THE REACTION OF THE HEART TO DIGITALIS WHEN THE AURICLE IS FIBRILLATING.*

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In a communication published in *Heart* in March of this year¹ it was shown that the completely irregular pulse,† which is so frequently encountered in clinical work, and which is peculiarly associated with advanced mitral stenosis and arterio-sclerosis, is the result of a condition

Fig. 1.—Venous and femoral curves from a dog during a period of auricular fibrillation. The venous curve is ventricular in form. The pulse is completely irregular.

well known to experimentalists—namely, fibrillation of the auricle.

I do not propose to reiterate at the present time the detailed evidence upon which this conclusion rests, but content myself by stating that the conclusion is in absolute accord with all the known characters of the experimental and clinical conditions. It may be stated that a similar irregularity of the heart occurs in horses, and since the publication of my full paper I have had a further opportunity of examining the heart of such an animal beating *in situ*. The auricle was fibrillating.

When the heart is inspected in an animal in which the auricle (speaking of right and left auricles as a whole) is fibrillating, this chamber is found to be in a state of continued diastole. No co-ordinate contraction of its walls interrupts its condition of distension, but careful examination discovers a flickering or tremulous state of the musculature. The muscle seems to be alive with the movement, yet no given point shows any appreciable excursion. The interpretation of the phenomena witnessed is a simple one. In a normally beating heart the auricle responds to rhythmic impulses generated in the neighbourhood of its junction with the superior vena cava,² and it contracts as

contractile substance of this chamber is thrown into delirium. There is no co-ordinate contraction, meaning by co-ordinate contraction universal contraction of the fibres in a definite order and eventually together. There is a condition of asystole.

Now, while the auricle is in this state the *individual* ventricular systoles are co-ordinate; but the chamber beats in a rapid and highly irregular fashion. Thus, while each contraction of the ventricle is of a similar nature to a normal systole, the sequence of contraction presents no rhythm, but has a completely disordered character. In explanation of this gross irregularity in the ventricle it is supposed that occasional impulses escape in a haphazard fashion from the turmoil in the auricle, and that, like normal impulses, they are transmitted across the junctional tissues, the auriculo-ventricular bundle and its arborizations, to the ventricle.

It is upon a heart whose mechanism is disturbed in this way that digitalis exerts its most conspicuous action. Given in full doses it frequently produces a marked retardation of the ventricular rate. In inquiring into the cause of the retardation it is essential, first, that the condition of the auricle should be remembered; and, secondly, that we examine the known ways in which ventricular slowing may be brought about when the auricle is fibrillating. In the experimental heart, when fibrillation of the auricle is present, retardation of the ventricular rate

Fig. 2.—Venous and femoral curves showing the effect of vagus stimulation. With the stimulation 2:1 heart-block appears.

follows certain definite procedures. It results from stimulation of the vagus nerve (Fig. 3), and it has been suggested by Professor Cushny³ that such slowing is the outcome of an increased obstruction to the passage of impulses across the auriculo-ventricular junction; for it is known that the conductive functions of the junctional tissues are markedly depressed by inhibitory impulses, and that heart-

Fig. 3.—Venous and femoral curves from a dog. The auricle is fibrillating throughout, and the venous pulse is of the ventricular form. When the vagus is stimulated the ventricle ceases to beat, but the auricle continues to fibrillate, and leaves its impress on the venous curve in the form of small and rapid oscillations.

a whole, expelling its contents into the ventricle. The movement of the auricle is a rapid one, and there is shortening of the muscle in every direction. It is supposed that in the fibrillatory state this normal impulse formation is in abeyance, and that in its stead numerous and small areas of the hyper-irritable musculature are building up independent and pathological impulses; it is further supposed that the resulting waves of contraction, pro-

block in an otherwise normal heart is a ready consequence of vagus excitation (Fig. 2).

