turpentine, in its physical properties, is considered unsuitable for medicinal use.

Oil of turpentine, when old, becomes ozonized by the formation of hydrogen peroxide in the presence of air and water and produces a characteristic bleaching action upon the cork stopper of the bottle containing it. Upon long exposure, ultimately, it thickens and partly resinifies by oxidation. Oil of turpentine is applied externally in liniment as a stimulant and counter-irritant Only the rectified oil of turpentine should be used internally. This is used as a stimulant diuretic carminative and expectorant and may be given in the dose of .3 cc. The purpose of this preparation is merely to provide a more pure form of oil for internal use. As this oil deteriorates upon keeping, by ozonizing and finally resinifying, it should not be kept on hand for too long a time before using.

5. Ammonia

a. Ammonia Water (Solution of ammonia) - dose, 1 cc.
b. Stronger Ammonia Water (Strong solution of ammonia)
c. Ammonium Carbonate - dose, 0.3 grams.
d. Aromatic Spirits of Ammonia - dose - 2 cc.

Ammonia water is occasionally employed hypodermically as a circulatory stimulant. It is also used for syncopal attacks by inhaling; it is rarely given by mouth, the aromatic spirits being preferred. The dose is .6 to 1.2 cc., largely diluted. Externally it is caustic and stimulating. It is a common ingredient in stimulating liniment. Pharmaceutically, ammonia water is frequently used to precipitate iron salts by combining with the acid radical, ferric hydroxide being thrown down. Its advantage over fixed alkalies, consisting of volatility, any excess being readily detected by the odor. It is largely used for cleaning fabrics. The stronger ammonia water is used only for chemical and pharmaceutical purposes and for making ammonia water by dilution, and in the preparation of the petroxolins of the N.F., where it forms an ammonium oleate, also in the spirits of ammonia. It is too strong for internal administration. Ammonium carbonate is given hypodermically as a circulatory stimulant. By mouth, it is used as an expectorant, especially for children. It is the basis of smelling salts so valuable as a restorative in hysterical syncope. The dose is .2 to .32 grams. It is generally administered in mucilaginous syrup. It is occasionally used as a leavening agent and in consequence is sometimes called 'Baker's Ammonia'. The aromatic spirits of ammonia is very valuable and is largely used as an antacid and stimulant. It is useful in cases of nausea, faintness, and other similar conditions. The dose is from 1.2 to 4 cc., largely diluted with water.

6. Cantharides (Spanish Fly)

a. Tincture of Cantharides - dose, 0.1 cc.
b. Cantharides Cerate (blistering cerate)

Cantharides is used as an aphrodisiac and is poisonous. When applied externally it produces vesication. Tincture of cantharides is used rarely as a diuretic uterine stimulant for it is extremely dangerous. Its chief use is as a scalp stimulant in hair tonic. The toxic effects which may arise after any mode of application of cantharides are all attributable to its very great power of irritation, especially on the kidneys and alimentary tract. The symptoms of poisoning are: burning sensation in the mouth and throat, thirst, but inability to swallow, nausea, voniting, possibly diarrhea, kidney pains, frequent urination, with casts and albumen, rapid pulse, then slow and weak, fainting, difficulty in breathing, and collapse. If recovery takes place, it is long delayed. Death is due to respiratory paralysis. The treatment for poisoning by this drug consists of washing out the stomach with a stomach

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9. Acetic Acid

a. Glacial acetic acid
b. Dilute acetic acid - dose, 2 cc.
c. Trichloracetic acid

Glacial acetic acid is an irritant and if left in contact with the tissues will produce blistering. It is sometimes applied cautiously over a long period of time to remove warts. Symptoms of poisoning are much the same as those for the alkalies and strong mineral acids.

Acetic acid is used in pharmacy as a solvent and menstruum and for making a diluted acetic acid. The crude acetic acid, called pyroligneous acid is sometimes put up under the name of 'liquid smoke', and sold for the purpose of preserving meat, fish, etc., which are dipped therein, then dried, instead of subjecting them to the customary smoking process. This use of pyroligneous acid is prohibited by most food laws. Acetic acid is also used as a starting point in the manufacture of many other organic compounds. It also finds many applications to the textile industry.

Glacial acetic acid is a solvent for fixed and volatile oils. As a medicinal aid it is a caustic and a vesicant when applied externally. It is often sold under various disguises as a corn solvent. It is also used in the synthesis of many organic substances.

Diluted acetic acid is superior to vinegar as a menstruum and is used officially because of its greater purity, more uniform strength, and freedom from color. It is of service as an astringent, as in sunburn, and as a styptic.

Trichloracetic acid is used as a caustic, in solution or in crystal form.

10. Lactic Acid

Lactic acid is similar in action to acetic acid but much milder. It is used chiefly to form the lactates which are believed to be more easily assimilated than most salts. It is rarely prescribed alone, but may be given in doses of 2 to 12 cc., largely diluted.

11. Nitric Acid

This was formerly used widely to remove such growths as warts, moles, etc., but recently has been replaced by substances which cause less pain and do not stain so badly. When nitric acid is used the area surrounding the part to which application is made should be coated well with petrolatum, or vaseline, to prevent burning. It is occasionally given internally in stomach and intestinal disorders, in doses of 0.3 to 0.6 cc.

B. ASTRINCENT

Astringents are drugs which contract tissues with which they come in contact. They are used to:

1. Check secretions and lessen diarrhea.
2. Allay inflammation.
3. To stop bleeding.
4. To harden tissue.
5. To promote healing by mild irritation.
6. To lessen the growth of microorganisms.

1. Tannic Acid - dose, 0.5 grams.

a. Glycerite of Tannic Acid - dose, 2.5 cc.
b. Ointment of Tannic Acid

Tannic acid produces its astringency by precipitating protein. It is a powerful astringent in doses of .2 to .6 grams. It is frequently employed as an astringent in the form of an ointment chiefly for hemorrhoids. Its solution in glycerine is a valuable liquid form of administration. It is quite frequently employed in cases of diarrhea. Through its astringent action upon the intestines, it oftentimes lessens the diarrhea and relieves the symptoms.

2. Zinc

a. Zinc acetate - dose, .125 grams.
b. Zinc chloride.
c. Solution of zinc chloride.
d. Zinc oxide.
e. Ointment of zinc oxide.
f. Zinc sulfate - dose, 1 gram.
g. Prepared calamine.

Zinc acetate is used locally for its astringent effect in eye washes, injections, etc. If used internally the dose is .125 grams. Zinc chloride is used in a one or two percent solution as a dental antiseptic and astringent. Zinc oxide is chiefly used externally as a desiccant and protective to inflamed surfaces. It may be dusted on the part or used in the form of an ointment. It is occasionally given internally in diarrhea, but not frequently. Zinc sulfate is the most important of the zinc salts. It is used medicinally as a prompt and certain emetic, in doses of .6 to 2 grams, as a tonic and astringent, .065 to .13 grams. It is also used locally for its astringent action. Prepared calamine is used similarly to zinc oxide, but it is employed chiefly in protective ointments and lotions. It is often prescribed by dermatologists to give color to lotions or ointments.

3. Alum (Purified alum) - dose, 0.5 grams.

a. Exsiccated alum (burnt alum)

Alum is a powerful astringent because of its precipitation of albumen. It is slightly antiseptic. When powdered, it is used as an emetic in croup, in doses of 1 teaspoonful. It is sometimes used as a local styptic, and is frequently employed in making astringent lotions and injections. Exsiccated alum is used as an escharotic and is more powerful than alum, not only because it is more concentrated, but it also absorbs water from the tissues because it is very hygroscopic.

4. Lead

a. Lead acetate (Sugar of Lead)
b. Solution of lead subacetate (Goulard's Extract)
c. Lead monoxide (Litharge)
d. Lead oleate plaster.

Lead acetate is a valuable astringent and sedative. It is used both internally and externally. The dose is from .065 to .2 grams. Its solution in water is usually turbid, due to the formation of a trace of carbonate through the carbonic acid present in the water. Diluted acetic acid dissolves the precipitates and makes a clear solution.

Solution of lead subacetate is sedative and astringent. It is employed externally as an application to bruises and sprains.

Lead monoxide is used officially for making several preparations, such as, lead oleate plaster and solution of lead subacetate.

5. Copper Sulfate - dose, 0.3 grams

Copper sulfate is called, commercially, blue stone, or blue vitrol. It is used internally as an emetic; as an astringent or tonic. It is used as an injection in gonorrhea and other diseases and also as a stimulant wash, and in substance, as an escharotic. It is also an antidote for phosphorus poisoning.

C. PROTECTIVE.

Protectives are drugs which are employed to cover tissue and usually soften and relax the tissue. Their action, when taken internally, is much the same.

1. Glycyrrhiza - dose, 2 grams

a. Fluidextract of glycyrrhiza - dose, 2 cc.
b. Extract of glycyrrhiza
c. Pure extract of glycyrrhiza
d. Mixture of opium and glycyrrhiza (Brown's Mixture) - dose, 4 cc.
e. Compound powder of glycyrrhiza - dose, 4 grams
f. Elixir of glycyrrhiza (Adjuvant Elixir)

Glycyrrhiza is valuable in pharmacy chiefly because of the sweet principle. It is one of the most efficient substances known for masking the taste of bitter substances like quinine. Acids precipitate the glycyrrhiza and should not be added to mixtures which the glycyrrhiza is intended to mask the disagreeable taste. The fluidextract is a pleasant flavor for use in syrups and elixirs to be employed as vehicles and correctives. The extract and pure extract are used as flavoring agents. Brown's mixture is an expectorant frequently used in bronchitis, often combined with ammonium chloride. The elixir is a pleasantly-flavored vehicle employed in the preparation of many other elixirs. The chief objection to its extensive use is the high alcohol content, which at times counteracts the effect of other medicines. The National Formulary offers several vehicle elixirs of low alcoholic strength, among them being Compound Elixir of Almond, about 5% alcohol, Aqueous Elixir, non-alcoholic, and the Compound Elixirs of Cardoman and Vanillin, both of about 10% alcohol.

2. Starch - Amylum

Starch is used in a number of official preparations, chiefly because of its absorbent properties, also used as a filler or diluent in pills and tablets and, in the latter, as a disintegrator. It is used externally as an absorbent and is applied to the skin by dusting. It is also used to make paste for applying in skin diseases.

3. Acacia (Gum Acacia, or Gum Arabic)

a. Mucilage of Acacia - dose, 15 cc.

In pharmacy, acacia is extensively used for the suspension of insoluble substances in water and for the formation of pills and troches. Two kinds of powdered acacia are used; one, a coarse powder called granulated, and the other finely dusted. The granulated dissolves more readily in water, because it has lost, during desiccation, only a part of its moisture, while in preparing the finely dusted powder, the high heat necessarily used to dry it thoroughly, dries out nearly all of the water. Its easy solubility and its absence of tendency to form lumps cause the coarse powder to be preferred for solutions, emulsions, etc. Acacia is used as a binding agent in emulsions, pills, and troches, etc. It is used for its demulcent action in inflammation of the throat or stomach. The mucilage of acacia is also employed as a demulcent and as an excipient in making pills and troches, and as an emulsifying agent for cod liver oil and other substances.

4. Tragacanth

a. Mucilage of Tragacanth.

Tragacanth, in the form of a glycerite, affords an excellent pill excipient. The powder itself is often used to stiffen a pill mass

and render it adhesive. It is also used as a suspending medium in lotions, mixtures, and in extemporaneous preparations and prescriptions. It is used with emulsifying agents, largely to increase consistency and retard creaming. It is sometimes used as a demulcent in sore throat. The mucilage is used almost exclusively as a pill excipient.

5. Bismuth

a. Bismuth Subnitrate (Bismuth) - dose, 1 gram.
b. Bismuth Subcarbonate - dose, 1 gram.
c. Bismuth Subgallate (Dermatol) - dose, 1 gram.
d. Bismuth Subsalicylate - dose, 1 gram.
e. Bismuth Magma (Milk of Bismuth) - dose, 4 cc.

Bismuth salts are not applied for any specific action, but usually to allay irritation to the inflamed surfaces to which they are applied internally and externally. They find considerable use in the treatment of syphilis. Bismuth subnitrate is largely used in intestinal disorders, but frequently as a dusting powder. The gastro-intestinal dose is from 3 to 15 grains, or .2 to 1 gram. The dose as an anti-syphiletic by parenteral injection, is 0.125 gram. Bismuth subcarbonate is used for its protective and antacid effect in inflammation of the stomach and bowels. It is also given in large doses for rendering the alimentary canal opaque to x-ray. It is employed for the same purpose as the subnitrate, but is to be preferred to the subnitrate in mixtures containing carbonate, as the acidity often noticed in the subnitrate, frequently causes decomposition, or explosion in capsules, pills, etc. The latter, however, is much more frequently used. Bismuth subgallate is used internally in diarrhea, externally as an application to wounds and ulcerations, and the treatment of eczema. Bismuth subsalicylate is used as an intestinal antiseptic and protective, and as an anti-syphiletic by parenteral injection. The milk of bismuth is used for the same purposes as bismuth subnitrate and subcarbonate.

6. Glycerin (Glycerol) - dose, 4 cc.

Glycerin is one of the most valuable products known to pharmacy. It is solvent and antiseptic, scarcely inferior to alcohol. Glycerin is useful in keeping substances moist owing to its tendency to absorb water from the air. It is a valuable emollient in many skin diseases, and its agreeable taste and non-poisonous properties adapt it for many purposes. When glycerin is acted on by nitric acid, nitroglycerin, a powerful explosive, is formed. This is used in preparation of dynamite and other high explosives. It is sometimes called glonoin, and trinitrin. A 1% alcoholic solution is official. Internally, glycerin is employed as a demulcent for coughs, sore throat, and hoarseness; as an adjuvant laxative and as a vermicide for intestinal trichinae, or muscle threadworm. It might be well to say that its chief uses are as a solvent, a vehicle, a flavor, as an excipient, and as a preservative for pharmaceutical preparations.

Administered in the form of a suppository, rectally, glycerin acts as a laxative. It should not, however, be employed too frequently as, in such cases, it ceases to be of value.

7. Petrolatum (Vaseline, Soft Paraffin, Petroleum Jelly)

a. White petrolatum
b. Liquid petrolatum (liquid paraffin, mineral oil) - dose, 15 cc.

Petrolatum is widely used as a base for ointments, although it is not so readily absorbed as are some other bases. Special trade-marked brands of petrolatum are known as cosmoline, vaseline, albolene, etc. White petrolatum is similar to yellow petrolatum in uses and characteristics. It is often preferred because of its freedom from color. It is employed as a basis for ointments and cerates. Liquid petrolatum is used as a basis for medicinal preparations, for spraying the nasal passages, and as a laxative, its efficiency being due to mechanical lubrication. The so-called 'Russian Oil' consists of naphthenes, instead of the homologues of methane, which occur usually in American petrolatum. There are some American oil wells which yield naphthene. It is said that the heavy oils, which consist of naphthene, are the only oils which will make a permanent emulsion, and give no effect of leakage. The lighter oils are used for spraying. Because of the widespread use of this oil as a laxative, it has been sold under many special names.

8. Almond

a. Sweet almond.
b. Expressed oil of almond.

Sweet almond finds its use in the form of the expressed oil of almond. This is used as an emollient and must never be confused with the essential oil. Many customers, wishing this oil, simply ask for almond oil and if the pharmacist dispenses the essential oil without asking any questions, an error is made which might have serious results. You will recall that the essential oil, or oil of bitter almond, contains the deadly poison, hydrocyanic acid. The expressed oil is very popular for use in hand lotions and ointment creams. The nutrient value is highly esteemed, especially in the form of almond bread for diabetics, since it contains comparatively little starch but plenty of fat and some protein.

II.

ALIMENTARY TRACT

A. CARMINATIVES

Carminatives are drugs which counteract flatulence and colic. Their method of action in connection with relieving the discomforts of gas, etc., is not clearly understood. All drugs of this class contain volatile oil and have a pungent, aromatic odor and taste.

1. Peppermint - dose, 4 grams

   a. Oil of peppermint - dose, 0.1 cc.
   b. Peppermint water - dose, 15 cc.
   c. Spirit of peppermint - (Essence of peppermint) - dose, 1 cc.
   d. Menthol - dose, 0.06 grams

   The properties of peppermint are due to the presence of about 2% of a volatile oil, which contains menthol. It is largely cultivated and is a very fine aromatic stimulant. It is used in making spirit of peppermint. The oil of peppermint is a local anesthetic, antiseptic, and carminative. It is much used in sick stomach, and also as a flavor and as an ingredient in the official preparations, such as, peppermint water, spirit of peppermint, etc. Peppermint water is used almost exclusively as a flavored vehicle. The spirit of peppermint is a valuable carminative, and a gastric stimulant, in flatulence and nausea. The oil is usually employed for flavoring. Menthol is largely used compressed into cones as a local remedy in neuralgia and headaches, and as a constituent in solutions for nasal and throat sprays, etc. It is also much used in throat lozenges and as a local application to relieve itching.

2. Spearmint - dose, 4 grams.

   a. Oil of spearmint - dose, 0.1 cc.
   b. Spearmint water - dose, 15 cc.
   c. Spirit of spearmint - dose, 1 cc.

   The spearmint is the mint of culinary use in preparing mint sauce and also well-known mint julep. The volatile oil is the only constituent of importance in this plant and the yield is from one-half to one percent. This oil is used sometimes as a carminative and very extensively as a flavoring agent, especially for chewing gum. Spearmint water, like peppermint water, is used almost completely as a flavored vehicle. The spirit of spearmint is used as a carminative.

3. Ginger - dose, 0.8 grams

   a. Tincture of ginger - dose, 2 cc.
   b. Syrup of ginger - dose, 10 cc.

   Ginger owes its virtues to about 4% of volatile oil which is soluble in alcohol and ether. Ginger is used as an intestinal stimulant and carminative in colic, diarrhea. The most commonly used form for this purpose is the tincture. The syrup is used largely as a vehicle in prescriptions for colic and diarrhea.

4. Capsicum (Cayenne pepper) - dose, 0.06 grams

   a. Tincture of capsicum - dose, 0.5 cc.
   b. Oleoresin of capsicum

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same combination, as was done in many compound digestive elixirs which are still in demand as physicians insist upon prescribing them however illogical their constitution. It should not be given in combination with acid because it is in this combination that its activity is destroyed. It performs its most valuable digestive action in the presence of weak alkalies. From this we may deduce that pancreatin performs its action in the intestines, which are normally alkaline in reaction, while pepsin is most active in the stomach which is normally acid.

C. SIMPLE BITTERS.

Bitters are agents which increase the appetite and the secretion of the digestive juices. The benefits derived from them are fully psychological.

1. Gentian - dose, 1 gram.

2. Quassia (bitter weed) - dose, 0.8 gram.

Both of these drugs are used mainly as simple bitter tonics. However, quassia is sometimes used in the form of an infusion; as an enema to destroy pinworm.

D. LAXATIVES.

1. Castor Oil -(Oleum Ricini) - 15-30 cc

The administration of this oil is greatly facilitated by adding the dose extemporaneously to a small amount of soda water, flavored with sarsaparilla syrup, as much foam as possible being developed. The glass should be well-wetted with water and the oil carefully poured into the center of the glass without touching the sides. It may also be administered in capsules, or by mixing it with an equal bulk of aromatic syrup of rhubarb and shaking thoroughly before administering.

2. Agar - dose, 10 grams

This drug is widely used in culture media for bacteriological work. It is also administered internally in doses of 8 to 12 grams, to give moisture and bulk to the intestinal contents in chronic constipation.

E. CATHARTICS

1. Cascara Sagrada - dose, 1 gram

a. Extract of Cascara Sagrada - dose, 0.3 gram
b. Fluidextract of Cascara Sagrada - dose, 1 cc.
c. Aromatic Fluidextract of Cascara Sagrada - dose, 2 cc.

Cascara, by action on the large intestine, serves as a very fine cathartic and produces little or no griping. For this reason, it has become a very popular remedy for chronic constipation. It is

as near the ideal cathartic as is obtainable. It produces its cathartic action through stimulating the peristaltic action of the intestines, and one of its finest features is that susceptibility is not lost by continued use, so that the drug may be gradually withdrawn if new habits are formed. The fluidextract is a form very commonly used as a cathartic. This particular form is intensely bitter, but it is sometimes desired for its stomachic effect. To overcome the bitterness of taste, the aromatic fluidextract is used. The uses are the same as for the plain fluidextract, but the dose is much larger.

2. Rhubarb - dose, 1 gram.

a. Extract of Rhubarb - dose, 0.5 gram
b. Fluidextract of Rhubarb - dose, 1 cc.
c. Tincture of Rhubarb - dose, 4 cc.
d. Aromatic Syrup of Rhubarb - dose, 10 cc.
e. Compound Powder of Rhubarb - dose, 2 grams.

The therapeutic properties of rhubarb depend upon the valuable natural combination of its cathartic and astringent constituent. In small doses, the astringent action predominates and can be used for diarrhea and other intestinal disorders as an astringent bitter. In larger amounts the laxative properties are shown in a movement after six to ten hours, with little or no colic. Rhubarb is, therefore, considered suitable to chronic constipation of children and weakened patients. The fluidextract, besides being used as a cathartic, is sometimes used in making other rhubarb preparations. Tincture is used almost exclusively in preparing the compound syrup of rhubarb. Aromatic syrup is a laxative of special value for children who suffer diarrhea because of the combined astringent and laxative action. It is especially valuable in the treatment of infants but is too weak for adults. When mixed with equal volume of castor oil, it makes a palatable laxative which is readily administered, even to children. The compound powder is used as a laxative and antacid.

3. Aloe - dose, 0.25 gram

a. Aloin - dose, 0.015 gram
b. Pills of Aloe - dose, 2 pills

Aloe contains aloin, traces of emodin, a trace of volatile oil and a substance which has been improperly called resin. It is used as a cathartic, this action being due to its active constituent, aloin. Aloe is a very old remedy, having been used by the Egyptians centuries ago. In very small doses it has been given as a stomachic, especially with iron, the constipating tendency is thus counteracted. In larger doses, it is very strongly laxative. It is said that the continual use of aloe does not lead to less efficiency and that it is of particular value in habitual constipation, but it probably has no advantage over cascara. Aloin is a pentoside or mixture of pentosides

obtained from aloe, it varies in chemical composition and in physical and chemical properties according to the variety of aloe from which it is obtained. It is used as a cathartic, and, as previously stated, in smaller doses as a laxative. The pills have exactly the same use as the aloe, the advantage being that they are in a little more palatable form, aloe itself being extremely bitter.

4. Phenolphthalein - dose, 0.06 gram

Phenolphthalein is largely employed internally as a cathartic and is a very common ingredient of proprietery preparations on the market. Its exact method of action is not clearly understood although has been known since 1900. It takes place partially in the small, and more in the large bowel. It has a disadvantage of having a tendency to become habit forming when used over a considerable period of time. This drug is widely used in chemistry as an indicator, especially in analytical work.

5. Senna - dose, 2 grams

a. Fluidextract of Senna - dose, 2 cc.
b. Syrup of Senna - dose, 8 cc.

Senna is the most drastic of this class of drugs, and because of this drastic action, and the griping it produces, is most often combined with aromatics or carminatives. It is used often in the form of an infusion as a cathartic. The fluidextract is also used as a cathartic and frequently produces griping when used alone. Its main use is to make other preparations. The syrup acts as a good laxative, frequently in combination with other drugs. Coriander is usually added to senna on the assumption that it lessens its griping action.

F. DRASTICS

1. Croton Oil - dose, 0.06 cc.

Croton oil is one of the most powerful purgatives known. As little as one drop causes a burning in the mouth and stomach, sometimes vomiting, and much pain in the abdomen. After an hour or two, repeated stools, which are first hard, then watery. Larger doses are usually fatal. When applied to the skin externally, it causes severe burning and blistering. It is very seldom employed in present day medicine as it is so dangerous.

2. Podophyllum (May Apple, Mandrake)

a. Resin of Podophyllum (Podophyllin) - dose, 0.01 gram

The use of this drug was handed down from the American Indians. In small doses the drug is much used as a laxative for chronic constipation. This drug seems to have the advantage over a num-

ber of other drugs used for the same purpose, in that it does not bring on a demand for its continued or habitual use, even though having been used for a long period of time. It must be used with caution, however, since in large doses it is a powerful substance, as little as a half a gram having been fatal in one case.

3. Jalap - dose, 1 gram

This is one of the most popular drastics. It is much milder than most of the others and also less disagreeable, and, at the same time, causes a very small amount of intestinal irritation.

G. SALINES

1. Magnesium

a. Magnesium Oxide (Light Magnesia) - dose, 0.25 gram
b. Heavy Magnesium Oxide (Heavy Magnesia)
dose - 0.25 gram
c. Magnesia Magma (Milk of Magnesia)
dose - antacid, 4 cc.; laxative, 15 cc.
d. Magnesium Carbonate (Light Magnesium Carbonate)
dose - antacid, 0.6 gram; laxative, 8 grams
e. Solution of Magnesium Citrate (Citrate of Magnesia)
dose - 7 fluid ounces
f. Magnesium Sulfate (Epsom Salts) - dose, 15 grams

Magnesium oxide, or magnesia, is popularly used as an antacid in doses of about 0.25 grams. In administering the magnesia, it should be added to the diluent whichever it be, water or milk, and not vice versa. If it fails to act when used as a laxative, it should be followed by lemon juice, or some other form of citric acid. The uses and doses of heavy magnesia are the same as those of the light magnesia.

Milk of magnesia is used as an antacid, as a laxative, and the addition of a flavor as suggested by some authors, renders it very acceptable when used as an antacid mouth wash, for which purpose it is frequently used under a dentist's orders. The usual dose as an antacid is 4 cc. and as a laxative, 15 cc. In small doses, magnesium carbonate is antacid and in larger doses is cathartic. It is also employed externally as an absorbent or drying powder. It was at one time largely employed in making medicated waters to assist in diffusing the oil used in preparing them, but, being slightly soluble, it always imparted an alkaline reaction to the water which is especially dangerous in dispensing, as aromatic waters made with it will cause a gradual precipitation of free alkaloids, like strychnine, atropine, etc., when a salt of the alkaloid is dissolved in such an aromatic water. Its use in this manner is not recognized by the U.S.P.

