MUTATIONS

Mutations

- Mutations are a change in the base sequence of DNA in an organism
- (eg) a gene sequence that should read:

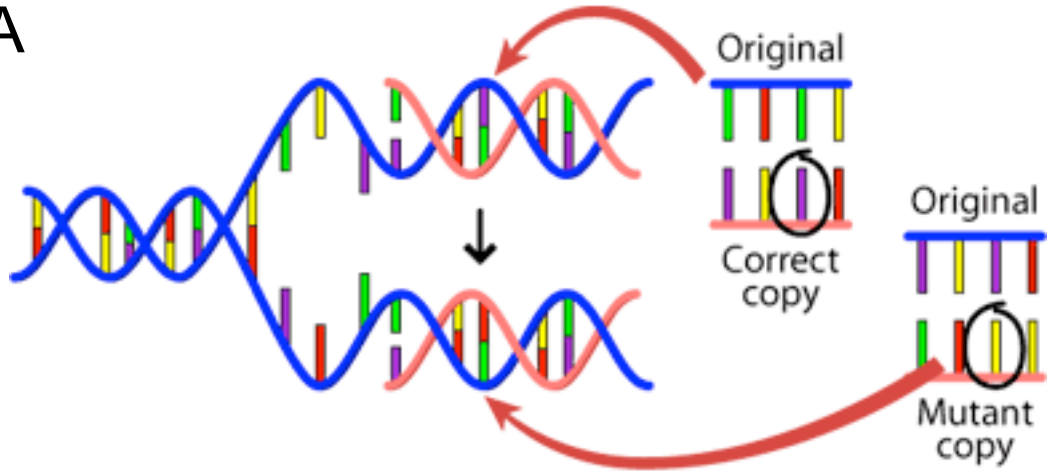
  ACG CCG TCA

  might change to:

  ACG **A**CG TCA

This may result in the mutation being:

1. HARMFUL
2. NEUTRAL
3. BENEFICIAL



Mutations

- Beneficial mutations
  - -Gives organism a selective advantage
  - -Tends to become more common over time
  - -Leads to new evolutionary change
- Harmful mutations
  - -Reduce an individual's fitness (health)
  - -Tends to be selected against (not used)
  - -Occur at low rates
- Neutral mutations
  - -No benefit nor a cost
  - -Not acted on by natural selection

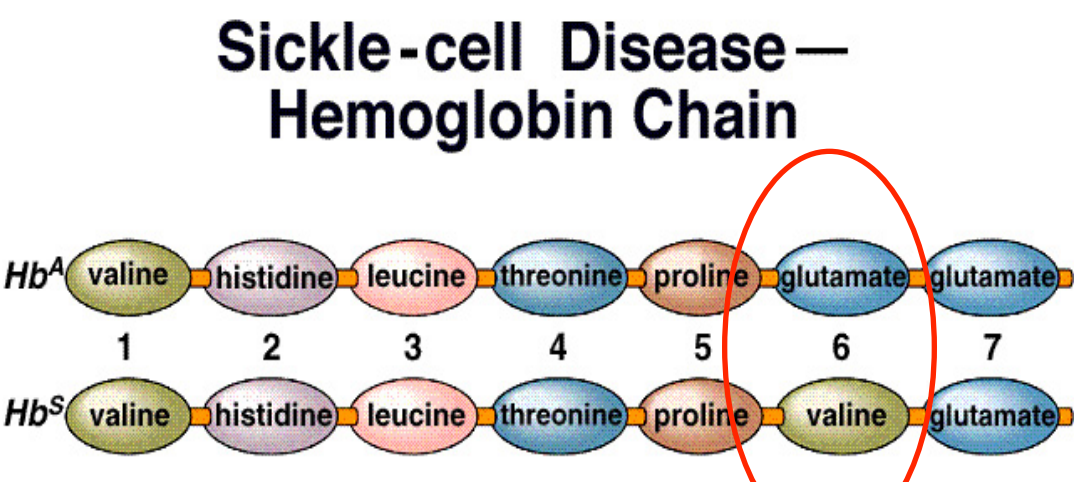
HARMFUL Mutations

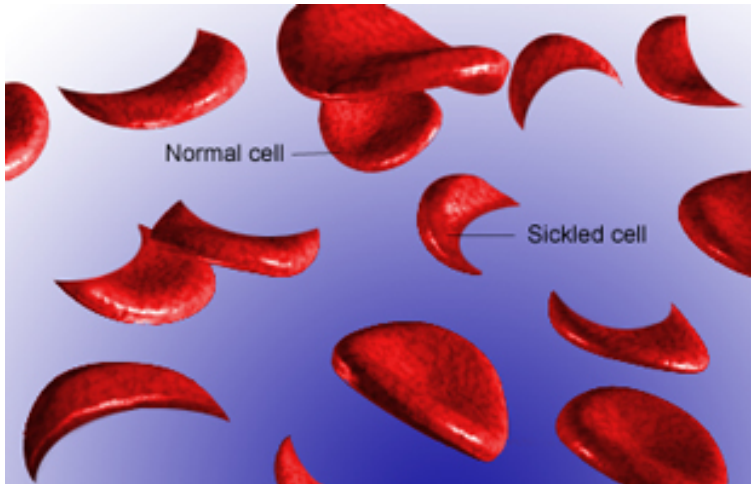
Sickle-cell Anemia

- Affects **hemoglobin** on **Red Blood Cell**
- Valine **replaces** glutamate as 6th amino acid in 1 of protein chains
- Red Blood Cell assumes a sickle shape

  -**Unable** to carry an adequate amount of O_2

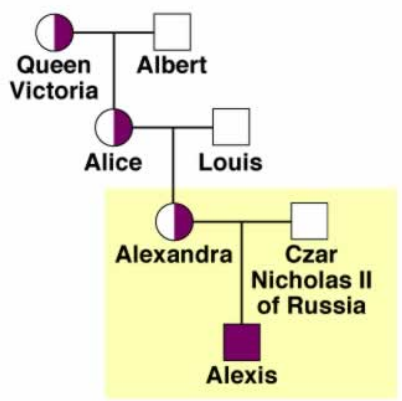
  -clog capillaries, starving body's tissues of O_2





Hemophilia

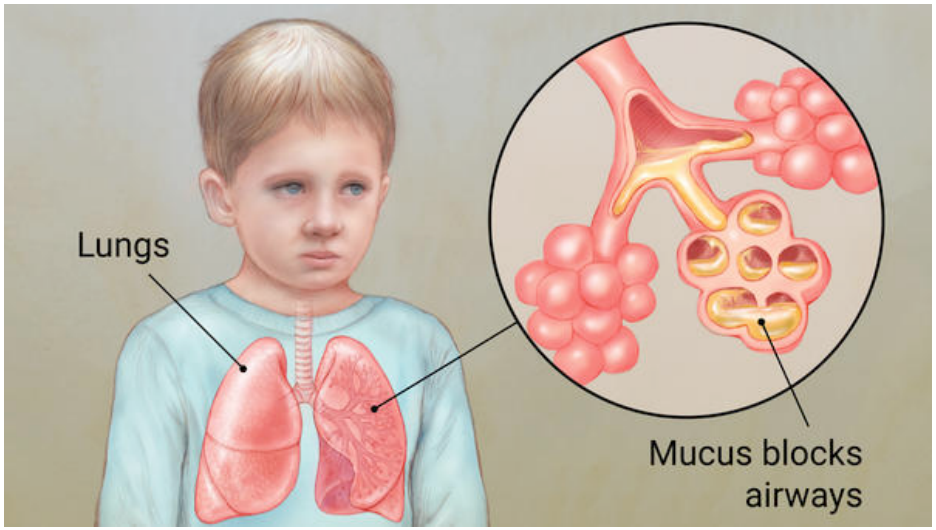
- **absence** of a certain protein, which is required for blood clotting
  - -Traced to a single defective gene



ALEXIS, SON OF CZAR NICHOLAS II OF RUSSIA, HAD HEMOPHILIA, A HEREDITARY DISEASE THAT IMPAIRS THE CLOTTING OF BLOOD. THE DISEASE PRIMARILY AFFECTS MALES AND HAS BEEN PASSED DOWN THROUGH MANY ROYAL BLOODLINES.

Cystic fibrosis

- **deletion** mutation
  - -Inability to produce a protein that regulates Cl^{1-} channels which regulate flow of mucus
  - -Lung secretions are thick and block airways



