

## ON THE ACTION OF TONICS.

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DURING the heat of summer many people feel limp and weak, and are disposed to sympathise, in imagination, with a collar which has just been washed, but not starched. They apply to their doctor for a tonic, take the medicine which he prescribes, and feel themselves much the better for it. There can be no doubt that the word "tonic" conveys a certain meaning both to doctor and patient, definite enough in one way, but very vague in another. Both understand that the tonic will increase the strength, and remove the weariness and languor, but how it does so probably neither has attempted to find out. On turning to Pereira we find that tonics are defined as agents which increase the tone of the system: but if we inquire further what is meant by tone, and what by the system, it will not be quite so easy to give a definite answer. Perhaps the easiest way of doing this is to take the want of tone, as we term it, for which tonics are administered, and to analyse the various symptoms which we find. First of all, then, there is a feeling of languor and disinclination to exertion, mental or bodily. The person may be roused by some excitement to make considerable exertions, but these are succeeded by a greater than usual feeling of fatigue; the appetite is generally diminished, the pulse is softer and more compressible than usual. Not unfrequently, too, there is less power than usual to resist the attack of disease. Want of tone, then, consists in diminished functional activity of the muscular, nervous, circulatory, and digestive systems, and a tonic is something which will increase this activity. Some tonics, however, act more on one system than another: and so we have vascular tonics, nervous tonics, and digestive tonics; as well as general tonics which seem to influence all the systems together. The functional activity of the body, and of the various organs which

compose it, depends upon the combustion which goes on in it and in them, and this combustion may be increased by increasing the nutriment, by quickening oxidation, or by removing more quickly than usual the products of waste, just as a fire may be made to burn more brightly by heaping on coal, by using the bellows, or by raking out the ashes. We may increase the functional activity of the body to a certain extent by increasing the food which a person takes, although there are limits to this, and an excessive quantity of food may prove injurious, just as one may smother a fire by heaping on too much fuel. The first class of tonics, gastric or digestive tonics, enable the patient to take more food, and with a greater relish. The most typical examples of this class are the so-called bitter tonics, such as calumba, quassia, gentian, cascarilla, and hops, either alone or in the form of bitter beer. In the mouth, these drugs produce a transient bitter taste, and increase the secretion of saliva. Thus they will tend to aid the digestion of starchy matters. In the stomach they cause a slight irritation, and the stomach, not having the same power of discriminating sensations that the mouth has, feels this, not as bitterness, but as appetite; unless the dose of the bitter should be too great, or too concentrated, and then it is felt as nausea, and is followed by vomiting. The appetite, however, which small doses excite, induces the patient to take more food, and to take it with greater relish. The increased relish is not to be disregarded. It would not be the same thing if the patient were simply to cram down, against his inclination, the same amount of food which he takes after his appetite has been excited by a tonic. We have not yet succeeded by pharmacological experiment in ascertaining precisely the effect of different emotions upon the stomach, but there can be little doubt that the pleasant feeling resulting from gratified appetite, aids digestion, while that of disgust and satiety interferes with it. Experiment has not shown that bitters increase the secretion of gastric juice in the same way that they do that of saliva, but they have an important action in lessening the tendency to putrefaction in the stomach. It is not impossible that in this way they prevent the formation during digestion of such substances as butyric acid, which is a direct nervous poison, and which, when absorbed into the circulation, would of itself tend to cause weakness and debility. It must not be forgotten that a man may be poisoned by substances formed in his own intestines, as well as by poisons taken into them by the mouth.

