EXPERIMENTAL SYPHILIS IN THE RABBIT.

VI. Affections of Bone, Cartilage, Tendons, and Synovial Membranes.

Part 2. Clinical Aspects of Syphilis of the Skeletal System. Affections of the Facial and Cranial Bones and the Bones of the Forearm.

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Plates 61 to 66.

(Received for publication, January 31, 1921.)

Syphilitic affections of the skeletal system were described in the preceding paper (1) from the standpoint of the pathological process, and it is the purpose of this paper to correlate these changes with clinical manifestations of the disease. This phase of experimental syphilis is of unusual importance on account of the widespread and frequently obscure nature of the infection. The subject will be dealt with, therefore, in somewhat greater detail than other groups of affections with the belief that the facts presented have an important bearing upon latent or obscure infections in the human subject and especially upon congenital forms of the disease.

The conditions to be described are numerous and it will be necessary to divide the material into two papers, the first of which will deal with affections of the facial and cranial bones and the bones of the forearm. The remaining subjects will be considered in the second paper.

Parts Involved and Character of the Affection.

The most obvious affections of the skeletal system were those of the face and of the feet and legs, but lesions were also found in many other parts of the body, such as the cranial bones, the cervical and

caudal vertebræ, the ribs, and the sternum. The proportion of focal infections which gave rise to clinical signs of disease cannot be estimated, but it seems probable that many obscure infections occurred which did not give rise to any obvious abnormality.

Bone infection was recognized in general by the development of visible or palpable enlargements over the surface of the bones, or, in the absence of these, by rarefication and the loss of structural detail as indicated by the radiograph, and eventually by necrosis and disintegration of the bone. The skin over the lesion was freely movable, while the nodular mass was firmly attached to the underlying bone. In rare instances, the skin might become adherent, but it is worthy of note that necrosis and ulceration of the skin were never observed in connection with lesions of either tendons or bones, with the exception of the phalanges. The diagnosis of these conditions as syphilitic affections was readily made by the demonstration of spirochetes in the lesions.

These were the general characteristics presented by all classes of bone infections, but the details of the processes as they occurred in different parts of the body were subject to considerable variation.

Facial and Cranial Bones and Cartilages.

Judged upon the basis of the occurrence of lesions which were sufficiently pronounced to be detected by ordinary methods of examination, the facial bones were more often the seat of syphilitic affections than those of any other part of the body, with the possible exception of the hind feet and legs. The bones usually involved were the nasals, the two lateral splints composed of the frontal process of the premaxilla and the maxillary process of the frontal, the turbinates, and to a lesser extent the maxillæ, the premaxilla, and the frontal eminences. These bones lie immediately around the nasomaxillary fossa, and, with few exceptions, the lesions of the facial area were confined to the region of this fossa and the bridge and sides of the nose. The most frequent locations were the bridge of the nose, the end of the nose, and the bony ridge extending from the naso-orbital angle along the sides of the nose, while young animals in particular showed a marked tendency to localization at the point of union of the frontal and maxillary processes.

The appearance presented by animals with well marked facial lesions of various types is shown in Figs. 1 to 7, 11, and 15. Fig. 1 represents a very common type of deformity due to a sharply circumscribed periosteal lesion on the bridge of the nose. Fig. 2 is a more pronounced condition of a similar character which involved the lower two-thirds of the nasal bones and the lateral splints and extended well down on the premaxilla.[1] The profile of the animal shows a gradual curve extending from just below the level of the eyes to the tip of the nose, the deformity being less abrupt than that in the preceding case, and hence not so noticeable at first.

A less common affection is that illustrated in Fig. 3. This was a multinodular lesion of the lower portion of the nasal bones and cartilages and was the most pronounced case of its kind which occurred in our series of animals, measuring 1.85 by 1.7 by 1.2 cm.

Another unusual type which was associated with a marked alteration of the profile is that shown in Fig. 4. The prominence seen above the eye of this animal was due to a large periosteal granuloma involving the supraorbital portion of the frontal bone. This process was bilateral.

