

**The action and uses of digitalis in cardiac failure : a clinical lecture delivered at the Hospital for Consumption and Diseases of the Chest, Brompton / by J. Mitchell Bruce.**

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# The Action and Uses of Digitalis in Cardiac Failure (2.)

## A CLINICAL LECTURE

Delivered at the Hospital for Consumption and Diseases of the Chest,  
Brompton

BY

J. MITCHELL BRUCE, M.A., LL.D.(Hon.), M.D., F.R.C.P.

*Consulting Physician to the Hospital and to Charing Cross Hospital*

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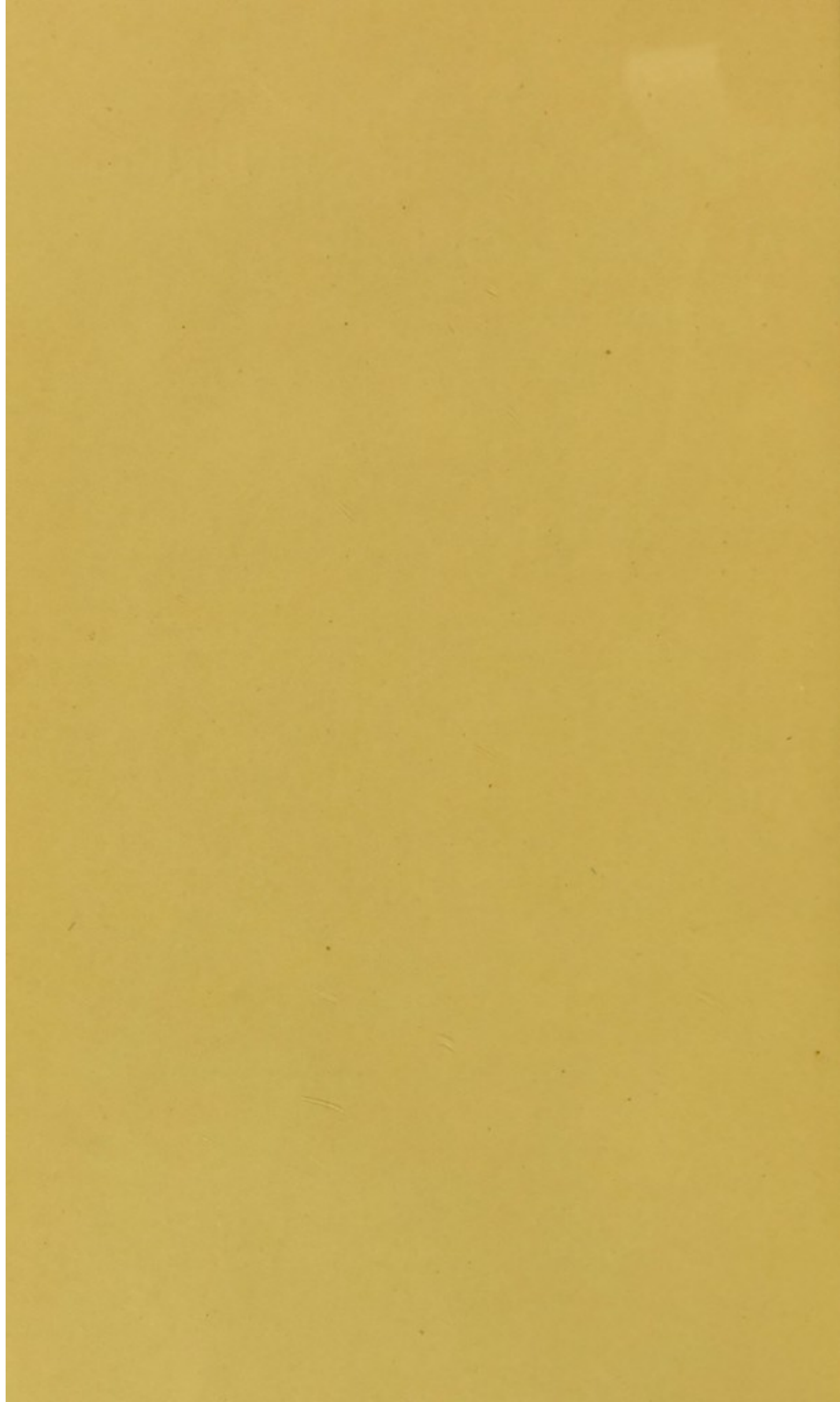


