

48. Observations on Osteomalacia in the Zoological Collections of Manchester and Cleveland. By T. WINGATE TODD, M.B., F.R.C.S., Professor of Anatomy, Western Reserve University, Cleveland, Ohio *.

[Received May 5, 1913 : Read June 3, 1913.]

(Plates LXXXVII.—LXXXIX.†)

It is the object of this communication to call attention to the widespread appearance of osteomalacia among animals in captivity, and to point out the opportunity afforded by the disease for the study of changes in formed bone-tissue.

Through the kindness of Messrs. Jennison of Manchester and Director Springborn of Cleveland, I have been enabled to study the disease as it exists in the Zoological Gardens of both these cities.

In Manchester, while the cercopitheques, macaques and small baboons were kept in a large cage in a moderately heated monkey-house, the animals sickened and died of miliary tubercle within a few months after their arrival. When, however, the glass was removed from the windows of the monkey-house and a free current of air permitted to pass through the building, the animals remained healthy for as long as three years. Eventually, however, most of them begin to show a disinclination to move about, crouching and walking with the aid of the fore-limbs—the hind ones being curled up beneath the body in squatting attitude. When attacked by healthy animals they seem unable to defend themselves, or, if they try to run away, they do so groaning with apparent pain. This is more marked if they are compelled to use their hind legs, as, for instance, in climbing. Left to themselves they are very much addicted to masturbation. Indeed, in Cleveland, my attention was first drawn to the condition by my being asked to inspect some macaques of both sexes which had developed this objectionable habit. As the disease progresses the joints become stiff and enlarged, although post-mortem joint-changes have not been present in the cases which I have examined. The disease is not of itself fatal and may last two years, although it is usually found necessary to destroy the animals after twelve months. If the animals die, there are frequently indications of broncho-pneumonia found at the autopsy. The food on which all the apes, healthy and diseased, are fed consists of rice-pudding, carrots, onions, potatoes, greens, apples, and bananas, with a little meat occasionally.

While suffering from the disease, the hair may become dry, ruffled, or fall out. This is more frequently the case in rabbits

* Communicated by the SECRETARY.

† For explanation of the Plates see pp. 859–860.

and rats than in monkeys. The disease seems to localize itself in different sites in different animals. In the macaques and baboons it usually affects the hind limbs, which are in consequence badly bent and twisted, but that the whole skeleton is affected is shown by the brittle character of all the bones. The ability of the bones to unite after fracture does not seem to be impaired. Fig. 4 (Pl. LXXXVIII.) represents the tibia of a young Anubis Baboon (*Cynocephalus anubis*) after healing of a fracture near the upper extremity. This bone was broken by a fall from a height of some three feet while the animal was attempting to escape from a pursuer. The animals may become affected by the disease while still young and before the epiphyses have joined, so that the disease is readily confounded with rickets. The lesions, however, are the same at whatever age the disease occurs. In some instances the bone-changes are found most marked in the fore limbs. This was the case in a peccary from the Manchester Collection. The animal struggled about with its fore limbs bent backwards beneath the body. In other animals the bones of the face are affected. The maxillæ are much enlarged and give a puffed-out appearance to the cheeks. This condition occurred in a horse, a leopard, a rabbit, and a chimpanzee. In some cases the necks of the teeth are decayed and the teeth may fall out. This was observed in the leopard and rabbit just referred to, and also in a Californian sea-lion from Cleveland. Ulceration and falling of the teeth has not occurred among the apes in Manchester since the glass was taken out of the windows of the monkey-house. The bones of the chest are frequently softened and deformed, which would seem to predispose the animal to respiratory disorders. The lungs of the sea-lion showed emphysema and patches of broncho-pneumonia, the latter being confirmed by histological examination.

Post mortem, the viscera show no lesion whatever in animals which have been intentionally killed. Nor are there any atrophic changes in the muscles of the disabled limbs.

