Three Cases of Rarefaction of the Skeleton in Africans

TWO ASSOCIATED WITH SEVERE URINARY BILHARZIASIS

BY

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Three Africans were admitted to hospital with rarefaction (osteoporosis) of the skeleton. Two, in addition, had a severe degree of urinary bilharziasis and the third child probably had renal disease, but not of bilharzial origin. Whether bilharziasis could have been responsible in some way for the osteoporosis in two of the subjects cannot be proven and this possibility is discussed.

Osteoporosis of a great part of the skeleton is not often seen in my experience in the African. Because he is subject to many forms of malnutrition, one could expect to meet more cases of osteomalacia or nutritional rickets in clinical practice, although in Johannesburg and Ibadan rickets is apparently commonly encountered.

Case 1

Clement, an adult African male, aged about 22 years, was admitted to the Salisbury African hospital on 3rd April, 1956, complaining of chest and general body pains for the previous one and a half years. At times these seemed to improve, but then they would become worse. The pains were not of a flitting character.

For the past two months he had been rising twice a night to pass urine. He complained of marked weakness of all his limbs and at times was unable to lift them. His appetite was good and he made no mention of cough, dyspepsia, nausea or abdominal pains.

On examination, little could be detected. His blood pressure was 110/80 and pulse 92 per minute and regular. The cardiovascular and respiratory systems were normal and no abnormality could be found on abdominal examination.

He was only able to walk with the aid of a stick. There was marked lordosis of the spine and he kept his back rigid and extended. The deck reflexes were present and brisk and the superficial reflexes normal. No sensory changes were noticed and the cranial nerves and function were normal. He had a normal intelligence. He was unable to lift his legs, and he lay in bed with his knees bent. If the knees were straightened, the spine became further extended.

He was admitted to hospital with the provisional diagnosis of tuberculous disease of the spine.

The following investigations were carried out:

Haemoglobin, 110 per cent. (16.2 g. per cent.); leucocytes, 10,200; neutrophils, 49 per cent.; lymphocytes, 42 per cent.; monocytes, 1 per cent.; and eosinophils, 8 per cent.

Serum calcium, 9.8 mg. per cent.; blood urea, 26 mg, per cent.; E.S.R., 12 mm. The Mantoux reaction (1/2,000) was negative. Serum alkaline phosphatase, 12.1 units per 100 ml. Serum inorganic phosphate, 3.2 mg. per cent. normal equals 2.7 to 3.7 mg. per cent.). Blood Wassermann reaction negative. Urine: urinary calcium normal (Sulkowitch test). Urine ova of *S. haematobium*. Stool: no ova or parasites detected. The urine was negative for porphyrins.

X-rays showed marked decalcification of the vertebral column and pelvis, with definite flattening and early wedging of the lumbar vertebrae. A periosteal line of calcification was noticed in the lower two-thirds of the right femur (Figs. 1 and 2).

An intravenous pyelogram revealed calcification of the bladder and lower right ureter, with a dilated and tortuous right ureter in its lower third. The left renal pelvis and ureter were normal (Fig. 3).

The urinary phosphate was 57.5 mg. per 100 ml. Urine volume in 24 hours, 610 ml. Total phosphate output in 24 hours, 351 mg. as P (average normal amount of phosphate passed in urine in 24 hours is 1 to 5 G). No abnormal amounts of aminoacids were present in a urine sample examined by Mr. W. R. Carr.

Mr. Honey carried out a cystoscopy and confirmed the presence of gross urinary bilharziasis. He found the bladder capacity to be normal.

A diagnosis of osteomalacia was made and Calciferol 40,000 units a day with calcium lactate gr. V three times a day were prescribed. For the bilharzial infestation sodium antimony tartate was commenced, but after six injections the patient refused to continue with them. He was persuaded, however, to remain in hospital, but after 21 days he sought his own discharge. No improvement was noticed when he left hospital.

CASE 2

Mtandwa, aged about six years, was admitted on 6th May, 1960, from the Enkeldoorn district. He was a full-term normal delivery, being the eighth child. All the family were said to be healthy. His diet consisted of mealie meal, meat and milk.

