BONE INFARCTS

CASE REPORT WITH AUTOPSY FINDINGS *

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Infarction of soft parts and especially of certain internal organs is a generally recognized condition, but infarction of bones, whether in its early or late stages, is a condition that is little known to the general medical profession. One looks in vain for more than a bare mention of this subject in textbooks on general and special pathology such as those of Kaufmann, Aschoff, MacCallum, Karsner, and Boyd. Since the publication by Kahlstrom, Burton, and Phemister [1] of the pathological and roentgenological findings in a series of cases of old bone infarcts, which made it possible to establish the diagnosis roentgenologically, numerous reports of cases have appeared in the literature.

The roentgenological recognition of old infarcts is based on the fact that when they are located in the heads of the femora and humeri, use leads to collapse, followed by organization of the dead bone bordering on the joints and deforming arthritis; and when they are located in the shafts and deeper portions of epiphyses, they become partly replaced by new bone and partly calcified, and cast blotchy medullary and linear peripheral shadows that are denser than those of normal cancellous bone.

The reported lesions have been confined to the long bones and have been either single or multiple. They have occurred in workers in compressed air as a sequel of the picture of caisson disease and also in an equally large number of persons, both male and female, who have never worked in compressed air and in whom the cause is usually obscure. No report has been found of bone infarction produced by nitrogen liberation from too rapid ascent in an airplane. Additional cases occurring in caisson workers and presenting the typical x-ray findings have been reported by Coley and Moore,[2] Walker,[3] Rendich and Harrington,[4] Bell, Edson, and Hornick,[5] Taylor,[6] and others. Of the 54 cases in Taylor's report on infarction, 13 were due to caisson disease and the remainder had no occupational history. Bell, Edson, and Hornick studied 32 compressed air workers, of whom 14 gave a history of bends, 1 of otalgia, and 4 of arthritis. Twenty-four, or 75 per cent of the number, showed typical changes of old infarction in one or more bones on x-ray examination.

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There is still a dearth of cases that have been studied pathologically. Tissue excised at operation confirmed the diagnosis in the case reported by Walker.[3] One of us (S. C. K.) has autopsied 3 cases in a 6-year period in a very limited service, which speaks for the relative frequency of this entity. The other [7] has had an opportunity to examine an infarct of the tibia obtained at autopsy and to confirm the diagnosis in case no. 4 of our original report (Part I) with Burton,[1] by examination of tissue since removed in an operation on the hip.

There are good reasons for the comparative silence on this subject in the literature of pathology. In the first place, many bone infarcts are entirely asymptomatic, especially for many weeks or months after their development and are therefore no cause for concern to the patient, the clinician, or the pathologist. Their discovery during life, as in the case here presented, is often entirely accidental. However, if they involve the end of the bone and lead to either collapse of the articular portion or to chronic arthritis, the pain and limitation of motion in the joints frequently lead to the establishment of the diagnosis by roentgenological examination. The striking absence or paucity of reports of infarction observed in either the early or late stages is related to the relatively infrequent examinations of the bones of the extremities at autopsy and to the infrequency with which operation gives an opportunity to obtain tissue for microscopical examination. There is every indication that if the large long bones of the body were routinely studied roentgenologically before autopsy and were sectioned longitudinally, there would be an enormous increase in the frequency of recognition of recent and old skeletal infarcts. The careful visceral necropsy usually suffices to explain the clinical manifestations and cause of death and this too often lessens the incentive to undertake the laborious task of removing the bones for further study. Roentgenograms are not taken because of the time and expense involved. The embalmer and the relatives often object to detailed skeletal examination because of mutilation of the body.

The more careful study, with sectioning of bones, of extremities amputated for arteriosclerotic gangrene would doubtless reveal evidence of blockage of blood vessels in the bones, now frequently overlooked. The departments of anatomy of medical schools have access to bones which could be routinely sectioned for gross examination, at least, without great trouble or expense. The material aid offered by x-ray examination of bone specimens in a study of this type would stimulate great interest in the correlation of the status of bone pathology with visceral pathology.

Report of Case

While the clinical and roentgenological characteristics of the following case have been reported previously,[8] the subsequent verification of the bone lesions by autopsy forms the basis for this paper.

J. K., a Polish male, 55 years of age, was hospitalized at U. S. Veterans Administration, Bath, N. Y., for the sixth and final time in September, 1942, for recurrent hemorrhages from the gastrointestinal tract. The diagnoses previously established were cirrhosis of the liver with esophageal varices, secondary anemia, diabetes mellitus, arteriosclerosis, coronary and general cardiac enlargement, bilateral varicose veins, and multiple old bone infarcts.

The family history was irrelevant. The patient's only occupation had been that of chef. There was no history of exposure to compressed air. He had at times been addicted to excessive use of alcohol.