The visible deformity in all these animals was quite apparent, but there were many instances in which little or no visible alteration in contour could be detected either on account of the size and form of the lesion or its location. This was especially true when the sides of the nose and the region of the nasomaxillary fossa were involved. Photographic reproduction of even large lesions in these locations was found to be extremely difficult. This class of affections is illustrated by two animals (Figs. 5 and 6) both of which represent very common types of facial involvement.

The lesions of the animal in Fig. 5 consisted of a multinodular mass which extended downward along the bony ridge at the sides of the nose from the region of the naso-orbital angle and then across the bridge of the nose. They were quite large and yet very little of the lateral deformity could be seen until the hair was clipped, disclosing the marked increase in breadth or fullness of the midnasal region which is fairly well shown in the photograph.

In Fig. 6, there is a large, flat, and slightly oval lesion covering the upper half of the right nasal bone and extending well back over the nasomaxillary fossa. It measured more than 0.5 cm. at its center (determined after resection), and yet no deformity of the face was apparent until the hair was removed.

In like manner, the symmetrical deformity produced by many bilateral lesions was even less evident than that of unilateral affections,

[1] See Brown, Pearce, and Witherbee (1), Fig. 28.

especially in the naso-orbital angles or along the upper portions of the nasal splints, which are frequently involved. The appearance presented in the majority of these cases was merely that of a fullness between the eyes or of a slight prominence in the naso-orbital curve.

Facial abnormalities were more apparent with periosteal lesions arising from the outer surface of the bones than with other forms of bone involvement, unless the lesions extended to the outer surface, in which case they frequently assumed an appearance similar to the conditions described.

The extent of the process and the damage produced by infections of the facial bones bore no particular relation to the size of the external growth. These changes could be gauged by palpation, by sounding the lesion with a pointed instrument, or by radiographs. The information to be derived from the use of the latter method of investigation may be illustrated by a series of animals in which the appearance of the lesion, the radiograph, and the bone specimen are compared (Figs. 7 to 16).

The first animal in this series had a marked diffuse periostitis of the nasal bones which produced a typical Roman nose deformity (Fig. 7). By palpation, it was found that the entire lower portion of the bone gave beneath the finger, and a radiograph taken at this time (Fig. 8) showed complete destruction of the mid-area of the nasal bones together with some clouding and loss of architecture in adjacent parts of the bone. After about 2 weeks, the lesion began to subside and regeneration of the bone could be detected. At the end of 6 weeks, a second radiograph (Fig. 9) showed a marked but irregular thickening of the nasal bones and an absence of the usual architecture. There was also a bony mass extending below the level of the nasal bones. The actual condition existing is shown by Fig. 10 which is a photograph of the dried skull.

A second, more significant case is illustrated in Figs. 11 to 14. This was an instance of diffuse periostitis which produced very little facial deformity. A slight thickening could be made out over the bridge and lower portion of the nose and a defect could be detected along the sides of the nasal bones near the end of the nose. The radiograph of these lesions showed very plainly that there was some bone destruction as indicated by the ragged appearance and the thinning out of the under side of the shadow near the end of the nose (*cf.* Fig. 13 which shows the normal appearance). The fine lines of shadow produced by the turbinates were also blurred, and there were clouding and loss of architecture throughout most of the nasal bone. When these findings were compared with the autopsy specimen (Fig. 14), it was found that the destruction was somewhat greater than might have been imagined from the radiograph.

The late effects following repair in a similar case of diffuse periostitis are shown in Figs. 15 and 16. In this animal, there was a permanent enlargement of the end of the nose (Fig. 15) due in part to a fibrous thickening of the periosteum and in part to a thickening of the nasal bones as shown in Fig. 16. The condition had existed for upwards of 2 years.

Infections arising from the interior of the nose were characterized clinically by one or more of three conditions: the presence of a nasal discharge containing spirochetes, necrosis of the outer covering of bone, and finally, the development of external granulomatous lesions. Few of these infections have been recognized clinically and our knowledge of them is mostly that of autopsy findings. Involvement of both the nasals and the turbinates has been demonstrated in this way, but it will be seen at once that in the absence of any external lesion, there is no simple method of recognizing affections of this class or of differentiating them from affections of the mucous membranes. It is not improbable, therefore, that many internal lesions may escape detection and that many instances of nasal discharges containing spirochetes and of obstructive phenomena of the nasal passages are referable to bone infection rather than to primary infection of the mucous membranes. This supposition is supported by abundant pathological evidence.

