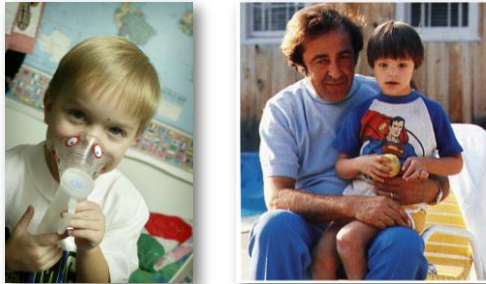
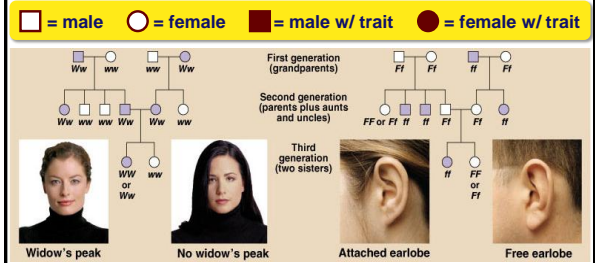


Studying Inheritance in Humans



Pedigree Analysis

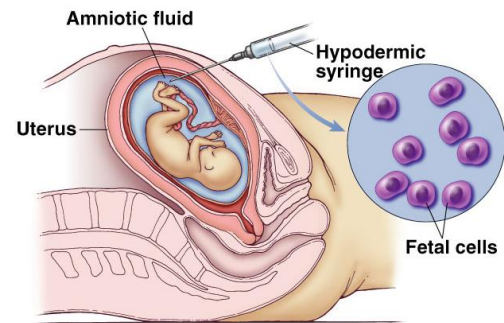
- Pedigree analysis reveals Mendelian patterns in human inheritance
- ◆ data mapped on a family tree



Genetic Counseling

- Pedigree can help us understand the past & predict the future
- Thousands of genetic disorders are inherited as simple recessive traits
 - ◆ benign conditions to deadly diseases
 - ◆ albinism
 - ◆ cystic fibrosis
 - ◆ Tay Sachs
 - ◆ sickle cell anemia
 - ◆ PKU

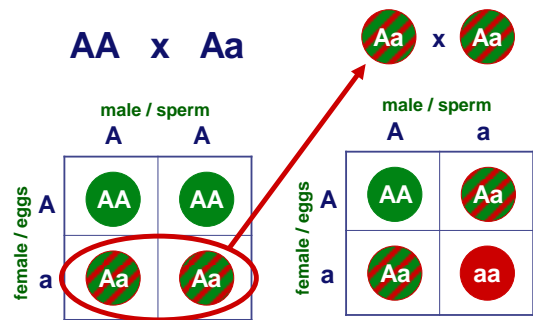
Genetic Testing



Recessive Diseases


- The diseases are recessive because the allele codes for either a malfunctioning protein or no protein at all
 - ◆ Heterozygotes (Aa)
 - carriers
 - have a normal phenotype because one "normal" allele produces enough of the required protein

A hidden disease reveals itself...



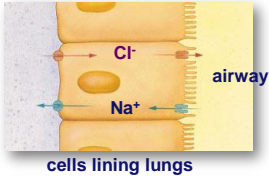
Cystic Fibrosis

- Primarily 'whites' of European descent
- strikes 1 in 2500 births
 - 1 in 25 whites is a carrier (Aa)
- normal allele codes for a membrane protein that transports Cl⁻ across cell membrane
 - defective or absent channels cause high extracellular levels of Cl⁻
 - thicker & stickier mucus coats around cells
 - mucus build-up in the pancreas, lungs, digestive tract & causes bacterial infections
- without treatment children die before 5; with treatment can live past their late 20s



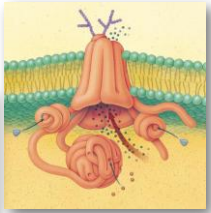
normal lung tissue

Normal Lungs



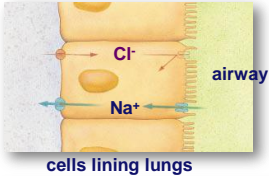
Cl⁻
Na⁺
airway
cells lining lungs

Chloride channel
Transports chloride through protein channel out of cell.
Osmotic effects: H₂O follows Cl⁻

