

Preventing Disease in Babies Before Birth

Dr. Jodie Benson

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Dr. Jodie Benson a specialist Obstetrician and Gynaecologist at University Hospital Geelong and a senior clinical lecturer at Deakin University in Australia. Here Dr. Benson discusses her research into vitamin D deficiency in pregnant women that might adversely affect their babies.

Why did you become interested in vitamin D deficiency in pregnancy?

My interest in vitamin D deficiency in pregnancy was almost accidental. Not until I spent time with an endocrinology colleague did I become aware of the full extent and seriousness of the problem, especially in newborns. My interest was further heightened by the patients who were at risk for this problem. In our clinic these women were often marginalized—not fluent in English and with poor social supports.

There was no consensus on how to screen for or manage the disorder in pregnancy. So in this era of evidence based medicine, the idea of studying vitamin D deficiency in pregnancy and preventing the birth of vitamin D deficient babies just jumped out at me.

What specific abnormalities in the newborn might someone see if the mother is vitamin D deficient herself?

Vitamin D deficiency impairs bone mineralization and leads to bone softening, but most vitamin D deficient newborns are asymptomatic. Softening of the skull bones may occur, but most alarmingly a neonate may suffer from hypocalcaemic seizures. Rickets—bowed long bones—is the typical manifestation of long-term vitamin D deficiency but isn't evident until weight bearing occurs. Other associated problems include thinning of bones—osteomalacia—as well as osteoporosis, increased fracture risk and muscular aches and pains. More recently, vitamin D deficiency has been linked to an increased risk of death from cardiovascular disease, as well as with cognitive impairment in older adults. Vitamin D deficiency is also associated with increased mortality from malignancies—such as colon, breast, ovarian, melanoma and prostate—as well as an increase in upper and lower respiratory tract infections. Vitamin D deficiency is also associated with an increase risk of depression and suicide. There is some evidence linking vitamin D to multiple sclerosis, type 2 diabetes, inflammation and the risk of allergies in children and adolescents.

Are there any specific racial, cultural or



socioeconomic factors that predispose pregnant women to have low levels of vitamin D in their blood?

Vitamin D deficiency can result from inadequate sun exposure and/or inadequate nutritional intake, as well as from diseases that impair vitamin D adsorption or conversion into active metabolites (e.g. liver and renal disease). Typically vitamin D deficiency occurs in populations with highly pigmented skin, as well as those with clothing practices resulting in minimal sun exposure.

Increasingly we are seeing maternal vitamin D deficiency in a more diverse population. As people spend more time indoors for both work and domestically, sun exposure is decreased. This can be compounded by the “sun smart” message and use of sunscreens. Vitamin D deficiency is also increased in the obese population.

How do you identify pregnant women with low levels of vitamin D and can you effectively remedy the problem to keep the baby healthy?

A simple blood test—either prepregnancy or in early pregnancy—can detect vitamin D deficiency. Oral supplementation can commence as soon as the diagnosis is made. Our study showed that if you adequately supplement vitamin D deficient women, they and their babies will have normal levels at birth.

The option of treating postnatally is also important. Breast milk is not a very good source of vitamin D—oral supplements must be given. Generally, breastfeeding is best for both babies and their mothers, but if the mother is at risk of



vitamin D deficiency this should be addressed with vitamin supplementation.

Do you think the public is aware of the potential problem low levels of vitamin D pose to the newborn? Should there be more public awareness of the issue?

I don't think that the generally public is aware of the potential problems that vitamin D deficiency poses to adults, children or newborns. There should be more public awareness in general.

Given that I'm an obstetrician and gynaecologist. I believe that the pregnant population should be targeted. Women are usually more highly motivated to change any behaviours or remedy any ills when they are pregnant. The family practitioner has the opportunity to screen and treat the entire family as well. This is important because studies have shown that if a pregnant woman is deficient, her family is also at risk and should be screened.

Do you have plans to extend this study in the future or focus elsewhere?