The probability of the occurrence of lesions other than those described must not be overlooked. Several instances of peculiar thickening of the frontal and parietal bones of rabbits with generalized syphilis have been noted, and there was one animal with a marked mandibular affection. These lesions were all inactive, and there was nothing present which would enable one to determine their cause with certainty. However, a case of necrosis of an occipital condyle was observed, in which the infection was still active. The circumstances in this case will be given later (2).[2]

The points of especial interest in connection with syphilis of the facial bones are the frequency, the location, and the destructiveness of the lesions. It is also important to note the close analogy which exists between certain of the nasal and supraorbital affections of the experimental animal and those of man, especially in the congenital form of the disease.

[2] Brown, Pearce, and Witherbee (2), p. 531.

Forearms.

Bone affections of the anterior extremities of the rabbit were, with one exception, represented by a periostitis involving the distal ends of the ulna and radius. The majority were situated on the extensor surfaces at or near the epiphyseal line, with an occasional lesion at a slightly higher level.

This type was of comparatively common occurrence. As a rule, the lesions were rather small and with the fur intact produced little or no alteration in the appearance of the affected part but were easily detected by palpation. Normally, the extensor surface of the forearm is either perfectly smooth or is marked by small cross ridges and angular projections at the epiphyseal lines and the heads of the radius and ulna respectively. When lesions develop at these points, oval or rounded nodules are formed which are very readily felt on examination and can be seen after removal of the hair.

A typical case of bilateral involvement of both ulna and radius is shown in Fig. 17 (*cf.* Fig. 18 in which the left forearm is normal). Three of the four nodes present were distinctly rounded, while that on the right radius was more oval and covered a greater area of the bone.

A second type of affection which was frequently encountered is that seen in Fig. 18. In this instance, there was only one lesion, which formed a rather large oval mass on the right ulna just above the carpus.

In exceptional instances, the lesions of these bones were much more marked than those described and produced very striking deformities, as in Figs. 19 and 20. This, again, was a bilateral affection of both the ulna and the radius. As may be seen from Fig. 20, the lesion of the ulna was very sharply demarcated and raised abruptly from the surface of the bone, while that of the radius was more diffuse and resulted in extensive necrosis of the distal end of the bone.

A second case of an even more marked character is illustrated in Figs. 21 and 22. This was a large oval lesion which arose from the ulna but extended to the radius by way of the interosseous membrane. It was one of the few instances in which definite necrosis of the bones of the forearm could be made out clinically. As shown in the accompanying radiograph (Fig. 22), there was necrosis of the lower end of the ulna as well as the contiguous margins of both the ulna and the radius. The lesion was of very rapid growth, reaching the stage shown within 9 days after it first appeared. The tissues surrounding it were of a violet-red color, and there was a pronounced edema of both the skin and subcutaneous tissues.

In addition to the affections described, mention may be made of an enlargement of the carpus, which was followed by a permanent deformity occurring among the first animals of our series, but the methods then in use were not sufficiently developed to enable us to determine the nature of this condition. From the circumstances, it seems probable, however, that this might have been due to syphilitic infection. No other case of the kind has come under our observation.

The examples of periostitis of the ulna and radius which have been cited were cases in which there was not more than one lesion on each bone. Multiple lesions of one or both bones were occasionally seen, but they were usually small. In many instances, only one forearm was affected, but more often the involvement was bilateral and symmetrical.

It was a notable feature of this group of lesions that they rarely led to extensive necrosis. Grossly, the surface of the bone was eroded or roughened, and obliteration or widening of the epiphyseal line could be demonstrated by use of x-rays. Similarly, when the lesion healed, the bone might show a slight roughening or increase in thickness with a few tiny nodes (see lateral margin of the ulna in Fig. 22), but rarely was there any considerable deviation from the normal. Microscopic examination showed, however, that the syphilitic process frequently extended through the entire thickness of the bone and that the effect produced was in general much greater than gross appearances would indicate.

