Crohn disease early in life and hypovitaminosis D: where do we go from here?1,2

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In a cross-sectional study of 112 patients (44 females) who had Crohn disease and were 5–22 y of age, Sentongo et al (1) evaluated each subject for hypovitaminosis D. They substantiate that Crohn disease early in life is associated with decreased serum concentrations of vitamin D. This observation has also been noted in older subjects with Crohn disease, among whom 30% have hypovitaminosis D (2). Among patients with Crohn disease who have had portions of their small intestine resected, 60% have hypovitaminosis D. Vitamin D deficiency contributes to the osteopenia and osteoporosis of Crohn disease. In young adults, osteopenia is defined as a bone mineral density (BMD) 1.0–2.5 SD below the peak bone mass, and osteoporosis is defined as a BMD >2.5 SD below the peak bone mass (3). The risk of a fracture approximately doubles for each SD below the peak bone mass (2).

Among subjects with inflammatory bowel disease (IBD), patients with Crohn disease are more likely to develop low BMD than are those with ulcerative colitis. The etiology of low BMD in Crohn disease involves many factors, including malabsorption, steroid therapy, inflammatory mediators, hyperalimentation, and hypogonadism. Patients with IBD may also be subject to the same risk factors for osteoporosis to which the general population is subject; these factors include female sex, increasing age, estrogen deficiency, white race, low weight and body mass index, family history of osteoporosis, smoking, and history of prior fracture. Other possible risk factors, such as the use of alcohol and beverages containing caffeine, are inconsistently associated with decreased bone mass. Levels of exercise in childhood and adolescence also correlate poorly with BMD later in life. However, late menarche, early menopause, and low endogenous estrogen concentrations are associated with low BMD (4). Osteoporosis associated with Crohn disease can occur as a presenting manifestation of the disease in children as young as 12 y who have no history of steroid use. The first sign of the disease may be multiple collapsed vertebrae (5). Although recommendations for the prevention and treatment of osteoporosis have been advanced for adult patients with CD (2, 6), recommendations need to be developed for young patients with this disease, who are at risk of osteoporosis and pathologic fractures.

Calcium supplementation may benefit BMD in healthy children. Calcium supplementation (1000 mg/d) enhanced the rate of increase in BMD in a 3-y, double-blind, controlled trial in which 70 pairs of identical twins aged 6–14 y received either calcium or placebo supplementation. The authors speculated that if the increase were to persist, adult peak bone density would increase and the risk of fracture would decrease with calcium supplementation in childhood (7). In another study, the frequency of unbalanced diets with low milk consumption in childhood was higher in adult osteoporotic patients than in control subjects (8).

A screening serum concentration of vitamin D is suggested for adult patients with Crohn disease who have small-bowel disease or malnutrition or have had upper intestinal resection (2). The overall vitamin D status is best determined by the serum 25-hydroxyvitamin D concentration. Once adults with Crohn disease have begun corticosteroid therapy, vitamin D3 supplementation (400 IU by mouth twice daily) should be initiated (2), and this regimen should be considered for younger patients.

Weight-bearing exercise is important for the maintenance of healthy bone. In a study of 117 older patients with Crohn disease, progressive low-impact exercise was shown to be a potentially effective method of increasing BMD (9); low-intensity exercise of moderate duration does not seem to be associated with an exacerbation of symptoms in patients with Crohn disease (10). Regular weight-bearing physical activity has been recommended for adults with Crohn disease, and smoking and excessive alcohol intake should also be avoided (2). These recommendations impose little risk on young patients and could easily be implemented in children and teenagers with Crohn disease.

It is reasonable to consider baseline dual-energy X-ray absorptiometry of the hip and spine in young patients with CD. Measurement of urinary N-telopeptide or of 24-h urinary calcium excretion should also be considered (2). Urinary N-telopeptide is a highly specific and rapidly responsive marker of osteoclastic activity in bone and can be measured in a spot urine sample. A decrease in the urinary concentration of this peptide is predictive of an increase in bone density. In adult patients who continue to have elevated urinary N-telopeptide or increased urinary calcium excretion, the addition of hydrochlorothiazide (25 mg once or twice a day), combined with dietary sodium restriction, has been suggested (2). Hydrochlorothiazide is beneficial in increasing intestinal calcium absorption and decreasing urinary calcium excretion.

When steroid therapy is initiated, the risk of osteoporosis increases dramatically. Thus, the use of long-term steroids is to be discouraged, and steroids should not be used for maintenance therapy. Once steroid therapy has begun, in addition to the
general measures noted above, the following measures are recommended to evaluate ongoing therapy in adults: serial dual-energy X-ray absorptiometry scans and measurement of urinary N-telopeptide and of urinary calcium excretion (2). At least one study has shown that supplemental fluoride, in combination with vitamin D and calcium, is an effective, well-tolerated, and inexpensive treatment to increase lumbar bone density in patients with Crohn disease and osteoporosis (11). However, meta-analysis of fluoride therapy has not shown that there is a protective effect on fracture risk in patients with osteoporosis who do not have Crohn disease (4). Finally, biphosphonates, calcitonin, and hormone replacement therapy are suggested for adults with IBD who are taking steroids (2). These therapies have not been studied in children and are not appropriate at this point in time for young patients with Crohn disease.

It is obvious that we have much to learn concerning calcium homeostasis, vitamin D status, and osteoporosis in children and young adults with Crohn disease. Sentongo and coworkers are helping us to better understand the pathophysiology of this disease process. Through continued research, perhaps recommendations can be established to minimize the adverse effects of Crohn disease on bone and mineral metabolism in young patients with IBD.

REFERENCES