

The role of cereals in the aetiology of nutritional rickets: the lesson of the Irish National Nutrition Survey 1943–8

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1. Review of the evidence of the Irish Nutrition Survey concerning a marked rise in the incidence of rickets in Dublin in 1942 concludes that a rise in the extraction rate of the national flour from 70 to 100% was principally responsible.

2. This rise and subsequent decrease in incidence as the extraction rate of flour was reduced is not explained by changes in the proportion of children protected by vitamin D supplements or by small changes in dietary vitamin D intake.

3. The evidence suggests that nutritional rickets in man cannot be explained on the basis of deficient vitamin D intake alone, whether derived from diet or u.v. radiation.

The prevalence of rickets and osteomalacia in the Asian population of the United Kingdom has renewed interest in the aetiological factors involved in these diseases (Ford *et al.* 1972; Holmes *et al.* 1973). In particular, the role of cereals in the aetiology of nutritional rickets, first suggested by Mellanby (1949), has been reconsidered. The issue has again been raised of whether high-extraction and wholemeal cereals may be rachitogenic or whether rickets and osteomalacia in man can always be explained by deficient vitamin D intake derived from either diet or ultra-violet radiation.

A marked increase in the incidence of rickets was observed in Dublin in 1942 when the extraction rate of the national flour was raised from 70 to 100%. The subsequent course of this outbreak of rickets was monitored by the Irish National Nutrition Survey from 1943 to 1948 and reported by Jessop (1950). We have re-examined this evidence and supplemented it with food consumption information from Ireland which the survey did not consider. The evidence has been re-interpreted in the light of recent dose-response studies relating oral vitamin D to serum 25-hydroxyvitamin D (25-OHD) levels.

MATERIALS AND METHODS

The Irish National Nutrition Survey

Details of the rise in the incidence of rickets in Dublin in 1942 and of its subsequent decline are contained in the report of the surveys of rickets in Dublin (Jessop, 1950). This report details the methods used to monitor the radiological incidence of rickets in Dublin children from 1943 to 1948, their consumption of vitamin D supplements and the changes in the extraction rate of the national flour over the period.

National food consumption information

Values for the *per capita* consumption of principal foods in Ireland were obtained from the Central Statistics Office in Dublin for the years 1935–44 and 1947–9. No values were available for 1945 or 1946. An individual dietary survey was carried out in Dublin in 1946 by the National Nutrition Survey and shows good agreement with the *per capita* consumption values for 1947 and 1948. Results were calculated as daily intakes of energy, protein, calcium and vitamin D. The diet was divided, somewhat arbitrarily, into 'animal' (beef, mutton, bacon, pork, poultry, fish), 'dairy' (eggs, milk, butter, margarine, cheese) and 'vegetable' (flour, bread, sugar, potatoes) foods in order to observe absolute and relative changes in these food classes over the period of the survey. Intakes were expressed as mg elemental phosphorus since this notation allows expression of the effect of changing the extraction rate of flour and there is a close relationship between the latter and its P and phytate content.

Relationship of oral vitamin D to serum 25-OHD

We have completed a number of trials in the elderly and in Asian families to establish the role of vitamin D supplements and vitamin D-fortified foods in the prevention of vitamin D deficiency in these vulnerable groups (Pietrek *et al.* 1976; Conely *et al.* 1977; Dunnigan & Ford, 1977; Dunnigan, 1977). Three trials have involved the administration of oral ergocalciferol to Asian families and white geriatric subjects within the range found in the normal diet (Table 3). In two trials, butter specially fortified to 'margarine' levels of 90 μg ergocalciferol/kg by the Scottish Milk Marketing Board was given to Asian families for 1 year (Dunnigan, 1977) and to geriatric subjects for 6 months and in one trial, weekly vitamin D supplements were given under supervision to Asian children for 6 months to provide the equivalent of 2.5 and 5 μg ergocalciferol/d. The response to the administration of the supplement or fortified food was assessed by the change in serum 25-OHD produced; this was measured by competitive-binding assay modified to include preparative chromatography (Belsey *et al.* 1974).

