

## Commentary

The positive effect of enzyme therapy on bone disease in adults with Gaucher disease Type 1 adds another important piece to the therapeutic puzzle for affected patients. Elstein, et al. (1) show that femoral cortical bone thickness can be improved in Gaucher disease Type 1 patients with mature skeletons following 2-4 years of regular alglucerase infusions. This study and that of Rosenthal, et al. (2) that focuses on the immature skeleton, provide a solid foundation for the use of enzyme therapy for skeletal involvement by Gaucher disease Type 1 at all ages.

Differences in bone assessments, study population ages, splenectomy status, and enzyme dosages complicate comparisons of Elstein, et al. and Rosenthal, et al. Three observations are apparent: 1) Rosenthal, et al. show dramatic improvements in cortical bone thickness in children, whose skeletons were immature, while receiving enzyme therapy. These data support Elstein's, et al. suggestion that early intervention with enzyme therapy may be the most efficacious treatment for the bone disease; 2) The nearly universal (13/14) improvement in adult cortical bone thickness in Elstein, et al. contrasted to no response in the three adults in Rosenthal, et al. This indicates, as with other response indicators, variable bone changes in adults receiving enzyme therapy. The contrasting results in adults clearly indicate that factors in addition to enzyme dose determine skeletal responses. Indeed, there is not a priori reason to expect a lower efficacy with more enzyme; 3) Lack of methodologic uniformity and, particularly, the skewing to children or adults, in Rosenthal, et al. or Elstein, et al., respectively, preclude direct quantitative comparisons of efficacy with the differing dosing regimens. Sensitive standardized methods are still needed to assess, not only cortical, but trabecular bone involvement as well as joint and growth plate effects of Gaucher disease. While cortical bone

thickness provides a measure of bone involvement, this single test does not reflect the general status of skeletal disease, nor the totality of bone response to enzyme therapy. There is a critical need to develop sensitive and general assessments, potentially chemical indicators, of bone and other organ involvement, to optimize therapy for individual patients. Finally, both studies suffer from the lack of appropriate controls that should include treated and untreated patients matched for age and disease severity. The efficacy of enzyme therapy potentially makes such a study unethical.

Elstein, et al. paraphrasing Grabowski (3) recommends: "...early administration of enzyme therapy to patients prone to developing skeletal complications." as potentially the most efficacious use of enzyme therapy. Defining the genetic and/or environmental factors that predispose to the varying degrees of severity and therapeutic response of Gaucher disease remains an open and rich avenue for research.

## REFERENCES

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