

intolerance did not develop in either group. The advancement in bone age over the 12 months was not different between the two groups.

The authors conclude that growth hormone therapy is of significant benefit to pre-pubertal children with CF in terms of their height, weight, body composition, pulmonary function, and number of hospitalizations.

Hardin DS, et al. *J Pediatr* 2001;139:636-642.

First Editor's Comment: *This study by Hardin and associates is the first randomized, controlled trial of growth hormone therapy in children with cystic fibrosis. The findings are highly significant, although they have only been collected for a single year. Many questions remain unresolved. It would be important for studies to be undertaken to determine whether or not the change in lean body mass was due to an improved use of ingested calories and protein as suggested by the authors. In addition, the long-term benefits of treatment need to be evaluated, and the optimal dose needs to be determined. Furthermore, it will be important to follow these children to determine whether or not they are at increased risk for glucose intolerance over time. Hardin and associates have provided the preliminary data necessary to undertake a much larger scale study of the use of growth hormone in these children.*

William L. Clarke, MD

Second Editor's Comment: *Growth Hormone treatment in patients with cystic fibrosis has been shown*

to be of benefit in various short-term trials.^{1,2} However this is the first randomized controlled trial of GH treatment in patients with this disease. Growth hormone resulted in improved clinical status and increased growth. In CF, malnutrition develops as a result of unfavorable energy balance caused by a combination of poor intake, malabsorption of nutrients, chronic pulmonary disease and increased energy expenditures. Malnutrition adversely affects the course of the disease as well as the survival of the patients. Therefore any means to improve the anabolic state of CF patients may be of benefit. In this study GH treatment also improved the quality of life. Nonetheless, detrimental effects of GH treatment could occur in patients with CF, as diabetes is prevalent among this population.³ Although in this study no patient developed this problem, the data cannot be extended to other patients or to those who would undergo a longer-term treatment. It should also be kept in mind that improvements in growth and nutrition status of CF patients may be accomplished with aggressive nutritional supplementation without GH treatment.⁴

Fima Lifshitz, MD

References

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2. Hardin DS, et al. *Horm Metab Res* 1998;30:636-641.
3. Lang S, et al. *BMJ* 1995;311:655-659.
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Intake of Vitamin D and Risk of Type I Diabetes: A Birth-Cohort Study

To ascertain whether vitamin D supplementation or vitamin D deficiency in infancy could affect the development of type I diabetes, a birth-cohort study was done in Oulu and Lapland, Finland. All infants born in 1996 were studied (n = 12,055). Data were collected on vitamin D supplementation and on the presence of suspected rickets during the first year of life. The primary outcome measured was the diagnosis of type I diabetes by the end of 1997 (30 year follow-up). Of the 10,366 children included in the analysis, 81 were diagnosed with type I diabetes. Vitamin D supplementation was associated with a decreased frequency of this disease. Children who took the recommended 2000 IU of vitamin D on a daily basis had a rate ratio of 0.22 of developing the disease, as compared with those who received no vitamin D. The rate ratio in those who received a lesser amount of vitamin D supplementation was 0.12. Children suspected of having rickets during the first year of life had a rate ratio of 3.0 as compared with those without

such diagnosis. The authors concluded that vitamin D supplementation was associated with a reduced risk of type I diabetes.

Hypponen E, et al. *Lancet* 2001;358:1500-1503.

First Editor's Comments: *This is a very provocative study implicating the deficiency of one hormone (vitamin D) on the development of another hormone deficiency (insulin). The mechanisms of such association were thought to be related to the triggering of an immune process resulting from the lack of vitamin D. This is consistent with data from animal studies, and with the observation that cod liver oil supplementation during pregnancy is associated with a reduced rate of type I diabetes in the offspring.¹ The Eurodiab study also showed that vitamin D supplementation in early childhood may prevent this disease.² However, only 0.3% of infants in the Eurodiab study were not given*

vitamin D during the first year of life, thus the comparative population was rather small. The increased prevalence of this disease (3x) among children in this Finnish study, who were suspected of having rickets, is impressive. However the data are not very compelling since there was no radiologic or biochemical evidence of rickets presented.

