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

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Mitral Obstruction.—In mitral obstruction the same series of symptoms present themselves as in mitral regurgitation. The obstacle here is in the entry of the blood into the ventricle; the orifice being narrowed, it is necessary that the blood be poured in under greater pressure. The feeble but regular pulse tells how imperfectly the ventricle is distended in each diastole. There are the necessary changes in the right ventricle and pulmonic circulation, and a general thickening from the ventricular wall to the smallest vessels, which ensue from the natural conservation of the system; and as long as these compensatory changes are kept up fairly, the sufferer is scarcely conscious of his injury. But, sooner or later, the compensation either fails, or secondary diseases follow the lesion and its sequelæ. We can only take the natural indication of compensatory hypertrophy, and aid it, so far as in our power lies, by administering agents which assist the natural attempts made in the manner explained in a previous section. We must keep up the powers which are to drive the blood through the narrowed orifice, and that can only be attained through increasing the pressure by an increased *vis a tergo*. The changes in the lung when the pulmonic congestion has led to disease further obstruct the flow, and impede the action of the right ventricle. Death is approaching from failure of the right ventricle, and its action must be kept up at all hazards. Increased action in it leads to a freer circulation through the lungs, the asthenic congestion being the cause of the dyspnoea. We must obviate the tendency to death, and meet its approach by appropriate means; and in this valvular lesion it is failure of the right ventricle against which we have to guard.

Mitral Regurgitation.—In this valvular lesion, even more remarkably than in mitral constriction, we find changes due to overcharge of the pulmonic circulation. The blood is driven into the ventricle without obstruction, but part is forced back at each ventricular systole. This regurgitation overloads the blood-vessels behind, and the blood is forced into the ventricle on diastole under increased pressure; the consequence is, that the left ventricle is over-distended, and a certain enlargement of the ventricular cavity follows, usually accompanied by hypertrophy. This change in the left ventricle is always to be borne in mind, and not to be overlooked in the question of administering a drug which produces increased ventricular contraction. For it is obvious that, while we might increase the power of the right ventricle, if the left remained unaltered and the agent acted equally on it, as it does, all our increased power might be met by an unnatural contraction of the left, more than negating the good to be got from the increased activity of the right ventricle. If the left ventricle remained without change, the administration of the drug would certainly be decidedly contraindicated; the danger of over-contraction of the left ventricle would constitute a more serious danger than the one we wished, as in mitral obstruction, to relieve. But the increased pressure under which the blood is poured into the left ventricle from the distended auricle and veins behind it, more than counterbalances that risk. In fact, the action of the agent on the left ventricle, is equally beneficial to prevent its becoming over-distended and yielding before the increased centrifugal pressure of the blood driven into it under greater pressure from behind. In mitral regurgitation, the benefit to be derived from the administration of digitalis is as manifest as in any condition of cardiac disease. The mode of repair which we find to have been set up by the natural efforts of the system in persons in whom valvular lesion has been discovered by some chance, is a compensatory thickening of the muscular fibre of the right ventricle and the pulmonic vessels, and an increase of the capacity of the latter to withstand the stress upon them from the addition of the blood which regurgitates to that which is sent in from an enlarged and more powerful ventricle. The vessels, though consisting of tissue not readily taking on increased growth, change gradually to keep pace with the increase in the power of the right ventricle, and retain this hypertrophy even when the efforts of the right ventricle are waning. The failure of the right ventricle is again the avenue by which death is advancing; and

