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Osteoporosis in childhood

C. E. DENT*
Ph.D., F.R.C.P., F.R.S.

Department of Human Metabolism, University College Hospital Medical School, London

Summary

Osteoporosis is defined as 'too little normal bone', the disorder being rarer in children than adults. The varied forms in childhood can be classified as those secondary to some other disease and primary forms of the disorder which include the genetically determined osteogenesis imperfecta types and idiopathic forms of osteoporosis. A plea is made for greater clinical application in attempting to discriminate differing forms of these primary disorders. Osteogenesis imperfecta it is argued is a heterogeneous condition with the evidence favouring both dominantly and recessively transmitted forms in different kindreds. Another possible osteogenesis imperfecta variant is characterized by dwarfing, scoliosis and peculiar cystic lesions of the proximal humeri. Idiopathic juvenile osteoporosis is a term reserved for the acute osteoporosis beginning in the immediate prepubertal years and may differ in its cause from idiopathic osteoporosis beginning rather earlier in childhood. It is emphasized that immobilization osteoporosis is of very great importance and may become superimposed upon other osseous dysplasias. A complete understanding of these conditions will be helped by elucidation of the basic underlying defects in collagen and other constituents of bone matrix.

ALTHOUGH osteoporosis in children is complex it is somewhat easier to recognize than in adults among whom it is much commoner and often associated with advanced age, post-menopausal changes and other factors. Being rarer, one's experience of osteoporosis in childhood is more restricted than in adults. Fortunately in children it is easily differentiated from the calcification defect of vitamin D deficiency because of the characteristic clinical and radiological features of rickets. In adults, osteoporosis and osteomalacia are more difficult to distinguish and radiologists examining radiographs will sometimes use the expressions 'a decalcified skeleton' or 'malacic bones' and it is quite uncertain what they actually mean.

Correspondence: Dr D. P. Brenton, Rayne Institute, University College Hospital, Medical School, London WC1.

*Professor C. E. Dent died September 1976. After his death this paper was written by Dr D. P. Brenton based on the transcript of Professor Dent's presentation at Bristol.

Osteoporosis is defined as 'too little normal bone' whether in a child or an adult. When there is deficiency of normal bone the pathogenesis is presumably too little matrix formation as suggested by Albright (1947). Such matrix that is laid down is normally calcified and matures to form histologically typical bone but is deficient in amount and distribution. This does not produce a striking or diagnostic histological picture, hence the great importance of radiographs especially as they permit studying the whole skeleton as well as an isolated bone. Bone matrix is a complex mixture of proteins and other substances, but is mainly collagen. It presents analytical problems for the clinician and biochemist, but work is well under way in several centres assessing certain properties of collagen, e.g. solubility and amino-acid content which may differ in various forms of osteoporosis (Bauze, Smith and Francis, 1975; Smith, Francis and Bauze, 1975).

There are no specific simple biochemical changes yet described in plasma or urine which are diagnostically helpful in osteoporosis. Since histology is not very helpful either, radiological and clinical differentiations are all important. The classification of osteoporosis in childhood (Table 1) needs refining. The need to identify well defined and homogeneous groups within the spectrum of osteoporosis is the main plea and purpose of this paper. The need is becoming pressing in several ways. Clinically, for example, it is necessary in differentiating that distressing social and medico-legal problem, the 'battered child', from the child with osteogenesis imperfecta. It is necessary for the improvement of genetic and prognostic advice and it is needed in the evaluation of treatment which may be effective in one kind of osteogenesis imperfecta and not in another. Finally, it is needed for the proper correlation of clinical features with sophisticated biochemical and biophysical studies on the constituents of bone matrix.