Mtandwa was well until October, 1959, when he began to complain of pain in his lower back in the left shoulder. At the same time he experienced pain on passing urine. He was found to have ova of *S. haematobium* in his urine and a course of treatment was instituted. At no stage had the child complained of pain in the arms and legs and the mother had not observed any deformity of the limbs. There was no history of a fracture. He had no cough. His appetite since he became ill had been poor. No attacks of carpopedal spasms or history of laryngismus stridulus were recorded.

On Examination

The boy was thin. His weight was 33 lb. and on admission to the ward he was in pain. He was unable to walk, due to the pain in his lumbar region. He was sweating profusely on

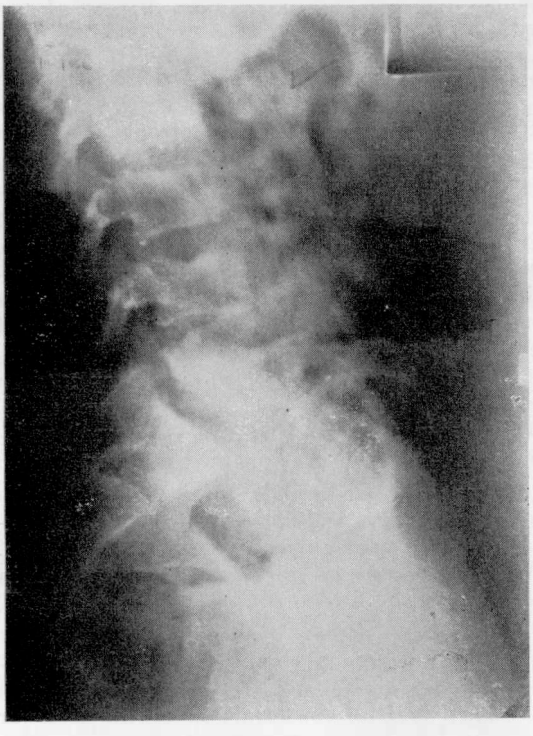

Fig. 1—Rarefaction of third and fourth lumbar vertebrae is well shown.

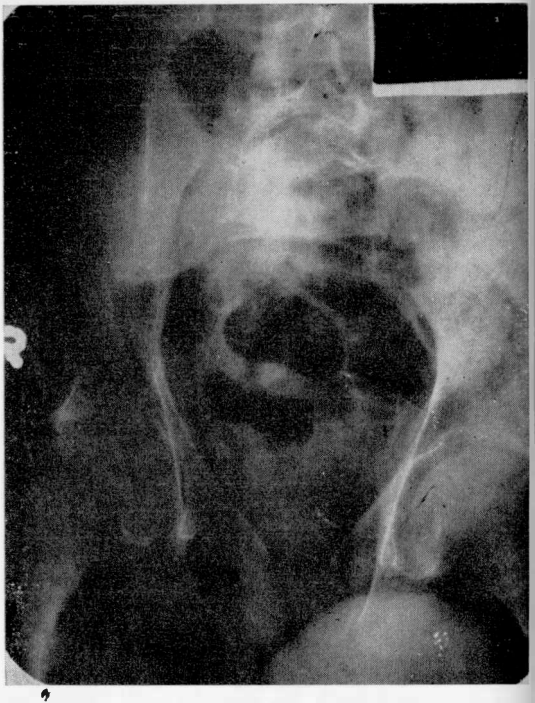

Fig. 2—Calcified outline of bladder due to bilharzial disease. There is also marked osteoporosis of the right femur and right side of the pelvis.

admission. His colour was fairly good. There was a mild purulent conjunctival discharge. The heart, lungs and abdomen were normal. The lymph nodes in the cervical, inguinal and axillary regions were just palpable, but mobile and not tender. There was wasting of the muscles of his legs and thighs and the child was unable to stand.

The tone in the arms and legs was normal, but the power weak. There was a rickety rosary in the chest wall, but the ends of the long bones appeared to be normal in shape. There were no tender areas in the long bones. There was a well marked lumbodorsal kyphosis.

