Section of Physical Medicine

President—A. C. BOYLE, M.D., M.R.C.P.

[*January* 9, 1957]

DISCUSSION ON GENERALIZED ACHES AND PAINS FROM METABOLIC BONE DISEASE

Dr. G. Alan Rose (University College Hospital): *Bone Pains in Steatorrhœa*

That a connexion exists between steatorrhœa and osteomalacia has been clear since the work of Parsons (1927) and of Bennett *et al.* (1932). In dealing with the individual patient, it may be obvious on clinical grounds that the patient is suffering from both of these conditions. Thus, he may present with the frequent, foul, frothy, offensive and bulky stools characteristic of steatorrhœa, and with gross bony deformities, and with tetany. In such a case the diagnosis will be easy, and is readily confirmed by biochemical and radiological investigations. The state of affairs may, however, be entirely different. The stools may have few or none of the characteristics mentioned. L. D., a patient recently described as "Case II" of Davies *et al.* (1956), had probably had steatorrhœa for very many years. She habitually used purgatives to obtain adequate bowel actions, and had never suffered from diarrhœa. This constipation may have been partly due in more recent years to a hypercalcæmia caused by a parathyroid adenoma, but this could not have been the whole explanation. V. M., a woman of 35, was found to have steatorrhœa at a time when she was having a bowel action once every three days. During the next ten years she developed frank diarrhœa, and finally osteomalacia. If the patient has a low intelligence quotient a history of diarrhœa may not be readily obtained. Patient L. B. was a girl of 17 when the diagnosis was made of steatorrhœa due to cœliac disease, with rickets and dwarfism. She had suffered from recurrent and severe attacks of diarrhœa from the age of 6 months; neither she nor her mother, however, worried much about these attacks, and her complaint on admission was that her knees were painful from banging one against the other (she had knock-knees). A patient with such an I.Q. may not appreciate the pallor of the stools, even if this is obvious to the doctor. Patient V. M. discovered by experience that a low fat diet tended to reduce her diarrhœa, when this finally developed. Others may find by trial and error that a low gluten diet helps them. Thus for various reasons, steatorrhœa may be present but not recognized.

The precise time relationships between the onset of steatorrhœa, and the onset of osteomalacia are not clear. Our present concept is that the steatorrhœa develops first, and is occult or overt. After a period of time, which is variable, but of the order of three to ten years, osteomalacia may develop. When this occurs, the steatorrhœa may still be occult. The onset of osteomalacia may be fairly sudden or it may be insidious. It is therefore possible that a patient with steatorrhœa may present only with the symptoms, either early or advanced, of osteomalacia. We may therefore hazard a guess that amongst the mass of patients presenting with general aches and pains, there will be some who are developing this syndrome. It is important to try and pick out these patients before they have developed crippling deformities, since therapy can prevent the deformities from occurring as well as curing the pains and other disabilities which precede them.

In our experience, patients with early osteomalacia due to steatorrhœa may often present with a certain pattern of symptoms whereby they may be recognized. The pains usually start in the lower half of the body, in the legs, thighs, pelvis or back. They are not sciatic in distribution and are frequently bilateral. The patient can usually clearly indicate that limb pains are between joints, and not in the joints themselves. After a period of time, the pains spread to other bones of the body, affecting the arms and shoulders. The bones may be tender to the touch. F. D., a woman of 58, had steatorrhœa with osteomalacia. The

lightest tap on her skull, long bones or thoracic cage caused her to wince. This may well suggest the diagnosis of "hysteria", but it should also suggest possible metabolic bone disease. The lower ribs may be tender. This was so in patients F. D., S. G., and V. M. Each of these patients stated that, on turning over in bed at night, she experienced pains in the lower ribs and in other bones. This was sufficiently distressing to make them arrange their bedding in ways calculated to prevent movements in their sleep. Muscular weakness is a feature frequently alluded to in various ways. A patient may develop a waddling gait, and this may be the first symptom recognized by him, or by his friends or relatives. Patient A. B., a woman with occult steatorrhœa, developed severe muscular weakness of the legs,

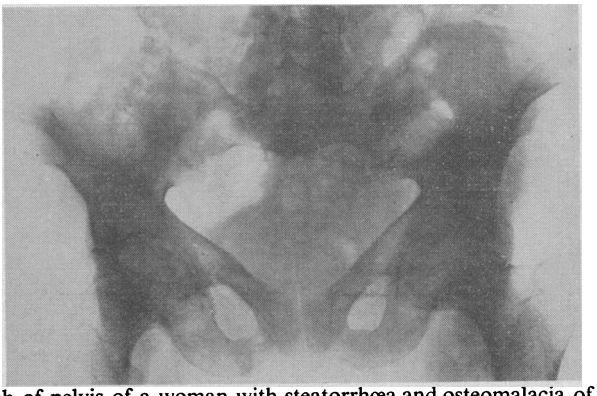

FIG. 1.—Radiograph of pelvis of a woman with steatorrhœa and osteomalacia of sudden onset, and with tetany. The bones are almost normal in shape, but show Looser zones in the pubic rami.