Osteogenesis imperfecta

This is a lifelong heritable syndrome almost certainly embracing several distinct types. The very

TABLE 1. Classification of osteoporosis in childhood: 'Fragilitas ossium'

1. Lifelong heritable syndromes	Osteogenesis imperfecta
2. Idiopathic juvenile osteoporosis	
3. Chronic acquired syndromes	Biliary atresia Cyanotic heart disease Other
4. Acute acquired syndromes	Immobilization
5. Acquired metabolic causes	Thyrotoxicosis Cushing's syndrome, Spontaneous and iatrogenic Calcium lack Scurvy
6. Neoplastic causes	Leukaemia Primary and secondary malignancy

variable clinical severity and differing radiological features are such that there might ultimately prove to be as many as six distinct forms. The commonest and best known form is inherited as a dominant associated with blue sclerae and, in some patients, deafness in later life. The clinical course is devoid of marked fluctuations but fractures are less frequent after puberty. Fractures do not usually occur until after birth and the severity is variable. The term 'osteogenesis imperfecta tarda' is descriptive of this onset of fractures after birth and should not be used as a term identifying osteogenesis with blue sclerae. Occasionally in families with osteogenesis imperfecta and blue sclerae fractures may be present in children at birth, so-called 'osteogenesis imperfecta congenita'. However, most children with fractures at birth do not have a family history and probably represent different forms of the disease.

Fairbank (1951) classified osteogenesis imperfecta (OI) with fractures at birth as either the thick bone type or the slender bone type. The former presents with short wide bones of extremely thin cortex and with multiple fractures, many probably occurring *in utero* (Fig. 1). Multiple rib fractures are associated with respiratory difficulties leading to an early death. The slender bone type presenting with multiple birth fractures may have a better prognosis and some may survive to adult life and employment. The skull vault at birth may be extremely thin and soft, rapidly ossifying in a month or so (Figs 2, 3). The tam-o'-shanter skull (Fig. 4) with the characteristic inverted triangular facies (see McKusick, 1972 for illustration) is a gross skull deformity probably arising from the soft skull of infancy. Its presence probably indicates survival from the less lethal slender bone form of osteogenesis imperfecta

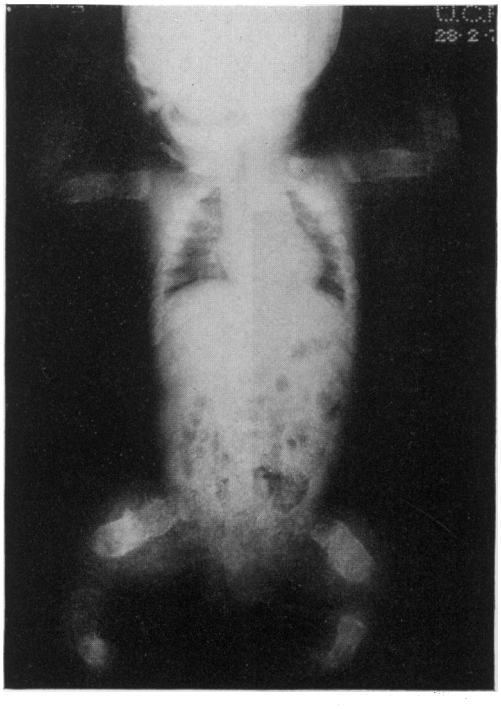

FIG. 1. Osteogenesis imperfecta congenita—thick bone type.

