

suggestive. From the examination of the urine he determined the proportion of uric acid to urea to have been 1 to 16. Uric-acidemia is productive of varied nervous symptoms, and it may not be unlikely that that was a provoking cause of the nervous symptoms in this particular case. It is very common, as all of us know, to see cases of vertigo that we attribute to the stomach and liver. I should say in these cases that there is some defect in the working of the liver. We may have failure of performance of some action of the liver, even if we do not have jaundice. The liver is intimately concerned in the formation of uric acid and urea, and where we find cases of excessive uric acid, the proper process of digestion of the intestines is not taking place, and also excretion is probably imperfect. It is very common to see persons affected with vertigo, who are quite comfortable in the supine position. They are not at all anemic; the blood examination shows that, and the pulse indicates that there is no lack of blood, but they become very dizzy upon rising. Treatment directed to the proper action of the liver, as for instance the administration of hydrochloric acid and strychnin, has afforded complete alleviation of this condition. Another question is whether vertigo may not be due to real ptomain poisoning. I think it sometimes is, but that hinges on one point, namely, imperfect disposition of the food in the alimentary canal. Unless we can limit the patient to one meal a day, we can not tell whether a certain meal is productive of certain symptoms. If we can give the patient one meal, and in six, ten, twelve, fourteen or twenty-four hours, regularly and uniformly, certain effects are produced, then we have a right to say that there are certain ill effects produced by that particular meal. A great many cases of vertigo are simply due to improper digestion.

DR. HUGH T. PATRICK, Chicago—I should like to ask Dr. McCaskey to state a little more carefully the character of the vertigo in this case. Probably I did not get it fully as he read it. It is exceedingly important, in writing of the nature, cause or origin of any case of vertigo, to very definitely define the vertigo itself. I should like to say, for myself, that I have come more and more to look with great skepticism on vertigo of gastric origin and on liver or intestinal vertigo, and symptoms coming under that general head. Where there has been a real turning or rotary sensation, with inability to stand steadily or at all, the cause has ordinarily been found in the ear or somewhere in the cranial cavity, or it has been a case of heart disease, or a bad case of anemia—in other words, something strictly and determinably of organic origin. I do not remember seeing a case of well-defined, unmistakable vertigo of gastric or abdominal origin. A general feeling of lightness in the head, a general feeling of uncertainty and discomfort, which patients describe as dizziness or as vertigo, as well as the cases spoken of by Dr. Wolfstein, approximating agoraphobia, in which the patient is terror-stricken or panic-stricken and can not find himself, are exceedingly frequent, but they are separate and distinct from real vertigo.

DR. G. W. MCCASKEY, Ft. Wayne, Ind.—Referring to Dr. Patrick's expression of his own skepticism as to the existence of vertigo of gastric or intestinal origin, I would say that the gentleman simply voices the sentiments of the average neurologist of to-day. This is undoubtedly the trend of neurologic thought, and in reaching a different conclusion I have done so on the basis of a rather large experience with gastric disease. A case which I have not quoted is one among a great many others I have seen—a case in which there was no suspicion whatever, of either cerebral or aural disease; one of the worst cases of gastro-intestinal disease I have ever seen. There was very intense gastric-motor insufficiency. That patient was taken into one of my rooms and placed on a table for examination, and it would take him two or three minutes to get up or lie down, the vertigo was so intense. So far as the adequacy of the gastric or gastro-intestinal causes is concerned, the patients have recovered without exception, and in this one the vertigo remained permanently cured upon curing the gastric disease. We must take into account the conditions to which Dr. Patrick has referred, as associated anemia, etc.—but why do they recover without recovery from the anemia? And why does the vertigo take place in the absence of anemia? I do not think it is fair on the part of physicians or neurologists to assume the existence of cerebral or aural disease, unless they can be positively demonstrated by examination. This case has been observed over a period of three years, and is absolutely well; no return of the vertigo or any development of what might have been at that time latent cerebral or aural disease. It is fair to assume that it does not exist in that case.

