

## Clinical and subclinical vitamin D deficiency in Bradford children

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*From the Divisions of Paediatrics and Medicine, Stobhill General Hospital, Glasgow; Children's Hospital and Environmental Health Division, Bradford; and Department of Medicine, Middlesex Hospital, London*

**Ford, J. A., McIntosh, W. B., Butterfield, R., Preece, M. A., Pietrek, J., Arrowsmith, W. A., Arthurton, M. W., Turner, W., O'Riordan, J. L. H., and Dunnigan, M. G. (1976).** *Archives of Disease in Childhood*, 51, 939. **Clinical and subclinical vitamin D deficiency in Bradford children.** A survey of the vitamin D status of Bradford schoolchildren was carried out in April 1973, employing conventional biochemistry, radiology, and measurement of 25-hydroxycholecalciferol levels. Biochemical evidence of rickets was present in 45% of the Asians. When re-examined in September, several children showed spontaneous biochemical resolution; nevertheless, radiological abnormalities were present in 12% of the original sample. No evidence of rickets was detected in the smaller White sample. Minor biochemical abnormalities were present in 9 of the 40 West Indian children.

A study of admissions to Bradford hospitals in the 4 years 1969-1972 inclusive confirmed that clinical vitamin D deficiency was confined to Asians except for a few cases of infantile rickets in White children. The probability that one Asian child in 40 may require admission during the period from birth to adolescence emphasizes the urgent need for the introduction of prophylactic measures.

Rickets and osteomalacia affecting Asian immigrants were first encountered in Glasgow in 1961 (Dunnigan *et al.*, 1962). Subsequent reports have confirmed that these conditions are common among Asians in Britain (Ford *et al.*, 1972; Holmes *et al.*, 1973; Cooke *et al.*, 1973). Neonates (Ford *et al.*, 1973; Moncrieff and Fadahunsi, 1974), infants (Arneil and Crosbie, 1963), adolescents, and pregnant women (Felton and Stone, 1966) are particularly affected. With one exception (Cooke *et al.*, 1973), significant vitamin D deficiency has not been reported outside infancy in otherwise healthy West Indian and White children.

We examined the prevalence of vitamin D deficiency among older children in the Bradford Asian community, the largest in the United Kingdom. Levels of circulating 25-hydroxycholecalciferol (25-OH-D) were measured as a sensitive index of vitamin D status in addition to conventional radiology and biochemistry. Hospital admissions with rickets were examined over a 4-year period as

a measure of the incidence of the more severe forms of the disease. A subsidiary aim of the study was to look for evidence of vitamin D deficiency in smaller samples of West Indian and White schoolchildren in Bradford using the same criteria.

### Subjects and methods

**Survey of hospital admissions.** With the consent of the consultants concerned, the case records of admissions with the diagnosis of rickets to all Bradford hospitals in the years 1969-72 inclusive were obtained for scrutiny from Leeds Regional Hospital Board. Multiple admissions and cases of rickets secondary to renal disease and malabsorption were excluded. Estimated numbers of Asian children from 0-16 years of age in Bradford were obtained from the Public Health Department and hospital admission rates for rickets calculated.

**Survey of schoolchildren.** After informed parental consent, 10 ml venous blood was taken from 156 Asian children (105 boys, 51 girls) attending Bradford schools in May 1973. Similar samples were taken from 40 West Indian children (20 boys, 20 girls) and 35 White children

(14 boys, 21 girls). The children, aged from 9 to 16 years, were selected at random from school registers and were in apparently good health. None admitted to taking any form of medication. 40 of the children in whom biochemical abnormalities had been shown were re-examined in Bradford Children's Hospital in September 1973 when they had a further venepuncture and x-rays of the wrists and knees. Those with radiological or biochemical abnormalities were then treated with vitamin D.

Blood samples were separated within one hour of withdrawal and the sera stored at  $-20^{\circ}\text{C}$ . Serum Ca, inorganic P, and alkaline phosphatase were estimated on a Technicon Auto Analyser. Based on a study of normal children and adolescents, the range of uncorrected serum Ca in our laboratory is 9–10.8 mg/100 ml (2.2–2.7 mmol/l) (95% confidence limits). No correction was made for serum albumin as the mean values of the three ethnic groups have been shown to be similar (Watney *et al.*, 1970). In the absence of comparable data for West Indian and Asian children, normal ranges for serum P and alkaline phosphatase were taken from the age- and sex-related data of Round (1973). While derived from White London schoolchildren, there is no evidence to suggest differences in either the age or rate of onset of pubertal changes between the three ethnic groups. Serum 25-OH-D was estimated by a competitive protein binding assay (Preece *et al.*, 1974). Based on a previous study of normal White children and adults living in London and Glasgow, the normal range was taken as 3.8–32.8 ng/ml (Preece *et al.*, 1975).