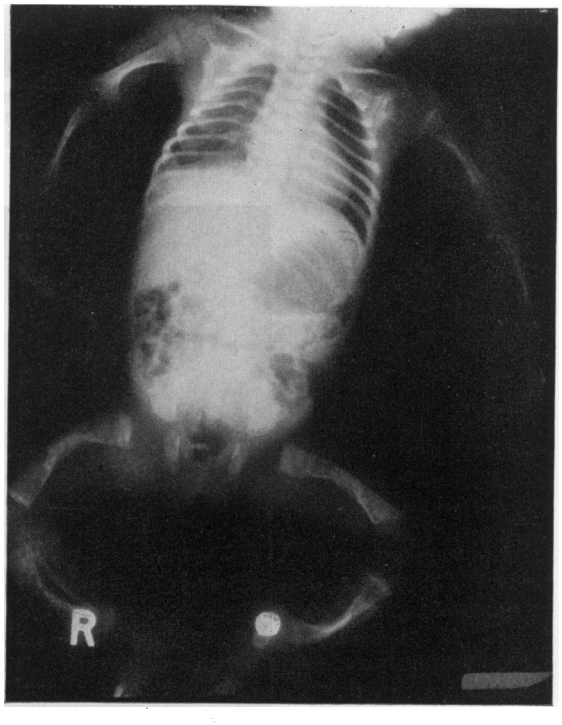

FIG. 2. Osteogenesis imperfecta congenita—thin bone type.

congenita. Two of the author's adult patients had this skull deformity with blue sclerae and lax ligaments. When there is no family history such patients may be new mutations of the dominant OI form with blue sclerae. However, that may not be true of all slender bone forms of osteogenesis imperfecta congenita and the thick bone type is very probably a separate genetic entity.

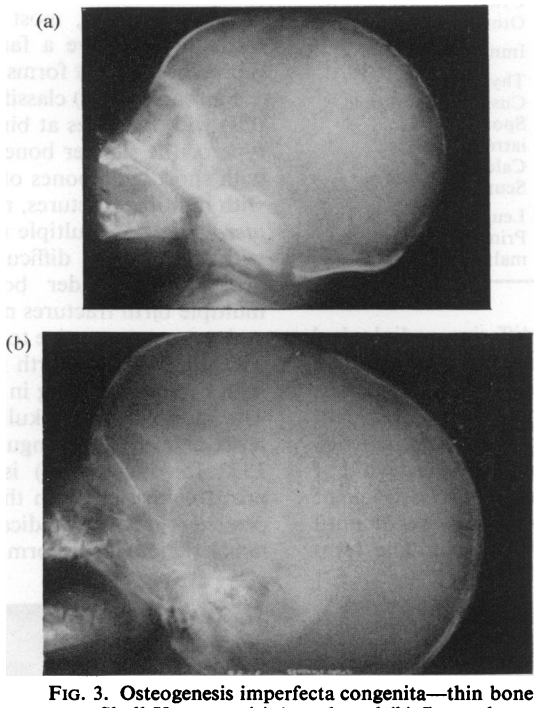

FIG. 3. Osteogenesis imperfecta congenita—thin bone type. Skull X-rays at (a) 1 week and (b) 7 months to show the very thin skull at birth which then rapidly ossifies.

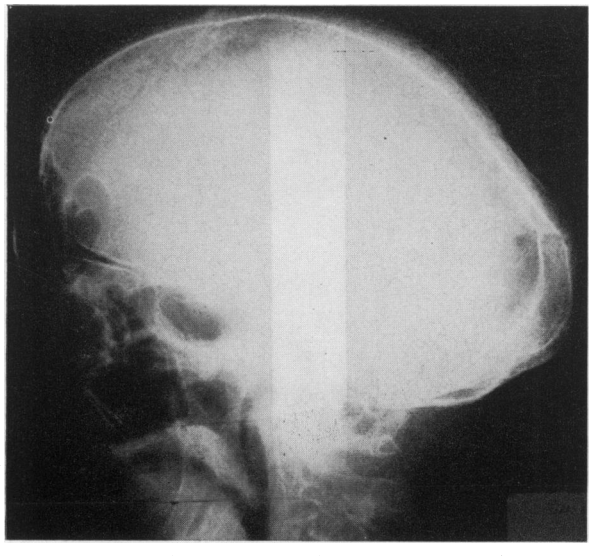

FIG. 4. Osteogenesis imperfecta with blue sclerae. Classical skull deformity presumably reflecting a very soft skull at birth.

