

Severe Hemoglobin H Subtype: A Class by Itself

BY MARY ANN MOON

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A subtype of hemoglobin H disease distinguished by life-threatening anemia during infectious illnesses should be recognized as a clinical entity distinct from other thalassemias, all of which are becoming more common in the United States, according to a single-center study.

Hemoglobin H Constant Spring (hemoglobin HCS) causes significant growth delay, causes repeated plunges in hemoglobin levels requiring urgent blood transfusions as early as infancy, and can lead to iron overload in early childhood, with its attendant sequelae. Most important, patients with HCS show acute, life-threatening worsening of anemia during common illnesses caused by viral or bacterial infections such as strep throat.

In contrast, other hemoglobin H disease does not cause growth deficits or iron overload during childhood, and it rarely causes severe anemia, said Dr. Ashutosh Lal of the department of hematology/oncology at Children's Hospital and Research Center Oakland (Calif.), and his associates.

The investigators were able to characterize the natural history of hemoglobin H disease and the subtype hemoglobin HCS among children in the United States for the first time largely because of newborn screening for the disorders, which has been done in California since 1998. They identified and followed 86 cases of hemoglobin H disease.

In the past, hemoglobin H disease has been prevalent in Asian and Mediterranean populations but rare in others. Now, however, it appears to be making inroads into the United States. In this study, many patients were of mixed ethnic backgrounds, including African Americans, who historically have a very low rate of alpha-thalassemias.

This finding supports the usefulness of universal newborn screening for hemoglobin H syndromes. "Life-threatening

anemia may develop in infants before the diagnosis can be made through conventional means in the absence of newborn screening," Dr. Lal and his colleagues noted (*N. Engl. J. Med.* 2011;364:710-8).

Among the 86 cases, 60 patients (70%) had hemoglobin H, 23 (27%) had the more severe HCS, and 3 (3.5%) had other, non-deletional hemoglobin H illness.

All of the episodes of acute worsening of anemia requiring blood transfusions occurred in the HCS group, while the children with hemoglobin H disease "had a predictably benign course." In HCS, the probability of requiring at least one transfusion before 1 year of age was 13%; this increased to 39% by the age of 5 years, 75% by the age of 10 years, and 80% by the age of 20 years. Thirty-seven transfusions (82%) were precipitated by infections.

Growth was significantly delayed in children with HCS but not in the other children. "This finding suggests that close attention to growth is required and that nutritional and hematologic associations with growth delay should be evaluated," the investigators said.

Patients with HCS required nearly twice as many clinic visits each year and nearly four times as many hospital admissions. In addition, "substantial fatigue was observed in a subgroup of older patients with HCS, a finding that raises concern that the quality of life of patients may deteriorate with age," Dr. Lal and his associates said.

Five patients with HCS underwent splenectomy between the ages of 3.9 and 13 years because of their need for frequent blood transfusions, while no children with hemoglobin H disease did. Splenectomy reduced or eliminated acute hemolytic episodes in four of the five children.

"We suggest that HCS be recognized as a thalassemia syndrome that is distinct from hemoglobin H disease, so that the appropriate treatment approach can be devised for each group," they noted.

This study was supported in part by the Maternal and Child Health Bureau of the U.S. Department of Health and Human Services. The authors reported no relevant financial disclosures.

Study Documents Need for Screening

The findings by Lal et al. "highlight the dynamically changing effect of globalization on public health, as genetic disorders indigenous to specific populations become more common in the countries to which they migrate," said Dr. Edward J. Benz Jr.

The study results "make a strong case for newborn screening for alpha-thalassemia, at least in states with a substantial increase in their Asian populations. The gene frequency for these disorders is high (up to 25% in some groups), and the screening tests are both inexpensive and virtually 100% accurate," he noted.

The study also documents the clinical

need to identify patients at highest risk – those with HCS – so that tighter surveillance and early intervention for infections can mitigate the need for excessive transfusions and the concomitant iron overload. "In some of these children, the use of appropriate hypertransfusion protocols with iron chelation might facilitate more normal growth and development," he added.

DR. BENZ is at the Dana-Farber Cancer Institute, Boston. He reported no relevant financial disclosures. These comments were taken from his editorial accompanying Dr. Lal's report (*N. Engl. J. Med.* 2011;364:770-1).

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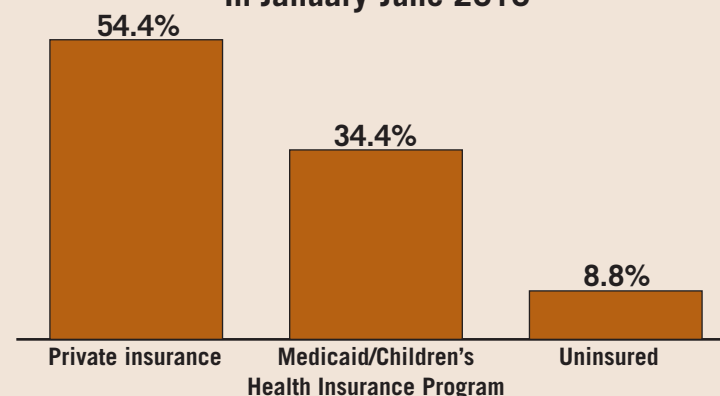


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VITAL SIGNS

Over One-Third of Children Had Public Health Insurance In January-June 2010



Notes: Data are for children 0-18 years old. Individuals may be counted in both the private and Medicaid/CHIP categories. Preliminary estimates for Medicaid/CHIP and uninsured are slightly lower than estimates expected from the final files.

Source: Centers for Disease Control and Prevention/National Health Interview Survey