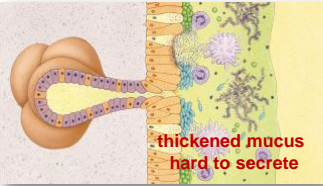


mucus secreting glands


Lungs with Cystic Fibrosis



Cl⁻
Na⁺
airway
cells lining lungs



thickened mucus hard to secrete



damaged lung tissue
bacteria & mucus build up


Tay-Sachs

- Primarily Jews of eastern European (Ashkenazi) descent & Cajuns
- strikes 1 in 3600 births
 - 100 times greater than incidence among non-Jews or Mediterranean (Sephardic) Jews
- non-functional enzyme fails to breakdown lipids in brain cells
 - symptoms begin few months after birth
 - seizures, blindness & degeneration of motor & mental performance
 - child dies before 5yo



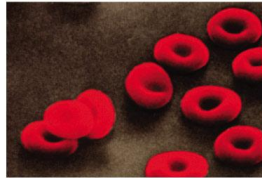

Sickle Cell Anemia

- Primarily Africans
- strikes 1 out of 400 African Americans
- caused by substitution of a single amino acid in hemoglobin
- when oxygen levels are low, sickle-cell hemoglobin crystallizes into long rods
 - deforms red blood cells into sickle shape
 - sickling creates pleiotropic effects = cascade of other symptoms



Sickle Cell Anemia

- Substitution of one amino acid for another in a polypeptide chain

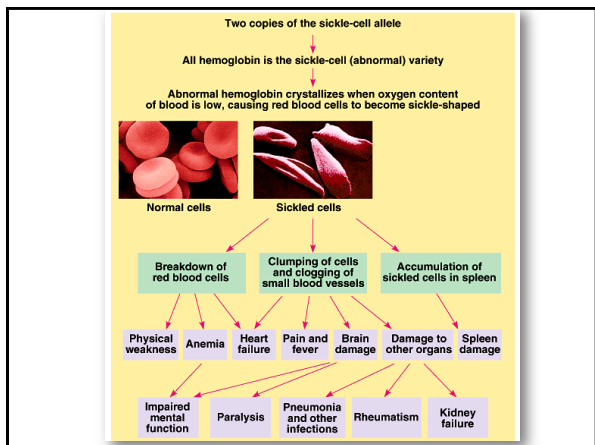
10 μm

Val | His | Leu | Thr | Pro | Glu | Glu | ...
1 2 3 4 5 6 7

(a) Normal red blood cells and the primary structure of normal hemoglobin

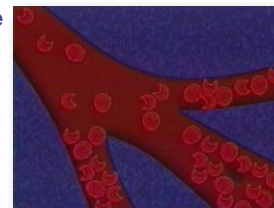
Val | His | Leu | Thr | Pro | Val | Glu | ...
1 2 3 4 5 6 7

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin



Sickle Cell Phenotype

- The 2 alleles are both represented...
 - ◆ both normal & abnormal hemoglobins are synthesized in heterozygote (Aa)
 - ◆ carriers usually healthy, although some suffer some symptoms of sickle-cell disease under blood oxygen stress
 - exercise



Heterozygote Advantage

- Sickle cell frequency
 - ◆ high frequency of heterozygotes is unusual for allele with severe detrimental effects in homozygotes
 - 1 out of 400 African Americans
- Suggests some selective advantage of being heterozygous
 - ◆ sickle cell: resistance to malaria?
 - ◆ cystic fibrosis: resistance to cholera?

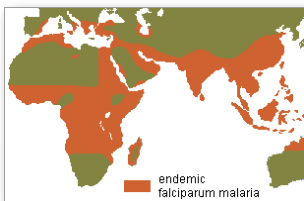


Heterozygote Advantage

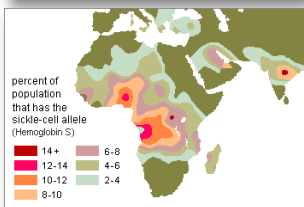
- Malaria
 - ◆ single-celled eukaryote parasite spends part of its life cycle in red blood cells
- In tropical Africa, where malaria is common:
 - ◆ homozygous normal individuals die of malaria
 - ◆ homozygous recessive individuals die of sickle cell anemia
 - ◆ heterozygote carriers are relatively free of both
- High frequency of sickle cell allele in African Americans is vestige of African roots



Prevalence of Malaria



Prevalence of Sickle Cell Anemia



Genetics & Culture

- Why do all cultures have a taboo against incest?
 - ◆ laws or taboos forbidding marriages between close relatives are fairly universal
- Fairly unlikely that 2 carriers of same rare harmful recessive allele will meet & mate
 - ◆ but matings between close relatives increase risk
 - consanguineous matings
 - ◆ individuals who share a recent common ancestor are more likely to carry same recessive alleles