Another possible variant of OI is a severe form of the disease with white sclerae, multiple fractures, gross bone changes, severe dwarfing and marked scoliosis. The teeth are transparent and yellowish in colour. Death usually occurs at an early age from respiratory infection. Four such patients have been seen at University College Hospital (UCH). All had normal parents and the inheritance may be recessive. In one of these patients with the most severe growth retardation, rounded almost cystic structures were seen at the proximal ends of the humeri (Fig. 5). This may be a separate disease. Fairbank (1951) illustrated similar abnormalities of the proximal extremities of the humeri and femora but with no specific comment. It is not the condition he referred to as 'osteogenesis imperfecta cystica' in which the lesions were more widely distributed. The clinical details of these four patients are emphasized to indicate that they are different from the commoner dominant form of the disease.

Apart from the possible varieties of osteogenesis imperfecta described above there may be yet others. These might include two forms unusual in showing more than the expected degree of recovery, one relatively mild and one much more severe. This suggestion is based on only two cases from UCH, so presumably both would be uncommon.

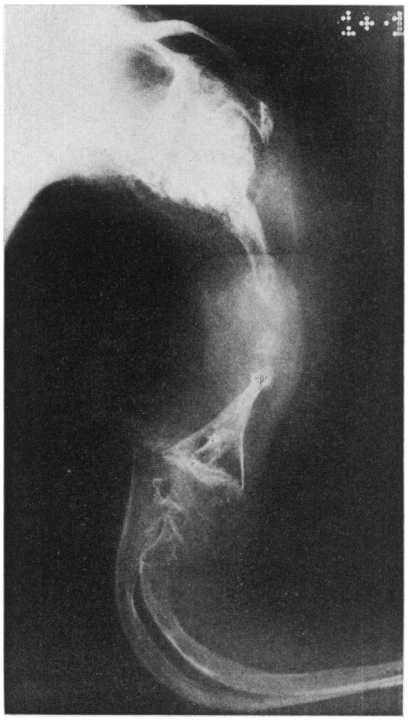

FIG. 5. Osteogenesis imperfecta. Severe form with white sclerae, gross dwarfism, scoliosis and abnormal teeth. Note the unusual changes around the upper end of the humerus.

Idiopathic juvenile osteoporosis

There is a distinct group of children who develop acute osteoporosis 2 or 3 years before puberty and who tend to improve spontaneously during their