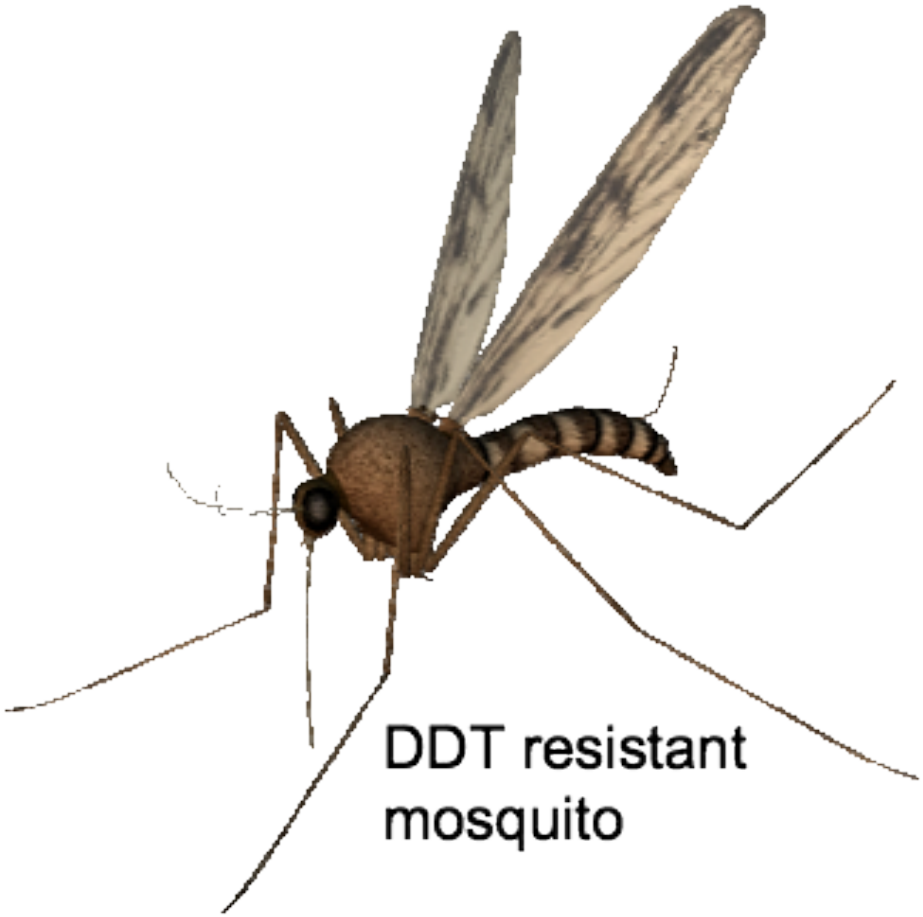
NEUTRAL Mutations

… no changes

BENEFICIAL Mutations

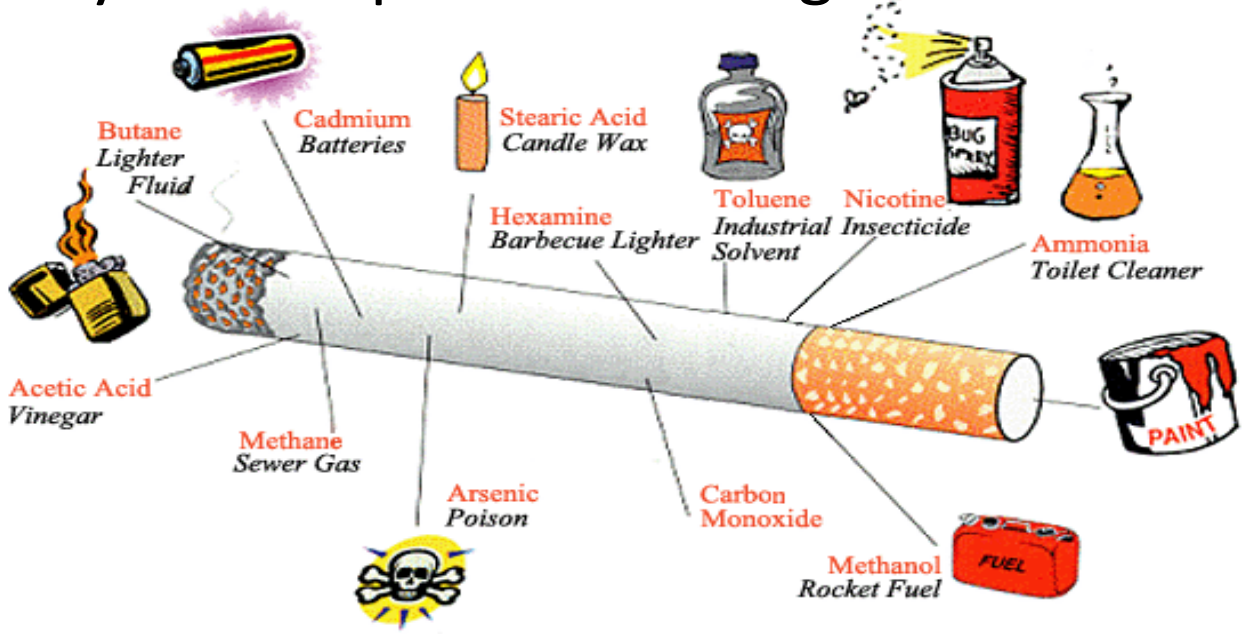
In Limone, Italy, some of its population have an extremely rare protein mutation shields people from cardiovascular disease.

BENEFICIAL Mutations



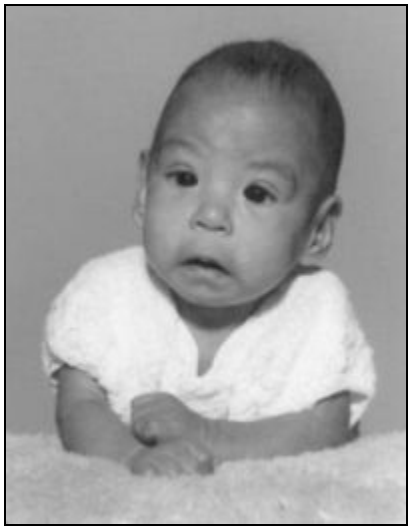
Mutations: CAUSES

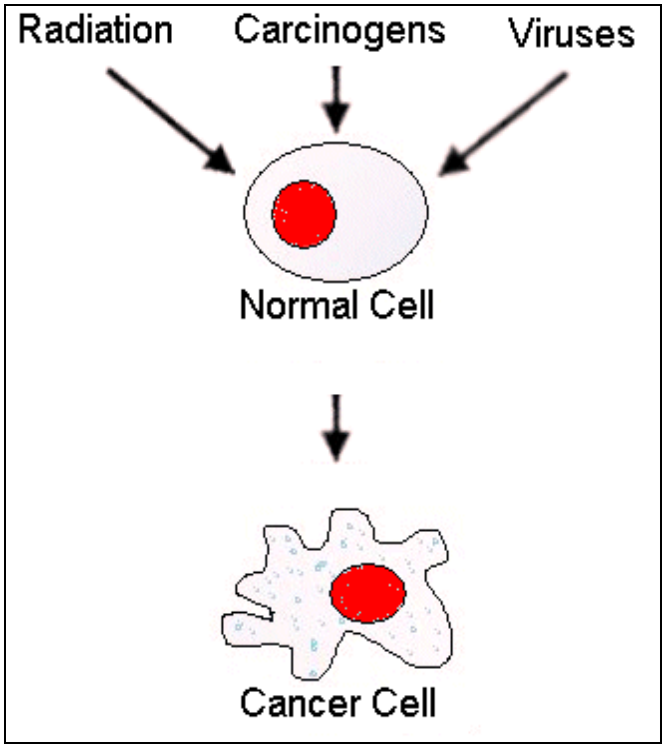
- Mutations can be spontaneous…OR… caused by mutagenic agents
- Radiation (ie. X-rays, UV radiation, Microwave radiation)
  - Do you fly a lot? Aviation workers are exposed to almost twice the radiation as a fuel – cycle worker in a nuclear power plant.
- Chemicals (eg. cigarette smoke, alcohol, drugs, pesticides, heavy metals etc.)
- micro-organisms (HPV, hepatitis virus can cause our immune system to produce mutagenic chemicals)



Mutations: CAUSES

- **MUTAGEN**: anything that causes **DNA to mutate**
  ex. radiation, chemicals, viruses (HPV), etc.
- **TERATOGENS**: mutagens that cross the placenta and **change the DNA of the developing embryo**
- **CARCINOGENS**: mutagens that cause **cancer cells** to form





MUTATIONS: CAUSES

My strange addiction (3 mins)

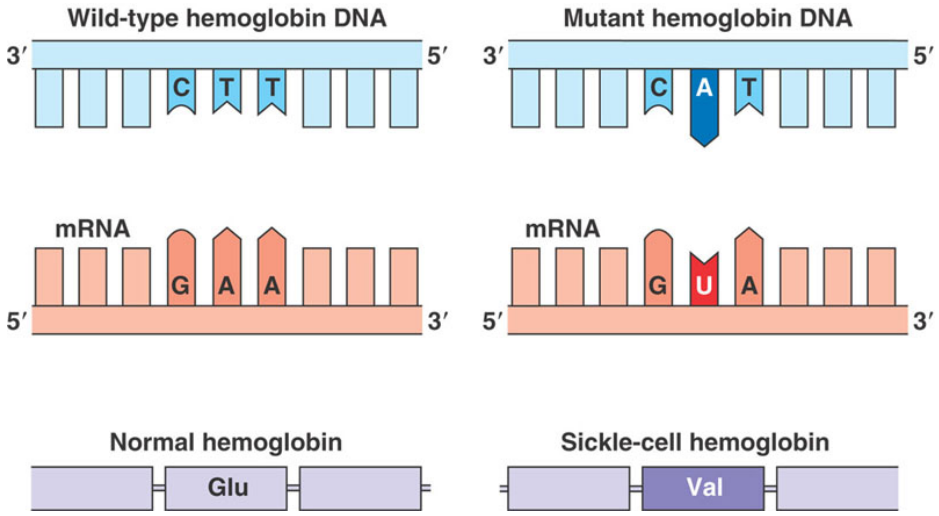
Using a tanning bed before age 35 increases you risk of skin cancer by 59%

