Safrolum, *Safrol*, $C_{10}H_{10}O_2$,—is the methylene ether of allyl pyrocatechol, found in oil of sassafras, camphor oil, and other volatile oils. It is largely used in the manufacture of soap to disguise the odor of the fatty bases. Dose, ♏j–x [av. ♏v].

Preparations.

Mucilago Sassafras Medullæ, *Mucilage of Sassafras Pith*,—has of the pith 2, in water 100. Dose, indefinite [av. ℥iv].

Oleum Sassafras, *Oil of Sassafras*, a volatile oil distilled from Sassafras,—a colorless or yellowish liquid, having the odor of Sassafras, a warm, aromatic taste and a neutral reaction, readily soluble in alcohol. Treated with cold nitric acid it becomes of a dark red color, and is finally converted into a red resin. Dose, ♏j–iv [av. ♏iij].

Infusum Sassafras, *Infusion of Sassafras* (Unofficial),—is a popular "tea" which may be taken *ad libitum*. When made from the bark, and taken internally as well as applied locally, it is almost a specific for the rash produced by poison oak (Hinton).

Sassafras is a constituent of the two compound Sarsaparilla preparations. It acts as a stimulant diaphoretic when used in quantity of the hot infusion. It enjoys a popular reputation as a "blood-purifier," and has a destructive influence on infusoria. It is employed chiefly in combination with Sarsaparilla and Guaiacum in cutaneous disorders and rheumatic and syphilitic affections. The mucilage of the pith is an excellent demulcent drink in acute gastritis and enteritis, or in poisoning by irritant and corrosive agents. It may be used in extemporaneous prescriptions to hold insoluble substances in suspension and for flavoring purposes. The oil is chiefly used for flavoring in mixtures and confectionery. The syrup popularly known as "Sarsaparilla" is composed of Oil of Sassafras and Oil of Gaultheria, in syrup.

Dr. J. Bartlett, of Chicago, in a paper on the toxic properties of Sassafras, published in the *Pharmaceutical Journal*, says that it appears to have some resemblance to three familiar drugs—opium, strychnine, and ergot; for it has a narcotic and sudorific action; a property of inducing tetanic and clonic spasms followed by paralysis, and a probable stimulant effect on the uterus.

SCAMMONIUM, Scammony,—is a gum-resin obtained by incising the living root of *Convolvulus Scammonia*, a plant of the nat. ord. Convolvulaceæ, growing chiefly in Syria and Asia Minor. It contains about 80 per cent. of *Resin*, with gum, sugar, starch, etc. The active principle, *Jalapin*, is probably identical with the Convolvulin of Jalap, and is contained in the root and the resin. Dose, gr. j–x [av. gr. iv].

Resina Scammonii, *Resin of Scammony*,—soluble in alcohol and in ether. Dose, gr. j–v [av. gr. iij].

Extractum Colocynthidis Compositum,—(see page 246) contains 14 per cent. of Resin of Scammony, and is an ingredient of the Compound Cathartic Pill, and the Vegetable Cathartic Pill.

Scammony is an active cathartic, stimulating the liver and the intestinal glands, and causing free purgation in a few hours with considerable griping. Its solution in the bile is necessary to its action, and it combines with the soda

in that secretion. Though quite drastic in action it is somewhat uncertain as a purgative and is generally employed in combination with similarly acting agents. It is anthelmintic against the tapeworm, and in overdoses produces a high degree of irritation. It is used as a drastic purgative for children with calomel or potassium sulphate, when an active cathartic is indicated. In the same way it is the appropriate agent on the principle of derivation in dropsies and cerebral affections, also in torpid states of the intestines with much slimy intestinal mucus; but it is contraindicated in cases attended by irritability of the stomach and bowels.

SCILLA, Squill,—is the sliced dried bulb of *Urginea maritima*, a perennial plant of the nat. ord. Liliaceæ, growing on the shores of the Mediterranean. It contains the glucosides—*Scillitoxin*, acrid and bitter, the most active principle; *Scillipicrin*, acting on the heart; and *Scillin*, causing numbness and vomiting; also *Sinistrin*, a mucilaginous principle. The *Scillitin* of the older writers is a complex substance. Dose of the powdered drug, gr. j–v [av. gr. ij].

Preparations.

Fluidextractum Scillæ, *Fluidextract of Squill.*—Dose, ♏j–v [av. ♏jss].