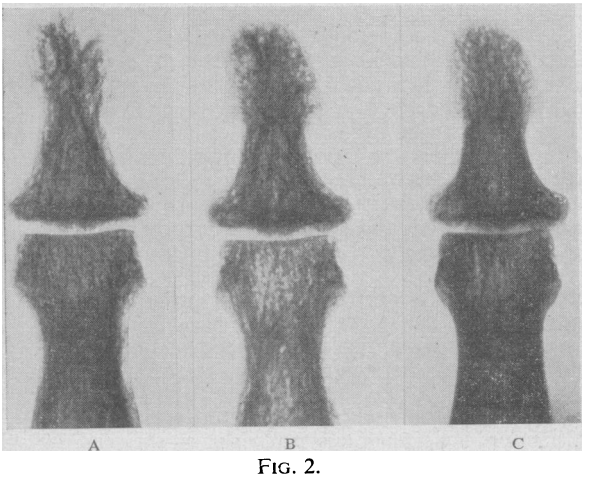

FIG. 2.

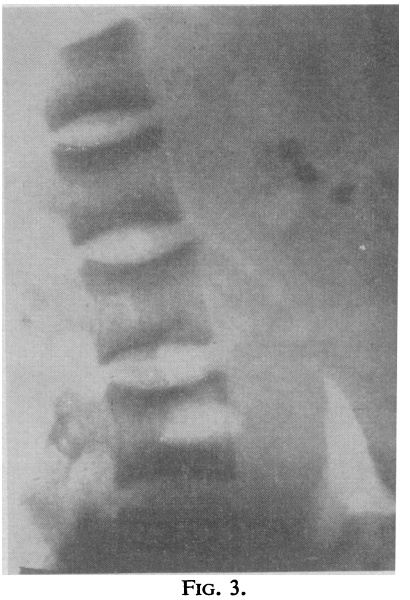

FIG. 3.

FIG. 2.—Radiographs of phalanges of a single finger of "Case II" of Davies, Dent and Willcox (1956). The patient had steatorrhœa and two parathyroid adenomata. A, before treatment (January 3, 1955) showing subperiosteal erosions. B, February 3, 1956, two months after removal of second adenoma. C, December 1956. The bones are now normal. This last follow-up radiograph was made after the paper of Davies, Dent and Willcox had gone to press. The others are taken from their paper, by kind permission.

FIG. 3.—Radiograph of lumbar vertebræ of "Case I" of Davies, Dent and Willcox (1956), reproduced by kind permission. Each vertebra is biconcave and shows two horizontal zones of osteosclerosis, between which is a less dense zone. The patient had steatorrhœa and radiological signs of hyperparathyroidism in the phalanges.

so that she was obliged to go up the stairs on all fours. Other patients have experienced feelings of "stiffness" in the legs on getting up, and which wear off with exercise. Others have felt unsteady on their legs, or unsure of themselves. These symptoms are not due to pain, or deformities, or general nutrition, and are reversed by treatment with vitamin D only. The other well-known symptoms of steatorrhœa may, of course, be present. There may for instance be nocturia due to delayed excretion of a water load. There may be a sore tongue, latent or overt tetany, or œdema.

The more fortunate patient who has developed osteomalacia due to steatorrhœa will be diagnosed before deformities occur. At this stage there may be no signs of old rickets, and the X-rays of the skeleton may appear entirely normal. Nevertheless, the diagnosis, when suspected, may be confirmed by a few simple tests. The urine calcium may be easily assessed in an out-patient department by the Sulkowitch test on any reasonably concentrated specimen of urine. The twenty-four-hour urine calcium provides the same information in a more precise manner. In the presence of normal renal function a very low urine calcium is suggestive of steatorrhœa. This may be so even if the plasma calcium is normal or high. Biochemical osteomalacia is demonstrated by the combination of a low plasma calcium and/or a low plasma phosphorus, with a raised plasma alkaline phosphatase. The diagnosis of steatorrhœa is confirmed by inspection of stools, by fat balance, glucose tolerance curve, water excretion test, blood count, and other tests.

