Milk Intake, Calcium and Vitamin D in Pregnancy and Lactation: Effects on Maternal, Fetal and Infant Bone in Low- and High-Income Countries

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Abstract

Calcium and vitamin D are essential for bone growth and maintenance. Among the bone-forming minerals, dietary calcium supply is close to biological requirements and may be limiting in some parts of the world where there are few rich dietary sources of calcium, particularly for children and women during pregnancy and lactation. Animal milk is a rich source of calcium and, in countries where milk is fortified with vitamin D, a contributor to dietary vitamin D intake. Current evidence indicates that, in the human, there are physiological mechanisms that support the necessary calcium fluxes across the placenta and mammary gland and that are unresponsive to increases in calcium intake. This applies across the range of dietary calcium intakes recorded in healthy individuals. In contrast, although there is unlikely to be an additional requirement for vitamin D during pregnancy and lactation, many women have poor vitamin D status. This places them at risk of osteomalacia and their infants at risk of rickets, osteomalacia, compromised skeletal growth and other outcomes. There needs to be increased awareness among policy makers, health professionals and the public about the importance of safe UVB sunshine exposure and consumption of dietary vitamin D by women of reproductive age at risk of vitamin D deficiency.

Introduction

Calcium and vitamin D are essential for bone growth and maintenance. Among the bone-forming minerals (Ca, P, Mg, Zn), dietary calcium supply is close to biological requirements and may be limiting in some parts of the world where there are few rich dietary sources of calcium, particularly for
children, and women during pregnancy and lactation [1]. Similarly, the vita-
min D status of many women and young children is compromised by low UVB
skin exposure and by factors that increase vitamin D usage, even in tropi-
cal countries with abundant sunshine [2]. Milk from domesticated ruminants,
primarily cow, sheep, goat, camel and buffalo, are major sources of dietary
calcium and, in countries where commercially available milk is fortified, of
dietary vitamin D. This short review summarizes the data on calcium and vita-
mmin D supply for mothers and young children in low- and high-income coun-
tries and considers the evidence on the implications for maternal, fetal and
infant bone health.

**Calcium as a Bone-Forming Mineral**

Bone consists of mineral embedded in a collagen matrix. The mineral
phase closely resembles hydroxyapatite, and is composed of crystals of pre-
dominantly calcium, phosphorus and water together with a number of other
components that are present in lower quantities, such as Mg, Zn, carbon-
ate and citrate. All but 1–2% of the body’s calcium is contained within the
skeleton, unlike the other bone-forming minerals which are widely distrib-
uted in many tissues [3]. Calcium forms part of essential cell-signaling sys-
tems throughout the body, and these are exquisitely sensitive to changes in
intra- and extracellular calcium concentrations. The skeleton acts as a buffer
to avoid life-threatening swings in calcium concentration elsewhere in the
body. The release and accretion of skeletal calcium is one arm of a physiologi-
cal response to maintain ionized calcium in the circulation within narrowly
defined limits and to smooth out the peaks and troughs of calcium flux that
occur naturally during 24 h, for example following a calcium-rich meal or an
overnight fast. Consequently, any factor that compromises the body’s supply
of calcium for a prolonged period is likely to affect the mineral content of
the skeleton, either by reducing the potential for bone mineral accretion and
repair, or by inducing bone mineral mobilization to meet the body’s extraskel-
etal requirements for calcium [4].