Special Investigations

Haemoglobin, 86 per cent. (Newcomer) 12.6 g. per cent.; leucocytes, 8,950; polymorphs, 51 per cent.; lymphocytes, 49 per cent. No sickle cells demonstrated.

Blood: Total serum calcium, 5.4 M. Eq. per cent. Serum inorganic phosphate, 2.6 mg. per cent. Serum alkaline phosphatase, 20 K.A. units. Blood Wassermann reaction was negative.

Total urinary calcium, 16 mg./24 hours. When repeated three months later, this figure was 10.4 m./24 hours. Two dimensional chromatography of the desalted urine showed normal spots of taurine alanine, valine, B. amino-isobutyric acid and glycine (Dr. A. Kinnear). No glucose was detected in the urine. Urine showed a trace of albumin, red blood cells and leucocytes +, casts absent; *B. haematobium* present. Culture of urine—no growth obtained. Blood sugar, 72 mg. per cent. Blood urea, 16 mg. per cent. Stool: No ova found. Fat analysis, 11.5 per cent. with normal splitting.

Long Bones: There was a gross generalised osteoporosis. A small zone of destruction about two inches from upper end of *L. humerus* was observed on its outer aspect, with periosteal reaction (Fig. 4).

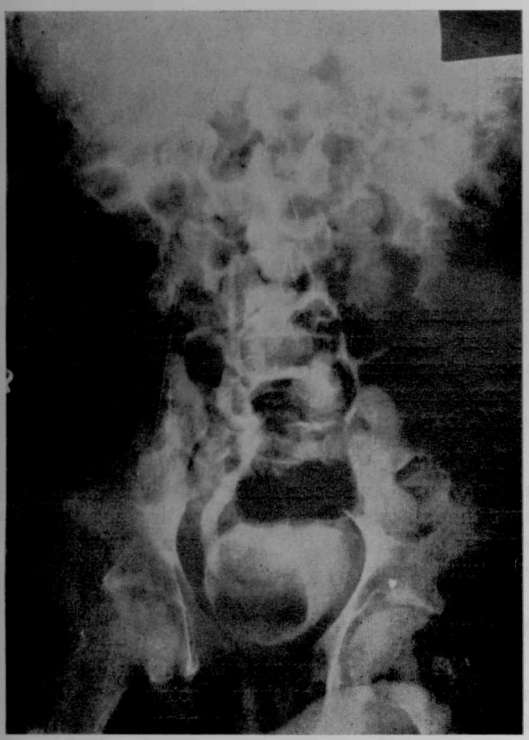

Fig. 3—A typical dilated and tortuous ureter on the right side due to bilharziasis.

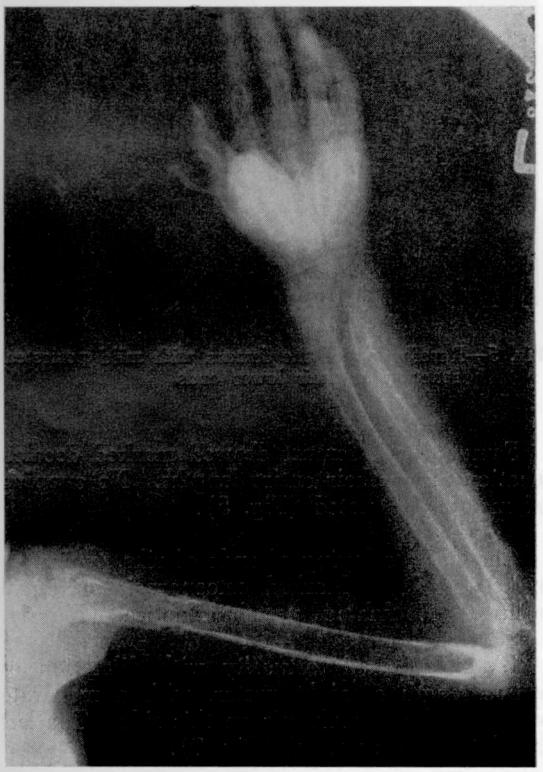

Fig. 4—Note the extensive osteoporosis of the bones of left upper extremity with periostitis and foci of bone destruction.

