The Journal of
Pathology and Bacteriology

Vol. LXIX, No. 1

FOCAL PAGET'S DISEASE OF THE SKULL (OSTEOPOROSIS CIRCUMSCRIPTA)

D. H. COLLINS * and J. M. WINN

From the Departments of Pathology and Radiodiagnosis, University of Leeds

(PLATES I-V)

THERE is a form of bone disease affecting the flat bones of the adult skull which causes softening and rarefaction of a large well-defined area of the cranium. The diseased bone, which usually covers a fan-shaped field spreading from either the frontal or the occipital pole, is sharply demarcated from the adjacent normal bone. The affected part is so translucent to X-rays that it often appears to be an absolute defect of the cranium (fig. 1), unless radiographed tangentially (fig. 2), when the finely stencilled outline of the inner and outer tables shows that this is some form of extreme osteoporosis without gross deformity. The Viennese radiologist, Schüller (1926) in an English paper first gave the name " circumscribed osteoporosis " to this condition. Since then, it has been widely recognised by radiologists, and the radiographic files of most large hospitals are likely to contain examples.

The pathological features of the lesion are much less well known, and no series of pathologically studied cases has yet been published. The opinion is generally held, we believe rightly, that this affection is a manifestation of Paget's osteitis deformans ; but this conclusion is not self-evident, for many of the well-recognised characters of Paget's disease are lacking. There is, for example, no deformity of the part, no appreciable thickening of the cranial bones, no total enlargement of the skull (which has been regarded as a classical feature of this disease since Paget's original description in 1877) and usually there are no foci of bony sclerosis to give rise to the characteristic cotton-wool mottling in the X-ray picture. Much of the evidence that osteoporosis circumscripta is a form of Paget's disease is derived from radiological studies. Although in many instances osteoporosis

* Present address: Department of Pathology, The University, Sheffield, 10.

circumscripta of the skull seems to be an isolated lesion in an otherwise normal skeleton, a number of cases have been recorded where the skull lesion has been seen in patients who, either at the time or subsequently, have manifested indubitable lesions of Paget's disease elsewhere (Kasabach and Gutman, 1937; Windholz, 1945; Hunter and Jupe, 1950, p. 445; Irvine, 1953). In a few cases, radiological follow-up has shown a gradual transition over the course of years from the purely porotic circumscribed lesion of the skull to the more usual mottled and blotchy X-ray picture of the skull in Paget's disease (Kasabach and Dyke, 1932).

Pathological studies have done less to identify osteoporosis circumscripta with Paget's disease. The first histological report (Sosman, 1927) was made by Wolbach on trephine biopsy material obtained by Harvey Cushing from a man aged 51. It reads "Simultaneous proliferation and degeneration of bone, with complete absence of haversian system, similar to Paget's disease". The X-ray reproduced (Sosman, fig. 3) seems to show a more mottled and less purely translucent focus of bone disease. Schüller (1929) quotes Sosman's case but states that osteoporosis circumscripta could be a mild form of either Paget's disease or an osteomalacia-like bone disease. Some doubt must exist whether Schmorl (1930, 1932) recognised osteoporosis circumscripta as a form of Paget's disease and whether it was this lesion that he described as hæmorrhagic infarction of the skull. Schmorl (1930) speaks of peculiar skull changes with expanded diploë, very dark red coloured patches, the sharp edge contrasting with the surrounding bone, the edges not keeping to the sutures; but histologically he found deeply situated masses of dead bone without nuclei although the surrounding marrow showed living cells. This seems to be a picture of avascular necrosis such as is not uncommonly seen in Paget's disease in many parts of the skeleton. Schellenberg (1931) found only a non-specific picture of osteitis fibrosa in the area of osteoporosis circumscripta of the frontal bone of a man aged 40. He thought that, though the lesion could be an early stage of Paget's disease, it was impossible so to classify it since, whatever it was, the pathological process was an early one which had not yet attained its definitive character. Erdheim (1935-36) examined the skull of a 79-year-old woman and concluded that the term osteoporosis circumscripta did indeed imply an early stage of Paget's disease. Kasabach and Gutman (1937) quote Schüller's observations on two post-mortem cases where the reddish areas of skull bone were so soft that they could be cut with a knife. Goldenberg (1951) classes osteoporosis circumscripta as one of the forms that Paget's disease takes in the skull, but Irvine (1953) raises the question whether some of the instances of circumscribed osteoporosis in persons younger than the usual age for Paget's disease might not be instances of fibrous dysplasia, especially since some such patients have associated tumour-like lesions of mandible or maxilla.

