A vital vitamin

Professor Carol Wagner is a paediatrician with expertise in neonatal-perinatal medicine. Here, she discusses how her research into the vitamin D status of pregnant and lactating women is filling a significant knowledge gap and fuelling innovative public health initiatives.

What inspired you to begin studying vitamin D status in pregnant and lactating women and how have your background and previous experiences helped your current research?

I was inspired to study vitamin D requirements during pregnancy and lactation because of my collaboration with biochemist Dr Bruce Hollis, one of the world’s leading scientists in vitamin D research. Back in 2000, we were discussing the vitamin D requirements of lactating women and the issue of supplementation in breastfeeding infants. I became intrigued by the fact that human milk, always viewed as the ‘perfect’ first food for babies, was deficient in vitamin D and began to question why this was the case. Together, Dr Hollis and I began to conduct vitamin D supplementation studies in lactating women in an attempt to answer this question. Later, we studied pregnant women in order to understand why vitamin D metabolism is so dramatically different during pregnancy. From that point on, I have not looked back.

Do you think that the impact of vitamin D deficiency on pregnant and breastfeeding women has been underresearched prior to your studies? Why do you think this is?

My answer to this is a resounding yes! Vitamin D deficiency during pregnancy and lactation has been understudied because until very recently it was thought that vitamin D was only involved with calcium homeostasis and bone integrity – and that beyond childhood there was little need for vitamin D. Now, with an exponential growth in vitamin D research, we are able to explore the mechanisms of action of vitamin D at the cellular level and, importantly, we see that it affects every cell in the body, just as other steroid hormones such as thyroxine and cortisol do. As a result of previous misunderstanding and a lack of robust research on the effects of vitamin D, there is much ‘catch-up’ that needs to be done in this area.

You and your team collaborate with non-profit organisation GrassrootsHealth. How is this partnership facilitating the translation of your research into public health initiatives?

It has been a tremendous experience to work with GrassrootsHealth. As a clinician scientist, I did not have any prior experience in translating research into practice. When speaking about our research findings, I would often communicate in terms that were not easily understood by nonmedical folks – and as a result this minimised the impact of our findings. Partnering with GrassrootsHealth – which is directed by Carole Baggerly – has allowed us to make the transition from using technical jargon to explaining health impact factors in terms that are accessible to everyone.

What do you see as the next steps in promoting vitamin D supplementation and adherence to supplementation programmes during pregnancy nationwide?

We are currently planning to launch community-based programmes in Charleston, South Carolina; San Diego, California; Chicago, Illinois; and Omaha, Nebraska, through our collaboration with GrassrootsHealth. Such programmes are important because they provide an educational forum for both healthcare providers and the women themselves. Additionally, the involvement and support of insurance companies – which shoulder the burden of escalating costs incurred with adverse pregnancy outcomes – will ensure the sustainability of these programmes. Indeed, with the US ranking much higher than many other countries for adverse pregnancy outcomes, there is an urgent need to turn the tide.
Spotlight on deficiency

Researchers based in the Division of Neonatology in the Department of Pediatrics at the Medical University of South Carolina in Charleston, USA, are investigating the optimal vitamin D status for the improved health of pregnant and lactating women and their babies.

LARGELY DERIVED FROM sunlight on bare skin, vitamin D is essential for human health – and recent years have witnessed enhanced interest in the many and varied functions of this vitamin. For instance, in addition to maintaining calcium homeostasis in the body – consequently preventing rickets and osteomalacia in children and osteoporosis in adults – the deficiency of vitamin D has been linked to multiple chronic conditions such as cancer, diabetes and the development of neurological diseases. Although it is possible for individuals with vitamin D deficiency to survive for many years, their quality of life and overall health status are often severely compromised.

Unfortunately, vitamin D deficiency is becoming much more common in the US and in many other nations throughout the world. This is largely due to modern lifestyle factors; for example, the prevalent indoor culture means that people are less likely to spend extended periods of time outside in the sun and, if they do, they will usually be covered with sunscreen, which prevents their skin from absorbing sunlight and making vitamin D. Additionally, because vitamin D is fat-soluble and can be stored in fat, overweight and obese individuals are prone to deficiencies due to reduced amounts of vitamin D circulating in their blood. Thus, the growing obesity epidemic – a trend that is particularly marked in the Western world – is also a contributing factor to the increasingly widespread phenomenon of vitamin D deficiency.