## Results

**Survey of hospital admissions.** In the 4-year period 1969–72, 22 Asian and 10 White infants (0–3 years inclusive) were admitted with nutritional rickets. No West Indian infants were admitted, though infantile rickets has been found previously in this ethnic group in Bradford (Dawson and Mondhe, 1972). Hospital admissions with late rickets occurring between 9 and 16 years of age were confined to Asian children. 23 children in this age range were admitted with rickets; 18 had rachitic deformity sufficient to require osteotomy. Based on the estimated Asian child population of Bradford at the time of the survey, the hospital admission rate for infantile rickets was 5.7/1000 infants per annum, and for late rickets 1.5/1000 children per annum.

**Survey of schoolchildren.** In May 1973, a high proportion (45%) of Asian children showed abnormalities of serum Ca, P, or alkaline phosphatase (Fig. 1A, B, C). In contrast, no White child was biochemically abnormal. 9 West Indian children showed abnormal alkaline phosphatase levels, while borderline hypocalcaemia was found in one child (8.9 mg/100 ml; 2.2 mmol/l). The mean level of serum Ca was significantly lower in

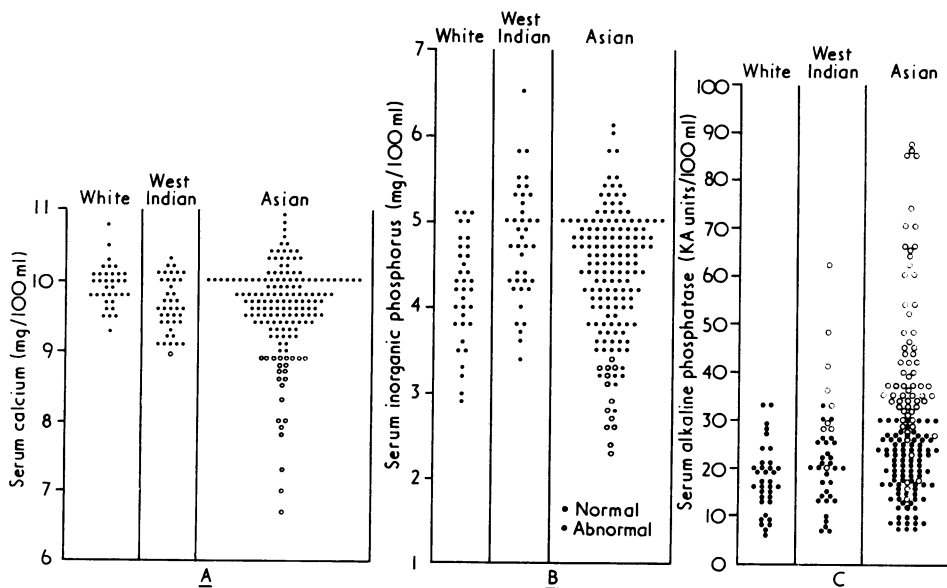


FIG. 1.—(A) Serum calcium, (B) inorganic phosphorus, (C) alkaline phosphatase levels in White, West Indian, and Asian children. Conversion factors: Traditional to SI units—Calcium: 1 mg/100 ml  $\approx$  0.25 mmol/l. Phosphorus: 1 mg/100 ml  $\approx$  0.323 mmol/l.

TABLE I

Serum calcium, inorganic phosphorus, alkaline phosphatase, and 25-hydroxycholecalciferol (25-OH-D) levels in Bradford children

