The attempt to eliminate the bacteria themselves, or even their toxins, by means of the emunctories, as we have seen above, is very unlikely to amount to much, and powerful cathartics, diuretics, and sudorifics are more likely to prove harmful than beneficial.

One further resource, however, holds out the brightest promise as a successful means of combating the difficulties in question, and its realization seems almost if not quite within our grasp; I refer to the injection of the serum of immunized animals. The uncertainty of the results obtained by Marmorek's antistreptococcic serum seems in a fair way to be rectified since the studies of Van de Velde have thrown more light on the probable reason for its occasional inefficacy in cases apparently well suited for its employ. Van de Velde, namely, has tried to determine by experiment[23] whether a serum produced by means of a given variety of streptococcus is efficacious against all other varieties of streptococcus pathogenic for man, or whether it is active only against a certain number of varieties. To decide this question he makes use of a serum produced by means of a streptococcus A, and he inoculates a horse with another variety of streptococcus, P, which coccus is chosen because, *in vitro*, its development is not inhibited by the serum A added to the leucocytes of a rabbit; from the horse he acquires another variety of antistreptococcus serum, serum P. Now he observes that serum A is very active when injected in doses of 5 c.c.; it annihilates the effects of five thousand pathogenic doses of streptococcus A, but is able to neutralize the effects of only one hundred doses of streptococcus P. On the other hand, the serum P is able to neutralize the effects of five thousand pathogenic doses of streptococcus P, but is completely inactive against streptococcus A.

These researches, conducted at the Bacteriological Institute of the University of Louvain, have led them, at that institution, to modify the technique of the vaccination of horses for the production of serum, and their immunizations are now made with a mixture of streptococci coming from as many different sources as possible. The serum thus prepared has received the name of "polyvalent serum," and it is anticipated that a serum thus prepared will be more generally and uniformly successful in practice than the antistreptococcic serum prepared in the usual manner.

In the presence of probable, if not indubitable, streptococcic infection of a grave type, especially in cases in which streptococci have been demonstrated in the blood, the question of the administration of large doses of a reliable antistreptococcic serum merits, to say the least, the careful consideration of the attending practitioner.

Zmigrodski, whose distressing personal experience with an operation wound has been detailed above, heads his report of his own case with a pertinent quotation from Dr. Parkes[24]; it will not be unfitting to repeat it here:

"I believe these cases of severe septic infection, if they do get well, scarcely ever do so because of the doctor, but by the grace of God." —*Leonard W. Bacon, Jr.*

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DISTOMA. See *Trematodes.*

DITA.—The bark of *Alstonia scholaris* (L.) R. Br. (fam. *Apocynaceæ*), a large tree of Southeastern Asia and the adjacent islands, especially the Philippines, yielding a valuable fine-grained timber. The bark and its alkaloid have been much used at home, and to some extent in this country, as an antiperiodic substitute for quinine. It is a very rough, coarse bark, occurring in pieces as large as the hand and larger, and a fourth to a half inch or more in thickness. The outer surface is coarsely fissured and of a dark-gray or brownish color, the inner is buff and coarsely striate. The texture is largely cellular and it is easily ground or powdered. It is odorless but very bitter.

Numerous crystalline principles have been extracted from it, among them several alkaloids. *Ditaïne* (or echitamine, $C_{22}H_{28}N_2O_4$) is the most important. It occurs in brightly shining, prismatic crystals, soluble in both water and alcohol. It is said to act like curare, but its use appears to have been purely experimental. Other alkaloids are *ditamine* ($C_{19}H_{21}NO_3$) and *echitenine* ($C_{20}H_{21}NO_4$). "Ditain," as said to be used in the Philippines in equal doses with quinine, is a very indefinite substance. It certainly is very different from the poisonous bases noticed above.

Dita has not been found of much value as an antiperiodic; it is useful, however, as a general tonic. It appears to be a rather powerful abdominal stimulant, of value in

severe diarrhœa. The dose of the powdered bark is 0.2 to 0.5 gm. (gr. iij.–viij.) or as many minims of the fluid extract.