Tinctura Scillæ, *Tincture of Squill*,—10 per cent. Dose, ♏v–xxx [av. ♏xv].

Acetum Scillæ, *Vinegar of Squill*,—10 per cent. Dose, ♏v–xxx [av. ♏xv].

Syrupus Scillæ, *Syrup of Squill*,—has of the Acetum 45, with Sugar 80 and Water to 100. Dose, ♏x–℥j [av. ♏xxx].

Syrupus Scillæ Compositus, *Compound Syrup of Squill*,—has of the fluidextracts of Squill and Senega, each 8, Tartar Emetic 0.2, Sugar 75, Water to 100. Is known popularly as *Coxe's Hive Mixture*, and contains less than one grain of Tartar Emetic to the fluid ounce (15 grains in 17 fl. ozs.). Dose, for children, ♏v–℥j, the latter being an emetic dose; for adults, as an expectorant, ♏xx–xlv [av. ♏xxx].

Incompatibles.

Incompatibles are: as for glucosides (see page 8), and in addition with the *Compound Syrup* those for Tartar Emetic (see page 139).

Physiological Action and Therapeutics.

In small doses Squill is expectorant, in larger doses emetic and diuretic, and in overdoses it is a violent irritant poison, producing nausea, vomiting, purging, gastro-enteritis, strangury, bloody urine, perhaps suppression of urine, paralysis and convulsions, with death by paralysis of the heart in systole. Medicinal doses slow the heart, making the pulse stronger and slower, raising the arterial tension, and increasing the flow of urine (like Digitalis). Its active constituents diffuse into the blood, and its systemic effects follow on its application to the skin and seem to be exerted upon the lining of the secretory organs, especially affecting the bronchial, gastro-intestinal and genito-urinary mucous membranes.

Squill is employed in medicine for its expectorant and diuretic effects. It is especially applicable in cardiac dropsy, combined with digitalis or the saline

diuretics, and in chronic bronchitis, in which it may be associated with ipecac, ammonia, asafetida, or benzoin. It is used in croup, but is usually combined in this affection with some other emetic, as tartar emetic in the compound syrup, a mixture which may produce very depressing effects and should be used with caution. In whooping-cough and other irritant coughs with tickling sensations in the throat the syrup or vinegar is often of great service.

The action and uses of Squill should be studied in connection with those of Digitalis and Ipecacuanha.

SCOPARIUS, Scoparius (Broom),—is the dried tops of *Cytisus Scoparius*, the Broom plant, a common garden shrub of the nat. ord. Leguminosæ, having small, downy leaves and numerous large golden-yellow flowers. It contains *Sparteine*, $C_{15}H_{26}N_2$, a volatile, liquid alkaloid, which contains no oxygen, but possesses very decided basic qualities; and *Scoparin*, a neutral principle. There are no official preparations. Dose, gr. v–xxx [av. gr. xv].

Sparteinæ Sulphas, *Sparteine Sulphate*,—white, prismatic crystals, or a granular powder, of slightly saline and bitter taste, very soluble in water and in alcohol. Dose, gr. $\frac{1}{16}$–$\frac{1}{2}$ [av. gr. $\frac{1}{5}$] hypodermically, gr. $\frac{1}{2}$–ij by the mouth. Small doses, gr. $\frac{1}{16}$–$\frac{1}{4}$, every 5 hours, for cardiac action; larger, gr. j–ij, for diuresis (Clarke). Larger doses are necessary, say gr. jss–iij, ter die (Prior).

Incompatibles are as for alkaloid (see page 6).

Physiological Action and Therapeutics.

Broom-tops are diuretic and laxative, also emetic and cathartic in large doses. Their diuretic power is believed to be due to Scoparin, which acts as a stimulant of the renal epithelium. In the form of decoction they have long been a favorite diuretic and vehicle for other diuretics in the treatment of dropsies, both cardiac and renal, and are considered most reliable in dropsy of renal origin, but are contraindicated in acute renal affections, and where pulmonary congestion or inflammation exists.