The bone lesions were discovered quite by accident, the left knee being radiographed following a minor injury in 1940. No fracture or dislocation was present, but large, irregular, mottled calcific deposits of increased density were present in the medullary portions of the distal third of the left femur and the proximal third of the left tibia. Following roentgenographic survey of the remaining skeleton, similar lesions were encountered in the distal third of the right femur and the middle third of the left humerus, the latter being but a small fleck of increased density.

The patient was rather stocky and well developed, but weak and quite anemic on this admission. The pulse was 92, respirations were 28, and the blood pressure was 94/70 mm. Hg. The physical examination further revealed a slightly enlarged liver, but was not otherwise remarkable. The stools were strongly positive for occult blood. The red blood cells numbered 2,700,000 with a hemoglobin of 45 per cent; the urine contained 1 per cent sugar while the blood sugar was 250 mg. per cent. As on many previous occasions, no source for the hemorrhage could be found in the x-ray examination of the gastrointestinal tract. Esophageal varices were looked for, but not found. The stomach was filled with a large blood clot.

The patient was given supportive treatment, including repeated blood transfusions, but continued to have hemorrhage and expired on October 21, 1942.

Autopsy disclosed a ruptured esophageal varix; cirrhosis of the liver; ascites; amyloidosis of the spleen, with perisplenitis; arteriosclerosis, coronary and generalized; cardiac enlargement (400 gm.); chronic interstitial nephritis; and an accessory kidney on the right side. The left tibia and each femur were removed. They were studied in the Laboratory of Surgical Pathology of the University of Chicago.

The external appearance of all three bones was not remarkable; the articular cartilages and synovia appeared normal. They were sectioned midcoronally. The proximal half of each femur was filled with red bone marrow, whereas the distal half contained fatty marrow except in the regions of the lesions. In the right femur, beginning 7 cm. above the lower end and extending upward for 2 cm., was a jagged, yellowish white, hard, amorphous area surrounded in most of its extent by a narrow, brownish, peripheral zone (Fig. 1). In the posterior half of the left femur, beginning 10 cm. above the lower end and extending

upward for 9 cm., the medullary content was dark gray with a mottled whitish streak of hard chalky material in the upper half (Fig. 2). Penetration with a needle revealed hard deposits in the posterior half at this level.

On section the left tibia contained yellow marrow throughout except in the upper third of the shaft. In the latter region a mottled lesion was encountered which filled the medullary canal irregularly for a distance of 10 cm. (Fig. 6). It was yellowish to gray in its mid-central portion. There were two dark brown patches, a large one superomesially and a small one inferolaterally, and a narrow dark brown zone lined the internal surface of the cortex along most of the involved segment. Roentgenograms were made of coronal sections cut approximately 0.5 cm. thick from the involved regions of the femurs (Figs. 3 and 4) and left tibia (Fig. 7). They bring out well the details of the dense mottle shadows of the lesions in the medullary canals. The slices were then decalcified and microscopical sections were made large enough to include the entire extent of the lesions. They were stained with hematoxylin and eosin. Figure 5 shows the unenlarged microscopical section of the left femur. In the upper half the marrow cavity is occupied by irregular islands of pale eosin-staining material surrounded by zones of blue-staining tissue of varying degrees of thickness. In the central portion of the lower half is a similar oblong lesion surrounded by normal appearing bone marrow. Under magnification it is seen that the pale central regions are necrotic and unorganized, while the hematoxylin-staining surrounding areas represent necrotic tissue that has been invaded by connective tissue which has become calcified in varying degrees and at the periphery has in turn been replaced by new bone or marrow.

Figure 9 shows a low magnification of the region indicated by "×" in Figure 5. Zone *a* is the outer cortex consisting of living bone which, from its normal arrangement, appears not to have been involved. Zone *b* is the inner cortex which is irregularly arranged and is composed principally of living bone and, to a small extent, of dead bone which is undergoing creeping substitution by new bone. In this region there appears to have been extensive necrosis which, for the most part, has been repaired. Calcium granules have been deposited in some of the haversian canals. At *c* is the zone of fibrous invasion of the necrotic endosteal and medullary region, with marked calcification along the inner margin. The old trabeculae are dead and surrounded by connective tissue. In the peripheral regions some of the calcified connective tissue is undergoing ossification and some of the dead trabeculae are being replaced by new bone. Zone *d* is the central necrotic

medullary region. It is, for the most part, filled with amorphous débris throughout which calcium granules are irregularly dispersed. Scattered, small, necrotic, bony trabeculae are present. Throughout the region there are vacuoles with calcium more densely concentrated at the periphery. Regions from the zones of Figure 9 are shown in detail in Figures 10 to 12. Figure 10 is from zone *b*. It shows dead bone, A, undergoing creeping replacement by new bone, B. Figure 11, from zone *c*, shows the dead trabeculae remaining, but the dead marrow is replaced by fibrous tissue, a part of which has become calcified. Figure 12, from zone *d*, shows calcium granules in the necrotic débris about vacuoles, and partly calcified connective tissue invading the periphery. In some regions the outlines of old fat cells are to be seen, with calcifying débris filling the space formerly occupied by the cytoplasm. Cholesterol slits are present in a few regions, suggesting the previous existence of hemorrhage.

