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ON DIGITALIS: ITS MODE OF ACTION
AND ITS USE.*

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Shock.—In temporary conditions of paralysis of the sympathetic, agents which act as stimulators to this nerve are of great importance. Thus in shock, which Romberg calls paralysis of the sympathetic, the use of these agents is beneficial. Whatever may be the mode of action of external impressions, physical or psychical, that produce shock, whether in altering the molecular condition of the nerve-cells, or some other subtle action, certain it is that we have a small feeble pulse, coldness of the skin, cold breath, diminished temperature, and other evidences of the organic system of nerves being acutely depressed. In this condition, the heart-walls contract ineffectively, and do not respond to the stimulus of their contents; there is failure of the heart's action—a species of paresis. In this condition, general stimulants act well; but the question of special stimulants to the sympathetic ganglia has scarcely ever been broached. In one case of shock following parturition with twins (a common cause of shock), where there was the utmost danger of the patient's sinking, and the pulse was feeble, fluttering, and almost imperceptible, the administration of digitalis was followed by the most satisfactory results. It may be perhaps better to give the experience of some one else on so intricate a subject. Thus, in a case under Dr. Wilks (reported in the *Medical Times and Gazette*, January 16th, 1864), the patient was literally restored to life under its use. She was apparently in *articulo mortis*—her limbs were cold, her body in a state of deathly clammy sweat; the face was livid, no pulse could be felt at the wrist, and a mere fluttering was heard when the ear was placed over the region of the heart. Brandy and ether had been given without any good effect; and, as dissolution was every moment expected, it was determined to try digitalis. Half-drachm doses of the tincture were given every hour; after four doses a reaction took place, and after seven doses complete recovery occurred. The lividity of the face showed that the blood was lying in the venous system, and that it was not absent altogether. In this condition of shock, there is every reason to believe that the condition is one of passing paralysis, and that the condition of the heart is one of distension. Were digitalis a cardiac sedative, death in the two above related cases should have inevitably occurred. From the question of cardiac inability and unquestioned asthenia, we pass on to the condition of palpitation.

Palpitation.—Palpitation is more nearly allied to asthenia than we are in the habit of commonly thinking. Taught to regard it as over-action, we have come to associate it with excess of power; yet nothing can be more fallacious. Palpitation is a laborious evident effort, and reveals that the heart is over-taxed. It is over-taxation, not over-action with which palpitation is associated. We know perfectly well how palpitation is evoked by exertion in persons with structurally altered hearts. Here we know well that it is an accompaniment of effort; but the so-called nervous palpitation has been a troublesome stumbling block. Violent action of the heart, with a small and reduced pulse, suggested a tumultuous contradictory action of the muscular fasciculi as the only explanation of the condition admissible in the then existing state of knowledge. A condition of augmented cardiac action with no effect upon the radial pulse, was an anomaly, until advancing knowledge let us into the secret of vaso-motor alteration of the calibre of arteries. Then we began to see light shining through the darkness. Direct experiment then showed how augmented action of the heart followed certain irritation of the medulla oblongata when all nerve-communication with the heart was severed. (See Carpenter's *Human Physiology*, 7th Edition, p. 269.) It was found that alteration in the calibre of the arteries, by offering opposition to the flow of blood, caused laborious action of the heart, *i.e.*, palpitation. This action of the heart was not apparent in the arteries, because occasioned by a condition of them, which neutralised the effect of the increased action of the heart; or, more