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# The Action and Uses of Digitalis in Cardiac Failure

## A CLINICAL LECTURE

*Delivered at the Hospital for Consumption and Diseases of  
the Chest, Brompton,*

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HOSPITAL

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GENTLEMEN,—It is but seldom that the record of the course of a single case of cardiac disease, or indeed of any disease, for a few weeks furnishes material for a clinical lecture to practical post-graduate medical men like you. I feel that I ought to introduce my subject this afternoon with an apology for such an attempt; and you will forgive me also, I trust, if I speak in a straight, plain, dogmatic fashion, treating you, as it were, like students round a bed. This is a necessary result of our having to consider the details of the treatment of an individual patient who has already left the hospital. I have not the patient here, but I have behind me a chart which exhibits graphically the course of his disease as far as it concerns us this afternoon, including more particularly the action and uses of digitalis. I propose



to demonstrate to you the observations thus recorded, and to discuss them serially and as a whole.

The case itself was full of interest pathologically, but I will not dwell on this aspect of it, except so far as is necessary to illustrate certain points in the action and uses of cardiac remedies. The patient was a man of 27, a 'bus conductor, who was under my care in Charing Cross Hospital from November, 1903, to February, 1904, suffering from failure of the heart with dropsy in connection with valvular disease of rheumatic origin. The valvular lesions were mitral incompetence, mitral stenosis and aortic incompetence, with well-marked physical signs, including the characteristic murmurs, in addition to which a tricuspid systolic murmur was also audible. On admission, November 23, the patient was cyanosed and suffered from orthopnœa, præcordial distress, and extensive œdema; the pulse was extremely irregular in force and rhythm, 94 beats reaching the wrist per minute; the liver enlarged and pulsating. You will observe that in every respect the case was an ordinary one, and I need only add that the evidence was that the heart had failed in consequence of exposure and exertion. This was the second occasion on which compensation had broken down within a few years.

The patient was at once put on what may be called our routine treatment for cases of the kind. He was in bed, and properly nursed; he had a somewhat dry, solid diet, including fish, chicken, bread and butter, and light pudding; and to this was added from  $1\frac{1}{2}$  ounces to 3 ounces of brandy per



diem. After an immediate dose of 3 grains of calomel, followed by white mixture, he was given half a drachm of compound jalap powder every morning, and he took 10 minims of tincture of digitalis with potassium acetate and tincture of nux vomica every four hours. A proper record was kept of the daily observations made in connection with the case, and those which were expressed numerically were represented in the form of a chart, which I will now show you, omitting the temperature curve, which does not concern us now. The two curves which you see represent respectively the pulse-rate and the volume of urine passed; and it is by these curves that I wish to order my discussion of the action of the remedies employed.

The first striking feature of the urine curve is its low range for the first week. It starts, you will observe, at 16 fluid ounces on the man's admission, reaches a maximum of not more than 30 fluid ounces on the fifth day of treatment, and falls again to 23 fluid ounces on the seventh day. This was a most disappointing result. After a whole week of thorough treatment with the remedies which I have mentioned there was no diuresis. It is true that, as you will see by the other curve, the pulse-rate had begun to fall, so that the digitalis appeared to have begun to act upon the heart, but so far no impression was made on the kidneys. I have called this a disappointing result, for our experience is that diuresis as the effect of digitalis in cardiac failure occurs by the middle of the first week of treatment. However, this dis-



appointment is a convenient feature of our case for my present purpose. It serves to demonstrate to us with uncommon clearness the first point which I desire to make in our discussion—namely, that the diuresis produced by digitalis in ordinary doses of the pharmacopœial preparations does not make its appearance for several days.

