Department of Health and Social Security

**Report on Health and Social Subjects**

19


# RICKETS AND OSTEOMALACIA

Report of The Working Party on Fortification of Food with Vitamin D
Committee on Medical Aspects of Food Policy

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# Preface

Until the first half of this century, rickets was known as the English disease. However, rickets and osteomalacia have never been confined to the United Kingdom and are found in many European and tropical countries even today. Examination of skeletal remains indicate that rickets occurred in ancient Egypt and other early civilizations.

The value of cod liver oil in the treatment of rickets has been known since the seventeenth century, but it was not until the 'vitamin era' of nutrition in the 1920s that the part played by vitamin D in the absorption of calcium from food and the deposition of calcium in bone was realized. The importance of ultra-violet radiation from direct sunlight for the synthesis of vitamin D by the body also became apparent at about the same time.

In the 1930s, malnutrition was not uncommon in Britain but, during the 1940s, at a time of national emergency, better sharing of staple foods and the provision of extra milk and vitamin supplements for those in special need made valuable contributions to public health, and in the course of the next decade rickets was virtually abolished.

The recent recrudescence of rickets and osteomalacia in Britain has been confined almost entirely to the Asian community and is a local problem limited to the areas in which Asians live. Information to date indicates that the battle against rickets can again be won if the known and well-tried methods of prevention and treatment are put into practice.

We are grateful to the expert Working Group and to the members of the Committee on Medical Aspects of Food Policy for giving so willingly of their time and expertise in order to consider the best way to deal with this present health problem.

**H Yellowlees**
Chairman—Committee on Medical Aspects of Food Policy

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# Contents

# 1. Introduction

## 1.1 The purpose of the Working Party

1.1.1 It has been known for several hundred years that cod liver oil could prevent and cure rickets. In the early 1920s the constituent responsible for this activity of cod liver oil was identified and called vitamin D and, at about the same time, ultra-violet radiation either from sunlight or from an artificial source, acting on the skin, was shown to have similar curative and preventive properties. Rickets used to be called 'The English disease' but had been almost completely eradicated in Britain by the 1950s (section 2). The occurrence at the present time of overt clinical rickets in children, and of osteomalacia in adults, in the population of the United Kingdom is therefore a challenge to all those with responsibilities for health and is rightly a subject which has been widely discussed.

1.1.2 Rickets in children has been the active concern of Government at various times for 40 years. The Panel on Child Nutrition, under the auspices of the Committee on Medical Aspects of Food Policy, in their Interim Report (Department of Health and Social Security, 1970), considered the evidence for the existence of overt rickets and concluded (p 5, para 16) that 'the distribution ..... in Britain appears to be in pockets, some geographical and some perhaps racial existing in the midst of areas of apparent freedom from the disease'. The report also stated (p 6, para 19) that 'The Panel is not in a position to produce evidence on the prevalence of sub-clinical deficiency. All that can be said is that its manifestations were such that radiologists disagreed and biochemists disputed as to whether it was or was not present.' In the opinion of the Panel there was no need for any change in the scheme of fortification of foods with vitamin D at that time.

1.1.3 With the resurgence of rickets in the last two decades, chiefly among the Asian section of the population, the Panel on Child Nutrition re-considered the situation and commissioned certain investigations. Since other age groups in the population besides children were affected by vitamin D deficiency, the matter held wider implications than those which concern the Panel on Child Nutrition. Therefore in March 1977, the Committee on Medical Aspects of Food Policy set up a Working Party to look into the question of a possible increase in the fortification of foods with vitamin D.

## 1.2 Terms of reference

The terms of reference of the Working Party were as follows:

> To advise the Committee on Medical Aspects of Food Policy about the fortification of foods with vitamin D.

## 1.3 Fortification past and present

1.3.1 About 40 years ago, with the advent of war, the Government took action to safeguard the nutritional status of the nation. Rationing, possible in a time of national emergency, ensured that essential foods were shared among all sections of the population according to need. On medical and scientific advice, margarine was required to be fortified with vitamin D and flour with calcium. Mandatory fortification of these foods as a means of preventing nutritional deficiency was justified at the time because a large proportion of the population was considered to be at risk. One question for the present Working Party to decide was whether or not the problem of rickets and osteomalacia in Britain now is of such dimensions that only further action by central government could provide the solution.

1.3.2 Recommendations about fortification must be based on a thorough examination of the extent of the problem and on estimates of the number of people likely to be affected. An assessment must also be made of the sources of vitamin D which exist in the United Kingdom and consideration given to other aspects such as possible toxicity. These matters are discussed in some detail in the report.

## 1.4 Form and scope of the report

1.4.1 The report is addressed to those who are responsible for the nutritional aspects of health, to specialist doctors and scientists who are concerned with nutritional deficiency diseases and to general medical practitioners, health visitors, dietitians and others who have to deal with the practical problems of health care in the community. The report sets out the evidence on which the Working Party has based its advice as to whether or not further fortification of food(s) with vitamin D is necessary.

1.4.2 The Working Party wished the report to be concise but considered that some historical background information would be relevant. This is set out in section 2. The problem of rickets and osteomalacia in young adults is chiefly confined to Asian newcomers to the United Kingdom. Therefore consideration has been given to the question of whether or not Asian people are at greater risk of developing rickets and osteomalacia in the United Kingdom than in the country in which they lived previously. The occurrence of rickets and osteomalacia in the United Kingdom is discussed in section 3 and in tropical and sub-tropical countries in section 4 of the report.

1.4.3 Rickets and osteomalacia develop when there is insufficient synthesis of vitamin D by the action of sunlight on the skin or as a result of an inadequate dietary intake of vitamin D. The relative importance of these two sources of vitamin D is discussed in section 6.

1.4.4 The remainder of the report sets out what is known about aetiology and recent trends in the disease in Britain and discusses the question of food fortification in the light of the available evidence. The decisions of the Working Party and recommendations are to be found in the last sections. Appendix A summarizes the clinical, radiological and biochemical characteristics of vitamin D deficiency, and Appendix B lists the vitamin D content of some natural foods and of fortified proprietary foods.

1.4.5 The report does not deal with vitamin D deficiency caused by prolonged use of anti-convulsant drugs or by abnormalities of vitamin D metabolism or by diseases of, for example, the gastro-intestinal system or the kidney.

# 2. Historical review

2.1 The discovery of vitamins and therefore the possibility of the existence of 'deficiency diseases' in the early part of this century led to what are now recognized as the classical researches of Mellanby (1921) and of Chick, Dalyell, Hume, Mackay, Henderson Smith and Wimberger (1923). Mellanby unravelled the relationship between calcium, phosphorus, the newly discovered fat-soluble vitamin D and bone growth. He showed that rickets was a disease in which calcification of growing bone was defective. Chick, Dalyell, Hume, Mackay, Henderson Smith and Wimberger (1923), working in Vienna, showed that very severe rickets in children could be cured either by giving cod liver oil (a rich source of vitamin D), or by exposing the skin to summer sunshine or to ultraviolet radiation from a suitable source.

2.2 At the beginning of this century, rickets was reported to affect 90% of black infants in New York (Hess and Unger, 1917) and Melvyn Howe in his description of conditions in late Victorian times in England states that 50% of children in the poor areas of Leeds had marked rickets (Melvyn Howe, 1976). In the period 1926—1942 studies in several large towns in Great Britain indicated a prevalence of radiological signs of rickets among young children of 2% to 8% and the evidence suggested that the figure for Glasgow was higher (British Paediatric Association, 1944). In 1943 a survey in 23 areas of Great Britain and Ireland showed that, on average, around 2% of infants aged between 3 and 18 months had radiological signs of rickets (British Paediatric Association, 1944). About 13% were judged in the same survey to show clinical signs of the disease, although it was stated that the severe form of rickets had almost disappeared. The disease was not restricted to the poor and in rural areas of the United Kingdom rickets was less common than in the cities.

2.3 At the beginning of the Second World War various measures were taken by Government to safeguard health. In 1940, on the recommendation of Sir Jack Drummond, Chief Scientific Adviser to the Ministry of Food, the addition of vitamins A and D to all margarine sold for domestic use was made compulsory. Vitamin supplements were introduced in 1941 as part of the Government Welfare Foods Scheme. Under this scheme children, at first up to the age of 2 years but from 1942 onwards up to the age of 5 years, could have, without cost, cod liver oil[1] which contained 2.5 μg vitamin D/g. Fruit juices[1] rich in vitamin C were also available free of charge as a protection against scurvy (Ministry of Food, 1946). Tablets which contained vitamins A and D, calcium phosphate and potassium iodide were provided free for all mothers during pregnancy and for 30 weeks after delivery. In 1942, the vitamin D content of cod liver oil was increased

[1]Cod liver oil and Welfare orange juice were replaced by Children's Vitamin Drops in 1971 (Statutory Instrument, 1971).

to 5.0 μg/g by fortification in an attempt to help those who took the vitamin irregularly. Some manufacturers had added vitamin D to infant milks before 1939, and from 1945 onwards National Dried Milk was also fortified with vitamin D. Manufacturers of other proprietary products soon followed by adding vitamins A and D to infant milks and also to infant rusks and cereals.

2.4 The acknowledged improvement in nutritional status and health of the population during and after the Second World War (Magee, 1946) was attributed to the better sharing of food by rationing, to full employment which allowed poorer people to purchase a more nourishing diet, to some decrease in pollution from smoke, and in part to the Welfare Foods Scheme and to school milk and meals. In 1946 the Government decided to continue Welfare milk and vitamin supplements, school meals and school milk as part of the peacetime social services.

2.5 In 1952 Lightwood described a newly recognized disease in infants and young children associated with a failure to thrive and hypercalcaemia which sometimes proved to be fatal. This was followed by suggestions that excessive intakes of vitamin D might be a causative factor (Stapleton, Macdonald and Lightwood, 1957). In 1955 the British Paediatric Association (British Paediatric Association, 1956) had expressed the view that there was a strong case for taking steps to safeguard infants against the possible risks of an unnecessarily high intake of vitamin D. Because the number of cases of hypercalcaemia was increasing, the Ministry of Health and the Department of Health for Scotland set up a committee in 1956 to advise on the continued need for Welfare vitamin supplements. The report of the Committee (Ministry of Health, and Department of Health for Scotland, 1957) suggested that, because of the system of food fortification, some children had unnecessarily high intakes of vitamin D. As a result of the recommendations of the Committee the amounts of vitamin D in cod liver oil, infants milks and cereals were reduced. (This subject is discussed in more detail in section 7.2).

2.6 Rickets did not return, as was feared, when fortification with vitamin D was reduced, and enquiries by the Ministry of Health in 1963 and 1966 confirmed a low incidence of the disease in some industrial cities, notably in Glasgow. However, the Panel on Child Nutrition (Department of Health and Social Security, 1970) recognized that there was a possibility of more widespread sub-clinical disease.

2.7 In 1964 Gough, Lloyd and Wills were the first to draw attention to the fact that nutritional osteomalacia may occur in the United Kingdom, although up to that time it had been thought to be very rare. Only 3 proven cases due to primary lack of vitamin D had previously been reported and Gough, Lloyd and Wills (1964) described 3 additional cases which were confirmed by bone biopsy. A study by Smith, Rizek, Frame and Mansour (1964) indicated that elderly women in Michigan had a much poorer vitamin D status as measured by bio-assay than women of similar age in Puerto Rico. Moreover, these authors also showed, for the first time, a seasonal variation in the concentration of vitamin D in the blood

of women in Michigan which was not a feature of the Puerto Rican women who had good exposure to sunlight all the year round. In Glasgow, Anderson, Campbell, Dunn and Runciman (1966) found that some elderly women, on admission to hospital, had osteomalacia. Since then, the results of nutritional surveys of elderly people have indicated that vitamin D deficiency contributes to the skeletal rarefaction which occurs in old age (Exton-Smith, Hodkinson and Stanton, 1966), and have revealed evidence of osteomalacia among the elderly, particularly among those who are housebound (Department of Health and Social Security, 1972 and 1979b).

2.8 Early in the 1970s reports in the medical press concerning rickets and osteomalacia in the United Kingdom became more numerous. The disease was said to be found chiefly among Asians and to be either clinically overt, occasionally with severe signs, or sub-clinical in that individuals were found to have abnormal biochemical or radiographical signs only. The disease was sometimes, but not always, associated with poor living conditions and other deficiency diseases such as anaemia. These reports are discussed in section 3.

# 3. Background to the present problem of rickets and osteomalacia in the United Kingdom

## 3.1 Introduction

3.1.1 Vitamin D deficiency is more likely to occur at times when the requirement for vitamin D is increased, such as the periods of rapid growth in infancy, early childhood and puberty. In adult women there is an increased need for vitamin D during pregnancy and lactation, and osteomalacia may develop in susceptible women during the reproductive years. Elderly people are also at risk of vitamin D deficiency because only a small amount of vitamin D is usually obtained from the diet, and decreasing mobility with advancing age means less outdoor activity and exposure to sunlight.

3.1.2 In this section reports of the occurrence of vitamin D deficiency in the United Kingdom over the past 15—20 years are reviewed. The most vulnerable age groups, infants and young children, school-children and adolescents, women of child-bearing age and the elderly, are considered separately.

## 3.2 Rickets in infants and young children

3.2.1 Rickets in the 1940s and 50s, as a disease affecting British children, did not completely disappear. A small number of cases continued to occur among infants and young children living in poor social conditions where mothers failed to appreciate the necessity for vitamin supplements when household milk, which contains relatively small amounts of vitamin D, took the place of human milk or the fortified artificial milks. This sporadic pattern of incidence has continued but, since the early 1960s an increasing number of cases from immigrant families, mainly Asians, has dominated the picture. Some evidence from Glasgow, where rickets has shown a greater tendency to persist, indicates that during the period 1960—1975 the yearly number of cases of rickets in the white indigenous population declined whereas the number from the Asian community increased (Goel, Sweet, Logan, Warren, Arneil and Shanks, 1976). Since about 1975 however there is some evidence that the yearly number of Asian cases has declined (Scottish Health Service Common Services Agency, Information Services Division, 1978 and 1980; Arneil, 1978, personal communication).

