ON THE NATURE OF NEUROPATHIC AFFECTIONS OF THE JOINTS *

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We are no further in our knowledge of the joint lesions accompanying nervous disease than we were twenty-five years ago. The best expositions of the subject date back to this time; more recent ones have added nothing new and have often left out of consideration facts of importance. Theories and speculation as to the etiology of nervous arthropathies began directly they were described by Charcot in 1868, and continue to this day. The whole discussion turns about the question, "Is the primary cause of these arthropathies to be sought in the nerve-lesion, is the nerve-lesion the primary exciting factor, or is it merely incidental and aggravating?"

Do the nerves exert some mysterious "trophic" influence on the bone, or will an alteration of the normal warning sense of pain suffice to explain the occurrence of osseous affections? Are we to seek the primary lesion in the bones, and to regard the nerve changes as merely incidental, and in certain cases as aggravating, perhaps? Are Charcot joints nothing but ordinary syphilitic deforming arthritides, and the spontaneous fractures of tabes nothing but ordinary breaks made painless by tabic analgesia, or do these bone changes, arthritides and fractures, merely serve as moments (auslösende Momente) inciting processes whose whole course and termination are determined by the accompanying nervous factors, trophic, analgesic, or what not? The problem is involved, it has too many uncertain quantities to admit of clinical solution. On the side of the nerves we have had the question: "*Are* there any trophic nerves?"—and we did not know. On the side of the bones we had the question: "What is a deforming arthritis, what causes it?"—and until recently we did not know. Twenty years ago Klemm, of Riga, recognized the difficulties of a clinical solution and proposed experimental work on the subject; but the time was not ripe. Barth asked how we could hope to explain a neuropathic deforming arthritis, when we did not even know the nature of an ordinary one. Now the last few years have brought us nearer to a solution, we at

*This paper was on the Program of the Orthopædic Section of the 1915 A. M. A. Meeting; a sudden departure for abroad prevented its presentation. Continued absence has made it impossible for me to consider literature later than May, 1915. The first part of the work was done in the Division of Surgery, University of California. The paper was read before the Stanford Clinical Society, October 9, 1916.

least have some knowledge as to the nature of an ordinary deforming arthritis, and have been able to produce it experimentally, and have thus eliminated one of the uncertain quantities. So that I set myself the problem of determining the cause of Charcot joints and went at it from various directions.

Let me first state the questions involved:

1. Are tabic arthropathies due purely to degeneration of certain nerves that cause the bone to atrophy? (Charcot's theory.)

2. Are they simple syphilitic arthritides, occurring sometimes in the course of a tabes, but not infrequently found in the absence of any nerve lesion? (Barré and Babinski.)

3. Are they due to the combined influence of nerve and bone lesions? If so, where does the primary change lie?—In the nerve or in the bone? What is the nature of the nerve-change? Is it merely a lack of sensibility, or is it the degeneration of some nerve assumed to exert a trophic influence? What is the nature of the bone-lesion? Is it an arteriosclerotic deforming arthritis, or a syphilitic one, or one the result of an unfelt trauma?

In order to answer these questions I aimed to produce lesions in cats simulating as nearly as might be tabes in man. I cut a series of posterior roots leading to a particular extremity, enough of them to make a total analgesia, anæsthesia and ataxy. This eliminated many of the factors complicating tabes; the underlying syphilis, for instance. Sections of cords from these cats show an ascending degeneration of the posterior columns corresponding to what would be in man a one-sided tabes (Figs. 1 and 2). Cutting one side only enabled me to have the other as a control. I watched the cats for a considerable period and had the satisfaction of seeing some of them under certain conditions develop what in man would be called a Charcot joint or a tabic fracture.

I then produced joint changes in another series of animals, and after waiting some time, cut the posterior roots, so as to see what effect the nerve-lesion might have on the process in the joint. Then I reversed the order of experiment; cut the roots first, let the cat accustom herself to the anæsthetic limb, and after a month or so induced a deforming arthritis, to see whether this lesion in an enervated joint would immediately assume the extravagant course of a tabic arthropathy. And finally, to refute those who might object that depriving a limb of its sensibility might cause its disuse, and that a possible atrophy might be due merely to inactivity, and not to a trophic nerve influence, I cut three dorsal roots, leading to as many ribs, in a further series of cats. As the ribs were moved along with the movements of their neighbors, there could be no assumption that any trophic change that might be found would be the result of muscular inactivity. All cats were operated on under full ether anæsthesia.

I am indebted to a number of friends for help in this work,—to the

late Dr. Painter, Drs. Howe and Markel for X-rays, to Prof. O'Neill, of Berkeley, for chemical analyses of bones, to Prof. Wing, of Stanford, for tests of tensile strength, to Mr. L. Heynemann, M.E., of San Francisco, for suggesting and giving me an apparatus for the determination of deflection under cross-strain, to Dr. Blaisdell for micro-photographs, and finally to the aid of my attendant, Mr. Moran.

