

Digitalis : its mode of action, and its use : an enquiry illustrating the effect of remedial agents over diseased conditions of the heart : the Hastings prize essay of the British Medical Association for 1870 / by J. Milner Fothergill.

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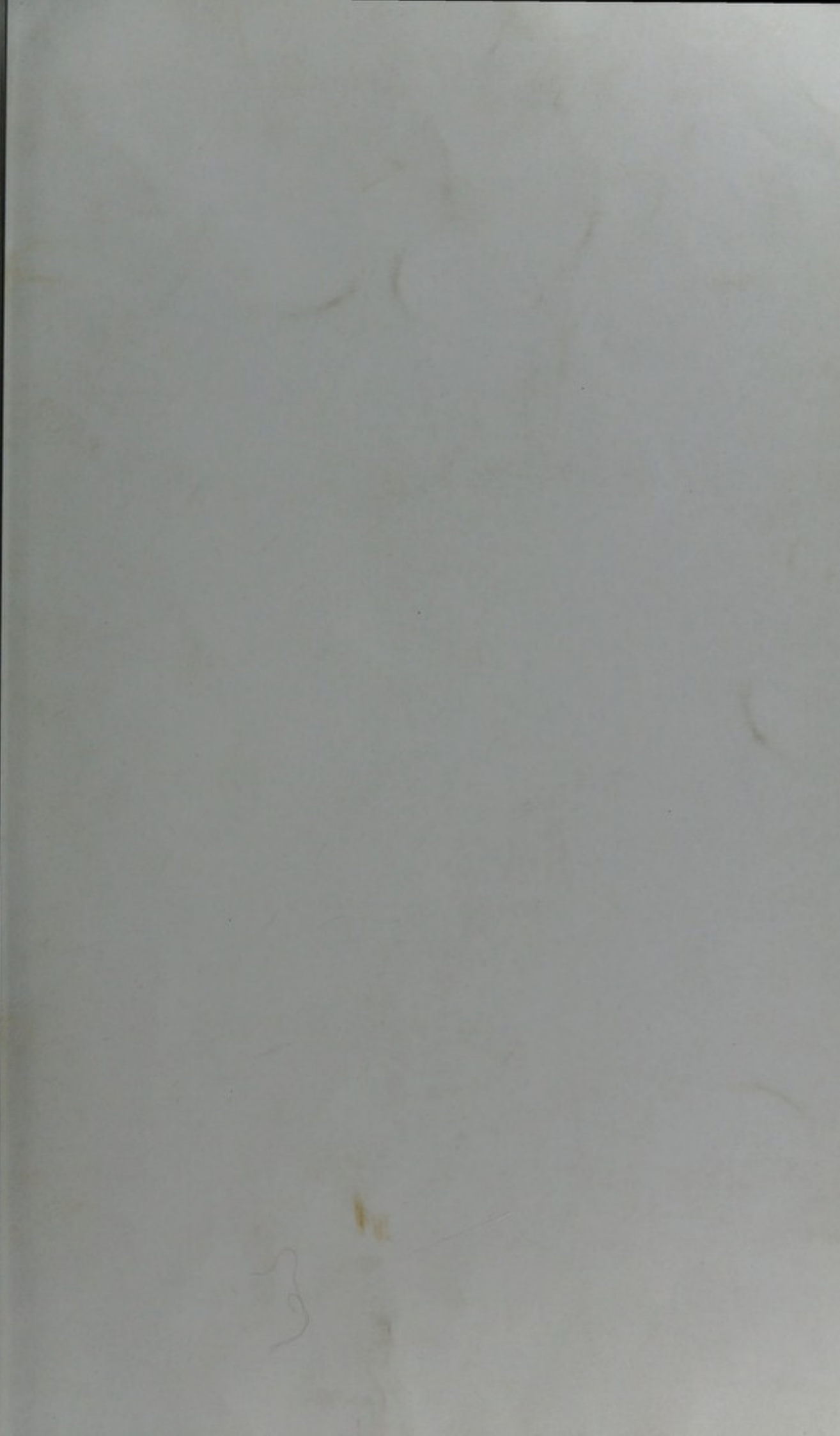
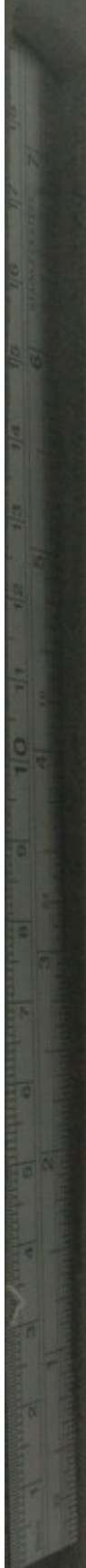
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DIGITALIS :

ITS MODE OF ACTION : AND ITS USE.

AN

ENQUIRY ILLUSTRATING THE EFFECT OF REMEDIAL AGENTS

OVER

DISEASED CONDITIONS OF THE HEART

THE HASTINGS PRIZE ESSAY OF THE BRITISH MEDICAL
ASSOCIATION FOR 1870

BY

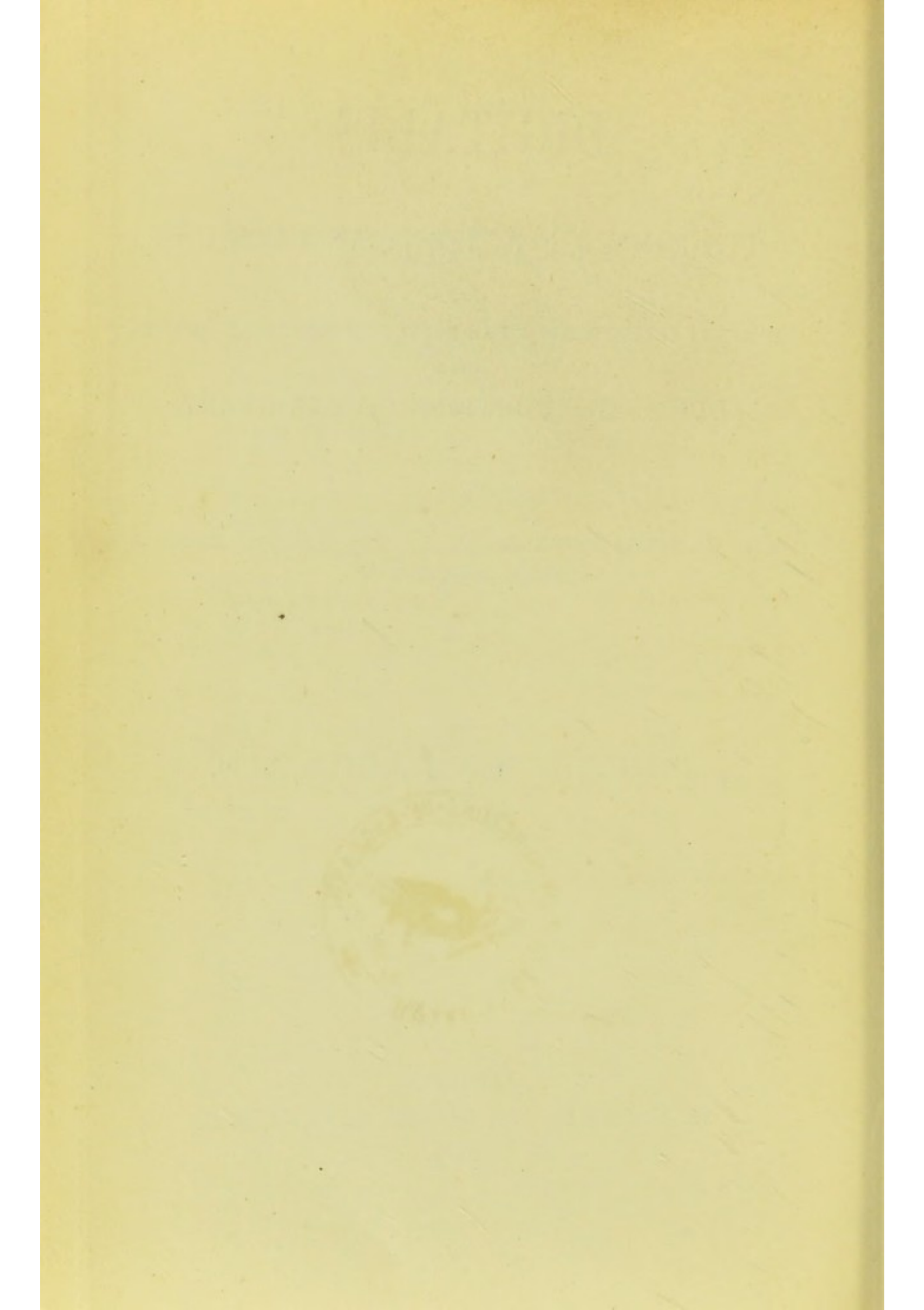
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LONDON :

H. K. LEWIS, 136, GOWER STREET, W.C.

1871.



PREFACE.

By the solicitation of friends and the permission of the Committee of Council of the British Medical Association, this essay is published in a separate form. Whether it contains matter entitling it to a permanent form, or not, time alone can say. But from the review of cardiac compensatory pathology, &c., which is unavoidable in discussing the action of digitalis the writer trusts it may be found to have some claim to so exist. It would be very gratifying to him to find this essay aid, however little, in diminishing the hopelessness with which diseases of the heart are too commonly regarded from a therapeutic point of view.

LONDON. September 15th, 1871.



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ON DIGITALIS:

ITS MODE OF ACTION AND ITS USE.

IN bringing forward a subject so debated as digitalis and its action, the only apology the writer can offer is, that for years he has studied its effects clinically, having had patients continuously under its use for no less a period than three years and a half uninterruptedly. He has tried to bring to the inquiry a mind free from prejudice on either side, and impressed with the wish to elicit the truth. Physiological experiment has been largely resorted to and carefully observed; and, finally, the writer has carefully striven to give his results honestly, and to record what he thinks digitalis can do, and what it cannot, and, further, why he thinks so. It may be desirable to commence with an account of the different experiments performed, and the results obtained; and all through the inquiry he will regard digitalis as a member of a group of agents, rather than as possessing any qualities which are unique or peculiar to itself.

On Plants.—Marcet and Brunton have separately tried the effects of digitalis on the haricot bean by watering the plant with an infusion, and found it to kill it by withering it up. The writer injected a strong infusion into the hollow stems of the ordinary bean without effect for days; in time, however, those so treated withered and died, contrasting with those not interfered with. Precisely the

same results ensued from similar injections into the orange lily. A lettuce was frequently watered, in a dry season too, with a strong solution, without any perceptible injury to it either soon or late. Another was then dug up by the roots, and placed in a large basin containing a strong infusion of foxglove, and for a day or two grew amazingly; on the fourth day, it commenced to wither, and died in a day or two. The first effect of the drug was to improve the appearance of the plants to which it was administered; an impression to the same effect remains in the minds of friends who witnessed the experiments. Strong infusions were injected into the stem of the rasp, and into holes bored into a plum tree without apparent effect.

On Invertebrata.—Snails, when touched with the tincture or strong infusion, took a contractile spasm, threw off a coating of mucus, and passed on apparently unaffected. Earth-worms, when placed in an infusion for a short time, did not appear incommoded. Wasps were not affected by it when applied to them.

On Fishes.—Minnows, when placed in an infusion of digitalis, a very weak one, for some minutes were not affected; then commenced a rapid movement of the gills, which lasted till death; they were also drawn to one side in dying. After death, the ventricle was found firmly contracted and glistening like a speck of gristle; and, on being examined under the microscope, no cavity was visible. The auricle was distended and vainly tried to drive any blood into the tightly contracted ventricle, the blood merely regurgitating into the venous sinus behind, and then flowing back again, from the venous distension relieving itself on the auricular diastole. On pricking the venous sinus so as to permit the escape of the contained

blood, the auricle soon also became firmly contracted, and no cavity was perceptible under the microscope. The quickened action of the gills was probably due to the accumulation of carbonic acid in the blood, giving rise to an increased necessity for breathing, while the firmly contracted ventricle prevented the flow of blood to the branchiæ, and cut it off from oxygenation.