The similar bark of *A. constricta* F. von Mueller, of Australia, has there a similar repute as an antiperiodic.
Henry H. Rusby.

DI-THIO-CALCIUM CARBONATE ($CaCS_2O$) is calcium carbonate in which two atoms of oxygen have been replaced by sulphur. It is a hygroscopic, orange-red, crystalline powder, slightly soluble in water and less so in alcohol. On exposure to light and air its aqueous solution is decomposed, with liberation of sulphur and sulphuretted hydrogen. On account of its large proportion of sulphur it was used by Tommasoli and Vicini in five-per-cent. ointment or freshly prepared solution as an application in psoriasis, lupus, eczema, and other skin diseases. Sabbatini has found that a one-per-cent. solution prevents the growth of pyogenic bacteria, but does not kill them. A twenty-per-cent. solution caused a vesicular and pustular dermatitis. *W. A. Bastedo.*

DITTANY.—American Dittany. The herb of *Cunila origanoides* (L.) Britton (fam. *Labiatæ*). This aromatic perennial, found abundantly in rich woodlands of the Eastern United States, is a more energetic carminative than many of its relatives which are more frequently employed. It has a biting, peppery, aromatic taste and contains an abundance of volatile oil. This oil is distilled for the market and appears to be very similar to oil of thyme. The drug and the oil are more stimulant to the perspiratory glands than are most of the aromatics. The dose of the dried herb is 1 to 4 gm. (gr. xv. to lx.).
Henry H. Rusby.

DIURETICS are medicines which increase the secretion of urine. They are divided into two classes, *direct* and *indirect*.

To the first class belong all medicines that produce an increase of diuresis by influencing the kidneys directly; to the second, those that accomplish this by augmenting the general blood pressure.

In order to have a clear conception of the practical bearing of this division, it is necessary to understand the conditions that modify the urinary secretion in health and disease.

The activity of the kidneys, in their healthy state, depends upon the quantity of blood flowing through the renal vessels, and the amount of urinable substances (that is, substances that are eliminated by the kidneys, such as water, inorganic salts, urea, uric acid, etc.) which it contains. As both the quantity and quality of the renal blood undergo marked changes, the urine secreted at different times by healthy persons presents striking variations in amount, color, and density. These variations are readily accounted for by the fact that the principal constituents of the urine, the water and the solids, are secreted in different parts of the kidneys—the Malpighian bodies and the uriniferous tubules. These two parts are not always equally active, and hence the normal variations in the composition and quantity of the urine.

The quantity of the water of the urine depends chiefly on the activity of the Malpighian bodies or glomeruli. They separate from the renal blood its surplus of water and those salts which it normally holds in solution, such as chloride of sodium, etc. From the glomeruli the water passes into the lumen of the uriniferous tubules, where it serves as a solvent or vehicle for any substance that may have been secreted by the epithelial cells of the tubules. The quantity of water yielded by the glomeruli is regulated, according to Ludwig, by the pressure of the blood in the capillaries of the glomeruli, but according to Heidenhain, by the velocity of the blood current. Ludwig holds that the passage of water through the walls of the capillaries and the simple layer of epithelial cells covering the tuft of capillaries, is merely a mechanical filtration. Accordingly, the greater the pressure in the capillaries, the more abundant the water that filters through them, and the more the pressure in the glomeruli exceeds the pressure in the tubules, the more rapid and extensive the process of filtration. Heidenhain, on the contrary, maintains that it is the velocity of the blood current that determines the quantity of water flowing from the glomeruli. The more rapid the blood current in the glomerular capillaries, the more copious the flow of water. When the blood current is very rapid, a larger quantity of water is brought into relation with the epithelial cells of the glomeruli in a given time, and hence their activity becomes augmented. Thus Heidenhain regards the removal of water from the blood of the glomerular capillaries to be a process of active secretion by the epithelial cells of the glomeruli.

Normally, blood pressure and rapidity of blood flow in the Malpighian bodies are simultaneously increased or diminished, but in some pathological states the pressure may be augmented while the flow is retarded.

