Ataxia: A Symptom

ATAXIA: A SYMPTOM.

BEING THE FIRST OF THE MORISON LECTURES, 1912.

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I.

MR. PRESIDENT, Fellows of the Royal College of Physicians,—My first duty—and it is a pleasant one—is to express my sense of the honour done me in inviting me to deliver this course of lectures. If I feel that honour deeply, so do I also feel, quite as deeply, the responsibility which has thus been laid upon me, for it is no light thing to address an audience such as this.

Nor was it easy to select a subject which should be fitting and appropriate for the purpose—one with which I was myself in some closeness of touch, and one with which I might venture to hope that this audience would be in full sympathy.

After careful consideration I resolved to take as the topic for discussion some special symptom, or rather some particular function of the body and the derangements to which that function is liable. It may be asked whether it would not have been simpler to have devoted our study to a particular nervous disease in which that function is characteristically disturbed. That would doubtless have been an easier course to take, but it would hardly have led us far enough, nor would it have served the purpose for which these lectures are designed.

In viewing a single function as a whole, we stand, as it were, further off. We can thus appreciate its bolder and broader outlines; we can see its true bearings and relationships. Moreover, when we examine the many different ways in which its disturbance is brought about, we are able to draw more accurate conclusions as regards the true origin and nature of such disturbances.

A simple example will show what is here meant. How much should we know of the true nature of the act of coughing were we to consider it only as a symptom of pneumonia? What should we know of ataxia if we thought of it merely as a symptom characteristic of tabes?

Moreover, when one comes to look at the matter closely, it
seems as if it were natural to study some one function of the body on an occasion such as this, for the diagnosis of nervous disease must always start from the evidence of derangement of function, and must therefore ever rest on the firm basis of known physiological fact. Only after that basis has been reached can our reasoning be transferred to an anatomical and pathological basis and a localising diagnosis be made, i.e. a judgment be formed as regards the actual lesion which is present and the exact tissue which is involved in the process.

If one takes the trouble to analyse the steps by which, consciously or unconsciously, the diagnosis in any particular case is arrived at, it will be found that the questions which one puts to one's self are in essence the following:—

A. Diagnosis by physiology—
   1. What function is deranged?
   2. What neurones subserve that function?

B. Diagnosis by anatomy—
   3. Where do these neurones lie, i.e. what are their anatomical relationships?

C. Diagnosis by pathology—
   4. What morbid processes are capable of affecting these particular neurones injuriously?

Thus we may speak of:—
   Clinical physiology.
   Clinical anatomy.
   Clinical pathology.

Of these, the last two are well-defined terms. The subjects with which they deal are constantly being referred to, constantly being taught in our schools. But how shall we define the first term—clinical physiology?

We shall see its meaning and scope best if we think of some particular function of the nervous system and ask ourselves the questions:—What are its normal clinical characteristics? What is the form and method in and by which that function expresses itself in the healthy human being? We may be sure that that will ever be something making for good—(a) in the building up or maintenance of the vitality of the individual, or (b) in guarding him against injury, or (c) in the perpetuation of the race to which he belongs.
To use clinical physiology for diagnosis, we must know:—

1. What tests we ought to apply in order to ascertain whether the function we may be investigating is or is not normal.

2. What deviations from the absolute normal standard are compatible with health.

Regarding the matter from this point of view, it seemed to me that these lectures might usefully be devoted to the study of some particular function of the body and the derangements of that function. The one chosen is co-ordination and loss of co-ordination, i.e. ataxia.

When the smooth, easy, exact, and delicate movement of perfect co-ordination gives place to one which is jerky, strained, inexact, coarse, and irregular, we speak of ataxia. By that term we mean a disturbance of innervation, other than paralysis, which prevents the proper carrying out of a movement. Ataxia in this sense is therefore equivalent to inco-ordination, and we can best reach a proper definition of that term by defining its opposite, namely, co-ordination.

By co-ordination we mean a harmonious muscular movement which is performed in the simplest and easiest way compatible with accuracy, so that its purpose is exactly fulfilled with the least possible expenditure of neuro-muscular energy.