As to the character of vertigo, in this case it was a very sudden loss of balancing power. The patient would have fallen

if he had not been supported, and when he had once lain down, he could not move his head from one side to the other. He could not look up suddenly without severe aggravation of the vertigo. Here is a case in which this symptom develops with the ingestion of a large quantity of food, and disappears with its rejection. I assume that we can attribute such a series of events one to another. I think the *post hoc* in this instance is fairly demonstrable to be a *proctor hoc*.

There was hepatic disease in this instance. There was bile pigment in the urine and feces, as demonstrated by the spectroscope. The presence of bile in feces is pathologic, not physiologic. The normal coloring matter present in the feces is not bile. There was no jaundice whatever. The only evidence of hepatic disease was enlargement and tenderness of the liver, with bile-pigment in the urine and fecal matter. I did not attach much importance to the large quantity of uric acid. The proportion of uric acid—the ratio—to urea was too large; it was 1 to 18. The absolute quantity was small, only 0.6 gram, which is less than 10 grains and is below the average. Even if it were 20 or 30 grains, I would regard it as a relatively unimportant phase of the case.

Dr. Wolfstein spoke of recurrence. I recognize the pertinence of that point, and I told this patient that, in my opinion, he was not well. He will return to me with this vertigo, because the gastric disease will recur. I confess that it is very difficult to determine the essential pathology of such a case, and yet, at the same time, I am forced by the honest study of the facts in these cases, to the conclusions that gastric disease is an efficient cause of vertigo, and while in this case there was associated aural disease, in many it does not exist, as far as examination will enable us to determine.

HEART TONICS.*

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In discussing the subject of this paper I must at the outset claim the license to consider it in its broadest sense, studying it from the standpoint of the clinician and therapist rather than from the technical ground of the physiologic action of drugs.

The term "tonic" should mean, when discussed in this way, the broad principle evolved by the therapy of any remedy, which shall have the power of regulating heart action, whether its irregularity be functional or organic or that modification of its conditions which renders the heart action a source of discomfort or danger to the patient. In dealing with functional disturbances which are the result of impaired reflexes, coming as they most commonly do, from disturbance of digestion or some uterine derangement, the indications for relief are plainly the removal of the gastric or uterine disorder back of the perturbation or irregularity, not forgetting that prolonged and persistent functional disturbance may result in organic change of the walls or valves of the heart.

Again, intelligent consideration of these agents and skilful exhibition must be absolutely based on an accurate knowledge of the pathology of the affection in which a heart tonic is indicated. A conviction that many times an improper drug for the fulfillment of the indications is selected and given, either with no benefit or with directly harmful results, has been the inspiration of this paper.

Selecting those drugs most popular as heart tonics, and most frequently exhibited, I shall consider their physiologic action and then the indications for their therapeutic application, reserving to myself, as I have already indicated, the right to discuss agents which, under a strict classification, are to be considered as cardiac depressants, but yet are, in the broadest sense, indirect heart tonics, because they regulate heart action.

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Why not if it be excessive and too strong. I emphasize this point, because it is not a new thing to see digitalis given to relieve a patient suffering from disturbed heart action, excessive in tension, because of hypertrophy—the result of valvular or renal lesion or of long-continued and excessive stimulation of the vagus due to excessive use of tobacco—when really it is emphatically contraindicated, and the truest tonic, calmative and comforting to the patient, is an agent like aconite, nitroglycerin or veratrum viride belonging to the class of pronounced motor depressants.

On the other hand, agents like these, nitroglycerin especially, are frequently exhibited to sustain heart action when strychnin or digitalis may be imperatively demanded to prevent sudden and absolute heart failure.

Digitalis.—Physiologic action is most pronounced in the beginning by slowing of the heart's action, increased arterial tension and lengthening of the diastole. These are due to the stimulation of the vagus, cardiac motor ganglia and inhibitory centers, though some authorities claim its action is directly on the muscular walls of the heart which act with increased power, filling the blood-vessels more perfectly and fulfilling the conditions of a perfectly normal circulation. But continued administration results in greater frequency and diminished arterial tension, due to exhaustion from over-stimulation of the vagus, etc. In the first stage of its action there is a contraction of the arterioles of the kidneys, diminished elimination, consequent on over-stimulation of the vagus, and secondary cardiac depression. As a result of these conditions, digitalis is a remedy of uncertain value, because a secondary condition of depression may result from its exhibition, and at a time when it would jeopardize the welfare of the patient.