Citrate of magnesia, or citrate, as it is usually called, is one of the most agreeable saline cathartics available. It was formerly given to adults in the quantity of the official formula, of 12 fluid ounces, although the U.S.P. 11 changed the average dose to 7 fluid ounces, which is more in harmony with the frequent practice of administering one half of the contents of the regular 12 ounce bottle. Magnesium sulfate, which at one time sold for a very high price, was first obtained from the celebrated spring at Epsom, the English Spa, hence the common name. In continental Europe it is frequently called Seidleitz Salt because it is the principal active constituent in the Seidleitz Spring of Germany. In America, it has been called Crab Orchard Salt, because it was obtained from the waters of a spring by that name in Kentucky.

Magnesium sulfate is a valuable hydragogue cathartic. If dissolved in ice water its nauseous taste is not so perceptible as when water of ordinary temperature is used. It may be still further disguised by the use of orange juice. Hot, concentrated, aqueous solutions of magnesium sulfate, (about 1 pound per pint of water), are extensively used in the treatment of deep seated infections, cloths being saturated and applied while hot. The action is much like that of a poultice and has the advantage of being sterile. All magnesium compounds can be used as laxatives, but some of them, like the nitrates, are readily absorbed to give toxicity. The carbonates, magma and oxide, are of less efficiency than the sulfate but have the advantage of being antacid, in fact, the usual aim in using them is to relieve dyspepsia, nausea, heartburn, sick headache, rheumatic and gouty pains, and other complaints attended with acidity, purgation being merely an additional quality. The carbonate may cause some flatulence from carbon dioxide, but the oxide is free from this possibility and is non-irritating. Both have been employed as dusting powders and pastes for ulcers and burns. The oxide is considered an antidote for arsenic poisoning. Magnesium citrate solution is a popular and agreeable laxative, and magnesium phosphate has been introduced as an antacid with the advantage of not causing systemic alkalinization.

2. <u>Sodium Sulfate</u> - (Glauber's Salt) - dose, 15 grams

This drug is widely used in veterinary practice for administration to animals, but its use as human medicine is somewhat limited, not because of its inefficiency, or lack of value, but due to its very disagreeable taste. The taste may be corrocted to some extent by acids and effervescing mixtures. However, the magnesium sulfate usually replaces this salt for human use.

3. <u>Tartrates</u>

a. Sodium Potassium Tartrate (Rochelle Salt) - dose, 10 grams
b. Compound Effervescing Powder (Seidleitz Powder, Effervescent Tartrated Soda Powder)

c. Potassium Bitartrate (Cream of Tartar, Acid Potassium Tartrate) - dose, 2 grams

The tartrates provide a means of administering a cathartic drug which, at the same time, has a pleasant taste due to the effervescence produced when dissolved in water. While the tartrates are used primarily for their cathartic action, they are quite readily absorbed by the system and hence, are also diuretic.

4. Sodium Phosphate - dose, 4 grams

a. Effervescent Sodium Phosphate - dose, 10 grams
b. Exsiccated Sodium Phosphate - dose, 2 grams

Sodium phosphate is used as a laxative particularly for children on account of its mild action and its lack of being disagreeable. The effervescent salt furnishes a pleasant means of administering sodium phosphate, as when it is dissolved in water, effervescence occurs, liberating carbon dioxide and producing a somewhat refreshing taste. The exsiccated sodium phosphate is used primarily in making the effervescent sodium phosphate, but should be freshly dried as it otherwise will be variable in its water content, since it rapidly absorbs water if exposed to moist atmosphere, as much as 15 to 20 percent often being present.

H. INTESTINAL ANTISEPTICS

Many investigators have tried, over long periods of time, to find a drug, which, when administered by mouth, will pass into the intestines and act as an antiseptic. However, very few drugs have survived the test. It seems reasonable, and has been generally accepted, that to find a drug or substance which is powerful enough in the intestine to destroy the bacteria, will also have an irritating and destructive action on the host tissue, and, too, in the normal intestine and bowel, there are bacteria which are necessary to proper putrefaction and elimination. These, too, would be destroyed if an antiseptic as we have been speaking of should be found. About all that can be expected from a drug classed as an intestinal antiseptic, is one which will perhaps restrict the growth of the undesirable bacteria which are present under certain conditions. By far the best measures to reduce putrefaction, are diet and purgation, and these are usually as efficient as is possible. If drugs are to be used, they must be so chosen that they will be little acted upon in the upper intestinal tract, otherwise they would be destroyed there, absorbed, or otherwise broken down until by the time they reach the lower intestines, the point for which they were intended, they will have lost their antiseptic value. The ideal substance should have maximum bactericidal character combined with minimum solubility and absorption, but should be free from irritating effects. Many have been tried, but as previously stated, few have survived the test. The ones now in common use are salol, and some phenols.

1. Phenyl Salicylate (Salol) - dose, 0.3 grams

In the body, salol is split into phenol and salicylic acid, obtaining its antiseptic action, of course, from the phenol. The drug itself is of no value until this action has taken place in the system. This drug is considered by some to be the best intestinal antiseptic obtainable and is probably as efficient as any that has been used, although many investigators do report no results whatsoever. This drug also gives some of the action of the salicylates, due to the formation of the salicylic acid upon the splitting of the drug in the system.

I. Antacids

1. Lime

a. Calcium oxide (lime) (slaked lime).
b. Solution of calcium hydroxide (limewater) dose 15 cc.
c. Lime liniment (Carron Oil)

Externally lime acts as an escharotic. In the pharmacopiea calcium hydroxide has replaced lime as it is more stable and more readily available and of a quality more suitable for medicinal use than the lime usually obtainable. Unless protected from air lime soon becomes unfit for use due to the action of carbon dioxide and partial hydration from moisture in the air. Calcium hydroxide or slaked lime is prepared by adding a calculated amount of water to especially prepared calcium oxide. This form of lime has replaced the freshly burned lime which was usually bought from some builders supply house and consequently was contaminated with impurities. This new product is readily available in an excellent quality. Solution of calcium hydroxide is prepared by adding a calculated amount of calcium oxide to distilled water, agitating for a period of hours, and then allowing the excess to settle out. The clear solution is decanted and used. Lime water is very extensively used in pharmacies. The object of keeping a supply of undissolved lime is to insure saturated solution. Lime is not very soluble in water and less soluble in hot water than cold, which is an unusual phenomenon, consequently when the solution is heated a deposition of lime takes place which is re-dissolved in cooling. In medicine lime water is used quite extensively to check nausea, although its value has been apparently over-estimated. The amount of lime the solution actually contains is so small that it would require almost 8 ounces to do any good at all. It is usually administered with milk when used for correcting acidity, especially in infant feeding. It is employed externally to allay inflammation and in washes of various kinds. It has been used extensively, but apparently without value to supplement infant feeding, the idea being that it aided in the formation of teeth. Limewater unites with carbon dioxide to

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4. Potassium bicarbonate - dose, 1 gram.

Potassium bicarbonate is used for much the same purposes as is the sodium bicarbonate. The latter, is much more extensively used, probably for the reason that it is found in every kitchen throughout the land in the form of baking soda. All of the bicarbonates render the urine alkaline and increase the total output. This may be useful in infectious diseases of the bladder and urethra and in preventing the formation of kidney stones. Although the bicarbonate has no effect directly on the oxidation and utilization of sugar, it is apparently useful in diabetis probably by furnishing a more alkaline medium which may favor glucose metabolism. Sodium bicarbonate is sometimes used to replace blood-loss in hemorrhage or operations, at times finding preference over saline solution.

EMETICS

Emetics are substances which produce an emptying or expulsion of the stomach's contents. This action may be induced by one of two different ways. It may be done by what is known as local action upon the stomach or alementary tract, or the emesis may be brought about by stimulating the vomiting center in the medulla. Undoubtedly most of them act in the former method. Accompanying vomiting there is always a feeling of weakness, paleness, increased perspiration of the patient followed by a feeling of depression. These may or may not be secondary symptoms. Emetics find their use mostly in cases of poisoning when it is desired to remove from the stomach anything which has been taken either accidentally or by an individual with the intent to end his life. Oftentimes one eats food, which for some reason upsets him and it becomes desirous of emptying the stomach contents.

The following is a list of the more common emetics which have proven effective:

1. Mustard
2. Zinc sulphate
3. Copper sulphate
4. Ipecac
5. Antimony and potassium tartrate (tartar emetic)
6. Warm water
7. Apomorphine

Of all the emetics listed above perhaps the one most readily available and consequently most commonly used, is mustard. Although this is a very unpleasant emetic, it is at the same time very efficient, and can be found in most household cabinets. A dose as an emetic ranges from 4 to 12 grams. Zinc sulphate is perhaps a better emetic than is mustard, but has the disadvantage of not being so easily obtained. When given in doses of 20 grains dissolved in water it usually produces the desired results in a very few minutes. If emesis does not occur within about five minutes, the dose may be repeated. Copper sulphate in doses of from 5 to 12 grains may be used, but is not so desirable. Ipecac is an efficient

emetic in doses of 1 gram. The fact that this drug is also an expectorant in smaller doses, makes it useful in treatment of paroxysms of whooping cough. While tarter emetic will work it is now rarely used as an emetic probably because of the fact that it is poisonous. It is now employed chiefly as a diaphorotic and expectorant.

Large quantities of tepid water will in most cases produce good results as an emetic. The water must not be hot nor must it be cold, but just the temperature in which it is sickening to drink.

Apomorphine, although obtained from morphine, is entirely devoid of narcotic properties. In doses of 1 milligram, it acts as an expectorant, but when the dose is increased to 5 milligrams. it is a powerful emetic. The emetic action is entirely a central action because it is not prevented by bismuth or other local anti emetics. The only thing that will stop the emesis in the administration of apomorphine is to give a dose of some narcotic such as morophine. Caution must be exercised in employing this drug as an emetic in order to avoid excessive emesis. Large amounts too give delirium and convulsions and then asphyxia. This is the most reliable emetic we have. It is administered by mouth or hypodermically. The action takes place within a very few minutes. It can rarely be used by other than a physician, for the reason that it is still on the narcotic list and can be obtained only on a prescription properly signed by a physician.

III

DRUGS ACTING LOCALLY ON THE DISEASE ITSELF

A ANTISEPTICS.

1. Boric acid, dose 0.5 grams.
2. Glycerite of boroglycerin (glycerin of boric acid)
3. Ointment of boric acid
4. Sodium borate (borax), dose 0.75 grams
5. Sodium perborate, dose 0.06 grams.

Boric acid is used as a mild dressing for inflamed surfaces either in the form of a wash or an ointment. It is very feebly germicidal, but is distincly an antiseptic and causes very little irritation. Its use as a preservative in beverages and food is prohibited by national and state legislation. The powdered boric acid may be employed as anon-irritant dusting powder in surgery and in skin diseases. Borax has much the same action as boric acid although it is used usually for different purpose. It is a common ingredient in many insect powders, but it is also used as a dressing, as an eye wash, and sometimes in the form of an ointment. Sodium perborate with water gives hydrogen peroxide which can be used for germicidal purooses. It is a very common ingredient in tooth powder, in fact some tooth powders have nothing but sodium perborate flavored with some flavoring ingredient. Cintment of boric acid is used in treatment

of mild skin diseases and also in treatment of burns. Sodium borate in addition to being used as mentioned finds considerable use as an antiseptic dusting powder or as a wash in aqueous solution for wounds. When used in treatment of Trench mouth two teaspoonfuls are dissolved in a tumbler of warm water and used as a mouth wash and gargle every hour.

2. Silver

a. Silver nitrate, dose 0.01 grams
b. Fused silver nitrate(moulded silver nitrate, lunar caustic)
c. Mild silver protein (mild protargin, argyrol, silvol, solar-gentum).
d. Strong silver protein (strong protargin, protargol)
e. Neo-silvol (colloidal silver iodide)

Silver nitrate is used externally as a caustic and germicide and in diluted solution is valuable for its antiseptic powers and is widly employed as a local application to inflamed mucus membranes as well as wounds. A one per cent solution is used to prevent eye infection in new born infants. Two drops are placed in each eye. The fused silver nitrate comes in forms of sticks and is employed as a caustic in the removal of warts and other skin growths. The mild silver protein and strong silver protein finds much the same uses as does silver nitrate. The mild silver protein is used quite extensively as eye drops and nose drops, in the form of usually a ten per cent solution. Strong silver protein is fairly efficient as an antiseptic for mucous membranes especially against gonococcus infection. It is less powerful than silver nitrate, but this disadvantage may be overcome by the use of stronger solutions. Solutions of 0.25 per cent to 2 per cent are used for injections, and 1:1000 and 1:2000 for irrigation purposes.

Neo silvol, another colloidal silver compound, is used mainly on mucous membranes, eye, urethra, bladder, nose, throat, etc.

Caution must be observed in the use of fused silver nitrate because of the fact that it is so powerfully caustic. As previously stated, this comes in the form of sticks or cones, and so the fingers must be protected while applying it.

Death has resulted more than once through the careless use of silver nitrate in cauterizing the throat, the cone having slipped out of the fingers and then been swallowed by the patient.

3. Phenol (carbolic acid) dose 0.06 grams

a. Liquefied phenol (liquefied carbolic acid) dose 0.06 cc
b. Ointment of phenol
c. Glycerite of phenol (glycerine of phenol)

Phenol is one of the most largely used disinfectants and because of this fact great caution must be observed in dispensing it as it is employed frequently for suicidal purposes. When applied to the skin or mucous membranes it cauterizes and produces blanching. Alcohol applied at once to the cauterized parts causes the disappearance of the white spot. When diluted with an equal volume of glycerine it becomes miscible with water in any proportion. Phenol is used internally in the treatment of various digestive disorders and as a urinary antiseptic. As an external remedy it is used for anaesthetic and antiseptic action in skin diseases. It is also largely used in local application in nose and throat infection as a surgical disinfectant. Liquefied phenol was introduced in the pharmacopiea to furnish a uniform and convenient method of using phenol in a concentrated liquid form. The practice of adding ten per cent water to crystallized phenol has long been followed, this liquid being more convenient for the compounding of prescriptions than crystals. In using it, allowance must, of course, be made for the presence of ten per cent of water. Phenol ointment finds its only use as an antiseptic dressing. Glycerite of phenol is used for preparing antiseptic dilutions of phenol. It mixes in any proportion with water. It is also used as an addition to gargle and mouth washes.

4. Picric acid Dose, 0.03 grams.

Picric acid is used as an antiseptic in the form of a one per cent aqueous solution for burns. Also used for an astringent and antiseptic effect in skin diseases. In urinalysis it is employed as an agent to detect and estimate albumin. It is very explosive when dry, therefore, great caution concerning transportation must be observed. It has been employed internally as an antipyretic.

5. Creosote dose 0.25 cc.

a. Creosote carbonate (creosotal) dose 1 gram.

Creosote is used internally as an expectorant in bronchitis and as a gastro-intestinal antiseptic. It is occasionally employed externally for its disinfectant action. It is applied upon cotton to exposed nerve tissue in teeth and used in packs as a local anaesthetic. It is also homostatic when applied to bleeding surfaces. When taken internally undiluted and in large doses it is a powerful poison. The administration of mucilagenous drinks and the prompt evacuation of the stomach by a stomach pump would be the best treatment, no antidote to poisoning by creosote being known. Creosote carbonate is claimed to be non-toxic and devoid of irritating properties. It is employed as an expectorant.

6. Guaicol, dose 0.05 cc.

Guaicol is employed internally as an expectorant in bronchitis and in tuberculosis.

7. Iodine, dose 0.01 gram.

a. Tincture of iodine, dose 0.1 cc.
b. Compound solution of iodine, dose 0.2 cc (Lugols solution)
c. Iodine ointment

Iodine is very largely used in medicine. Internally it is a valuable alterative useful in goiter, syphilis, rheumatism and other chronic diseases. Locally it is used as a counter irritant and is a germicide for sterilizing the skin and wounds.

The tincture of iodine is very widely used. Applied locally as a counter irritant and also for its affect in sprains, chronic rheumatism, gout, chilblains, enlarged glands and under many other conditions. It should not be used on the skin in repeated applications as the evaporation of the alcohol leaves almost pure iodine which is very irritating and caustic. It is extensively used to sterilize the skin for minor operations or injections, for disinfecting wounds and in treating erysipelas. For these purposes a half strength preparation is usually employed. The new USP mild tincture of iodine is intended as a first aid antiseptic dressing, and for use in preparing the field for operation, and will faithfully replace the half strength tincture now so widly used. The compound solution of iodine affords a most efficient means for administering iodine internally. And whenever internal administration is indicated this form is used. Ointment of iodine is antiseptic. It is used mainly for its counter irritant action.

8. Chlorine

a. Solution chlorinated soda (Labarraque's solution)
b. Surgical solution of chlorinated soda (modified Dakin's solution)
c. Chlorinated lime (calx chlorinata, chloride of lime, bleaching powder)
d. Chloramine powder (chloramine-T, chlorazene)
e. Dichloramine (Dichloramine-T)

Labarraque's solution is used as a cleansing agent for such purposes as to wash floors, disinfect the hands, disinfecting excreta and sputum, etc. This solution corrodes metals and bleaches and otherwise injures fabrics. Surgical solution of chlorinated soda or modified Dakin's solution is now official under the name of diluted solution of sodium hypocholrite. This solution is a rapid germicide and an

efficient antiseptic for infected wounds when it is used after free incision in cleansing and applied by practically continuous irrigation. Its strength and reaction are easily adjusted so as to be practically non-irritant to wounds. The skin, however, is subject to irritation and must be protected by petrolatum.. The solution does not precipitate protein, but on the contrary dissolves necrotic tissue and thus helps to keep the wound clean. On the other hand it dissolves silk ligatures and loosens cat-gut thus favoring secondary hemorrhage.. The solution is practically non-toxic when used externally. It should not be injected into the peritoneum. For external use it is full strength. It is claimed that below a 0.4% solution of sodium hypochlorite the clinical effect of the hypochlorite solution is nil, while above 0.5% the irritating effect on the skin becomes serious. A SOLUTION CHLORAMINE-T IN WATER IS NOT IDENTICAL WITH DAKIN'S SOLUTION, AND SHOULD NOT BE DISPENSED AS SUCH.

Dichloramine-T an effective germicide through its content of active chlorine is only sparingly soluble in water but soluble in chlorinated eucalyptol or chlorinated paraffin. Chlorinated paraffin or chlorcosane of the USP is a solvent of the latter type. The solution produces a gradual sustained antiseptic action. It is more irritant than chloramine-T but also more solvent. It should not be administered internally. Dichloramine-T is claimed to be useful in the prevention and treatment of diseases of the nose and throat. It has been used with success when applied to wounds. Dichloramine-T dissolved in chlorinated paraffin is used in concentrations from one half to ten per cent. In nasopharyngeal work from one to two per cent solution is employed. For application to wounds five per cent solution. Solution of dichloramine in chlorinated paraffin is not very stable and should not be kept for more than two or three days. At times the solution may become irritating to the skin because of the formation of hydrochloric acid. Both dichloramine-T powder and solution should be protected from the sunlight to prevent decomposition.

9. Manganese.

a. Potassium permanganate, dose 0.06 grams.
b. Zinc permanganate.

As a therapeutic agent potassium permanganate is employed as a disinfectant and deodorant. Also as an antidote to morphine, strychnine and snake poison. Formerly it was employed internally for menstrual disorders, but is of little value. It is one of the most powerful oxidizing agents known Chemically; it is used as a volumetric test and oxidizer for which it is admirably adapted on account of the distinctness of its color reaction. Although the difficulty of keeping the solution from partial decomposition is a serious annoyance and interferes with the accuracy of the estimation. When potassium permanganate comes in contact with organic

matter it is decomposed with a liberation of oxygen.

Zinc permanganate is used as an antiseptic and astringent and is used in urethritis as an injection or douche in 1:400 solution.

10. Iodoform dose, 0.25 grams.

a. Iodoform ointment

Iodoform is used very largely as an external application for wounds and ulcers. It is also employed in supositories for hemorrhoids and occasionally internally as an alterative. Iodoform ointment is used in the treatment of wounds, ulcers and other old sores.

11. Formaldehyde

a. Solution of formaldehyde (formalin)

Formaldehyde being a gas, it is rarely used except in the form of solution. This solution is externally used as a disinfectant and deodorant. It was formerly employed for preserving milk, meat and other articles of food likely to spoil through fermentation, but its use is now prohibited by national and state laws. It is, however, used for disinfecting apartments which have been subjected to infection by spraying it on sheets and in the room, or a vapor may be conducted into the room from a generator of which there are numerous forms on the market. The most common of these forms is known as the formaldehyde candle.

12. Resorcinol

a. Mild resorcinol paste (Lassar's mild resorcinol paste)

Resorcinal is an antiseptic resembling phenol in its physiological action, but is much less powerful. It is used mainly externally as a gastric antiseptic. It is quite a common ingredient in hair and scalp preparations and used for scalp diseases and infection. Lassar's paste is used in the treatment of minor skin diseases and irritation.

13. Sulphur

a. Sublimed sulphur (Flowers of sulphur) dose, 4 grams.
b. Sulphur ointment.
c. Compound sulphur ointment. (Wilkinson's Ointment, Hebra's itch Ointment).
d. Washed sulphur (Sulphur lotum) dose 4 grams.

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3. Sodium Nitrite, dose 0.06 grams
4. Spirit of Ethyl Nitrite (spirit of nitrous ether, sweet spirit of nitre), dose 2 cc.

The Nitrite group as used in medicine comprises salts or esters of nitrous acid and certain organic nitrates which are reduced to nitrite in the organism. The chief members have been listed above. The characteristic action of this group is vasodilation, with a fall of the blood pressure. The members differ chiefly in the promptness and duration of their effect, Amyl nitrite being the quickest, though its action is of correspondingly short duration.

When given by inhalation, amyl nitrite produces almost instantaneous dilatation of the peripheral blood vessels, shown by redness of the skin, beginning in the head and neck, rapidly spreading over the body, and sometimes extending to the lower extremities. This is promptly followed by dilatation of other vessels so that the blood pressure soon falls. The lowered pressure increases the heart rate. There is a feeling of fullness in the head, often accompanied by headache; the breathing is rapid. With excessive doses, or over-susceptibility, unconsciousness may supervene; and convulsions occasionally occur after toxic doses. Large doses kill by respiratory paralysis. It may produce methemoglobin in the blood and cause the excretion of sugar in the urine. It is used chiefly in angina pectoris, which is a neuralgia of the heart. It is also employed to some extent to relieve spasm in epilepsy. Amyl nitrite is given to reduce the blood pressure in hemorrhage due to rupture of the blood vessel in the lungs, brain, or other organ, in consequence of elevated blood pressure, but in hemorrhage with normal blood pressure it may do harm. It is also used in bronchial asthma. Although nitroglycerin is a nitrate, it has the physiological action of nitrite, but acts more slowly than amyl nitrite. Glyceryl trinitrate may be given when it is desired to effect a reduction of the arterial pressure, but it becomes inefficient with continued use. It may be prescribed in arteriosclerosis, and in nephritis, in which high blood pressure is a common symptom. It is used with success in some cases of angina pectoris. It is sometimes used with digitalis, when it is desired to produce vasodilatation, and thus lessen the work of the heart. Sodium nitrite has the characteristic properties of the nitrites, and resembles nitroglycerin in its action, though its effect is manifested more slowly and is somewhat more lasting. It sometimes produces gastric disturbance.

Spirit of ethyl nitrite is chiefly employed as a diaphoretic in mild fever, and is a diuretic, especially for children.

B VASOCONSTRICTORS

Vasoconstrictors are drugs or substances which cause a constriction of the blood vessels.

1. Ephedrine
   a. Ephedrine hydrochloride, dose 0.025 grams.
   b. Ephedrine sulfate, dose 0.025 grams.

2. Epinephrine (Adrenalin, suprarenin) dose 0.0005 grams.

Ephedrine excites the sympathetic nervous system and produces effects resembling those of epinephrine. It differs from the latter in that it is slower to act and its effect is more prolonged. It also exerts a direct depressent action on smooth and cardiac muscle. It produces a rather lasting rise of blood pressure on intravenous or intramuscular injection, due mainly to vasoconstriction. Other effects, similar to those of epinephrine, are dilatation of the bronchi, and mydriasis, which means dilatation of the pupil of the eye, after local, or systemic administration. Thus far, the most definite indications for the usefulness of ephedrine, are for its local use to shrink the nasal membrane. Ephedrine has proved effective in some cases of asthma, but in a considerable proportion of cases it has failed partially or completely. Moreover, its oral administration generally causes symptoms of the anxiety complex, and this may constitute a definite contraindication to its use. The administration of epinephrine causes a sudden rise of blood pressure by contraction of the arteries. The pulse is slowed as the result of the increased blood pressure. The heart is stimulated directly, but the resistence offered by the contraction of blood vessels is such that at times the heart is unable to overcome it and suffers passive dilatation. Intravenous injections of epinephrine are sometimes useful to stimulate the heart action and raise the blood pressure in various forms of collapse. Its efficacy, however, is limited by the brief action. It may cause delirium if injected during chloroform anesthesia. It relaxes bronchial spasms. When given by mouth in moderate doses it seldom causes any perceptible effect on the general circulation, but it is readily absorbed by mucus membrane of the nose and mouth, urethra, vagina, and rectum, producing local constriction of the blood vessel. Epinephrine acts promptly after intravenous injection, but it is destroyed rapidly. Intravenous injection is dangerous unless the dose is very small and unless it is given in great dilution and very slowly. The effect following intermuscular injection are intermediate between those following subcutaneous and intravenous injection. The chief use of epinephrine is to constrict the blood vessels by local application. For arresting hemorrhage it must be applied directly to the bleeding vessel or congested area. If the blood washes it away, the application may fail because the drug has not had time to act. Epinephrine is employed in conjunction with local anaesthetics to delay

the absorption to secure more efficient local action. It has proved very useful in relieving paroxysms of asthma for which it is applied in a spray to the nose or throat or by hypodermic injection.