OSTEOPOROSIS CIRCUMSCRIPTA OF THE SKULL

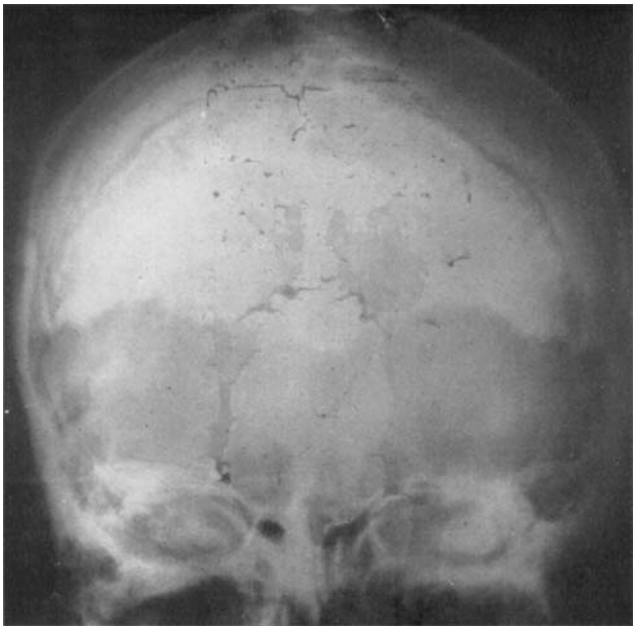


FIG. 1.—Typical radiograph of osteoporosis circumscripta, antero-posterior view (reduced), revealing a sharply outlined defect of the frontal bone. Male, aged 43, who came to hospital because of pain in the shin. The characteristic radiographic changes of Paget's disease were seen in one tibia and in the pelvis. This case was not studied *post mortem*.

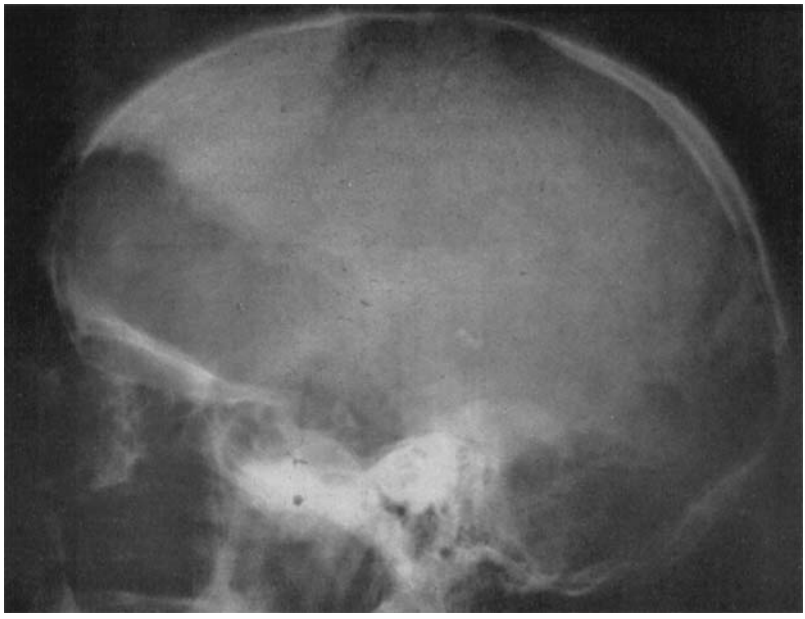


FIG. 2.—Lateral radiograph (reduced) of the same skull as in fig. 1, showing in the tangential view the finely stencilled outlines of the inner and outer tables.

The purpose of this paper is to describe the pathological features of five cases of circumscribed osteoporosis of the skull studied *post mortem*.

Personal observations

Five cases of circumscribed porotic disease of the skull came to light at necropsy in the course of about 22 months at the Leeds General Infirmary, during which time every calvarium removed in the post-mortem room which was abnormally thick or thin, soft or blue, was reserved for our personal inspection. Cases 1 and 5 were separated by a total of 1632 necropsies, of which 1369 were on persons of 40 or more years of age. The likelihood of finding the lesion in the post-mortem room is therefore something of the order of once in every 350 or 400 necropsies.

The ages of the five patients, four men and one woman, were 43, 57, 61, 78 and 80 years. In one man, Paget's disease of the usual pattern was identified in the bones of the pelvis. In the other four cases no focus of Paget's disease was found elsewhere in the skeleton. Two of the five patients, as it happened, had had radiographs of the skull during life.

Radiography of the skull vault after death included macro-radiography. This technique gave clear enlarged pictures showing changes in texture but yielded no information of special value.

Ordinary histological methods were used after formic-citric-acid decalcification, and blocks were selected from many parts of each skull. Sections were also made from one or more lumbar vertebræ and sometimes from the bones of the pelvis.

Case 1

S. B., man, aged 78. Uræmia, acute retention of urine, prostatic enlargement. At necropsy, the only abnormalities of the skeleton seen were in the skull and lumbar vertebræ.

