Approach to Thalassemia: Part 1

These slides are not comprehensive and are meant to use as a visual aid for specific topics within these thalassemia podcasts.

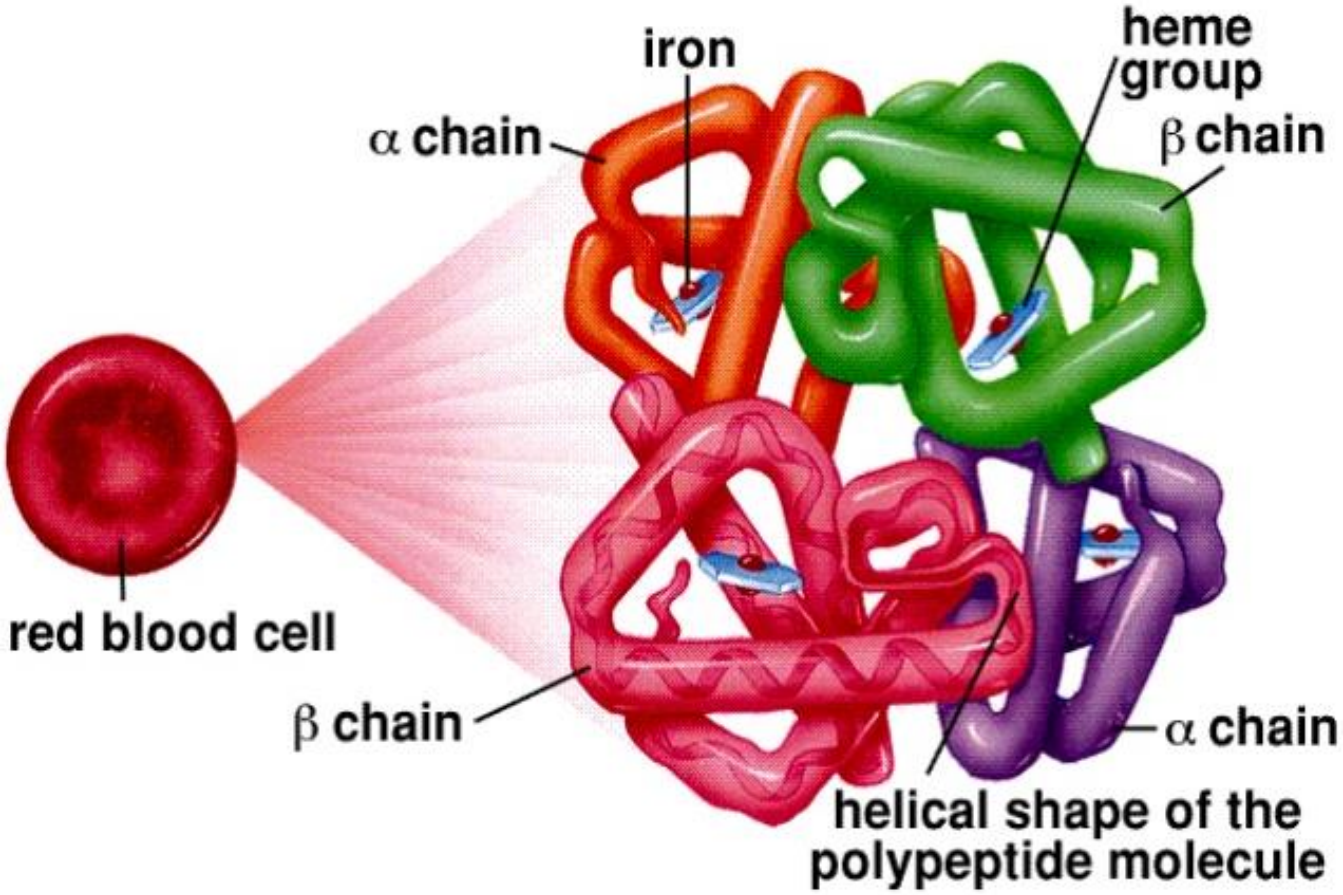
Case 1

You are in a medical genetics clinic meeting Tahir and Nafia. They are both 26 years old and immigrated from Turkey in their childhoods.

They are referred to you because they are planning on having their first child and Nafia has heard thalassemia is present in her family.

They deny any past medical history.