RESULTS

Rickets survey in Dublin: 1940–2

The number of instances of rickets referred to the radiological departments of children's hospitals more than doubled between 1939–40 and 1941–2 (Jessop, 1950). This increased incidence coincided with a gradual increase in the extraction rate of the national flour from 70% in September 1940 to 100% in February 1942. Daily *per capita* intakes of vitamin D fell from 1.9 μg in 1940 to 1.5 μg in 1942 due to wartime restrictions on imports of fatty fish and margarine (Table 1).

There was no significant change in the *per capita* consumption of any other food over this period (Table 2).

The children who developed rickets in 1941–2 were not taking a cod-liver-oil supplement. Jessop (1950) observed, however, that their older siblings had consumed the same basic diet of bread and butter; although unprotected by a cod-liver-oil supplement they had shown no signs of the disease while consuming 70% extraction flour in the period before 1941.

Rickets surveys in Dublin: 1943–8

In the spring of each year of the period 1943–8 inclusive, the incidence of radiological rickets was estimated from samples of Dublin children between 3 months and 4 years old; in all 2580 children were examined.

In children of 1 year and under the incidence of rickets varied little in 5 of the 6 years between 1943–8. A significant increase ($P < 0.01$) from 173 to 285 per 1000 (SE 39 per 1000)

Table 1. Incidence of rickets in Dublin children 1940-8, their uptake of vitamin D supplements (as cod-liver-oil) the extraction rate of the national flour and national per capita intakes of vitamin D and calcium

Year	Incidence of rickets* (per 1000 children)		Extraction rate of flour (%)*	Vitamin D supplement* (% uptake)		Dietary vitamin D‡ ($\mu\text{g}/\text{d}$)	Dietary Ca‡ ($\mu\text{g}/\text{d}$)
	≤ 12 months	13 months- 4 years		≤ 12 months	13 months- 4 years		
1940		} †	70 → 75	—	—	1.9	658
1941			80 → 100	—	—	1.8	702
1942			100	—	—	1.5	699
1943	174	173	100 → 85	85	71	1.6	726
1944	250	139	85	66	66	1.5	695
1945	133	79	85 → 80	60	51	—	—
1946	173	85	80 → 90	72	60	2.3§	954§
1947	153	47	90 → 85	81	65	2.3	903
1948	166	27	85	77	56	2.1	873

→, Direction of change.

* Jessop (1950).

† Hospital referrals 'more than doubled' (Jessop, 1950).

‡ Central Statistics Office, Dublin.

§ Individual survey; Irish National Nutrition Survey.

Table 2. Principal components of the Irish diet, 1940-8*

Year	Energy (MJ)	Protein (g)	Food (mg phosphorus)		
			'Vegetable'‡	'Dairy'‡	'Animal'‡
1940	12.6	80	222	440	281
1941	12.2	84	1002	452	270
1942	12.2	84	1036	461	285
1943	12.6	90	1129	466	308
1944	13.0	93	679	477	306
1945	—	—	—	—	—
1946†	13.4	98	820	490	336
1947	12.7	96	662	482	357
1948	12.7	91	640	519	345

* Central Statistics Office, Dublin.

† Individual survey; Irish National Nutrition Survey.

‡ For details, see p. 18.

occurred from 1943-4. In contrast, in children between 13 months and 4 years inclusive, the incidence of rickets showed a progressive and significant decrease ($P < 0.01$) from 179 per 1000 (SE 22 per 1000) in 1943 to 29 per 1000 (SE per 1000) in 1948 (Table 1). During the period 1943-8 there was a reduction in the extraction rate of flour from 100% in early 1943 to 85% in December 1943 at which level, with minor variations, it was maintained until the end of the study in 1948 (Table 1). These changes are reflected in the changing per capita intakes of vegetable P (Table 2).

Vitamin D intake showed no significant increase from its 1942 level of 1.5 $\mu\text{g}/\text{d}$ until 1946 when it increased to 2.3 μg due to increased availability of fatty fish and margarine at the end of the war (Table 1).