Skull. There was an area of purple-red bone, 10-12 cm. in diameter, centred on the occipital pole but spreading on to the posterior part of each parietal bone. The abnormal bone was sharply demarcated from the normal by a serpentine frontier where the colour changed abruptly from purple to the normal ivory of the unaffected parts of the skull (fig. 3). The occipital bone, though slightly thicker than the rest of the cranium, was nowhere greater than 11 mm. in thickness. A horizontal arc of the lateral part of the occipital and parietal bones, when macerated (fig. 4), showed abnormal porosity of a relatively wide-mesh pattern and attenuation of the tables, especially the inner, but a less abrupt change from bone of normal to bone of abnormal texture than appeared from the colour change on the surface. There were a few discrete areas of more compact or sclerotic bone, and, histologically, these reveal a characteristic picture of Paget's disease with a prominent mosaic of cement lines intervening between blocks

of lamellar bone disorientated one from another (fig. 5). Elsewhere, the enlarged marrow spaces contain many wide vascular channels and there is an endosteal lining of fibrous tissue. General fibrosis of the marrow is no longer visible. Between the blood channels are sparse islets of hæmopoietic tissue and some adipose tissue. Osteoblasts and osteoclasts are seen here and there, but the general picture is to be interpreted as a quiescent phase of Paget's disease in which porosis is more advanced than sclerosis.

Lumbar vertebral bodies were soft and spongy, with widely dispersed delicate trabeculæ. Histological examination confirms the presence of simple osteoporosis of senile type and shows no evidence of Paget's disease.

Case 2

J. H., man, aged 43. Choroidal papilloma of 4th ventricle. Death shortly after air encephalogram. The ante-mortem X-ray examination showed circumscribed osteoporosis of the frontal bone (fig. 6).

Skull. Necropsy revealed a corresponding lesion of the frontal bone when the calvarium was lifted and the dura mater stripped (fig. 7). The affected bone was soft enough to be sliced with a knife. It was highly vascular, of cyanotic hue and sharply demarcated from the normal bone by a frontier of scalloped outline. The purple discolouration was most obvious when the skull was viewed from the inside, but was also seen from the outside after peeling the aponeurosis from the vault. The blue colour showed through the bone in the walls of the frontal air cells and was evident throughout the orbital plates and anterior fossa, including part of the lesser wing of each sphenoid bone and the anterior clinoid processes. The floor of the sella turcica and middle fossa and all the posterior parts of the skull were normal. There was no gross deformity of skull, face or jaws.

Lumbo-sacral vertebræ, iliac bones and right tibia. These were opened with the saw. No disease was seen and there was no evidence of Paget's or other bone disease elsewhere in the skeleton. Histologically, various parts of the diseased skull bones show a wide-mesh cancellum of irregularly constructed trabeculæ, a generally fibrous and richly vascular marrow, and patchy endosteal activity, sometimes osteoblastic sometimes osteoclastic. No wide osteoid margins are seen, there are no sclerotic foci and no areas of predominant osteogenesis. These features, together with occasional trabeculæ that show a clear mosaic structure, indicate Paget's disease in a predominantly resorptive phase.

Case 3

H. B., man, aged 80. Bronchopneumonia; thrombosis of right common carotid artery. At necropsy there was no obvious deformity of the skull or of any other part of the skeleton of this much wasted old man.

Skull. This was very easily sawn through, except in the frontal region, where the bone was of normal texture. On lifting the calvarium,

OSTEOPOROSIS CIRCUMSCRIPTA OF THE SKULL

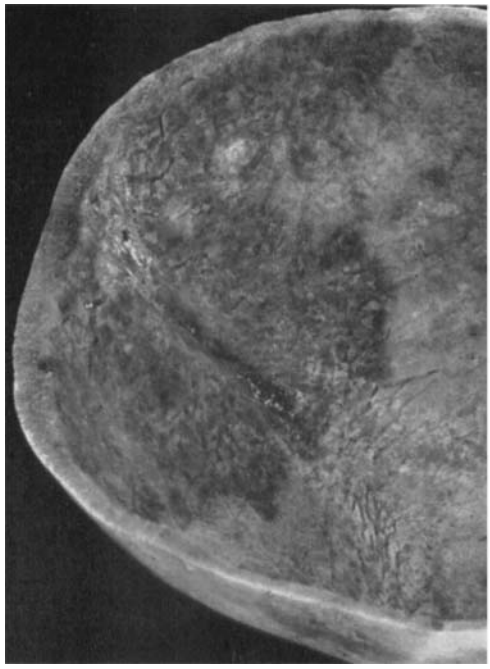


FIG. 3.

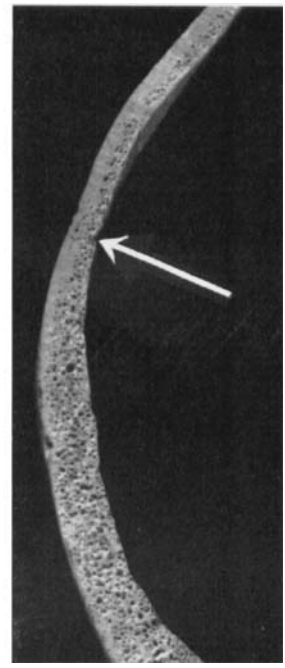


FIG. 4.

