A Lecture

ON

THE DYSTROPHY OF TABES AND THE PROBLEM OF TROPHIC NERVES.

DELIVERED AT THE NATIONAL HOSPITAL FOR THE
PARALYSED AND EPILEPTIC.

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THERE are regions of mortality of which the Registrar-General takes no cognizance; one is that which relates to scientific theories. Their death-rate is high. Some perish early, launched into existence with defective vitality. Others, more robust, come to a sudden end, done to death in controversial contest. Others, again, at first seem vigorous, but afterwards slowly fade, from inanition. Growing knowledge ceases to furnish them with support. The facts on which they seemed to rest are found to have different relations, and that which the theory was framed to explain is found to be otherwise intelligible.

Such seems to be the fate of the theory that the nutrition of the tissues is governed by special trophic nerves and centres distinct from those which influence their general functions. It has always been a theory; progressive research has afforded no direct evidence of such nerves or centres. It was once invoked and held to explain muscular atrophy, but the relation of this to disease of the purely motor nerves and motor cells has been so firmly established that the theory has quietly dropped out of sight so far as this disease is concerned. But it still lingers, and is still reasserted, as an explanation of the affections I propose to consider to-day—the remarkable derangement of nutrition which occurs in some cases of tabes. This is seen in the cutaneous tissues and their appendages, and is especially conspicuous in the joints and bones. In these, as you know, it is called “tabetic arthropathy,” or “osteo-arthropathy,” and it has also been termed “Charcot’s joint-disease,” from its first thorough describer. Of late, all these nutritional disorders have been included under the convenient designation “tabetic dystrophy.”

Look at the knee of this tabetic patient. You see how greatly it is enlarged. There is some effusion into the joint, but this is not the chief cause of its increase in size. The tissues about the joint are thickened by a peculiarly firm oedema, especially above, where the condition extends into the lower part of the thigh. But the chief cause of the enlargement is an increase in size of the ends of the bones entering into the joint, especially of the head of the tibia and the external condyle of the femur. Besides this, a separate small mass of bone has formed in the capsule of the joint on the outer side. Some grating can be felt on movement, showing erosion of the articular surfaces. This condition came on gradually a year ago, and was thought to be due to a strain.

In the other tabetic patient before you, a definite, rather severe sprain of the ankle started the morbid process in the joint. The end of the tibia is much enlarged, and there is also increase in the astragalus. Little effusion can be discovered, but the fibrous tissues about the joint are all thickened. In the third patient there is only a slight enlargement of the tarsal bones. You may have noted that in each case manipulation of the joint caused no pain or even discomfort. That is the rule in this malady. Yet you know quite well what acute pain would be felt if the joint were the seat of an ordinary inflammation, whether rheumatic or the result of injury. Such passive movement would be unbearable, though it here causes no distress. From this it is evident that sensitiveness to pain is lost in the deeper nerves. That it is also lost in the skin you perceive. In each patient, if I prick the skin, no pain is felt. The prick seems like a touch.

Arthropathy is not frequent in tabes. It has been said to occur in 10 per cent., but I think that the proportion is even less. Since tabes also is absolutely uncommon, an instance of the joint affection will come under the notice of only a few of you who engage in general practice. Hence the importance of fixing its features in your mind lest error take you unawares. If the symptoms of tabes have not been recognized, the joint may not suggest

even a search for its symptoms, and is easily ascribed to pure trauma, to rheumatism, or gout—the more readily because the latter are so often thought to be the cause of tabetic pains. Yet the cases are few in which the error is excusable. A spontaneous arthritis in one joint only should always excite suspicion, just as does bronchitis limited to one lung. When not spontaneous, but excited by an injury, its degree is generally in great excess of the cause, and enlargement of the bones should always suggest this disease. These symptoms are not conclusive, but a practitioner who is in the habit of noting all points, and also of comparing them—a habit which can be acquired—cannot fail to be struck by the absence of pain, or its insignificant degree, in a malady in which movement or simple handling usually causes sharp distress.

