



Chapter 14.

**Studying Inheritance
in Humans**

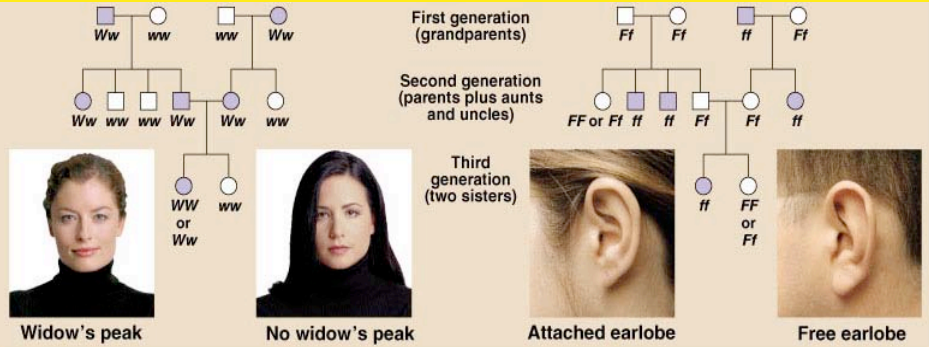
AP Biology

2004-2005

Pedigree analysis

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

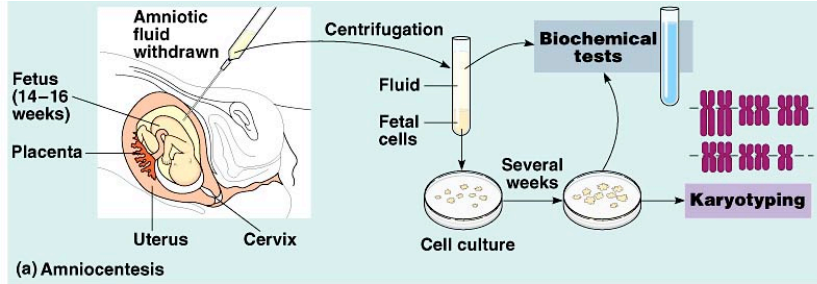
□ = male ○ = female ■ = male w/ trait ● = female w/ trait



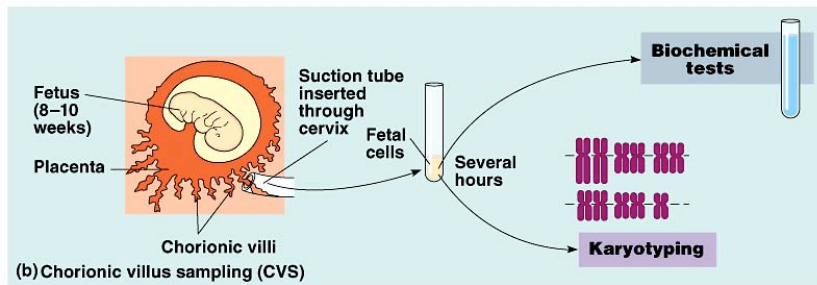
Genetic counseling

- 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

Genetic testing



(a) Amniocentesis



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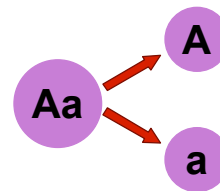
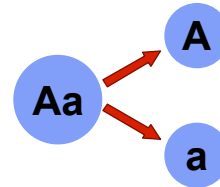
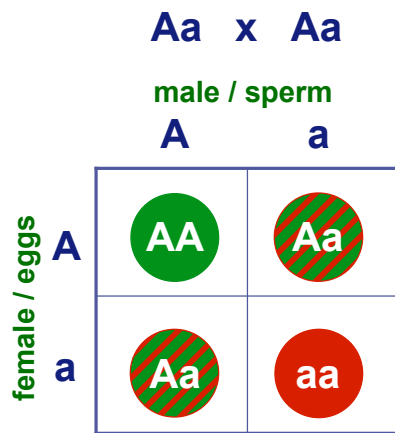
(b) Chorionic villus sampling (CVS)

