Non-Disjunction, Aneuploidy & Abnormalities in Chromosome Structure

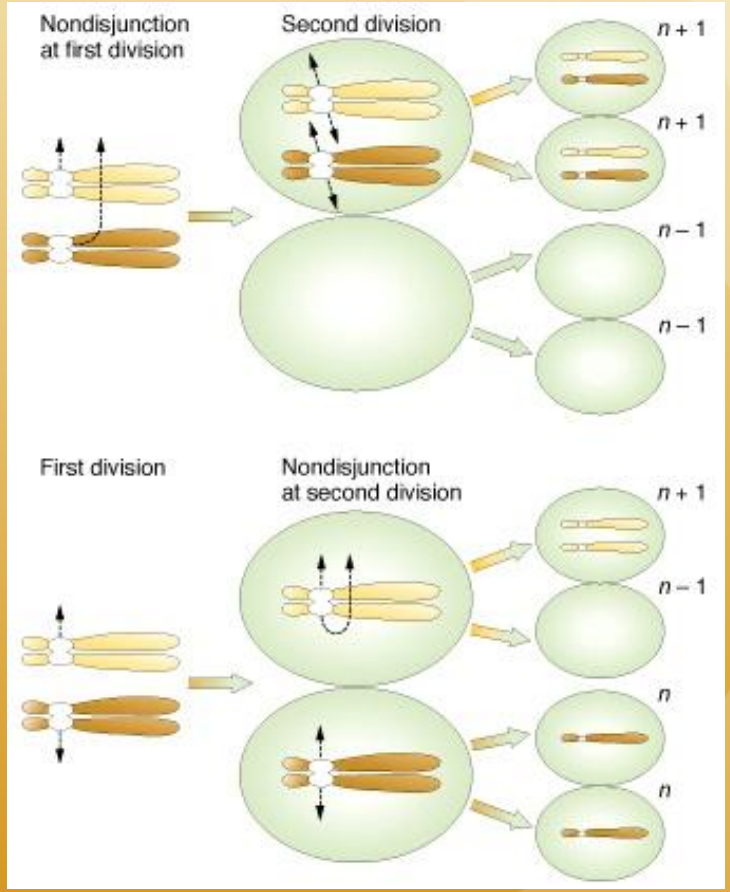
Packet #16

Introduction I

- Ploidy
  - Degree of repetition of the basic number of chromosomes
    - Diploidy
      - Chromosomes repeat 2X
        - Remember, in humans, you have one copy of a chromosome from the maternal father and one from the maternal mother
- Euploidy
  - "True" ploidy
    - In the case of somatic human cells, euploidy occurs when the cell is diploid.

Aneuploidy

- "Not True" ploidy
  - Having too many or too few chromosomes.
- Non-Disjunction
  - An event that occurs occasionally during meiosis in which a pair of chromosomes fail to separate so that the resulting germ (sex) cell has either too many or too few chromosomes