Sparteine resembles Coniine in action, paralyzing the peripheral terminations of the motor nerves, though affecting the central nervous system but slightly. It depresses the heart, showing its rate and weakening its contractions. When injected intravenously it produces a slight rise of arterial tension for a short time, but has no effect on the blood-pressure when given internally. It is much less poisonous than coniine or gelsemine, and proves fatal to animals by paralyzing the end-organs of the phrenic nerves in the diaphragm. It was formerly supposed to act similarly to Digitalis on the heart and kidneys, but experimental and clinical observations have shown that it possesses no such power comparable with that of the latter agent. It has been extravagantly praised as a remedy in cardiac affections requiring stimulation of the heart's action with the slightest possible increase of arterial tension, in mitral and aortic regurgitation, mitral stenosis, cardiac palpitation and arrythmia, chronic Bright's disease, exophthalmos, and asthma. In the treatment of the opium habit Jennings found

it serviceable at the periods of depression, to overcome the plateau shown in the sphygmographic trace by stimulating the cardiac force. The claims made for it by enthusiastic reporters have not been substantiated generally, and it is no longer used to any great extent in practice.

SCUTELLARIA,—is the dried plant *Scutellaria lateriflora*, Skull-cap, an indigenous, perennial herb of the nat. ord. Labiatæ, growing in moist places and along ditches. It contains a little volatile oil, traces of a bitter principle, besides fat, tannin and sugar. Dose, gr. x–xxx [av. gr. xv].

Fluidextractum Scutellariæ, *Fluidextract of Scutellaria*.—Dose, ♏x–xxx [av. ♏xv].

Scutellaria produces no very obvious effects when taken internally. By some practitioners it is said to have tonic, nervine and antispasmodic powers, and it has been used in domestic practice to calm the nervous system in diseases characterized by restlessness, tremors, spasms, twitching of the muscles, and hyperesthesia, as chorea, delirium tremens, nervous exhaustion from fatigue or over-excitement, hydrophobia, hysteria and epilepsy. The Scutellarin of the eclectics is not a proximate principle, but an extract precipitated by alum from a concentrated aqueous tincture. It is given in dose of gr. j–iv.

SENEGA,—is the dried root of *Polygala Senega*, an indigenous, perennial plant of the nat. ord. Polygalaceæ, having small, white flowers in a close spike at the summit of the stem. Its principal constituent is the glucoside *Senegin*, $C_{32}H_{54}O_{18}$, which is identical with Saponin (see page 410), and closely allied to Digitonin. It is a white, amorphous powder, readily soluble in alcohol and hot water, forming a soapy emulsion when mixed with boiling water, and decomposed by HCl into sugar and *Sapogenin*. Dose of Senega, gr. x–xxx [av. gr. xv].

Preparations.

Fluidextractum Senegæ, *Fluidextract of Senega*.—Dose, ♏x–xxx [av. ♏xv].

Syrupus Senegæ, *Syrup of Senega*, has of the fluidextract 20, Syrup 80. Dose, ʒj–ij [av. ʒj].

Syrupus Scillæ Compositus, *Compound Syrup of Squill*,—contains 8 per cent. of Senega. (See under Scilla, page 435).

Incompatibles are as for glucosides (see page 8).

Physiological Action and Therapeutics.

Senega is a stimulating expectorant, a diuretic and a diaphoretic. It causes irritation of the throat, with some salivation and gastro-intestinal irritation, an inclination to cough, increased bronchial secretion, and perhaps some diuresis and diaphoresis. Inhaled as a snuff it is very irritant to the mucous membrane of the nose, causing cough, sneezing and nasal catarrh. Senegin is violently irritant and a powerful depressant of the heart, and the vascular, nervous and muscular systems. It is excreted by the bronchial mucous membrane, the kidneys and the skin, all of which it stimulates and in large quantity irritates.

The use of Senega is chiefly that of a stimulating expectorant in chronic bronchitis, the second stage of acute bronchitis, typhoid pneumonia, asthma and croup, also as a diuretic in dropsy due to renal disease. It removes the tightness and oppression experienced in the subacute chest affections, relieves

cough and rapidly promotes expectoration. When the mucus is tough and scanty this remedy is of no value. It has been used with benefit in amenorrhea, given in saturated decoction for two weeks before the expected period. In chronic rheumatism and in rheumatic paralysis its stimulating and diaphoretic powers have been of value. Senegin has been successfully used in 2-grain doses as a remedy for uterine hemorrhage.

SENNA,—the dried leaflets of *Cassia acutifolia*, Alexandria senna, or of *Cassia angustifolia*, India senna, shrubs of the nat. ord. Leguminosæ, growing in Egypt and India. They contain an amorphous glucoside, *Cathartic Acid*, which forms salts with bases and may be decomposed into glucose and cathartogenic acid. Other constituents are *Sennapicrin* and *Sennacrol*, both glucosides; *Catharto-mannit*, a peculiar, unfermentable sugar; also *Chrysophanic Acid* in small quantity, sugar, and various salts. Dose ʒss–ij [av. ʒj].