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

Heterozygote crosses

- Heterozygotes as carriers of recessive alleles



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Cystic fibrosis

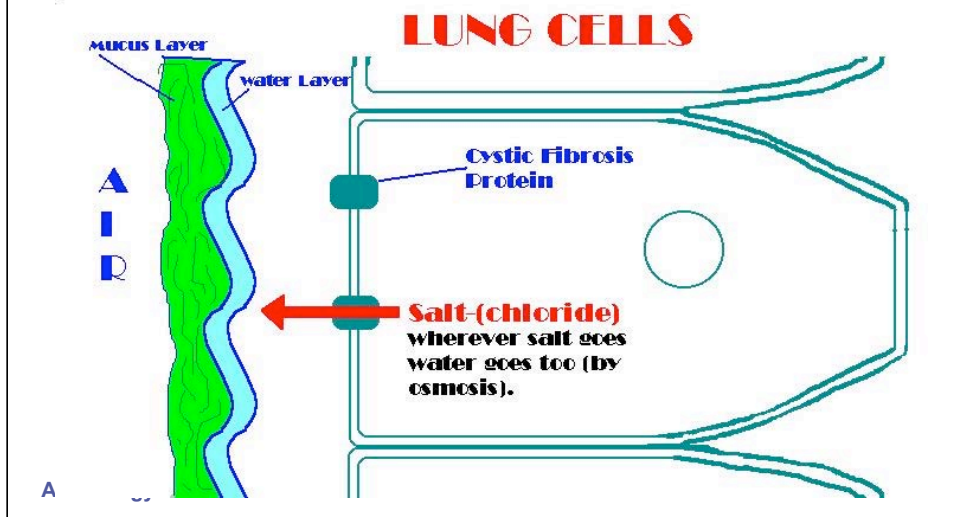
- **Primarily whites of European descent**
 - ◆ strikes 1 in **2500** births
 - 1 in 25 whites is a carrier (Aa)
 - ◆ normal allele codes for a membrane protein that transports Cl^- across cell membrane
 - defective or absent channels cause high extracellular levels of Cl^-
 - thicker & stickier mucus 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

Cystic fibrosis is an inherited disease that is relatively common in the U.S. Cystic fibrosis affects multiple parts of the body including the pancreas, the sweat glands, and the lungs. When someone has cystic fibrosis, they often have lots of lung problems. The cause of their lung problems is directly related to basic problems with diffusion and osmosis in the large airways of the lungs.

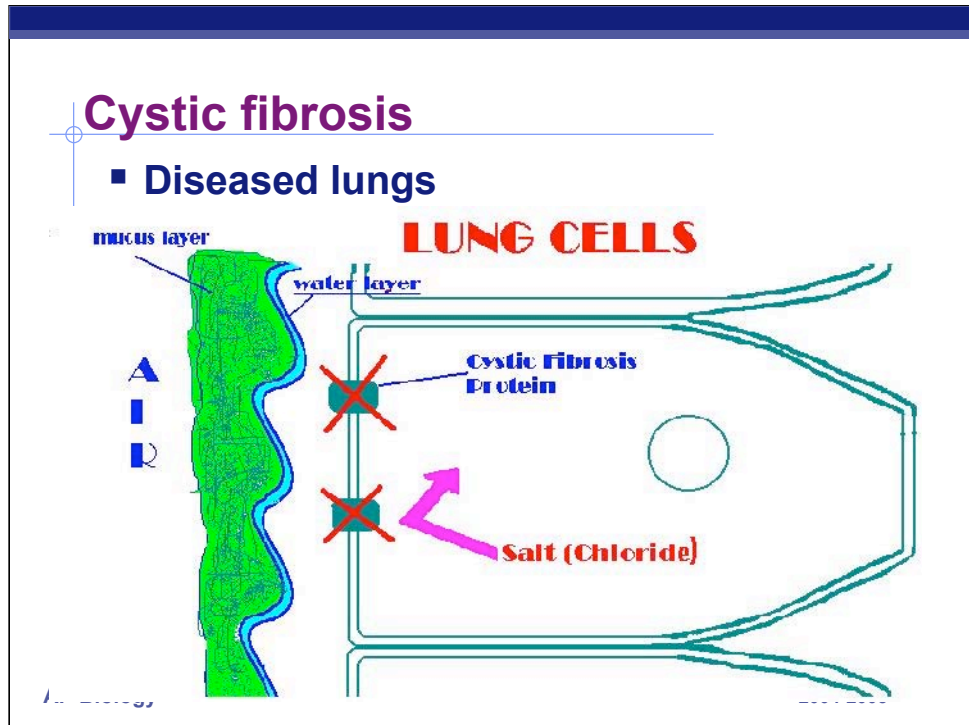
People without cystic fibrosis have a small layer of salt water in the large airways of their lungs. This layer of salt water is under the mucus layer which lines the airways. The mucus layer in the airways helps to clear dust and other inhaled particles from the lungs.