In the less fortunate patient, there will be advanced bone changes before the diagnosis is made. These changes follow along certain now well-defined lines. If the osteomalacia is of relatively sudden onset, it will be characterized by the development of pseudofractures or "Umbauzonen" of Looser (1920). These zones of decalcification are considered by Dent and Hodson (1954) to occur in any relatively acute osteomalacia. Fig. 1 shows such pseudofractures in the otherwise apparently normal pelvis of a woman with steatorrhœa. If the osteomalacia is of more gradual onset, as has occurred in most of our cases, then the characteristic deformities of the chest, pelvis and legs will develop. Clinically relative trunk shortening will be found and X-rays will show that the bones are rarefied. The clavicle will droop, the tri-radiate pelvis will be seen, and there may be marked coxa vara. The X-rays of the lateral spine will show the biconcave "cod-fish" vertebræ, plus signs of decalcification. Each vertebra will have collapsed to the same extent as its neighbours. The osteomalacia of steatorrhœa may, as can occur in renal failure, be accompanied by radiological signs of secondary hyperparathyroidism. This has been described recently by Davies *et al.* (1956). One such sign is the "rugger-jersey spine" in which there are horizontal bands of sclerosis and porosis in each vertebra, as can be seen in Fig. 3. The subperiosteal erosions (Pugh, 1951) may be present. Fig. 2 shows the phalanges of a single finger of "Case II" of Davies *et al.* (1956) on three separate occasions. This patient had steatorrhœa and osteomalacia; subsequently she was presumed to have developed primary hyperparathyroidism following prolonged secondary hyperparathyroidism. These X-rays show the complete reformation of bone following removal of two parathyroid adenomata and massive vitamin-D therapy.

We now have good therapy for these cases of osteomalacia. A gluten-free diet is given if the patient has been shown to be gluten-sensitive and if he will be able to continue this as an out-patient. It is supplemented with folic acid, and with a form of vitamin D, in suitable dose. At present, we use calciferol, or dihydrotachysterol, or vitamin D_3. It is our hope that it will be possible to pick out more cases of osteomalacia with occult steatorrhœa who present with generalized aches and pains before they develop deformities, in order that early treatment will prevent these deformities from ever occurring.

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Dr. F. H. Lumb (University College Hospital): *Pain in Renal Osteodystrophy*

Like steatorrhœa, chronic renal failure may be the cause underlying a variety of skeletal aches and pains which are diagnosed for long periods as fibrositis or rheumatism. It would be wrong to claim that renal osteodystrophy is a common cause of such symptoms, though this does not detract from the importance of its diagnosis. That this is so is shown by the very satisfactory response to treatment of patients with this condition, both in terms of prolongation of life, and of symptomatic relief. Once a renal cause for skeletal pain is suspected, a few simple observations and investigations go far towards establishing the

diagnosis. Furthermore, treatment other than that based on an attempt to correct the underlying biochemical disorder is of little value, failing to affect the discomfort and incapacity, which gradually increase in severity. It would thus seem reasonable to attempt to define the main clinical characteristics of the renal osteodystrophies, as they often remain for long unrecognized, even in patients already known to be suffering from chronic renal failure.

Various types of renal disease may be associated with bone abnormalities. In general, predominantly glomerular failure, as in chronic nephritis, is associated with nitrogen retention, and with raised serum phosphorus and low serum calcium levels. Bone pain may occur in such cases, and some show radiological evidence of secondary hyperparathyroidism, though not necessarily so. Tubular defects, as in the Fanconi syndrome, may also be associated with bone pain, though in these cases nitrogen retention may not be marked, and the initial radiological changes are more those of osteomalacia (Albright and Reifenstein, 1948). Whatever the underlying renal disease, or type of bone change present, the symptoms tend to follow a common pattern. Also as the bony abnormality is due to biochemical disturbance and therefore generalized, it is hardly surprising that the patient's complaint should resemble those described in other forms of metabolic bone disease, as discussed by Professor Dent and Dr. Rose.

Both history and physical examination may greatly assist in the diagnosis of renal osteodystrophy. Obviously the clinical picture is greatly affected by the age of the patient, for in children chronic renal disease produces stunting of growth and deformity as its main skeletal manifestations, and such cases often present at orthopædic centres. Here, however, we are mainly concerned with adults, in whom bone pain is often the only presenting feature. Before discussing this symptom, however, another common aspect of the patients' disorder deserves mention. This concerns their previous contact with doctors and hospitals, where they have been seen on account of their increasing discomfort. In their attempts to obtain relief from pain they have often received treatment in various departments of physical medicine, orthopædics and sometimes psychiatry, not to mention general medical and other clinics. In one instance, a 35-year-old woman with a renal tubular defect and severe skeletal pain remained undiagnosed for six years, during which time she received a varied assortment of treatments which ranged from plaster casts to Evipan narcosis. The discovery of aminoaciduria in 1949, whilst she was undergoing neurological investigation, led to the diagnosis being established, and measures to correct her disturbed biochemical state have been associated with a most satisfactory symptomatic improvement. She is now in full-time employment as a shorthand typist.