by increasing its efforts we increase the blood-pressure, and increase its opposition to the regurgitation, and thus more blood is thrown into the aorta at each ventricular systole, while increased arterial tension leads to better tissue-nutrition. Of course the condition of the vessels must be taken into consideration, as will be considered more at length under the head of contraindication. Even pulmonary congestion does not militate against the exhibition of digitalis in mitral insufficiency; in fact, usually it is much relieved by the increased action of the right ventricle. The effect of compensatory change, and, of course, of artificial aids to it, is much more obvious in mitral than in tricuspid insufficiency. The increased action of the right ventricle is not lost over the length of the pulmonic circulation, as in the increased action of the left ventricle in tricuspid regurgitation. In fact, in mitral regurgitation, we see most constantly the effect of conservative compensatory changes behind the lesion; and thus, of course, agents aiding in effecting that compensatory change are of the greatest value. It is clear, too, from the tendency of the left ventricle to yield to the increased centrifugal pressure of the blood driven in by the distended auricle and veins behind, that the stimulated contraction in it from the action of the drug does not constitute an objection to its use. It is only by observing what changes have gone on spontaneously in individuals suffering from mitral insufficiency, and yet capable of sustained exertions, and further observing how that compensation commences, that we can get a clear idea of what to attempt to achieve, and of the mode by which relief can be afforded. These indications we must carefully follow if we expect to give any therapeutic aid to the sufferer, either during the disturbance which follows the first appearance of the lesion, or when the compensatory change is failing.

Aortic Obstruction.—In aortic obstruction, a totally different change takes place from what goes on in mitral disease; and as long as the mitral valve remains perfect, the change is confined to the muscular walls of the left ventricle. It is a simple question of increased power; and as the contracting action of interstitial inflammation of the valves and orifice is very gradual, the muscular change can keep pace with the changes. Thus we see in aortic obstruction usually a simply hypertrophied left ventricle. There is not dilatation, because there is no increase in the centrifugal pressure of the blood poured into the ventricular chamber. A natural increase in the muscular power allows an equal quantity of blood to be driven through the orifice, now narrowed, in an equal time; there is no disturbance of balance; the hypertrophy here is most commonly perfectly compensatory, and the compensation lasts longest. The existence of aortic obstruction is most frequently discovered casually, and not by any heart-symptoms on the part of the patient. In conditions of failure of the ventricle, from general debility or atheroma of the aorta interfering with the propulsion of the blood into the coronary vessels, and consequent imperfect nutrition, increased ventricular contraction at once relieves the patient, and tends to produce a comparatively permanent improvement. My reasons for regarding the improvement following the use of digitalis in this affection to consist in increase in the driving power, rather than in slowness of the ventricular contraction, as stated by Sir Dominic Corrigan, have been given above, and need not be repeated. It may not be out of place to add here that hypertrophy is the mode of repair adopted by the efforts of nature, and not any reduction of the number or the rapidity of the contractions. Reilef, too, follows the use of digitalis when there is no appreciable retardation of the pulse. As to the question, it is merely one of time or power, and the latter is evidently the correct explanation. The effect of digitalis would depend largely on the condition of the muscular fibre. If there were only a passing disturbance, and the muscular fibre were fairly structurally sound, small doses alone would be required; if the hypertrophy were passing into degeneration, much larger doses would be called for. In aortic obstruction, the therapeutic aid to be given is: very simple question; and increased ventricular contraction, however produced or attained, at once restores the disturbed equilibrium and gives relief.

Aortic Regurgitation.—In aortic regurgitation, however, it may be made a matter of great question how far any interference can be beneficially available. In this affection, we meet with the true *co. bovinum*, an excessive enlargement of the left ventricle, both in thickness and cubic space and cavity. The regurgitation through the aortic valves produces increased and sustained contraction of the ventricle. The backward flow on the arterial recoil is no longer caught and arrested by the semilunar valves, but falls on the fundus of the ventricle, and thus normal contraction is prolonged into sustained contraction. On the diastole, however, the blood flows through the insufficient semilunar valves, as well as through the mitral valve; the quantity regurgitating being added to the normal amount from the auricle, and then the centrifugal pressure is increased and dilatation follows. At the same time a great increase of the muscular walls follows the increased necessi-

* Continued from page 89 of last number.