This slowness of action of digitalis must be distinctly appreciated. We must be prepared for this, powerful and trustworthy drug as it is. As we have just seen, it begins to steady the heart meanwhile and to relieve distress; but that striking change in the whole aspect of the case which attends profuse diuresis does not occur for the first two or three days. Two practical considerations follow on this fact. The first of these is that during this preliminary period, or period of suspense, other more rapidly active drugs usually have to be given, including caffeine, ether, ammonia and strychnine. The second practical consideration is that we must be prepared to wait patiently for the diuretic action of the drug to be displayed. We must not hastily conclude that it is useless if it have not produced a rapid effect like strychnine subcutaneously or a dose of ether. Digitalis takes days to increase the flow of urine. To convince yourselves on this point you have only to look at the smaller charts which I hand round. In all of these you will observe that the urine curve invariably remains low for two or three days.

But to return to our own case. The fourth, fifth, sixth and seventh days passed, and no diuresis had



made its appearance. If one feel anxious and become sceptical of the value of digitalis, as one may be tempted to do, on the third day, what was one to think of a drug that had made no impression on the kidneys by the seventh day? It would not have been altogether unreasonable to conclude that it was useless and that it must be dropped for something more efficacious.

This brings me to the second phase of the case. On the seventh day, instead of removing the digitalis, from distrust of it, I gave it more freely. Finding the volume of urine only 23 fluid ounces, I raised the dose of tincture of digitalis by one half—that is, to 15 minims every four hours. The effect was striking. Next day 35 fluid ounces were secreted; on the following day 70 fluid ounces; and after keeping on this level for four days the amount rose to 80 and then to 100 fluid ounces. Thus my action was justified by the result. The end that we had been working for from the first was attained: the kidneys were rapidly clearing off the arrears of excretion; the dropsy disappeared, and the patient was relieved. We had learned another lesson—that digitalis to be useful must be given freely.

This is an all-important point. If we are to get real good from digitalis in cardiac failure, it is very little use giving a moderate dose. If we are to get real good from it, we must not be afraid to use enough. I insist on this point because I find it is quite usual for digitalis to be given in 5 minim doses three times a day, or perhaps six times a day. Un-



doubtedly 10 minims every four hours in the majority of cases should and do suffice. But here is an instance where it required a much larger dose, and from which we are justified in coming to the conclusion that the discredit into which digitalis has fallen amongst certain authorities may have been due to their not having given enough.

But there is another aspect of this part of our subject. When a full dose of digitalis, such as 10 minims of the tincture every four hours, has been given for several days, and the pulse is found small, irregular and frequent, the drug might be regarded as not only useless, but as worse than useless—as positively dangerous, and accountable for the wretched state of the heart and pulse. The toxic action of digitalis might be believed to have been developed: the patient supposed to be being poisoned by a drug that kills by paralysing the heart. This would be an entire error, and an unfortunate one. I have just shown you the effect of the largely increased dose on the urine curve; now look at the pulse curve. Instead of remaining frequent and feeble and irregular, the pulse, you observe, fell to 50 when the excretion rose to 100 fluid ounces, and at the same time it became more ample in its wave and more regular.

This is entirely in accord with my experience. I believe that I can recognise what may be called a digitalis heart and pulse when I meet with them—the effects of prolonged free administration of this remedy. Along with the characteristic pulse there is a sort of sledge-hammer quality of the cardiac



impulse and first sound; the ventricle bangs, as it were, against the chest wall and the stethoscope. The acceleration and irregularity of the heart which characterise the toxic degree of digitalis action of the textbooks are not met with clinically. Therefore, my rule, and the rule I would recommend you to follow, in cardiac failure is not to be deterred by a small irregular pulse from pushing your remedy, and, instead of cutting off the digitalis, to give more. When digitalis does not produce diuresis in cardiac failure, do not discard it lightly: continue it in increased doses.

