THE SENSATIONS AS REFLEX MANIFESTATIONS OF DISEASE.

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

IN a recent communication Sir James Mackenzie¹ has put forward the thesis that the early symptoms of disease reveal themselves in a disturbance of the normal reflexes. This hypothesis, which was arrived at by the members of the St. Andrews Institute for Clinical Research, involves a wider conception of what is meant by "reflex" than the term is usually held to denote. Any definition of reflex action has to be an elastic one, comprising as it must such widely differing varieties as the axon reflex and the conditioned reflex of Pavlov, but the whole subject of reflex action must be viewed from a different standpoint if sensations are to be included in the same category.

According to this theory the body is regarded as a highly complex and efficient mechanism, the actions of which are co-ordinated and controlled by innumerable reflexes. In a state of health the reflexes are nicely balanced and in constant play one with another. Variations of balance in either direction occur within certain limits and provide for the physiological necessities of the organism as a whole. Symptoms of disease show themselves by a disturbance of balance which in the initial stages may be similar to that occurring in normal physiological conditions, the difference being that in the case of disease the physiological stimulus is absent or is insufficient to account for the altered condition.

As an example may be cited the breathlessness, increased cardiac action, and other phenomena associated with severe and prolonged muscular exertion. These are physiological variations of balance in a number of reflexes. The same disturbance occurs more readily with increasing age and may still be regarded as physiological, though it reveals a failing power of response in the various organs of the body. In certain diseased conditions—for example, in hyperthyroidism, the same disordered reflexes arise from a stimulus which in the normal condition is ineffective. The injurious agent acts upon some portion of the arc of one or more of the reflexes, and the normal balance is disturbed.

The symptoms of disease are illimitable, just as the reflexes are, and many of them are common to a number of different conditions. They tend, however, to group themselves in a definite manner, and it is hoped that by careful study and long-continued observation it may be possible to classify these groups and to arrange them upon a scientific basis. This can best be done by observations on the behaviour of the body itself in the earliest stages of disease. The body furnishes an apparatus more sensitive than any laboratory instrument, and the slightest deviation from the normal reveals itself in altered reflexes before the most elaborate physical and chemical tests are applicable. Further, the body, in its response to an injurious agent, indicates, in a manner which no laboratory test can do, its capacity for successful resistance, and so furnishes the skilled observer with material for prognosis as well as diagnosis. It consequently falls to the lot of the general practitioner, who most frequently sees the earliest symptoms of disease, to detect the meaning of symptoms as revealed by this most elaborate and sensitive of all mechanisms—the living body.

In order to understand the meaning of symptoms it is first of all essential that there should be a clear knowledge of the structures and mechanism on which they are based. The reflex arc in its simplest form consists of a receptor, afferent nerve fibre, nerve centre, efferent nerve fibre, and an effector. Disease may alter the normal reflex by attacking any one or more of these parts of the reflex arc.

For practical purposes one may divide the arc into three parts—the receptor, the centre, and the effector. The reflex, however, is probably in all cases much more complex than is usually represented, and this complexity is determined by the nature and extent of its connexions in the

central nervous system. The reflex centres are all more or less linked up together. Interconnecting neurones with their synapses largely determine the special characters of reflex action as worked out by Sherrington. Even in the simplest reflex involving muscular movement there is co-ordination, a function which is exercised by the reflex centre. An afferent impulse on reaching the reflex centre passes to one or many neurones, the extent of its spread varying according to the character and strength of the stimulus. The activity of some nerve cells is increased while others are inhibited. Thus in a reflex producing flexion of a limb the efferent neurones of the flexor muscles are stimulated, but the efferent neurones of the antagonistic extensors are inhibited. Reciprocal innervation exists, and the impulse is so co-ordinated in the reflex centre that a co-ordinated response takes place in the effectors. Physiological evidence is lacking as to the exact nature of the mechanism involved in the visceral reflexes, but there is some reason to believe that reciprocal innervation is of very general occurrence.

The most common of the early symptoms of disease are sensations, especially those of exhaustion and pain. The ordinary physiological conception of the reflex finds no place for these sensations, but from a clinical point of view they may be regarded as reflexes provided one adopts a wider conception of what the reflex really signifies.