3.2.2 Hospital admissions in Glasgow (Ford, Colhoun, McIntosh and Dunnigan, 1972a) and in Bradford (Dawson and Mondhe, 1972) over the period 1968—72 indicated that Indian, Pakistani and West Indian children were those

most at risk of rickets. According to Gertner and Lawrie (1977) rickets continues to occur among several different immigrant groups: in a hospital in East London between 1970 and 1976 there were 22 cases, 18 of them being under 31 months of age. Singleton and Tucker (1978) called attention to the low vitamin D intakes of Asian infants in Southall, Middlesex, after the age of 6 months.

## 3.3 Rickets in schoolchildren and adolescents

3.3.1 Rickets in Asian adolescents in Britain was first described in 1962 in a study of Pakistani families in Glasgow (Dunnigan, Paton, Haase, McNicol, Gardner and Smith, 1962). When the community was resurveyed 10 years later, Ford, Colhoun, McIntosh and Dunnigan (1972a) again found 'clear biochemical evidence of rickets' in 17 out of 29 children between the ages of 9 and 14 years. Three boys and 3 girls also showed radiological evidence and complained of pain. In a study of Bradford schoolchildren aged 9—16 years in 1973, biochemical findings again indicated that rickets was a problem primarily among Asians and to a lesser degree among West Indian children (Ford, McIntosh, Butterfield, Preece, Pietrek, Arrowsmith, Arthurton, Turner, O'Riordan, and Dunnigan, 1976).

3.3.2 A study in Birmingham of 569 Asian, white and West Indian schoolchildren aged 14—17 years also produced biochemical evidence which suggested a high prevalence of rickets among the Asians. Further investigation by radiography of some of the children with increased alkaline phosphatase activity in their blood indicated a minimum prevalence of rickets of 8% among the Asians and 3% among West Indians (Cooke, Swan, Asquith, Melikian and McFeely, 1973). Response to vitamin D therapy was taken to confirm that vitamin D deficiency existed among some Asian and West Indian teenagers (Cooke, Asquith, Ruck, Melikian and Swan, 1974). A later survey of adolescent boys in the same area showed that concentrations of serum 25-hydroxyvitamin D (25-OHD) were significantly lower in Asian boys than in their West Indian or European classmates, and were sometimes within the range found in rickets and osteomalacia. However, there were no cases of florid rickets and concentrations of 25-OHD showed some improvement at the end of the summer. The mean ages, heights and weights were essentially the same in the 3 ethnic groups (Ellis, Woodhead and Cooke, 1977).

3.3.3 Cooke, Asquith, Ruck, Melikian and Swan (1974), on the basis of abnormal biochemical findings, had suggested that white schoolchildren were also affected by vitamin D deficiency but to a lesser degree than coloured children. This suggestion was taken up by the Panel on Child Nutrition, who, in collaboration with Professor T P Whitehead's Department of Clinical Chemistry, Queen Elizabeth Hospital, Birmingham, organized a survey of white, Asian and West Indian schoolboys aged 13—16 years in Coventry. Measurements on blood samples taken from these boys did not support the finding that biochemical rickets occurred in white teenage children (Culank and Whitehead, 1974). However, 9 Asian boys in the survey had low serum calcium

concentrations combined with high alkaline phosphatase activities and were investigated further. Although some of them also showed radiological signs of active or healed rickets and had some degree of knock knees, their physical condition was good. It was agreed by the Panel on Child Nutrition that a dietary investigation should be made of these boys. No outstanding differences were detected between the diets of the 9 boys and those of 9 other Asian boys who were without signs of rickets (O'Hara-May and Widdowson, 1976).

3.3.4 Occult rickets in children was described in a survey of Asian families in Rochdale (Holmes, Enoch, Taylor and Jones, 1973), and both overt and sub-clinical rickets were found in schoolchildren as well as pre-schoolchildren in Glasgow (Goel, Sweet, Logan, Warren, Arneil and Shanks, 1976).

3.3.5 A number of Asian children with rachitic deformities severe enough to warrant osteotomies were seen in Glasgow (Ford, Colhoun, McIntosh and Dunnigan, 1972a) and in Bradford (Ford, McIntosh, Butterfield, Preece, Pietrek, Arrowsmith, Arthurton, Turner, O'Riordan and Dunnigan, 1976) between the years 1968 and 1972. On the other hand much of the evidence for a high prevalence of rickets among Asian schoolchildren was based primarily on biochemical abnormalities, some of which are difficult to interpret in this age group, when pubertal growth affects the biochemical picture.

## 3.4 Osteomalacia in women of child-bearing age and neonatal rickets

3.4.1 Clinical signs of osteomalacia associated with vitamin D deficiency have been reported in 3 European women who excluded vitamin D-containing foods from their diets and also in 4 Indian women who were strict vegetarians (Dent and Smith, 1969). Osteomalacia has also been reported in Asian women of child-bearing age who had lived for some years in Britain (Stamp, Walker, Perry and Jenkins, 1980), and in pregnant Asian women in Rochdale (Holmes, Enoch, Taylor and Jones, 1973). Felton and Stone (1966) suggested that pregnancy could precipitate florid osteomalacia and reported the disease in 3 pregnant Asian women who responded to treatment with vitamin D and bore healthy babies.

3.4.2 Very low concentrations of 25-hydroxyvitamin D (25-OHD) have been found in the plasma of Asian women throughout pregnancy especially in vegetarians (Dent and Gupta, 1975) and after parturition (Brooke, Brown and Cleeve, 1979; Heckmatt, Peacock, Davies, McMurray and Isherwood, 1979). 25-OHD concentrations in blood from the umbilical cord at birth were also low and significantly less in Asian compared with non-Asian women.

3.4.3 Watney, Chance, Scott and Thompson (1971) attributed the neonatal hypocalcaemia, which sometimes gave rise to convulsions in Asian babies, to the low calcium intake and vitamin D deficiency of the mothers during pregnancy. Neonatal rickets in two Asian babies has been described in association with maternal vitamin D deficiency (Ford, Davidson, McIntosh, Fyfe and Dunnigan, 1973; Moncrieff and Fadahunsi, 1974), and fetal rickets has also been reported

in a Pakistani woman in Manchester (Russell and Hill, 1974). Hypoplasia of the dental enamel which accompanied neonatal tetany was thought also to be a consequence of maternal vitamin D deficiency (Purvis, MacKay, Cockburn, Barrie, Wilkinson, Belton and Forfar, 1973). Recently neonatal tetany and craniotabes have again been found to occur more frequently in Asian than in non-Asian babies (Heckmatt, Peacock, Davies, McMurray and Isherwood, 1979).

## 3.5 Osteomalacia in the elderly

3.5.1 Osteomalacia has been described as the most disabling and at the same time the most remediable bone disease of the elderly (Smith, 1976). It is more common in elderly women than elderly men (Chalmers, Conacher, Gardner and Scott, 1967). Anderson, Campbell, Dunn and Runciman (1966) found that 4% of elderly women admitted to the geriatric department of a Glasgow hospital had osteomalacia. Leeming (1973) reported the incidence to be 1% in geriatric hospital admissions in the south of England.

3.5.2 The incidence of fractures of the femoral neck increases steeply after the age of 60 (Knowelden, Buhr and Dunbar, 1964), and the possible importance of osteomalacia in the pathogenesis of this type of fracture was noted by Aaron and her colleagues (Aaron, Gallagher, Anderson, Stasiak, Longton, Nordin and Nicholson, 1974). They found that 20—30% of women and 40% of a smaller sample of men with fractured femurs in Leeds had histological evidence of osteomalacia. Faccini, Exton-Smith and Boyde (1976) also reported an association between fracture of the femoral neck and an increase in the proportion of osteoid as well as with a reduction in the quantity of bone (osteoporosis).

3.5.3 The possible importance of vitamin D deficiency in the aetiology of some fractures was again suggested by the lower concentrations of 25-OHD in serum from patients with fractured femurs compared with controls of a similar age (Brown, Bakowska and Millard, 1976; Baker, McDonnell, Peacock and Nordin, 1979). In Britain, 25-OHD concentrations are known to be lower in the elderly than in younger persons (Stamp and Round, 1974) and to show a seasonal variation (Lester, Skinner and Wills, 1977). Aaron, Gallagher and Nordin (1974) found the prevalence of histological signs of osteomalacia among patients with femoral neck fracture, and Baker (1980) the incidence of this type of fracture to be highest during the winter months.

## 3.6 The overall picture

3.6.1 It appears that in the United Kingdom rickets now affects predominantly infants, young children and schoolchildren of Asian origin. The disease is usually relatively mild. Rickets severe enough to cause lasting deformities is not common. Osteomalacia in women of child-bearing age and neonatal rickets have

been reported from a number of centres and appear to be confined to Asians, particulary vegetarians. The elderly of all races constitute a group at risk of osteomalacia, particularly if they are housebound or living in institutions.

3.6.2 In the spring of 1976 the Panel on Child Nutrition organized a nationwide enquiry into the occurrence of rickets and osteomalacia to ascertain whether the impression gained from the literature was confirmed. Under a covering letter from the Chief Medical Officers of England, Scotland, Wales and Northern Ireland, a questionnaire was sent to Area Medical Officers in England and Wales and Chief Administrative Medical Officers in Scotland and Northern Ireland asking whether, over the previous 3 months, February—April, clinical evidence suggestive of vitamin D deficiency rickets or osteomalacia had been seen in their areas, and if so in which age groups the disease occurred. There was a full response and the replies confirmed that rickets in children and osteomalacia in pregnant women were limited to the areas with a large Asian community, while osteomalacia in the elderly had a more widespread distribution throughout the country.

# 4. Rickets and osteomalacia in tropical and sub-tropical countries

## 4.1 Introduction

4.1.1 A question which needed study was whether the occurrence of rickets and osteomalacia in Asians in Britain results from the circumstances of their life here, or whether these diseases occur with similar frequency in the countries from which they came. This section of the report examines information about the distribution of rickets and osteomalacia in India and other tropical and sub-tropical countries.

## 4.2 Rickets in infants and young children in India.

4.2.1 Many reports of rickets in young children have come from different parts of India. Fifty years ago in the Bombay area rickets was more prevalent in children of upper class families, where the mothers observed purdah, than in lower class children who lived an outdoor life (Hutchison and Shah, 1922). In more recent times, rickets has been reported in 3—5% of young children in both rural and slum areas around Delhi, although other diseases such as anaemia, vitamin A deficiency and protein-energy malnutrition were more widespread than rickets (Ghosh, Sarin and Shegal, 1962; Ghosh, 1969; Gupta and Agarwal, 1972; Datta Banik, Nayar, Krishna and Raj, 1973). Other workers in Delhi regarded rickets as a national problem, often affecting children from families where there was a known case of osteomalacia (Rizvi, Chawla, Sinha, Malhotra, Gulati and Vaishnava, 1976).

4.2.2 A similar incidence (about 5%) of rickets has been reported from Bombay (Mankodi, Mankikar, Shiddhye and Shah, 1974), but among pre-school-children in Hyderabad the frequency of clinical signs was much lower (0.5%), probably because so many of these children were also malnourished and therefore not growing normally (Rao, Singh and Swaminathan, 1969). In a nutritional survey of pre-schoolchildren in Calcutta nearly 2% were found to have radiological evidence of rickets (Chaudhuri, 1975); anaemia and helminthic infestation were much more common. Bhattacharyya (1978), referring to this work, commented that rickets was a significant problem in India, and that errors in diet, inadequate exposure to sunlight and ascariasis were important causes in Calcutta. Protein-energy malnutrition was occasionally associated with rickets, but less frequently than in Delhi, and could greatly modify the clinical, biochemical and radiological features. Bhattacharyya pointed out that, for treatment, adequate calcium intake must be ensured, and that rickets should not be regarded simply as a result of vitamin D deficiency.

## 4.3 Rickets in other tropical and sub-tropical countries

4.3.1 Although rickets was common in Singapore among young Chinese children in the late 1930s and early 1940s (Williams, 1946), according to Hutchison (1978) it is now rare in Hong Kong, because of the widespread use of milks fortified with vitamin D for infant feeding.

4.3.2 In Nigeria, rickets was reported to be not uncommon in children up to 4 years of age (Jelliffe, 1951; Antia, 1970). According to local custom, babies may be covered up with clothes and may be secluded with their mothers in purdah if they are Moslems. In recent years rickets has been seen in children aged between 3 and 8 years at a hospital in Jamaica (Miller and Chutkan, 1976). Rickets had hitherto been thought not to exist in the West Indies (Jelliffe, 1971).

4.3.3 In spite of an abundance of sunshine, rickets is common in Tehran (Salimpour, 1975). The incidence in patients admitted to one hospital was 15% based on radiological criteria; malnutrition almost certainly masked biochemical and radiological changes in many more children. In Haifa, Israel, 16% of a series of children under 2 years of age examined post mortem had histological rickets (Griffel and Winter, 1958), and clinical and radiological rickets has also been reported from Iraq (Nagi, 1972). In Algeria, Libya, Morocco and Tunisia, 3—18% of children from birth to 5 years of age, who were examined in 1965 by a World Health Organization consultant, had clinical signs of severe rickets. The disease was more common and more severe in towns than in rural areas (FAO/WHO, 1967).

4.3.4 In South Africa, rickets has been frequently found among non-European infants in Johannesburg (Feldman, 1950). Dancaster and Jackson (1961) also described radiological rickets among Bantu and Coloured children in Cape Province. These authors claimed from their experience that the idea held by many that lack of growth protects from rickets in incorrect.

