when damaged, seriously hamper individual activity and utility, and collectively tend to undermine our national vigour, prosperity, and well-being.

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THE NATURE AND SIGNIFICANCE OF HEART SYMPTOMS.

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II. THE REFLEX PROCESS AND THE HEART BEAT.

As disease is only recognized by the symptoms it produces, a knowledge of symptoms is a necessary preliminary to an intelligent investigation of disease. This knowledge of symptoms is necessary not only to the diagnosis of a patient's complaint but for a prognosis and a rational treatment. The symptoms of disease even in one sick individual may be numerous and varied, so that it is impossible to study every symptom with that care and insight which are necessary for understanding its use in the practice of medicine. The search for symptoms by new methods leads to the discovery of many, but the result is often but to add to the mass of details which obscure the problems of disease, and some other method of investigation is urgently needed.

Phenomena in nature, however numerous and varied, are subject to definite laws. Progress in every branch of knowledge which deals with these phenomena is hampered until these laws are discovered. The symptoms of disease are natural phenomena, and the vital processes concerned in their production are certain to be few in number, and the nature of symptoms will not be understood until these vital processes are discovered.

Recognizing that a knowledge of symptoms was the first step in the investigation of disease, the staff of the St. Andrews Institute for Clinical Research began their work by a search for the laws governing the production of symptoms.

In the course of this inquiry it was found that a great mass of symptoms were produced by disturbance of a single vital process—that which includes what is known as reflexes. The term "reflex" had been restricted to a few manifestations of a vital process, so that its affinity to other manifestations had not been recognized.

Though reflexes had received much attention, yet the manner in which they were modified by disease had received little attention. We therefore have devoted a good deal of study to the process as it concerns different organs, and in this article I deal with the light which the recognition of this process has thrown upon the mechanism of the heart beat.

The Nature of the Reflex Process.

We tried to look at the reflex acts from the point of view of the vital process. We analysed the parts concerned in a reflex arc. The arc consists of cells that are capable of stimulation connected in some way with cells that are capable of producing an effect. In some instances we can recognize the stimulus and the cells stimulated, but as a rule we can only recognize the effect. In the vast majority of reflexes we can only infer or guess at the nature of the stimulus, while of the manner of conduction from the cells stimulated (receptor cells) to the cells activated (effector cells) we have only the vaguest notion.

The parts concerned in a reflex act are the stimulus, the cells receiving the stimulus, the cells concerned in the conduction of the stimulus, and the cells which respond and produce an effect.

It will be seen that this process includes a great variety of responses or manifestations widely different in character and appearance, as contraction of muscle, secretion of glands, sensations, etc. For this complicated process we required a term, and we attempted to get one which would be compre-

hensive, but on consideration we found that no term could convey so much of the process as the term "reflex." To avoid confusion we tried to give a clear description of what was meant by the term. The meaning we attach to the term "reflex" is *that vital process by which a stimulus passes from one tissue or organ to another, resulting in a response.* The nature of the response depends on the function of the organ stimulated.

In this definition of the reflex process the manner in which the stimulus is conveyed from the receptor cells to the effector cells is not mentioned. Hitherto it has been assumed to be by nerves, but nerves are not necessary to the process, for other tissues may convey the stimulus, as will be realized when the evolution of the nervous system and the movements of the heart are described.

The Origin and Evolution of the Reflex Process.

The test of a new conception is the light that it throws upon obscure problems. The application of the theory of disturbed reflexes led to an examination of the mechanism of the heart beat—a mechanism which depends upon this vital process which we call reflex, and it fulfils the test of a true conception, as it presents the whole subject of the heart beat and its disorders in a new and better light. It also provides an interpretation of many facts which had either been misunderstood or overlooked, and gives a guide in which direction to look for other facts.