On Birds.—About half a drachm of strong infusion of digitalis was passed down the throats of two sparrows, some being spilled during the process. The animals soon became unable to move much, and gasped for breath most vigorously. The hen died first, and the cock died hard in about half an hour. On opening them immediately on death, the left ventricle in each was found firmly contracted; the lungs so congested as almost to be hepatised, the right ventricle full of blood. It was evident that the condition of the lungs and right ventricle was due to inability to drive the blood into the contracted left ventricle. The gorged condition of the lungs accounted for the gasping respiration observed. Side by side with them, ten drops of Fleming's tincture of aconite were administered to a third sparrow, who became convulsed, and died in about one minute and a half. In it, the lungs were pale, and the heart completely paralysed and distended, looking like a small Barcelona nut. The contrast between the two conditions was marked.

On Mammals.—Experiments have been made on the higher animals by Handfield Jones and Fuller, with similar effects as regards the state of the heart after death.

On Frogs.—These have purposely been put last, on account of the large number of experiments to which they have been subjected by various writers. Frogs have been made much use of by experimenters, on account of their

great susceptibility to medicines, and the ease with which experiments could be carried on. Dybkowsky and Pellikan abroad, and Hilton Fagge and Stevenson in England, experimented largely on them, with uniform results as regards the state of contraction of the heart observed. The manner in which the writer experimented was this: The frog having been firmly secured to a piece of lath by a bandage, leaving the chest exposed, the chest was then opened with a pair of scissors up the middle; the heart usually appeared through the incision, and was readily cleared of its pericardium. It thus beat with much regularity, apparently not much affected by temperature or air. It may not be out of place here to state that, when thus exposed, the cardiac contraction was clearly seen to be a swiftly passing peristaltic action, commencing in the auricle (as first described by Schiff and corroborated by Valentin), and passing rapidly on to the ventricle. The complete distension of the auricle stimulated it to contract in the direction towards the ventricle; this action, driving still more blood into the already distended ventricle, produced such distension of it as stimulated it to contraction; after the systole came a period of muscular rest, during which the blood poured from the distended veins into the lax chambers, until the the distension of the auricle led to a general systole. Digitalis was then administered by the mouth, or hypodermically, and its effects were quickly apparent. First, the contractions became somewhat quicker, and the contraction more complete; and here it may be stated that, whatever may be the normal state of the human heart in systole, certainly the frog's is not thoroughly emptied, and is still dark coloured from the colour of the contained blood, showing through the transparent walls, which are quite white

when thoroughly contracted. Soon the peristaltic action became more marked, the systole being longer and more perfect. Then the distension became less complete, especially at the apex, which remained white and firmly contracted. Here and there were little sections, apparently belonging each to a separate cardiac ganglion, which did not seem affected, and in the general contraction pouched out, contrasting in colour, too, with the other contracted and whiter portions: these are the crimson pouches of Dybkowsky and Pellikan. The action of the ventricle became almost vermicular in its slowness, and the diastole was most imperfect, till the ventricle came ultimately to a standstill in firm contraction, the heart being much diminished in size—and in size, shape and colour, much resembled an unripe apple-pip. The frogs did not seem much affected otherwise, the poison seeming to be confined, as regarded its action, purely to the heart. If released, they hopped about unconcernedly, nor did the removal of the contracted heart by scissors cause them any apparent inconvenience. They merely seemed to die ultimately from the arrested respiratory changes; a slow mode of death in cold-blooded animals. In accordance with the observations of the above mentioned experiments, my results were uniform as regards the contracted condition of the ventricle. To other frogs were administered belladonna, caffeine, strychnine, and aconite. The first produced rather marked contraction, caffeine somewhat less so. Strychnine produced no perceptible effect, contrary to anticipation. Aconite produced paralysis and arrest of the heart in diastole. A still more interesting series of experiments was performed. To some frogs, digitalis and aconite were administered, side by side, and the opposite actions contrasted. The experi-

ment was then varied ; and, after the action of each drug was well established, the other was administered,—*i.e.*, after the effects of digitalis were well established, aconite was administered ; and to others, after the action of aconite was well brought out, digitalis was given. Over the action of digitalis, aconite certainly had an influence, but it could scarcely be called a marked one, and did not ultimately arrest the contraction produced, even when pushed. On the contrary, the administration of digitalis was followed by the most marked results, when aconite had been given, and the ventricle had become gradually more and more distended, and its contractions more and more imperfect, each contraction merely expelling a small quantity of blood off the top of the distended ventricle, the contractions becoming slower and slower, and less and less perfect, until a condition of advanced dilatation had been artificially produced ; and even when the heart seemed to have given up all action, and remained in diastole, distended with blood and inert. When all action had apparently ceased, the first effect was to produce an imperfect contraction at long intervals ; then the intervals became shorter and the contractions more complete, some irregularity both as to time and amount of contraction being observed. Slowly and gradually, however, the distended ventricle recovered itself under the action of digitalis, the contractions being more rhythmical and perfect, and the distension less and less pronounced, until a return to normal contraction and distension was brought about. If the administration of digitalis were then continued, the same appearances were brought out as when no aconite had been previously given. This interesting experiment was frequently performed before other medical observers, and can be readily repeated. In all the ex-

perimemts the ventricle was the most affected; in the frog, where there is only one ventricle, the auricle could only remain distended behind it, incapable of getting rid of its contents into the firmly contracted ventricle in front, and of course it could not contract unless its contents could be disposed of: if the venous sinuses behind were pricked, as in the case of the minnows, the auricles soon became contracted. As regards the effects upon the rhythm, the general results may be stated broadly thus: at first there were occasional slow beats, interposed without any exact order; and then, as the effect became more marked, the slow beats preponderated, until the contractions were only occasional before complete cessation in systole. During an experiment on a dog by Brunton and Gamgee, a temporary murmur was observed, which they concluded was due, and apparently with good reason, to an irregular action of the muscoli papillares, producing imperfect closure of the mitral valve.

In these experiments on the frog, sometimes the tincture of digitalis was used, and at other times the infusion. In some instances, a solution of digitalin was used, but its effect in producing increased contraction was certainly not so marked as when a preparation was used which contained the other principles. It is not intended that this statement should convey the impression that there exists any good reason for supposing that digitalin is not the active principle in digitalis; but such is the writer's experience.

Hilton Fagge and Stevenson found that, sometimes, the ventricle makes only one pulsation for two of the auricle, the number of its contractions being therefore lessened one half (*Transactions of the Royal Society*, May, 1865, Conclusion 3). Reid seems to think that some-

times more than one auricular systole is necessary to produce such ventricular distension as would excite contraction. This seems in accordance with reason and fact.

Composition.—The leaves of digitalis have been subjected to repeated chemical examination, chiefly by foreign investigators. It has been found that there are various substances, which can be separated from one another, contained in them. The principal of these is digitaline. Indeed, by some it is considered the active principle; but of this I am not convinced; certainly it did not act on frogs so powerfully as the tincture of the leaves did. It is, however, frequently used. Digitaline is light yellow, inodorous, and crystallises with difficulty, and presents the appearance of very imperfect crystals, if crystals at all, under a pretty high magnifying power ($\times 250$). It does not contain nitrogen, nor does it neutralise acids. It is a principle, not an alkaloid. It is soluble in sulphuric acid, and also in hydrochloric acid. The solution in hydrochloric acid passes from yellow to a fine green. Homolle considered this reaction sufficiently delicate for medico-legal purposes. It is scarcely necessary to state that it is not generally accepted as being so. There are also digitalic acid, digitalin, digitalose, digitalide, of whose qualities we know nothing. There are also tannic acid, sugar, and a substance named pectin, chlorophyll, and woody fibre.

Chemical Characteristics.—A dark precipitate (tannogallate of iron—Pereira) is formed on the addition of sesquichloride of iron to the decoction, or to a mixture of the tincture and water. A solution of gelatine causes a scanty precipitate (tannate of gelatine). Tincture of nutgalls merely causes a slight turbidity. There is no reason to suppose that any of the active principles are affected by these combinations; or that the drug is rendered inert by

anything that we know. For a fuller account of its principles, the reader, if curious, can consult Pereira, or the thesis of Brunton.

On the Blood.—Magendie and Thackrah thought the addition of a decoction of digitalis interfered with the coagulation of the blood. Davy states that the addition of a large quantity of watery extract to blood gave it the consistence of paste. So far as I know, no English observers have recently noticed anything peculiar in the blood of animals experimented upon. And in the large number of animals experimented on by me, there never was any appearance about the blood which made it different from any other blood. No scientific observations of any kind have yet been instituted as to the action of digitalis or any of its constituents on the blood, such as have been performed by Harley, Bernard, Fraser and Crum Brown, and Broadbent, on some other therapeutic agents, by which their action has been much elucidated. At this point, it may be desirable, in order to elucidate the subject thoroughly, to take a bird's-eye view of the manner in which the heart's action is maintained: the manner of its disorder, the mode of production of its affections of its vascular walls, and the mode of action of the drug.

The Heart's Mode of Action. The heart, as has been shown by Pettigrew, consists of several folds of organic fibre-tubing folded on each other; it is thus capable of distension and rhythmical contraction. For this purpose, a singular system of innervation, motor and co-ordinating, is provided. The real motor power of the heart is under the control of minute ganglia, each with a morsel of muscular fibre under its direction, which are alone capable of carrying on the action of the heart, but only in a tumultuous manner, as seen after section of the vagi. As with

all other accumulations of organic fibre, the distension by contents leads at length to contraction in a more or less rhythmical manner. The vagus exercises over this a co-ordinating (von Bezold), or even an inhibitory action; *i.e.*, the application of a stimulus, as electricity, for instance, to the vagus, retards the cardiac contractions, and, if the stimulus be powerful enough, arrests the heart's action in diastole. The vagus then normally acts against the first impressions of distension, and only permits contraction when the distension is sufficient to produce uniform contraction, which then goes on in a truly peristaltic manner, but so swiftly as to be easily mistaken for a simultaneous general contraction. Thus, to some extent, distension and the action of the vagus balance each other; any disturbance of that balance, then, would produce irregularity, no matter in what direction the disturbance might lie. There lies, too, in organic muscular fibre, an inherent power of growth to meet demand; thus, if increased strain be thrown upon the heart, increased growth of muscular tissue, in health, takes place, and again the balance is restored between the blood to be driven and the power to drive it. When, however, from any cause, there is a deficiency in the compensatory nutrition, a species of balance is again struck, but of a lower form, by distension of the fibres, or, in other words, dilatation. In fact, there is planted on this comparatively simple cardiac innervation, a more complex one of contraction and reduction of the ventricular cavity on the one hand, and a species of normal distension on the other. These actions are regulated by nerves which have been dissected out in the rabbit, and experimented on by MM. Cyon, Claude Bernard, and others. The one which calls into action an increased action against obstruction is called the *accelerator nerve*;

and the other, which admits a normal distension of the walls, is called the *depressor nerve* of the heart. Claude Bernard has even gone so far as to state it as his opinion that, through the action of the latter, a species of distension may so take [place in accommodation to existing circumstances as to convert the cardiac chambers into temporary blood-reservoirs. This their construction as organic fibre would permit; for organic fibre permits great distension without abolition of function. Thus, while carrying on the circulation by expelling a quantity only of the contained blood off the top of the ventricle, and permitting a large portion to remain on each systole, this accommodation is allowed without bad results. This is undoubtedly no rare occurrence, if clinical observation were exact enough. Thus, between the ordinary balancing powers of the obstacle of the blood to be driven, and the muscular power to drive it, of the stimulating effects of distension in producing contraction, and the controlling action of the vagus, the heart's action ordinarily rocks; but, in addition to that, there is a more complex system of accommodating distension on the one hand, and an accelerating contracting action against an obstacle on the other: which exercise a regulating power according to special circumstances. Ordinarily, however, the action lies between the first set of nerves, with the driving power, and the work to be done. With their disturbances of balance, we are now more especially engaged.