Preparations.

Fluidextractum Sennæ, *Fluidextract of Senna.* Dose ♏x–ʒj [av. ♏xxx].

Syrupus Sennæ, *Syrup of Senna,*—has of the fluidextract 25, Oil of Coriander ½, Syrup to 100. Dose, ʒss–ij [av. ʒj].

Confectio Sennæ, *Confection of Senna,*—has of Senna 10, Cassia Fistula 16, Tamarind 10, Prune 7, Fig 12, Sugar 55½, Oil of Coriander ½, Water to 100. Is sold under the trade names *Tamar-Indien*, and *Tropical Fruit Laxative.* Dose, ʒss–ij [av. ʒj].

Infusum Sennæ Compositum, *Compound Infusion of Senna* (*Black Draught*),—has of Senna 6, Manna 12, Magnesium Sulphate 12, Fennel 2, Boiling Water 80, Cold Water to 100. Dose, ℥ij–vj [av. ℥iv].

Pulvis Glycyrrhizæ Compositus, *Compound Licorice Powder* (See under GLYCYRRHIZA),—contains 18 per cent. of Senna. Dose, ʒss–ʒjss [av. ʒj].

Syrupus Sarsaparillæ Compositus, *Compound Syrup of Sarsaparilla* (See under SARSAPARILLA),—contains 1½ per cent. of the fluidextract of Senna. Dose, ʒj–℥j [av. ʒiv].

Incompatibles.

Incompatible with *Senna* are: Mineral Acids, Carbonates, Cinchona infusion, Lead Acetate, Lime-water, Mercuric Chloride, Silver Nitrate, Tartar Emetic.

PHYSIOLOGICAL ACTION AND THERAPEUTICS.

Senna is a very efficient and safe cathartic, producing copious yellow stools in about 4 hours, with considerable griping and flatulence, which may be lessened by combining it with carminatives. Its action is expended chiefly on the small intestine, and it increases both peristalsis and intestinal secretion. It has no irritant quality in ordinary doses, and does not produce hypercatharsis, or leave constipation as an after-result. Its infusion injected into the veins causes both vomiting and purging; and in large doses by the mouth it produces nausea, vomiting, flatulence, excited pulse and drastic purgation with severe tenesmus, but its effects are never poisonous. It may cause hemorrhoids and increase the menstrual flow in women. Given to a nursing mother her milk will acquire purgative powers. In some very susceptible persons the odor of the leaves or the infusion will cause an evacuation of the bowels. Its odor

and taste are particularly disagreeable, especially when administered in infusion.

Senna would probably take rank as our best and safest cathartic but for the nauseousness of its smell and taste. It is a favorite laxative in England for children, and is used with great benefit in habitual constipation or where prompt evacuation of the bowels is required. In hemorrhoids and anal fissure it is employed to produce soft and easy motions; but if a tendency to hemorrhoids exists, the use of this drug in cathartic doses will cause irritation of the part and induce an acute attack. For the same reason it is contraindicated in hemorrhage or inflammation of the intestinal mucous membrane, menorrhagia, and abortion. The least disagreeable of its preparations are the confection and the compound licorice powder.

SERA, Serums. Serum-therapy proper is the prophylactic and curative treatment of certain infectious diseases by the subcutaneous or intravenous administration of a blood-serum containing an antibody (antitoxic, bactericidal, etc.) which is specific to the particular disease. As generally used however, the term includes also the treatment of some of these affections by the toxic products (toxins) of attenuated cultures of their respective microbes; but these toxins, though sometimes grown on blood-serum, may be produced on other media, and are never administered in a serum, as the antibodies invariably are. Bergey classifies these agents as follows:—

Toxins,—including tuberculin and other bacterial products employed for immunizing purposes. The attenuated virus of rabies, and the toxins of streptococci, bacillus prodigiosus, bacillus mallei, bacillus lepræ, and the cholera spirillum have been used for their respective diseases.

Antitoxic Sera,—including those of diphtheria and tetanus, the only ones in general use; though antitoxins for cholera, typhoid, tuberculosis, and other diseases, have been used with more or less benefit.

Bactericidal Immune Sera,—including those for typhoid, dysentery, tuberculosis, and cholera.