The nature of the process we call a reflex can be gathered by the description given in Bayliss's *Principles of General Physiology* of the evolution of the nervous system. This system begins in the conduction of a stimulus in the lowest multicellular organisms, where the communication passes from cell to cell without any intermediate mechanism. The next stage may be seen in the sea anemone, where projections of the cutaneous cell are connected with muscle fibres. The next stage may be considered to be that when a nerve cell is interposed the stimulus arising in one cell (the receptor or A part of the reflex) passes to a nerve cell (the centre or B part of the reflex) which is connected with the organ which gives the response (the effector or C part of the reflex). This stage, simple at first, as in the earthworm, becomes extremely complicated, especially in the central or B part of the reflex, which is situated in the central nervous system, where the stimuli are rearranged and guided into the paths for the production of their effects. The portion of the reflex in the central nervous system is that generally spoken of as "centres"—as the centre for vomiting, for respiration, for micturition, etc.

It will be seen that this description of the evolution of one part of the nervous system deals with the passage of a stimulus from one tissue to another, corresponding with our conception of a reflex.

The Reflex Process and the Movements of the Heart.

In the different rhythms of the heart we find variations in the reflex process, corresponding in a curious manner with Bayliss's description of the evolution of the nervous system. In certain abnormal conditions the muscle cells of the auricle and ventricle may contract independently of the control of the normal mechanism. The contraction of one cell stimulates its neighbour to contraction, and hence we get that remarkable condition called fibrillation. In this condition the muscle wall, though as a whole it stands still, is seen to be in continuous movement on account of the inharmonious contractions of the individual muscle cells. No sooner does one cell contract than it is again stimulated to contraction by its neighbour—that is to say, the stimulus evoked by one cell passes directly to another, in the manner described as the first stage in the evolution of the nervous system.

The stimulus for contraction of the ventricle passes from the auricle to the ventricle along the auriculo-ventricular bundle. (See Fig. A.) If this be cut or a portion destroyed by disease the ventricle no longer responds to the stimulus from the auricle. The ventricle, however, does contract at a slower and different rate from the auricle. There is good reason for assuming that the stimulus arises in the remains of the bundle and passes to the ventricle by the Purkinje cells. Thus we have an illustration of the reflex process where the stimulus arises in the Purkinje cells and is conveyed by them to the effector organ—that is, to the muscle cells of the ventricle.

The process is similar, though a little more complex, when the stimulus arises in the auriculo-ventricular node or in the auricle. The stimulus for contraction arises normally in the

sino-auricular node, passes directly to the auricle, causing it to contract, is taken up by the cells of the auriculo ventricular node, which reproduce the stimulus and send it by the bundle to the ventricle, thus giving rise to that regular sequence of auricular and ventricular contractions which facilitates the work of the heart.

It is to be observed that in this description of the conduction of the stimulus the stimulus is not conveyed by nerve fibres but by the Purkinje cells, the stimulus passing from cell to cell. Comparisons have been made of the rate of conduction along nerve fibres with that along the auriculo-ventricular bundle, but the conditions are not comparable because the nerve fibre is a continuation of one cell, while in the bundle the stimulus passes through a great number of cells. Above the sino-auricular node, and modifying its activities, are the vagus and sympathetic nerves. It is through these that the heart's action is reflexly affected by agents outside the heart. We thus see that the heart's rate and rhythm, both normal and abnormal, are governed by variations of the same vital process. How the recognition of this fact leads to a fuller understanding of the variation of the heart beat and the factors engaged in modifying it will be seen in the account which follows.

The Practical Application of the Reflex View of the Mechanism of the Heart Beat.

This description of the mechanism of the heart beat may appear to be of the nature of an academic disquisition and of little practical value. On the contrary, this appreciation of the factors concerned is essential to the understanding of the signs and symptoms of disease and of the action of remedies. Indeed, the reason of the backward state of cardiology and of our knowledge of the action of remedies is due to the failure, to grasp the principles involved in this aspect of the subject.

In the last article it was shown that there were two kinds of tissue concerned in the movements of the heart: (1) that concerned in the production and the conduction of the stimulus which regulates the contraction of the chambers (the conducting, or, as we may also call it, the reflex system—Fig. A); (2) that concerned in the contraction of the chamber—the muscle cells of auricles and ventricles (the contracting system).

