CASE XXX (Reported by Mr. Connell, F.R.C.S.E., Surgeon, Sheffield Royal Infirmary).

Married woman, supposed to have intestinal obstruction following recent abortion. Mr. Connell, called in consultation, found marked blue line, constipation, anaemia, etc. The woman admitted having taken "6r pills" in one week.

REFERENCES.

¹ BRITISH MEDICAL JOURNAL, 1893, vol. ii, p. c. ² *Lancet*, 1898, vol. ii, p. 255. ³ *Ibid.*, p. 742. ⁴ BRITISH MEDICAL JOURNAL, December, 1899. ⁵ *Ibid.*, June and July, 1900. ⁶ *Ibid.*, 1901, vol. ii, p. 72. ⁷ *Quarterly Medical Journal*, February, 1902. ⁸ BRITISH MEDICAL JOURNAL, 1903, vol. i, p. 242. ⁹ *Ibid.*, 1903, vol. i, p. 849. ¹⁰ *Allbutt's System*, vol. ii, p. 964, Lead Poisoning, by Thomas Oliver.

NEW METHODS OF STUDYING AFFECTIONS OF THE HEART.

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II.—THE ACTION OF DIGITALIS ON THE HUMAN HEART.

CONSIDERING the number of years during which digitalis has been employed in the treatment of affections of the heart, and considering the great number of experiments that have been performed on animals to determine the action of digitalis, it might be assumed that the nature of the action of the drug was sufficiently well known. But if one critically examines the results of these observations, clinical as well as experimental, no clear conception of the manner in which this drug acts can be obtained. The study of its effect upon my own patients has engaged my attention for many years, and I have collected a large number of observations which show its effect on the movements of the heart. The correct interpretation of these observations baffled me for a long time, but at last two events happened which threw a flood of light upon this subject. The first of these events was the observation that in a large class of patients, for whom digitalis is frequently prescribed, the rhythm of the heart does not proceed from the auricle to the ventricle, but originates in the fibres joining auricle and ventricle (remains of the canalis auricularis), or in the ventricle itself. The reaction to digitalis varies greatly, but the arrhythmia produced by the drug in a heart with the ventricular rhythm differs markedly from the arrhythmia produced in a heart with the normal rhythm. The fact that the rhythm of the heart may be ventricular in origin is beyond the ken of the physiologist and experimental pharmacologist, inasmuch as it is the result of long-standing changes in the heart impossible to produce experimentally; but it must be taken into consideration by all who desire to study the effect of digitalis in the human heart. The second event which enabled me to get a clearer insight into the mode of action of digitalis was the perusal of Professor Wenckebach's book on *Arrhythmia of the Heart*. This author, who had made himself familiar with the most minute details of the action of the individual functions of the heart muscle fibres, drew my attention to the exact meaning of many forms of arrhythmia which I had found resulted from the administration of digitalis. Pursuing the inquiry on the lines laid down by him I was able to explain satisfactorily the mode of action of digitalis in many of the most common and most striking irregularities.

I do not for one moment suggest that I have found out the whole matter of the action of digitalis, because there are many phenomena produced by digitalis with which I do not deal. This paper is concerned mainly with certain modifications of the heart's action produced by digitalis. The interpretation here given may not be found sufficient, because my knowledge is very limited and new facts are cropping up continually, so I have endeavoured as far as possible to give a careful record of the facts with such interpretations as appear most reasonable in my present state of knowledge. In doing this I place on record numerous tracings, for by these only can a true conception of the forms of arrhythmia be acquired. It is surprising how much of the literature on digitalis is taken up with the description of its action on the movements of the heart; the writers contenting themselves, as a rule, with minute verbal descriptions, the result of these descriptions being such a curious mixture of fact and fancy that no accurate notion of the real nature of the arrhythmia can be grasped. When in rare instances tracings have been given I have had no difficulty in recognizing the nature of the arrhythmia.

