

crease or decrease the functions of those parts. We can depress the functions of the motor nerve endings with conin, and the sensory nerve endings with aconite. We can paralyze the involuntary muscle fibers directly with the nitrites, or indirectly by chloral hydrate, which depresses the functions of the vasomotor center. We can stimulate or depress the functions of cardiac muscle and dilate or contract the blood vessels. The tissues of the various glands may likewise be stimulated or depressed. We can improve the nutrition and therefore the function of almost all the tissues by iron, cod-liver oil and lime; and indirectly we can produce the same effect by the gastric tonics and digestives which promote the taking and absorption of food.

Dr. Albert Abrams, in a paper entitled "The Employment of Drugs in Diagnosis," alludes to the administration of certain drugs as a means of diagnosis. Amyl nitrite, for instance, relieves anemic headaches and intensifies those of hyperemic origin. Migraine of spastic origin is relieved, whereas paralytic migraine is aggravated. He claims that the phenomena of auscultation are in many instances brought out after inhalation of amyl nitrite. The antitoxins are of value as a means of diagnosis in diphtheria, cryptogenetic septicemia, hydrophobia, etc. Anesthetics are invaluable often in the examination of joints and to determine whether tumors, contractures, etc., are due to hysteria. Arsenic is of value in aiding a physician in the diagnosis of many neuroses. It is also an efficient aid in excluding tuberculous adenitis from Hodgkin's disease.

The diagnostic value of atropin in ophthalmic medicine is well known; colchicum in gout; potassium iodid in neuralgias, ulcerations, paralysis, etc., of suspected syphilitic origin, intoxication from mercury, lead, zinc, etc., and in actinomycosis; quinin in intermittent fever; salicylic acid in atypical manifestations of presumable rheumatic origin; salol for determining the motor activity of the stomach. Thyroid feeding constitutes an invaluable diagnostic means in the recognition of all cases of myxedema, whether the disease be the true form, sporadic cretinism or cachexia strumipriva. Thy-mol is especially destructive to the parasite of ankylostomiasis and is of undoubted value both as a means of diagnosis and cure.

Therapeutics implies more than the mere administration and local application of drugs. Climate and artificial aëro-therapeutics or medicated atmospheres are often important adjuncts in the treatment of disease. Balneology and hydrotherapeutics are immensely important and are increasing in popularity, and deservedly so. This subject alone requires our most careful thought and investigation. It is wonderful what results may be obtained by the proper use of water externally or internally, or both.

Equally important are the medical applications of electricity. No less an authority than H. Lewis Jones says there is no manner of doubt that electrical currents produce definite physiologic effects. The most obvious physiologic action of electricity is its power of stimulating living tissues. The metabolic activity of the tissues can be considerably increased by electricity, as Gautier and Larat have shown in their experiments on the elimination of carbonic acid gas and urea under electrical treatment, when it was found that an increase of 40 or 50 per cent. could be produced by general electrification.

Massage or "mechano-therapy" is another invaluable means of treating many diseases, particularly when applied by an expert. The practice of massage by people

quite ignorant of medicine, certainly with no scientific training, and independent of proper diagnosis and directions from a physician, is altogether to be deprecated, and is one of the great sources of the prejudice against the method still existing in the minds of medical men.

I must not fail to mention "suggestive therapeutics." The fact that the condition of many patients is influenced favorably or otherwise by their mental condition is well known. Drugs are not all that is necessary in the treatment of disease, and one is a very narrow therapist indeed who seeks for no means of relief outside of a drug store. There are limits to the utility of drugs, and the want of belief in them is largely due to the fact that they are expected to achieve the impossible.

THE FUTURE OF THERAPEUTICS.

I believe with Brunton that the prospects of therapeutics are very bright. "I think it is highly probable," says Brunton, "that before long we shall have a series of drugs which will stimulate the biliary secretion of the liver or modify its glycogenic function, arranged in order of their comparative strength, in much the same way we now have the class of antipyretics. We may also fairly expect to obtain a series of remedies which will act on the spinal cord in such a way as to enable us to treat a number of diseases which are at present altogether beyond the reach of our remedies."

The grandest principles that challenge human investigation center round the subject of therapeutics. Let us master every phase of it, that we may be better enabled to relieve our suffering patients. It is to be hoped that the therapeutic researches of the present generation will be followed by yet more brilliant achievement and by its light the darkness of passing illusions be happily dispelled.

Original Articles.

CARDIAC STIMULANTS.*

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The group of drugs which in therapeutic nomenclature is included under the head of cardiac stimulants or cardiac tonics—the so-called digitalis group—has not yet, as applied to the treatment of cardiopathic states, been displaced by hydrotherapeutic, aërotherapeutic or mechanical therapeutic measures, efficient as these latter means may be. The great practical, as well as therapeutic interest, attached to this oft-discussed group of drugs is sufficient excuse for their present consideration to which this paper is limited. In this connection the terms tonic and stimulant have acquired a synonymous usage, a custom not strictly to be commended, because, while the principal cardiac stimulants have also tonic properties, and may correctly be so employed, there are certain well-recognized cardiac tonics, such as the iodids, which are not available for stimulant purposes. Again, the chief clinical application of this group of drugs is for the purpose of stimulating an incompetent heart. That these drugs exert a tonic effect at the same time is not forgotten; indeed, such an effect is postulated by efficient stimulation, but the former effect is incidental and secondary to the latter in the absence of which is not obtainable at first. Our dosage in the presence of evidence of failing muscle power, is

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based on the stimulant properties of these drugs. The term stimulant, therefore, appears proper in this connection.

