Gaucher Disease

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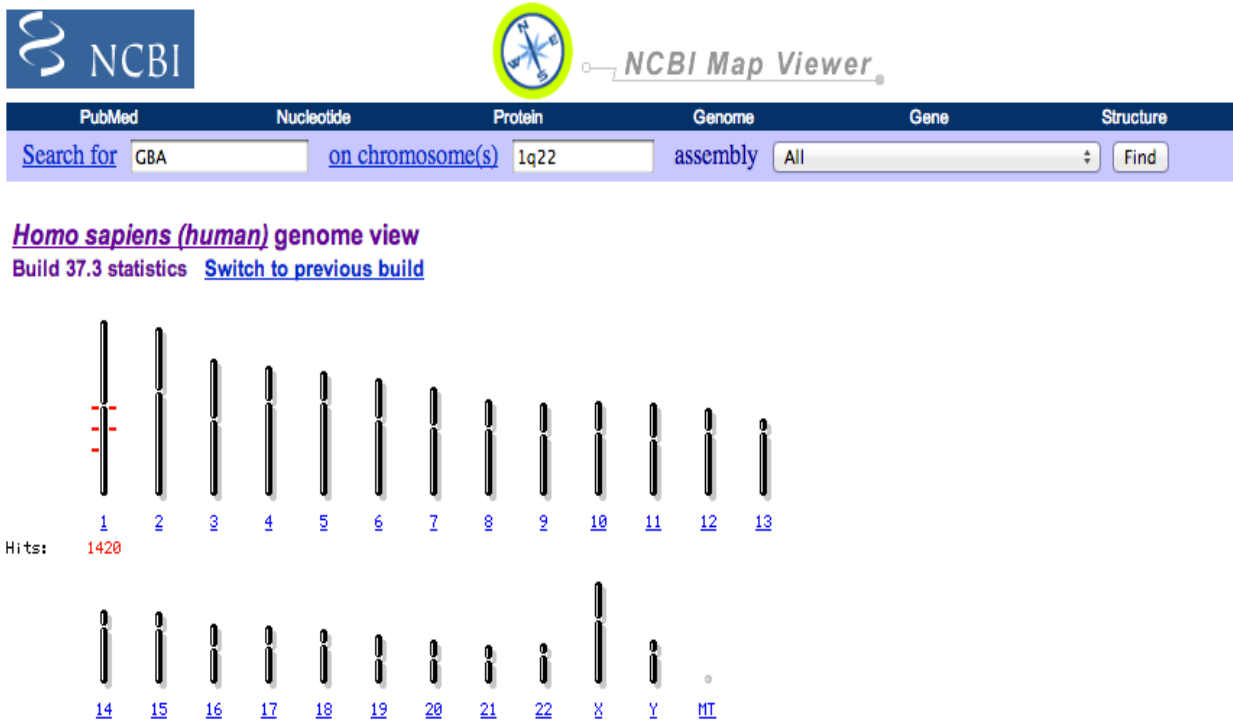
BioChem 118

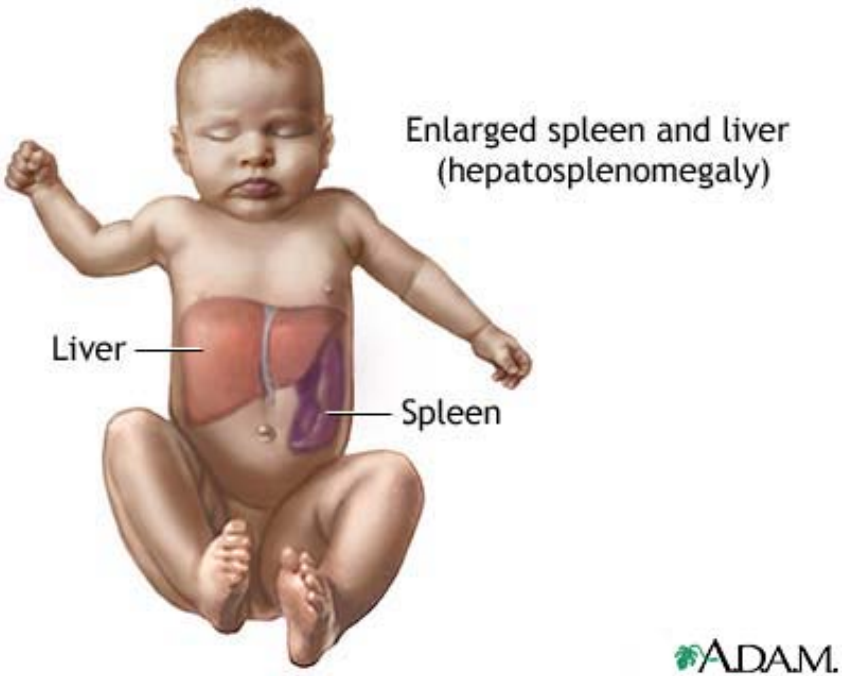
What is Gaucher Disease?