PREGNANCY AND LACTATION

Two particularly worrying subpopulations subject to large-scale vitamin D deficiency are pregnant women and breastfed infants – a number of observational studies have revealed correlations between low vitamin D levels and comorbidities in pregnancy including preeclampsia, lower birth weight and a higher rate of preterm delivery. Unfortunately, these patterns have been vastly underresearched to date, largely due to the mistaken association between vitamin D and toxicity during pregnancy. Based on observations that hypercalcaemia led to facial and other deformities in the foetus following the supplementation of milk and other food sources with vitamin D, in the past the root cause of these deformities was wrongly attributed to vitamin D. In fact, the problem of metabolising vitamin D is a symptom of Williams syndrome, a genetic disease. Vitamin D has nothing to do with causing this condition, yet even today many clinicians remain reluctant to prescribe vitamin D supplements to pregnant women.

Motivated by the lack of research and the misconceptions surrounding vitamin D deficiency and supplementation in pregnant and lactating women and their infants, Professor Carol Wagner is attempting to

VITAMIN D: FACING THE FACTS

- The active form of vitamin D is produced from previtamin D3, derived from sunlight, dietary supplements or certain foods. Before it becomes biologically available, D3 must be metabolised in a series of steps, first in the liver, then the kidneys, and finally released into the circulation in its active hormone form (1,25(OH)2D).

- Vitamin D enables the body to use calcium ingested in the diet. More recently, research has emphasised that, due to its effect on both innate and adaptive immunity, vitamin D has multiple roles in protection against a plethora of chronic conditions.

- The populations at highest risk of vitamin D deficiency are those of African, Hispanic and South Asian origin because the melanin in their skin reduces their ability to make vitamin D in response to exposure from sunlight.
A number of observational studies have revealed correlations between low vitamin D levels and preeclampsia, lower birth weight and a higher rate of preterm delivery.

For a deeper understanding of the optimum vitamin D dosage for these populations, as a prominent clinician-researcher in the Division of Neonatology at the Medical University of South Carolina (MUSC), Wagner has devoted the past 15 years to studying the benefits of vitamin D supplementation in both lactating and pregnant women and, more recently, to begin to explore the role of vitamin D in early infancy. Her innovative research has benefited from her longstanding collaboration with Dr Bruce Hollis, an expert in vitamin D and Professor in the Department of Pediatrics at the MUSC Children’s Hospital. “The importance of vitamin D in health has expanded in the last decade as we have deciphered the role of this steroid hormone in cellular metabolism that includes, but goes well beyond, bone and calcium metabolism,” Wagner points out. Indeed, recent studies have highlighted that vitamin D plays a key role in immune function and general health throughout life.

**FAR-REACHING FINDINGS**

In order to determine the effectiveness of vitamin D supplementation in pregnant and lactating women, Wagner and Hollis have conducted important clinical trials. Funded by the National Institute of Child Health and Human Development and the Thrasher Research Fund, the data from their studies on pregnant women suggest that maternal supplementation with high doses of vitamin D leads to a reduction in risk of infection, preterm labour and preterm birth. As for the lactation trial, the results showed that high-dose maternal supplementation of vitamin D during lactation could substantially improve both maternal and neonatal nutritional vitamin D status. “Significantly, we found that if the mother is vitamin D replete, which can occur with 4000 IU vitamin D3/day, then her milk is replete and her infant’s vitamin D status will be similar to those infants who receive 400 IU vitamin D3/day as a supplement,” Wagner elucidates. “Thus, when mothers have adequate vitamin D status, their milk is enriched with vitamin D and their infants achieve healthy vitamin D levels without any need for supplements.” Importantly, this finding helps to dispel the myth that human milk is an inherently poor source of vitamin D.

**FORGING A FULLER UNDERSTANDING**

So far, Wagner’s cutting-edge research has helped to address a significant knowledge gap regarding the role of vitamin D in pregnancy, lactation and early childhood. Yet much more work remains to be done in this field and, together with her colleagues, she is currently seeking to establish the mechanisms that underpin the link between vitamin D deficiency and the risk of complications in pregnancy. Moreover, Wagner is also eager to translate her research findings into practice; to this end, she has partnered with a not-for-profit health organisation to run community-based programmes that educate women and healthcare professionals about vitamin D supplementation during pregnancy and breastfeeding.

Excitingly, Wagner and her research team have recently been awarded a grant by the Kellogg Foundation to embark on a study that aims to prevent health disparities in pregnancy outcomes through the supplementation of vitamin D. “This project involves a comparison between women who are receiving the current standard of care for vitamin D of 400 IU received in a prenatal vitamin with women receiving the much higher dose of 4000 IU/day,” she explains. “We are focusing on immune function – T cell morphology, inflammatory and anti-inflammatory cytokine profiles and placental changes – as a function of maternal vitamin D status.” Looking ahead, the hope is that the completion of this project will result in a more in-depth understanding of the mechanisms exerted by vitamin D during pregnancy and, ultimately, that this knowledge will generate wider acceptance of the importance of maintaining vitamin D sufficiency in pregnant women.