As the quantity of water flowing from the glomeruli depends upon the abundance of blood in their capillaries, it is evident that the quantity of urine secreted must be controlled by the general arterial blood pressure. When the blood pressure is high, the urinary secretion is abundant; when it is low, the secretion is scanty. In the normal state of the organism the general blood pressure is such as to supply the kidneys with an abundance of blood, so that they can rapidly remove from it the urinable substances it may contain. Some of the ordinary changes in the quantity of urine are attributable to variations of the general blood pressure. Thus, when the surface of the body becomes cold the vessels of the skin contract, and the general blood pressure slightly increases; the urine then becomes more abundant, less dense, and light-colored. On the contrary, when the surface of the body is exposed to a very warm atmosphere, the superficial vessels dilate, and the blood pressure falls somewhat; as a consequence the urine becomes scanty, dense, and high-colored.

But the quantity of water flowing from the glomeruli depends also upon the concentration of the renal blood. When the renal blood contains a minimum of water, the glomerular epithelium can remove or secrete but little, and the urine becomes dense, scanty, and high-colored. On the contrary, when the renal blood contains a maximum of water, the renal epithelium removes the surplus rapidly, and the urine becomes copious and light-colored. This is well illustrated in health by the variations in the quantity of urine resulting from the amount of fluid ingested. Soon after imbibing large draughts of water, a copious flow of light-colored urine takes place.

The indirect diuretics have been defined as medicines that increase diuresis by augmenting the general arterial blood pressure. This results from their action on the heart, whose energy becomes increased. They do not, it is now held by most authorities, exert any direct action on the kidneys, since they are incapable of augmenting the flow of urine when they fail to increase the force of the heart's action. In the normal state of the organism, they do not markedly augment the quantity of urine, evidently because the blood pressure is generally at its maximum height. But when the blood pressure is abnormally low from inefficient heart action, and the secretion of urine has abated in consequence of scanty supply of arterial blood, they display great power over the secretion of urine, often in a short time producing a copious flow.

The quantity of the solids of the urine depends upon the activity of the epithelial cells of the uriniferous tubules. All authors accord to these cells an active secretory function. They take from the blood in the capillaries surrounding the tubules the urea, uric acid, kreatinin, and other products of metabolism, and probably foreign substances such as medicines and poisons, and discharge them into the channels of the tubules. The activity of the epithelium depends upon the quantity of such urinable substances contained in the renal blood, increasing when they are abundant and diminishing when they are scanty. It depends also upon the velocity of the blood current, since with an accelerated flow a

larger quantity of urinable substances is brought into relation with them in a given time. When the blood flowing into the kidneys contains a large amount of such substances and a minimum of water, the urine becomes dense, scanty, and high-colored. On the contrary, when the renal blood contains only a minimum of them and a maximum of water, the urine becomes pale, less dense, and very copious. It is evident, therefore, that the degree of activity of the two secreting structures of the kidney is dependent primarily on the quality of the renal blood.

The kidneys, like all other organs, in a measure regulate their own blood flow. When they are active, they contain an abundance of blood; when inactive, they are comparatively bloodless. When, for instance, the activity of the epithelium becomes excited by the presence of urinable substances, there quickly takes place a more abundant flow of blood to the kidneys, or rather to the secreting apparatus, in consequence of dilatation of the renal arterioles. This statement does not rest merely on general principles. Heidenhain found, as a result of his experiments, that a very dilute solution of nitrate of sodium, or urea, injected into the blood, greatly increased the flow of urine, when it had abated in consequence of low blood pressure. No change of the blood pressure resulted from the injections, and hence the augmented flow of urine could not be attributed to rise of the general arterial pressure. That it was solely due to an increase of the local pressure in the vessels of the kidneys, and augmented velocity of the blood current, is evident from the experiments of Cohnheim and Roy. These investigators found that small quantities of a very dilute solution of urea, or of chloride of sodium, injected into the circulation, which in no wise influenced the general blood pressure, soon caused a very decided increase of the bulk of the kidney. This shows that the amount of blood flowing through the kidneys—that is, the degree of dilatation of the renal arterioles—depends upon the quantity of urinable substances in the renal blood and the activity of the renal epithelium. Augmented activity of the epithelium is hence always attended by an active physiological hyperæmia.

