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SYMPOSIUM ON 'OSTEOMALACIA AND RICKETS'

Nutritional rickets in children in Glasgow

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Descriptions of infantile rickets were attributed to Homer in 900 BC and to Hippocrates but Findlay (1917) dismissed these claims as unproven. Soranus Ephesius (*c.* 130 AD) is credited with the classical description of rickets, referring to 'the backbone bending' and 'legs twisted at the thighs' in a disease noted to be commoner in smoky cities than in the country. Later, in Leyden in 1645, Daniel Whistler drew attention to rickets in a dissertation '*De morbo puerili Anglorum*' (Whistler, 1645), which probably led to the later eponym for rickets of 'Die englische Krankheit' (the English disease). The classical English description by Glisson (1650) provided not only a monument to English medicine, but a graphic warning of the potential perils of runaway inflation, debasement of the currency, depression and collapse of export markets in the 17th century. A wage-freeze as the price of food rose rapidly led to widespread poverty, undernutrition and rickets. It all sounds very topical.

By the 17th century the disease was recognized in the west of Scotland, and the value of treatment with cod-liver oil was known: this was used as what must have been a truly nauseous medication. By 1807 cod-liver oil had been used in England for the treatment of malacosteon (osteomalacia) and was the subject of a book by Bennet (1841). Glisson (1650) had clearly differentiated between rickets and scurvy, but confusion returned and this was not cleared up until the last 25 years of the 19th century. The recorded story of rickets in Glasgow dates from that period.

Rickets in Glasgow

The classical survey of Owen on the distribution of rickets began in 1884 and was reported in 1889 (Owen, 1889). He drew vivid attention to the very high

prevalence of infantile rickets 'in the industrial zone between the Firths (estuaries) of Clyde and Forth preponderating markedly in the Clyde Valley and northern Ayrshire and all but universal in Glasgow and its suburbs'. These findings were corroborated by Palm (1890).

The detailed studies of the diet and social conditions prevailing in Glasgow during the early years of the 20th century carried out by Findlay, Lindsay and others are a fascinating series of papers which reflect fully the abject povery of diet, the squalor and deplorable social background in which the great mass of Glasgow families lived at that time and for 3 further decades. In 1918 Findlay recorded that 'it was only with the greatest difficulty that Sister Elinor could find amongst patients at the Dispensary (out-patients) of the Royal Hospital for Sick Children (Glasgow) a sufficient number of non-rachitic children for the needs of the present research' (Findlay & Ferguson, 1918). It seems that whatever the nature of their complaint, medical or surgical, the vast majority of the out-patients suffered incidentally from florid clinical rickets. It was no wonder that many of Glasgow's children grew into the 'wee, bowly-legged bachles' (stunted, bow-legged weaklings) which characterized many citizens at that time. It was an era when osteotomy to correct gross deformity flourished and in one year (1908) more than 1000 osteotomies were performed on children by Drs Nicoll and McEwan at the Royal Hospital for Sick Children (Glasgow) mainly on out-patients. The less publicized but more heroic operation of thymectomy was carried out upon at least one rachitic child as an out-patient by the more adventurous surgeons of Glasgow, an operation whose rationale was later to be condemned in the same city (Renton & Robertson, 1916).

A fascinating argument then began between Findlay, Paton and Lindsay in Glasgow and Mellanby from the south. Not until Chick's work (Chick, Dalyell, Hume, Mackay, Henderson Smith & Wimberger, 1923) was the position clarified as to the links between ultraviolet radiation and dietary anti-rachitic factors. The story of Findlay's fixation on fresh air and exercise to prevent rickets without appreciating the concomitant introduction of ultraviolet light to the exercising group is a classic example of misinterpretation (Findlay, 1908, 1915, 1922; Findlay & Ferguson, 1918).

With the synthesis of ergocalciferol, a cheap and abundant source of vitamin D became available. Despite this potential preventative therapy, the fall in the incidence of infantile rickets in Glasgow during the 20 years from 1923 to 1943 was gradual and disappointing. Insensitivity on the part of doctors resulted in persistent attempts to coax or coerce mothers to use cod-liver oil. This product had a taste that mothers wholeheartedly disliked, its smell repelled many mothers and Its effect on precious woollen baby-clothes was disastrous. Failure to understand that 'a little bit of sugar makes the medicine go down' or that conscious, sustained administration of any vitamin tonic by every mother (or even every second mother) was an unrealistic goal, resulted in thousands of unnecessary cases of rickets. It is almost incredible that, despite repeated criticisms, cod-liver oil was still in official favour until the 1970s.

