The Epidemiology of Vitamin D and Calcium Deficiency

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At the time of weaning, the infant’s food and nutrient intake changes radically from that derived from breast-milk to that derived from complementary foods. In developing countries particularly, this change may have serious consequences for the provision of nutrients, especially for micronutrients and vitamins. Two nutrients of particular importance for bone health are calcium and vitamin D. At the 52nd Nestle Workshop on Micronutrient Deficiencies, I discussed the pathogenesis of rickets in young infants due to maternal and infant deficiencies. Here I will discuss the epidemiology of vitamin D and calcium deficiency in the infant older than 6 months of age and young children.

Vitamin D Deficiency

Although classified as a nutrient, vitamin D should rather be considered a prohormone, as the typical diet of most populations contains insufficient vitamin D to maintain vitamin D sufficiency unless foods are fortified with the vitamin. The vitamin D status of an individual is largely maintained through the conversion of 7-dehydrocholesterol to vitamin D in the skin under the influence of ultraviolet light.

Vitamin D is the generic term for a number of different compounds, the most important of which are vitamin D$_2$ or ergocalciferol and vitamin D$_3$ or cholecalciferol. Both forms are found in the circulation in humans, although the amounts of each are dependent on the diet and the amount of skin exposure to ultraviolet light. Vitamin D$_2$ is formed by the ultraviolet irradiation of the sterol, ergosterol, in plants and is ingested by humans mainly through
the fortification of foods with vitamin D. Vitamin D on the other hand is generally derived from its formation in the skin under the influence of ultraviolet light, although dietary intakes may contribute as there is a move towards the fortification of foods with vitamin D rather than vitamin D, which was the custom in the past.

A number of factors influence the amount of vitamin D formed in the skin; these include the duration and intensity of ultraviolet light exposure, the surface area of skin exposed, the degree of melanin pigmentation in the skin, and the amount of substrate available in the skin for conversion to vitamin D.

The wavelength of ultraviolet-B radiation needed for the formation of vitamin D is between 290 and 315 nm. The amount that reaches the earth's surface is dependent on the zenith angle of the sun, the amount of atmospheric pollution and the degree of cloud cover. Thus the further one moves from the equator, the less UV radiation that is able to reach the earth. Consequently vitamin D formation is reduced in countries of high latitude, and during the winter months. This has been well shown, for example, in South Africa, where in Johannesburg at 26°S there is good vitamin D formation throughout the year, while in Cape Town at 32°S there is limited vitamin D formation during the winter months from April through September [1]. That study also highlighted the importance of the time of the day, with maximal vitamin D production occurring between 10.00 and 15.00 h in the summer months. Similar but more extreme results have been obtained from Boston at 42°N, where during the winter months of November through February no significant production of previtamin D occurred, and from Edmonton (52°N), where no vitamin D synthesis occurred between October and April [2].

Ozone pollution in the air of industrialized cities could have a significant impact on the amount of UV-B reaching the earth, as it effectively absorbs UV radiation. Thus it could reduce the amount of cutaneous synthesis of vitamin D. Although the size of this effect has not been quantified, it could increase the risk of vitamin D deficiency in young infants and the elderly living in the industrial cities of North America and Europe [3].

Melanin granules, which are produced by melanocytes within the stratum basale of the epidermis, very effectively absorb UV-B radiation in the range of 290–320 nm, thus reducing the amount of UV-B available for vitamin D synthesis [4]. Thus the darker the skin pigmentation is, the greater the amount of sunshine that is required to produce a given amount of vitamin D. This is the likely explanation for the higher incidence of vitamin D deficiency in African-American infants in North America and other countries at high latitudes.

Another factor that is of considerable importance in determining the cutaneous synthesis of vitamin D is the surface area of skin exposed to UV radiation. In adults, even light clothing (with arms and legs exposed) as might be worn in summer significantly reduces the amount of vitamin D formed,
while autumn clothing (with arms and legs covered) almost completely prevents the expected rise in serum vitamin D in response to whole body UV irradiation [5].