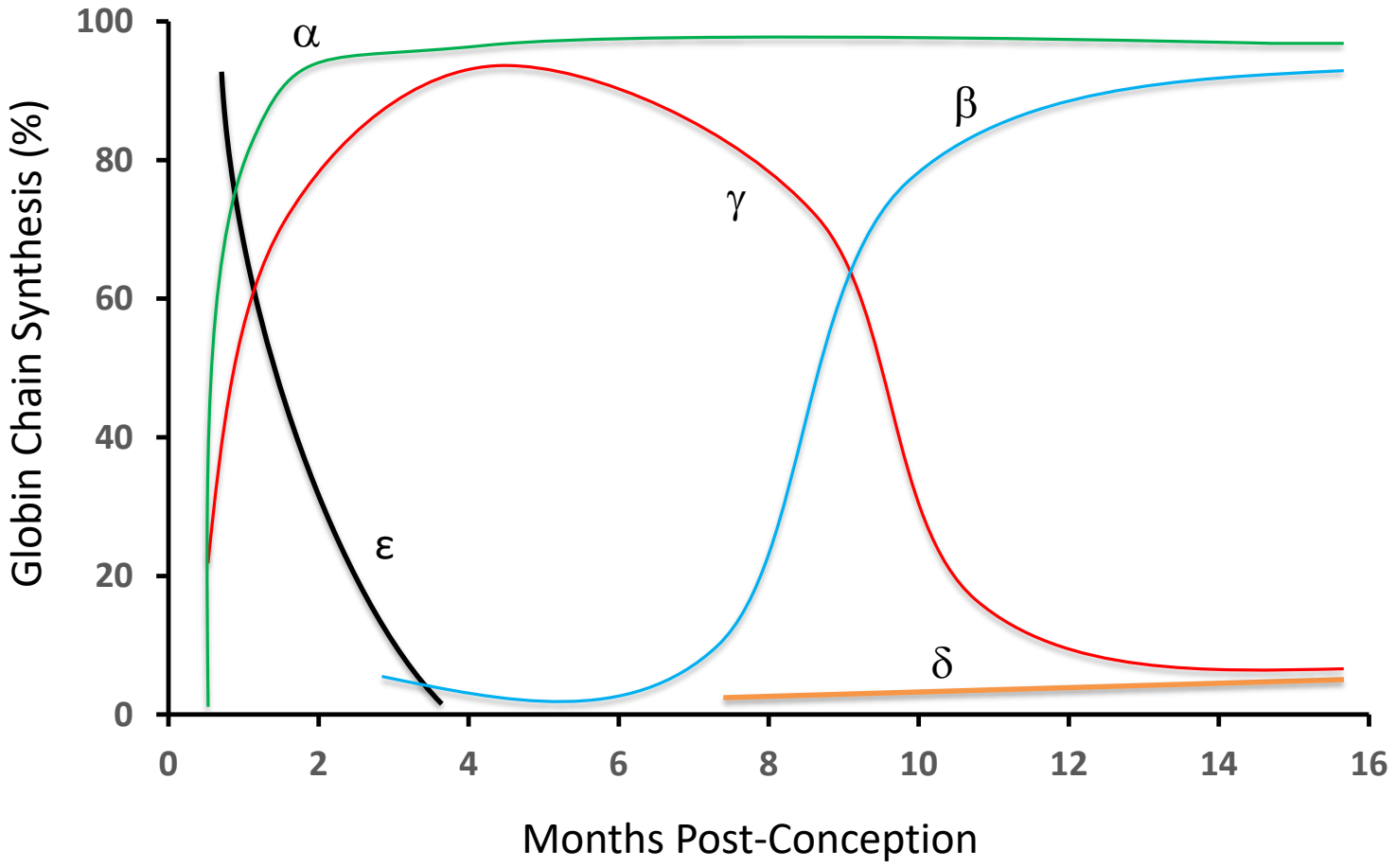
Hemoglobin Molecule



Tetramers	Hemoglobin Type
αααββ	Hb A
αααγγ	Hb F
αααδδ	Hb A_2

Zeb A. Structure and function of hemoblogin. 2015 June 19 [cited 2017 Apr 6]. In: Slideshare [Internet]. Lahore: Slideshare.net; c2017. Available from: https://www.slideshare.net/asifzeb2/structure-and-function-of-hemoglobin