Cystic fibrosis

Normal lungs



In people without cystic fibrosis, working cystic fibrosis proteins allow salt (chloride) to enter the air space and water follows by osmosis. The mucus layer is dilute and not very sticky.



In people with cystic fibrosis, non-working cystic fibrosis proteins mean no salt (chloride) enters the air space and water doesn't either. The mucus layer is concentrated and very sticky.

People with cystic fibrosis have lung problems because:

- Proteins for diffusion of salt into the airways don't work. (less diffusion)
- Less salt in the airways means less water in the airways. (less osmosis)
- Less water in the airways means mucus layer is very sticky (viscous).
- Sticky mucus cannot be easily moved to clear particles from the lungs.
- Sticky mucus traps bacteria and causes more lung infections.

Therefore, because of less diffusion of salt and less osmosis of water, people with cystic fibrosis have too much sticky mucus in the airways of their lungs and get lots of lung infections. Thus, they are sick a lot.

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



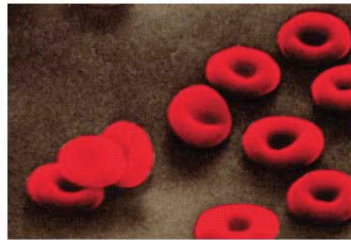
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Sickle cell anemia

- **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

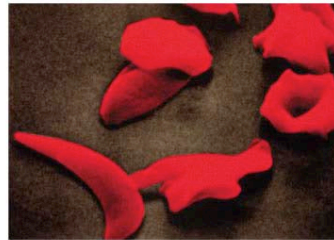
Sickle cell anemia

- Substitution of one amino acid in polypeptide chain



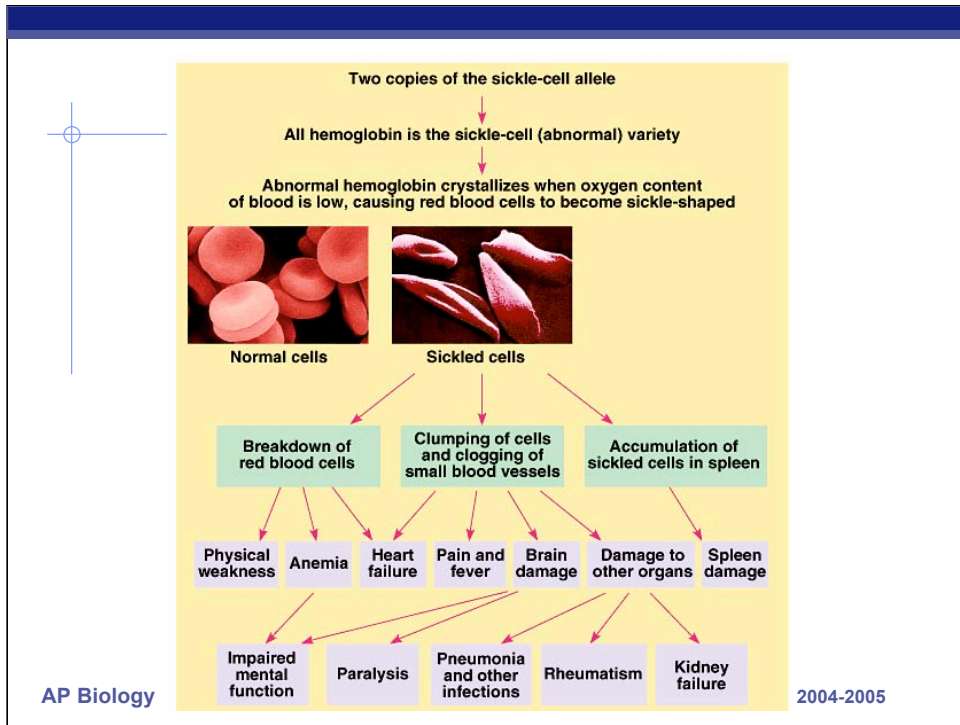
Val	His	Leu	Thr	Pro	Glu	Glu	...
1	2	3	4	5	6	7	

