Cancer Link?  
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In controlled trials of adults, there were no cases of lymphoma or malignancies. The Remicade prescribing information also includes information about the risk of hematopoietic T-cell lymphoma in children and young adults treated with the biologic and other immunosuppressive drugs for Crohn’s disease. Of the four TNF blockers approved by the FDA, three were approved for pediatric indications: Enbrel in 1999 for the treatment of moderate to severe JIA in children aged 2 years and older; adalimumab in February 2008 for moderate to severe JIA in patients aged 4 years and older; and infliximab for treating children with Crohn’s disease. The agency has requested that makers of these products provide it with information about all cases of cancer in children and young adults who were treated with TNF blockers. Dr. Edward H. Giannini, professor of pediatric rheumatology at the Cincinnati Children’s Hospital Medical Center, said, “Further investigation [of the cancer risks associated with TNF blockers] is necessary and is in the best interest of all concerned.” However, there is a background rate of cancer among children. Whether the rates among those treated with TNF blockers are higher than rates among children in the same age group must be studied, he said in an interview.

Controlled data from studies conducted by Dr. Giannini and his associates indicate that cancer rates were not higher than expected among etanercept-treated patients compared with other indications, including adult indications. In a registry study of 601 JIA patients, aged 2-18 years, treated with methotrexate, etanercept, or both, there were no cases of lymphoma or malignancies over a total of 1,200 patient-years of follow-up, said Dr. Giannini, the study’s principal investigator. Dr. Giannini has served as a consultant to Amgen while developing study protocols. Dr. Lehman is a speaker or consultant for Amgen and Wyeth, which markets etanercept with Amgen; and Humira manufacturer Abbott Laboratories.

Low Vitamin D Seen in Young Musculoskeletal Pain Patients

**BY JANE SALODOF MACNEIL**  
Senior Editor

**ALBUQUERQUE —** A prospective pilot study of 41 children with complaints of nonspecific musculoskeletal pain found their average levels of vitamin D were low even though the youngsters lived in the sunny southwest of the United States.

The mean level of serum 25-hydroxy vitamin D was lower in a group of 35 children with vague pain than in 6 children found to have diagnostic conditions that explained their pain: 28 ng/mL vs. 38 ng/mL. While this difference was statistically significant, average vitamin D levels in both groups of children (aged 2-17 years) met the study’s definition of hypovitaminosis D.

Moreover, when eight children were given vitamin D supplements, five had “marked subjective improvement or complete relief” from pain. Those making a recovery included one of two children with documented hip effusion as well as children with back pains and leg pains that had lasted, in some cases, for years. “I am certainly not saying growing pains are caused by vitamin D deficiency, but it is something we are exploring,” Dr. Elizabeth A. Szalay said in an interview after presenting the data at the annual meeting of the Pediatric Orthopaedic Society of North America.

What was, perhaps, most remarkable, was that the children lived in New Mexico—an area not typically used in vitamin D studies, because it has abundant sunshine year round. The National Health and Nutrition Examination Survey III suggests that 17% of healthy adolescents at a higher latitude have vitamin D levels below 10 ng/mL, while 1% have levels below 5 ng/mL during summer, she said. In the New Mexico study, 30% of the youngsters in pain had vitamin D levels below 25 ng/mL, she said.

Dr. Szalay, an orthopedic surgeon at the University of New Mexico and Carrie Tingley Hospital, both in Albuquerque, and her coinvestigators Ellyce B. Tryon used a local laboratory’s classification of vitamin D levels in their analysis. Ranges were presented as 0-5 ng/mL for deficiency, 5-20 ng/mL for insufficiency, 20-40 ng/mL for hypovitaminosis D, 40-100 ng/mL for sufficiency, and more than 100 ng/mL for toxicity.

The highest level recorded was 47 ng/mL. It was seen in both subgroups: those with vague complaints and those with objective explanations of their pain (Legg-Calvé-Perthes disease, arthrogryposis, and chondrolysis). The lowest level in the majority with vague complaints was less than half of that of the children with diagnostic conditions. One child had 12 ng/mL, she said.

Dr. Szalay speculated that the low levels of vitamin D could be attributed to a convergence of factors. Sunlight is a prime source of vitamin D and 15 minutes of exposure a day is sufficient, she said, but many children do not play outside. They don’t walk to school and may spend as much as 44 hours a week on electronic media such as video games. Diet by itself is unlikely to provide enough vitamin D, she continued. Milk is fortified with vitamin D, but consumption is down, compared with years past. "In 1970, children drank twice as much milk as soda," she said. "In 2000, children drank twice as much soda as milk.

While children benefit from the calcium in other dairy products, she added, these do not contain vitamin D and are usually not fortified. "Eggs have vitamin D, if they feed it to the chickens and, even then, it is a very small amount," she said. "There are only 25 units in an egg. You’ve got to eat a lot of eggs to get to 800 to a thousand units.

Children’s multivitamins, likewise, do not make up for vitamin D deficiency, according to Dr. Szalay. Some only contain 64 U a day, she said, recommending that children at risk take both a multivitamin and a chewy calcium-plus-D supplement plus two glasses of milk a day. For children without pain, she said, she recommended that, if children at risk take both a multivitamin and a chewy calcium-plus-D supplement plus two glasses of milk a day. For children without pain, she said, they should get at least 1000 U of vitamin D, in addition to any other medication that did not contain it.