The elongated island in the center of the medullary cavity in the lower part of Figure 5 was similar to the lesion above it, to which it was attached in a posterior plane as revealed by the roentgenograms. There is evidence that in places it was still being very slowly reduced in size and replaced by fatty marrow and fine bony trabeculae about the periphery. Blood vessels were relatively sparse throughout the entire section and no old obstructed vessels were seen.

Sections of the smaller lesion in the right femur showed changes identical with those of the left femur.

Figure 8 shows a microscopical section of the tibial lesion which measured 8 cm. in length and filled almost the entire medullary canal for a length of 6 cm. Its upper and lower limits are jagged and there is a small, similarly involved island 1 cm. above the mass on the mesial side of the bone. There is a bluish-staining calcified zone about its periphery which in some places borders on the cortex of the shaft and in others is separated from the shaft by a narrow zone of marrow. The contents within its calcified zone are dark brown about the periphery and gray to brown in the central region. Microscopical examination shows them to be composed of necrotic fat, partly calcified and with the outlines of many of the cells preserved, old blood pigment especially abundant about the periphery, cholesterol slits, coarse calcium granules, necrotic bony trabeculae, and invading connective tissue. Figure 13 is a low-power view extending through cortex, calcified zone, old blood pigment containing cholesterol slits, and necrotic and partly calcified marrow. Figure 14 is a higher power showing old pigment containing cholesterol slits, necrotic and partly calcified fat, and necrotic bone trabeculae. The blood vessels of the bone outside the

infarct are small and there are no signs of obliteration or of arteriosclerosis.

Discussion

The three lesions which have been described are the remains of old aseptic infarcts which have been somewhat reduced in size by connective tissue invasion, absorption, and replacement by new bone and marrow at the periphery. The reparative stimulus appears to have been long since almost completely exhausted and the unreplaced portions have undergone partial calcification and encasement by a calcified fibrous wall. There was no appreciable change in the x-ray appearance between the first examination and that at death 2 years later. The presence of much blood pigment and of cholesterol slits in the tibial lesion, especially peripherally, is evidence that it was a hemorrhagic infarct. Cholesterol slits in a few regions of the left femoral lesion are suggestive of old hemorrhage there.

The location of the infarcts suggests that they arose from blockage of the branch of the nutrient artery supplying the involved end of the respective bone. The large size of the lesions in the left femur and tibia suggests that the entire branch may have been blocked, although the anteroposterior and lateral roentgenograms reveal that the posterior portion of the bone was the more extensively involved in each case. The small size and eccentric location of the lesion of the right femur would indicate blockage of only a portion of the inferior nutrient branch. The evidences of necrosis and creeping substitution of internal cortical bone in the left femur speak for nutrient artery blockage since it supplies the internal portion of the cortex.

The exact cause of this multiple infarction cannot be stated. There was no history of work under compressed air. The structure indicates that the lesions are all of the same vintage and that they are many years old. Because of the arteriosclerosis, both generalized and coronary, one must think of vascular blockage from intimal thickening, embolism or thrombosis. The absence of infarcts in the spleen and kidneys militates to some extent against that explanation. There was no evidence of old valvular lesions. The cirrhosis of the liver should be considered since Axhausen [9] reported fresh infarcts in a patient dying with portal cirrhosis. The absence of recent infarcts speaks against cirrhosis as a causative factor.

Summary and Conclusions

Autopsy studies are reported of another case of ancient infarction in multiple bones of the extremities which was diagnosed roentgenologically before death by the presence of blotchy medullary shadows

of increased density produced by calcification of the unresolved portions of the infarcts.

The exact cause of the infarction was undetermined although it may have been related to the accompanying generalized and coronary arteriosclerosis.

A review of the recent literature indicates that old calcified bone infarcts, both multiple and single, are being diagnosed frequently by the blotchy shadows and evidences of collapse and deformity of articular surfaces shown in roentgenograms.

Failure to examine the long bones routinely at autopsy is responsible for nonrecognition of a great many infarcts.

Routine roentgenography of the bones of the extremities preceding autopsy would assist greatly in the recognition of old infarcts.

A diligent routine search for bone infarcts at post-mortem examination would lead to the discovery of lesions in the early stages and help to arrive at the cause in those cases which remain unexplained.

