MALABSORPTION OF VITAMIN B₁₂ FROM THE INTESTINE IN A CHILD WITH cblF DISEASE: EVIDENCE FOR LYSOSOMAL-MEDIATED ABSORPTION

To the Editor:

The original child with cblF disease demonstrated an accumulation of unbound and nonmetabolized vitamin B₁₂ (Cbl) in the lysosomes of cultured fibroblasts, and the absence of enzyme-bound Cbl in either the cytoplasm or the mitochondria. The defect is presumed to involve a failure to Cbl to get from lysosomes into the cytoplasm. This infant girl developed stomatitis, glossitis, convulsions, and hypotonia at age 12 days, and methylmalonic aciduria was detected on newborn screening. She was originally treated with both oral and systemic hydroxocobalamin (OH-Cbl), but subsequently was treated only with systemic OH-Cbl. By the age of 3 1/2 years, her development was delayed only 2 to 4 months and her EEG pattern showed improvement. She was receiving 1 mg systemic OH-Cbl administered by her mother every 2 to 3 weeks.

At age 3 1/2 years, we studied Cbl absorption in this patient. She was withdrawn from Cbl injections for 21 days, and received a mixture of 0.25 μg (0.5 μCi) [⁵⁷Co]-cyanocobalamin (CN-Cbl) mixed with intrinsic factor with 0.25 μg (0.8 μCi) [⁵⁸Co]-CN-Cbl in 20 mL water. CN-Cbl (1 mg) was injected intramuscularly 90 minutes later and the urine volume collected over the subsequent 24 hours was 900 mL. Excretion of [⁵⁷Co] was 0.57% and that of [⁵⁸Co] was 0.50%. The batch of commercially prepared vitamin and intrinsic factor appeared to be of acceptable activity.

The test of intestinal Cbl absorption was repeated at age 8 years. The child has continued to develop well on OH-Cbl injections every 2 to 3 weeks. The last dose of OH-Cbl was administered 1 month before this second test. Excretion of [⁵⁷Co] was 0.56% and excretion of [⁵⁸Co] was 0.76%.

Both of these tests, performed several years apart, indicate that this child with cblF disease is unable to absorb vitamin B₁₂ from the gut, whether bound to intrinsic factor or not.

The injections of OH-Cbl were interrupted for the test to reduce the chance that biliary Cbl would dilute the radioactivity entering the intestine. However, this would not explain the low excretion because absorption of radioactive Cbl is little affected by injection of the flushing dose simultaneously with the oral radioactive tracer.

An unresolved question is which intracellular compartments are involved in the transfer of Cbl from intrinsic factor to transcobalamin II in intestinal cells. The studies on this child with cblF strongly suggest that normal Cbl absorption involves transit through the lysosomes of the enterocyte.

RACHEL LAFRAMBOISE
Ontogénese et Génétique Moléculaire
Centre de Recherche du CHUL
Quebec, Quebec, Canada

BERNARD A. COOPER
Hematology-Oncology
Department of Medicine
Royal Victoria Hospital
McGill University
Montreal, Quebec, Canada

DAVID S. ROSENBLETT
MRC Genetics Group
Centre for Human Genetics
Division of Medical Genetics
Department of Medicine
McGill University
Montreal, Quebec, Canada

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Malabsorption of vitamin B12 from the intestine in a child with cblF disease: evidence for lysosomal-mediated absorption [letter]

R Laframboise, BA Cooper and DS Rosenblatt