The one indication for the employment of this class of drugs is insufficiency of the heart muscle—a minus dynamic force with reference to the demand. The efficiency of these drugs may be modified by the nature of the specific cause of the insufficiency, which in certain instances may contraindicate certain members of this group. A relative insufficiency depending on increase in exocardial resistance does not necessarily indicate this group of remedies, or, if so, only in connection with agents which remove such peripheral resistance to blood movement. In some instances the latter agents are all that is necessary to allow the heart to perform its work, as was the case with a patient in whom considerable dropsy of the limbs and congestive enlargement of the liver were removed by five drops of tincture of opium thrice daily. In these cases such true cardiac tonics as strychnia or the iodids have their proper application.

It is not necessary at this time to discuss the physiologic action or the toxicology of these medicaments. The practical questions are, when and how to give them, and when to stop them. In some instances the latter question is more difficult to decide than the former, and imperfect results are often more due to faulty judgment on this question than to indecision on the others. The principles which govern the employment of the chief of this group—digitalis—also apply, with individual modifications, to the entire group.

DIGITALIS.

Digitalis easily maintains its position as the chief cardiac stimulant for general efficiency, reliability, and, numerically speaking, applicability. The indications and contraindications for its use have always been more or less in dispute, and probably will always constitute points of controversy. The limitation of Porter, who says that digitalis is useful only in lesions of the mitral valve, and there only for a short time, is too narrow. On the other hand, we may agree with Bartholow that the doctrine that digitalis is suitable for all kinds of weak heart is fallacious. Abstractly, the statement of Washburn, that broken compensation always demands digitalis, may be accepted in the sense that the one indication of its employment is dynamic insufficiency of the heart muscle without reference to the nature of the valvular lesion or other cause for such insufficiency. Practically, however, we find that individual causes of this insufficiency may so modify the effects of digitalis as to constitute a contraindication to its use. It is not necessary to say here that the mere presence of a murmur constitutes no evidence for or against the administration of digitalis, however frequently such evidence has been accepted. The real question rests on the inability of the heart muscle with respect to the presence or absence of features contraindicating digitalis. These features contraindicating digitalis may be due to intrinsic cardiac conditions, or may arise from causes exocardial in nature.

The cardiac conditions which may contraindicate digitalis are certain mechanical conditions of the heart, arising in consequence of valvular lesions, which operate as contraindications, even though the muscle may respond to the action of digitalis, also advanced degrees of myocardial changes. In the first class comes marked mitral stenosis, extensive aortic regurgitation and excessive degrees of aortic stenosis. Pronounced stenosis of the mitral opening contraindicates digitalis because

of the overdilatation of the left auricle during the longer diastole and, if the heart is slowed too much, the danger of the high pulmonary pressure causing pulmonary edema. Ewart points out that the drug should be at once suspended in these cases when the pulse slows down to 85 per minute, and that the rapid, irregular heart of these uncompensated cases is less likely to be mistaken for cumulative drug action because its danger comes at an early period from undue slowing of the heart.

Some cases of moderate stenosis, though, perhaps, with loud murmur, and many cases of double mitral lesion respond to digitalis better than to any other cardiac stimulant. The presence of mitral regurgitation is practical assurance of the safety of digitalis in cases with stenosis, while its absence should indicate caution in the use of the drug because of the danger of increasing too much the pressure behind an obstruction which does not lessen, and in a cavity whose walls have little resistance. According to Sansom, digitalis is often harmful in mitral stenosis by increasing ventricular action, which is not necessary on the left side, and results in overstretching of the right ventricle.

Aortic disease has been largely regarded as a contraindication for digitalis, especially regurgitation. According to Potain the latter condition is a contraindication unless the pulse is rapid. Peacocke states that digitalis is useful in uncomplicated aortic stenosis, and is generally indicated in double aortic disease, though there may be sudden syncope. The alleged pernicious effect on the left ventricle of prolongation of the diastole has been the basis of the complaint against digitalis in aortic regurgitation. Corrigan discouraged its use in his original memoir, and was followed by Fothergill and others. That this view as a generalization was not well taken is shown by the opinion of later authorities, such as Balfour, who says that digitalis or its congeners is imperatively demanded in failures from aortic incompetence, or of Broadbent, who says that the aortic cases with mitral symptoms should be treated as mitral cases. Washburn's approval is endorsed by Ewart with reservations, anginal pain being the main indication for its avoidance. He thinks digitalis dangerous in marked degrees of aortic stenosis except when there is acute dilatation with rapid running pulse. Groedel says that there is no indication that digitalis should be excepted in a whole class of valvular diseases, such as the stenotic lesions of the aortic opening.