|                            | Serum calcium<br>(mg/100 ml)<br>Mean $\pm$ SEM | Serum inorganic<br>phosphorus<br>(mg/100 ml)<br>Mean $\pm$ SEM | Serum alkaline<br>phosphatase<br>(KA units/100 ml)<br>Mean $\pm$ SEM | Serum 25-OH-D<br>(ng/ml)<br>Mean $\pm$ SEM |
|----------------------------|--|--|--|--|
| White (n=35)<br>(1)*       | 9.93 $\pm$ 0.05<br>NS                          | 4.19 $\pm$ 0.10<br>P < 0.001                                   | 17.62 $\pm$ 1.18<br>P < 0.01   | 15.10 $\pm$ 0.94<br>P < 0.001              |
| West Indian (n=40)<br>(2)* | 9.64 $\pm$ 0.05<br>NS                          | 4.75 $\pm$ 0.11<br>P < 0.01                                    | 22.75 $\pm$ 1.76<br>P < 0.01   | 9.59 $\pm$ 0.73<br>P < 0.001               |
| Asian (n=156)<br>(3)*      | 9.59 $\pm$ 0.05<br>P < 0.01                    | 4.37 $\pm$ 0.06<br>NS  | 29.81 $\pm$ 1.34<br>P < 0.001  | 5.23 $\pm$ 0.37<br>P < 0.001               |

\*Student's 't' test: (1) White—West Indian; (2) West Indian—Asian; (3) White—Asian.

Note: For conversion factors from traditional units to SI for calcium and phosphorus, see legend to Fig. 1.

Asian children than in White children, while that of serum alkaline phosphatase was higher (Table I). The mean serum Ca in West Indian children did not differ from that in White or Asian children. Serum alkaline phosphatase levels were significantly higher in West Indian children than in White children and lower than in Asian children. Curiously, serum P levels were significantly higher in West Indian children than in either the White or Asian groups. No differences related to age, sex, or religion were found within or between the racial groups.

The mean serum 25-OH-D levels were lowest in Asian children and highest in White children, but were intermediate in the West Indian group. The mean values were significantly different from one another (Fig. 2, Table I). Of 139 Asians in

whom serum 25-OH-D levels were measured, 57 (41%) had very low levels < 3.8 ng/ml. 4 Asian children with subnormal levels of serum Ca and P, including 3 with radiological rickets, had serum 25-OH-D levels (3.9–4.4 ng/ml) in excess of the lower limit of our derived normal range. As noted by Mawer *et al.* (1975), the presence of rickets or osteomalacia cannot be equated with particular absolute levels of serum 25-OH-D. No White child had an abnormal serum 25-OH-D level but 2 West Indian children with normal biochemistry had levels below the lower limit of the normal range (both 3.5 ng/ml). Levels of serum 25-OH-D in 8 West Indians with raised alkaline phosphatase levels ranged from low normal (4.7 ng/ml) to well within the normal range (14.8 ng/ml).

Levels of serum Ca, P, and alkaline phosphatase improved in the 40 Asian children with abnormal biochemistry re-examined in September 1973 (Table II). In 9 children biochemical values returned to normal. Of the 30 children for whom paired 25-OH-D values were available, 15 were below 3.8 ng/ml in April while only 8 remained below this level in September. Despite this biochemical improvement, 20 of the Asians investigated in September (12% of the original sample), showed unequivocal radiological evidence of active or healing rickets. Of 5 West Indian children re-examined in September, none was found to have radiological changes of rickets.

### Discussion

In evaluating the severity of vitamin D deficiency in an ethnic group of population it is important to distinguish between clinically overt rickets and osteomalacia, and subclinical vitamin D deficiency as judged by conventional criteria, and,

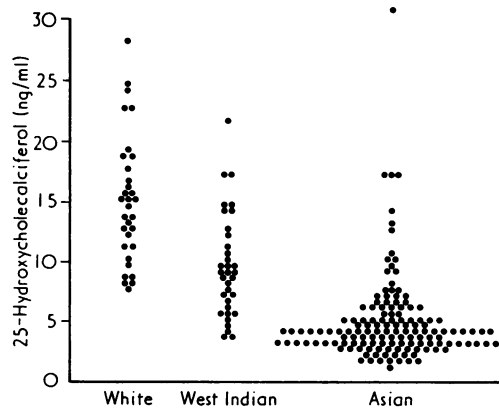


FIG. 2.—Serum 25-OH-D levels in White, West Indian, and Asian children.