Table 3. *Response of serum 25-hydroxyvitamin D (25-OHD) to low-dose supplements of ergocalciferol in Asian children and geriatric patients*

No. of subjects	Average ergocalciferol supplement ($\mu\text{g}/\text{d}$)	Duration of trial (months)	Mean serum 25-OHD (ng/ml)		Change in serum 25-OHD (ng/ml) SEM
			Initial	Final	
Asian Children					
14	0	13	3.16	6.60	0.96
18	4.9†	13	5.96	7.85	0.94
17	0	7	11.08	10.37	1.80
12	2.5‡	7	9.42	9.87	1.71
11	5.0§	7	14.41	14.01	3.87
Geriatric Patients					
20	0	6	5.42	7.16	0.60
16	2.3†	6	6.35	9.09*	0.85

* $0.01 < P < 0.05$.

† Average intake *per capita* of butter fortified to 90 μg ergocalciferol/kg.

‡ Given as 17.5 μg weekly supplement.

§ Given as 35 μg weekly supplement.

The percentage of children taking vitamin D supplements decreased significantly ($P < 0.01$) between 1943 and 1945 and did not show a significant increase until 1946, both for children under and over 1 year (Table 1).

The only other significant changes ($P < 0.01$) in the Irish diet over this period occurred in 1946 when there were increases both in Ca intake, associated with the fortification of flour, and in the intake of 'animal' foods due to increased meat consumption (Table 2).

The relationship between oral vitamin D and serum 25-OHD

In Asian children and in the elderly the provision of additional oral vitamin D equivalent to 10 μg daily produced a significant rise in serum 25-OHD whether provided as a weekly supplement, in the form of fortified butter or in chapatty flour (Pietrek *et al.* 1976; Conely *et al.* 1977; Dunnigan & Ford, 1977; Dunnigan, 1977). Additional vitamin D equivalent to 2.5 μg and 5 μg daily either in fortified butter or as a weekly supplement produced no significant rise in serum 25-OHD in Asian children (Table 3). Indeed, this level of supplementation did not prevent a small winter fall in serum 25-OHD levels from the above average values attained after the unusually sunny summer of 1976.

Geriatric patients, in conditions of u.v. deprivation, given an average supplement of 2.3 μg ergocalciferol daily in fortified butter had a final mean serum 25-OHD level of 9.09 ng/ml compared to 7.16 ng/ml for a similar control group, a small but significant rise of 1.93 ng/ml ($0.01 < P < 0.05$).

DISCUSSION

In man, the greater part of serum 25-OHD is derived from skin synthesis in response to u.v. irradiation; only a small fraction is derived from dietary sources (Poskitt *et al.* 1979). Direct enquiry in Dublin suggests that no changes in social behaviour sufficient to alter the outdoor exposure patterns of Dublin children occurred in Ireland during the Second World War in which Eire was not involved. Thus, changes in u.v. exposure can be discounted as a causal factor in the increased incidence of rickets in 1942.

During the period 1943–8, the incidence of rickets fell in children between 1 and 4 years from 173 per 1000 to 27 per 1000. This decline commenced in the year 1943–4. Of the changes in diet over this period, the percentage of children taking vitamin D supplements

continued to decrease until 1945–6; national vitamin D intake fell slightly in 1942 and remained at this reduced level in 1943 and 1944, increasing significantly by $0.8 \mu\text{g}$ in 1946; the extraction rate of flour decreased from 100 to 85% in the year 1942–3. Hence the only dietary factor whose change preceded the decline in rickets was the reduction in the extraction rate of the flour.

During the period 1940–2, the doubling of incidence coincided with an increase in the extraction rate of flour from 70 to 100% and a decrease in vitamin D intake by $0.4 \mu\text{g}/\text{d}$.

The case for considering vitamin D intake as a causative factor in the increased incidence of rickets must therefore rest on the changes in serum 25-OHD which would follow a fall in daily vitamin D intake of $0.4 \mu\text{g}/\text{d}$. This value is based on adult consumption and the changes in dietary vitamin D applicable to the young children in this study would be even less than this.

The dose-response studies detailed previously indicate that only in the case of geriatric patients who had been deprived of sunlight was any significant change in serum 25-OHD observed when a daily supplement of $2.5 \mu\text{g}$ ergocalciferol was given. Over all these dose-response studies indicate that insignificant changes in serum 25-OHD would result from changes in dietary vitamin D intake of less than $1 \mu\text{g}$ daily. The recent observations of Poskitt *et al.* (1979) that a mean rise in serum 25-hydroxyergocalciferol of only 1.4 ng/ml resulted from a supplement of $5 \mu\text{g}$ ergocalciferol in white children support these conclusions.