Immune but not Bactericidal,—including the anti-pneumococcus, anti-streptococcus, and anti-staphylococcus sera.

This separation of the products of immunity is wholly artificial, and it may be that the sera act upon the toxins or upon the micro-organisms, or upon both.

Toxins are specific poisons produced by bacterial growth in suitable media, and when circulating in the organism they are the immediate causes of the acute infectious diseases. After the discovery of the bacillus tuberculosis other micro-organisms were found constantly associated with certain infectious diseases, notably tetanus, diphtheria, cholera, pneumonia, erysipelas and typhoid fever. The specific microbes of these affections were at first believed to be the immediate cause of their respective disorders, but later researches have shown that such diseases are due to the action of chemical poisons (toxins)

produced by their specific bacteria growing on suitable soils either within the animal organism or outside it. The toxin produced by any particular bacterium varies greatly in power through very slight circumstances. It may be weakened or increased in virulence by the cultivation of its bacteria on different culture media or on the same media with different surroundings as to oxygen, temperature, etc.; also by passing successive generations of these organisms through a definite series of animals, chosen for their natural insusceptibility or susceptibility thereto. The pathogenic microbes of several diseases may be cultivated in test-tubes, forced to acquire an increased or lessened degree of virulence or toxin-producing power as required, separated from the poisonous products of their metabolic life-work, and by the inoculation of either their progeny or their chemical products (toxins) the corresponding diseases may be reproduced upon healthy animals in almost any desired degree of intensity.

The treatment of diseases due to pathogenic microbes by the toxic products of their own particular bacteria is based upon the theory that these germs produce substances in their culture media which are inimical to their own life. The treatment of tuberculosis by Koch's tuberculin and the inoculations of Haffkine against cholera are examples of true toxin treatment. The vaccinations of Jenner for variola and of Pasteur for rabies are of the same nature when employed as remedial methods, the material being obtained from a morbid product of the disease in the one case and from the diseased tissue itself in the other, the culture medium in both being the blood and tissues of the infected animal organism. It has been frequently observed that patients afflicted with malignant disease have been greatly benefited by an intercurrent attack of erysipelas, in consequence of which the tumors seemed to undergo retrogressive changes. This has suggested the employment of the toxins of streptococcus erysipelatis and bacillus prodigiosus in inoperable cancer, and may lead to the treatment of other diseases by the toxins of bacteria hitherto unassociated with them.

The injection of a toxin, in gradually increasing doses at proper intervals, will confer immunity in many cases upon the animal so treated against the corresponding disease and its particular bacteria. This immunity may be transferred to another animal by injecting into its cellular tissue the blood-serum of the immunized one, and this serum will also act remedially on a subject of the disease if administered early in its course (Behring). The immunizing and curative action of the serum is believed to be due to the existence of an antibody in the blood of the inoculated animal, elaborated by the living cells of its tissues as a defence against the action of the toxin. These facts and hypotheses form the basis of the treatment of certain diseases by antitoxic and bactericidal sera.

Antitoxins are suppositious substances, assumed to exist in antitoxic sera, and believed to be produced by the cells of the blood or tissues for the defence of the organism against foreign bacterial toxins. *Alexins* are similar substances,

natural antitoxins, which are supposed to exist in the blood of naturally immune animals. An Antitoxic Serum is a blood-serum containing antitoxin, produced therein by the cells of the organism as a result of the repeated injection of a toxin into the tissues of the animal from which the serum is taken.

It was shown by Von Fodor in 1887 and subsequently by Nuttall that the blood-serum of healthy animals is naturally bactericidal, that it possesses this quality in varying degrees of efficiency, and that it may be sufficiently powerful in this respect to prevent certain pathogenic bacteria from gaining lodgment in the organism, thereby conferring *natural immunity* against a particular disease upon the individual so protected, and in some cases even upon the pecies. Further study and experiment established the fact that temporary *artificial immunity* against certain diseases may be imparted to a susceptible animal by repeated inoculations of the specific bacteria or their toxic products in gradually increasing degrees of virulence (Behring, Kitasato, Roux). The crowning discovery that the blood-serum of such an immunized animal may be successfully employed for curative as well as prophylactic purposes against its particular disease upon other animals of the same or different species, was made by Professor Emil Behring of Berlin, in 1891. This was no chance discovery but was the legitimate result of logical reasoning and hard work, and is formulated under the title *Behring's Law*, as follows: The blood-serum of an animal which has been artificially rendered immune against a certain infectious disease, when injected into the body of another animal, has power to protect the latter individual against the same disease and to cure the disease after infection has occurred.