The curve now demonstrated (Fig. 4) strongly supports this view. It shows simultaneous venous and arterial curves from a dog in which the auricle is fibrillating. Accompanying stimulation of the vagus the ventricular rate is diminished, while the fibrillation, identified by the small and rapid oscillations in the venous curve, proceeds. A few seconds later the fibrillation terminates, and the normal and co-ordinate auricular contractions

Fig. 4.—The end of a period of auricular fibrillation. Its termination results from vagus stimulation. The oscillations cease where the fibrillation ends, and from this point co-ordinate auricular contractions are represented. A condition of 2:1 heart-block is present. To show that the ventricular slowing while the auricle is fibrillating is the outcome of heart-block.

pagated from each and all of the new impulse centres, meet each other in the walls of the auricle without travelling far, and that as a consequence the whole of the

are re-established. When these rhythmic contractions of the auricle appear, it is seen that only one in two transmits an impulse to the ventricle and excites a response. The slowing of the ventricle at this stage is the result of heart-block; the presumption is that the slowing previously manifested was of similar origin.

It has been shown by Fredericq⁴ that the ventricle beats slowly and regularly when the auriculo-ventricular

* A paper read in the Section of Pharmacology at the annual meeting of the British Medical Association, July, 1910.

† Or "pulsus irregularis perpetuus." The rhythm of the heart has passed under the terms "arrhythmia perpetua," "nodal rhythm," and chronic arrhythmia.

bundle is transected, and while the auricle is fibrillating—a fact which demonstrates that all auricular impulses to it are impeded by such a procedure. As a consequence the ventricle assumes its own spontaneous slow and regular rhythm. Partial heart-block is readily induced by asphyxia, and, in conjunction with Dr. Mathison, I have utilized this fact to show that when a condition of heart-block is present, the production of auricular fibrillation, while disturbing the regularity of the ventricular contractions, fails to bring about the marked increase of rate which usually accompanies its onset in the normal animal. It may be similarly shown that when the auricle is fibrillating the production of partial heart-block reduces the rate of the ventricular responses (Figs. 5 and 6).

The clinical condition, auricular fibrillation, has been seen in association with heart-block of several grades; with partial heart-block in the curves of Dr. G. A. Gibson,⁶ by Dr. Mackenzie,⁸ and myself; in all these cases the ventricular rate was slow; and a case of auricular fibrillation has been recently reported in which complete heart-block in an epileptic and syphilitic subject was probably present.⁷ In this case the ventricle beat regularly at a rate of approximately 30 per minute.

We see, therefore, that the known ways in which the ventricular action may be retarded, whether the fibrillation is clinical or experimental, are of one type; in all instances heart-block is either probable or proved. What more natural than to suspect that digitalis acts in a similar manner when it produces ventricular slowing in the clinical condition? For digitalis has been found to induce heart-block experimentally,⁹ and clinically a similar action has been described by Mackenzie,⁹ and has been fully substantiated by a number of more recent workers.

The case for which I plead—that digitalis slowing is a result of heart-block when the auricle is fibrillating—is very materially strengthened when the following facts are considered: The type of case in which, with the normal or co-ordinate contraction of the auricle present, heart-block is readily provoked by digitalis administration, is the advanced rheumatic heart, and a *fortiori* the heart affected by mitral stenosis. It is a striking fact that of all cases of clinical auricular fibrillation, those which are of rheumatic origin, and a *fortiori* those affected by mitral stenosis, show the characteristic slowing of digitalis to most advantage. This is the type of case in which digitalis acts in so magic a fashion, and in which the rate of the ventricle is set by the dosage employed; it is the type of case in which the ventricular rhythm may be sometimes reduced to regularity, and in which the rate may be reduced to that consistent with a true ventricular rhythm.

On the other hand, there is the type of patient in whom no reaction ensues upon the exhibition of the drug. Now Mackenzie has shown that digitalis produces heart-block in those patients in whom a previous defect of conduction exists. The proposition I put to you is a parallel one, namely, that the ventricle is retarded in auricular fibrillation by digitalis when there is a pre-existing damage of the junctional tissues, a damage which is frequently demonstrable in cases of rheumatic heart affection.*

The complete evidence in support of this proposition will require time for its collection. We require observations upon patients in the early stages of the affection. It is requisite that it be demonstrated that a large proportion of the cases which react to digitalis had a deficiency of auriculo-ventricular conduction *before* the onset of fibrillation. I can offer the facts in regard to three cases¹⁰ only at the present time. In these three cases the heart-rhythm was observed before the onset of fibrillation, or during the intervals of rest between attacks. The cases were thoroughly tested with digitalis during the stage of fibrillation. Two cases, in which no previous defect of conduction could be demonstrated, failed to show a trace of reaction to the drug. The third case in which deficiency of conduction was clearly established reacted repeatedly and in the most typical manner.