FIG. 3.—Case 1. Male, aged 78. Posterior part of vault of skull viewed from within, showing the sharp but irregular frontier of the discoloured abnormal bone, which is little if any thicker than the normal occipital squama at this level. Slightly reduced.

FIG. 4.—Case 1. Horizontal arc of the lateral part of occipital and parietal bone (macerated). The arrow marks the point at which the colour change appeared in the fresh specimen, but the transition between normal and abnormal bone is less sharp in this preparation. Note the increased porosity and slight thickening of the diseased occipital bone and the attenuation of the inner table of the skull. Natural size.

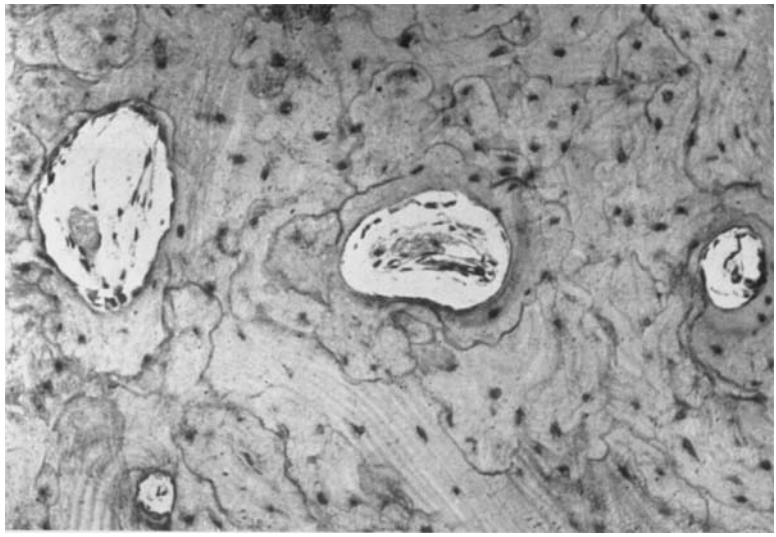


FIG. 5.—Case 1. A small focus of sclerosis in the occipital bone, showing the mosaic of cement lines and disorientated lamellar systems characteristic of Paget's disease. Hæmatoxylin and eosin. ×160.

the dura mater peeled away cleanly to reveal extensive reddish-purple discolouration in the bone of the posterior four-fifths of the skull vault (fig. 8). The same colour contrast was seen on the convexity of the vault only after careful removal of the epicranial aponeurosis and the pericranium with the aid of a periosteal elevator (fig. 9). When the brain was removed and the dura mater stripped from the bones, it was seen that about four-fifths of the bones forming the base of the cranium were similarly affected and discoloured. The only unaffected parts were the orbital plates in the anterior fossa, the frontal eminences and about two-thirds of the squama of the frontal bone below the coronal suture. Diseased and normal bone were joined in the vault along a sharply defined serrated line 1·4 cm. anterior to the coronal suture, and in the base by a similar but rather less distinct frontier line traversing the lesser wings of the sphenoid near the ridge. The skull was neither enlarged nor deformed and was increased in thickness to a barely perceptible extent (11 mm.) only at the occipital pole.

Other bones seen with the naked-eye to be the seat of Paget's disease were the right pelvis and right and left ilium. There was no deformity of the long bones, and the ribs, sternum, clavicles and vertebral bodies appeared normal.

Histologically most parts of the skull show a wide-mesh porosis with little active production of new bone (fig. 10). The marrow spaces lying between coarse trabeculæ are filled with loose fibrous tissue that encloses many blood-vascular spaces. Both tables of the skull are greatly reduced in thickness, the inner to merely a thin plate of continuous bone. Most of the trabeculæ show a mosaic pattern. Some osteoblasts and osteoclasts appear along the endosteal borders but there is little general activity of bone cells. A few marrow spaces contain hæmopoietic and adipose tissue cells. Other parts of the skull, especially towards the occiput, show equally great porosis but also some discrete foci of woven-bone production along the inner face of the bone (fig. 11).

Sections of the junction between normal and abnormal bone reveal a frontier zone of osteoclastic activity, more advanced on the inner table than the outer (fig. 12). Original compact bone in process of destruction gives place abruptly to cellular and vascular fibrous tissue and is faced by many osteoclastic giant cells but no osteoblasts. A narrow zone of bone-free tissue lies between the excavated face of the old bone and the new feebly osteogenic tissue, but there is continuity of the thin plate of inner-table bone and the old dense table, and it is not certain whether old bone is totally or only mostly destroyed. An oblique or dove-tailed junction between a focus of Paget's disease and normal bone is usual. In this skull the greater advance of resorption of the inner than of the outer table gives rise to a striking double outline to the lesion in the X-ray picture (fig. 13). What is unusual is the paucity of new bone formation in the area of Paget's

disease. Only a few widely spaced trabeculæ appear within the vascular fibrocellular tissue and the total effect is one of atrophy rather than hypertrophy of the bone.