When we consider the direct nature of the pressure in the left ventricle and its mechanical effects in aortic lesions, especially regurgitation in which dilatation is primary and progressive, it is not surprising that digitalis should be on the whole less effective than in mitral lesions. In the earlier stages of aortic lesions, when the heart muscle has stretched but is not markedly degenerated, we obtain relatively as good results from digitalis as in other lesions, but in later stages, when the muscle has degenerated as a result of imperfect nutrition, it is not reasonable to expect such results. We must remember that the hyposystolic period of aortic lesions, the period of the passive congestions that are so generally recognized as clinical evidence of the demand for digitalis, do not, as a rule, present until the heart muscle has undergone these degenerative changes to an extent sufficient to allow of stretching the mitral ring. If the drug fails here it is to be charged against the myocardial degeneration. And yet, even here we often have marked results which, unfortunately, are too

often but temporary because of imperfect coronary blood supply from imperfect filling of the aorta in the one case and too rapid emptying in the other. It is usually necessary to give relatively larger doses of digitalis in aortic regurgitation to produce effects, but the pulse reduction can not be safely carried to the same extent as in mitral lesions.

Acute myocardial inflammation, as a rule, contraindicates digitalis, always if extensive. According to Thompson, digitalis is absolutely excluded in acute degenerations of the heart. In many cases, however, of endomyocarditis of rheumatic origin digitalis, in suitable doses, may be of considerable service.

Chronic myocardial inflammations and degenerations present the most difficult class of cases in which to determine the eligibility of digitalis. The difficulty of distinguishing clinically between interstitial, granular and fatty changes is recognized by all clinicians and by some the differentiation is considered impossible. We are often obliged to adopt Huchard's plan of feeling our way with digitalis, even though we are inclined to be positive in our diagnosis. It is in this class of cases that various subjective as well as objective signs obtain a value as contraindications for the use of digitalis in vitium cordis of indefinite clinical outline. Potain says that myocardial lesions strongly contraindicate digitalis; that it may be dangerous, and that senile cachexia and fatty degeneration call for great care in using digitalis. On the other hand, Beates insists on the value of digitalis in the cardiac lesions of senility. Groedel says continuous small doses of digitalis are of use in slight fatty degeneration from alcohol and tobacco.

The presence of such extrinsic causes of relative or actual cardiac incompetence as atheroma, sclerosis of the vessels, or arterial spasm are by many regarded as contraindications for digitalis. Undoubtedly this is often correct, and yet if the heart be actually incompetent, even though it be through degenerative changes in the heart muscle, much good may be obtained by the careful exhibition of the drug. The argument is advanced that if the muscle has sustained degenerative changes how can it be expected to respond to the stimulating effect of digitalis? Very true, and yet we expect and obtain good results from strychnia and the iodids. Now if the circulation in and the nutrition of the muscle is good enough to respond to the tonic action of these remedies it will also respond to and be benefited by the action of digitalis, provided the latter be administered with due regard to the conditions present and its action be guarded by proper regulation of its action on the vessels. Clinically we often obtain remarkable results in cases where we have reason to expect failure, judging from our estimate of the heart muscle, and so one becomes impressed with the extreme difficulty of estimating the integrity of the muscle and the results to be obtained.

The large class of so-called muscular mitral insufficiencies are often much benefited by small and continued doses of digitalis in conjunction with strychnia and the iodids, and the action of the latter remedies are thus much enhanced, the above objection as urged by many to the contrary notwithstanding. Digitalis is of special adaptability in these cases because of the convenience of administration, the lack of stomach disturbance and the ease with which it may be administered in connection with vaso-dilators, cholagogues or laxatives. The doses of digitalis advocated by Beates in senile cardiac lesions present a startling contrast to

the conservatism with which digitalis is administered by those who have less faith in its utility and who emphasize its dangers. He recommends $1/10$ to $1/2$ grain from 3 to 6 times daily if necessary, and, if dissolution threatens, $1/2$ grain by hypodermic, repeated in an hour, and then $1/4$ grain by mouth every 2 hours till 2 grains are given. He claims that the blood tension is lowered rather than increased; that it can not be increased when the propelling function of the arteries is lessened, and that increased tension in old people does not contraindicate heart stimulants.

Recently, when recommending $1/8$ grain of digitalis every 6 hours for a man 76 years old, I was asked by the attending physician to assume the entire responsibility of so doing. A few days later I found him assuming the entire responsibility of giving the same dose to the same patient every 4 hours.

When exocardial resistance to the circulation from general vascular disease is marked it has been generally accepted as contraindicating digitalis. Bartholow's statement that digitalis is justified when arterial tension is low may be taken as supporting this view. The same view is variously stated by many observers. Arteriosclerosis is not confined to the aged, is not always a general process, and the tension is not always increased. The heart may or may not be directly concerned in the general vascular changes, hence its incompetence may be actual or relative. In the latter instance the vaso-dilating remedies—the hypotensive medication of Huchard—have their most successful application. In the former instance a combination of this form of medication with heart tonics and probably stimulants is necessary. Digitalis as a vaso-constricting cardiac stimulant has been much objected to in this connection. If, however, degenerative changes in the heart have not progressed too far, digitalis combined with vaso-dilators is not only safe in most cases of vascular disease, but is markedly efficient. The best dilators are opium, nitrite of sodium and nitroglycerin. The latter is best for marked cases of vascular sclerosis with increased tension. Its fault is rapid and transitory action, developed in about twenty minutes and lasting about one hour and a half. Its administration in connection with digitalis should be delayed about three-quarters of an hour. Opium is an ideal dilator as regards reliability, length of action and adjustment of effects, but in many cases has its objections. Nitrite of sodium is reliable and without objection in this class of cases, barring individual susceptibilities. The relative quantities necessary to affect the vascular action of a dose of any preparation of digitalis equal to from 10 to 15 drops of the tincture would be, in the average case, of opium, $1/3$ grain of powdered opium, from 3 to 5 drops of tincture, or $1/16$ of a grain of morphia; of sodium nitrite, from 3 to 5 grains; of trinitin, from $1/200$ to $1/100$ of a grain.