Globin chain production



Symbol Legend	
α	Alpha
β	Beta
γ	Gamma
δ	Delta
ε	Epsilon

Hemoglobinopathy

- Inherited disorders affecting quantitative and/or qualitative globin chain production

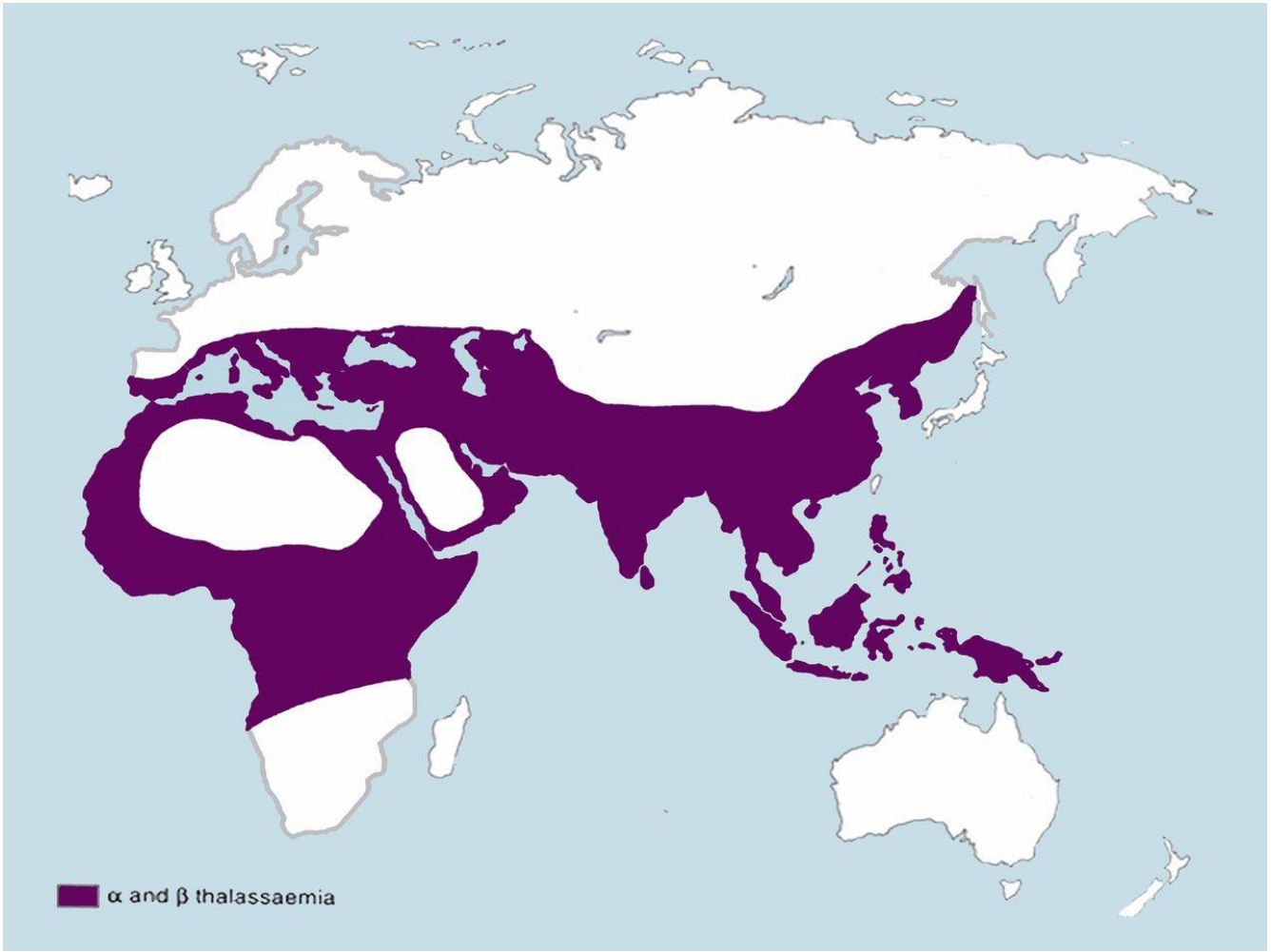
Nomenclature

- Silent carrier
- Thalassemia trait
- Thalassemia disease

→ Non-transfusion dependent thalassemia