Distension.—The first action of disturbance of this balance is engorgement or distension. When much blood has been located in the ventricles, and they are not capable of completely emptying themselves, a portion remains at each systole. At each diastole, however, an equal quantity of blood is again thrown into the ventricle, and thus at

the next systole a larger quantity remains unexpelled; and this process goes on until death, or until some compensatory relief is attained. This relief is usually attained by congestion of the veins, and the system suffering. This distension or, if chronic, dilatation is produced in many ways, thus: 1. Pouring in of the blood under increased pressure, as in the enlargement of the left ventricle, which follows in time on mitral regurgitation, and increased action of the right ventricle and thickened pulmonary vessels; 2. Muscular failure from defective nutrition, as in fevers, in coronary atheroma, or pericardial adhesion; 3. Obstruction to the flow of blood forwards, as in deposit of fibrine on the semilunar valves, diseased vessels, etc.; 4. Disorder of innervation, as a disturbance of the balance between the sympathetic ganglia and the action of the vagus; 5. Excessive exertion and consequent cardiac exhaustion; 6. Valvular insufficiency. This condition may pass on to permanent dilatation.

Mode of Repair.—The ordinary modes of repair of this condition are two: first, relief of the condition on which it depends, where practicable; and, second, hypertrophy, when it is due to increased difficulty in the flow forwards, or to valvular insufficiency, by that power of self-increase which is allowed to all muscular fibre, but with which organic muscular fibre is endowed *par excellence*. Restoration of the balance may take place in three modes, of higher and lower grades: 1. The highest, restoration of the cavity to normal size; 2. Hypertrophy, by increase in number of fibres (Forster) and thickening of existing fibres (Bamberger and Rokitsansky)—a compromise; 3. Dilatation, a permanent distension—the lowest restoration of balance, and entailing diminished vital capacity to a point proportioned to the heart's lowered power.

The signs of this disturbance of balance, or partial asthenia, are three—palpitation, irregularity, intermittency.

1. *Palpitation*.—The first evidence of failure of power is palpitation. It is undistinguishable from increased action, except in deficiency of results. When there is excited action, as in exertion or excitement, it is perceptible in the bounding pulse, or, with the sphygmograph, in the increased apex-beat. Palpitation is not so accompanied; and though to auscultation and percussion the heart-stroke may appear identical, it is in the results the real difference lies. Palpitation is a laborious heart-stroke, but not a stronger one. It is the evidence of effort, not of capacity. It is barren in result—a laborious stroke in place of a normal one, but not of more effect, not always of so much. It is intimately associated and commonly mixed up with the next form—irregularity. Palpitation may be engrafted on symptoms of chronic insufficiency as a temporary condition; as, for instance in the palpitation of Bright's disease, or of slight exertion in a dilated heart from valvular insufficiency. Palpitation is a violent effort of the heart-walls to overcome the action of the vagus, *plus* the obstructed flow.

2. *Irregularity*.—Irregularity of the bulk of blood transmitted into the arteries is one thing, and is due to auriculo-ventricular incompetence. Irregularity in time is another. The latter is under consideration here. Irregularity of rhythm is not due to disordered innervation, but to obvious debility. It is an arrest in the commencement of the peristaltic contraction or heart-stroke. The controlling action of the vagus arrests the contraction until such time as the layers of fibres acting early on the systole ought normally to have acted; and then a sharp, almost

simultaneous contraction takes place, with an increased thud against the chest-walls. This action is homologous with the increased action of the muscular fibres, under the control of the cardiac ganglia, when the systole has been retarded by stimulation of the vagus. Sometimes it appears as if the action of these layers, acting early in the systole had been lost; and there is a perceptible change of action in the heart, as if the contraction were commencing from a new layer or set of fibres. Richardson has compared this to a change in order of a number of strikers on an anvil. It always reminds the writer of a horse changing its feet when cantering. This is a more serious evidence of over-taxation of the heart, and is often found mixed up with palpitation. It is often the result of over-exertion, and affords strong suspicion of ventricular distension. Chronic irregularity may have engrafted upon it a passing palpitation from an intercurrent additional disturbance of balance. Nervous irregularity and palpitation will be considered in a future section.

3. *Intermittency*.—This is sometimes purely nervous, and is inexplicable. When persistent, it is usually associated with an impaired first sound, defective apex-beat, and and other signs of degeneration. The occurrence of palpitation during this condition sometimes clouds the diagnosis, and makes it very difficult. Intermittency of ventricular contraction is not identical with intermittency of radial pulse, though related to it. In some cases of intermittency of the radial pulse, if the stethoscope be applied while the pulse is held, a ventricular contraction will be distinguished when there is no evidence in the pulse; but it is a feeble contraction. In other cases, the ventricle does not perceptibly contract. Whether there

is a very abortive contraction, or not, is doubtful. Certain it is, that in some cases the ventricular contraction can be detected when too feeble to produce a pulse wave; in other cases no ventricular contraction can be perceived. Intimately connected with this condition, is true angina pectoris, and, finally, cessation in diastole.

After this brief *resumé*, we can now consider the mode of action of digitalis, in what manner it acts; and from that, again, get an idea of its therapeutical value.

Manner of Action.—We have seen in a previous section how the administration of digitalis in physiological experiments is followed by increased contraction. It is obvious that this can only take place in one of two ways, viz., by stimulation of the cardiac ganglia, or by paralysis of the fibres of the vagus. These are, then, the two theories which exist. We will consider, first, the theory of Traube—that of paralysis of the pneumogastric fibres.

1. *Theory of Traube.*—This theory took its rise in the tumultuous movements which result from the section of the vagi. When both vagi were cut, tumultuous and irregular vermicular action was observed to result. That is, the nerve-force was still passing into the sympathetic, which were in full activity, while no longer was there any co-ordinating power in action. It must be admitted on the side of Traube, that certainly digitalis did not act so rapidly on animals where the vagi were cut (see the experiments of Handfield Jones); but, on the other hand, it is more difficult, on his theory, to see how it could act at all after that. Also, section of the vagi only produces death slowly, and that by hepatisation and disorganisation of the lungs; and the most complete paralysis could not be more effective than section. Now, the administration of digitalis in full doses brings the heart to a standstill as

a primary action, and that, too, at an early period. There is no apparent connexion between the administration of digitalis and section of the vagi, except an increase in arterial tension, as tested by the hæmadynamometer—the test used by Traube. Winogradoff, from a similar series of experiments to those of Traube, came to opposite conclusions. Niemeyer states that he has clinically been compelled to emancipate himself from the bonds of Traube's theory.

2. *Theory of Stimulus to Cardiac Ganglia.*—This theory was announced by Dybkowsky and Pellikan abroad, and supported by Handfield Jones, with Fuller and others in this country. This theory is, that digitalis acts as a stimulus to the cardiac ganglia, and thus produces the increased muscular contraction. It is almost needless to remark here, that in no way could the stimulus to the nerve-ganglia manifest its results except in muscular energy—*i.e.*, increased action of the muscular fibres under their control. The increased action and irregularity can as easily be conceived to result from a disturbance of balance through over-action of the cardiac ganglia, as in paralysis of the opposing fibres of the vagus. That this irregularity does result, is unquestioned by either side. In order to settle the question of these opposing theories, Eulenberg and Ehrenhaus took out the heart of a frog, and dipped the lower end, or apex, into a solution of digitalin; the rhythmical action which goes on under the action of the cardiac ganglia, when the heart of a cold-blooded animal is cut out of the body, and when no longer any nerve-force is coming in from vagus or sympathetic fibres, and which contrasts with the tumultuous action which follows section of the vagi when the other nerves are intact, was interfered with; if the solution were weak, the action was

rendered slow and irregular; if strong, the motion was stopped. Some light, too, is thrown on this intricate subject by observing the effects of digitalis on other organs where no inhibitory action of the pneumogastric exists. Dickinson found the action of digitalis beneficial in menorrhagia, from its contractile effect on the arterioles. Malan watched the contraction of the capillaries (to dispute whether they are capillaries or arterioles would be out of place here) of a frog's foot under the microscope—an experiment corroborated by the writer. On the application of an aqueous infusion of digitalis leaves, a contraction of the vessels of the web was found to follow, and to proceed to such an extent as to interfere materially with the circulation, bringing it nearly to a standstill: of this some further account will be given in the section on the action of digitalis on capillaries. The inhibitory action of the pneumogastric could have no place in these last named observations. And from the obvious difficulty attending Traube's theory, and the direct evidence in favour of the other, I am led to unhesitatingly side with the latter. The action of the stimulated cardiac ganglia is too much for the action of the vagus; and thus, instead of an almost synchronous contraction, as is normal, the action is seen to be distinctly vermicular. A long peristaltic contraction is followed by an imperfect diastole and distension, until a state of permanent systole is attained, exactly corresponding to the process of the application of electricity to the sympathetic, and in no way analogous to the results of section of the vagi—than which no paralysis could be more complete as regards abolition of function. The results, too, of the administration of digitalis after aconite poisoning had been established, would necessitate the theory of aconite acting as a stimulus to the fibres of the

pneumogastric, if Traube's theory of the action of digitalis were true—a conclusion which is not warranted by what we know of aconite.

Action on Capillaries.—The action of digitalis on the capillaries, as observed by M. Malan and the writer, is in unison with the above mentioned theory of its action on the cardiac ganglia. From the same portion of the splanchnic system arise the vaso-motor system of nerves, regulating the size of the lesser arteries and arterioles, but not capillaries. Be this as it may, and granting that capillaries do not possess the power of contraction, and that, therefore, the vessels must have been arterioles if they contracted, unquestionably the application of infusion of digitalis to a frog's foot produced contraction of the vessels of the web. While the corpuscles had before been coursing down them in single file, they were now arrested and passed with great difficulty, in many parts of the field being arrested altogether. The flow through the capillaries was no longer a continuous flow, in which the impulse of each ventricular contraction was lost; the circulation was by pulses corresponding to each beat of the heart, during which each corpuscle moved about twice its own diameter forwards. On the application of digitalis systemically, consequent increased ventricular contraction became conspicuous, each corpuscle now travelling about four times its own diameter; but the general condition was not altered. Further observations as to its effect on the capillaries may lead to further knowledge; and the writer regrets that circumstances have interfered with his prosecution of this branch of the inquiry. Enough, however, has been observed to demonstrate that digitalis has a direct action on the minute vessels; and in practice that fact must not be forgotten when digitalis is administered

for the sake of its effects on the muscular walls of the heart, and the condition of the vessels between the heart and small vessels—viz., the arteries—is registered.

