HUMAN GENETICS & MUTATIONS

MUTATIONS = CHANGES in DNA

Upon completion of this section the student will:

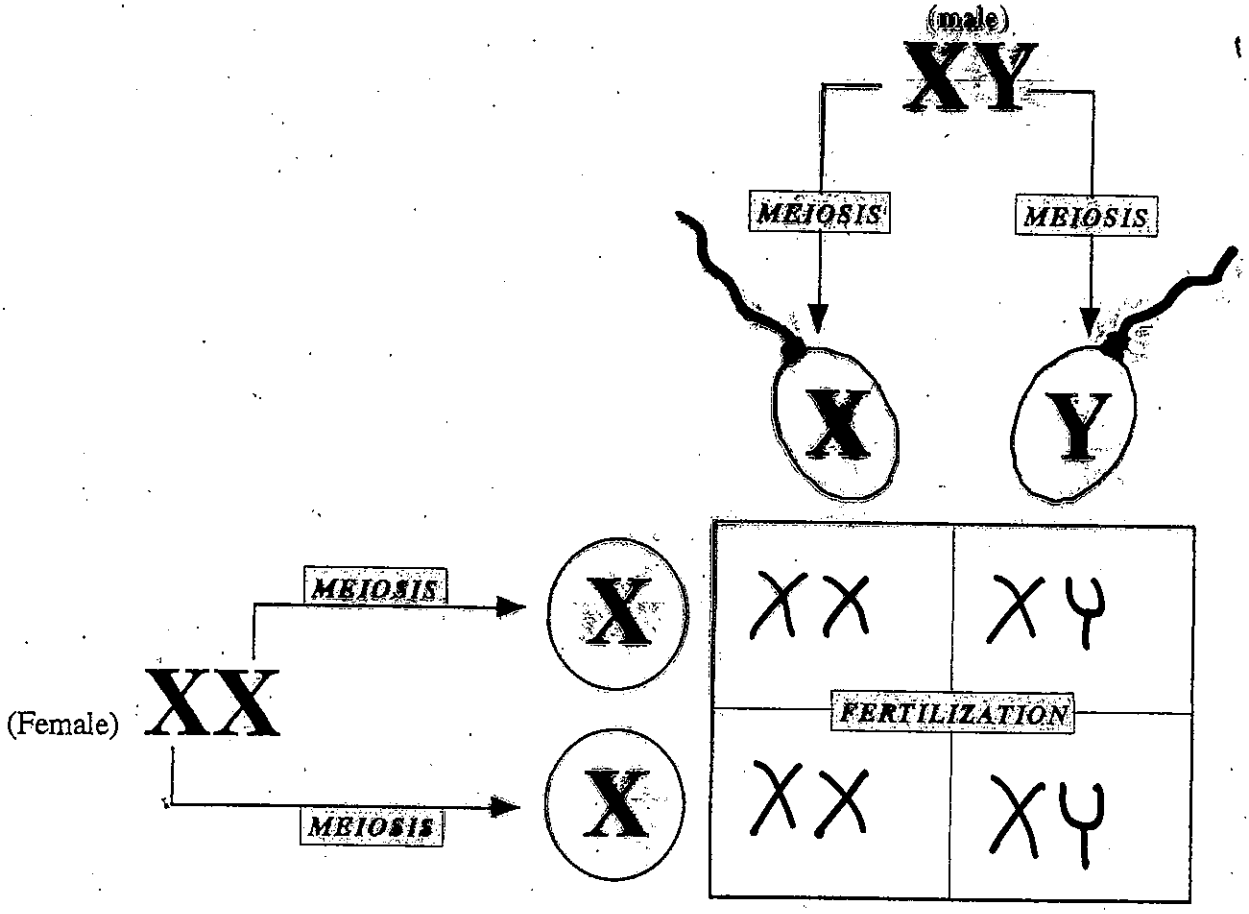
__ 1. recognize that it's the male that determines the sex of of the offspring.
__ 2. define **MUTATION**.
__ 3. distinguish between chromosomal and gene mutations.
__ 4. identify Downs Syndrome as a chromosomal mutation.
__ 5. recognize that each gene carries a separate piece of information that codes for a particular trait (protein).
__ 6. list and briefly describe **FOUR** types of gene mutations.
__ 7. recognize that sickle cell anemia is a ***RECESSIVE*** genetic condition.
__ 8. describe the genetic and physical causes of ***sickle cell anemia***.
__ 9. using Punnett squares, predict the probability of having a child with sickle cell anemia when given the genotype and/or phenotype of the parents.
__ 10. explain the molecular basis of ***diabetes***.
__ 11. explain some of the difficulties that arise in studying human genetic.
__ 12. describe the processes of ***amniocentesis*** and ***chorionic villus sampling*** and how they can be used to diagnose some human genetic disorders.
__ 13. construct a ***karyotype*** and explain how it can be used to diagnose some human genetic disorders.