## 4.4 Late rickets in India and South Africa

4.4.1 There is very little information about rickets in schoolchildren and adolescents in tropical countries. In the early 1920s late rickets was said to be found among the upper class children in the Bombay area with a peak in incidence around the ages of 12—13 years, a time when many young females entered purdah and a life of seclusion within dark rooms (Hutchison and Shah, 1922).

4.4.2 Active rickets in South African black children aged 4½ to 13 years has been described (Pettifor, Ross, Wang, Moodley and Couper-Smith, 1978). Contrary to usual experience, these children were well exposed to sunlight and had normal serum concentrations of 25-OHD, but their calcium intake was low, that is to say, between 175 and 475 mg daily. The children all improved on a

normal hospital diet containing about 900 mg calcium daily without supplementary vitamin D.

## 4.5 Osteomalacia in women in India, Pakistan and Israel

4.5.1 In the Kangra district of the Punjab, Taylor and Marshall Day (1940) found 40% of the women had osteomalacia which they concluded was due to severe calcium deficiency. Wilson and Widdowson (1942) observed that, among all classes of women in North India, want of sunlight was associated with severe bony deformities.

4.5.2 Vaishnava (1975) reported on 593 cases of osteomalacia admitted to the metabolic ward of Irwin Hospital, New Delhi, during the period 1962—74. These were mostly women between the ages of 13 and 30 years. The majority were poor and lived in urban slums which lacked sunlight. Their diet was low in vitamin D and calcium and high in phytate. Aches and pains were constant complaints; multiple pregnancies and prolonged lactation were also common. Large doses of vitamin D (about 1,250 $\mu$g/day) were required to achieve positive calcium balance and were sometimes given for as long as 2 years. No signs of toxicity were noticed and no explanation for the apparent vitamin D resistance was found. The author said that osteomalacia was the commonest metabolic bone disease seen in Delhi and perhaps in the Northern part of India. Evidence suggested that osteomalacia was rare in the South, although rickets appeared to be as common there as in the North.

4.5.3 A recent report from Meerut, India, described the very low vitamin D intakes of 500 pregnant women examined between 1973 and 1978; clinical manifestations of vitamin D deficiency were found in 80% of them. Among 110 babies born to these mothers, 2 had congenital rickets and 2 hypocalcaemic convulsions (Teotia, Teotia and Singh, 1979).

4.5.4 Rab and Baseer (1976) reported that the incidence of symptomatic osteomalacia was low among women in Karachi, Pakistan, although biochemical abnormalities suggestive of vitamin D deficiency were found. The authors commented that the number of cases reported had declined in recent years, except in the North where the women were still veiled.

4.5.5 A detailed account has been given of osteomalacia among the Bedouin women of the Negev desert (Groen, Eshchar, Ben-Ishay, Alkan and Ben Assa, 1965). At that time custom demanded that the women lived inside tents or that when they went outside they were fully covered in black clothes. The diet consisted mainly of unleavened wholemeal bread, and the calcium intake was about 500 mg a day or less. Many pregnancies alternated with prolonged periods of lactation. Ill health and inability to work created a vicious circle leading to almost complete confinement and sometimes neglect. A change in social behaviour seems to have occurred and Bedouin women nowadays work near their tents unveiled with their faces, forearms and feet exposed to the sun (Shany,

Hirsh and Berlyne, 1976). Serum concentrations of 25-OHD in a small sample of healthy Bedouin women were well above the range typical of osteomalacia.

## 4.6 Conclusion

4.6.1 These reports indicate that rickets in children and osteomalacia in women of child-bearing age are not uncommon and are sometimes important health problems among inhabitants of parts of Asia, Africa and the Middle East. The most frequent and severe disease appears to occur in the northern part of the Indian sub-continent. The diseases are associated with the following health and social factors: female seclusion (purdah); poverty, over-crowding, bad sanitation, sunless dwellings; frequent pregnancies, prolonged lactation, infant seclusion, late weaning; predominantly vegetarian diets, especially those based on coarsely milled wheat and pulses; generalized malnutrition and associated gastro-intestinal and chest infections, and worm infestations.

# 5. Recent trends in rickets and osteomalacia among Asian people in Britain

5.1 It has been suggested in several reports that Asian migrants from the Indian subcontinent experience an increase in the risk of developing rickets or osteomalacia on entering Britain (Hodgkin, Hine, Kay, Lumb and Stanbury, 1973; Preece, Tomlinson, Ribot, Pietrek, Korn, Davies, Ford, Dunnigan and O'Riordan, 1975; Hunt, O'Riordan, Windo and Truswell, 1976). This was considered to be due largely to the smaller quantity of sunlight available in the United Kingdom.

5.2 Present public health practice for the prevention of these diseases among Asians has been questioned on the grounds that it is relatively ineffective and fortification of chapatti flour was suggested as an answer (Pietrek, Windo, Preece, O'Riordan, Dunnigan, McIntosh and Ford, 1976).

5.3 The case for food fortification would be strengthened if the incidence of clinically overt disease were tending to rise; whereas if the incidence were declining as the Asian people settled down in Britain, as more of them were born here, and as the number of new immigrants decreased, this measure would be less attractive and there would be good reason to persevere with existing methods of prevention.

5.4 A study was therefore made to try to answer, at least partially, these key epidemiological questions. The following is a summary only of the main results that were obtained.

5.5 The study material included information from Hospital Activity Analysis (HAA) (Rowe and Brewer, 1972) in four regions, the Hospital In-Patient Enquiry (HIPE) (Department of Health and Social Security/ Office of Population Censuses and Surveys/ Welsh Office, unpublished), the results of special enquiries into rickets and osteomalacia in selected areas (unpublished) and statistics on the Asian population and Asian immigration for Great Britain (Office of Population, Censuses and Surveys, 1975, 1977 a, b, 1979, and personal communication; Central Statistical Office, 1980). Further evidence has been obtained from general practitioners who were selected because they were expected to have a large proportion of Asian people in their practices.

5.6 Since rickets in children and osteomalacia in women of childbearing age mainly affect Asians, the number of cases each year must be related to the size of the Asian population in Britain. Figures 5.1 and 5.2 show the growth in the Asian population and Asian immigration into Britain in the period 1962—1978. Changes in the age and sex structure of the population were assessed in the second half of the period and were found to be small. Figures 5.3 and 5.4 indicate, from HIPE and HAA figures, the general trend in the crude hospital admission rate for rickets and osteomalacia for Asians in Britain in the period 1962—1978 expressed as a crude incidence ratio.[1] Table 5.1 shows additional material from general practitioners in areas which have large Asian communities.

5.7 Evidence from the various sources suggests a gradual decline in the incidence rate for rickets over the last 10 to 15 years. For osteomalacia there is less information: overall, that which is available suggests that the incidence has remained rather steady, although the HAA analysis shown in Figure 5.4 indicates the possibility of a slight increase in the 1970s. In recent years the estimated number of hospital admissions for rickets has been similar to the estimated number of admissions for osteomalacia (Asians). It is of interest that there is some suggestion of a positive relationship between hospital admission rates and immigration.

5.8 From somewhat limited information on the ratio of hospital in-patients to out-patients with rickets, and making some allowance for cases not seen in hospitals, a rough estimate of the incidence of clinically overt rickets among Asians in the age group 0 to 16 years was calculated for the year 1977. For the Midlands and North of England the figure suggested was around 10 cases per 1000, and for London around 4 cases per 1000.

[1]Crude incidence ratio (hospital admission rate).

Regional statistics of numbers of Asian persons are usually not available except for census years and so yearly regional admission rates could not be calculated from the HAA figures. To enable a better comparison of numbers of hospital in-patients each year, a crude 1973 related incidence ratio (1973 = 1.0) was calculated which utilizes national statistics on numbers of Asian persons. These ratios relate to the crude hospital admission rate for the disease, and are therefore useful for direct comparison and examination for trends. However, use of the ratio involves the assumption that the regional proportional changes in numbers of Asian persons during a period are closely similar to that for the whole of Great Britain.

$$\text{Crude incidence ratio (1973 = 1.0)} = \frac{Ny}{Py} \times \frac{P73}{N73}$$

Ny = estimated number of cases in a particular year
Py = Asian population for Great Britain in that year
N73 = estimated number of cases in 1973
P73 = Asian population of Great Britain in 1973

**Figure 5.1.** *Asian population of Great Britain, 1962-1978. (based on OPCS† estimates).*

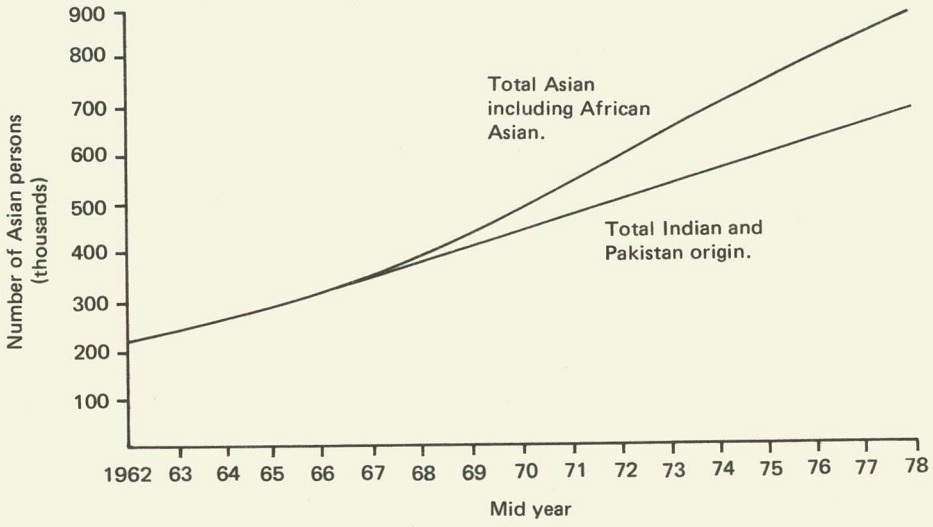
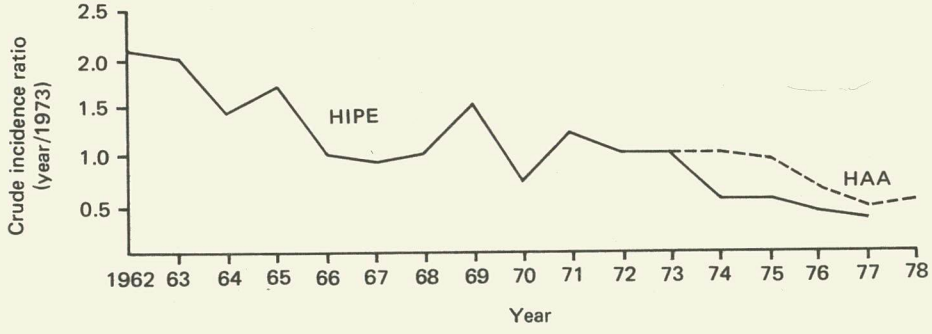



**Figure 5.3.** *Rickets: hospital admission rate: crude incidence ratio by year. (HIPE and HAA data).*




† Office of Population Censuses & Surveys.

**Figure 5.2.** *Number of Asian migrants entering Great Britain, 1964-1978. (based on OPCS estimates).*

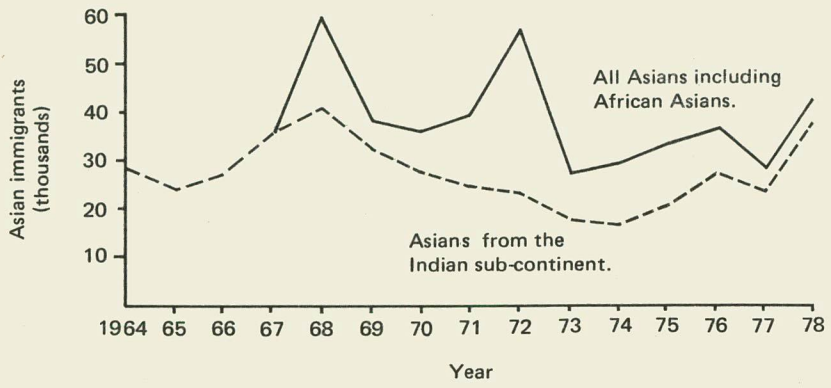
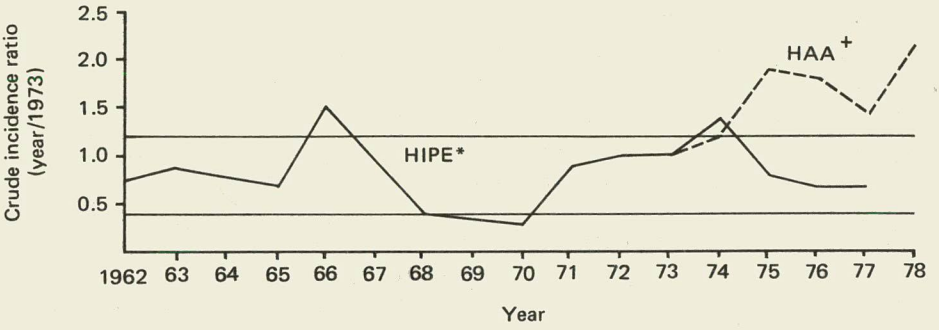



**Figure 5.4.** *Osteomalacia (Asians): hospital admission rate: crude incidence ratio by year. (HIPE and HAA data).*




* HIPE estimates are based on a 10% sample of all hospital discharges in England and Wales and are therefore subject to sampling error. In Figure 5.4, 95% confidence limits for no change in admission rate are indicated by horizontal lines at 0.4 and 1.2.

+ A standard error cannot easily be assigned to the HAA estimates. Although these are based on near actual numbers (HAA coverage was generally above 75%), this part of the study was confined to certain areas and hospitals serving large Asian communities.