**Vitamin D Sufficiency, Vitamin D Insufficiency and Vitamin D Deficiency**

The classical presentation of vitamin D deficiency in infants and young children is rickets. Clinical and radiological rickets may take several months to develop depending on the growth rate of the child, the degree of vitamin D deficiency and the calcium content of the diet, even though biochemical abnormalities, such as hypocalcemia, hypophosphatemia, and elevated alkaline phosphatase and parathyroid hormone concentrations, may occur much earlier.

A more accurate assessment of vitamin D status is the circulating level of 25-hydroxyvitamin D (25-OHD). It is generally accepted that levels of $<12$ ng/ml (30 nmol/l) in children are indicative of vitamin D deficiency, however in the adult literature particularly, there is considerable controversy around the level that constitutes vitamin D sufficiency as it is suggested that levels above 12 ng/ml (30 nmol/l) may be inadequate to maintain bone health and biochemical normality although manifestations of osteomalacia or hypocalcemia do not occur. The serum concentration of 25-OHD above vitamin D deficiency levels but below that which is needed to provide optimal health is termed vitamin D insufficiency [6]. In children, there is less discussion and little evidence to suggest that values above 12 ng/ml may be inadequate. Thus in the pediatric literature, there is no clear indication that a situation of vitamin D insufficiency occurs. Further it must be understood that levels within the vitamin D deficiency range may not be associated with clinical, radiological or biochemical abnormalities, particularly if they are of short duration, as may occur during the winter months in countries at high latitude.

**Vitamin D Deficiency in Infants and Young Children**

From the above discussion, it is clear that the vitamin D status of infants and young children is determined by the combination of the dietary intake of vitamin D and of that produced in the skin under the influence of UV light.

The natural dietary sources of vitamin D for the infant or young child are limited as few unfortified complementary foods contain significant quantities of the vitamin. For this reason, all infant milk formulas are fortified at a level of approximately 400 IU (10 μg)/l and a number of other foods designed for infant feeding, such as infant cereals, may also be fortified by manufacturers. In North America, liquid cow's milk is also fortified, but a study has found that the amount of vitamin D actually present in milk is very variable ranging from $<5$ to $>120\%$ of the stated amount on the package label [7]. Breast milk too has only a limited vitamin D content (between 20–60 IU/l) [8, 9], which is inadequate to maintain vitamin D sufficiency in the infant.
Thus, unless the infant is drinking reasonable quantities of infant milk formula or fortified cow's milk (approximately 500–600 ml/day), vitamin D sufficiency will not be ensured unless cutaneous synthesis of vitamin D supplements the dietary intake. Several factors may hasten the onset of vitamin D deficiency in the young infant, these include: (1) the global recommendation that breast-feeding should be exclusive and the preferred method of feeding for the first 6 months of life, thus precluding the intake of vitamin D-fortified infant foods in the early months of life, and (2) a low vitamin D status in the mother at the time of birth, as the placental transfer of vitamin D, in particular 25-OHD, from a replete mother to the fetus helps protect the infant from vitamin D deficiency in the first couple of months [10].

It is thus apparent that many infants and young children are dependent on the cutaneous synthesis of vitamin D in order to maintain vitamin D sufficiency. This has been highlighted by a study in Cincinnati by Specker and Tsang [11] who showed that in breast-fed infants the serum concentrations of 25-OHD correlated with sunlight exposure rather than with the vitamin D content of maternal breast milk.

Globally, vitamin D deficiency is characteristically a disease of infants and young children. The reasons for this are apparent if one considers the importance of UV light exposure in maintaining vitamin D sufficiency. Deficiency occurs typically in countries at high latitudes, where winter months are cold, and in countries where for social and religious reasons children are precluded from sunlight. The peak incidence of vitamin D deficiency occurs between 6 and 18 months of age and has a strong seasonal variation with the disease being most common in the late winter and early spring months [12].

The prevalence of vitamin D deficiency has been greatly reduced in a number of countries from that occurring at the end of the 19th and beginning of the 20th centuries, when in northern Europe the disease was almost universal in young children [13]. This has been achieved through health education, the use of vitamin D supplements and the introduction of food fortification. However vitamin D deficiency remains a problem in a number of developing countries and there has been a resurgence in several developed nations. A number of studies over the past 20–30 years have highlighted the continued high prevalence of vitamin D deficiency among the Asian communities in the United Kingdom [14], and among young children in countries such as Turkey, Greece, Mongolia, Tibet, China, Ethiopia [15], Saudi Arabia [16], Iran, Kuwait, the United Arab Emirates, India [17], and Pakistan. Furthermore there have been an increasing number of reports of vitamin D deficiency in dark-skinned immigrant communities in Australia [18], New Zealand and Europe, and in African-American infants in the USA [19].

