A NEW OUTLOOK IN CARDIOLOGY.

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(From the Institute for Clinical Research, St. Andrews.)

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AURICULAR FLUTTER.

MACWILLIAM,⁹ in his experiments on the mammalian heart, artificially produced auricular fibrillation. He was also able to produce another form of contraction which he called flutter. In fibrillation the individual muscle cells are contracting independently of one another, with the result that the movement of the auricle is a continuous quivering. In flutter certain of the muscle cells contract simultaneously, but at a great rate, and are ineffective so far as giving rise to a beat capable of emptying the auricle. The condition is closely allied to and probably of the same nature as fibrillation, and the one passes readily into the other. Langley has described a similar condition in the paralysed voluntary muscle where the fibrillating muscle may take on large rhythmic movements.

In my earlier observations I came across a number of patients with this condition, but I was not able to differentiate them until Jolly and Ritchie¹⁰ described the condition in the human subject. The study of auricular flutter also reveals a number of instructive features. One advantage is that we can count the number of impulses which the auricle discharges, and we can recognize the number to which the auriculo-ventricular node responds. Here again we find the node in the same extremely susceptible condition. The auricular waves are usually somewhere in the neighbourhood of 300 a minute. It is only on rare occasions that the auriculo-ventricular node responds to each auricular beat.

More frequently it responds to every second beat. Occasionally when the body is at rest it may respond to still fewer beats, and irregularly. This is shown in the series of tracings in Figs. 8, 9, and 10. In the first of these tracings the pulse rate is 150 a minute, while the auricular waves are double that number. These are represented by the downstrokes in the space *As* of the diagram (Fig. 8). In the

and the shading after the response represents the refractory period which persists till after the next auricular beat comes down, so that every second auricular wave falls during the refractory period and is blocked, and the pulse (ventricular) rate is only half the auricular. The tracing (Fig. 8) was taken as soon as the patient lay down. In the course of a few minutes the pulse became slower and irregular, as shown in the figure (Fig. 9). After ten minutes the pulse became still slower but more regular (Fig. 10). In this tracing are shown the jugular and auricular waves at the rate of 300 a minute, while the pulse rate is 50. The diagram (Fig. 10) shows that the difference in rate of the auricle and ventricle was due to prolongation of the refractory period of the auriculo-ventricular node so that the impulses from the auricle failed to reach the ventricle. The slightest effort, such as standing up and walking a few paces, immediately raised the rate of the pulse to 150 beats, as in Fig. 8. More effort, and even violent effort, failed to increase the rate beyond this, and the reason is to be seen

in the fact that the refractory period of the auriculo-ventricular node could not be shortened.

THE ACTION OF
DIGITALIS IN AURICULAR
FLUTTER.

While I was groping amongst these cases I had one case which puzzled me at the time, and which I described in 1905.¹¹ I had put it down as a case of auricular paralysis. The rate was rapid, and on giving digitalis the rate of the pulse speedily fell to 50 beats a minute. One day, though the patient was under digitalis, the pulse rate suddenly increased to 80 beats a minute. The digitalis was continued, and the doses increased, but the rate of the pulse did not decrease. A tracing taken of the radial and jugular pulses showed that the rhythm had become normal. When auricular flutter was recognized as a distinct entity, it was found a common experience for auricular flutter to pass into fibrillation and the rate of the ventricle to become very slow on the administration of digitalis, and on stopping the heart

frequently reverted to normal rhythm. This action is shown in Figs. 11, 12, and 13. When these three tracings are reproduced in the form of the diagram we have before us a number of interesting facts. The auricular waves in the space *As* in Fig. 11A give place in Fig. 12A to the short strokes representing the impulses of the fibrillating auricle; and at the same time there is shown the extraordinary refractory state of the auriculo-ventricular

FIG. 8.—Tracing of the radial pulse during auricular flutter. The diagram shows the parts concerned in producing this type of pulse. The sino-auricular node is out of action as in Fig. 5A. The auricle is beating at twice the rate of the ventricle, as every second auricular impulse falls on the auriculo-ventricular node when it is refractory.

