

peripheral-blood smear showed macroovalocytes (Fig. 1A, arrowheads) and hypersegmented neutrophils (Fig. 1A, arrow). A bone marrow aspirate, performed to evaluate pancytopenia, showed megaloblastic erythroid precursors (Fig. 1B, arrowheads) and giant bands (Fig. 1B, arrow). The patient was treated with folic acid, 5 mg daily by mouth for 2 months, and vitamin B₁₂ replacement. A complete blood count obtained 7 months later showed a normalization of the red-cell count indexes. Pernicious anemia is suspected but has not been confirmed.

Julia M. Braza, M.D., M.S.
Parul Bhargava, M.D.

Beth Israel Deaconess Medical Center
Boston, MA 02215

1. Braza JM, Bhargava P. A medical mystery — a 71-year-old man with pancytopenia. *N Engl J Med* 2008;359:1941.

EDITOR'S NOTE: We received 1520 responses for this medical mystery, from 86 countries. Sixty-five percent of respondents were practicing physicians, 20% were physicians in training, 11% were medical students, and the remaining 4% were other readers. Overall, 77% of respondents identified some type of megaloblastic anemia, and two thirds of this group specifically suggested a diagnosis of vitamin B₁₂ deficiency or pernicious anemia. The remaining 23% of respondents suggested other diagnoses: 17% suggested an alternative hematologic process, such as an acute or chronic leukemia, multiple myeloma, Waldenström's macroglobulinemia, or polycythemia vera, and 6% suggested other conditions, including babesiosis, malaria, parvovirus B19, leishmaniasis, or poisoning with lead or arsenic.

More on Propranolol for Hemangiomas of Infancy

TO THE EDITOR: The response of infantile hemangiomas to propranolol reported in the letter by Léauté-Labrèze et al. (June 12 issue)¹ catapulted the use of this treatment to first-line status among physicians managing this disease. Not included in their letter was a discussion about initiating and monitoring propranolol use, or about potential risks, which may be unique among these patients. The most common serious adverse effects are bradycardia and hypotension. Infants with very large hemangiomas or miliary hemangiomatosis are at risk for high-output cardiac compromise.² Propranolol may mask the clinical signs of early cardiac failure and diminish cardiac performance. Propranolol may also blunt the clinical features of hypoglycemia. Sustained hypoglycemia in infancy has been associated with long-term neurologic sequelae.³ We know of two infants who had unrecognized side effects from propranolol.

We developed a treatment protocol to optimize safety: baseline echocardiography and 48-hour hospitalization or home nursing visits to monitor vital signs and blood glucose levels. Medica-

tion is given every 8 hours, with an initial dose of 0.16 mg per kilogram of body weight. If the vital signs and glucose levels remain normal, the dose is incrementally doubled to a maximum of 0.67 mg per kilogram (to a maximum daily dose of 2.0 mg per kilogram). Propranolol should be gradually tapered over a period of 2 weeks.

Elaine C. Siegfried, M.D.
William J. Keenan, M.D.
Saadeh Al-Jureidini, M.D.

Saint Louis University School of Medicine
St. Louis, MO 63104
siegfried@kidsderm.com

1. Léauté-Labrèze C, Dumas de la Roque E, Hubiche T, Boralevi F, Thambo J-B, Taïeb A. Propranolol for severe hemangiomas of infancy. *N Engl J Med* 2008;358:2649-51.
2. Gottschling S, Schneider G, Meyer S, Reinhard H, Dill-Mueller D, Graf N. Two infants with life-threatening diffuse neonatal hemangiomatosis treated with cyclophosphamide. *Pediatr Blood Cancer* 2006;46:239-42.
3. Burns CM, Rutherford MA, Boardman JP, Cowan FM. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics* 2008;122:65-74.

THE AUTHORS REPLY: After more than 40 years of clinical use in infants, there is no documented

case of death or serious cardiovascular disease as a direct result of exposure to a beta-blocker.¹ Side effects of beta-blockers are well known; these include transient bradycardia and hypotension that warrant close monitoring at the onset of treatment. Bronchospasm is usually seen as an exacerbation in patients with underlying reactive airways; a family history with regard to atopy or repeated wheezing should be obtained. Beta-blockers decrease lipolysis, glycogenolysis, and gluconeogenesis that predispose patients to hypoglycemia. They also mask some beta-sympathetic-related hypoglycemic symptoms. The first week of life is a critical period when neonates gradually reach their optimal milk intake and spontaneous hypoglycemia is more likely to develop; beta-blockers clearly should be avoided during this period. Most infants treated for an infantile hemangioma are older and have a normal food

intake, and the conditions described in the article by Burns et al.² do not apply.

A large multicenter study is in the planning stage. We hope that this study will lead to elaborate, reasonable, and objective recommendations concerning the use of beta-blockers in this indication.

Christine Léauté-Labrèze, M.D.
Eric Dumas de la Roque, M.D.
Alain Taïeb, M.D.

Bordeaux Children's Hospital
33 076 Bordeaux, France
christine.labreze@chu-bordeaux.fr

1. Love JN, Sikka N. Are 1-2 tablets dangerous? Beta-blocker exposure in toddlers. *J Emerg Med* 2004;26:309-14.
2. Burns CM, Rutherford MA, Boardman JP, Cowan FM. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics* 2008;122:65-74.

Cardiac Amyloidosis with the E526V Mutation of the Fibrinogen A α -Chain

TO THE EDITOR: Proteinuria developed in a 48-year-old man in 2003. His mother had died 10 years earlier from renal amyloidosis. Laboratory tests showed isolated nephrotic-range proteinuria (urinary protein excretion, >7 g per 24 hours) with normal creatinine clearance (estimated glomerular filtration rate with the use of the Modification of Diet in Renal Disease equation, 96 ml per minute per 1.73 m² of body-surface area); no monoclonal gammopathy was found. A specimen from a renal biopsy contained amyloid deposits located exclusively in the mesangium of the glomeruli (Fig. 1A). The hereditary transmission of the disease led us to perform a molecular analysis for hereditary amyloidosis (associated with transthyretin, fibrinogen, apolipoprotein, or lysozyme); only the E526V mutation of the α -chain of fibrinogen A, the most frequent mutation resulting in fibrinogen amyloidosis, was identified.

Three years later, the patient reported dyspnea (New York Heart Association class II), which gradually increased; 4 years later, a cardiac arrhythmia necessitated implantation of a defibril-

lator. The patient had no family history of heart disease. Cardiac ultrasonography suggested cardiac amyloidosis, with septal hypertrophy, a left intraventricular gradient of 40 mm Hg, and filling impairment.¹ Circumferential thickening of the left ventricle was observed on cardiac magnetic resonance imaging, with focal late-phase contrast enhancement of the posteroseptal territory of the midventricular region. Whereas diffuse enhancement is characteristic of AL amyloidosis,² focal enhancement suggests non-AL amyloidosis.³ Specimens from multiple myocardial biopsies showed amyloid deposits in subendocardial and perivascular areas (Fig. 1B), definitively establishing the diagnosis of cardiac amyloidosis. This amyloid material was specifically labeled with anti-fibrinogen antibodies (Dako F0111), whereas the results of staining with antibodies against λ -chain and κ -chain were negative (Fig. 1C).

Since fibrinogen A α -chain amyloidosis was first described in 1993,⁴ about 40 cases have been reported. Renal involvement is always present,