The reasons for vitamin D deficiency in countries, such as China, Mongolia and Tibet, are clearly related to the high latitude and long and cold winters reducing the UV light exposure of the skin. In the Middle East, however, other mechanisms have been shown to play major roles. These include religious and
social customs, such as purdah and the tradition of veiling, which preclude the mother and young infant from sunlight, and prolonged breast-feeding without vitamin D supplementation [20]. In Ethiopia, vitamin D deficiency is associated with protein-energy malnutrition and the lack of sunlight exposure [15]. In the USA, rickets occurs characteristically in African-American infants who are breast-fed, thus melanin pigmentation and the lack of vitamin D in breast milk appear to be major factors, although recently DeLucia et al. [21] have suggested that low dietary calcium intakes associated with weaning may play a role. The reasons for the high prevalence of vitamin D deficiency and rickets in Asian children in the UK have been extensively researched. Melanin pigmentation, extensive skin coverage by clothing, and low calcium and vitamin D intakes associated with vegetarian diets have all been indicted. Clements [22], some 15 years ago, provided a convincing explanation by which the low calcium intakes and decreased bioavailability of calcium in the traditional vegetarian diets were responsible for exacerbating vitamin D deficiency in the Asian community. In rat studies, he showed that low calcium intakes increased the catabolism of 25-OHD to non-active metabolites, thereby increasing the requirements of vitamin D to maintain vitamin D sufficiency.

It is thus clear that vitamin D deficiency remains a global problem and that many infants and young children are at risk of the consequences of the disease, which is only now beginning to receive attention from international agencies.

**Dietary Calcium Deficiency**

The estimation of the dietary requirements for calcium is difficult in humans in general, but even more so in infants and young children. As deficiency syndromes are not clearly defined, there are no biochemical tests which indicate the nutritional status for calcium, and dietary requirement studies are notoriously difficult to conduct in children of this age. These difficulties are highlighted if one compares the recommended dietary intakes made by various national bodies (table 1).

In adults, dietary calcium requirements may be calculated from that which is required to maintain the calcium balance at zero, however in children this is not possible as growing children should be in a significantly positive balance to allow for bone growth in particular. Furthermore intestinal calcium absorption varies not only with the nature of diet, but also with the adaptation of the body to calcium requirements and dietary calcium content.

The exclusively breast-fed or formula-fed infant is assured of an adequate calcium intake to meet the requirements for growth, however once weaning occurs and the consumption of milk drops off, the reduction in calcium intake associated with this decline in milk intake must be made up by weaning foods.
In developed countries, where dairy products are readily available, calcium intakes are generally maintained and there is little evidence of dietary calcium deficiency in the infant and young child populations. In the United Kingdom and the USA, it is estimated that dairy products provide over 60% of the calcium intake in young children [23, 24] and total calcium intakes exceed 600 mg/day.

In developing countries, the situation is often very different; the weaning diet is mainly cereal based and is often high in phytates, dairy products are frequently scarce and priced out of the reach of the average family, and the diet lacks variety. These factors coupled with frequent bouts of diarrhea and intestinal infections result in calcium intakes being low and possibly poorly absorbed. In a study of calcium intakes in toddlers in Egypt, Kenya and Mexico, mean daily intakes of 218, 210 and 735 mg, respectively, were obtained [25]. The reason for the higher intake in Mexican toddlers was because of the addition of lime to tortillas during their manufacture. Intakes similar to those in Egypt and Kenya have been found in young children in Nigeria [26] and South Africa [27]. In The Gambia [28], India and China intakes of around 300 mg/day are not unusual.

Thus calcium intakes of infants and young children differ markedly between developed and developing countries, yet is there any evidence that the low calcium content of the diets in developing countries is detrimental to health? This question has not been answered with certainty, and will be discussed in more detail elsewhere, however there is evidence to suggest that very low calcium intakes in growing children are responsible for rickets in the face of vitamin D sufficiency.