Ehrlich has shown that Behring's law is valid also for the chemical poisons, *Ricin* and *Abrin*, the respective toxalbumins of the ricinus palm and the jequirity bean. The blood of animals slowly immunized by increasing doses of these toxins contains antitoxic substances named *Antiricin* and *Antiabrin*, which, if added to their respective poisons, will attenuate and even neutralize the latter. These facts are advanced as proof that the slowly increasing artificial immunity is not a simple tolerance acquired by the organism, as Sternberg taught, but is due to the production of new antagonistic and defensive substances by the living cells of the organism. The weight of evidence seems to favor the doctrine that the leucocytes are stimulated to the increased secretion of specific antagonistic and bactericidal substances by the repeated inoculation of the micro-organisms or their toxins.

Theories deduced from the observed facts are as follows: As the various pathogenic bacteria produce the causative toxins of their respective diseases, so the organic cells of the body, reacting under the stimulus of the poisons thus introduced, immediately proceed to elaborate defensive bodies, which if produced in sufficient quantity will neutralize the effects of the toxins. Residual antibodies remaining in the blood after recovery render the animal immune for a time against the disease. The immunizing and curative effects obtained by the injection of the blood-serum of an immunized animal into the circulation of another animal are due—either to direct chemical neutralization of the toxins themselves by the antibodies so introduced (Behring, Kitasato), or to a particular influence exerted by the antibodies upon the living cells of the organism, which, being affected in two opposite directions, remain neutral to the disease

(Buchner). Some authorities hold that these results are due to the conjoint action of leucytic and chemical forces. Ehrlich's side-chain theory assumes that every toxin contains *toxophore* molecules having direct toxic action, and *haptophore* molecules which combine the toxophores with a similar combining group of molecules in the tissue cells of the attacked organism. The tissue-cell molecules being destroyed by the toxophores, a rapid and profuse regeneration of similar molecules occurs in side-chains; and these molecules overgrowing, are carried into the circulation, becoming the antitoxin, which acts by combining with the haptophores of newly arrived toxin, using up their combining power before they can reach the tissue cells.

Antitoxins are, with perhaps a few exceptions, characterized by possessing *specific action*, which means that the serum from an animal inoculated with the toxin of the diphtheria bacillus is effective only against diphtheria, and the tetanus antitoxin only against tetanus. A dose of an antitoxin followed by a dose of the corresponding toxin produces no effect from either, the action of the one being rendered ineffective by that of the other. The corresponding toxin and antitoxin may be mixed together outside the body and then injected with like result, though of course there must be a certain amount of antitoxin present to counteract a given dose of toxin. The immunizing or vaccine property of the antitoxins, though transient, is probably destined to be of considerable importance. Instances are recorded in which epidemics of diphtheria in schools were apparently stopped by vaccinating all the children therein with diphtheria antitoxin.

Serum obtained from human subjects suffering from bacterial diseases has been used for therapeutic purposes. In some cases the serum was secured by blistering the patient during convalescence, in others by taking blood by venesection or by leeches. This has been done in cases of pneumonia, yellow fever, scarlet fever, erysipelas, syphilis, and whooping-cough.

Antitoxic Serum is prepared as follows: A highly virulent culture of the specific microorganism of the particular disease, or still better, a strong toxin of tested strength prepared therefrom, is injected into the cellular tissue of a suitable animal, generally a horse, at first in very small quantity. The effect is soon shown by the onset of fever and other symptoms of acute disease, which are known as the "reaction." After an interval of time sufficient for recovery from these symptoms, the injection is repeated with a stronger toxin or with a culture of greater virulence, or with a larger quantity of the original toxin. This process is continued for several months, or until the animal no longer "reacts" to the poison, and then sufficient antitoxin is presumed to exist in its blood to render it immune to the toxin and to the disease. After each inoculation the animal's blood serum is tested as to its value by experiment on guinea-pigs of definite weights. When the desired degree of immunity is reached the animal is bled from the jugular vein under strict aseptic precautions, from 6 to 12 pints being taken from a horse, according to his size and general condition. The blood is received in sterilized flasks, which are carefully stoppered and stored on ice until the clot has separated from the serum. The latter is tested to determine its value in antitoxin, has phenol added to it in the proportion of 0.5 per cent., and is bottled in vials which contain in each the dose for one patient. The vials are labeled with a statement of the number of normal antitoxin units per Cc. of the contents, expressed in multiples of a standard normal serum.