**Calcium Requirements for Infancy, Pregnancy and Lactation**

Calcium is an essential nutrient, provided purely from dietary sources.
There are two routes of calcium absorption from the intestine: active absorp-
tion under the control of the active metabolite of vitamin D (see below) and
passive absorption. There are obligatory endogenous losses of calcium from
the intestinal secretions, urine and sweat. Excess calcium is excreted into
urine, and renal calcium reabsorption also becomes more efficient when
physiological needs for calcium retention increase [5].
The skeleton of a neonate contains about 25 g of calcium and that of an adult woman contains about 800–1,000 g of calcium [1, 3]. The accretion of calcium by the fetus occurs predominantly in the second half of pregnancy with the highest rates of 200–300 mg/day occurring in the last trimester. Similar daily accretion rates occur in the first weeks of life and gradually decrease during infancy. These are mirrored by the calcium supply from breast milk which averages around 200–300 mg Ca/day during exclusive breastfeeding [1]. A woman who delivers a singleton infant and breastfeeds exclusively for 6 months therefore transfers about 200–300 mg Ca/day to her infant either in utero or via breast milk for around 9 months of the reproductive cycle, and continues to transfer significant quantities for as long as breastfeeding is continued. This represents more than 100 g for a typical Western woman who has 2 children and exclusively breastfeeds each for at least 6 months and around 1,000 g for a mother who breastfeeds each child on demand for 2 years with complementary feeding from about 6 months and who has 7 or more children, as is typical in many low-income countries.

**Vitamin D Requirements for Infancy, Pregnancy and Lactation**

Vitamin D is a prohormone which is converted in the body to an active metabolite, 1,25-dihydroxyvitamin D \(1,25(\text{OH})_2\text{D}\) that is essential for maintaining calcium homeostasis by the orchestration of intestinal calcium absorption, bone mineral turnover and renal calcium reabsorption [2, 6, 7]. There are two forms, vitamin D\(_3\) (cholecalciferol) and vitamin D\(_2\) (ergocalciferol), that differ in some aspects of structure and metabolism, but both have prohormone activities. Vitamin D\(_3\) is produced in the skin under the action of UVB light of wavelength 290–315 nm. It enters the circulation bound to D-binding protein and is transported to the liver where it is converted to the long-lived metabolite 25-hydroxyvitamin D (25OHD). This also circulates bound to D-binding protein and is converted to 1,25(OH)\(_2\)D in the kidney and is then secreted and has endocrine action in those tissues involved in the regulation of calcium and phosphate homeostasis (intestine, skeleton, parathyroid glands and kidney). 1,25(OH)\(_2\)D is also involved in cellular processes in many other tissues, and 25OHD is taken up by these cells for intracellular production and utilization of the active metabolite.

For those individuals that have regular exposure to adventitious UVB sunlight exposure on face, hands and lower arms, endogenous synthesis of vitamin D\(_3\) is the primary source of vitamin D [4, 7, 8]. However, in temperate countries, UVB is not present in sunshine during the winter months, and there are other factors, such as pollution, indoor lifestyle and conservative dress, that also reduce an individual’s UVB skin exposure, even in tropical countries where UVB is present in sunshine year-round [4]. In addition, melanin reduces the penetration of UVB into the skin, and people with darkly pigmented skin
require longer periods of UVB exposure to achieve an equivalent amount of cutaneous vitamin D synthesis to fair-skinned people. Dietary sources of vitamin D₃ and vitamin D₂ are important providers of the prohormone when skin exposure to UVB sunlight is limited [7]. After absorption, oral vitamin D is transported to the liver where it is converted to 25OHD.

During gestation and breastfeeding, vitamin D and its metabolites are transferred by the mother to her offspring via the placenta and breast milk. These are relatively small quantities compared to maternal concentrations, and there is no evidence that the requirement of the mother for vitamin D is increased in absolute terms by pregnancy and lactation [9, 10]. However, hypovitaminosis D [a plasma concentration of <25 nm (10 ng/ml) 25OHD] is common in many parts of the world, including among pregnant and lactating mothers and young children [2]. This increases the risk of rickets and osteomalacia, and high prevalence rates of clinical vitamin D deficiency are widely reported, particularly among people originating from Africa, Asia and Middle East living in temperate countries and those living in tropical countries who have limited skin exposure to UVB sunshine [2].

**Dietary Sources and Intakes of Calcium**

Ruminant milks are among richest sources of dietary calcium when expressed as a percentage of weight consumed; cow’s milk contains approximately 120 mg Ca/100 g. Other calcium-dense sources include small fish consumed with bones and materials used as condiments and culinary ingredients, such as lime used for the production of tortilla in Central America, dried baobab leaf used to prepare steamed millet and dried baobab fruit used to flavor porridges in West Africa [11]. Some cereals, such as tef, green leaves, seeds, nuts and fruits also contain measurable amounts of calcium, all of which make small but useful contributions to the overall calcium intake in populations where milk and milk-products are scarce or not part of the local cuisine.