Sections of the pubic bone, on the other hand, show thick bony trabeculæ, which are so closely set as almost to form compact bone, and a prominent mosaic of cement lines. There is little fibrosis of this marrow and little activity of the endosteal cells.

Case 4

J. L., man, aged 61. Coronary thrombosis.

Skull. The posterior half of the skull, including the posterior fossa, was purple, very slightly thickened but not otherwise deformed. It was soft to saw and highly translucent to X-rays. A sharply defined line of junction between normal and diseased bone ran across the vault a little distance behind the coronal suture.

Histologically the affected skull bone is composed of an open mesh-work of rather broad trabeculæ, all of it showing a prominent mosaic pattern. The wide marrow spaces contain sparse fibrous tissue and many large blood-filled vascular channels. There is little activity of endosteal cells, but some short rows of osteoblasts and an occasional osteoclast are seen.

Lumbar vertebræ and *crest of right ilium.* Both show simple osteoporosis of senile type with no fibrosis of the marrow, no bone-cell activity and no cement-line mosaic in the attenuated trabeculæ.

Case 5

D. P., woman, aged 57. Diffuse cerebral glioma.

Skull. At necropsy this was soft and of a deep purple-red colour throughout its posterior part. The sharply outlined limits of the lesion approximated to the coronal suture anteriorly and to the line of the lateral cranial sinus posteriorly and below. The maximum thickness in the occipital bone was less than 1 cm. Large pieces of this skull were used for the estimation of the specific gravity and calcium content with the following results :—

	Normal bone (frontal)	Diseased bone (occipital)
Specific gravity	1·82	1·49
Calcium content after oven drying and extraction of fat	27·4 per cent.	23·3 per cent.

These results indicate that, though the bone mass is greatly reduced in proportion to the soft tissues in the skull, its calcium content lies within normal limits. In other words, the softness and radiolucency of the affected bone are the result of an osteoporotic rather than of

OSTEOPOROSIS CIRCUMSCRIPTA OF THE SKULL

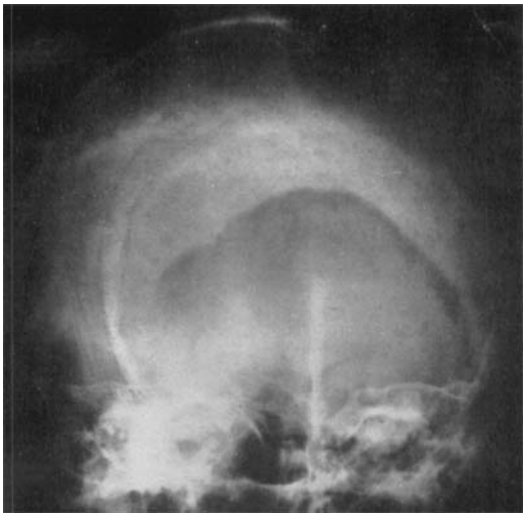


FIG. 6.—Case 2. Radiograph of skull made before death, showing circumscribed osteoporosis of the frontal bone. Antero-posterior view, reduced.

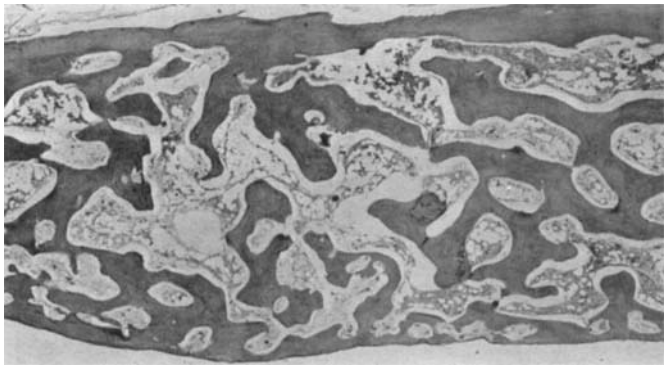


FIG. 10.—Case 3. Section of parietal bone in affected area. Wide-mesh porosis. Vascular fibrous marrow with some hæmopoietic tissue below outer table. Little active bone production. H. and E. ×12.