This inquiry suggests a probable explanation for the curiously discordant results obtained by observers, experimental and clinical, inasmuch as it has been overlooked that digitalis has a peculiar tendency to affect primarily those functions of the heart muscle fibre that have been previously damaged, the result being the production of an arrhythmia due to further depression of those functions. I have found, for instance, that in hearts where the function of conductivity

was normal digitalis has no effect upon this function, though it may materially affect other functions of the heart muscle. But in cases where conductivity could be shown to be depressed digitalis very speedily exaggerated this depression and produced the characteristic dropping out of ventricular systoles. In the handling of the heart in experiments one can readily conceive how easily the delicate organization of the heart may be injured by some trivial accident, and the results obtained by experiment may thus vary according to the nature of the function injured.

Writers frequently urge that certain forms of the drug are more potent or more reliable than others. I have found all forms of the drug equally potent in suitable cases, and equally inefficacious in others. I have usually employed the digitalis in the form of the *B. P.* tincture, of the well-known squill, calomel and digitalis pill, and of the digitaline granules (Nativelle's). It might seem that the advocates of special forms of the drug have unwittingly prescribed it to patients whose hearts were peculiarly susceptible, and have attributed the very striking results to the nature of the drug rather than to the susceptibility of the organ.

Another point which shows the susceptibility of the organism to digitalis is this, that the drug affects all non-striated muscle fibre, and before it can have an appreciable effect on the heart it may grievously affect other muscular organs. I have collected sufficient evidence to incline me to the belief that the "gastric irritation" so frequently produced by digitalis is really due to the action of the drug in the musculature of the digestive tract.

A.—ACTION OF DIGITALIS WITH THE NORMAL RHYTHM OF THE HEART.

1. *Effect of Digitalis on Stimulus Conduction (Dromotropic Effect).**

In a paper recently published in this JOURNAL I described how the stimulus for contraction was conveyed from muscle fibre to muscle fibre. The stimulus arises at the mouths of the great veins, passes over the auricle, and reaches the ventricle by the fibres joining auricle and ventricle. By observing the time that elapses between the systole of the auricle and the systole of the ventricle we can gauge the rate of conduction along these fibres. This is shown in tracings of the jugular and carotid pulses, when in the jugular a wave, *a* (Fig. 1), due to the auricle, is frequently present, and is immediately followed by a wave, *c*, due to the carotid. The time between *a* and *c* represents the time that the stimulus takes to cross the fibres between auricle and ventricle. The conductivity may be considered normal when the *a-c* interval does not exceed one-fifth of a second. When this function is normal, it is doubtful if digitalis can effect it. At all events, I have pushed it in many cases until other functions of the heart were affected, and until severe gastric disturbances resulted, without the slightest sign of conductivity being delayed. But when conductivity is depressed—that is to say, when the *a-c* interval is more than one-fifth of a second—then digitalis may depress this function with great readiness. Patients may have a slight depression of conductivity for years, and during that time the rhythm of the heart may be invariably regular. Such patients are, however, exceedingly susceptible to the influence of digitalis, and a very small quantity of the drug may produce an arrhythmia due to the dropping out of ventricular systoles. The auricle will continue to contract with perfect regularity, but the stimulus occasionally fails to cross the fibres that connect auricle and ventricle.

CASE I.

Female, aged 24. She was under my care in 1900, and I had prescribed digitalis, and phenomena similar to what I am about to describe supervened. She had rheumatic fever in 1902. She married early in 1903,

Fig. 1.—Simultaneous tracings of the jugular and carotid pulses with the radial, showing that the *a-c* interval (Space A) is twice the normal period (two-fifths of a second in place of one-fifth), indicating a delay in the stimulus passing from auricle to ventricle. The time marking here and in the other figures represents one-fifth seconds.

and consulted me on October 4th, 1903, being at that time four months pregnant. The heart's dullness was only slightly increased.

* This and kindred terms used afterwards have been employed by Engelmann, and are bound to be permanently used in the literature on the heart.

