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HST.161 Molecular Biology and Genetics in Modern Medicine  
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Lecture 5                                      Thalassemias  
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What is thalassemia?

- red blood cells have little/no/badly functioning hemoglobin; abnormal RBCs ; so have no or diminished capacity for carrying oxygen

Where do we see thalassemia?

- southern Europe, Middle East, southern and southeast Asia and India, northern half of Africa
- heterozygous thalassemia mutation grants some resistance to malaria – so see lot of overlap in malaria prone regions

Genetics:

- chromosomes 16 and 11
- alpha and beta globin gene clusters

Development of erythropoiesis: [see chart on slide 7] [repeated on slide 5 of lecture 06\_housman]

Chart shows the different timelines during development for alpha, beta, and gamma thalassemia gene induction.

Three different kinds of thalassemia disease:

- alpha: obvious right away; babies have no ability to make hemoglobin. Usually these babies are born very badly damaged, but sometimes they come out undamaged, just anemic.
- beta: non-well-functioning hemoglobin; severity depends on homozygosity.
- gamma: also no hemoglobin; anemic, jaundiced. Severity depends on homozygosity.
- Many variations on these themes; interactions between types can be good or bad (for instance, a thalassemia that causes alpha chains to be harmful to RBCs combined with one that knocks out alpha activity, and therefore lessens the mutated alpha's harmful effects)

The standard of care used to be to not give transfusions due to fears of iron poisoning causing death later down the line. Later care did advise giving transfusions (because the iron was able to be removed), and children tended to look and feel more normal.

Transfusion-dependent complications:

- iron overload (heart, liver, endocrine complications => death)
- infections – hepatitis, HIV
- immunization issues (allergic reactions, alloimmunization)

How to deal with iron overload? You need something with an enormous iron affinity in order to pull it out of your blood...

- iron chelators (a few different types)