KILLER WORDS

sex chromosomes	mutations	chromosomal mutations
gene mutations	Downs syndrome	trisomy 21
Sickle Cell Anemia	Cystic Fibrosis	Huntington Disease
substitution	deletion	addition
inversion	hemoglobin	red blood cells
diabetes	insulin	pancreas
amniocentesis	karyotype	chorionic villus sampling

I. SEX DETERMINATION IN HUMANS

• *FEMALES* = XX • *MALES* = XY



RESULTS: 50% MALE

50% FEMALE

- Since women are *XX*, the EGG can only contain an X chromosome.
- Since men are *XY*, the SPERM can carry an X or a Y chromosome.
- For this reason, the MALE (SPERM) determines the sex of the offspring.

II. *MUTATIONS* → CHANGES in DNA

MUTATIONS IN BODY CELLS	*MUTATIONS IN SEX CELLS*
• CANNOT be passed on to offspring	• CAN be passed on to offspring

A. TYPES OF MUTATIONS

1. *Chromosomal Mutations*

- Usually involve changes that effect the entire CHROMOSOME

a) *Mutations Involving Chromosome Number*

(1) Downs Syndrome

- Discovered in **1866** by English physician J.L. DOWN
- Occurs when a person is born with an extra chromosome 21.
  (Instead of 2, people with Downs Syndrome have 3 of chromosome #21)
- Medically referred to as TRISOMY 21
- Because chromosomes are made up of thousands of GENES, this mutation causes many changes is a person's physical make up or PHENOTYPE.

2. *Gene Mutations*

- Involves changes in individual DNA segments or GENES.
- Some are not very harmful.
  EXAMPLES: COLOR-BLINDNESS, ALBINISM
- Some are not as visible but are more LETHAL or DEADLY
- *Deadly* mutations are called LETHAL.

EXAMPLES: TAY SACHS
ALD
CYSTIC FIBROSIS

a) *Types of Gene Mutations*

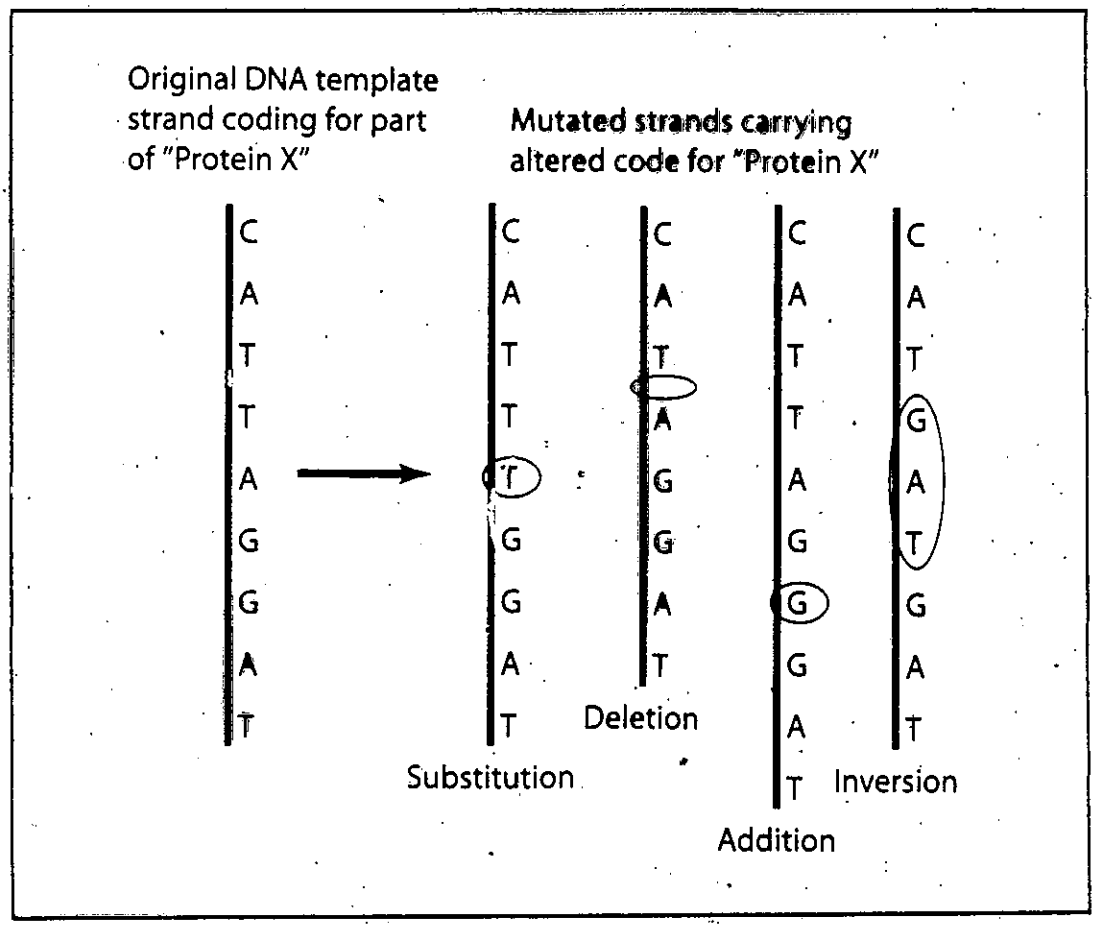
(1) **Substitution** - - - occurs when one base (**A,T,C,G**) is ***substituted*** or ***replaced*** by another in a DNA segment or GENE.