We all greatly dread the inhalation of sewer-gas into the lungs, but probably very few of us think that noxious gases formed in the stomach and intestines are readily absorbed by the blood, sometimes producing very serious results, and probably in many other cases leading to weakness and depression, the cause of which is never suspected. Experiment has shown that bitters, if they do not increase the secretion of gastric juice, at least tend to diminish the secretion of mucus, and lessen in this way, as well as by the antiseptic action just mentioned, the fermentation which mucus is apt to set up. It has been found by Köhler that even simple bitters in large doses will raise the blood-pressure by acting on the vaso-motor centre. It is doubtful whether they do so in the small doses usually administered or not, but there are other remedies—so-called vascular tonics—which combine this action to a considerable extent with one upon the stomach. Thus, infusion of digitalis does not greatly increase the secretion of saliva, nor produce a feeling of appetite in the stomach. It acts, after its absorption, upon the vaso-motor centre and upon the heart, rendering the cardiac pulsations slower, and more powerful by contracting the vessels, and thus making the pulse firmer and less compressible. This improvement in the circulation makes itself felt in every organ of the body. Thus the stomach is relieved of congestion, digests the food more easily, is less liable to secrete mucus, and is much less apt to be distended by flatulence. This is perhaps best marked in cases of mitral disease, where the venous congestion which accompanies such a condition often leads to an accumulation of flatus, sometimes termed by patients heart-wind. The pathology of this condition has not been precisely made out, but we must not forget that interchange of gases goes on between the blood in the capillaries of the stomach and the gas contained in its cavity in the same way, though to a much less extent, as between the blood in the capillaries of the lung and the air contained in the pulmonary alveoli. The action of another drug, very different from digitalis, namely, charcoal, upon flatus of the stomach, is very marked, and is usually ascribed in text-books to the power which the charcoal possesses of absorbing gas. But charcoal only does this when it is dry; it loses its power when moist, and it seems incredible that a teaspoonful of charcoal swallowed after a meal and mixed with the contents of the stomach, including perhaps a pint of beer, in addition to all the gastric juice, should, after being churned up with the food in the stomach, absorb so

much gas as to have any effect whatever upon the flatulent distention. It seems much more probable that its action is simply mechanical, and that by the small insoluble particles acting upon the mucous membrane, the circulation through it is so stimulated that the blood, flowing more rapidly through the vessels, absorbs and carries away a part at least of the accumulated gases. In respect, then, of its action upon the circulation in the stomach, charcoal may have some similarity to digitalis, but here the similarity ends. Charcoal has no action upon the heart. It cannot restore the balance of the circulation like digitalis, and it has none of the general effects upon the heart and vessels produced by the friction in the wet sheet so well described by Dr. Winternitz.

The improved circulation produced by vascular tonics makes itself felt in the liver and intestines as well as in the stomach. The yellow tinge, indicating biliary congestion, will disappear from the eye, and hæmorrhoidal engorgement will be lessened or removed. The brain and nervous centres, under the influence of a freer current of blood, act more readily and powerfully, thought comes with less effort, and exertion, both mental and bodily, can be continued for a much longer time, without any sense of fatigue. Two conditions also disappear, which, although apparently contradictory, afflict debilitated persons at the same time. These are drowsiness and sleeplessness. Frequently do we hear debilitated patients complain that they are so heavy for sleep that when sitting in their chairs or going about their work an irresistible drowsiness comes over them, and they fall asleep in the midst of an unfinished task, but when they lay their heads on the pillow and seek rest the conditions are at once reversed, drowsiness disappears, they toss about from side to side in the vain attempt to fall asleep, and perhaps it is not until they get up and walk about for a little that they are able to effect their purpose. Both of these conditions, apparently so dissimilar, depend upon the atonic condition of the vessels, so that instead of resisting the pressure of blood within them, they yield before it. In consequence of this the blood gravitates, while they are in an upright position, to the vessels of the abdomen and legs, leaving the brain anæmic and thus inducing sleep. On the other hand, when the horizontal position of the patient allows the blood to flow more easily to the head, the carotids and their branches, instead of contracting and keeping back the blood, allow it to circulate rapidly through the brain, and thus the unfortunate patient, unable to think at the time

when he wishes to, is plagued by a rapid and incessant flow of ideas at the very moment when he least desires them. By giving digitalis so as to excite the vaso-motor centre the vessels are made to contract moderately, they no longer yield to the pressure of the blood, and thus the blood is prevented from gravitating to the abdomen and lower limbs, and a free circulation through the brain enables it to discharge its functions satisfactorily, notwithstanding the force of gravity which in the upright position always tends to make it anæmic. Again, when the patient retires to rest, the blood, which tends in a horizontal posture to rush towards the brain, is checked in its course by the carotids and their branches, which under the influence of the vaso-motor centre, stimulated by the vascular tonic, contract and regulate the cerebral circulation so as to allow only sufficient blood to pass to the brain for the purpose of nutrition, but not enough for functional activity.