**Table 5.1:** *Distribution of information* from general medical practitioners in Birmingham, Bradford, Manchester, Ealing and Newham about the trend of incidence of rickets and osteomalacia in Asians.*

| Trend in incidence | Number of replies (areas combined) | |
|---|---|---|
| | Rickets | Osteomalacia |
| Decreasing | 40 (31%) | 24 (18%) |
| Steady | 36 (28%) | 34 (26%) |
| No cases | 34 (26%) | 47 (36%) |
| Not known | 15 (11%) | 19 (15%) |
| Increasing | 5 (4%) | 6 (5%) |
| Total | 130 (100%) | 130 (100%) |

*The material was obtained by questionnaire in January 1979 to which the response was 86%. The information obtained was mainly, but not entirely, subjective.

5.9 Information from HAA indicates that at least 70% of patients admitted to hospitals in Britain during 1973—1977 with either rickets or, in the age group 20—47 years, osteomalacia were of Asian origin, and that a majority of those with osteomalacia were females. Most of the children with rickets were between 0 and 3 years of age with the largest number between 1 and 2 years. The data show a second peak of rickets in adolescence. Contrary to expectation, there was no seasonal variation in the number of admissions for either rickets or osteomalacia, suggesting that climate or latitude may not be of primary importance in the aetiology of these diseases among Asians in Britain. Evidence for a south to north gradient in incidence within the country might be accounted for by factors concerned with general living conditions. A similar gradient exists for infant mortality and neonatal deaths in the general population.

5.10 Rickets and osteomalacia are not uncommon in parts of the India sub-continent from which Asian families living in Britain have come (section 4). It could be expected that if a problem of rickets and osteomalacia existed among Asian people before they came to Britain, after their arrival here rickets in children would be the first to decline and osteomalacia in women would be more persistent.

# 6. Aetiology of rickets and osteomalacia in the United Kingdom

## 6.1 General

6.1.1 The risk factors mentioned in para 4.6.1 do not necessarily continue to apply when Asians come to live in Britain. However, national customs may persist and traditional habits of clothing, diet and seclusion are probably those to which Asians adhere most firmly. These may play an important part in the aetiology of rickets and osteomalacia in the United Kingdom. There may also be genetic characteristics which render Asian people more susceptible to rickets and osteomalacia than other groups, for example, their darker skin colour (see para 6.3.1.).

## 6.2 Lack of sunlight

6.2.1 The vitamin D status of most people is determined largely by the action of sunlight on the skin when 7-dehydrocholesterol is converted to cholecalciferol. A noticeable feature of vitamin D status in British people is the seasonal variation in plasma 25-OHD concentration (Stamp and Round, 1974; McLaughlin, Raggatt, Fairney, Brown, Lester and Wills, 1974). In Britain the average concentration reaches a maximum in late summer and a minimum in the early months of the year. The variation is correlated with daily hours of sunshine (Poskitt, Cole and Lawson, 1979; Lawson, Paul, Black, Cole, Mandal and Davie, 1979). Only solar radiation of wavelength less than 313 nm is effective in forming vitamin D (Knudson and Benford, 1938; Kobayashi and Yasumura, 1973), and the average intensity of this declines with distance from the equator (Schulze and Grafe, 1969; Johnson, Mo and Green, 1976; Scotto and Fears, 1977). The decline is such that no radiation of less than 313 nm reaches Britain from the end of October to early March and consequently no vitamin D can be formed during these months. Thus it seems that much of the vitamin D utilized by the body in winter has been synthesized in the previous summer.

6.2.2 In addition to the variation with latitude the intensity of solar ultra-violet radiation (UVR) at the earth's surface varies with time of day. Of the total available radiation in summer, the proportion reaching the earth's surface between 9.30 am and 3.00 pm, local standard time, is 68% in Dundee (latitude 56°) and 77% in North Dakota (latitude 47°) (Scotto and Fears, 1977; Frain-Bell, 1979). Periods out of doors at other times will therefore in general yield less vitamin D. Maximum cloud cover reduces the intensity of solar UVR by about 50% (Schulze and Grafe, 1969; Johnson, Mo and Green, 1976).

6.2.3 There is very little detailed information on the length of time different groups of the population spend out of doors, the distribution of this time throughout the day or its variation with age and sex. Time out of doors needs to be considered in relation to the area of skin exposed, although very little is known about the rate of vitamin D synthesis which can be achieved by skin. The relatively low vitamin D status of elderly people in Britain may be due to less time spent out of doors. Many people over 70 years old, who live a 'normal' life, spend less than 2 hours weekly outside (Lawson, Paul, Black, Cole, Mandal and Davie, 1979), but this may also apply to many younger people.

6.2.4 It has proved difficult to make any quantitive assessment of how much Asian women and children allow direct sunlight to fall on their unclothed skin compared with their European or West Indian counterparts (O'Hara-May and Widdowson, 1976), but there is a general impression that Asian children tend to spend less time out of doors than white children. There is also a general feeling that Asian women and children tend to have more of their bodies covered, although as the children adopt Western style clothing the difference will disappear. Dunnigan, Childs, Smith, McIntosh and Ford (1975) found no significant difference between the outdoor exposure of Asian children and of white children in either summer or winter.

## 6.3 Skin pigmentation

6.3.1 Black skin is more dense than white skin to ultra-violet radiation (UVR) of the wavelength required for skin synthesis of vitamin D (Thomson, 1955; Everett, Yeargers, Sayre and Olsen, 1966; Pathak, 1966). In temperate climates, where sunlight and UVR are relatively weak for much of the year, skin colour might therefore be of some importance in determining vitamin D status. The fact that, in Britain, West Indian people have an average blood 25-OHD concentration which is higher than that of the less pigmented Asians, though lower than that of white people (Ford, McIntosh, Butterfield, Preece, Pietrek, Arrowsmith, Arthurton, Turner, O'Riordan and Dunnigan, 1976; Ellis, Woodhead and Cooke, 1977), would suggest that the influence is not a major one. Studies which have shown a similar response in blood 25-OHD to irradiation with UVR lamps in groups of black, white and Asian subjects (Stamp, 1975; Davie and Lawson, 1980) are open to some criticism because a higher intensity of UVR might have exceeded the barrier effect of the skin pigment, or there might have been differential destruction of vitamin D by shorter wave radiation (Knudson and Benford, 1938). In general it would seem that for the majority of deeply pigmented people in Britain any effect of skin colour on their health is insignificant, but that when there is a higher risk of rickets or osteomalacia for other reasons, a dark skin may add to the total risk and predispose to the development of overt disease.

## 6.4 Diet

6.4.1 A second source of vitamin D is from some foods. Fatty fish (herring, mackerel, salmon, pilchard, sardine and tuna) are the only common natural foods which contain appreciable amounts, but may not always be acceptable to Asian people. Eggs, butter, cheese and milk contain only small quantities of the vitamin. These are likely to be taken by many Asian people but not by those who are strict vegetarians. Margarine and some proprietary products are fortified with the vitamin (see Appendix B).

6.4.2 Deficiencies or excesses of other substances in the diet may increase the requirement for vitamin D, and so render a diet low in vitamin D more rachitogenic than it would otherwise be. Of known importance in this connection are calcium and phytate (McCance and Widdowson, 1942). Phytate, or inositol hexaphosphate, which occurs in whole cereal grains, interferes with the absorption of calcium by forming insoluble calcium phytate in the intestine. A diet high in phytate and low in calcium and vitamin D is more rachitogenic than one with the same amount of vitamin D, but with more calcium and less phytate. A high fibre intake might also under certain conditions reduce the availability of calcium in the diet (Reinhold, Faradji, Abadi and Ismail-Beigi, 1976; James, Branch and Southgate, 1978; Kelsay, Behall and Prather, 1979).

6.4.3 There has been a suggestion that rickets, at ages other than infancy, occurs almost invariably in those Asians who eat chapattis (Dunnigan, McIntosh and Ford, 1976; Robertson, Kelman and Dunnigan, 1977). These are made without yeast, and much less phytate is destroyed than during bread-making when the dough is set to rise (Widdowson, 1941). In at least one study, individuals with late rickets and osteomalacia showed biochemical improvement when chapattis were replaced by white bread (Ford, Colhoun, McIntosh and Dunnigan, 1972b) but in another study, an Asian boy did not respond when chapattis were omitted from his diet, although treatment with UVR led to rapid healing of his rickets (Dent, Round, Rowe and Stamp, 1973). Consumption of chapattis is likely to be associated with vegetarianism and the consumption of other foods rich in phytate and fibre.

6.4.4 The amount of chapattis consumed by Asians ranged widely from about 30 g to about 400 g of flour a day (Hunt, O'Riordan, Windo and Truswell, 1976; O'Hara-May and Widdowson, 1976; Dunnigan, 1977; Goel, 1979). Chapattis are made in the United Kingdom from white flour which contains the statutory additions of calcium carbonate, thiamin, nicotinic acid and iron, together with a variable amount of the bran-containing fraction of the wheat according to the preferences of local Asian communities.

6.4.5 The dietary intake of phytate phosphorus by Asian schoolboys was found to be over 200 mg a day (Cooke, Asquith, Ruck, Melikian and Swan, 1974; O'Hara-May and Widdowson, 1976), which was considerably more than West Indian or white schoolboys were consuming. However, the calcium intakes of the same groups of Asian adolescents were surprisingly high, 850 mg a day

(Cooke, Asquith, Ruck, Melikian and Swan, 1974) and 1200 mg a day (O'Hara-May and Widdowson, 1976). In the latter study about 50% of the calcium came from milk and nearly 20% from the calcium carbonate in the chapatti flour. In both groups there should have been more than enough calcium available for absorption over and above the amounts that might have been rendered unavailable by the phytate.

6.4.6 In all the dietary studies vitamin D intakes were found to be low and less than 2 $\mu$g a day (Cooke, Asquith, Ruck, Melikian and Swan, 1974; Hunt, O'Riordan, Windo and Truswell, 1976; O'Hara-May and Widdowson, 1976) compared with the dietary intake of 2.5 $\mu$g recommended at that time (Department of Health and Social Security, 1969). This is not peculiar to Asians, however, for schoolchildren of other ethnic groups (West Indian and white) were found to have intakes of the same order (Cooke, Asquith, Ruck, Melikian and Swan, 1974).

6.4.7 Asian infants and young children do not eat enough chapattis for the phytate in them to interfere with calcium absorption. Their intake of vitamin D may, however, be low if they are breast-fed by mothers who are deficient in the vitamin or if they are weaned early on to 'doorstep milk' and have no supplement of vitamin D.

## 6.5 Conclusion

6.5.1 There are two main factors involved in the aetiology of rickets and osteomalacia in the United Kingdom. The first is the reluctance or inability of some Asian people and the elderly to take full advantage of the effect of sunlight on their uncovered skin. The second contributory factor is not only the low vitamin D content of the diet, which applies to many people of all races, but in the case of Asians, other characteristics of their diet which may confer some additional rachitogenic property. These two influences which predispose the Asian people to rickets and osteomalacia would be expected to become less as they settle down to the way of life in Britain.

# 7. Toxicity of vitamin D

## 7.1 Introduction

7.1.1 It is known that prolonged consumption of large amounts of vitamin D, in excess of about 2,000 μg a day, is harmful. Such over-consumption can cause hypercalcaemia, calcification of soft tissues and serious damage to the kidneys and cardiovascular system.

7.1.2 The difference between the amounts recommended for health or prophylaxis and that which used to be regarded as likely to cause poisoning is large. For example, the estimated daily recommended amounts for health ranges from less than 2.5 μg to 10 μg per day (Smith and Dent, 1968; Department of Health and Social Security, 1969 and 1979a) and the daily intake likely to be toxic about 3,750 μg (British Pharmaceutical Codex, 1973). However, during the last 30 years evidence has appeared which suggests that some individuals are at risk of adverse effects from intakes which are close to those recommended for prophylaxis.

7.1.3 This chapter examines the evidence for harmful effects arising from the prolonged consumption of relatively small excesses of vitamin D of about 25 μg to 100 μg a day and is concerned mainly with evidence relating to two disorders, infantile hypercalcaemia and coronary heart disease.

## 7.2 Infantile hypercalcaemia (IH)

7.2.1 There is evidence that IH is the result of a comparatively rare degree of sensitivity to moderately excessive intakes of vitamin D during the first nine months of post-natal life and sometimes by the mother during pregnancy.

7.2.2 The mild form of the disease has a good prognosis, is characterized by hypercalcaemia and 'failure to thrive' and is of sudden onset between three and nine months of age. The severe form has a bad prognosis and has additional features which include mental defect, impaired kidney function, a peculiar facial appearance, and supra-aortic and pulmonary stenosis. Serum cholesterol concentration is usually increased in the severe form but is only occasionally increased in the mild form of the disease. It is not clear whether the two forms are degrees of severity of the same condition or whether the difference is more fundamental. There is reason to believe that the severe form frequently has its inception *in utero* (Fraser, Langford Kidd, Kooh and Paunier, 1966). More than 90% of cases in the United Kingdom 'outbreak' of the 1950s were of the mild form.

7.2.3 In 1953 and 1954, when around 100* new cases of IH were being recorded annually in Great Britain, a normal infant might easily have consumed 100 $\mu$g of vitamin D daily in fortified milk, cereals and cod-liver oil compound (British Paediatric Association, 1956). However enquiry indicated that not all infants who developed IH had consumed this much; in one study of 38 patients, 26 (68%) had apparently taken less than 50 $\mu$g and 8 ( 21%) less than 25 $\mu$g daily (Graham, 1959).

7.2.4 In 1957, as a result of recommendations by the British Paediatric Association, the Ministry of Health and the Department of Health for Scotland (British Paediatric Association, 1956; Ministry of Health and Department of Health for Scotland, 1957), appropriate reductions were made in the vitamin D contents of infant milks, cereals and cod-liver oil compound. The reductions were estimated to have approximately halved the vitamin D intakes of young infants by the end of 1958.