MUTATIONS: 2 CATEGORIES

1

Point

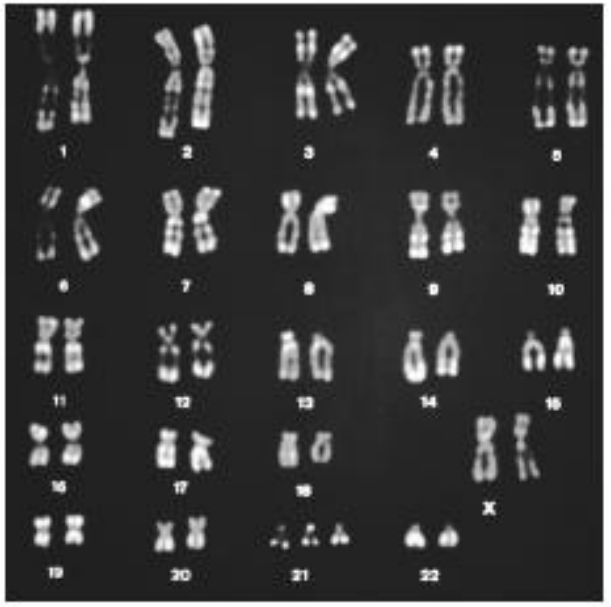
Changes in part of DNA



2

Chromosomal

Changes in structure Or number of chromosomes



Inheritable changes in DNA

Point Mutations

1. Arise from *mistakes in* replication which change the genetic code
2. An incorrect mRNA built using altered DNA as template
3. Ribosome reads wrong code and **builds wrong protein using wrong amino acid**
4. Most produce adverse effects but can also be a source of genetic variability

So basically, wrong proteins are built because of changes to the nitrogenous bases in DNA…

…but not always…
some mutations have have a neutral effect

POINT MUTATIONS

A.) POINT MUTATIONS

- Changes in a single base pair of a DNA sequence
- May or may not change the sequence of amino acids

TYPES of POINT MUTATIONS

i.) Same-sense (Silent) mutation

-No effect on operation of cell

-**No change in amino acid** coded for

ii.) Mis-sense mutation

-Results in a single **change of 1 amino acid** in the polypeptide (protein may still be usable)

iii.) Non-sense mutation

-premature STOP codon stops DNA sequence so protein **no longer functions**

-Often lethal to cell

POINT MUTATIONS

B.) GENE mutations

-Changes the amino acids specified by DNA sequence

TYPES

i.) Deletion – 1 or more nucleotides are removed from DNA sequence

-RESULTS in changes to the protein

ii.) Addition (insertion)

– Placement of an extra nucleotide in a DNA sequence

- **RESULTS** in different amino acids to be translated

iii.) Substitution

-a base is changed (eg) "C" to a "A"

(may or may not change the amino acid)

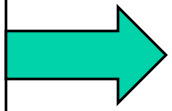
POINT MUTATIONS

Both insertions and deletions are:

Frameshift Mutations

Change in sequence base number results in a shift of the reading frame of codons (the genetic code is read wrong)

Example: "Sometimes the error may arise"



becomes "Someimest hee rrorm aya rise

Original DNA order: A**A**C CTG TGT

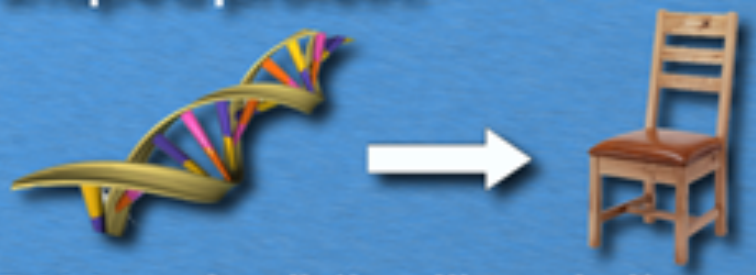
…if 1 base is taken out or added it changes the triplets…

With the "A" removed the codons are now…

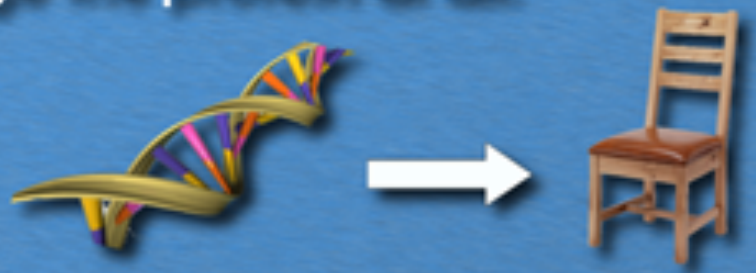
ACC TGT GT_

Genetic Mutations

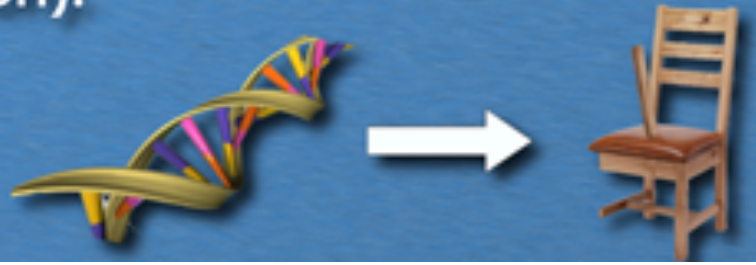
Suppose there is a strand of DNA that codes for a chair-shaped protein:



If that DNA got a "silent" mutation, it would not change the protein at all.



However, if a "missense" mutation occurs, a single portion of the protein's structure would change (which can massively alter the function).



In the case of a "nonsense" (or chain-termination) mutation, the translation into a chair would be stopped early, leading to an incomplete structure.

But a "frameshift" mutation turns the rest of the information into a completely different sequence, resulting in the creation of an entirely different protein.

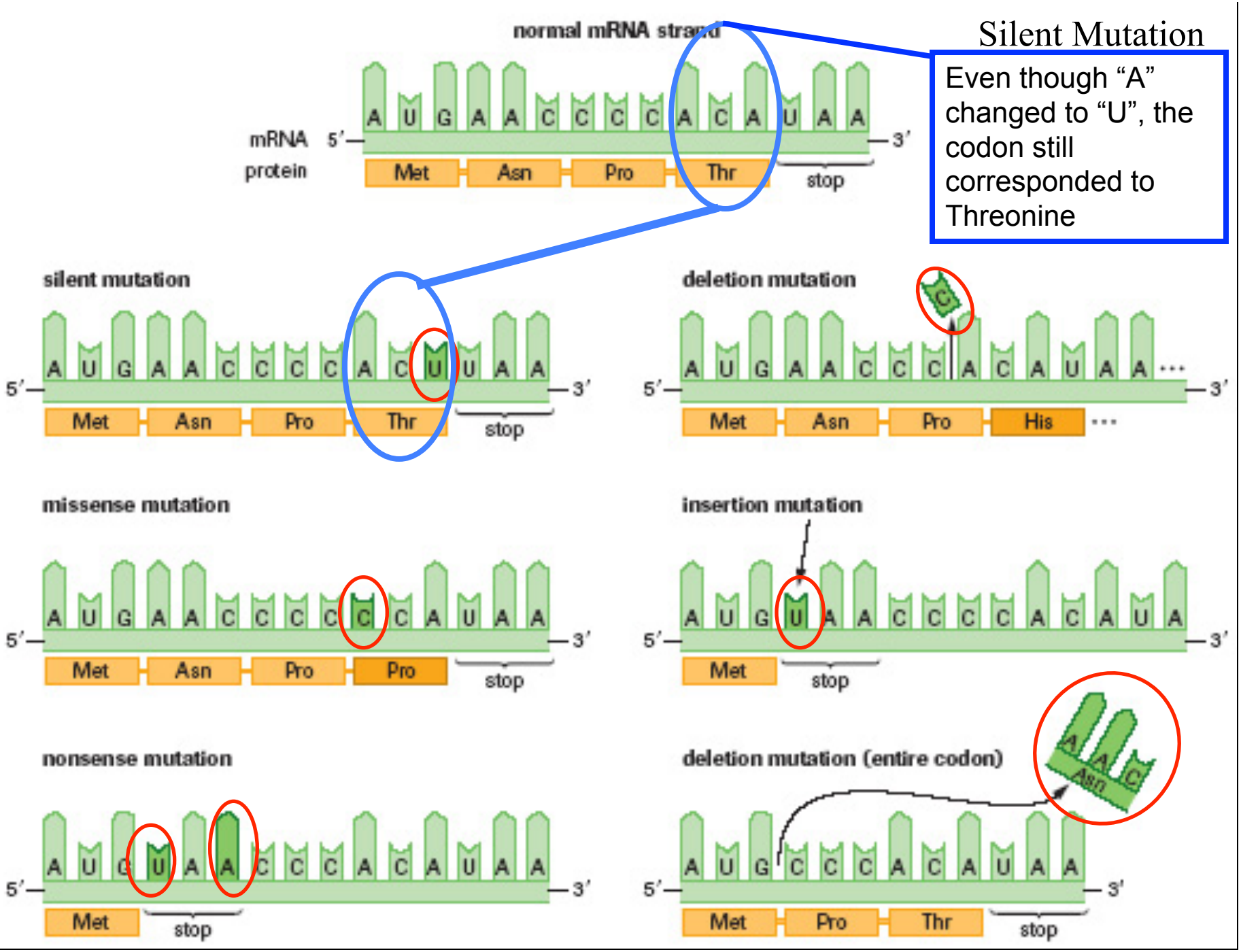
POINT MUTATIONS

Normal DNA Strand:	**AAC TCG ACC CGC**
Normal mRNA strand:	**UUG AGC UGG GCG**
Normal Amino Acids	**leu ser try ala**

Original DNA Strand:	AAC TCG ACC CGC
DELETION	AAC CGA CCC GC_
mRNA	UUG GCU GGG CG_
Amino acids	leu ala gly …

Original DNA Strand:	AAC TCG ACC CGC
ADDITION	ACA CTC GAC CCG C_ _
mRNA	UGU GAG CUG GGC G
Amino Acids	cys glu leu gly

Original DNA Strand:	AAC TCG ACC CGC
SUBSTITUTION	AAC TCT ACC CGC
mRNA	UUG AGA UGG GCG
Amino Acids	leu arg try ala


normal mRNA strand
mRNA
protein
5′
3′
A U G A A C C C C A C A U A A
Met Asn Pro Thr
stop
Silent Mutation
Even though “A” changed to “U”, the codon still corresponded to Threonine
silent mutation
A U G A A C C C C A C U U A A
Met Asn Pro Thr
stop
deletion mutation
C
A U G A A C C C A C A U A A
Met Asn Pro His
missense mutation
A U G A A C C C C C A U A A
Met Asn Pro Pro
stop
insertion mutation
A U G U A A C C C C A C A U A
Met
stop
nonsense mutation
A U G U A A C C C A C A U A A
Met
stop
deletion mutation (entire codon)
A A C
Asn
A U G C C C A C A U A A
Met Pro Thr
stop

LETS DO SOME EXAMPLES

Using the following DNA sequence, write a new DNA sequence that would result from each type of point mutation. Show the corresponding polypeptide. Are they non-sense, same-sense or mis-sense?