But there is a limit to the usefulness and safety of the most valuable of therapeutic measures, and I thought so in this patient's case when I had reached the fourteenth day of treatment, when the diuresis was profuse, and the pulse had fallen to 50. My house physician, Dr. C. F. Day, my students and myself were impressed all the more strongly with the conviction that we had gone far enough in this direction when we tested the condition of the heart with the stethoscope. You remember that the patient had aortic regurgitation (with other lesions); and now that the heart was so infrequent, we heard the period of normal diastolic silence filled by an extremely prolonged blowing murmur, which brought home to us not only that digitalis "slows" the heart by lengthening diastole, but that in doing so it increases the duration (and therefore the amount) of diastolic reflux if the aortic valves be incompetent. The demonstration in our patient was extraordinarily complete. Although I



am not one of those who dread giving digitalis for failing heart in aortic incompetence, I felt that the time had come to reduce the dose; and I did so, giving but 5 minims instead of 15 every four hours.

We now enter upon the third phase of our observations, and we shall find it as instructive as the first and second phases. To begin with, the volume of urine steadily fell off to 80, 60, 50, 40, and finally to 30 fluid ounces. I questioned whether this fall could be solely referred to the reduction of the diuretic drug. The dropsy had been practically removed by this time, and since there was no effusion to remove, and as the diet remained "dry," the urinary excretion necessarily declined. That this was the correct explanation appeared to be proved by the striking fact that the pulse continued to be infrequent, usually under 60, for about another week, and, indeed, at the end of that time fell to 48. The dose of digitalis, smaller though it was, appeared to maintain such an amount of the drug in the body (once it had been, as it were, saturated with it) that the heart remained under its influence. Accordingly, on the twenty-second day of our observations, trusting that we had overcome the dropsy, I removed digitalis entirely, nux vomica alone being given.

Let us consider the phenomena of the phase which we had now reached, the fourth phase of the case. The pulse rose steadily from 48 through 54, 78, 90, and 106 to 124, and became irregular and smaller. In the same time the excretion of urine remained constant for a few days, rose to 40 fluid ounces for



two days only, and then fell steadily to 26 fluid ounces—the same amount as on the day of the patient's admission. He became ill again, and dropsy reappeared in the lower limbs. Manifestly the influence of our treatment on the heart and kidneys, whilst it had been very powerful, was not maintained. It had sufficed to clear off the arrears, but it had not sufficed to establish the smallest reserve, nor indeed to supply an ordinary amount of what might be called working capital. Within a few days of its deprivation of the assistance of digitalis the heart was already in fresh difficulties, although in every other respect the treatment remained unchanged; and after eleven days it was failing rapidly.

It appears from this observation that digitalis, although its action on the heart persists for days after its reduction, must be continued for a certain length of time if the benefits it has effected are to be maintained. It ought not to be suddenly withdrawn. We removed it in the present instance, as I have said, because the pulse had fallen to 48, and the diastolic pause with its striking murmur of aortic reflux somewhat alarmed us. We departed from the rule which the practitioner had learned long ago to observe, to reduce slowly the dose of digitalis after relieving with it the urgent manifestations of cardiac failure, and we believed at the time that we were right in departing from it, but now we found that we were wrong. We therefore determined to correct our error by resuming digitalis; and accordingly, on December 25 (the thirty-third day of treatment) the



patient was once more ordered 10 minims of tincture of digitalis every four hours, the dose, you will observe, with which the treatment had been begun.