In some instances other members of the group of cardiac stimulants will give better results in cardiac inability associated with vascular disease than will digitalis because of difficulty in modifying the vascular effect of the latter, or because it is not well borne by the stomach.

General symptoms contraindicating digitalis or indicating its suspension are, according to Potain, nocturnal delirium, pallor, cold extremities, trembling, and contracted pupils. Generally we find that intolerance of digitalis, or too large dosage, is manifested by sensations of oppression or disturbance about the pre-

cordium, dizziness, faintness, and, at times, irregular heart action.

The cumulative action of digitalis has long been a bugbear to its administration. Personally, I have never observed it, and I have been in the habit of giving moderate doses of the drug for from four to six weeks without interruption. Porter claims that cumulative effects result from interference with nutrition from the constricting action of digitalis on the arterioles. If so, the effective combination with vaso-dilators might tend to restrict cumulative effects. I have regarded these effects as the result of improperly selected cases or to faulty methods of administration. MacLaren thinks the toxic effect of digitalis is overestimated.

The best preparations of digitalis are the infusion made from the fresh English leaf, the tincture made from an assayed drug (Squibb's) and a reliable digitalin—such as Merck's digitalinum Germanicum. According to Arnold and Wood the latter preparation is stable and 1 grain equals 70 c.c. of the tincture of digitalis. Digitoxin is the most active as well as the most poisonous element of digitalis. Solomon says digitoxin is the chief ingredient of the leaves, is superior to digitalis as a diuretic and is more prompt and certain in its action in doses of from 1/1000 to 1/250 of a grain. Zeltner believes digitoxin to act better in primary cardiac disease and in secondary disease from emphysema and nephritis than digitalis leaves. He advises its administration by mouth, hypodermically, and by the rectum, and says there is no more danger from disturbance of the stomach or from poisoning than from digitalis. The latter part of this assertion certainly can not be accepted at present.

Digitalin (Merck) is a safe, reliable and eligible preparation. Providing its dose is properly adjusted and vascular effects properly controlled, its effects on the heart can not be excelled by other preparations of digitalis or equaled by other cardiac stimulants. Imperfect effects are generally due to too small dosage. From 1/12 to 1/8 of a grain represent, in the average case, a dose of from 10 to 12 drops of a reliable tincture. The extremes of life do not present the same susceptibility to digitalis that we are accustomed to allow for with other drugs. Jacobi has pointed out that children bear digitalis better and in comparative larger doses than adults. His allowances are: for an infant of one month, 1/10 adult dose; 6 months, 1/5; second year, 2/5; 4 to 14 years, 7/10. Early adult life generally presents more or less marked susceptibility to the action of digitalis. Old age requires practically as large a dose as maturity.

Continued administration of moderate doses of digitalis for periods of from three to four weeks, followed by interruption for like or lesser periods in order to obtain the full tonic possibilities of the drug, is a method whose value is generally underestimated, but properly carried out the asystolic period of chronic cardiopathies may be often considerably postponed. Groedel says that digitalis does not lose its effect by continuous use, and is useful in continuous small doses in heart lesions from overexertion. This method of using digitalis is particularly applicable in senile cardiopathies.

STROPHANTHUS.

Strophanthus, while a heart stimulant of value, is not to be depended on, in the presence of marked muscular failure, to the same extent as digitalis. It is valuable in regulating functional ataxia, or that due to

mild degrees of muscular insufficiency. Its special clinical application is in relation to the latter condition in association with mitral stenosis. Here it is both safer and more efficient than digitalis except when there is dilatation of the right ventricle. Aside from a tendency to produce gastric disturbance it is well borne at all ages. The dose of the tincture (P. D. & Co.'s) is from 8 to 12 drops. It is best given in laurel-cherry water.

Fraser stated that strophanthus acted mainly on the heart and slightly on the arteries, which he considered an advantage, but which Balfour doubts, as the blood pressure is more variable and metabolism uncertain. The action of strophanthus on the heart is more transient than that of digitalis and its tonic effects are therefore less marked. Strophanthin fairly represents the action of the drug and is considered reliable by most observers. My own results have been best with the tincture when it was well borne. The dose of strophanthin is from 1/200 to 1/60 of a grain. The former quantity may be used hypodermically. The diuretic action of strophanthus is decidedly uncertain. In vascular diseases with relative cardiac insufficiency it often acts well when digitalis fails or aggravates existing conditions.

SPARTEIN.

Sulphate of spartein is valuable, both as a regulator of functional ataxia and as a stimulant in muscular inefficiency. It is adapted to the treatment of nervous irregularity in drug habitués. In myocardial weakness following acute diseases, especially influenza, it is useful. Its special field of usefulness, however, is in the continued treatment of various degrees of myocardial weakness and ataxia associated with myocardial degenerations of toxic origin, and in the various chronic degenerations which may be grouped under the head of senile cardiopathies. Voight thinks it indicated in weakness of the right heart. Thomas and Cushing, and Matthews think it acts directly on the myocardium. Heffron thinks it a reliable stimulant for weak heart walls. Chapman recommends it in dilatation of the heart, and in dropsy from dilatation of the right ventricle. The action of spartein is rapid and it may be used to sustain the heart until digitalis has had time to produce effects. The drug is soluble and may be used hypodermically. The dose of the sulphate is from 1/2 to 2 grains.