DNA: AAT CGG CTC AAC GGT AAA

Substitution

New DNA Sequence

mRNA

Polypeptide

Type of mutation:

Addition

New DNA Sequence

mRNA

Polypeptide

Type of mutation:

LETS DO SOME EXAMPLES con't…

DNA: AAT CGG CTC AAC GGT AAA

Deletion

New DNA Sequence

mRNA

Polypeptide

Type of mutation:

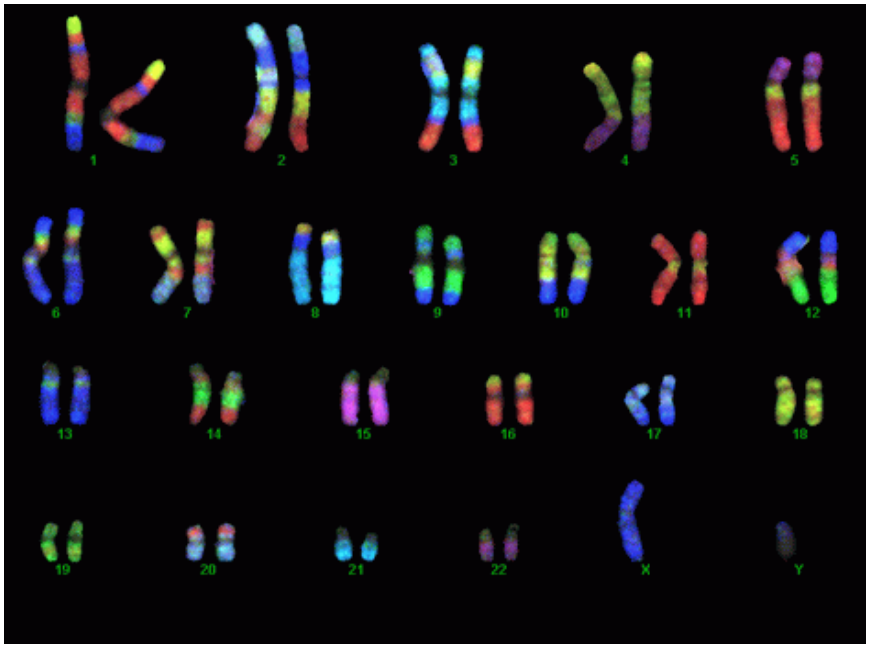
2/3 of Cancers Caused by Bad Luck

http://www.cbc.ca/news/health/two-thirds-of-cancers-caused-by-bad-luck-not-heredity-environment-1.2888125

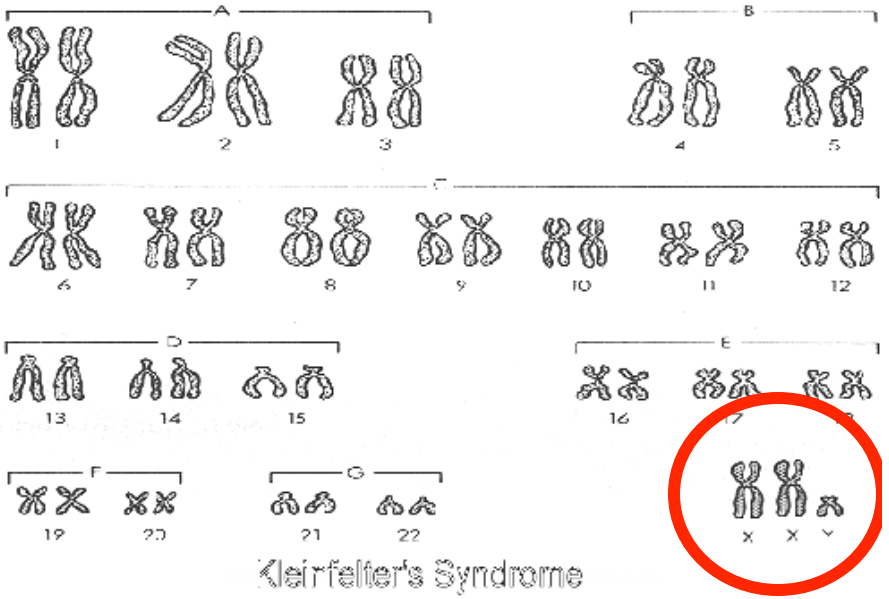
Chromosomal Mutations

- Changes in **structure** and/or **number** of chromosomes
- Normal number of chromosomes in each human cell is 46 (23 pairs and 2n = 46)

These chromosomes are all taken from a **2n** cell



Vs



Karyotyping

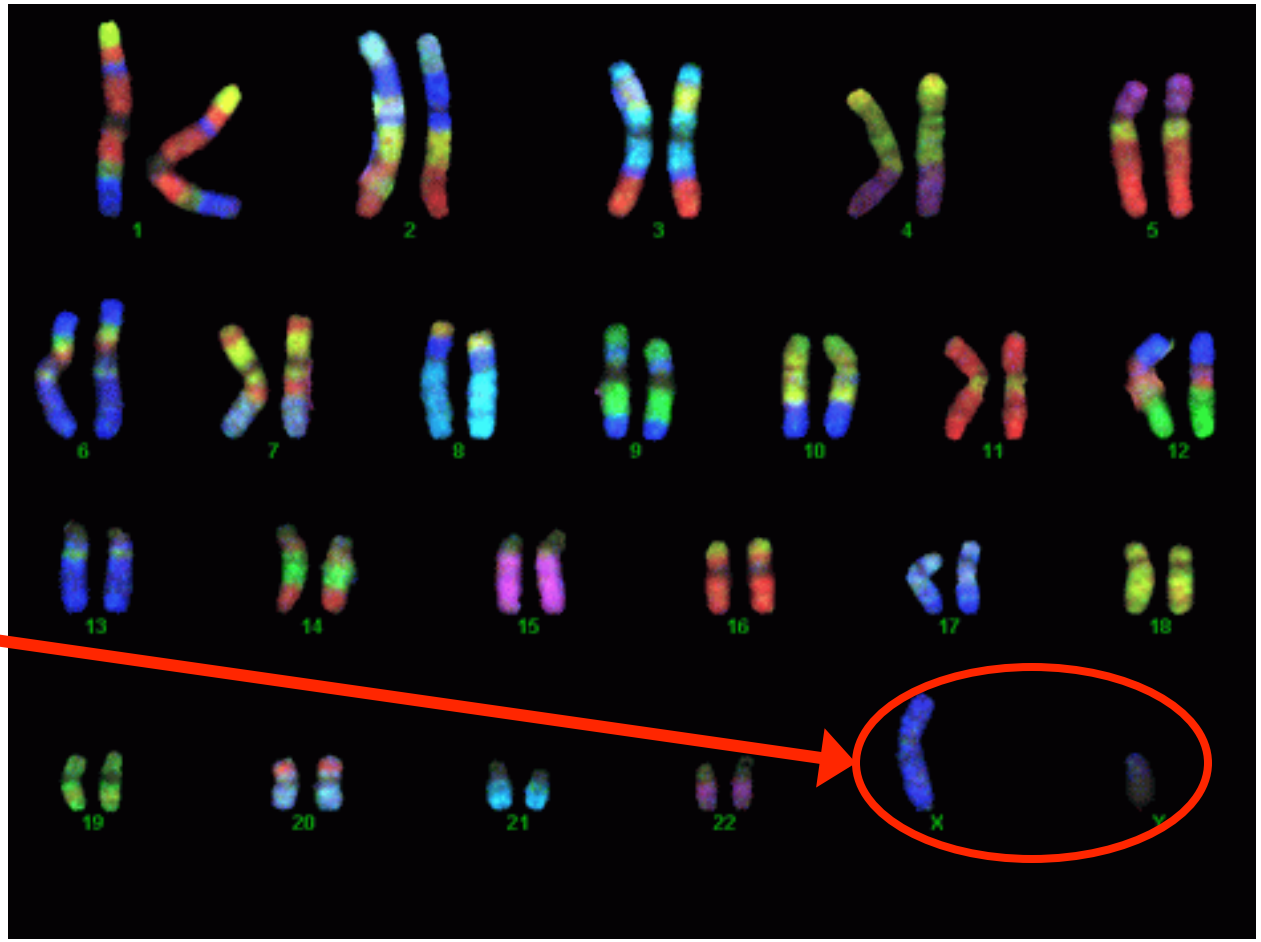
- Used for detecting chromosomal abnormalities (mutations)
- Chromosomes are organized according to 3 characteristics