These two systems are quite distinct in function, and the manifestations in health and disease of the one system are quite distinct from the other, and the kinds of information yielded by the symptoms of the two systems are also quite distinct.

The conducting system, with the sympathetic and vagus nerves, is concerned with the regulation of the rate and rhythm of the heart's contraction. The agents of disease readily affect some parts of this system, and in consequence we get the symptoms which are peculiar to this system—that is, variations in the rate and rhythm.

The contracting system, on the other hand, is concerned with the output of blood from the heart—that is, with maintaining the functional efficiency of the heart. When the heart begins to fail—that is to say, when its functional efficiency becomes impaired—the symptoms belong to quite a different category from that of the conducting system.

If this distinction is kept in mind it will be realized that attempts to find out the functional efficiency of the heart by observing the variations in the rate and rhythm of the heart are bound to fail, for the simple reason that information of a kind is sought from a source that cannot yield it.

The introduction of auscultation was followed by long and careful research to find out the cause of murmurs. The excellent results were vitiated by the failure to recognize the kind of information which had been obtained. It was thought that the functional efficiency of the heart could be ascertained from the modified sounds of the heart. To-day we find the modified sounds used as a guide in treatment and prognosis—a kind of knowledge they are incapable of supplying.

The interpretation of variations in the rate and rhythm of the heart has been misapplied in the same way, for the kind

of knowledge they reveal has not been understood. That the functional efficiency of the heart depends on the integrity of the heart muscle is such a commonplace that it seems unnecessary to mention it; but we find that the information of functional inefficiency or heart failure is sought for in signs which have nothing to do with the functional efficiency of the heart muscle, while the signs peculiar to the inefficiency of the heart muscle are overlooked.

It is true that certain murmurs may indicate valves so damaged that they impede the work of the heart muscle. But it must be realized that they only oppose a hindrance to the contracting system, and it is the exhaustion of the contracting system that produces the symptoms of heart failure—that is to say, while heart murmurs may indicate conditions that may lead to heart failure, they do not of themselves give the signs of heart failure. In the same way the conducting or reflex system may occasionally give certain signs which we associate with heart failure, or which may lead to heart failure (as an excessive increased or diminished frequency), but these are not the signs of heart failure.

The variations of rate in response to effort, which are so often taken as evidences of functional efficiency, are thus seen to be due merely to a susceptibility to stimulation of some part of the conducting or reflex system which may have nothing to do with the heart's state of efficiency. Thus as the signs of damaged valves give one kind of evidence, so does the manifestation produced by the conducting or reflex system give another kind, and the signs of the contracting system give information distinct from the other two.

The Kind of Information Yielded by Dis- turbance of Rate and Rhythm (the Reflex or Conducting System of the Heart).

The phenomena produced by disturbance of the reflex system of the heart can best be described by recognizing two different kinds of mechanism which regulate the heart beat—(1) when the rhythm starts at the sino-auricular node (the normal rhythm), and (2) when the heart's contraction starts at some other place in the heart (abnormal rhythm). I propose to deal very briefly with the evidences, merely showing how the recognition of the disturbances throws light of a valuable kind on diseased states and on the effects of remedies. The knowledge acquired so far is limited, but such as it is it shows the lines on which more valuable knowledge can be acquired.

The normal heart beat starts at the sino-auricular node, where the stimulus for contraction is produced. The stimulus passes to the auricle and ventricle in the manner already described. It will thus be seen that in the normal heart beat the variations in rate and rhythm of the pulse are entirely dependent on the sino-auricular node. The cells of the sino-auricular node, after the discharge of a stimulus, are exhausted and remain quiescent for a short period, during which they recover from the exhaustion. As this period of recovery lengthens they become more and more susceptible to stimulation, until they again discharge their stimulus. What it is that excites them to "go off" is not quite clear, but certain agents have the power of increasing or diminishing their susceptibility—as heat, which causes an increase in the rate, or cold, which causes a decrease. It is possible also that agents circulating in the blood may affect the cells in a similar fashion; certain agents like alcohol seem to increase their sensibility, while others like digitalis may decrease it. In like manner the agents of disease may act, by the increase in temperature or by the toxic products.