C. LOCAL ANAESTHETICS

1. Cocaine, dose 0.015 gram
2. Ethyl Aminobenzoate (benzocaine, anesthesine), dose 0.3 grams
3. Procaine hydrochloride (Novocaine)
4. Butyn

Local anaesthetics are substances which are applied to inactivate the ends of sensory nerves, with the intention to prevent pain which may be subsequently produced as in minor operations. The most efficient agents for either purpose are cocaine and its substitutes. The most important action of cocaine is the paralysis of sensory nerves for direct application resulting in local anesthesia.
Cocaine is the oldest representative of the group of local anaesthetics. Numerous synthetic drugs have nearly identical action and have advantages especially in certain fields. They may be discussed together. They all have a selective depressant action on nerve fibres, especially on those of sensory nerves resulting in temporary loss of sensation but complete recovery when the drug is eliminated. The localanaesthetics, therefore, lose their local action when they are absorbed into the circulation, but if absorbed rapidly, may induce toxic or poisonous effects. It is therefore, desirable, to use smallest quantity of anaesthetic that is effective, and to confine it as close as possible to the place of operation by delaying its absorption into circulation. Toxic effects are likely to occur if the drugs are absorbed rapidly whereas slower absorption is relatively harmless. The safety depends on the prompt destruction of these substances in the body. The destruction of cocaine in the body is relatively slow and this accounts for the more frequent accidents with it. The toxic symptoms are similar for all the local anaesthetics. They begin with excitement, palpitation and fainting progress rapidly to collapse, sometimes in brief convultions. Death may occur in a few minutes. Poisoning is treated by artificial respiration and the injection of epinephrine. Cocaine was formerly used for its stimulant properties, as it produces a condition of psychic excitement in susceptible individuals. Such use, however, easily leads to habituation. The cocaine habit is very difficult to cure. Sudden withdrawal is followed by distressing symptoms, and continuance of its use results in chronic poisoning, especially characterized by mental deterioration. The Harrison Narcotic Law, a law passed by Congress in 1915 includes cocaine in its group of restricted drugs, or those which cannot be sold

except on a physician's prescription. This has done much to reduce the number of cocaine addicts in the various cities and communities. However, due to the fact that there are some individuals who are constantly trying to do anything to make money, or it seems to beat the law, there is a certain amount of cocaine and other narcotics bootlegged and so we do find some addicts, especially in the larger cities.

Procaine hydrochloride is probably the safest of the local anaesthetics, especially for injection anaesthesia. Its action is practically identical with cocaine so far as its anaesthetic value and properties are concerned. Ethyl Aminobenzoate or benzocaine is used for application to painful wounds and ulcers, etc., of the skin and accessible mucus membranes, for instance, after dental operations. It has been used to relieve pain of some gastric disturbances for which, however, it has little or no value.

Butyn is a local anaesthetic proposed as a substitute for cocaine particularly in surface anesthesia as for the eye, nose and throat. It has a special advantage of acting through intact mucus, almost effectively as cocaine. On the normal human eye a 0.5% solution of butyn is less effective than a one per cent solution of holocaine but more efficient than a one per cent of cocaine. Butyn solutions are non-irritant.

D. ANESTHETICS GENERAL

1. Ether, dose 1 cc
2. Chloroform, dose 0.3 cc
3. Nitrous oxide (Nitrogen monoxide, laughing gas)

General Anesthesia is useful in obliterating the perception to pain and abolishing reflexes and voluntary movement, chiefly to permit surgical operation. The ideal anesthetic would paralyze temporarily the cerebral motor and perception centers and the spinal reflexes without affecting the control of vital functions. It would be capable of easy administration and rapid recovery and would involve no after effect. However, such a substance is as yet unknown. Those which approach nearest to this are, ether, nitrous oxide, and chloroform. Ether is used mainly by inhalation for the production of anesthesia. It depresses all parts of the central nervous system, causing loss of sensation and consciousness, and abolition of the reflexes. The vital centers of the medulla are involved late in anesthesia, a fact which enchances the safety of this anesthetic. The respiratory center is the first of these to be affected. Later there is depression of the vasomotor center, and

a consequent fall of blood pressure. Ether does not produce a severely toxic action on the heart, its first effect being a moderate reflex stimulation. In the administration of ether as an anesthetic, caution should be exercised to have the ether at a distance from, and, if possible, lower than any fire or flame to avoid setting fire to the heavy, inflammable vapors. It is occasionally administered internally, particularly in the form of a spirit as an anodyne, sedative, carminative, and antispasmodic. It is sometimes mixed with oil and administered by the rectum. For anesthesia, a pure ether should be used. The U. S. Pharmacopiea contains the following warning or caution in regards to the use of ether: "CAUTION: ETHER TO BE USED FOR ANESTHESIA MUST BE PRESERVED ONLY IN SMALL, WELL CLOSED CONTAINERS AND IS NOT TO BE USED FOR THIS PURPOSE IF THE ORIGINAL CONTAINER HAS BEEN OPENED LONGER THAN 24 HOURS." However, many specimens of ether sold in larger containers meet the Pharmacopeial requirements for ether for anesthesia so far as purity is concerned.

Chloroform is administered chiefly by inhalation for the production of general anesthesia, The excitement stage resembles that of ether but it is of shorter duration. It is much more dangerous, however, many fatalities occurring by stoppage of the heart early in the administration. The anesthetic stage is also more dangerous than with ether, there being a gradual, progressive fall of the blood pressure, even if the administration is managed carefully. The fall is due to the depression of the cardiac muscles, and possibly, to that of the vasomotor center. The respiratory center is also depressed. If an excessive concentration is given, death occurs in this stage, usually by stoppage of respiration, but since the circulation is also greatly weakened, recovery is less frequent than with ether. Sometimes, especially in cardiac disease, the heart may be the first to fail. Prolonged administration is especially dangerous, often producing death after the lapse of several days, by so-called delayed chloroform poisoning. This is characterized by general fatty degeneration, especially marked in the liver and resembling acute yellow atrophy,

Chloroform is distincly less safe as an anesthetic than ether and should be employed only when ether is unavailable, or its use, for some reason, is inadmissible.

Chloroform acts locally as a penetrating and fairly powerful irritant, which may blister, if its evaporation is prevented. It is used in liniment. Taken by mouth, small doses are carminative and anodyne. It is therefore

used in gastric fermentation and colic. Excessive oral doses produce unconsciousness and coma similar to the results of its inhalation. Analgesia, for painful dressings and short operations may be produced by the inhalation of a fixed dose of 5 cc. of chloroform, which the patient administers to himself, but this is dangerous.

Nitrous Oxide causes anesthesia by its direct influence on the central nervous system. After a few, deep inspirations, the face assumes a deathly pallor and the patient becomes unconscious. Nitrous Oxide and oxygen are most frequently used as a means of producing anesthesia for brief operations and in obstetrics.

E. STIMULATION OF SECRETIONS

1. Pilocarpine

a. Pilocarpine Nitrate, dose 0.005 grams.
b. Pilocarpine Hydrochloride, dose 0.005 grams.

2. Physostigmine

a. Physostigmine Salicylate (eserine salicylate), dose 0.002 grams.

Pilocarpine finds its uses usually in the form of the nitrate or the hydrochloride. The action of both being the same. This drug stimulates the ending of the nerve. It increases secretion of the salivary, mucous, and sweat glands. It stimulates the smooth muscles of the body, generally, including the motor system of the intestines, and the bronchi. The stimulation of the cardiac branch of the vagus produced by it is unimportant in man, as it is soon followed by vagus depression, with an accelerated pulse rate. It contracts the pupil of the eye and causes spasm of the muscles of accommodation in the eye. Pilocarpine is administered internally chiefly for its diaphoretic affects, especially in nephritis. It may also be of service in certain diseases of the skin. In diseases of the eye, such as glaucoma, pilocarpine is applied locally as a weak myotic.

Physostigmine, which is practically always administered in the form of a salicylate, increases the intestinal peristalsis, and produces contraction of the pupil of the eye by local action. When instilled into one eye, it causes contraction of the pupil of that eye only. Toxic, or poisonous doses, cause slowing of the pulse, dizziness, and faintness. It is sometimes used in paralytic form of constipation. Overdosage of this drug is counteracted by atropine.

F. UTERINE STIMULANTS

1. Ergot, dose 2 grams

a. Fluidextract of ergot, dose 2 cc.

Ergot causes powerful contractions of the uterus. It tends to slow the pulse by stimulating the cardio-inhibitory center. It also produces contraction of other involuntary muscles, such as those of the blood vessels, bladder, stomach and intestines. The principal use of ergot is to prevent postpartum hemorrhage. For this purpose, a full dose is sometimes given as soon as the second stage of labor terminates, but it should not be given until the placenta has been expelled. Its use during labor should be avoided as it may cause rupture of the uterus or asphyxia of the child. It is employed as a prophylatic for after pain. The fluid-extract is a convenient form for administering ergot.

2. Pituitary, dose 0.03 grams

a. Solution of pituitary (pituitary extract), dose 1 cc.
b. Pituitary extract obstetrical, dose 1 cc.
c. Pituitary extract surgical, dose 1 cc.

3. Cotton Root Bark, dose 2 grams.

4. Hydrastis (Golden Seal), dose 2 grams.

The pituitary may be divided into three parts; anterior, intermediate, and posterior, each of which apparently liberates one or more different endocrine principals. As yet, none of these secretions have been obtained in the pure form. Their ultimate chemical nature is therefore unknown. Solutions prepared from the posterior lobe of the pituitary injected subcutaneously, are employed in postpartum as well as in other forms of uterine hemorrhage. They should not be injected during the first stage of labor because if the cervix be not fully dilated, energetic contractions may cause rupture of the uterus. The extracts have also been recommended in shock and in various other conditions of temporary low blood pressure, but they would be ineffective in advanced shock, and at best, only of temporary benefit in complete shock. The extracts should always be injected hypodermically or intramuscularly, although some activity has been seen when they are applied to the mucous membrane.

Therapeutic application of the anterior pituitary preparations are at present in a very unsettled condition. While their actions in animals are fairly well known, they have been used only to a very limited extent in human beings. It appears, therefore, that all such products until more is known about them, should be used with great caution, clinically, particularly, as it is possible for some of them to produce serious pathological state,

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The therapeutic action of belladonas is due to its content of the alkaloid atropine consequently, the action and uses are very similar to those of atropine which will follow shortly.

The application of belladona plaster to the skin induces a local anodyne effect which is employed to relieve rheumatic and neuralgic pain and soreness. It is a serviceable application in acute inflammatory conditions.

Atropine and related alkaloids depress or paralyze the endings of the vagus and other nerves of the parasympathetic system and of the nerves supplying the sweat glands. Atropine checks the secretion of the saliva so that the mouth and throat become dry. This dryness is due to some extent to a similar effect on the mucous secretions of the mouth, throat and nose. As an application of this action the drug is occasionally used to check excessive secretions of saliva in cases where such action is desired: It is also used in coryza especially in the first stage to diminish the congestion of the excessive secretions of the nasal mucous. It is said to be useful in sore throat. It is used in cases of excessive expectoration, in bronchitis etc. It also checks the secretion of saliva and mucous during anesthesia. In moderate doses atropine relaxes the blood vessels of the skin, especially that of the face and upper extremities, which become red, sometimes showing an eruption closely resembling that of scarlet fever. In larger doses it contracts the vessels and raises the blood pressure. In still larger doses a general fall of blood pressure occurs accompanied by a very rapid and feeble pulse.

The secretion of sweat is reduced by atropine. It is used for the suppression of night sweats, especially in pulmonary tuberculosis. A single dose given at night may be followed the next night by a larger dose if the first dose is not effective. The use of atropine for this purpose should be deferred as long as practicable and discontinued as soon as possible on account of its disturbing influence on digestion. This drug produces a dilatation of the pupil of the eye and paralyzes the accommodation. To produce these actions on the eye atropine is employed as a solution dropped in a conjunctival sac for the purpose of facilitating the examination of the eye with the instrument called the Ophthalmoscope. Atropine is sometimes used externally in the form of ointment of belladonna for the relief of neuralgia, especially those in which pain results from local conditions of the nerves or surrounding tissues. It has been recommended for local use in the rectum to relieve pain of hemorrhoids or fissure for which purpose it is commonly prescribed in the form suppositories.

2. Stramonium (Jimson weed, Jamestown weed), dose 0.075 grams

a. Extract of stramonium, dose 0.02 grams
b. Tincture of stramonium, dose 0.75 cc
c. Fluid extract stramonium, dose 0.075 cc

Stramonium sometimes replaces belladonna for local sedative effect and stramonium leaves are usually preferred to relax bronchial spasms in asthma where they are mixed with potassium nitrate and smoked in cigarette form.

3. Hyoscyamus (henbane), dose 0.2 grams

a. Extract of hyoscyamus, dose 0.05 grams
b. Fluid extract of hyoscyamus, dose 0.2 cc
c. Tincture of hyoscyamus (tincture of henbane), dose 2 cc

The action and uses of hyoscyamus are similar to those of belladonna.

I ANALGESICS

Analgesics are agents which abolish pain perception. They are also known as anodynes or sedatives. The alagesics, such as morphine, are usually narcotic, effecting the perception centers of the brain, but some of them like acetanilid relieve the pain by different mechanism which is unknown.

1. Opium, dose 0.06 grams

a. Powdered opium, dose 0.06 grams
b. Granulated opium, dose 0.06 grams
c. Tincture of opium, (Laudanum), dose 0.6 cc
d. Camphorated tincture of opium (Paregoric) dose 4 cc
e. Syrup of ipecac and opium (Syrup of Dover's powder) dose 4 cc
f. Compound mixture of opium and chloroform (Squibb's diarrhea mixture), dose 2 cc
g. Expectorant mixture (Stokes expectorant), dose 4 cc
h. Lotion of lead and opium (lead and opium wash)
i. Morphine sulphate, dose 0.008 grams.

j. Pantopon, dose 0.005 grams
Pantopon is a mixture of the hydrochlorides of the alkoloids of opium in the proportion in which they exist in opium and containing 50 per cent of anhydrous morphine.
k. Ethyl morphine hydrochloride (dionine), dose 0.015 grams
l. Codeine, dose 0.03 grams.

(1) Codeine sulphate, dose 0.03 grams.
(2) Codeine phosphate, dose 0.03 grams.

The group of opium alkaloids undoubtedly represents the most important class of all drugs. Altogether the opium of commerce contains more than 25 bases of which morphine is the largest in amount and the most useful, but which also contains such drugs as codeine and papaverine. The uses to which opium is put are based on its content of the various alkaloids, principally morphine.

Morphine causes a specific central analgesic action, a depressant effect on the respiratory center, a stimulation of the vomiting center, followed by depression, a descending depressed action on the entire central nervous system, and a constipating effect resulting from a combination of central and local action. Morphine is practically devoid of local action except on the gastro intestinal tract. This local action is a subject of much debate, but it seems certain that it plays a part in the causation of the constipation which results from the administration of the drug. The systemic actions of morphine are generally dependent on the dose used. The smallest doses producing therapeutic effects result in the relief of pain. Somewhat larger doses cause definite cerebral depression leading to more or less profound and prolonged sleep. Some persons react peculiarly to morphine showing one or more of the following symptoms:

Excitation, more common, perhaps in women than in men, but usually mild and of short duration soon giving place to the depressed action of the drug; nausea and even vomiting which not infrequently result in the systemic action of a small dose. In some persons nausea has a very pronounced after affect of the drug lasting at times for hours. The drug exerts a decided effect on the heart through the vagus mechanism chiefly influencing the rhythm which may become irregular. The rate may be slowed considerably after large doses, but morphine does not endanger life through its heart action. Morphine causes a constriction of the pupils of the eye when given in moderate doses and this phenomenon is often used as a gauge for the cessation of its administration, in cases in which large doses are necessary. It has no local myotic action when dropped into the eye. The respiratory center is depressed by relatively small doses of morphine

such as are too small to be hypnotic. Use is made of this action in the treatment of persistent and troublesome coughs, but it should be remembered that if the cough is productive the depression of the cough reflex may lead to a dangerous retention of the secretion of the inflamed mucosa. Morphine may be used to relieve the attacks of asthma and to lessen other similar troubles, but caution should be exercised and the slowing of the respiration should not be so great as to embarrass the heart. Asthmatic attacks are better relieved by epinephrine which was studied a short time ago. It should be used cautiously in the pain of uremia as it interferes with the elimination by the intestines. Morphine is used chiefly as an analgesic in conditions of severe acute pain, but even here its use should be very guarded for various reasons, but chiefly on account of the great danger of the formation of the morphine habit. In surgical conditions in which the alleviation of severe pain may obscure the course of the disease and lead to the unwarranted postponement of an operation, morphine should not be used, or it should be employed only in very small doses and with great care. In chronic conditions associated with pain morphine should not be used as the formation of the habit is almost certain to result from its prolonged administration. Exceptions to this generalization are to be found in such conditions as cancer, etc. in which the condition is hopeless and at the same time, the cause of much suffering. In general it may be said that morphine should not be used for relief of pain when any satisfactory relief can be obtained by the use of other remedies. Since the introduction of the coal-tar analgesics and of the hypnotics of the chloral group, the use of morphine as a pure hypnotic has become exceptional but it is extremely useful in inducing sleep and in violent pain. Habituation to morphine is readily established and is most difficult to relieve. Over doses of morphine lead to intoxication which may result fatally. The symptoms begin with the usual depression which deepens into sleep. The pupils become extremely constricted, the respiration becomes slow; the sleep deepens into coma from which the patient can be aroused with difficulty at first, later he cannot be aroused at all and the respiration falls and may be as slow as three or four in a minute. The heart is somewhat weakened and the rate is slowed. Death results from respiratory failure. Morphine is excreted promptly from the alimentary tract. Some of the morphine thus excreted may be reabsorbed into the circulation. Even after the hypodermic administration of the drug it is excreted in part by the way of the intestinal tract. Morphine is also used to lessen secretion and check perstalsis in diarrhea. For this purpose opium appears to be more efficient than does morphine.

Tincture of opium is employed whenever opium is indicated.

It relieves violent pain, produces sleep, allays inflammation and irritation and reduces secretions. The latter property explains its use in many diarrhea mixtures.

Paregoric is a mild anodyne in coughs, nausea, and abdominal pain. It should never be used to quiet restless infants, as a habit may be induced. It contains four tenths of one per cent of opium. Paregoric is one of the exempted preparations under the Harrison Narcotic Act, but its sale is subject to strict regulation and the pharmacist is held strictly accountable for its legitimate distribution.

Syrup of ipecac and opium, or syrup of Dover's powder is used as a diaphoretic and sedative expectorant.

Lead and opium wash is applied externally as an astringent and sedative for sprains and bruises.

Pantopon produces essentially the effect of opium, but being devoid of its extractive it may be used for hypodermic administration. It is probably absorbed rather more promptly and is free from the nauseant odor and taste of the ordinary preparations. It is used in the same conditions as those in which opium is indicated.

The systemic action of dionin is intermediate between the action of morphine and that of codeine. It is claimed that dionin does not produce constipation nor nausea. The conclusion of careful observers, however, is that for internal use it possesses no advantage over codeine.

When applied to the eye this drug causes local vasodilation. It is employed for its analgesic curative effect in conjunctivitis, corneal ulcer, acute glaucoma and other inflammatory diseases of the eye. Codeine although less actively analgesic, hypnotic, and sedative than morphine is preferable to the latter whenever doses of codeine are effective because it is less likely to produce habit and is less constipating. Its usefulness in replacing morphine is limited by the necessity of avoiding overdosage.

Codeine is especially useful in coughs where average doses are generally effective. If overdoses are given this makes the cough worse. It must be remembered that serious sequelae may result from stopping a cough where there is copious secretion which requires coughing for its removal. It is largely used as an agent to reduce pain previous to operations, or allaying nervousness and some authorities prefer codeine for the relief of cardiac pain. Codeine is

practically always used in the form of a sulphate or phosphate.

2. Alcohol (ethanol)

a. Diluted alcohol.

Externally alcohol is a rubefacient and astringent and by its evaporation a refrigerant. It is used to harden and cleanse the skin as a mild counter irritant in the form of soap liniment. In the concentration of 70 per cent it is markedly antiseptic and is employed as tincture of green soap in surgery especially to cleanse the skin of the patient and operator. Internally alcohol is a narcotic. Excessive doses depress and paralyze the nervous system. Small doses stimulate respiration reflexly dilate the cutaneous vessels moderately and modify the circulation. It is oxidized in the body and thus serves to a restricted extent as a source of energy. Alcohol is employed as a stimulant, diaphoretic and hypnotic. In patients accustomed to its use it may be very valuable, otherwise it is apt to do more harm than good. It is usually administered in the form of whiskey, brandy or wine.

Alcohol is used as a solvent in pharmacy and in the form of aromatic elixir as a vehicle for medicine. Diluted alcohol is used in pharmacy as a menstruum.

3. Cannabis. (Mariahuana, Hashish, and Bang).

a. Extract of cannabis, dose 0.015 grams.
b. Fluid extract of cannabis, dose 0.1 cc.

Aside from a slight local irritant effect the action of cannabis seems to be limited almost exclusively to the higher nerve centers. In man this is first manifested by a peculiar delirium which is accompanied with exaltation of the imaginative senses and later by a remarkable loss of the sense of time. The delirium is often accompanied with motor weakness and diminished reflexes and generally followed by drowsiness.

Cannabis is used in medicine to relieve pain, to encourage sleep and to soothe restlessness. We have very little definite knowledge of the effect of therapeutic quantities, but in some persons it will often relieve migrain headaches.

This drug was widely used as a coloring agent in corn remedies, coloring them green. In the last few years, however, a Federal law has been passed which restricts the use, sale, growth, or in any way dispensing of this drug. In fact, so rigid are the restrictions on this preparation, that it is doubtful if it will be found in any store throughout the United States at the present time. There is, however, some still in the various Army institutions, supply depots, hospitals, etc., but its use

is practically discontinued. The uses formerly claimed for it have been found not to be so valuable and there are other drugs which will take the place of this narcotic type drug without the danger attached to the use of cannabis. The extract and the fluid extract were merely convenient forms for administering and using the drug.

4. Acetanilid, dose 0.2 grams

Acetanilid is an analgesic, antipyretic and in excessive doses a cardiac depressant.

Moderate doses have little effect on the temperature of the normal animal and man, but such doses cause a marked reduction of the temperature in fever.

In poisonous doses acetanilid produces cyanosis, abnormal reduction in temperature, coldness of the extremeties and a profuse sweating. In individuals with an idiosyncrasy for the drug similar actions may be produced by small doses. It should be avoided or used cautiously in patients who are debilitated from any cause, especially those with heart disease.

Acetanilid is effective for the relief of headache, neuralgic pain and for the aches and pains of the febrile patient, but is not suited to the treatment of pain caused by inflammation. It has been exploited widely as a universal analgesic in various mixtures and under different names. Many so-called headache powders contain it. Its indiscriminate use in such forms is highly dangerous. In the first place, acetanilid is to be ranked among the habit-forming drugs. There are a number of well, authenticated instances on record of acetanilid habit. In the second place, the prolonged use of the drug, leads to chemical changes in the blood. When acetanilid is taken regularly, and frequently, these changes in the blood are frequently manifest, even to the casual observer, by a peculiar, dusky, cyanotic color of the skin, and especially of the lips. Probably because of the diminished oxygen-carrying power of the blood, there is a tendency toward degenerative changes in various organs, especially the heart muscle, and sudden death from slight over-exertion, is liable to occur.

5. Acetphenetidin (phenacetin), dose 0.3 grams

The action and uses of acetphenetidin are similar to those of acetanilid. The analgesic, antipyretic, and cardiac depressant effects of acetphenetidin, like those of acetanilid, are due to the formation of another compound which is para-aminophenol, and its possible advantage over acetanilid is probably due to the fact that this decomposition occurs more slowly. It is

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spasms of tetanus. Potassium bromide is also useful for quieting nervous excitability in neurasthenia and hysteria. It may be given as an adjunct to hypnotics such as chloral hydrate. It is said to be of value for the prevention of sea sickness. The therapeutic effects of potassium bromide are also produced by sodium bromide, but the latter salt is often preferred because it is probably less irritating to the stomach. The ammonium and calcium bromides are used for the same purpose as is potassium bromide and usually combined with potassium and sodium to form a sedative mixture. The Elixir of Three Bromides contains a combination of ammonium, sodium, and potassium bromides. The Elixir of Five Bromides contains, in addition to the above three, calcium bromide and strontium bromide; they are merely a convenient means of administering the bromides in treatment of nervous conditions, the action of both being very similar to that of potassium bromide previously discussed.

K. HYPNOTICS

Hypnotics are agents which produce sleep. This action is brought about by a depressant effect on the psychic centers. An ideal hypnotic would be one which would be agreeable to take, would act promptly and persistently, and be free of any depression of the vital functions, or from any other than the hypnotic action, and give no after-effect.

It seems needless to say that this ideal hypnotic has not yet been found.

1. Barbiturates

a. Barbital (veronal), dose 0.3 grams
b. Soluble barbital (barbital sodium, medinal), dose 0.3 grams
c. Phenobarbital (luminal), dose 0.03 grams
d. Phenobarbital sodium (luminal sodium), dose as for luminal
e. Isoamylethylbarbituric acid (Amytal), dose 0.1 gram
f. Allylisopropylbarbituric acid, (allonal), dose 0.03 gram

Barbital is an effective sedative hypnotic hence it is used in simple insomnia and hysteria and in epilepsy in the intervals between the seizures and to allay nervousness before surgical operations. It augments the action of analgesics such as aminopyrine especially in the relief of neuralgic pain. It is more actively hypnotic than chloral hydrate and a margin between the therapeutic dose and the toxic is somewhat wider, but there is no satisfactory evidence that this margin is wider in the case of any of its derivatives than in that of barbital itself.