The ductless glands are apparently normal. Pathological appearances are to be found only in the nervous system and the bones. As regards the former opinion is very varied. Gayet and Bonnet describe an increase in volume of the nerves with an overgrowth of the fibrous tissue between the nerve-bundles and disappearance of myelin in certain cases. The blood-vessels of the nerves exhibit endarteritis (1). They found no cellular lesion nor any alteration in nerve-fibres in the spinal cord. Morpurgo, on the other hand, describes diffuse chromatolysis in the cells of the anterior horns of the cord, but denies any change in the cells of the spinal ganglia (2). These changes occur very early in the course of the disease, but there would appear to be no definite evidence to show that they initiated the disease (3).

It may be that these different histological pictures were

produced by differences in the ætiology of the disease. For the bone-changes can only be a symptom, caused, perhaps, in many different ways.

The bone-marrow in osteomalacia is much modified. The marrow-cavities of the long bones are enlarged and filled with a gelatinous fatty tissue and by bright red marrow. Marrow is divided microscopically by Ziegler into splenoid and fine-fibred constituent factors (4). Of these the latter form is much increased, partially filling up the marrow-cavity and penetrating the bony tissue.

In early cases the compact bone is invaded by this vascular fibrous tissue, which has already replaced to a large extent the spongy bone and which is not preceded by osteoclasts. The same observation has been recorded by Morpurgo (3).

In later stages the whole of the compact tissue of the shaft has disappeared and is replaced by fibrous tissue, in which are to be found discreet areas or islets of osseous material (see Pl. LXXXIX. figs. 5, 6). There is meanwhile no subperiosteal deposit of new bone. The histological picture of the bone closely resembles that seen in *ostitis fibrosa*. The remaining islets of bone lose their ossein and become transformed into a tissue which, from its staining properties, appears to be hyaline in character. But, at the same time, in other situations the regressing bony substance exhibits a fibrillar change of the ground-substance similar to that described by Retterer as the basis of normal bone (5).

Cells with similar staining reactions to osteoblasts may still be seen bordering the islets of bony tissue (see Pl. LXXXIX. fig. 6). In many places so-called "osteoclasts" are observed. But, on examining several slides one is struck by the comparative infrequency of these cell-masses. As Gayet and Bonnet remark (1) it is difficult to believe that osteoclasts can play more than a very subsidiary part in the destruction of bone, because of their scarcity when compared with the extent of the process. It would appear that osteoclasts are not at all necessary for the production of change in bone-substance.

As the bony tissue becomes transformed or replaced by the fibrous material, the Haversian systems disappear. The periosteum becomes intimately united to the mass of fibrous tissue which remains in place of the true bone. I have not observed hæmorrhages in subperiosteal or other localities. The joints were unaffected. At the diaphyso-epiphyseal junction, changes similar to those in rickets were observed.

The theories of causation of osteomalacia have been well reviewed by Morpurgo (2), who, among others, has succeeded in producing the disease by inoculation of a micro-organism (6).

The detailed histological changes have been discussed by Basset (7), whose description is amply borne out by my own slides.

The disease is one which may be secondary to some other

lesion, and therefore localised, as in the variety appearing after trauma.

It may develop in connection with giant-celled sarcoma and be more generalised in type (Schönenberger, 8).

It may occur in the so-called spontaneous form, such as is seen in animals in captivity.

The last-mentioned variety is certainly not a simple decalcification. There is absorption of osseous substance with rarefaction of the tissue. The process starts from the marrow-cavity and involves first spongy and later compact bone. The Haversian systems disappear and the bone becomes fibrillar in character and later is transformed into fibrous tissue.

An intermediate hyaline change is shown in places. All these changes point to a revolution in the constitution of bone as a whole, which is accompanied by changes in the marrow and periosteum, as already described. Similar changes in bony tissue are to be observed in *ostitis fibrosa* and *leprosy*. For it has been my good fortune to be able to investigate all three diseases at the same time. The clinical symptoms in these cases of generalised bone-softening, which I have described as *osteomalacia*, suggest a nervous origin. The obvious inference to be drawn from the histological picture in *leprosy* is that in the last-named disease the bone-changes are certainly trophic in character. I would emphasise the fact that we are as yet ill-acquainted with the symptoms consequent on lesions to the sympathetic nervous system. But there would seem to be ample confirmation of nerve-lesion in the histological changes found in the nerve-bundles by Gayet and Bonnet (1). Moreover, the intimal proliferation described by these authors in the vessels of the nerve-trunks may be produced by a lesion in the sympathetic nerves, as I have recently been enabled to show (9).