General Observations as to its Effects when Administered Clinically.—It may be well to give a summary of the effects of digitalis when clinically watched, before proceeding to instances of particular disease. The early administration of digitalis was conducted on the theory of its being a cardiac sedative. The reason for this theory was, that palpitation and irregularity were relieved by its administration; and hand in hand with this went on the theory of these derangements, especially palpitation, being over-actions of the heart. That in reality they are evidences of deficiency rather than excess of power on the part of the heart, we now all know. With the exception of excitement, which is visible in its effects on the pulse, we now know that there is no such thing as over-action of the heart. Hypertrophy is, without exception, a compensating growth to overcome some obstacle; though Niemeyer would except one class of cases where he considers it a mere result of plethora. We can no more imagine a heart undergoing spontaneous uncalled-for hypertrophy, than we can fancy a similar action going on in the bladder or bowel. It is too obvious that the increase in muscular tissue is called forth only by a necessity for it. Palpitation may occur with hypertrophy; but it merely gives evidence that that hypertrophy is insufficient. Palpitation is an evidence of over-taxation, whether it occurs in hypertrophy or in dilatation. Nevertheless, the administration of digitalis is followed by a quieter action, but that is by its restoration of the conditions to the norm, or an approach to it. Under digitalis, the pulse becomes steadier, firmer, and less compressible; the excited stroke of

palpitation is steadied into the normal, quiet, effective contraction; the system is relieved; dyspnœa, the external witness of pulmonary congestion, is abated; the deficient secretion of the urine, which tells us that the pressure on the glomeruli of the Malpighian bodies is lessened, is improved, and free secretion takes its place: dropsy is thus often relieved. The general condition of cyanosis is abated; there is evidence of a better circulation throughout the system generally. Frequently, the gradually widening circle of troubles which are involving the patient's existence, gradually diminishes after an improvement is inaugurated in the circulation. The spell which bound the system in a load of ever-increasing fetters is broken by the administration of a drug whose action is unquestionably to produce better, more complete, ventricular contraction; and in that, and that only, I believe the magic lies. When we consider the extreme tendency there is for a condition of cardiac engorgement, or distension to result from any prolonged debilitating cause, or acute disorder, and that, too, especially in the right or truly venous side of the heart; when we consider how that again tells on every excretory organ, from the lungs in front to the kidneys behind, and how that leads directly to non-excretion, and how blood-poisoning is engrafted on partial blood-stasis; how the left side of the heart is encumbered between the two burdens of poisoned blood and venous congestion—we can readily appreciate a drug which will enable these chambers to more completely empty themselves, and thus to direct better blood-propulsion, and can understand its extreme therapeutical importance. It is of the utmost importance that we really understand in the administration of digitalis what we can fairly expect of it, what it may be fairly presumed to be able to do, and what experience

tells us it has done before. It is obvious that when all is well, neither we nor any patient would wish to administer it or any other drug; we now know that there is no deviation from health except in a downward direction. It is obvious that the most perfect action of the heart is when we are unconscious of its labours. It is equally obvious that those symptoms which tell us that it is at work, are really evidences that the heart is labouring, in both senses of the word. It is for a condition of inability on its part that the physician is consulted by the patient; and though it is possible that now and then its efforts can be strangled by a sedative, or allayed by a narcotic, it is equally obvious that neither can be styled a scientific treatment; for permanent relief we must look for something which will really aid its efforts; and to this, and for the condition under which digitalis ought to be administered according to the experience of the writer, the next section will be devoted.

General Considerations continued.—The conditions under which the physician finds his patient run somewhat in this fashion. The patient complains of a feeling of anxiety about the precordia, with a general unaccountable anxiousness—a sense of difficulty of breathing, which is notably increased upon exertion; he has fluttering about the left breast amounting to palpitation upon effort or exercise; the pulse is irregular, or may be regular but compressible; then come a dusky complexion and impeded respiration. Here, then, is a condition of cardiac engorgement which would scarcely be disputed, whether as a passing condition or as one in a series of similar attacks. On examination of the case, there can usually be found a feeling of diffused impulse on palpitation, a large mass apparently being thrown into contact with the thoracic

walls; percussion reveals an increased general dulness, frequently in the direction of the right side of the sternum. Auscultation communicates to us the further information that there is a short slapping sound, with or without irregularity, or, perhaps, evidence of laboriousness—a heaving swell with obvious effort, which, however, is not followed as effect by that impression on the arteries we might look for: and, finally, there is a something beyond this utterly undescribable by words: a peculiar significant information conveyed, which experience and repeated observation alone can understand or interpret. Those who have made heart disease a study will readily understand and supply that which I feel incompetent to convey. Or, in other circumstances, the patient has a tickling cough, feels short of breath on exertion, has a slight attack of bronchitis, or may be no particular ailment; the pulse is small or feeble, but, on casually applying a stethoscope, there is found a state of cardiac excitement with some irregularity in time—action, like imperfect palpitation, but without any evidence on the radial pulse. It is nevertheless there, and percussion soon demonstrates that there is increased dulness to the right side of the sternum, and auscultation reveals corroborative information in adding a marked accentuation of the second sound at the pulmonary valves. The aggregation of sounds demonstrates that there is embarrassment and also laboriousness in the right ventricle; it is not likely to be accompanied by any effect on the radial pulse; and even the discriminating sphygmograph is thrown out, for there is no increased arterial tension anywhere where it can be applied. The trouble is going on in the right side, the diminished amount of blood passing into the left ventricle is insufficient to allow any impression to

be made on the arteries even if, as is very probable, the left ventricle is acting somewhat excitedly. From the number of fibres which belong equally to the right and left ventricles, and can be traced into each (see the works of Searle and Pettigrew), such community of action, even where there is no call on the left ventricle, is almost unavoidable. These conditions, and more so the latter one, are common enough when searched for, especially among the out-patients of a public institution; in fact, we are learning that a condition of engorgement of the cavities of the heart is quite usually met with; and, in fact, if we are to believe MM. Cyon, von Bezold, and Claude Bernard, a special innervation is in action to permit it. How far this condition may be a necessary one in the present state of science, we are unable to determine; we can, however, readily discover this condition, and more easily calculate the amount of mischief which is actually present therefrom, or likely to result from its continuance. Without entering here into the troubled waters of a consideration of the existence and importance of a condition of temporary distension in acute disease or passing conditions, which is reserved for a later section, we are familiar enough with this condition when fully established as dilatation, with or without hypertrophy. A permanent enlargement of the ventricular cavities, and more commonly so of the right one, is a condition the reverse of rare. While frequently found among persons advanced in life, it is far from uncommon among younger people. These are the conditions which physiological research has pointed out as suitable for the administration of digitalis as a therapeutic agent; and clinical observation confirms the view. It is proposed, then, to consider the general condition of distension or dilatation; the manner in which the drug

acts; the other conditions, causal or consequential, with which the condition is connected; and the especial circumstances in each condition which would encourage or forbid its use.

Mode of Action in Distension or Dilatation.—It is in this condition of distension that the advantages of the administration of digitalis are most evident. In this condition of deficiency of expulsive power, the heart-walls yield. The heart is distended, and in contraction only gets rid of a little blood off the top, remaining more or less full in systole. It is more or less full before the distended auricle and veins behind pour in their contents under the increased pressure of distension. It is in the partially filled condition of the ventricle that the difficulty lies essentially. If the ventricle were not partially full, the auricle and veins would be somewhat relieved; but there is what would fill well an empty ventricle waiting to be discharged into one more or less full to begin with. The action may be moderately regular on quiet being maintained, but it is at once disturbed on motion, especially if this be at all active; and then we get palpitation and irregularity or even intermittency, the regular action being again restored by quiet. There is a constant contest going on between the stimulus of the contained blood and the inhibitory action of the pneumogastric fibres. The distension excites the muscular walls to overcome the restraining influence; for, without the stimulus of distension the walls could never overcome the inhibitory action of the pneumogastric, *plus* the *vis inertiae* of the blood to be driven; and action still further deranges the balance by making still greater calls on the muscular walls. In fact, the heart is in a state of over-distension, and in a condition both analogous to, and homologous with, an hyper-

trophied bladder attempting to overcome the obstruction of an enlarged middle lobe of the prostate. The over-distension goads the organ to such a contraction as shall relieve that over-distension, but only so far, and no further; there is no complete contraction. An incessant play goes on between the condition of over-distension and the restraining fibres of the vagus; the balance between the muscular walls and their work remaining confessedly disturbed. In this condition, the administration of a drug whose physiological action is to stimulate the sympathetic ganglia, and thus the muscular fibres under their control, into excessive contraction, is almost the only means of restoring the equilibrium. This is beautifully exemplified in the heart of a frog, when paralysed and almost brought to a standstill in diastole by aconite; the heart is distended, globular, and, in every respect but that of chronicity, in the condition of a dilated or distended heart. Then administer digitalis, and watch the result. The distended globe, just pumping painfully a little off the top of the contained blood, and that at long and irregular intervals, begins to contract with more vigour; each ventricular systole is more and more complete; and the bulk of blood remaining unexpelled—and that is the great point—becomes less and less in quantity. Shortly, the distension in diastole is shortened, the distension and contraction come gradually back to the norm, the irregularity in time is lessened, and a complete restoration results. But if the experiment be carried still further, spasmodic contraction or the condition of concentric hypertrophy sets in, irregularity again makes its appearance—for the balance is now disturbed in the opposite direction; in fact, the symptoms of digitalis-poisoning are brought out, and ultimately the heart is brought to a permanent standstill in systole.

Thus in a distended heart, only a longer time is requisite, and, of course, the cause of the original distension must be overcome; so that the conditions are scarcely equal, and longer time and an artificial compensatory hypertrophy is necessary to maintain the balance thus temporarily restored. When this condition of distension is only of short duration, as seen in people who have been overworked and overtaxed for a short period only, but presents all the appearances, signs, and symptoms of cardiac dilatation, the restoration of the natural balance by digitalis may be quick and withal permanent. Certainly I have seen such cases. The experiments of W. T. Gairdner on Groux, the man without a sternum, show that the ventricular chamber undergoes a certain amount of expansion under passing circumstances, a normal distension in fact; for distensibility without abolition of function is a peculiar property of involuntary muscular fibre; but when distension is excessive, or the tissue degenerate, however, abolition of function may, and certainly does, take place. The experiment may be tried on any thin muscular man—viz., place the tip of your finger on the exact apex-beat, and bid him hold his breath; the right ventricle dilates until the apex-beat is lost behind the distended ventricle, which acts like a water-cushion between the left apex-beat and your finger. Still keeping your finger in its place, tell the man to breathe again; the distended condition passes away, and soon no trace of it remains. Now, all the time the heart has been beating away, and there has been no abolition of function. Claude Bernard has gone so far as to suggest that a normal distension of the heart takes place through the action of the depressor nerve of the heart of Cyon and Ludwig, and that the heart can undergo a certain amount of accom-

modation to the blood-vessels, and by dilatation become, for the time being, a regulating reservoir. Without endorsing the theory of Claude Bernard, it must certainly be admitted that the condition is unquestionably common enough, and is not detected because, probably, it is not sought for: it is intimately related to the short, weak, fast pulse, which in a remarkable manner is rendered slow by digitalis, with great improvement in the systemic symptoms. Now, what has gone on? The condition is one of distension; the ventricle, just at the point of distension always, from inefficient contraction, soon becomes so over-distended as to be excited to contraction in spite of the vagus; the pulse-wave is feeble, for only a small quantity of blood is thrown into the aorta, and the elastic walls are not sufficiently distended to bring out a good pulse; the needs of the circulation are not properly supplied, and the body generally partakes of the feebleness of the circulatory centre. Then administer digitalis, and soon the pulse falls, say from 130 to 72; the radial pulse is much improved, being fuller and more sustained, and relief of the system is attained. Sometimes, but rarely, we read of a curious irregularity of rhythm accompanying the alteration, viz., sometimes a series of beats at the rate of 130 per minute, and then another series at the rate of 72; it seems as if it were some time before the old habit was broken. Never having met with such a case, I cannot explain the condition. The slow pulse is due to the ventricle making a more complete contraction, taking up, of course, more time over it, and requiring longer time for distension again. In fact, to again use our old simile of the bladder, the condition of distension is like the bladder behind the enlarged prostate, only contracting to the extent of over-distension—soon full, because never empty;

while the altered condition bears more resemblance to the normal bladder capable of complete contraction, and consequently requiring longer time for distension. The heart in distension is incessantly at the point of over-distension, and is acting unnaturally quickly; the administration of digitalis, by producing more perfect contraction, relieves this condition of irritable, or, rather, irritated distended ventricle, while, at the same time, more complete contraction produces more thorough aortic distension, and thus brings out more thorough arterial recoil or systole; that, again, gives relief generally to the systemic symptoms, and also permanent benefit as an ulterior result. It must be borne in mind here that the contraction of the ventricle fills the vessels and distends them; the recoil of the elastic arteries completes the propulsion of the blood. The series of altered actions consequent upon increased contraction, run in the following order or sequences; and it may be desirable for the sake of lucidity to arrange them in a series of propositions, each depending on the one before, like a logical syllogism. The effects of increased contraction are, then:—

1. Increased arterial distension and tension, which give relief to the systemic symptoms, and further causes

2. Increased arterial recoil. This is the propelling power for the coronary arteries; and thus arterial recoil means

3. Increased or improved coronary circulation; and that, in its turn, produces

4. Increased nutrition of the heart, which results in

5. Compensatory hypertrophy. In connection with these, we have also to consider

6. Atheroma and fatty degeneration of the heart-fibres.

We will now proceed to the consideration of each proposition in detail.

