

- 56 **Judkins A**, Eagleton C. Vitamin D deficiency in pregnant New Zealand women. *N Z Med J* 2006;**119**(1241):U2144.
- 57 **Hollis BW**, Pittard WB. Evaluation of the total fetomaternal vitamin D relationships at term: evidence for racial differences. *J Clin Endocrinol Metab* 1984;**59**:652–7.
- 58 **Pawley N**, Bishop NJ. Prenatal and infant predictors of bone health: the influence of vitamin D [review]. *Am J Clin Nutr* 2004;**80**(6 Suppl):1748S–1751S.
- 59 **Nicolaïdou P**, Hatzistamatiou Z, Papadopoulou A, et al. Low vitamin D status in mother-newborn pairs in Greece. *Calcif Tissue Int* 2006;**78**(6):337–42.
- 60 **Bodnar LM**, Simhan HN, Powers RW, et al. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr* 2007;**137**(2):447–52.
- 61 **Hoogenboezem T**, Degenhart HJ, de Muinck Keizer-Schrama SM, et al. Vitamin D metabolism in breast-fed infants and their mothers. *Pediatr Res* 1989;**25**:623–8.
- 62 **Hollis BW**, Wagner CL. Nutritional vitamin D status during pregnancy: reasons for concern. *CMAJ* 2006;**174**(9):1287–90.
- 63 **Namgung R**, Tsang RC, Specker BL, et al. Low bone mineral content and high serum osteocalcin and 1,25-dihydroxyvitamin D in summer- versus winter-born newborn infants: an early fetal effect? *J Pediatr Gastroenterol Nutr* 1994;**19**:220–7.
- 64 **Hollis BW**, Wagner CL. Vitamin D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D in both mother and nursing infant. *Am J Clin Nutr* 2004;**80**(Suppl):1752S–1758S.
- 65 **Cancela L**, LeBouch N, Miravet L. Relationship between the vitamin D content of maternal milk and the vitamin D status of nursing women and breastfed infants. *J Endocrinol* 1986;**110**:43–50.
- 66 **Atiq M**, Suria A, Nizami SQ, et al. Vitamin D status of breastfed Pakistani infants. *Acta Paediatr* 1998;**87**:737–40.
- 67 **Gartner LM**, Greer FR. Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. *Pediatrics* 2003;**111**:908–10.
- 68 **Wharton B**, Bishop N. Rickets. *Lancet* 2003;**362**(9393):1389–1400.
- 69 **Nozza JM**, Rodda CP. Vitamin D deficiency in mothers of infants with rickets. *Med J Aust* 2001;**175**:253–5.
- 70 **Dawodu A**, Agarwal M, Sankarankutty M, et al. Higher prevalence of vitamin D deficiency in mothers of rachitic than nonrachitic children. *J Pediatr* 2005;**147**(1):109–11.
- 71 **Greer FR**. Issues in establishing vitamin D recommendations for infants and children [review]. *Am J Clin Nutr* 2004;**80**(6 Suppl):1759S–1762S.
- 72 **Delvin EE**, Salle L, Glorieux FH, et al. Vitamin D supplementation during pregnancy: effect on neonatal calcium homeostasis. *J Pediatr* 1986;**109**:328–34.
- 73 **Mallet E**, Gugi B, Brunelle P, et al. Vitamin D supplementation in pregnancy: a controlled trial of two methods. *Obstet Gynecol* 1986;**68**:300–4.
- 74 **Cockburn F**, Belton NR, Purvis RJ, et al. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *BMJ* 1980;**5**:11–14.
- 75 **Datta S**, Alfaham M, Davies DP, et al. Vitamin D deficiency in pregnant women from a non-European ethnic minority population: an interventional study. *Br J Obstet Gynaecol* 2002;**109**:905–8.
- 76 **Vieth R**, Chan PCR, MacFarlane GD. Efficacy and safety of vitamin D₃ intake exceeding the lowest observed adverse effect level (LOAEL). *Am J Clin Nutr* 2001;**73**(2):288–94.
- 77 **Heaney RP**, Davies KM, Chen TC, et al. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. *Am J Clin Nutr* 2003;**77**:204–10.
- 78 **Saadi HF**, Dawodu A, Afandi BO, et al. Efficacy of daily and monthly high-dose calciferol in vitamin D deficient nulliparous and lactating women. *Am J Clin Nutr* 2007;**85**(6):1565–71.
- 79 **Ala-Houhala M**, Koskinen T, Terho A, et al. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 1986;**61**:1159–63.
- 80 **Wagner C**, Hulsey T, Fanning D, et al. High dose vitamin D₃ supplementation in a cohort of breastfeeding mothers and their infants: a six-month follow-up pilot study. *Breastfeed Med* 2006;**2**:59–70.

Vitamin D

Vitamin D in pregnancy: an old problem still to be solved?