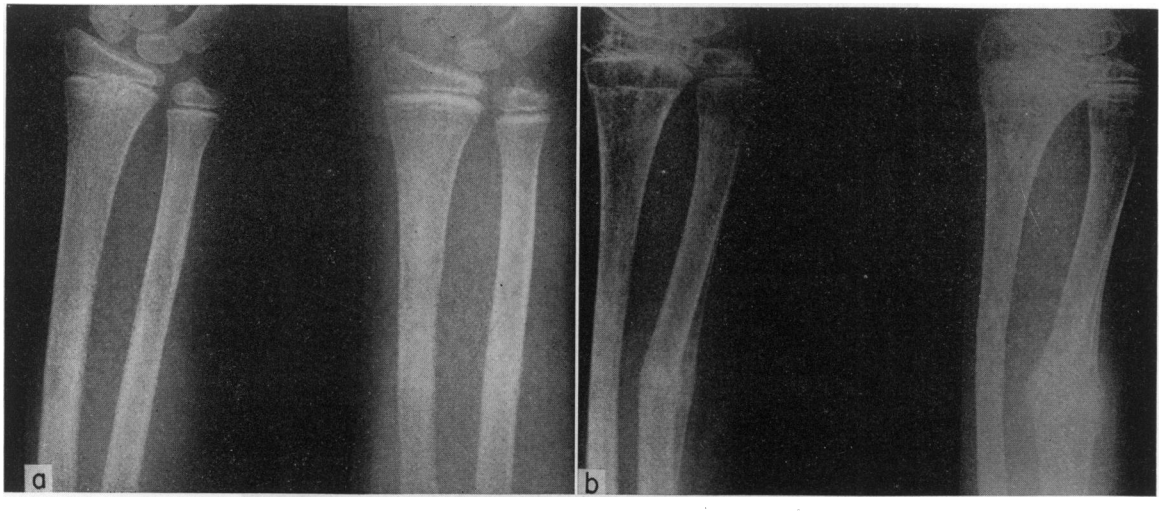

FIG. 6. Idiopathic juvenile osteoporosis. Serial X-rays of the same forearm and wrist. (a) March 1956 (L) December 1956 (R). (b) December 1957 (L) and March 1968 (R). The first X-ray is essentially normal. The second shows a translucent band across the distal metaphyses of radius and ulna (neo-osseous porosis). Osteoporosis is gross in the third film and recovering in the fourth.

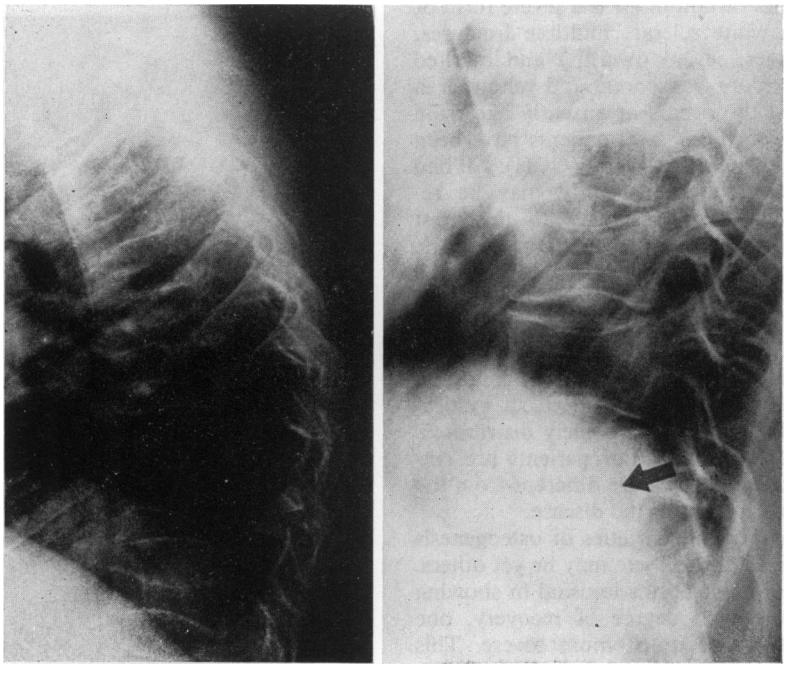

FIG. 7. Idiopathic juvenile osteoporosis. Extensive vertebral collapse with subsequent improvement.

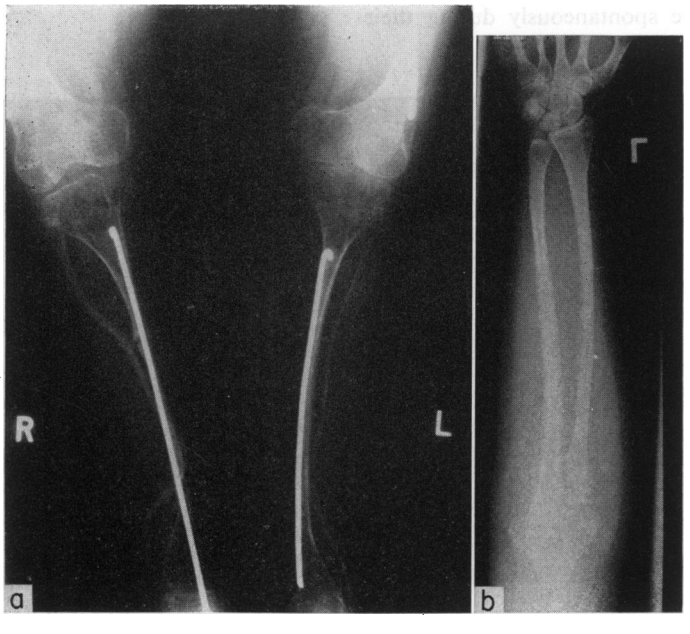

FIG. 8. Osteogenesis imperfecta. The X-ray appearances are much more severe in the legs (a) than the arms (b) most probably as a result of immobilization of the legs due to fractures and surgery.