Note also, as a symptom especially significant in the early, dubious stage, the thickening of the tissues outside the joint, and often, as we see here, beyond it. It looks like oedema, but it is firmer and may develop rapidly. The increase in the ends of the bones occurs more slowly, and yet is often distinct when the patient first complains of his joint, so little pain is there to make him seek advice. The enlargement is generally irregular, and often so great at spots as to give rise to projections—“osteophytes,” as they are termed. It is strange that in spite of this surface growth the substance of the bone becomes rarefied, and less opaque to the Roentgen rays, by a process that the Germans call “*Kalkschwund*,” for which we have no English equivalent. Inside the joint, villous projections form and may become loose; the cartilage becomes first roughened and then wastes, and the bony substance may ultimately be exposed and its rarefied texture readily worn down. In the thickened capsule, bony nodules may develop, as in the patient here.

The knee and the ankle are the joints most frequently affected, and next the tarsus. The hip suffers more frequently than the shoulder, the elbow rarely, the wrist and fingers still more rarely. The vertebral column has been thought to be the least frequent seat, but I think it is affected more often than the hand. In the hip the effects produced may be perplexing. The head of the femur generally wastes rapidly when the spongy substance of the bone is exposed, and hence, although the ring of the acetabulum may be thickened, dislocation readily occurs, commonly on the dorsum of the ilium; there is sometimes fracture of the neck. No doubt, as the head of the femur is reduced in size, a great strain is thrown on the ligaments, which yield, and fail to keep the diminished head in place. In the shoulder the changes may be similar and dislocation may occur from the same causes. The compact elbow-joint is seldom affected, unless as the sequel to considerable injury, and then the degree sometimes attained may be great.

The condition in the knee I have pointed out from the case before you. Nowhere else is so high a degree of change so frequent, or osteophytes and osteoid nodules so common. Subluxation, the head of the tibia going back, frequently occurs. But it is important not to mistake for special arthropathy the very common retroflexion of the joint which results from simple stretching of the ligaments. The support to the knee largely depends on the tendons of the muscles that pass by it, and especially on the tendon of the rectus, in which the patella is situated. The support thus furnished depends on the steadiness with which the muscular contraction is maintained; its irregularity in tabes, alternately giving way and overacting, throws undue stress on the fixed ligaments and capsule of the joint. These yield in consequence, and become so stretched that the joint bends forwards in increasing degree (the “*genu recurvatum*”) without any true arthropathy. The affection of the ankle-joint is much more frequent than that of the wrist, and the tarsus more often suffers than the carpus. The finger and toe joints are seldom affected. In association with ulceration of the toes there may be atrophy of the terminal bones of the phalanges. A rare seat for tabetic arthropathy is the spine, usually in the lower dorsal or lumbar region. It may produce considerable thickening of the bones, with displacement and deviation of the spine. Often the latter is due to fracture of the bodies, the result of some traumatic influence, and then crepitation may be felt. Unless the occurrence of spinal dystrophy is known, the condition may be puzzling, but

in most cases the primary malady has been already discerned.

The impaired nutrition of the bony tissues which causes "rarefaction," may involve the shafts of the bones as well as their ends, and renders their fracture easy. The man before you, with the tarsal arthropathy, who has also optic nerve atrophy and universal analgesia, has a fracture of both bones of the forearm. It is like a "green-stick fracture" of childhood, and was produced by moderate force in a lesson his son was giving him in the Japanese art of "Jiu-jitsu." More than one fracture may occur in tabetics from falls, and even from strenuous muscular effort; it is often difficult to secure union of the bones.

Similar changes in nutrition occur in one other chronic malady, syringomyelia, and in the minor degrees of spina bifida, which alone survive. Arthropathy is rare, but sometimes characteristic. I have elsewhere¹ described a case in which the shoulder-joint suffered. Cutaneous dystrophy is more common. I was lately asked to see a young man, aged 26, to decide whether his left foot should be amputated. Perforating ulcers began on the toes at the age of 11, and first one and then another toe had to come off until all were gone, and he now had similar ulceration of the ball of the foot. The bones of his ankle-joint were distinctly enlarged. Over the whole of this leg sensibility to pain was almost lost, while a touch was felt everywhere. This isolated loss of pain, as you know, is a characteristic of these defects of development of the cord as well as of tabes. On inspecting the patient's back a huge scar was seen, occupying the whole lumbar region, about 8 in. wide, and on its margin were some of the large coarse hairs which, in this region, often accompany "spina bifida occulta." The lumbar spine seemed duly closed, but I learned that at the age of 8 months a hairy mole had been destroyed there. The trophic and sensory changes in the limb made unilateral defect of development in the cord almost certain, and the characteristic congenital abnormality of the surface removed all doubt. Such a condition is really a variety of syringomyelia, and thus the trophic changes were explained.