FIG. 9.—Shows an irregular radial pulse—the auricular waves are constant, and the pulse irregularity is seen to be due to variations in the length of the refractory period of the auriculo-ventricular node. The radial tracing is a continuation of that in Fig. 8.

FIG. 10.—The tracing is a continuation of Fig. 9, and shows that the radial pulse has decreased still further in rate, due to a still greater increase of the refractory period of the auriculo-ventricular node. All these variations in the pulse rate happened during a period of ten minutes and the tracings are parts of that continuous record. When the patient exerted himself the pulse increased in rate at once to 150 as in Fig. 8. The jugular tracing shows some of the small auricular waves (*a*) and are represented in the diagram by the downstrokes in the space *As*. The *c* waves are due to the carotid.

node. The diagram representing the normal rhythm (Fig. 13A) shows the disappearance of this extraordinary refractory state, which, be it observed, occurs as soon as the sino-auricular node has resumed its activity, shown by the shaded areas in the upper space S.A.N., notwithstanding that the heart was under the influence of digitalis.

It may be remarked in passing that there is something about this effect of digitalis which we do not understand. The effect is not only upon the auriculo-ventricular node, but also on the auricle which passes from flutter to fibrillation. Following the auricular fibrillation which has come out of auricular flutter, the sino-auricular node resumes its function and the heart returns to the normal rhythm. It is to be noted that such a result only occurs in that form of auricular fibrillation which follows flutter. I had hoped that, by pushing the digitalis in ordinary cases of auricular fibrillation, a similar result would follow, but although I have tried it in hundreds of cases I have had not a single success. In a few cases of advanced disease of the heart digitalis has produced auricular fibrillation, and a stoppage of digitalis has been followed by a resumption of the normal rhythm. We are therefore forced to the conclusion that auricular fibrillation in these cases is different in some way from the more common kind.

THE USE OF INSTRUMENTS.

About the time that it was recognized that the auricle had passed into fibrillation the electro-cardiograph came into use. I was amongst the first, if not the first, to see the value of this instrument in throwing light upon some forms of irregularity of the heart. In 1906 I proposed to the late Professor Waller to bring some of my patients from Burnley to London to get a record of the condition I called auricular paralysis, but he said it was not feasible. At that time few people accepted my teaching that the auricle had ceased to function. When I went to London in 1908 I was fortunate to meet Thomas Lewis and to interest him in the subject of heart irregularities, and drew his attention to the possibilities of the electro-cardiograph. It is not necessary at this time of day to dwell upon the splendid work he has done on this subject.

At the outset I foresaw the limitations of the method, in that it would be of little use beyond revealing the nature of certain disturbances of rhythm. As I have said, the object which from the outset of my investigations chiefly interested me was the functional capacity of the heart or heart failure, and it was clear to me that the electro-

cardiograph would be of little or no help in this matter. The inability to realize this has been the cause of the failure of all attempts to estimate the functional capacity of the heart by the use of this instrument.

The reason for this failure becomes quite evident if we but realize what it is the instrument shows. There are two great systems in the heart, one concerned in regulating the function of the heart, and the other concerned in supplying the organs of the body with blood.

The electro-cardiogram reveals disturbances of the regulating processes, but throws no light upon functional capacity.

In contrast with the usefulness of the electro-cardiogram for this purpose we have in the sphygmograph an instrument which reveals facts of a valuable kind in that the sphygmogram is a record of the output from the heart, and is therefore a manifestation of the functional activity of the heart.

FIG. 11.—Tracing of the jugular and radial pulses during auricular flutter (auricular rate, 280; ventricular, 140). The reason for the varying height of the *a* wave is that every second auricular contraction falls during ventricular systole, so that more blood is thrown back into the veins, and the *a* waves are therefore larger.

FIG. 11A.—Diagram representing the events in Fig. 11. The auricular waves fall on the auriculo-ventricular node, which responds to every second impulse as in Fig. 8, with the result that the ventricular rate is half the auricular one.

The Radial Pulse as an Indicator of the Output of the Heart.

