THALASSEMIA QUIZ

A 26-year-old woman comes to the office due to progressive tiredness. Physical examination shows facial changes & Poor growth. The patient does not use tobacco, alcohol, or illicit drugs. Peripheral smear shows severe microcytic, hypochromic anemia with target cells. She is also having hepatosplenomegaly

Complete blood count is as follows:

- Hb= <7 g/Dl
- MCHC = 32% Hb/cell
- MCV = 70 μm^3

Fecal occult blood test is negative. Iron therapy is initiated. When the patient returns 6 weeks later, her laboratory findings are unchanged, the patient should be started immediately on which of the the following?

- Continue Iron therapy
- Splenctomy
- Folic acid
- Transfusion therapy
- Observation

- A 32-year-old Italian-American man comes to the office for a routine checkup. The patient is a business executive and has been under significant stress recently. He drinks alcohol occasionally and has a 10-pack-year smoking history. Laboratory results are as follows:
- Hb = 10.8 g/dl
- RBC count= 5.7 million cells/mm^3
- MCV = 61 μm^3
- WBC count = 5,500/mm^3
- Platelets = 170,000/mm^3
- Serial fecal occult blood tests are negative. Peripheral blood smear show target cells, Which of the following is the best treatment for this patient?

- Cobalamine
- Deferoxamine
- EPO
- Observation with no therapy required
- Hydroxyureas
- Iron
- Prednisone

- Thalassemia minor is usually asymptomatic and **no treatment is required.** Patients typically have mild anemia, low mean corpuscular volume (55-75 μm^3), target cells on peripheral smear, and disproportionately high red blood cell (RBC) count. Iron deficiency anemia is associated with low RBC count and no microcytosis until hemoglobin is <10 g/dL.

- A 20-year-old girl is brought to the clinic by her mother because she noted that her skin is getting pigmented progressively. The patient's family is from Greece, and her mother and maternal uncles have chronic anemia. Menarche was at age 13 with Menses occur regularly each month, lasting 5-6 days with heavy bleeding and passage of clots, requiring her to wake up multiple times each night to change pads. The patient is also having Diabetes mellitus. Cardiac examination shows dilated cardiomyopathy. The patient appears pale. Serum ferritin levels are elevated. The patient is a known case of Thalassemia & is on chronic transfusions. Which one of the following is the best treatment for this patient

- Folic acid
- Continue transfusion therapy
- Splenectomy
- Deferaserox

- An 8-month-old girl is brought to the clinic by her mother for posthospitalization follow-up. She was admitted and discharged last week due to fatigue and anemia requiring transfusion of packed red blood cells. Since going home, the patient has had no issues. On examination, she is alert and interactive. Cardiopulmonary examination is unremarkable. The spleen is palpated 2 cm below the costal margin. Hemoglobin electrophoresis performed prior to her initial transfusion shows 5% hemoglobin A2 and 95% hemoglobin F. Her mother asks about the long-term outcome. It is discussed that the patient will need chronic red blood cell transfusions to maintain her hemoglobin at an appropriate level, but individuals are now able to survive into the fifth and sixth decades of life with supportive management. In addition to chronic transfusions, the patient will require which of the following supportive medications to improve long-term survival?

- Chelation therapy
- Hydroxyurea therapy
- Iron replacement
- Penicilline prophylaxis
- B12 supplementation

↳ Anemia

Transfusion therapy [9][10][14]

This is the mainstay of management for thalassemia major and intermedia (see "Transfusion" for more information about pretransfusion testing and transfusion reactions).

- **Transfusion dependency**: can fluctuate for individual patients depending on the subtype, severity, and external factors.
- **Non-transfusion-dependent patients**: only require either occasional or short-term regular blood transfusions for acute needs.
- **Transfusion-dependent patients**: require lifelong regular transfusions (e.g., every 2–5 weeks).

Transfusion therapy in thalassemias

	Non-transfusion-dependent thalassemias (NTDT) [9]	Transfusion-dependent thalassemias [10]
Subtypes	• Alpha/beta-thalassemia intermedia • Mild to moderate hemoglobin E/beta thalassemia	• Alpha/beta-thalassemia major • Severe hemoglobin E/beta thalassemia
Indications for transfusion	• Hb < 5 g/dL • Anticipated acute physiological stress	• Persistent Hb < 7 g/dL • Facial changes

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Indications for transfusion	• Hb < 5 g/dL
	• Anticipated acute physiological stress
	• Declining Hb with continuous splenic enlargement
	• Frequent hemolytic crises
	• Delay in:
	  ◦ Growth
	  ◦ Cognitive development
	  ◦ Secondary sexual development
	• Signs of bone changes
		• Persistent Hb < 7 g/dL
		• Facial changes
		• Poor growth
		• Fractures
		• Significant extramedullary hematopoiesis

Goals of therapy	• Specific short-term clinical benefits (indication-dependent)	• Maintain Hb 9–10 g/dL

Additional therapies

- **Folic acid** should be considered in patients with: [14]
  - Thalassemia major or intermedia: regular supplementation
  - Thalassemia minor during periods of acute physiological stress (e.g., infections): episodic supplementation
- **Fetal hemoglobin induction**: hydroxyurea may help induce fetal hemoglobin, reducing symptoms and the need for transfusions

Splenectomy [9][10]

- **Limited use**: risks may outweigh benefits (see "Asplenia").
- **Indications** include:
  - Hypersplenism causing recurrent infections or bleeding
  - Clinically significant splenomegaly
    - Symptomatic (e.g., abdominal pain)
    - Massive splenomegaly (> 20 cm) at risk of splenic rupture
  - Uncontrollable iron overload disease
  - Uncontrollable anemia affecting growth and development
- **Post-operative care**: See "Management of asplenic patients."

Iron overload disease

All patients receiving transfusion therapy should be periodically evaluated for iron overload disease and subsequent organ damage. [9][10][12]

- **Clinical features of iron overload diseases**: e.g., bronze skin, growth delay, signs of organ damage
- **Diagnosis of iron overload diseases**
  - Liver biopsy (gold standard test)
  - MRI (noninvasive alternate test)
- **General monitoring:** serum ferritin
- **Monitoring for organ damage**
  - Endocrinopathies: Screen patients for the following conditions and refer to endocrinology as needed.
    - DM
    - Hypothyroidism/hypoparathyroidism
    - Hypogonadism
    - Osteoporosis
  - Liver cirrhosis and hepatocarcinoma: liver chemistries (every 3 months) and MRI (annually)
  - Cardiac siderosis: regular imaging (echocardiogram or MRI) [10][15]

- **Treatment:** Chelation therapy is typically recommended when iron accumulates to toxic levels and may be required from a very early age. [9][10][12]
  - Deferasirox (first-line)
  - Deferoxamine
  - Deferiprone

Iron overload can seriously affect the liver and cardiac function, as well as several endocrine glands, and is potentially lethal in the long term. Once organ damage occurs, it is often irreversible.

The objective of chelation therapy is to prevent organ damage resulting from iron overload disease and requires good adherence to treatment, continuous monitoring by specialists, and frequent dosing adjustment.