Barbital is absorbed quickly and within half an hour it causes a sleep which usually lasts from four to eight hours. The patient usually awakens refreshed, but lassitude, headache, nausea, etc., may occur on the following day even after moderate doses. Skin

eruptions are sometimes induced in which case the administration should be stopped. Toxic doses lower the temperature, depress the respiration and circulation and weaken the heart. They induce long continued stupor sometimes interrupted by excitement. This condition has been confused with certain diseases or other conditions and with opium poisoning. Barbital is excreted slowly and cumulative toxic effects may be induced unless the administration is interrupted occasionally. Its continued use may lead to habitual addiction. Fairly large doses are effective against poisoning by the local anesthetics such as cocaine and procaine and also against poisoning by strychnine. Soluble barbital has the same properties as barbital except so far as greater solubility may affect the rapidity of absorption. Phenobarbital, like barbital, is a hypnotic and sedative. Phenobarbital has a sedative action on respiration and lessens the frequency of breathing. It kills by respiratory paralysis. It is eliminated by the kidneys and a certain portion being probably decomposed in the organism. It does not cause gastric disturbances but it sometimes causes skin eruption. Phenobarbital is used as a hypnotic in nervous insomnia and conditions of excitement of the nervous system. It is also used as a sedative and antispasmodic in the treatment of epilepsy. The drug is also used in other conditions of a chronic character and it is well to bear in mind that its effects are purely those of relief and never curative. The sodium salt of phenobarbital, phenobarbital sodium, is readily soluble and its solution may be used on occasions where the imperitive need of prompt action necessitates intravenous injection.

Amytal was originally introduced as a surgical anesthetic, especially by intravenous injection as for reasons pointed out by the council on pharmacy and chemistry, the intravenous injection of this group of drugs is not to be recommended except in great emergencies and the clinical experiences have shown that with permissible doses the anesthesia is uncertain. It is, however, valuable as a preliminary sedative allaying nervousness and giving a smoother more pleasant anesthesia. As a somnifacient it is useful in cases where prompt action is desired. As a means of controlling convulsions it is without doubt one of the most valuable remedies that we possess.

2. Chloral Hydrate, dose 0.65 grams.

Chloral hydrate is applied locally and usually in a concentrated solution for its irritant and anesthetic purposes. When taken internally its most important effect is the depression of the centers of consciousness, and it produces a sleep the soundness of which depends upon the size of the dose administered. In somewhat larger doses it acts as a depressant to the motor side of the spinal cord and the respiratory center, but usually the sensory apparatus is unaffected. Large doses lower the blood

pressure, chiefly through an action upon the vaso motor center, and in poisonous doses a profound coma with anesthesia is produced. Chloral hydrate finds its main use in medicine as an agent to produce sleep, as a preventative for convulsions and externally as a local anesthetic and disinfectant. It is one of the most important and effective somnifacients that we have in sleeplessness in which there is no pain involved. Its action is very prompt - sleep generally beginning within ten minutes or a half an hour after the oral administration. The action is usually of short duration from three to four hours. When the sleeplessness is caused as the result of pain chloral hydrate is very much inferior to the opiates for the production of sleep, but it does work well as an adjuvant in such cases as tetanus and strychnine poisoning in which death is often caused by spasms. However, in conditions such as epilepsy in which the convulsions are of little importance the drug seems to have no effect and consequently is not used for this purpose.

Occasionally the administration of chloral hydrate will produce very unpleasant symptoms such as various skin lesions or circulatory failure. Such conditions are cause for alarm, and death has resulted from as little as thirty grains of the drug. The most common symptoms of chloral poisoning are deep sleep, passing into coma, the pupil, at first contracted, later dilates, the respirations fall in number, the pulse is weakened and rendered slower, but later may become rapid and irregular, the temperature is reduced, the muscular system is relaxed, and both sensibility and reflex actions are diminished, or sometimes completely abolished. The immediate cause of death is generally respiratory paralysis. In the treatment, if action is taken early in the poisoning, the stomach should be thoroughly emptied by a stomach tube, and atropine, strychnine, cocaine and caffeine, employed as respiratory and circulatory stimulants. In conjunction with this, heat should be applied externally to the body to maintain the normal temperature, and efforts made to keep the patient from going to sleep. It must be remembered, however, that for this latter purpose, the patient must <u>not</u> be walked around, as this would put too much of a strain on the heart and cause death. Chloral hydrate is best administered in the form of a solution, usually in some such preparation as Syrup of Orange, or other simple aromatic preparation. Since chloral hydrate solutions decompose rapidly with the production of hydrochloric, trichloracetic, and formic acid, upon standing, or exposure to the light, they should be very freshly prepared before being used and should be well-protected from the light.

3. <u>Scopolamine Hydrobromide</u> (Hyoscine Hydrobromide), dose 0.0005 grams.

Scopolamine resembles atropine in its influence on the nerve endings, but differs from it in having a sedative instead of a stimulating effect on the brain. It is used as a cerebral

sedative in many forms of insanity but it is not used routinely in the better hospitals for this purpose. It must be employed with caution as it sometimes induces a rapid fall in blood pressure and collapse. It has been used extensively in conjunction with morphine for the production of surgical anesthesia as a preliminary to the use of ether or chloroform or without other anesthetics for operation. Doses of morphine and scopolamine, sufficiently large to produce anesthesia, however, are likely to cause dangerous depression of the respiration. Experience with these methods of anesthesia has not been satisfactory. The mixture has been employed as a partial anesthetic in labor, but the effect on the fetus is sometimes disastrous, many children being born cyanosed or dead. Scopolamine hydrobromide is frequently used in eye work for the purpose of dilating the pupil of the eye and is regarded by some ophthalmologists as preferable to atropine because it is less irritating and its action is less prolonged than that of atropine.

4. Paraldehyde, dose 2 cc.

Paraldehyde is a hypnotic and antispasmodic. It has little or no direct action on the circulation, except that it does dilate the blood vessels. In moderate doses, it produces in both man and animals a normal sleep which is hard to detect from ordinary slumber and is unaccompanied with any marked change in circulation, respiration, or sensibility. Its prompt, efficient, action and low toxicity make it a valuable hypnotic despite its disagreeable odor. After taking this drug the odor persists on the breath for quite some time and often, for this reason, interferes with the use of the drug. Caution must be exercised in the administration of paraldehyde because of the fact that it will produce a habit similar to that caused by alcohol.

L. STIMULANTS

1. Strychnine, dose 0.0015 gram

a. Strychnine Nitrate, dose 0.002 grams.
b. Strychnine Sulfate, dose 0.002 grams.

Strychnine acts as a stimulant to the spinal cord and is also a respiratory stimulant, increasing the rate of respiration, but the effect is of very short duration. In larger doses, bordering on to those of being poisonous, it raises the blood pressure by stimulating the vaso-constrictor center. It has little or no direct action on the heart.

Poisoning by strychnine is characterized by a tetanus of the back, resulting in a condition such that when the patient is laid on his back, his heels and his head will touch and the back will be arched. Also accompanying this poisoning, is a silly grin on

the face. Death may occur after one or several convulsions, due chiefly to fatigue of the respiratory center, resulting from over-stimulation of this apparatus. Perhaps the most important antidote for strychnine poisoning is barbital or ether, which abolishes many of the sensory impulses and permits recovery, after more than the average fatal dose has been given. Strychnine is very widely used as a bitter tonic, usually in the form of a preparation of nux vomica, the drug from which it is obtained. Strychnine also acts as a tonic to the muscular system, for the reason that it increases the response to stimuli. It has been very widelyused in a number of other conditions, such as circulatory stimulant in pneumonia and other infections, shock; has been used for treatment of some forms of paralysis, but its value is very doubtful, in fact, some careful observers consider that its use for any purpose, other than as a simple bitter tonic, is superfluous. It is added to cathartics in the treatment of chronic constipation, but probably without advantage, and it is not at all uncommon to read in papers of accounts where laxatives left carelessly laying around within reach of children have been the cause of death in many instances. Strychnine is usually administered in the form of the sulfate or the nitrate; rarely is the alkaloid itself used.

2. Nux Vomica, dose 0.1 gram.

   a. Extract of Nux Vomica, dose 0.015 gram.
   b. Tincture of Nux Vomica, dose 1 cc.

   The properties and uses of nux vomica are the same as those of its chief constituent, strychnine. The preparations of nux vomica are used as stomachic tonics. Some physicians believe that nux vomica acts more favorably as a bitter tonic on the stomach than does strychnine. The reason for this belief is undoubtedly that, because it is absorbed much more slowly than strychnine, it so acts locally somewhat more persistently.

III

RESPIRATORY TRACT

A. EXPECTORANTS

Expectorants are agents which are used to aid in the removal or expulsion of mucous from the respiratory tract and, in this way, alters favorably the course of the bronchial disease for which it is used. The term is now broadly used to include any remedy employed for the relief of cough; hence, according to the common understanding of the term, any cough remedy is an expectorant. Technically, however, this is incorrect because there are cough remedies which do relieve the cough without aiding expectoration in any manner.

The whole group is divided into three main classes, which are, sedative, anodyne, and stimulating. The sedative cough mixtures produce their action through relaxing of the vessels and by increasing the secretions in the bronchi. The anodyne type cough mixtures are those which deaden the nerves and so inhibit the cough reflex. The stimulating expectorants are those which restore tone to the bronchial muscles and, in this manner, decrease the amount of mucous and they irritate sufficiently to stimulate the growth of new tissue.

1. Terpin Hydrate, dose 0.25 grams

a. Elixir of Terpin Hydrate, dose 4 cc.
b. Elixir of Terpin Hydrate and Codeine, dose 4 cc.

Terpin hydrate finds its chief use as an expectorant in bronchitis and other cough conditions. This drug is largely used in the elixir of terpinhydrate and codeine, in which case, it is undoubtedly the action of the codeine rather than that of the terpin hydrate which produces the favorable result when used as cough sedative or anodyne.

2. Antimony

a. Antimony and Potassium Tartrate - (Tartar Emetis), dose 0.003 grams.
b. Compound Syrup of Squill, dose 2 cc.

Antimony and potassium tartrate is given as an expectorant with the object to increase secretions and facilitate the expulsion of mucous. Care must be observed in the administration of this drug because of its very poisonous nature. Also, if too large a dose is given, when used as an expectorant, it will produce nausea and vomiting, which are undesired. There are other agents which can be used to produce nausea and vomiting which are to be preferred over this drug. Antimony preparations are used now almost exclusively in the treatment of certain diseases most frequently encountered in the tropics.

Compound Syrup of Squill contains, in each cc., 0.002 grams of antimony and potassium tartrate. This syrup has expectorant and diaphoretic properties, both of which depend upon its nauseating action. This preparation, although formerly very widely used in the treatment of cough, is now very seldom used. It seems that the use of drugs possessing such powerful systemic nauseating effects, or actions, as do squill and antimony can be replaced by more suitable drugs.

3. White Pine, dose 2 grams.

White Pine bark is used as an ingredient in numerous cough syrups

and its preparations are very popular vehicles for cough mixtures. The white pine itself is probably worthless as an expectorant and its present use is probably due to tradition.

4. Ipecac, dose expectorant 0.06 grams, emetic, 1 gram

a. Fluidextract of Ipecac, dose 0.06 c.c., as an expectorant, and 1 cc. as an emetic.
b. Syrup of Ipecac, dose 0.75 cc. as an expectorant, and 15 cc. as an emetic.
c. Tincture of Ipecac (Wine of Ipecac), dose 1 cc.
d. Powder of Ipecac and Opium (Dover's Powder), dose 0.3 grams.
e. Emetine Hydrochloride, dose 0.02 grams.

Ipecac is, in large doses, emetic; in smaller doses, diaphoretic and expectorant; and in still smaller doses, stimulant to the stomach, exciting the appetite and facilitating digestion. In quantities not quite sufficient to cause vomiting, it produces nausea and frequently acts on the bowels. As an emetic it is mild but tolerably certain and free from corrosive or narcotic properties.

As an emetic ipecac is rarely used merely for the purpose of evacuating the stomach, but when an action upon the circulation is desirable, and in the so-called biliousness, or acute alcoholism, it is often of service. By virtue of their nauseating effect, small doses of ipecac tend to increase various secretions of the body. Thus, it is widely used as a diaphoretic, especially in combination with opium in the early stages of acute coryza, and other mild infections. In the same way it acts as an expectorant and in the early stages of acute bronchitis it is one of the most valuable remedies we possess. The fluid extract and syrup of ipecec provide convenient means for administering the drug, and although the syrup possesses all of the virtues of ipecac, it is used almost exclusively as a nauseating expectorant in acute bronchitis.

Emetine hydrochloride is emetic and amebacidal, but it is seldom used as an emetic or for the routine treatment of amebiasis, but it is valuable in association with other amebacides. Emetine is useful for surgical amebic lesion in which it affords relief of symptoms and, too, permits the use of other amebacides which effect a cure. When there is doubt concerning the co-existence of bacillary and amebic infection emetine is used to control the amebic portion of the infection. It is often indispensible in amebiasis in those patients in whom the existence of liver damage precludes the use of other amebacides. It is also possible that emetine may be useful in other diseases due to pathogenic amebas. Its toxicity interferes with the continued administration of sufficiently large doses to eradicate the amebas in most cases and when it is injected subcutaneously it often fails to destroy the ameba in the intestinal wall, especially in chronic cases of carriers

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employed as an addition to expectorant mixtures in chronic bronchitis, but the proportion of alcohol is too large to allow of its advantageous use in some cases. It is used in preparing the syrup of tolu. In small quantities it is often employed to flavor cough mixtures. In the use of this tincture it must be borne in mind that it is precipitated by aqueous liquids. Syrup of tolu balsam is used chiefly to impart its agreeable flavor to mixtures, while balsam of tolu possesses therapeutic properties, but not enough is dissolved by the syrup to have any perceptible effect. If a stronger preparation is desired, the tincture of the balsam may be added in the desired quantity directing the bottle to be shaken.

VI

GENITO-URINARY

A. DIURETICS

The diuretics are substances which increase the amount of urine excreted. This may be accomplished in a variety of ways because of the complicated structure of the kidneys and because of their susceptibility to foreign influences. As a matter of fact, it is difficult to state positively in what manner a given diuretic acts and in many cases, the effect may have been gained by a combination of conditions. The most common methods of inducing diuresis, however, are:

1. Changes in the circulation.
2. Local stimulation of the renal structure.
3. Osmosis or salt action.

An alteration in circulation which would cause a greater output of urine may consist of general vasoconstriction with a minimum effect in the kidneys, or of increased heart action with a consequent rise in blood pressure. The administration of any solid which can be carried in the blood stream will increase the excretion of urine by salt action. Any large excess of fluid in circulation will accomplish the same effect. Lowered osmotic pressure expands the blood vessels, increases the glomerular pressure and probably also gives reabsorption from the tubules. Any soluble material will be effective in this manner, but in practice, water, salt, sugars or other harmless substances are most often employed. Of the inorganic salts those of potassium are considered best, combined with the anions, chloride, nitrate, or iodine. The bromides, because of their cerebral action, are not so useful. That class of diuretics which stimulate locally, contains a large number of drugs whose action is little understood. The majority are known to be irritant to mucous membrane and especially to the renal structure, where they are supposed to cause some dilation and possibly also to stimulate the functional activity of the filtration cells. Any irritant will, in moderate amount, produce

an increased output of urine, but excessive doses are very harmful. The essential oils, alcohol, glucosides, cantharides, acids, calomel, etc., probably act as diuretics by such irritation.

1. Water

After water has been absorbed into the blood stream, it has a profound influence in increasing all the bodily secretions, notably those of the kidneys, and sweat glands. It is therefore frequently used as a diuretic when it is desired either to wash out the toxic substances from the system or by dilution to make the irritating urine more bland. It has been found that the drinking of large amounts of water tends to increase the elimination of urea and sulfates, and to decrease the acidity of the urine, but that the excretion of certain other substances, is not affected. Water is readily absorbed from mucous membranes in general but very little, or not at all in the stomach. It thereby increases fluid in the blood stream, and leads to interchange of material and increased activity of the excretory organs. With sufficient quantity, even the normal bowel movement will be stimulated. Diaphoresis and, to a less extent, salivation, and expectoration are also enhanced. Abnormal temperature is lowered by sweating and by mechanical heat consumption so that drinking large amounts of fluids, or cold baths, may be effective antipyretic measures.

In pure forms, water is not absorbed by the skin but is capable of giving a mild irritation and even softening and swelling. In the form of baths this may be utilized as a local stimulant measure in certain skin diseases, improving the circulation and nutrition of the epidermis, thereby removing the adverse condition. Furthermore, the local irritation, especially if the bath is hot, will reflexly stimulate in such a way as to counteract pain leading to circumstances which promote a normal sleep. The same reflex stimulation from a hot bath, particularly with added irritants, can be employed to reestablish menstruation. It is also said that baths of body temperature are the best remedies in nervous insomnia. If tepid water is taken into the stomach in sufficient quantities, it will act as an efficient emetic. Ice, applied to small cuts, will prove an effective hemostatic because of the local vaso-constriction.

2. Ammonium Salts

a. Solution of Ammonium Acetate (Spirit of Mindererus), dose 15 cc.
b. Solution of Iron and Ammonium Acetate (Basham's Mixture), dose 15 cc.

The ammonium salts produce their diuretic action mostly due to salt action and to the resulting irritation. At the same

time, intravenous injection gives respiratory and circulatory stimulation, with slowed pulse, increased blood pressure, and enhanced respiratory rate. The solution of ammonium acetate is used as a saline diaphoretic and diuretic, especially in febrile conditions. Basham's Mixture is an active diuretic and also astringent and is very largely used in chronic Bright's Disease. There has arisen a popular superstition that it exercises a curative effect in nephritis, which its originator, Dr. Basham, never claimed for it. Its value is probably simply that of a builder of red blood and not superior to other forms of iron.

3. Potassium Salts

a. Potassium Acetate, dose 1 gram
b. Potassium Chloride, dose 1 gram
c. Potassium Citrate, dose 1 gram
d. Effervescent Potassium Citrate, dose 4 grams
e. Potassium Nitrate, dose 0.3 grams

Potassium citrate is a type of those drugs which increase various secretions by what is known as salt action. This group of drugs which includes most of the non-toxic crystalloids act by increasing the saline concentration of the blood, disturbing the osmotic balance between this fluid and the surrounding tissues, thereby attracting water into the vessels, and tending toward an increase in the volume of the blood. Not only is the secretion of urine greater but there is also an increase in the bronchial, sweat and other glands. The therapeutic uses of potassium citrate, however, are not due alone to this action, the citrates being oxidized in the body into carbonates, the salt tends to correct any systemic hyper-acidity and the potassium apparently increases the completeness of bodily combustion. This combination of actions makes the drug of particular value in those forms of metabolic disturbances accompanied with the over-production of uric acid, such as acute or chronic rheumatism and gout. Probably the most frequent use of potassium citrate today is an expectorant in the early stages of acute bronchitis. By increasing the secretion of the mucous glands, it indirectly exercises a sedative action on the inflammatory mucous membrane. It is valuable as a sudorific in the early stages of the milder infections. It is sometimes of service as a diuretic, although caution must be observed in its use when there is serious disease of the kidneys because of the possible poisoning from retention of potassium. In cases of cystitis when the urine is excessively acid, it is especially valuable. It may be most pleasantly exhibited in conjunction with lemon juice which does not lessen the alkalizing effect.

The effects of potassium acetate upon the system are very similar to those of the citrate, except that it is less likely to act upon the bowels. Like the citrate, it is oxidized in the system and appears in the urine as a carbonate and therefore tends to render this secretion alkaline. It is usually less acceptable to the palate than the citrate. It is especially employed in the treatment of rheumatic fever and other forms of rheumatism for its alkalizing effect on the system. It is also sometimes used for its diuretic effect in dropsies and nephritis. Some investigators have found it useful in several skin diseases, such as, eczema.

Potassium chloride is recognized by the N. F. because of its presence in certain mineral waters, imitations of which are official. There is no reason to believe that the small amount of potassium chloride present in these compound salts modify materially their action.

The official effervescent potassium citrate affords an agreeable mode of administrating potassium citrate. It is more prone to exert a laxative effect because of the sodium tartrate formed in its manufacture.

As a therpeutic agent the potassium nitrate is of very little importance. Its former use as a diuretic, and in rheumatism, have passed into a well-deserved oblivion. Locally it has been used in the place of potassium chlorate in some conditions, but is even less efficacious than that feeble remedy.

In asthma, nitrous fumigation is often useful, performed by inhaling the fumes from burning torch paper, prepared by dipping blotting paper in a saturated solution of potassium nitrate and afterwards drying it. It is habitually added to strammonium leaves in the preparation of the so-called "asthmatic powders" but it is used, under these circumstances, more for its oxidizing effect in encouraging the combustion than for its own therapeutic action.

In pharmacy, potassium nitrate was formerly employed to form crocus of antimony to procure nitric acid and sometimes in the preparation of the spirit of nitrous ether.

4. <u>Sodium</u>

a. Sodium Chloride (Salt) - dose, 15 gms.

b. Physiological Solution of Sodium Chloride.

c. Sodium Acetate - dose - 1.5 gms.

d. Sodium Citrate - dose, 1 gm.

As sodium chloride constitutes over 90% of the inorganic constituents of the blood serum, it is usually the salt of preference for making solutions isotonic with the blood. The official preparation "liquor sodii chloridi physiologicus", is a solution of this type. Because of the large amount of this solution which can be introduced into the body without serious distur-

bance of its function and because of the power of the healthy body to adjust itself to enormous variations in the daily ingestion of sodium chloride, the importance of salt metabolism in many disease processes has not been appreciated until comparatively recent times. When the intake of the chloride ion is less than its excretion there will occur: first, a failure of the stomach to elaborate hydrochloric acid and, secondly, a relative increase of the bicarbonates of the blood, producing the condition known as alkalosis. Another well-marked group of symptoms, the explanation of which is not at present understood, are nausea and vomiting, associated with the increased irritability of the muscles, as shown by cramps or even convulsions. It is well known that sweating will cause muscle cramps which can be completely relieved by the use of a weak salt solution, instead of plain water, for quenching the thirst.

Besides its internal uses, salt is employed for various external purposes. The application of saturated solutions of sodium chloride tends to relieve congestion and exudation, and is a useful therapeutic measure in sprains, bruises, and the like.

Salt baths are used for their tonic and exciting effect in various diseases, especially when attended with weakness of the circulation. A pound of salt to 4 gallons of water forms a solution of about the strength of sea water and suitable for a bath.

When given by mouth in large quantities, sodium chloride is emetic and in proper dilution is laxative.

Sodium citrate, like potassium citrate, is oxidized in the system and appears in the urine in the form of a carbonate, and may therefore be used to overcome excessive acidity of the urine. Sodium citrate is also used, like the potassium salt, as a diuretic, expectorant, and sudorific, although generally esteemed as somewhat less efficient.

When added to the blood outside of the body it prevents coagulation, presumably by the formation of non-ionizing calcium citrate. In the same way it prevents the curdling of milk by rennin, the sodium caseinate which is formed by this ferment after the addition of the citrate being soluble.

As an anti-coagulant, sodium citrate is used very largely in transfusion of blood from one individual to another. This salt is also employed pharmaceutically as a buffer agent in such preparations as glycerite of phenol and glycerite of tannic acid to prevent such preparations from becoming discolored.

Sodium acetate is diuretic, acting much like potassium acetate, but is rarely used as a medicine. It is employed principally to yield acetic acid by the action of sulfuric acid. In prescribing this salt, the fact should not be forgotten that the mixture of equal parts of it with potassium nitrate, if heated, explodes with great violence.

5. Caffeine Group.

1. Caffeine - dose, 0.15 gm.

a. Citrated Caffeine - dose, 0.3 gms.

b. Caffeine Sodio-benzoate - dose, 0.3 gms.

2. Theobromine - dose, 0.35 gms.

a. Theobromine Sodio-salicylate - dose, 1 gm.

3. Theophylline (Theocin) - dose, 0.25 gm.

Caffeine occurs in tea and coffee, and less abundantly in cocoa. Theobromine is more abundant in cocoa, but it is prepared synthetically. Theophylline occurs in small amounts in tea but it is also prepared synthetically.

Theophylline is probably the most active diuretic, but this action is brief. It sometimes causes gastric disturbance and renal irritation. Caution is necessary, therefore, when large doses are given to patients who suffer with nephritis. Theobromine is about as effective as theophylline when the prolonged action is considered. It is less prone to cause unpleasant effects than caffeine or theophylline, and it is probably the most useful diuretic of this group. Caffeine is usually said to be the least active diuretic of the three but testimony is conflicting. It has the disadvantage of causing insomnia, nervousness, cardiac irregularity and gastric disturbances.

Small doses of caffeine act on the nervous system, stimulating the psychic center, the respiratory and vasomotor center and the reflexes. It modifies the circulation by stimulating the heart and relaxing the vessels by direct action. The flow of urine is increased, muscular traction is facilitated and fatigue lessened. Excessive doses produce insomnia, nervousness, headache, palpitation, and nausea or vomiting, especially in susceptible persons. It may lessen the capacity for mental or muscular work. Toxic doses may produce tetanic convulsions and cardiac dilitation.

Caffeine has rather complex, and therefore, somewhat inconsistent actions on the circulation. After therapeutic doses the pulse may be quickened or slowed. The blood vessels tend to dilate by the peripheral action and to contract by the central action. The dilitation probably predominates in the kidneys in most cases, but the blood pressure may rise slightly by increased force and output of the heart. This increased output and lessened resistance tends to produce a more rapid flow of blood, resulting in an increased flow of urine. These effects make caffeine especially efficient in some cases of cardiac dropsy, although it is generally inferior to digitalis. A disadvantage in the use of large doses is the cerebral stimulation produced, which often prevents sleep.