- Inherited disorder caused by a gene mutation
  - Autosomal recessive pattern
- Lacks enzyme called glucocerebrosidase
  - Needed to break down glucocerebroside
    - Fat build up in liver, spleen, and bone marrow
- Many types
- Possible link to Parkinson's Disease
- Affects 1 in 100,000



Classical Diagnosis

- Blood test
  - enzyme activity
  - white blood cell count
- enlarged organs
  - spleen
  - liver
- Bone marrow test
  - Look for Gaucher cells



Gaucher: Type 1

- Also called non-neuronopathic Gaucher disease
  - Central nervous system usually not affected
- Symptoms appear anytime from childhood to adulthood
  - Symptoms include:
    - hepatosplenomegaly (enlargement of liver and spleen)
    - Anemia
    - Thrombocytopenia (decrease in blood patelets)
    - Lung disease
    - Bone abnormalities
- Range from mild to severe

More Types

TYPE 2

- neuronopathic form
  - Affects the central nervous system
- In addition to symptoms from type 1, type 2 also includes:
  - Seizures
  - Brain damage
  - Abnormal eye movements
- usually life-threatening medical problems
  - Start from infancy

TYPE 3

- Also a neuronopathic form
  - Affects nervous system
- Progresses more slowly than type 2
- Also has symptoms from type 1