CAFFEIN.

Caffein has been recommended by Beaumetz, Huchard and Semmola in asystolic conditions, arrhythmia and cardiopathic conditions of bulbar origin as a cardiac stimulant and diuretic. In some instances it is efficient. It appears to be adapted to cardiopathic states associated with nephritis or with vascular disease, or both. In asystolism due to valvular lesions it is not, as a rule, effective, though it may be of use as a diuretic. In too large doses it causes dizziness, faintness and irregular pulse. Heffron recommends it in dropsy from parenchymatous nephritis when the heart is involved. Zenetz condemns it as having a poisonous action on the spinal cord, striated muscle and cardiac muscle like strychnia; as accumulating in action, of slow elimination (lasting from ten to fifteen days after last dose); as causing a slow rise in blood pressure, which culminates in cardiac and renal diseases, in from four to six days in symptoms of impending cardiac tetanus; and as showing marked individual variations as to the toxic dose. He thinks all renal or cardiac diseases associated with atheroma or arteriosclerosis absolutely forbid its administration.

Huchard is not afraid of the toxic effects of caffein, and recommends it when digitalis fails to act on a damaged myocardium, in cardiac weakness from infective diseases, and as superior to digitalis in renal diseases. I have employed it in cardiopathies of renal origin or association with good results, using a salt prepared by combining equal parts of the alkaloid caffein and sodium benzoate, two or three drams of each to three ounces of distilled water, giving a teaspoonful every six hours.

STRYCHNIA.

Next to digitalis, strychnia is the most useful of cardiac remedies. As a cardiac stimulant it is useful in the hypostolic period of all lesions, and is the only stimulant which can safely be used as such in connection with digitalis in any lesion at any stage. It is essentially the best stimulant when the right ventricle is overtaxed from rapidly developed strain. Its frequent hypodermic use is a most valuable means of stimulation in emergencies. The dose is from 1/25 to 1/15 of a grain. J. Basil Hall recommends large doses as a prophylactic against surgical shocks. He gave 1/4 of a grain in two cases of impending death from air embolism with recovery. He thinks it futile in such cases to give less than 1/10 of a grain. Baumgarten thinks that in cardiac weakness the best results are obtained from small doses of strychnia, because large doses, besides having undesirable effects on the entire spinal cord by raising blood pressure, immoderately increase resistance to the heart's action long before it can assist it indirectly; that it must be used before the strength of the heart has sunk too low, because on Binz's statement that strychnia raises blood pressure by increasing reflex irritability of the vasomotor center, and not by stimulation, thus necessitating peripheral impulses to accomplish contraction of the vessels, strychnia must fail in the very conditions of collapse for which it is so much depended on; that moderate doses should not be long continued, because, like digitalis, it may accumulate. He charges clinicians with not being as well acquainted with the cumulative effects as physiologists and pharmacologists. Lauder Brunton says strychnia is a "cumulative poison," as it contracts the renal arteries and thus prevents its own excretion. A. H. Carter admits the utility of strychnia as a heart tonic for occasional use, but thinks its prolonged administration not justified except in the smallest doses.

The clinician is forced to deal with conditions of disease as he finds them, and is not always able nor does he always attempt to reconcile clinical results with physiologic argument—a privilege I will here avail myself of. The dosage of such remedies as strychnia must ever be a relative matter. I have administered strychnia continuously in 1/30 grain doses thrice daily for periods of from 6 to 8 weeks with results which I believe to be satisfactory in every respect. Also, I have given 1/15 of a grain hypodermically every 2 hours for 48 hours, and for 2 or 3 doses every hour, in critical collapse in pneumonia, with prompt response to every dose and final recovery. I have seen prompt and effective results from 1/10 of a grain in traumatic and surgical shock, and I am therefore not prepared to accept the second conclusion of Baumgarten.

Strychnia, in small doses, is the most valuable heart tonic we possess, and is particularly adapted to the treatment of senile lesions by continuous administration over periods of several weeks. During the second and third decades of life strychnia is not as well borne as it

is later, being likely to excite and irritate the nervous system.

OTHER DRUGS.

Convallaria majalis, cactus, grandiflora, adonis vernalis, nerium oleander, coronilla scorpeoides are all cardiac remedies whose stimulant action is less valuable than those already considered. Canadian hemp has recently been recommended by Golubinin as a valuable cardiac stimulant. He recommends 5-drop doses of the fluid extract three or four times a day.

Suprarenal substance has obtained some use as a cardiac stimulant as would naturally follow from its effect on the vasomotor system. S. Florsheim says the drug acts quickly and causes rapid improvement in flaccid and fluttering hearts, arrhythmia disappears and the heart remains in better condition. The substance appears to have a tonic action on the heart muscle, causes more regular action, increased force and fuller, stronger pulse. Florsheim noted best effects in cases of dilatation with weak pulse, diffuse apex beat and fluttering, irregular action. Two cases showed contraction of the heart with stronger and more localized apex beat. I have employed adrenalin to raise blood pressure in conditions of collapse, and during the critical period of pneumonia when the blood pressure was low and the heart's action weak. In such instances the action of adrenalin is prompt and effective. Three or four drops of a 1:1000 solution may be administered hypodermically. As a cardiac stimulant the use of this substance has as yet been too limited to form definite conclusions as to its full clinical value or application.