A F Williams

Perspective on the paper by Dijkstra *et al* (see page 750)

In this issue Dijkstra *et al* describe the high incidence of hypovitaminosis D (serum 25-hydroxyvitamin D <25 nmol/l) amongst infants born in Rotterdam, the Netherlands (latitude 52°N). Babies born to veiled or dark-skinned mothers were significantly more likely than those of white mothers to have a low 25-hydroxyvitamin D (25OHD) concentration in umbilical cord blood. Similarly, a recent study of pregnant women in the Hague found that 56–66% of women of Moroccan and Turkish descent had 25OHD levels <25 nmol/l, compared with 8% of women of Western origin.¹ Given that mainland United Kingdom lies at a latitude of 50°–58°N and the populations of its large cities show similar ethnic and cultural diversity, these findings are very relevant to Britain. Indeed amongst Cardiff women from ethnic minority groups attending their first antenatal appointment, half showed a serum 25OHD concentration <20 nmol/l.² Those of Indian or African origin were most likely to be affected, especially women who had arrived in the UK within the last 3 years. Interestingly these problems are not confined to northerly latitudes but occur in sunnier climes as well.³

We have known for over 30 years that hypovitaminosis D is common amongst pregnant women in ethnic minority groups, particularly those of Asian origin.⁴ Intervention studies, including a randomised placebo-controlled trial (amongst women of south Asian origin living in South London) showed that infants of vitamin D supplemented mothers were less likely to be small for gestational age, less likely to develop neonatal hypocalcaemia, and had better tooth enamel mineralisation.^{5,6} Recent epidemiological data have added another perspective to maternal vitamin D status in pregnancy and challenge the widely held assumption that suboptimal vitamin D status in pregnancy is a problem confined to at risk ethnic groups. Amongst white women living in Southampton (at one of the most southerly latitudes of the United Kingdom) maternal 25OHD concentrations in the third trimester of pregnancy correlated significantly with the child's whole body and lumbar spine bone mineral content at the age of 9. Eighteen per cent of these mothers showed a 25OHD concentration <28 nmol/l at parturition. Although no national data exist for pregnant women, the low status of UK women of childbearing age

is borne out by the National Diet and Nutrition Survey of British adults: 28% of women aged 19–24 and 13% of those aged 25–34 had plasma 25OHD concentrations <25 nmol/l. These findings suggest that infants who present clinically with vitamin D deficiency, either in the neonatal period or later with clinical rickets, represent only a small proportion of those with suboptimal vitamin D status.

How can the risk of vitamin D deficiency in pregnancy, and by implication in infancy, be reduced? In 1991 the Committee on Medical Aspects of Food and Nutrition Policy (COMA) set a reference nutrient intake (RNI) of 10 µg/day (400 IU/day) vitamin D for women who are pregnant or breast feeding.⁷ This amount was chosen as sufficient to maintain plasma 25OHD >20 nmol/l during the winter months in Scotland and was endorsed by COMA as recently as 1998.⁸ Whilst sunlight exposure is generally of greater importance than diet in the maintenance of vitamin D status, there is no ambient ultraviolet light of the appropriate wavelength at UK latitudes during the winter months. For this reason maintenance of adequate vitamin D status in pregnancy is best achieved through dietary means. However, the average dietary vitamin D intake of young women in the UK approximates 3 µg/day and fewer than 1% consume more than the 10 µg RNI.⁹ Achieving the RNI therefore necessitates supplementation. The advice applies to all women and not merely those in ethnic minority groups, yet very few women take a vitamin D supplement during pregnancy and an individual woman's risk of deficiency in pregnancy seems rarely to be assessed.

Unfortunately there have been many barriers to policy implementation. These

include a lack of public and professional awareness, limited availability of suitable supplements which omit retinol (vitamin A) and inconsistency in guidance. In 2003 NICE concluded that "vitamin D supplementation should not be offered routinely to all pregnant women".¹⁰ This view clearly conflicts with the COMA opinions cited above and was based on a meta-analysis of two randomised trials, one of which was conducted in the UK and showed important effects.⁵ The Department of Health later stressed the continued importance of offering vitamin D supplements to pregnant women, particularly those in vulnerable groups.¹¹

Some time ago a public education campaign conducted amongst at risk groups in Glasgow demonstrated effectiveness in terms of both increased uptake of supplements and a reduction in rickets,¹² but a recurring and commonly cited concern has been the lack of a suitable low cost and palatable preparation. Fortunately this has recently been rectified in the process of reforming the welfare food scheme as *Healthy Start*. A single tablet providing vitamin D (10 µg) with folic acid (400 µg) and vitamin C is now available free to pregnant or breastfeeding mothers who are eligible for *Healthy Start* benefits, and can be prescribed at low cost for those who are not.