More Types

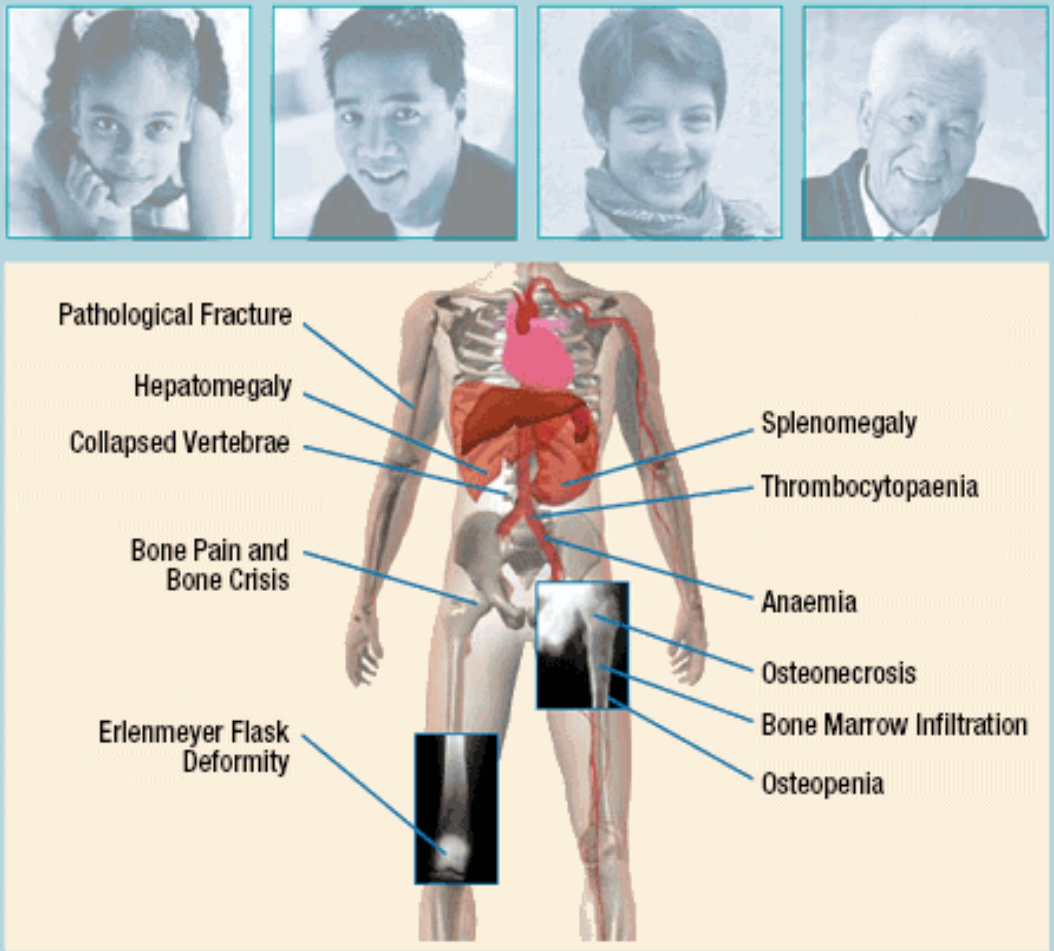
PERINATAL LETHAL FORM

- Most severe type
- Life-threatening complications
  - Start before birth or in infancy
- Symptoms:
  - Hydrops fetalis: extensive swelling caused by fluid accumulation before birth
  - Ichthyosis: dry, scaly skin
  - Hepatosplenomegaly
  - Distinctive facial features
  - Severe neurological problems
- Most infants survive only a few days after birth

CARDIOVASCULAR TYPE

- Affects the heart
  - Causes heart valves to calcify
- People with this form also usually have:
  - splenomegaly
  - eye abnormalities
  - bone disease

Multisystem Involvement in Type 1 Gaucher Disease Can Manifest **at Any Age**



Treatment

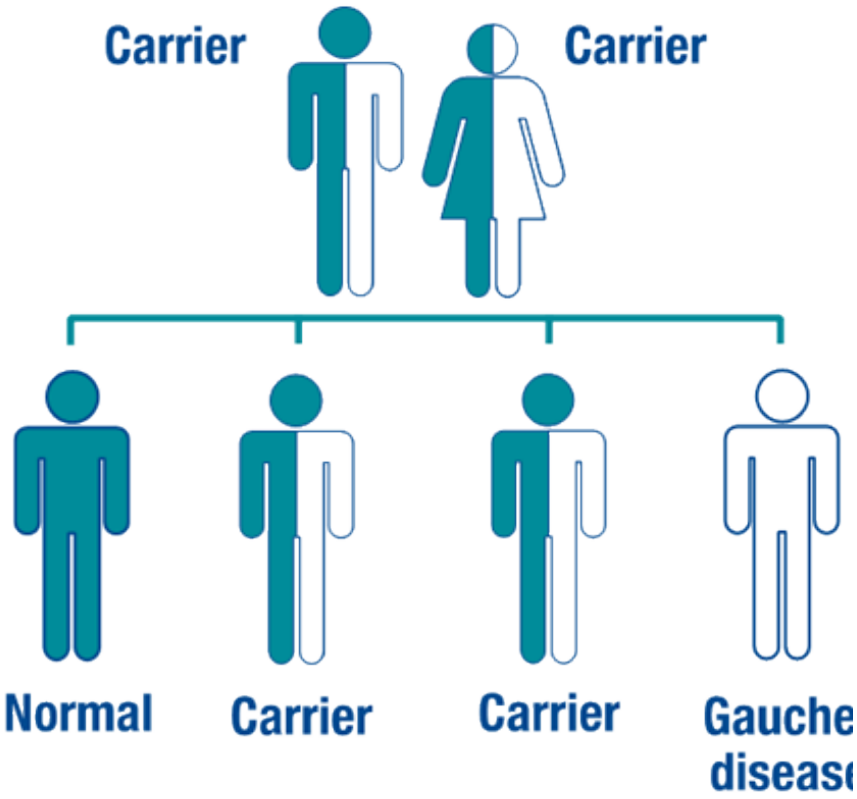
- Enzyme Replacement Therapy (ERT)
  - Consists of a modified form of the glucocerebrosidase enzyme -> given intravenously
  - stops and often reverses the symptoms
- Can also have symptomatic treatments if don't take ERT
  - Such as splenectomy, transfusion of blood products, and analgesics for bone treatment

Treatment (continued)

- Substrate Reduction Therapy
  - Treatment with N-butyldeoxynojirimycin (NB-DNJ) = an inhibitor of glucosylceramide synthase
  - Treatment over 24 months
  - decreased liver and spleen volumes
- Bone Marrow Transplantation
  - Gaucher cells disappeared from bone marrow
  - Liver size back to normal

Novel Treatment

- Gene Therapy (future)
  - introduction of GBA into hematopoietic stem cells
  - Enzyme production does not appear to be sustained
- Genetic counseling
  - Targeted Mutation Analysis
    - Used to detect carriers in high risk populations (4 common mutations)
      - Can be insufficient
- Sequence Analysis
  - nucleotide sequence is determined for a segment of DNA,
    - done in the GBA coding



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