DISCUSSION.

DR. HENRY BEATES, JR., Philadelphia—The phenomena of normal circulation depend on a relation of intracardiac pressure or tension with that of the blood vessels, and there also exists a constant relation between arterial and venous tension. I would lay down the rule that all lesions of the heart must be viewed from the standpoint of their being especially local, while all disturbances of the circulatory system, in which the one great result, disturbance of equilibrium, results, are due to either exocardial conditions, local and, frequently, influences operating from both. It is, however, the disturbance of equilibrium which all treatment is intended to overcome, and to restore lost circulatory equilibrium is the one grand object, whether it be by the use of so-called cardiac stimulants, or, as is sometimes necessary, the combined exhibition of these and sedatives.

In every lesion of the heart, there must be, for physiologic reasons, consequent exocardial change. This generally occurs in the arterial side first, and, sooner or later, in the venous also. When these two conditions obtain, the lymphatic disturbances next follow, and these require the observance of the same principle for successful treatment. It is these exocardial secondary lesions and the consequent inability for the disturbed equilibrium to be overcome that indicated, not the diminution of the dose of the cardiac so-called stimulant, but bold and heroic exhibition of increased doses. A moment's thought discloses the fact that, if the vis a tergo is greater than the vis a fronte, the heart feels no strain when its ventricle empties its contents into the aorta, and if it is weakened from a local lesion, there is not that intensified and fatiguing force necessary to be exerted, which adds to an already failing heart. But if the vis a fronte be much increased, it is necessary not only to give strength to the already tiring heart, but to remove the load from in front. There is not sufficient importance accorded to the part played by the arterial system in the work of carrying on the circulation of the blood mass. The importance of thoroughly appreciating the condition of the arteries is not comprehended by the profession generally as it should be, and it is only when the clinician will recognize that each artery is practically a heart for the part it supplies, there

will be a clearer understanding of the application of the principles involved, in the treatment of these conditions. When we give digitalis, or any other so-called heart stimulant (I prefer the term "circulatory" to "heart") we do not, by its administration, act alone on the heart but, let it be emphasized, on the blood vessels also (arteries and veins), and from what has been briefly said, it is evident that the object in view, being to restore equilibrium to the circulation, necessitates aid being given to the blood channels as well as to the heart. It is by this powerful influence on the vessels that digitalis proves so useful in these conditions. It removes the great load from before the heart, and enables the well-nigh exhausted viscus to pulsate, and thus digitalis saves life.

Referring to the mentioned cumulative action of digitalis, the somewhat extended studies of its derivatives lead me to the conclusion that these effects are due to the derivatives known as digitalin Belgic or chloroformique, and digitoxin; they have never occurred after years of continued exhibition of the use of digitalin Germanic Merck. I advocate, therefore, the use of that digitalin known as Germanic Merck. Another point: when any of the galenic preparations of digitalis are given, all therapeutic deductions which may be reached are necessarily unreliable. We know that any drug derived from the vegetal materia medica, in its crude condition, represents a feature characteristic of every vegetal organism. It is that principles or derivatives vary in their percentage presence and solubility; thus, one unit of digitalis leaves might represent 10 per cent. of this, 8 per cent. of that, 2 per cent. of the other, and so on, derivative, and these themselves vary in their percentage degree of solubility in alcohol, ether, chloroform and water. Indeed, some are insoluble in one or the other of these latter, and thus it is that tinctures, infusions, etc., cannot possibly represent a unit of therapeutic strength. The natural result, therefore, of galenic official preparation of digitalis, as well as the rest, is difference in clinical action. Digitonin is soluble freely in water, and hence the infusion contains this derivative in considerable quantity. The digitalin Germanic Merck is also soluble in water, therefore in the infusion we have a preparation that approximates a unit of strength, and for those rare conditions of disturbed circulatory equilibrium, where the action of the medicament is so pronounced on the vasoconstrictors as to produce local peripheral ischemias, and it is sometimes necessary to overcome this by the judicious use of a cardiac so-called sedative, and digitoxin possessing this property preëminently, we have, in the infusion, a very desirable remedy for this particular group of cases.

This point Dr. Patton has very clearly indicated, and brings forth the fact that there are conditions in which both stimulation and properly adjusted sedation may be required, and in these the infusion of digitalis answers a purpose second to none. Numerous cases are characterized by the cardiac musculature being weak, while the arterial tension is increased. In such cases, contrary to the usual teaching, digitalis is not only not contraindicated, but most emphatically demanded. It acts by restoring the propelling power to the arterial system, and removes from before the organically weakened viscus a great and almost insurmountable burden. In these conditions the preternaturally distended side of the circulation will rapidly disappear after full doses of digitalin Germanic Merck, gr. $\frac{1}{2}$ from 3 to 6 times daily, in emergency cases, and a conspicuous great venous tension will, in the course of a few hours, disappear as equilibrium is restored.