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[*Illustrations follow*]

DESCRIPTION OF PLATES

PLATE 176

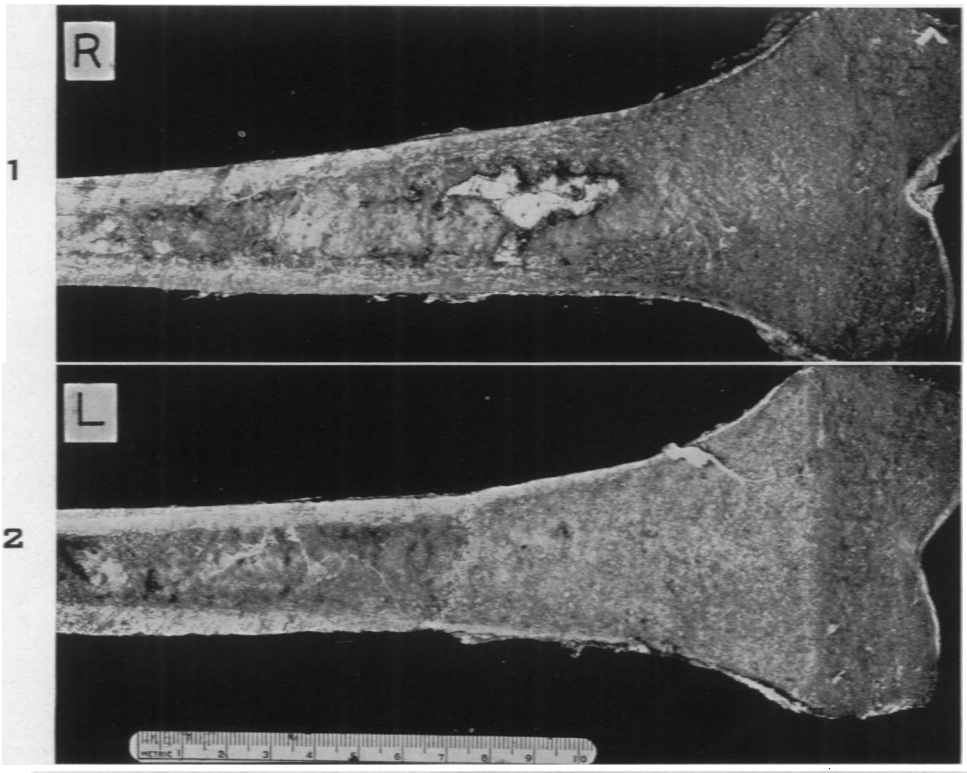
FIG. 1. Yellowish white, calcified infarct in right femur.

FIG. 2 Grayish white, calcified areas in left femur.

FIG. 3. X-ray shadow of calcified infarct in right femur.

FIG. 4. X-ray shadow of calcified infarct of left femur.

FIG. 5. Microscopical section of calcified medullary infarcts of left femur.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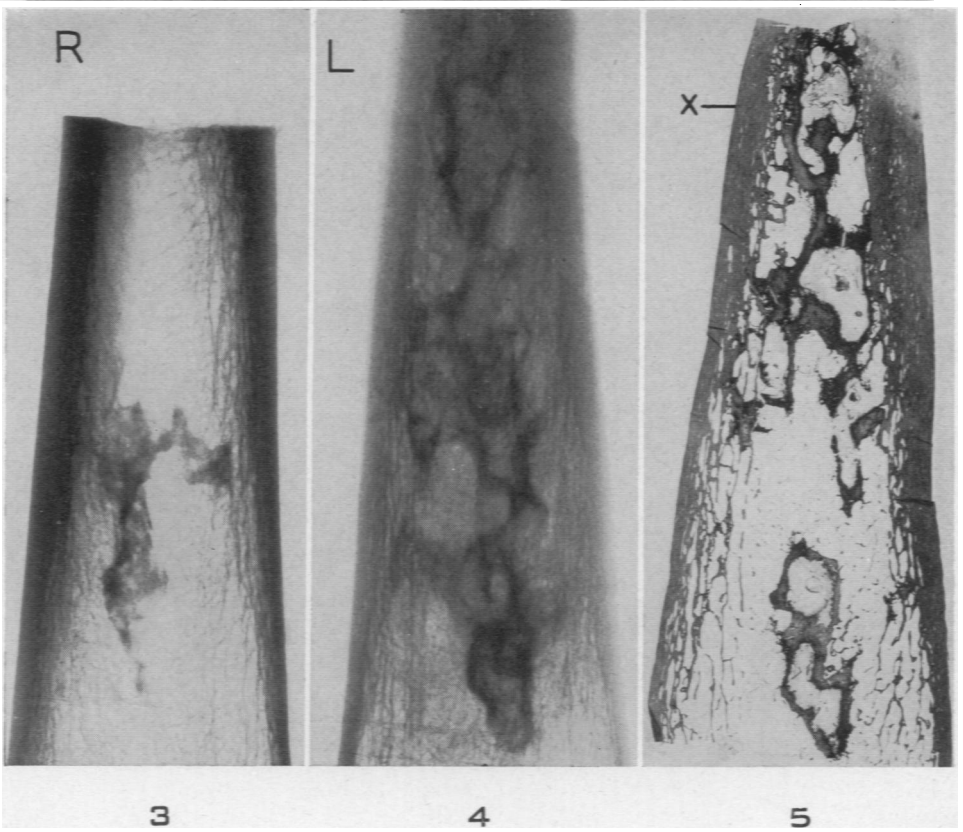
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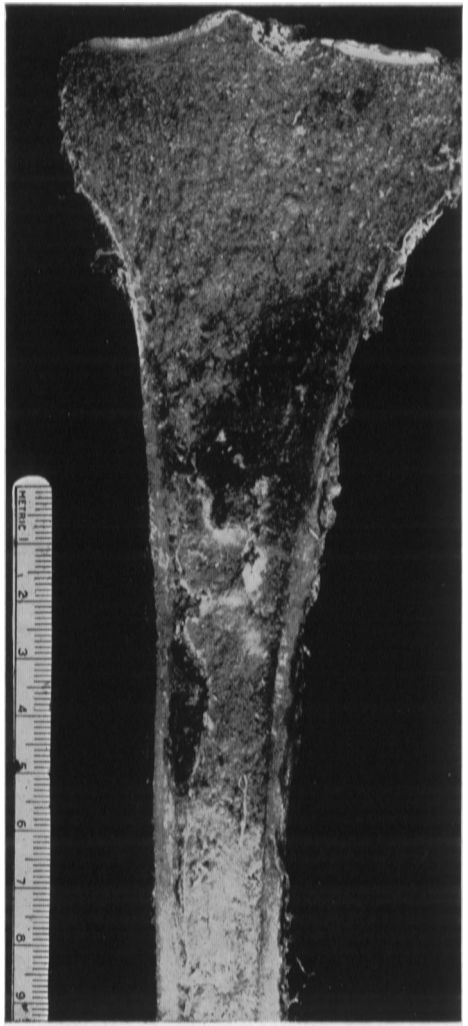
PLATE 177