Proteidin of immunizing and curative powers is produced by cultivating bacteria on suitable media, and collecting the specific bacteriolytic enzyme produced, which when combined with blood albumins, furnishes a specific immunizing and curative substance. The culture medium contains asparagin, peptone, bouillon, potassium biphosphate, magnesium sulphate, sodium chloride, and distilled water. This product has been used in anthrax and hog cholera with results which warrant the belief that it will supplant the antitoxic sera (Emmerich).

Bactericidal Sera are used with the object of reinforcing the natural bactericidal power of the blood. This is best accomplished by a mixture of normal serum with immunized serum, the former furnishing an additional quantity of bactericidal ferment, the so-called complement; while the latter supplies the binding material or immune body (the *amboceptor*), which unites the complement to the bacteria and enables it to destroy them. Some of the bactericidal sera have shown marked antitoxic qualities, particularly the antityphoid and antidysenteric sera.

Nonbactericidal Immune Sera include those obtained by inoculation of the pneumococcus, the streptococcus, and the staphylococcus toxins. As at present produced these sera have no definite antitoxic or bactericidal powers, but they possess protective and curative properties as shown by laboratory tests and clinical experience. They are supposed to exert their influence by stimulating cell-proliferation in the marrow of the long bones, and by increasing the phagocytic power of the leucocytes.

Diphtheria Antitoxin, though not the first antitoxin discovered, is by far the first in practical importance. The bacillus of diphtheria was discovered by Loeffler and Klebs in 1884, its toxic products were isolated by Roux, and Sidney Martin demonstrated the chemical identity of the toxins produced in culture media with those produced by the bacillus in the human organism. In 1891 Behring discovered the antitoxin and established its preventive and curative properties. The clinical results obtained thereby were announced by Roux at the Buda-Pesth Congress of Hygiene in 1894, and attracted universal attention. Since then the statistics of diphtheria serum-therapy have grown voluminous, have included a large number of reports from official and private sources of the highest professional authority, and the weight of evidence has steadily grown more and more favorable to this treatment of the disease. It is now generally conceded that under antitoxic treatment the mortality in all forms of diphtheria has been reduced from 40 per cent. and more to 15 per cent. and less, and if laryngeal and operative cases are excluded to less than 5 per cent. In laryngeal diphtheria the former mortality of 73 per cent. has been reduced to about 27 per cent., thus almost completely reversing the figures representing the deaths and recoveries from this form of the disease. These statistics include over 68,000 cases reported on since 1894, by Roux, Welch, Virchow, the American Pediatric Society, and the Boards of Health of the German cities, Massachusetts, New York, London, Chicago, Boston, Baltimore, Washington, and Denver. A few writers contend that much of this decrease of mortality is due to improved hygienic surroundings, and deny the value of antitoxin treatment, claiming that under it the deaths from pulmonary and renal complications are more common than formerly. Dr. Lennox Brown maintains that in London the diphtheria mortality without antitoxin treatment rarely

exceeds 20 per cent., and Bayeux states the mortality of this disease throughout the world as only 16 per cent. The general professional opinion agrees with that of Professor Klein, who stated at a meeting of the British Medical Association, in reference to this disease, that "the scientific basis for the application of antitoxic serum is as firmly founded and as thoroughly established as the use and application of any known drug."

The clinical history of the disease under the antitoxin treatment, as recorded by its observers, shows an extraordinary decrease in the severity of the symptoms. A marked improvement in both the local and general symptoms is usually noticed within 24 hours after the injection of the serum. The membrane loosens and clears off rapidly, high temperature is lowered, and the pulse slows and gains in force (Washbourn). Evident signs of distress vanished within 24 hours, and apparent strength and good-humor took the place of a previously low mental and physical condition (Kossel). In no case did the larynx become involved after the use of the serum if not so previously, and many cases showing laryngeal symptoms recovered without tracheotomy. Even in the fatal cases life was prolonged (Caiger). The remedy has decided power to prevent the spreading of the false membrane into the larynx and trachea. It is powerless to repair damage already done to the tissues by the diphtheria toxin, hence the earlier the serum is administered the better are its results. It is decidedly more efficient in the fibrinous form of the disease than in the septic form, and in cases of simple infection than in those of double or mixed infection. The liability to paralysis and albuminuria is not lessened but is perhaps somewhat increased by this treatment, though genuine nephritis is less frequently seen under its use than in cases treated by other methods. The serum may cause certain untoward symptoms, as cutaneous eruptions, swellings, etc., but these are not serious and are not attended with danger to life. Its injection is very rarely followed by serious local disturbances, as abscess, and probably would never be complicated thereby if the serum were always pure and used with strict aseptic precautions. Welch states that in over 100,000 injections the serious mishaps directly attributable to the serum can be counted on the fingers.