My interest has recently shifted to perinatal loss. I sit on the Consultative Council on Obstetric and Paediatric Mortality and Morbidity Stillbirth Subcommittee, convened by the Department of Health. We review all cases of stillbirth in Victoria. My recent research interest looked at the feasibility of CT scan versus autopsy in the investigation of stillborn babies. This is a terribly sad topic and we have to learn more to help and counsel families affected by the loss of their unborn baby.

Fighting Vitamin D Deficiency Before Birth

Vitamin D deficiency isn't just a thing of the past. Dr. Jodie Benson's research shows that identifying and treating vitamin D deficiency in pregnancy can prevent vitamin D deficiency in the newborn.

AN OLD DISEASE REARING ITS HEAD AGAIN

Rickets—fractures and bony deformities in infants and young children due to poor calcification of the bones often caused by vitamin D deficiency—was probably known at least by the first or second century A.D. However, rickets was not formally described as a specific malady until a treatise in 1645 by Daniel Whistler, an English physician. In fact, the term “orthopaedics” was coined by the French professor Nicholas Andry—derived from Greek words for “correct” or “straight” (“orthos”) and “child” (“paidion”)—in his 1741 book Orthopaedia: or the Art of Correcting and Preventing Deformities in Children. By 1918, Kurt Huldshinsky, a German paediatrician, successfully showed that rickets could be treated by exposure to ultraviolet lamps. This made sense, since vitamin D is produced in the skin from the conversion of 7-dehydrocholesterol by UV radiation. By 1945, rickets had all but been eliminated in developed countries by the enrichment of food, especially of milk, with vitamin D via UV irradiation. But rickets, and vitamin D deficiency generally, seems to be making a comeback of late.

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Dr. Jodie Benson and her colleagues have observed that vitamin D deficiency seems to be on the rise in some populations in Australia and elsewhere. They note that lifestyle factors, such as increased time spent indoors and increasing use of UV-blocking sunscreens, effectively decrease UV light absorption, hence

vitamin D production. Obesity is also a risk factor for vitamin D deficiency. The problem is compounded in darker pigmented individuals and people whose cultural practices include extensive body covering, both situations decreasing UV absorption by the skin. What most concerned Dr. Benson, an obstetrician, was the problem of vitamin D deficiency in the pregnant women for whom she cared. Since foetal vitamin D is acquired transplacentally from the mother, low maternal vitamin D levels lead to vitamin D deficiency in the foetus. Further, breastfeeding does not supply sufficient vitamin D—especially if the mother is vitamin D deficient to begin with—so babies who have low levels of the vitamin at birth cannot catch up with breast milk alone.

25 HYDROXY VITAMIN D LEVELS IN PREGNANT WOMEN

To investigate the prevalence of vitamin D deficiency in pregnancy and the possibility of prenatal treatment, Benson and her group designed and carried out a study of pregnant women attending a routine outpatient antenatal clinic in a tertiary referral centre in Melbourne, Australia. Relevant demographic information was obtained from the women, including socioeconomic status, lifestyle factors such as clothing preference and sun exposure habits. Vitamin D levels were measured by measuring serum levels of 25-hydroxy vitamin D—also known as 25-hydroxycholecalciferol, a precursor of vitamin D considered the best indicator of a person's vitamin D status—and women with low serum vitamin D levels were included in the study. Measurements were taken both initially and at intervals thereafter, including at delivery, as well as from the baby after birth. The vitamin D deficient women were initially divided into two groups and randomised to receive either vitamin D supplementation during their pregnancy versus non-treatment. Since there was no standard recommendation for vitamin D supplementation during pregnancy, the withholding of treatment was not ethically

objectionable. However, after delivery any women in the non-treatment arm were offered treatment with vitamin D for themselves and their newborns.

FACTORS ASSOCIATED WITH VITAMIN D DEFICIENCY

Benson's study initially enrolled and randomised 78 pregnant women, although at the end of the study 45 women were available for data analysis, 22 in treated and 23 not treated, some women being lost due to compliance and other issues. The women in both groups were similar in age, 28-29 years, and had only been in Australia for 6-8 years. Thus, younger immigrants represented a goodly portion of the study population. Perhaps as expected, approximately 75% of these vitamin D deficient women were dark skinned and about 15% wore veils and extensive body coverings. Both of these situations are associated with low levels of vitamin D. Also, dairy intake—including vitamin D fortified milk—was similar, at about 8-9 servings per week. Importantly, about a fourth of the women had a previous history of vitamin D deficiency.