Caffeine is useful in collapse by causing rise of blood pressure and stimulating respiration. It may be used in organic poisoning in the form of hot coffee which may be administered by rectum, if the stomach is to be washed out meanwhile. It is especially valuable in opium poisoning and it may be used in alcohol poisoning. It relieves some forms of headaches, but in the conjestive form it may increase the pain.

Caffeine is excreted by the kidneys partly unchanged, and partly as a mono or di-methylxanthine. It does not increase the amount of uric acid in the urine.

What has been said might then be summarized by saying that caffeine has three important physiological actions, namely: a stimulating effect on striated muscles; a stimulating action upon a large group of centers in the cerebro-spinal axis; and a stimulating effect upon the kidneys.

Citrated caffeine is possessed of the physiological and therapeutic properties of caffeine, but is more liable to disagree with the digestive functions. Citrated caffeine is a mixture of caffeine and citric acid in equal proportions.

Caffeine sodio-benzoate, or technically more correct, caffeine with sodium benzoate, which is the new title in the U.S.P. 11, has the physiological effects and therapeutic uses of caffeine. It has the advantage over the alkaloid of being freely soluble in water, and over the citrated caffeine, of being less irritant to the stomach; whenever it is desired to exhibit caffeine in solution, the preference should be given to caffeine and sodium benzoate. It is especially suitable for hypodermic administration, for which purpose it may be dissolved in 3 parts of water and from 10 to 20 minums (0.6-1.3 cc.) of this solution injected at a dose.

The actions of theobromine on the kidneys and heart are similar or practically identical with those of theophylline and caffeine, but it is possible that theobromine dilates the coronary arteries somewhat more than caffeine, and that it may be useful in some cases of angina pectoris.

Its effect on the central nervous system is much less than that of caffeine. Its relative freedom from side action makes it preferable to caffeine as a diuretic. It is not irritating to the kidneys and is employed as a diuretic in all forms of dropsy. It is only very slightly soluble in water hence it is used in the form of the freely soluble theobromine with sodium salicylate.

Practically, then theobromine may be said to find its main use as a diuretic, a stimulant to the heart muscle and dilator of the blood vessels, especially the coronary artery.

In a general way, the physiological actions of theophylline are similar to those of its chemical relative, caffeine, except that it has very slight influence on the nervous system. For this reason, although it is of no particular value for those effects which, like respiratory stimulation, depend upon a nerve action, it is superior as a remedy in circulatory and renal disorders. In cases of cardiac insufficiency, whether the result of acute depression or chronic heart disease, it is often a remedy of great service. In the latter group of disorders, while it does not increase the muscle tone like digitalis, its action in dilating the coronary arteries is often of great benefit, especially when used in conjunction with digitalis. It has been highly recommended by numerous clinicians in the treatment of angina pectoris and other forms of heart disease. It is of great service as a

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per day in the treatment of cystitis.

When given in very large doses too, it often causes violent inflammation of the urinary tract. As these irritations are due to an excess of formaldehyde liberative, the treatment consists of the administration of sufficient doses of bicarbonate of soda or citrate of soda to keep the urine alkaline and large amounts of water to dilute it.

An interesting and novel use of methenamine is afforded by its ready inflammability and the fact that it burns with a smokeless flame. In the absence of a Bunsen burner, or an alcohol lamp, a five-grain tablet of methanamine placed upon a metal or some other non-inflammable surface and ignited will develop sufficient heat to boil a test tube full of water, to sterilize a hypodermic needle, or to make a test for albumen in the urine.

The oil of sandalwood is used largely as a perfume. In medicine, its chief use is in gonorrheal urethritis, although it is sometimes employed in chronic bronchitis and cystitis. Its general antibacterial power is comparatively weak, but it has special relation toward certain micro-organisms; thus, 20 minums of oil of sandalwood three times a day seems to have no effect on the growth of the B. coli in the urine, but markedly retard the multiplication of the staphylococci.

Copaiba is gently stimulant, diuretic, laxative, and in very large doses, often actively purgative. It is used as a stimulant in chronic inflammation of the mucous membrane, such as chronic cystitis, chronic diarrhea, hemorrhoids, and chronic bronchitis. The complaint, however, in which it is most employed, is gonorrhea. It should not be administered in the first stages, when the inflammation is severe and acute, nor is it applicable to very chronic forms of the disorder, such as gleet. It was formerly much esteemed as an application to ulcers but it is now seldom used externally.

It may be given dropped on sugar but in this form is often so exceedingly offensive as to render some concealment of its nausea qualities necessary. A less disagreeable form is that of emulsion, sweetened with sugar, and flavored with some aromatic water, such as that of mint or cinnamon.

When taken internally, methylene blue is absorbed and eliminated chiefly from the kidneys, coloring the urine blue or greenish. In therapeutic doses, it produces no symptoms except occasionally some irritation of the bladder. It is a feeble antiseptic, and has been used to a considerable extent in gonorrheal and other inflammations of the urinary tract.

In the past few years, methylene blue has attracted much attention as a remedy against those poisons which stop internal oxidation, such as the cyanides and carbon monoxide. There is abundant evidence, both experimentally and clinically, of its value in cyanide poisoning.

Methylene blue is preferably administered in capsules. In malaria, from 10 to 20 grains (0.65-1.3 gm.) may be given in the course of a day for 10 days and after this, 0.4 to 0.65 grams a day for two weeks. In obstinate cases, a full dose of quinine may be exhibited every seventh day, the methylene blue being omitted. The staining action of methylene blue upon any portion

of the body or clothing with which it may come in contact, and its color effect upon the urine should always be explained to the patient.

VII

MISCELLANEOUS

Under the heading of miscellaneous, we will study those drugs which have not heretofore been classified and studied under any other heading.

A. ALTERATIVES

Alteratives have been defined as substances which alter the course of morbid conditions in some indefinite way. It can thus be seen that the term was probably used to conceal ignorance as to the manner of action. According to the definition, any drug could be used as belonging to this class since the improvement or alteration of disease is the primary purpose of medicine. As a matter of fact, however, the old alteratives were presumed to exert their favorable action on the general metabolism or nutrition. They were commonly employed in those diseases which were mysteries or for which no other drug had been found useful.

1. Sarsaparilla.

    a. Fluidextract of Sarsaparilla - dose, 2 cc.

    b. Compound Syrup of Sarsaparilla - dose, 15 cc.

Sarsaparilla was one of the earliest of the New World drugs to be used by European physicians. In the 16th century it was employed quite extensively in the treatment of syphilis but fell into disuse until revived in 1757.

It continued to be highly regarded as an alterative not only in syphilis but in various skin diseases and chronic rheumatism for more than a hundred years. In the latter part of the 19th century, its employment was almost universally regarded as a survival of ignorant superstition and it would have entirely disappeared from the medical field had it not been for the valuable property as a vehicle of the compound syrup.

While the day has gone by when compound syrup of sarsaparilla is regarded by the medical profession as an active therapeutic agent, it has a wide and proper use as a vehicle, especially for the iodides and other saline drugs. It is also widely employed, especially in extemporaneous mixtures to mitigate the unpleasant flavor of castor oil. The fluidextract of sarsaparilla finds its main use as an ingredient in the compound syrup of sarsaparilla.

2. Guaiac - dose, 1 gram.

    a. Tincture of Guaiac - dose, 4 cc.

Formerly, guaiac was included in that mysterious group of drugs previously mentioned under 'alteratives', which were used in all sorts of chronic diseases, for which there was no satisfactory treatment, such as syphilis, chronic rheumatism, etc. Because of its local irritant action upon the stomach, in full dose it may cause some nausea which will increase a tendency to sweat, but it is doubtful whether it has any therapeutic virtue beyond that of other nauseants. It has been almost completely abandoned in the treatment of skin diseases but some physicians still consider it useful in rheumatic affections. As an ingredient in many mouth washes and throat gargles, it still finds a place in pharmacy, for there are a number of physicians who insist upon its use. Guaiac is usually in the form of the tincture.

B. ANTISYPHILITICS

1. Mercury

a. Mercury with Chalk (Gray Powder) - dose, 0.25 grams..

b. Mass of Mercury (Blue Mass, Blue Pill) - dose, 0.3 grams.

c. Mild Mercurial Ointment (Blue Ointment)

d. Stronger Mercurial Ointment.

e. Ointment of Yellow Mercuric Oxide.

f. Mild Mercurous Chloride (Calomel) - dose, 0.15 grams, usually given in a series of small doses.

g. Compound Pills of Mild Mercurous Chloride (Compound Cathartic Pills, CC Pills) -dose 1 or 2 pills.

h. Corrosive Mercuric Chloride (Corrosive Sublimate, Bichloride of Mercury) - dose, 0.004 grams.

i. Ammoniated Mercury (White Precipitate)

(a) Ointment of Ammoniated Mercury (White Precipitate Ointment)

j. Mercuric Salicylate - dose, 0.06 grams. - intramuscularly twice a week.

k. Mercurochrome.

Mercury with chalk is a very mild mercurial, similar in property to the blue mass, but much weaker. It is sometimes used as an alterative, but is most frequently employed as a cathartic, particularly in the complaints of children attendant with deficient biliary secretion, indicated by white or clay colored stools. The chalk is antacid and though in small quantities may sometimes be useful as an accompaniment of mercury in

diarrhea. It should not be given in pill, the substance of which becomes hard on keeping, as the contraction of the mass presses together the particles of mercury which in time appear in globules in the interior of the pill.

Blue mass has the therapeutic properties of the mercurials but is today chiefly employed for its cathartic action. It seems to be somewhat less irritant than calomel and the purgation caused is less frequently accompanied with griping. When used as a cathartic, it is sometimes necessary to follow it after some hours with a saline.

Mild mercurial or blue ointment is intended only for the destruction of parasites and vermin on the skin; for anti-syphilitic inunctions, the strong mercurial ointment should be employed.

The strong mercurial ointment is intended for the introduction of mercury into the general system, especially for the treatment of syphilis. There has been some question as to the method of absorption of mercury after inunction; there can be no question of the fact of absorption. Some of the older writers believed that the mercury was volatilized and entered the system largely by being inhaled, but the investigation of numerous authors have shown that this view is untenable. It has been found that when there are daily applications of mercurial ointment to the skin the absorption increases progressively. In practicing mercurial inunction those areas of the body should be selected where the skin is comparatively thin, as the inner surface of the elbows or thighs, the groins, and the flanks. The ointment should be vigorously rubbed in for twenty or thirty minutes, applying from two to four grams at each inunction. It must be remembered that too large doses of mercury by inunction may cause Mercurial poison just as certainly as by mouth. The inunction should not be repeated at too short intervals in the same area of the body on account of the danger of causing inflammation of the hair follicles. Mercurial ointment has been recommended to prevent the maturation of the small-pox pustule and the consequent pitting. For this purpose it may be applied to the face or other parts thickly spread on a patent lint or muslin, care being taken to prevent the access of air to the covered parts. To be successful it must be applied before the third or fourth day of the eruption.

The ointment of mercuric oxide possesses distinct antiseptic properties. It was originally introduced as a remedy for conjunctivitis and is still extensively employed for this purpose. However, there are some investigators who believe that its value is greatly over-estimated. Mild mercuric chloride finds its main use as a cathartic, diuretic and antiseptic. As a laxative it is slow but thorough in its action affecting both upper and lower bowels. While the former belief that it was a stimulant to the hepatic secretions has been shown to be incorrect, it in some way increases the bile in the intestinal tract, perhaps through an action on the bile passages or perhaps through its antiseptic effect preventing the decomposition of the natural bile. It is, therefore, preferred in cases where there is an absence of this secretion, as shown by light colored stools, and in biliousness. It is also a valuable agent to cleanse the intestines in enteritis, both because of the thoroughness of its effect and of its

antiseptic action. When used as a purgative better effects may be obtained with less discomfort by giving it in divided doses; thus a quarter of a grain may be given every half hour until three or four grains have been taken. It is usually advisable to follow it the next day with a saline laxative for the reason that if it should fail to operate, sufficient mercury may be absorbed to cause salivation.

Externally, calomel is used for a dusting powder in various infections of the eye, and in venereal ulcers and in the form of an ointment in various ulcerated conditions of the nasal or other mucous membranes.

Compound pills of mild mercurous chloride were first made official in the second edition of the United States Pharmacopoeia. Although it is an active purgative the combination of so many drugs seems unnecessary and a bit irrational. Their use has greatly diminished in recent years and it is to be hoped that they will soon be altogether forgotten. They should never be used in habitual constipation because of the calomel contained in them.

Corrosive sublimate is a powerful mercurial and may be used for the various systemic effects for which the other preparations of this metal are employed. When administered in large doses it is prone to irritate the stomach and intestines and therefore, such large quantities of mercury cannot be introduced into the system as of some other salt. It is, however, one of the best preparations of mercury for hypodermic use in syphilis.

Externally employed, corrosive sublimate is stimulant, escharotic, and germicidal. The powdered chloride has been used as an escharotic but is, in general, inferior to silver nitrate or potassium hydroxide.

Corrosive sublimate is one of the most powerful of known chemical germicides. Solutions containing one part in 20,000 are sufficient to destroy the vitality of the most non-sporulating bacteria while one in 1,000 will kill the most resistant sporulating organism. The practical utility of mercuric chloride as a disinfectant, is however greatly limited by its chemical instability and its injurious effect on human tissues.

It has a strong affinity for albumen and although the precipitated form is redissolved in an excess of albumen the disinfectant power of mercury is very much reduced. Moreover, it attacks most metals which are used in surgery and is, therefore, unsuitable for disinfecting instruments. Nevertheless, because of its convenience, as well as its powerful action, it is very widely employed as a germicide for surgical purposes. The solution of 1:1000 may be used for washing the hands, disinfecting furniture etc., and is even employed in the disinfecting of wounds; usually, however, a much weaker solution than that just mentioned is employed by the surgeon. It is rarely, if ever, justifiable to use upon a mucous surface or wound a solution stronger than 1:2000 and if the solution is to be used freely and continuously 1:10,000 is as strong as should be employed; indeed, the employment of this chemical for such purposes has been followed by a violent poisoning.

Ammoniated mercury is used only as an external application. It is a valuable remedy in parasitic skin diseases, such as ring worm, and is also em-

ployed for destruction of lice. Ammoniated mercury is highly poisonous, producing gastric pains, nausea and purging. It has been known to have been swallowed by mistake.

The ointment of ammoniated mercury is used chiefly as a stimulant and a parasiticide in cutaneous eruptions such as scabies, ring worm and chronic eczema. The U.S.P. ointment, which is ten per cent in strength, may require dilution for some conditions, such as when it is to be used on infants or small children and those individuals who have a highly sensitive skin, especially toward the action of mercury.

Mecuric salicylate is used chiefly in the treatment of syphilis especially by intramuscular injection. The advantages claimed for it are that it is locally non-irritant and that it does not salivate. The first of these is due to its insolubility and the second is an evidence of its slow absorption. Mercuric salicylate is also used locally for its germicidal effect either as a dusting powder in the strength of ten per cent or as an injection in gonorrhea, one part of the drug being suspended in three hundred parts of mucilage.

Mercurochrome is used almost exclusively for its anti-bacterial properties. It has been used extensively as a surgical disinfectant especially in the treatment of small wounds for its lack of irritant action and its beautiful color, increases popularity for surface disinfections. It has also been used as a disinfectant to mucous membrane, including the throat and mouth. Mercurochrome has been highly lauded as a blood disinfectant for treatment of some conditions, but the evidence concerning its value is somewhat contradictory. The fact of the matter is, that the report of investigators who have studied the use of mercurochrome as a skin disinfectant are so conflicting that it is hard to say whether or not it is of any value.

2. Arsenic.

   a. Arsenic trioxide (arsenous acid) - dose, 0.002 grams.

   b. Solution of arsenous acid (Solution of arsenic chloride) - dose 0.2 cc.

   c. Solution of potassium arsenite (Fowler's solution) - dose 0.2 cc.

   d. Sodium cacodylate - dose 0.06 grams.

   e. Arsphenamine (Salvarsan) - dose caution, intravenous, 0.4 grams.

   f. Neoarsphenamine (Neosalvarsan) - dose, caution, intravenous 0.6 gms.

Arsenic trioxide applied to denuded or ulcerated tissue has a mildly caustic action which is quite painful. It has been used as a caustic especially for malignant growths but the painful character of the application, the danger of the absorption and the uncertain extent of the destructive action have limited its use.

Taken internally arsenic trioxide irritates the mucous membrane of the stomach and intestines. Toxic doses cause nausea, vomiting, diarrhea of a watery character, resembling that of cholera, and fatty degeneration of the liver and other internal organs.

Arsenic is employed in the treatment of neuralgia. It is thought to be especially adapted to cases of periodic character. It is also used in the treatment of chorea. Arsenic stimulates the action of the blood-forming organs, especially the bone marrow. It is considered useful in the treatment of anemia. While improvement often occurs under the use of arsenic for this condition it is usually only temporary. In such conditions it is best administered in the form of solution of potassium arsenite or arphenamine.

Many skin diseases are favorably influenced by proper doses of arsenic. It acts by stimulating the skin in those cases which require external stimulating applications. It is also of service in lesions due to disturbances of the system in which the skin is usually poorly nourished. The following skin affections may be benefited by arsenic; psoriasis, chronic eczema, and others which are not quite so common. On the other hand, acute inflammatory conditions of the skin are made worse by arsenic. Arsenic has also been used in chronic respiratory infections such as chronic bronchitis, asthma and tuberculosis. It may have some indirect benefit as a general tonic but much dependence cannot be placed upon it.

The medicinal properties of the solution of arsenous acid are much the same as those of Fowler's solution with which it corresponds in strength. It should be remembered, however, that it is incompatible with alkalies.

Fowler's solution has the general action of the arsenical preparations on the animal organism. In this liquid form it is more convenient for gradually increasing the dose and this is the preparation generally resorted to when arsenic is given internally. In malarial affections and chorea it should be administered in ascending doses until the puffiness about the eyes or disturbance of the bowels betrays the arsenical impression. Ordinarily in administering this preparation the patient is started out with taking three drops daily, increasing the dose one drop per dose per day until ten-drop doses have been reached, at which time the dose is then decreased by one drop per dose per day until the minimum dose of three minums or drops is reached. This then constitutes what is known as a course of arsenic.

The range of demonstrated therapeutic usefulness of sodium cacodylate is similar to that of arsenic. Its early popularity was achieved chiefly in the treatment of skin diseases, especially psoriasis and in tuberculosis. In the latter condition it seems to act precisely as does arsenic simply by improving the general nutritive state of the patient. There is also much clinical evidence of its value in various forms of anemia, asthma, chronic bronchitis, malaria, and various other conditions in which arsenic is useful. It is especially employed in those conditions such as pernicious anemia in which it is desired to give very large doses of arsenic. This preparation has been tried in the treatment of carcinoma, leprosy, and pellagra, but not to sufficient extent to allow of a positive conclusion as to its value. The advantage of cacodylic acid over arsenous acid lie not merely in the fact of its lowered toxicity but especially in that it can be given hypodermically. When given by mouth it generally imparts such a strong garlicky odor to the breath that this method of using the drug is rarely available.

Arshphenamine is a specific remedy for syphilis in all stages, but is the

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2. Quinine - dose, Tonic - 0.1 gm. - Antimalarial - 1 gm.

a. Quinine Sulfate - dose, as for Quinine.

b. Quinine Bisulfate - dose, as for Quinine.

c. Quinine Tannate - dose, 0.2 grams.

d. Quinine Hydrobromide - dose, as for Quinine.

e. Quinine Hydrochloride - dose, as for Quinine.

f. Quinine and Urea Hydrochloride - dose, hypodermic, 1 gm. in a single dose daily.

g. Coco-Quinine.

In large doses, cinchona exerts an irritant effect on the stomach and may occasion nausea and even comiting, especially if the stomach was previously inflamed. If the dose of the cinchona bark has been large enough, the symptoms of cinchonism may result. At one time, cinchona bark and its preparations were used as antiperiodics, but at present for such purpose, one or another of its alkaloids is always selected. Various attempts to determine the relative antimalarial efficiency of the cinchona alkaloids have resulted in discordant results. The whole bark, usually in the form of a tincture, is sometimes used as a bitter stimulant to gastric digestion and appetite.

The fluidextract of cinchona is an ineligible preparation. It is not strong enough to be a useful means of obtaining the systemic action of its alkaloid and is too strong to be frequently useful as a stomachic bitter.

Compound tincture of cinchona is an excellent bitter tonic, useful for its local effect on the stomach, but too feeble in the principals of cinchona to serve when the systemic action of the drug is required.

Quinine is a protoplasm poison, affecting the protozoa more than bacteria. It is somewhat irritant to the stomach and intestines, and when absorbed it may cause ringing in the ears, but usually moderate doses produce no other marked effects in healthy persons, though hypersensitiveness to quinine is not rare. In patients with fever it acts as an antipyretic.

It is used chiefly as a specific antimalaria. In this disease it should be given in large doses several hours before the time of the expected chill. Toxic doses may produce depression of the heart and respiration and collapse. Such doses may produce more or less complete blindness, terminating in a permanent loss of sight. Moderately large doses of quinine act as a stimulant to the uterine muscles, but do not produce such spasmodic contractions as ergot. Quinine may be used as a tonic, as are the simple bitters, for the improvement of digestion and nutrition. Its solutions produce local anesthesia, especially the solution of quinine and urea hydrochloride. The ordinary quinine salts are irritant.

The actions and uses of quinine bisulfate are similar to those of quinine, over which it has the advantage of being freely soluble in water.

Perhaps one of the least efficient of the quinine preparations is quinine tannate; not only does it contain less than one half the amount of alkaloid than the other salts, but because of its slow hydrolysis and consequently delayed absorption, has a still lower index of therapeutic activity.

It is useful, however, as a means of administering quinine to children who are not able to swallow pills, because of its comparative tastelessness. It has, to a considerable extent, been replaced even for this purpose, by some of the synthetic compounds, such as, the ethylcarbonate.

There is a widespread belief that quinine hydrobromide acts somewhat differently from the other preparations of quinine. The preportion of hydrobromic acid is, however, too small to exert any influence upon the system; 10 grains of quinine hydrobromide represent less than 2 grains of hydrobromic acid. The salt has achieved a high reputation in the treatment of Graves' Disease, and certainly in many cases will cause at least a temporary improvement of many of the nervous manifestations of this disorder.

Quinine hydrochloride finds much the same uses as do the other salts of quinine, but it has a decided advantage over the sulfate in its greater solubility in water. It is, however, less soluble than the acid quinine hydrochloride.

Quinine and urea hydrochloride is the most suitable of all the official salts of the alkaloid for hypodermic administration on account of its free solubility and on account of its neutral reaction. It is, therefore, widely employed in the treatment of the severe types of malaria, where the drug must be given parenterally, as well as in other conditions where large doses are required. For some time quinine and urea hydrochloride was quite extensively used as a local anesthetic. It has, however, the disadvantages that it does not easily penetrate mucous membrane and, therefore, of low efficiency when applied as a wash and, when injected, is liable to produce extensive sloughing. In recent years it has been used as a sclerosing agent for the treatment of varicose veins.

3. Cinchonidine Sulfate - dose, 0.15 grams.

4. Quinidine Sulfate - dose, 0.3 grams, with caution.

So far as our knowledge goes, this alkaloid influences the system, similarly to quinine; there is difference of opinion as to its relative efficiency.

Quinidine, like quinine, is a protoplasm poison, affecting protozoa more than bacteria. Quinidine acts on the heart in such a manner as to bring about the cessation of fibrillation of the auricles in a certain proportion of instances. The pharmacology of the drug has been investigated extensively. It has been shown that quinidine increases the refractory period of auricular muscles and decreases its irritability and rate of conductivity. Quinidine sulfate is used to restore the normal rhythm of the heart in cases of auricular fibrillation. This has been brought about in approximately 50% of the reported cases in which the drug was used. It appears to be the most efficacious in the treatment of cases of fibrillation of short duration

or those of the paroxysmal type. It is least useful in cases of fibrillation with marked cardiac insufficiency. Quinidine however is not without untoward, and even dangerous effects. There is danger that while the quinidine abolishes the auricular fibrillation the ensuing contraction of the auricle may dislodge a clot, causing sudden death. Some patients are much more susceptible to its toxic action than others. The untoward symptoms brought about by its use in these patients, are nausea, vomiting, convulsions, headache, faintness, and flushing. Quinidine sulfate has the antimalarial action typical of quinine and it may be given to patients who do not tolerate quinine.

D. ANTIRHEUMATICS

1. Salicylates.

a. Salicylic acid - dose, 0.75 grams.

b. Sodium Salicylate - dose, 1 gram.

c. Ammonium Salicylate - dose, 1 gram.

d. Strontium Salicylate - dose, 1 gram.

e. Salicin - dose, 1 gram.

f. Methyl Salicylate - dose, 0.75 cc.

g. Acetylsalicylic acid - (Aspirin) - dose, 0.3 grams.

The physiological action of salicylates is the same for all the compounds but there are quantitative differences. The acid is markedly irritating to mucous membranes and abraded surfaces and, on the skin, produces a gradual destruction of tissue without pain, an action which prevents its internal administration. It is about equal to phenol in antiseptic power and has the advantage of not being volatile. The salts are scarcely irritating to any surface and not greatly antiseptic, but oral injestion is followed by liberation of some free acid in the stomach and in the urine, if acid, producing weakly germicidal qualities and some irritation.

All of the compounds are rapidly absorbed from the alimentary tract and the more volatile penetrate the skin more or less readily. They are transported by the blood as sodium salts and excreted within 48 hours, unchanged, chiefly in the urine but somewhat in the milk perspiration and bile. Except for osmotic action, therapeutic doses have no significant effect on normal persons but idiosyncrasies to the drug are fairly common consisting of the usual effect of small amounts of tolerance to large quantities. When the temperature is high it is promptly reduced to normal by an increase of heat loss and by dilation of the cutaneous vessels accompanied by sweating. When certain forms of pain exist they are dulled or abolished by salicylate. The excretion of nitrogen and sulphur is greatly increased but it is not known if this is accompanied by a larger amount of basal metabolism.