→ Transfusion dependent thalassemia

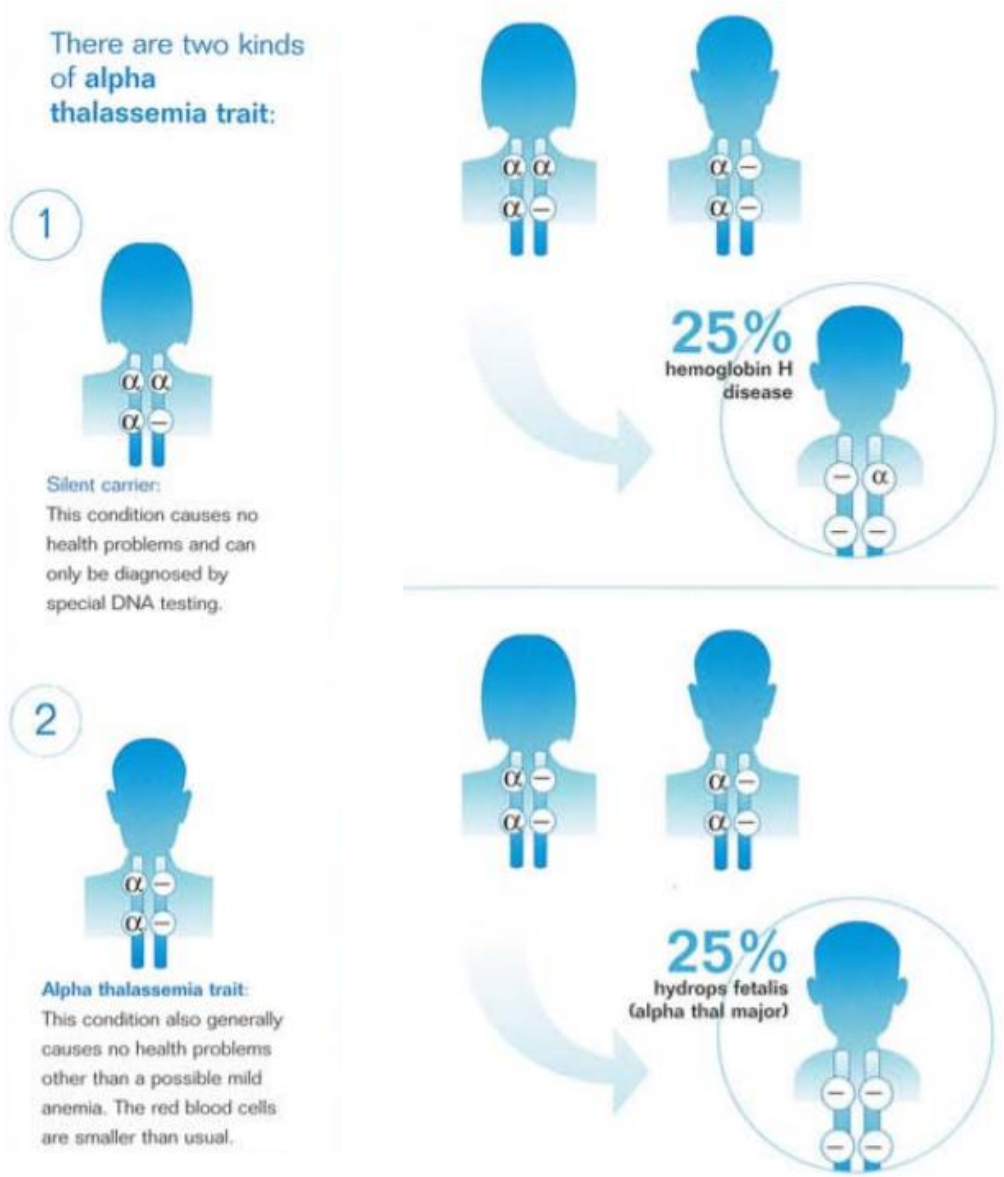
Epidemiology



Amid A, Saliba AN, Taher AT*, et al.* Thalassaemia in children: from quality of care to quality of life. Archives of Disease in Childhood. Published Online First: 19 August 2015. doi: 10.1136/archdischild-2014-308112