At the first visit—between 12-16 weeks of gestation—the 25-OH vitamin D levels in these two groups of women was approximately the same and low. In the treatment group, the serum level averaged 32 nmol/l, while in the placebo group it was 33 nmol/l. Although no official recommendations existed at the time for vitamin D levels in pregnancy, Benson and her colleagues used clinical guidelines published in 2011 by American endocrinologist Michael Holick and his colleagues that considered the normal level of 25-OH vitamin D to be >75 nmol/l, while deficiency was defined as a level <50 nmol/l. Clearly, both of Benson's patient groups were significantly deficient in vitamin D, putting themselves and their babies at risk for the adverse effects of vitamin D deficiency. Benson and her co-workers found what they had expected—pregnant women with recognized risk factors having significantly low levels of vitamin D. So did the vitamin D supplementation work?

SIGNIFICANT RISE IN VITAMIN D LEVELS

When Benson analysed the 25-OH vitamin D levels over the course of the pregnancies in both groups, she found the very answer she was looking for. While both groups had levels of 32-33 nmol/l at the beginning, both in the

deficiency range, when levels were drawn at 28 weeks of pregnancy—when other routine blood work was drawn—the treatment group was now up to an average of 65 nmol/l, while the untreated women had average levels of 41 nmol/l. The untreated women were still deficient, below 50 nmol/l, while the treated women were now in a borderline zone between 50-75 nmol/l. And at that point, the dosing of vitamin D supplementation in the treatment group could be doubled—from 2000 IU of ergocalciferol (vitamin D3) to 4000 IU—to see if more was better, and also to see if a higher dose was tolerated in pregnancy.

At delivery, the level in the treatment group had risen to 71 nmol/l, now in the recommended normal range, while the level in the untreated group was still in the deficiency range, at 36 nmol/l. Beyond that and most importantly, the vitamin D levels in the newborn babies correlated with the maternal vitamin D levels. In the treatment group, the 25-OH vitamin D levels averaged 81 nmol/l, compared to 42 nmol/l in the untreated group, a significant difference. The treated babies had normal vitamin D levels—presumably keeping them safe from rickets and other manifestations of vitamin D deficiency—while the levels in the untreated group were in the deficient range. Benson's hypothesis was confirmed—treating the mother with vitamin D before pregnancy significantly improves the mother's vitamin D levels, but it also raises her baby's levels so it can be born with normal levels of vitamin D. Screening and treatment appears to be a reasonable strategy to combat maternal and foetal vitamin D deficiency.

Benson admits that this is a small study and technically not extremely rigorous. However, the results speak for themselves and, combined with research by other groups, the study gives clear evidence that supplementing vitamin D in pregnancy remedies vitamin D deficiency in pregnant women themselves and prevents neonatal vitamin D deficiency. The results of Benson's study indicate that larger studies are needed to verify the results, determine the optimum levels of vitamin D in pregnancy and how much supplementation should be given, and generate guidelines that can then be applied to all prenatal patients. But the die is cast in this battle against the resurgence of neonatal vitamin D deficiency.

Researcher Profile



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Dr. Jodie Benson received her Bachelor of Medicine & Surgery from the University of Melbourne. She completed formal specialist training in Obstetrics & Gynaecology at Monash Medical Centre, being elevated to Fellow in 2011. Her early career featured international experience including a Fellowship in Robotic Gynaecological & Endoscopic Surgery. This time abroad also ignited a passion for intrapartum care and labour ward teaching, having worked in a busy obstetrics unit in Ireland delivering close to 10,000 babies a year. She returned to Australia in 2010 and worked at South West Health care and Deakin Warrnambool, where she was the Women's Health rotation coordinator, before moving to Geelong. Dr. Benson combines her clinical role at GUH, with RANZCOG training supervision, Deakin medical student teaching as well as sitting on the Consultative Council on Obstetric and Paediatric Morbidity and Mortality (DHS).

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