Sixty-nine cats were used for the experiments, and 42 of them were observed for greater lengths of time, from 3 months to over three years. The rest died of intercurrent diseases, sepsis in the anæsthetic limbs, or other complications. After cutting a sufficient number of roots the affected limbs showed the clinical picture of advanced tabes. They were atactic and their muscle-sense was gone. The gait was unsteady, the cats would frequently paw the air a few times before setting the limb to the ground, as though to make sure of its position. Often, in the attempt to make a step, instead of bringing the leg forward the cat would extend it stiffly in all joints, and would drag the limb rigidly after it for a few paces before moving it again. The awkwardness and spasm were atactic, not paralytic. Many of the cats got deep ulcers on the dorsum of the foot from dragging it along the ground. Muscular hypotony was marked; many of the cats walked with an outward rotation of the hip which may have been the cause of the dislocations of the hip-joint noted in some of the animals. Ataxy and atony were less strong in the unilateral resections than in the double ones. For days and sometimes weeks, the cats with bilaterally resected roots would make but few attempts to use their hind-legs. They would hold them extended backward stiffly, and would slide along the floor with their groins and knees touching the ground, as though they did not know that they had hind-legs. They were not paralyzed, however, since they would kick vigorously if lifted by the nape of the neck. The unilateral resections rarely caused bladder disturbances, the bilateral ones were often followed by fecal incontinence, and sometimes by a fatal cystitis. In all successful resections there was complete loss of the sense of pain, both in the soft parts, the skin, and the bone. The periosteum of the affected leg could be pricked with a pin without the cat's evidencing discomfort. The knee-jerk on the affected side was lost. A cross reflex might be obtained by tapping the sound patellar tendon, when both knees jerked, but on tapping the affected tendon no knee-jerk appeared on either side.

Now as to the results of the resections: Nineteen cats with unilateral resections of posterior roots were observed for periods of from three months to three and a quarter years. Of these, two got a fracture of the head of the femur, one a fracture of the great trochanter, three a coxa vara, three had dislocations of the hip, one a fracture of the tibia, one a fracture of the fibular malleolus, one a Pott's fracture, and six showed various lesions about the ankle-joint, fractures of the bones of the foot, etc.; some of these animals had multiple bone and

joint lesions; in six of them no abnormalities of the bones or joints could be found.

Three cats with a bilateral rhizotomy were followed for over six months. Of these one showed an arthritis of both hips with coxa vara, one merely a metatarsal fracture, while the third got a fracture of the head of the femur on one side and on the other a fracture of the middle of the femur, a typical Charcot knee with luxation of the tibia, and a Charcot ankle with fracture of the os calcis.

Sixteen further cats that died of intercurrent disorders could be observed but for a shorter period of from four to ten weeks. Of these two had pus joints, both of them a hip that was dislocated and full of pus, one of them a purulent Charcot knee besides; one of them had a fracture of the neck of the femur, two fractures of the tibia and fibula, five others had tarsal fractures or joint lesions, in five the bones and joints seemed intact, but even of these, two were noted as having but little anæsthesia of the side whose roots had been resected. So, out of thirty-eight cats with disturbances of sensibility of the legs, twenty-seven developed spontaneous lesions of the bones or joints.

It is difficult to know how much stress to lay on changes at the ankle. Disintegration of the metatarsal or tarsal joints and fractures of the bones about them were common, and occurred in fourteen cases out of the thirty-eight; sepsis from an open ankle-joint was a frequent cause of death. Almost all the cats had ulcers of the anæsthetic foot, and it may be that changes at the ankle-joint were effects of the suppuration near by; however, lesions of the hip, femur, knee and tibia being uncomplicated by suppuration, were characteristically neuropathic. It is noteworthy that all the eight joints showing the periarticular ossifications and destructive arthritis typical of Charcot's arthropathies were seats of a fracture that ran into or near the joint.

The mere production, therefore, of these bone and joint changes in healthy animals has disproven some of the theories as to the cause of tabic arthropathies, viz.: the theory of a luetic origin, and that of a primary deforming arthritis.

To see whether there was any change in the composition of the bones following root-resection I had bones from the affected and from the sound side analyzed chemically. They showed no chemical difference. Prof. Wing, of Stanford, was so good as to have tensile strength tests made for me; these, however, presented such technical difficulties and were so full of sources of error that we gave them up, and at the suggestion of Mr. L. Heynemann, M.E., tried measuring the deflection of the bones under a given load, as being easier and giving a more useful criterion of their strength and elasticity. Mr. Heynemann had built for me the little apparatus shown in Figure 14. The ends of the bone are supported by two narrow pieces of metal, over the middle of the bone is placed a hook from which a weight may be

hung. The deflection of the bone under the load of a given weight is measured by the vernier riding overhead on a slotted bridge. Tests both of the ribs whose nerves had been resected as mentioned before, and of the bones of the leg, showed certainly that the bones from the affected side were not weaker than the controls from the sound side. In fact, both these strength tests and the X-ray seem to show that the bone on the enervated side is usually a little stronger than on the sound one. We may assert then, as a result of forty determinations on some thirty-two ribs and fifty-three determinations on various other bones, that there is no osseous *atrophy* produced by a disturbance in conduction along the posterior roots. These determinations make untenable Charcot's theory that a trophic disturbance causing a *wasting* of the bone is at the root of these arthropathies.