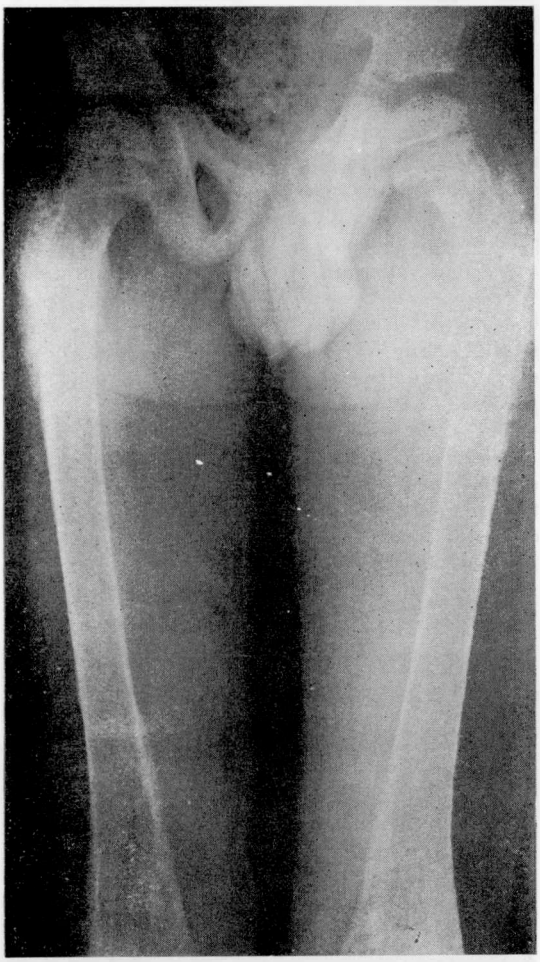

Fig. 5—Rarefaction of the femurs with mild periosteal reaction at their lower ends.

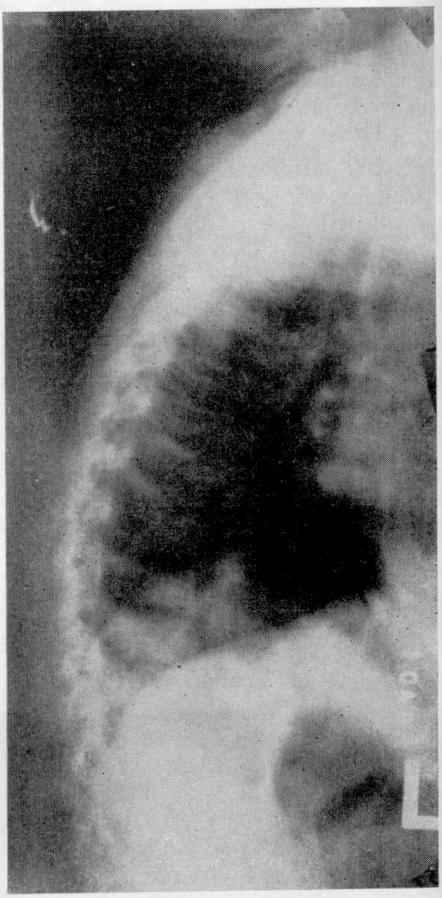

Fig. 6—This illustration shows the extent of the osteoporotic changes in the dorsal column.

Femur: Both femurs showed marked decalcification along their entire lengths. No cupping of metaphyses noted (Fig. 5).

Chest: No splaying of ends of ribs, typical of rickety rosary. Marked osteoporosis of dorsal column. No fish cod vertebrae noticed (Fig. 6).

I.V.P.: Marked tortuosity with dilatation of entire length of right ureter, with a moderate degree of hydronephrosis on this side. The left renal tract was normal (Fig. 7).

On 29th July, 1960, Dr. A. Kinnear kindly carried out tests to determine glomerular and tubular functions. These were normal. The blood urea was 23 mg. per cent; urea clearanc 93 per cent. average normal maximum clea ance; glomerular filtration rate = 96 ml/minut Phenolsulphonphthalein excretion = 6 per cen in 24-hour period.