It seems highly probable that a similar action is exerted upon the vessels of the spinal cord, and that thus the patient feels increased muscular power and is equal to more prolonged exertion.<sup>1</sup> But this is not all, for the subcutaneous cellular tissue, and probably also the muscles themselves, are also benefited by the improved circulation. In the case of the subcutaneous tissue, the improvement is visible and palpable, as it is also in the muscles, though perhaps rather less plainly. In persons suffering from debility, even although there be no cardiac disorder, we find the feet swollen at night, so that the patients complain of their boots being too tight, and the ankles may be seen to pit upon pressure. Under the action of vascular tonics this condition will disappear, the ankles no longer swell, and deep and continuous pressure produces little or no mark upon the skin. The muscles, too, which were previously soft and flabby, seem to undergo a similar change, and become firmer, harder, and more elastic. The mode in which this is effected seems to be twofold—less fluid is poured out from the vessels into the tissues, and more is absorbed from the tissues into them. Thus, instead of plasma stagnating in the intercellular places of the muscles and connective tissue, a brisk circulation is kept up, by which fresh oxygen is

<sup>1</sup> For a fuller explanation of the *modus operandi* of contraction of vessels in the cord in increasing muscular strength, we may refer to a paper on the curative effects of mild and continued counter-irritation of the back in cases of general nervous debility and in certain cases of spinal irritation, by Arthur Gamgee, M.D., F.R.S., in the *Practitioner*, vol. xviii. p. 113.

supplied, and the products of waste are removed. The tissues are thus put into the most favourable condition for performing their functions, for, as we have already stated, functional activity depends upon the rapidity of combustion which goes on within the tissues or organs. It is quite possible to paralyse a muscle by stopping the supply of blood to it, and thus preventing it from obtaining oxygen, but it is still easier to paralyse the muscle by allowing the products of its own waste to accumulate within it. The easiest way to stop combustion in the muscle is, so to speak, to smother it in its own ash. It has been shown by Kronecker that if we remove the products of waste from a muscle which has been kept in a state of tetanus until it refuses to contract any longer, we can restore its contractile power even although we supply no fresh oxygen to it. In all probability it is the accumulation of the products of waste in the muscles in debilitated persons, which is, to some extent at least, the cause of the languor which they feel. That such is the fact, is, I think, shown by the feeling of comfort which they experience when the legs are gently shampooed, the pressure being always exerted upwards so as to favour the return of the fluids from the tissues. Such a procedure tends to give a lightness and corkiness to the limbs, which can hardly be attributed to any change in the nervous system generally, but must rather be ascribed to the removal from the muscles of those waste products which were partially paralysing them.

In talking of the nervous system, of the brain, and of the spinal cord, we have not taken into account this action of vascular tonics increasing combustion and removing waste from the nervous tissue, but probably, although we cannot see it so readily as in the connective tissue and muscles, the same process goes on in the nervous centres, and has much to do with the beneficial action of tonic remedies. I have stated that the action of tonics upon the intercellular fluid in the tissues is probably twofold—that they prevent excessive exudation from the vessels at the same time that they produce increased absorption. The reasons for believing that they lessen the exudation of fluid from the vessels are derived from a consideration of the pathology of œdema as made out by Ranvier. The first experiments upon the subject of œdema were made by Lower, who, in 1680, tied the vena cava, and found that œdema appeared in the lower extremities. A similar condition was noticed by Bouillaud in patients suffering from thrombosis of the iliac veins, and thus it appeared clear that the occurrence of