FIG. 6. Old hemorrhagic and calcified infarct of tibia.

FIG. 7. Roentgenogram of specimen illustrated in Figure 6, showing mottled increase in density of involved medullary region.

FIG. 8. Microscopical section of tibial lesion.



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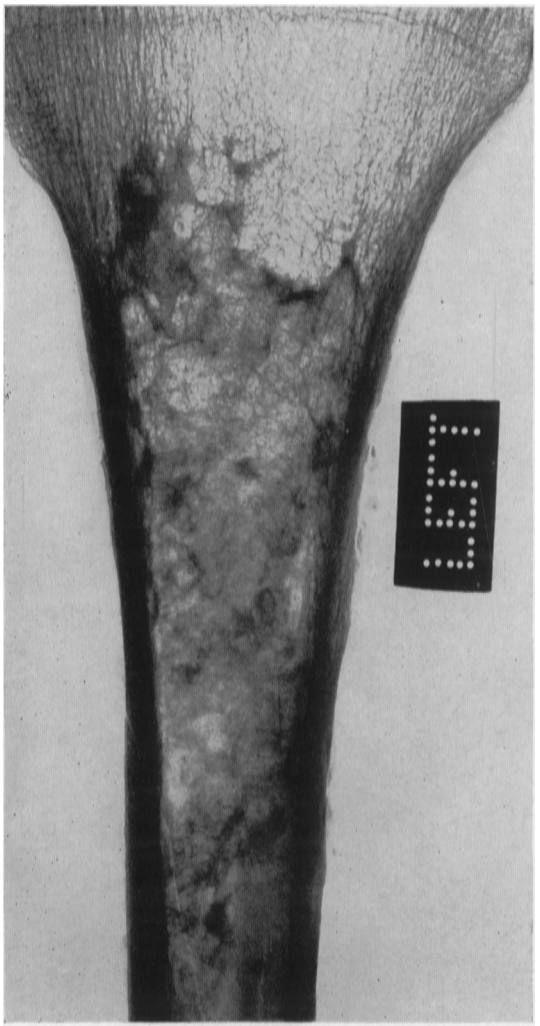

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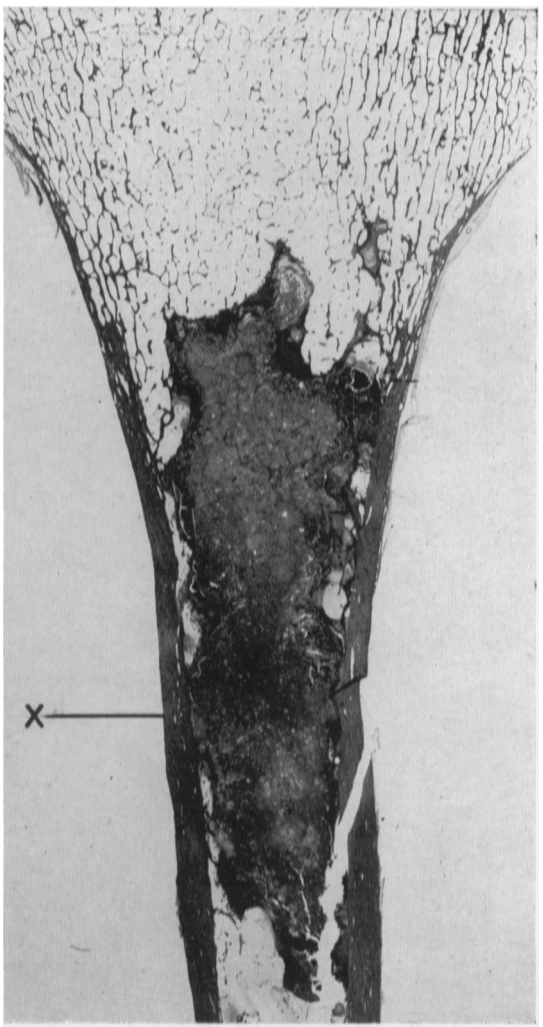