The sino-auricular node has inherently a pace which is modified by certain circumstances. It is under the domination of the nervous system by means of the vagus and sympathetic nerves. The vagus maintains such a control over the sino-auricular node in health that it is never free from its inhibitory influence. A relaxation of vagal activity is followed by an increased rate of the pulse. The sympathetic acts in the opposite manner to the vagus, and an increase in its activity leads to an increase in the rate of the

FIG. A.—Diagram representing the two main systems concerned in the heart beat. (1) The conducting system, represented by the sino-auricular node (S.A.N.) and the auriculo-ventricular node (A.V.N.) and bundle (A.V.B.). In both auricles and ventricles are also Purkinje fibres which belong to this system, represented by the scattered cells (P) in the auricle. The vagus (vag.) and sympathetic (sy.) also belong to this system. (2) The contracting system, represented by the muscle cells of the auricle (A) and ventricle (V).

heart. Here is where the great difficulty in interpreting variations of rate comes in. The sino-auricular node without vagus influence would cause an increase in the heart's rate. When, then, we find an increase in rate, we have to ask whether it is due to the sino-auricular node being freed from vagal activity, or to an increase of the sympathetic influence, or to a direct effect of some agent (temperature, toxins, drugs) on the sino-auricular node itself. These are the types of questions that require settling before we can understand the action of remedies or the symptoms of disease.

We know already a little, but that little indicates that there is much more to be known. We know, for instance, that the increased heart rate that follows the administration of atropine is due to a suspension of vagal activity, and that the increase in rate is different from that which follows a rise of temperature or effort, or the administration of alcohol. It is also known that digitalis may have a definite effect on the vagus, stimulating it and so restraining the activity of the sino-auricular node.

Varied as are the effects of drugs diseased states have effects as distinctive, for agents of disease affect the reflex system in diverse places and diverse ways, and it is by the recognition of these diverse modifications that the different diseased states can be recognized. We know that the reaction is different in pneumonia from that in typhoid fever, and these again from that in rheumatic fever. During some infections the conducting system may be affected, as shown by the temporary presence of partial heart-block.

But there is more than that, for the agent of disease modifies or counteracts the action of drugs. Thus, though in the normal heart atropine increases the rate, yet in certain diseased states it may slow the heart's rate. In some forms of disease digitalis will slow the heart rate, in other diseased states it is without effect. The recognition of these facts explains the reason of the confusion which reigns in the therapeutic field. A great deal of work has been done in testing the action of drugs on the healthy heart, but it has not been realized that the diseased condition modifies the effects of the drug. When it is realized that it is chiefly on some part of the reflex process that most drugs act the importance of a better understanding of this process will become apparent, all the more so when it is further realized that it is also by the modification of some parts of this process that many symptoms of disease arise. If these points are grasped it will be seen that in the sick man the agents of disease have affected the parts on which the drugs act, and therefore we can state as a principle which must be recognized in the investigation of the action of drugs that *the effect of a remedy is modified according to the nature of the disease*. It is the neglect of this principle which keeps therapeutics in the state of confusion in which they are at present.

Other reactions have to be considered. R. M. Wilson has lately drawn attention to a factor that has not been recognized—the secondary reaction to a stimulus. In a balanced reflex, when an act is regulated by two nerves acting the one in opposition to the other, the excitation of one is accompanied by the diminished action of the other. When the excitation ceases the nerve whose activity was diminished may greatly increase its activity. Thus a temporary slowing of the heart by stimulation of the vagus may be followed by a great increase in the rate of the heart by secondary reaction of the sympathetic (a reflex stimulation of the sympathetic by the vagus).

Abnormal Rhythms.