for contraction. There is not here simple dilatation, for the ventricle can empty itself without impediment, and the sustained contraction calls out more muscular effort. Between the two forces of increased distension and increased and sustained contraction, the ventricle becomes both enlarged and thickened. But the increased volume of blood thrown at each ventricular systole into the aorta, and over-distending it, leads sooner or later to endo-arteritis; the aorta is not only enlarged, but its walls become diseased and lose their elasticity; thus goes one element in the propulsion of blood in the coronary arteries. At the same time, the regurgitation takes off from the arterial recoil, as is well seen in a sphygmograph tracing, and the recoil no longer fills the coronary arteries, but is lost in the regurgitation; this adds further to the diminished flow through the coronary arteries. Sooner or later, the hypertrophy passes into degeneration, and the muscular walls lose their structural integrity, and with it their compensatory usefulness. The more diseased and less elastic the aorta, the more defective becomes the coronary circulation, and the tissue-nutrition connected with it. It would be difficult, then, to move in this complicated condition without finding the risks increased in strict proportion to any benefit that might accrue. Increased ventricular action might produce increased tension, and consequent better heart-nutrition; but then there is the increased danger of rupturing the diseased arterial coats. The benefit is not without alloy; and it may be made a matter of question how far we can safely interfere at all. Each case must stand on its own peculiarities, and the treatment be adapted to the patient's special requirements; but digitalis can rarely be indicated. In the earlier stages it is contradicted by the hypertrophy and sustained contraction. Its administration is hazardous; and the risk of driving the ventricle into a contraction which may never be relaxed, and of bringing the heart to a standstill in systole, is greater than any risk accruing from inefficient contraction; in fact, in this lesion the hypertrophy is usually so extreme as to need no abetting.

Disease of the Right Side.—The effect of disease of the right side, as regards the muscular walls, has been considered above. In valvular disease of the right side, we do not know any peculiarities connected with the pulmonary orifice: disease here is rare, and the same indications and contra-indications would not exist as in aortic disease. It is widely different in the affections of the right auriculo-ventricular valves.

Tricuspid Regurgitation.—In tricuspid regurgitation, repair is almost forbidden by the anatomical arrangement of the parts. There is no possibility of compensatory change, at a little distance behind, coming to the rescue and backing up the insufficiency, as in mitral disease. The tricuspid is far removed from any force which could in any way make up for its deficiencies. As to the theory of the tricuspid being naturally and normally imperfect, and admitting regurgitation on any distension of the right ventricle or obstruction before it, or what was called "safety valve" action, it is now generally abandoned. It would, if it existed, militate strongly against any compensatory change in the right ventricle, which never takes place without some enlargement of the cavity of the ventricle. It would be a most common thing to find jugular pulsation, cyanosis, dropsy, etc., on any stress falling on the right ventricle, which we know only to occur when the tricuspid has become incompetent. These evidences of tricuspid incompetence are of portentous moment, and are the ordinary harbingers of serious danger to the organism, and only too commonly of approaching dissolution. If the "safety valve" theory were a correct one, they should follow inevitably in any pulmonary affection which might try the right ventricle. Instead of that, their appearance during a chronic cardiac affection is usually the precursor of death: showing that the last anchor, the tricuspid valve, has given way. It occasionally happens that a lesion in the tricuspid occurs as a primary affection. The progress of the case is rapid and downward; the venous engorgement and its concomitants are present at the first, and not at the last of the case. Dropsy sets in while there may be a fair amount of vigour, and the patient going about. There is a rapidly accumulating coma from the venous congestion of the encephalon; there is asthenic congestion of the lung; there is engorgement of the liver and kidney, and from it, again, uræmia. The patient's troubles come upon him in quick succession, and the last change is not long delayed. All art seems useless; there is no ventricle at a little distance behind, to back up the lesion, and no compensatory change can be organised. The administration of digitalis is apparently of no benefit whatever; the increased action of the left ventricle is too far distant to be of any avail. The action seems lost over the length of the systemic circulation, and in the dilatability of the veins. This is the only action available. Purgation may relieve the venous engorgement; but

nothing can compensate the lesion. The prospect is hopeless; and though we may try to be of service to the patient, it is with a painful consciousness of the futility of our efforts. The free use of digitalis was of no apparent use in a case where it was given unsparingly enough, in order to ascertain if any good could accrue from its empirical use; though reason could advance nothing in its favour. When the tricuspid fails in chronic cardiac disease, the patient's prognosis is hopeless, and relief of some of the most urgent symptoms is all that we can hope for.