Relative absorption efficiency from most diets is generally around 30% or less, but is greater when calcium intakes are low and during times of high physiological need [5]. Calcium absorption from animal milks is considered to be high relative to most other sources, averaging around 30–35%; the absorption of calcium from breast milk exceeds that from animal milks [5]. Calcium absorption from plant sources is considered to be low compared to animal sources because of the chelation properties of phytates and oxalates present in a plant-based diet. Calcium-rich water is also a significant source of dietary calcium, with an absorption similar to milk in healthy individuals with normal gastric acid production, but this fact is not widely appreciated and calcium from drinking water is generally not recorded in dietary surveys. Some countries require or permit calcium fortification of the food supply, for example in the UK there is mandatory fortification of white flour with calcium, and many
food products contain calcium as a fortificant. Dietary calcium supplements in tablet or powder form are also sold in many countries. Dietary calcium intakes vary widely between individuals in the same population and between different populations, generally reflecting the consumption of animal milks (see below): a typical adult range is 300–1,500 mg Ca/day and is proportionately lower for children. Intakes at the low end of the range are well below international recommendations and are close to the biological calcium requirement for pregnant and lactating mothers and their offspring [1, 11].

Breast milk is the sole source of calcium for the exclusively breastfed infant and remains the predominant source after the introduction of complementary foods in populations where animal milk and milk products are not commonly available or avoided [12]. As described earlier, intakes of breast milk calcium average around 200–300 mg/day. However, there is considerable variation between women and between different parts of the world [13], such that the intake of calcium by healthy exclusively breastfed children can range by as much as 5-fold [13]. The accumulating evidence from observational and intervention studies has shown that the concentration of calcium in breast milk does not reflect the mother’s dietary calcium intake during pregnancy or lactation [1] even among women with a very low calcium intake [14, 15] but is related to the concentration of other constituents of human milk, notably casein, phosphate and citrate [16].

**Dietary Sources and Intakes of Vitamin D**

There are few rich dietary sources of vitamin D that are eaten regularly [2]. Among the most common are oily fish, egg yolks and to a lesser extent, meat. Fish liver oils and synthetic preparations of vitamin D are used as a dietary supplement; these make a significant contribution to vitamin D intakes in those individuals who use them regularly [17]. Many countries have mandatory or voluntary fortification of the food supply with vitamin D, although the fortification vehicle varies: for example, in the US and some other countries ‘door-step’ milk is fortified; in the UK, there is mandatory fortification of margarine [7, 17]. Animal milks contain small, but measurable, quantities of vitamin D and its metabolites. However, unless fortified with vitamin D, animal milks are not a rich source of vitamin D and make only a small contribution to overall dietary intakes. Other commercially available products, such as breakfast cereals and fruit juices, and aid foods, such as wheat-soy blend and multiple micronutrient mixes, are also often fortified with vitamin D.

The intakes of vitamin D vary between individuals and populations depending on the consumption of these rich sources of vitamin D: an average of 4 µg/day in the UK from a variety of sources including fortified margarine and cereals compares with 7 µg/day in the USA and Japan, the former largely due to the significant number of consumers of vitamin D supplements and
vitamin D-fortified milk in the USA, the latter because of the high consumption of oily fish in Japan [2, 17]. Dietary intakes of vitamin D from the plant-based diets of subsistence-farming populations in low-income countries are likely be very low.

Breast milk contains measurable quantities of vitamin D and its metabolites, but the predominant sources of vitamin D for the exclusively breastfed infant in the first months of life are from body stores built up in utero and later from skin exposure to UVB sunshine. The concentrations of vitamin D and its metabolites appear to be unrelated to the vitamin D status of the breastfeeding mother, except when she consumes high doses of supplemental vitamin D [7, 9, 10].