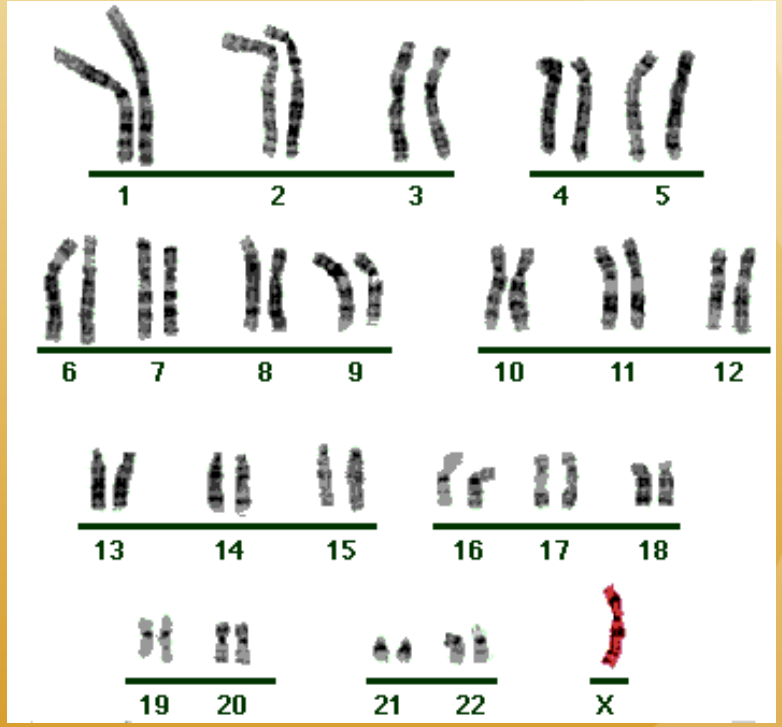


Genetic Disorders Caused by Sex Chromosome Aneuploidy

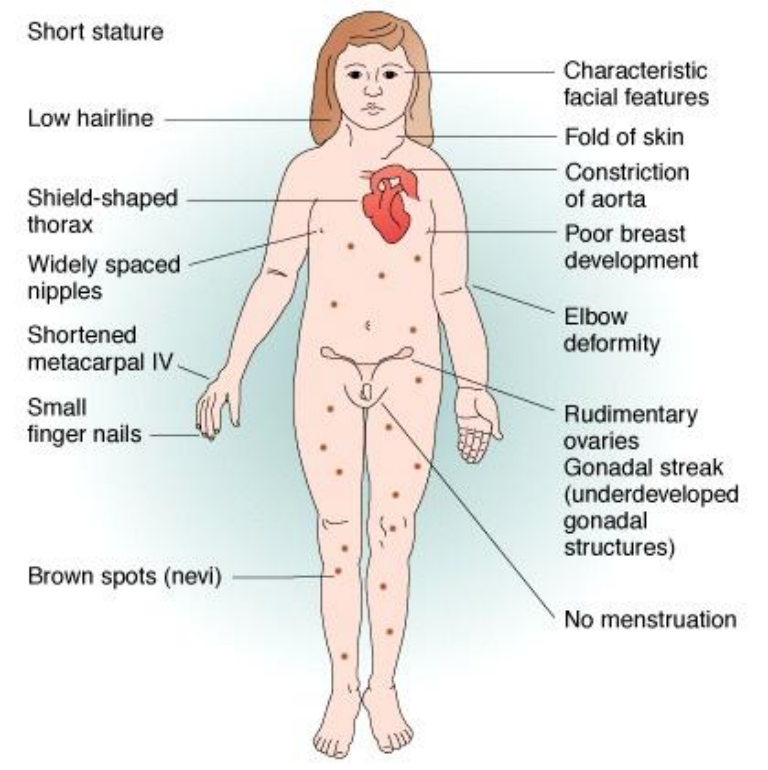
Sex Chromosome Aneuploidy

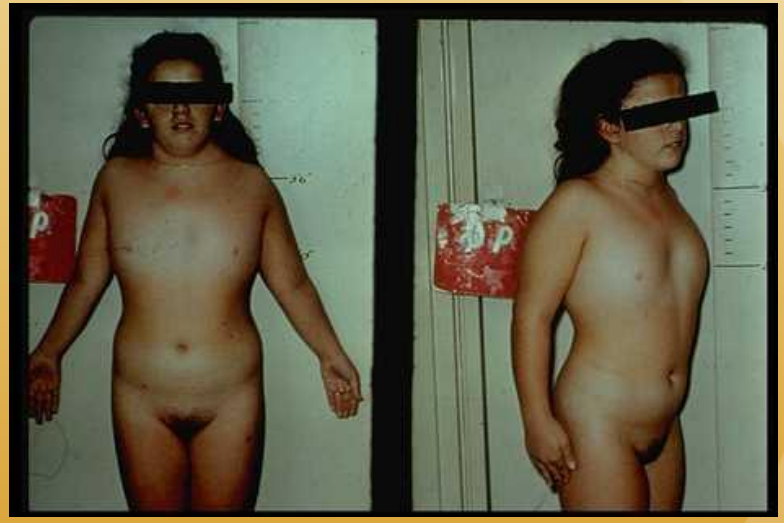
Turner Syndrome

- 2n - 1
  - 45 XO
    - 44 autosomes + 1 X chromosome
      - There is the absence of a sex chromosome
- Female in appearance but their female sex organs do not develop at puberty and they are sterile
- Short in stature; swelling; broad chest; low-set ears; webbed necks
- Shows normal intelligence but some cognitive functions are defective
  - Difficulties in mathematics and memory
- 1 in 5000 female births show Turner Syndrome