Tricuspid Obstruction.—The existence of this affection is questioned, so rare is it; but that is no proof of the impossibility of its occurrence. When it does occur, digitalis and all other cardiac neurotics would be useless, for the same reasons as in tricuspid insufficiency.

In all valvular affections, digitalis is useful or useless entirely as it is possible to produce conservative compensatory changes in the muscular walls. In disease of the left side, by following the indications thrown out by spontaneous accessory growth, we may be of the greatest service in either aiding the production of the compensatory change, or assisting in its continuation when beginning to fail.

Degeneration of the Walls.—This was once considered to negative any recourse to digitalis, when it was regarded as a cardiac sedative; and this was quite consistent. Our modern acquaintance with its action tells us, that in degeneration we may resort to it without alarm, and not only that, but with confidence. In degeneration of muscular fibre, no action can affect those fibrillæ which are converted into fat-globules; any action must affect the sound fibrillæ only. It is obvious, then, that digitalis may, by stimulating the sound fibres, produce not only relief to the general symptoms, but may even aid in somewhat improving the structural condition. Of course this will depend to a great extent on the causation of the degeneration. If it be connected with atheroma of the aorta, and thus a preservative lesion consequent on that atheroma—if the degeneration arise from impeded circulation through the coronary arteries from loss of arterial recoil, due to the loss of arterial elasticity, then the administration of digitalis will, while obviating one risk, increase another. But, if it be due to other causes, as pericardial adhesion along the track of the coronaries, then digitalis will assist us in our efforts to bring about improved tissue-nutrition, by improved ventricular action. The degenerate walls yield to centrifugal pressure, and do not contract completely, and dilatation follows. Then digitalis will be useful, as described in an early section; and the condition of the muscular fibres will not affect the treatment, except in so far as it diminishes the prospect of success. The possibility of effect on the capillaries, and of their contraction offering an opposition to the flow of blood, is put forth by Brunton as an objection to its use. But this is practically no objection to the use of digitalis, as clinical observation has convinced me. The increased action of the heart more than counterbalances the capillary contraction. Thus in a frog, when a watery infusion of digitalis was applied to the web of the foot, the contraction following almost completely arrested the circulation through the part. The administration of digitalis by the mouth restored the circulation. If, then, the increased action of the heart was visibly efficacious where the infusion, applied locally, produced contraction of the vessels, and the increased ventricular action was apparent in so small a section of the circulation, the fear of any stress thrown on the heart by capillary contraction, affecting its power to contract, must be a hypothetical one only. The frequent administration of the drug in liberal quantities has never yet in my experience been followed by any untoward result.

Angina Pectoris.—In angina pectoris, the use of digitalis is novel. Fuller, from his conviction of the tonic action of digitalis, proposes its employment in angina, but gives no experience of his own, merely suggesting its use. Many views exist as to the nature of angina pectoris, as to whether it occurs in healthy hearts and is merely neural, a hyperæsthesia of the cardiac plexus (according to Romberg), or one of the most important symptoms of muscular degeneration, being in fact pathognomonic of it; hence this is a very difficult subject to approach in the direction of therapeutics. In true angina pectoris, certainly not mere cardiac asthma, occurring in a patient where there was strong reason to regard it as in its nature neural, and where the attack was usually produced by passion, lasting two or three hours, and little if anything relieved by diffusible stimulants, as ammonia, chloric ether, etc., the addition of thirty minims of tincture of digitalis, repeated at the end of half an hour, gave great relief; and so different was the result of the treatment when the digitalis was added, that there could be little or no doubt of the connexion being consequential. Further use of it in these attacks in the same person corroborated that belief. The next case which occurred was in a patient where there was strong reason to suspect the existence of fatty degeneration. In a paroxysm of angina, encouraged by the success in the other case, I gave

* For an able investigation of this subject, see T. W. King's article in *Guy's Hospital Reports* for 1837.

digitalis with very satisfactory results. Of course, the question of a rational conception of its action is difficult in the presence of so many various views as to its pathology; the old idea of spasm is now giving way to an idea that it is arrested, or nearly arrested, ventricular contraction, which is the real state of the matter. There are those who believe that angina pectoris is connected with spasm of the coronary vessels, or with bony plates in the sinuses of Valsalva getting across the mouths of the coronary arteries and obstructing them, or, rather, the circulation through them. Certain, however, it is, that whatever the exact neurosal condition may be found to be, or even if angina may arise from temporary action not neurosal, it is commonly associated with hearts that give at other times evidences of impaired tissue-integrity. Whatever it may consist in, my experience in these two cases shows, firstly, that the administration of digitalis is not harmful, and, secondly, that there appears to be such benefit following its administration as to lead me to the conclusion that it exercises a remedial action over this condition.