Other aspects of the subject of syphilis of the skeletal system will be presented in Part 3 of this paper (2).

BIBLIOGRAPHY.

1. Brown, W. H., Pearce, L., and Witherbee, W. D., *J. Exp. Med.*, 1921, xxxiii, 495.

2. Brown, W. H., Pearce, L., and Witherbee, W. D., *J. Exp. Med.*, 1921, xxxiii, 525.

EXPLANATION OF PLATES.

All illustrations are reproductions of photographs or radiographs which have not been retouched and represent objects at their natural size. Statements of time are estimated from the date of inoculation unless otherwise indicated.

FIGS. 1 to 6. Appearance presented by animals with syphilitic affections of the facial and cranial bones.

PLATE 61.

FIG. 1. 146 days. Nodular periostitis, bridge of the nose.

FIG. 2. 105 days. Marked diffuse periostitis of the lower two-thirds of the nasal bones.[1]

FIG. 3. 159 days. Marked nodular periostitis and perichondritis of the nasal bones and cartilages.

FIG. 4. 71 days. Marked periostitis of the supraorbital region.

PLATE 62.

FIG. 5. 110 days. Multinodular periostitis of the nasomaxillary fossa, the sides and bridge of the nose. The lesions were very pronounced.

FIG. 6. 92 days. Periostitis of the right nasal bone and splint. The lesion formed a broad flattened mass which covered the upper half of the bone and adjacent portions of the fossa.

FIGS. 7 to 16. A comparative study of clinical and pathological conditions in syphilitic affections of the nasal region.

PLATE 63.

FIGS. 7 to 10. Marked diffuse periostitis of the nasal bones and splints with necrosis and regeneration.

FIG. 7. 68 days. The deformity of the nose. The lesion was centered over the bridge of the nose and extended from just below the level of the eyes to the tip of the nose.

FIG. 8. 68 days. Radiograph showing complete necrosis of the bone at the center of the process. The turbinates are also involved.

FIG. 9. 6 weeks later. Regeneration of bone. The nasal bones are considerably thickened, irregular, and devoid of architecture. There is also an irregular osteoid mass beneath the nasal plates.

FIG. 10. 121 days. Lateral view of the skull showing the regenerated bones.[3]

[3] For frontal view see Brown, Pearce, and Witherbee (1), Fig. 29.

PLATE 64.

FIGS. 11, 12, and 14. Diffuse periostitis which produced very little alteration in the facial contour.

FIG. 11. 102 days. A slight prominence towards the end of the nose was the only visible abnormality. Palpation showed necrosis of the margins of the nasal bones.

FIG. 12. 116 days. Radiograph showing clouding of the nasal bones and erosion of the under side near the end of the nose. There are also a marked clouding and loss of finer shadow details throughout the nasal chambers and parts of the maxilla and premaxilla, indicating an extensive involvement of these parts.

FIG. 13. Normal radiograph for comparison.

FIG. 14. 123 days. Skull of the animal in Figs. 11 and 12.[4]

PLATE 65.

FIGS. 15 and 16. 2 years and 2½ months. Chronic fibrous periostitis with bulbous thickening of the end of the nose—a permanent condition. The enlargement of the nose was due in part to fibrous tissue and in part to thickening of the bone. In the radiograph (Fig. 16) note the change in shape and prolongation of the nasal bones, eburnation, and increase in osteoid tissue on the under side of the nasal bones and throughout the nasal region.[5]

FIGS. 17 to 22. Syphilitic affections of the radius and ulna.

FIG. 17. 61 days. A typical bilateral periostitis of the radius and ulna.

FIG. 18. 92 days. A typical case of unilateral periostitis of the ulna (right) with extension to the interosseous membrane and the adjacent margin of the radius. The left forearm is normal.

PLATE 66.

FIG. 19. 76 days. An unusually marked affection of both the ulna and radius. The condition was bilateral.

