

Medical Update Memo

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GENETIC STUDY SUPPORTS VITAMIN D DEFICIENCY AS AN ENVIRONMENTAL FACTOR IN MS SUSCEPTIBILITY

Summary

Researchers funded by the MS Society of Canada have found evidence of an interaction between vitamin D and a common genetic variant which may alter the risk of developing multiple sclerosis. The research, published in the Feb 5 edition of the open access journal *PLoS Genetics*, suggests that vitamin D deficiency during pregnancy and the early years may increase the risk of a child developing the disease.

Details

The causes of MS are unclear, but it has become evident that both environmental and genetic factors play a role. Studies have shown that MS is more common in areas of less sunshine, such as Canada and Northern Europe. It has also been shown that fewer people with MS are born in November and more in May, supporting a gestational risk effect of diminished sunlight. These findings suggest a possible link between deficiency in vitamin D, which is produced in the body through the action of sunlight, and increased risk of developing the disease.

The most striking illustration of this is the geographical distribution in populations matched for ethnicity. This has further advanced the proposal that sunshine, and in particular, a deficiency in vitamin D, is an environmental factor influencing the risk for developing MS. Circumstantial evidence supporting this comes from studies showing the involvement of vitamin D in immune and nervous system function.

Now, in a study funded by the MS Society of Canada, the UK MS Society, the Wellcome Trust and the Medical Research Council, researchers at the University of Oxford have shown that there is a direct relationship between *DRB1*1501* and

vitamin D with a receptor (a DNA sequence responsive to vitamin D) largely restricted to chromosomes bearing the *DRB1*1501* variant.

"We found that vitamin D affects the expression of this particular genetic variant – in other words, adequate vitamin D must be present for the variant to do its normal job," explains Dr Julian Knight from the Wellcome Trust Centre for Human Genetics, University of Oxford. "This effect only appears to occur in people carrying the *DRB1*1501* variant associated with MS".

"We have known for a long time that genes and environment determine MS risk," says Professor George Ebers, University of Oxford. "Here we show that the main environmental risk candidate – a deficiency of vitamin D – and the main gene region are directly linked and interact." Professor Ebers and colleagues believe that vitamin D deficiency in mothers or even in a previous generation may lead to altered expression of *DRB1*1501* in offspring.

In the current paper, researchers show that vitamin D binds to a receptor on the *DRB1*1501* variant. They hypothesise that this is necessary for the thymus, a key component of the immune system, to perform its regular tasks.

The thymus produces an army of T cells, which act like soldiers to identify invading pathogens, such as bacteria and viruses, and then attack and destroy them. There are millions of different T cells, each designed to recognise a specific pathogen, but the sheer number of T cells presents a risk that one type might mistakenly identify one of the body's own cells or proteins as an invader and attack it with "friendly fire".

Ordinarily, the thymus will regulate the T cells and delete those that pose the greatest risk of attacking the body's own cells and proteins. However, the researchers believe that in people who carry the variant, a lack of vitamin D during early life might impair the ability of the thymus to delete these T cells, which then go on to attack the body, leading to a loss of myelin on the nerve fibres.

"Our study suggests the possibility that taking vitamin D supplements during pregnancy and the early years may reduce the risk of a child developing MS," says Dr Sreeram Ramagopalan, first author of the study. "Vitamin D is a safe and relatively cheap supplement with substantial potential health benefits. There is accumulating evidence it can reduce the risk of developing cancer and offer protection from other autoimmune diseases."

"This research represents an important development in our understanding of the cause of MS" says Dr. Paul O'Connor, national scientific and medical advisor for the Multiple Sclerosis Society of Canada.

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The Multiple Sclerosis Society of Canada is an independent, voluntary health agency and does not approve, endorse or recommend any specific product or therapy, but provides information to assist individuals in making their own decisions.

"The evidence implicating vitamin D deficiency as a key factor in MS continues to mount," says Dr. O'Connor. "Vitamin D insufficiency is emerging as a key factor of MS in children, and in adults. This finding links important work in two streams of research, namely genetics and epidemiology, and illustrates the important role the MS Society plays in solving what is a very complex disease."

Dr. O'Connor cautions that the study does not provide guidelines on vitamin D dosage and that any decisions on treatment or supplementation should be made in consultation with a trained physician.

National Research and Programs

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