Salicylic acid is an antiseptic. It is quite irritant to mucous membrane and is somewhat corrosive. Internally it has the actions described under

sodium salicylate, in which form it is commonly employed. Externally it has been used as an application in pruritus and in some forms of eczema; also in the form of ointments and collodion to cause the removal of corns and warts.

The action of sodium salicylate upon the system and its therapeutic use are precisely those of salicylic acid except that the salt is not locally irritating and being soluble, is more rapidly absorbed. When salicylic acid is administered it is mostly converted into sodium salicylate before it is absorbed into the blood. Four grams of the salt contain about three and one half grams of the acid. Sodium salicylate is an analgesic, antipyretic, and a feeble antiseptic but it is in no sense a specific remedy. It is irritant to mucous membrane and may cause pain and even vomiting when large doses are administered while the stomach is empty. Large therapeutic doses produce ringing in the ears, nausea and sometimes vomiting, occasional sweating and an increase in the amount of urine; it also may cause albuminuria and renal irritation which, however, generally disappear after the drug is excreted. In very large doses it may produce depression of the central nervous system, rarely convulsions, a slowing and depression of the respiration and collapse from depression of the circulation. Large doses may produce abortions hence they are contraindicated in pregnancy. It is sometimes administered for headaches or neuralgic pain but it is chiefly used for its effect in rheumatic fever, in which it is highly efficacious. It promptly relieves all the local joint symptoms and the fever but does not affect the endocarditis, which is the inflammation of the epithelial lining membrane of the heart. Its effects last only while the medication is continous. It is useful in tonsilitis but has not the decided action in the ordinary infections that it has in rheumatic fever.

Ammonium salicylate is one of the best forms of administering salicylic acid. Its actions are the same as those of the acid.

Strontium salicylate, when taken internally, is slowly decomposed in the alimentary canal with the liberation of salicylic acid which acid can be detected in the urine shortly after administering. Of the salicylates, the strontium salt is of especial value in subacute rheumatic affections acting more slowly and persistently than most of the other allied salts. By some it is believed to have less tendency to disturb the digestion but others have reached the conclusion that the toxic dose of the strontium salt is the same as that of the sodium salt, and that the strontium salt has no advantage in any way. It may be administered in capsule or solution.

Salicin acts upon the stomach probably as a simple bitter and, after absorption, as a feeble and uncertain form of salicylic acid. Since it is rapidly, although not completely, decomposed in the system, the products of its change appearing in the urine fifteen to thirty minutes after the injection of a single dose. The elimination is partly as salicin, partly as salicylic acid and partly as other compounds. It has been recommended as a substitute for salicylic acid in rheumatism by some, but since it owes its activity to its conversion in the blood into salicylic acid, and since this conversion is uncertain, salicin is inferior in power to the salicylate By some, however, it is believed to be less liable to upset the stomach. Salicin has also been used as an antiperiodic, but is probably of no value for this purpose.

Methyl salicylate is used chiefly in the treatment of various forms of rheumatism in which other preparations of salicylic acid are of service. It has the advantage over the inorganic salicylates of being less unpleasant to the taste but usually seems to cause digestive disturbances. Because of its volatility, it is capable of being absorbed through the skin and is frequently applied externally for its systemic effect. For this purpose it may be mixed with equal parts of lard and a small amount spread over the surface about as large as the palm of the hand and covered with an impermeable dressing to prevent evaporation. It is also employed for its counter-irritant action in various liniments. As a flavoring agent two minums may be used for each fluid ounce. Internally, it is best administered in emulsion although sometimes taken by dropping into a teaspoonful of sugar. The custom of giving it in capsules is to be avoided and frowned upon, as it is much more likely to irritate the stomach under these circumstances.

Although it has been shown that the salicylic acid occurs in the urine within from twenty minutes to half an hour after the injection of acetyl salicylic acid, there is strong reason to believe that the drug circulates in the blood in large part unbroken; in other words, the action is not purely that of salicylic acid but there is also a different effect of aspirin.

Acetylsalicylic acid has been used in medicine as an antirheumatic, as an analgesic, as an antipyretic and for its local action. In inflammatory rheumatism it is generally of less value than ammonium or sodium salicylate. On the other hand, in those neuralgias of dubious origin, commonly diagnosed as chronic rheumatism, aspirin is often of great usefulness. In a general way it may be said that the more nearly these types of pain approach to true rheumatism, the more likely it is that sodium salicylate will be a superior drug to aspirin. As an analgesic, acetysalicylic acid comes in competition with acetanilid and other coal tars for the relief of headaches, neuritis and similar painful conditions, but is distinctly inferior. As an antipyretic, it has been shown that it far exceeds the salicylate in power but, like acetanilid, is liable to produce serious collapse. Locally it has been recommended in acute tonsillitis and it appears to exert a local anesthetic effect in various forms of sore throat. For this purpose it may be used as a gargle in saturated aqueous solution, or a tablet may be allowed to dissolve in the mouth and the aspirin swallowed slowly. It has also been employed to a lesser extent in eczema and other skin diseases.

2. <u>Cinchophen</u> (Phenylcinchoninic Acid, Atophan) - dose, 0.5 grams.

   a. Neocinchophen - dose, 0.5 grams.

Neocinchophen has action and uses nearly similar to those of cinchophen, over which it has the advantage of being nearly tasteless; and there is some evidence that neocinchophen is less likely to prove toxic, but this evidence is not conclusive and the same contra-indications and precautions should be observed in its use as in the case of cinchophen. The precautions which should be observed are: to avoid its use in any one who has had symptoms of liver disorder; not to give it in excessive doses over long periods of time; and to immediately withdraw the drug on the slightest jaundice or other evidence of hepatic disturbances.

Neocinchophen, like cinchophen, increases the permeability of the kidneys

selectively to uric acid and greatly increases the execretion of urates, thus tending to lower their concentration in the blood. The action is similar to that of salicylates, but it is more prompt and greater. It ceases within a few hours after the administration is stopped. There is no important effect on other metabolites. Among the toxic effects (more frequently reported after cinchophen) are a sense of oppression in the gastric region, with acid eructation, or belching, and diarrhea. In cystitis, there may be pain in the bladder; occasionally there is a scarlet and urticaria-like rash; it sometimes induces cardiac distress attended with dizziness. The appearance of skin rash, vomiting, heartburn, diarrhea, or jaundice demands the immediate discontinuation of the drug. Relatively small doses have occasionally caused symptoms and it is impossible that an attack of hepatitis renders the patient extremely susceptible to these drugs at a later date. Great caution is also necessary in their use in patients who have renal insufficiency. The promiscuous use of cinchophen and neocinchophen (which are the bases of numerous proprietary preparations) by the public is obviously dangerous. This fact has been thoroughly realized by the government and so recently a law was passed which forbids the sale of these and other similar drugs to the laity over the counter without a prescription properly filled out and signed by a registered physician.

3. Colchicum

a. Colchicum Corm - dose, 0.25 grams.

1. Strong Tincture of Colchicum Corm (Colchicum Wine) - dose, 0.6 cc.

2. Fluidextract of Colchicum Corm - dose, 0.2 cc.

b. Colchicum Seed - dose, 0.2 grams.

c. Colchicine - dose, 0.0005 grams.

Colchicum Seed produces marked irritation of the intestines, leading to looseness of the bowels with much pain and watery stools. It may result in severe enteritis and collapse. The collapse is believed to be due to the intestinal irritation and not to a central action. It also produces irritation of the kidneys which may lead to severe nephritis. Colchicum seed is said to be antineuralgic and analgesic. By many it is considered to be a specific in acute gout, controlling the pain and cutting short the attack. It may be given to prevent the occurrence of gouty attacks and it is recommended by some to continue it in smaller doses after the attack, but it often fails. Colchicum seed is of little or no value in rheumatic fever.

The medicinal properties of colchicum corm are precisely the same as those of colchicum seed, but the latter is less variable and therefore usually to be preferred. The tincture of colchicum seed possesses the properties of colchicum and may be given whenever that medicine is indicated.

The alkaloid, colchicine, acts like colchicum, producing violent diarrhea, with diminished urinary secretion; causing some abdominal disturbance with increased diuresis, depending on the size of the dose administered.

E. Insulin is an aqueous solution of an active principal from the pancreas which affects sugar metabolism. The great value of insulin in medicine is in the treatment of that increasingly common metabolic disorder known as diabetes mellitus. It is no exaggeration to say that this drug has completely revolutionized the treatment of this disease. On the other hand, it must be remembered that the use of this extract simply provides the system with an absent hormone; it has no effect in restoring health to the diseased cells of the pancreas. In other words, it is not properly to be regarded as a curative agent and it does not tend toward a restitution of normal function.

Diabetes mellitus is a disease marked by the passage of an excessive amount of urine, containing an excess of sugar. It is attended by thirst, enormous appetite, and lack of strength. It may occur in a temporary form after the use of certain foods, with certain nervous diseases, and with congestion of the liver; but the disease is usually chronic and fatal without the use of either a proper diet or insulin. In individuals who suffer from this type of diabetes, or cannot handle the sugars, insulin is injected into the muscles, and by supplanting this hormone which is absent in the person suffering from the disease, proper metabolism of the sugar takes place and the individual goes on living very similar to a normal person.

The reduction in blood sugar which is caused by the injection of insulin, may give rise to serious symptoms, and, if the dose be large enough, to death. In rodents, the toxic effects are manifested chiefly by convulsions, collapse, and when the dose is sufficient, from death by respiratory failure. These symptoms may be immediately abolished by the intravenous injection of glucose. In human beings, the symptoms caused by overdoses of insulin are great prostration, profuse sweating, and unconsciousness. In cases where individuals have taken an overdose of insulin, about the only thing necessary for them to do to overcome the bad effects, is to eat some sugar or glucose or candy, and in a very short time the excess insulin in the system will be used up in the metabolism of the injested sugar.

Until a short time ago, it was necessary for the users of insulin to inject the proper dose immediately following each meal or at any time when food was taken into the system. Now, however, there has been introduced onto the market, a combination of protamine and zinc with insulin. This combination is absorbed very, very slowly and, as a result, ordinarily, one injection each 24 hours, is sufficient to carry the diabetics over for that period of time. Obviously, this is a great aid to the sufferer of diabetes.

F. IRON

1. Reduced Iron - dose, 0.6 grams.

2. Solution of Ferric Chloride - dose, 0.1 cc.

3. Ferrous Sulfate (Copperas) - dose, 0.1 gram.

4. Solution of Ferric Subsulfate (Monsel's Solution) - dose, 0.2 cc.

5. Pills of Ferrous Carbonate (Blaud's Pills)

Metallic iron is used pharmaceutically in making preparations of iron, but in medicines it is used chiefly in the form of reduced iron.

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yellow phosphorous matches phosphorous poisoning has become very rare but an occasional case from roach poison or other vermin exterminator may occur. The symptoms usually do not manifest themselves until some hours after the ingestion of the phosphorous. The symptoms are nausea, vomiting, abdominal pain followed the second or third day by abdominal tenderness and some fever. Later the patient becomes jaundiced and severe vomiting of a coffee-ground liquid free from bile and similar to the black vomit of yellow fever; the urine is scanty and albuminous and often it may finally be suppressed. Frequently there is wild delirium. The temperature falls markedly and the patient sinks into a coma which ends in death. After death a peculiar fatty degeneration is found affecting almost all of the soft tissues. The parts which suffer first are the liver, the gastro-intestinal mucous membrane and the kidneys.

The pills of phosphorous offer a convenient means of administering this drug as does the elixir. Great caution is necessary in the use of phosphorous and its effect should be very closely watched.

VIII

BIOLOGICAL PRODUCTS

A line of products including serums, small-pox and rabies vaccine viruses, bacterial vaccine, antigens, and extracts, toxins, etc., which are used for prophylaxis, treatment and diagnosis of infectious diseases and the manufacture of which depends upon the use of bacteria and bacterial products are known as biologics or biological products.

The production of biological products involves the exercise of the skill of expert laboratory technicians and the practical application of the principles of the science of bacteriology and related branches of knowledge. Their preparation requires;

a. The growing and handling of mass cultures of bacteria.

b. Their treatment by technical processes so that they can be made into vaccine.

c. The separation and refinement of the toxins or poisonous products elaborated.

d. The production of serums, antitoxins and antibody solution.

e. The preparation of attenuated viruses.

f. The preparation of protein extracts, etc. by scientific methods.

These will be outlined below under the description of each product.

The pharmacopoeia says that diphtheria and tetanus antitoxin should be preserved at a temperature between 2°C. and 10°C. (35.06°F. and 50°F) and that small-pox vaccine must be kept at the lowest possible temperature, preferably below 0°C. and never above 5°C. (32° F. and 41° F.)

These products are usually stored in electric refrigerators maintained solely for that purpose in order to insure against loss of potency of the product. Expiration dates on biological products are purely arbitrary and are not a guarantee against loss of activity caused by improper storage. If a preparation is subjected to high temperature it may be rendered inert within a few hours; but if properly stored it will retain its potency for a much longer period than that indicated by the dating.

Small-pox vaccine is particularly susceptible to heat. Body temperature, 98° F., not only weakens the virus very promptly but will kill it in three or four days. At 70° F. the virus is materially weakened in one to three weeks. At sufficiently low temperature, below freezing, it has been found active after several years.

Similarly, but in lesser degrees the potency of all biologicals is adversely affected by improper storage.

The use of biological products in medicine rests entirely upon the science of immunology which is the science which treats with the defensive and offensive reaction of the body to infectious or parasitic micro-organisms and to foreign proteins. It is, therefore, necessary to understand something of the processes of immunity before one can appreciate why the so-called biological products have attained such an important place in the prevention and treatment of disease.

Immunity is the state or condition of the body which exempts it from contagious diseases or which enables it to resist infection effectively. It is sometimes called <u>resistance</u>. The opposite is called <u>susceptibility</u>. More simply, immunity may be defined as the resistance which one has or may acquire toward a disease or disease organism.

Immunity may be antitoxic immunity or antibacterial immunity.

<u>Antitoxic immunity</u>.

Many organisms excrete very poisonous substances known as toxins. The exact composition of toxins is unknown, but they are known to be nitrogenous and very complex. Most of them are unstable and readily destroyed by heat.

There are two types of toxins, exotoxins or true toxins and endotoxins. Exotoxins are formed as a natural metabolic process of the organism and are excreted from the cells during life. Examples of true toxins are; diphtheria toxin, tetanus toxin, botulinus toxin and scarlet fever toxin. Endotoxins are formed in the cells of the organism but are not liberated until after the death of the cell. A good example of an endotoxin is tuberculosis toxin. There is a difference between endotoxins and exotoxins which is very important; exotoxins when injected into an animal organism stimulates the formation by that organism of antitoxin, a substance which neutralizes or inactivates the toxin. Endotoxins do not stimulate the formation of antitoxin. This immunity produced by the formation of antitoxin is known as antitoxic immunity.

While some organisms secrete the substance which stimulates the formation of antibodies which inactivate the secreted poisonous substance, other organisms by virtue of their own composition stimulate the formation of anti-

bodies to destroy the organism. These organisms and any substance which can stimulate the formation and appearance of specific antibodies in the circulation of animals is termed an antigen. Chemical protein structure is the necessary criterion for an antigen. The important structural unit being the aromatic amino acid. Antibodies which have the property of destroying bacteria are called antibacterial antibodies and the immunity which results from these antibodies is called antibacterial immunity.

Immunity is further broken down into natural immunity and acquired immunity. The immunity which exists normally in an animal or human being is termed natural immunity. Certain persons appear to have a definite immunity to scarlet fever and diphtheria although they have never had the disease; others repeatedly pass through epidemics of various infections such as measles and pertussis (whooping cough) without becoming infected. Man is immune to fowl cholera, swine plague etc. Acquired immunity is the resistance to a disease which exists after an attack or subattack of the disease or after vaccination against the disease with a specific vaccine or virus. Example of the first is the immunity following a small-pox attack, or the immunity that comes in later years of youth and adult life to diphtheria; of the second the immunities following vaccination against small-pox and diphtheria.

Natural immunity is a condition which usually stays with an individual throughout his lifetime. Acquired immunity may be subdivided into active and passive immunity. Active immunity is that which an individual acquires by either having the disease or being vaccinated. In either event the individual because of proper stimulation produces his own antibodies and the immunity is more or less of a permanent nature lasting from two years to a lifetime. A good example of this active immunity is that produced by either being vaccinated against or by having small-pox. This acquired active immunity serves to protect the individual against the disease against which he has been vaccinated.

Passive immunity is that which is produced in an individual as the result of injecting into him antibodies which have been produced in some other animal organism. It is usually administered in the form of a serum or antitoxin and normally is of short duration. This type of immunity is employed usually in conditions when there is an epidemic of a disease prevalent, or after a person has been exposed to a certain infectious or contagious disease and it is desired to protect that person from becoming infected.

Antibodies are substances occurring in the blood stream of individuals who have either had a disease or have been vaccinated, or they may occur naturally, which enables that individual to resist the particular disease for which the antibodies are specific.

A serum is the clear amber portion of the blood separated from it by allowing the blood to stand until clotting takes place. The clot is generated by what is known as the clot ferment, or fibrinogen. It might be said that serum in blood minus the serum and fibrin.

Serum are divided into two classes - immune and normal. Normal serum is obtained from normal healthy animals that have not been subjected to any active immunization. Immune serums are serums which contain antibodies and are derived from animals which have been actually immunized against a

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ly large dose is injected, symptoms of a more or less violent character appear. The reaction is manifested chiefly by the contractions of the involuntary or smooth muscles. In the guinea pig this affects particularly the smooth muscle fibers of the bronchi, producing marked respiratory distress and perhaps resulting fatally. In the rabbit, the reaction apparently selects the smooth muscle fibers in the walls of the arterial system of the lungs, with the effect that circulation through the lungs is stopped and the animal dies through oxygen starvation of the remainder of the body. Other animals react in other ways. The animal is said to be "sensitized" by the first injection, with the result that a second dose of the same protein in a sub-lethal quantity for a normal control, and given after a suitable interval, will cause the death of the animal.

Although easily produced in animals, anaphylaxis is fortunately rather rarely observed in the human subject.

There are, however, many other manifestations of protein sensitization of a less severe type. Hay fever, urticaria, serum sickness, asthma, eczema, etc., are examples. A long list of proteins - food, animal, epidermal, bacterial, and pollen - have been incriminated as the inciting agents. One authority estimates that about one per cent of the population of the United States suffers from hay fever. It is the most prevalent form of sensitization. The main factors in this disorder are the wind-borne pollens. When present in inspired air they impinge upon the mucous membranes of the nasal passages and some of their soluble substances are absorbed. This sets up a train of symptoms in pollen-sensitive individuals, marked by congestion and irritation of the respiratory mucous membranes and by catarrh, paroxysmal sneezing, itching, etc. Some are sensitive to one or more of the tree pollens, such as the willow, oak, walnut, maple, and others which pollinate in the early spring. Other patients are sensitive to one or more of the grass pollens, especially timothy, and suffer from hay fever during the pollinating period of this plant in the latter part of May and June. A still larger group is sensitive to some one or more of the numerous wind-borne pollens of late summer and autumn, particularly the ragweeds in Eastern United States and the wormwoods and sagebrush in the western half. There are certain localities, as for example, in the Southwest, where climatic conditions permit plant growth throughout the year, with a succession of pollinating periods, so that sensitive individuals are in discomfort practically the year round. This is the so-called perennial hay fever. Many of the common weeds which pollinate in the late summer and early fall are factors in hay fever of a mixed type. While some hay fever sufferers are sensitive to but one pollen, the majority are sensitive to two or more, but these are usually closely related botanically.

Asthma, in some of its forms, constitutes another example of protein sensitization. A large number of inciting factors have been identified in this disease. Some patients, for example, are found to be sensitive to house dust or mill dust. Others are sensitive to horse dander and cannot enter a stable without developing an attack. Some asthmatics suffer acute attacks if they have to sleep on a feather pillow. Others are sensitive to sheep wool, and in some, the asthmatic symptoms are caused by pollens.

Serum sickness is a manifestation of protein sensitization with which the physician is frequently concerned. The ordinary form of serum sickness ap-

pears usually from eight to thirteen days after the injection of the serum, and is characterized by a rash and skin eruption together with some edema or swelling and joint pains and sometimes a slight fever. Sometimes it manifests itself by an immediate stormy reaction resembling shock. Such immediate reactions occur usually after the first dose of the serum and develop only in those individuals who are naturally sensitive to horse serum. Natural sensitiveness to horse serum is fortunately rare - about one patient in twenty thousand according to one authority. Most individuals are normal with respect to sensitivity to horse serum and can be given a dose of antitoxin or serum without any immediate or severe reactions. These patients are more likely to show more pronounced symptoms of serum sickness following a second dose of serum than after the first.

The mild, delayed form of serum sickness is not serious and excites no alarm The immediate or shock reaction, however, must be avoided as far as possible Physicians should take the precaution to determine, before giving the first injection of a serum, whether the patient is sensitive to horse serum. This is particularly important if the patient gives a history of asthma, for it may be that the asthma is a symptom of sensitiveness to horse protein In any case, sensitiveness can be readily determined by making a preliminary skin test. This is done, a) by injecting a very small amount, 1/20 to 1/10 of a cc., between the layers of the skin. If the patient is sensitive a noticeable reaction will appear within twenty minutes to one-half hour, in the nature of an area of redness with development of a wheal around the site of injection. One who is not sensitive to horse serum develops no reaction and may safely be given ordinary therapeutic doses of serum; or b) a drop of horse serum, diluted 1 to 10, or a drop of the serum product to be used (diluted 1 to 10) is placed in the lower conjunctival sac; if no reaction (itching, burning, congestion and lacrymation) occurs within fifteen minutes, it is believed that the presence of a dangerous hypersensitivity is excluded. A positive reaction indicates a dangerous degree of sensitivity and constitutes a definite contraindication to the injection of even small doses of horse serum. A positive reaction may be neutralized by placing a drop of 1 to 1000 epinephrine solution in the eye.

Serum treatment of those who show a positive reaction must be carried out very carefully, usually beginning with a very small dose, a fraction of a cc., and gradually increasing this at hourly intervals, until 1 cc. can be given without causing a reaction. Doses may then be more rapidly increased, until the required therapeutic dose has been administered.

Remedy for Anaphylaxis - It is important, when serum is to be administered to have a sterile epinephrine solution, 1 to 1000, ready for instant use in case of an allergic reaction. This can be injected subcutaneously in doses of 0.5 to 1 cc. and repeated at intervals as indicated by the patient's condition. The effect of epinephrine is increased by massage at the site of injection.

Treatment of the many forms of protein sensitization may be carried out along different lines. The simplest method, of course, is to avoid or remove the specific cause of illness. If this cannot be done, specific protein treatment is the method of choice. Specific protein treatment means the partial or complete relief of the symptoms by subcutaneous injections of a suitable preparation of the specific protein, found by test to be the causa-

tive factor. It is necessary to begin the injections with very small subtoxic doses. These can be increased very gradually. Usually they must be continued over a considerable period of time. The doses may be given at short intervals, with the object of increasing the patient's tolerance as rapidly as possible. The duration of the immunity or tolerance gained by this method of treatment varies greatly. In hay fever, for example, one authority states that one cannot rely upon the duration of tolerance lasting more than six to eight weeks. For this reason hay fever sufferers usually have to repeat the treatment preceding the onset of symptoms each season.

In the treatment of other forms of protein sensitization there are marked irregularities in the results, which may be accounted for by difficulties in making accurate specific diagnosis, by differences in the degree of the sensitiveness of the patient and by differences in the intensity of exposure. Developments in this branch of Immunology are appearing rapidly and the pharmacist who makes some effort to keep in touch with them will be in the best position to render service on biological products.

Labeling, Dating, Preservation, Storage, and Dispensing - There are some practical points which apply to all biological products and are of great importance to the pharmacist, both in his professional capacity and as a means of preventing unnecessary losses.

Legal Control and Labeling - Biologicals must be prepared in an establishment licensed by the Secretary of the Treasury of the United States. The requirements for labeling are that the outside label must bear the name of the antitoxin and the minimum number of units in the package, the lot number of the antitoxin, the name, address, and license number of the manufacturer, and a statement of the date beyond which the minimum potency may not be maintained. This date is one year from date of issue from the manufacturing establishment if an excess of 20 per cent over the minimum potency has been placed in the container, two years for a 30 per cent excess, three years for a 40 per cent excess, or four years for a 50 per cent excess.

The strength shall be expressed in antitoxic units, and the unit shall be that of the standard antitoxin distributed by the National Institute of Health of the United States Public Health Service.

The potency of biological products in general tends to decrease or fall off more or less rapidly with the lapse of time. Their period of potency is greatly prolonged by preserving them at low temperatures. This is nowhere more clearly shown than in the data which was first worked out by Dr. W. F. Elgin for smallpox vaccine. It was found that the potency of vaccine virus was lost within three or four days by exposure to temperatures of 98° F. (37° C.); it was greatly weakened or lost by one to three weeks exposure at 70° F. (21° C.); at ordinary refrigerator temperatures of 50° F. (10° C.), the virus was still active after three or six months; at 10° F. (-12° C.) it remained active for four years.

Smallpox vaccine, as indicated above, should be kept as cold as possible. When kept in a refrigerator cooled with ice, smallpox vaccine should be stored in a metal container in direct contact with the ice. When stored in a mechanical refrigerator, the vaccine should be kept in one of the compartments inside the freezing coil.

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glycerin, 1 month.

Tuberculins - concentrates, containing at least 50 per cent of glycerin, 5 years; dilutions, 1 year.

Bacterial Vaccines - 18 months.

Sensitized Vaccines (Serobacterins) - 18 months.

Modified bacterial derivatives - 18 months.

Diphtheria Toxin-Antitoxin Mixtures - 6 months.