œdema was due to the absorption of the intercellular fluid being prevented by venous congestion. Lower's experiments, however, were repeated by Valsalva, Hewson, and others, without producing œdema, and the cause of its production therefore remained obscure. It was reserved for Ranvier to clear up this question, and to show that the occurrence of œdema usually depended upon increased exudation from the vessels as well as diminished absorption by the veins. He tied the vena cava in the abdomen of a dog, and found, like Valsalva, that œdema did not come on. The quantity of fluid exuding from the arteries was so small that the lymphatics were able to absorb it without any assistance from the veins, and thus it did not accumulate in the tissues, but on cutting the sciatic nerve on one side, intense œdema occurred in the corresponding leg. Venous congestion was equally present in both legs as the vena cava itself had been tied, but in one the nervous influence proceeding to the arteries through the sciatic nerve kept them contracted and prevented the exudation of more fluid than the lymphatics could absorb. In the other leg, however, where the nerve had been paralysed by a division, the vessels dilated, the limb became rosy and warm, and so much fluid was poured out that the lymphatics alone could not absorb it without the aid of the veins. Ranvier next proved that this dilatation of the arteries was due to paralysis of the vaso-motor and not of the motor fibres contained in the sciatic, by cutting, in different experiments, the motor and the vaso-motor nerves in the lumbar region before they had united to form the nervous trunk. When the motor strands were divided, as they issued from the lumbar vertebræ before they had been joined by the sympathetic fibres, complete paralysis of the leg was produced but no œdema occurred; but if, on the other hand, he divided the sympathetic fibres, passing to the sacral plexus, there was no motor paralysis—the animal could still use its limb, but the vessels dilated and œdema occurred.

These experiments show pretty conclusively that dilatation of the vessels by paralysis of the vaso-motor nerves is one factor in the production of œdema. In them, of course, we see in an exaggerated condition the same phenomena which are observed in cases of debility, because in these experiments the vaso-motor nerves were completely paralysed, whereas in our patients they are simply weakened. We may sometimes see very clearly in persons whose vascular system is deficient in tone, the effect of dilated vessels in causing œdema even when there is no great

obstruction to the return of blood. Such persons, when walking about in a warm day, with their arms hanging by their sides, sometimes find their hands become so swollen that they can hardly close their fists. The combined effect of heat and exercise upon their already debilitated vascular system, aided by the effect of gravitation, has caused so much fluid to escape into the tissues of their hands, that the veins and lymphatics are together unable to absorb it, and thus the fingers become swollen. The absorption of fluid from the tissues is, like its exudation into them, greatly controlled by the central nervous system. This is shown by some experiments of Goltz and Nasse. The former found that when a fluid was injected under the skin of the back of a frog, it was rapidly absorbed so long as the brain and spinal cord were uninjured, but when they were destroyed, little or no absorption took place. As the ordinary action of the nerve-centres causes absorption to go on, we would naturally expect that any increase in their activity would quicken the absorptive process, and this indeed was actually shown by Nasse to occur. It is well known that irritation of a sensory nerve stimulates the vaso-motor centre reflexly, and causes the vessels to contract. But, in addition to this action, Nasse found that irritation of a sensory nerve also caused increased absorption. It has not yet, so far as I know, been proved experimentally that such a drug as digitalis, which undoubtedly stimulates the vaso-motor centres, has a similar action to stimulation of that centre by irritation of a sensory nerve. Some time ago I made a few experiments upon this subject, but from imperfect graduation of the dose, the results I obtained were unsatisfactory, as the heart was too much affected by the drug, and the circulation became entirely arrested. There seems, however, no reason to believe that direct stimulation of the vaso-motor centre by digitalis will have a different action from its reflex stimulation through a sensory nerve, and we may therefore, I think, confidently assume that vascular tonics like digitalis increase the absorption of fluid from the tissues. They will thus remove the products of waste, and by keeping up a constant circulation of fresh intercellular fluid will assist combustion and functional activity in the tissues.