On 13th June, 1960, Mr. Honey carried ou a cystoscopy and found active bilharzial lesion over the lateral wall and vault, with right ureteri stenosis. Culture of a mid-stream urine speci men was sterile.

Treatment

Despite a long course of Calciferol, 20,00 units daily, plus calcium lactata tablets b mouth for 12 weeks, no improvement in th condition of the patient was noticed. As he wa so ill we found it difficult to decide on a treat ment for his bilharziasis. I first tried a ne

Parke Davis preparation, but this was ineffective. Next a course of Nilodin tablets was given, but he continued to pass active bilharzial ova. He continued to pass active bilharzial ova until we decided to treat him with Anthiomaline by the intramuscular route, and this seemed to have been successful and he appears to have stopped excreting ova.

CASE 3

Sinoya, aged five years, was brought into hospital in October, 1960, by his father, who said that his child was well until six weeks before, when he began to complain of pain in his legs and was unable to walk. He could stand with support.

On his admission to hospital it was observed that he sat erect in his bed for long periods without moving his buttocks and lower limbs, although he moved his neck and arms freely. He was thin and had a mild conjunctivitis. He was not pale. A few tiny lymph nodes could be felt in his neck.

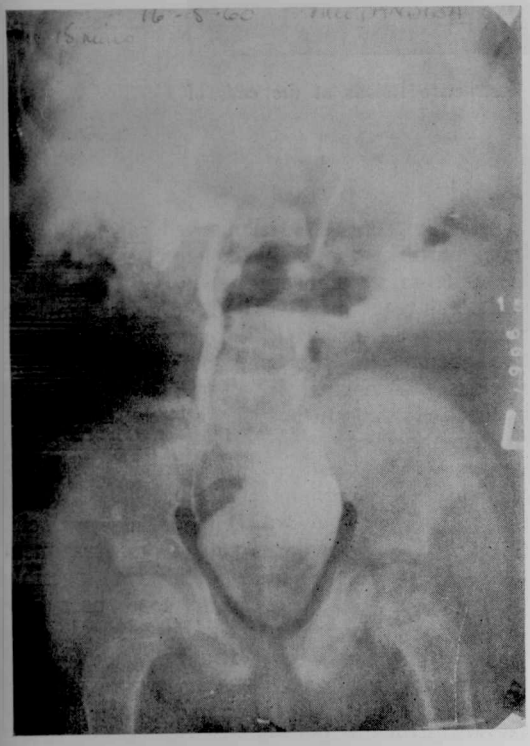

Fig. 7—In this illustration there is dilatation of the right ureter and pelvis from bilharzial infestation.

The pulse rate on admission was 102 per minute and regular. His temperature fluctuated between 99° F. and 100.50° F. for almost two weeks after his admission, and after this returned to normal. The heart was normal. The lungs were clear; and although he had a pot belly, the liver and spleen were not palpable. The costochondral junctions were enlarged (rickety rosary), but there was no tenderness in the bones and no definite enlargement of the metaphyseal ends of the long bones.

Both legs were weak and wasted and his power was poor. The reflexes were brisk, sensation was normal and joint movements normal.

Initial X-ray showed marked rarefaction of the whole skeleton. In addition to the rarefaction of the long bones, there were signs of periostitis and also small islands of necrosis or destruction of the metaphyses. The X-rays of the chondral ends of the ribs showed the cup-like concavities found in rickets (Figs. 8, 9 and 10). An intravenous pyelogram showed both renal tracts to be normal.

Biochemical Results

Blood sugar, 52 mg. per cent.; blood urea, 31 mg. per cent.; serum calcium, 9.6 mg. per cent.; serum inorganic phosphorus, 2.5 mg. per cent.; serum alkaline phosphatase, 10 King-Armstrong units. Wassermann reaction of blood negative. Urine clear of albumin and sugar on chemical examination. No abnormality seen microscopically. Total urinary calcium = 20.2 mg./24 hours. Two dimensional chromatography of the urine showed spots of taurine, cycline, alanine, beta-aminobutyric acid and methyl histidine in normal amounts. Urinary total glucose, 0.3 g./24 hours. (Dr. A. Kinnear kindly carried out this investigation.) Blood count: Hb. 72 per cent. Leucocyte count, 9,300 (polymorphs 58 per cent., lymphocytes 42 per cent.).