The 1939–45 war was the stimulus that led to the disappearance of widespread rickets. First, mothers on war work switched from breast-feeding to cow's-milk feeding. Secondly, fear of the calamitous effect on morale if enemy bombing disrupted the milk supplies for babies led to a cheap supply of National Dried Milk (NDM) being widely distributed, and a strictly rationed population snapped it up eagerly. Thirdly, ergocalciferol was added to NDM near the end of the war. The vast majority of mothers unknowingly gave their children ergocalciferol in NDM and rickets abruptly receded. In one medical unit in a Glasgow hospital the admission rate fell from an average of 20/year during the period 1937–44 to 6/year during 1945–7. This reflects the over-all fall in the much greater number of rachitic children seen and treated as out-patients. Very few reliable national or regional statistics are available since no proper surveys were conducted.

The consequences of ergocalciferol supplementation

Enthusiasm outpaced reason. NDM in 1948 contained a minimum of 0·25 μg ergocalciferol/g dry weight ('not less than 280 i.u. of ergocalciferol per dry ounce') but there was no upper limit, and uniformity of distribution was doubtful. Cod-liver oil was fortified with ergocalciferol to provide a total of 5 μg/g ('700 i.u. per teaspoonful'). Ergocalciferol was added to infant cereals in quantities as great as 0·27 μg/g. The over-all and reasonable intention of ensuring 17·5 μg/d gave way to an uncontrolled situation in which daily intakes of 100 μg and even higher were not uncommon. The inevitable ergocalciferol overdosage, euphemistically labelled 'idiopathic hypercalcaemia', became more and more common. Nobody knows how common.

No government or other agency seems to have carried out a suitable random study of the infant population, apart from a small study in Glasgow which gave disturbing results in 'normal' infants. Undoubtedly many healthy babies were stricken and died unnecessarily with renal medullary calcinosis. Disquiet was growing at this plague of idiopathic hypercalcaemia, largely localized in Britain, and by 1956 publications were calling for action. A daily intake of 17·5 μg ergocalciferol having been proposed, and inadequate regulations and misjudgment having led to many thousands of babies receiving about 100 μg/d (British Paediatric Association, 1956), an inevitable backlash occurred. In 1957 a joint sub-committee recommended reduction of the ergocalciferol content of NDM from a minimum of 0·25 μg/g to an average of 0·09 μg/g (from 280 to 100 i.u. per ounce of powder) (Ministry of Health, 1957). The total vitamin D content of cod-liver oil was reduced from 5 to 2·5 μg/g. The ergocalciferol content of infant cereals was reduced. Not unnaturally there was a widespread loss of enthusiasm for vitamin D administration, and uptake rates of cod-liver oil at clinics slumped to below 10% of the desired value.

In retrospect the consequence was predictable. The average admission rate for infantile rickets to the Royal Hospital for Sick Children (Glasgow) had steadily fallen. For the period 1948–52 it was 9/year and for 1953–8 it was 1·8/year. In 1959–62, as ergocalciferol intake declined, it rose again to 8/year (peaking in 1964

at twenty-four cases). In 1963 we drew attention to these problems and to rickets occurring in immigrant children (Arneil & Crosbie, 1963). The Medical Officer of Health for Glasgow was convinced, but higher official reaction was rather complacent scepticism. Infantile rickets was officially no longer a problem in Britain, so clearly the Glasgow paediatricians must be wrong or deluded, or alternatively the city was 'a special case'. The fact that the children in question were gross clinical, radiological and biochemical cases, nearly all unrecognized by their general practitioners, and admitted by 'accident' (implying unrecognized cases in the community) was largely ignored.

Survey work

Five surveys have been carried out by the staff of the Department of Child Health of the University of Glasgow. The first two were aimed at proving the existence of florid, undetected rickets in the community, the third at investigating the underlying dietary pattern in a Scottish context, and the fourth and fifth at demonstrating that florid cases were the 'tip of the iceberg', with subclinical cases of hypovitaminosis D more frequent in the childhood population.