In the 1970s several isolated case reports appeared of infants developing rickets after having been placed on very restricted calcium intakes for the treatment of chronic diarrhea [29, 30]. In the same decade, we suggested that rickets in older children living in rural areas of South Africa might be due to dietary calcium lack as all had normal circulating levels of 25-OHD and elevated 1,25-(OH)₂D concentrations, and all responded to an improvement
in calcium intake. Their calcium intakes were estimated to be between 150 and 200 mg/day, their diet being mainly corn based with no dairy products whatsoever [31]. Since then, a number of reports from Nigeria have indicated that low dietary calcium intakes might be associated with rickets in that country [32–34], and a similar etiology has been postulated as being responsible for rickets in Bangladesh [35]. In all of these studies, calcium intakes of approximately 200 mg/day have been measured. It is highly likely that low dietary calcium intakes are primarily responsible for the development of the bone disease, however other factors such as phytates, which influence the bioavailability of dietary calcium, might exacerbate its development, as no difference was found in calcium intakes between children with and without rickets in one case-controlled study.

An interesting report originating from the east coast of the USA has recently suggested that dietary calcium deficiency may play a role in the pathogenesis of rickets, particularly in African-American infants and toddlers [21]. Although calcium intakes were not measured, they were reported as being low with many of the children being weaned onto diets which contained little or no dairy products after prolonged breast-feeding.

Thus it is apparent that dietary calcium deficiency as manifested by clinical rickets is being recognized in several areas of the world. It is unclear, however, how widespread the problem is, as vitamin D deficiency and dietary calcium may coexist. Furthermore, treatment of rickets often comprises both vitamin D and calcium supplements which treat both conditions effectively. The picture is complicated further by the role of low dietary calcium intakes in increasing the catabolism of vitamin D through the elevation of serum 1,25-(OH)2D levels, resulting in increased requirements of vitamin D in children on low calcium intakes [36].

Here the presence of rickets due to low dietary calcium intakes has been used as a measure of dietary calcium deficiency. It is likely, however, that the clinical manifestation of rickets is the tip of the iceberg and that disturbances in the biochemical markers of mineral homeostasis are much more common findings. How common or widespread the biochemical changes of hypocalcemia, and elevated alkaline phosphatase, PTH and 1,25-(OH)2D levels are, is unknown, although in one study from South Africa these findings were frequently found in a rural community [37].

The assessment of the prevalence of dietary calcium deficiency worldwide is complicated further by the lack of a clear understanding of what calcium intakes are necessary to promote optimal bone health in growing children, which in the Caucasian population in industrialized countries has been a subject of much research. Maximizing peak bone mass, which is achieved during the third decade of life, is considered to be an important objective, as bone mass at this time of life might influence the incidence of minimal trauma fractures in later life. Although a few studies have suggested an improvement in bone mass through calcium supplementation during childhood in Caucasian
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children, no information is available on the effect of the supplementation of the generally lower calcium intakes in children in the developing world. Further the relevance of such supplementation is unclear as the incidence of minimal trauma fractures in the elderly in the developing world is generally considered to be very much lower than that in the developed world.

It is thus apparent that much research needs to be done to clarify the indicators of dietary calcium deficiency worldwide, and to assess the role of current dietary calcium intakes on the prevalence of these indicators.

References

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Discussion

Dr. Guesry: I believe in the role of latitude to explain differences in synthesis in vitamin D in the derm. But with all due respect, I doubt that the difference in latitude that you mentioned between Johannesburg and Cape Town would explain more than 5–10% of the difference you showed us, and the rest is probably due to altitude, cloudiness.

Dr. Pettifor: I think that is right, we are talking about season. It is not just latitude, it is also the issue of cloud cover which makes a major difference.

Dr. Guesry: You could ask a specialist to calculate the angle and to extrapolate on the maximum effect and it is probably something like 5%.

Dr. Pettifor: I accept that seasonal weather changes are relevant.

Dr. Castillo-Durán: Infants born preterm or small-for-gestational age can be a very highly prevalent group in many developing countries, from 50 to 60%. How can this be included as a risk factor for rickets?