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PLATE 178

FIG. 9. The are marked "×" in Figure 5 at 8½ ×:

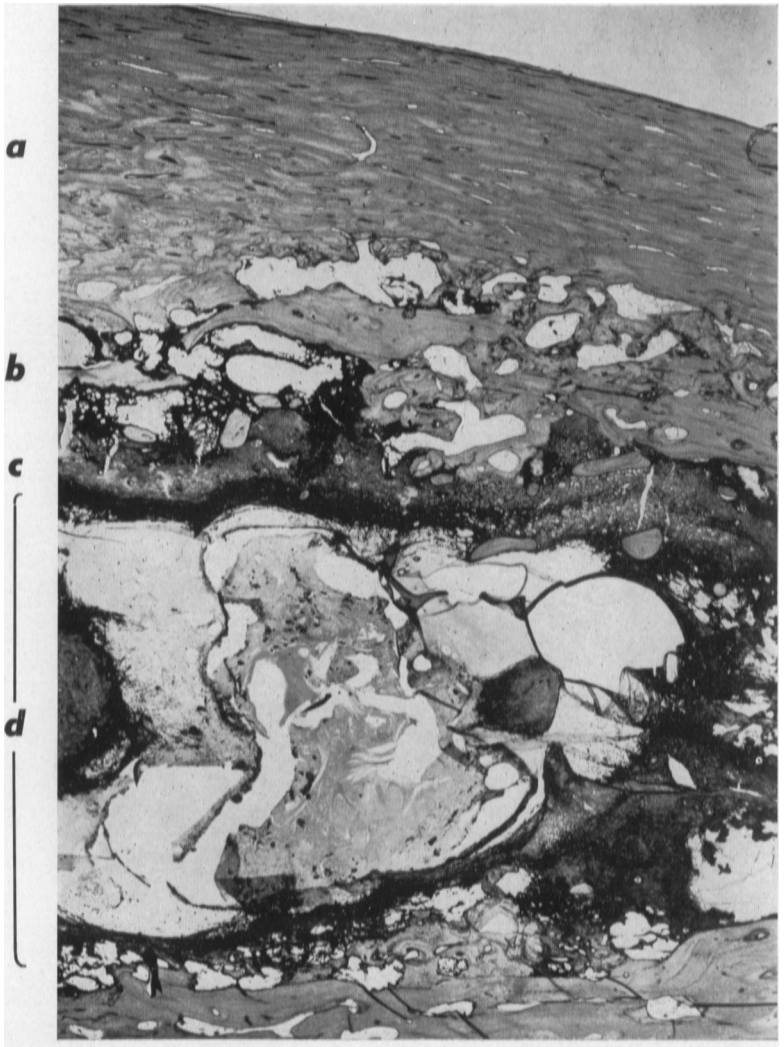
a. Unaltered superficial cortex.

b. Deep cortex, necrotic, and partially replaced by new bone.

c. Fibrous invasion and calcification of necrotic medullary region.

d. Liquefaction and calcification of medullary region.

FIG. 10. Zone *b*, Figure 9, at 190 ×, showing dead bone, A; being replaced by living bone, B.