**Animal Milk Consumption in Low- and High-Income Countries**

Animal milks and milk products are major contributors to calcium intakes; populations with a ready supply of animal milks have considerably higher average calcium intakes than those where the supply is limited. The most reliable information about the likely contribution of animal milks to the diets of people in low- and high-income countries comes from the regular reports from the Food and Agricultural Organization on supply per capita in different countries of the world. The most recently available was conducted in 2005 (http://faostat.fao.org/site/368/). These demonstrate wide disparities in the availability of animal milks around the world, with the supply per capita in many African and Asian countries being very low. Calculating the potential amount of calcium that could be provided by animal milks in each country demonstrates that, when averaged over all members of the respective populations, there is sufficient animal milk available in countries of North America, Europe and Australasia to provide most, if not all, of the calcium needed to meet international dietary recommendations but that this is not the situation in most countries in Africa and Asia [18]. In such countries, the average total calcium intake from all sources generally falls well below international recommendations. As described earlier, the consumption of animal milks makes only a small contribution to dietary vitamin D intake, unless the country has a program of fortifying purchased animal milks and milk products with vitamin D.

**Implications of a Low Calcium Intake for Maternal and Infant Bone Health**

In theory, the additional calcium required by a pregnant or lactating mother to support the skeletal growth of her fetus during gestation and her infant during breastfeeding could be obtained by an increase in one or more of the
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following: dietary calcium intake, intestinal calcium absorption, renal calcium reabsorption and maternal bone mobilization. Also plausibly, maternal physiological adjustments to provide the essential supply of calcium to the offspring could be compromised in women with a low customary calcium intake with potential health consequences for herself and her baby. In the last 10–15 years, there have been a number of detailed studies that have investigated calcium and bone metabolism in human pregnancy and lactation and the extent to which mothers on a low calcium intake would benefit from greater calcium intakes during their reproductive lives. As has been summarized in detail elsewhere [1, 19–21], these studies have demonstrated that both pregnancy and lactation are associated with increased maternal bone turnover and a net efflux of bone mineral into the extracellular compartment, combined with enhanced intestinal calcium absorption in pregnancy and greater renal reabsorption in some women during lactation. Measurable decreases in whole-body and regional bone mineral content are observed [13, 22, 23]. Such decreases are of sufficient magnitude to make a significant contribution to the calcium required for fetal bone accretion or breast milk production [1, 21, 23]. These changes appear to be reversed, and bone mineral replenished, once breastfeeding becomes less intensive or is stopped altogether. By the time a woman has ceased breastfeeding for several months, there is little evidence of a lasting reduction in skeletal mineral content that can be related directly to pregnancy or lactation rather than to changes in bodyweight or advancing age [23, 24].

These studies have found no evidence of a relationship between the magnitude of these changes and the mother’s calcium intake [22, 23, 25]. Decreases in parathyroid hormone, bone resorption markers and small increases in maternal bone mineral density have been reported in pregnant and lactating women receiving calcium supplements, but these are in line with the expected biological response to the ingestion of additional calcium and are of a similar magnitude to the changes observed in control women given calcium supplements [21, 25]. Most intervention studies among pregnant and lactating women with very low calcium intakes have not identified any benefit of the extra calcium for fetal bone mineral accretion, birth size or infant skeletal growth and development [14, 15]. Some studies have suggested a temporary increase in bone mineral density immediately after birth in the infants of mothers with a low calcium diet supplemented with calcium during pregnancy, but these increments have not been observed in infants studied some weeks after delivery [14, 26]. A very low calcium intake in early life may also be implicated in the development of rickets reported among young African and Asian children where primary vitamin D deficiency has been discounted and calcium deficiency is suspected [18, 27]. Other health detriments unrelated to the skeleton have been hypothesized for mothers with a very low calcium intake and their offspring, most notably an increased risk of pre-eclampsia and eclampsia during pregnancy and a greater prevalence of cardiovascular
risk factors later in childhood: the limited data are summarized elsewhere [28, 29], but definitive comment awaits further evidence from ongoing studies.

