

## ELEVATED FETAL HEMOGLOBIN

An elevated level of fetal hemoglobin (Hb F) in an adult may result from a genetic disorder of hemoglobin production or from various acquired hematological conditions.<sup>1</sup>

### Genetic

- hereditary persistence of fetal hemoglobin (HPFH)
- sickle-cell anemia
- beta-thalassemia
- delta-beta-thalassemia
- unstable beta-globin chain variants

### Acquired

- pregnancy
- recovery from marrow hypoplasia
- leukemia, especially juvenile chronic myeloid leukemia
- aplastic anemia and paroxysmal nocturnal hemoglobinuria
- thyrotoxicosis
- hepatoma and choriocarcinoma

An infant at birth has 70-90% Hb F, at 6 months < 8% Hb F, and by a year < 2% Hb F. Normal adults have 0.3 to 1.2% Hb F, < 3.5% Hb A<sub>2</sub> and the remainder Hb A.

### Hereditary persistence of fetal hemoglobin (HPFH)

A patient identified as having hereditary persistence of fetal hemoglobin (HPFH) trait is characterized by moderate elevation of fetal hemoglobin (usually > 10%) but no elevation of hemoglobin A<sub>2</sub>. Typically the red cell mean corpuscular volume (MCV) is normal. Kleihauer-Betke staining of a blood smear reveals fetal hemoglobin distributed *evenly* throughout the red cell population. Both heterozygous and homozygous forms are asymptomatic.

### Sickle cell anemia

The level of Hb F in individuals with sickle cell anemia varies. Among African-Americans with sickle cell anemia, the mean level of Hb F is 6-10 %<sup>2</sup>. Elevated levels of Hb F may be due to the preferential survival of Hb F-containing red cells.

### Sickle/hereditary persistence of fetal hemoglobin

A child who inherits a sickle gene from one parent and an HPFH gene from the other parent will have *sickle/HPFH, an asymptomatic condition*. This genotype can be misdiagnosed as sickle/beta-thalassemia, a symptomatic condition. The best way to distinguish the two is to test the parents. If the parents are not available for testing, retesting the infant at 1 year of age or older is recommended since by then the Hb F will be reduced to the level the child will exhibit as an adult. A child with sickle/ $\beta$ -thalassemia, like all infants with sickle cell disease, requires penicillin prophylaxis. A child with sickle/HPFH will not experience the symptoms of sickle cell disease and penicillin prophylaxis is not required.

### The thalassemias

The thalassemias are characterized by a reduced rate of production of one or more of the globin chains of hemoglobin. **Beta-thalassemia** ( $\beta$ -thal) **trait**, resulting from a reduction in  $\beta$  chain synthesis, is characterized by a **normal level of Hb F**, an elevated Hb A<sub>2</sub> ( $\alpha_2\delta_2$ ), and a low MCV. **Delta-beta thalassemia** ( $\delta\beta$ -thal) **trait** results in a reduction of both  $\beta$  and  $\delta$  chain synthesis and is characterized by an **elevated amount of Hb F**, a normal to low Hb A<sub>2</sub> and a low MCV. Kleihauer-Betke staining of a blood smear reveals fetal hemoglobin distributed *unevenly* throughout the red cell population.

### Elevated Hb F in pregnancy

If a pregnant woman is found to have elevated hemoglobin F, the partner should have hemoglobin electrophoresis. If the partner has sickle cell trait and the child inherits both sickle gene and the elevated F the newborn screen will identify the child as having sickle cell disease. The child should be tested after 1 year of age. If the Hb F is still elevated the child may have sickle/HPFH (asymptomatic) or sickle/ $\delta\beta$ -thalassemia (a mild clinical disorder)<sup>3</sup>.

1. Weatherall and Clegg: *The Thalassemia Syndromes*, p.72-76

2. Powers, D.R. et al. *Blood* 63:921, 1984

3. Weatherall and Clegg, p. 353