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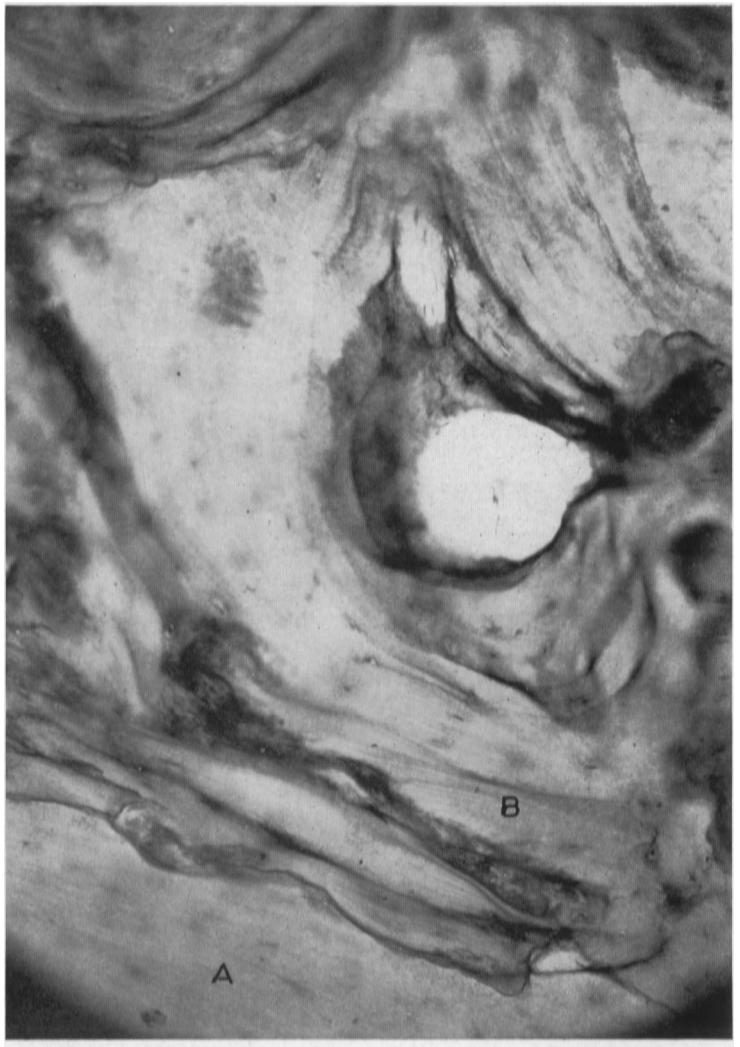

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PLATE 179

FIG. 11. Zone *c*, Figure 9, at 70 ×, showing fibrous replacement and calcification.

FIG. 12. Zone *d*, Figure 9, at 45 ×, showing necrosis, liquefaction, calcification, and connective tissue invasion.