Survey 1 (1964). Two areas were surveyed, one (Bridgeton) largely a slum, the other (Springburn) of average type. Children (200 from each area) were selected by random numerical sampling of the birth register. Of the children surveyed, 300 (75%) were found to have an unsatisfactory dietary intake of vitamin D. Their mothers were asked to bring them to the out-patients department, and 101 did so. Seventy-six mothers allowed their children to have X-ray examination of the wrist and venepuncture. Five children were found to have clinical rickets, seven florid radiological rickets and three gross elevation of serum alkaline phosphatase (*EC* 3.1.3.1) level (Arneil, 1969). Three of the seventy-six thus satisfied all three criteria for gross active rickets, giving an incidence of 4% in those fully investigated.

Survey 2 (1964). The subjects were 100 slum children aged 1–3 years, selected by health visitors as at risk (the youngest children in families, and in poor homes in central Glasgow). Clinical, radiological and biochemical rickets were present together in two children (2%) (Arneil, McKilligan & Lobo, 1965).

Survey 3 (1965). With support now given by the Scottish Home and Health Department, an extensive survey of the dietary pattern of 4365 children throughout Scotland was carried out. A total of 3743 children (85·8%) were successfully investigated and results computed. The children were selected by random numerical sampling of the birth register in nine areas of Scotland: Aberdeen, Dundee, Edinburgh, Glasgow, Greenock, Paisley, Ayrshire, Renfrewshire and Wigtownshire. A full report has been published (Arneil, 1967).

There were three relevant facts arising from this survey.

(1) In some areas 15·3% of infants received unfortified 'doorstep' (i.e. cow's) milk from birth, and 27·7% by the age of 1 month.

(2) Over-all, 29% of infants received no vitamin D supplements from the age of 3 months onwards; 60% of these received vitamin C tonics.

(3) The percentage of infants receiving less than 2·5 μg cholecalciferol daily from

all sources (except solar radiation) was 4·3% aged 3 months, 8·2% aged 6 months and 24·8% aged 1 year.

Survey 4 (1966). Glasgow children (a total of 202) were selected by random sampling (to yield one in sixty of the population aged 12–24 months in Glasgow at a specified period in 1966). Their wrists were X-rayed and serum alkaline phosphatase was measured, as a result of which thirty-nine of the 202 children were referred to the Royal Hospital for Sick Children because of abnormalities. Seven of these defaulted. An X-ray of wrist was repeated in all thirty-two who attended; seventeen showed minimal active rickets or minimal healing rickets. This amounts to 8·5% of the original 202 children. We have published the diagnostic criteria (Richards, Sweet & Arneil, 1968). Of these children, 33% were receiving less than 2·5 μg cholecalciferol/d from all dietary sources, and 26% aged 18–24 months were ingesting less than 1·25 μg/d.

Survey 5 (1966). Glasgow children (a total of 501) were selected by numerical random sampling (to yield one in ten of the population aged 1–2 years) (Richards, Hamilton, Taylor, Sweet, Bremner & Price, 1968). Loss of metaphyseal definition was seen in 2% (minimal active rickets) and metaphyseal bands were seen in 7% (minimal healing rickets). Serial radiological examination showed that minimal healing progressed to normal, and the minimal active condition progressed through minimal healing to normal, when vitamin D supplements were given.

We believe that the earliest manifestation of hypovitaminosis D is a loss of calcification in a normally shaped bone with loss of definition at the normal metaphyseal edge (minimal active condition). If vitamin D intake then exceeds requirement, healing begins at the extreme edge of the bone, where a dense white line is seen (minimal healing). As healing progresses, the density of the remainder of the shaft increases and the definition of the band disappears. It is our view that a considerable proportion (25–33%) of Glasgow children 1–3 years old suffer chronically from inadequate vitamin D intake from alimentary sources. When the sun shines or vitamin D is ingested, and when growth is less, the bones heal up and calcify. In winter, or during growth spurts, minimal active lesions result. These heal by a terminal metaphyseal band appearing transiently, and the pattern then returns to normal. On the other hand, if at the minimal active stage vitamin D deficiency persists and growth occurs, then it is assumed that, as the Ca^{2+} level falls in plasma, the parathyroid glands overproduce and the gross, distorted osteoid of florid rickets becomes a feature. Richards, Hamilton *et al.* (1968) pointed out the unreliability of serum alkaline phosphatase levels in the diagnosis of hypovitaminosis D. Dunnigan & Smith (1965) had previously pointed out the pitfalls of relying on alkaline phosphatase levels as a guide to minimal rachitic activity, and our survey confirmed this view.