1) centromere position

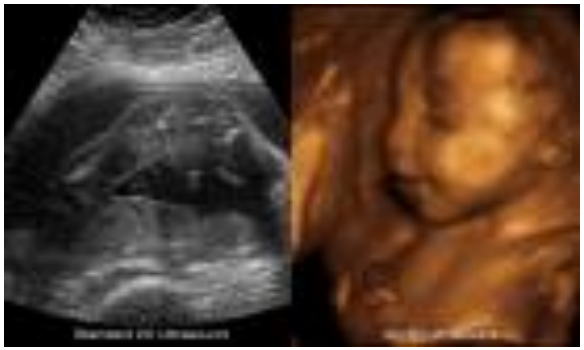
2) , banding pattern

3) Size,

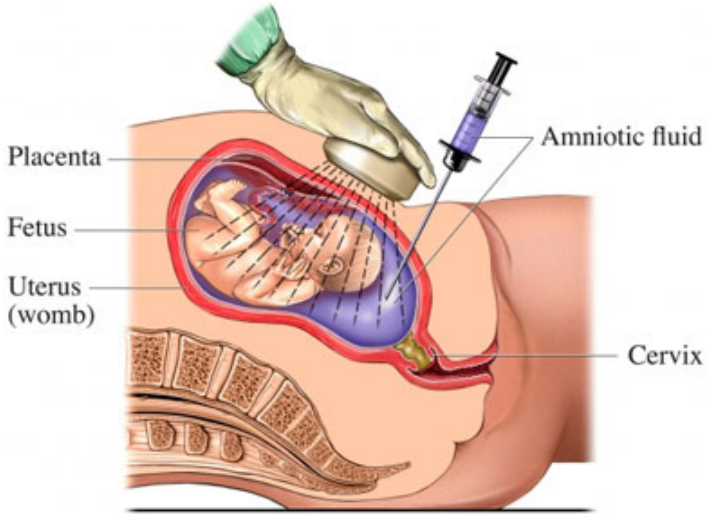
Sex?



Cells for karyotypying



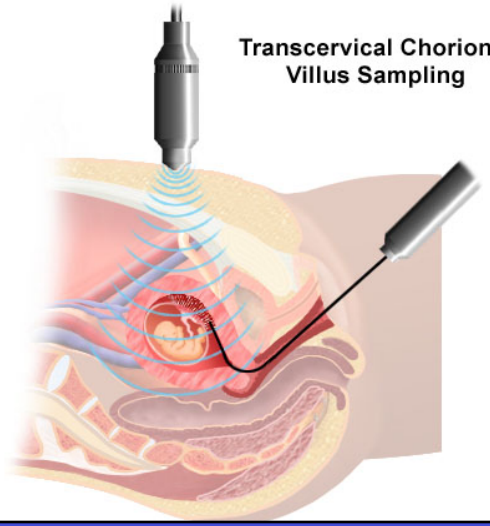
Ultrasound locates position of fetus



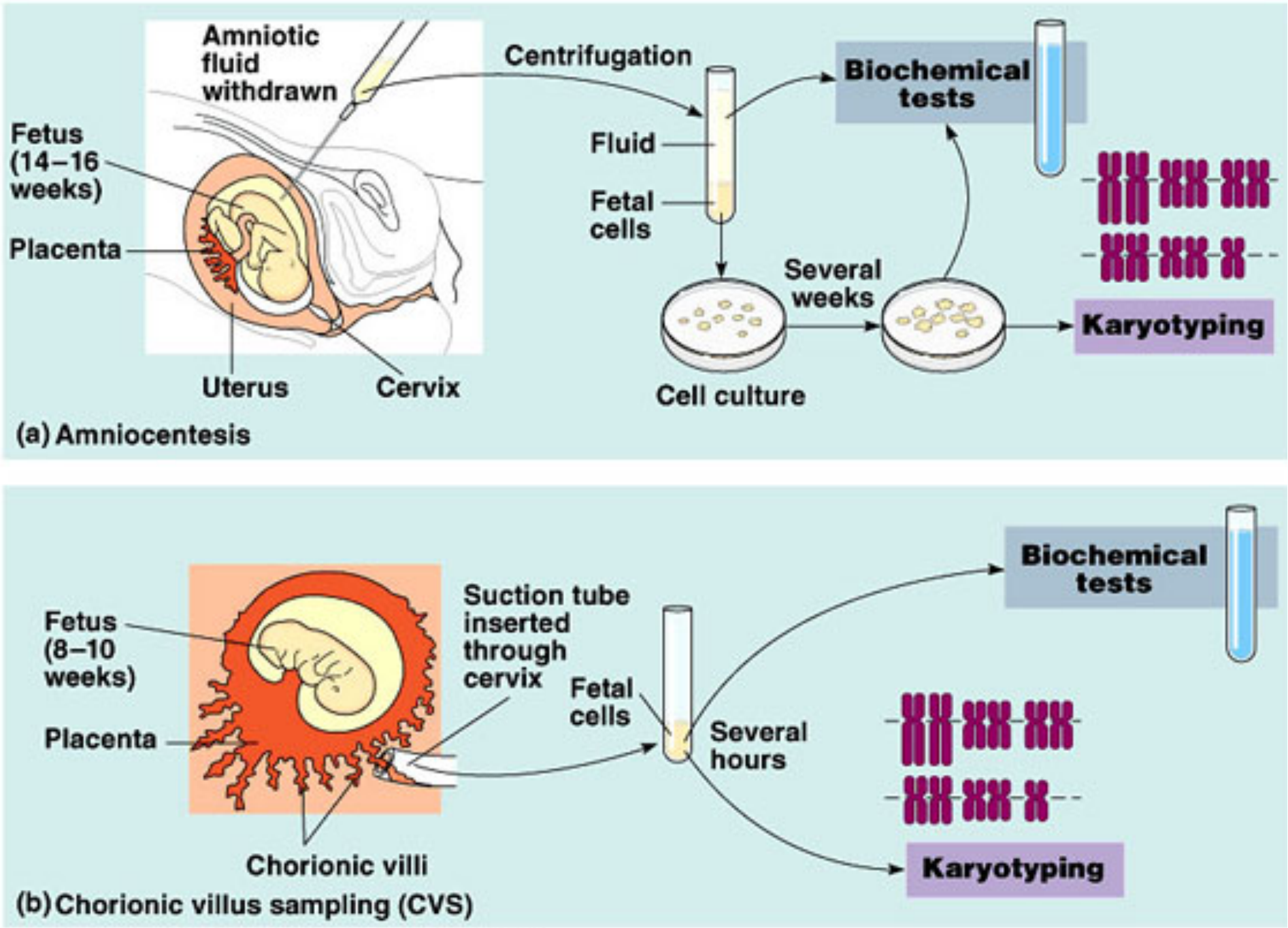
Chorionic Villus Sampling (CVS)

draws cells from outer membrane of embryo

- CVS can be used as early as 8 weeks of pregnancy



Amniocentesis uses a needle to withdraw some amniotic fluid from around fetus in the uterus.



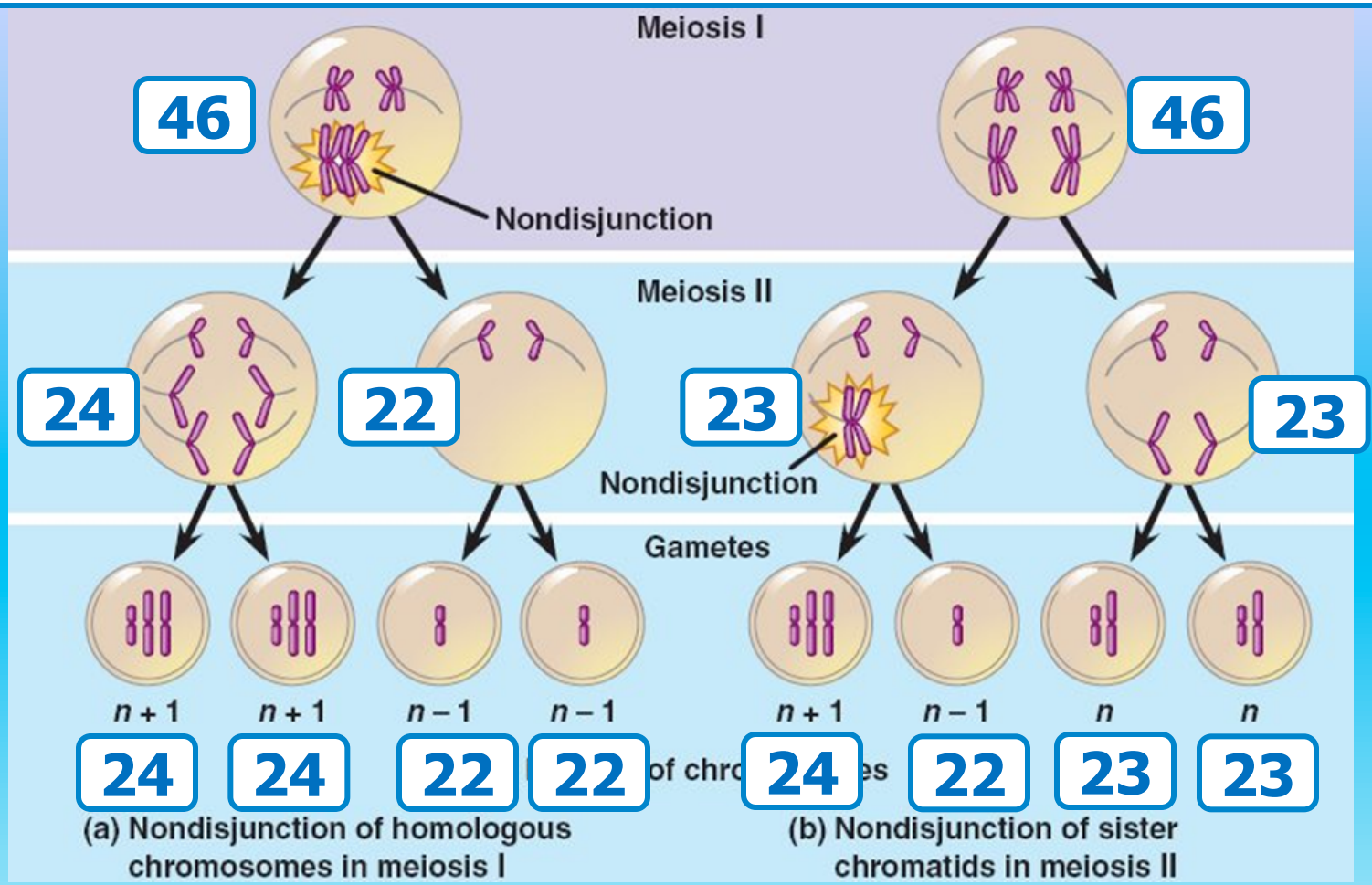
How do we prepare a Karyotype

1. Blood is centrifuged to separate out blood cells
2. WBC'c are transferred & treated to stop cell division
   - Which stage would we observe the cell? **PROPHASE**
3. Sample is fixed, stained and spread on a microscope slide
4. Slide of 2n cells is examined
5. Chromosomes are photographed
6. Computers are used to arrange chromosomes into pairs

Abnormal Meiosis

- **Chromosomal abnormalities result when chromosomes and chromatids do not separate as they should during meiosis**
  - **This is called nondisjunction**
- **Nondisjunction can occur at 2 times:**
  1. **Anaphase I** - homologous chromosomes move to the same pole
  2. **Anaphase II** – sister chromatids don't separate and move to the same pole

In humans, diploid number is 46 and haploid number is 23.



