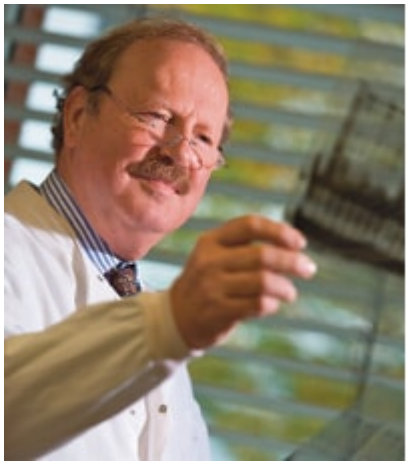
The Ebers effect: Unraveling the MS and vitamin D connection



Canadian professor receives the 2013 John Dystel prize for research on MS and vitamin D.

by Elinor Nauen

Doctors and medical researchers are often compared to detectives, tracking down clues—not to solve a crime but to make a diagnosis and suggest treatment. Professor George C. Ebers, MD, of the University of Oxford in London, is one such detective, investigating the case of multiple sclerosis.

He has made extensive contributions to understanding the disease, shedding new light on factors such as genes that contribute to susceptibility to MS, as well as other factors that influence who eventually gets MS.

For this work, Dr. Ebers was awarded this year's John Dystel Prize for MS Research. The $15,000 prize, given jointly by the National MS Society and the American Academy of Neurology, has been awarded since 1995 in honor of John Dystel, a young lawyer—and one-time patient of Dr. Ebers—whose career and life were cut short by progressive MS. The prize is given to a scientist who has made significant, wide-ranging and exciting contributions to the understanding, treatment or prevention of MS.

Science sleuth

Dr. Ebers followed clues to tease out the link between sunlight and MS. "In 1987, in **The New England Journal of Medicine**, I said the geography of MS had to be determined by climate or diet or both," he says. "Vitamin D was attractive because it was sourced via both climate and diet." His continuing investigation throughout the subsequent decades has clarified the connection.

The biggest clue to the vitamin D and MS correlation, Dr. Ebers says, “was that the risk of MS was determined very strongly by where you live. We knew that if English, Welsh or Irish people moved to South Africa or Australia, their risk for MS would go down 80 percent. But studies of families, adoptees, stepchildren and half-siblings raised together and apart all exonerated the effect of family and household conditions. Risk appeared to be determined by the place, acting at a broad population level, in much the same way as a local virus.”

Dr. Ebers sifted through the evidence. “For 3 million years humans were naked on the plains of Africa, and plenty of vitamin D was made in the skin from sunlight.” As humans migrated northward, they became deficient in vitamin D, which led to evolutionary changes toward lighter skin. “The frequency of MS increases with distance from the equator,” he continues, “suggesting that one risk factor may be vitamin D, which is only synthesized in the body when sunlight is of sufficient strength.”

Take Scotland, for one example. Unlike countries with year-round sunshine—and fewer cases of MS—Scotland has too little sunlight for people to make adequate amounts of vitamin D. The typical Scot shows evidence of vitamin D deficiency having influenced his or her appearance: The light skin, reddish hair and freckling are all genetic adaptations aimed at maximizing vitamin D production in the skin. The Scots’ diet used to contain higher levels of vitamin D, but in the 50 years since their diet changed, MS levels in Scotland have tripled. There are some exceptions to this latitude effect, but they seem to still correlate with low vitamin D levels.

The genetic component

Even if it turns out that sunlight/vitamin D level does determine the geography of MS, it is not the only environmental factor, Dr. Ebers notes. Smoking, virus infection and early-life hygiene all influence disease susceptibility within the context of genetic factors. “Indeed, we showed several ways in which vitamin D interacts with the genetics,” he explains. “The old argument about genes versus environment has been settled: It is both, and they interact.”

Other research found that both the main genes and a number of the small genes that predispose a person to MS are regulated by vitamin D. Dr. Ebers’ group discovered that people who have a genetic deficiency of an enzyme called 1,25-alpha-hydroxylase, which converts vitamin D to the active form, were more likely to develop MS.

Dr. Ebers previously practiced at the London (Ontario) Health Sciences Centre, where he conceived and initiated the Canadian Collaborative Project on Genetic Susceptibility to MS. This project comprises data and DNA on some 30,000 people with MS and their families.

For 25 years, starting in the early 1980s, Dr. Ebers also followed about a thousand people with MS in Canada. These people had received no treatment for 20 years or more, in most cases because disease-modifying treatments were not yet available. “It’s important to understand the disease course without treatment,” he notes, in order to compare the long-term effects of treatment, given the short-term nature of clinical trials. These studies of the “natural history” of MS have also led to important insights, such as understanding the

average number of MS relapses a person may experience; the predictive value of the early course of MS; and the features of primary-progressive MS.

D is for determination

Dr. Ebers thinks it eventually may be possible to prevent MS by adding vitamin D to foods to increase people's intake of the vitamin. "Unexpectedly, there are hints that vitamin D may help people who already have the disease, as small studies show some MS improvement in people with MS taking high doses of vitamin D," he says, "but there is much more work needed to substantiate this."

Some research suggests the possibility that vitamin D supplements taken during pregnancy and the early years may reduce the risk of a child developing MS later on. "In fact, if you do supplement with vitamin D, it may change the risk for your children or grandchildren," he says, "and there is good evidence for effects from exposure in previous generations, which ramps up the stakes in any decision about supplementing on a large scale." Similar efforts, such as folic acid supplementation to reduce certain severe birth defects, have been successful.

Dr. Ebers says he has been interested in MS ever since he was a neurology resident at Cornell University in the 1970s. Thirty-five years later, "I'm still at it," he says. And although he hasn't broken the case entirely, "We've covered a lot of ground," he says. "There's lots of progress!"

Elinor Nauen is a health writer based in New York City.

Learn more about the John Dystel Prize for Multiple Sclerosis Research.