correctly speaking, the heart's action was called out to neutralise the condition of the arteries. Thus without muscular effort, which necessitates augmented action of the heart, perceptible in the radial pulse, an evident laborious stroke of the heart may be evoked by a spasmodically contracted condition of the arteries and arterioles. Thus we have palpitation very common among the sufferers from chronic Bright's disease, in whom structural changes in the heart are most common. The diseased condition, according to Dr. George Johnson, is a thickened muscular tunic of the arterioles. The arterioles, by contraction, oppose the entrance of the blood, altered by excessive quantity of the products of retrograde tissue-metamorphosis. This contracted condition, when long continued, generates hypertrophy of the muscular tunic, and chronic opposition to the flow of blood, and then leads to changes in the heart-walls. Thus a species of balance is struck between the arterioles and the heart; cardiac compensatory hypertrophy endowing the sufferer with power to move and act; dilatation admitting a crippled existence only. Any unusual accumulation of the products of histolysis then evokes palpitation. That is, excess of the irritant provokes contraction of the hypertrophous muscular tunic, and that in its turn affects the heart; accumulating demands on it evoke laborious effort or palpitation, and this, too, more in the dilated than in simply hypertrophied conditions of the heart. Palpitation occurs commonly in such people, along with other evidences of an uremic condition of the blood. So, also, in the palpitation of jaundice, the arterioles, by contraction, oppose the entrance of the poisoned blood, and, by the obstruction thus offered, evoke palpitation. Further acquaintance with the finer processes of pathology are doing much to enlighten us as to cardiac (so-called) functional disorders. But it is the effort at compensation which is apparent, not the disordered condition, which is the real cause. Thus hypertrophy, the evidence of constant call on the heart, was at first thought the disease; now we know that it is a reparative proceeding. Palpitation, the evidence of over-taxation, will soon be relegated to its proper position as a symptom, not as a disease. A proper knowledge of palpitation can alone tell us what agents are likely to relieve it. It is evident, then, that the means of relieving palpitation will be found in the rank of agents, which increase the ventricular contraction. It is obvious that the obstruction of a constricted aortic orifice is analogous in its action to the contracted condition of the arteries. The agents which relieve one condition must act in the other. Thus the agents which have empirically been found to exercise the strongest influence over palpitation are found to be drugs—as digitalis, belladonna, caffeine, and others—which physiological experiment demonstrates to possess the power of increasing the ventricular contraction, and which clinical observation has shewn to be of service in other conditions of cardiac asthenia. Palpitation is intimately connected with ventricular engorgement, and the means of relief are only to be found in the list of agents which augment ventricular contraction. The strangling the heart's efforts by a direct sedative like prussic acid, or allaying them by a narcotic like morphia, does not militate against this view; the one is a lowering of all vitality till the heart is equal to its work, or the general lethargy produced by a narcotic; and so the most complete cessation of palpitation could be procurable by death. The means of relief of palpitation, which leave the general system unaffected, are those which enable the heart to act more efficiently; and of these, digitalis is the chief. The whole question of temporary failure of the heart's action is scarcely yet even *sub judice*. The subject is only a promising one, and one of the deepest interest and importance; but sufficient is known to be most encouraging, and only those, who have dived deepest into the recesses of therapeutics, can estimate the amount of good which may result from the prosecution of the inquiry. The conclusions given above are not supposed to be complete; but such as they are, they have appeared to me as the result of careful thought and investigation. Better results have certainly followed, and that, too, with a greater certainty since the foregoing conclusions have shaped themselves; and in venturing to recommend them to the notice of others, the writer must deprecate any idea of a wish to proselytise. The questions are questions of fact, not questions of opinion; and though to some readers the conclusions may appear somewhat startling, they are given in all good faith; and with a strong trust that trial will be favourable, and not unfavourable, and that therefore it is to be courted. The conclusions are laid open to the verdict of the profession with all humility. It would be vain, as it would be unprofitable, to hope that the conclusions will be wholly or universally accepted. But if personal success in treatment is to be a valid test, the writer could appeal triumphantly to his experience. But it is not to record the fortunate cases here that these conclusions are fairly stated, but in the hope that, by attracting attention to this wide but little explored field of therapeutics, future benefit to sufferers may accrue.