To be more explicit, in mitral regurgitation, the lesion in which it is conceded to be most useful, in the earlier stage when we wish to sustain heart action until compensation is established by a physiologic hypertrophy, I question whether the drug can be limited to its first effect until compensation is established; and in the later stage, when compensation fails and the heart is already depressed and exhausted, digitalis is evidently contraindicated. Digitalis is, to say the least, a remedy of transient benefit in mitral regurgitation and may be positively harmful in its ultimate results. But this is the most favorable standpoint from which to consider the drug. In fatty change in the heart walls, the stronger contraction of the heart in systole on the contained blood results in a muscular strain, thus increasing the dangers of rupture of the cardiac wall.

In the threatened heart failure of typhoid fever, benefit must accrue from the exhibition of such an agent as can be continued long enough to tide the patient over the critical period. The heart muscle, as the result of long-continued high temperature and impaired nutrition, is in a condition of granular, degenerative myocarditis. Any agent which stimulates the cardiac ganglia, inhibitory center or vagus under such conditions must be harmful to the patient in the highest degree; and when the exhaustive stage is reached, serious danger of fatal syncope may be expected as a legitimate consequence. Hence in fevers, septicemia and like affections, digitalis and all agents of similar physiologic action are positively contraindicated. Nor is this all: Careful observation has demonstrated that digitalis does not increase

pulse tension in pneumonia. It is suggested because of the febrile condition. But another patent fact must be considered, namely, that with the lesion in the lung—hepatization, most probably—the threatened heart failure is the result of exhaustion. The heart tires from an ineffectual effort to keep up the circulation through solidified lung, and the compensatory respiration carried on by the remaining or partially congested tissue does not aerate the blood rapidly enough to save the strain on the tired heart muscle. It is like lashing a foundered horse to force him to renewed exertion of which he is incapable.

Again, in mitral stenosis, benefit is to be expected from the exhibition of digitalis because prolonged diastole allows the ventricle to receive a larger quantity of blood. Its greatest field of usefulness is in lesions of the mitral and tricuspid valves, with their resulting secondary lesions. But in aortic stenosis, the forcible contraction of the ventricle during systole, with obstruction ahead of the column of blood, is risky, because rupture of the heart wall may result. Nor is the danger less in aortic insufficiency. Lengthened diastole permits overloading of the ventricle, and again danger from heart rupture is at the maximum. I believe that it is commonly routine practice to prescribe digitalis or kindred remedies when valvular lesions are detected, without making a discriminating diagnosis, and this ought not to be.

Convallaria.—In its action this drug is similar to digitalis and it is used under similar therapeutic indications. A fact of some importance is that it may be used as supplemental to digitalis. Its advantages over the latter are: 1. It is more strictly limited to the heart. 2. It does not prolong the diastole to the same extent, but slows cardiac action while augmenting the force of ventricular contraction. 3. It is probably free from the danger of cumulative action, and therefore may be given for a longer period. 4. It is probably better borne by the stomach, though the experience of observers differs in this respect. 5. Its diuretic action is not so distinct as digitalis. 6. It is of value in correcting cardiac rhythm. It must, however, be acknowledged that it is not so strong or reliable as digitalis.¹

Sparteïn.—This is a true stimulant to the muscular substance of the heart, acting through the cardiac ganglia, and in my hands has been valuable, when the heart walls were flabby and weak. It has been recommended as a heart stimulant in anesthesia.² Sparteïn, too, has the advantage of being slowly eliminated.

Strophanthus.—There is diversity of opinion among observers as to the true physiologic action of strophanthus; some claiming that its effect is less permanent than that of digitalis. If it be given in combination with strychnin, this objection is obviated, and it possesses the advantage of acting on the heart muscle and muscular coat of the blood-vessels, thus avoiding the reaction which comes from exhaustion of the vagus when digitalis is used. I am not, however, prepared to admit, as the result of my observation, that its action is less permanent than digitalis. After compensation has failed, stimulation of the tired heart muscle by strophanthus, while the vagus is still active, is of considerable value. In the threatened heart failure of typhoid fever and the

1. Westbrooke: *Foster's Practical Therapeutics*.

2. Cotton, G. C.: *N. Y. Med. Jour.*, Nov. 26, 1896. *Foster's Practical Therapeutics*.

septicemias, given with strychnia, it will be found a very useful agent.