In considering the case histories of those patients with renal osteodystrophy who have been under the care of Professor Dent at University College Hospital, the following features emerge. Pain, as mentioned previously, is the dominant symptom. As would be expected in a condition where the bones are generally affected, the pain is mainly referable to those parts of the skeleton which are subject to maximum stress and trauma. Thus pain affecting the lower limbs or lumbosacral region is a common complaint. It is often described as a severe, constant, nagging ache, difficult to alleviate, and of gradually increasing severity since its onset. It differs from sciatic pain in its usually bilateral distribution, and though it may be felt down the back of the thigh, it rarely spreads below the knee. Sometimes it is more definitely localized, coinciding under these circumstances with the presence of a stress fracture. Some patients notice marked bony tenderness, especially affecting the shins and ribs.

Characteristically, any increase in local stress is associated with an exacerbation of the pain. Almost always it is intensified by weight-bearing, and walking becomes more and more painful, resulting in restriction of activities and final immobility. Even the latter, however, may not give relief, as in the absence of treatment, the pain becomes more generalized, and even slight movements may become intolerable. Changing their position in bed is dreaded by some of these patients, who are wakened from their sleep by sudden movements, so much so that they not infequently go to considerable lengths to immobilize themselves by particular arrangements of pillows and bolsters. Similarly, if the ribs are affected, and stress fractures present, the patients will go to considerable lengths to suppress coughing on account of the discomfort which ensues.

Difficulty in walking may be due to the pain described, but occasionally seems to occur in the absence of the latter, or at least before pain is severe. The patient may describe a sensation of stiffness around the hip-joints and a feeling of uncertainty when on his feet. Such symptoms are usually associated with an obvious disorder of gait, best described as a waddling gait. One patient described a sensation of stiffness in the thighs, which limited walking in the absence of actual pain. Muscular weakness is often prominent in cases of renal osteodystrophy and may be extreme. It seems to be something more that the general lassitude of chronic uræmia and associated anæmia, and is a further reason why walking

may be difficult. As is well known, in those cases where potassium loss occurs consequent on a tubular lesion, periods of actual muscular paralysis may occur.

The combination of the pain, difficulty in walking, and muscular weakness described, should raise the diagnostic possibility of a renal osteodystrophy, and indicate the lines for further enquiry. The clinical picture described may long precede the malaise, vomiting and pruritus which signalize the terminal phase of renal failure, and these manifestations should not necessarily be expected. The osmotic diuresis, which, however, occurs at an earlier stage, gives rise to polyuria, nocturia and thirst, and such symptoms are worth enquiry.

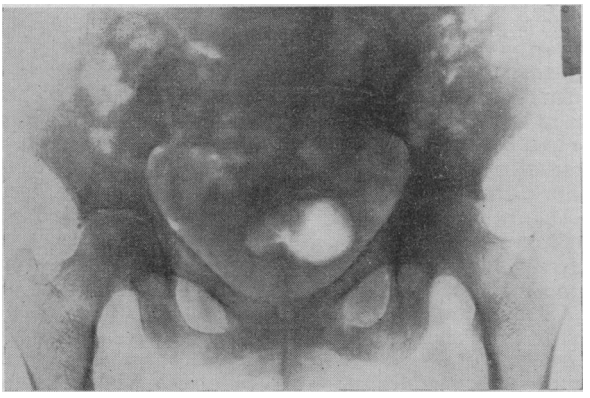
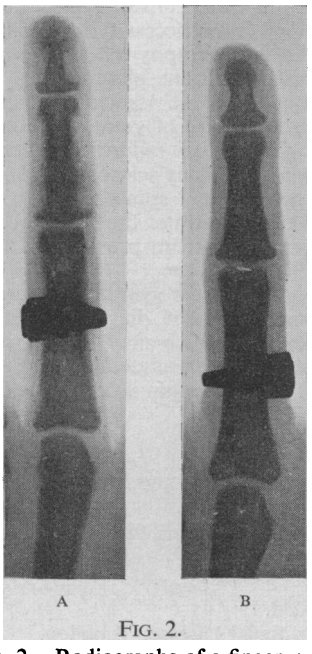


FIG. 1.—Radiograph of the pelvis, showing stress fractures in the pubic rami of a patient suffering from chronic renal failure. The fractures healed with subsequent treatment.