From this it follows that all medicines which increase the flow of urine by a direct action on the kidneys cause more or less active hyperæmia. Some of the direct diuretics, if given in large doses, diminish the quantity of urine and render it bloody and albuminous, which shows that they may so greatly irritate the secreting epithelium and the walls of the capillaries as to produce inflammation, and thus retard and even completely arrest the blood flow of many parts of the kidney.

Direct Diuretics.—Some of the direct diuretics produce a change in the chemical reaction of the urine, rendering it less acid or even alkaline. They are called *saline diuretics*. Numerous diuretics, when administered in excessive doses, diminish the quantity of urine, and cause other symptoms characteristic of irritation or inflammation of the kidneys. Hence they are distinguished as *irritant* or *stimulant diuretics*.

Saline Diuretics.—To this group belong many of the salts of potassium, sodium, lithium, calcium, and magnesium. The salts of potassium cause a more decided increase of the urinary secretion than the other salts, and hence are always preferred when an increase of the quantity of urine is indicated.

Of the salts of potassium the acetate, citrate, and bitartrate seem to possess equal diuretic power. This is readily explained by the fact that in the organism they are all converted into the carbonate, and as such are eliminated by the kidneys.

Doubtless, in being eliminated, they excite the renal epithelium to increased activity, in consequence of which an active hyperæmia results, and hence an augmented flow of watery urine. That the increase of diuresis is not due to an augmentation of the general blood pressure is proved by the fact that injections of dilute solutions of chloride of sodium into the veins are rapidly followed by an increase of the bulk of the kidneys and a free flow of urine, although the general blood pressure is not altered. The action of salines is held by many physicians to be due in part to changes of the general circulation, and, in febrile diseases, to lowering of temperature. If they are capable, as claimed by some recent writers, of producing antipyretic effects, their diuretic action in fevers may partly result indirectly. For it has been found experimentally by Mendelson that in fevers the kidneys become diminished in bulk, in all probability in consequence of the action of the hot blood on the vaso-motor centres. Husemann recommends nitrate of potassium, even in small doses, in inflammatory diseases, on the ground that it lowers the febrile temperature and improves the general condition of the patient.

Indications for the Use of Saline Diuretics. The saline diuretics are employed to meet two indications: first, to remove morbid accumulations of serum; secondly, to neutralize an excess of acid in the urine.

Excessive accumulations of serum occur in a variety of pathological states, diseases of the heart, liver, kidney, and as a consequence of inflammations. When the morbid condition giving rise to the dropsy is amenable to treatment, the diuretic action of the salines is often followed by rapid absorption of the effused liquid. This is especially the case when an abundant effusion occurs in consequence of inflammation of serous membranes, as in pleuritis, pericarditis, peritonitis, etc. After the symptoms of active inflammation have subsided, the use of salines is generally followed by rapid absorption.

Their utility is less evident in dropsies dependent upon organic diseases of the heart, lungs, liver, and kidneys; but when associated with other therapeutic means indicated by the pathological condition giving rise to the dropsy, they often greatly hasten absorption. Thus, in cardiac dropsy the chief indication is an increase of the arterial blood pressure. This the saline diuretics cannot accomplish. But when they are combined with the indirect diuretics, which augment the force of the heart's action, they promote the diuretic action of the latter and thus accelerate absorption.

In renal dropsy saline diuretics may be useful or harmful, according to the condition of the kidneys. In the dropsy attending acute nephritis, they will do harm as long as the inflammation is the cause of the diminished secretion of urine. The kidneys, when inflamed, like all other organs, require rest. The administration of salines may not only cause injury to the kidneys directly by augmenting the quantity of blood in them, but may hasten the appearance of uræmic symptoms. When, however, the inflammation has subsided, and the free flow of urine is prevented by the presence of tube casts and masses of blood in the uriniferous tubules, they may become useful by hastening the removal of these impediments.