Diphtheria Toxin for Schick Test - to be diluted before use - 6 months.

Diphtheria Toxin for Schick Test, diluted, ready for use - 1 year. The words "if kept between 0° C. and 8° C. (32° to 46.4° F.)" must appear on the labels of both products.

In dispensing biological products the pharmacist is dealing with preparations, most of which are intended for use by injection, either subcutaneously, intramuscularly, or directly into the vein. It is therefore of paramount importance that the sterile condition of the preparations be maintaine up to the time they are actually injected. Sterility is assured by the processes used in the manufacturing establishments, and no product is released until repeated tests have shown it to be safe in this respect. The pharmacist contributes his part to the maintenance of potency of the product and safety to the patient by observing the requirements of the U. S. P. XI, for the official antitoxins, viz., that they must be preserved at a temperature between 2° and 10° C., preferably at the lower limit and that they must be dispensed in the unopened glass containers in which they were placed by the manufacturers.

BIOLOGICAL PRODUCTS USED FOR PASSIVE IMMUNIZATION

Antitoxins

Antitoxins are antitoxic serums, usually more or less concentrated and purified by the removal of some of the non-essential serum constituents. They confer passive antitoxic immunity and are used in the specific treatment of the acute manifestations of disease.

Official Products - Three antitoxins are recognized by the U. S. P. XI, namely, Diphtheria Antitoxin, Scarlet Fever Streptococcus Antitoxin, and Tetanus Antitoxin, now official only in the refined or concentrated form.

ANTITOXINUM DIPHTHERICUM

Diphtheria Antitoxin

Diphtheria Antitoxin is a sterile aqueous solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal of the genus Equus, which has been immunized against diphtheria toxin. After the serum

or plasma from the immunized animal has been collected, the antitoxin bearing globulins are separated from the other constituents of the serum or plasma and dissolved in freshly distilled water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. Diphtheria Antitoxin has a potency of not less than 500 antitoxic units per cc.

Description and Physical Properties - A transparent or slightly opalescent liquid, of a faint brownish, yellowish, or greenish color, nearly odorless, or having an odor due to the presence of a preservative; it may have a slight granular deposit. Diphtheria Antitoxin must be free from toxins, and must not contain an excessive proportion of preservative (not more than 0.5 per cent of phenol or 0.4 per cent of cresol, if either of these is used) and its total solids must not exceed 20 per cent.

Uses - Diphtheria Antitoxin is the specific curative agent in the treatment of diphtheria. Its administration accomplishes two things, provided it is given in adequate dosage and sufficiently early in the course of the disease. (1) It neutralizes diphtheria toxin in the blood and body fluids and possibly the toxin which is in contact with, or united to, the tissue cells. (2) Adequate dosage supplies the patient with an excess of antitoxin, which serves to neutralize any further toxin production as long as virulent diphtheria bacilli remain. The antitoxin also influences the destruction and removal of the bacilli which produce the toxin.

Benefit from the use of Diphtheria Antitoxin depends largely on the method and time of administration and the size of the dose. All authorities emphasize the importance of introducing the Diphtheria Antitoxin into the circulation as soon as possible after infection has occurred. In view of the importance of the time factor it is generally recommended that antitoxin be given to every patient upon the mere suspicion of diphtheria, making bacteriological diagnosis afterward.

With reference to the methods of administration, the subcutaneous route is used only in the treatment of mild cases. Any part of the body where there is an abundance of subcutaneous cellular tissue may be selected. The intrascapular region is usually preferred. In moderate cases intramuscular injections are recommended. The gluteal region or the anterior part of the thigh offer suitable sites. Absorption is three to four times more rapid than from subcutaneous injections. Intramuscular injections if properly carried out, are no more painful than subcutaneous injections, and because of the more rapid absorption are recommended for routine use. In severe and malignant cases and in all cases seen late in the disease it is important to introduce the antitoxin into the circulation at the earliest possible moment. Intravenous injection is therefore the method of choice.

Diphtheria Antitoxin is also used for prophylactic or protective purposes. To those who have been exposed to diphtheria by contact with cases and have not themselves developed the symptoms, immediate though temporary protection is conferred by the injection of 1000 units Diphtheria Antitoxin. This gives a temporary, passive immunity which protects the individual against infection for a short time. This protection lasts little more than two weeks, and is therefore limited to prophylaxis in persons actually exposed to the disease and finds its chief value in the presence of epidemics. A more or less per-

manent active immunity to diphtheria is conferred by the use of diphtheria prophylactics--diphtheria toxin-antitoxin mixture or diphtheria toxoid.

Dose--The Pharmacopoeia states the average dose as follows: "By parenteral injection, Therapeutic, 10,000 units. Prophylactic, 1000 units." In practice, physicians gauge the curative dosage by the severity of the symptoms and the stage of development of the disease. In very mild cases, treated early, 3000 to 5000 units is often sufficient. An average dose of 10,000 units should be regarded as a minimum initial dose in severe cases and in those seen late. The dosage may be repeated at short intervals, if indicated. There is apparently no danger of an over-dose. It is the practice to reduce the dosage by one-half for infants under twenty pounds, and a one-third reduction is recommended for children under fifty pounds. Otherwise the dosage given applies to all age groups. The protective or preventive dose of 100 units is standard practice.

DOSAGE FORMS AVAILABLE--Commonly supplied in 1000-unit, 3000-unit, 5000-unit, 10,000- unit and 20,000-unit containers.

ANTITOXINUM SCARLATINAE STREPTOCOCCICUM

Scarlet Fever Antitoxin.

Scarlet Fever Antitoxin is a sterile aqueous solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal of the genus Equus which has been immunized against the toxin or toxin-like substance produced by the streptococcus regarded as causative of scarlet fever. After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in freshly distilled water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. Scarlet Fever Antitoxin has a potency of not less than 400 antitoxic units per cc.

Description of Physical Properties--A transparent or slightly opalescent liquid, of a faint brownish, yellowish, or greenish color, nearly odorless or having an odor due to the presence of a preservative; it may have a slight, granular deposit. Scarlet Fever Antitoxin must be free from toxins, and must not contain an excessive proportion of preservative (not more than 0.5 per cent of phenol or 0.4 per cent of cresol, if either of these is used), and its total solids must not exceed 20 per cent.

PREPARATION--Normal, full-grown horses are used, after a ten-day period of observation in quarantine has shown them to be free from disease. The horses are injected subcutaneously with toxin from broth cultures of the scarlet fever streptococcus. The injections are increased gradually up to the limit of tolerance. When potency reaches a satisfactory stage, the horses are bled regularly until large amounts of serum have been collected. The serum or plasma is then purified and concentrated by the method used for the concentration of diphtheria

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a potency of not less than 300 antitoxic units per cc.

Description and Physical Properties.--A transparent or slightly opalescent liquid, of a faint brownish, yellowish, or greenish color, nearly odorless, or having an odor due to the presence of a preservative; it may have a slight granular deposit. Tetanus Antitoxin must be free from toxins, and must not contain an excessive proportion of preservative (not more than 0.5 per cent of phenol or 0.4 per cent of cresol, if either of these is used) and its total solids must not exceed 20 per cent.

USES--Tetanus Antitoxin must be considered rather as a preventative than as a curative agent, as best results are obtained when the antitoxin is routinely administered before the tetanus toxins have invaded the motor nerve cells. Conditions favoring the growth of tetanus bacilli are found in contused, lacerated wounds, in which destruction of tissue and blood has occurred.

"It should be the universal rule to give a prophylactic dose of 1500 units of antitoxin to all patients who have received lacerated or penetrating wounds. If the wounds contain necrotic tissue or a suspected foreign body, the dose should be repeated in ten days and subsequently if operation on the wound is contemplated." Deeply seated wounds which heal on the surface are especially dangerous, as also puncture wounds from nails and Fourth of July accidents. Statistics of its use in armies have fully demonstrated the protective value of tetanus antitoxin in wounds occurring in warfare. Wounds occurring in or about stables or on the farm, where manure, one of the best carriers of tetanus bacilli, is present, should be treated as soon as possible, and the injection of an immunity dose of Tetanus Antitoxin should be regarded as standard routine practice.

Treatment of tetanus is not as satisfactory as the protective use of the serum. Tetanus toxin has a special affinity for nerve tissue, and eventually fixes itself to a nerve cell of the spinal cord. Since this fixation of the toxin in the nerve cell cannot be reversed, the object of treatment is to administer large quantities of antitoxin at the earliest possible moment in an attempt to neutralize the toxin before fixation has had time to proceed to a dangerous extent. Therefore, if the symptoms of the disease have appeared, an attempt should be made at once to saturate the patient with antitoxin by the quickest possible method. For this reason authorities recommend either intravenous or intraspinal injections or both.

Dose--The curative dose stated by the Pharmacopoeia is 20,000 units by parenteral injection. This is usually greatly exceeded. Therapeutic doses of from 30,000 to 40,000 units, repeated daily, are often given, and occasionally even larger doses have been used.

The protective or prophylactic dose is 1500 units. This dose should be repeated every eight to ten days, as long as the condition of the wound indicates the possibility of the continued presence therein of tetanus bacilli or its spores.

DOSAGE FORMS AVAILABLE--Commonly supplied in 1500 units, 5000 units, and 10,000 unit containers.

ANTIBACTERIAL SERUMS

Antibacterial serums are antagonistic to bacteria. They attack the germs themselves and for this reason are to be clearly distinguished from the antitoxic serums or antitoxins. As noted in the preceeding section, antitoxic serums neutralize the toxin or poison produced by certain germs. Antibacterial serums, on the other hand, contain antibodies which act in a very different way. They contain one or more of several kinds of antibodies, of which the better known are briefly defined as follows:

BACTERIOLYSINS--Bactericidal antibodies which kill by actually dissolving or disintergrating the bacterial cells. They act only in the presence of complement--a substance which is present in fresh blood.

BACTERIOTROPINS--These antibodies do not destroy bacteria by direct action but promote phagocytosis, that is, they in some way affect the invading bacteria so that they are rendered defenseless and are taken up easily by the phagocytes or white blood corpuscles. Bacteriotropins are not injured by moderate heat.

OPSONINS--Antibodies similar in function to the bacteriotropins but different in that they are easily destroyed by moderate heat.

AGGLUTININS--Agglutinins are antibodies which act directly on the bacteria without complement, causing them to come together in clumps.

PRECIPITINS--Precipitins act on solutions of bacterial substances causing them to precipitate.

It will be seen, from the number of different kinds of antibodies, that the action of antibacterial serums is much more complicated and in most cases less effective than that of the antitoxins. The production of potent antibacterial serums is correspondingly difficult. Their therapeutic value is not so clearly defined nor as well established as that of the antitoxins. There are several reasons for this. One is found in the fact that antibacterial antibodies are associated with a different serum globulin, and, up to this time, it has not been found practical to concentrate them successfully. The antibacterial substances cannot, therefore, be prepared in the degree of purity and concentration which characterizes the antitoxins. The antibacterial serums are unconcentrated and, comparatively speaking, low in antibody content. Specificity of the antibodies must be taken into account in preparing and using antibacterial serums. This is nowhere more clearly seen than in the case of meningococcus and antimeningococcic serum. Four distinct types of the meningococcus have been found and it has been shown that serum containing antibodies against one of these types is not effective against the other three. So with antipneumococcic serum. Type I antipneumococcic serum is not effective against Type II or Type III organisms. In other words, antibacterial serums are ef-

fective, as a rule, only against the particular strains or types of the organism used in producing the serum.

SERUM ANTIMENINGOCOCCICUM. Antimeningococcic Serum.

Serum Antimeningococcic - Antimeningococcus Serum; Meningococcus Serum; Meningitis Serum:

Antimeningococcic Serum is obtained from the blood of an animal of the genus Equus immunized with cultures of the several types of meningococci (Neisseria intracellularis) which prevail in the United States.

Description and Physical Properties - A yellowish, clear, or slightly turbid liquid having a faint odor of horse serum or having an odor due to the presence of a preservative; it may have a slight, granular deposit.

Antimeningococcic Serum must come from healthy animals and must be sterile. It must not contain an excessive proportion of preservative (not more than 0.35 per cent of phenol or cresol if either of these is used).

PREPARATION - Cultures of a number of strains representing the four different types of the meningococcus are mixed in one emulsion. Horses are given regularly graduated doses of this suspension at fixed intervals, until trial bleedings show that the serum of the horse is at least equal in agglutinin content to that of a standard control serum distributed by the National Institute of Health. Then regular bleedings are made and the serum is recovered, sterilized, tested and filled into market containers in the usual way. Since the antigens used in immunizing the horses contain representative strains from each of the four principal types of meningococcus, the resulting serum contains antibodies specific for the four types and the serum is therefore described as polyvalent.

USES-- Specific in the treatment of meningococcus meningitis. In the first or carrier stage the germs are found in the mucous membranes of the nose and tonsils and in the sinuses. Treatment in this, the initial stage, is almost entirely local.

In the second stage of the disease, that is, in septic cases, there is a blood stream infection. This occurs before the meninges are affected. Sterilization of the blood stream is attempted at once by giving large doses of Antimeningococcic Serum, preferably by vein. Intravenous use is also advisable when the meningococci persist or reappear in the blood during the third stage, that is, after the localization of the infection in the membranes of the brain and spinal cord, but the precaution must be taken to desensitize the patient before giving the first intravenous injection after intraspinal injection has been done. Treatment of the third stage requires the introduction of the serum into the spinal canal. This is done by lumbar puncture. Directions for making lumbar puncture and introducing the serum intraspinally usually accompany packages of Antimeningococcic Serum.

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USES--Investigations have shown that pneumococci of several serological types may cause lobar pneumonia. In addition to the fixed Types I, II, and III originally recognized, sub-divisions of Type II have been described. The previously heterogeneous group IV has been partially resolved into a number of serological types. Only products containing Type I and/or type II pneumococci have been shown to be therapeutically useful. If a definite diagnosis of acute lobar pneumonia is made within two days of the onset and rapid typing is not possible, treatment with antipneumococcic serum containing Types I and II may be instituted without waiting to determine the pneumococcus type, but it should be realized that this treatment will be of no value in about half the cases. Intravenous injection is recommended. If this method is not practicable, as in very young children or in obese patients, intramuscular injection should be resorted to. Subcutaneous injections are not recommended.

DOSE--An initial dose of 10,000 units of the serum, intravenously, as soon as possible after diagnosis, and a second dose of 20,000 units in 1 hour; the second dose may be repeated at intervals of 2 - 4 hours until fall of temperature and relief of symptoms indicate the control of the infection.

DOSAGE FORMS AVAILABLE--Supplied in bottles and syringes containing 10,000 units and 20,000 units.

NORMAL HORSE SERUM

Serum Equinum--Although not a specific immunizing product, Normal Horse Serum may conveniently be placed in the general group of the serums. Normal Horse Serum is that separated from the freshly drawn blood of normal horses and sterilized by filtration. It is called normal serum because it contains no anti-bodies or antitoxins produced artificially by the injection of antigens into the horse. It is therefore to be distinguished from the curative serums which contain antitoxins, or antibacterial bodies, or both.

Uses--Its principal use is to increase the coagulability of the blood and is employed in the treatment of hemophilia and other hemorrhagic conditions; for example, hemorrhages following wounds and fractures and during or following surgical operations. It has also been used in non-specific protein therapy. Like other foreign proteins, injected hypodermically, sufficient doses of Normal Horse Serum are follow ed by a shock reaction, which has been considered of benefit in the treatment of many conditions.

Dose. May be applied locally to any bleeding surface by means of sterile cotton saturated with the serum. It is recommended for use subcutaneously in doses of 20 to 30 cc. or intravenously in doses of 10 to 20 cc. as a means of increasing coagulability of the blood and of preventing hemorrhage.

Serum Poisoning or Anaphylaxis--The following special precaution when administering horse serum is given by the N.N.R.

If horse serum is applied liberally to a burn or an open wound on a patient who is sensitive, there is danger of a severe if not a fatal reaction. Before administering horse serum or a preparation containing it to a patient, whether topically, intracutaneously, subcutaneously, or intravenously, the physician should obtain a history of the patient as regards serum administration. The safest procedure is to make a test of sensitiveness by injection of not more than 0.05 cc. of a 1 in 10 dilution of the serum in the skin of the forearm or the instillation of a drop of the same dilution into the conjunctival sac. No patient showing sensitiveness should be given the serum without previous desensitization.

Most cases of this poisoning have occurred after the use of antitoxic serums; but emphasis should be laid on the fact that these symptoms are not caused by antitoxin, but are due to hyper-susceptibility to the proteins of horse serum in which it is contained.

Atropine and epinephrine, hypodermically, should be used for the severer manifestations of serum poisoning.

Dosage Forms Available--Commonly supplied in 10 cc. syringes or ampuls, in 20 cc. syringes or vials, in 25 cc., 50 cc., and 100 cc. ampuls, in 30 cc. and 50 cc vials., and in 50 cc. and 100 cc. bottles.

BIOLOGICAL PRODUCTS USED FOR ACTIVE IMMUNIZATION.

Following recovery from many of the acute infections, such as scarlet fever, typhoid fever, and others, a more or less well-developed and lasting immunity appears. This is a matter of common knowledge. The condition represents an acquired active immunity resulting from the stimulation of the body cells by the infecting agent and the excess production of specific antibodies. But in this chapter we are interested in the possibility of protection without infection, that is, the artificial production of an active immunity without subjecting the individual to the disease itself. Such use for biological products follows from the early observations on vaccination against smallpox and against rabies. Jenner's observations and experiments proving that cowpox virus or vaccina, inoculated into the human subject, gave immunity to smallpox, and was followed some eighty years later by the discovery by Pasteur that a disease virus or germ could be so modified or attenuated that its inoculation into the human subject did not cause the actual disease yet it would stimulate the body cells to produce specific antibodies and thus give rise to active immunity. Upon this fundamental observation the whole theory and practice of prophylactic immunization has been built. Pasteur himself early devised a method of attenuating the virus of rabies (hydrophobia) and a method of immunizing against this disease.

The historical importance of smallpox vaccine and of rabies vaccine and the effective immunity induced by them gives them first place in the discussion of biological products used for active immunization.

Vaccinum Variolae: Smallpox Vaccine

Smallpox vaccine consists of a glycerinated suspension of the vesicles of vaccinia or cowpox which have been obtained from healthy vaccinated animals of the bovine species. The vesicles must be removed and the vaccine must be prepared under aseptic conditions.

The vesicles must be removed from the animal at the time of maximum potency, thoroughly triturated and made into a smooth suspension with an aqueous solution of glycerin. This solution shall not be acid to bromcresol purple T.S. and not distinctly alkaline to phenol red T.S.

Description and Physical Properties.--Smallpox Vaccine is a gray-ish turbid suspension; it may have an odor and a trace of color due to the presence of a preservative.

Smallpox Vaccine must be prepared in an establishment licensed for the purpose by the Secretary of the Treasury of the United States.

The following precautions must be observed in licensed establishments:

No Vaccine shall be prepared from any animal having a communicable disease other than vaccinia. Animals used for propagating Smallpox Vaccine must have responded negatively to a tuberculin test and, prior to vaccination, must have evidenced no ill health while in quarantine for at least seven days under daily veterinary inspection. After the vaccine pulp has been removed from each animal, a necropsy shall be performed, permanent records of which shall be kept. Each lot of Smallpox Vaccine shall be examined to determine its freedom from undue bacterial content, and a special examination shall be made of each lot to determine the absence of tetanus organisms and other pathogenic anaerobes. Permanent records of these examinations must be kept. The finished product must be placed in sterile containers that comply with the requirements of the law of the regulations established by the United States Public Health Service.

The outside label must bear the name Smallpox Vaccine, the name, address, and license number of the manufacturer, and the date beyond which the Vaccine may not be expected to retain the potency prescribed by governmental authority. The label must also bear directions concerning storage of the package below 5 degrees C.

Storage--Preserve and dispense Smallpox Vaccine in hermetically sealed, capillary glass tubes.

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.

USES--Smallpox Vaccine has amply demonstrated its efficacy in producing an effective immunity against smallpox. Human beings of both

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ment, not to the skin. Rarely a severe "take" may require antiseptic dressings.

ADVANTAGES OF PRESSURE METHODS

1. Virus may be wiped off immediately after vaccination; no waiting for wound to dry before clothing touches it.

2. Least painful method.

3. Leaves practically no scar-hence is an added advantage when vaccinating girls.

4. Insures greatest freedom from sore arms and infection.

5. Safest procedure in vaccinating infants and small children.

REACTIONS

If the vaccine has been properly kept and applied, one of three forms of "take" will appear in every case. If no reaction occurs, it does not indicate that the subject is immune, but rather that the virus is inactive and worthless and is therefore incapable of protecting against smallpox.

(a) The typical "take". If the person has not been previously immunized the reaction will appear as a primary "take" or vaccinia. On the third or fourth day after vaccination, a papule appears which becomes vesiculated on the next day and is surrounded by a red margin or areola which rapidly extends to a wide area about the seventh or eighth day. The maximum size of the vesicle and area is reached on about the ninth or tenth day, after which the area rapidly fades and the vesicle becomes brown and crusted. If kept dry, the crust will separate in approximately three weeks from the day of vaccination.

(b) The "accelerated reaction." If the person retains some degree of immunity, either from previous vaccinations or an attack of smallpox, the reaction will appear sooner and last a shorter time. Such a reaction is termed a "vaccinoid," or accelerated reaction.

(c) The "immune reaction." If the immunity is high, the acceleration may be so great that the reaction consists only of a papule with areola reaching its maximum size in 12 to 60 hours after vaccination. Under such conditions, usually no vesicle forms, and the reaction is termed "immunity reaction" or "immediate reaction".

DOSAGE FORMS AVAILABLE--Supplied in hermetically sealed capiliary tubes and in combination capillary tube and scarifying point. May be obtained in packages of 1, 5 and 10 vaccinations.

UNOFFICIAL SMALLPOX VACCINE DRIED

Many attempts have been made to prepare a smallpox vaccine which would withstand the effects of higher temperatures and one that would be suitable for shipment to, and use in, tropical and sub-tropical countries. A dried smallpox vaccine for such use has been supplied for some time by two or more European laboratories. Dried Smallpox Vaccine was successfully produced on a manufacturing scale in the United States as early as 1922 and has found a considerable field of usefulness in torrid countries. License for its regular production was issued by the U. S. Public Health Service in 1925 but it is supplied chiefly in export trade to those regions of the world where the temperature conditions or lack of refrigeration facilities render the use of glycerinized vaccine virus impracticable.

VACCINUM RABIES RABIES VACCINE

Rabies Vaccine is a sterile suspension of the attenuated, diluted, dried, or dead, fixed virus of rabies. The virus is contained in the tissue of the central nervous system of an animal suffering from, or dead of, fixed virus rabies infection.

DESCRIPTION AND PHYSICAL PROPERTIES--A more or less turbid, white or whitish liquid nearly odorless or having an odor due to the presence of a preservative. Rabies Vaccine must come from animals that are healthy excepting for rabies infection. It must not contain an excessive proportion of preservative (not more than 0.5 per cent of pheno or 0.4 per cent of cresol if either of these is used.)

Rabies is an acute infectious disease caused by the filterable virus. It is one of the diseases most dreaded by the laity. The virus or causative agent is contained in the saliva of the rabid animal. Infection takes place through abrasions or punctures of the skin following bites or scratches. The virus shows a special affinity for the nervous system and makes its way along the nerve tracts to the central nervous system, the involvement of which causes the distressing symptoms. Fortunately, the incubation period is a long one, varying from fourteen to ninety days, and it is possible to develop a protective immunity before the symptoms of the disease appear. Pasteur was the first to demonstrate the protective value of Rabies Vaccine. The method which he devised and modifications thereof have been almost entirely supplanted by the Semple, Fermi, and other methods.

PREPARATION--Rabies Vaccine is attenuated or rendered practically non-virulent for man by repeated passage through rabbits, and is treated in various ways to decrease or destroy infectivity.

Methods of treating the virus before inoculation, are (a) the dilution method--Hegyes, (b) low temperature method--Harris, (c) dialyzing method--Cummings, (d) phenol-treated or killed virus--Semple and Fermi.

In the dilution method of Hogyes, the brains of rabbits dead from rabies are preserved in glycerin. Emulsions of the brain substance

are prepared beginning with a 1 in 20,000 dilution and increasing the strength until a 1 in 100 dilution is given. The Harris low-temperature method involves freezing the emulsion of the brains and spinal cords and desiccation in vacuum. The result is a dried powder which is standardized, and emulsions in graded doses are prepared for injection. The method of dialysis or Cummings' method is applied by dialyzing a 1 per cent suspension of brain tissue against running distilled water until the active virulent virus is destroyed.

The phenol-killed virus, Semple and Fermi, calls for the preparation of an emulsion or standard suspension of the brain and cord substance killed by treatment with phenol.

USES--Rabies Vaccine is used to establish an immunity to rabies (hydrophobia) by treating the individual after the bite of a rabid animal, but before the incubation period is completed. The injection of attenuated, or modified or killed virus during the period of incubation stimulates the production of antibodies so that the infecting virus of the wound is neutralized or destroyed. The efficacy of rabies vaccine is demonstrated by the statistics which indicate the reduction in the death rate from 15 to 20 per cent to less than one-half of 1 per cent (0.5 per cent). The immunizing treatment, to be effective, must be instituted as soon as possible after the bite has been inflicted. The treatment is without effect after the symptoms of rabies have appeared. The resulting immunity is not regarded as very durable and the recommendation is that if the person is bitten a second time by a rabid animal one or more years after an immunizing treatment, a complete series of prophylactic injections should be repeated.