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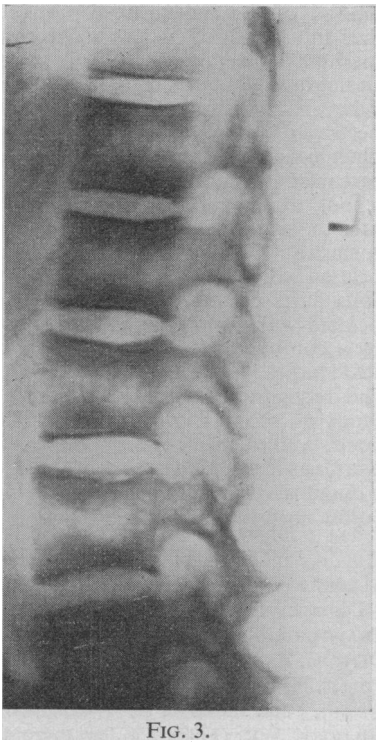

FIG. 3.

FIG. 2.—Radiographs of a finger, A before and B after treatment, showing the subperiosteal erosions associated with secondary hyperparathyroidism, in a case of chronic renal failure.

FIG. 3.—Radiograph of the spine, from the same patient as Fig. 2, showing the increased density of the upper and lower parts of the vertebræ—the "rugger-jersey" appearance.

They are especially marked in patients with tubular defects, even though in these conditions there may be little associated nitrogen retention. Such polyuria may occasionally determine an undue persistence of enuresis.

The past history may be helpful in various ways, especially if revealing a previous illness likely to have been responsible for chronic renal impairment. Long-standing renal dysfunction, present from childhood, may have produced disturbance of growth, the patient having been left behind by his younger siblings. The family history also repays investigation —similar cases in the patient's generation may indicate a Fanconi syndrome—whilst the affection of several generations with similar symptoms directs attention to such possibilities as polycystic disease of the kidneys.

The examination of these patients may afford further information of diagnostic value. Often they show an earthy pallor, in association with an anæmia, though in some cases well-marked brownish pigmentation may be present. This appearance is especially marked where there is tubular dysfunction and electrolyte loss and the pigmentation is essentially similar to that seen in chronic adrenal insufficiency, being well marked in the skin creases, over pressure areas and sometimes affecting mucous membranes. It is of interest to note that patients with renal osteodystrophy are not usually hypertensive, the blood pressure being often normal, or even low. This is perhaps important in the genesis of their disability, as marked skeletal lesions depend for their production on a renal failure of long standing, which is more likely to occur in the absence of hypertension and its complications.

If long-standing renal impairment has been present from childhood proportional dwarfism is the rule, though in some cases surviving puberty the limbs have been described as disproportionately long in comparison with the trunk—perhaps due to inhibition of epiphyseal fusion by some factor associated with chronic renal failure. Where tubular dysfunction presents in middle age, loss of height may be apparent. Further examination may disclose other suggestive features, such as marked bone tenderness, while such features as palpable polycystic kidneys would be of obvious diagnostic importance.

With a suggestive history and corroborative signs as described, the diagnosis may be further confirmed by simple investigations. A simple examination of the urine is of first importance. A dilute urine, containing protein and perhaps glucose, greatly increases the likelihood of a renal cause for vague skeletal pain. The Sulkowitch reaction requires further interpretation in the renal cases, where calcium excretion may be lowered, as in glomerular failure, or raised, as in states where tubular function is abnormal.

Radiography may be of value, though not necessarily so, as pain from bone involvement may be present before visible X-ray changes occur. Where there are clinical grounds for suspecting renal osteodystrophy, a negative X-ray does not abolish the necessity for further biochemical investigation. This does not imply, however, that radiography may not be of the greatest assistance (Dent and Hodson, 1954). Various different bone pictures may be seen, but, in general, the tubular defects as in the Fanconi syndrome are associated with a greater or lesser degree of skeletal rarefaction, and stress fractures are of great diagnostic importance (Fig. 1). Secondary hyperparathyroidism in glomerular failure is usually associated with visible radiological change (Fig. 2) and the interesting bony sclerosis affecting various parts of the skeleton being responsible for the "rugger-jersey" spine seems to be associated with this condition (Fig. 3) (Crawford *et al.*, 1954). Sometimes the X-rays may show a combination of these various changes, as would be expected from previous pathological studies (Gilmour, 1947; Follis and Jackson, 1943; Follis, 1950).

The recognition of renal osteodystrophy in patients with suggestive symptoms mainly depends on the possibility being borne in mind. Confirmation of the diagnosis is not difficult, and is rewarded by the excellent symptomatic response which may follow such measures as large but cautious doses of vitamin D and the correction of an associated acidosis. The diagnosis deserves consideration in all cases where pain of skeletal origin is not explicable on other grounds.