Non-disjunction

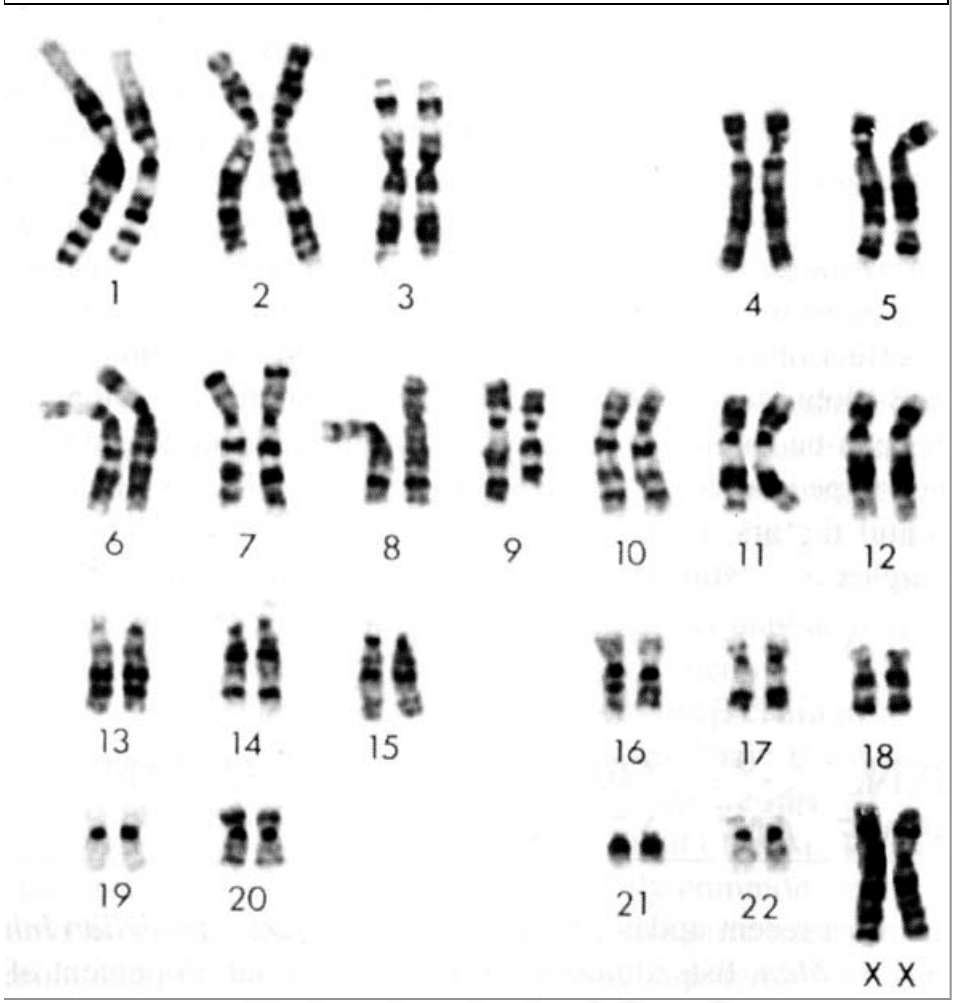
- **Normal gametes have 23 chromosomes**
  - **Abnormal gametes form when there is either one more (24) or one less (22)**

- **Trisomy – three homologous chromosomes (47 chromosomes total)**
  - **Ex. Down's Syndrome: trisomy of chromosome #21**

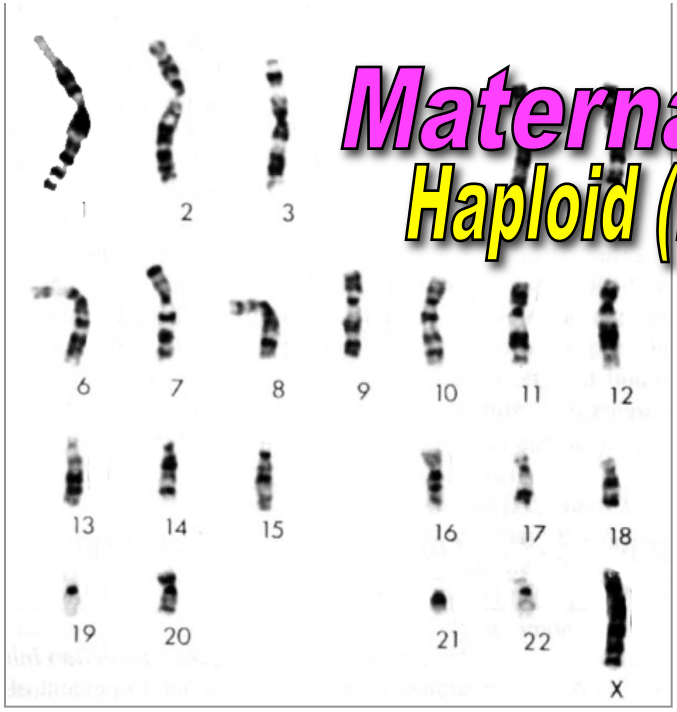
- **Monosomy – a single chromosome instead of a homologous pair (45 chromosomes in total)**
  - **Ex. Turner's syndrome: monosomy of chromosome # 23 (XO)**

NORMAL KARYOTYPES

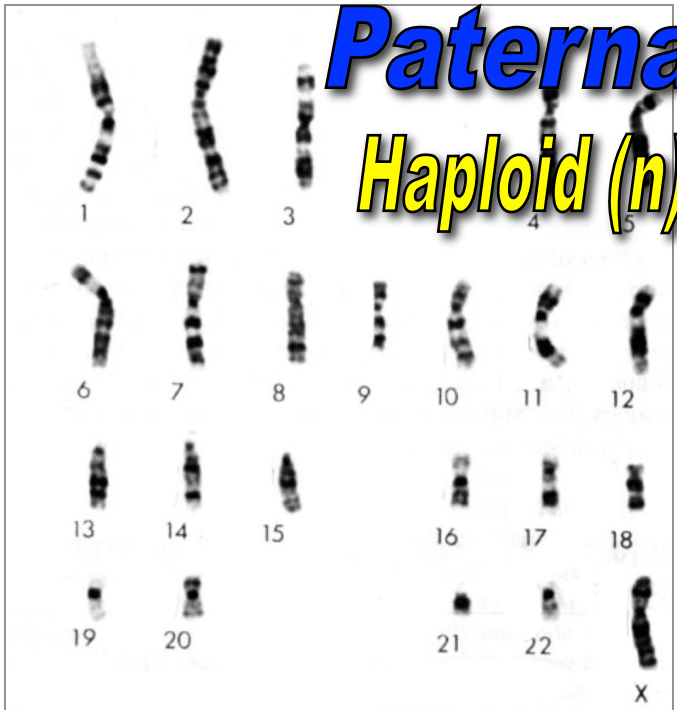
23 from each parent (46 total)



Diploid (2n)



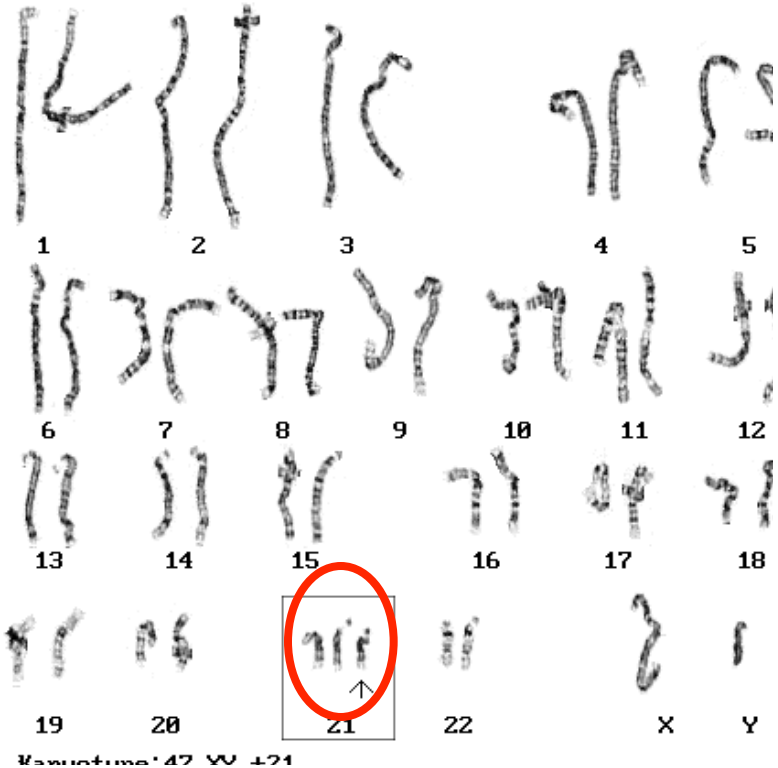
Maternal
Haploid (n)