1. *Increased Arterial Distension and Tension.*—The immediate effect of increased contraction of the ventricle and more complete emptying of the chamber is, that a greater volume of blood is thrown into the aorta, and a more perfect arterial tension produced. Thus we have improvement in the whole circulation, and relief of the systemic symptoms. Cyanosis or blood-stasis is relieved by the more perfect delivery of blood, by increasing the *vis a tergo*; while the emptying of the distended veins assists in inducing a more perfect general circulation. The pulmonic circulation shares in this improvement, and thus the congestion is abated, and with it the dyspnœa. For, when there is so much extra bulk of blood within a given thoracic space, there must be less room for the reception of air on inspiration. When there is an accumulation of carbonic acid in the blood, the improved circulation brings it more rapidly into contact with the pulmonary membrane, and a more perfect interchange of carbonic acid and oxygen takes place, the blood is more thoroughly purified, and the condition of carbonic acid poisoning—the result of wear within the organism—is relieved; thus one of the most dangerous sequelæ is, for a time at least, held at bay. Relief of other consequences, as dropsy, etc., follows for the same reason. The relief thus obtained is the direct result of a larger volume of blood being thrown into the aorta; for after that the arterial recoil completes the propelling impulse. As long as the arterial coats are sound and retain their elasticity, the ventricular contraction merely produces arterial tension; the arterial recoil is the propelling power after that. When the arteries are rendered less elastic by atheroma, or endarteritis deformans,

hypertrophy of the ventricle follows, and the blood is propelled by a sustained effort, very evident in a good sphygmographic tracing, and evident in the pulse at the wrist. Ordinarily, however, the arterial elasticity and recoil complete the impulse received from the ventricular contraction. The greater, then, the distension, the greater the arterial recoil. We thus come to—

2. *Increased Arterial Recoil.*—The arterial recoil, besides completing the impulse received from the ventricular contraction, has an action which is rarely sufficiently recognised. The propelling power through the coronary circulation is the arterial systole. Contrary to other arteries, the propelling power into the coronary arteries is solely the arterial recoil or systole; opening out from the sinuses of Valsalva, they run in a direction opposite to the current occasioned by the ventricular contraction. But the arterial recoil, arrested in the backward direction by the semilunar valves, fills the coronary arteries, and that, too, during the diastole, or heart's period of rest. The question of arterial tension and recoil thus bears directly on the circulation through the coronary arteries—the nutrient arteries of the heart. Thus, too, the blood-supply is secured to the muscular walls of the heart during their period of rest, and not during their activity, which would oppose an obstruction to the circulation, and which would be the case if the ventricular systole were the propelling power through the coronaries. It is thus easy to see how the blood-supply of the heart itself is more perfect, from its being associated with the arterial, rather than the ventricular, systole. Thus increased arterial recoil leads directly to—

3. *Increased or Improved Coronary Circulation.*—It being thus seen how the coronary circulation takes its rise in the

arterial recoil, it is easy to see how an improvement in the arterial distension leads to a more perfect circulation through the coronary arteries, and thus to a more perfect supply of blood to the heart's structure, and a freer supply of nutrition to it. The condition of the muscular structures is intimately associated with their blood-supply. Whenever the blood-supply is defective, the muscles deteriorate, and their efficiency is interfered with. However rich the blood may be, and supplied with nutritive material by perfect digestion, if the circulation through any part be interfered with, that part suffers, and does not benefit by the abundance of nutritive material in the blood. If the blood be impoverished, then, of course, the nutrition of every part is interfered with, but still more so in the part also labouring under obstructed local flow. The arterial recoil has much to do with the general circulation, no doubt, and the unsustained pulse of unfilled—that is, undistended—arteries is well known; the sphygmograph shows a rapid fall after the rise of the systole. This unfilled condition affects all parts; but the heart-structure, through which the coronaries run, is most affected. Their impulse being solely that of arterial recoil, the want of it is a serious drawback to the coronary circulation; while, at the same time, the incessant action of the heart demands a very perfect nutrition to preserve its integrity. Thus, then, improved action of the ventricle leads to increased arterial tension, and through that, by its increasing recoil and improved coronary circulation to more perfect self-nutrition. Thus hypertrophy tends to perpetuate itself, though to an inferior extent, where there is aortic regurgitation or atheroma; that is, loss of arterial elasticity. In these conditions the recoil no longer fills the coronaries, and a deficient flow sooner or later impairs the structural

integrity of the heart. When, however, the dilated or distended heart, accompanied by a rapid, feeble pulse, evidencing a diminished arterial tension, is just pumping a little off the top of the contained blood, there is an inherent probability of tissue-degeneration following at no distant date. The feeble impulse and lessened recoil do not fill the coronary arteries; while the rapidity of the contractions, by infringing on the heart's period of rest between the beats, does not afford the pause during which the coronary arteries supply the heart-walls with nutrition. Thus we see how the improved ventricular contraction leads directly to a better tissue-nutrition; that is, to a consequent hypertrophy. Thus a more perfect action of the ventricle leads to a more perfect nutrition of itself by a special provision, as well as by the general law of increased action leading to increased nutrition, which holds good in all parts of the body equally.

4. *Increased Nutrition of the Heart.*—The improvement in the circulation by supplying more nutritive material to the muscular structure of the heart, and, at the same time, a more perfect removal of waste material, furnishes one factor in the question; the increased systole and lengthened diastole furnish a prolonged period of rest—another factor; and the increased muscular activity, a greater demand for nutrition. There are thus aggregated all the circumstances favourable to improved nutrition.

5. *Compensating Hypertrophy.*—This increased nutrition leads in a direct manner to hypertrophy. The well-known instances of the arm of the blacksmith and the leg of a ballet-dancer demonstrate the growth which accompanies activity with a good supply of nutritive material. For, without the nutrition, the activity leads to degeneration, as seen in the muscles of the top-sawyer mentioned in

Chambers' *Clinical Lectures*. But, with the improved circulation, all parts are improved; there is better appetite, and more perfect digestion. The relief of the systemic symptoms has set every organ into more perfect action. A more perfect elaboration furnishes more nutrition to the blood, now more rapidly circulated through every organ. From a widening circle of troubles, there is now a widening circle of improvement felt everywhere. The muscular activity, causing a greater demand for formative material, finds it provided by the very action that now calls for it, and tissue-activity leads directly to improved tissue-growth. It matters little whether this be by reduplication of fibres, or increase in length and strength; sufficient that it exists. Thus the muscular walls are better enabled either to resist the distending action of the blood forced in under greater pressure, or to overcome an obstruction to the flow of blood forward. Hypertrophy of muscular tissue is the restoration of the balance, as the result of natural processes. Compensatory hypertrophy frequently enables serious lesion to be borne without any great constitutional embarrassment. It is the way in which the system again strikes the balance in well-nourished individuals; and, as a natural process, it is only too desirable to imitate it and favour it. Compensatory hypertrophy, again, restores a balance between the opposing forces of propulsion and obstruction. When hypertrophy is sufficiently pronounced, an almost perfect compensation may be said to exist. Niemeyer states that a huntsman in Griefswald, who suffered from "extensive stenosis and aortic insufficiency, and immense eccentric hypertrophy of the left ventricle, performed all the manœuvres and forced marches of the army without difficulty" (vol. i, fol. 347). Compensatory hypertrophy is Nature's mode of repairing injuries to the

heart's integrity ; and in treatment I have striven to make it mine, and certainly not without success. By a proper recognition of this principle, and of the means by which it may be obtained, a much more effective treatment of heart-lesions may be resorted to than is currently believed. *Experte credo.*

6. *Considerations on Atheroma and Fatty Degeneration.*—The question of atheroma, however, materially interferes with these changes at every step. It may be desirable, and not uninstrusive, to follow for a while this interference. Atheroma is essentially a parenchymatous inflammation of the inner arterial tissues, and may either exist in patches or be more general, leading to dilatation of the arteries, and loss of elasticity. When the arterial elasticity is impaired, the artery distended by the ventricular systole is unable to recover itself. It thus remains more and more distended, and when possible, elongated—*i.e.*, tortuous. This impaired elasticity then lessens the recoil ; the distension and elongation of the arteries interfere with the recoil, and instead of perfect recoil, the artery remains permanently enlarged. This change goes on gradually, incessantly aggravated by exertion and all calls on the heart for increased action. The arteries become elongated and distended, from the aorta to the tortuous temporal artery ; they are increased in length and breadth ; they become, too, more brittle and more easily ruptured by strain. Here, now, we see a wonderful instance of conservative change, tending directly to prolong the existence of the organism. The diseased arteries recoil less perfectly, and thus the coronary circulation becomes involved and its circulation diminished, and thus impaired nutrition of the heart ; and from that, again, lessened and impaired activity, and thus diminished risk of the heart rupturing

the diseased and friable arteries. Thus we see that not only is fatty degeneration a preservative lesion, as Sir William Jenner showed at Leeds, but that that very change which is preservative in its action, is entailed by the diseased condition of the arteries, which the very want of that lesion would endanger. Thus the changes go on, hand in hand; the more diseased, brittle, and non-elastic the arteries, the less their power of recoil, and thus impaired structural integrity of the heart and impaired contractile power. The diseased arteries thus fortunately lead to the very muscular change imperatively necessary in order to prevent the heart from rupturing them. Where the atheroma is general, there is a stronger probability of fatty degeneration following, and thus this condition is more favourable to life than when the atheroma is in patches. Where the atheroma is deposited in ring-like, annular patches, encircling the aorta at the branching off of some smaller artery—its favourite seat—it is more fraught with danger. The hypertrophy consequent on the obstruction, to the flow, and increased tension resulting from the obstruction does not so soon undergo preservative degeneration, as the sound parts preserve their elasticity and recoil fairly. Thus the obstruction of the isolated masses, especially if annular, keeps up the hypertrophy by increasing the tension behind them and the results of increased arterial tension, and thus endangers the patient's existence by the increased risk of some degenerate mass giving way. In these conditions, increased ventricular action could only render them more and more dangerous; the greater contraction and distension would try still farther the degenerate vessels, and could only slightly improve the coronary circulation, and thus only to a small extent diminish the risk of arrest of the heart's

action, while it would certainly greatly enhance the more imminent risk of arterial rupture. If ever hypertrophy is to be regarded as otherwise than an unalloyed good, it is in these conditions. Certainly any attempt to secure it artificially in the manner discribed, would be detrimental to the patient's real interests; as the attempt to extenuate one danger would greatly enhance the hazard of another.