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Professor C. E. Dent (University College Hospital): *Pain in Some Metabolic Bone Diseases Not Due to Steatorrhœa or Renal Failure*

Before describing further types of adult bone disease, I will review briefly our general experience of all types at University College Hospital during the last five years. During this period our metabolic ward has been functioning and nearly all the cases I will mention have been admitted there and have been very thoroughly investigated. This data is summarized in Table I. It will be seen that, apart from steatorrhœa and the various forms of renal

TABLE I.—CASES OF METABOLIC BONE DISEASE (ADULTS) STUDIED IN THE LAST FIVE YEARS IN WHICH THE MAIN COMPLAINT WAS OF GENERALIZED ACHES AND PAINS

Ætiology	Number of cases	Pathognomonic radiological signs present in	Presenting symptoms	Plasma biochemistry abnormal in
Steatorrhœa	10	8	Most of the following: Vague generalized "rheumatic" pains Waddling gait Muscular weakness Pain in low back and/or both thighs Tender ribs Stiffness of joints (rare)	All of these
Renal-glomerular failure	7	6		
Renal-tubular failure	7	5		
"Vitamin-D resistant" osteomalacia	9	7		
True adult vitamin-D deficiency	3	2		
Ureterosigmoidostomy	2	2		
Primary hyperparathyroidism with bone disease	4	4		
Osteogenesis imperfecta tarda	2	0	Low back pain Hip pain	None of these
Idiopathic osteoporosis	7	7	Severe back pain, loss of height, rib fractures	
Senile osteoporosis	innumerable	all	Backache, more rarely rib pain	

failure which have been already discussed by Drs. Rose and Lumb, we have also studied some metabolic bone diseases due to several other causes. The most common is probably that usually described under the name "vitamin-D resistant" osteomalacia. This condition is also associated with a renal-tubule leak for phosphate with few, if any, other signs of renal dysfunction. This group is certainly heterogeneous (Dent and Harris, 1956). Our 3 cases of vitamin-D deficiency require commenting upon. It is hardly possible to believe that this can occur in adults in this country since adult requirements are so small and the general level of nutrition adequate enough. For the same reasons, but with reference to the U.S.A., Albright and Reifenstein (1948) have stated "The authors are cognizant of no single case of osteomalacia in the United States due to simple vitamin-D lack. . . ." However, we have no doubts about the authenticity of our 3 cases and as all of them had reasonable worldly means but suffered only from curious ideas about food, further cases could presumably occur anywhere, even (perhaps especially) in the U.S.A. One of these cases will be mentioned in more detail below: the diet of another with brief clinical details has been described by our dietitian (Hill, 1956) and a brief reference to the third has been made by McCance (1953). As to the other diseases, the bone disease complications of ureterosigmoidostomy and of primary hyperparathyroidism are now well known. Although Table I is made out in the hope of giving some idea of frequency of incidence in the various kinds of bone disease, it is, of course, very inaccurate in this respect, as, apart from their small numbers, there is considerable selection in submitting patients to us.

It will be seen from Table I that the general symptomatology of the further bone diseases I am now introducing is similar to that described by Dr. Rose and Dr. Lumb for the special cases of steatorrhœa and renal dysfunction. Indeed, as far as the particular bone manifestations are concerned there may be no difference at all. However, associated additional findings in the history and clinical examination may be diagnostic. Note especially that in a small proportion of cases the skeletal X-rays appeared quite normal. Some

of these had very severe symptoms. The X-ray changes of the further cases shown in the bracket in Table I, when present, were usually indistinguishable from those in steatorrhœa and renal failure (Figs. 1 and 2A, B). An interesting additional point can, however, be made,

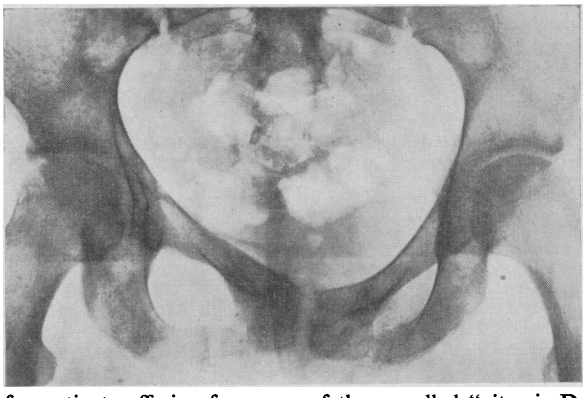

FIG. 1.—Pelvis of a patient suffering from one of the so-called "vitamin-D resistant" forms of osteomalacia. There are Looser zones in both ischiopubic rami and a further small one on the inner rim of the pelvis opposite the right femoral head. The patient was severely crippled by the pain but fortunately was diagnosed before symptoms had been present for long: there is therefore not much deformity. The clinical history of this patient was described by Rose (1956).

