

Bone Marrow Transplantation in the Maroteaux-Lamy Syndrome (Mucopolysaccharidosis VI)

The authors report the use of bone marrow transplantation as treatment for the severe form of Maroteaux-Lamy syndrome in a 13-year-old girl who continues to show improved biochemical and clinical status 24 months after transplantation.

Bone marrow transplantation is now the treatment of choice for many leukemias, aplastic anemias, and immunodeficiency disorders. In experienced hands, when using marrow from HLA-MLC-matched sibs, complication rates and survival times have become quite acceptable. The possibility of using bone marrow transplantation for in-born errors of metabolism has been discussed for many years. Recently, bone marrow transplantation has been used, with encouraging results, for one form of osteopetrosis (an inherited disorder with osteoclast dysfunction) to restore the marrow's osteoclast-monocyte population.

Selective enzyme deficiencies such as Maroteaux-Lamy syndrome would appear to be candidates for

this type of treatment. Maroteaux-Lamy syndrome, for which there is an animal model, is a lysosomal disorder that spares the CNS. Using the feline mucopolysaccharidosis VI model, bone marrow transplantation experiments demonstrated that transplanted reticuloendothelial and hematopoietic cells could return to almost normal the biochemical and clinical abnormalities present in affected animals.

With this background, a 13-year-old girl with the severe form of Maroteaux-Lamy syndrome was identified for bone marrow transplantation. Her disease had become life-threatening with the development of frequent apnea episodes and severe congestive heart failure. Her sister, who was HLA-DR-identical, was the bone marrow donor. The patient was pretreated with busulfan and a graft-versus-host preventive regimen.

Her response to therapy was monitored by clinical response, liver biopsy changes, white cell enzyme assays, urinary mucopolysaccha-

ride output, and electron microscopic (EM) studies of liver cells, bone marrow cells, peripheral blood leukocytes, and platelets. After engraftment, blood-group studies demonstrated the presence of only donor cells.

Peripheral leukocytes, which had been severely deficient in arylsulfatase B prior to bone marrow transplantation, showed normal activity by two months after transplantation and remained normal for the 24-month observation period. Liver biopsies revealed apparent repopulation with Kupffer's cells after bone marrow donation, with the ratio of arylsulfatase B to arylsulfatase A activity increasing from 3% to 16% of normal activity. Accumulation of mucopolysaccharides in hepatic Ito cells decreased so that no storage material was seen 148 days after transplantation. No storage material was seen on EM studies in hepatocytes, Kupffer's cells, or endothelial cells in posttransplantation biopsy specimens. Urinary excretion of mucopolysaccharides decreased and was within normal limits by 100 days after transplantation.

Pulmonary hypertension, cardiomegaly and thickening of ventricular walls, and congestive heart failure had been present prior to transplantation, but resolved completely 15 months after transplantation. Pulmonary function also returned to normal by this time, and apneic episodes ceased. No change in radiologic abnormalities of the bones could be demonstrated, but there was subjective improvement in the range of motion in most joints. Visual acuity improved, but glaucoma and corneal clouding remained unchanged. There was a marked decrease in hepatic mass, and the spleen returned to normal size post-transplant. Intellectual status remained normal, but the general sense of well-being was markedly improved. Now 24 months post-transplant, the patient has shown remarkable improvement in severely affected areas without any evidence of deterioration in new areas.

Krivit W, Pierpont ME, Ayaz K, et al: *N Engl J Med* 1984;311:1606.

Editor's comment—This report describes an exciting new mode of therapy for some inherited disorders with inborn errors of metabolism. However, it is important to emphasize that this mode of therapy will be appropriate only in selected diseases that involve either bone marrow elements or reticuloendothelial cells which, when transplanted from an unaffected individual, can redistribute themselves in the liver, lung, and intestines of the recipient. Thus, disorders involving CNS deterioration are probably not appropriate candidates for treatment with bone marrow transplantation. The long-term outcome for an individual treated with this mode of therapy is

still unknown. There is no question that the natural history of diseases treated in this way will be altered. A new set of complications will arise.

As the authors also point out, bone marrow transplantation entails considerable risks of morbidity and mortality, as well as a large commitment of medical, financial, psychosocial, and other resources. A comprehensive evaluation and the presence of an HLA-identical sib are essential. Nevertheless, the morbidity or predictable mortality of the individual patient may be dramatically improved as in this reported case. This mode of therapy gives hope for previously hopeless disorders.

Growth Retardation in Crohn's Disease: The Merits of Aggressive Nutritional Therapy

Growth retardation, defined as a cessation or slowing of linear growth to a rate below that expected for age and pubertal stage, occurs in 30% to 85% of children with Crohn's disease of prepubertal onset.

The author reviews several possible reasons for growth failure. Malabsorption does not seem to be a significant cause since most growth-retarded children have normal D-xylose absorption and minimal fat malabsorption. Decreased nutrient intake has been reported, with anorexia being an important component of Crohn's disease as well. Many patients experience early satiety or abdominal pain after meals, thus making it necessary for them to eat small, frequent meals. However, not all observers have reported low nutrient intake in all growth-retarded children with Crohn's disease. Of the hormonal factors studied in these children, somatomedin-C has been low. Zinc deficiency also does not account for growth retardation in all patients. The role of enteric protein loss is not understood, but many growth-retarded children are in positive nitrogen balance.

While the exact energy and protein requirements of growth-retarded patients with Crohn's disease are not known, the home use of nutritional support permits intake of adequate energy and protein to restore growth.

The author offers four methods for nutritional intervention: (1) increased oral intake, (2) supplementary formulas, (3) supplementary parenteral nutrition, and (4) total parenteral nutrition. The method chosen should depend on the individual patient and his needs. Lactose intolerance could restrict the range of oral formulations, but the author suggests that this can be overcome by adding commercial lactase preparations to the formulas. In the author's own experience, increased growth velocity (amount not specified) occurred when the caloric intake was raised from a mean of 1,245 kcal/d to the recommended 2,400 kcal/d.

Kirschner BS: *Manual of Clinical Nutrition* (suppl)1983; 2(4):26.

Editor's comment—This paper is a good review of state-of-the-art approaches to nutrition and growth retardation in Crohn's disease. While the ultimate cause of the poor growth remains unresolved, nutrition appears to be an important component. Nutritionally induced remission of the disease after bulk nutritional supplementation, as well as improvement in growth, has been documented. More must be learned about specific nutritional deficiencies, (ie, magnesium and zinc) and ways to deal with the patient's inability to ingest adequate calories for growth.