If we look at such a tracing of the radial pulse as shown in Fig. 14 we see some remarkable variations in rhythm and in the size of the beat. With the sudden onset of this type of pulse the patient from whom this tracing was taken became weak and breathless, her face in a few hours became dusky and puffy, the heart dilated, and the liver enlarged, and she could not lie down because of breathlessness. After ten hours the pulse suddenly altered, as shown in Fig. 15, and at once the patient experienced a sense of relief, and in a few hours the dilatation of the heart and liver had dis-

appeared, and the duskeness left her countenance, and from that moment she could go about her work with ease and comfort. The interpretation of the sphygmograms explains the whole matter, and in so doing reveals some of the most important things connected with vital processes.

The pulse tracing in Fig. 14 is typical of auricular fibrillation, and occasionally a similar type of tracing is

FIG. 12.—Tracing of the jugular and radial pulses from the same patient as Fig. 8, after digitalis. Auricular fibrillation is present, and the ventricular rate is 40 per minute.

FIG. 12A.—Diagram of Fig. 12 showing the auricle has now passed into fibrillation, and that the refractory period of the auriculo-ventricular node is greatly prolonged and variable in duration, giving rise to ventricular beats at rare and irregular intervals.

found, as in Fig. 9, in auricular flutter, but in no other condition. The cause is the same in both auricular fibrillation and flutter.

Where this radial tracing differs from all other forms is in the fact that in all other irregularities of the pulse the size of the beat has a distinct relation to the length of the pause that precedes it—the longer the pause the bigger the pulse beat. This is due to two things: (1) the length of the pause enables more of the fibres of the ventricle to recover and to take part in the contraction, and (2) during the longer pause more blood has accumulated in the ventricle. While this also occurs in auricular fibrillation, there is often

present another peculiarity in that there is no such relation—and a small beat may occur after a long pause, and a large beat after a short pause. This is a peculiarity which is distinctive of the pulse in auricular fibrillation and flutter. A similar peculiarity is found in the pulsus alternans, but there the rhythm is not irregular; moreover, it is frequently present in auricular flutter.

When we consider all the possibilities we are forced to the conclusion that in producing such pulse beats the ventricle is varying in the strength of its contraction, and this can only be due to the fact that only a portion of the fibres participate in the contraction of the ventricle which produces the smaller beats, while more fibres participate in the contraction which produces the larger beats.

When we come to inquire why the ventricle should behave in this way, we must recognize that the ventricular contraction is entirely under the control of the auriculo-ventricular node. We know that the stimulus for contraction in auricular fibrillation originates in the auriculo-ventricular node, and the question arises, How comes it that the auriculo-ventricular node should act in this way? Here again it is necessary to revert to one of the laws that have emerged from our investigations in St. Andrews—the Law of Fluctuation.

I have already pointed out that the cell activity varies in a remarkable manner under the influence of agents that hasten or delay the metabolic processes which restore the functional energy of the cell. When the cells are grouped together this increase and decrease of the rate of restoration is shown by an increase or decrease of function. This is diagrammatically illustrated in the sino-auricular node in Fig. 4A, where the variations of the pulse rate are shown to be due to variations in the rate of recovery of the sino-auricular node.

I pointed out at the same time another result of this variation in cell activity, in that all the cells did not recover at the same rate. As a consequence of this, in an organ, some cells are active while others are inactive. When those that are active cease to function, the inactive ones become active. In this way there is a continual fluctuation in cellular activity.

In the diagram Fig. 14A the shading of the auriculo-ventricular node represents variations of the time of recovery. The downstrokes, representing the ventricular systole (space Vs), are shown to vary in length, representing the variations in the size of the pulse beats in Fig. 14. These variations in size indicate not only variation or fluctuation of ventricular activity, but of the activity of the auriculo-

ventricular node. When the ventricle produces the smaller beats only a few cells of the auriculo-ventricular node are active and send impulses which affect a few fibres of the ventricle. In producing the larger beats more cells send impulses to the ventricles, while in producing the biggest beats all the cells of the node may send impulses to the ventricle.

This point of view assumes that a contraction of the ventricle is under the control of the auriculo-ventricular node and that when there is an imperfect action of the node there results imperfect contraction of the ventricle.