(2) **Deletion** - - - - - - occurs when one base (**A,T,C,G**) is ***deleted*** or ***missing*** from a GENE.

(3) **Addition** - - - - - - occurs when one base (**A,T,C,G**) is ***added*** to a GENE.

(4) **Inversion** - - - - - - occurs when a group of bases (**CCATG**) is removed from a gene and put back in reverse order (**GTACC**).

EXAMPLES OF GENE MUTATIONS



The piece of DNA on the left is part of a gene that codes for protein X. The four strands on the right show the DNA that would result from the 4 types of gene mutations discussed above.

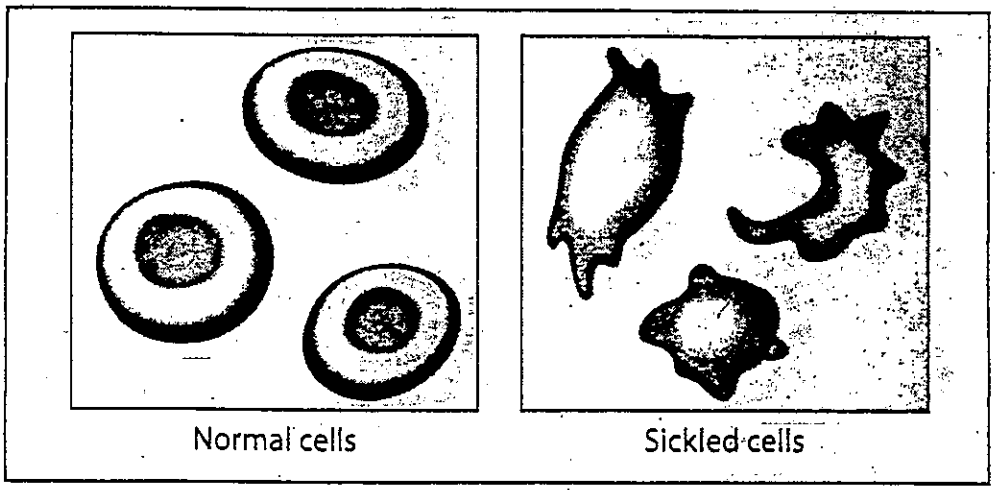
III. *Human Genetic Diseases*

REMEMBER: DNA → RNA → PROTEINS

Our GENOTYPE determines our PHENOTYPE.
Random changes in our *genetic make up* or ***genotype*** are called: MUTATIONS
Mutations change our *physical make up* or ***phenotype*** by affecting a cells ability to synthesize specific PROTEIN MOLECULES.

