Enzyme Replacement Therapy
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Lysosomal Storage Diseases (LSD)

- Lysosome = organelle responsible for catabolyzing macromolecules
- Characterized by deficiency of lysosomal enzyme
- Group of over 40 diseases
- Most are autosomal recessive
- Combined incidence of 1:6500 – 7500 live births
Enzyme Replacement Therapy (ERT)

- Cultivate missing enzyme outside the human body and then administer it to patients as treatment
- Can be used for diseases besides LSD
- First suggested in 1960s by Roscoe Brady
- Treats the cause, not just the symptoms
Currently ERT for 6 Lysosomal storage diseases
Gaucher’s Disease

- 1st developed ERT
- Most common of the lysosomal storage diseases
- Deficient enzyme: Glucocerebrosidase (catabolizes glucoceramide)
- Affects spleen, liver & bone marrow
- 3 clinical subtypes
- Gaucher Disease type 1: lethal by 2 years old
- Cerezyme
- ERT reverses pathologies → near normal lives

http://geneticpeople.com/?p=276
Fabry Disease

- X-linked inheritance
- Deficient enzyme: α-galactosidase (catabolizes globotriaosylceramide)

Symptoms:
- Usually begin in adolescence
- Acroparesthesias
- Pain and gastrointestinal problems

Fabrazyme
- Prevents but does not reverse damage
- Pain remains
Pompe Disease

- A.k.a. Glycogen storage disease type II
- Deficient enzyme: α-glucosidase
- Onset infant – adulthood
- Skeletal muscle problems
- Myozyme
- ERT prolongs infant life, increases motor abilities
- Clinical trials still in process for late onset Pompe


http://www.joemcdowellphotography.com/Haley/Haley/1903403_Mpc3n/3/97982714_W9w3V#97982714_W9w3V
Mucopolysaccharidoses (MPS)

- Group of 6 diseases
- Glycosaminoglycans accumulate
- 3 types have treatment
- **MPS I**
  - Hurler or Hurler-Scheie syndrome
  - α-L-iduronidase
- **MPS II**
  - Hunter syndrome
  - X-linked inheritance
  - Iduronate sulfatase
- **MPS VI**
  - Maroteaux-Lamy syndrome
  - Arylsulfatase
Mucopolysaccharidoses

- Common symptoms: coarse facies, deafness, cardiac disease, delayed development, neurologic problems (I & VI)

- Bone marrow transplant (Hurler)

- Enzyme replacement therapies
  - Aldurazyme (Hurler) – 2003
  - Elaprase (Hunter) – 2006
  - Naglazyme (Maroteaux-Lamy) – 2005

- http://www.maroteaux-lamy.com/English/hcp/AboutMPS.aspx
- http://www.metabolica.org/start/node/8
- http://chad-pyper.last-memories.com/
Non lysosomal storage diseases

- Can correct symptoms, not disease
  - Cystic fibrosis – has problems with pancreatic ducts that prevents enzymes from reaching gastrointestinal tract
  - Pancreatitis
  - Pancreatic and periampullary cancer
Shortcomings of ERT

- Administered via IV once every 2 weeks
  - Infusions last 2 – 6 hours

- Side Effects
  - Allergy symptoms, respiratory distress
  - Long term effects not yet known
  - Gaucher’s: treated for 15 – 20 years with no severe side effects

- Antibody responses
  - IgG – binds to drugs → allergy symptoms
  - IgE – increased risk of anaphylactic reaction

- Cost = $200,000 - $300,000 per year
  - Can max out health insurance in 2 – 5 years

- Affects employment
Sources