Atropin.—Its physiologic action is to stimulate the cardiac sympathetic, the accelerator apparatus of the heart, producing increased frequency and increased tension and at the same time to lessen the inhibitory apparatus. It must not be pushed to the point of exhaustion. Its greatest usefulness is in tiding the patient over an emergency, in cases of sudden collapse and threatened heart failure. Some of the cases of flabby, fatty heart, especially those in which we have bronchorrhea as a sequence of the impaired action of the heart, and in which also there is risk to the patient from threatened stoppage of the heart, and from interference with respiration by the flooding of the bronchial tubes with mucus, are peculiarly benefited by atropin because it deals with both these conditions. A respiratory stimulant as well as a cardiac, it strengthens respiration and stops the effusion of mucus by its drying effect on the bronchial mucous membrane. I think, however, it is always important that it should be combined with strychnin. Potter recommends its use hypodermically in threatened heart failure from chloroform narcosis.³

Caffein.—Caffein stimulates and then depresses the cardiac ganglia as well as the cardiac muscle. Its chief field of usefulness is in functional heart affections, or as an adjuvant in those cases of organic heart trouble in which the function of the kidneys needs to be stimulated, to get rid of dropsical effusion. It is not curative in this instance but adds much to the comfort of the patient and aids in prolonging life. I have found caffein, when given in combination with benzoate of lithium and sulphate of spartein, especially useful in the dropsical conditions of parenchymatous nephritis, associated with secondary heart involvement.

Strychnia.—Close clinical observation has constantly increased my confidence in this agent, and demonstrated its reliability for definite results. Not the least part of its adaptability as a heart tonic is that, like other bitters, it is a stomachic tonic also, strengthening digestion and improving assimilation and nutrition. "It stimulates the motor nerve cells of the spinal cord, the cardiac motor ganglia, the respiratory and vasomotor centers in the medulla, and the sensory nerves and their terminal elements. The result is that respiration is deepened and quickened, the action of the heart is increased and the blood-pressure raised."⁴ In the enfeebled heart action from chloroform narcosis, it is a valuable remedy, and it has become almost routine practice with me to precede the administration of chloroform by giving, hypodermically, 1/30 to 1/20 gr. of nitrate of strychnia. Its value, administered as a safeguard, will be appreciated, when we remember that death from chloroform is due to paralysis of respiration, or paralysis of the heart, or to the two combined plus the shock of operation. Strychnia directly antagonizes these conditions. In the enfeebled heart of typhoid fever, the septicemias and pneumonia, or in the syncope due to heart failure I know no remedy so potent and prompt to sustain heart action. In functional reflex cardiac disturbance, weakened irregular heart action, the cardiac disturbances of the climacteric complicated by exhausting hemorrhage; in the weakened heart action in the later stage of Bright's disease, after compensation has

failed and arterial tension has given way, resulting in an ischemic condition of the blood-vessels; strychnin in all these conditions fortifies heart action. The superiority it has over digitalis and other heart tonics of its class is demonstrated by the fact that there is no cumulative depressant second or third stage. Nor will its ability be disappointing in organic valvular lesions of the heart when the heart muscle needs support in the performance of its function. The fact that it may be pushed for a longer time and gives satisfactory and definite results places it at the head of heart tonics.

Nitroglycerin.—We hear this agent spoken of, and see it mentioned in many articles of current medical literature, as a heart tonic. Experiment has demonstrated that it produces death by general paralysis, especially of the muscular system; and autopsy shows the ventricles of the heart unequally dilated, the right more so, and the venous system engorged with blood. It lowers arterial tension, and in an engorged right heart is useful, combined with strychnia. Physiologically we have languor, nausea, rapid, weak, dicrotic pulse. It also impairs muscular contractility. Its most beneficial action is found in angina pectoris, both true and pseudo. I am persuaded that its use is contraindicated in the weak and impaired heart of typhoid fever, septicemia, and surgical shock. No agent can be safely administered to sustain heart action, and avert death from heart failure whose physiologic action is known to be first, depression of the medullary center, consequent threatened paralysis of respiration and marked paralysis of the muscular system.