Cerebrospinal fluid: White cells less than 1; sugar, 53 mg. per cent.; chlorides, 760 mg. per cent.; protein, 20 mg. per cent.; Nonne-Apelt, negative.

On 3rd December, 1960, 4,000 units of vitamin D were given orally per diem. On 22nd December, 1960, the child developed a brisk haematuria which lasted two days and then cleared completely. On 20th December, 1960, it was decided to add vitamin C, 250 mg. b.d., to the treatment.

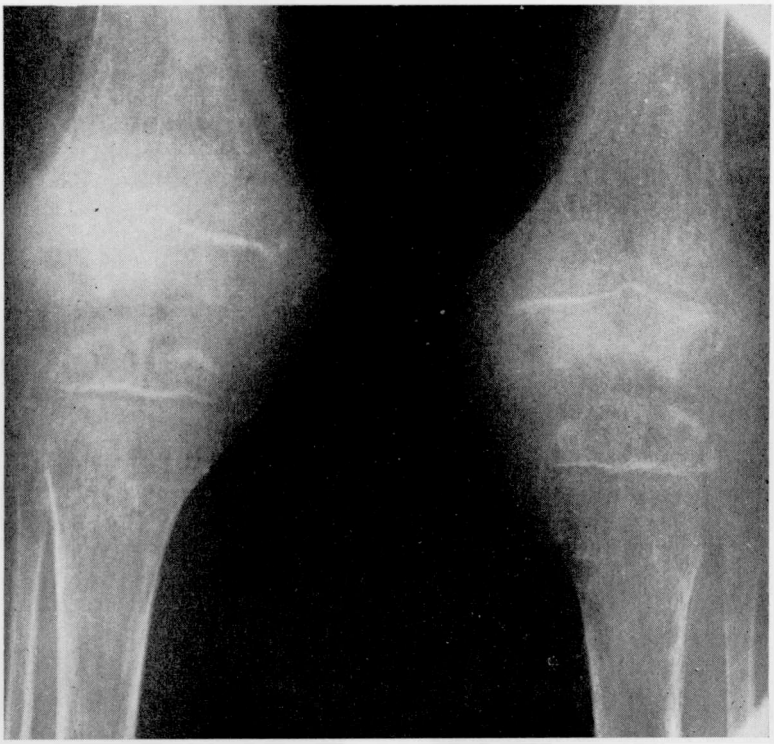

Fig. 8—Besides the rarefaction there are destructive lesions at the ends of the bones.

No radiological improvement followed these therapeutic measures, and vitamin D was increased to 20,000 units daily. On 23rd January, 1961, calcium lactate gr. V, 1 tablet t.i.d. p.c., were added, but still no improvement was noticed. On 28th February, 1961, the calciferol intake was increased to 200,000 units daily. The child was no better during February and he still could not leave his bed. The X-rays showed no real improvement. On 14th February, 1961, he developed signs of vitamin D excess such as increased weakness and tenderness in the muscles of his limbs, with nausea.

His blood urea was now 40 mg., but three weeks later it had risen to 52 mg. per cent. The serum calcium on 14th February, 1961, was 11 mg. and the serum inorganic phosphorus 3.5 mg. per cent. The serum potassium was 18 mg. per cent. (4.5 meg.), serum sodium 350 mg. (152 m. eq.) and serum chlorides 640 mg. (110 m. eq.).; 17 oxysteroids excreted—1 mg. calculated as dehydroepianrosterone. Sickle cells were not found in his blood.