Dose--Dosage recommendations vary considerably, according to the method of preparation and the amount and condition of the virus in the suspension injected. Rabies Vaccine (Pasteur) consists of 21 to 25 doses. The doses are graded so that the first contains virus of the greatest attenuation, while the last dose in the series represents the least attenuation. Doses are injected at 24-hour intervals. Rabies Vaccine prepared by the dilution method (Hogyes) is supplied in a treatment of 18 doses, each dose varying in quantity from 3 to 5 cc. the first one consisting of a 1 in 20,000 dilution, and the last a 1 in 100 dilution. Rabies Vaccine (Harris) is given in daily doses over a period of 10 days or more, the dosage increasing gradually up to a maximum at the tenth day which may be supplemented if desired. Rabies Vaccine (Cummings' method) is available in 14 or 21 dose treatments. The 21 dose is recommended for the more severe cases, the 14 dose is the less severe. A 2 cc. dose is given each day. Rabies Vaccine, phenol-killed, is available in 14-dose treatment packages. It possesses better keeping qualities than the attenuated living virus; and therefore can be stocked by pharmacists, and the entire treatment can be put up and dispensed in one package. The doses are the same size and strength which avoids the necessity of following out a fixed schedule of increasing doses.

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The refined toxoid (Havens) is given subcutaneously in 0.5 cc. or 1 cc. amounts as indicated on the label. One dose constitutes a complete treatment. Due to the presence of potassium aluminum sulfate in the refined toxoid, absorption is delayed and a nodule persists at the site of inoculation for several days.

TOXINUM SCARLATNAE STREPTOCOCCICUM. Scarlet Fever Streptococcus

Toxin (Toxin. Scarlet. Streptococ.--Scarlet Fever Streptococcic Toxin, Scarlet Fever Toxin for Immunization and for the Dick Test).

Scarlet Fever Streptococcus Toxin is a sterile solution in beef-broth of certain products including a soluble toxin, resulting from the growth in the broth of suitable strains of hemolytic streptococci (Streptococcus Scarlatinae)

DESCRIPTION AND PHYSICAL PROPERTIES--A transparent liquid having the color of the broth in which it is made (usually straw to brownish in color) and having a broth-like odor which is often altered somewhat by the antiseptic used as a preservative.

No horse blood or other foreign blood shall be added to the culture medium used for the preparation of the Toxin.

Scarlet Fever Streptococcus Toxin must be prepared in an establishment licensed for the purpose by the Secretary of the Treasury of the United States.

The potency of the Toxin shall be expressed in terms of the skin test dose, which is that quantity of toxin which will give positive reaction in all persons susceptible to scarlet fever and negative reactions in persons immune to scarlet fever, when injected intracutaneously.

Average Dose--For determining susceptibility (Dick Test), intracutaneous, 0.1 cc. of the dilution representing one skin test dose.

For active immunization--For this purpose the Toxin shall be dispensed in a series of graduated doses of such potency and number that on the average, when the series has been injected hypodermically at proper intervals, into a toxin-susceptible individual, that individual will not react positively to one skin test dose of the Test Toxin, injected intracutaneously.

SCARLET FEVER IMMUNITY TEST OR DICK TEST--Approved products, under license from the Scarlet Fever Committee, Inc., are supplied under the name Scarlet Fever Streptococcus Toxin for the Dick Test. It is a soluble toxin derived from the hemolytic streptococci of scarlet fever. Intradermal injections of this toxin, properly diluted, give positive skin reactions in susceptible persons, but no reaction in those immune to scarlet fever. The nature of the reaction is quite similar to that produced by Diphtheria Toxin in the Schick

Test, except that it produces somewhat less inflammation of the skin and the reactions are more transient. An area of redness is the principal characteristic of a positive reaction, and the rule is to regard any reddening of the skin, however faint, measuring over 1 cm. in diameter, as a positive reaction. The reaction reaches its height in from eighteen to twenty-four hours, and the reaction is read and recorded within that period.

PREPARATION--Scarlet Fever Streptococcus Toxin for the Dick Test is prepared by the proper dilution of the toxin obtained from cultures of scarlet fever streptococci, and standardized so that 1/10 (0.1) cc. contains one skin test dose. Standardization is done by comparison with a toxin of known strength distributed by the U. S. Public Health Service.

Dose-- 1/10 (0.1) cc. injected intradermally (intracutaneously).

DOSAGE FORMS AVAILABLE--Marketed in 1 cc. containers sufficient for ten tests, and in 10-cc. containers sufficient for 100 tests.

BACTERIAL VACCINES

Bacterial vaccines, or bacterins, are sterile suspensions of bacteria in physiological salt solution. Ordinarily, some preservative is added, such as tricresol, phenol, or glycerin; organic mercury compounds are also being used extensively. When injected into the body, the bacterial substance tends to stimulate the tissues to the production of antibodies.

PREPARATION--The preparation of bacterial vaccines demands careful technic and the experience of trained bacteriologists. The first step is to procure the infecting agent or causative organism in pure culture. These may be isolated from pus collected from an abscess or sinus, or they may be taken from nasal secretion, or from sputum, or from urine, or blood, or direct from an infected lung, etc.

When this is done, the isolated strains may then be maintained as "stock cultures". In the preparation of a vaccine, the stock culture is used. After a suitable interval at controlled temperature the growth is collected and emulsified. Purity tests are made to determine that the suspension contains none but the desired organism. If this test is satisfactory, the suspension is killed by exposure to heat or by other means. The killing temperature is carefully controlled, the degree and time of exposure varying for different types of vaccines. A preservative is then added and the vaccines standardized by bacterial count and dilution to the required strength, placed in the final containers, and released for distribution only after satisfactory tests show the product to be sterile.

All manufacturers of biological products for human use licensed by the Federal Government are required to place on the labels of bacterial vaccines the name of each organism used in the preparation of the material and the number of each organism contained in each cc.

The statement "No U. S. Standard of Potency" must appear on the labels of those products for which no potency standard has been adopted.

USES--As antigens capable of producing active immunity, some of the bacterial vaccines have proved of great value in prophylaxis. The prophylactic use of typhoid bacillus vaccine is the outstanding example.

The employment of these vaccines in the treatment of disease has been extensive, not only in chronic infectious diseases, but even in the acute stages. No general statement can be made of their value in this connection, except that subacute and chronic cases seem to be more amenable to treatment. Some have apparently given much more favorable results than others. Specific indications are mentioned under the individual products following.

Dose--For prophylactic (preventive) immunization, three to five gradually increasing doses are given at intervals of three to seven days.

For treatment of acute conditions, no scheme of dosage can be stated definitely, for the reason that no two individuals react alike to the same dose of a given bacterin, and because reactions produced by different bacterins are not the same, owing to inherent differences in the germs themselves. The initial dose is arbitrarily selected, the physician being guided by the thought that, in general, the severer the disease the smaller the first dose. Subsequent doses are controlled as to amount and interval by the results obtained from preceding doses. The clinical symptoms which physicians look for in controlling dosage of bacterial vaccines have been summarized as follows:

A sub-minimal dose has no perceptible effect.

A minimal dose is rapidly followed by a feeling of well-being on the part of the patient, and a transient fall in temperature, if in a febrile case.

A medium dose may induce some local reaction at the site of injection and a slight reaction at the focus of infection, and possibly a slight general reaction which may show itself by a rise of temperature of not more than 1°C., accompanied by a slight malaise and some increase in pulse rate. This may be followed; in twenty-four hours, by a fall in temperature and a general improvement in the condition.

A large dose is followed by a local reaction and by a severe reaction at the focal of infection, and symptoms of a general reaction (malaise, rise of temperature, etc.) may persist for some time without evidence of improvement.

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will not permit detailed information concerning each one. Formerly, a considerable number were admitted and described in the N.N.R., but of recent years many of them have been dropped from the book on the grounds that there was not sufficient acceptable clinical evidence to warrant retaining them.

In one instance, however, a mixed vaccine has proved of very great value and has practically supplanted the use of the single vaccine. This is the Typhoid-Paratyphoid Vaccine, or Typhoid Bacterins, Mixed.

VACCINUM TYPHO-PARATYPHOSUM. Bacterial Vaccine made from the Typhoid Bacillus and the Paratyphoid "A" and "B" Bacilli

Bacterial Vaccine made from the Typhoid Bacillus and the Paratyphoid "A" and "B" Bacilli is a suspension in physiological solution of sodium chloride of killed typhoid bacilli (Eberthella typhi) and killed paratyphoid "A" bacilli (Salmonella paratyphi) and killed paratyphoid "B" bacilli (Salmonella schottmulleri).

The Vaccine shall contain in 1 cc. at least 1,000,000,000 typhoid organisms and at least 500,000,000 of each of the paratyphoid organisms.

Description and Physical Properties--A more or less turbid, whitish fluid; nearly odorless or having a faint odor due to the presence of a preservative. Bacterial Vaccine made from the Typhoid Bacillus and the Paratyphoid "A" and "B" Bacilli must be sterile and must not contain an excessive amount of preservative (not more than 0.5 per cent of phenol or 0.4 per cent of cresol when either of these is used).

Bacterial Vaccine made from the Typhoid Bacillus and the Paratyphoid "A" and "B" bacilli must be prepared in an establishment licensed by the Secretary of the Treasury of the United States.

AUTOGENOUS VACCINES

In protective immunization in general, stock vaccines are used, and in most instances notably in the case of typhoid vaccine, results are entirely satisfactory. In the treatment of acute infection stock vaccines are required so that time shall not be lost from treatment while awaiting the isolation and identification of the infective agent. On the other hand, in some chronic infections of long standing, it sometimes happens that after a slight initial improvement following the use of stock vaccine, the condition will remain practically stationary, in spite of repeated injections. Substitution of an autogenous vaccine is then indicated.

Autogenous vaccines are those prepared from bacteria isolated from the patient. Their use has the advantage of bringing to the patient an antigen calculated to stimulate antibodies specific for the infecting organism. Their use is indicated particularly in chronic

conditions where vaccine therapy is plainly indicated and where stock vaccines have failed to bring about the desired improvements.

TUBERCULINS

Tuberculins are extracts or suspensions of the tubercle bacillus substances. A large number of preparations have been advanced from time to time, for each of which, special advantages or properties have been claimed. Only those which have been accepted and described in New and Non-official Remedies will be mentioned here. These are often designated by symbols, as follows: "O.T"--Koch's Old Tuberculin; "T.R."--Tuberculin Residue, Tuberculin Ruckstand, Koch's New Tuberculin; "B.E."--Bacillen Emulsion; "B.F."--Tuberculin Denys or Bouillon Filtrate.

The official tuberculin is as follows:

TUBERCULINUM PRISTINUM Old Tuberculin

(Tuberculin. Prist.--Tuberculin-Koch, Concentrated Tuberculin, Crude Tuberculin)

Tuberculin is a sterile solution in a special liquid culture medium of the soluble products of growth of the tubercle bacillus (Mycobacterium tuberculosis) and should contain about 50 per cent of glycerin.

Description and Physical Properties-- A clear, brownish liquid, readily soluble in water and having a characteristic odor. Tuberculin must be prepared in an establishment licensed for the purpose by the Secretary of the Treasury of the United States.

Tuberculin must be capable of effecting a general and local response in tuberculous guinea pigs.

Average Dose--By intracutaneous injection, 0.001 cc.

PREPARATION--Tuberculin O.T., which has received official recognition, is essentially a glycerin bouillon extract of tubercle bacilli. The culture is grown in glycerin bouillon and this is sterilized by heating with steam, and reduced by evaporation to one-tenth the original volume. The bacilli themselves are removed by filtration. The filtrate is a brownish colored liquid and keeps indefinitely.

Tuberculin, T.R. or Tuberculin Residue is made from living dried tubercle bacilli which are thoroughly ground and extracted in water. By centrifuge, extractives contained in the supernatant fluid are separated. The sediment is reground, extracted, and centrifuged as before, the process being repeated until practically no sediment remains. Fluid portions are combined and diluted with glycerin until the solution contains the residue of 10 mg. of dried tubercle bacilli per cc. It is a colorless liquid.

Tuberculin B. E. or Bacillen Emulsion is a suspension of dried, pulverized tubercle bacilli in equal parts of water and glycerin. Sediment is removed and the emulsion standardized to represent 5 mg. of the tubercle bacilli per cc.

Tuberculin B. F., Bouillon Filtrate or Tuberculin Denys is a culture of tubercle bacilli from which the bacilli are removed by filtration. It contains all the soluble products of the growth of the tubercle bacillus, but differs from Tuberculin O. T. in that no heat is applied during the course of preparation.

ACTION AND USES--The tuberculins are not toxins, like the Diphtheria Toxin or Scarlet Fever Streptococcus Toxin. This is proved by the fact that relatively large amounts may be injected into a healthy non-tuberculous subject, without any ill effect. On the other hand, very small amounts will produce a reaction in tuberculous subjects. Tuberculins have little or no antigenic power and are of negligible immunizing value. Nevertheless, they have in the opinion of those who have used them a definite place in the treatment of selected cases of tuberculosis, especially in those of a chronic and localized character. The benefit derived from their use must be ascribed to the tuberculin reaction.

So small an amount as 0.00,000,01 of a cc. of tuberculin may cause symptoms of illness in a tuberculous subject. The tuberculin reaction is accompanied by local reactions and also a focal reaction is employed as a means of diagnosis.

Recovery from tuberculosis is commonly regarded as resulting from the formation of fibrous tissue around the foci of infection, or tubercles, thus forming a dense capsule within which the tubercle bacilli are imprisoned. There is some evidence that the administration of tuberculins in suitable dosage set up a slight inflammation and chronic local congestion at the site of the lesions, and that this congestion favors the formation of fibrous tissue, thus promoting the walling-off of the lesion. Tuberculin therapy is therefore considered most promising in chronic tuberculosis with localized lesions. The use of tuberculins in treatment requires special knowledge and experienoe, the great danger being in the administration of too large doses. Doses that are too large produce severe reactions with ill effects on the patient. Physicians applying tuberculin therapy realize that the susceptibility to tuberculin in different patients varies considerably, and they take every precaution not to exceed the patient's tolerance.

Dose--In treatment an initial dose may consist of 0.00,000,001 to 0.00,000,01 cc. Not more than two doses per week should be given. No fixed dosage schedule can be given because different patients vary greatly in their sensitiveness to tuberculin. Subsequent doses are gradually increased but always keeping them low enough to prevent any marked constitutional disturbances. Tuberculin therapy should be accompanied by the usual measures of rest, diet, and proper hygiene.

Different kinds of tuberculins vary in strength and even different lots of the same tuberculin may vary somewhat. It is a wise precaution therefore, during the course of treatment when a package of tuberculin bearing a new laboratory number is first used, to reduce the dosage one-half, in order to guard against possible change in strength.

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	Maximum	Average
	Metric	Metric
Cinchophen	1.0	0.5
Cocaine and salts	0.06	0.03
Colchicine	0.001	0.0005
Colchicum Corm	0.5	0.25
Colchicum corm strong tincture	2.0	0.6
Colchicum extract	0.12	0.06
Colchicum seed	0.3	0.2
Colchicum tincture	3.0	2.0
Colocynth	0.3	0.1
Colocynth extract	0.12	0.03
Conium	0.5	0.2
Conium extract	0.06	0.03
Copaiba	4.0	1.0
Copper sulphate	0.6	0.25
Cotarnine chloride	0.2	0.06
Creosote	0.5	0.25
Cresol	0.2	0.06
Croton oil	0.12	0.06
Diamorphine hydrochloride	0.015	0.005
Digitalis	0.2	0.1
Digitalis tincture	2.0	1.0
Emetine hydrochloride	0.03	0.02
Ephedrine and salts	0.2	0.06
Epinephrine	0.001	0.0005
Ergot	4.0	2.0
Ether	4.0	1.0
Ethylaminobenzoate	0.5	0.3
Ethylmorphine hydrochloride	0.045	0.015
Ethyl nitrite spirit	4.0	2.0
Ferric chloride tincture	3.0	0.6
Ferrous carbonate mass	1.2	0.25
Ferrous iodide syrup	2.0	1.0
Gaultheria oil	2.0	0.5
Gelsemium	0.12	0.03
Gelsemium tincture	1.2	0.25
Gentian	2.0	1.0
Glyceryl trinitrate spirit	0.12	0.06
Guaiacol	0.6	0.5
Hexyl resorcinol	1.0	0.5
Homatropine hydrobromide	0.002	0.0005
Hydrastine hydrochloride	0.06	0.01
Hydrastis	3.0	2.0
Hydriodic acid diluted	2.0	0.5
Hydrochloric acid diluted	2.0	1.0
Hydrocyanic acid diluted	0.3	0.12
Hyoscyamine salts	0.001	0.0006
Hyoscyamus	0.03	0.2
Hyoscyamus extract	0.12	0.05
Hyoscyamus tincture	3.0	2.0
Iodine	0.03	0.01

	Maximum	Average
	Metric	Metric
Iodine compound solution	0.6	0.2
Iodine tincture	0.3	0.1
Iodoform	0.3	0.25
Ipecac	2.0	0.06
Ipecac syrup	4.0	0.75
Lead acetate	0.3	0.06
Lobelia	0.6	0.1
Lobelia tincture	2.0	1.0
Mercuric iodide	0.015	0.004
Mercuric oxycyanide	0.015	0.004
Mercurous chloride	0.6	0.15
Mercurous iodide	0.06	0.01
Mercury and chalk	0.6	0.25
Mercury mass	0.6	0.3
Methenamine	2.0	0.3
Methyl salicylate	2.0	0.75
Morphine and salts	0.03	0.008
Mustard volatile oil	0.03	0.008
Neocincophen	1.0	0.5
Nux vomica	0.25	0.1
Nux vomica extract	0.06	0.015
Nux vomica tincture	2.0	1.0
Opium	0.2	0.06
Opium extract	0.06	0.03
Opium and ipecac powder	1.2	0.3
Opium tincture	2.0	0.6
Ovarian substance	1.0	0.3
Oxgall extract	0.6	0.4
Papaverine salts	0.5	0.06
Pelletierine tannate	0.6	0.25
Phenobarbital (and sodium salt)	0.12	0.03
Phenol and liquefied phenol	0.2	0.06
Phenolphthalein	0.2	0.06
Phenyl salicylate	2.0	0.3
Phosphorous	0.002	0.0006
Physostigmine salts	0.006	0.002
Pilocarpine salts	0.015	0.005
Pituitary	0.25	0.03
Potassium arsenite solution	0.6	0.2
Potassium chlorate	1.2	0.25
Potassium hydroxide solution	2.0	1.0
Potassium iodide	2.0	0.3
Potassium permanganate	0.2	0.06
Quinidine and salts	1.0	0.3
Quinine salts	1.0	0.3
Quinine urea hydrochloride	1.0	1.0
Resorcinol	0.6	0.12
Salicylic acid	1.2	0.75
Santal oil	2.0	0.5
Santonin	0.3	0.06

Scopolamine Hydrobromide
Silver nitrate
Sodium bromide
Sodium cacodylate
Sodium hydroxide solution
Sodium iodide
Sodium nitrite
Sodium salicylate
Squill
Squill tincture
Stramonium
Stramonium extract
Stramonium tincture
Strontium salicylate
Strophanthin
Strophanthus
Strophanthus tincture
Strychnine and salts
Sulphonethylmethane
Sulphonmethane
Sulphuric acid aromatic
Sulphuric acid diluted
Terebene
Terpin hydrate
Thymol
Thyroid
Thyroxin
Trinitrophenol
Veratrum viride
Venatrum viride tincture
Volatile oils except as given otherwise
Wild cherry
Zinc acetate
Zinc sulphate

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ARTHRITIS.--Inflammation and swelling of the joints.
ASPHYXIA.--Condition caused by absence of oxygenation by the blood.
ASTRINGENT.--That which produces contraction of tissue.
CARMINATIVE.--Agent used to prevent or dispel gas in the intestines.
CATHARTIC.--A purgative of fairly high power.
CAUSTIC.--That which destroys tissue.
CAUTERIZER.--A caustic.
CHOLAGOGUE.--That which promotes formation or flow of bile.
COMA.--Abnormally intense sleep or stupor.
CORRECTIVE.--That which modifies side effects, particularly griping of purgatives.
CORROSIVE.--A caustic.
COUNTER-IRRITANT.--An agent used to produce irritation in one part in order to give improvement in condition at some more remote part.
CYSTITIS.--Inflammation of the bladder.
DEMULCENT.--That which softens, relaxes, and protects the mucous membrane.
DENTIFRICE.--A cleanser for the teeth.
DEPILATORY.--A material used to destroy hair.
DEPRESSANT.--Diminishing functional activity.
DERIVATION.--The process in which a counter-irritant is employed.
DERMATITIS.--Inflammation of the skin.
DETERGENT.--A cleanser.
DIAGNOSIS.--Determination of cause from a knowledge of effects.
DIAPHORETIC.--That which produces increase of perspiration.
DIASTOLE.--The period of dilation, particularly of the heart.
DIGESTANT.--Anything which aids in processes or speed of digestion.
DISINFECTANT.--That which can remove infection.
DIURETIC.--That which promotes increase of urinary output.
DRASTIC.--A powerful purgative.
ECBOLIC.--That which produces abortion or aids in delivery of child.
ECCOPROTIC.--A mild purgative.
ELIMINATION.--The process of leaving the blood stream.
EMETIC.--An agent which causes vomiting.
EMMENAGOGUE.--Agent which stimulates menstrual flow.
EMOLLIENT.--That which softens, relaxes, and protects the external tissue.
EMPIRICAL.--Use of a drug because of experience without reasons.
ENDOCRINES.--Glands of internal secretion.
EPISPASTIC.--A blistering agent.
ERRHINE.--That which increases nasal discharge.
ESCHAROTIC.--That which produces an eschar, or dry crust of dead tissue.
EVACUATION.--Expulsion of contents, particularly of the stomach.
EXCRETION.--The process of leaving the body.
EXPECTORANT.--That which modifies bronchial secretion for the better.
FLATULENCE.--Formation of gas, particularly in the intestine.
GALACTAGOGUE.--An agent which stimulates the flow of milk.
GALACTOPHYGE.--An agent which decreases the secretion or flow of milk.
GASTRITIS.--Inflammation of the stomach.
GASTRO-ENTERITIS.--Inflammation of the alimentary canal.
GERMICIDE.--That which kills germs.
GLYCOSURIA.--A condition of sugar in the urine.

HELIOTHERAPY.--Treatment of disease by means of light.
HEMATINIC.--That which improves the quality of blood.
HEMOSTATIC.--An agent which arrests hemorrhage.
HEPATITIS.--Inflammation of the liver.
HORMONES.--The potent substance in a secretion, chiefly of the endocrines.
HYDRAGOGUE.--A purgative causing watery discharges.
HYPERTHYROIDISM.--A condition in which the thyroid gland is overfunctioning.
HYPNOTIC.--An agent which causes sleep.
HYPODERMIC INJECTION.--Injection of a drug by means of a needle.
HYPOTHYROIDISM.--A condition in which the thyroid is underfunctioning.
IDIOSYNCRASY.--Individual peculiarity in reactions to a drug.
INCRETIONS.--The secretions of a gland of internal secretion.
INHIBITION.--The restraint of organic or drug activity.
INSECTICIDE.--That which is used to kill insects.
INTRAMUSCULARLY.--Injected directly into muscles.
INTRAVENOUSLY.--Injected directly into a vein.
INUNCTION.--Medication by rubbing into the skin.
LAXATIVE.--A mild purgative.
LENETIVE.--A mild laxative.
LETHAL DOSE.--A dose which is fatal.
LITHONTRIPTIC.--That which removes calculi or stones.
LOCAL ANESTHETIC.--An agent which paralyzes the sensory nerves locally.
LOCAL ANODYNE.--That which abolishes pain by local application.
LOCAL SEDATIVE.--That which relieves pain or discomfort by local application.
LOCAL STIMULANT.--An agent which stimulates repair by causing irritation.
MASTICATORY.--A remedy to be chewed to improve local conditions in the mouth.
MAXIMUM DOSE.--The largest amount consistent with safety.
MINIMUM DOSE.--The smallest amount which will give a desired effect.
MYDRIATIC.--That which dilates the pupil.
MYOTIC.--That which contracts the pupil.
NARCOTIC.--An agent tending to paralyze the nervous system, and producing, in sufficient doses, sleep, stupor, and death.
NECROPSY.--Examination of a dead body.
NEPHRITIS.--Inflammation of the kidneys.
NUTRIENT.--A medicinal food.
ORAL ADMINISTRATION.--Given by mouth.
OXYTOCIC.--An agent which promotes uterine contraction.
PARASITICIDE.--That which kills parasites.
PARENTERAL ADMINISTRATION.--By other routes than the mouth.
PARTURITION.--The process of giving birth to a child.
PATHOLOGY.--The science of diseases.
PEDICULOSIS.--The condition of infection with lice.
PROGNOSIS.--Prediction of ultimate outcome.
PROPHYLACTIC.--That which prevents.
PROTEOTHERAPY.--Treatment by injection of proteins.
PURGATIVE.--Anything which tends to produce bowel movement.
PUSTULANT.--An agent used to produce pustules for counter-irritation.
PYELITIS.--Inflammation of the pelvis of the kidney.
RADIOTHERAPY.--Treatment by means of radium or of X-ray.

SORBEFACIENT.--A drug producing absorption of exudates.
STERNUTATORY.--That which causes sneezing.
STIMULANT.--That which increases functional activity.
STOMACHIC.--A drug which increases appetite and production of gastric juice.
STOMATITIS.--Inflammation of the mouth.
STYPTIC.--An hemostatic.
SUBCUTANEOUS INJECTION.--Introduction by needle just under the skin.
SUDORIFIC.--A diaphoretic.
SYNERGIST.--An agent which supplements another.
SYSTEMIC ACTION.--Action after absorption.
SYSTOLE.--The period of contraction, chiefly of the heart.
TOLERANCE.--Decreased susceptibility to reaction.
TONIC.--An agent used to increase bodily tone.
TOXIC DOSE.--An amount which will be poisonous.
VAGUS.--The pneumogastric nerve which controls the functions of various organs, chiefly of interest in pharmacology because of relation to the heart.
VASOCONSTRICTOR.--A drug which constricts the blood vessels.
VASODILATOR.--A drug which dilates the blood vessels.
VESICANT.--An agent which produces blistering.