The results of our five surveys have led to several conclusions.

(1) A substantial proportion of Glasgow infants were receiving a grossly inadequate dietary intake of vitamin D, some from birth, and 25–33% at 1 year.

(2) Florid, active rickets existed undetected in indigenous white Glasgow children (1–3 years old), probably less than 2% being affected. Since it was not

recognized by general practitioners, rickets probably existed in other cities.

(3) A considerable percentage of children (9%) had subclinical, radiologically detectable bone lesions resolved by vitamin D supplements ('subclinical rickets' or the preferred term, 'hypovitaminosis D').

Fortunately, gross rickets was found mainly in the 1–3 year age-group so that almost complete recovery was possible with adequate vitamin D therapy. The extent of healing is often remarkable. A campaign was mounted using television, press, health visitors and clinic and other medical and nursing staff to encourage vitamin D supplements. Early 'doorstep' milk feeding was discouraged. It was advocated that fortified dried milk be given to infants up to 1 year, fortified cereals to 2 years and 'tonics' of cholecalciferol and ascorbic acid combined (e.g. Vitavel; Bencard Ltd, Brentford, Middx.) to 3 years of age. After nearly 10 years of repeated campaigning (since 1963), a single vitamin product containing ascorbic acid and cholecalciferol has at last been provided nationally (Children's Vitamin Drops; Welfare Foods) to replace the unpopular cod-liver oil and orange juice which had proved a relative failure, and had been rejected by the mothers of Glasgow in favour of rose-hip syrup and other palatable vitamin C products. Rickets has not entirely disappeared in indigenous white children, but these measures, together with slum clearance and a smoke-free zone over the city, has steadily reduced the problem.

'Immigrant' rickets

As the indigenous problem came under control, a new problem became more apparent. During the period 1928–55 there were 560 children with active rickets admitted to the Royal Hospital for Sick Children (Glasgow). All were white. During 1966–71 forty-one children were admitted, of whom twenty (49%) were coloured and three (7%) were half-caste (Arneil, 1973). As early as 1963 we had drawn attention to this problem, and had written saying the problem of this racial group is circumscribed and ought to be evanescent (Arneil & Crosbie, 1963). The solution seemed to lie in adequate education of Asian women immigrants, first in the English language, and secondly in the elements of child nutrition in this climate. 'It was revealing to have an Asian child with nutritional rickets translate into English the answer of the mother to a question about the child's diet' (Arneil & Crosbie, 1963). Clearly we were over-optimistic.

The age distribution of the 'immigrant' children is interesting. From 1928 to 1971, 642 white children were admitted with nutritional rickets, and only two were more than 8 years old. From 1960 to 1971 there were thirty-four coloured children admitted with rickets; seven were more than 8 years old (Arneil, 1973). Rickets in coloured children has become biphasic, with one peak corresponding to that of indigenous slum children (9–36 months) and the other related to the pubertal growth spurt.

The bulk of the work on coloured adolescents in Glasgow has been carried out by Dunnigan and his team of co-workers: contrary to popular belief that adolescent Asian rickets is the new 'English disease', the original observations

were made in Glasgow in 1962 (Dunnigan, Paton, Haase, McNicol, Gardner & Smith, 1962). Similarly Dunnigan's team described the first cases of congenital rickets which derived from pregnant osteomalacic Glasgow mothers. Further research by Dunnigan's team has included efforts to test fortification of flour (and chupatties) with extra calcium and with vitamin D. They have also studied the value of plasma 25-hydroxycholecalciferol (25-HCC) levels in assessing latent rickets (M. G. Dunnigan, unpublished results).

The Glasgow observations were followed some years later by the first (Felton & Stone, 1966) of a series of papers from English cities as awareness of the situation spread. A wide range of centres including London have now recognized the problem as existing in their communities. Rickets is now officially back on the list of problems officially requiring solution.