These tabetic dystrophies are so mysterious, and the arthropathy is often so great in degree, that we cannot wonder if it seems to need an influence of special nature, a derangement of special nerves and centres. But the fact that these have never been discerned, either positively by their presence or negatively by their absence, compels us to ask whether the theory of their existence and influence is really needed, whether some other mechanism may not induce the changes of nutrition in these diseases of the nervous system. If we scrutinize carefully the conditions under which these local dystrophies occur, we find that there is always some impairment of the nerves of ordinary function, the nerves of motion or sensation. In muscular atrophy the motor nerves have suffered. In tabes we usually have clear evidence of an affection of the sensory nerves, in the defective perception of pain in the skin, that the slightness of pain in the affected joints shows always that the deeper nerves have also suffered. Sometimes the affection of the sensory nerves is very great. In a patient in whom all the teeth fell out, the jaw had become absolutely insensitive to touch as well as to pain. This loss of sensation depends on degeneration of the nerves. We can, indeed, only see this with the microscope when the change has reached a high degree, but it is doubtless effective long before it can be thus discerned. This constant concomitant compels us to consider whether the altered nutrition of the common nerves can be the cause of the altered nutrition of the tissues.*

What can we learn from other changes in nutrition dependent on the ordinary nerves? That in the muscles is particularly instructive. If a motor nerve is simply divided, there is degeneration of the fibres down to the

muscle. The muscular fibres undergo very slow wasting, so slow that months pass before there is much visible change, and voltaic excitability is long preserved; but if the nerve is interrupted by causing irritant inflammation, as by passing through it a thread dipped in a solution of chromic acid, the degeneration of the nerve below seems to share the irritant character of the lesion, and the process invades the substance of the muscle fibres. They undergo rapid granular and fatty degeneration, and in a week or two they lose all excitability, even to voltaism. It is lost, never to be regained, for the fibres perish. We see the same difference in cases of anterior poliomyelitis. Usually the degeneration of the nerves is not irritant, and the muscles long preserve their voltaic excitability. But in some cases the inflammation seems more intense in character and the descending change in the nerves partakes of it, and is such as to cause the rapid degenerative destruction of the muscle fibres I have mentioned. Voltaic excitability ceases in a few weeks, and there is no recovery. This transfer of nutritional tendency from nerve to muscle takes place, although the nerve ending has no direct continuity with the muscular protoplasm. Just as the intervening sheath does not prevent the stimulation of the muscle substance by a nerve impulse, so it does not prevent the muscle substance sharing the nutritional state of the nerve fibre. When this is a quiet degeneration, the independent vitality of the muscle seems to maintain its nutritional integrity, but it is insufficient to resist a change of invasive intensity. Note this indication of a double influence—an inherent vitality and a relation to the vital state of the nerve fibres.

The same lesson is taught by the cornea. The peculiar relations of this structure render its inherent vitality low, readily disturbed by an affection of the fifth nerve, on which it depends. The vitality of fibres of the fifth nerve is dependent, as you know, on the cells of the Gasserian ganglion. As in all sensory nerves, a change in nutrition passes from these cells down the nerve, although it conducts upwards. Disease of the ganglion or of the nerve in front of it readily entails keratitis and ulceration. Disease behind the ganglion has not this effect, unless it is intensely irritant in nature. Then it invades the ganglion and damages the cells sufficiently to lead to irritant degeneration of the fibres in front, and inevitable inflammation of the cornea and eye. The conditions on which keratitis depends are significantly shown in the removal of the ganglion for neuralgia. Done, as the operation is, with strict antiseptic precautions, the degeneration of the fibres is simple, not irritant. Yet, during the first week or two, it is extremely difficult to prevent keratitis. The cornea has lost sensitiveness, and dust and other particles falling on it do not excite movement of the eyelids to remove them. If the eyelids are fixed together, so as to protect the cornea, inflammation does not occur. But this is not all, because a week or two after the operation the eyelids may be left apart with safety. The cornea is still insensitive; particles of dust still fall on it, but have no effect. The danger exists only during the period in which the secondary degeneration is taking place. It is the changing state of the nerve fibres which renders the nutrition of the cornea so unstable. When the process is over, although the loss of sensation continues, the disturbing influence ceases and the inherent vitality of the tissue is sufficient to maintain its integrity.* The facts surely constitute proof that the trophic state is influenced by the transmission to the tissues of that of the nerve.