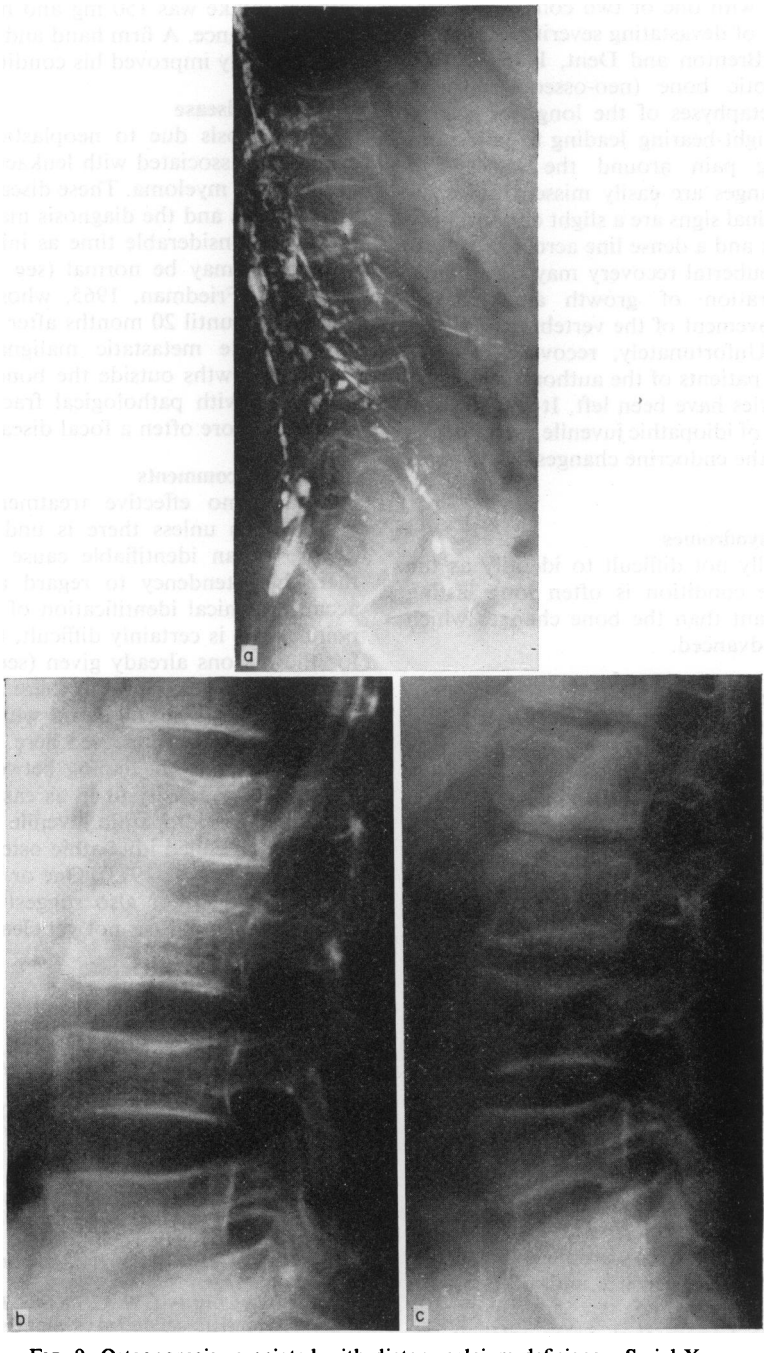

FIG. 9. Osteoporosis associated with dietary calcium deficiency. Serial X-ray of the spine ((a) May 1958; (b) August 1961; and (c) April 1964) showing severe osteoporosis with vertebral collapse and gradual improvement.