Dr. W. J. ROBINSON, New York—I wish to endorse what has been said about digitalin. There can be no doubt at all that the cumulative effect of digitalis must be due to some other agent than the principle digitalin. Disappointment in the use of digitalin is often due to the fact that the dose is too small; indeed, this must be so if we can give digitalin in doses as large as $\frac{1}{2}$ grain three times a day, for days at a time, as we know has been done, and with good results. A prescription that I frequently use consists of 1/12 of a grain of digitalin, 1/60 of a grain of strychnin, and 1/100 of a grain of nitroglycerin. I have had patients take this pill for months without causing distress, or gastric disturbance, or bad results

of any kind. I have found this combination a useful stimulant to the circulation, for prolonged use.

Among cardiac stimulants I would include camphor, the value of which is but little known in this country. The best method of administration is in the form of a solution (10 per cent.) made with pure olive-oil, to be given hypodermically. The usual dose of camphor is 1 or 2 decigrams ($1\frac{1}{2}$ to 3 grs.), or 1 to 2 c.c. (15 to 30 minims) of the solution. When this is given to a patient in a state of collapse the results are simply marvelous. In such a condition one or two hypodermics will produce most satisfactory results.

With regard to the use of adrenal substance as a cardiac stimulant, its effects are too evanescent for us to rely on it in cases of chronic disease of the heart.

Dr. HEINRICH STERN, New York—I take exception to the statement that *Adonis vernalis* is inferior in the general run of cases to digitalis as a cardiac stimulant. I wish to know whether or not the author of the paper bases his opinion on personal experience with adonidin? Basing my conclusions on an experience with several hundred cases treated with adonidin, I maintain that adonidin is not a mere succedaneum of digitalis or its alkaloids, but that its action is in many instances markedly superior to that of the latter drug. Adonidin is more rapid in action than digitalin or digitoxin, and it may be given without hesitation in a number of instances in which digitalis or its preparations should not be prescribed, as a rule. In fatty degeneration of the heart, in various atheromatous conditions, etc., adonidin acts safely and efficiently. In rapidity of action adonidin excels most of the other heart remedies, as digitalin or digitoxin, strophanthus, spartein, etc. In certainty of action it is also superior to these drugs. It is more permanent in action than any of these medicines, without possessing the well-known accumulative properties of digitalis. It is especially useful if kidney disease is accompanying the heart affection. The diuretic qualities of adonidin in the normal kidney are little pronounced; it exerts very great diuretic activity, however, in conditions concurring with dropsy and low arterial tension.

Dr. H. C. WOOD, JR., Philadelphia—With regard to the point made by Dr. Beates, I wish to confirm the statement that in the condition called "heart-failure" the heart is not solely at fault, the symptoms are due to circulatory failure. In such cases it is important to see that the vasomotor apparatus does its work. As digitalis acts also on this vasomotor apparatus, there arises a tendency in the minds of the profession generally to overestimate this action of digitalis and to avoid its use as a cardiac stimulant because it increases the resistance in front of the heart, so that the heart being compelled to act more powerfully and to do more work, the drug might fail to accomplish the purpose if the heart should be too weak to overcome the force in front of it. The use of digitalis in acute endocarditis has been advocated by some and condemned by others. In nephritis, we hesitate to give diuretics, because of their action on the kidney structures; but in endocarditis we do not hesitate to give digitalis, for its action is on the myocardium and not upon the endocardium.

With regard to the use of suprarenal extract, or adrenalin, it is to be observed that, when given by the mouth, it is too rapidly eliminated to produce any physiologic action on the circulation. In the laboratory it has been found that the only way to produce any effect on the circulation by this agent is to throw it into a vein. Even then the effect passes off in a few minutes. It is possible that suprarenal extract, or adrenalin, may prove of use in an emergency as a cardiac stimulant in very acute conditions, if used intravenously.

Dr. S. SOLIS-COHEN, Philadelphia—The profession owes a great debt of gratitude to Dr. Beates for his patient insistence on the value of digitalinum verum, or Germanic of Merck. After becoming familiar with Dr. Beates' observations, I diminished my use of the common preparations of digitalis and used as much as possible the Germanic digitalin, which permits accuracy and regulation of dosage and is satisfactory in its results. Dr. Beates has also taught the profession that the dose of Germanic digitalin is not 1/60 grain, but more

nearly 1/6 grain, as the rule, and even much larger doses may be given with advantage and safety.

The point that Dr. Robinson mentioned deserves attention; and in order to be clear on the subject we must discriminate more closely between cardiac stimulants—temporary and quick in their action—and those drugs that have a sustained or tonic effect. When we wish to apply a quick spur to a flagging heart, we should give camphor or musk; for tonic action slowly developed and long continued we should turn to digitalis, strophanthus, adonidin, or spartein sulphate; while atropin stands between the two classes. Bartholow used to say to his pupils that we give digitalis to-day and get effects to-morrow. He taught that the stimulant effect of the tincture of digitalis given hypodermically was due to the alcohol rather than to the digitalis. This may have been an exaggeration, but it expressed his estimate of digitalis. The effects of spartein and adonidin on the heart are even more slowly developed than those of digitalis; while strychnin is the most prompt in action of the tonic class, especially as a vasomotor stimulant. The combination of strychnin, atropin and digitalin thus has a special value.