Contraindications.—It is necessary to review the circumstances which may modify our views as to the desirability of administering or with-

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holding digitalis. We have seen that it acts by producing contraction of the heart, and, to some extent, contraction of the capillaries (or arterioles and venules). It is obvious, then, that an increased arterial tension resulting therefrom will test the integrity of the structures intermediate—namely, the arteries. It is, then, of primary importance to ascertain and bear in mind the condition of the arterial system, and to conduct our treatment accordingly. Thus, atheroma or endoarteritis is commonly associated with cardiac complaints; and more especially with those manifestations of over-taxation for which the patient consults us. The primary consequence of atheroma is hypertrophy, which sooner or later yields to fatty degeneration, in the manner described in an early section. This exceedingly complicated condition is frequently presented to us, and increases the difficulty of adopting a treatment which secures the maximum of good, and the minimum of risk. Thus, whilst the increased action of the heart (the hypertrophy) supplements the inelastic condition of the arteries, and restores the balance of the circulation, it is in itself not without an alloy, for the atheroma is most marked at those points where there is the greatest pressure; and thus the increased action tests these weak points most severely. Thus in the thin-walled vessels at the base of the encephalon, we have often rupture. So in our treatment of cardiac debility with or without hypertrophy, we must be guarded and watch the effect of our remedies most narrowly. In the palpitation of hypertrophy, this is especially necessary. It is, however, possible with care to get at what is desired without any imminent risk, but small doses alone are admissible; and until the practitioner has familiarised himself with all the complex relations of this condition, and can wield his remedy with skill and confidence, it may be safer to resort to some other agent. It is within the limits of possibility to reach the honey and yet avoid the sting, but the attempt must only be made after careful calculations as to the force of the pulse, the state of the vessels, the amount of palpitation or irregularity, and a critical weighing of the different factors. The presence of atheroma to any extent is the contra-indication *par excellence* against the use of digitalis. In considering the conditions which contraindicate the use of digitalis, it is necessary to investigate the importance of fatty degeneration of the heart itself. Brunton has, from a consideration of the increased capillary opposition, warned us against its use in fatty degeneration; his objection is, however, only a theoretical one, though unquestionably rational. Reith and Gull have also made a similar objection, but on other grounds. It may, then, not be out of place here to investigate the subject critically. Firstly, the increased action of the muscular walls resulting from its use has always more than counterbalanced any capillary opposition; and the possibility of death resulting from the enfeebled heart being unable to act against the opposition so offered, may be questioned; it is only where the coronary arteries alone are the subject of disease that this could occur. In the usual condition of general atheroma, the contractility of the arterioles would also be impaired, and not respond to the stimulus of the drug. But of more serious moment is the question of partial or localised degeneration—that is, where some portion of the ventricles are more degenerate than others. This is beyond our diagnostic powers, and is therefore a purely speculative consideration. There is no question about the existence of this condition, which apparently depends on the greater or lesser amount of disease in the walls of the small nutrient arteries. It is obvious, then, that if we act on the muscular fibre remaining at all strongly, we must increase the pressure on the non-contractile degenerate portions. If we increase the centripetal action of certain portions of a hollow globe on fluid contents, we must increase the centrifugal pressure on the non-contracting portions. Thus if we produce an increased opposition to the flow of blood, and stimulate only certain portions of the ventricle, we must endanger the degenerate portions, *i.e.*, we must increase the risk of rupture through the thinned and degenerate portions of the wall. Thus the treatment may become a nice calculation of probabilities, guided by the lessons of the deadhouse. We must remember that there are numerous cases of cardiac asthenia for one of rupture through a degenerate portion of the ventricular wall; and that, as physicians, we have to obviate the tendency to death. It is being of no use to allow the patient to die of asthenia, from a hypothetical risk of rupturing a rotten section of the heart-wall. The probabilities must guide us. The variation between the sounder and more diseased parts can rarely be so great as to make this a practical danger. The difficulty of acting on the walls at all reduces even the possibility of the risk. This condition, too, is usually associated with advanced disease of the arteries; and thus we have the practical danger of rupturing them to estimate, as well as the hypothetical one of increased centripetal action of one acting section of a hollow sphere increasing the centrifugal pressure of the fluid contents on the non-acting sections.