**Implications of a Low Vitamin D Supply for Maternal and Infant Bone Health**

Vitamin D deficiency causes rickets in children and osteomalacia in children and adults. Both are disorders of poor mineralization of collagen, of the growth plates at the end of long bones and bone osteoid, respectively. Other sequelae include hypocalcemia, cardiac complications, myopathy, poor dental development and, in the newborn, craniotabes [10]. Vitamin D deficiency in the mother during pregnancy is associated with vitamin D deficiency in the infant [7, 10]. There is also evidence to suggest that poor vitamin D status of the mother at levels above those associated with clinical deficiency are associated with small birth size of the offspring, reduced linear growth in infancy and lower bone mineral accretion by 9 years of age [1, 7, 30]. Other health detriments have been suggested in terms of immune function and insulin sensitivity/glucose handling, and are currently being explored in a number of detailed intervention studies which will report in the next few years.

**Animal Milk Intake in Pregnancy and Lactation**

It is well recognized that generalized maternal undernutrition affects the size and development of the fetus, and hence the bone mineral accretion of the offspring. Infants born in less affluent societies tend to be smaller and have lower bone mineral content than their more affluent peers [14, 21]. There are data that suggest an association between the consumption of calcium-rich foods, including dairy products, in pregnancy and fetal growth [31, 32] and the bone mineral density of the offspring aged 6 years [33]. It is difficult to distinguish between the effects of these foods on the nutrient quality of the whole diet and those of calcium per se, given that animal milks are rich sources of growth factors and many essential nutrients such as Mg, Zn, essential fatty acids and water-soluble vitamins. Interpretation is even more complicated in studies from the USA, Canada and other countries where commercially available animal milks are fortified with vitamin D and where the regular consumption of such products may partly determine maternal vitamin D status.

**Conclusions**

Calcium intake and vitamin D status are low in many parts of the world. Animal milks make valuable contributions to dietary intakes of many nutri-
ents, including calcium. Skin exposure to UVB sunlight is the predominant source of vitamin D for most people, but dietary sources of vitamin D are important when UVB exposure is limited due to climate, latitude or lifestyle; milk and milk products that are fortified with vitamin D contribute to vitamin D intakes. Calcium is a bone-forming mineral, and vitamin D is required for regulation of calcium homeostasis and bone mineralization; both calcium and vitamin D are essential for the growth and maintenance of a healthy skeleton. Current evidence indicates that, in the human, there are physiological mechanisms that support the necessary calcium fluxes across the placenta and mammary gland and that are unresponsive to increases in calcium intake during pregnancy and lactation. This applies across the range of calcium intakes recorded in healthy individuals. In contrast, although there is unlikely to be an additional requirement for vitamin D during pregnancy and lactation, many women around the world have poor vitamin D status, which places them at risk of osteomalacia and their infants at risk of rickets, osteomalacia, compromised skeletal growth and other outcomes of vitamin D deficiency. There needs to be increased awareness among policy makers, health professionals and the public in both low- and high-income countries about the need for safe UVB sunshine exposure and provision of dietary vitamin D to women of reproductive age at risk of vitamin D deficiency.

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References

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Discussion

Dr. Mølgaard: Concerning calcium, as far as I can see there is nearly no relation between calcium intake and the outcome in these studies. What is the mechanism behind this utilization of calcium, or are there any factors that have an influence on it like vitamin D? Could there be other nutrition factors or other things that have an influence on this regulation, because it’s a huge difference in calcium intake and you have the same outcome.

Dr. Prentice: There are two parts to the answer to that question, I think. One is about what the mechanism is, and that is still being examined at the moment. It is clear that a whole range of different hormones that are specific to pregnancy and lactation, prolactin for example, are part of this story, as is the hypogestrogenemia of lactation. Parathyroid hormone-related peptide, which is produced by the mammary gland in late pregnancy and lactation, appears to be at least one component of the mechanism that drives the skeletal changes, but the likely mechanism is really very complex. The other part of the answer is the relatively small biological stress on the mother of pregnancy and lactation per unit time in relation to her own size. The results from human and animal studies have shown large species differences in the amount of calcium that needs to be transferred each day during pregnancy and lactation relative to maternal size. For small mammals, the amount is huge in relation to the calcium in the mother’s skeleton, and these animals are very dependent on the dietary calcium intake for reproductive success. These animals also have physiological changes including bone mobilization, but these are very dependent on calcium supply, and there are mechanisms to bring in more calcium, such as increases in parathyroid hormone production, if it is needed. That does not appear to be the case in the human for calcium, in common with several other aspects of human nutrition in pregnancy and lactation. One can rationalize this in terms of the fact that the amount of calcium needed on a daily basis is actually very small compared to the mother’s own size, but the mechanism has still yet to be fully understood [1–3].