It therefore appears likely, as Jessop (1950) suggested, that the major change in the extraction rate of the flour used as a staple item of diet in Ireland was responsible for a marked simultaneous rise in the incidence of rickets, independent of changes in vitamin D intake. This hypothesis is supported by the subsequent decline in the incidence of rickets in older children between 1 and 4 years as the extraction rate of flour was reduced. The observation that the incidence of rickets changed little in children under 1 year who consumed little or no bread is consistent with this hypothesis; there is no obvious explanation for the significant rise in incidence between 1943 and 1944.

The role of diets containing wholemeal and high-extraction cereals and pulses in the aetiology of nutritional rickets and osteomalacia is disputed. As noted above, dietary vitamin D plays an insignificant part in maintaining serum 25-OHD levels even in Northern latitudes such as the United Kingdom (Haddad and Hahn 1973; Preece *et al.* 1975; Poskitt *et al.* 1979). If dietary components other than vitamin D are excluded from consideration, 'nutritional' rickets must therefore be attributed to ultra-violet deprivation and this is certainly evident in certain circumstances such as the osteomalacia of the institutionalized or housebound elderly. Ultra-violet exposure may be normal, however, in a number of situations where rickets and osteomalacia are prevalent. In each case the diet has been observed to contain a high proportion of high-extraction or wholemeal cereals and pulses.

Adolescent rickets and osteomalacia have been found in Asians in Britain whose outdoor exposure did not differ from their white counterparts (Dunnigan *et al.* 1975; Dunnigan, 1977; Compston, 1979). The traditional Asian diet contains much unleavened high-extraction cereal as chapatty and a variety of pulses. In Iran Amirhakimi (1973) and Rheinhold (1971) found rural rickets in children whose sunshine exposure appeared normal but whose diets contained large quantities of unleavened wholemeal bread as tanok. In rural Kashmir Wilson (1931) found severe osteomalacia in field workers who spent many hours a day outdoors but whose diets were exclusively vegetarian, consisting almost entirely of rice, lentils (dal) and wholewheat flour (atta). Pettifor *et al.* (1978) found severe adolescent rickets in rural Bantu children in Natal whose diet consisted almost exclusively of maize and green vegetables; their sunshine exposure was high. The evidence of the Irish National Nutrition Survey supports the epidemiological evidence that high-extraction and wholemeal cereals

may be rachitogenic and is particularly significant since the Irish diet was in other respects entirely adequate.

The mechanism of the possible rachitogenic action of cereals is uncertain. It seems unlikely that dietary phytate by itself is responsible and it has been suggested that phytate-derived polyphosphate esters may be rachitogenic (Van den Berg *et al.* 1972). Since nutritional rickets and osteomalacia are associated with low levels of serum 25-OHD and respond to treatment with vitamin D, interactions between u.v.-derived vitamin D and dietary factors other than vitamin D may be important. Evidence for an entero-hepatic circulation for metabolites of vitamin D provides a mechanism for such interactions (Arnaud *et al.* 1975; Rosenberg *et al.* 1979). Interruption of the entero-hepatic circulation of metabolites of vitamin D by constituents of high-extraction cereals and pulses may be important in the aetiology of nutritional vitamin D deficiency. Lignin, an important component of wheat fibre, combines with bile acids and increases their excretion (Eastwood *et al.* 1968). Rheinhold (1976) has suggested that should vitamin D become attached to the fibre-bile acid complex, which is chemically likely, it may be transported through the gut. High fibre diets may thus lead to enough wastage of vitamin D and its metabolites, derived mainly from u.v. radiation, to produce rickets or osteomalacia.

The Irish National Nutrition Survey has shown that there is no racial predisposition to nutritional rickets produced by intakes of high-extraction cereal and warns against the uncritical advocacy of the consumption of wholemeal and high-fibre diets, particularly at times of rapid growth. Children and women on such diets, particularly where u.v. exposure is limited by latitude, an urban environment or social custom should be protected by vitamin D supplements providing the equivalent of not less than 10 μg of vitamin D daily (Dunnigan & Ford, 1977).

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