To attain this symphony of movement the muscles engaged must act harmoniously, certain contracting, certain relaxing, and contracting or relaxing, in certain groups, in a certain order or sequence, in a certain rhythm, and with a certain strength. Moreover, this strength is not uniform, but is smoothly graded, increasing or diminishing as the action proceeds.

We shall appreciate more fully the enormous complexity of the subject if we remember that in some actions hardly a muscle throughout the body is not engaged. A swordsman, in the quick play of the rapier, must use not merely his hand, arm, and shoulder as the steel flashes out, but he must balance his body with a delicate precision. He must throw his whole weight into the thrust and yet not overbalance. He must hold himself in instant readiness to parry. Eye, hand, foot, trunk must all engage, must each play its part, so that his aim may be sure and his attack effective. The complex multiplicity of even everyday actions is so great, the varieties of muscular combination so infinite, that it has been said, probably with close approach to
truth, that never in one's whole life does one perform the same action in every detail twice.

To direct such complicated movements there must obviously be controlling and guiding centres, and these centres are mainly (1) in the anterior horns of the cord and the homologous cranial nuclei; (2) in the cerebellum and basal nuclei; (3) in the cerebral cortex.

These centres must possess accurate knowledge as regards the position of the limb, the degree of flexion or extension, of pronation or supination, and, generally, the condition of the muscles, whether they are contracted or whether they are relaxed. And this knowledge must cover the condition of these structures, not merely before a movement has commenced, but also from instant to instant throughout the whole performance of that movement.

Obviously, therefore, afferent, informing impressions are necessary, not merely one or two but a multitude of them. These impressions are for the most part subconscious. They are proprioceptive in Sherrington's nomenclature—that is, they are such as are excited by changes going on in the organism itself, chiefly mechanical strains and stresses, movements of muscles, pressure. These impressions we group together under the term "muscular sense," using indeed the very words which Charles Bell employed when he first described what he quite logically called the sixth sense.

We shall presently define that term by endeavouring to show what varieties of stimuli it includes, from what receptors these arise, what is the adequate stimulus in each case, by what paths these stimuli proceed, to what centres they make their way, by what efferent tracts these centres act, and by means of what terminal apparatus their stimuli become effective and are translated into action.

In the meantime, however, we shall simplify and, I hope, clarify the problem before us if we turn aside for a moment to consider certain simple actions and their mechanism. We cannot, it is true, attain complete simplicity, however much we may strive to do so, for, so far as I know, there is no instance in which one voluntary muscle acts normally by itself alone—no action in which one muscle, only, takes part.

To Sherrington, in one of the earliest of that brilliant series of researches on the neuro-muscular apparatus with which he has enriched science, we owe our knowledge that if a muscle is made to contract, its antagonist relaxes. If, for example, in a decere-
Fig. 1.—The Normal Grasp.

Fig. 2.—Grasp in a Case of Tabes.
brate preparation—that is an animal in which trans-section has been performed just above the pons—the purely muscular nerve from one of the flexors of the knee be cut and its central end stimulated, an instantaneous change takes place in the extensors of the knee. These, which had previously been in a state of tonic spasm, now suddenly relax. This most interesting phenomenon, this reciprocal innervation as Sherrington calls it, is an important, even an essential, element in the scheme of co-ordination. It is quite independent of consciousness, and without any sort of doubt is regulated from spinal cord centres.

On careful investigation it has been found that this relaxation of the antagonist is simultaneous with, possibly even precedes, the contraction of the agonist. It cannot therefore be reflex in origin, and indeed the mechanism of its production is not definitely known. Apart from the possibility of the presence of inhibitory fibres, we may consider the possibility of a stimulus passing from the dendrites of one motor cell to those of another in its near vicinity, either directly or by means of an intercalary neurone. But whatever be its exact mechanism, it is easy to convince oneself clinically of this antagonistic relaxation. If the foot be strongly dorsiflexed and the sole pressed at the same time against a firm resistance, then when an attempt is made to extend the foot, the muscles of the calf will be felt to contract, while their antagonists on the front of the leg relax. So far as my observations go, this reciprocal innervation is not disturbed in cases of tabes.