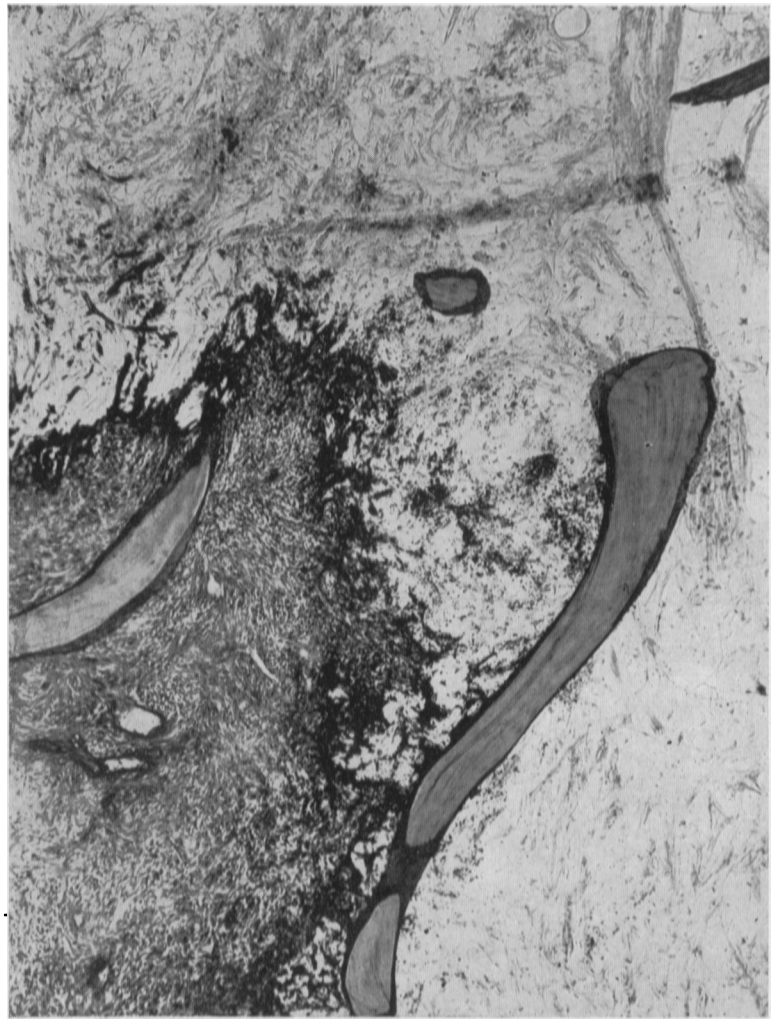

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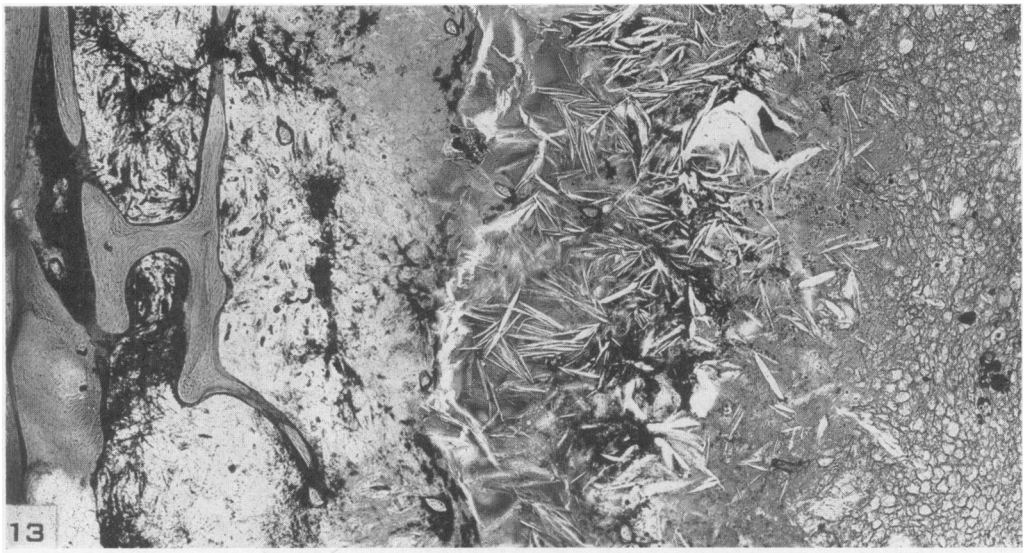
PLATE 180

FIG. 13. Level "×" of Figure 8, at 18 ×, passing through cortex, *a*; calcified zone, *b*; old blood pigment and cholesterol slits, *c*; and necrotic and partly calcified marrow, *d*.

FIG. 14. The central region of Figure 8, at 50 ×, showing necrotic fat with regional calcification, *a*; and old hemorrhage and cholesterol slits, *b*.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b
c
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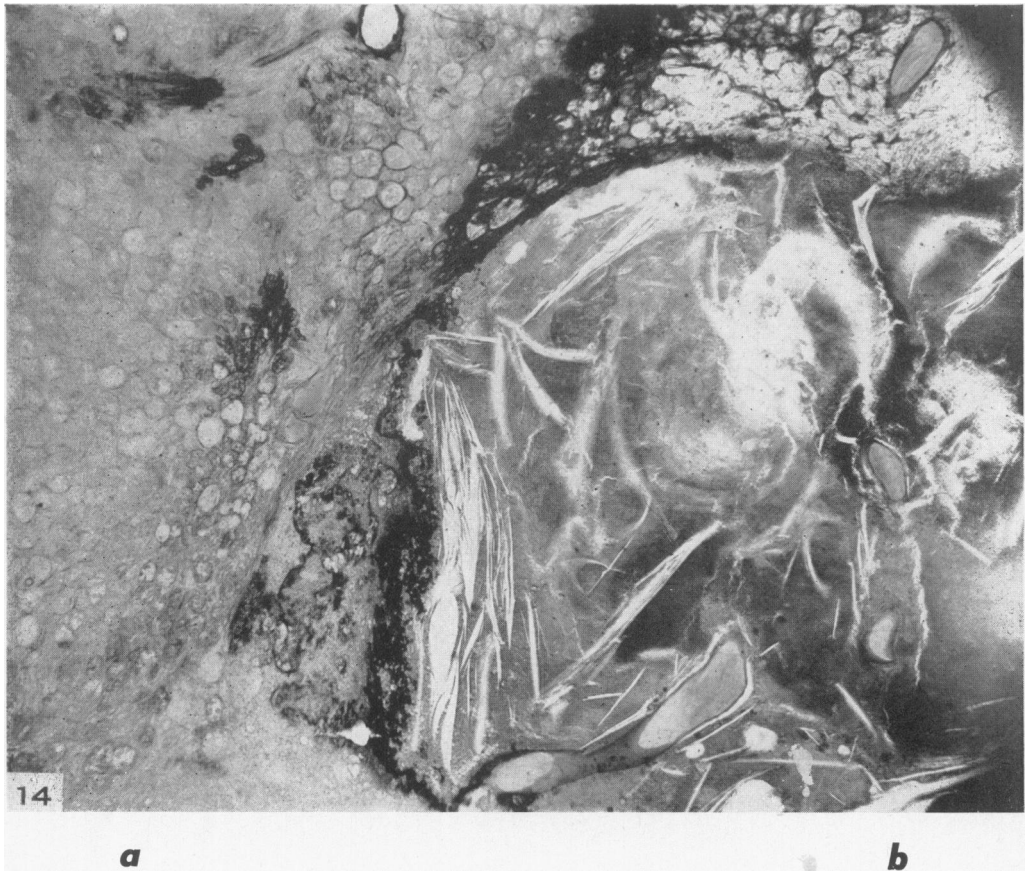
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