Beta-thalassemia

Genetics

-HBB (11p15.4)

-AR

Clinical findings/Dysmorphic features

-Reduced synthesis of the hemoglobin subunit beta --> microcytic hypochromic anemia:

1) Major: Severe anemia and hepatosplenomegaly; medical attention within the first two years of life; w/o treatment: affected children have severe FTT and shortened life expectancy

2) Intermedia: present later, mild anemia

Etiology

-The highest incidences are reported in Cyprus (14%), Sardinia (12%), and Southeast Asia

Pathogenesis

-Absence of globin beta chains --> reduced amounts of hemoglobin A (2xalpha + 2xbeta)

-Non-assembled globin alpha chains that result from unbalanced globin alpha chain/non-globin alpha chain synthesis precipitate in the form of inclusions --> damage the erythroid precursors in the bone marrow and spleen, causing ineffective erythropoiesis

Genetic testing/diagnosis

-Diagnosis of β-thalassemia:

--> Red blood cell indices: microcytic hypochromic anemia, nucleated red blood cells on peripheral blood smear

--> Hemoglobin analysis: decreased amounts of HbA and increased amounts of hemoglobin F after age 12 months

-In each at-risk population, 4-10 mutations account for the large majority of HBB disease

Others

-Treatment with a regular transfusion program and chelation therapy (to reduce transfusion iron overload) --> normal growth and development and extends life expectancy (30s-50s)

-High frequency of β-thalassemias: most likely related to selective pressure from malaria

-Increased HbA2 (alpha2delta2)