But while this beautiful mechanism will be found to prevail generally throughout the body, there are certain apparent exceptions which require passing notice. The grasp of the hand is one of these. Duchenne first pointed out many years ago that in this action not only do the flexors contract, but also the extensors; that is, the antagonistic muscles instead of relaxing, as is the general rule, contract (see Fig. 1). Opinions differ as regards the exact meaning of this synergic contraction, but all agree that the contraction of the extensors is designed to assist the action of the flexors in the grasp. The rule seems to be that when, in the case of any particular movement, relaxation of the antagonists will help, they relax. When, on the contrary, a synergic contraction is needed to steady a joint or to increase the energy of the contraction, then that synergic contraction will take place.

The reflex centre for the flexor part of the grasp of the hand
lies probably in the spinal cord. It certainly cannot lie above the pons, for grasping movements have been observed to take place in anencephalous monsters. The synergic portion of the grasp is probably cortical in origin. It is absent in infants until about the third or fourth month.

These synergic movements, and there are many of them, are apt to be disturbed by diseased processes. To a want of synergy, to a failure in the exactitude of the contraction relations of agonist and antagonist, has been ascribed the volitional or intention tremor of disseminated sclerosis. These characteristic movements are, without doubt, movements of inco-ordination, and it seems highly probable that the method of their production is that just mentioned. We shall see, later, that cerebellar control has some special relation to synergic movements, and it is well known that the cerebellum is frequently and deeply involved in multiple sclerosis.

In some cases of tabes the synergy in the action of grasping just described is lost, and I show you a photograph of the hands in a case of this kind which has quite recently come under my observation (see Fig. 2).

Let us now turn to the consideration of the reflex arc. From it, from its behaviour, its properties, its characteristics, its performances, we shall obtain some light on the problems of co-ordination and on those pathological changes which give rise to ataxia.

In so far as muscular sense is concerned, the component parts of the reflex arc are as follows:—There is, in the first place, the afferent neurone leading from the muscle. The centre of nutrition of this neurone is the cell in the corresponding spinal ganglion. Of these cells there are, as we all know, many varieties. Dogiel recognises at least eleven different kinds, and their differences are
not merely morphological, but in all likelihood express differences in function as well. Of this neurone we must regard the fibre leading from the muscle as the dendrite, and the posterior root fibre we must look upon as the axone of the cell. It is perhaps worth noting that the fibres of this neurone differ morphologically from those proceeding from the receptors of the skin, their fibres being larger and coarser than the latter. Entering the spinal cord the posterior root fibres divide into ascending and descending branches, both of which give off many collaterals. The one with which we have to deal at present is the reflex-collateral, which curves through the posterior column of the cord to reach the grey matter, through which it passes to the anterior horn (see Fig. 4).

The efferent or motor neurone, which forms the other side of the reflex arc, consists, as we all know, of the motor cell in the anterior horn of the cord with its dendrites and its axone, the latter forming the motor fibre by means of which the muscle is set in action. This motor neurone forms the "final common path," as Sherrington, with happy terminology, has styled it. By it, and by it alone, can stimuli reach the muscle. Whether such stimuli originate in the cerebral cortex, in the basal ganglia, in the cerebellum, or in the cord, they must each and all pass through that one terminal tract leading to the muscle—the final common path.

The transmission in the reflex arc is therefore from the muscle through the fibrils of the afferent neurone, thence through the synapse in the grey matter of the anterior horn to the fibrils of the efferent neurone, and so back to the muscle again. The rate of transmission through such a reflex arc as this is notably slower than that through nerve-fibre alone, and there is ample evidence to show that the retardation takes place at the synapse. It is also just at this synapse that certain poisons such as strychnine and tetanus act, disturbing the co-ordinating mechanism. As is well known, these neurones—afferent and efferent—though so closely related in function, have no structural connection, the fibrils of the one ending in minute bulbous swellings which lie very close to those of the other.

In so far as concerns co-ordination and its reverse, ataxia, the afferent neurone is the one chiefly, if not entirely, concerned, for by it the impressions, which we group together as those of muscular sense, are conveyed towards the centres. Its degeneration and consequent loss of function is the essential lesion of tabes.

How, then, does it reveal its function? It does so clinically,
by reason of the effects it produces on the efferent or motor neurone; and these again we can gauge by observing the results on the muscle. Of those effects which are clinically observable the most important is tonus.