The issue of hypovitaminosis D in pregnancy must also recognise current uncertainty about the meaning of "normal" in the context of vitamin D status. Population reference ranges are influenced by a number of biological and lifestyle influences, most importantly sunlight exposure. However, in the twenty first century "sun shy" culture of industrialised nations¹³ they may not be indicative of optimal health. Indeed 25-OHD concentrations encountered in people liberally exposed to sunlight (such as lifeguards) exceed by 5–10-fold the lower limit of "normal" (25 nmol/l) cited above.¹³ Several authorities in the United States now argue that maintenance of a 25OHD

concentration above 75–80 nmol/l is associated with improved health, citing the associated reduction in parathyroid hormone concentration and increased calcium absorption and bone mineral density.^{13 14} Interestingly, the achievement of such plasma levels through high dose supplementation (50 µg, 2000 IU vitamin D per day) in breastfeeding mothers also increases both antirachitic activity in breast milk and plasma 25OHD concentration in their infants.^{15 16} The National Diet and Nutrition Survey of British adults suggests that if such a threshold were applied to UK population data, some 80–90% would be considered at risk of deficiency.¹⁷ This is potentially therefore a population health issue of considerable importance and its significance and implications require careful thought.¹⁸ Currently the 25-OHD concentration of <25 nmol/l cited by Dijkstra *et al* as a threshold of deficiency risk remains widely adopted but may prove conservative to say the least.

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REFERENCES

- 1 van der Meer IM, Karamali NS, Boeke AJ, *et al*. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutr* 2006;**84**(2):350–3.
- 2 Datta S, Alfaham M, Davies DP, *et al*. Vitamin D deficiency in pregnant women from a non-European ethnic minority population—an interventional study. *BJOG* 2002;**109**(8):905–8.
- 3 Nicolaidou P, Hatzistamatiou Z, Papadopoulou A, *et al*. Low vitamin D status in mother-newborn pairs in Greece. *Calcif Tissue Int* 2006;**78**(6):337–42.

- 4 Dent CE, Gupta MM. Plasma 25-hydroxyvitamin-D levels during pregnancy in Caucasians and in vegetarian and non-vegetarian Asians. *Lancet* 1975;**2**(7944):1057–60.
- 5 Brooke OG, Brown IR, Bone CD, *et al*. Vitamin D supplements in pregnant Asian women: effects on calcium status and fetal growth. *BMJ* 1980;**280**(6216):751–4.
- 6 Cockburn F, Belton NR, Purvis RJ, *et al*. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *BMJ* 1980;**281**(6232):11–14.
- 7 Committee on Medical Aspects of Food Policy (COMA). *Dietary reference values for food energy and nutrients for the United Kingdom*, Report on Health and Social Subjects No 41. London: HMSO, 1991.
- 8 Committee on Medical Aspects of Food and Nutrition Policy. *Nutrition and bone health*, Report on Health and Social Subjects No 49. London: Stationery Office, 1998.
- 9 Henderson L, Irving K, Gregory J, *et al*. *The National Diet and Nutrition Survey: adults aged 19 to 64 years*. Vol 3. Vitamin and mineral intake and urinary analytes. London: Stationery Office, 2003:1–160.
- 10 National Institute for Health and Clinical Excellence. Antenatal care: routine care for the healthy pregnant woman. In: *Compilation: summary of guidance issued to the NHS in England and Wales*, Issue 7. London: NICE, 2003, 127–60. See also <http://guidance.nice.org.uk/CG6> (accessed 20 June 2007).
- 11 Anon. Meeting the need for vitamin D. *CMO Update* 2005;**42**:6.
- 12 Dunnigan MG, Glekin BM, Henderson JB, *et al*. Prevention of rickets in Asian children: assessment of the Glasgow campaign. *BMJ* 1985;**291**(6490):239–42.
- 13 Hollick BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr* 2005;**135**(2):317–22.
- 14 Hollick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *Am J Clin Nutr* 2004;**80**(6):1678S–88S.
- 15 Ala-Houkala M, Koskinen T, Terho A, *et al*. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 1986;**61**:1159–63.
- 16 Hollick BW, Wagner CL. Vitamin D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. *Am J Clin Nutr* 2004;**80**(6 Suppl):1752S–8S.
- 17 Ruston D, Hoare J, Henderson L, *et al*. *The National Diet and Nutrition Survey: adults aged 19 to 64 years*. Vol 4. Nutritional status (anthropometry and blood analytes), blood pressure and physical activity. London: Stationery Office, 2002:1–156.
- 18 Scientific Advisory Committee on Nutrition. Update on vitamin D. London: Stationery Office, 2007:1–68. <http://www.sacn.gov.uk> (accessed 28 June 2007).

Vitamin K deficiency

Vitamin K deficiency bleeding: the readiness is all

Paul Clarke, Martin J Shearer

Perspective on the papers by Busfield *et al* and McNinch *et al* (see pages 954 and 959)

Over 10 years ago, William Hathaway described the 50-year chequered history of the association

between a neonatal bleeding disorder and vitamin K deficiency and its prevention as a splendid example of the cyclical nature of

discovery–rediscovery in medical science.¹ The lessons that should have been learnt from the extensive body of early work were reiterated in a recent lively review in this journal.² In the UK these forgotten lessons first resurfaced in a 1983 *Lancet* article entitled "Haemorrhagic disease of the newborn returns".³ Of course this rare deficiency syndrome, now more accurately termed vitamin K deficiency bleeding (VKDB), had never gone away but had merely been rediscovered at a time of a progressive trend towards exclusive breast feeding. The latter had long since been established as an important risk factor for neonatal hypoproteinaemia.⁴