The view suggested, therefore, is that the ventricular rate is retarded in clinical auricular fibrillation by the action of digitalis upon the junctional tissues, the functions of which are already in a depressed state; and this view

is put forward, together with an indication of the direction from which the evidence will come, which, if favourable, should convert what may be now regarded as a proposition into a well-established conclusion.

REFERENCES.

- ¹ Lewis, *Heart*, 1909-10, i, 306. ² Lewis, *ibid.*, 1910-11, ii, 23. ³ Cushman and Edmunds, *Amer. Journ. Med. Sci.*, 1907, cxxxiii, 66. ⁴ Fredericq, *Archiv. Internat. d. Physiol.*, 1904-5, ii, 281. ⁵ Gibson, *BRITISH MEDICAL JOURNAL*, 1906, ii, 1113. ⁶ Mackenzie, *Heart*, 1909-10, i, 23. ⁷ Lewis, *ibid.*, 1909, i, 349; and Lewis and Mack, *Quart. Journ. of Med.*, 1909-10, iii, 273. ⁸ Cushman, *Journ. Exper. Med.*, 1897, ii, 233. ⁹ Mackenzie, *BRITISH MEDICAL JOURNAL*, 1905, i, 587. ¹⁰ Lewis, *Heart*, 1909-10, i, 306 (cases 2, 10, and 11).

VARIATIONS OF THE FERMENTATION PROPERTIES OF THE *B. TYPHOSUS*. *

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Lactose.

DR. TWORT has shown that the *B. typhosus* can be made to ferment lactose-peptone water. He found that two years' growth on lactose-peptone water was necessary to produce this strain. I have examined this new variety and find: (1) It is a genuine *B. typhosus*. (2) On plating on lactose it always gives rise to mixed plates of fermenting and non-fermenting colonies. Subculture of fermenting colonies on lactose plates gives again a mixture of fermenting and non-fermenting colonies, so that the character is always tending to disappear and requires constant growth on lactose for its retention.

If the atavistic non-fermenting colonies are retrained on lactose-agar slopes, after a variable number of subcultures they take on the fermenting power again. In this process of training, when the efficient fermenting strain is arising they show papillae-formation on the lactose, the papillae being very large and acid in reaction as indicated by neutral red.

I have attempted the complete training of a large number of strains myself, and have only got one to the stage of very slightly fermenting lactose-peptone water in two days. I have not yet got red colonies out of it. This has required sixteen monthly subcultures.

Dulcitol.

I have shown † that *B. typhosus* requires about ten days to produce acidity in dulcitol-peptone water. The period can be readily shortened to one day by one to three subcultures on dulcitol media at monthly intervals. Normal *B. typhosus* produces neutral or alkaline colonies on dulcitol agar. About the fifth day, in one-third of the strains papilliform projections arise on the colonies, which become acid in a day or two. Subcultures from these papillae give rise to fermenting colonies. Other strains of *B. typhosus* give papillae about eight to ten days after inoculation. These do not acquire an acid reaction. Occasionally strains do not show papillae on this medium.

Plating on dulcitol agar daily from dulcitol broths of *B. typhosus* shows the history of the variation. It usually takes two to ten days to produce fermenting elements on dulcitol agar. Then, some time later, all the non-fermenting elements are killed off suddenly, and the broth contains only fermenting elements.

This new fermenting character tends to recede after its first selection, but if continuous growth on dulcitol is undertaken for two to three months, the character remains permanent. A strain so trained and selected about nine months ago gave on plating out within the last few days pure plates of fermenting colonies.

Thus apparently two years' growth on lactose selects out a strain acting similarly to a dulcitol strain selected in about a week. How long will a pure permanent lactose strain require for its selection?

Arabinose.

B. typhosus does not ferment arabinose on neutral red arabinose agar plates and ferments arabinose peptone water very slowly and irregularly. After three months'

* The view that digitalis acts by the production of heart-block was originally put forward in the *BRITISH MEDICAL JOURNAL* of November 2 th, 1909, and was more fully considered in *Heart*, 1909-10, i, 349.

† A paper read in the Section of Bacteriology at the annual meeting of the British Medical Association, London, July 29th, 1910.

† Penfold (1910), *Journ. of Path. and Bact.* vol. xiv., p. 406.