Whether there may not be some nerve influence, a "trophic" influence (whatever that may be), that causes a change in the metabolism of the bone, causes it to become more dense, more sclerotic, more liable to arthritis, and more rigid, more liable to fracture, I should not like to say. Especially the case of cat No. 32, where one rib of the three anæsthetic ones was found broken at autopsy, might make one suspect some such factor. There are, however, so many agencies at work in a tabic limb that might produce fractures,—the sudden pull of atactic muscles, the lacking muscle sense which brings the limb into unnatural positions little adapted to resist strain, the anæsthesia and analgesia,—that I do not see why it is necessary to have recourse to the assumption of a mysterious and unproven "trophic" influence in order to explain tabic fractures. The denseness of the tabic bones seen in the X-ray plates might also well be merely a response to added demands, to increased sudden stresses and strains arising from the ataxy, lacking muscle-sense and analgesia previously mentioned.

Some of the cats showed coxa vara, a number of them an obviously traumatic one, but some hips were without the least evidence of fracture or other injury,—it was, however, noted that just these cats walked with rigidly outstretched legs or with an uncertain and wobbling gait, treading now on the sole, now on the dorsum of the deflected foot, so that their varus deformity may as well have been a static one as due to some particular nervous "trophic" cause. In short, there is nothing in our findings that proves the existence of changes in the texture of the bones that may not be accounted for by conditions arising solely from an altered function dependent on a lack of sensibility, nothing in these findings that gives proof of the existence of "trophic" nerves.

We have then to look for the cause of these joint affections in influences due to some combination of both the nervous and the bony lesions. Can we find it in an ordinary deforming arthritis aggravated by a lack of a warning sense of pain? To answer this question I induced a deform-

ing arthritis with the thermocautery after the method of Axhausen, in both knees of thirteen cats, waited for the wounds to heal soundly and the inflammatory reaction to disappear and followed the operation on the knees by a unilateral root-resection. Six of these animals were observed for over four months. In five of them no characteristic difference could be seen in the degree of arthritis on the analgesic and the sound side; one of them (Figs. 6 and 7) developed a typical Charcot knee in the joint which was at the same time arthritic and analgesic. In this cat it was noted from the beginning that the leg was carried awkwardly, with the knee doubled under. This proportion of one cat in six proves nothing, as an equal proportion of cats in the series where the joints were not made arthritic artificially developed spontaneous joint-lesions.

The presence, therefore, of a moderately severe arthritis is not sufficient to make an analgesic joint develop a characteristic arthropathy. Furthermore, we cannot explain the cause of an arthropathy by the assumption of an atrophying influence of degenerated nerves. And finally, we cannot see in these lesions simply an aggravated form of a luetic arthritis. Where have we then to look?

As a companion-piece to the last-named order of experiment I resected the posterior roots in three further cats, and after waiting a number of weeks, opened the joints and seared a spot on the femoral condyles with a thermocautery. *Within three weeks every one of these three cats developed a Charcot joint* with a huge joint hydrops, deformity and grating of the joint surfaces (see Figs. 16 and 17). This, then, was not a slow aggravation of a pre-existing deforming arthritis; it was the sudden response of an anæsthetic joint to the acute trauma of operation, a rapid reaction to bone injury by the production of a typical Charcot joint.

Moreover, it was not only in this last series of experiments, where the limb was purposely subjected to trauma, but in all the experiments as a whole that we find that the cats that were the ones to develop arthropathies, spontaneous luxations of the hip, Charcot knees, or spontaneous fractures were those that did not suffer from operation, those that were lively and active, and we find particularly noted that it was those that held their limbs in awkward and unnatural positions that developed bone and joint lesions. Hence it was the animal most subject to trauma that most often suffered bone or joint trouble. The joint lesions themselves were visibly of traumatic origin, eight of them still showed fractures near the joint, others dislocations such as the joints shown in Figs. 3, 4, 5, 8, 9, 10, 11, 12, 13 and 17. This agrees with clinicopathological observations in man, with the fact that arthropathy is a lesion of *early* tabes, a lesion occurring during the time when the tabetic is still subjecting himself to trauma, and is much rarer in the late atactic or paralytic stage when the patient is weak and confined to

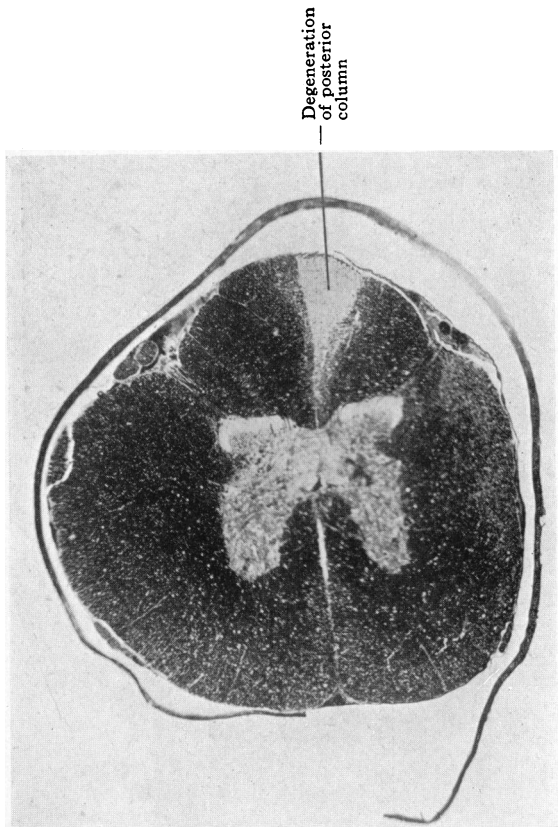


FIG. 1.—Spinal cord of cat No. 33. Weigert stain. Microphotograph by Dr. Blaisdell.