Use in Hypertrophy.—In hypertrophy of the heart, perhaps, the action of digitalis was first, and is perhaps most readily, observed. For, hypertrophy being essentially compensatory, the balance between the blood to be driven and the power to drive it is being already re-established by the efforts of nature. Of course, the effect of a drug whose action is to drive the ventricle into contraction, would be most quickly and evidently apparent in this condition, where a restoration of the balance is being wrought out, than in dilatation where no such compensatory change is being attempted. In hypertrophy, no great amount of the drug would disturb the balance in the opposite direction, and then the symptoms of digitalis poisoning—*i.e.*, of the drug driving the ventricle into an abnormal state of contraction—would be readily produced. This condition was thought to be due to the drug producing a marked sedative effect on the heart, and was considered the strongest proof of its sedative action. The condition of collapse is due to a defective arterial distension, and if that is brought about by a small bulk of blood being thrown into the aorta at each ventricular systole, it matters not whether it be due to a distended ventricle just pumping a little off the top of the contained blood (as was thought the case,) or to its being in a state of unnatural contraction, and only admitting partial distension on the

auricular contraction. Of course, in dilatation much larger doses are not only tolerated, but required; and from there being no attempt at compensating hypertrophy to restore the disturbed balance, a greater stimulus to contraction is necessary to produce the desired results. It is thus comparatively easy to understand here how the early observers, who perceived such marked results follow the use of small doses of digitalis in hypertrophy, conceived the idea of its being a sedative, and dreaded its use in dilatation; in fact, regarding the use of large doses in dilatation as open heresy. A knowledge of its real action, however, explains in a satisfactory manner the apparent anomaly, and explains its effects in each condition; its almost magical effect in hypertrophy in small doses; its tolerance in large doses in dilatation. Thus we see how digitalis is tolerated in large doses for months—nay, years—in cases of confirmed dilatation, where its action, or that of some substance of similar property, is necessary to the preservation of the organism. In dilatation, where the system is confessedly unequal to the establishment of compensatory muscular hypertrophy—of a balance again being struck between the forces of obstruction and the power to overcome it—the use of a drug whose action is to throw the ventricle into a state of tonic contraction is readily understood as being of the greatest service; and this also explains how its use in large and continued doses is not only not productive of symptoms of poisoning—*i.e.*, of ventricular spasm, which was once imagined to be due to an accumulation of the drug in the system in some mysterious inexplicable manner—but is even necessary to the continuance of life. Without it, or some similarly acting drug, dilatation must become only more and more extensive, and hand in hand with that extension must be

an increasing inability on the part of the heart to recover itself; hence still more enfeebled circulation, blood-stasis and its consequences, until the widening vicious circle ends in somatic death. In hypertrophy, where the system is equal to an attempt at restoring the disturbed balance by increasing the muscular driving power, and where occasional palpitation alone reveals the remaining inequality, the use of digitalis soon enables the sympathetic ganglia, and their muscular servants to get over the difficulty, and tides on the system, until a more perfect histogenesis has again struck a balance, and a permanent equilibrium is established. In this condition of compensatory growth and power, the continuance of the drug would soon be fraught with a new danger from the ventricular contraction becoming excessive. This, I believe, is the true explanation of an apparently opposite action of digitalis, which has long divided the ranks of medicine.

It is not that hypertrophy is any bar to its administration, only it is required in less doses. As long as a heart is equal to its work, neither patient nor physician would interfere; but when its inability is revealed by palpitation and the other evidences of over-taxation, hypertrophy does not forbid the use of digitalis, but it is only required in small quantities, as by these small quantities the desired results can be obtained. But it must not be given on any idea of its tranquilising action being in its nature allied to that of a narcotic or a sedative; it is by enabling the heart to contract without laboured effort that it calms excitement. Niemeyer states: "Digitalis in pure uncomplicated hypertrophy is unsuitable. As has been brilliantly demonstrated by Reich, the results of experiments with this medicine on dogs stand in glaring contradiction to the conclusions drawn from experience at the bedside.

(On the Employment of Digitalis in Disease of the Heart. Inaugural address under Professor Niemeyer, Tübingen, 1864.) The action of digitalis, under the use of which innumerable cases of disease of the heart, cyanosis, dropsy, hepatic engorgement, and suppression of urine have been made to subside, is not to lower the centrifugal pressure of the arteries, but rather to increase it. Its use is indicated in diseases in which the action of the heart is weakened, but never in cases where it is augmented" (vol. i, fol. 315) *Text-book of Practical Medicine*.

In Valvular Disease.—In valvular disease, no effect must be expected from digitalis, except so far as it acts on the muscular walls. It happens, however, that alteration in the muscular walls is compensatory; in injured valves so much so, that life may be maintained for years, and sometimes with a fair share of activity, in the presence of serious valvular mischief. Dr. Chambers (*Clinical Lectures*) states "The existence or non-existence of valvular disease lies not so much in the injury it inflicts itself, as in the likelihood of the induction of other lesions of the heart. If the muscular structure remain healthy, injured valves do not appear capable of causing death." In obstructive disease this is readily comprehended, for it can be reduced to simply this. It is necessary for the wants of the system that so much blood be driven through a certain orifice in a given time; and if that orifice be narrowed or otherwise partially occluded, for this to be accomplished it is imperative that the driving power be increased. In fact, hypertrophy is compensatory, and enables this to be done; and where there is this hypertrophy, the patient himself may not be conscious that any morbid change has gone on in him. In fact, between hypertrophy and dilatation again does the balance rock, and with it the

prognosis ; in hypertrophy, as long as it can be maintained, the patient's chance of life is a good one ; in dilatation the aspect is clouded, and an artificial hypertrophy must be attempted. Artificial hypertrophy is no therapeutic fiction, and can be produced by more or less time and perseverance, in a great many cases, by administering agents which produce a better ventricular contraction, and a system of nutritive support ; for the law of increased action being followed by increased tissue nutrition in normal texture is unalterable, if healthy blood be furnished. The good effect of change in the muscular walls in regurgitant valvular disease is not at first sight so preceptible as in regurgitant mitral, for instance, where the question is far from an uncomplicated one. No observer of much experience will have any difficulty in recalling numerous instances of mitral regurgitation with hypertrophy, or dilatation, or both, of the left ventricle, and where the ventricular change is consequent. Let us see how, where no drug has been administered, the system's power of repair has set up compensatory changes. Valves, it must be remembered, are not found in hearts of the lowest grade, and are only belonging to complicated and involved hearts ; the primitive heart is a mere "pulsatile sac", a thickened and dilated section of a tube. So, when the valves are injured, the heart is reduced to a lower type ; that is, the muscular walls no longer get that aid from the valves to which they have been accustomed, and consequently augmented work and increased growth are entailed. In fact, the muscular structure is no longer aided by this beautiful mechanical contrivance, and so change in itself is necessitated. The blood is no longer thrown forward into the aorta at each ventricular systole completely, but a portion regurgitates through the imperfect auriculo-

ventricular valve, and thus overloads the venous system behind. The pulmonic system and the right ventricle undergo compensatory changes of dilatation with thickening; the power of the pulmonic system, in fact, is generally increased; the blood pours into the left ventricle on its diastole, under great pressure, and thus distension of it follows, with hypertrophy or dilatation as its usual concomitants; the usual question of restorative power of the system deciding whether. The consequence of this change is one little to be expected by any one who has not given the subject of compensatory changes its proper consideration. It is this; that, in spite of the regurgitation of a considerable amount of blood, it (the ventricle) remains capable of filling the aorta (Niemeyer). That it does so with more or less success is evidenced by the irregularity of the pulse—not irregularity in time, but irregularity in volume, sometimes nearly the whole amount of blood passing forward, and then again a great portion passing backwards. But to achieve this change in the left ventricle, increase of growth behind the lesion is unavoidably necessary; without the opposition of the blood in the pulmonic system, and the hypertrophied right ventricle, this would be unattainable. Thus we see that muscular change is compensatory in regurgitant disease behind, as well as obstructive disease before.

Sir Dominic Corrigan considered the advantage of administering digitalis (and the fact of relief being afforded by it is unquestionable, however defective the explanation) to lie in its rendering ventricular action slow. Thus in aortic obstruction it allowed the ventricle more time to perfectly empty itself into the aorta; that is, compensation took place by more time being allowed for the passing of the blood into the aorta through the narrowed orifice.

The objection to this theory lies here : there is a diastole, as well as a systole, and a prolonged systole must necessitate a shortened diastole, or no compensatory good can accrue. For the ventricle must be filled before systole, and that requires time ; so that if the advantage lies in the retardation, it is difficult to see how it is any advantage. There must, on this explanation, be so many fewer contractions in the minute, and the wants of the system would be as unsupplied as ever. It is not, and cannot be, a question of time, but of power. What comes of the hypertrophy which occurs in obstruction ? To what is it compensatory on the theory of time ? After the ventricular action has been rendered slow, the hypertrophy ought to pass away, as it does in a parturient woman. Whether it does so or not, I cannot tell, as I have not found the pulse made slow in aortic obstruction in my experience. So in mitral obstruction it was supposed to be beneficial by allowing the auricle more time to empty itself into the ventricle. But, unfortunately, the same objection meets us here, and, further, the ventricle is nearly full when the auricle contracts. It is the distension of the auricle which evokes contraction ; its contraction produces distension of the ventricle, which distension then provokes ventricular contraction, but the ventricle is nearly full when the auricle contracts. In mitral regurgitation, the retardation could have no good effect. The question is not one of time, but of power. In obstructive disease, a simple hypertrophy enables the ventricles to throw an equal quantity of blood through a narrowed space in a given time. In order that an equal quantity of blood may be driven through a narrowed orifice in an equal time, we must have increased power. No other arrangement could possibly achieve the result. In regurgitant disease, the

question is not nearly so simple ; and in order to comprehend exactly how digitalis can give relief in mitral regurgitation, a digression for a little time is absolutely necessary, so that we may review the changes which the normal conservative power of the system, unaided by art, can produce ; and it is in imitating or assisting these changes that we can alone hope to be of service. The effect, then, of mitral insufficiency is regurgitation into the pulmonary veins. The lung-space is unduly filled with blood, and therefore has not sufficient space for air ; hence the dyspnœa commonly found as a symptom of this lesion. The circulation is impeded, and the blood is imperfectly aerated, and flows less readily into the pulmonary veins from the capillaries.* Thus there is further tendency to pulmonary engorgement and obstructed flow. This impediment to the flow of blood from the right ventricle entails in it changes. The right ventricle becomes dilated and hypertrophied. First there is dilatation, and then hypertrophy comes to the rescue. The overloading of the pulmonic circulation leads directly to changes in the muscular walls, and again the battle of life or death rests on the power of self-growth in the involuntary muscular fibre. If the yielding lead to degeneration, sudden death is the probable result at no distant period ; if to a lesion in the tricuspid, then the stress falls back on the veins, and dropsy results, with all its train of troubles. The temporary effusion through the walls of the veins or venous capillaries often gives great relief to the patient ; in fact, the blood, overladen with water, is relieved of part of its burden, the overcharged circulatory system is somewhat eased, and the improvement of all the systemic symptoms

* The question of the readier flow of blood containing oxygen is not one to be entertained here.

is consequent. But it has added another trouble in the future, and the passing relief is embittered by the reflection that it is a mere bill of accommodation that will soon be due again. The relief to the distended venous and pulmonary systems sometimes admits of their recovering themselves to some extent, but this is unfortunately only a rare occurrence. Dropsy, that is effusion from distended capillaries, is also taking place into the pulmonary tissues, and pulmonary œdema increases the patient's woes; blood even may be effused when the distension is great, and there is no more alarming consequential symptom of mitral regurgitation than hæmoptysis. The stress on the systemic veins directly affects the systemic circulation, and increases the stress on the left ventricle; increased difficulty of flow is superadded, and the pulmonary engorgement is redoubled. In addition, the liver is gorged, and the spleen distended; the kidneys are in a condition of asthenic congestion, and the pressure on the glomeruli is lessened; thus the flow of water by dialysis is interfered with, and the bulk of urine radically lessened; and thus we have an extended circle of mischiefs aiding and abetting each other, acting and reacting till it becomes difficult to ascertain the starting point. This is no exaggerated or even highly coloured picture of the condition of the patient suffering from mitral insufficiency and its consequences. But against this train of troubles must be set the power of hypertrophy in the right ventricle. If there be sufficient compensatory change, then all this may be arrested for a long period of time. Increased activity of the right ventricle gives relief to the general symptoms. The blood pouring into the left ventricle under greater pressure, and its reflux being opposed by a greater *vis a tergo*, more blood is thrown into the aorta, and thus better aortic

distension follows the muscular activity as a necessary consequence. Thus the action of digitalis on the right ventricle is of the utmost importance, while its effects on the capillaries aid in sustaining the increased pressure on the pulmonic circulation. By its use, we aid that natural thickening and increase of substance which the system spontaneously sets on foot on its balance being disturbed. In some conditions, aid is unnecessary for years, or may only be required during some debilitating action, but it must never be withheld when a trying affection like bronchitis is testing to the utmost the patient's power of resistance. In other cases where the natural efforts are visibly unequal to the demand, and the struggle is being abandoned, the aid we can furnish may be less effective, and the restoration of balance more imperfect; still it is worth the trial, and tends to prolong the existence of the organism. We must never forget that, in regurgitation through the mitral valve, the condition of the right ventricle and its allies is the only hope of the physician. It is, then, to the action of the right ventricle that we must look for assistance when trouble is due to the mitral insufficiency; and it is by augmenting the contractile action of the ventricular fibres, and its effect on the capillaries by opposing their distension, that digitalis can be useful in mitral disease; for the troubles of mitral obstruction are those of mitral regurgitation. It is to the loss of compensatory action, or, rather, the inefficiency of it, that we must attribute the want of success in our treatment of tricuspid regurgitation. The increased action of the right ventricle is not lost over the short length of the pulmonic circulation, while the increased action of the left ventricle is lost over the length of the systemic circulation, and therefore exercises no useful effect in opposing the regurgitation of the blood in tricuspid insufficiency.