later pubertal development. The osteoporosis may be relatively mild with one or two collapsed vertebrae, or it may be of devastating severity (Dent and Friedman, 1965; Brenton and Dent, 1976). Newly formed osteoporotic bone (neo-osseous porosis, Fig. 6) in the metaphyses of the long bones may collapse when weight-bearing leading to impaction fractures, causing pain around the knees and ankles. These changes are easily missed radiologically, but the cardinal signs are a slight discontinuity of the bone cortex and a dense line across the metaphysis. The late pubertal recovery may be remarkable with restoration of growth and marked radiological improvement of the vertebrae and long bones (Fig. 7). Unfortunately, recovery has not been good in two patients of the author's series and crippling deformities have been left. It seems likely that the causation of idiopathic juvenile osteoporosis is bound up with the endocrine changes of the onset of puberty.

Chronic acquired syndromes

These are usually not difficult to identify as the primary causative condition is often long lasting and more important than the bone changes which are seldom very advanced.

Acute acquired syndromes

Immobilization is a well known cause of osteoporosis, but it is not so universally appreciated that the bone changes can develop very rapidly when there is some underlying intrinsic skeletal disorder. Several cases have been seen in which this has been striking when superimposed upon osteogenesis imperfecta and this may cause diagnostic confusion (Fig. 8). Immobilization certainly aggravates idiopathic juvenile osteoporosis just as it aggravates osteoporosis in adult life.

Acquired metabolic causes

Osteoporosis occurs in thyrotoxicosis but has never been the presenting feature of the endocrine disorder in the author's experience with one odd exception. A 5-year-old boy treated for cretinism had been chronically overdosed with thyroid by his mother in a well intentioned attempt to secure normal mental development. When first seen he had fragile bones owing to osteoporosis. It is much more common to see osteoporosis complicating steroid treatment of asthma or eczema and of course it occurs in Cushing's syndrome.

It is not widely known that gross calcium deficiency during the growth period may lead to osteoporosis and not to rickets. It is extremely uncommon but was observed in a 6-year-old boy who had been seen by many neurologists for difficulty with walking. Radiographs of his spine revealed striking osteoporosis (Fig. 9). His total daily calcium intake was 150 mg and he was in negative calcium balance. A firm hand and adequate calcium intake greatly improved his condition.

Neoplastic disease

Osteoporosis due to neoplastic disease is most commonly associated with leukaemia or lymphoma or in adults, myeloma. These diseases can present as osteoporosis and the diagnosis may not be detected for some considerable time as initial bone marrow aspirations may be normal (see case David L. of Dent and Friedman, 1965, whose leukaemia was not evident until 20 months after the onset of back pain). While metastatic malignant disease from primary growths outside the bone marrow may be associated with pathological fractures, the disease is usually more often a focal disease.

Concluding comments

Because no effective treatment is known for osteoporosis unless there is underlying neoplastic disease or an identifiable cause such as steroids, there is a tendency to regard attempts at more accurate clinical identification of the syndromes as pointless. It is certainly difficult, but it is necessary for the reasons already given (see introduction). It should be pointed out that there are certainly cases of osteoporosis in childhood which are difficult to fit in the classification used here. Some generalized cases, apparently beginning between 3 and 8 years of age, do not easily fit in as cases of osteogenesis imperfecta or idiopathic juvenile osteoporosis, and can only be called idiopathic osteoporosis of childhood (Kooh *et al.*, 1973). One or two other patients seen by the author also suggest strange forms of localized osteoporosis not yet clearly defined.

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