UCSF Benioff Children's Hospitals
Fetal Treatment Center

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Prenatal Screening for Thalassemia

Thalassemias are inherited anemias caused by mutations in either the alpha of beta globin genes. These mutations result in decreased hemoglobin synthesis. If both parents carry mutations in the same globin gene each of their children has a 25% chance of inheriting a severe form of that thalassemia. Both alpha and beta thalassemia major require treatment with serial blood transfusions. Alpha thalassemia major is unique in that treatment, if pursued, should be initiated prenatally.

Globally, 5% of people carry a thalassemia trait. For people whose ancestry traces to Asia, the Pacific Islands, the Mediterranean, the Middle East, or Africa, carrier rates can be as high as 45%. Most people do not know their carrier status.

Types of Thalassemia

β Thalassemia Trait (β/-)
1 of 2 functioning beta globin genes
- Can lead to slight microcytic anemia
- Parents who are both positive for this trait are at risk for having a child with beta thalassemia major

β Thalassemia Major (-/-)
0 of 2 functioning beta globin genes
- Individuals born with beta thalassemia major have severe anemia and require treatment with serial blood transfusions
- These patients may be eligible for curative treatment with bone marrow transplant

α+ Thalassemia Trait (α-/α-)
2 of 4 functioning alpha globin genes, one on each chromosome
- Can lead to slight microcytic anemia

α-0 Thalassemia Trait (αα/--)
2 of 4 functioning alpha globin genes on the same chromosome
- Can lead to slight microcytic anemia
- Parents who are both positive for this trait are at risk for a pregnancy with alpha thalassemia major

α Thalassemia Major (--/--) or Hb Bart's Hydrops Fetalis
0 of 4 functioning alpha globin genes
- Leads to severe anemia in fetuses and can be fatal unless treated with in utero blood transfusions
- Individuals born with alpha thalassemia major require treatment with serial blood transfusions and may be eligible for potentially curative bone marrow transplant

Diagnostic Codes and Parameters

Complete Blood Count	
85025	• Hemoglobin <11 g/dL indicates anemia • Mean Corpuscular Volume <80 fL indicates microcytic anemia • Mean Corpuscular Hemoglobin <27 pg indicates hypochromic anemia

Hemoglobin Analysis	
83021	• Hemoglobin Electrophoresis/HPLC Hb A2 >3.5% indicates beta-thalassemia trait ≤ 3.5% rules out beta thalassemia but does exclude alpha thalassemia

Imaging for ATM (Hb Bart's Hydrops Fetalis)	
76811	• Fetal Ultrasound to assess for signs of hydrops or evidence of cardiomegaly concerning for alpha thalassemia major
76821	• Middle Cerebral Artery Doppler Ultrasound MCA peak velocity >1.5 MoM indicates fetal anemia

Iron Studies	
82728	• Serum Ferritin <30 ng/mL indicates iron deficiency anemia with or without thalassemia

Genetic Analysis	
81364	• Beta Globin Complete Gene Sequencing
81257	• Alpha Globin Common Deletions/Mutations Analysis If negative consider alpha globin gene sequencing

Thalassemia diagnosis ICD-10 Codes	
D56.3	Diagnosis of Parental Alpha or Beta Thalassemia Trait
D56.0	Diagnosis of Alpha Thalassemia Major
D56.1	Diagnosis of Beta Thalassemia Major
O35.8XX0	Maternal care for suspected fetal condition

Prenatal screening for thalassemia

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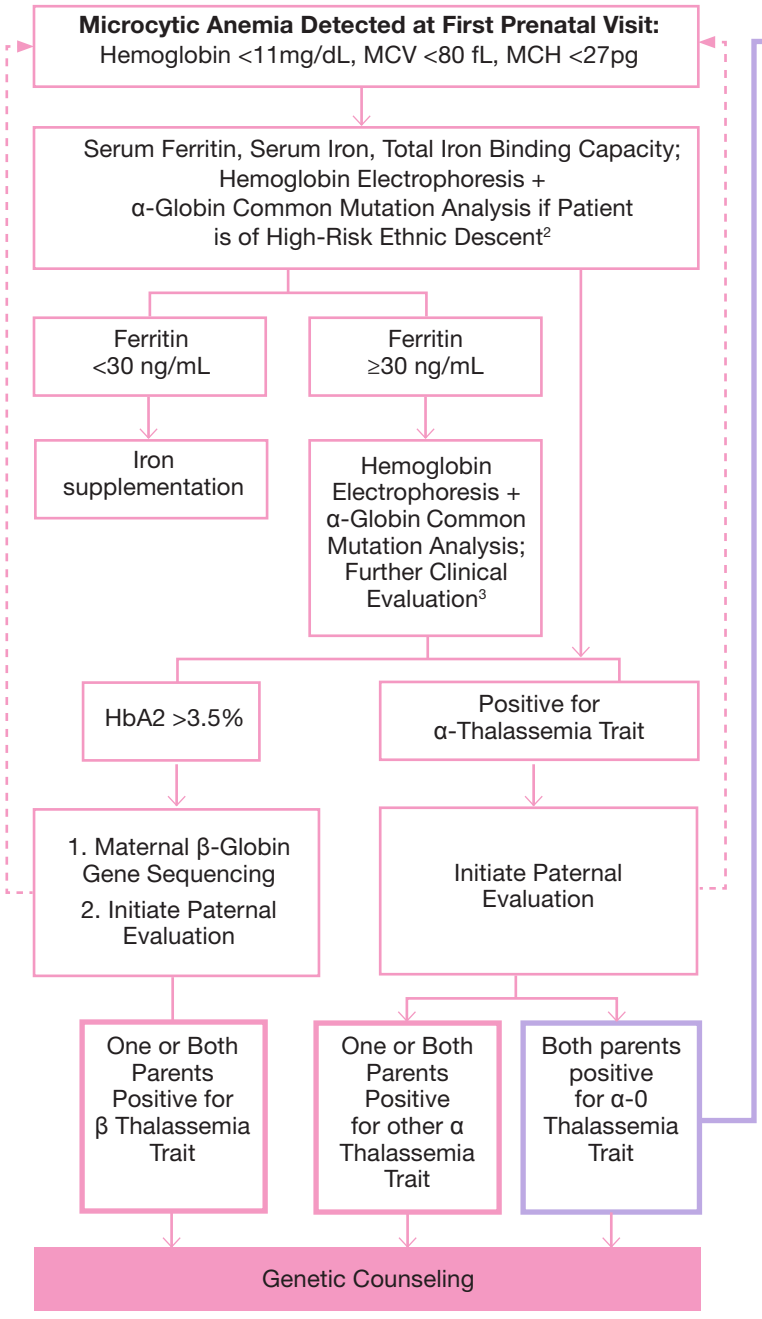
Maternal and Paternal Screening for Thalassemia Trait[1]