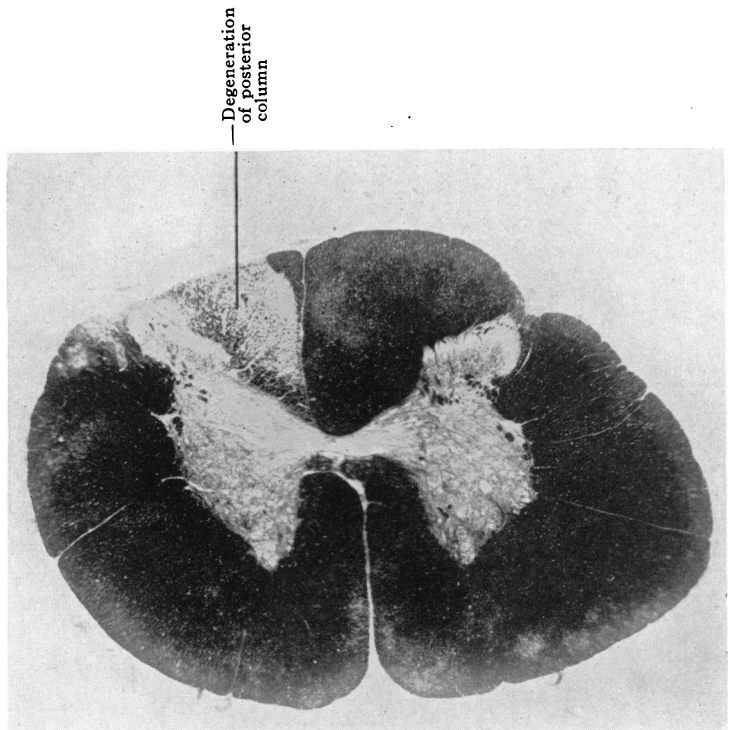


FIG. 2.—Spinal cord of cat No. 48, Weigert stain. Microphotograph by Dr. Blaisdell.

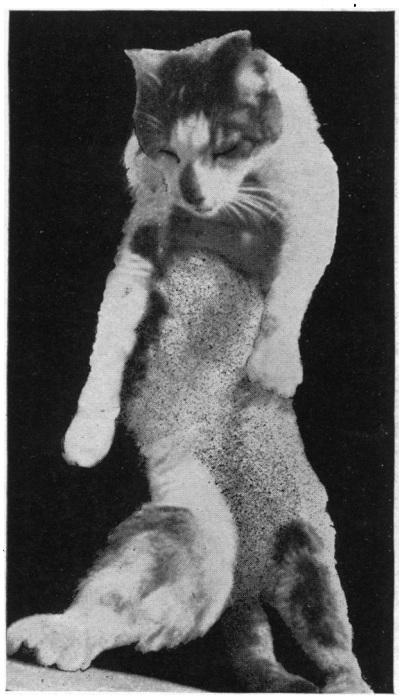
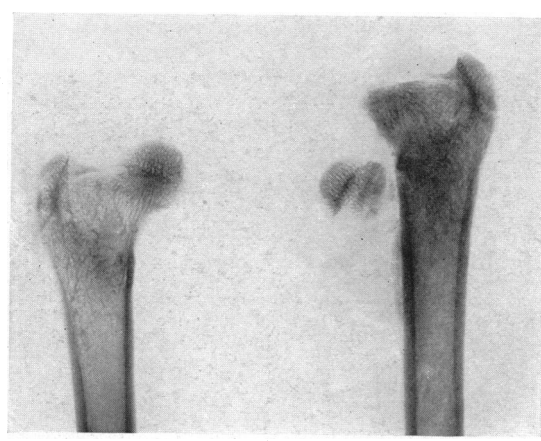


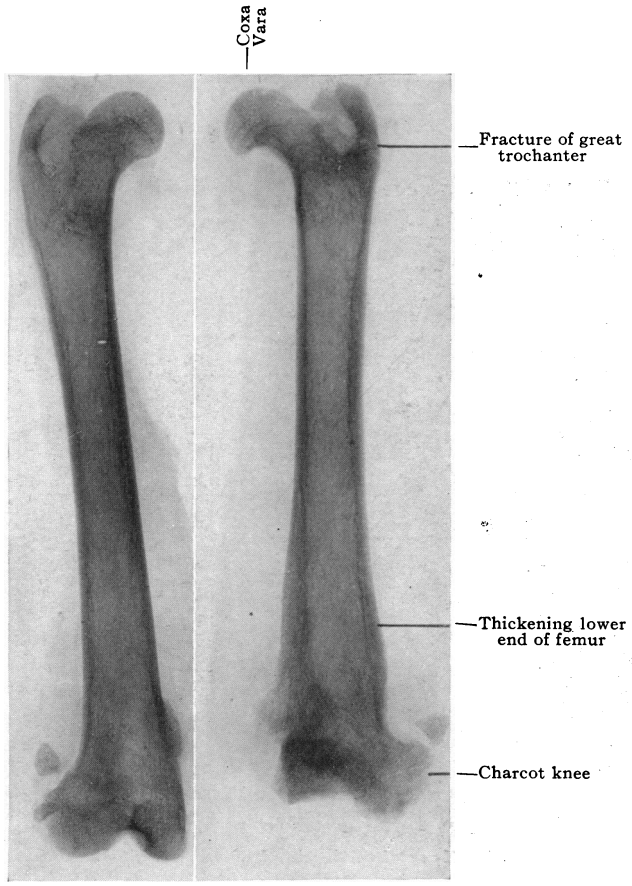
FIG. 3.—Cat No. 52, Charcot knee with dislocation.

