

Sickle Selections

a quarterly newsletter from the University of Rochester Sickle Cell Program

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Differential Diagnosis of Hemoglobin S but no A at Birth

New York State Newborn Screening identifies in infants with sickle cell disease. An infant identified as having hemoglobin F, S and no A can have any of the following genotypes:

- symptomatic
1. Sickle cell anemia (S/S)
 2. Sickle/ β^0 -thalassemia (S/ β^0 -thal)
 3. Sickle/ β^+ -thalassemia (S/ β^+ -thal)
- or
- asymptomatic
4. Sickle/hereditary persistence of fetal hemoglobin (S/HPFH)

Clearly the way to distinguish among these is to test the parents. If one parent is not available, retesting the infant at 1 year of age or older is recommended.

Only in the 3rd type, sickle β^+ -thalassemia, would you expect to see hemoglobin A at birth. (The β^0 thal mutation turns off β -globin synthesis; the β^+ -thal mutation merely turns down β -globin synthesis.) However as the second article shows, sometimes hemoglobin A is not detected at birth in β^+ sickle thalassaemia, and retesting the infant at a later age may be required.

A higher hemoglobin level or lower mean cell volume than expected in sickle cell anemia are reasons to consider sickle β^+ -thalassaemia.

Misdiagnosis of Sickle β^+ -thalassaemia

A recent article by Kinney* and colleagues at Duke University reports the misdiagnosis of 20 newborns as having sickle cell anemia; later testing revealed the correct diagnosis to be sickle β^+ -thalassaemia.

Newborn testing may not detect hemoglobin A because the β^+ globin gene produces an amount of A too low to be detected or is delayed in expression.

Six of the infants were tested up to 5 times before HbA was detected, and the oldest age at which HbA was still undetected was 14 months.

The original diagnosis of sickle cell anemia in these infants was doubted because in each case the hemoglobin level was higher or the mean cell volume was lower than expected in sickle cell anemia.

Why is it important to distinguish sickle β^+ -thalassaemia and sickle cell anemia? Because infants with sickle β^+ -thalassaemia have better preservation of splenic function, a later onset of vaso-occlusive crises, and a lower incidence of pneumococcal sepsis than children with sickle cell anemia.

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Infants with sickle β^+ -thalassaemia, like all infants with sickle cell disease, require penicillin prophylaxis.

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ROCHESTER
MEDICAL CENTER

Regarding treatment contact:

Dr. Norma Lerner or Pat Lamarche R.N., P.N.P. Department of Pediatrics 275-2981
Dr. Karen Kaplan, Department of Medicine 275-3761

Regarding laboratory diagnosis, newborn screening and genetic counseling, contact:

Dr. Peter Rowley, Sandra LaBella or Starlene Loader, Division of Genetics 275-4602

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