By *tonus* is meant a slight, steady, nearly continuous muscular contraction, which is due to a stimulus from the afferent neurone of the arc playing upon the efferent or motor neurone. (Later we shall see the important influences which stimuli from the semicircular canals exert on this condition.) On the presence of muscular tonicity depend the phenomena of the knee-jerk and of the other so-called deep reflexes. Section of the afferents from the skin receptors of the same segment does not affect it, but it at once disappears if the afferent from the muscle is cut. It is for this reason that the knee-jerk is lost in cases of tabes, the afferent neurone having degenerated and being therefore incapable of fulfilling its function.

Obviously there are many points connected with the reflex arc which have an intimate bearing on the present subject. The grading of the agonist, as contrasted with the antagonist, is an important function of the reflex centre, for the relaxation and contraction of these respectively ought to be suitably balanced. If the relaxation were not sufficient the contraction would be impeded, whereas if it were too great there might be a corresponding degree of looseness or shakiness about the subsequent movement.

It must be clearly understood that the afferent neurone from the muscle to the cord is special in function, bringing stimuli from the muscle to the centre. These stimuli have been selected by special receptors, which are tuned, as it were, to receive these specific stimuli alone and to reject all other stimuli which are not in harmony—much as wireless instruments are tuned to answer to special wave-lengths. These stimuli, carried to the spinal cord through these special afferents, reach the reflex centre, which is itself specially arranged for co-ordination. The movement, thus co-ordinated, is effected through the lower motor neurone—the final common path.

The afferent innervation from the muscle is therefore designed for the purposefulness of movement, that is, for perfect co-ordination. If these fibres degenerate, then that co-ordination is no longer possible and ataxia results. Ataxia so brought about is typically seen in cases of tabes and in certain forms of peripheral neuritis, particularly that produced by alcohol.
Fig. 4.—REFLEX COLLATERALS OF POSTERIOR ROOT (LENHOSSEK).

Fig. 5.—MICRO-PHOTOGRAPH OF SPINAL GANGLION CELL IN TABES. \( \frac{1}{12} \) OIL IM.
It will be necessary to refer so frequently to tabes that a brief statement regarding its pathology may now be made, in so far as the ataxic symptoms of that disease are concerned. The more recent work, especially that of Spielmeyer on experimental tabes, leaves us in no doubt as to the essential nature of the process. Without any question we have to deal here with a primary elective toxic degeneration of afferent fibres. This degeneration no doubt affects the whole neurone more or less, but the place of least resistance is to be found in the collateral of the posterior root, and therefore it is there that the signs of degeneration first show themselves as a patch in the column of Burdach. The old view that this was the result of a meningitis, and directly due to pressure on the fibres of the posterior root as they traverse the pia, is quite untenable.

As in all such toxic processes, the function of the neurone is affected before morphological changes have had time to show themselves. Just as in amyotrophic lateral sclerosis the morphological changes in the pyramidal tract can first be detected in the distal part of that long neurone where its vitality is lowest and the axone least resistant, so here the degenerative change appears first in that portion of the axone which is furthest removed from the cell.

Presently, as the disease progresses, the cells of the spinal ganglia begin to exhibit signs of morbid change (see Fig. 5). Fatty degeneration of the protoplasm commences, the satellites of Cajal accumulate, the cells vacuolate, break down, and ultimately the remains, surrounded by a ring of satellites, form the nodules résiduels of Nagotte.

These satellite cells are extremely interesting. In health they show themselves as flat, usually triangular, plate-like bodies, with long branching pseudopodia. They are probably the homologues of the cells of Schwann in connection with the nerves. Present normally in small numbers, when degeneration commences they draw in their pseudopodia and crowd to the injured point. Their action is believed to be rather histolytic than phagocytic.

To return to the spinal cord as a centre of co-ordination, it has to be observed further that section of all the afferent nerves of a limb does not render the limb incapable of voluntary movement in the rough. The results of electrical stimulation of the cortex, for example, are not materially affected thereby. But, as Sherrington and Mott have shown, when the posterior roots have been cut in a monkey, the animal will not voluntarily
use the apæsthetic limb. I am aware that H. Munk has controverted this statement, but unquestionably it is correct. Indeed the observation in its essence is an old one for Charles Bell showed long ago that if the supramaxillary division of both fifth nerves were cut in the ass, the use of the upper lip for prehensile movement was lost. The reason why the deafferented limb is not used is probably that the tonus of the muscles is completely lost and that therefore the motor neurone no longer receives the stimulus of afferent muscular impressions.