Dr. Pettifor: The infants that are born in many developing countries, the low birth weight group of infants, are in fact mainly small-for-gestational age rather than premature. We have looked at the problem of rickets in these children, and if they are breast-fed then the problem appears to be mainly phosphate deficiency rather than calcium deficiency, and it tends to occur in premature rather than small-for-gestational age babies. I don't have any data on what the long-term effects of perhaps mild
biochemical changes such as elevated alkaline phosphatase or low phosphorus levels are during this period. They certainly may be present with rickets during this period, although it is relatively uncommon. We see very little rickets due to what we think is hypophosphatemic rickets in this age group.

*Dr. Endres:* You showed nicely that the renal excretion of calcium increased when you gave calcium. I think most of us know as pediatricians that, when we are treating rickets, not only should vitamin D be given but also calcium because otherwise tetany might occur in these hypocalcemic infants. Did you investigate this in your studies when you gave vitamin D to these children?

*Dr. Pettifor:* In the calcium-deficient group the children were randomized to either receive calcium, vitamin D, or calcium and vitamin D. We didn't find any difference in calcium excretion in urine. Calcium excretion in these children is very low once they become calcium-deficient; it is 1 or 2 mg/day basically, which is very low indeed. When we talk about raising urine calcium, that calcium rise is relatively small as well. I haven't studied this problem in vitamin D-deficiency rickets, so I really can't answer the question as it relates to vitamin D deficiency. We generally do not give calcium supplements to infants who have vitamin D deficiency because we believe that their milk intake is generally adequate to meet the calcium demands of the growing child. So calcium is not supplied, except if the infants have tetany in the early stages of presentation. But if they have rickets, they should just be given a normal milk intake and vitamin D. We haven't run into tetany problems in these children. Whether it slows down the healing, I don't know.

*Dr. Gebre-Medhin:* I very much enjoyed your presentation and your words are well taken that to extrapolate from different populations to others leads to a lot of problems. My question is what do we know now about the body's ability to store vitamin D during periods of plenty, for instance the summer months, then use it towards the end of the year when there is less sunshine? I am asking you this question because in the early 1970s vitamin D-deficiency rickets was very prevalent in highland Ethiopia, I would say close to 80%. We have not changed the vitamin D supply program, protein energy malnutrition has not changed but rickets is now very rare, even in highland areas, and the main reason for this has been a huge program encouraging mothers to take their children outside during the sunny months. Does this mean that the body is capable of storing quite a lot for later use?

*Dr. Pettifor:* It appears that vitamin D is stored in fat and muscle and 25-hydroxyvitamin D may also be stored. The duration of storage is difficult to assess because it certainly depends on whether it is stored in the fat and how fat an individual is. If you take individuals who have vitamin D toxicity, the duration of vitamin D toxicity may persist for many months after cessation of giving vitamin D. So there is good evidence that vitamin D is continuously being pulled out to produce the effects of vitamin D toxicity. I am not sure if Dr. Specker has an answer to the actual half life of this in a normal individual. Certainly if you take individuals who have reasonable vitamin D sufficiency during the summer, their 25-hydroxyvitamin D levels fall during the winter, but not to the same level as in an individual who starts off relatively vitamin D insufficient during summer. These individuals tend to develop vitamin D deficiency during the winter months. So to answer your question, I am not sure I can give you an actual figure.

*Dr. Specker:* We found, at least in newborn infants, that the maternal and infant 25-hydroxyvitamin D levels correlate up until about 8 weeks of age in the baby [1]. So if you assume that this is placental transfer, it appears that the storage in the infant lasts about 2 months, which can also explain why you see vitamin D deficiency rickets at higher latitudes around March, the very end of winter or early spring. So as a sort of consensus, if there is one out there, it is that the half life is about 8 weeks.

*Dr. Pettifor:* The neonate may of course be a different issue because the major transfer across the placenta is 25-hydroxyvitamin D, and we know that the half life is

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about 2–3 weeks. So as we saw from the studies that we did in Johannesburg, the levels dropped significantly by 6 weeks of age, but these concentrations protect the infant from rickets in the first 3 months of life unless the mother is vitamin D-deficient.