Dr. Thorsdottir: I have a question about parathyroid hormone levels as an indicator for vitamin D deficiency. What could you tell us about this possibility?

Dr. Prentice: Obviously secondary hyperparathyroidism, high PTH, in white elderly women particularly, is a well-recognized risk factor for osteoporosis. As I illustrated during my talk, parathyroid hormone will increase when any aspect of the calcium-phosphorus-vitamin D physiological system is perturbed such that calcium is needed to maintain homeostasis, and this can lead to bone mineral loss. So in an elderly person, high PTH is a risk factor for osteoporosis, and for people living in European countries that is often associated with poor vitamin D status as opposed to low calcium intake, and so it has been used as a marker as you say. However, the reason for a high PTH is very variable from one person to another. For example, it is highly dependent on calcium intake. Women in The Gambia have an elevated parathyroid hormone concentration all through life, which is not related to vitamin D status or to fracture risk. So, across populations PTH is not useful as a marker of vitamin D sufficiency. In pregnancy and lactation it is not useful. Parathyroid hormone is suppressed during pregnancy and suppressed during lactation, because parathyroid hormone-related peptide
has taken over. Therefore, using PTH as a marker of nutritional status in that situation is hopeless. In adolescence, PTH will rise because calcium requirements go up and calcium absorption needs to go up. Physiologically you would expect so see high levels of PTH, so it is not a marker of status in adolescence either [4].

Dr. Anderson: Concerning the 25-hydroxy levels, is there a downside to getting much above the 70 nM level? The other thing that puzzles me is fortification. You mentioned that the UK, US, and Japan have very different levels in plasma. Is there any population health evidence that that makes a difference? The third question then is why is not vitamin D fortification of milk much more widely used, especially in the UK?

Dr. Prentice: The first question was on toxicity or at least on detrimental/adverse effects of high levels of 25-hydroxy vitamin D. I don't actually have any evidence to go into that particular discussion. The Gambian people have abundant tropical sunshine and relatively little restrictions on skin UVB exposure because of local customs of dress. This is changing at the moment, but certainly in the years when I have been studying there the people are out in the sunshine most of the day with their face, arms and parts of their upper bodies uncovered, so they have 25-hydroxy vitamin D levels which I believe reflect endogenous skin synthesis in somebody with unrestricted year round UVB exposure. We rarely see a 25-hydroxy vitamin D level in those individuals who have a concentration of above 150 nM, so I have expressed concern that moving the lower level for defining sufficiency to 80 or 90 nM, which is an average figure for The Gambia would mean that the average level required for a healthy population would exceed the upper range that I see in endogenous synthesis. As to whether that is toxic or not, I know there are many people who are looking very hard at that question at the moment. Your third question was about fortification with milk and why we do not do it in the UK. What was the middle question? Health consequences of the differences in dietary intake? These are very difficult to tease out because the data I presented were from national surveys in the three countries, and they don't tell you anything about 25-hydroxy D status. However, in the US, we certainly know that 25-hydroxy vitamin D concentrations of the general population are much better than in the UK, but then it is a sunnier country, at a lower latitude. I do think this helps to put into context the debates that there are between the Americans and Europeans about defining vitamin D adequacy, because we still have such a major problem of rickets and osteomalacia which is hardly seen in the US, although in Canada you are seeing it again. In the US, the debate has shifted from how we can prevent rickets/osteomalacia to how we can optimize health, whereas in Europe we have got a frank clinical problem that needs to be addressed and I think that changes the rhetoric. Why don't we fortify milk? You almost have to go back 50 years and ask the recommendation committees at the time but it was to do with quality control or the difficulty of controlling the quality, with respect to the amount of vitamin D that was put into milk. There were some cases of hypercalcemia in infants that occurred at about the time that milk was fortified in the UK, which at the time were put down to the fortification. This assumption has been challenged since, but nevertheless vitamin D was taken out of milk because they felt it was not possible to maintain consistent levels in milk, but that by adding it to margarine you could even out any peaks and troughs. I have to say having seen some of the data from the US, quality control of vitamin D fortification of milk is a problem there too. However, milk is still a vehicle that could be used for population fortification in the UK, but it would not reach our ethnic minorities, because they don't traditionally drink milk. So, if we are going to fortify the food chain for them, we need to think of something else [5–7].