Why, then, one may ask, is voluntary movement not usually lost in tabes? The explanation obviously is that all the afferents have not degenerated.

In so far as the motor side of the reflex arc is concerned, the results of diseased processes are well known. A lesion of this kind gives rise to a paralysis of the lower motor neurone type with all its characteristics. These, however, do not specially concern us now.

But before leaving the consideration of the reflex arc there is, in the normal state, a special function connected with the reaction of that arc which is peculiarly interesting in view of co-ordination, i.e. the reversal or Umkehr. This remarkable phenomenon was first observed by v. Uexküll in the starfish. He found that when an afferent stimulus played upon a group of motor nerve-centres certain of these centres responded, while others did not do so. He was able to show that the determining factor is the momentary condition of the muscles innervated by those centres, and that the centres which answer to the stimulus are those corresponding to muscles which are most on the stretch at the time. The same law holds good in the vertebrates, and the most complete demonstration of its truth is that which has recently been given by Magnus.

In a spinal dog, one in which trans-section of the cord has been made between the eighth and twelfth dorsal segment, if a patellar tendon—say, the left—is tapped, the stimulus produces a jerk in both legs. Magnus shows that the result in the case of the right leg depends upon the passive position in which that limb happens to be at the moment when the tap is given. If that position is one of extension then the movement is flexion, whereas if the limb is flexed then extension follows the stimulus; that is, one and the same stimulus will produce opposite effects according to the passive position of the limb at the time. This singular phenomenon is what
is known as the reversal effect, and there is conclusive proof that this effect depends upon the afferent neurone from the muscles concerned. The play of the afferent neurones of a stretched muscle appears to tune up the motor neurone and to render it more susceptible to respond to the stimulus than is that of the relaxed muscle.*

No doubt this takes place clinically and under our very eyes, but it is then so veiled by other motor phenomena that it is not readily perceived. We may see, however, an indication of its

* What is true as regards the passive position of the limb has been recently shown by T. Graham Brown to be true also of the active.
presence in connection with the conditions which determine the crossed adductor jerk.

From every point of view, therefore, it is evident that the important thing for us to consider in connection with the present subject is the stimulus which the afferent neurone brings from the muscle to the spinal cord; and we now turn to ask ourselves the question, Whence does this stimulus arise, and what receptors has Nature attuned to receive it? In connection with the muscles and tendons of the mammal there exist two such specialised receptors—(1) the muscle-spindle; (2) the Golgi tendon-organ.

The muscle-spindle was first observed in the year 1862 by Kölliker, who took it to be identical with Weismann's embryonic fibre. In the following year Kühne discovered spindles in the mammalian muscle, and from this date onwards these most interesting structures have been studied by Golgi, by Kölliker, by Krause, and by many others. As regards their function very different views prevailed. They were thought by some to be centres of new growth in the muscles, by others they were looked upon as lymphatic structures, by yet others they were regarded as pathological, as foci of inflammation. It was not till the year 1888 that Kirschner, in the course of an article on the subject, hazarded the suggestion that muscle-spindles might possess a sensory function. Six years later, in 1894, Sherrington, by conclusive experiment, proved that they were afferent receptors.

The muscle-spindle is fusiform in shape (see Fig. 6 and Fig. 8), its long axis lying more or less parallel with the muscular fibres in which it is embedded. It consists of a many-layered fibrous capsule enclosing a lymph space which is crossed by fine membranous septa and filaments. Then comes a delicate axial sheath enclosing the intrafusal muscular fibres, which are markedly embryonic in character with abundant protoplasm. These intrafusal fibres, usually tendinous at one or other extremity, split up into numerous daughter fibres, and towards the equatorial region of the spindles they lose their striation. At this point they are surrounded by many nuclei, spherical or oval in shape, and clear in appearance.

Round the fusal fibres there wind, in spiral form, large myelinated posterior root fibres, of which several subserve each spindle. As they enter the spindle their sheath of Henle becomes continuous with the capsule. They then divide dichotomously and, in the case of each fibre, after losing its
Fig. 6.—Muscle-Spindle, Diagrammatic (after Regaud).