**Mr. Parvanta:** In South Africa do you have a national recommendation with regard to vitamin D supplementation for breast-fed infants? In relation to the data you showed in which the controls had a better calcium intake than the children with rickets; can you give us a description of what the primary dietary sources of calcium were in that population?

**Dr. Pettifor:** To answer the first question about the vitamin D supplementation policy in South Africa: no, there isn’t one. The pediatric community is divided as to whether we should be recommending vitamin D supplementation to breast-fed infants or whether the amount of sunlight that we have is adequate for a small daily exposure to maintain vitamin D supply. Certainly vitamin D deficiency is an uncommon problem in infants in South Africa these days. In the 1960s when breast-feeding was not as prevalent and the infant food that was given at that time was diluted cow's milk (two thirds cow's milk and a bit of sugar), rickets was very common particularly in Cape Town with 15% of children presenting with rickets, but that has almost disappeared completely now. However, we are seeing it now in the inner city areas where parents are living under poor socioeconomic conditions, where there is a lot of crime, and children and mothers are not getting outside. Thus it is a problem in the high-rise, high-density residential areas, but otherwise not. To discuss the issue of the difference in calcium intakes between the children who presented with dietary calcium deficiency, the only difference in the diet was that those who had calcium intakes of 300–400 mg/day had some sort of dairy product on a reasonably regular basis. So the parents may have kept cows; they may have had family members sending back milk powder to those families, so that they may have been drinking a little bit of milk in their tea or half a glass of milk a day, and that was the only difference. Otherwise the diet is very similar, it is mainly a corn maize-based diet with vegetables and occasional meat.

**Dr. Zlotkin:** I think the vitamin D issue is a wonderful example of the problematic application for the prevention of a micronutrient deficiency, and let me just give you Canada as an example. In the 1930s at the Hospital for Sick Children the most frequent diagnosis for children admitted to our hospital was actually rickets, and in the 1930s the first fortified food was developed. This is a great example of the use of fortification to solve a micronutrient problem. It was for young children but not for children of school age. 50 years ago, when I was a child, we used a supplementation to prevent rickets. As children many of my friends and I took cod liver oil because the liver of the codfish has a very high concentration of vitamin A and vitamin D. Again it is a good example of supplementation, the prevention. The next step of course was the use of foods for children, that is formula and infant cereals with calcium and vitamin D concentrations. But there was general recognition that, for infants who are exclusively breast-fed, fortification would not work because their needs are different, and possibly 10 years ago there were recommendations for vitamin D supplementation of all exclusively breast-fed infants. In Canada the prevalence of vitamin D deficiency rickets is very low and there is a strong voice among pediatricians in Canada that we no longer need supplementation because the prevalence of this entity is so low due to the successful supplementation program. So I think it is an interesting case model of how fortification and supplementation work to prevent the disease. In Canada there is a new recommendation that all infants after 6 months of age should not be exposed to sunlight in the noon hours or if they are going to be exposed to sunlight they be provided with sunscreen. So my question is: is it likely that the provision of sunscreen to infants is going to increase the prevalence of rickets? What is the effect of the sun blockers on the endogenous synthesis of vitamin D?
Dr. Pettifor: I think you have actually written a paper on the issue of sunscreens as a factor in the causation of vitamin D deficiency [2]. I think there is a lot of ambivalence about what we should be recommending to mothers. Certainly I think the dermatologists would scream blue murder if one recommended any sunlight exposure to infants. The recommendation now is that as soon as a baby is put outside, it is to be covered from head to toe with sunscreen. I do believe we are going to run into problems, and we are seeing an increased prevalence of rickets in the US and Canada, although it happens particularly in the dark-skinned African-American population. Whether this is only due to vitamin D deficiency or whether there is also a role for dietary calcium deficiency in this situation is not clear. Certainly the data from DeLucia et al. [3] suggest that calcium deficiency may well be a factor here because calcium intakes drop after weaning because of the introduction of mainly nondairy low calcium-containing foods. They suggest that dietary calcium deficiency plays a significant role. If we accept this then you have a synergistic effect of dietary calcium deficiency plus vitamin D insufficiency leading to an increased prevalence of rickets, and we need to look at both of these. We should look at either increasing calcium and/or providing an adequate vitamin D intake to optimize calcium absorption during these periods.