With regard to the suprarenal gland and its various preparations, after a rather extended experience I can not agree with Dr. Wood that when given by the mouth these agents are always inert. It is true that in many cases I have seen no result, but in some cases I have seen decided results which I could attribute properly to them. This might be the result of the method of administration adopted. My instruction to my patients is to allow the drug to dissolve in the mouth, and not to swallow it immediately. From observation of its effects on other mucous membranes, I am led to believe that effects on the general circulation can result from this manner of administration. A drop of adrenalin solution on the conjunctiva will sometimes produce a remarkable effect on the heart. I have made some clinical tests of the effects of this drug in various heart and circulatory disorders. In the Polyclinic and in the Philadelphia hospitals I have employed suprarenal extract in a large series of cases. In exophthalmic goiter it is frequently curative, as in certain types of cardiovascular asthma and albuminuria. In valvular disease of the heart, I have obtained little definite result. In a case of bradycardia, due to Stokes-Adams disease, of which I have notes of the autopsy, I administered suprarenal extract by injection into the conjunctiva; each injection being followed by transient increase in strength of the heart's action. This observation was confirmed by several other physicians who saw the case under treatment. I merely mention this experience to show that as yet the exact value of adrenalin in cardiac disorders has not been determined. We are in a position to say, however, that in some cases it will produce marked transient effects. I believe that when collapse seems to be impending, danger may be averted by this agent. It is certainly worthy of further study.

DR. W. W. TOMPKINS, Charleston, W. Va.—The value of rest in cases of disturbance of the circulation and cardiac weakness is almost as important as the therapeutic agents just considered. It is of prime importance to lessen the work of the heart, and this can be done by rest; in the more aggravated cases absolute rest in the recumbent posture, in the milder cases relative rest obtained by reducing bodily activity. As to the form of digitalis to be used, it depends to a great degree on the idiosyncrasies of the patient. The pharmacopeia directs that its preparations shall be made from leaves of the second year's growth; and we are told that they contain nine alkaloids, each one exerting different physiologic effects. As far as my own experience goes, I regard the infusion as of most value, principally on account of its diuretic action. I think that in many of the cases of this character it is well to combine some form of iron with the digitalis, because these patients are generally very anemic. As a cardiac tonic, strychnia is most effective, and I frequently combine it with the digitalis and the iron. I believe, however, that, to a great degree, each case is a law to itself, and the method of treatment and the drugs employed must be selected according to the requirements of the individual cases.

PROF. C. S. N. HALLBERG, Chicago—I wish to make a simple suggestion. Empirically, it is generally stated that there should be a distinction made between the infusion of digitalis and the tincture. The difference between the two preparations is unquestionably due to the fact that the active principles of digitalis are glucosids. Like all glucosids they are apt, in the presence of water, to decompose and to split into glucose and other principles, but in alcohol this does not occur and they retain their original character. This is of importance to pharmacists, as it bears on the question of the propriety of making the infusion from the fluid extract. The great difficulty with digitalis is—and we have the same with ergot—that sufficient attention has not been paid to this splitting of the active principles in the presence of water. We know that in the presence of water, amygdalin and emulsin in wild cherry and bitter almond form hydrocyanic acid, and that in many other glucosidal drugs there is probably a similar reaction, and that it is very important. In all these preparations of similar character, the method of manufacturing must have a great influence upon the therapeutic value of the product. The committee on revision of the pharmacopeia wished to make a standard for the preparations of digitalis, but found it impracticable to do so. Our knowledge is not sufficiently advanced at present to permit this to be done. It is the same with ergot. I mention this fact in order to indicate the necessity for a more thorough knowledge of the constituents of these plants, so that their active principles may be of more uniform potency and strength.

DR. JOS. M. PATTON, Chicago—The point of Dr. Beates on the pharmacodynamic relations between disorders of the circulation, diseases of the heart, and digitalis, was explained in a lucid manner. The opinion has been expressed that digitalin is a safe, reliable and effective agent in relatively large doses and the statement made that it can be given in such doses for a considerable period of time, in appropriate cases, without danger. I concur in this opinion, but think that patients should be kept under careful observation, when such unusual doses are given.

In reference to the remarks about camphor, in my paper I did not take up that class of remedies but only the direct cardiac stimulants. In cases where a prolonged effect is required, we use digitalin because its action is more sustained. It not only increases the power and action of the heart, but keeps it up. If we wish to have only a temporary stimulating effect we use ammonia, alcohol or some other article of that class; but for a sustained effect we give digitalis.

In reply to the gentlemen who spoke of *Adonis vernalis*, my paper was confined to the statement of the results of my own experience, and I have had no experience with adonidin. I feel satisfied, however, that where a heart-muscle is degenerated or weakened I can not get the results from adonis that I can from digitalis. My experience does not confirm the claim that has been made on behalf of other drugs that were said to be as good as digitalis, although I would be very glad to have something as valuable as digitalin to use in the class of cases needing a heart tonic. I confirm the remark of the gentleman from West Virginia about adjusting our remedies to suit the individual case. He was also perfectly correct in saying that rest is one of the most important cardiac remedies. There is no reason, however, why the infusion should be different in its effects from other preparations of the drug, if the others are given in corresponding dosage. In some patients the infusion is preferred, in others the tincture may be more suitable. Personally I have been in the habit of relying on the digitalinum verum for the reason that it is reliable. It also agrees with the stomach better than the other preparations and the dose can be regulated more accurately to suit the needs of the case than any other form in which this remedy can be administered.

Ice for Respiratory Hemorrhages.—Ice applied to the external genitals—the scrotum in men, the labia in women—is said to the best and simplest method for controlling blood-spitting and nose-bleed.—*Canada Medical Record*.