FIG. 20. 77 days. Autopsy specimen of the same lesions. That of the ulna is seen to be a sharply demarcated periosteal granuloma, while that of the radius is an osteitis of the head of the bone.

FIG. 21. 60 days. Marked periostitis and osteitis of the distal ends of the ulna and radius.

FIG. 22. 61 days. Radiograph of the same lesions. Note the irregularities and rarefication of the lower ends of the bone and the fusiform enlargement of the radius.

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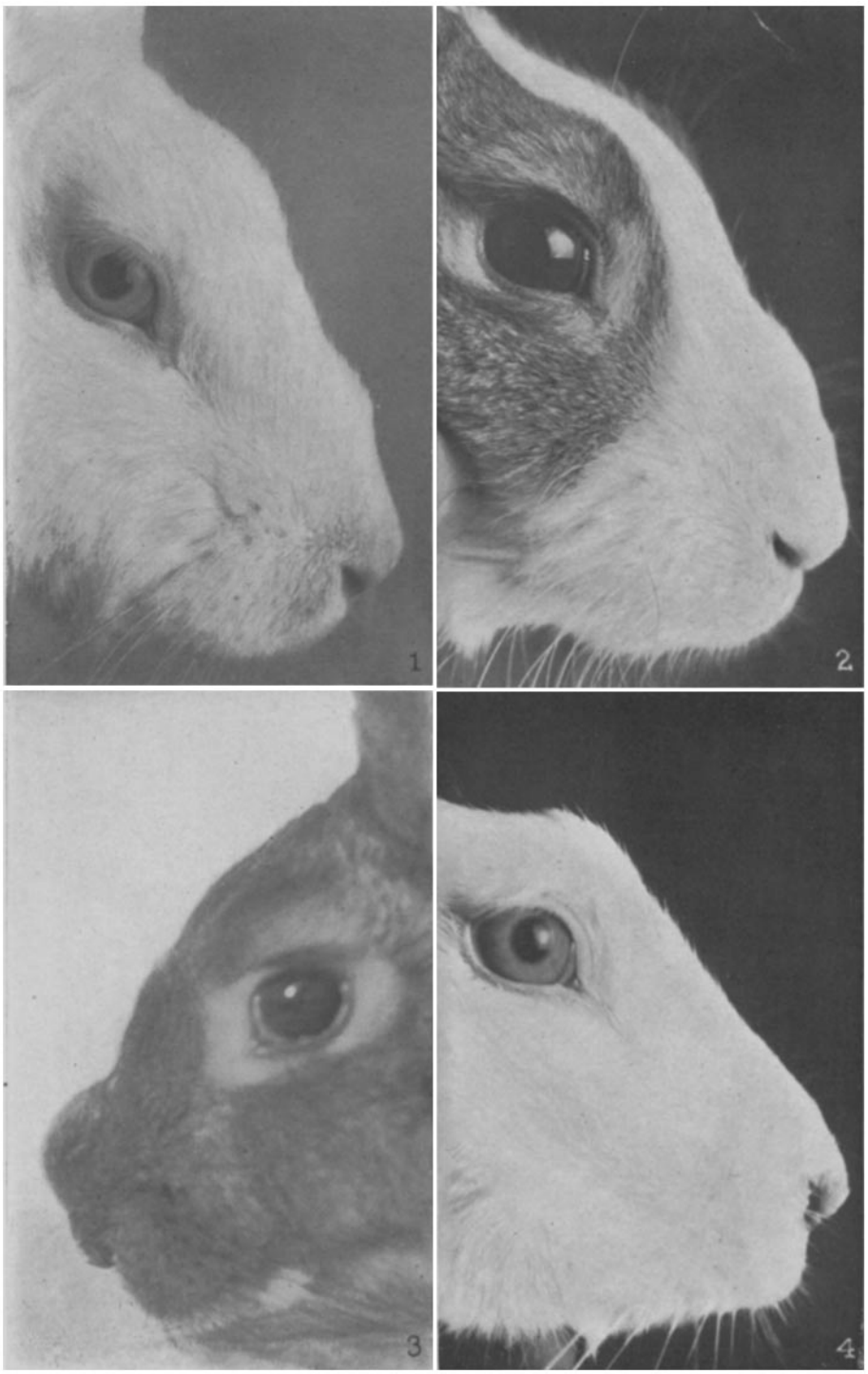
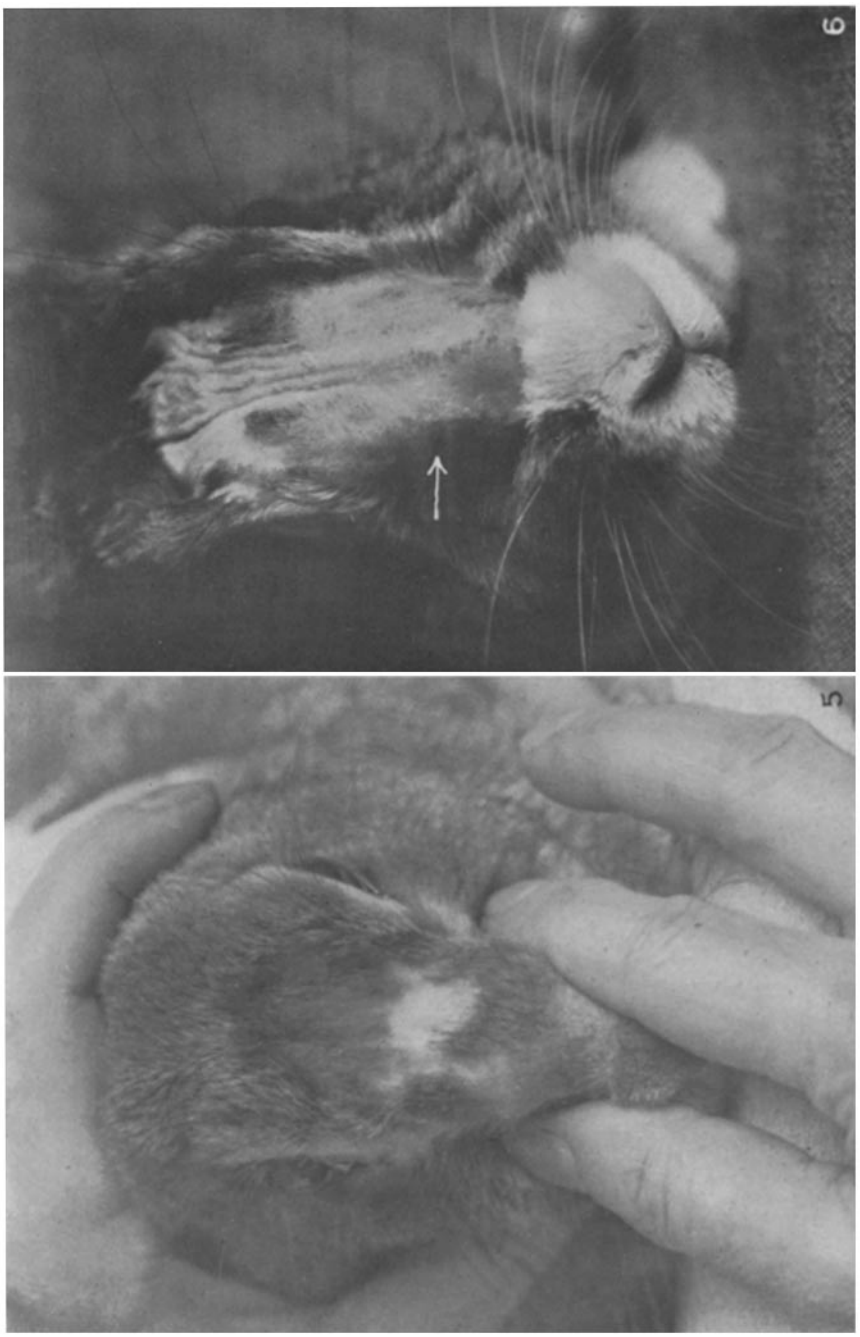
[4] For frontal view see Brown, Pearce, and Witherbee (1), Fig. 27.