FIG. 4.—Cat No. 52 (same as Fig. 3).



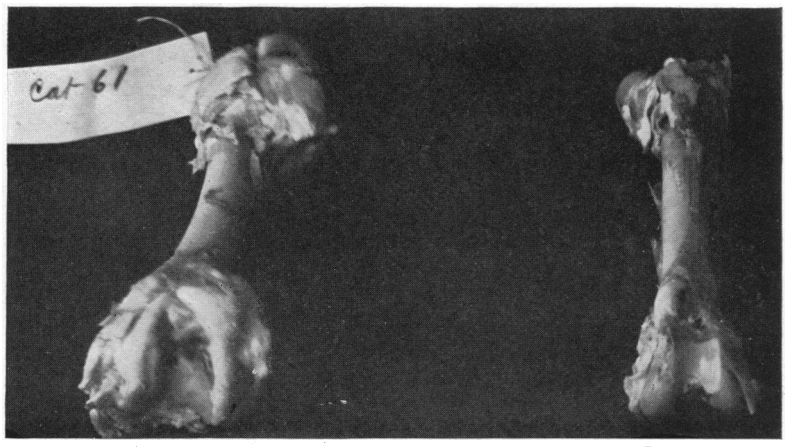
A *B*

FIG. 5.—X-ray of cat No. 1. Fracture of the neck of the femur. The bone on the affected side, *B*, is denser than on the sound side, *A*, as was the case in many of the cats with bone and joint lesions.



A *B*

FIG. 6.—X-ray of femurs, cat No. 61. The affected side, *B*, shows coxa vara, fracture of the great trochanter, much thickening of the lower end of the femur and a Charcot knee with marked deformity of the condyles. See photograph of knees, Fig. 7.



A *B*

FIG. 7.—Cat No. 61. *A*, right femur: Condyles show hypertrophic ossifications and extravagant changes in form incident to Charcot knee. *B*, left femur: Condyles (upper anterior part) show erosions of deforming arthritis after thermocauterization.

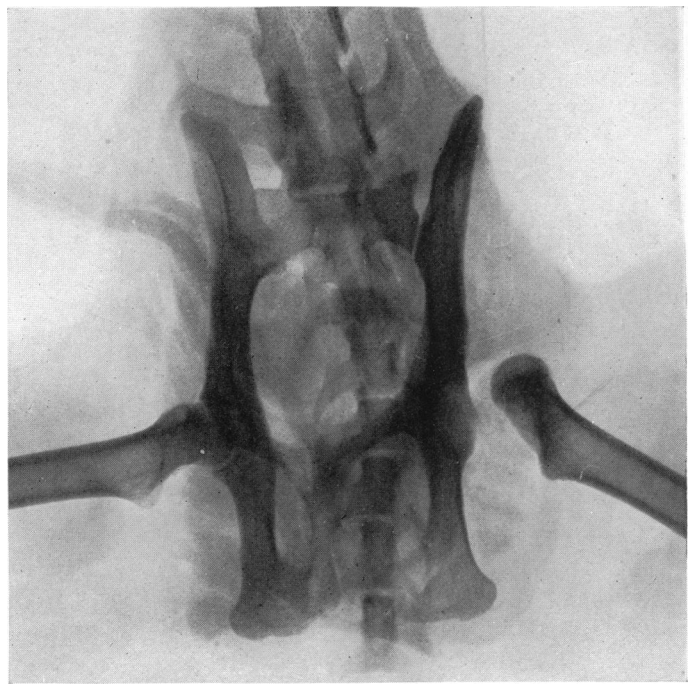


FIG. 8.—X-ray of pelvis with dislocation of hip-joint. Cat No. 42.

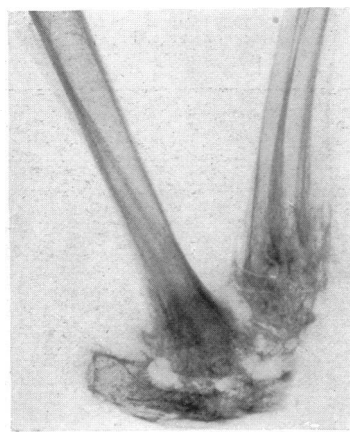


FIG. 9.—X-ray of ankle, cat No. 25, showing disintegration of the ankle-joint. ("Pied tabétique.")