If the disease is infectious, the incubation-period must be considerable, for it seems to appear spontaneously in animals which have been isolated for a long while. After inoculation, Morpurgo found the animal became ill in a week or two. Such evidence as we have points to the nervous system as the seat of primary disease, whether it be infectious or not, and suggests that the bone-changes are consequent on nervous lesion. Treatment is unsatisfactory. Dr. Fox, of Philadelphia, has recently administered calcium lacto-phosphate and adrenalin, separately and in combination, to animals suffering from the disorder in the Philadelphia collection, but without success (10).

In making observations on the living animals Messrs. Antliff and Readinger, keepers of the monkey-houses at Manchester and Cleveland respectively, have rendered generous assistance. The histological sections are the work of Mr. Gooding, of the Anatomical Department of Manchester. Mr. J. C. Miller, of the Laboratory here in Cleveland, has assisted me in gathering and abstracting the literature. To all these gentlemen, I would therefore express my obligation.

Summary.

1. Osteomalacia, or so-called spontaneous generalised bone-softening, is not a simple decalcification of bone, but a re-organisation of bone as an organ, in which the loss of osseous tissue is not brought about by osteoclasts.

2. From this it is evident that the cell-masses known by the name of "osteoclasts" are not indispensable in the transformation of bone to less specialised tissue.

3. The disease may be infectious in origin. If so, the evidence at our disposal points to the nervous system as the site of infection. The bone-changes appear to be the symptoms consequent on the nervous lesion.

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EXPLANATION OF THE PLATES.

PLATE LXXXVII.

Fig. 1. Right Radius from young Anubis Baboon (*Cynocephalus anubis*). Advanced stage of osteomalacia.

Note large size and dark colour of marrow cavity. The dark appearance is due to the large quantity of red marrow. The rarefaction of bone and the progression of the osteoporosis from marrow-cavity outwards is well shown in this photograph. The compact tissue can be seen to have been replaced by spongy bone.

- Fig. 2. Right Ulna from same animal. Here and there are districts of gelatinous fatty marrow giving rise to lighter areas between the dark-coloured sites of red marrow. The thickened periosteum and its intimate union with the tissue composing the bone can be seen well, especially near the centre of the shaft. In this situation the bone was accidentally broken while stripping off the muscles.

PLATE LXXXVIII.

- Fig. 3. Right Humerus of same animal.
Note the irregular diaphyso-epiphyseal junction at the upper end of the shaft. The extreme brittleness of the bones resulted in the fracture of the surgical neck of this humerus while the muscles were being removed. There is no sharp line between the articular cartilage of the condyles and the underlying spongy bone. This photograph shows clearly the articular cartilage being destroyed on its bony aspect.
4. Right Tibia and Fibula from same case.
Note extreme recurved upper portion of tibia. The bone had been fractured some time previously and had united in this position. The union is complete. The fibula was likewise bent, its lower extremity is cut obliquely and is shown behind the lower portion of the tibia.

PLATE LXXXIX.

- Fig. 5. Longitudinal section of shaft of Left Ulna from the same animal. $\times 40$.
Note the entire disappearance of Haversian systems from the bone and the replacement of osseous tissue by fibrous material. The bony substance is here shown broken up into islets. The section represents what once was the compact bone layer of the shaft.
6. Longitudinal section of shaft of Left Ulna from the same animal. $\times 206$.
A bone-islet is shown surrounded by non-osseous tissue. Note the gradual transition of the bone into fibrous tissue. There is no sharp line of demarcation, and no osteoclasts are to be observed. The decalcification progresses from the centre of the illustration to the periphery. Intermediate between bone and fibrous tissue is a zone where the nuclei are surrounded by considerable non-calcified protoplasm. This corresponds in appearance to the pre-osseous stage in Retterer's description of bone (5).



Todd, T. Wingate. 1913. "Observations on Osteomalacia in the Zoological Collections of Manchester and Cleveland." *Proceedings of the Zoological Society of London* 1913, 855–860. <https://doi.org/10.1111/j.1469-7998.1913.tb06157.x>.

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DOI: <https://doi.org/10.1111/j.1469-7998.1913.tb06157.x>

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