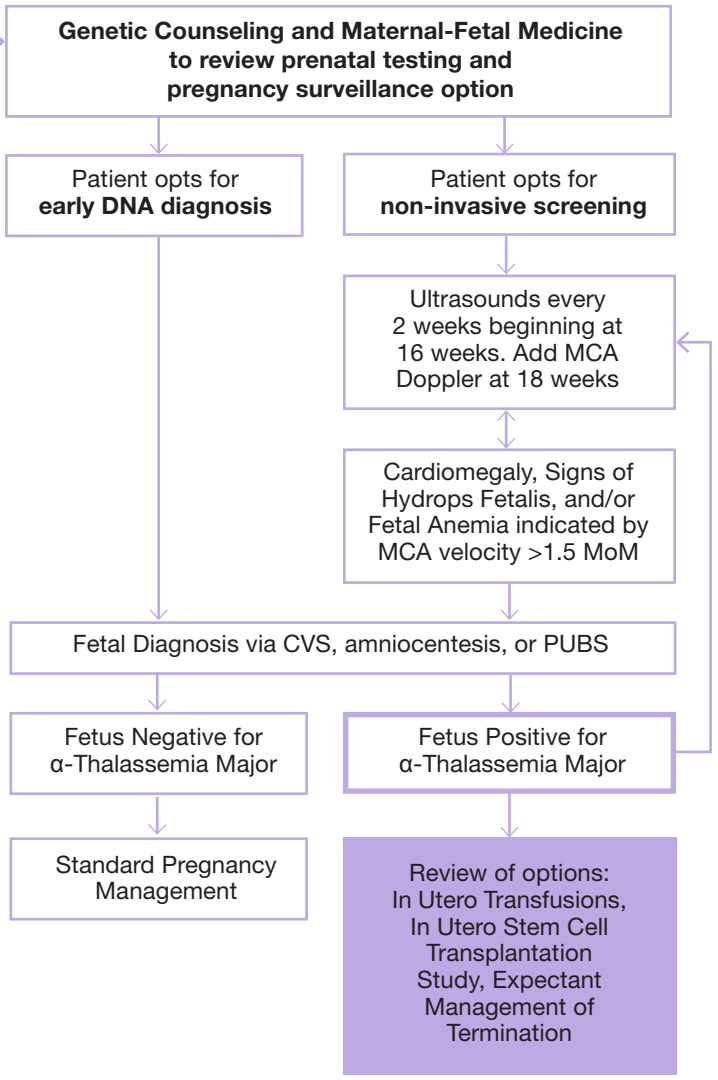
Most couples are unaware of their risk for thalassemia in pregnancy. **Screening for thalassemia trait ideally occurs preconception or with the initial prenatal labs by assessing the patient's CBC.** When microcytic anemia is detected, we recommend simultaneous maternal hemoglobin electrophoresis/HPLC and alpha globin gene sequencing, as **normal hemoglobin electrophoresis/HPLC results do not exclude alpha thalassemia.**



[1]This tool is not a replacement for referral to genetic counseling, which may happen at any time in this pathway. Genetic counseling provides guidance for genetic testing and management options for families with pregnancies at risk for severe forms of thalassemia.

Prenatal Monitoring for ATM (Hb Bart's Hydrops Fetalis)

If alpha-0 thalassemia trait is identified in both parents, education related to options including prenatal diagnosis and pregnancy management is essential. Because fetuses affected with alpha thalassemia major develop severe anemia and hydrops fetalis, monitoring the pregnancy for these complications (below) is necessary to mitigate risk to the motherand adverse sequalae to the fetus.



[2] Ethnicities at high risk for thalassemia include: Asian (South, Southeast, Chinese), Pacific Islander, Mediterranean, Middle Eastern, and African

[3] Rare mutations, such as delta -beta thalassemia, non-deletional alpha thalassemia, and others, may not be captured in this algorithm. In high-risk cases, or where hemoglobin electrophoresis is abnormal, consultation with a genetic counselor and/or hematologist is recommended.