Such a view is contrary to accepted beliefs of the manner in which the ventricle contracts; but it must be recognized that these beliefs are based upon a very imperfect understanding of the heart's contraction. It has not yet been found out

in what way an adequate knowledge of the heart's contraction can be acquired, and we are searching for the appropriate method. There are two ways which help to throw some light upon the subject. As I have stated, the part played by one element of the reflex arc cannot be recognized when all elements are working harmoniously in normal activity. A defect or disturbance in the action of an element in the arc will often reveal the part it plays. In disease we get a fertile source for the disturbances of the different elements of which the arc is composed. So far, many of these disturbances cannot be explained by the limited knowledge we possess at present, and some new conception is necessary for their interpretation. The analysis of the

phenomena on the lines indicated in this paper has resulted in the conception that the ventricle is completely under control of the auriculo-ventricular node, and that the small beats are due to participation of only a portion of the fibres of the ventricle in the contraction, and this again is due to impulses being discharged from the auriculo-ventricular node which affect only a portion of the

fibres of the bundle which convey impulses to the ventricle.

Another method of studying the subject is to be found in the recognition of the laws which govern other muscular organs. We know the activity of such organs as the bowel and the uterus is variable, and the variation depends upon the number of fibres that participate in the contraction of the muscle of these organs. The same principle applies to the contraction of voluntary muscles; the number of fibres participating in a contraction may vary—the number depending upon the number of neurones which convey the impulses to the muscle. This principle is well illustrated by

FIG. 13.—Tracings showing the normal rhythm, which varied with auricular fibrillation, as shown in Fig. 12. The heart rate is 70 per minute, and the a-c interval normal.

FIG. 13A.—Represents the events in Fig. 13. The rhythm is shown to be regular and the sino-auricular node is active, and governs and controls the auricle, the auriculo-ventricular node, and the ventricle.

FIG. 14.—Simultaneous records of the jugular and radial pulses. The radial pulse is irregular, of a kind typical of auricular fibrillation, inasmuch as there is no relation between the length of the preceding pause and the size of the beat. The waves (v, c, v) in the jugular tracing are due to the ventricle, and are characteristic of auricular fibrillation in that they show no auricular wave. At times there is no evidence of a beat in the radial, but there is one v wave in the jugular, showing that the ventricle contracted, but so feebly that the wave in the radial was not sufficient to raise the level of the sphygmograph. (See diagram Fig. 14A.)

FIG. 14A.—A diagram representing the events in Fig. 14. In the sino-auricular node space there is no sign of activity. The short strokes in the space As represent the impulses from the fibrillating auricle. The space A.V.N. represents the auriculo-ventricular node and shows its varying activity, and the irregularity of the pulse is seen to be due to the varying periods of recovery of this node. The downstrokes in the space Vs represent the ventricular systoles as shown in the radial pulse. These systoles vary in size and in force. The length of the strokes represents the output of the heart as shown in the radial tracing.

the action of the diaphragm where the movements are regulated by impulses which reach it by the phrenic nerve. At the beginning of inspiration a few fibres contract, and as the inspiratory movement increases a greater number of fibres are involved. At any time these numbers can be controlled by the will. In this instance we see how completely muscle contraction is under the control of the regulating process. This control cannot be demonstrated by experiment, for we cannot imitate the normal stimulation of the phrenic nerve; in an experiment when the phrenic nerve is stimulated there is no gradation in the contraction of the diaphragm.

Seeing, then, that there is a law applicable to muscular organs, both voluntary and involuntary, we can reasonably conclude that the same law applies to the heart, although it is masked by the peculiarities of development, and at first sight is difficult to recognize. The interpretation I have given of the action of the heart brings it within the same law that governs the action of other muscles.

THE CAUSE OF HEART FAILURE.