Receptors are universally distributed throughout all living structures in the body, and each is normally excited by an adequate stimulus differing in character according to the structure of the end organ excited. The nerve impulse travels by afferent nerve fibres to some part of the brain stem and its prolongation the spinal cord. The true reflex centres are found in what is developmentally the oldest portion of the central nervous system, and with the possible exception of the senses of smell and sight, all afferent impulses pass to that portion of the nervous system which is represented by the mid-brain, pons Varoli, medulla oblongata, and spinal cord. Many of the important visceral centres have been roughly localized, but it is a mistake to regard them as separate units. The centres are frequently diffuse, freely connected, and more or less interdependent. A powerful stimulus, such as that occasioned by the spasm of a ureter endeavouring to get rid of a calculus, provides an impulse which sets up a number of reflexes. The predominating result is pain referred to certain areas of the outer body wall, but the impulse spreads widely, producing vomiting, vasomotor, cardiac, respiratory and other disturbances. The sensation of pain is just as clearly a reflex as is the occurrence of vomiting. In the case of sensations the effector organ is the cerebrum, whether one regards their perception as taking place in the cortex or in one of the cerebral basal ganglia. The cerebrum is to be looked upon as a distinct organ with very definite functions, not the least of which is the translation of afferent impulses into sensations. The cerebrum responds to the impulse, and is in this case the effector organ; its response is the sensation of pain, or whatever sensation the afferent impulse evokes. The response by the cerebrum is as a rule only one of the results of an afferent impulse; even the sense of pain, although the most obvious symptom, may not be the essential part of the reflex. Sherrington has shown that in the spinal animal the painful stimulus is prepotent, although in this animal it cannot evoke the sensation of pain. In other words, the painful stimulus gives rise to an impulse, which, by virtue of its special character or strength, commands the pathways in the reflex centres involving many neurones and producing a great variety of responses or symptoms.

But the cerebrum can act as a receptor as well as an effector, that is to say, it can, in response to an adequate stimulus, initiate a reflex. The perception of sensation excites a number of special processes, including, it may be, memory, judgement, or other phenomena associated with cerebration. Such activity may result in an impulse which, from the point of view of the present argument, must be regarded as afferent in that it goes to the reflex centres. It is there co-ordinated and distributed to the effectors. In this sense the conditioned reflex of Pavlov is a double reflex. In the first the receptor is at the periphery and the effector is the cerebrum, in the second the cerebrum acts as the receptor and the impulse passes through the reflex centres to bring about the final response in a peripheral effector.

This conception of the central nervous system is an unusual one, but provides a working hypothesis which appears of value from a clinical point of view. It exalts the importance of the reflex centres, the really vital portions of the central nervous system. The cerebrum, and the same is true of the cerebellum, is looked upon as a distinct organ which can receive and initiate impulses, but these impulses are sorted and to a large extent co-ordinated in the lower reflex centres. The thesis, pushed to its logical conclusions, involves one in seeming absurdity. Voluntary muscular action becomes in this sense a reflex. Initiated in the cortex cerebri, it passes as an afferent impulse to some part of the reflex centre, and is there translated into efferent impulses which result in co-ordinated movement.

Voluntary muscular movement cannot be classified as a reflex in the restricted physiological sense of the term, and it might be better to employ some other term to denote the conception the wider view requires. It is difficult to find a term which expresses the general meaning so well as that ordinarily implied by "reflex," and it is at least open to question whether one cannot justifiably extend its scope to include the greater part of the mechanism whereby voluntary muscular contraction is produced. Mental processes can initiate visceral reflexes. Recollections of various kinds, mental excitement, anger, shame, and other conditions provide impulses which provoke widespread activity of the reflex centres. The resulting cardiac, vasomotor, and other visceral phenomena are undoubtedly reflex, and why should not the simultaneous contraction of voluntary muscle be included in the same category? It is true that the contractions of striped muscle can be inhibited by the will, while there is no such control over the visceral responses; but this power of inhibition is largely acquired by education and is not always complete. Many voluntary actions have much in common with the reflex. The proper swing of a golf club, and in fact skilled movements generally, show many of the characteristics of reflex action, and it is possible that they actually are reflexes. It is, indeed, in many cases difficult to determine when an action ceases to be voluntary and becomes a reflex.

There is ample reason to believe that voluntary movement and the reflex action of voluntary muscles do in many instances make use of essentially the same mechanism, and this is all that the St. Andrews view of the reflex requires. Whether all voluntary action is to be regarded as reflex involves serious problems with which we are not concerned.