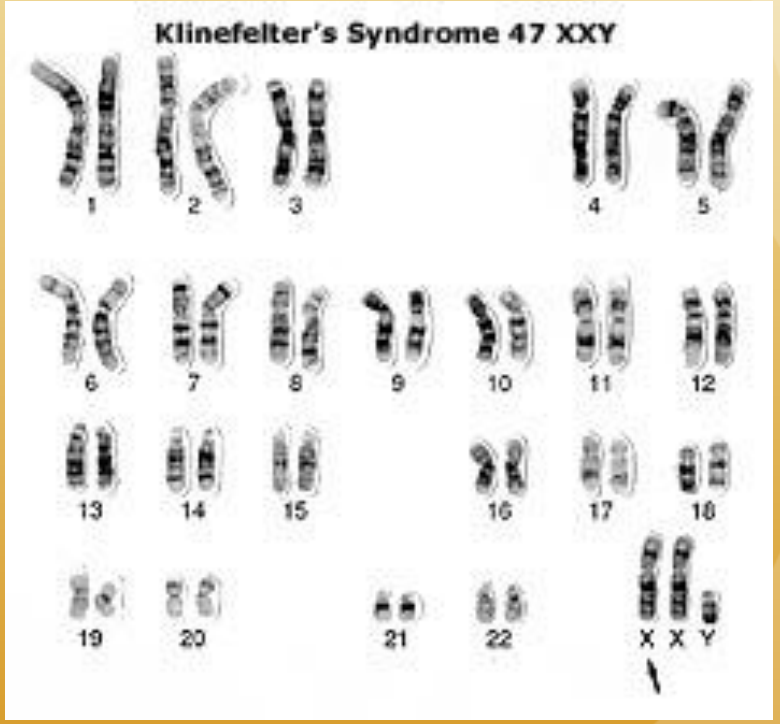
Turner Syndrome II



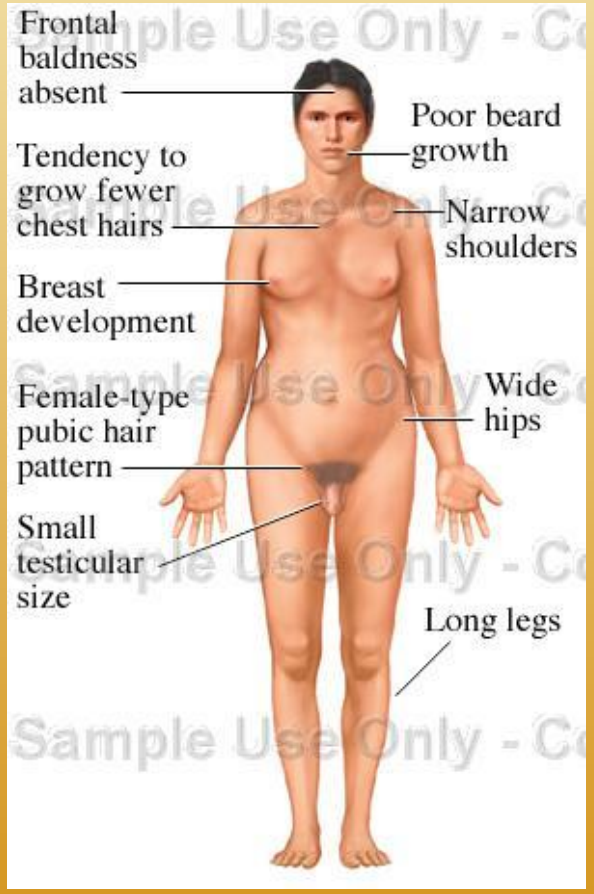


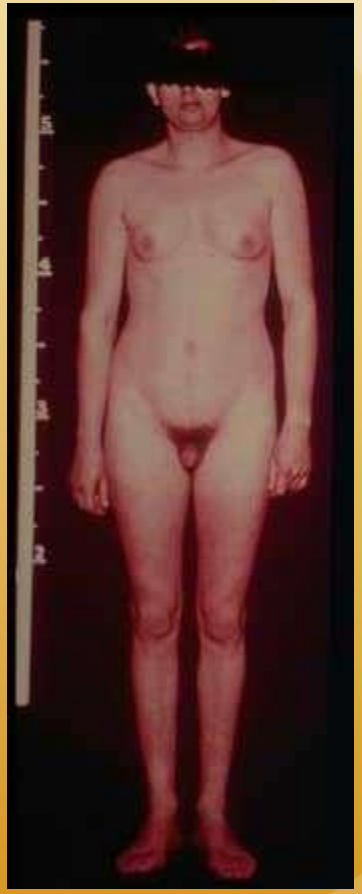
Klinefelter Syndrome

- 2n + 1
  - 47 XXY
    - 44 autosomes + 3 sex chromosomes
      - There is an extra X chromosome
- Male in appearance and they too are sterile
- Female type pubic hair pattern
- May have breast development