The relation of the cornea to the fifth nerve is a type of that which obtains in the case of all the tissues of the body except the muscles. Their nutrition is related to that of the sensory nerves. In a traumatic lesion of a mixed nerve, or severe neuritis, the inherent vitality of the skin is sufficient to maintain it intact, but its nutrition is readily disturbed by causes insufficient to have the same effect in health. You know that in neuritis, hot water, quite bearable to a normal hand, will cause troublesome blisters difficult to heal. When the deranged nutrition of the nerve has become stationary, slow chronic change in the nutrition of the skin may supervene, as in the familiar "glossy" skin so often met with.

* Sherrington, in Schäfer's *Physiology*, vol. ii, p. 876, says that "There is no proof of nerves having a special trophic influence. The evidence seems to show that every nerve centre that can influence the proper and specific activity of a tissue possesses in so far a trophic influence on that tissue." He finds (p. 878) a difficulty in trophic influence being in a direction contrary to the ordinary function. But the vitality of a nerve is from its ganglion cell, irrespective of the direction of conduction, and if it is conceived (as maintained here) that the influence on tissue nutrition is simply a communicated state, depending on the vital state of the nerve, and not a transmitted energy, the difficulty disappears.

* The fact that division of the inner fibres of the fifth nerve has a special effect on the nutrition of the eyeball seems to me to afford evidence of trophic nerves only to those who are already sure of their existence. So with similar observations on division of the posterior branches of the spinal nerves.

Some forms of myelitis seem specially irritant. When these involve the posterior columns, either because transverse, or because foci of that specially active form, disseminated myelitis, are seated in these columns, loss of sensation in the legs is attended with an intense tendency to trophic disturbance. The inflammation seems to have a strong invasive tendency; it spreads down the posterior roots, overcomes the stability of the ganglia, doubtless invading their structure, and passes down the posterior roots to the structures related to their endings. Hence bedsores form on the least excitant; slight pressure causes a bulla. The eruption of herpes zoster, as you know, seems to depend on a special form of inflammation of the ganglia, and its significance accords with the facts I have mentioned.

I might multiply these examples, but they are sufficient for my purpose. Their indication is that the state of nutrition of the nerves influences that of the structures related to them. So far as our present knowledge goes, no other conclusion is warranted than that there is an inherent vitality of the tissues, but that this is also influenced by disturbance of nutrition of the nerve fibres. In the case of muscle, the influence is exerted by the motor nerves, in other tissues by the sensory nerves. Of the visceral organs I do not speak, for I at least know too little of such trophic disturbance in them.

It may be urged, How are we to explain the lessened growth of limbs in infantile paralysis, whether due to spinal poliomyelitis or to a cerebral lesion? The question suggests another: If trophic nerves and centres are to be invoked to explain this effect, how is the theory to be reconciled with the facts that the result occurs equally with a lesion of the anterior grey substance of the spinal cord and of the motor region of the brain? The problem is made more difficult by the fact that the hindered growth occurs in structures the nutrition of which we know to be independent of the anterior nerve roots. The effect is related in degree to the early age at which the paralysis occurs. It is during the first few years of life that the chief deficiency in growth results from paralysis. Do not these facts suggest that the effect may be directly due to some local interference with the process of growth rather than to an impairment of a nervous influence on nutrition? May not this interference be found in the imperfect approximation of the epiphyses to the shafts of the bones consequent on the muscular paralysis? The loss of power, the cessation of movement and of all muscular contraction must change the condition under which normal growth occurs. Even partial loss of power must modify them. It must lessen the stimulus to the general circulation in the limb, and especially it must lessen the relation of the epiphyses to the shafts of the bones. This mechanical influence is certainly a condition of the normal development of the cartilage into bone, and its loss must surely have a considerable influence on the process by which the shaft increases in length. It is said that mere inability to move one leg for six weeks, due to untreated fracture of the femur, so that the lower leg was hanging motionless, distinctly influenced the growth of the tibia and fibula.² We may, therefore, conceive that the hindrance to the growth of the bones in a paralysed limb may be independent of any direct nerve influence. Disturbance of the circulation may play a minor part in hindering the supply of nutrient material, but the old view that the vasomotor nerves and the state of the vessels played a dominant part in producing trophic changes has been long relinquished.