Alpha-thalassemia

Chromosome 16



Cooley's Anemia Foundation [Internet]. New York: c2017. About thalassemia. Available from: http://www.thalassemia.org/learn-about-thalassemia/about-thalassemia/

Clinical Features

Symptoms (non-specific)

- Fatigue
- Dyspnea
- Irritability

Signs

- Failure to thrive
- Jaundice
- Pallor
- Hepatosplenomegaly
- Bone deformities *(late findings)*: skull bossing (prominent forehead), maxilla, flat nasal bridge, long bone deformities

Investigations

CBC

- Menzter Index: MCV/RBC

>13 suggests iron deficiency anemia

<13 suggests thalassemia

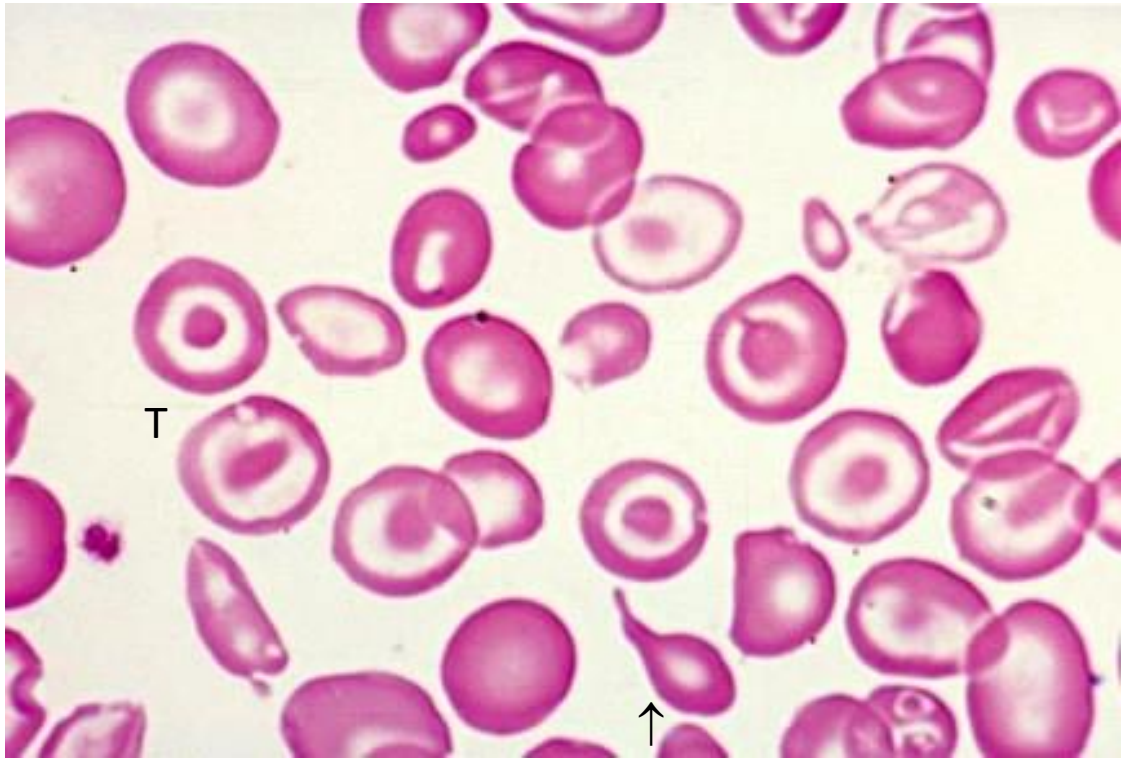
Peripheral blood smear

Fe Studies

Hemoglobin investigations

- *Usually normal in alpha-thalassemia*

Genetic testing



A peripheral blood film showing target cells (T), teardrop cells (↑) and a variation of red blood cell shapes (poikilocytosis) and sizes (anisocytosis).

Krafts K. Pathology Student [Internet] Minnesota: c2009 Jul 27. Thalassemia. Available from: https://www.pathologystudent.com/?p=1233

Case 1 continued

Lab Investigations

Lab Parameter	Nafia	Tahir
Hb (g/L)	108	140
MCV (fL)	70	78
Peripheral Blood Smear	Hypochromic, microcytic red cells Target cells	-

Case 1 continued

Genetic Testing

Nafia's Genotype: αα/- -

Tahir's Genotype: αα/α -

Possible Genotypes for Their Child

Inherited Chromosomes	αα	- -
αα	αα/αα	αα/- -
α -	α -/αα	α -/- -

Approach to Thalassemia: Part 2

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Case 2

You meet Kal in the pediatric emergency room.