The manifest and distinctive evidences of heart failure to which reference has been made, as following the onset of auricular fibrillation, can be explained when the character of the pulse tracings in Figs. 14 and 15 are compared. The movement of the blood from the left ventricle to the right auricle is mainly dependent upon the force of the ventricular systoles. The action of only a few fibres of heart muscle is bound to throw out blood with a force barely sufficient or insufficient to carry the blood round the circuit. As a result of this the blood gradually stagnates in the parts where the pressure is least, as in the extremities. The blood to the liver by the portal system has to pass through one set of capillaries before it reaches the liver, and in consequence the force of the ventricle is here at its weakest, and hence the reason for the engorgement of the liver which is so frequent an accompaniment of heart failure in auricular fibrillation.

This explanation of heart failure shows that the view so long held of "back pressure" is not true. The back pressure view was based upon the evidences of stasis to which I have just referred, and on the notion that when a murmur revealed a leaking valve, that leaking valve accounted for back pressure. Anyone who takes the trouble to study his patients and watch the gradual onset of heart failure will have no difficulty in realizing the fallacy of the back pressure theory.

RECOVERY FROM HEART FAILURE.

In the description I gave of a patient from whom Fig. 14 was taken it was shown that extreme heart failure followed speedily on the onset of auricular fibrillation, and this figure was taken while she was suffering from this cause. The sudden resumption of the normal rhythm which is shown in Fig. 15, taken a few hours after the normal rhythm was resumed, was accompanied by a rapid disappearance of all signs of heart failure.

From these two tracings, and from the conditions in which the patient was while they were taken, we can recognize the reason for heart failure and its disappearance. In Fig. 14 most of the heart beats were weak and imperfect on account of the participation of a few fibres only in the ventricular contraction. In Fig. 15 the contractions are full and complete.

Fig. 16 was taken from a man 37 years of age. He was a gamekeeper, and was in a good state of health, and led a vigorous life. He had had an attack of rheumatic fever in boyhood, from which he had apparently made a good

recovery. On two occasions a month before I saw him he had been seized with attacks of great prostration and breathlessness. These attacks lasted a few hours and suddenly ceased. Three days

before I saw him he had had another attack which had not ceased but had continued. When I saw him he was very breathless and had to sit upright in bed, breathing in a laboured fashion. His face was dusky, and his lips and ears slightly cyanosed. The pulse was small and so rapid that it could not be counted by the finger. A tracing was taken with considerable difficulty, which showed the imperfect beats in Fig. 16. The rate was 160 a minute. The heart was only slightly increased in size. For two days this greatly increased rate continued, and he was then put upon digitalis. After a couple of days the rate began to decrease until it fell to 50 beats a minute on the sixth day of taking the digitalis (Fig. 17). The digitalis was stopped, and resumed when the rate began to increase until the dose was found which kept the rate about 60 beats a minute. With the fall of rate all signs of distress disappeared, and within three weeks he was able to resume his work and

experienced no inconvenience so long as he took the digitalis.

In this instance we find that the recovery was due, not to the cessation of auricular fibrillation, but to the disappearance of the imperfect beats, and we can infer how this was brought about. The digitalis acted by rendering the auriculo-ventricular node less excitable, so that although the impulses from the auricle continued undiminished, the node did not re-

spond to these so readily. With the longer rest the cells of the node probably all participated in sending impulses to the ventricle.

It is probable that this effect was brought about by the action of the digitalis upon the vagus nerve. The slowing of the rate of the ventricle and its more complete contraction is sufficiently explained in this way without assuming that the digitalis had any effect upon the ventricular muscle, just as the disappearance of the symptoms of heart failure followed the more efficient ventricular contractions when the normal rhythm was resumed, as shown by Fig. 14. In many cases bodily inactivity results in great slowing of the pulse rate with disappearance of the imperfect beats in both auricular fibrillation and flutter and at the same time the symptoms of heart failure subside. The process of recovery is the same as by the action of digitalis.

FIG. 15.—Tracings of the radial and jugular pulses with the normal rhythm. In the jugular tracing the waves *a* are due to the auricle and the waves *c* to the carotid.

FIG. 16.—Tracing of the jugular and radial pulses three days after the onset of abnormal heart action and great heart failure. The radial pulse was scarcely perceptible to the finger, and the tracing was got with difficulty. The jugular pulse is of the ventricular type, each wave corresponding to a radial pulse beat. The rate is 170 beats per minute.