Opium.—In conclusion, I would say a word on opium as a reliable heart tonic. The clinical significance of its beneficial action on the weak heart I have seen repeatedly exemplified. When, after a long continuance of typhoid fever, the stage of coma vigil, vasomotor paresis, general, but especially marked in the accumulation of gas in the intestines; feeble, dicrotic pulse; dusky hue of the cutaneous surface, especially the face; in fine, that clinical picture so familiar to us all, and indicative of the great jeopardy of the patient, opium in a commanding dose, repeated in a few hours if necessary, has changed the whole aspect of the case, and proved the pivot on which the case has turned to a prompt and sure convalescence.

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DISCUSSION.

DR. W. D. GARLOCK, New York City, said that there is one point which is frequently overlooked in the treatment of weak heart, i. e., the state of the blood. We have a mechanical problem of an engine—the heart—driving a weight of blood through the blood-vessels. If the blood is poor, the required quantity of the blood is increased, and the weight being thus increased, more work is thrown on the heart. If we, by appropriate treatment, improve the quality of the blood, we to that extent reduce the labor of the heart, for the tissues will not demand so much blood for their nutrition.

DR. REILLY, New York City, asked if the reader had an opinion to communicate as to the value of *cactus grandiflora* as a heart tonic?

DR. J. N. UPSHUR said that his experience with *cactus grandiflora* had been very slight. He had used it, especially in one condition in which there was a condition of debility, a depressed condition of the heart, the result of excessive use of tobacco. In his part of the country he often sees cases of tobacco heart. He likened it to the fiddler who keeps constantly tightening up the string, until the string snaps. In the same way, the persistent overstimulation of the heart by the tobacco finally leads to heart failure. In the case of a prominent clergyman in Richmond, who did not respond well to strychnin, he had given *cactus*, but it did not give him as

3. Potter: Practical Therapeutics, p. 131.

4. Potter: Foster's Practical Therapeutics, p. 26.

much relief as it should and he finally got relief from strychnin in large doses. We see so many patients who are stimulated too much with tobacco, but none of them will admit that they are slaves to the habit. He has one challenge by which he can prove to them that they are taking too much and are under its stimulating effects. He challenges them to stop using tobacco, for a time, to see what an outcry there will be of the system against the stoppage, and the consequent gain in the pulse-beat after using the tobacco. If you take any machine and constantly drive it from one-third to one-half above its capacity it will break down. In the heart we have the same thing. There is a certain influence of the living tissue against the tobacco, but it will finally break down. The consequence is depressed action of the heart, and especially in young men, and particularly from excessive cigarette smoking. When such a person is taken sick with some serious illness, like pneumonia, then the heart tonics fail us, and they die of heart failure, when they should get well.

DR. J. T. MELVIN, Saguache, Colo., said that he had used cactus as supplementary to strychnin, but not as a substitute for it. His own experience is that the best results from cactus are obtained when the disturbance of the heart is functional. In all cases in which the disturbance is unconnected with organic disease, we have in cactus a useful agent. In digestive and genital disorders we often have reflex disturbance of the heart, also in tobacco and coffee habits. He gives, in such cases, the fluid extract in five-drop doses several times a day.

DR. LEONARD CORNING, New York City, said that he had used strychnin and found it beneficial on a smoker. The only objection is that when using strychnin he smokes twice as much.

DR. HEINRICH STERN, New York City, said that the author of the paper under discussion had omitted any reference to adonidin. In his investigations adonidin proved the very best and the most efficient of the so-called heart tonics we possess. Adonidin is not a mere succedaneum of digitalis. It is true, the physiologic action of both agents is identical to a certain degree. However—and this part he wished particularly to emphasize—adonidin, in spite of its more prompt and energetic action, may be safely administered in such cases where digitalis and the so-called other heart tonics can not be employed at all or only with the greatest caution; such, for example, as fatty degeneration of the heart, pericarditis, atheroma and heart lesions accompanying chronic cases of nephritis. He said he had never noticed a cumulative action of the drug, and in all instances in which he employed it, whether it was administered in the form of powders, tablets, pills or solution by the mouth, or in that of suppositories by the rectum, or by hypodermic injection, it was always well borne. The dose of the drug varies, according to the object desired, from .002 gm. to .01 gm. Those who are interested in the subject were referred to his original article, in *Merck's Archives*, April and May, 1900. He said, too, that adonidin deserves a place right on top of our list of heart remedies.