Fig. 7.—Tendon-Organ, Diagrammatic (after Regaud).
Fig. 8.—Muscle-Spindle (Dogiel).

Fig. 9.—Tendon-Organ (Dogiel).
myelin, the axone constricts, flattens out into a ribbon, and applies itself in an intricate spiral interlacement round and between the fusal fibres. Such, then, is the commencement of the afferent muscular neurone.

Motor fibres branching from the ordinary motor muscular nerve also reach the muscle-spindle. They pierce the capsule and end in motor platelets at one or other extremity of the fusal fibre.

Connected with these singular receptors there are many interesting points, one or two of which may be mentioned here. They develop during the fourth intra-uterine month, that is at a period considerably earlier than that of ordinary muscular fibre. Moreover, singularly enough, the muscle-spindles do not degenerate after section of both anterior and posterior nerve-roots, neither do they hypertrophy after exercise, as ordinary muscular fibres do, and lesions which are fitted to cause degeneration of muscle do not affect the spindles; these remain intact.

The tendon-organ of Golgi is formed much on the same plan (see Fig. 7). There, also, we find a capsule enclosing a lymph space in which, however, lie, not muscular fibre, but delicate embryonic tendon fibres, which are attached at one end to the tendon, at the other to the ordinary fibres of the muscle in question. The afferent fibre of this receptor is much like that of the muscle-spindle. It forms irregular ribbons, which are rolled in spirals round and between the tendon fibres. These spiral terminations are found, when carefully stained, to consist of ramifications of fine neuro-fibrils (see Fig. 9).

It remains for us to consider how these receptors are stimulated. As regards the tendon-organ, it seems clear that it is placed there for the purpose of measuring traction, i.e. that the adequate stimulus is the pull on the tendon. But with regard to the muscle-spindle there are many theories, all of which, however, agree in this, that that receptor is designed to measure muscular contraction. In what way, however, it does this is a matter of considerable dubiety. It has been assumed that the stimulus which excites this form of receptor is due to external pressure exerted on the capsule by the contraction of the muscle in which it lies. Others believe that the pressure within the capsule is raised by the contraction of its fusal fibres; others, again, conceive that the stimulus arises by reason of the pressure of the contracting fusal fibres upon the spiral nerve fibres which
surround them, or that these are stimulated by the action-current in these fusal fibres as they contract. It seems to me probable that one or other of the two last theories is likely to be correct.

There is one other point in connection with this subject to which passing allusion may be made. In the last few years there has been much discussion and much theorising with regard to that singular structure in the wall of the heart, the atrio-ventricular bundle, which is generally regarded as a mechanism by means of which the rhythm of the heart is controlled and regulated. Anyone who examines with care this remarkable bundle of His must be struck with certain peculiarities which it possesses. The muscular fibres of which it is composed are notably embryonic in character and structure. They, like the intrafusal fibres of a muscle-spindle, are surrounded by a fibrous capsule. Penetrating this capsule and spirally surrounding these fibres numerous nerve-fibres can be traced. The resemblance is therefore singularly close, and I think we may well consider the possibility, nay, even the probability, that the atrio-ventricular bundle is in reality a mass of highly differentiated receptors tuned to perceive the commencement of contraction in the wall of each cavity of the heart, which stimulus, transmitted to local centres, would serve to regulate rhythmically the contraction of each chamber.

ACUTE MYELOCYTHÆMIA ASSOCIATED WITH OSTEOSCLEROSIS AND OTHER UNUSUAL FEATURES OCCURRING IN AN INFANT.*

By ALEXANDER GOODALL, M.D., F.R.C.P.

A female child aged 10 weeks was admitted to the Royal Hospital for Sick Children, under the care of Dr. J. S. Fowler, on the 12th of March 1912. She was suffering from bleeding at the nose and diarrhoea.

History.—The patient had spent the greater part of her life in a kitchen bed-closet, but the hygienic surroundings were otherwise fairly good. Her father, aged 43, and mother, aged 38, were both strong and healthy. Patient was the seventh child. The second child died at the age of 10. He had been blind, and was said to have been born "with a clot on the brain." The third child died

* A paper read before the Edinburgh Medico-Chirurgical Society, 1st May 1912.