Poisonous symptoms are not believed to be caused by the antitoxin, but are due to some other constituent of the serum, for they may occur when the simple blood-serum of another species of animal is injected into the human subject. The most common one is a rash, usually an erythema, but sometimes papular or urticarial, which occurs in about 35 per cent. of the cases, generally appearing about a week after the injection. Pains in and swelling of the joints are occasionally experienced, and symptoms of septicemia have occurred, with irregular temperature, nephritis, and death.

Clinically most cases of diphtheria are of mixed infection, and as the antitoxin is effective only against the toxin of the Klebs-Loeffler bacilli, the local antiseptic treatment of the throat is still insisted on. If thoroughly carried out in the incipiency it may destroy the dangerous streptococci and other microbes, thereby preventing the mixed infection which proves so virulent; if continued throughout the case and during convalescence it will minimize the danger of infecting other persons. In some instances bacilli were found as long as two months after recovery.

Diphtheria antitoxin has been employed with good results in the treatment of pneumonia, typhoid fever, pertussis and asthma, in which it is supposed to act by increasing leucocytosis and hastening the elimination of toxic material.

The *antitoxic unit* generally recognized is 1 Cc. of an antitoxic serum which will counteract ten times the minimum fatal dose of toxin in a guinea-pig. The *prophylactic dose* for children is 500 to 1,000 units, to be repeated after two or three weeks if the case is still exposed to infection. The immunity so conferred is only temporary, its duration depends on the quantity of antitoxin administered, and it gradually decreases as the antitoxin is eliminated, but can be maintained for a long time by the repeated use of smaller doses at short intervals. The *therapeutic dose* recommended by the committee of the American Pediatric Society is 1,000 units as the initial dose for children under two years of age and for mild cases; 1,500 to 2,000 units for older children, severe cases, and all laryngeal cases. Many physicians administer 2,000 to 4,000 units in severe pharyngeal cases, or 3,000 to 6,000 units in laryngeal cases, the higher doses when the case is not seen until the third or fourth day. In all cases the initial dose should be repeated or doubled if favorable results do not follow within 6 or 8 hours after the first injection. The necessary amount for any case can be determined only by estimation of the quantity of toxin present as indicated by the symptoms; remembering that this quantity increases rapidly with every day after infection. The prognosis is unfavorable if the case is so far advanced before treatment that the toxin has had time to accumulate and to exert its paralyzing influence on the nervous apparatus of the heart.

Diphtheria Antitoxin is now prepared in all European countries and in the laboratories of several boards of health, manufacturing druggists and others in this country. A concentrated serum is recommended by the committee of the American Pediatric Society, in order that the requisite number of antitoxic units may be administered in small bulk, and such sera have been produced, containing as many as 1,750 units in 1 Cc., but they are unstable, and soon lose their power. The sera in general use contain from 200 to 500 units to the Cc. In all cases the dose should be regulated by the number of units required, not by the quantity of serum. Diphtheria Antitoxin is official in the U. S. Pharmacopœia under the title—

Serum Antidiphthericum, *Antidiphtheric Serum, Diphtheria Antitoxin,*—a fluid separated from the coagulated blood of a horse, immunized through the inoculation of diphtheric toxin. It should be kept in sealed glass containers, in a dark place, at temperatures between 40° and 59° F. Average dose, 3000 units; immunizing dose for well persons, 500 units.

Double Diphtheria Antitoxin is a serum obtained from a horse which has been immunized against streptococcus virus after having been previously rendered immune against the diphtheria toxin. It is supposed to contain both the diphtheria and streptococcus antitoxins, and is intended for the virulent cases due to a mixed infection with these two poisons, but it may be used in any case of diphtheria.

Tetanus Antitoxin.—Tetanus was one of the first diseases to be studied successfully by the bacteriologists, and its antitoxin was the first one prepared. Breiger in 1880 showed that a crystalline substance of high toxicity could be