The fifth phase of observations was thus commenced. For three days the pulse remained uninfluenced, running at 135, irregular, small, and feeble. Still, its rise was checked. But the volume of urine, instead of rising, continued to fall, until it reached 22 fluid ounces. Thus once more we learned that digitalis does not appreciably influence the urinary secretion for two or three days. At this point in the history of the case an interesting observation was made. In my absence from the wards on December 28—that is, on the fourth day of return to the drug—my colleague, Dr. Galloway, substituted 2 fluid drachms of the infusion of digitalis for the 10-minim dose of the tincture, giving it, like the other, every four hours. The pulse now improved, falling to 96. But there was no diuresis; and on the seventh day from the return to digitalis, first as tincture and then as infusion, the volume of urine was only 20 fluid ounces, after falling, indeed, to 16 fluid ounces.

Thus the experience of the very first week of treatment was exactly repeated: you will remember that that also was nothing better than a secretion of 23 fluid ounces on the seventh day of the use of the same dose of digitalis. Once more, then, we learned the lesson which was taught us by the first phase of this case: that less than a certain dose of digitalis (different, no doubt, in different instances) fails to produce diuresis in cardiac dropsy. We had hoped



that a more moderate dose might suffice in the second course of the drug, but we were disappointed. I therefore ordered once more, on the forty-first day of our observations, the dose which had proved successful originally—15 minims of the tincture every four hours ; and therewith we commenced the sixth phase of the case.

The effect of the increased dose was very striking, as you will see by the chart. The pulse fell and continued to fall in frequency, until on January 9 (forty-eighth day) it was as low as 65. The dropsy again disappeared. Most striking of all, the amount of urine secreted immediately rose, until on the forty-fourth day it had again reached 96 fluid ounces, from which high level it naturally fell after a few days, maintaining, however, the excellent volume of about 65 ounces for nearly a fortnight. Cardiac distress and dyspnœa subsided, and the whole condition of the patient improved steadily, this time, happily, to remain satisfactory until he left the hospital several weeks later, able to resume work. Thus the diuretic action of a sufficient dose of digitalis was clearly demonstrated a second time. On this occasion we were careful not to try to be independent of it prematurely. We remembered the lesson we had learned : we reduced the dose very gradually, and continued to give the drug for weeks on end, with the free diuresis which I have just mentioned as a result. We had in this a demonstration of the fact that the effect of digitalis, once obtained, can be maintained indefinitely—that (in contrast with morphine, for



example) digitalis in its action is not characterised by toleration but by accumulation.

I have conducted you through the ups and downs of this interesting chart, and have submitted the different observations, of which it is a graphic record, as simply as possible to your consideration. Let me now collect in systematic order the conclusions which we have felt ourselves justified to reach, and which I believe to be legitimate and temperate.

The first conclusion is obvious—that digitalis is a diuretic in cardiac dropsy. I suppose there is no one here who entertains a doubt on this point after noting the very low ebb of the urine in certain phases of the case and the profuse diuresis in the others ; but, lest there be a sceptic among you, I will return to the subject presently.

Our second conclusion was that the diuresis produced by digitalis in ordinary doses of the pharmacopœial preparations of the drug does not make its appearance before the third or fourth day of administration. The third conclusion, you remember, was that digitalis to be useful in cardiac dropsy is to be given in full doses. The next lesson that we learned was that when digitalis fails to produce diuresis in cardiac dropsy the use of it is not to be abandoned, but it is to be given in larger doses. The small irregular pulse which is met with in cases of cardiac failure under treatment with digitalis is not an effect of an excessive but evidence of an insufficient dose of the drug, and, instead of being a contraindication, is an indication for its continued administration, pro-



bably in larger doses. This is an extremely important conclusion, and one which in practice you may hesitate to follow. When you find your patient still very ill, the dropsy increasing, and the pulse very frequent and irregular, you may well ask yourselves the questions, "Have I given too much? Is not this the toxic action of digitalis?" You can unhesitatingly answer "No." The toxic effect of digitalis clinically is an entirely different one from that.<sup>1</sup>

Another practical consideration that we reached was that digitalis which is acting or has acted as a diuretic in cardiac failure must not be suddenly removed, and must be slowly, not rapidly, reduced in dose before its final removal—that is, continued for some time after the disappearance of dropsy. If in our case, instead of reducing the dose, as I did, at once to 5 minims, and then removing it altogether, I had reduced it first to  $12\frac{1}{2}$  minims, and then to 10, and so on, the probability is that we should have had no return of the dropsy.