7.2.5 Although, by 1960, there was an impression among paediatricians that the incidence of IH had declined, the recorded average monthly number of cases did not show a decline until 1960—61, about 2 years after the reductions had been made. This apparent inconsistency led to some reservations on the evidence for a causal relationship between IH and vitamin D excess (British Paediatric Association, 1964; Fraser, 1967), although others continued to regard the evidence which incriminated vitamin D as strong (Bransby, Berry and Taylor, 1964).

7.2.6 A reconsideration of the details relating to the apparent lack of correspondence between the timing of the vitamin D reductions and the decline in IH suggests that much of the difference might be resolved. The average numbers of cases per month recorded in 3 surveys (British Paediatric Association, 1964) were 7.2 between 1 January 1953 and 30 June 1955, 6.8 between 1 January 1959 and 31 December 1959, and 3.0 between 1 January 1960 and 31 May 1961. Since the age of onset is 3 to 9 months, the vitamin D content of foods given to infants in the second half of 1958 could have influenced morbidity in the first few months of 1959. Also as the figure shown for 1959 is a monthly average it is possible that the number of cases in the second half of that year was significantly lower than in the first half. Furthermore, there was the possibility that complete replacement of old products containing larger amounts of vitamin D was not achieved until some time in 1959 (Department of Health and Social Security, 1970).

*The incidence of reported cases of IH in 1953—55 was about 1 in 8,000 live births. In 1960 to 1961 the reported incidence was about 1 in 20,000 live births. Although these figures indicate a rare condition, because of the general nature of the illness in the mild form and the fact that the incidence estimates were based on reports from hospital doctors only, there is the possibility of under-reporting. The scale of morbidity due to this condition in Britain in the 1950s is therefore somewhat uncertain.

7.2.7 A further point in favour of a causal relationship is that the amount of vitamin D consumed from cod liver oil and fortified products at different ages in the first year of life (Ministry of Health and Department of Health for Scotland, 1957) appears to correspond well with what has been reported on the age distribution of IH (Stapleton, Macdonald and Lightwood, 1957; British Paediatric Association, 1964; Black, 1964; Fourman and Royer, 1968).

7.2.8 A comparison of the features of IH with those seen in known cases of vitamin D poisoning in infants provides further evidence that IH is due to an intake of vitamin D which is excessive for the individual. The same symptoms and kidney damage occur in both conditions (Black, 1964). However, the dose of vitamin D is typically very large in classical poisoning, usually hundreds or thousands of $\mu$g a day for several months (Black, 1964; Najjar and Yazigi, 1973), whereas it appears to be often within the range of 20 to 100 $\mu$g a day in IH (Black, 1964). This discrepancy might be explained on the basis of normal variation in sensitivity or by development of abnormal hypersensitivity. When vitamin D is withdrawn the hypercalcaemia declines more rapidly to normal in known intoxication than in either type of IH (Black, 1964). Black thought there was little doubt that chronic overdosage with vitamin D could produce the clinical and radiological features of the severe type of IH.

7.2.9 A report by Ćurčić and Ćurčić (1975) is possibly relevant to the problem of IH. They describe increases in the serum cholesterol and blood pressure in children under 3 years of age who were being treated for rickets with 75 to 300 $\mu$g vitamin D daily. The findings however need comparison with measurements from healthy children, since patients with active rickets may be generally undernourished and might be expected to show increases in some physiological values on rehabilitation.

7.2.10 Some experimental work in animals suggests that hypersensitivity to vitamin D in the offspring might be induced by giving very large doses to the mother during gestation (Taussig, 1966).

## 7.3 Coronary Heart Disease

7.3.1 Prolonged consumption of 1000 to 3000 $\mu$g vitamin D daily is known to cause hypercholesterolaemia (Fleischman, Bierenbaum, Raichelson, Hayton and Watson, 1970), hypercalcaemia, and cardiovascular and renal damage (Fourman and Royer, 1968). Comparable doses produce similar effects in animals including arterial lesions similar to human atherosclerosis (De-Langen and Donath, 1956; Gillman and Gilbert 1956; Taura, Taura, Kamio and Kummerow, 1979). There is also some evidence that, in the presence of hypercholesterolaemia, small prolonged excesses of vitamin $D_3$, of about 12.5 $\mu$g to 25 $\mu$g/day, can give rise to atherosclerosis-like lesions in squirrel monkeys (Peng, Taylor, Tham and Mikkelson, 1978). However the lowest daily intake that would contribute to cardiovascular damage among a large group of normal people is not yet known.

7.3.2 Linden (1974) concluded, in a retrospective case control study of vitamin D consumption and myocardial infarction in a northern part of Norway where consumption of dietary vitamin D was exceptionally high, that about 30 μg a day might be a critical amount above which there is a significant addition to the risk of developing myocardial infarction. Some support for this finding appears in another study in which a group of farmers taking vitamin D supplements of between 17 and 62 μg a day had a significantly higher serum cholesterol than another group not taking supplements (Dalderup, 1968 and 1973). However other studies do not confirm these findings. Serum 25-OHD was measured in patients with myocardial infarction and found to be no higher than in controls (Lund, Badskjaer, Lund and Soerensen, 1978; Schmidt-Gayk, Goosen, Lendle and Seidel, 1977; Vik, Try, Thelle and Førde, 1979). In another study 25 μg of vitamin D daily did not cause an increase in serum cholesterol, but the trial was complicated by the use of a multi-vitamin preparation (Carlson, Derblom and Lanner, 1970).

## 7.4 Discussion

7.4.1 Except in infancy and sometimes in old age vitamin D appears to be obtained mainly from the action of sunlight on 7-dehydrocholesterol in the skin. With the exception of certain groups deprived of sunlight or who consume a rachitogenic diet the need at other ages for a dietary source is not well established. A low degree of dependency on the diet might have developed in populations in temperate latitudes, and industrial development and smoke pollution appear to have caused a special need in the past. However, the amount of vitamin D obtained from food is usually small and only a few μg a day.

7.4.2 What is known of the physiology of vitamin D is consistent with these facts and suggests that the body is better adapted to handle vitamin D which is derived from sunlight (Fraser, 1980). Vitamin D is probably formed in the skin and transferred to the blood at a controlled rate (Holick, Holick, NcNeill, Richtand, Clark and Potts, 1979); when taken by mouth it is more rapidly absorbed, gives rise to wider fluctuations in plasma 25-OHD and is less well conserved. When large amounts are ingested much of the vitamin may be transported in the blood bound to lipoprotein and albumin instead of the specific globulin, and this may lead to uncontrolled transfer in the tissues (Silver, Shvil and Fainaru, 1978).

7.4.3 A consideration of the evidence on adverse reactions to between 25 and 100 μg of vitamin D a day leads to the question of whether such reactions depend on normal variation in sensitivity or on abnormal hypersensitivity. At present it seems that either might apply. There are the epidemiological studies suggesting a dose response type of risk relationship, or experimental and clinical observations (Fleischman, Bierenbaum, Raichelson, Hayton and Watson, 1970; Leeson and Fourman, 1966; Taussig, 1966) that suggest hypersensitivity might be induced by a large overdose of vitamin D.

7.4.4 Concerning present consumption of vitamin D by the population in Britain, there may still be a small risk from excess consumption among some infants during the first year of life, which is associated with the rather high variability of intakes (Department of Health and Social Security, 1970). There has been some concern in the past that further action to eliminate this possible risk would result in a large number of infants with low intakes and an increase in rickets. Nevertheless in a recent review of infant feeding practice a change in the dose of Children's Vitamin Drops is recommended (Department of Health and Social Security, in press). At ages other than infancy and early childhood it is difficult to assess whether there is any health risk from excessive consumption of vitamin D. For the population in general the dietary intake appears to be low and on average about 2.5 μg a day with the majority of intakes falling within the range of 1 to 7 μg. New evidence on the vitamin D content of cows' milk and other animal produce (Lakdawala and Widdowson, 1977; Kummerow, Cho, Haung, Imai, Kamio, Deutsch and Hooper, 1976; Bille, Carstensen, Leerbeck and Sondergaard, 1976) may mean there is some underestimation of intakes. Although it appears unlikely that there is any widespread problem of prolonged high intakes, the subject requires further study since there seems to be a small chance that a high intake might result occasionally from certain foods and/or medicinal products. More information is needed on the vitamin D content of the diet and the use of vitamin D containing medicines by different groups of the population.

## 7.5 Conclusion

7.5.1 The question examined here is whether habitual daily consumption of 25 to 100 μg of vitamin D is harmful in normal individuals (para 7.1.3). The evidence considered does not allow a conclusive answer but does indicate a risk to health in respect of infantile hypercalcaemia. Concerning coronary heart disease there is no convincing evidence that intakes as low as this predispose to the disease although in view of various epidemiological and experimental studies it is important to bear in mind the possibility that they might. Vitamin D when given in high dosage over long periods can cause serious damage to the cardiovascular and renal systems; what is unknown is the level of dosage at which this property first becomes manifest among normal individuals.

# 8. Fortification of foods with vitamin D

## 8.1 Introduction

8.1.1 Fortification is the addition of a nutrient to a widely consumed food which acts as a vehicle for increasing the daily intake of the nutrient. As a public health measure, fortification can be used to supplement the diet with a nutrient, lack of which has been shown to cause a deficiency disease. The statutory fortification of margarine in 1940 with vitamins A and D was introduced to ensure that adequate intakes were maintained at a time when other sources might be in short supply.

8.1.2 In 1940 Government was also concerned that decreased imports might jeopardize national supplies of milk and cheese and that the rationing of these foods might lead to a shortage of dietary calcium. National flour, which had been introduced as a wartime measure in May 1941, contained greater amounts of phytate than white flour. For these reasons, all flour (except wholemeal flour) was fortified with calcium carbonate. This fortification became mandatory in 1942. These actions by Government were taken because they were deemed necessary for the protection of the health of the large majority of the population. Apart from the fortification of National Dried Milk with vitamin D in 1945, and later, the partial restoration (not fortification) of iron and two of the B vitamins, thiamin and nicotinic acid, to white flour from which these nutrients had been removed in milling, there has been no compulsory addition of any nutrient to a food.

8.1.3 In the United Kingdom, manufacturers may fortify their products voluntarily with any nutrient, including vitamin D. The Labelling and Claims Regulations (Ministry of Agriculture, Fisheries and Food, 1979 and 1980a) ensure that the public can be aware of the amount of any nutrient added to the food for which the manufacturer makes a claim because this amount is declared on the label. Under this system there can be no accusation of compulsory medication of individuals. A list of some foods which are voluntarily fortified with vitamin D is given in Appendix B.

8.1.4 The Working Party set up by the Committee on Medical Aspects of Food Policy in 1977 had the task of assessing whether or not the recrudescence of vitamin D deficiency in Great Britain was of such proportions that only some action by central government could abate the problem, or whether a disease for which the cure and preventive measures are known, and which has been virtually eradicated in the past, could be better dealt with by local action. If Government action were considered necessary then the question arises whether one of the

foods eaten by most of those persons who are at risk of deficiency should be fortified and to what extent, or whether an increase in the fortification of foods already fortified with vitamin D would be justified.

8.1.5 The foods considered by the Working Party were household milk, chapatti flour, all flour (other than wholemeal), butter and margarine. Since vitamin D deficiency occurs chiefly among Asian infants and children, young Asian women, and the housebound elderly of all races it is important that the foods to be discussed are those which are usually included by these people in their diet.

## 8.2 Household milk

8.2.1 In the United States of America fortification of foods with any nutrient is a matter for voluntary action by the food industry although it is controlled, as in the United Kingdom, by Labelling Regulations. Milk is no exception, and for some 30 years about 85 per cent of household milk has been fortified with about 10 μg vitamin D/US quart (6.25 μg/Imperial pint; 11 μg/litre). The American Academy of Pediatrics (1963) reported that the fortification of milk was an effective method of preventing rickets. Nevertheless, there are groups which are not effectively reached by this measure (Bachrach, Fisher and Parks, 1979).

8.2.2 In Canada, fortified household milk has been available for some time and, since March 1976, the addition of vitamin D to milk has been mandatory. The amount added varies from 7.5 to 10 μg vitamin D/Imperial quart (6.6—8.8 μg/litre). At the same time the addition of vitamin D to all other foods was prohibited with the exception of margarine and baby milks. No information is available about the effect of this measure on public health.

8.2.3 In Britain ordinary cows' milk contains only about 0.1 to 0.3 μg vitamin D/litre associated with the fat, and some water-soluble vitamin D sulphate (Lakdawala and Widdowson, 1977), the biological activity of which has not yet been fully investigated. Most people, including Asians, drink some milk daily and the small amount of vitamin D thus ingested is likely to be of some significance for their health. Milk is also a good source of protein, calcium and phosphorus, all of which are necessary for the growth and maintenance of bone. In a special study from 1971 to 1978 of milk drunk by individuals, the National Food Survey found an average weekly intake of 4—5 pints/person, that is to say, about 365 ml/person daily (Ministry of Agriculture, Fisheries and Food, 1980b). Dietary surveys suggest that Asian adolescents also drink similar quantities of milk (Hunt, O'Riordan, Windo and Truswell, 1976; O'Hara-May and Widdowson, 1976).

8.2.4 According to National Food Survey findings, the average amount of vitamin D in food purchased for domestic use, excluding meals eaten outside the home, is 2.7 μg/person daily. If milk were fortified here as in the United States of America to 6.25 μg vitamin D/Imperial pint, about 4 μg vitamin D/person daily

would be added to the average dietary intake. Such an amount would be of benefit to young Asian women during pregnancy if milk were included in an otherwise vegetarian diet, especially if the women remained indoors for much of the time and were not taking the supplements which can be provided on the advice of general practitioners and obstetricians. The amount would also benefit many young Asian children, or any child who was on the borderline of deficiency, and probably many household elderly people. However, beside all those in particular groups who would derive benefit from additional vitamin D there remain the majority in the general population who appear to have no need for any extra, and some individuals who habitually drink exceptionally large quantities of milk would have intakes considerably in excess of their requirements over long periods of time.