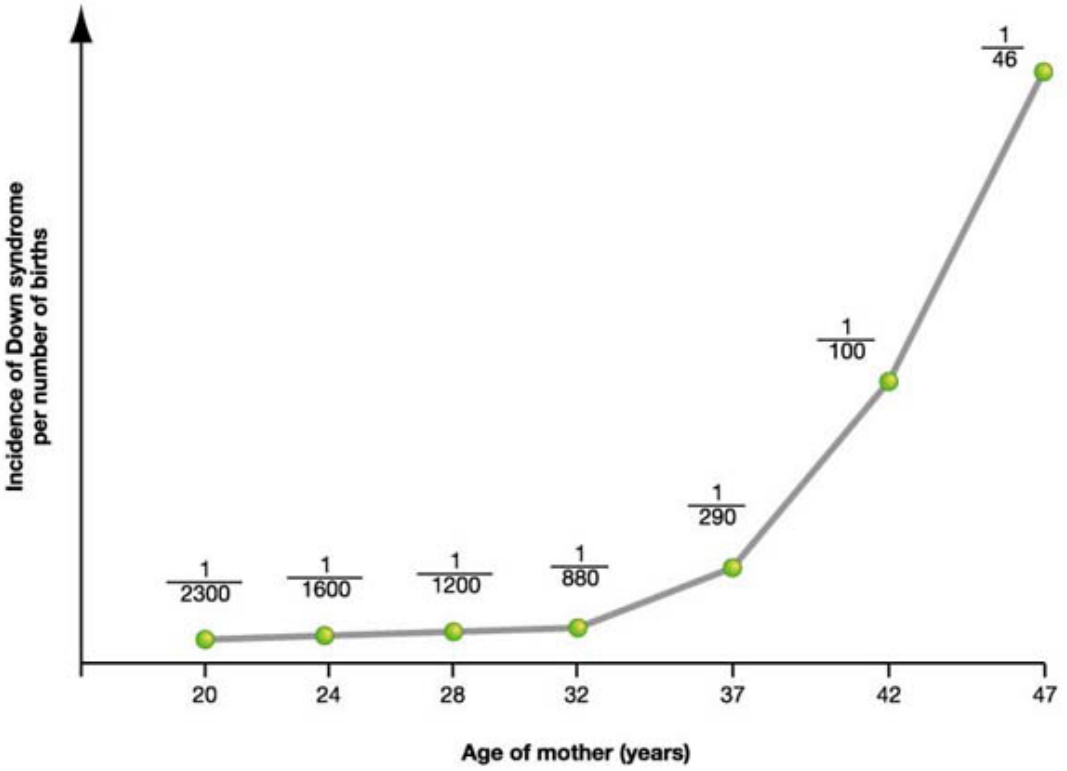


Paternal
Haploid (n)

Down Syndrome

-Also known as **trisomy 21** – 3 of chromosome 21
-47 chromosomes in each cell
-1 in 800 babies have Down syndrome
- Incidences increase as mothers age increases
- Exposure to **radiation** results in increased chance of Down syndrome
- Lower mental ability, physical growth delays, facial difference

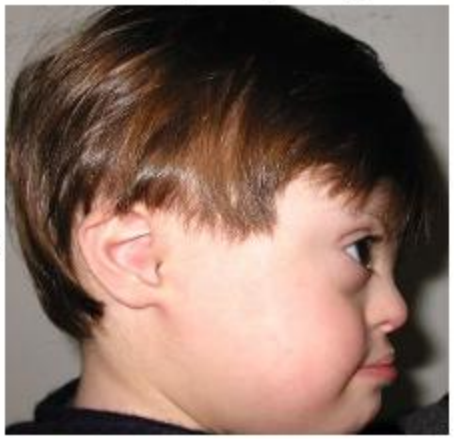




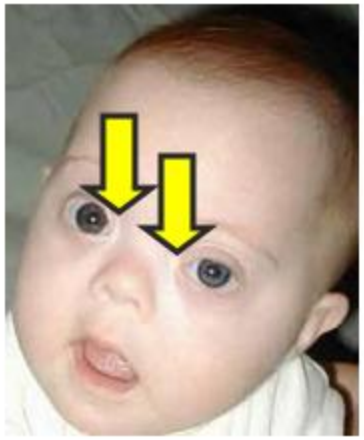
Down Syndrome
Features

Upslanting palpebral fissure

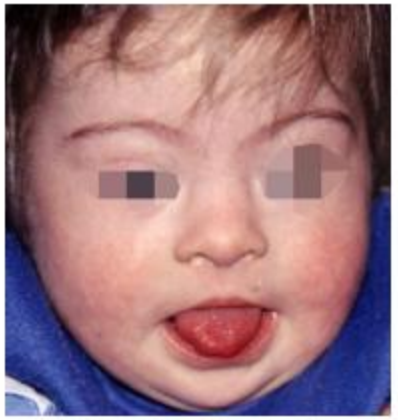
Brachycephaly



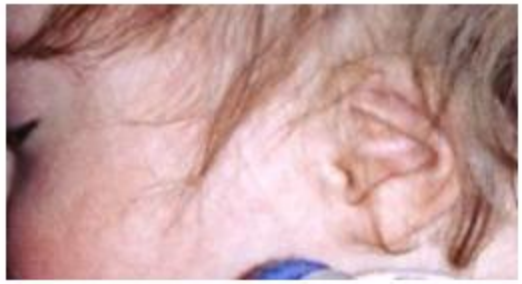
Flat nasal bridge, hypoplastic maxilla



Epicanthus

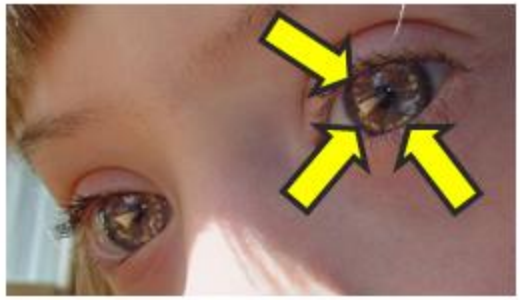


Macroglossia, glossoptosis

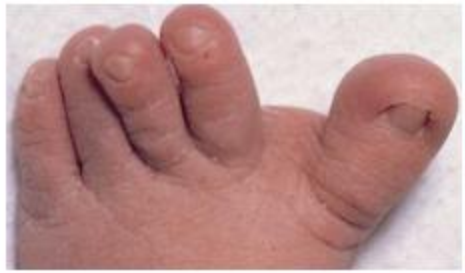


Microtic, low-set ears

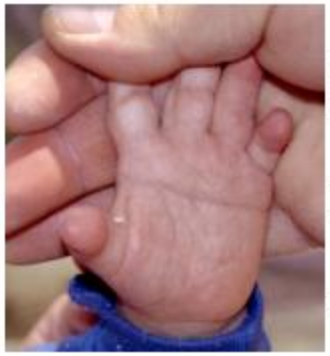
(Dourmishev, 2009)



Brushfield spots

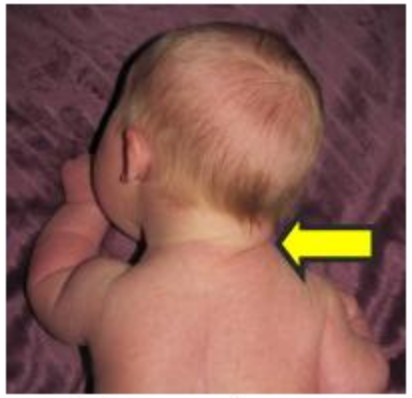


Sandal deformity



Simian crease

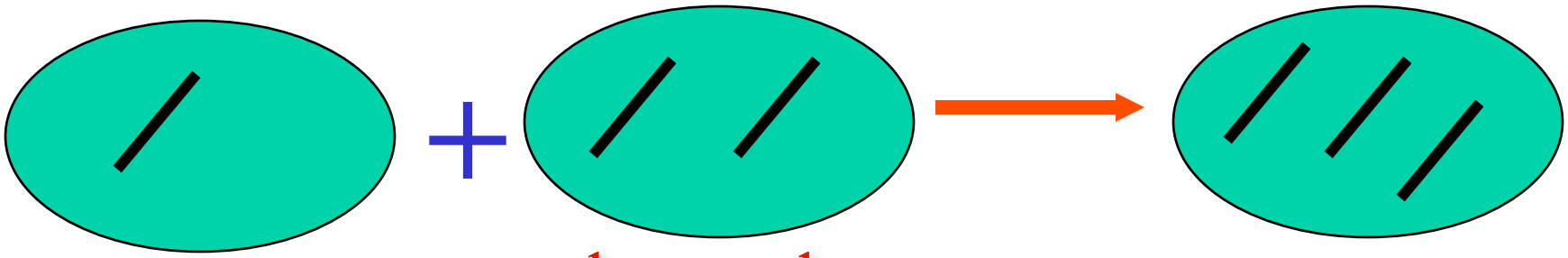
(Dourmishev, 2009)



Excessive nuchal folds

Down Syndrome

- 2 #21 chromosomes fail to separate (they head to the same pole) during anaphase I or II
- Happens in production of one gamete …sperm or egg....not both
- One gamete ends up with 2 # 21's