ID: He is a 6 month old male who was born at 39 weeks via an elective C-section. The pregnancy and birth were uncomplicated.

HPI: increasingly irritable with difficulty feeding recently. He has been gaining weight and his growth curves have been normal but he is smaller than his two siblings. He drinks breastmilk and has just started trying cereals. His vaccinations are up to date and there has been no travel.

Case 2

Physical Exam

Vitals

BP 75/45, HR 150, RR 30, SpO_2 95% RA, Temp 37.8°C

General appearance: alert, slightly pale

Cardiovascular: systolic murmur and hyperdynamic precordium

Respiratory: unremarkable

Abdominal: soft, non-tender and distended with mild splenomegaly

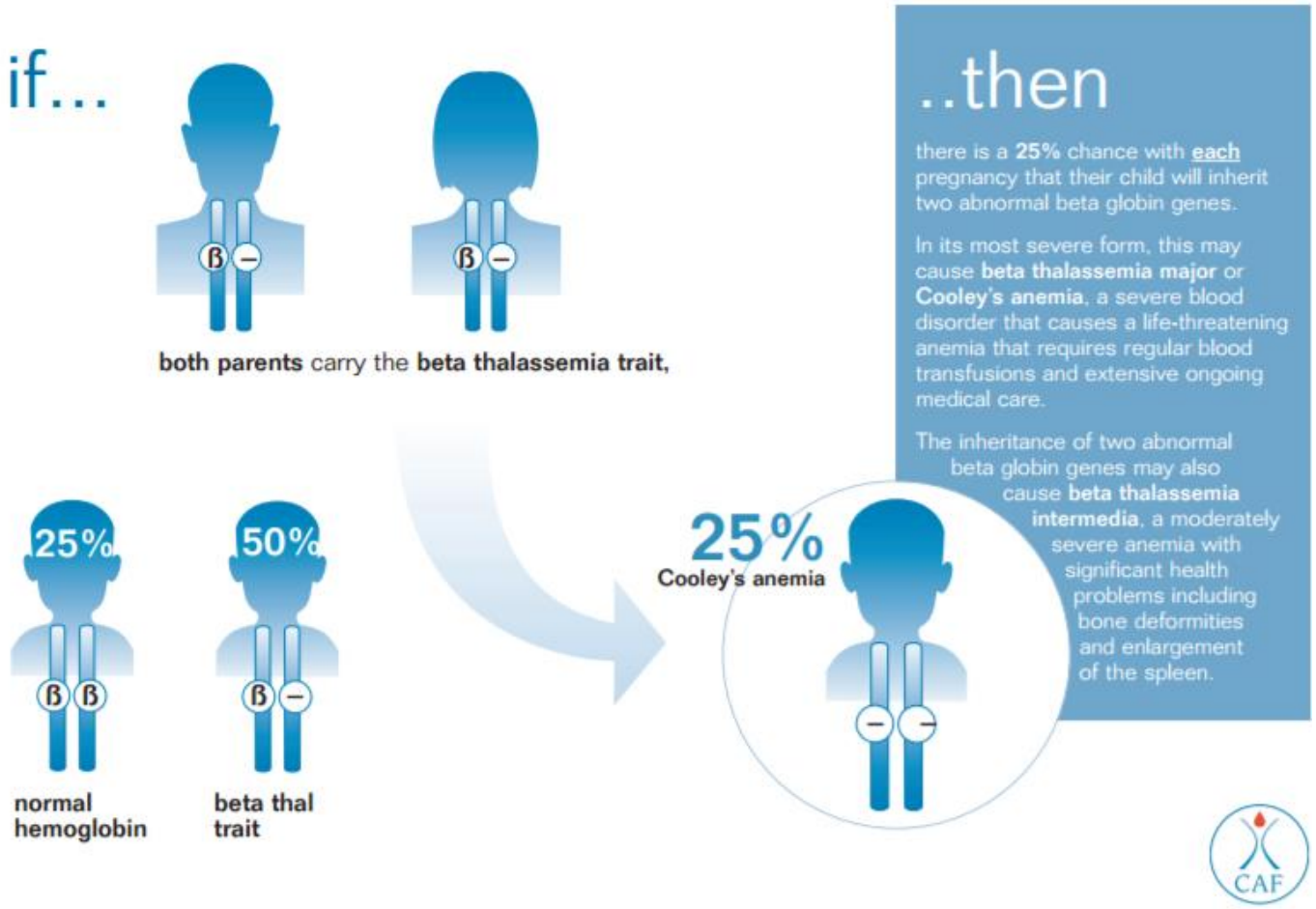
Case 2

Lab Investigations

Lab Parameter	Result
Hb (g/L)	60
MCV (fL)	50