8.2.5 In order to ensure an even dispersion of vitamin D in liquid milk, homogenization would probably be necessary. Homogenized milk has different physical properties and a slightly different taste from ordinary household milk which make it unpopular with some people. An educational programme would be necessary to persuade those in need of milk fortified with vitamin D to persevere with the homogenized product.

8.2.6 Mandatory fortification of liquid milk would entail negotiation, not only with the British authorities, but also with the European Economic Community. No other member country of the Community fortifies milk with any nutrient. Voluntary fortification and the marketing of a specially named product, which could not be called 'milk' unless other regulations were altered, would almost certainly lead to an increased cost compared with household milk. The problem would remain of teaching those at risk of vitamin D deficiency to purchase the specially fortified and named product.

## 8.3 Chapatti flour

8.3.1 Some, but not all, Asians eat chapattis made from flour sold for the purpose (paras 6.4.3 and 6.4.4). There has been considerable enthusiasm, from some people who are concerned about rickets in the Asian population, for chapatti flour to be fortified with vitamin D. The suggestion arose after a study carried out in Glasgow (Pietrek, Windo, Preece, O'Riordan, Dunnigan, McIntosh and Ford, 1976) in which chapatti flour fortified with vitamin D was provided for 6 Asian families for 6 months. The flour contained 125 $\mu$g vitamin $D_2$/kg, the object being to supply approximately an extra 10 $\mu$g (400 iu)/person daily, allowing for 50% of the vitamin to be lost on cooking. Four other families received a capsule containing 75 $\mu$g (3000 iu) vitamin D weekly. A third group of 4 families acted as a control and received no supplement. In the control group mean concentrations of calcium and 25-OHD in the blood fell during the winter months. In the other 2 groups the concentrations increased, but the pattern of change in those receiving capsules was not consistent, possibly because the supplement was not always taken. The number of children with biochemical changes suggestive of rickets increased in the control group during the 6 months, but in both groups receiving vitamin D the number decreased. The vitamin D

fortified chapatti flour was uniformly effective in increasing the plasma 25-OHD concentration, and it was therefore concluded that this was one suitable means of introducing supplementary vitamin D into the Asian diet. The study was carefully supervised and there was every inducement to eat the fortified flour.

8.3.2 Tests which have since been conducted under the auspices of the Panel on Child Nutrition, in collaboration with the millers, showed that the stability of vitamin D added to flour in normal storage was satisfactory, but in one standard method of cooking chapattis about 50% of the added vitamin was destroyed (Hartley, 1977, personal communication). There may be considerable variation in cooking losses according to different culinary methods, different size of chapattis and different ingredients.

8.3.3 The intake of chapatti flour, like that of other cereal and vegetable staples, characteristically increases with age to adulthood and then declines slowly through maturity to old age. This age consumption pattern is not favourable to the aims of fortification, for the intake is low in young children and high in physically active young men. There is considerable variation between different Asian groups in the average amount which is consumed each day. The overall range of individual consumption varied from about 30 g to around 400 g (Hunt, O'Riordan, Windo and Truswell, 1976; O'Hara-May and Widdowson, 1976; Dunnigan, 1977). In the Glasgow trial (para 8.3.1), the average consumption was taken as about 200 g, which would have ensured an intake of about 10 $\mu$g vitamin D (Dunnigan, 1977). Cooking losses might be less than 50% and intakes considerably greater so that at this level of fortification some individuals would ingest 20 $\mu$g or more of vitamin D daily. On the other hand, young children aged 2—3 years would eat only about 20 g flour a day, and, allowing for cooking losses, would obtain only about 1 $\mu$g vitamin D in addition to their customary intake. Another difficulty is that not all Asians eat chapattis.

8.3.4. Fortification of chapatti flour with vitamin D on a voluntary basis would be permissible under the present legislation provided that the labelling of the product complies with the Labelling of Food Regulations (Ministry of Agriculture, Fisheries and Food, 1979). However it seems that wholesale and retail distributors would be reluctant to handle two sorts of flour, fortified and unfortified. For the addition to be made compulsory, the present Bread and Flour Regulations would require amendment and there would have to be an appropriate procedure for testing and enforcement. Ministers and Parliament would have to be convinced by expert advisers that such measures were essential as a solution to the problems of vitamin D deficiency in Britain.

## 8.4 All flour (other than wholemeal)

8.4.1 The addition of nutrients to any flour is controlled by the Bread and Flour Regulations which at present require the addition of calcium, iron, thiamin and nicotinic acid to all flours except wholemeal. The same considerations apply to the voluntary fortification of all flour as to the

fortification of chapatti flour. Convincing reasons why extra vitamin D is needed by the general population would have to be demonstrated before the addition of the vitamin could be made compulsory.

## 8.5 Butter

8.5.1 Another food which is a possible carrier for vitamin D is butter, but fortification of butter would present difficulties since much of the butter sold in the United Kingdom is imported.

## 8.6 Increased fortification of margarine

8.6.1 At present margarine contains 71—88 μg vitamin D/kg, that is, a vitamin D content about 10 times that of butter. Many Asians do not eat margarine, and to increase the amount of vitamin D in it would not be of great benefit to the Asian community.

## 8.7 Conclusion

8.7.1 The fortification of all liquid milk offers the advantage that it would be a potential solution to the problem of rickets and osteomalacia in all groups of the population. The quantities of milk consumed and the age pattern of consumption would comply with the aims of fortification. However, there is little reason to believe that any more than a minority of the population are in need of the benefit that fortified milk would confer.

8.7.2 Compulsory fortification of all flour with vitamin D would similarly supply additional vitamin D to millions of people who do not need it. Moreover the Bread and Flour Regulations would have to be amended before this could be done, and there would have to be procedures for regular assessment for enforcement of the addition of vitamin D. Chapatti flour could be fortified with vitamin D but there are difficulties in setting the desired concentration because Asians who are likely to need vitamin D are to be found among several different groups and the intake of chapatti flour by these groups is very variable. The administrative problems concerning compulsory fortification of chapatti flour are similar to those which would apply to all flour.

8.7.3 Milk or chapatti flour could be fortified on a voluntary basis but an extensive programme of health education, commercial advertising and propaganda would be necessary in order to ensure, as far as this is possible, that those at risk of deficiency obtained the food which had been fortified.

8.7.4 The fortification of butter presents difficulties because much butter is imported, and the increased fortification of margarine would be unlikely to solve

the problems of deficiency because both Asians and elderly people seem, in general, to prefer butter.

8.7.5 One of the decisions to be taken if any food were to be fortified is whether the addition of vitamin D should be to all or only some of that food on sale. Experience with the fluoridation of water suggests that the compulsory fortification of all flour or all milk might meet with much opposition. A likely reason for objection would be interference with the composition of a staple item of diet which might have unsuspected effects on health. Another objection might be on the ground of mass medication since the intakes of many people not in need of additional dietary vitamin D would be increased.

8.7.6 Vitamin D is known to be severely toxic when consumed in large quantities (para 7.1.1.), but it is unlikely that fortification of food would lead to such large intakes. However, there is some evidence that intakes which appear to be only slightly excessive are not without harm. The evidence has been reviewed in section 7. Evidence with respect to idiopathic infantile hypercalcaemia is more convincing than that for coronary heart disease. For present health problems, further fortification of food with vitamin D is undesirable if there is any possibility of doing harm, particularly as there are already effective measures for prevention available.

8.7.7 For all these reasons the Working Party does not consider the mandatory fortification of milk, flour or butter with vitamin D, or any increase in the compulsory fortification of margarine or any other food which is at present so fortified (Appendix B), a satisfactory solution to the present problem of vitamin D deficiency which is confined to a relatively small section of the population.

8.7.8 In addition, the Working Party considers that manufacturers should consult the Health Departments and the Ministry of Agriculture, Fisheries and Food as to the amount of vitamin D to be added to any product which they propose to fortify, in order that excessive intakes derived from a combination of several fortified foods in the diet may be avoided.

# 9. Other preventive measures

## 9.1 Sunlight and ultra-violet radiation (UVR)

9.1.1 An important aspect of the prevention of rickets and osteomalacia among Asians, and of osteomalacia among all elderly people, is that these people should appreciate the importance of sunlight on the uncovered skin as the means whereby the body obtains enough vitamin D.

9.1.2 Some Moslem and Hindu women and their infants and female children are screened from much of the available sunlight by customs of clothing and confinement indoors. These customs may be slow to change, but as the new generation of young women and mothers grow up, many of them will have lived all or most of their lives in the United Kingdom and it seems likely that female seclusion will be less strictly observed. Asian schoolchildren still seem to have more of their bodies covered with clothing than West Indian or white children, but there is evidence that they are adopting more and more the way of life typical of British schoolchildren. Many elderly people are also only rarely exposed to outside sunlight; they tend to wear more clothes and some, by reason of infirmity, are forced to remain indoors.

9.1.3 To ensure an effective response in the amount of vitamin D formed in the skin it is necessary for people to spend some time out-of-doors during the spring and summer (para 6.2.1). Solar UVR does not penetrate ordinary window glass and therefore people who are confined indoors do not benefit from it. Windows made of glass which transmits UVR, and fluorescent lighting which emits more UVR (Corless, Gupta, Switala, Barragry, Boucher, Cohen and Diffey, 1978), have both been suggested as possible ways of improving the vitamin D status of elderly people who live in institutions, hospital wards or ordinary homes. The Working Party recommends that more research, in collaboration with industry, is required before such methods could be advocated.

## 9.2 Foods containing vitamin D

9.2.1 Nutrition surveys of groups of the indigenous population have recorded average intakes of vitamin D of about 1.5—3.5 $\mu$g daily (Table 9.1) mainly obtained from margarine and eggs.

9.2.2 The dietary requirements of individuals for vitamin D are not known, partly because the amount derived from the action of UVR on the skin cannot at present be measured. For adults, a dietary intake of 2.5 $\mu$g vitamin D daily is suggested as likely to be enough, but 7.5 $\mu$g and 10 $\mu$g daily are suggested for infants and young children and 10 $\mu$g daily during the winter months for older

**Table 9.1**: *Average daily intakes of vitamin D by different population groups*

| Group | Age (yrs) | μg vitamin D/day | |
|---|---|---|---|
| | | males | females |
| Preschoolchildren | 1½—2½ | 3.17 | 3.84 |
| | 2½—3½ | 2.22 | 2.66 |
| | 3½—4½ | 1.94 | 1.91 |
| Schoolchildren | 10—11 | 1.66 | 1.44 |
| | 14—15 | 1.46 | 2.18 |
| | 14—15 | 2.12 | 1.74 |
| Pregnant women (indigenous) | | — | 2.28 |
| Elderly people | 65—74 | 3.33 | 2.31 |
| | 75 and over | 2.68 | 2.09 |

Source: Department of Health and Social Security, 1972, 1975 and unpublished data.

children (Department of Health and Social Security, 1979a). It would be difficult to achieve these amounts from the diet alone, and therefore supplements are necessary (section 9.3).

9.2.3 The use by Asian people of foods such as milk, eggs and cheese, and the occasional consumption of fish and meat, if these are acceptable, is to be encouraged, since these foods may have a protective effect against rickets and osteomalacia for reasons other than their usually small or negligible vitamin D content. They will provide high quality protein, calcium and phosphorus needed for growth and maintenance of healthy bone, and will also tend to displace any excess of plant staple that has a possible anticalcifying effect.

## 9.3 Vitamin D supplements

9.3.1 Cod liver oil has been known for three centuries to protect from and cure rickets. This has been recognized in more recent times to be due to its high content of vitamin D (para 1.1.1). Unfortunately the fishy taste is objectionable to most adults and older children, although the young child will often take it by mouth without any apparent distaste. Pleasant tasting preparations of vitamin D can now be obtained. These may be proprietary products, or Children's Vitamin Drops and Vitamin Tablets for expectant and nursing mothers supplied by the Health Departments and available under the Welfare Foods Scheme.

9.3.2 By the Welfare Foods Scheme, tablets containing vitamin D are available from maternal and child health clinics and Welfare Foods distribution centres for expectant mothers and for lactating mothers up to 30 weeks after parturition. The supplements are supplied either at low cost or free of charge to poor families. Since relatively few pregnant women choose to receive ante-natal care from community health-care clinics, and the vast majority attend hospital clinics at least once to make a booking for the birth, some consideration should be given to making the vitamin tablets also available at hospital clinics so that Asian women can be given a supply.

9.3.3 Children's Vitamin Drops are available free or at reduced price from Welfare Foods distribution centres for children up to 5 years of age. In a recent review of infant feeding practice the Committee on Medical Aspects of Food Policy has recommended that all children should have a daily dose of **5 drops** of the supplement from about one month of age until at least 2 years and preferably until 5 years of age (Department of Health and Social Security, in press). The rule that all infants should receive the supplement may be relaxed on professional advice if the vitamin D status is considered to be satisfactory.

9.3.4 Within the National Health Service proprietary vitamin preparations containing vitamin D can be prescribed by general medical practitioners. Exemption from prescription charges applies to children and adolescents up to the age of 16 years, to women during pregnancy and until the children are one year old, and to all elderly persons (women of 60 years and over, men of 65 years and over).

9.3.5 General practitioners, hospital doctors and local health authority clinic doctors and nurses are reminded of the possibility of vitamin D deficiency in Asian women, children and adolescents who complain of minimal non-specific symptoms (Appendix A). For other high risk Asians, who in the normal way rarely see a doctor or nurse, some additional means is required to contact them. Those most likely to need such attention, especially during the winter months, are adolescents and women of child-bearing age. Health Authorities should consider the provision of supplements to high risk Asian adolescents.