A. SICKLE CELL ANEMIA

- a genetic disorder caused by a SUBSTITUTION mutation in the gene responsible for synthesizing the protein HEMOGLOBIN in RED BLOOD CELLS.
- the abnormally shaped HEMOGLOBIN molecule changes the shape of the RED BLOOD CELL affecting its ability to carry O_2.

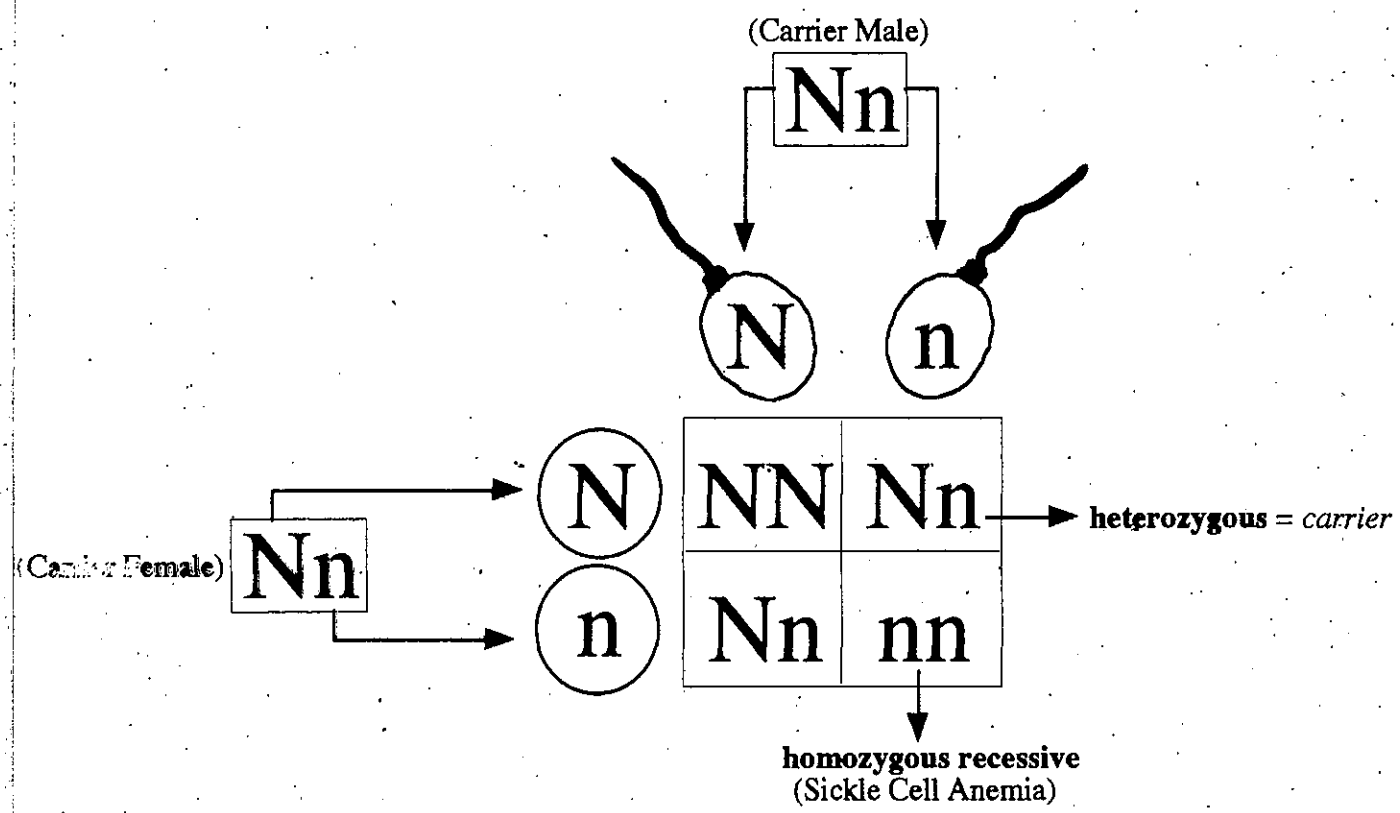


Effects of a Substitution Mutation: *Normal red blood cells are round and capable of carrying oxygen. Sickled red blood cells have an abnormal shape and are incapable of carrying oxygen. This abnormal cell shape is due to a substitution mutation that forms a defective hemoglobin molecule (protein) which changes the cell's shape.*