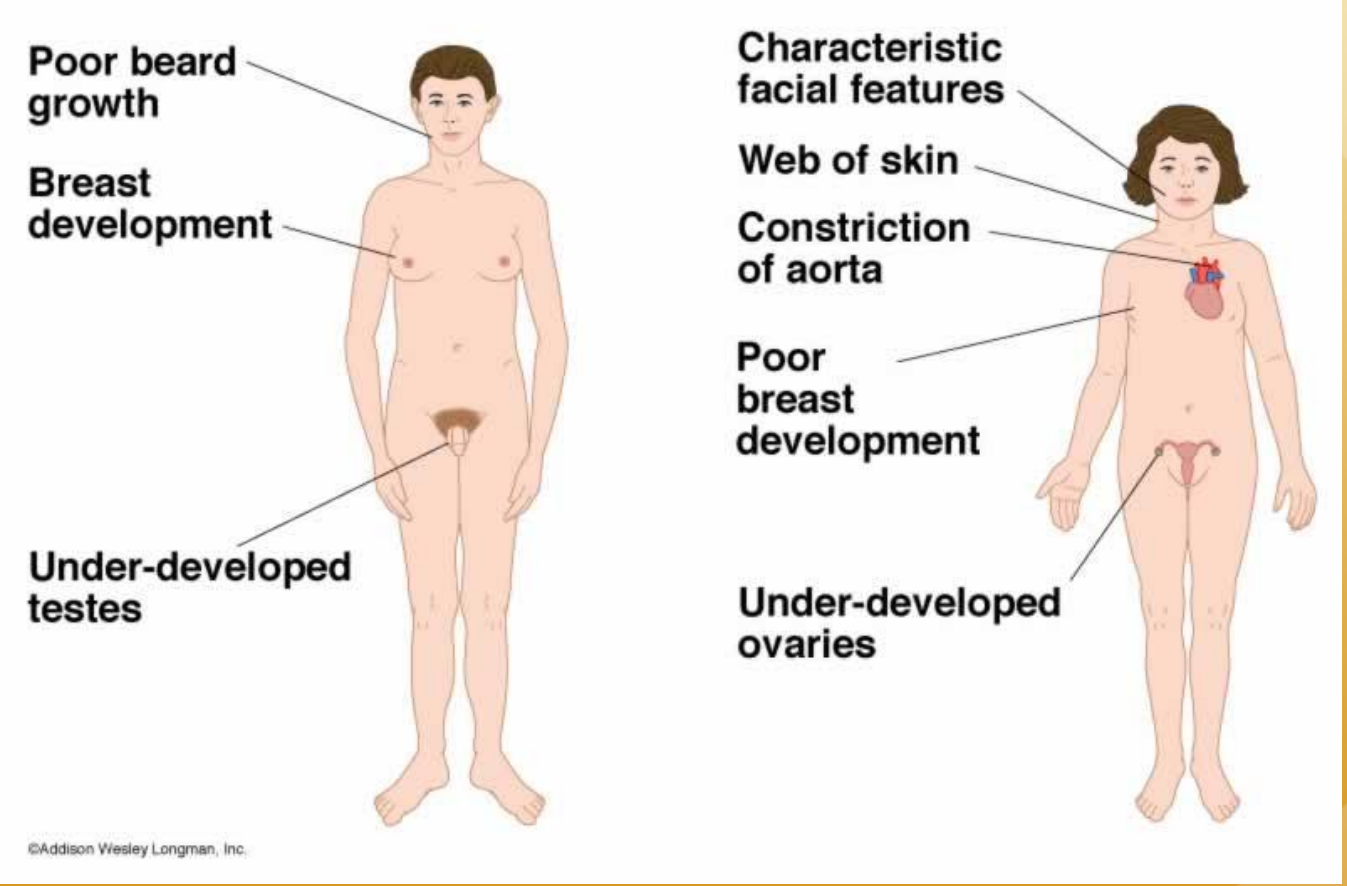


Klinefelter Syndrome II





Comparison of Turner & Klinefelter Syndromes

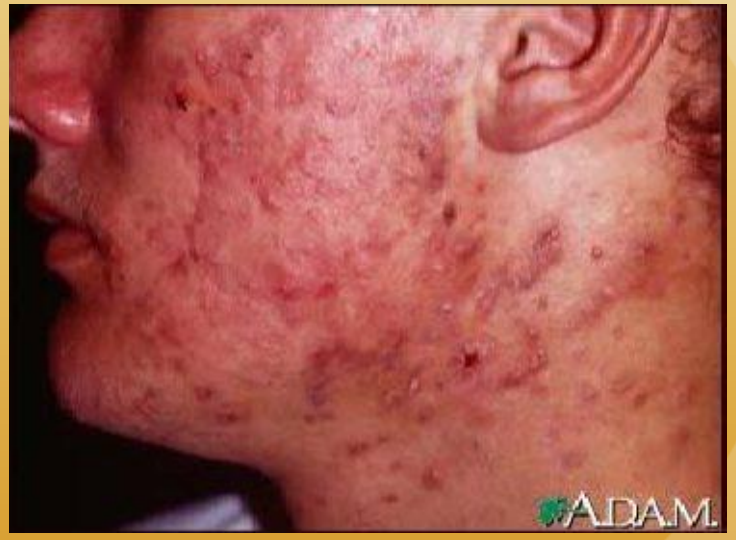


Jacob's Syndrome (YY Syndrome)

XYY

1/1000 newborn boys

- Tall and thin males
- Males have normal sexual development and are able to create normal gametes.
- Increased risk of learning disabilities and delayed speech and language skills.
- In some cases, individuals develop behavioral problems such as explosive temper, hyperactivity, impulsivity, defiant actions, or, in some cases, antisocial behavior.
- After age of 35, extra Y chromosome often degenerates and is not passed onto offspring