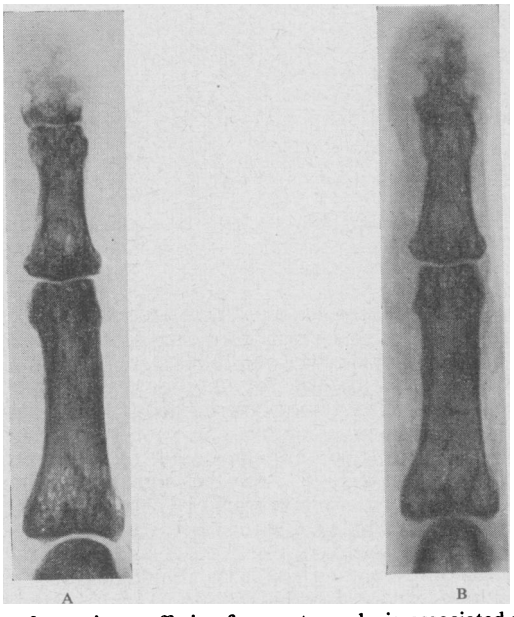

FIG. 2.—Index finger of a patient suffering from osteomalacia associated with neurofibromatosis. In A, taken before treatment with vitamin D began, gross erosion of the terminal phalanx is visible and also subperiosteal erosions in the mid-phalanx, both of which we now interpret as being due to secondary hyperparathyroidism, a rare feature in this form of osteomalacia. In B we see the beginning of reformation of the phalanx after some months' treatment with vitamin D. This patient had also developed an osteoclastoma in her maxilla, which is a further sign of hyperparathyroidism.

namely that mixed osteomalacic and hyperparathyroid changes were comparatively uncommon in any of the ætiologies shown in Table I except in the case of renal-glomerular failure, when they were usually present together. The importance of the plasma biochemistry is well shown. It is mainly by this means that the cases have been diagnosed in the first place. I have also added to Table I three other kinds of bone disease which may also present in somewhat similar ways, although the symptoms are usually less generalized. Unfortunately our treatment for these is much less satisfactory.

Perhaps it would be simpler now to stress the clinical resemblance to steatorrhœa and renal disease, shown by one of these further causes of osteomalacia, by describing the relevant case history:

Mrs. L. R. A housewife, aged 46, referred to me by Dr. Cedric Shaw for investigation of "a great variety of skeletal and muscular pains coupled with increasing lassitude and embellished by a multiplicity of symptoms relevant to every single one of her visceral systems". Dr. Shaw added that she was clearly a very hysterical type of person and that no definite physical signs could be elicited apart from tenderness over the whole thoracic spine and a flinching whenever her abdomen was palpated. There was obvious dramatization and a long history of marital disharmony. X-rays, B.M.R., E.S.R. and full blood count were normal but, "as an afterthought", Dr. Shaw had determinations done of her plasma calcium, phosphorus and phosphatase levels. These showed abnormalities which suggested the possibility of metabolic bone disease being present.

On admission to the metabolic ward we fully confirmed the presence of plasma abnormalities. Her calcium was 8·8 mg./100 ml.; phosphorus 1·8 mg./100 ml.; alkaline phosphatase 20 units (K–A). Other electrolyte levels and blood tests gave normal results. Renal function was normal but urine calcium excretion averaged only about 20 mg./24 hours. Her bone X-rays and fat balance were normal.

Her history was interesting. It began with pain in her left hip twelve years previously: this was treated with heat and massage, but after a brief improvement pains returned and spread also to the right hip. She was otherwise fairly well till two to three years ago, when aches and pains began in other parts—arms, hands, thighs, ankles, chest, and the whole of the spine. Her bones became tender to touch and she suffered particularly from chest pain, especially when turning over in bed at night. To avoid being awakened by involuntary movements during sleep she had had to arrange her bed with bolsters on either side of her. She slept flat on her back in the groove thus formed. Nevertheless, on waking she felt as if she had been "beaten all over". It took her about an hour to get dressed. Her pains prevented her from going shopping or walking freely. She had noted muscular weakness, especially on going upstairs, when she needed to pull herself up by the banisters.

Our diagnosis on the basis of history, clinical and biochemical findings (and in spite of the normal X-rays) was of osteomalacia, but we were much puzzled as to its ætiology; but further study of her history revealed that although she ate well, and indeed looked very well nourished, she had always rigorously avoided fatty foods such as margarine, eggs, milk, oily fishes, &c., and had also avoided exposure to the sun in recent years. We estimated that her chosen diet had contained less than 20 units daily of vitamin D. Our suspicion that her bone disease was due to defective oral intake was subsequently fully confirmed by our studies of her metabolic and clinical changes before and after small oral doses of vitamin D. She is now almost symptom free, although still as peculiar as ever mentally.