In the dropsy of chronic renal disease the saline diuretics rarely possess much utility. But in some cases their administration is followed by increased diuresis. This is observed especially when the dropsy results from failure of the compensatory action of the heart. Combined with digitalis, or other medicines that augment the force of the heart's action, they often cause a copious flow of urine. So, too, in the hydræmic dropsy following exposure to cold, or disorder of digestion, the saline diuretics, associated with such remedies as the special pathological condition indicates, are often followed by efficient action of the kidneys.

In any case of chronic renal dropsy the use of saline diuretics, if they do not produce an increase of diuresis, should not be long continued; for if the kidneys have become so severely damaged that they cannot remove the surplus of water from the renal blood, they will also be unable to eliminate these medicines. Their persistent employment will, therefore, soon be productive of serious disorder, especially feebleness of the heart's action and symptoms of uræmia.

For the purpose of increasing diuresis, the acetate, citrate, bitartrate, and nitrate of potassium are given in doses of gr. x. to xxx. every two or three hours.

The acetate and citrate may be administered in several tablespoonfuls of water, to which may be added a small amount of orange or lemon syrup. The nitrate, if given in large doses, should be administered in more water, say a wineglassful, lest it act injuriously on the gastric mucous membrane. On account of its slight solubility the bitartrate also requires a large amount of water.

To meet the second indication for the use of saline diuretics, namely, to neutralize excessive acidity of the urine, and thus to prevent the irritation resulting from excess of uric acid and its deposition in the urinary passages, the salts of potassium are generally preferred, especially the acetate and the citrate. This preference depends upon the fact that the urate of potassium formed under these circumstances is a very soluble salt. Should it, however, be necessary to employ remedies for a long time, and evidences of gastric disorder become manifest, the salts of sodium would be more eligible, as they are better borne by the stomach.

Recently the salts of lithium, especially the carbonate and citrate, have been much used to prevent deposits of uric acid and urates in the urine. Experimentally it has been found that they are more powerful solvents of uric acid than the salts of potassium and sodium. They seem also to dissolve, to some extent, the deposits of urate of sodium occurring in gouty subjects.

The carbonate of lithium is given in doses of gr. iij. to x., in a tumbler of water, several times daily. It may be ordered as follows: ℞ Lithii carbonatis, ʒij.; sacchari albi, ʒiv. M. Div. in partes æquales No. viij. Sig.: One powder three times a day. The citrate of lithium is preferable to the carbonate, and may be given in doses of gr. v. to x., in a tablespoonful of sweetened water, three times a day.

Caffeina.—This alkaloid acts as a decided diuretic in some forms of dropsy, especially those resulting from cardiac disease. For some years it has been freely employed by French and German physicians in cardiac dropsy, when digitalis had failed. It has been strongly recommended by Gubler, Dujardin-Beaumetz, Riegel, and Binz. According to these observers it regulates the heart's action, slows the pulse, and augments the arterial blood pressure. It produces these effects more rapidly than digitalis, has no cumulative action, and is usually well borne. Often it succeeds after digitalis has been used in vain.

Caffeine is indicated in cardiac and hydræmic dropsy, especially when the heart is fatty.

The citrate or hydrobromate may be given in doses of gr. ij. every three hours, or from gr. v. to xx., in divided portions, in twenty-four hours. The following formulæ are recommended by Riegel: ℞ Caffeinæ citratæ, gr. iv.; sodii salicylatis, gr. iiiss.; aquæ, ʒi. M. For one dose, internally. ℞ Caffeinæ citratæ, gr. xx.; sodii salicylatis, gr. xviiss.; aquæ, ʒi. M. Dose, from ɱi. to vi., subcutaneously.