9.3.6 The elderly who are housebound usually have some disability which keeps them indoors and consequently they are under the supervision of a general medical practitioner. No special arrangement is necessary to provide supplements for the elderly housebound, since these may be obtained on prescription free of charge.

9.3.7 Any preparation of vitamin D carries instructions which have been carefully drawn up to provide the correct dose. No risk of taking too much is incurred if the instructions are followed, but only **one** preparation should be used.

## 9.4 Additional measures

9.4.1 The importance of vitamin D and the effects of deficiency need to be brought to the attention of all at-risk groups and those responsible for them, together with information about available preventive measures. In this connection health education has a valuable part to play. Much has already been done in the field of health education in many large cities. In Glasgow, a working group which includes two community physicians, a paediatrician, a general physician, the area nursing officer (child health), the health education officer, the area pharmacy officer and a general administrator has put into operation an effective programme of health education for the prevention of rickets and

osteomalacia among Asians (Dunnigan, 1979, personal communication). The Glasgow experience should prove of value in other areas.

9.4.2 As with many other diseases, improvements in general nutrition and general living conditions are likely to reduce morbidity from rickets and osteomalacia.

# 10. Summary and conclusions

## 10.1 Incidence of rickets and osteomalacia

10.1.1 In the last 20 years an appreciable number of cases of rickets and osteomalacia in Asian people has been seen in Britain. Rickets has affected infants, children and adolescents, and osteomalacia has occurred in women of child-bearing age. Rickets has also been reported in infants of other dark-skinned races living in Britain. Both rickets in infants and children and osteomalacia in young women are now rare in the indigenous population of Britain, although osteomalacia in elderly people who are housebound or who live in institutions is not uncommon.

10.1.2 Rickets and osteomalacia are not notifiable diseases and there is no national information about incidence except that from records of hospital in-patient treatment which can be obtained from Hospital Activity Analysis and the Hospital In-patient Enquiry, and information obtained directly from local health professionals. These sources of information are subject to a number of limitations but they indicate that, during the last 10 years, the incidence of rickets among Asians in Britain has declined. The situation regarding osteomalacia among Asian women is less certain although most of the evidence indicates that the incidence has remained fairly steady. These trends should be observed over the next few years.

10.1.3 A decline in rickets among Asians appears to be occurring as they settle down in Britain and as the existing health measures and efforts in prevention take effect. Rickets and osteomalacia are not necessarily a result of coming to live in Britain since these diseases occur in the countries from which the Asian people have emigrated. However, it is possible that the smaller quantity of ultra-violet radiation (UVR) available from sunlight in this country may add to the risk of developing disease in some individuals. Rickets and osteomalacia are more likely to arise among women and children who remain secluded to some degree and when very little of the skin is left uncovered and exposed to sunlight; among vegetarians whose diet is made up largely of chapattis, legumes and vegetable curries; among those whose living conditions are poor due to dark rooms, over-crowding, bad housing and physical environment; among newly arrived immigrants from a poor socio-economic background; and among individuals whose families have a history of rickets or osteomalacia. In infancy, rickets is also associated with artificial feeding if there is an early change from infant formula, which is fortified with vitamin D, to cows' milk which contains little vitamin D unless a supplement of vitamin D is given. These characteristics are useful for identifying women and children at higher risk of developing osteomalacia and rickets, and will also help to identify those with other associated causes of poor health such as anaemia.

10.1.4 Osteomalacia among elderly people, especially the housebound, is a more widespread problem, and may have a bearing on the frequency with which fractures of the neck of the femur occur among the elderly. Members of the Working Party agree that more information is needed about the vitamin D status of the elderly and particularly about those who sustain a femoral fracture.

## 10.2 The question of fortification

10.2.1 Action by Government in Britain in 1940, at a time of war and restraints, had a favourable effect on the incidence of rickets, which was then not uncommon, and led to a very marked decline in the disease by the 1950s. The increase in incidence which has been reported in several parts of the country since 1962 has been caused by a special problem in a small section of the population.

10.2.2 Deficiency of vitamin D in an otherwise healthy person is the result of insufficient exposure of the skin to sunlight and/or an inadequate intake of the vitamin in the diet. Rickets and osteomalacia can be prevented by consumption of the few foods which either naturally contain the vitamin or which have been fortified with it. Since the best sources of vitamin D are often not included in the diet by Asians, consideration has been given to the fortification of flour, milk or butter with vitamin D and to an increase in the fortification of margarine.

10.2.3 There has been much enthusiasm to add vitamin D to the flour used by Asians to make chapattis. However, not all Asians eat chapattis, and the amount of vitamin D to be introduced into the flour presents some difficulty because of the variation in consumption. Children who eat few chapattis would not be provided with enough vitamin D and adults who eat large amounts of chapatti would necessarily have relatively larger intakes of vitamin D. Not only would these intakes be unnecessary but there is some evidence that intakes could approach amounts which might be harmful for some individuals. Mandatory fortification of any food which is a common constituent of the diet cannot be recommended if there is any evidence of possible harm, especially when other means of dealing with the problem of deficiency are available and have proved in the past, and are proving now, to be effective.

10.2.4 Fortification of ordinary liquid milk presents similar problems, arising from variation in consumption, to the fortification of chapatti flour. There would also be legal and administrative difficulties including the need to persuade the British people to accept compulsory medication in order to treat what appears to be a declining problem among a small section of the population. Asians do not generally eat margarine, and much of the butter which is used to make ghee is imported.

10.2.5 The Working Party unanimously decided not to recommend the mandatory fortification of any sort of flour, milk or butter with vitamin D or any increased fortification of margarine.

## 10.3 Ultra-violet radiation (UVR)

10.3.1 For the synthesis of vitamin D, UVR of wavelength less than 313 nm is required. Almost no solar radiation of this wavelength reaches the United Kingdom in winter, and synthesis is therefore limited largely to the spring and summer months provided that cultural habits do not prevent the radiation from reaching the skin by a full covering of clothing or by confinement indoors. Housebound persons, whether old or young, cannot obtain this benefit because ordinary window glass is opaque to UVR. A possible remedy for this situation would be to fit windows which are transparent to UVR or to have fluorescent lighting which emits radiation of the necessary wavelength in homes for people whose infirmity keeps them indoors and in hospitals. Some discussion with industry and further research are required before any decision can be taken on this.

## 10.4 Existing preventive measures

10.4.1 Vitamin supplements under the Welfare Foods Scheme are at present available to infants and children up to the age of 5 years, and to pregnant and lactating women for 30 weeks after the birth; they are not at present supplied to adolescents and the housebound elderly. The Working Party suggested that supplements should be made available to Asian adolescent schoolchildren and to non-pregnant Asian women who are at higher risk, and that consideration should be given to this matter by Health Authorities. General practitioners can prescribe proprietary vitamin preparations and exemption from prescription charges applies to all children and adolescents up to the age of 16, expectant mothers, mothers who have a child under one year of age and to women over 60 and men over 65. Thus, all age groups who are at risk of deficiency can obtain supplementary vitamin D either cheaply or free, with the exception of non-pregnant women below the age of 60.

## 10.5 Conclusions

10.5.1 The Working Party unanimously agreed that the present problem of rickets and osteomalacia appeared to be confined to certain areas and to relatively small, well-defined groups of the population and did not call for any major change on a national scale in the measures available for prevention. The problems can best be solved, not by the fortification of any new food or by increasing the fortification of any food which is at present fortified with vitamin D, but by local action so that available preventive and therapeutic measures are fully utilized. This will involve a programme of education both of health professionals and of the 'at-risk' groups.

10.5.2 For the Asians who are likely to be at risk, the importance of the action of sunlight on bare skin, of a generally nutritious diet and of the correct use of medicinal preparations containing vitamin D must be realized. The problem of

reducing the risk of osteomalacia among Asian women is likely to be a more difficult task than reducing the risk of rickets among infants and children.

10.5.3 For the elderly, the judicious use of supplements of vitamin D would be a more appropriate preventive measure than a system of food fortification. Education is also necessary so that the nutritional problems associated with being housebound are remembered as well as all the other problems of infirmity. If UVR can be introduced in the ways previously specified (para 10.3.1) this could alleviate the problem in the future; for the present such benefits are not available.

# 11. Recommendations

## 11.1 General considerations

11.1.1 After careful consideration of the available evidence about the present distribution and frequency of rickets and osteomalacia in Britain and recent trends in the incidence of these diseases; the dietary, technical, organizational and legal aspects of adding vitamin D to various foods; the possible harm from a relatively small excess consumption of vitamin D; aspects of the distribution and aetiology of rickets and osteomalacia in India and other warm countries; and previous experience in the prevention and treatment of these diseases in Britain, members of the Working Party make the following recommendations.

## 11.2 Fortification of foods

11.2.1 Milk, butter and flour, including chapatti flour, should not be compulsorily fortified by the addition of vitamin D.

11.2.2 The mandatory fortification of margarine with vitamin D should be continued, as at present, but not increased.

11.2.3 The voluntary fortification of certain proprietary foods which is permitted at present, should be allowed to continue.

11.2.4 Decisions about the possible fortification of any other foods should be made only after consultation between manufacturers, the Health Departments and the Ministry of Agriculture, Fisheries and Food.

## 11.3 Education

11.3.1 Those responsible locally for the health of Asian members of the population should give priority to the education of health professionals and to the Asians themselves about the importance of vitamin D for health; the need for out-of-doors exposure to sunlight on part of the uncovered skin during the spring and summer months; the dietary sources of vitamin D; and the need of individuals, who are at higher risk of deficiency and therefore of disease, to take supplements of vitamin D.

11.3.2 The risk of osteomalacia among persons who are housebound (confined indoors), particularly elderly people, advice about diet, and the use of small supplements of vitamin D, are also matters for the education of the individuals at risk and of both professional and lay people who are responsible for their welfare.

## 11.4 Supplements of vitamin D

11.4.1 The present provision, under the Welfare Foods Scheme, of vitamin supplements, which contain vitamin D, namely Children's Vitamin Drops for children up to the age of 5 years, and Vitamin Tablets for expectant and nursing mothers for 30 weeks after parturition, should continue.

11.4.2 Consideration should be given by Health Authorities to making the Vitamin Tablets of the Welfare Food Scheme available in hospitals for those who attend the ante-natal clinics.

11.4.3 Consideration should also be given by Health Authorities to making supplements of vitamin D available in winter to those Asian adolescent school-children who are selected as likely to benefit from the supplement.

11.4.4 The attention of health professionals should be drawn to the greater risk of vitamin D deficiency among vegetarian Asian women who spend little time out-of-doors and whose living conditions are poor. Health Authorities should consider the need to provide supplements for these women.

## 11.5 Trends in rickets and osteomalacia

11.5.1 The incidence of rickets and of osteomalacia should be monitored and the situation reviewed from time to time.

## 11.6 Research

11.6.1 The amount of vitamin D, both water soluble and fat soluble forms, in foods should be measured and the total intake, both dietary and from supplements, and its seasonal variability in different age/sex groups of the population should be investigated.

11.6.2 The possible toxicity of relatively small doses of vitamin D should be investigated further.

11.6.3 The association between vitamin D deficiency and fracture of the neck of femur in the elderly should be investigated further.

11.6.4 Further research should be promoted into the synthesis and metabolism of vitamin D in the human body, and methods of measuring the concentration of vitamin D metabolites in the blood should be standardized.

11.6.5 In collaboration with industry, research should be promoted into the production of window glass which is transparent to ultra-violet radiation of wavelength less than 313 nm and of fluorescent lighting in which radiation of this wavelength is emitted.

# Appendix A: Clinical, biochemical and radiological aspects of rickets and osteomalacia

## A.1 Clinical Aspects

A.1.1 *Diagnosis*

A.1.1.1 The clinical diagnosis of rickets is not always definitive by itself, but can usually be confirmed by radiographic examination of the bones of the wrists and knees, the bones most commonly chosen for this purpose in children, and by various biochemical measurements (see later). Radiography also provides an estimate of the activity and severity of the disease. More refined techniques include studies with radioactive isotopes and histological examination of a biopsy specimen of bone, but such studies are not easily made and cause a degree of disturbance to the patient which is not justifiable. A number of investigations may need to be performed in order to establish whether or not rickets is secondary to endogenous disease. These investigations lie outside the scope of this report.

A.1.1.2 The clinical picture produced by vitamin D deficiency in children is modified by the stage of development and the general health and nutrition of the child. The age-related features are important in differential diagnosis because unrelated conditions, which may occur in the same age group, may be confused with rickets or osteomalacia.

A.1.2 *Infantile rickets*

A.1.2.1 It is rare in Britain to find young infants with large mis-shapen heads, beading of the costo-chondral junction and thickened wrists and ankles which are the classical skeletal signs of florid rickets. The weakness, sweating and developmental delay or regression, which are the accompanying general manifestations, are also not often seen.

A.1.2.2. In Britain there are two groups of infants in whom signs of vitamin D deficiency may be encountered in the first few months of life. The first group, which is the most pertinent to this report, consists of infants born to osteomalacic or vitamin-D deficient mothers, the majority of whom are of Asian origin. Such infants may show signs of rickets at or soon after birth. The signs noted most often are softening of the bones of the skull (craniotabes), and hypocalcaemic convulsions (neonatal tetany). Neither of these signs is specific for rickets but, when they are associated with other evidence, there is little doubt that maternal vitamin D deficiency is the cause. Such infants are unlikely to receive an adequate supply of vitamin D from breast milk unless the mother's

vitamin D status is improved. The second group of young infants who are likely to have rickets are those born very prematurely and who have a vitamin D requirement in excess of that supplied by parenteral nutrition, breast milk or infant formulae. These very small rachitic babies are identified by radiological investigation which often reveals multiple fractures as well as typical changes at the metaphyses of the long bones. The condition is important, but these infants require special nutrition and are supervised by experts in neonatal medicine, they do not concern this working party.