Peripheral Blood Smear	hypochromic, microcytic red blood cells anisopoikilocytosis with target cells

Beta-thalassemia

Chromosome 11



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Clinical Features

Symptoms (non-specific)

- Fatigue
- Dyspnea
- Irritability

Signs

- Failure to thrive
- Pallor
- Hepatosplenomegaly
- Bone deformities *(late findings)*: skull bossing (prominent forehead), maxilla, flat nasal bridge, long bone deformities

Investigations

CBC

- Menzter Index: MCV/RBC

>13 suggests iron deficiency anemia

<13 suggests thalassemia

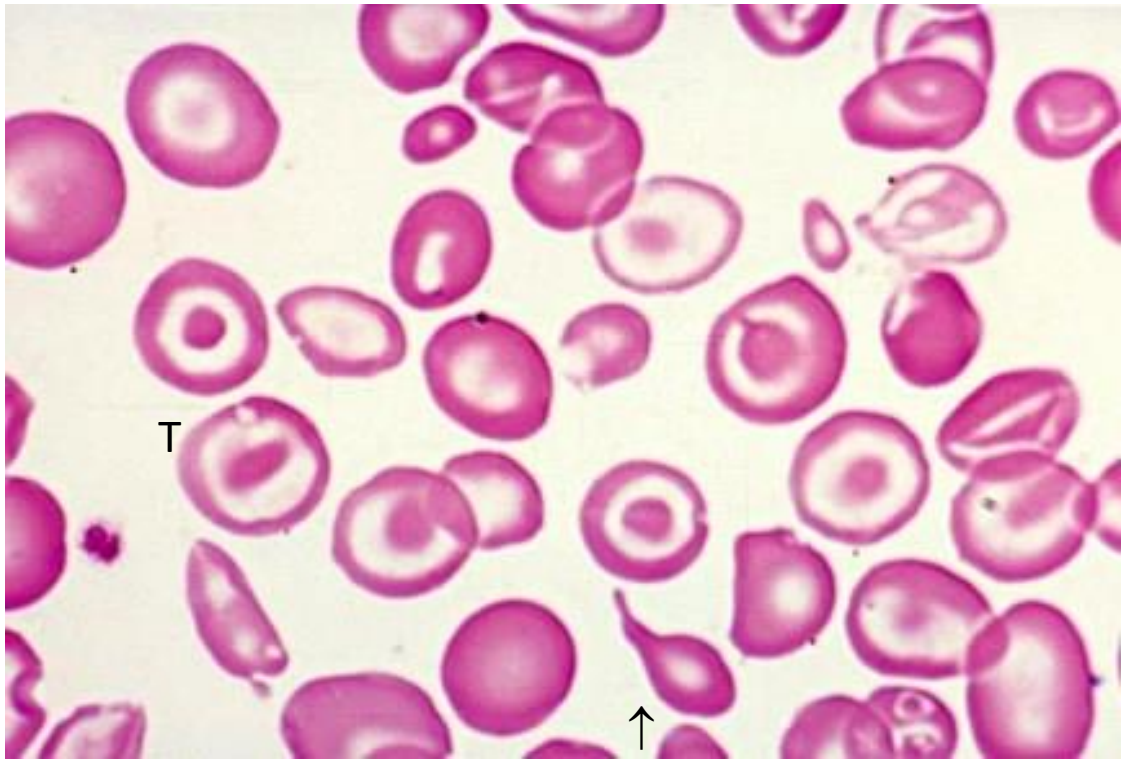
Peripheral blood smear

Fe Studies

Hemoglobin investigations

- ↓ Hb A *(or absent)*
- ↑ Hb F, Hb A_2

Genetic testing



A peripheral blood film showing target cells (T), teardrop cells (↑) and a variation of red blood cell shapes (poikilocytosis) and sizes (anisocytosis).