Adonis vernalis.—This plant, long used in Russia as a popular remedy for dropsy, was recommended by Bubnoff in 1879, and again in 1882, as a succedaneum of digitalis. He carefully investigated its action and uses, and found it to produce the following effects in cardiac disease with dropsy: the heart's impulse became decidedly stronger; its dimensions were markedly lessened; the heart sounds and murmurs, especially the præsystolic and systolic murmur of aortic stenosis, became better defined; the rhythm was rendered more regular and mostly slower; and the pulse was correspondingly influenced, becoming slower, stronger, and fuller. The flow of urine was decidedly increased, sometimes, in the course of twenty-four hours, from ten to eighty or one hundred ounces. Its diuretic action was equally marked when cardiac failure occurred in chronic kidney disease, but only when the dropsy resulted from the weak heart action.

Nothnagel tried adonis in cardiac dropsy, and generally found it to increase the general blood pressure and the flow of urine, sometimes acting after digitalis had failed. More frequently the reverse was the case, adonis failing and digitalis succeeding.

The action of adonis on the heart is due to a glucoside, *adonidin*, isolated by Cervello in 1882.

Adonis has no cumulative action, but it often causes nausea, vomiting, and diarrhœa.

Bubnoff usually gave an infusion containing from ʒ i. to ij., of adonis in six ounces, in doses of a tablespoonful every two hours.

Convallaria majalis.—This drug contains a glucoside, convallamarin, which was found by Marmé to act on the heart like digitalin. Both convallaria and its active principle have been tried in cardiac dropsy, with varying results. Thus Leubuscher, who administered as much as 1 gm. of the active principle in twenty-four hours, in no instance observed an increased flow of urine, a fall of the œdema, or a rise of the blood pressure. Hiller also reported unfavorably. Maragliano, on the contrary, found convallaria and its active principle useful in mitral disease with cardiac failure, the heart's action becoming stronger and more regular, and the urine increased. It had no cumulative effect. Frederick Roberts also succeeded with convallaria. In a case of mitral obstruction the heart's action became more regular and efficient, the thrill and murmur more evident, the quantity of urine progressively increased, and the dropsy disappeared. But in some other cases its action was less satisfactory. Falkenheim tried convallaria in eight cases of heart disease, and found it to exert a decided control over the heart's action and diuresis, but it seemed less certain than digitalis. He gave a tablespoonful of an infusion of the strength of one part of the flowers in twenty parts of water every two hours. Roberts used a liquid extract in doses of ten minims every four hours.

Apocynum cannabinum.—It has long been known that this medicine produces infrequency of the pulse and, in some forms of dropsy, copious diuresis. From its botanical relations Husemann supposed that it contains an active principle affecting the heart in the same manner as digitalin. Schmiedeberg has since isolated two active principles, apocynin and apocynein, which resemble digitalin in properties.

It seems very probable, therefore, that apocynum increases diuresis by acting upon the heart, and that it is specially adapted to dropsy resulting from inefficient cardiac action.

Usually it is administered in the form of an infusion made with a drachm of the bark of the root in eight ounces of water, of which the dose is a tablespoonful at intervals of four to six hours. Excessive doses cause nausea, vomiting, and purging.

Calomel.—The diuretic power of calomel was discovered by Jendrassik and announced by him in 1886. It had, however, been observed long before that calomel, in cases of dropsy, sometimes caused very profuse diuresis; but this was forgotten, and the writers on therapeutics in the two previous decades either entirely ignored the use of calomel as a diuretic, or recommended it only as an adjuvant to squill and digitalis.

The polyuria does not begin on the first day of administration, but usually on the second, the third, the fourth, or the fifth day. The quantity of urine then augments very rapidly, is most profuse on the second day, and subsequently slowly diminishes. As a rule, the polyuria continues until the symptoms of dropsy have completely disappeared. In cases of extensive dropsy the maximum quantity of urine voided in one day was twenty pints.

As the quantity of calomel necessary to produce such profuse diuresis is quite large, the ordinary effects of large doses supervene, unless prevented by prophylactic measures. Diarrhœa nearly always results. If not more than two or three stools occur daily, diuresis may still take place; but if the stools are very numerous no increase of the quantity of urine will result, doubtless because the calomel is expelled from the intestines before absorption can take place. To prevent such rapid discharge of the medicine, opium in small doses should be combined with it.

To prevent the effects upon the mouth, prophylactics should be used from the beginning of the treatment.