[5] For skull see Brown, Pearce, and Witherbee (1), Figs. 6 and 7.



(Brown, Pearce, and Witherbee: Experimental syphilis in the rabbit. VI.)



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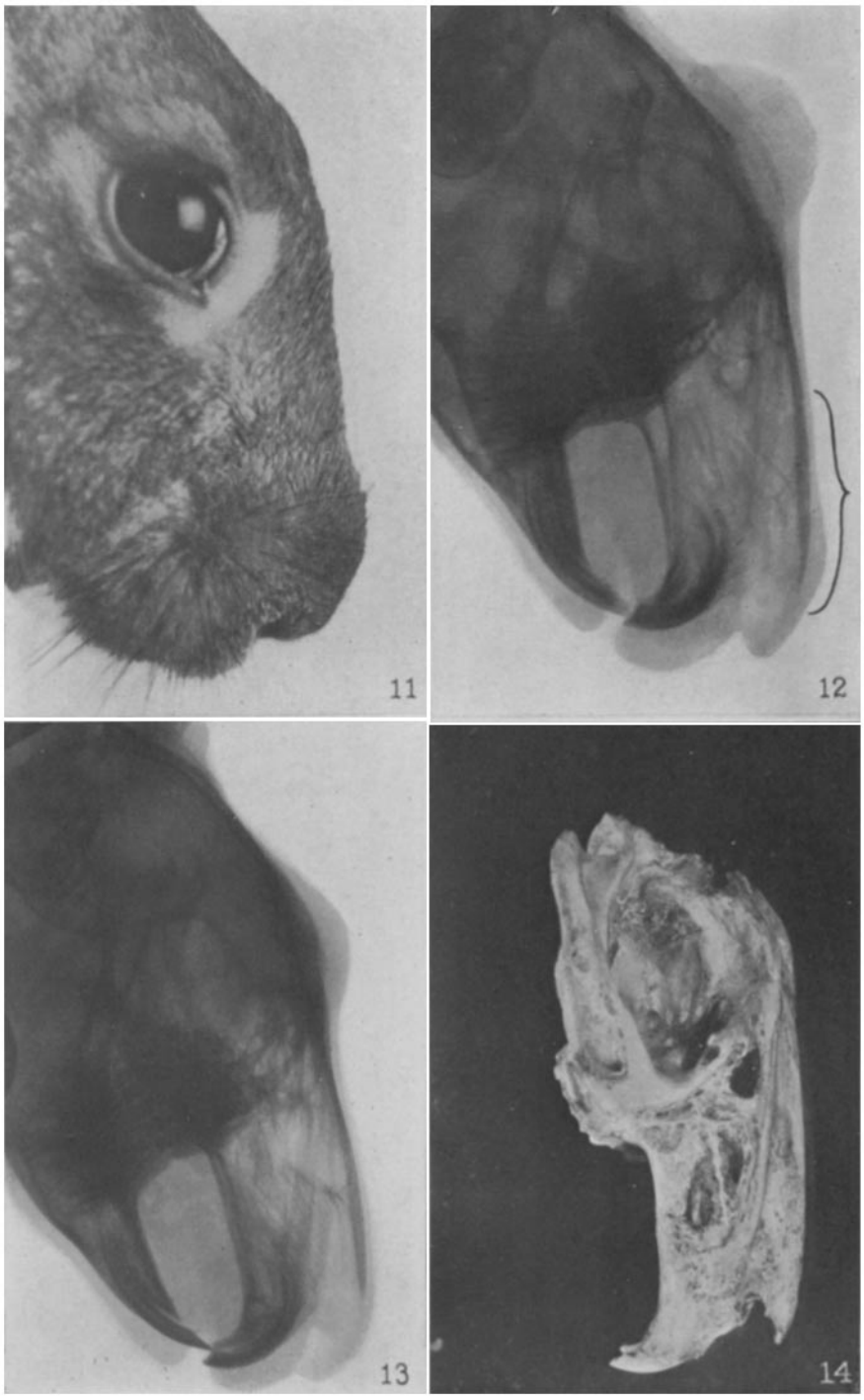