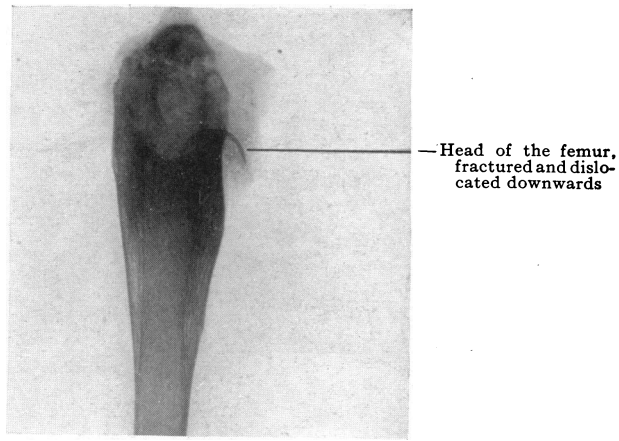


FIG. 10.—X-ray of Charcot hip with fracture of the head of the femur and much thickening of the bone. Cat No. 13.

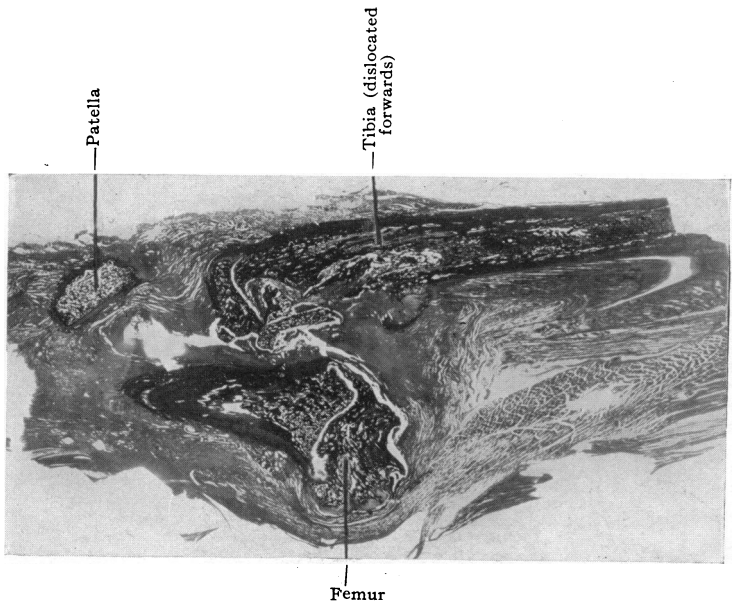


FIG. 11.—Microtome section through Charcot knee with dislocation of the tibia. Cat No. 13.

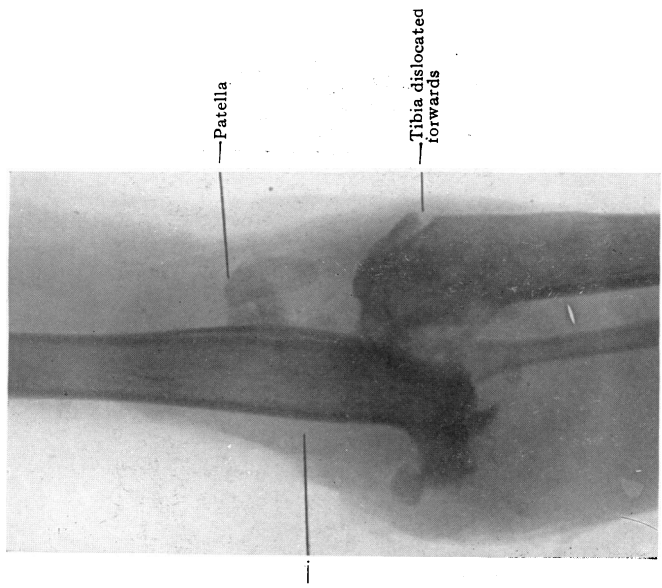


FIG. 12.—X-ray of same joint as Fig. 11.

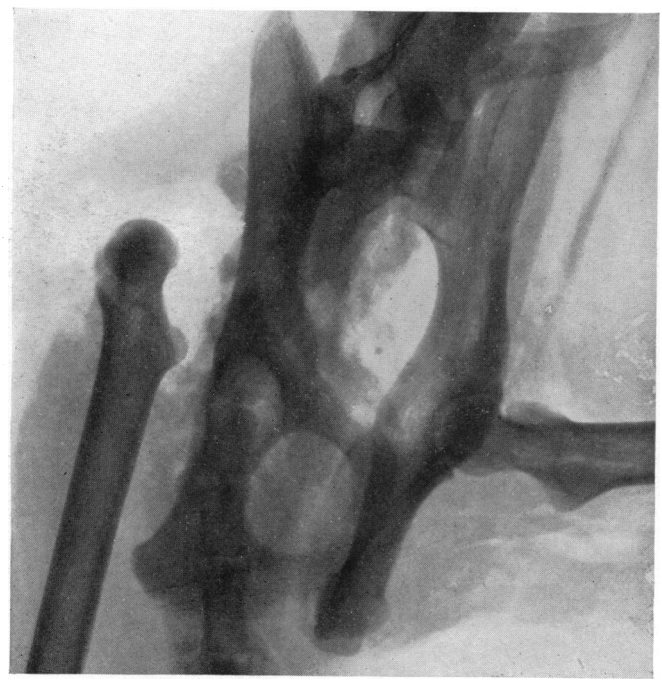


FIG. 13.—X-ray of pelvis with dislocation of hip-joint. Cat No. 51.