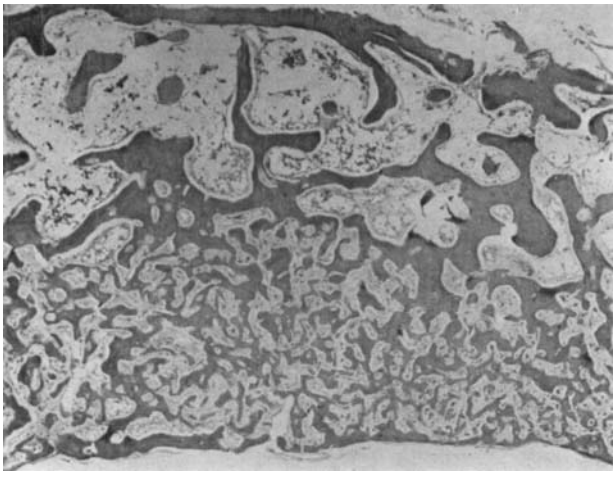


FIG. 11.—Case 3. Occipital bone. Advanced porosis of outer table in this area, but with production of close-set discontinuous trabeculæ of coarse-fibred primitive bone in place of the inner table. H. and E. ×9.

an osteomalacic change. This conclusion is in accord with the histological findings, for wide osteoid borders are never seen.

Histologically the skull is seen to be affected by a porotic type of Paget's disease, where resorption has advanced while new bone production has been limited.

Dorsal and lumbar vertebræ and pelvic bones. These are the seat of a moderately severe simple osteoporosis. No other focus of Paget's disease was detected in the skeleton.

Discussion

These five case records illustrate the pathological features of the bony lesion of the skull which radiologists recognise as osteoporosis circumscripta. The lesion is evidently not rare, occurring in this series in about 1 in 400 adult necropsies. It is probable that many cases are overlooked by pathologists who do not observe or who fail to recognise these peculiar circumscribed colour changes in the skull.

Our study confirms the view that circumscribed osteoporosis in the adult skull is usually to be regarded as a localised manifestation of Paget's disease, and that it is not infrequently the only focus present. It is nothing like so common as Paget's disease in general, which Schmorl (1932) found in 3·5 per cent. of necropsies on persons aged 40 or over. We do not pretend that focal Paget's disease is the only disease which may cause a single large confluent and sharply defined area of translucency in the X-ray picture of the skull but it is the most frequent. Among other, much rarer, causes of circumscribed osteoporosis are hyperparathyroidism (Kasabach and Gutman, 1937; Windholz, 1945), and xanthomatosis (Hunter and Jupe, 1950, p. 405). Most rarefying lesions of the skull are small and multicentric or but poorly circumscribed.

Some authors (Kasabach and Gutman; Windholz) believe that osteoporosis circumscripta is identical with Schmorl's hæmorrhagic infarction of the skull, to which reference has been made earlier in this paper. Schmorl did not state whether the affected bone was rarefied, but this seems unlikely, since infarcted bone is usually of greater radiographic density than its surroundings. More significant still is the fact that we see no dead bone in these skulls in any of our sections, whereas Schmorl described indubitable bone necrosis, such as we have ourselves seen in Paget's disease of different type in various other sites. We may therefore conclude that Schmorl's hæmorrhagic infarction of the skull is not the same process as osteoporosis circumscripta, where the bone, though engorged with blood, is not infarcted.

Much interest is attached to the fact that this circumscribed and focal form of Paget's disease of the skull is predominantly rarefying and not hyperplastic and deforming. It would be wrong to regard it as a separate type of Paget's disease, for occasional areas of sclerosis (fig. 5) and foci where bone is being actively produced (fig. 11) may be encountered, and all the histological characteristics of Paget's

disease are to be found if enough blocks of tissue are prepared. Sosman's view, however, seems reasonable. He suggests that osteoporosis circumscripta " may well be . . . the absorptive or destructive phase of Paget's disease at work, with the productive phase held in abeyance ". That is just what our histological investigations seem to show it to be.

We have ample evidence to support Reifenstein and Albright (1944) in their belief that the initial lesion in Paget's disease is bone destruction. They cut sections of the margins of circumscribed areas of bone destruction in the skull in Paget's disease and saw, like us, that the sharply defined margin of the lesion showed normal bone being destroyed and lying in contact with an advancing zone of cellular tissue in which were many osteoclasts, but no osteoblasts and no bone formation. In most other circumstances in Paget's disease the resorptive advance-guard of osteoclastic tissue is quickly succeeded by a formative osteogenesis, causing enlargement of the diseased part of the bone. Why is this not so in osteoporosis circumscripta of the skull ? Reifenstein and Albright suggest that it is mainly mechanical stresses and strains that stimulate osteogenesis, and that in the skull, since there are fewer stresses and strains, one frequently sees bone destruction divorced from over-production. This argument is weakened by the fact that the skull in most cases of Paget's disease is thickened and enlarged by copious over-production of new bone and that it shows great osteoblastic activity. One observation in our series might be significant. In three of the cases, a simple osteoporosis of senile type was noted in the vertebræ, both macroscopically and microscopically. Might it then be that the same influence that impairs osteogenesis in senile osteoporosis has also restrained osteoblastic activity in these porotic foci of Paget's disease in the skull ?