There was a well-marked systolic murmur at the apex (in 1900 I had noted a presystolic murmur). There was marked pulsation in the veins of the neck, a tracing of which shows an abnormal wide *a-c* interval (Space A, Fig. 1). Being in a fair condition of health, I advised her as to the avoidance of any means whereby the heart's work might be increased. On November 4th she consulted me for extreme weakness and shortness of breath. I prescribed her tincture of digitalis (B.P.), 15 minims, three times a day. On November 8th, when she had taken 3 drachms of the tincture, she complained of shortness of breath and great precordial distress—not pain, but a feeling of oppression over the front of the chest. The heart's action varied in a curious manner. For a few minutes the pulse would be perfectly regular, beating at the rate of 60 beats per minute, then it would suddenly become irregular and slow for a few minutes, then again resume the more rapid and regular rhythm. The digitalis was at once stopped, but the irregular action of the heart persisted until the 11th of November. From that date I kept the patient under constant supervision until a month after her confinement in February, 1904; I took tracings of her jugular and radial pulses at every visit and a very large number while she was in labour and under chloroform; I have seen her at intervals during the past year, and I have never found a single instance of the dropping out of the ventricular beat, or any resemblance to the irregularity which occurred from November 8th to November 11th. (On November 10th she fell for two hours into a curious mental condition, her memory for recent events being quite gone, talking in a slow hesitating manner, scarcely understanding what was said to her. The attack suddenly passed off, and never returned.)

I took a large number of long tracings during the days when the pulse was irregular, and the analysis of the short examples given in Figs. 2 and 3 applies equally to the whole of the tracings I obtained.

Fig. 1 shows the widened *a-c* interval, which is even yet (January, 1905) a constant phenomenon in tracings from this patient. Figs. 2 and 3 are instances of the different forms of irregularity that occurred after the administration of the digitalis. It will be noticed that the auricular wave, *a*, is perfectly regular in its appearance, whereas the radial pulse and the carotid (wave *c*) is markedly irregular.

Fig. 2.—Tracings of the radial taken at the same time as the jugular and carotid. The waves *a* and *a'* are due to the auricle, and appear with perfect regularity, while the radial pulse and carotid (wave *c*) appear irregularly—a beat missing after each auricular wave *a'* (see the diagram of the tracing, Fig. 4).

Further, it will be seen that the relationship of the radial and carotid to the auricular wave is a curiously varying one, approaching near to the auricular wave after a long pause, and receding from it after the next beat.

Fig. 3.—Shows the same thing as Fig. 2, except that here there is a tendency to a rhythmical irregularity (see the diagram, Fig. 5).

It will also be seen that after the auricular wave *a'* no radial or carotid beat follows—that is, a ventricular systole drops out, and the arrhythmia is really due to the occasional dropping out of ventricular systoles. The nature of the arrhythmia will be more apparent if a diagram be constructed to show the auricular and ventricular systoles and the passage of the stimulus along the fibres uniting auricle and ventricle. In Fig. 4 the downstrokes in the upper division, *A*, represent the auricular waves (*a*) of Fig. 2, occurring at exactly the same intervals. In the lower division, *V*, the downstrokes represent the carotid pulse beats (or radial pulse beat), and

occur at exactly the same intervals as the carotid waves (*c*) in Fig. 2.

Fig. 4.—Diagram constructed to demonstrate the action of the heart when Fig. 2 was taken. The downstrokes in the upper division, *A*, represent the auricular systoles, and correspond with the waves *a* and *a'* in Fig. 2, while the downstrokes in the lower division, *V*, represent the ventricular systoles, and correspond to the radial and carotid pulses in Fig. 2. The short thick lines connecting these downstrokes represent the passage of the stimulus through the fibres joining auricle and ventricle, and show a slant varying according to the rate of conduction. The occasional absence of this line means that the stimulus has failed to pass these fibres, and hence a ventricular systole drops out.