Another most valuable tonic, strychnia, has an action even more widely extended over the body than digitalis. It is at once a gastric, vascular, and nervous tonic. It aids digestion like other simple bitters in the way already described. It has, with the

exception of quinine, a more powerful action than most other bitters in preventing putrefaction. It excites the sensibility of the vaso-motor centre, thus exerting a beneficial effect upon the circulation, and likewise directly stimulates the nervous tissue of the spinal cord itself. So great is its effect upon the vaso-motor centre that by its means physiologists have discovered that instead of being confined to the medulla oblongata, as was formerly imagined, this centre extends down the spinal cord. It has just been said that an impression made upon the sensory nerves, reflexly stimulates the vaso-motor centre, contracting the vessels and raising the blood-pressure, but when a cut is made across the spinal cord just below the medulla oblongata this result is not produced. From this experiment it has been concluded that the vaso-motor centre was entirely confined to the medulla oblongata above the place of section; but if a little strychnia be now injected into the veins of an animal in which the cord has been thus divided, and a sensory nerve be then irritated, the vessels will contract and the pressure of the blood will rise. It thus becomes evident that the vaso-motor centre extends down the cord from the medulla, although its spinal portion is so feebly developed that under ordinary circumstances it has no power to contract the vessels when reflexly excited by stimulation of the sensory nerve. But strychnia has the power to increase its excitability so much, that reflex stimulation in this way will produce through it a decided effect. Now when we consider that sensory impulses are proceeding every moment from the skin to the vaso-motor centre, we can readily perceive how a slight increase in susceptibility produced by strychnia will have a wonderful effect in raising the tone of the vessels, and aiding the circulation. The mode in which quinine acts is not so clear, but we know from observation, that it also, in small doses, renders the pulse stronger and less compressible.

We have now seen how tonics may increase the quantity of nutriment taken into the body generally, how by their action on the vessels they quicken the circulation of inter-cellular fluid in the tissues, and by thus aiding its oxidation, and removing the products of waste, they greatly increase the functional activity of the various organs of the body.

We have now to consider how they affect the removal of waste from the body generally. The inter-cellular fluid in which these products are contained is absorbed into the general circulation

by the veins and lymphatics. Unless some provision were made for its removal, it would soon accumulate in the blood and arrest the functional activity of the various tissues, beginning with the most susceptible of all, the nervous tissue, and causing death. But these substances in all probability undergo further oxidation in the blood after their absorption and before they are finally excreted. This oxidation will be assisted if the respiratory movements by which oxygen is taken into the lungs are rendered deeper and more frequent, and also if the blood itself should acquire greater power to absorb this oxygen. Now strychnia has an action upon the respiratory centre in the medulla oblongata similar to that which it exerts upon the vaso-motor centre, and under its action respiratory movements become both quicker and deeper. No such effect is produced on the medulla by such a tonic as iron, but under the influence of this remedy the blood corpuscles not only become greatly increased in number, as was shown by Dr. Gowers in a paper in the *Practitioner*, vol. xx. p. 1, but they also contain a greater amount of hæmoglobin. Oxygen is thus more rapidly carried from the lungs to the tissues, and the process of combustion can thus go on more readily, both in the tissues themselves and in the minute blood-vessels into which the products of waste have been absorbed.

The rise in blood-pressure which occurs under the influence of tonics not only affords, as we have just seen, the most favourable conditions for oxidation in the tissues and for the removal of the products of waste from them, but it also assists in their elimination from the body itself. It has been shown by Ludwig and his scholars that the secretion of urine is, generally speaking, proportional to the pressure of blood in the renal glomeruli, and thus the pressure would rise along with the tension in the vascular system generally. The contraction of the vessels which tonics produce will therefore raise the tension in the kidney as well as in other parts of the body, and thus aid in the elimination of the products of waste.

From what has just been said, then, it would appear that strychnia or nux vomica is one of the most valuable tonics which we possess. When combined with nitro-hydro-chloric acid it is perhaps one of the most efficient remedies that we can give for the debility which is so often noticed in warm weather, and when the ordinary tonics, such as gentian, calumba, cascarilla, or quinine do not produce the desired results, the addition of a little nux vomica or strychnia to them may give us the wished-for effect.