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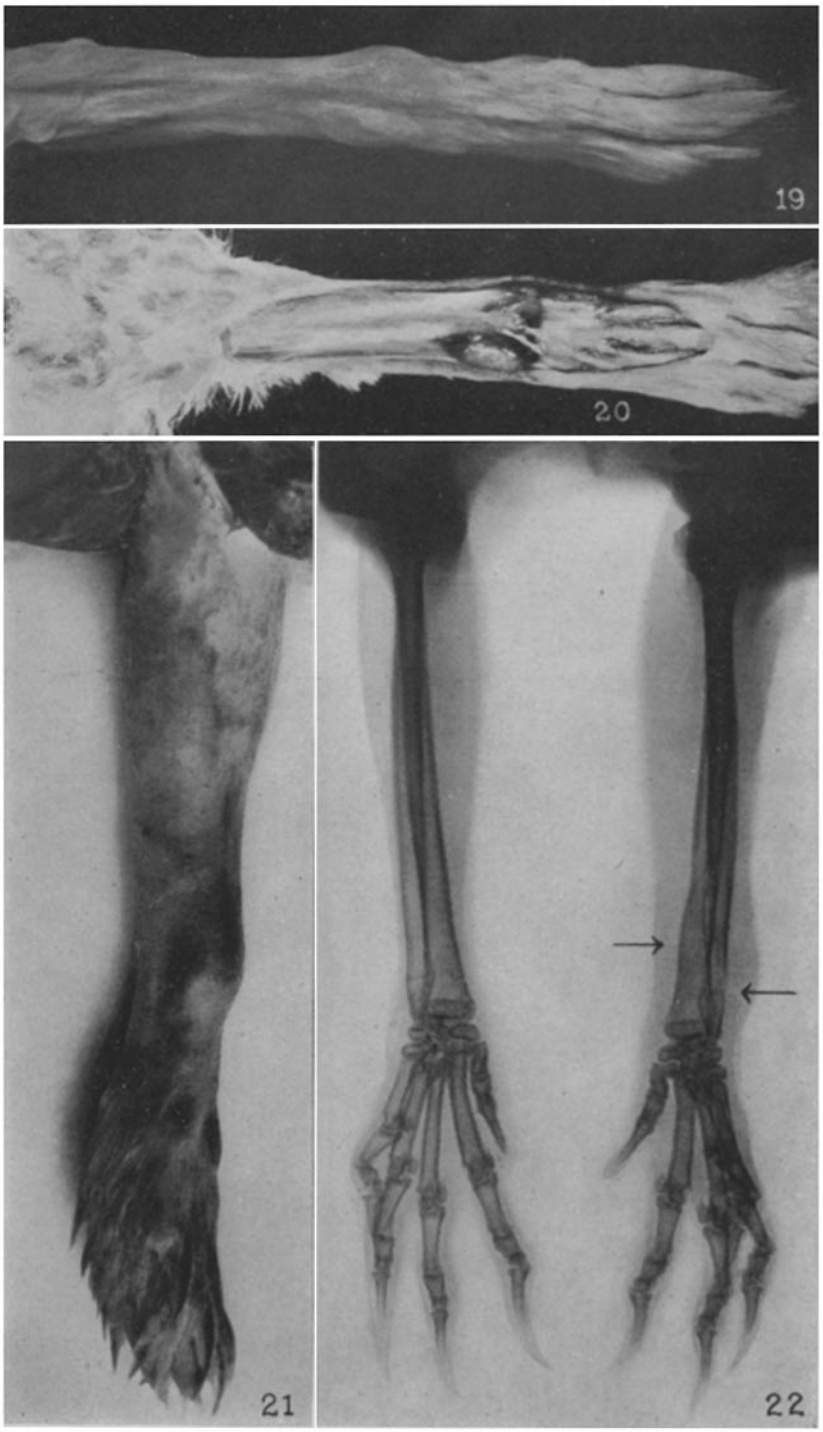

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