The cerebrum and cerebellum occupy a very special position. While capable of acting as effectors and as receptors in the reflex arc they have their own distinctive functions, and, moreover, they exercise a control over the lower reflex centres. The control exercised by the cerebrum is mainly that of inhibition, that of the cerebellum is a reinforcement of the activity of the reflex centres. The response of the body to a given stimulus is greatly complicated by the controlling influence of these organs and the same influences complicate the altered reflexes brought about by the action of injurious agents in disease.

Reflexes are frequently grouped in pairs, the one being antagonistic to the other. Examples are seen in the voluntary muscles which are grouped to form opposing forces: the heart has accelerator and inhibitor nerve fibres, the blood vessels vaso-constrictor and vaso-dilator fibres, and so on. Opposing reflexes are nicely balanced one against the other, but the balance is in some cases influenced by this third factor acting upon the centre—namely, a control by the cerebrum and cerebellum. The influence of the cerebellum is mainly concerned with the postural reflexes, and the importance of the reflex in the maintenance of posture is well known. In a recent article Blundell Bankart² has given an excellent description of the postural deformities which arise from alterations in the normal reflexes. Slight postural changes may be early indications of disease, and their production is the result of a disturbance of balance of certain reflexes. Temporary alterations may be physiological, as in fatigue, but they may be pathological, and if the conditions persist actual structural deformity may ensue.

Head,³ in a Croonian lecture upon diseases of the nervous system, points out that the manifestations of disease comprise both loss of function and outbursts of

excessive activity. He ascribes these phenomena to a "release of function," and divides them into categories entitled "disintegration" and "escape from control." It may be true that, as Hughlings Jackson taught, "destructive lesions never cause positive effects, but induce a negative condition which permits positive symptoms to appear." By the impairment or destruction of one reflex arc a negative condition is produced, the normal balance of the reflexes is disturbed, and positive symptoms arise from over-action of other reflexes which are no longer held in check. The same results are shown even more strikingly outside the central nervous system. If the activity of the vagus nerve is impaired by the use of atropine the heart beats more rapidly. The heart is released from the function of vagus control, but the real interpretation of the condition lies in a disturbance of the reflexes controlling the organ, impairment of vagus activity resulting in over-action of the accelerator mechanism. Many examples of a similar nature might be given. The term "release of function" may be more appropriate to some of the conditions described by Dr. Head, but the principle underlying them is the same, and Sir James Mackenzie's theory of disturbed reflexes provides a working hypothesis of wider application.

The theory is being tested at the St. Andrews Clinical Institute, and is found to be of great value in the elucidation of the early symptoms of disease. It enables the drawing up of a rational classification of symptoms, and gives a clue to their relative importance.

Incidentally it has revealed to members of the institute, and to others who have attended the clinics, the necessity of a closer correlation between the teaching of anatomy and physiology. Both subjects form the basis of any rational conception of the problems which have to be solved in medicine, and a thorough grounding in the anatomy and physiology of the mechanism of the living body is the first essential of medical education.

REFERENCES.

- ¹ Mackenzie, BRITISH MEDICAL JOURNAL, January 23rd, 1921, p. 147.
² Blundell Bankart, BRITISH MEDICAL JOURNAL, April 23rd, 1921, p. 587,
and April 30th, 1921, p. 636. ³ Head, *Proc. Roy. Soc., B*, vol. 92, p. 184,
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ON

SOME POINTS IN ABDOMINAL DIAGNOSIS.*

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WE all know the admirable lists of physical signs and symptoms carefully compiled in textbooks, the perusal of which makes differential diagnosis appear so straightforward and almost infallible, but we know, and to our cost, that in actual practice we find ourselves at our wits' end to make a diagnosis, and that the difficulty arises from overlapping of the signs and symptoms of widely different lesions and of what are called atypical cases. So instead of adding to the lists compiled in this manner I will discuss some of the difficulties we encounter, and try to give some hints whereby we may learn to avoid in future those failures we have all perpetrated. In brief, were we able to ascertain and elucidate in our minds those small warnings which precede nearly all acute lesions we would be led naturally and spontaneously to the climax they inevitably end in, and the crisis ceases to be a matter of doubt and is revealed as a clear inevitable event; it becomes a logical deduction. Much as is the bursting of an explosive charge inevitable when the lighted fuse reaches the detonating charge, so a gastric ulcer or chronic appendicitis or a gall stone inevitably flares up into a crisis. The exceptions to an inevitable flare-up are few and far between, and our proper mode of conduct is to advise an early operation and not to rely upon the very doubtful chance of a "flare-up" not occurring. Where we find our real difficulty is in unravelling the warnings, since so often various acute "crises" in their early stages have

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