FE (HbEE or HbE/Beta Zero Thalassemia)  
EE or Hb E/β0 Disease

Differential Diagnosis: Hemoglobin FE pattern on newborn screen is highly suggestive of homozygous hemoglobin E or hemoglobin E/beta zero (β0) thalassemia.

Condition Description: A red blood cell disorder characterized on the newborn screen by presence of fetal hemoglobin (F) and hemoglobin E in the absence of hemoglobin A. The hemoglobins are listed in order of the amount of hemoglobin present (F> E).

You Should Take the Following Actions
- Contact the family to inform them of the screening result.
- Evaluate infant, assess for splenomegaly, and do complete blood count (CBC) for Hb, and mean corpuscular volume (MCV) at the initial visit and at six months to differentiate hemoglobin EE from hemoglobin E/beta zero thalassemia.
- Contact a pediatric hematologist to determine need for further testing.
- Initiate timely confirmatory/diagnostic testing as recommended by consultant.
- Report findings to newborn screening program

Diagnostic Evaluation: CBC and MCV. Hemoglobin separation by electrophoresis, isoelectric focusing (IEF), or high performance liquid chromatography (HPLC), which shows FE pattern. DNA studies will usually confirm genotype.

Clinical Considerations: Hemoglobin EE is clinically benign. Individuals with Hb EE are not anemic, but have microcytosis and target cells on blood smear. Clinical expression of Hb E/β0 thalassemia is variable. Most individuals with Hb E/β0 thalassemia have moderately severe anemia, hepatosplenomegaly, intermittent jaundice, growth retardation, and overexpansion of the bone marrow. Severely affected individuals require lifelong transfusion, splenectomy and treatment for iron overload.

Additional Information:
American College of Medical Genetics and Genomics website  
https://www.acmg.net/StaticContent/ACT/Hb_(FE).pdf

Utah Department of Health  
http://health.utah.gov/newbornscreening/Disorders/HB/Hb_E_Disease_EE/FactSheet_Provider_HbEE_En.pdf

Hemoglobin Disorders (Grady Comprehensive Sickle Cell Center)  
http://scinfo.org/additional-online-books-and-articles/hemoglobins-what-the-results-mean

Thalassemias  
http://kidshealth.org/parent/medical/heart/thalassemias.html

Genetics Home Reference  

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What is Hemoglobin?
Hemoglobin is a protein in the red blood cells. It carries oxygen from the lungs to all parts of the body and gives blood its red color. There are many hemoglobin types (this is not the same as a blood type). Hemoglobin is inherited through genes, one from each parent. Most people have hemoglobin A, also called adult hemoglobin.

What is Hemoglobin E Disease (EE)?
Hemoglobin E in the red blood cells is responsible for causing hemoglobin E condition (EE). Children inherit this condition from their parents as a recessive genetic disorder. This means a hemoglobin E gene is passed from both mom and dad to the baby causing EE. Persons with EE have only hemoglobin E and no adult hemoglobin. When both parents have one hemoglobin E gene, there is a 1 in 4 or 25% chance with each pregnancy that an infant will inherit two hemoglobin E genes. There are no serious health problems associated with EE, but the gene for hemoglobin E is passed on from your child to your future grandchildren. EE is not contagious. Most people with EE have mild anemia and occasionally may have a slightly enlarged spleen, but usually they do not have disease symptoms and do not require treatment. Persons with EE have red blood cells that are smaller than normal and have an irregular shape.

What Problems can EE Cause?
EE red blood cells are not very flexible in moving through blood vessels and have a smaller outside surface area to carry oxygen. EE red blood cells are very small, unstable and have a reduced ability to hold onto oxygen. The lifespan of these red blood cells is also slightly shorter than normal (normal blood cells live about 120 days).

What is the Frequency of EE?
EE affects both sexes equally and is the second most common abnormal hemoglobin in the world. It is very common among persons from Southeast Asia or have ancestors from Cambodia, Laos and Thailand. EE is also found in people who live in Vietnam, Malaysia, northeastern India, Bangladesh, Pakistan and Sri Lanka and their descendants.

What can be done to treat EE?
Treatment is usually not necessary. Folic acid supplements may be prescribed by your child’s doctor to help his or her body to produce normal red blood cells and improve the symptoms of anemia. People with hemoglobin E disease can expect to lead a normal life.

What is Hemoglobin E/Beta Zero Thalassemia Disease?
Hemoglobin E/beta-thalassemia disease is a more serious disease than EE. Children with hemoglobin E/beta-thalassemia inherit one gene for hemoglobin E from one parent and one beta-thalassemia gene from the other parent. The beta-thalassemia gene causes the body to make less than the normal amount of hemoglobin. Persons who are affected may have a more severe anemia which can be life threatening, depending on the severity of the beta-thalassemia. If not treated, this disease can lead to heart failure from the severe destruction of red blood cells. It also can lead to severe enlargement of the spleen and liver, changes in bones and poor growth. Treatment may include repeated blood transfusions. Your baby’s doctor will do a complete blood count (CBC) and smear of the red blood cells to look for beta-thalassemia when your baby is approximately 6 to 9 months of age.

What are the Most Important Things to Remember about EE and Hemoglobin E/Beta-Thalassemia Diseases?
Work very closely with your child’s doctor and hematologist (a doctor who is a blood specialist). Make sure your child has regular checkups with them. Call your child’s doctor when you have questions and have your child seen if you have any medical concerns.

How Do I Get More Information about Hemoglobin E Disease?
Talk with your baby’s doctor. You may also want to have a genetic consultation for you and your family to see how these diseases might affect future children or grandchildren.