Thus the only certain element in tabes with which we can associate its dystrophy is the altered state of nutrition of the sensory nerves. The only mechanism for the perverted nutrition we can conceive which harmonizes with other known facts is that this determines an alteration in the processes of nutrition, disturbing that which is primarily due to the vitality of the tissues themselves. It induces a derangement which, once set up, continues and increases. In all cases of tabes there is reason to believe there are such changes in the deeper nerves, and, as I have said, it is very rare to meet with a case of pronounced arthropathy in which they are not evident in the cutaneous nerves. If this influence should seem insufficient to produce such colossal results as we often meet with, and as I show you here, we must remember how often we meet with vast effects from influences that seem in themselves altogether trivial. It

may also be urged that these trophic changes are rare events in cases in which the alteration in the nerves seems the same. This difficulty we must recognize, but should remember also that the precise change in the nerve-endings may vary when its manifestations, in its effect on function, seem to us the same. The effect of slight traumatic influences, in affording the opportunity for derangement of nutrition, may also be variable, and the peculiar distribution of the arthropathy is strong evidence of the frequency of such an excitant, even when unnoted. A local cause is suggested by the fact that usually only one joint is affected, and seldom more than two. It is also possible that rarely a true rheumatic affection may be the excitant. An inflammatory process, however excited, may be, as it were, misguided by the influence of the impaired nutrition of the nerves. Once excited and thus perverted, it progresses, in morbid form, growing more and more, to such results as you see here.

The slighter changes in the skin and its appendages, and the obstinate ulceration which is usually set up by the unwise use of a knife to a corn, are open to the same explanation. The normal processes of healing are defective by reason of the deranging influence of the altered nerves, and healing is hindered in proportion; but it is rendered difficult by another cause, the effect of which we seldom adequately recognize—the secondary result of the absence of pain. In consequence the parts are kept under influences which give the tissues no chance.

If better conditions are secured, the independent vitality of the tissue will generally suffice, except in the active stage of nerve disturbance, as in myelitis. If arthropathy has gone far, the changes are such that they cannot retrocede, but a perforating ulcer generally heals if pressure, motion, or mechanical congestion are prevented. Some time ago I was anxious to test the influence of electricity on these ulcers. To test an agent effectively it must be the only new condition introduced into the state of the morbid process to be dealt with. Every case of perforating ulcer was therefore kept at rest, and the ulcer carefully dressed and kept clean, in the expectation that it would soon become stationary, and refuse to heal; then electricity could be tried fairly. But the attempt had to be given up. In every case the ulcer was healed in a fortnight, although it had gone on for months while the patient was walking about, and the ulcer had been continually exposed to mechanical disturbance and mechanical congestion.

In like manner, although not in the same degree, even tabetic arthropathy would, I am sure, often be arrested if wisely dealt with in its early stages. The malady varies so much in character that it is unwise to be dogmatic, but I believe that most cases begin as a slight acute process, whether due to a traumatic influence or not, and much may be done to promote its subsidence by rest and the measures suited to any acute arthritis; but these measures are scarcely ever adopted or thought of. The malady is painless, and scarcely attracts even the patient's notice until enlargement becomes obtrusive. Then, too often tissue changes are established which have a tendency not only to persist but to spread. If considerable effusion is the chief element, it may need aspiration followed by elastic compression, which, even alone, has often a great influence on such cases. How considerable an effect may be obtained by suitable measures was shown by a patient in the first stage of tabes, but with definite analgesia, who presented enlargement of the left knee, ascribed to over-walking. The enlargement was chiefly of the head of the tibia, and made its circumference exceed that of the right by an inch. Although complete rest could not be secured, under relative rest and an elastic bandage the difference was reduced to half an inch, and a year later there was no sign of increase.

The conditions which would not prevent the recovery of a joint with normal nerves may be persistently harmful to one that is inflamed, however slightly, in a subject of tabes. The absence of pain permits the perpetuation of harm, and is to us a grave misfortune. With pain to emphasize our advice we can often secure rest when it is needed; without it, we too often fail. It is seldom recognized how good a friend pain may be to those who suffer it.

REFERENCES.

- ¹ Syringal Haemorrhage into the Spinal Cord. Lectures, Series II.
- ² Kawka, Aertz Ver. Hamburg. *Neur. Centralbl.* 1902, p. 372.