Dr. Lozoff: Although the pediatric recommendations are for calcium and vitamin D supplementation, some advocates of exclusive breast-feeding find this recommendation problematic. I was wondering if you could comment on this.

Dr. Pettifor: That is true. There are groups that say breast milk and breast milk only, and one doesn’t need to supplement with anything. In that situation there are some studies suggesting that if one supplements the mother with adequate levels of vitamin D, sufficient vitamin D will cross in the breast milk to prevent vitamin D sufficiency or insufficiency in this age group. Some researchers are recommending 4,000 units of vitamin D/day. Now I may be wrong, it may be 2,000, but I think it is about 4,000 that it is being recommended for supplementation of the mother, which is quite a high dose actually.

Dr. Guesry: I would like to come back to the data that you showed from Dibba et al. [4] who collected data on the dairy calcium intake in Africa and Asia. We have to be careful in these countries that there are other sources of calcium and that dairy calcium is not the only source of calcium intake. We also have to balance these calcium intake data by a coefficient of bioavailability, and you know better than me that when less calcium is given, it is usually better absorbed.

Dr. Pettifor: I would argue that the form in which the calcium exists in many of the developing countries is in fact relatively non-bioavailable because of high phytates and other factors, so I am not sure.

Dr. Specker: One of the things that is also important is that people forget about phosphorus in the diet, and when you get calcium from dairy products you also have phosphorus. This might also be an explanation for why we see higher rates of rickets in exclusively breast-fed infants. I think that in the 1-year-old child who is exclusively breast-fed the phosphorus content in human milk has dropped significantly since birth, whereas the calcium content stays the same. You have proposed this idea about calcium deficiency, but we should not forget phosphorus, and we should think more about the calcium phosphorus product in the etiology of rickets. Perhaps that could explain the Nigerian results with phosphorus.

Dr. Pettifor: We looked at phosphorus intake in these groups and could not find a difference. In fact the phosphorus intake is very good in these groups because their diets are all cereal-based with a high phosphorus content. I accept that some of this is phytate phosphorus which may not be absorbed. But even then there is still a significant amount of phosphorus. The serum phosphorus values are all over the place in affected children, but they are not generally severely hypophosphatemic, which I think
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in the issue of phosphate depletion is a factor. But having said that, Greek research
done some 20 or 30 years ago suggested that there are two different types of rickets
in the infant period [5]. One was a phosphate depletion rickets that was seen in the
older children and the other was vitamin D deficient.

Dr. Albar: I want to ask you about the supplementation of calcium to pregnant
mothers because some milk products contain calcium, and it is advised that it be given
to the mothers during pregnancy and 6 months after delivery. According to the rec-
ommendations you mentioned, the mother’s calcium content level does not influence
the level of calcium in the baby. What is your comment about obstetric products for
pregnancy and lactation including milk or vitamin-mineral supplementation, especially
calcium and vitamin D, that advertise that during pregnancy and lactation mothers
should consume these products to prevent their babies from developing rickets? An
example of an advertisement for obstetric products goes as follows: Best assurance for
a healthy baby is a healthy mother – special milk or vitamin-mineral supplement for
pregnancy and lactation.

Dr. Pettifor: I think the data suggesting that calcium supplementation is beneficial
in either pregnancy or lactation is negligible. In fact, the British recommendations
have not increased the calcium intake during lactation [6]. They suggest that there is
no need for that. Prentice et al. [7] studied calcium supplementation in the Gambia
where calcium intakes were very low, and were unable to show any effect of calcium
supplementation during that period on the mothers, on breast milk calcium levels or
on the well-being of the babies. The issue though is whether long-term calcium sup-
plementation may influence breast milk calcium levels, and there are no data on that.
But the issue of vitamin D supplementation might be more relevant in those commu-
nities where vitamin D insufficiency is a relatively common problem. Most of Europe
and the Middle East need to make sure that the mother’s vitamin D status is adequate
during pregnancy and lactation.

Dr. Albar: Do you agree on giving calcium supplementation to malnourished preg-
nant mothers?