As well as these contraindications which present themselves as pathological conditions modifying our views as to the desirability of ad-

ministering digitalis, there are others which present themselves as connected with the diagnostic indications, as, for instance, intermittency. The occurrence of intermittency during the administration of this agent has hitherto been deemed a valid contraindication; and certainly if we feel assured that it is the consequence of the drug, it is an evidence of its physiological effects being reached. Thus, if along with it we find the pulse becoming thready, the heart's action becoming a steady thud, a diminution in the bulk of urine, showing a lessened pressure on the glomeruli of the kidney, then it may be necessary to withdraw the digitalis. It may, however, not only be no contraindication to its use, but even be the strongest evidence of the need for its administration in increased quantity. Thus, where any obstacle is presented at all suddenly to the circulation, and digitalis is given, intermittency may come on as the result of the heart's inability, in spite of the stimulus to contraction to struggle against it; and the administration of the agent in increased quantity may be clearly indicated. This is no imaginary condition. Some months ago, the writer attended an old gentleman of ninety, suffering from an acute affection of the aortic orifice, accompanied by dropsy, orthopnoea, and feeble pulse. Digitalis was given by him as usual; and after a day or two the pulse commenced to intermit, and there was evident increasing circulatory debility. It was with great difficulty the scruples of the consulting surgeon could be overcome, and his permission gained to give the digitalis in double doses. After that, the pulse improved; the intermittency took its departure; the dropsy declined; the old gentleman could again lie down, after sitting in an arm-chair three weeks without intermission; the digitalis was continued, and the old gentleman was once more walking about in his garden. Thus we see that intermittency and the other evidences of cardiac debility coming on during the administration of digitalis may not only not be contraindications against its use, but may even be the strongest evidence in favour of the administration of it in increased quantities. The diagnosis as to whether the intermittency be due to the drug, or to the necessities of the patient being aggravated, would rest to a great extent on the conditions under which the drug was given. Thus, if it were given to allay the palpitation in hypertrophy, and in a healthy person, there would exist an *à priori* probability that it was due to the action of the drug; if digitalis were administered in great cardiac debility and growing obstruction, or obvious failure of the heart's action, the occurrence of intermittency may be the evidence of an imperative necessity for an increase in the dose. The occurrence of persistent vomiting, loss of appetite, noises in the head with flashes of light, or other symptoms of the system being fully under the action of the drug, or of some idiosyncrasy on the part of the patient, would suggest to us instinctively its withdrawal; and either the use of some similar agent, or its administration in some other form or combination. Thus patients who soon show an intolerance of digitalis if given on an empty stomach before food, tolerate it if given an hour or so after meals. The occurrence of attacks of syncope or other cardiac failure cannot be said to be any valid objection to its use; in fact, like intermittency, they may indicate the necessity for more of it. In some persons it is desirable certainly to give it along with diffusible stimulants. But failure of the heart under its use will be found to be the result of the affection, not the drug. Thus persons with fatty or otherwise degenerate hearts, where it is given, are subject to the attacks as the result of their ailments. "Such patients are liable to die suddenly, and will do so now and then whether digitalis be given or not." (Gull and Wilks, *Medical Times and Gazette*, July 1865.)

Antidotes.—Though digitalis-poisoning is no longer so common since a more accurate knowledge of its action has lent precision to its administration and its use, still cases might occur where, through misadventure or oversight, or perhaps some peculiar susceptibility in the patient, a condition of danger might arise from its administration. Such a condition must carefully be distinguished from attacks of cardiac syncope, the result of disease. If it were once ascertained that the danger was due to the drug, it would be necessary at once to stop its use; if it resulted from one huge dose producing acute poisoning, it might be advantageous to empty the stomach; in chronic poisoning, sickness is spontaneous. The use of agents must be resorted to which are known to paralyse the heart—for instance, aconite. In experiment on the frog, though aconite did act on the heart after the poisonous effects of digitalis had been induced, still its action was far from being so marked as when digitalis was given in aconite-poisoning. In digitalis-poisoning, aconite may be resorted to as an antidote. From the action of the Calabar bean, as described by Dr. T. R. Fraser, of Edinburgh, it is highly probable that it would act beneficially in the excessive action of digitalis. From the consideration of antidotes, it may not be out of place to consider the question of agents of similar action.

[To be continued.]