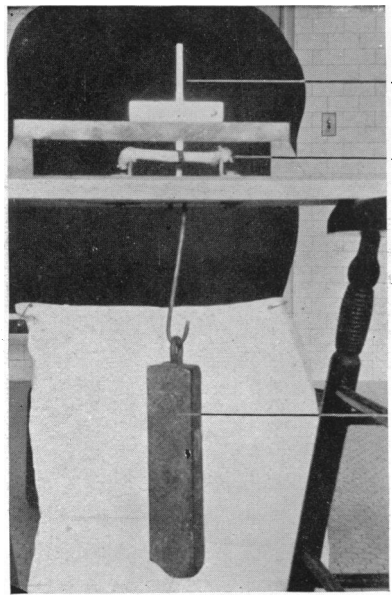


FIG. 14.—Apparatus for measuring deflection of bone under a given load.

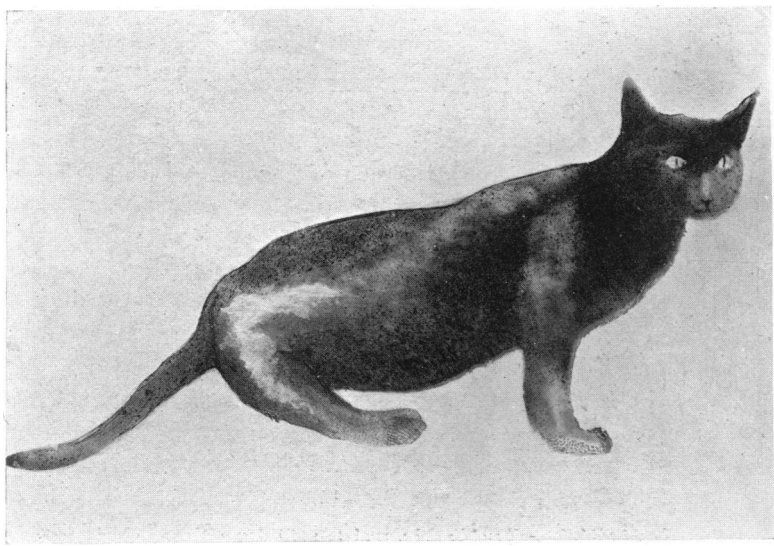
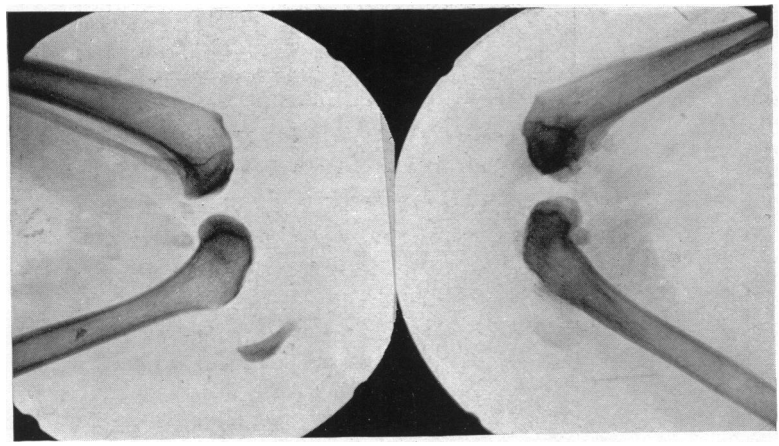
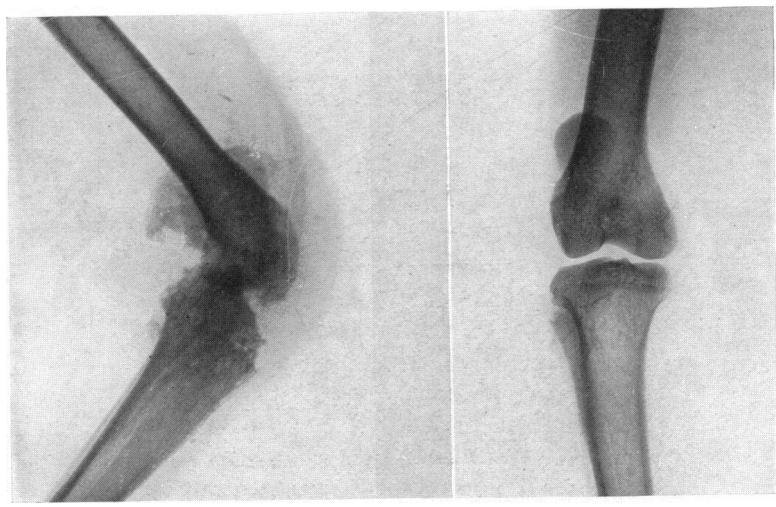


FIG. 15.—Cat No. 48, Charcot knee and eversion of hip-joint (see Fig. 16).



A *B*

FIG. 16.—X-ray of Charcot knee, cat No. 48. *A*, sound side; *B*, affected side.



A *B*

FIG. 17.—X-rays of Charcot knee in cat No. 33. *A*, affected side; *B*, sound side.