The narrow division (*A-v f*) in the middle represents the fibres joining auricle and ventricle, and corresponds to the *a-c* interval in Fig. 2. The thick line passing through the *A-v* fibres slants at different degrees, and this varying slant represents the varying rate which the stimulus takes to pass through the fibres from auricle to ventricle. Before the first ventricular intermission this slant is the greatest, after a ventricular intermission the slant is always the least. The increase in the slant represents an exhaustion in the power of conduction, and this exhaustion becomes ultimately so great that, after a systole of the auricle, the stimulus fails to reach the ventricle, and so a ventricular systole drops out. This failure of the stimulus to affect the *A-v* fibres permits them to have a long rest, so that when the next physiological stimulus comes from the auricle the conductivity is so much restored in the *A-v* fibres that the stimulus is conveyed to the ventricle with greater rapidity, as is shown by the shortened *a-c* interval in the tracing (Fig. 2) and by the diminished slant of the thick line in the diagram (Fig. 4).

Fig. 5.—Diagram constructed to demonstrate the action of the heart when Fig. 3 was taken. For explanation, see Fig. 4.

In 1900 this patient showed a more profound reaction to digitalis, inasmuch as at times every second ventricular beat dropped out and the ventricular systoles were exactly half the number of ventricular systoles (Fig. 6).

(In my book on the pulse I described the attack from which this patient suffered in 1900, but at that time I was not acquainted with Wenckebach's researches, and, therefore, did not realize the significance of the tracings which I got, but supposed, erroneously, that the ventricles were pursuing a rhythm apart from the auricles.)

I have had several patients who have shown this reaction to digitalis, in whom a jugular pulse was present, and the relationship between the auricular and ventricular systoles was similar to that which I have just described. In all these cases it could be demonstrated that the *a-c* interval was abnormally increased when the heart was regular in its action. When this affection of conductivity is present we have usually no means of detecting its presence except by the venous pulse. (In rare instances it may be detected by the effect of the left auricular systole on the radial pulse, or by the seemingly too early occurrence of the presystolic murmur before the apex beat.) But in

Fig. 6.—Slowing of the pulse due to digitalis depressing conductivity so that the ventricle does not respond to every second stimulus from the auricle. While the ventricle contracted 48 times per minute the auricle contracted 66 times.

patients with no venous pulse the effect of digitalis in depressing conductivity can be recognized by the finger or by a tracing of the radial. I think I can assert with confidence that in any given case, when the auricles are active, when, in response to the administration of digitalis, the pulse becomes irregular, with long pauses, these pauses are due to the propping out of ventricular systoles, because the stimulus has failed to pass from auricle to ventricle. To my mind, the only other cause which could occasion these long pauses is the occurrence of extra systoles, but on listening over the heart the sounds of the heart are absent when a ventricular systole drops out; whereas, with extra systoles, the characteristic short, rapid sounds can be heard, due to the premature contraction of the ventricles.

I quote the following case to show how the nature of the arrhythmia can be proved with fair probability without the presence of a venous pulse to guide us:

Female, aged 53. She has suffered from attacks of palpitation, for which I have attended her at intervals for many years. She consulted me in April, 1904, for great shortness of breath and violent throbbing in the neck and upper part of the chest. The pulse was usually from 90 to 100 beats per minute, full and forcible. There was marked pulsation in the carotid, but no venous pulse. There was a faint apex beat in the fifth interspace, and the heart's dullness extended to the left 1 in. beyond the nipple. There was a rough systolic murmur at the apex, also well heard at the base. I was doubtful whether there was not also a slight aortic systolic murmur. There were no murmurs during my previous attendances on this patient. Notwithstanding rest and appropriate treatment she did not improve, and in June she visited Nauheim, and there underwent a six weeks' course of treatment—baths and exercises—followed by a visit to Switzerland. She returned to Burnley distinctly worse, very much thinner, less able to undertake exertion because of the palpitation and breathlessness, and the pulse rarely under 100 beats per minute. I tried her with various remedies, including digitalis; but in a few days this drug produced such gastric derangement that I had to stop it. She steadily got worse, and, as there was sleeplessness and much muscular tremor I prescribed ammonium bromide. In a few days she had an extensive attack of erythema nodosum on both legs. She recovered from this in a fortnight, being kept in bed and gently massaged. I resolved again to try the effect of digitalis. She began with three granules of digitalin a day on September 18th. No effect was observed till September 20th, when her heart began to intermit very frequently, sometimes she said she could feel it miss every second beat for hours. When I examined her on September 26th the pulse-rate varied in its rhythm, periods of perfect regularity varying with periods of irregularity as in Figs. 7 and 8.