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 indications 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 dyspnœa. 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 the interstitial inflammation of the valves and orifice is very gradual, the muscular 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. Relief, 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 a 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 *cor bovinum*, an excessive enlargement of the left ventricle, both in thickness and

cubic space of cavity. The regurgitation through the aortic valves produces increased and 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 necessity 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. In-

creased 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 contra-indicated 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 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 distention 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

* For an able investigation of this subject, see T. W. King's article in *Guy's Hospital Reports* for 1837. This subject and the function of the "Moderator Band of Reil" are discussed by the writer in a paper in the *Edin. Med. Journal*. December, 1870.

be organized. 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 complete-

ly 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 neurosal, 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 neurosal, 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 a 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 connection being consequential. Further use of it in these attacks in the same person corroborated that be-

lief. 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 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 muscu-

lar 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 dyspnœa, 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 com-

paratively 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 vasomotor 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*, 1867-68.

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 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 illuminating 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 unmistakeably 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.

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 neu-

tralised 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 uræmic 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 shown 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 enquiry. 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 desira-

bility of administering or withholding 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 contraindication *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 administering 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.

Drugs of similar Power.—The whole question of agents acting upon the heart so as to increase its power of contraction is comparatively new. With the exception of digitalis we are, generally speaking, scarcely acquainted with their names. The agents are either entirely new,

or nothing has hitherto been known of their secondary effect upon the heart. The list of them is a short one, and will not take up much space in the enumeration. Thus Dr. Clifford Allbutt has advocated the use of Virginian cherry-juice (*Prunus Virginiana*) in cardiac affections; Dr. John Harley has investigated the action of belladonna; Dr. Braidwood the action of dajasck, or arrow-poison of Borneo (*Tanghanina venenifera*); Drs. Hilton Fagge and Stevenson have investigated the action of the *Scilla maritima* and the *Helleborus viridis*; and Leven has investigated caffein and thein. Of these, the writer has only experimented on digitalis, belladonna, and caffein. There is thus plenty of opportunity for investigating further the action of these drugs, and adding to what we already know of their action; while there is a ground for hope that to this list may be added new agents more certain, more effective, and more manageable than those we as yet possess. It is, then, with the hope and expectation that such will be the case that the writer has devoted so large a space to the consideration of the mode of action of digitalis. He has striven to aggregate what is known of the subject, and his own more recent conclusions, in order that the question may be regarded as broadly as possible. The frequent digressions and the consideration of the action of the morbid process have sometimes been considered at greater length than the administration of the agent; as, once admitting the increase in the activity of the ventricular contraction as the chief therapeutic action of the agent, the question of the value of the agent must rest on the question as to how far increased ventricular contraction may or may not be beneficial. By thus treating digitalis as a member of a class of agents, it will much facilitate the investigation into the usefulness, or uselessness, of a drug

as a cardiac neurotic. It is obvious that other agents which increase the ventricular contraction and bring the heart to a standstill in systole must necessarily possess a therapeutic value allied to that of digitalis. In prosecuting such an enquiry, it will be easy to ascertain to what extent the action is common to that of the whole class, or in what it is singular. This grouping of agents as to action will assist us in aggregating a number of agents with either a primary or secondary effect upon the heart; in time this will constitute a group, and in practice the remote effect of an agent upon the heart will be taken into consideration in the choice of therapeutic agents. Thus, we as yet can merely guess to what extent the different actions of opium and belladonna, as hypnotics, may be dependent, as regards the success or non-success following their administration, on the vascularity of the brain. How far the beneficial effect of belladonna, at times when opium has failed to relieve, may rest directly, not on the different hypnotic alkaloid, but on the vascular supply of the brain being augmented by its use, we know not. Thus a series of experiments with belladonna in delirium tremens, similar to those of Mr. Jones of Jersey with digitalis, when the pulse is feeble and fluttering, would be of the greatest practical interest. These might then be contrasted with a series with opium; and thus from a few facts we might attempt to build up a principle, and the application of that again to cases would in time furnish us with a law worth any amount of empirical guessing. It is only by the grouping of agents and then testing them by clinical experience and physiological experiment, observing the successes, the failures, and their causes, that we can expect to emerge from our present therapeutical chaos. Thus, under our old plan of empirical testing of agents, colchicum

has six or eight (I forget which) times been removed in and out again of our *Pharmacopæia*. The same, to a less extent, has occurred to numerous other agents of no trifling activity. It is obvious that the use of these agents has been conducted on nothing approaching a law, else some definite conclusions one way or the other must have been arrived at. Without some definite idea of what it is we want exactly to attain, and by what action our agent is likely to achieve the desired result, we cannot be said to do anything more than—to use a vulgarism—“make shots.” The experiments of Crum Brown and Frazer into the physiological and chemical agency of drugs, and Broadbent’s valuable speculations on chemical tension, and the question of the retardation or aiding of oxidation as a mode of explaining the action of many agents, are steps in the right direction, the value of which we are scarcely yet in a position to correctly estimate. The advance of therapeutics hand in hand with increasing knowledge of physiological and pathological processes is much to be desired. It is scarcely cheering to find men who are teachers telling us that they have found rest in bed the only useful treatment in diseases of the heart. What, then, must become of those who must work or hunger? A hopeless therapeutical scepticism will never solve the problem how to enable those injured by rheumatic fever to be still useful members of the community. If rest in bed were all that modern medicine can do for these supplicants, many of them valuable lives, with good work in them, then we need not wonder at their regarding it as giving them a stone when they ask for bread, and at their trying hydropathy or homœopathy in sheer despair. The question is, how far can we not only enable them to live, but endow them with capacity to labour. This utilising a large number of lives which

would otherwise be rendered inutile, is a problem which it is in the province of medicine to solve. That even with our present imperfect knowledge of these agents, much has been and is being done by numbers of enthusiastic workers at this field of inquiry, is unquestionable. In the present consideration of the mode of action of digitalis, the writer has striven so to arrange his materials as not only to elucidate the agency of it, but also to establish some broad rules applicable to the agents as a class, if once the action of the drug, as being capable of increasing ventricular contraction, be established. In order, then, to elucidate as far as possible this subject both particularly and generally, the action of morbid processes and the mode by which Nature proceeds to spontaneously repair them, or to compensate the lesions, have been subjected to critical review, and their indications recorded. The subject is one which must necessarily require great labour and pains to bring to anything like perfection, and anything written here must be considered as necessarily incomplete. The consideration of the question of increased ventricular contraction has been so conducted as neither to include nor exclude the question as to whether this group of agents are cardiac sedatives or tonics; in fact, it becomes more and more difficult to draw a distinction betwixt the two. The writer has thus striven to avoid all controversial enquiry on these heads, and by laying down the increased ventricular contraction as the action *par excellence* of digitalis, has striven so to conduct the investigation as not only to fix, to some extent at least, the action of the agent, and to demonstrate how it affects morbid conditions, but also to clear so much ground towards the successful investigation of allied agents, and the establishment of a new class of agents whose importance

in the future we cannot estimate, but about the value of which we may at least be permitted to hope.

Its Action in Nervous Affections.—From the unquestionable benefit resulting from the administration of digitalis in some nervous affections, an impression has existed that it exercises a neurotic action, or to be more explicit, that it has some more specific action over the nerve-centres. Like all powerful therapeutic agents, it has enjoyed an ephemeral reputation in the treatment of epilepsy; and from the undoubted influence it possesses over the vasomotor system from the heart to the capillaries, it is conceivable enough that in some cases, its use was followed by benefit, but only it is improbable that it possesses any influence other than that it exerts over the circulation. Serré used Debout's pill, consisting of four-fifths of a grain of digitalis, and one grain and a half of quinine, in the treatment of hemicrania, continuing it for long periods together. The success which followed the treatment was greatly influenced no doubt by the quinine; in fact, it is difficult to rid oneself of the impression that the quinine had the most to do with the result. Lockhart Robertson found that in certain cases of maniacal excitement in general paresis of the insane, its use was attended with marked benefit. He states: "It acts in every case of the kind in which I have given it as a specific, calming the excitement, and enabling the patient to pass without wear or irritation through this stage of the malady. Its action has been to steady the pulse, and thus apparently to supply the brain better with blood, and so obviate the tendency then existing to effusion of serum."

In Delirium Tremens.—The use of digitalis in heroic doses by Mr. Jones, of Jersey, with marked success, is one of the extraordinary facts of therapeutics. The

administration of the tincture in half-ounce doses, and repeated, too, at short intervals of time, was found to exercise an action that was almost amazing in delirium tremens. It was attempted to make out that this was due to the half ounce of proof spirit; but that was simply preposterous. The amount of digitalis in four drachms of the tincture must have exercised an influence of some kind. Neither has it been found to be universally successful in attaining the desired result. From personal experience, I may state that it is when the pulse is compressible, rapid, fluttering—in fact, when there is evidence of cardiac distension accompanied by great nervous prostration, that its administration is followed by beneficial results. The condition of the brain is one of anæmia from cardiac feebleness; while that feebleness is no doubt occasioned by the exhaustion of nerve-force, by the continued administration of the alcoholic stimulus. The sympathetic is exhausted, and cardiac distension follows; from that, again, imperfect circulation and cerebral anæmia; the exhausted brain is deprived of its blood-supply to a great extent; less and less nerve-force is evolved; the sympathetic is still further enfeebled; and the condition of a complex cerebral anæmia, called delirium tremens, ensues. The administration of digitalis in heroic doses produces a decided effect on the circulation, and that, again, relieves the brain, in a manner strictly analogous to that described above by Dr. Lockhart Robertson. When the pulse is full and sustained, and there is no great prostration, its use is not followed by any desirable result.

In Anæmia of the Brain.—In some conditions of cerebral anæmia dependent on disease at the aortic valves, digitalis exercises a decided beneficial action; so much so, indeed, that it is easily conceivable that it might be regarded as a

nervine tonic. In speaking of anæmic conditions of the brain, Todd in his *Cyclopædia*, Art. Abnormal Anatomy of Nerve-Centres, states—"It is also present when the heart, oppressed by some disease affecting its own structure fails to propel the blood with its proper force into the brain." A most interesting instance of this has fallen under my notice. An old and visibly feeble lady of 70, was subject to attacks coming on suddenly, during which she fell, but did not lose consciousness. This at once cleared away any suspicion of epilepsy, and suggested the condition of acute cerebral anæmia. That is, the supply of blood to the brain became so interfered with, that the brain was unable to evolve the normal amount of nerve-force, and the patient fell just as in swooning; in fact, it was syncope. The falling thus took off the weight of the blood-column above the heart, and thus gave relief to it; while at the same time, the head falling as low as any other part, the blood gravitated into it as readily as into the rest of the body. There was aortic obstruction, and, after some careful watching, it became apparent that the attacks came on whenever there was any approach to exhaustion, either from physical or mental effort. That is, the amount of blood passing out of the narrowed outlet was sufficient to maintain a species of integrity of nerve-manifestation for the wants of the system when all was quiet; but exertion, by overtaking the power of the heart, led to anæmia of the organ placed highest up in the organism; and then the fall, by restoring the circulation through the encephalon, and permitting to the heart a period of comparative rest, comes to the rescue and allows of readjustment. The administration of digitalis and consequent improvement of the heart's action, invariably gave her relief, and enabled her to undergo more exertion with-

out the attacks of syncope, and relieved her from them when recurring after any exhaustion. The period of benefit lasted for some time—in fact, as long as any evidence of its action on the heart remained. The beneficial effect of its use in cerebral affections can only, I believe, be explained after this fashion. Cerebral disorder is frequently due to cardiac disease; and when it is so related, and the nervous affection can be regarded as a sequel to the cardiac impairment, whether to persistent disease or debility referable to passing circumstances—when the head-symptoms can be clearly attributed to failure in the heart's power of blood-propulsion—then the administration of digitalis may fairly be calculated upon to be beneficial. When cerebral anæmia has a cardiac origin, then, and then only, I believe that digitalis is of service.