Dr. Mohan: There has been a concept that low maternal calcium intake affects the growth of the baby, but the study which you presented fails to show a response of
calcium supplementation. Is it then necessary to supplement mothers with calcium? What are the data from countries other than Gambia?

**Dr. Prentice:** In my talk I described the results from my studies, but also showed you a summary table of studies that have been conducted in lactation elsewhere. Most of the women in these studies would have had good vitamin D status. In the UK, our pregnant women would have had reasonable vitamin D status, but it would have been seasonal, it would have been low in the winter and high during the summer. In The Gambia, vitamin D status would have been high as I was just explaining to Dr. Anderson. The aspect of whether our conclusions about low calcium intake in pregnancy and lactation hold in the face of low vitamin D status is a very important question that needs to be answered. But the studies that I think you may be referring to are from India. There is a very famous study from Pune that has looked at providing calcium-rich foods during pregnancy on the growth of the child. However, calcium-rich foods provide the mother with many other aspects of good nutrition, including calories and protein and I think we would all expect an undernourished fetus to grow better under those circumstances. The studies that I have been showing have been trying to tease out whether it is calcium itself that is limiting. Now, if you increase the nutrition of everything else and don't increase calcium you are likely to run into problems as well and so thank you for raising the question. 30 min isn't very long to talk about all these things, but adequate nutrition throughout pregnancy and lactation is essential, calcium is part of that. It was whether a woman's needs for calcium go up even higher that I was addressing [1, 8].

**Dr. Mouane:** Is there an optimal body skin exposure to sunshine? We have more and more women with Islamic clothes, and these women often ask about that.

**Dr. Prentice:** Of course 'optimal' is always a very difficult word because it implies that you know where the peak comes before it starts to become a problem again but if you ask me about 'minimum' I could possibly answer that question a little better. One of the misconceptions I think is that one needs to have a lot of UVB exposure on 100% of the body, I mean that you have to be immodest and out in the sunshine, increasing the risk of burning and melanoma, especially for fair skin people. Neither of those is true because regular, adventitious (in other words walking about doing your every day business) UVB exposure on the face, top of the head, hands and lower arms, should be sufficient. It is very difficult, because the evidence is really not there, to put it down to minutes but 'approximately 15 min a day in summer sunshine, don't go pink; if you are beginning to go pink, put your sunscreen on', that is the message [7].

**Dr. Sankaranarayanan:** Could you explain dietary interference in calcium absorption?

**Dr. Prentice:** In terms of the absorption pathway, calcium shares it with iron to some extent, so iron and calcium are thought to be antagonistic to each other. There are many components particularly from plant sources, that chelate calcium in the gut and prevent it from being absorbed. We have Lindsey Allen in the audience, and she has much more knowledge of this than I have, so maybe you could ask her outside of the session? Nevertheless, for the people that I work with in Sub-Saharan Africa, most of the calcium comes from plant foods which are likely to bind calcium and there clearly must be mechanisms where their bodies release this calcium and absorb it. So I think to some extent the absorption of calcium must be regulated by the gut and by physiological needs as well as by dietary factors such as the composition of the food that the calcium is delivered with, but I absolutely take your point that absorption may be a problem for some individuals [9].