COMMENT

All three cases showed marked rarefaction of large parts of the bony skeleton, especially of the vertebral column and pelvis, together with periosteal reaction of limited extent in the long bones and, in the two children, marked destructive changes in the metaphyses. The serum calcium was normal in all three subjects, but in the two children the phosphorus was reduced. All three subjects, despite large doses, failed to improve with Calciferol or vitamin D. The two children had bone changes consistent with rickets and the adult with those of osteomalacia. All, however, proved resistant to the treatment given. One of the children (Sinoya) possibly had renal rickets, since his blood urea was elevated and he had a brisk but short haematuria. Bilharzial disease could not be demonstrated in him. In the other two cases—the adult and the child (Mutundya)—gross bilharzial disease of the bladder and of one ureter, the other ureter and kidney being apparently normal. One has to consider whether bilharziasis could in any way have led to a chroni

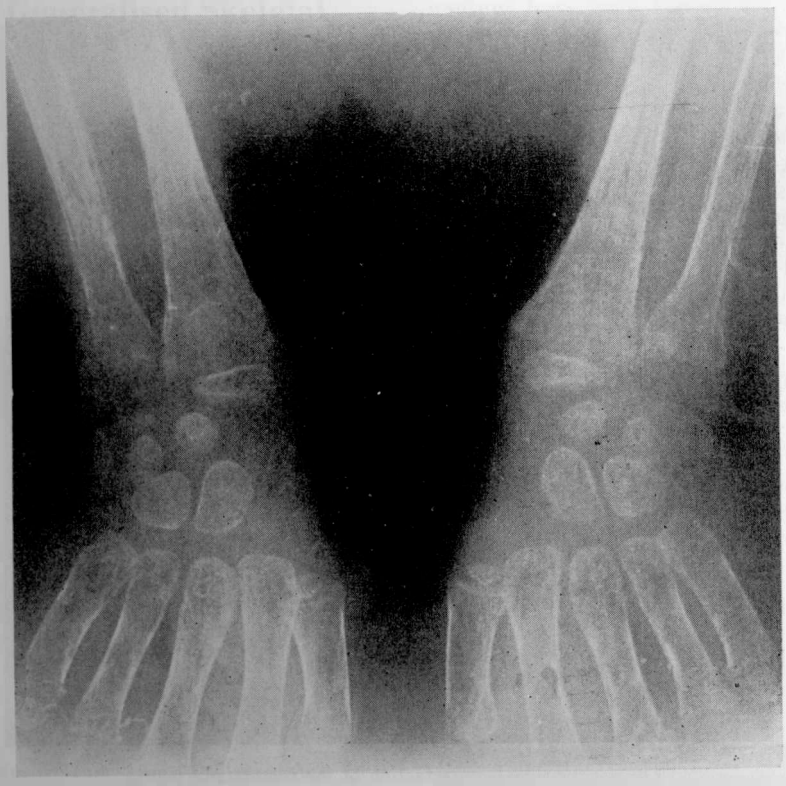

Fig. 9—Generalised osteoporosis of the bones of lower part of forearm, wrist and hand. Observe the periosteal reaction in the ulna and radius on each side, with destructive changes in the metaphyseal regions.

pyelonephritis from an ascending secondary infection, which in turn led to a loss of phosphates from the blood and, by altering the Ca x P product, induced the osteoporotic changes in the skeleton. The biochemical determinations in themselves did not, however, suggest any definite disturbance of tubular function and thus a renal osteodystrophy seemed to be unlikely.

Whether severe bilharziasis of the bladder and ureters may be responsible in some way for decalcification of the bones through an effect on the renal tissue is not known, but the evidence in these two cases is insufficient to assume this effect. The most one can do at the present time is to note how often severe bilharzial disease and decalcification in the skeleton occur in the same patient.

I have considered at times whether the calcified bladder of bilharziasis could be the result of metastatic calcification from loss of the calcium from the body as a result of renal changes induced by the disease. Against this, however, is that African subjects with the calcified bladder do not show osteoporosis in any part of the skeleton. There is inadequate evidence to blame the osteoporosis or the ricketic changes in the bones to bilharzial disease in the first instance, as it could be argued that as urinary bilharziasis is so common in Rhodesia, sooner or later the two diseases would occur together.

In none of the three cases was there anything to denote a decreased absorption of calcium from the bowel. Diarrhoea was not a feature. At first, nutritional rickets of osteomalacia from a lack of vitamin D seemed very possible, but in none of the cases, more so in the two children, did we observe any improvement, despite adequate amounts of it.