The infants who took 2000 IU of vitamin D as a daily supplement had a 78% lower risk of developing diabetes. This dose of vitamin D, however, is high and not recommended by most authorities. (The Committee of Nutrition of the American Academy of Pediatrics, among others, state that an adequate intake of this vitamin is 200 IU per day.) Others have recommended dosages ranging from 400 to 1000u per day,³ where there may be lack of sunlight exposure, particularly during the long winter months in the northern hemisphere. Although there is no single recommendation for the amount of vitamin D supplemented, exposure to the sun usually will satisfy the requirements to prevent rickets and vitamin D deficiency. As little as 1 minimal erythemal dose (MED) of sunlight is equivalent to ingesting about 10,000 IU of vitamin D. Simple exposure of hands and face two or three times per week provides a third to a half of the MED (about 5 minutes for fair-skinned people) is more than adequate. Moreover, sunlight is without risk of hypervitaminosis D which may occur when large amounts of vitamin D supplements are ingested. Thus, caution should be exercised to the possible temptation of increasing vitamin D supplementation in an attempt to prevent type I diabetes. Further studies are needed

to assess if there are other factors to ascertain why there is a high prevalence of type I diabetes among populations who also are exposed to insufficient sunlight such as found in Finland.

Fima Lifshitz, MD

References

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3. Canadian Pediatric Society *CMAJ* 1988;138:229-230.

Second Editor's Comment: In the early 19th Century, cod liver oil was given to prevent rickets. The classical role of vitamin D in the prevention of rickets is to assist absorption of calcium and phosphate. Vitamin D also appears to play a role in preventing some cancers and autoimmune diseases. Ideally, in a study such as the one reported here, evaluation would include plasma 25(OH) D or 1,25(OH) 2D₃ concentrations. When sun exposure is limited, as in northern Finland, supplementation or dietary intake is an important source of vitamin D. Breast milk does not contain enough vitamin D to cover an infant's needs. The role of vitamin D in the pathogenesis of type 1 diabetes certainly deserves follow-up. If vitamin D does impair the immune system functioning in infancy, there may be other long-term effects. Interesting as well, Finland has the highest incidence of type 1 diabetes in the world.

Judith G. Hall, OC, MD

Beneficial Effects of Intensive Therapy of Diabetes during Adolescence: Outcomes after the Conclusion of the Diabetes Control and Complications Trial (DCCT)

The DCCT, in 1994, reported the results of intensive diabetes therapy of adolescents (age 13-17 years at the time of enrollment into the study). Those results demonstrated a significant reduction in the risk for the development, and progression of retinopathy and microalbuminuria. Since that time, subjects from both the intensive and conventional therapy groups have been offered the opportunity to participate in the epidemiologic study of diabetes interventions and complications (EDIC). EDIC is a long-term observational study of the DCCT cohort. In this manuscript the DCCT/EDIC research group presents their latest findings. Of the original 195 adolescents, 175 agreed to participate in the EDIC study. At the end of the DCCT all subjects returned to their health care providers in the community for continuing diabetes care, and all conventionally treated subjects were offered instruction in the use of

intensive therapy. Approximately 50% of the subjects continued to receive their care at a DCCT/EDIC site. Subjects were seen on a yearly basis for determination of HbA1c and the recording of severe hypoglycemic episodes. Retinopathy was assessed by stereoscopic fundus photography at year 4, and classified according to the criteria described in the DCCT trial. A 3-step or more progression was classified as significant. Renal function was determined every other year by measurement of albumin excretion.

At year 4, 1/3 of the subjects who were originally randomized to conventional therapy continued to use 1 or 2 injections a day. The rest switched to multiple daily injections or insulin pump therapy. Ninety percent of former intensive therapy subjects continued to use multiple daily insulin injections or pump therapy. Total insulin doses and frequency of blood glucose monitoring