Cardiac Asthma.—In cardiac asthma or false angina pectoris, where there is evident distension of the right ventricle accompanied by palpitation, dyspnoea, and lividity of the face, frequent use of digitalis has led me to a conviction that it is certainly our mainstay. I have learned in this condition to give it freely and fearlessly, with confidence, the result of experience; and I have not yet been disappointed. The stimulating action on the sympathetic cardiac ganglia, and the effect on the muscular fibres under their control, is just the exact action which it is imperatively necessary to rouse in order to overcome the train of accumulating evils, as pulmonary congestion, cyanosis, and carbonic acid poisoning, which wear out the patient's existence, if he do not die of the more rapidly acting blood-stasis. Theoretically, this is the action of digitalis as learnt from physiological experiment; clinical observation demonstrates the soundness of the view, and further indicates it as a valuable addition to our means of controlling a condition which always is one of imminent danger in itself, tending to cut off the organism suddenly, and which, when repeated or long continued, certainly produces secondary derangements and complications, as emphysema, dilatation of the right side of the heart, with further pulmonary congestion, more frequent and prolonged dyspnoea, œdema of the lung, and, in fact, a constantly widening vicious circle of troubles, which render the patient's last days an intolerable misery to him. The relief of this terrible, and by no means uncommon condition, lies in rousing the action of the distended right ventricle; and that this may be done without bringing the left ventricle to a standstill in systole, is certain. For an explanation of this apparent anomaly, see the section on mitral regurgitation.

Temporary Cardiac Conditions.—From cardiac asthma we may pass on to the consideration of passing or temporary cardiac conditions, and to the means of treating them. For instance, in failure of the right ventricle in fevers, and in pulmonary affections, in shock, in palpitation, we must first satisfy ourselves as to the condition before proceeding to treat it; it is on our knowledge of the exact pathological condition that the efficiency of our remedies must depend. The whole question is a comparatively new one, and is most important; no more important addition could be made to our stock of therapeutic knowledge than a proper insight into these conditions, and the means of acting on them. We will first take failure of the right ventricle in acute asthenic conditions, commonly called cardiac asthenia.

Cardiac Asthenia.—In this condition we find the pulse furnishing us with the precursory evidences of approaching death. We find the pulse mounting in number, and its strength in inverse proportion; after a while there is an occasional intermission or irregular beat; then the intermissions come more frequently, and in time in clusters; the breathing is hastened and rapid, even out of proportion to the pulse; and we all know that the patient is in imminent danger, and usually dying. Now, of what are these symptoms indications? For, on the diagnosis must rest our only rational expectation of being of real service to the patient. Well! what does the *post mortem* table say? Usually in these conditions the left ventricle and the arterial system are empty and contracted, the right ventricle and venous system turgid and distended with blood. This throws some light on the symptoms. The right ventricle has become distended and contracts inefficiently; the blood is not circulating freely through the lungs, they are asthenically congested, partly from vaso-motor paralysis, partly from an altered condition of the blood itself. The quantity of blood pouring into the left ventricle is only equal to imperfect distension. The ventricles ordinarily act synchronously, in consequence of a large number of fibres being common to both ventricles, describing a figure of 8; and the left must keep time with the right ventricle. Thus, as the distended right ventricle always full is acting inordinately fast, expelling a small quantity of the top of the ventricular contents, the left is contracting on its diminished contents; consequently, we have a small