B. PREDICTING SICKLE CELL ANEMIA

- Sickle cell anemia is a RECESSIVE condition.
- Like ALL ***recessive*** traits, in order to suffer from this disease a person **MUST** be HOMOZYGOUS RECESSIVE for the sickle cell trait.
- And, like **ALL** recessive traits, individuals **MUST** get one recessive allele or gene from **BOTH** parents. (*See Punnett square below*)

SYMBOLS: **N** = *normal red blood cell*
n = *sickle cell anemia*



RESULTS:

	GENOTYPE:		PHENOTYPE:
NN =	$\frac{1}{4}$ = 25% HOMOZYGOUS DOM. "CARRIERS"	→	"NORMAL" RBC SOMETIMES HAVE SICKLE CELL ANEMIA
Nn =	$\frac{2}{4}$ = 50% HETEROZYGOUS	→	
nn =	$\frac{1}{4}$ = 25% HOMOZYGOUS REC.	→	SICKLE CELL ANEMIA

C. PUNNETT SQUARES: SICKLE-CELL ANEMIA

DIRECTIONS: Complete the following genetic crosses involving the gene for sickle-cell anemia.

1. A women ***heterozygous*** for the sickle-cell anemia trait marries a man who is also ***heterozygous*** for the sickle cell anemia trait. What are the chances that their first-child will die at a very young age of sickle-cell anemia (***homozygous recessive***)?

N = NORMAL
n = SICKLE-CELL

Heterozygous (carrier) Man X Heterozygous (carrier) female

SYMBOLS: Nn x Nn

RESULTS:

GENOTYPE:
¼ = 25% HOMOZYGOUS DOM.
½ = 50% HETEROZYGOUS
¼ = 25% HOMOZYGOUS REC.

PHENOTYPE:
¼ = 25% NORMAL RBC'S
½ = 50% CARRIER
¼ = 25% SICKLE-CELL ANEMIA

	N	n
N	NN	Nn
n	Nn	Nn

What are the chances that their first child will die at a very young age of sickle-cell anemia? (***homozygous recessive***)

25%

IV. THE MOLECULAR BASIS OF MUTATIONS ↓↑ GENETIC DISEASES

REMEMBER: DNA ⟶ RNA ⟶ PROTEINS

- *A great number of diseases that affect human beings are due to the body's inability to properly synthesize or make a specific **protein** molecule. The body's inability to make **proteins** results from mistakes or mutations in our **DNA**!*

A. HUMAN GENETIC DISEASES AND THE PROTEINS RESPONSIBLE.

DISORDER	PROTEIN	CLINICAL FEATURES
Sickle-Cell	Hemoglobin	Abnormally-shaped red blood cells causes clumping and severe pain in muscles and joints. RBC's also loose the ability to carry oxygen resulting in weakness.
Phenylketonuria	Enzyme (phenyalanine hydroxylase)	Inability of the body to break down the amino acid phenylalanine causes it to build up in the brain and cause mental retardation.
Tay-Sachs	Enzyme (hexosaminidase)	Lipid (fat) build up in the brain causes brain damage.
Cystic Fibrosis	Membrane Protein	Thick mucus build up in the lungs makes breathing difficult.
Diabetes	Hormone (Insulin)	Glucose is NOT able to enter the cells and therefore remains in the blood where it causes numerous circulation disorders.
Hemophilia	Blood Protein (Clotting Factor VIII)	Inabiility of the blood to clot resulting in excessive bleeding.

V. *MUTAGENIC AGENTS*

- MUTAGENS are factors in the environment that cause MUTATIONS

> Since most cancers have a ***genetic*** component, most mutagens are also referred to as CARCINOGENS or cancer-causing agents.

A. KNOWN MUTAGENS INCLUDE...

(1) Radiation:

- X-RAYS (don't forget about that lead apron)
- ULTRAVIOLET (UV) RADIATION -----> Sunlight?
- ELECTROMAGNETIC RADIATION -----> cell phones?

(2) Chemicals:

- CIGARETTE smoke has been proven to contain over 150 cancer-causing mutagenic agents.

- **P**oly**C**hloro**B**iphenols (**PCBs**) -----> To dredge or not to dredge?