No increased calcium excretion could be demonstrated in the two children; indeed, the reverse would appear to be the case. Thus "idiopathic osteoporosis," of which cases were recently described by Jackson (1958), would seem to be excluded.

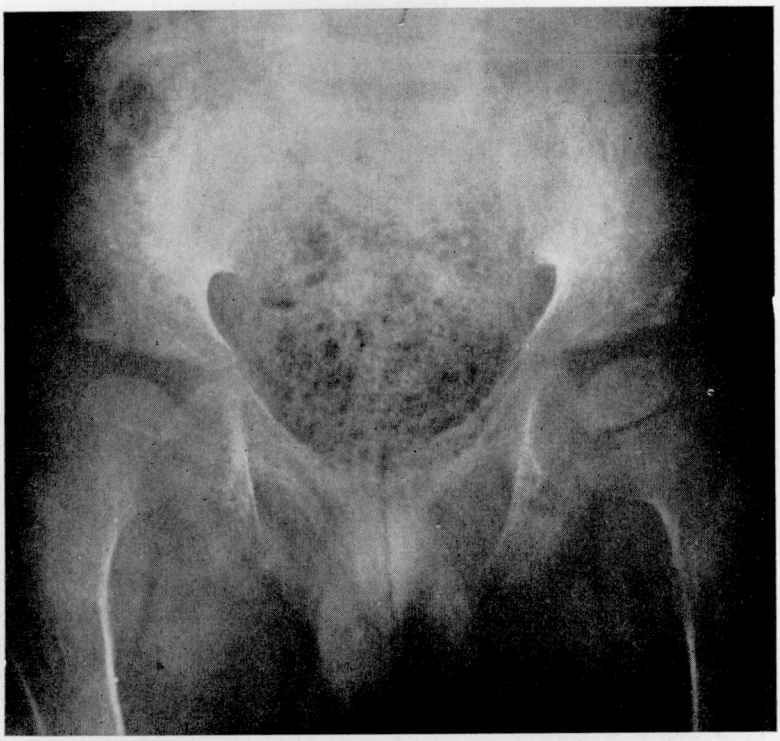

Fig. 10.—Extensive rarefaction of the femurs and pelvis.

None of the cases displayed an endocrinal abnormality such as Cushing's syndrome, a pituitary or thyroid disorder. As the serum calcium levels were normal, hyperparathyroidism could be excluded.

Despite the many cases of malnutrition one encounters in African practice, particularly pelagra, kwashiorkor, hypoproteinaemia and vitamin A deficiency, osteoporosis is not a feature and one is therefore not justified in linking the present reported series with a dietetic deficiency, even though it is a very difficult factor to exclude. From the studies carried out by Walker, Arvidsson and Pollitzer (1954) in Johannesburg, osteomalacia should be encountered not uncommonly in Africa, since they found that the serum calcium values in a group of Bantu children and adults in good outward health were low. They were inclined to attribute this to a relatively low intake of calcium.

Osteomalacia in the African, however, appears to be rare. Jelliffe (1952) found it to be very uncommon in Ibadan and that gross deficiency of vitamin D played little part as a cause of nutritional disorder in tropical Africa. Jelliffe, however, described a case of what he refers to as "juvenile osteomalacia" in a Nigerian chil aged eight, who was mentally defective.

SUMMARY

Three Africans—one adult and two childre —had severe osteoporosis. The cause in eac could not be determined. One child probabl had a form of renal rickets, and in the othe two cases fairly advanced bilharzial disease wa observed in the urinary tract, but no positiv relationship between it and the osteoporosi could be drawn. Nevertheless, it is considere worthy to draw attention to the possible relation ship between severe urinary bilharziasis an osteoporosis of the skeleton.

REFERENCES

JACKSON, W. P. U. (1958). *J. Bone & Joint Surger* 40, 434.

JELLIFFE, D. B. (1952). *J. trop. Med. & Ugy.*, 55, 21

WALKER, A. R. P., ARVIDSSON, U. B. & POLLITZE W. M. (1954). *S. Afr. med. J.*, 28, 48.

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