HEMOGLOBIN E AND RELATED CONDITIONS

A BRIEF EXPLANATION FOR HEALTH CARE PROFESSIONALS AND PARENTS

With the immigration of many thousands of individuals from Southeast Asia (particularly Cambodia, Laos, and Vietnam) to the United States during the past three decades, health care workers now encounter several categories of hematologic conditions which were once considered extremely rare. One such example is hemoglobin E, which may occur with or without various forms of thalassemia.

Hemoglobin E is an inherited abnormality due to a genetic defect which results in an amino acid substitution in the β globin chain of the hemoglobin molecule. This abnormality is easily identified on a routine hemoglobin electrophoresis test, in which the abnormal hemoglobin resembles hemoglobin C, a common hemoglobin variant in persons of African ancestry.

Hemoglobin A is the predominant hemoglobin in individuals of all races. In nearly all Northern European whites, hemoglobin A constitutes most of the hemoglobin in the red blood cells. In African Americans, hemoglobin S (sickle) trait and hemoglobin C trait are seen with some frequency (in 8% and 3% of persons respectively). Hemoglobin E, however, is restricted primarily to individuals from Southeast Asia. In certain areas of Thailand and Cambodia up to 30% of the population has hemoglobin E trait – i.e., one of their two β-globin genes has the defect.

Also extremely common in individuals from Southeast Asia are various forms of thalassemia, genetic conditions in which there is a decrease in the amount of hemoglobin produced in the red blood cells. These are classified either as α-thalassemia or β-thalassemia depending upon the particular globin chain which is reduced. Either α or β thalassemia may occur in combination with hemoglobin E trait or disease, resulting in a wide array of unusual combinations. Fortunately, most of these conditions are benign and do not cause problems.

The following is a brief description of each condition. Also attached is a laboratory summary describing the hematologic and hemoglobin electrophoresis findings.

Hemoglobin E Trait (AE): These individuals have no anemia but may have a slightly reduced mean cell volume (MCV) and target cells on the peripheral blood smear. The hemoglobin electrophoresis shows hemoglobin A and E (except in newborn infants, in which case the hemoglobin F is predominant) in a ratio of approximately 2:1. The condition is benign. No treatment is necessary.

Hemoglobin E + α-thalassemia: Individuals with this combination of two mild disorders are similar to those with E trait except that they have a lower percentage of hemoglobin E (A to E ratio 3:1 or 4:1) on the electrophoresis. This heterogeneous condition, usually associated with a low MCV and perhaps mild anemia, is also usually benign and does not require therapy.

Homozygous Hemoglobin E Disease (EE): These individuals may have mild anemia (but sometimes no anemia at all), a moderately reduced MCV, and numerous target cells on the blood smear. The hemoglobin electrophoresis shows (except during the newborn period) exclusively hemoglobin E. These individuals have no signs or symptoms. The condition is benign. No treatment is required.

Hemoglobin E β-thalassemia: This is the only potentially serious condition among the hemoglobin E disorders. Such patients nearly always have anemia, and sometimes it is quite severe, resembling that seen in thalassemia intermedia. For instance, such patients may have intermittent jaundice, splenomegaly, progressive bony deformities, aplastic crises, and need for transfusions. Increased iron

absorption (as well as blood transfusions) may result in iron overload. In addition to variable degrees of anemia and reduced MCV, such patients have abnormal peripheral blood smears, usually including nucleated red blood cells. The hemoglobin electrophoresis pattern shows predominately hemoglobin E and may resemble homozygous E disease (although hemoglobin F is usually elevated too). This condition is differentiated from homozygous E disease by physical examination, the hematologic findings, and family studies, since one parent has E trait and the other β-thalassemia trait. Children with hemoglobin E β-thalassemia, unlike the other conditions mentioned above, should be referred to and followed by a pediatric hematologist.

In addition to the conditions mentioned above, a number of other hematologic problems may exist in the Southeast Asian population. Dietary iron deficiency (resulting in microcytic anemia) is extremely common in infants and young children and must always be excluded (or treated empirically with a therapeutic course of iron) prior to exhaustive evaluation for hemoglobin E and thalassemia. In addition, glucose-6-phosphate dehydrogenase (G6PD) deficiency may cause episodic hemolytic anemia in Southeast Asians, particularly Chinese males. Finally, various forms of α and β-thalassemia – often without consistent hemoglobin E – are extremely common and result in anemia and microcytosis. Hemoglobin H disease, a form of alpha thalassemia, can be especially problematic.

This brochure prepared by:

George R. Buchanan, M.D.
The University of Texas Southwestern Medical Center at Dallas
Center for Cancer and Blood Disorders, Children's Medical Center Dallas
Tele: 214/456-2382
Fax: 214/456-6133

Rev: June 2008

LABORATORY DIAGNOSIS OF THE MOST COMMON HEMOGLOBIN E DISORDERS

Diagnosis	Hgb	MCV	Hemoglobin Electrophoresis				Clinical Problems
	(gm/dl)	(fl)	A	E	F	A_2	
E-trait	11-14	65-80	65	30-35	-	-	0
E-trait + alpha thalassemia *	10-12.5	55-70	70-80	20-30	-	-	0
Homozygous hemoglobin E disease	11-13	55-70	0	100	-	-	0
E-beta thalassemia	5-10	50-65	0-20	70-95	0-10	-	+ to +++
Beta thalassemia trait	9.5-11.5	55-70	90	0	2-3	4-7	0
Alpha thalassemia trait **	9.5-11.5	55-70	95	0	2-3	2-3	0
Normal	11-14	72-85	95	0	2	3	0

For a more detailed description of these disorders, standard hematology reference books should be consulted.

* one or two gene deletion
** two gene deletion

Revised
June 2008