Summary

A sharply outlined area of soft, rarefied and congested bone, corresponding to the lesion radiologically identified as osteoporosis circumscripta, was found incidentally at necropsy in the skull of five patients dying in hospital from causes unrelated to the bone disease.

The histological characters of the lesion in each case showed it to be a form of Paget's disease in which bone resorption greatly exceeded new bone formation. The skulls were little, if at all, thickened and were not deformed. The vault was generally affected more than the base, and the disease seemed to have spread fan-wise from either the frontal or the occipital pole.

The ages of the patients ranged from 43 to 80. Four of the five were men.

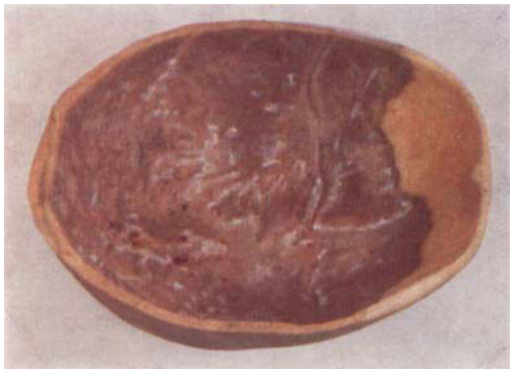
The incidence of osteoporosis circumscripta proved to be about 1 in every 350 or 400 adult necropsies. It is much less common than Paget's disease of the more usual pattern.

Paget's disease was found elsewhere in the skeleton in only one

OSTEOPOROSIS CIRCUMSCRIPTA OF THE SKULL

FIG. 7.—Case 2. Vault of skull viewed from within after stripping the dura mater. The colour contrast and sharp outline are the most striking pathological features of the focal lesion, which is in the frontal bone. The affected bone could be cut with a knife. Ektachrome.

FIG. 8.—Case 3. Male, aged 80. Vault of skull viewed from within. Four-fifths of the specimen are affected by hyperæmic and resorptive Paget's disease. There is no appreciable increase in thickness and no deformity of the skull. Part of the frontal bone is unaffected and the frontier is sharply defined. The silvery streaks are adherent shreds of dura mater. Ektachrome.



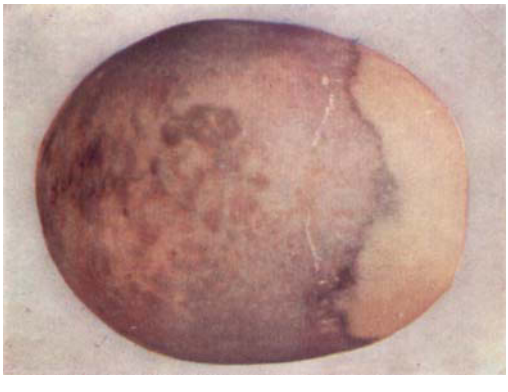


FIG. 9.—Case 3. Vault of skull viewed from without. The colour contrast and the sharply defined limits of the diseased bone can be seen only after stripping the epicranial aponeurosis and pericranium. Note that the disease has advanced without regard to the cranial sutures. Ektachrome.

OSTEOPOROSIS CIRCUMSCRIPTA OF THE SKULL

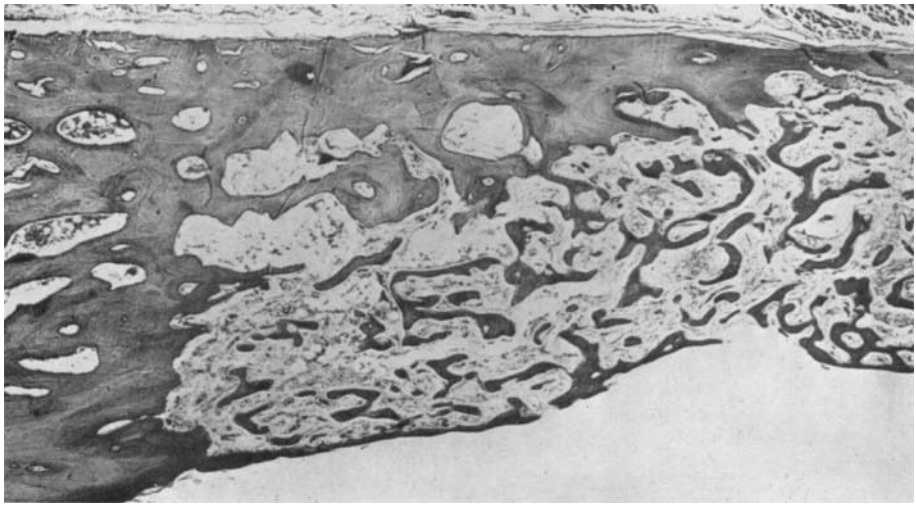


FIG. 12.—Case 3. Junction between normal and diseased bone at front of skull. The first change is osteoclastic resorption of original compact bone, a process which has pushed further forward into the inner than into the outer table. This is succeeded by osteogenesis in the vascular fibrous tissue, but new bone-formation is so limited that the total effect is one of great osteoporosis. H. and E. ×15.

