Osteoporosis in childhood

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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.

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'

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
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<tbody>
<tr>
<td>1. Lifelong heritable syndromes</td>
<td>Osteogenesis imperfecta</td>
</tr>
<tr>
<td>2. Idiopathic juvenile osteoporosis</td>
<td>Biliary atresia</td>
</tr>
<tr>
<td>3. Chronic acquired syndromes</td>
<td>Cyanotic heart disease</td>
</tr>
<tr>
<td></td>
<td>Other</td>
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<tr>
<td>4. Acute acquired syndromes</td>
<td>Immobilization</td>
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<tr>
<td>5. Acquired metabolic causes</td>
<td>Thyrotoxicosis</td>
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<tr>
<td></td>
<td>Cushing's syndrome, Spontaneous and iatrogenic</td>
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<tr>
<td></td>
<td>Scurvy</td>
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<tr>
<td>6. Neoplastic causes</td>
<td>Leukaemia</td>
</tr>
<tr>
<td></td>
<td>Primary and secondary malignancy</td>
</tr>
</tbody>
</table>

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.

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**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.

![Figure 3](image1.png)

**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.

![Figure 4](image2.png)

**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.

**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. 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 verte-
brae, 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 radiologi-
cally, but the cardinal signs are a slight discontinuity
of the bone cortex and a dense line across the meta-
physis. The late pubertal recovery may be remark-
able 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 osteo-
porosis, 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 idio-
pathic 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 Cushings syndrome.

It is not widely known that gross calcium de-

iciency 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
calium intake was 150 mg and he was in negative
calium 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
only be called idiopathic osteoporosis of child-
hood (Kooch 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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