Discussion

I hope that by now the point Drs. Rose, Lumb and I are trying to make has been made clear. It is that many cases of metabolic bone disease for which there is excellent treatment may in adults (the equivalent children's diseases usually present first with visible deformity) present with generalized aches and pains, usually rather vaguely localized and without any other obvious clinical features. These patients may be severely disabled, and although the diseases are all uncommon, they are gratifying to diagnose and treat. The problem therefore remaining is the very difficult one of picking out the one or two patients with metabolic bone disease (especially those without gross deformity or body disproportion) from the hundreds of others who also have aches and pains for other reasons. I can only suggest the following course of action as being practicable, as well as reasonably likely to succeed.

In the first place the clinical evolution common to all these cases should be very closely studied and remembered, bearing especially in mind the grave danger that the whole thing may appear to be entirely psychological. If the history is suggestive, and there will be many such cases, I think the urine should be tested routinely for the presence of protein (to pick out the renal cases) and for calcium with the Sulkowitch reagent (to pick out the low calcium excretions of many forms of osteomalacia). In both these cases the problem of urine concentration must be borne in mind for a very dilute urine cannot be properly tested and it is worth getting the patient to return with a morning specimen if necessary. (It is usually sufficient to look at it and only test specimens that appear reasonably yellow.) A case of severe renal damage will, of course, be unable to pass a strongly yellow urine, which in itself should arouse suspicion and be specially looked for. If there is still anything suspicious about the patient's history and preliminary urine tests, then further skeletal X-rays should be done, as well as blood tests, along the lines previously described (Dent, 1956), namely with respect to the plasma calcium, phosphorus, phospatase, bicarbonate and urea levels, and urine calcium output. If any of these are definitely abnormal, full and thorough investigation is justified and will not be too much of a burden since only a very small number of patients will survive this sorting and they will nearly all be genuine cases for whom we can do a great deal by medical treatment.

The treatment of these cases may sound surprisingly simple. It mainly comprises vitamin D with or without alkalis. There are serious dangers, however, of wrong dosage, the

required amounts varying considerably from case to case. Patients receiving treatment must therefore be carefully supervised. There is sufficient in the literature already about the treatment of steatorrhœa and of renal-tubular osteomalacia (Albright and Reifenstein, 1948). The renal-glomerular cases are more difficult and are not adequately covered as yet. We have considerable unpublished work on this subject which awaits longer follow-up of our cases. The treatment of so-called "vitamin-D resistant" ones has been reviewed recently by Dent and Harris (1956). There is still some doubt as to whether all the cases can, as we ourselves believe, be cured; and indeed Brailsford (1952) has described a case of typical osteomalacia that could not be cured with vitamin D, coining for it the new name of "osteogenesis exhausta". We have not yet come across such a case ourselves.

This review does not include all known causes of metabolic bone disease. Many interesting further examples such as that, for instance, following partial gastrectomy (Pyrah and Smith, 1956), or chronic liver disease (Atkinson *et al.*, 1956), or neurofibromatosis (Swan, 1954) have been briefly described already or are currently being further investigated. We have deliberately made no mention of other endocrine disorders such as Cushing's syndrome, acromegaly or eunuchoidism, all of which may present occasionally with pain due to bone disease. There is usually, however, in these cases much to take note of that would lead the patient to be first referred to an endocrinologist or general physician. Our attempt in this symposium was to describe cases very likely to be referred for treatment to Physical Medicine departments in view of the fact that the associated features which could lead to a correct diagnosis may require considerable looking for, and are never obvious at sight.

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SUMMARY

(1) Osteomalacia may be a cause of severe, vaguely localized, generalized aches and pains in a patient not otherwise presenting notable clinical signs. While osteomalacia of a particular ætiology may be rare, there are many different ætiologies which together provide us with a moderate number of cases.

(2) An attempt has been made to define more closely the clinical features of osteomalacia. The history may sometimes be characteristic and the X-ray signs often pathognomonic and accompanied by the signs considered specific for hyperparathyroidism.

(3) Whatever the ætiology, the clinical signs and skeletal X-rays may be indistinguishable.

(4) The existence of occult forms of renal failure and steatorrhœa presenting only as osteomalacia is stressed.

(5) In all these cases the bone disorder and associated symptoms can be cured independently of the progress of the renal or other disease.

(6) Rough methods are suggested for distinguishing these cases from the large number of other patients with aches and pains.