Fig. 7.—Tracing of the radial pulse, showing irregularity due to digitalis. The nature of this irregularity is shown in Fig. 9. The minute elevation preceding the fall at x is due to the systole of the left auricle.

Fig. 8.—Shows the same as Fig. 7. The nature of this irregularity is shown in Fig. 10.

During the intermissions no sounds could be detected in the heart. The digitalis was stopped, and the arrhythmia daily got less until the 4th of October when it had entirely disappeared. Since that date the pulse has never shown a single irregularity, the heart has become much quieter, the rate gradually falling as low as 72 beats per minute. The heart's dullness is now within the nipple line, the murmurs are still present, but the patient's general health has wonderfully improved. Although the improvement dates from the period of arrhythmia, the patient has a horror of the digitalis.

While the absence of a venous pulse deprives us of the absolute proof of the nature of the arrhythmia we can infer that depression of conductivity was the cause from the similarity of the irregularity to that shown in Figs. 2 and 3. The nature of this arrhythmia becomes all the more evident if we construct diagrams on the basis of the two tracings Figs. 7 and 8.

Fig. 9.—Diagram constructed to show the action of the heart when Fig. 7 was taken. For explanation see Fig. 4.

Fig. 10.—Diagram to show the action of the heart when Fig. 8 was taken. For explanation, see Fig. 4.

Fig. 10 is a diagram representing Fig. 8, and shows the nature of the arrhythmia in this instance. In constructing these diagrams, I have represented the auricular systole as appearing with mathematical regularity. As a matter of fact, however, there is usually a slight variation in the rhythm of the auricular systole, and a slight delay in its occurrence might slightly modify the time represented as having been spent by the stimulus crossing the A-v fibres. Further facts connected with this form of arrhythmia will be found in Wenckebach's book. This author had predicted that if digitalis were employed in a case of irregular pulse due to depressed conductivity, it might depress the conductivity to a dangerous extent.

On March 7th, 1905, this patient developed again this arrhythmia and at the same time a venous pulse appeared in the neck. I have taken numerous tracings of the jugular pulse and on analysis find that the above interpretation is verified in every particular.

The Milroy Lectures

ON

INDUSTRIAL ANTHRAX.

Delivered before the Royal College of Physicians of London.

By T. M. LEGGE, M.D. OXON.,

H.M. Medical Inspector of Factories.

LECTURE II.

[ABSTRACT.]

TREATMENT OF EXTERNAL ANTHRAX.

THE treatment of anthrax until recently has either been merely expectant or consisted in cauterization or other allied treatment of the local pustule. But the use of a serum derived from an immunized animal is coming more and more into use, especially in Italy and South America. Since in external anthrax spontaneous cures are frequent, a consideration of mere case-mortality will not suffice to establish the relative value of the three methods of treatment mentioned. Other points must be considered, such as (1) the relative amount of scarring or of deformity left; (2) the applicability of the form of treatment to the different types assumed by the disease and the stage which it may have reached; and (3) the length of time which elapses from the beginning of the treatment to resumption of employment. The third point is of especial moment in connexion with an industrial disease.

Muller¹ has described 13 consecutive cases treated successfully in Jena by rest, fixation, and elevation of the part affected, stimulating diet, and the local application of grey ointment. Ramstedt² from the same clinic, has adduced more recently other 7 consecutive cases (one very severe), in which nothing but the same expectant treatment was pursued. And, similarly, Fr. Schultze³ of Bonn has cited a case of extremely severe malignant pustule of the cheek, with extensive oedema of the eyelid, neck, and chest, which was cured after a plastic operation on the eyelid without other operative treatment. Muller, too, considers that the adoption of expectant treatment may be defended on the ground that any operation may facilitate the distribution of the bacilli throughout the system.

Surgical interference usually takes the form of free excision, dissecting out the pustule from the healthy tissues beneath, swabbing the wound out with pure carbolic, and allowing the wound to granulate up from the bottom. Subcutaneous injections of 5 per cent. carbolic acid around the malignant