From this hospital we recently mounted a survey into the continued incidence of undetected rickets in adolescent children of various races attending school. These are (a) Indian and Pakistani, (b) Chinese, (c) African and (d) 'poor whites'. Their dietary and nutritional states are being compared. It is already clear that in 1974, with all the propaganda of a decade behind us, many florid clinical cases remain undetected in 5–10% of Asian adolescents. That this is so indicates delay in effective action by the preventive health services concerned and by the general practitioners, failure of school health services to detect and deal with these cases and inability of us all (as teachers) to stimulate activity by these rather slow-moving bodies.

For years Glasgow has provided instructions to mothers on infant feeding in a wide range of languages. This is clearly not enough. Now we have co-operated with the Glasgow Community Relations Council to produce a cartoon film dubbed in five languages to be shown between main features in cinema shows provided for immigrant families, each in their own dialects. We believe that if coloured mothers are educated in the need to give vitamin D supplements they will do so. The cause of pubertal rickets in coloured children is unsolved. We are convinced that a major factor lies in the diet, and it is probably not phytate alone. Many adolescent white children rarely go outside the home to play and are never unclothed in the open, yet they do not contract rickets. Asian children who go out to play frequently and are lightly dressed may nevertheless contract the disease.

The fact that Asian children eating an Asian diet and living in Asian sunshine do not develop rickets does not prove that lack of sunshine is the cause. One could advance exactly the same argument for a child given cod-liver oil, i.e., that lack of cod-liver oil causes rickets. It is almost certain that sunshine plays a part and phytates play a part but that some other factor, probably dietetic, awaits discovery.

It is fascinating that just as bow-legged (genu varus) childhood rickets was not recognized by general practitioners because the age-group (9–36 months) was older than previously involved, so adolescent rickets in immigrants is missed because teachers, nurses and school health doctors fail to recognize the typical knock-knee deformity (genu valgum) (Dawson & Mondie, 1972). This is partly because of lack of interest, partly failure to note compensatory stance (knees lightly crossed and

feet near each other) and unusual gait. In contrast, late rickets (e.g. renal osteodystrophy) in white children produces bow legs. There has been only one case of bow-legged adolescent rickets in an Asian seen in Glasgow so far.

Nutritional rickets in Glasgow in 1974 falls into four groups: (1) congenital rickets in children born to immigrant mothers with osteomalacia, first recorded in Britain by Dunnigan's team in Glasgow (Ford, Davidson, McIntosh, Fyfe & Dunnigan, 1973); (2) premature babies in the early weeks of life with craniotabes (it may be that low-solute, low-phosphorus, vitamin D-fortified milk will change this); (3) white and coloured children given insufficient fortified milk, vitamin tonics and vitamin D-containing foods such as margarine, eggs, butter and oily fish; (4) coloured adolescents, whose diet and deficient vitamin D intake (in common with those of white adolescents) fail to cope with the pubertal growth spurt (many have been born in Glasgow).

All are preventable, and all should have been prevented. Ample supplies and varieties of fortified foods are present, but a clear policy and education are lacking. Education of schoolgirls, mothers, teachers, nurses and many medical practitioners and auxiliary staff provides the only long-term solution. In the meantime, latent fortification of baby-milks and of cereals, together with palatable vitamin preparations, are the measures minimizing the problem, which is still largely unrecognized and undetected. The only quick solution to rickets in coloured adolescents is vitamin D supplements either as a 'tonic' or in the food, possibly the chupatty flour.

Education is the long-term solution. A positive lead from health administrators should ensure that all School Health doctors and teachers know that every coloured schoolboy or girl requires extra vitamin D. It is intolerable that congenital rickets and girls with deformed osteomalacic pelves have returned to Glasgow. A rapid solution to the problem must be found. Our instructional cartoon film dubbed in Asian dialects may help.

The fascinating studies of ergocalciferol and cholecalciferol metabolism such as those of Dunnigan & co-workers (Preece, Ford, McIntosh, Dunnigan, Tomlinson & O'Riordan, 1973) have, paradoxically, probably delayed effective action against this unnecessary illness in our coloured adolescents. Nevertheless they have shown that variations in 25-HCC levels may be a much better indicator than alkaline phosphatase of hypovitaminosis D.

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