FIG. 17.—Tracing of the radial pulse from the same patient as Fig. 16, showing the effect of digitalis. The rate is 65, and the beats are now full and effective, and all signs of heart failure have disappeared.

THE IMPERFECT BEAT IN AURICULAR FIBRILLATION.

The increase in rate which so frequently occurs in auricular fibrillation has led to the conclusion that the increase in rate was the cause of the heart failure. This view has seemed justified by the fact that with the slowing of the heart the evidences of heart failure gradually disappeared.

A fuller investigation, however, has revealed that the mere increase in rate is not sufficient to account for the heart failure, for we find many instances of great increase in rate of the normal rhythm with no signs of heart failure. In other words, a great increase in the rate may be accompanied by an efficient output of blood, while a similar increase in rate with auricular fibrillation is accompanied by a deficient output of blood.

From what has been said it will be seen that the reason for this difference is the efficient contraction of the ventricle in one case, and the imperfect contraction of the ventricle in the other case.

When we look at a great number of cases of auricular fibrillation we find variations that follow its onset, which can be placed in three groups. In one group the onset is accompanied by no increase in the rate—indeed, the rate may become slightly slower. The irregularity of the heart is characterized by a relation of the size of the beat to the length of the pause which precedes it. In these patients the onset is not followed by any sign of heart failure, and they may pursue laborious occupations without discomfort. In them effort does not cause any unusual increase in the rate, and the pulse beats are full and effective.

There is another group in whom the pulse rate is not increased at the onset of auricular fibrillation, but may even be decreased so long as the body is at rest (Fig. 18). The pulse beats in these cases are also full and efficient. When, however, effort is made, the rate becomes abnormally increased and the pulse beats weak and ineffective (Fig. 19). When the body is at rest the rate gradually falls and the ineffective beats become fewer until they disappear (Fig. 18).

There is a third group in whom from the outset the pulse is rapid and the beats in the main small and ineffective (Fig. 16), and in these cases heart failure may set in at once; the patient may become unconscious and even die, but as a rule the patient only suffers great breathlessness and weakness. In some, within a few hours of the onset, cyanosis, dilatation of the heart and liver, with orthopnoea, may set in. This condition may persist for days and weeks, but there is generally a tendency for the rate to decrease. Some of these patients are extremely susceptible to digitalis. Digitalis acts not only by slowing the rate, but causes the small imperfect beats to disappear and, with their disappearance, all signs of heart failure also disappear (Fig. 17). So long as digitalis is taken in sufficient doses and the pulse rate kept moderate, the patient may be able to undertake laborious work.

These are the main groups, but there are a great many variations which belong partly to one group, partly to another. So long as it is possible to keep the heart from running away with the imperfect beats it may show little impairment. The heart failure which follows the onset of auricular fibrillation and flutter is due to the impaired out-

put of blood, brought about by the imperfect contraction of the ventricle. The varying degrees of heart failure are due to other factors, such as the absence of disease of the muscle fibres of the ventricle or its presence in varying degrees, and such diseases of the valves as embarrass the ventricles in their work.

VENTRICULAR FIBRILLATION.

The disturbances in the auricle (fibrillation and flutter) which follow on the cessation of the activity of the sino-auricular node find a parallel condition in the ventricle. When the auriculo-ventricular node and bundle cease to control the ventricle, the ventricle at once passes into fibrillation, and, as MacWilliam¹² has so clearly demonstrated, the ventricle becomes ineffective with each fibre rapidly contracting independently of other fibres. As a consequence there is a total cessation of the output of blood from the ventricle, the patient becomes unconscious, and if the fibrillation is continued beyond a few seconds death ensues. The question arises, Where does this change take place?

If we look at the parts concerned

in regulating the function of organs we find one part very sensitive to agents. This is the junction of the efferent neurone with the cells of the organs—such as the neuro-muscular junction of muscle. It is in the terminal branches of the nerve, or the receptors of the muscle cells, that such agents as atropine and curare act in producing paralysis, and it is also in these structures that agents like adrenaline act.