arterial distension as felt at the radial pulse. It is clear that the more distended the right ventricle, and the more imperfect its contractions, the less blood flows into the left ventricle, and thus the rapidity and feebleness increase hand in hand. The symptoms are plain enough, and the fuller the venous system the emptier the arterial; the more distended the right ventricle, the more imperfectly filled is the left. The intermission is connected with the state of the right ventricle, not so much with any difficulty in the left. And long before the intermission in the radial pulse is apparent, an intermission can be felt on applying the ear over the heart; the intermission can be heard before the condition of the right ventricle so affects the left as to be felt in the radial pulse. This condition is common in acute asthenic disease as well as in diseases of the respiratory organs. In disease of the respiratory organs the engorgement on the right side is most readily apparent, but not so in acute asthenic disease. In bronchitis, for instance, the original obstruction is almost mechanical in its operation, but it soon leads to chemical alterations. These chemical alterations and their consequences are of the highest importance; and more especially in their bearing on the right ventricle. Both in disease of the respiratory organs and in acute asthenic conditions, we have an accumulation of carbonic acid in the blood. In respiratory affections the injured organs do not admit perfect oxygenation; in acute asthenic disease we have not only a well known tendency to acute asthenic congestion, hypostatic or other, but also an increase in the products of waste. We have thus the venous blood more than ordinarily laden with carbonic acid, an agent which has a direct effect in paralysing the heart when brought into contact with the endocardium. Thus Cyon so arranged a stream of serum made to flow through a heart, as to be able to add a quantity of carbonic acid or to withdraw it from the serum. When the carbonic acid was added, cardiac paralysis came on; when withdrawn, the cardiac contractions were resumed. For a short account of this most interesting and instructive experiment, the reader can consult the Sydenham Society's *Year-Book*, 1867-1868.

Here we see experiment corroborating what clinical experience had taught. The right ventricle, as being connected with the venous system, is also more distensible, and is commonly distended, as a matter of habit; every severe exertion or shortness of wind congests or distends the right ventricle. There is thus a readiness of distension about the right ventricle which allows the chemical agent to act effectively. Thus the blood, more and more laden with carbonic acid, acts on a ventricle becoming more and more distended, and tends still further to paralyse any power of contraction remaining; while increasing inability to contract leads to further and more imperfect oxygenation. Under this action and reaction, the condition is commonly followed by cessation of the ventricle and death. The frequency of this condition is such as to prompt our most active interest in it, and to strive earnestly after some means of acting upon it. The failure of the right ventricle is the door by which death enters; and it is our duty to obviate the tendency to death, by all means in our power. Even bleeding, on account of its temporary agency in relieving the distended ventricle has been advocated by no less an authority than Dr. B. W. Richardson. Stimulants have been largely resorted to; and in the treatment of typhoid pneumonia, where the condition is well-marked, Dr. Hughes Bennett has advocated them most warmly and perseveringly. The fact of the great and extreme danger of this condition has always been recognised; but it is only now, when the effect of agents on the heart is being investigated, that a ray of real light is illumining the question. This use of agents affecting the heart is of the greatest importance, and is one of the great questions of the future. The effect of digitalis on the right ventricle in acute distension of the right side in cardiac asthma has inspired me with hope in the treatment of this condition when arising in the course of acute affections. It is, however, a question of fact, not of theory. But a man slings no worse for having a target to aim at, and a rational comprehension of what we stand in need of, and of the exact action of the agents we employ, will assist us in our efforts. The practical success of these efforts can alone tell us unmistakably what is their real value. As in the treatment of chronic cardiac affections, no attempt is being made here to extol digitalis as possessing powers either unique or peculiar to itself. It is merely the most active and best known agent of this class as yet. In time we may find agents more powerful and rapid in their action, but at present we can get results from it that we cannot get from other agents.

[To be continued.]

ERRATA.—In the portion of the Essay which appeared in the JOURNAL of July 8, the following errors require correction. Page 27, column 2, twenty lines from bottom, for "sufficient", read "insufficient". Page 28, column 1, line 22 from bottom, for "palpitation", read "palpation". Page 28, column 2, line 36, read "inhibitory action of pneumogastric plus the vis inertia of the blood". Page 29, column 1, line 10, for "junction", read "function".