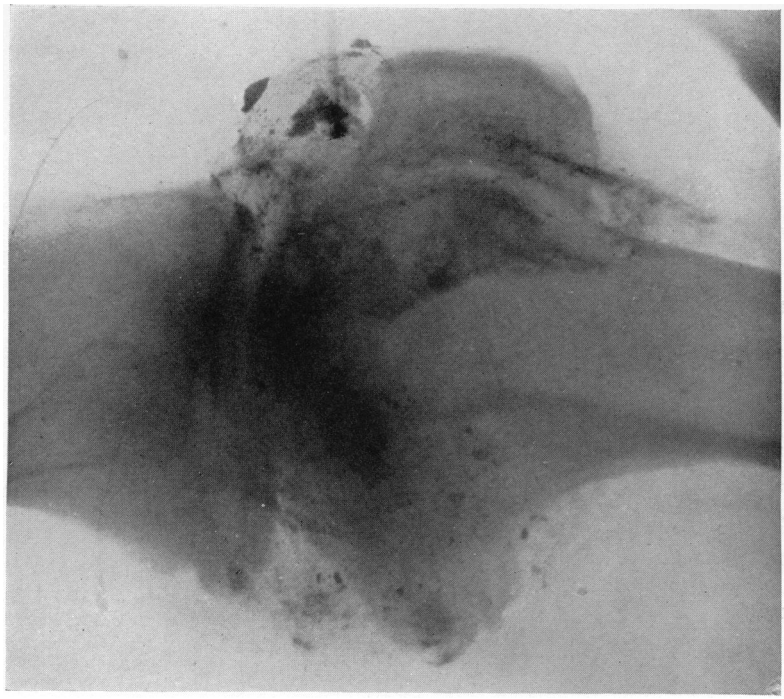


FIG. 18.—X-ray of Charcot joint following old gunshot wound of the knee. The blotchy shadows around the joint are caused by lead from the bullet deposited in the tissues of the joint-capsule.

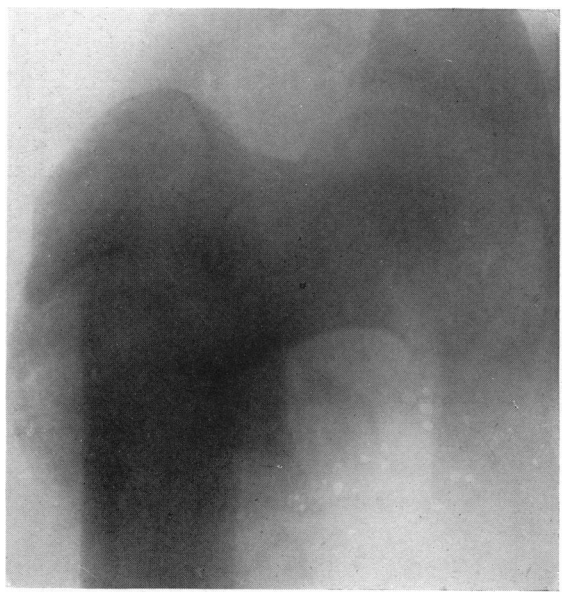


FIG. 19.—X-ray of Charcot joint following subtrochanteric fracture of the femur.

bed. It agrees with the findings in man, where in many Charcot joints we see evidence of old trauma, such as in the case shown in Fig. 18, where a Charcot followed an old gunshot injury; or in the case of a Chinaman in the University of California Service at the San Francisco Hospital, where it followed an evident fracture of the head of the tibia; or in the case of Fig. 19, where it followed a subtrochanteric fracture of the femur. The assumption of a trauma also explains the great para-articular ossifications and proliferating periostitides characteristic of these joints, comparable to the hypertrophic callus that MacEwen found in his fallow deer. All of these are findings inexplicable under the assumption of an atrophying nerve influence, which to explain them all simultaneously would have to be at once atrophying and hypertrophying. The trauma may be slight, but lacking the protecting sense of pain, a simple lesion may turn into a graver one from the added insult of unwholesome use.

I think, therefore, that in the assumption of trauma, grave or slight, plus lack of the protecting sense of pain, we have sufficient explanation for the origin of most Charcot joints.

CONCLUSIONS

1. Bone and joint lesions corresponding to those found in tabes dorsalis may be induced experimentally in the limbs of cats by severing the posterior nerve roots (the sensory fibres) leading from the limb.

2. Severing the posterior roots causes no atrophy of the bone.

3. Tabic fractures and arthropathies have been produced in healthy animals, hence they cannot be ascribed primarily to lues or other infectious causes.

4. The course of a deforming arthritis is not characteristically altered by the addition of an analgesic factor, hence the cause of the Charcot joint is not to be sought in a simple deforming arthritis occurring in a tabetic.

5. Nothing in these experiments gives proof of the existence of trophic nerves.

6. Of three animals whose joints were subjected to operative trauma after having been previously rendered anæsthetic by resection of posterior roots, all rapidly developed Charcot lesions. Trauma in a limb rendered anæsthetic and analgesic experimentally leads to grotesque lesions of the bone and joints, which are in every way the counterparts of tabic fractures and arthropathies; *trauma and lack of the warning sense of pain are the cause of most tabic bone and joint lesions.*