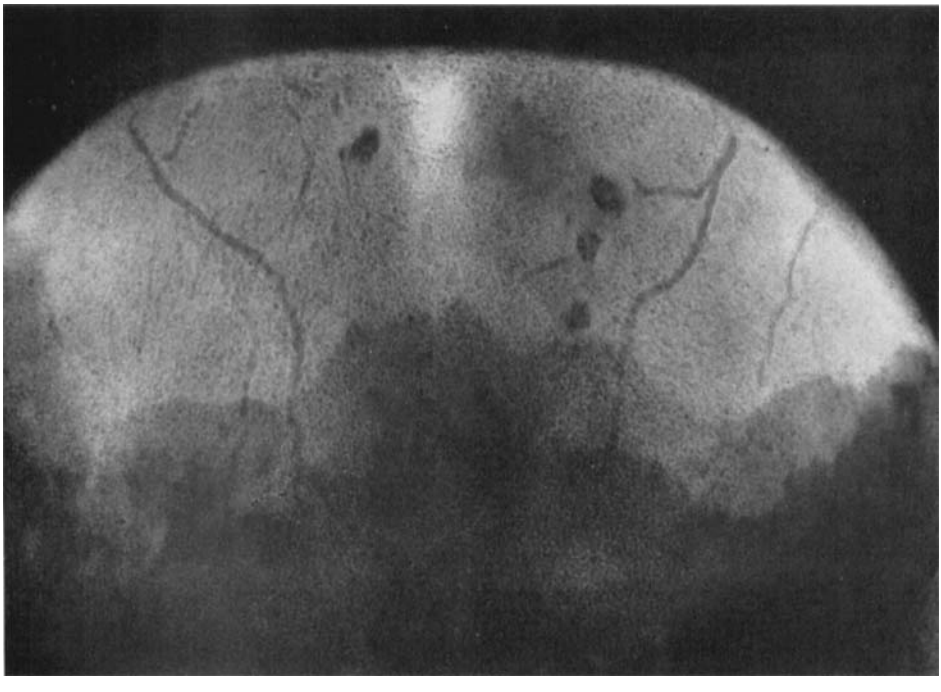


FIG. 13.—Case 3. X-ray of frontal region of specimen of skull vault. The double outline of the edge of the lesion results from the greater advance of bone resorption along the inner table, *cf.* fig. 12. The diseased bone is severely porotic. The discrete small translucent spots are pits that lodged arachnoid granulations. Slightly reduced.

of the five cases, but simple osteoporosis of senile type in the vertebræ was proved in three cases.

Our studies support the contention that the initial lesion of Paget's disease is bone destruction. We tentatively suggest that the failure, in osteoporosis circumscripta, of the productive phase that generally follows in Paget's disease may be associated with the same influences that impair osteoblastic activity in senile osteoporosis.

We are grateful to Mr C. N. England for the Ektachrome photographs and for the photomicrographs.

REFERENCES

ERDHEIM, J.	1935-36.	*Beitr. path. Anat.*, xcvi, 1.
GOLDENBERG, R. R.	1951.	*J. Bone and Joint Surg.*, xxxiiiA, 911.
HUNTER, D., AND JUPE, M. H.	1950.	*In* A text-book of X-ray diagnosis, ed. by S. C. Shanks and P. Kerley, *London*, 2nd ed., vol. iv.
IRVINE, R. E.	1953.	*J. Bone and Joint Surg.*, xxxB, 106.
KASABACH, H. H., AND DYKE, C. G.	1932.	*Amer. J. Roentgenol.*, xxviii, 192.
KASABACH, H. H., AND GUTMAN, A. B.	1937.	*Ibid.*, xxxvii, 577.
PAGET, J.	1877.	*Med.-Chir. Trans.*, lx, 37.
REIFENSTEIN, E. C., JR., AND ALBRIGHT, F.	1944.	*New Engl. J. Med.*, ccxxxi, 343.
SCHELLENBERG, W.	1931.	*Frankf. Z. Path.*, xli, 423.
SCHMORL, G.	1930.	*Verhandl. dtsch. path. Gesellsch.*, xxv, 205.
,,	1932.	*Arch. path. Anat.*, cclxxxiii, 694.
SCHÜLLER, A.	1926.	*Brit. J. Radiol.*, xxxi, 156.
,,	1929.	*Med. Klin.*, xxv, 631.
SOSMAN, M. C.	1927.	*Radiology*, ix, 396.
WINDHOLZ, F.	1945.	*Ibid.*, xliv, 14.