We are still profoundly ignorant of the connexion between the cells of the auriculo-ventricular bundle and those of the ventricular muscle, but it is probable that there is here a sensitive part which is susceptible to agents which interfere with the passage of impulses from the bundle to the

muscle. Reasoning from analogy, the suggestion arises that it is here that the disturbance occurs which produces ventricular fibrillation.

The purpose of making this suggestion is to draw attention to a part of the heart which needs further examination, in order not only to demonstrate the anatomical relation of parts but also the part they play in the functioning of the muscle.

THE ACTION OF REMEDIES.

This way of looking at affections of the heart has a significance applicable to a great many other organs. It can safely be said that the principles which have guided to the revelation of the features of heart failure are applicable to the study of affections of other organs. But this study has shown principles which have a still wider application. In pharmacology, for instance, and the use of remedies in general, the principles revealed here are of special importance. It has long been a matter of humiliation that the action of drugs has never been understood, even when they acted beneficially. The work of experimental pharmacologists receives little consideration from the physician, for the latter finds that his results seldom agree with those of the laboratory. The reason for this divergence became clear to me when I was engaged in the investigation of auricular paralysis. For ten years I gave digitalis freely to all sorts and conditions, and when I collected and analysed the results in only a few cases could its effect be demonstrated.

FIG. 18.—Simultaneous tracings of the jugular and radial pulse when at rest. The diagram shows sino-auricular node inactive, the auricle in fibrillation, the auriculo-ventricular node varying in activity, giving rise to the peculiar radial pulse. All the radial beats are full and effective. Compare with Fig. 19. Note the fibrillation (f) waves in the jugular pulse.

FIG. 19.—Tracing of the radial pulse taken from the same patient as Fig. 18 after slight exercise. The rate is 170, and the pulse beats are imperfect. The nature of the condition is shown by the diagram.

These cases were chiefly patients with auricular fibrillation, and patients with a slight impairment of conduction between auricle and ventricle. In both instances digitalis was often remarkably effective in producing a slowing of the pulse. I recognized in both cases that there were present forms of disease which favoured the action of the drug, and I put forth the view that the action of digitalis was modified by the disease that was present. The idea underlying this statement seems so simple and reasonable and so obvious that it may appear not worth discussing. But as a matter of fact it is one of those fundamental principles the neglect of which accounts for the deplorable state of therapeutics to-day. This will be realized when the principle of the reflex arc is understood. I have pointed out that the agents of disease in producing the symptoms of disease and the phenomena of ill health do so by acting on certain parts of the reflex arc or regulating processes. Drugs and other therapeutic measures act in the same way and affect the same structures. It is manifest, then, that if a drug which acts upon a certain structure be administered to a patient in whom that structure is already disturbed by the agent of disease, the action of the drug would be different from that on structures which are unaffected. As the experimental pharmacologist deals only with healthy structures, we see why his results differ from those of the physician. The recognition of this principle in therapeutic investigation will do a great deal to give precision to our practice, as it has done in the treatment of auricular fibrillation, and do away with that prescribing of useless remedies which is one of the least creditable features of modern medicine.

The failure to recognize this principle leads to many enterprises being undertaken without the knowledge necessary for their success, such as the investigation into the dangers of anaesthetics and of anaphylaxis.

CAPILLARY PARALYSIS.

In one of our discussions at the St. Andrews Institute I raised a question which had long puzzled me—the nature of heart failure, so called, which occurred in acute infections, as in puerperal fever, and the rapidly fatal infection that followed some surgical operations. The pulse in these conditions becomes extremely feeble, while the heart does not dilate. When I mentioned this and wondered why the pulse became so small, Professor Herring suggested that there might be no blood in the heart to pump out. I was struck by this suggestion, and my mind immediately reverted to the observations of Bayliss¹³ upon wound shock, and Dale¹⁴ upon histamine shock. In both these conditions there was a resemblance to what I had recognized in the malignant infections, and the phenomena in histamine shock has a remarkable resemblance to the features present in this condition. Dale has shown that in histamine shock the blood accumulates mostly in the capillaries of the extremities. I recalled a *post-mortem* examination I once made upon a woman who had died from puerperal fever. It was one of those painful and tragic experiences which every now and again confronts a doctor. A colleague who had been in consultation upon a woman with puerperal fever, whom he had examined, was met upon his way back and asked to attend a primipara in labour. She was successfully delivered, but took ill the following day and speedily died. The same night he was called out to another confinement, with the same disastrous result. At the *post-mortem* examination on one of them we could find nothing to account for the death. The heart contained but little blood, and showed no signs of damage. There was no stasis of blood anywhere, and the reason for death was inexplicable.