Dr. Pettifor: If we talk about malnourished pregnant mothers, I am not sure that
calcium supplementation is the answer. What the mother needs is a general improve-
ment in the diet, and if that actually happens to include increasing the calcium intake
that is well and good, but calcium supplementation is not the major factor in impro-
ving the nutritional status one hopes to achieve for the baby at birth.

Dr. Albar: There are a lot of milk products fortified with calcium and vitamin D whose
advertising is directed toward pregnant and lactating mothers, but calcium supplemen-
tation to the mothers has no effect on their babies. So it is useless for the mothers to
consume these products to prevent their babies from calcium deficiency.

Dr. Pettifor: I think the issue of protein or nutrient supplementation during preg-
nancy, except in the very severely malnourished mother, makes very little difference
on the birth weight of the infant.

Dr. Hurrell: I would like to come back to the phytic acid question and the absorp-
tion of calcium. In adults phytic acid has been shown to reduce calcium absorption
slightly, not as much as iron, and I don’t know of any studies in infants which have
shown that phytic acid reduces calcium absorption. It reminds me of a study we did
several years ago with a high phytate infant cereal in which we measured calcium
absorption in infants. We compared Cerelac with a very high phytate cereal, and there
was no difference in calcium absorption between the high and the low phytate cereals,
and the absorption was about 80% in these infants who were 5–8 months old. So I
would say that there is no evidence that phytic acid reduces calcium absorption other
than in adults, and there the reduction is not so high.

Dr. Pettifor: Perhaps Dr. Abrams might want to comment on that as well. We are
busy planning a study in Nigeria to look exactly at this, using stable isotopes in the
children that we see there. For instance whether the children who develop rickets are less able to adapt to the low calcium intakes is a question, and if a child already has a low calcium intake, whether the addition of phytate or oxalate for that matter may just drop calcium absorption enough to produce rickets on the long-term basis, I don’t think we know.

*Dr. Hurrell:* Obviously oxalate has a big impact on calcium absorption, it is not very well absorbed, but phytate I am not so sure.

*Dr. Abrams:* In Nigeria we measured calcium absorption because we thought that perhaps these children with rickets can’t absorb calcium very well, and we found that their calcium absorption is completely normal. So we were wondering if there is a critical value by which certain children get rickets, it is not very obvious at all. In general in developing weaning foods, calcium has been consider to be kind of a bad guy and it hasn’t been used for the most part, except in some commercial foods, because of larger concerns about iron, zinc and vitamin A. Given the considerable prevalence of calcium-deficiency rickets, do you think this should be reconsidered as a public policy matter?

*Dr. Pettifor:* I would take issue with your statement about the considerable prevalence of dietary calcium deficiency. I don’t think that dietary calcium deficiency, certainly clinical rickets, is that prevalent. The issue of whether there is a subclinical situation is another question: we have certainly suggested that children on low calcium intakes in some communities have biochemical perturbations with elevated alkaline phosphatase and low serum calcium, but did not have any radiological evidence of rickets [8]. Whether these children are disadvantaged long-term, we don’t know. So to make recommendations on a policy of calcium supplementation or fortification of foods, particularly in developing countries where it is very difficult or very expensive for the families to buy ready-prepared, ready-made food, I am not sure. I think it may well be appropriate to supplement with micronutrients at the moment. I am not sure that we should be recommending a broad spread of calcium supplementation at this stage. I am not sure that we should be recommending a broad spread of calcium supplementation at this stage. I am not sure that we should be recommending a broad spread of calcium supplementation at this stage.

*Dr. Mannar:* A few years ago in Bangladesh there was a sudden increase in the prevalence of rickets, probably calcium deficiency induced, and I was wondering whether there are any underlying factors that increase the prevalence of rickets in children?

*Dr. Pettifor:* In fact, a study was reported recently at the NIH Conference on Vitamin D Requirements, and I am afraid there is no conclusive evidence that it is dietary calcium deficiency. There is evidence that it might be that supplementation improves the condition. There are data suggesting that it is of recent onset. There may be many factors: one that has been put forward is related to the increased irrigation of rice fields and therefore being able to get more rotations of rice in any given year, and thus the diet has become very much more monotonous than it used to be 20 or 30 years ago. Whether this is a factor, we don’t know.

**References**