TABLE II

*Seasonal variation in serum calcium, inorganic phosphorus, alkaline phosphatase, and 25-hydroxycholecalciferol (25-OH-D) levels*

|                      | Serum calcium<br>(mg/100 ml)<br>Mean $\pm$ SEM | Serum inorganic<br>phosphorus<br>(mg/100 ml)<br>Mean $\pm$ SEM | Serum alkaline<br>phosphatase<br>(KA units/100 ml)<br>Mean $\pm$ SEM | Serum 24-OH-D<br>(ng/ml)<br>Mean $\pm$ SEM |
|----------------------|--|--|--|--|
| April 1973<br>(n=40) | 9.28 $\pm$ 0.09<br>P < 0.001                   | 4.14 $\pm$ 0.19<br>P < 0.001                                   | 40.07 $\pm$ 2.63<br>P < 0.001  | 4.20 $\pm$ 0.36<br>P < 0.001               |
| September 1973       | 9.82 $\pm$ 0.06                                | 4.55 $\pm$ 0.15  | 34.65 $\pm$ 2.38   | 7.31 $\pm$ 0.69                            |

more recently, by serum 25-OH-D concentrations.

The survey of admissions to Bradford hospitals over a 4-year period provided a crude measure of the incidence of the more severe forms of infantile and late rickets among Bradford children and has shown that this is overwhelmingly an Asian problem. A few cases of infantile rickets were found in White children, while the West Indian community contributed no hospital admissions in the period studied. Based on the hospital admission rates quoted above, approximately one Bradford Asian child in 40 can expect admission to hospital with rickets between birth and 16 years of age. Comparable figures calculated from a survey of admissions with rickets to Glasgow hospitals in the years 1969–71 inclusive indicate that approximately one Glasgow Asian child in 25 may be hospitalized with infantile or late rickets up to 16 years of age.

Cases of Asian rickets requiring hospital admission represent the tip of a much larger iceberg of vitamin D deficiency, the extent of which is measured by the finding of abnormal biochemistry or abnormally low serum 25-OH-D levels in approximately one Asian schoolchild in 2 in Bradford in the spring of 1973. Vitamin D deficiency was considerably ameliorated by increased exposure to ultraviolet light over the summer months as described previously by Gupta, Round, and Stamp (1974). Despite this improvement, one Asian child in 10 showed radiological rickets in the autumn of 1973 while a significant proportion continued to show biochemical rickets and low serum concentrations of 25-OH-D.

As judged by a few children with serum 25-OH-D levels at the lower limit of normal, the West Indian sample showed some evidence of borderline vitamin D deficiency. Whether the intermediate vitamin D status of Bradford West Indian children *vis-à-vis* their Asian and White counterparts is representative of this ethnic group in the country as a whole is at present unclear, since no other studies of serum 25-OH-D levels in West Indian subjects have been

reported. Cooke *et al.* (1973) reported no difference in the incidence of raised alkaline phosphatase levels in West Indian and White schoolchildren in Birmingham. Holmes *et al.* (1973) reported no clinical experience of overt rickets in West Indian children in Lancashire but did not include a sample in their Rochdale survey.

The small sample of White children showed no abnormality of any parameter of vitamin D deficiency. Evidence for such deficiency in older White children in the United Kingdom is conflicting and difficult to interpret, again because of the absence in earlier studies of serum 25-OH-D levels. Dunnigan and Gardner (1965) found that a small number of White children living in central Glasgow had slightly raised serum alkaline phosphatase and subnormal levels of serum inorganic phosphorus and concluded that these represented evidence of mild vitamin D deficiency; a comparable group of semirural schoolchildren examined at the same time showed no biochemical abnormality. Holmes *et al.* (1973) found similar abnormalities in a group of White schoolchildren in Rochdale and reached similar conclusions. On the other hand, no such abnormalities were shown in a large group of London schoolchildren whose exposure to ultraviolet light was almost certainly greater than that of children living in Rochdale or Glasgow. Cooke *et al.* (1973) have reported a much higher incidence of raised alkaline phosphatase levels in Birmingham schoolchildren, irrespective of race, than in other surveys. On balance, most currently available evidence would suggest that a variable minority of older White and West Indian children may suffer from a mild degree of vitamin D deficiency during the adolescent growth spurt. In the present United Kingdom situation of marginal vitamin D self-sufficiency, this finding is perhaps not surprising.

In marked contrast, the situation in the Asian community is of a different order of magnitude. A significant minority of Asian children develop severe rickets in infancy and adolescence. Similar-

ly, a significant minority of Asian women develop osteomalacia during pregnancy and give birth to children with neonatal rickets or hypocalcaemic tetany. A much larger number of Asian children suffer lesser degrees of disability, characterized mainly by limb pains of varying degrees of severity; in many of these children the diagnosis of rickets is never made. Unless measures to increase the vitamin D intake of the Asian community are implemented, the clinical reports of Asian rickets which have appeared over the last decade will continue unabated as a distressing reminder of a failure of preventive medicine.

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