Is Digitalis a Diuretic?—If by a diuretic is meant an agent eliminated by the kidneys, and producing increased secretion in the true sense of the word, then certainly digitalis is not a diuretic. If by a diuretic is meant an agent which increases the renal secretion by some special action, as juniper or cantharides, irrespective of an alteration in the arterial tension, digitalis can lay no claim to the appellation. Digitalis is not a true diuretic, though perhaps no material in the *Pharmacopœia* produces such decided increase in the renal flow as it does; but only under certain conditions. An alteration in the blood-pressure on the glomeruli of the kidney affects the flow; if that pressure be decreased, as in advanced cardiac disease, with enfeebled circulation, then a small quantity of urine is passed. If that pressure be increased, no matter how, increased flow follows. Thus, for instance, a large imbibition of water, by passing into the circulation and producing increased pressure on the glomeruli, will soon

affect the renal flow unless some other excretory organ be very active. When the skin is acting freely, and a large quantity of blood is located in the vessels of the skin, a sudden cooling of the skin is followed by diuresis, the cold contracting the cuticular vessels, and thus driving the blood internally, and increasing the pressure on the vessels of the viscera. Interstitial nephritis or cirrhosis of the kidney acts as a diuretic in the same manner. So much of the structure of the kidney is destroyed for all useful purposes; and therefore, as no diminution takes place in the calibre of the renal artery, there is increased pressure on the remaining uninjured portion, and thus there ensues increased diuresis—one of the prominent early symptoms of cirrhotic kidney. So, also, the flow of limpid urine in hysteria. We know that in hysteria there is a diminution of the calibre of the arteries, due to derangement of the vaso-motor system, and accompanied by increased action of the heart to overcome that condition, so much so as often to bring out palpitation; thus the pressure is again increased, and diuresis follows. But these conditions, though producing an increase in the renal flow, are not true diuretics. Digitalis in a similar manner acts as a diuretic in enfeebled conditions of the circulation, by increasing the arterial tension, as described in a preceding section. When administered to people in health, it does not increase the flow of urine proper—that is, of salts as well as water. Stadion put himself upon a strict diet, and took digitaline, and his urine was diminished. Wino-gradoff gave digitaline to several persons for five days, and found no results, except in one, and then there was diminution. Brunton, who experimented on himself freely, found increased diuresis; but on the day marked “intoxication,” there was a distinct fall. The case of poison-

ing related by him illustrates the effect of digitalis well. He says: "The amount of urine in my own case was markedly diminished during the period of intoxication, when the gastro-intestinal canal was most affected; and in the case of Daniel G., when the pulse was most affected, it fell from an average of between 40 and 50 ounces to 30 ounces on December 2nd, 25 to 26 ounces on the 3rd and 4th, and 18 ounces on the 5th and 6th; again slowly rising, till on the 10th it rose from 25 to 44 ounces, and then remained at its normal standard." Christison and Mazel both noticed suppression in cases of poisoning by it. Boulby and Reynal found a temporary suppression in the horses experimented on by them. In fact, when digitalis is producing those symptoms of intoxication which accompany a too firmly closed ventricle, a diminution in the flow of urine is one symptom. But then that is merely again a question of arterial tension. If a small quantity of blood only be thrown into the aorta at each ventricular systole, it makes no difference whether it be due to a state of over-contraction and imperfect distension of the ventricle, or to an imperfect systole. The effect is the same, whether due to the imperfect contraction of distension, or to the imperfect dilatation in the unnaturally contracted condition of the ventricle, which takes its rise in the excessive administration of digitalis. When the digitalis is given beyond the point of maximum arterial tension resulting, then the urine is diminished in quantity; the flow and the arterial tension being indissoluble. Thus, when given in cardiac disease, when an imperfect systole does not produce arterial tension, it increases the flow of urine which had previously been defective. When administered to poisoning, even total suppression may follow. In fact, my opinion is identical with that of Dr. Germaine: "there

is no proof that digitalis possesses diuretic properties, the reputation conferred upon it to this effect by Withering having been accepted without discussion; and the diuresis which often follows when an amelioration of the condition of the circulation has been produced by it in organic disease of the heart, is only a mediate effect, resulting from the return of the circulation to its normal condition." On the other hand, the flow of urine following its administration in enfeebled conditions of the heart, is so affected as to be, in one case at least the writer knows of, in itself a source of danger.

The Use of Digitalis.—Like other vegetable substances, digitalis is prepared for use by either tincture, infusion, extract, or separation of the active principle digitaline. The extract is little used, and personally I know nothing about it. The tincture is the most convenient form ordinarily, but throws down a dark green precipitate with iron, which detracts from its desirability. For general use, it can be given along with the ammonio-citrate of iron, or, still better, the potassio-tartrate. It is better kept in a dark cupboard or wrapped in a dark coloured paper, as light is supposed to act deleteriously upon it, weakening it and lowering its activity. The infusion is a good preparation for use along with potash or diuretics, and is conveniently added to vegetable infusions. Digitaline in solution may be the most elegant form, and perhaps may be found ultimately to be the most exact form for accurate administration; but a strong impression against it was left on my mind from experiments on frogs, when a solution of digitaline did certainly not produce such a decided effect as the tincture upon the ventricular contractions. It is certainly possible that the other constituents, digitalose, digitalic acid, etc., may possess properties peculiar to

themselves; and when the importance of a knowledge of the action of different agents on the heart-walls becomes fully recognised—for as yet we are only on the threshold of the inquiry—a careful investigation of them may not be barren in results. This field of inquiry is a most promising one; and no more important addition could be made to the present usefulness of medicine than a perfect knowledge of the action of agents on the heart, either in the chronic condition of persistent alteration—either as a primary or secondary lesion, or in passing conditions. We have long been acquainted with the frequency with which cases occur when, in chronic disease, the question of the integrity of the muscular walls of the heart, or of structural change in them, guides our prognosis as to how long the struggle may be maintained. We are, too, gradually recognising the failure of the right side of the heart in asthenic disease or affections of the respiratory organs, as the channel through which death commonly approaches; we can calculate how certainly the right ventricle, taxed to the utmost, becomes gradually paralysed by the carbonic acid of its contained blood anæsthetising its action. If we can find means to keep up its action, we may tide that patient on to recovery; while in the present state of our knowledge, the condition is only recognized by a few, and the means of producing any impression upon the condition by therapeutic agents confined to the hopefulness of only a very few. In the treatment of chronic conditions, when it is necessary to keep up the administration of digitalis until structural changes are produced, perhaps the powdered leaves are the most desirable form. In this form, it can be given in pill with the dried sulphate of iron, carminatives, laxatives, or both, and in this form will keep some time, and can be

given twice a day without causing the patients to revolt at its nauseous taste, or creating any aversion, on æsthetic principles, to its muddy-looking combination with iron. For long, a favourite form of pill with me for persistent use has been a combination of half a grain to a grain of powdered digitalis, with an equal quantity of the dried sulphate of iron in powder, and a morsel of cayenne, in extract of gentian, or aloes and myrrh pill. Thus we secure at one cast an action on the circulation, the addition of iron in a form which will act locally on the stomach, and thus act as an astringent in the gastric catarrh so common among the sufferers from heart-disease; while the carminative action of the cayenne is useful, and also takes off the griping from the action of the laxative, when an action is also necessary, as is commonly the case, on the bowels. I have had patients for months, and in some cases even years, thus under its influence in the most satisfactory manner. With their box of pills they can go anywhere, can take them about, and have a reserve stock if necessary; and then, twice a day or so, a pill can be taken without any inconvenience or parade of medicine-taking. One point of some importance must not be forgotten in this mode of its use, viz. that the pill must be taken shortly after food, otherwise it may be pouched in a fold of the stomach, and lie dormant, or it may be passed at once into the bowels, and its good effects lost. The pill is an artistic application of scientific research to the food, and must be regarded as such essentially, as, in fact, must all restorative remedies. In the use of digitalis, the addition of iron is of great importance. Some may raise objections that the good effect is due solely to the iron; but surely the constant administration of so potent an agent as digi-

talís cannot be without some effect. The results thus attained appear too early to be the mere effect of the iron. While the attempt to produce better nutrition of the heart from its use, as we saw in a preceding section, does actually succeed, the addition of iron, from its hæ-matic properties, aids us most materially. From the cheering results which I have witnessed in numerous cases of chronic cardiac disease, and the great alteration effected in the patient's condition, both as regards comfort, or, rather, relief from discomfort, ability to take more exercise, and even to undergo more exertion in those cases where the patient's circumstances necessitated labour, I can urge most honestly and conscientiously its use, and especially in this combination.

Another application of it is very important, and that is its absorption through the skin. In many instances, it is desirable to bring out the action of the digitalis when the risk of disordering the stomach may act as a check, or even when there is already great gastric disturbance. Here it may be used by either poultices of the leaves, or flannels soaked in the infusion, or a mixture of the tincture and water applied to the abdomen and thighs. Cases are given by Christison of such use of it. Trousseau relates a very interesting case where very decided results were thus obtained (vol. i, chap. xxxv). Some cases were recently detailed in the journals of such use of it. This manner of administering digitalis should never be lost sight of, as it may now and then enable us to do what we cannot accomplish by the mouth.

Hypodermic injection is another mode of administering it which should not be overlooked. Certainly, in the experiments on frogs, this was chiefly resorted to on account of its convenience. Bouillaud pursued an endermic

treatment by dusting a blister over the heart, with from six to fifteen grains of powdered digitalis. These various modes of administering digitalis have each their advantages according to peculiar circumstances. No one plan of action must bind the practitioner's mind in fetters. He must be ready and willing to use each in its place, or even to substitute for digitalis some drug of similar action. From the known intolerance of mercury in some constitutions, and notably in those suffering from cirrhosis of the kidney, which is often followed by consequent heart-mischief, with its train of sequelæ, the old combination of digitalis, squill, and blue pill may have to be abandoned, and for the blue pill iodide of potassium substituted. Patients' prejudices, as well as their needs, must be consulted. It is much to be desired that some drug may be discovered with equal properties to digitalis, and about whose action no preconceived opinions, based on imperfect observation, may bias the minds of medical men. It would be easier to establish the use of such an agent especially in this experimental age, than to war against a settled impression. And though at present the list of agents possessing an action on the heart, and through it a control over the circulation, may be a very limited one, but at the same time very important, the day is not far distant when the importance of inquiry in this direction will make itself felt. I have not claimed for digitalis anything for which it cannot fairly substantiate its claim, nor have I accorded to it any mystical action, differing from that of any other therapeutic agent. I have striven, as far as possible, to exercise the functions of a judge, as well as of an advocate, and tried fairly to lay down what, in the present state of our knowledge, digitalis can do, and what it cannot. And I am quite willing to labour under the disadvantage of

being regarded as an enthusiast, if only the subject can get that attention paid to it that it deserves; and my experience tells me in language that is unmistakeable, that the effect of agents upon the heart, of which digitalis is the most powerful one with which we are yet acquainted, can no longer be overlooked by any one in the profession who regards either his own interests or those of his patients.