The next point of which I would remind you is that the change in the characters of the pulse, particularly the reduction of its frequency, in response to digitalis precedes the appearance of diuresis, and persists after its disappearance.

We have now arrived at a subject on which there is a division of opinion. In our case I demonstrated to you that failure of the heart in association with aortic incompetence was beneficially, as well as safely,

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<sup>1</sup> Koehnhorn, *Viertsschr. f. gerichtl. Med.*, Neue Folge, 1876, p. 278.



treated with doses of digitalis sufficiently large to reduce the frequency of the pulse to 48 and greatly lengthen diastolic reflux.

You are aware that it has been maintained by some authorities on disease of the heart that digitalis should not be given in aortic incompetence, because the diastole may become so much prolonged by slowing of the cardiac rhythm that regurgitation is dangerously increased, and the patient may perish of circulatory failure by "bleeding from the aorta into the left ventricle." All I need say at present is—there are the facts before you: a man whose pulse was reduced to 48 by digitalis, and who had an extremely loud and long diastolic murmur, was safely and perfectly relieved by the treatment; and this experience is confirmed by that of authorities equally as good as those who maintain that digitalis is dangerous in these cases. If you have a patient with a failing heart in aortic incompetence do not hesitate to give him digitalis.

To these conclusions I may now add one or two of a more general character.

All the incidents of the course of this case go to support the view that digitalis has what is called a "cumulative" action, or, more correctly, that it has to accumulate in the body, and reach either a certain amount or a sufficient degree of activity before its diuretic effect is appreciable. This has long been recognised. The question naturally arises whether the same degree of activity might not be secured far more quickly, say within one day instead of three



days, or in an hour, or in a few minutes, by giving heroic doses of the tincture or of the infusion, or by administering digitalin or other of its constituents. Dr. Alexander Morison<sup>2</sup> has recently recommended the first of these methods, giving up to half-drachm doses of the tincture "every four hours until a definite effect is produced upon the action, force, and capacity of the dilated and failing heart." This, he says, may require the continuous administration in such doses of the combined tinctures of strophanthus and digitalis, until 200 to 300 minims have been taken. Dr. Morison would appear to have found that, after all, the administration of a 30-minim dose does not produce diuresis short of thirty-six hours, that is, before the third day.

Digitalin is said by the French authors to be highly efficacious. I show you here the curve of the diuretic effect of Nativelle's crystallised digitalin in a case of cardiac failure in chronic valvular disease and adherent pericardium. You will observe that diuresis was not established before the sixth day, and not until the ordinary (but of course moderate) dose of  $\frac{1}{160}$  gr. once a day had been doubled. The curve as a whole bears a close resemblance to our ordinary digitalis curve. Here I may as well say that experiments on animals have demonstrated that of the three most important active principles of the digitalis group in ordinary doses commonly tested, and occasionally used therapeutically, as diuretics, digitoxin is the slowest, taking sixty hours to affect the secre-

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<sup>2</sup> Morison, *Lancet*, January 30, 1904, p. 291.



tion sensibly (whilst it is exceedingly toxic); that digitalin takes twenty-four hours; and strophanthin only a few hours. The rate of accumulation is, therefore, different in the three substances. Thus, strophanthin would appear to be the body that we are in search of when we wish to obtain a speedy result.<sup>3</sup>