A.1.2.3. As long as the child is too young to stand, crawl, shuffle or walk, no weight is borne on the pelvis and lower limbs, and the bones are not subjected to much modelling from the play of muscles involved in locomotion or manipulation. However, at this stage growth is rapid, and exposure to sunlight is often restricted for climatic or cultural reasons. Dietary sources of vitamin D are therefore important and the vitamin may be supplied either naturally by breast milk from a well-nourished mother, or artificially from an infant formula, or in vitamin drops given as a dietary supplement.

A.1.2.4. After the first 4-6 months of age, the infant may become vitamin-D deficient because the milk taken may be mostly household milk, the solids introduced into the diet may contain little vitamin D, no supplements of vitamin D are given and the child is not out in the sunshine. Signs of deficiency may not appear for several months.

A.1.3 *Toddler rickets*

A.1.3.1. Very often the signs of rickets are delayed until the child begins to walk, and the characteristic deformities appear in the lower limbs. The rachitic child when in the erect posture shows bow legs or knock knees and, because of muscular weakness, a lordotic stance and somewhat waddling gait. Thickening at the wrists and ankles and a 'rickety rosary' may be seen. Severe rickets should not be difficult to diagnose, but milder cases may be confused with the much larger number of normal toddlers who show a degree of femoral bowing or tibial torsion as a result of minor postural abnormalities. The possibility of rickets is increased when the infant or young child is of Asian origin, and when other nutritional disorders, particularly iron-deficiency anaemia which may be associated with rickets, are present. Treatment of nutritional rickets in toddlers is simple and effective, healing of the active disease is prompt, but it may take some time before the legs become straight.

A.1.4 *Juvenile rickets*

A.1.4.1. Rachitic deformities and stunting of growth, which are legacies of undiagnosed or inadequately treated toddler rickets, may be encountered in shoolchildren before adolescence, although active disease is rare in this age group. Vitamin D deficiency is uncommon, partly because most normal school-aged children are out of doors for some part of the day, and partly because growth is slower than in early childhood.

A.1.5 *Adolescent rickets*

A.1.5.1. The predominant symptoms of clinical disease in the adolescent and young adult are vague aches and pains in the back, joints and limbs and some feelings of weakness. As is well known, these complaints are so common and are so often associated with non-organic illness that they are often managed without specific investigation. In some cases, however, there are physical signs of skeletal deformity (knock knees or bow legs) which suggest the diagnosis.

A.1.6 *Osteomalacia in pregnancy and fetal rickets*

A.1.6.1. There is little systematic information regarding vitamin D deficiency in the pregnant Asian woman in Britain. Symptomatic osteomalacia does occur and generally presents with back pain and muscular weakness. Investigations to confirm the diagnosis and to detect asymptomatic degrees of vitamin D deficiency in pregnancy are complicated by the alterations which occur in the physiological amounts of blood constituents and by the need for discrimination in the use of x-rays.

A.1.7 *Osteomalacia in the elderly*

A.1.7.1. Osteomalacia is very difficult to diagnose in the elderly. There is no single clinical sign, and biochemical results and radiology are often equivocal. The calcium infusion test and a bone biopsy taken from the iliac crest are probably the only reliable procedures for confirmation of the diagnosis. Muscle weakness, skeletal pain, bone tenderness and backache are all common among the elderly, but a waddling gait is characteristic of osteomalacia. Occurrence of fracture of the femoral neck in association with vitamin D deficiency and in the absence of the usual clinical signs of osteomalacia may be of considerable importance clinically.

A.1.8 *Sub-clinical rickets and osteomalacia*

A.1.8.1. The concept of sub-clinical (asymptomatic) rickets or osteomalacia implies that there are individuals in whom the abnormal physiological processes associated with rickets and osteomalacia exist in the absence of clinically recognisable manifestations of disease. Such individuals would be expected to be at risk of developing symptomatic disease at times of any increased demand for, or insufficiency of, vitamin D. The existence of sub-clinical rickets has been demonstrated by surveys of predisposed groups of individuals with the use of x-rays and biochemical tests to identify those with abnormal findings. Results suggest that vitamin D deficiency may be more prevalent than is indicated from the number of people who have clinical evidence of active rickets or osteomalacia.

## A.2 Biochemical changes in rickets and osteomalacia

**A.2.1** *Abnormal biochemistry*

A.2.1.1. Rickets and osteomalacia are diseases in which bone metabolism is impaired. The biochemical changes which are most readily detectable in these conditions are therefore in those blood constituents which are required for the

calcification of bone, that is, calcium and phosphorus. The activity of the enzyme alkaline phosphatase, which is present at the site of bone formation, may also increase. Changes in these blood components together with clinical and radiological signs help to confirm a diagnosis of rickets or osteomalacia or, by themselves, may be the first indication of sub-clinical disease. The term 'biochemical rickets' is sometimes used to describe a result which indicates abnormality in individuals who have no clinical signs or symptoms of overt rickets.

A.2.2 *Changes in serum calcium*

A.2.2.1 Vitamin D deficiency affects the absorption of calcium from the intestine, and the concentration of calcium in circulating blood tends to fall below its normal value of about 2.4—2.6 mmol/l (9.5—10.5 mg/100 ml). However, the maintenance of the calcium concentration in blood is so important to the body that the calcium may be withdrawn from the skeleton in order to preserve homoeostasis by a mechanism which is regulated by parathyroid hormone and through the influence of vitamin D metabolites. Patients with rickets or osteomalacia may be hypocalcaemic but not invariably so. A low blood calcium concentration possibly indicates an advanced stage of the disease. In pregnancy total plasma calcium falls in association with the reduction in plasma albumin due to haemodilution, and allowance must be made for this before a diagnosis of hypocalcaemia is given.

A.2.3 *Changes in serum inorganic phosphorus*

A.2.3.1 A decrease in the concentration of serum inorganic phosphorus below 1.3 mmol/l (4 mg/100 ml) in children is said to be a better indication of rickets than a lowered calcium concentration. The phosphorus concentration falls because parathyroid hormone, in its action to restore the serum calcium concentration, also increases the excretion of phosphorus in the urine. Thus, whereas the serum calcium returns to normal levels, the serum phosphorus may remain low. In adults the customary decrease in phosphorus concentration with age must be taken into account.

A.2.4 *Changes in serum alkaline phosphatase*

A.2.4.1 Alkaline phosphatase is present in osteoblasts at the growing ends of the bones. The activity of the enzyme circulating in the blood is increased during periods of rapid new bone growth, such as in childhood or at puberty. However, when excess osteoid tissue is being laid down without sufficient calcium present to ensure proper mineralization into bone, as happens in rickets and osteomalacia, the activity is similarly increased.

A.2.4.2 There is more than one alkaline phosphatase enzyme and the activity in serum may originate from a number of different tissues: in children the activity comes from the enzyme present in the bone, in healthy adults it is mainly from the liver, and in pregnant women, from the placenta. Increased activity in serum from adults may therefore indicate disease of either the liver or bone, or in the case of young women may be a natural consequence of pregnancy. In sera from pregnant women, the contribution from the placental enzyme, which is

completely stable to heat treatment at 55°C, can be measured and any residual increase due to bone disease can be estimated.

A.2.4.3 For adults, a value above 92 international units (IU), or above 13 of the traditional King Armstrong units, is probably sufficiently abnormal to merit further investigation of the subject. For children, the upper limit is much less well defined and may be as high as 200-300 IU. There is a marked increase in the values around the ages of 8-12 years in girls and 10-14 years in boys (Round, 1973). In young children very high values sometimes occur without any explanation (Stephen and Stephenson, 1971).

A.2.5 *Serum 25-hydroxyvitamin D*

A.2.5.1 In recent years great advances have been made in our knowledge of vitamin D metabolism, which have led to the development of methods for directly assessing vitamin D status. Vitamin D either from the action of sunlight on the skin or from the diet is hydroxylated in the liver to a 25-hydroxy derivative, and is then further metabolized in the kidney to several dihydroxy compounds, one or more of which is responsible for the biological activity of vitamin D. These dihydroxy compounds, and in particular 1,25-dihydroxy-cholecalciferol, are present in circulating blood in very small amounts and require sophisticated equipment for laboratory measurement. Their precursor, 25-OHD, on the other hand, is present in measurable amounts in sera or plasma from healthy people and can be estimated by techniques of competitive protein binding assay. 'Normal' values are available, for certain age groups, in the sense that the mean and variation about the mean have been established at various seasons of the year, but no absolute limits have been defined which can be related precisely to either clinical or sub-clinical rickets and osteomalacia. Since sunlight has such a strong influence on vitamin D status and can rapidly alter the concentration of 25-OHD in the blood, it is clearly important to ensure that the season of the year and the degree of outdoor exposure are taken into account when comparisons are made.

A.2.6 *Conclusion*

A.2.6.1 These biochemical measurements may confirm clinical or other diagnoses of rickets or osteomalacia, or they may identify groups of children or adults at risk. However, none of the changes in calcium and phosphate concentration or in alkaline phosphatase activity is specific for vitamin D deficiency states, and there is considerable overlap between values which may be normal and those indicative of sub-clinical disease. Of these three blood measurements, one or even two may be within acceptable limits in elderly people with osteomalacia (Anderson Campbell, Dunn and Runciman, 1966). In very young children malnutrition may mask biochemical changes; thin, malnourished children with obvious clinical signs of rickets may have normal serum concentrations of calcium, phosphorus and alkaline phosphatase (Salimpour, 1975). Although it has been shown that no 25-hydroxyvitamin D is detectable in the sera from children with overt rickets (Preece, Ford, McIntosh, Dunnigan, Tomlinson and O'Riordan, 1973), very low values hitherto considered indicative of osteomalacia have been found in elderly subjects in the

absence of any clinical signs (Lawson, Paul, Black, Cole, Mandal and Davie, 1979).

## A.3 Radiological changes in rickets and osteomalacia

A.3.1 *X-ray appearances of the bones*

A.3.1.1 The characteristic X-ray appearances in a child with rickets are the flaring and cupping of the epiphyses at the growing ends of the long bones, and the widening of the cartilaginous growth plate in a longitudinal direction. The zone of calcification is ragged instead of being smooth and even. The radiological features of sub-clinical rickets have been described as 'minimal active rickets' and 'recently healed rickets' but, as might be expected, the differentiation between the X-ray appearances of normally calcifying bone and milder rachitic changes is difficult and subject to observer variation.

A.3.1.2 In adults with osteomalacia the bones become more translucent than normal. The bone cortex is less dense and the trabeculation more apparent by contrast. There may also be areas of more severe rarefaction called Looser's zones or pseudo-fractures.

# Appendix B: The average vitamin D content of some foods

## 1. Natural foods

| | *μg Vitamin D/100 g* |
|---|---|
| Herring — raw | 22.5 |
| Mackerel — raw | 17.5 |
| Salmon — raw Pacific | 12.5 |
| raw Atlantic | trace |
| Pilchards — canned in tomato sauce | 8 |
| Sardines | 7.5 |
| Tuna | 5.8 |
| Egg — whole | 1.75 |
| Butter | 0.76 |
| Milk — summer | 0.03 |
| winter | 0.01 |
| Cheese — Cheddar | 0.26 |

## 2. Proprietary foods which are fortified with vitamin D

(a) *Foods prepared especially for infants*

Baby milks—all brands when reconstituted with water according to the manufacturer's directions on the pack yield artificial feeds which contain about 1 μg vitamin D/100 ml feed.

If sold as ready-to-feed the concentration of vitamin D is also about 1 μg vitamin D/100 ml feed.

| | |
|---|---|
| Baby cereals— | |
| Rusks | 15—18 μg vitamin D/100 g |
| Baby rice | 10—18 μg vitamin D/100 g |
| Other baby cereals | 5—18 μg vitamin D/100 g |

(b) *Other foods*

| | |
|---|---|
| Breakfast cereals | 0—2.8 μg vitamin D/100 g |
| Evaporated milk—unsweetened | 2.6 μg vitamin D/100 g |
| Evaporated milk—reconstituted (by addition of water to give the equivalent of cows' milk) | about 1μg vitamin D/100 ml |

| | |
|---|---|
| Branded food drinks— | |
| as powder | 1.4—8 μg vitamin D/100 g |
| reconstituted | 0.04—0.08 μg vitamin D/100 g |

Instant dried skimmed milk powders—most do *not* contain vitamin D

| | |
|---|---|
| Yoghurt—branded products with | |
| added vitamin D | about 2 μg/100 g |
| natural products | contain small variable amounts of vitamin D |
| Margarine—for domestic use | 7.15—8.82 μg/100 g |
| for non-domestic use | not fortified |

Slimming foods—a wide variety of slimming biscuits and a smaller range of special omelette mixes, cereals, fruit and nut mixtures, and a diet chocolate for slimmers are fortified with vitamin D. An indication of their vitamin D content is given below.

| | *Vitamin D* μg/100 g |
|---|---|
| (a) slimming biscuits | 0.9—7.49 |
| (b) special omelette mixes and soup powders | 5—8 |
| (c) cereal, fruit and nut mixtures | 1—2 |
| (d) diet chocolate | 1.5—6.7 |
| (e) meal replacements based on skimmed milk solids | 0—3.5 |

## 3. Liver oils which can be obtained from some fish

Liver oils which can be obtained from some fish are very rich in vitamin D. They cannot be considered as foods but are used medicinally as sources of vitamin D.

| | |
|---|---|
| Tunny liver oil | 40,000—625,000 μg vitamin D/100 g oil |
| Halibut liver oil | 500— 10,000 " |
| Cod liver oil | 125— 625 " |

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