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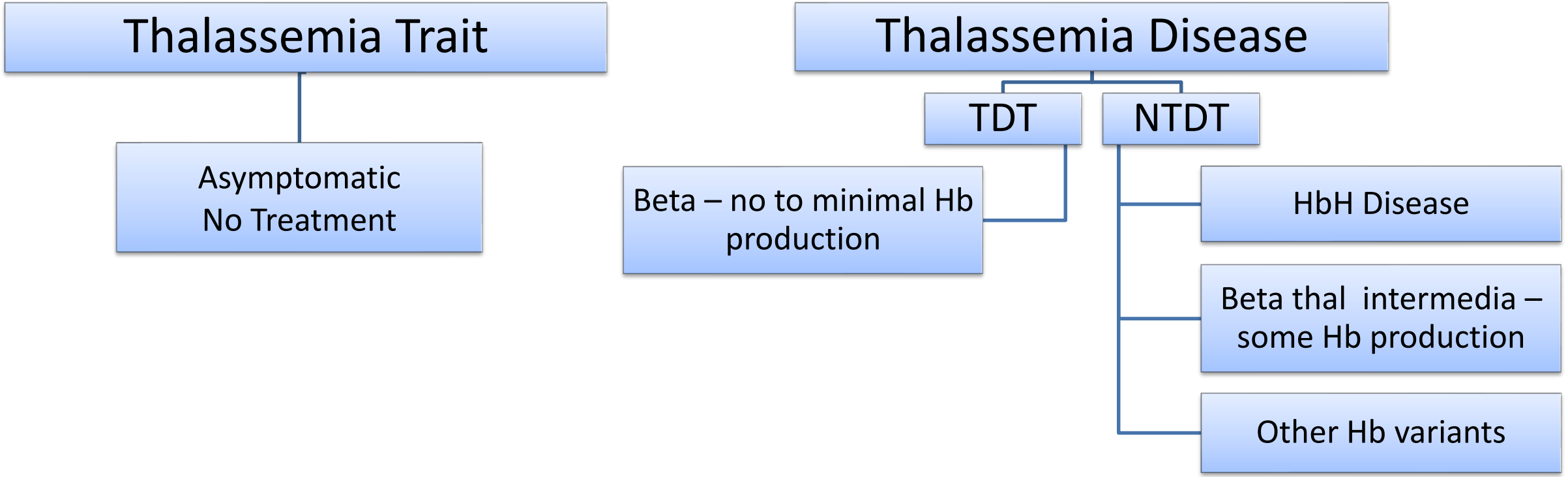
Case 2 continued

Kal was transfused 15mL/kg of packed red cells while you were interpreting his findings.

* * *

Two years later you meet him again as a pediatrics resident and find out he was eventually diagnosed with transfusion dependent beta-thalassemia.

Thalassemia Phenotypes



Transfusion dependent thalassemia (TDT): requires life long red cell transfusions to sustain life

Non-transfusion dependent thalassemia (NTDT): may have episodes requiring red cell transfusions but patients do not require chronic transfusions to sustain life

TDT Treatment

Transfusions

Iron Chelation

Hematopoietic Stem Cell Transplant

Long-Term Monitoring for Complications includes (not a comprehensive list):

- Hepatic and cardiac MRI for iron overload
- ECHO for cardiomyopathy
- etc.

Take Home Points

1) Keep thalassemia on the differential for a microcytic anemia
2) Thalassemia presentations can be variable; history includes ethnicity and parental consanguinity
3) Physical exam findings can be non-specific including: dyspnea, irritability and pallor
4) Important investigations and findings for the work-up of thalassemia includes:

- CBC: low MCV, high RBCs, with or without decreased hemoglobin in trait
- CBC: low MCV and variable Hb in disease depending on its severity.
- Peripheral blood smear: hypochromic, microcytic, poikilocytosis with target cells +/- nucleated red blood cells
- Hemoglobinopathy investigations Genetic testing for beta or alpha globin genes

5) Thalassemia disease is sub-categorized into TDT and NTDT

6) Management for TDT patients requires lifelong transfusions and iron chelation to prevent severe consequences of iron overload.

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