In our investigations in St. Andrews we had recognized that the capillaries of the skin were in a state of fluctuation. Among certain individuals, at times, the skin of the arms or legs becomes mottled, showing patches of a dark colour and patches of a paler hue. By encircling these patches with a ring of ink, in a few minutes we found that the dark patch became pale, and the pale patch became dark. There was evidently some influence at work which produced this variation, and it indicated the capacity of the capillaries to dilate and contract. Subsequently, we found that Krogh¹⁵ had made an elaborate investigation of this capillary fluctuation,

and demonstrated that the capillary field, if fully dilated, had an enormous capacity so that a portion of the capillaries could contain all the blood in the body.

In studying the heart failure which follows auricular fibrillation, we cannot but be struck with the condition of the peripheral circulation. In many cases the face and lips become dusky and blue, and there is oedema of the dependent parts. The contrast between this condition of the peripheral circulation and that which precedes death from a malignant infection is striking. Here the face is pale and sunken, and there is no oedema.

The reason for this difference seems to be that in the former case the capillaries are in no way affected and that they retain their contracted or controlled condition, and the stasis is due to a deficient force of the ventricular contraction. In the infections, on the other hand, the capillaries are greatly dilated and the blood is retained within them, so that only a portion of it circulates.

So far we have had little opportunity of testing this view, but I tried it in the following observation. A girl suffered from acute pneumonia with high fever and delirium. On the seventh day she seemed to collapse and the parents were in great distress; the face, which had been flushed, had become pale. The pulse had become small, though not very rapid, and the child had sunk into stupor, which the parents feared heralded the onset of death. I considered the condition to be a consequence of the crisis, and it occurred to me that it might be possible to differentiate this from shock and the condition of collapse that follows malignant affections. I thought that if it were the latter condition the functions of the brain would be suspended. So I poked the girl in the ribs, and told her to open her eyes. This she did; then I asked her to smile, and she smiled, and I concluded that the condition was not one of capillary paralysis, and that she would recover, which she did. The collapse which follows the malignant infection shows pallor, stupor, and a feeble pulse, but in the latter case the patient cannot be roused to give an intelligent response.

The purpose of this reference to capillary paralysis is to direct attention to a field for exploration which has been almost entirely overlooked. Though capillaries are such simple structures we are ignorant of the many parts they play in the economy. It is manifest that they are subject to variations in activity like all other organs consisting of active cells. There are processes concerned in regulating their activity, and we know so little of them that we are not able to recognize, and far less interpret, many of their most distinctive manifestations. It is necessary here also that new methods of research be employed, and, so far as we have gone, the application of the principle of the reflex arc promises to be as fruitful here as in its application to the interpretation of cardiac phenomena.

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THE first lecture of the course for 1924 at the Royal College of Surgeons of England will be given on Monday, January 21st, by Mr. R. St. Leger Brockman (Sheffield), on drainage in acute appendicitis. Other lectures will be given on January 23rd by Mr. R. M. Handfield-Jones, on retroperitoneal cysts; on January 25th by Mr. Sidney Forsdike, on cancer of the cervix; on January 28th by Mr. Frank Cook, on the toxæmias of pregnancy; and on January 30th by Mr. Alexander Fleming, on antiseptics in local and general infections. The first lecture in February will be given on February 1st by Mr. Geoffrey Jefferson (Manchester), on injuries of the cervical spine. The lectures, which will be given at 5 p.m. on each day, will be continued during that month. Further particulars will be published later.