THE THERAPEUTIC APPLICATION OF THE ORGANIC EXTRACTS.*

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A few years ago we listened with interest, wonder, and often incredulity to a paper on organic extracts, but since that time we have heard so many papers and read so much on the use and abuse of these extracts, that one feels like apologizing for talking on this subject.

We can no longer treat of these internal secretions together, but each one now claims a separate discussion, and if you will bear with me I will try to present a few facts and thoughts concerning the thyroid, thymus, pituitary and suprarenal glands.

Though Schiff had experimented in 1859,¹ he did not impress upon the profession, the scientific value of his experiments on thyroidectomized dogs until 1884.² Horsley and other observers³ have confirmed Schiff's

work, and Halsted⁴ has shown the interesting fact that removal or injury of a portion of the thyroid can stimulate the rest of the gland to furnish secretion enough for the whole body. In 1878, Ord⁵ showed the relationship between the thyroid gland and myxedema. Horsley, in monkeys, and Reverdin,⁶ in man, described the symptoms of operative myxedema, while Kocher⁷ noted these symptoms of operative myxedema did not occur when the thyroid was removed in old age; a very interesting fact.

Schäfer⁸ describes the symptoms of operative myxedema as tremor, mental apathy, unsteadiness of gait, diminution of the cutaneous sensibility, lowering of the temperature, drying of the skin, falling out of the hair, and an increase of mucin in the connective tissue, especially of the skin. These symptoms known to be caused by the removal of the thyroid, are all exceedingly interesting when we realize that a diminished secretion of the thyroid in man can be the cause of similar symptoms and yet the diminution of secretion perhaps not be sufficient to cause an actual myxedema. It is also therapeutically noteworthy that all of these symptoms can be prevented in thyroidectomized animals and men by feeding thyroid extracts.

In 1895 Baumann discovered iodine in the thyroid, which has since been proved to be the only part of the human body in which the iodine is normally contained, and Weiss⁹ estimates that the adult thyroid contains .004 of this element, the amount varying at different times and in different localities and at different ages, the greatest amount being found between the ages of 25 and 55.¹⁰

The feeding of thyroid extract or Baumann's iodo-thyrin causes loss of weight and an increased nitrogen, sodium chlorid and phosphorus— P_2O_5 —excretion and marked diuresis.—Ross.¹¹ It is very probable that this diuretic action is due to the increased amount of urea excreted, although all of the nitrogen increase is not in urea formation.

Cyon,¹² finding vasodilator fibers in the thyroid nerves and that their stimulation lowers the pressure in the carotid arteries, infers that a function of the thyroid is to regulate the circulation and prevent hyperemia of the brain.

Oliver and Schäfer¹³ have shown that the thyroid contains a substance which will cause marked fall of the blood-pressure, and J. L. Smith¹⁴ says that thyroidectomized animals show abnormally rapid reaction to changes of temperature, in other words, show a disturbance of the heat-regulating mechanism. This latter is to me a very important fact when we consider the lack of development of the thyroid in the young child and the child's susceptibility to every change in the atmospheric temperature.

The thyroid also seems to be a regulator of connective-tissue formation, and the less the thyroid secretion in the adult, the greater the connective-tissue growth.

In partial support of the theory that it is the purpose of the thyroid gland to render innocuous certain toxic substances circulating in the blood, is the fact that the urine of animals after removal of the thyroid becomes more toxic than that of normal animals.

So much for thyroidal experiments, but unlike other drug investigations we have the pathology of the thyroid to aid us in formulating the therapeutic indications. In cretins this gland is either absent, very small, or cystic, and the colloid material, the representative of thyroid activity, is absent from most of the alveoli—de Coulon.¹⁵

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