Lastly, I have already asked whether I have amongst my audience a thoroughgoing sceptic of medicinal treatment in general, and of the action and uses of digitalis in particular. It is quite open to him to question the whole of these results as far as I have attributed them to digitalis. He might contend with some show of reason that this case would have done just as well without digitalis at all—that is, on rest, nursing, warmth, proper diet, and attention to the elementary functions of life. This at least is a favourite position for some of our friends to take up with respect to drugs; nor can we always deny the impeachment, and prove that they are wrong. But we can do so in the present instance without hesitation. Let me refer once more to our chart. You observe that for the first seven days the patient enjoyed the advantages of those non-medicinal measures, the value of which I am the last person in the world to question, and yet the urinary secretion did not exceed a good pint. That did not look like a useful or indeed a promising effect of rest, comfort, nursing, and diet; and it was not bettered until the larger dose of digitalis was introduced into the system.

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<sup>3</sup> Fraenkel, A. (Badenweiler), Vergleich. Untersuch. u. d. kumulative Wirkung d. Digitaliskoerper, *Arch. f. Exp. Path. u. Pharm.*, Bd. li.



And if our supposititious friend be still sceptical, let me direct his attention to the fourth phase and to the fifth and sixth phases of the case, as I have numbered them. In the fourth phase the only variation in the patient's circumstances was removal of digitalis ; the nursing, feeding, and his other surroundings remained unchanged. But the diuresis ceased, the pulse rose, and the dropsy returned. In the next two phases, the only variation in the patient's circumstances was the restoration of digitalis, first in moderate and then in full doses. But the pulse fell, the diuresis returned, the dropsy disappeared for good, and eventually compensation was restored.

This evidence is incontrovertible. It fulfils both the positive and the negative conditions of proof. Let me repeat, however, that I do not undervalue the actions of non-medicinal remedies in failure of the heart. To do so, or to overestimate in the smallest degree the benefit to be looked for from drugs in this morbid condition, would prove our ignorance of the elementary principles of the management of what is in great measure a mechanical problem—the restoration of the capacity of the heart to carry on the circulation from a condition of insufficiency. More than that, I maintain that in every case of cardiac failure our investigation of it ought not to stop short at the diagnosis of failure (far less at the diagnosis of a particular lesion), but should include the determination of the cause of failure ; and that the particular cause, when it has been determined, must be dealt with, whether it be physical exertion,



starvation, dissipation, emotional distress, heart poisoning (for example, with tobacco), functional strain, or what not. In a certain number of cases it will be found that no digitalis whatever is required.

It is only a corollary to this conclusion to add that when compensation has been restored in chronic valvular disease of the heart, the non-medicinal measures to which I have just referred must be intelligently continued for a considerable length of time in order to establish it. As I have already said, a reserve must be accumulated in the myocardium—that natural reserve of force, that normal capacity for work other than a minimum, without which compensation after being restored cannot be maintained. Here is a great difficulty with us as practitioners. Our patients are naturally desirous—and, unhappily, many of them are compelled—to resume work prematurely; and the invaluable effects of treatment, including those of digitalis, are too often thrown away. A store of energy can never be reacquired until the heart has had a certain number of weeks of complete rest after the disappearance of the last trace of dropsy.

I desire to conclude this very elementary discourse with one more bit of practical advice which our chart fully endorses. This advice is expressed in three words, which though thus few appear to be easily forgotten—*Measure the urine*. The volume of urine proves to be a ready, accurate, and sufficient index both of the patient's condition and progress, and of the value or usefulness of your remedies, yet the

measurement of it is strangely neglected in family practice. Now you and I might often be in doubt about our cardiac patient's physical signs and symptoms, and about his state as a whole, and we might differ with each other in our interpretation of his pulse, for the characters of the pulse are often exceedingly difficult to estimate and to employ as therapeutic guides, but there can never be any question about the amount of urine secreted. It is easily measured ; it is expressed numerically ; its variations are delicate in degree and yet readily appreciated and significant ; and I trust that I have been able to show you by this chart that it is a true index of the progress of your case, particularly of the action and use of digitalis.