**Dr. Johansson:** Among the varieties of dietary calcium sources, which ones course over the other?
Dr. Prentice: For an individual who has a normal gastric acid secretion, the evidence would suggest there is very little difference between them. There may be very small differences but they are only very small differences. For elderly people who have problems secreting enough acid, that is not the case, but in pregnant and lactating women that shouldn't be an issue [9].

Dr. Johansson: The variation of calcium in saliva is also very narrow. It is very close to 1 mM independent of the status of the person. So there seems to be a similar mechanism for the secretion of all these fluids.

Dr. Prentice: As I was saying, there is now a mechanism to explain why the concentration of calcium drawn into the mammary gland ready for breast milk production is independent of extracellular calcium concentration and therefore of dietary intake. This is because the calcium is incorporated into casein and citrate complexes, and these are the drivers apparently [10].

Dr. Makrides: Is there a difference in the metabolism or utilization of the vitamin D that is produced in the skin and vitamin D taken orally?

Dr. Prentice: Thank you very much, fascinating question and one that there is not an answer to. We know that, in terms of vitamin D3 and vitamin D2 that are taken orally, they are both absorbed in a very similar way but that the metabolism is different, involving different pathways. However they are both antirachitic, i.e. they prevent rickets. The question whether oral vitamin D3 is different from synthesized D3, I am sure that it is unlikely that by the time it has reached the liver and has formed 25-hydroxy vitamin D3 the body could tell the difference. But the absorption of oral vitamin D3 is into the chylomicron transport system, whereas endogenously synthesized D3 diffuses out of the skin into the circulation where it is transported bound to D-binding protein. So, although the metabolism and utilization of 25-hydroxy vitamin D3 is probably the same from both sources, the mode of delivery to the liver is different. Whether this affects the efficacy of oral D3 vs. skin D3 has not, as far as I know, been looked at, and it would be good for somebody to answer that question [11, 12].

Dr. Adrianasolo: Is calcium deficiency in the lactating mother affecting her breast milk calcium?

Dr. Prentice: As far as we can tell from our evidence the answer is no, the breast milk calcium concentration of the mother is being determined by other factors in her milk, the protein and citrate content particularly, and not by the mother’s dietary calcium intake [10].

Dr. Haschke: I was interested in your data on calcium content in breast milk. As you indicated, there is a continuous decline in the concentration until 72 weeks of age. Are we doing something wrong when we increase the calcium concentration in follow-up formulas because of the (CODEX-based) regulatory environment in most countries?

Dr. Prentice: It’s a very interesting question. We did a study in Nigeria amongst families where there was a child with probable calcium deficiency rickets as opposed to vitamin D deficiency rickets, and looked at the breast milk of the mother when she was suckling a younger sibling, compared to age-matched women in the community. We did show a small but significant difference in breast milk calcium concentration between those mothers. So there may be something in the variation from one mother to another that might predispose a child to calcium deficiency rickets, and we are looking at that at the moment. However, your question about the physiological change in breast milk composition, it is not just calcium that goes down over time, of course, it is protein and many of the other nutrients. For a child who is exclusively breastfeeding, the volume will be going up at the same time and so the total amount of calcium that a child is consuming at 6 months from breast milk will be similar or greater than at 1 month and will tail off as breastfeeding begins to tail off. So, the extent to which
formula milks mimic those changes would need to factor in volume as well as concentration, but I have no experience in the setting of Codex recommendations [13].

*Dr. Boukari:* My question is about calcium and vitamin D status and the development of chronic disease. I know that the topic is huge, but can you just give us some evidence about, for example, the role of calcium and vitamin D in the development of immune or allergic disease?

*Dr. Prentice:* This is in relation to calcium and vitamin D intakes in pregnancy and the programming of the child for later disease. The evidence on vitamin D is associational largely, there have been relatively few supplementation studies, there are some ongoing at the moment in the UK and the US that are looking at this in a prospective fashion. The answers have not come out. There really isn’t a short answer for me to give you, and maybe we can talk about this later, but I think the best answer I can give is that there are plausible mechanisms that are being actively looked at, and this is an area of huge intense research at the moment and we just have to wait for the results.

**References**