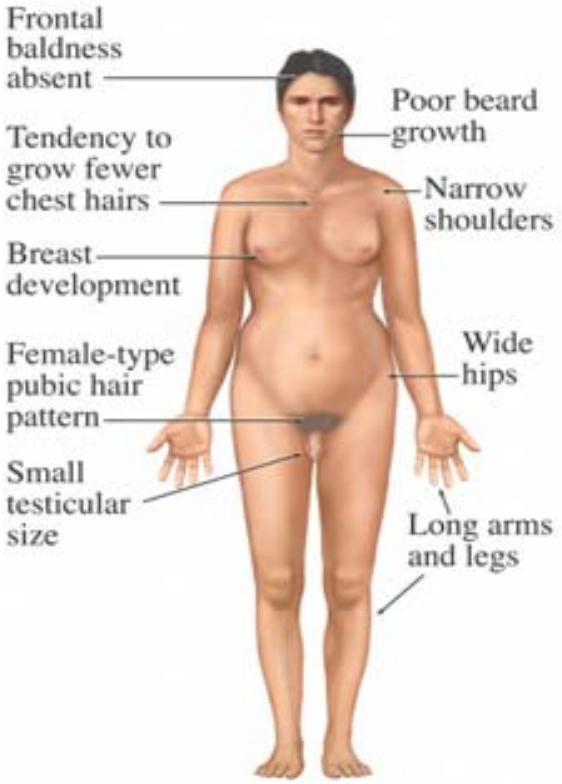


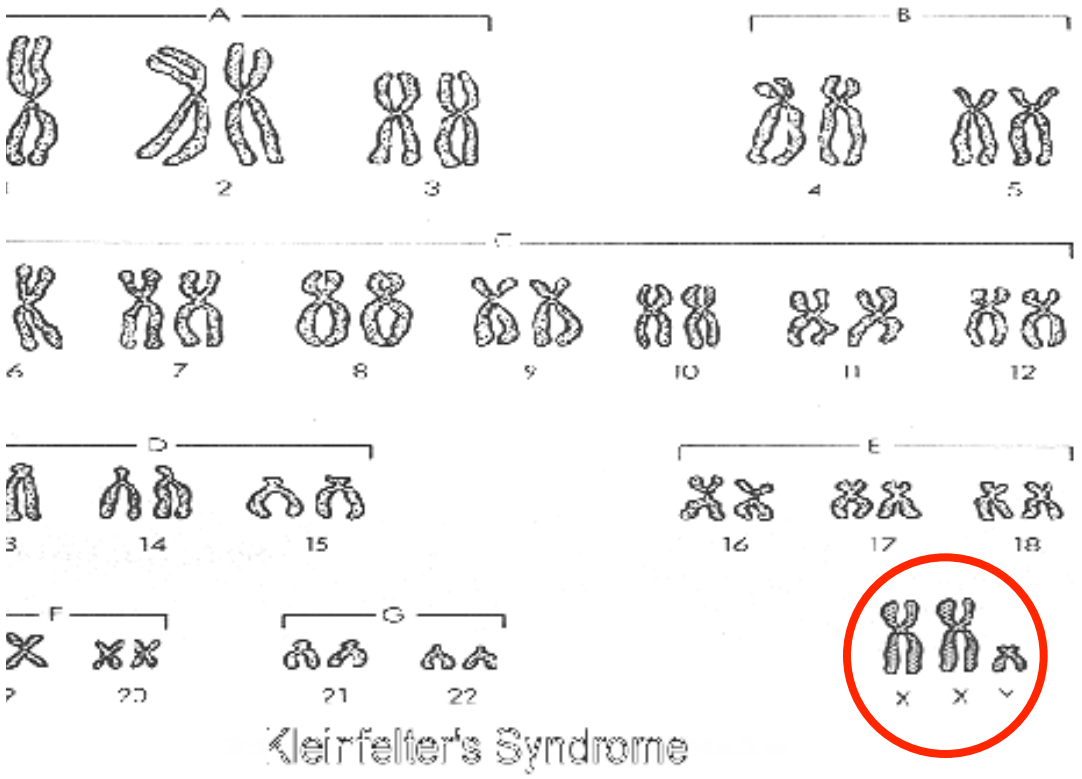
normal gamete with a single 21

abnormal gamete with 2 #21's

3 #21's

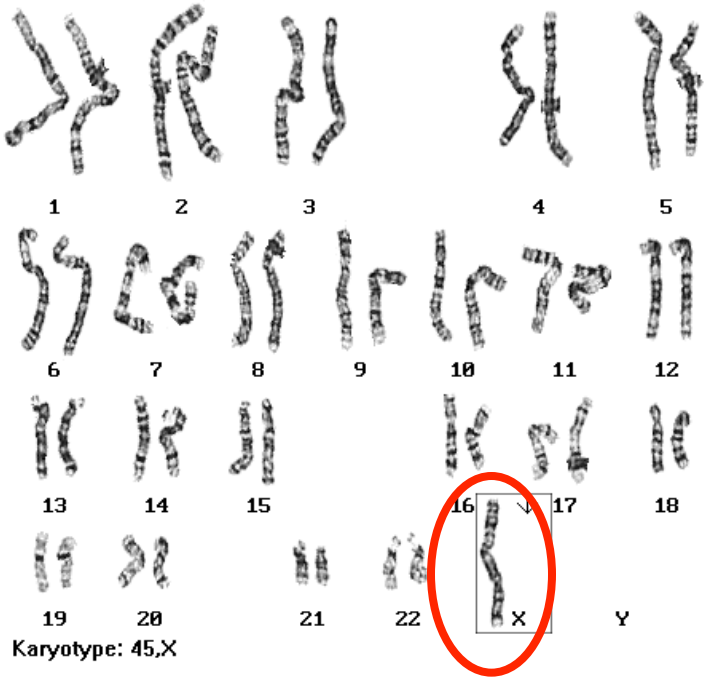
Klinefelter Syndrome - XXY



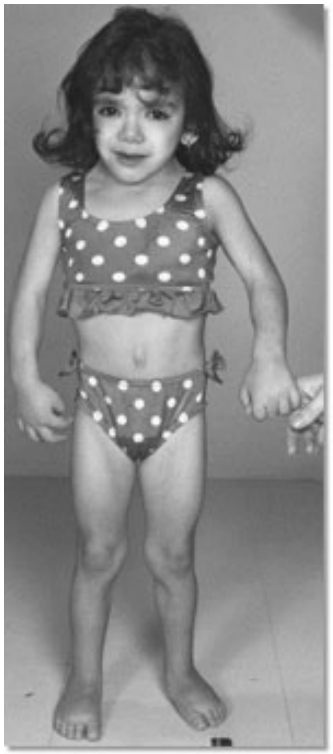


- Due to nondisjunction in the sperm or egg
- one gamete contains 2 X's, other contains only a Y (this is the normal one)
- Male at birth, but sterile and produce female hormones
- 1 in 10000 births

Turner's Syndrome - XO



1 in 10000 births



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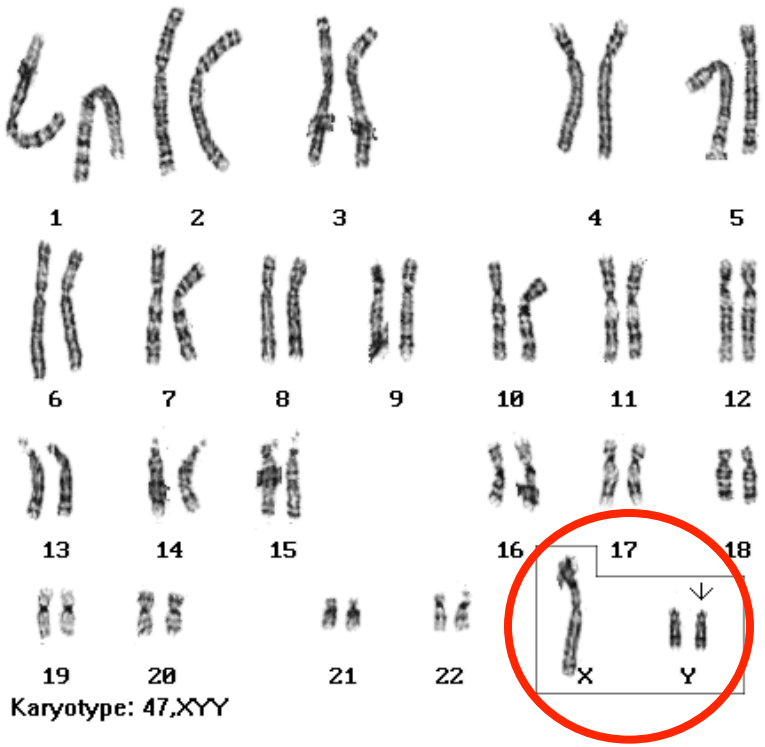
- Female only has **1 X chromosome**
- Due to nondisjunction during egg formation
- One egg gets both X chromosomes, other egg gets no X chromosome

Jacobs Syndrome - XYY



- "Supermale" due to two Y chromosomes
- Male, mostly normal
- Sometimes excess acne, very tall
    - Sometimes more aggressive

Variables Review

Manipulated variable the component or variable of the experiment we change or 'manipulate'. The thing being tested

Responding variable

the component of the experiment we plan to measure (the results)

Controlled variables the component(s) or variable(s) the experimenter keeps the same

1. A scientist wanted to see if nicotine causes cancer, so he exposed some bacterial cells growing on agar in a petri dish to nicotine and then tested to see if they had uncontrolled growth. He compared these cells to bacterial cells growing on agar in a petri dish that were not exposed to nicotine.

Manipulated variable nicotine

Responding variable – growth of bacteria

Controlled variables type of bacteria

time

temperature

Type of agar