(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	

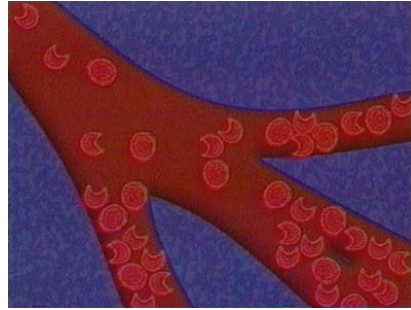
(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin



Doctors can use regular blood transfusions to prevent brain damage and new drugs to prevent or treat other problems.

Sickle cell phenotype

- **2 alleles are codominant**
 - ◆ 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



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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?

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Sickle Cell:

In tropical Africa, where malaria is common, the sickle-cell allele is both an advantage & disadvantage. Reduces infection by malaria parasite.

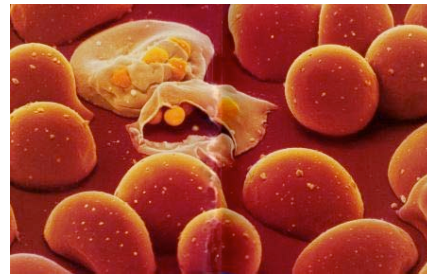
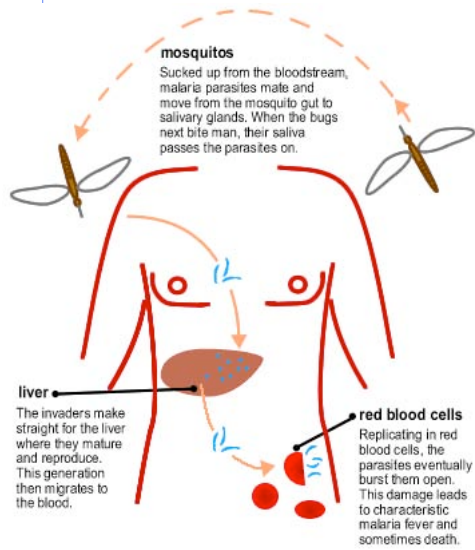
Cystic fibrosis:

Cystic fibrosis carriers are thought to be more resistant to cholera:
1:25, or 4% of caucasians are carriers Cc

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**

Malaria

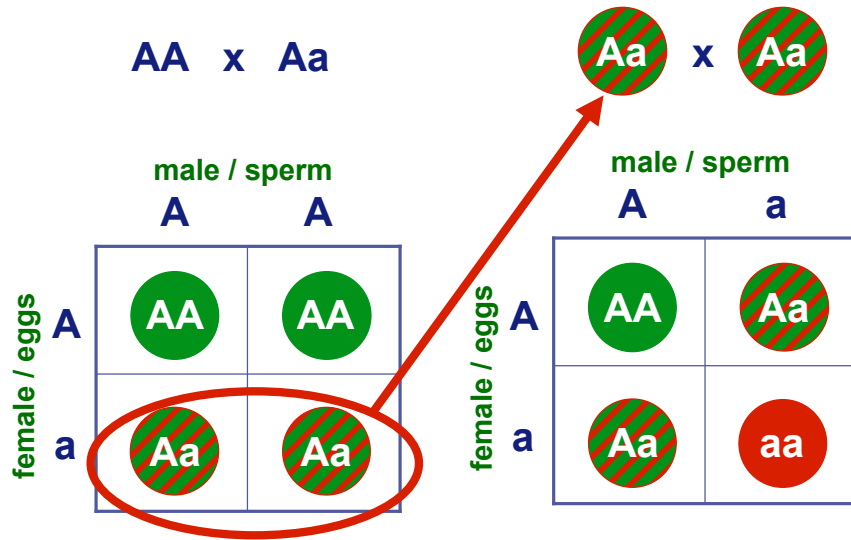


2004-2005

Genetics & culture

- **Why do 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**
 - ◆ individuals who share a recent common ancestor are more likely to carry same recessive alleles

A hidden disease reveals itself



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