If the understanding of the reflex system is of importance with the normal rhythm, it is evident that with an abnormal rhythm it is of still greater importance. The various places where the heart beat may start are different in structure and in function from that of the normal starting place (the sino-auricular node), and in consequence the effects upon the ventricles are different. This was so fully dealt with in the previous article that I need not dwell upon it here, save to refer to the differences which follow effort in the cases, say, of the normal rhythm, auricular fibrillation, and heart-block, and to the difference of the effect of drugs like digitalis. Moreover, the fact that the stimulus which is produced by the cells of the contracting system—as in auricular fibrillation, flutter, and the idio-ventricular rhythm—is different from that which arises in the cells of the conducting system calls for a reconsideration of the mechanism of these abnormal rhythms and of their relation to the various agencies (effort, drugs, heat, toxins of disease) which act upon them.

SUMMARY.

1. The mechanism concerned in regulating the heart beat belongs to the vital process included under the term "reflex."
2. The cells taking part in this mechanism belong to two groups: an extrinsic, connected to the nervous system by the vagus and sympathetic nerves, and an intrinsic, which includes the sino-auricular and auriculo-ventricular nodes, and the Purkinje cells in the bundle and auricles and ventricles.
3. Agents of disease (toxins) which modify the rate and rhythm act on different parts of this mechanism, and certain disease agents produce characteristic effects.
4. Drugs that influence the rate and rhythm of the heart act in the same way, some of them also producing characteristic effects.
5. As toxins act on the same parts as drugs the effects of drugs will be modified by the effects of the toxins.
6. Before the effects of a remedy can be investigated it is necessary to know if the toxins have not already produced an effect which will interfere with the action of the remedy.
7. The kind of knowledge which disturbances of the reflex process reveals is limited to the variations in rate and rhythm, and they give no information regarding the functional efficiency of the heart.

THE PEPTIC ULCER.

WITH A REVIEW OF TWELVE MONTHS' SURGICAL TREATMENT (1921).

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To obtain control over any disease it is necessary to possess means which can be safely employed to eradicate it when established, and a knowledge of its etiology such as will enable us to prevent its occurrence or recurrence. Surgical experience has made a very substantial contribution towards the mastery of peptic ulcer. It has contrived means of dealing radically with ulcers which are safe, at least in practised hands and when employed with discrimination. In the course of arriving at its technique it has thrown a great deal of light on the conditions which determine peptic ulceration, and which, if undisturbed, will tend to its recurrence. I will argue later that with the assistance of radiology it has now actually reached an understanding of the immediate cause of ulcer, and has determined, although not exhaustively, the ulterior causes.

Among the contributions which radiology has made to medicine none is more brilliant than that which it has made to the diagnosis of gastric disorders. Without its assistance the diagnosis of ulcer uncomplicated by penetration or haemorrhage or stenosis was only a matter of suspicion. Now suspicion can be put to a test in which the margin of error is, in my experience, extremely small. I wish to express my gratitude to my colleagues, Dr. Oram and Dr. Mather, to whom I owe the reports on the cases which I propose to review.

Of these cases, 48 in number, on whom I operated in 1921, 41 were men, 7 women. In 34 instances the ulceration was gastric, in 8 duodenal, and in 6 jejunal. These figures do not include other simple disorders of the stomach, such as those which depend on adhesions or those due to pylorospasm without ulcer, but I wish to refer shortly to these two classes.

Adhesions Involving the Stomach.

One is impressed with the gross disturbance of function and the simulation of visceral disease which may be caused by such adhesions. I have opened the abdomen on four occasions during the year in cases of this kind, the patient in each case being incapable of following any occupation. In all four the adhesions were chiefly between the stomach and the anterior abdominal wall deep to an operation scar. According to the histories obtained the earlier operation had been as follows:

1. For gastric ulcer (evidence of operation on pylorus).
2. For perforated gastric ulcer (suture).
3. For gastric ulcer (gastro-enterostomy).
4. For perforated duodenal ulcer (suture).

Infection is the cause of such adhesions. When formed between the stomach and the abdominal wall they may cause