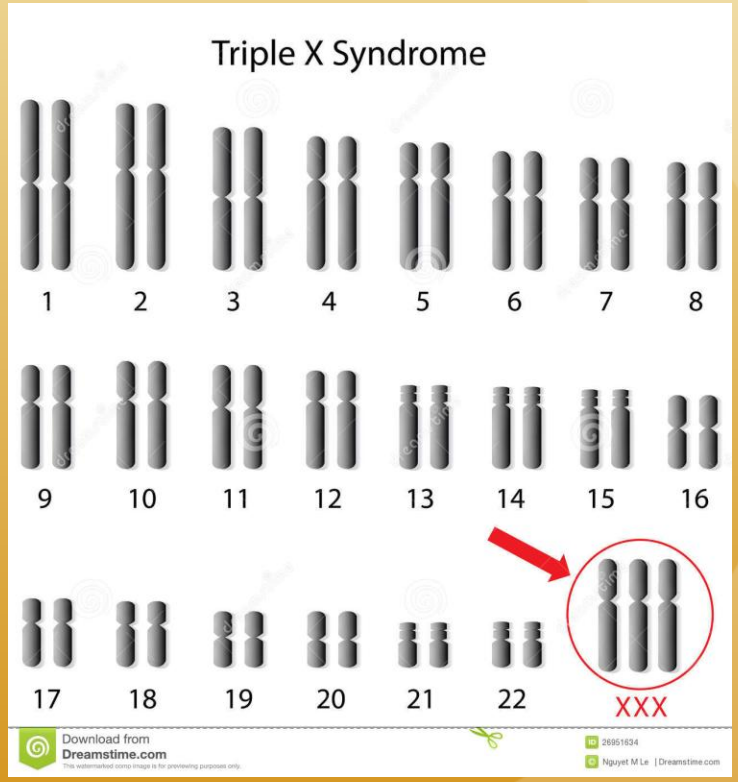


Triple X Syndrome

XXX

1/1500 births

- Increased risk of learning disabilities and delayed development of speech and language skills.
- Delayed development of motor skills.
- Behavioral and emotional difficulties are possible.
- Fertile females with normal gametes.

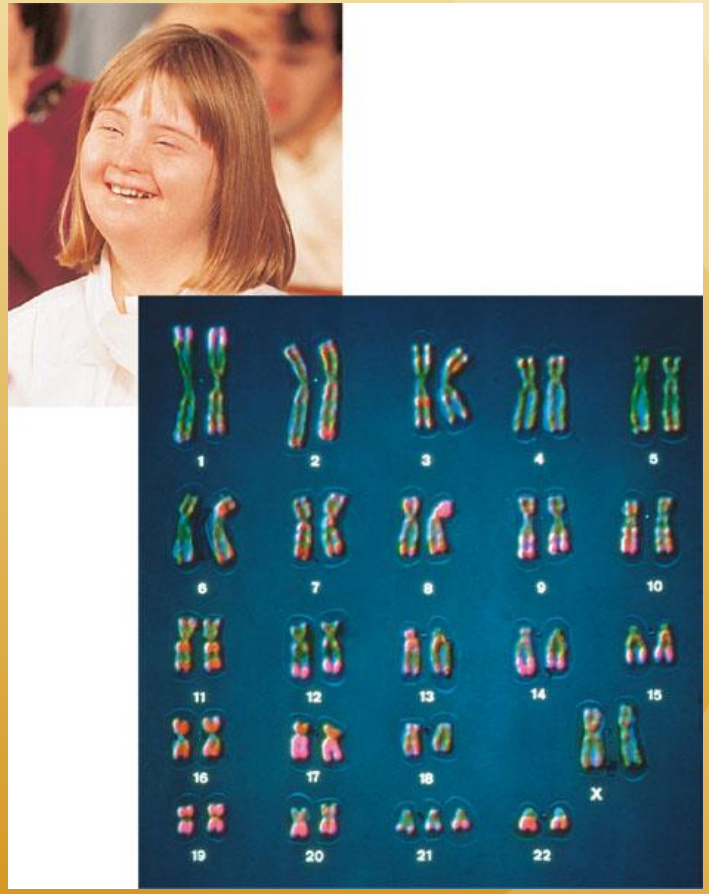


Genetic Disorders Caused by Autosomal Aneuploidy

Autosomal Aneuploidy

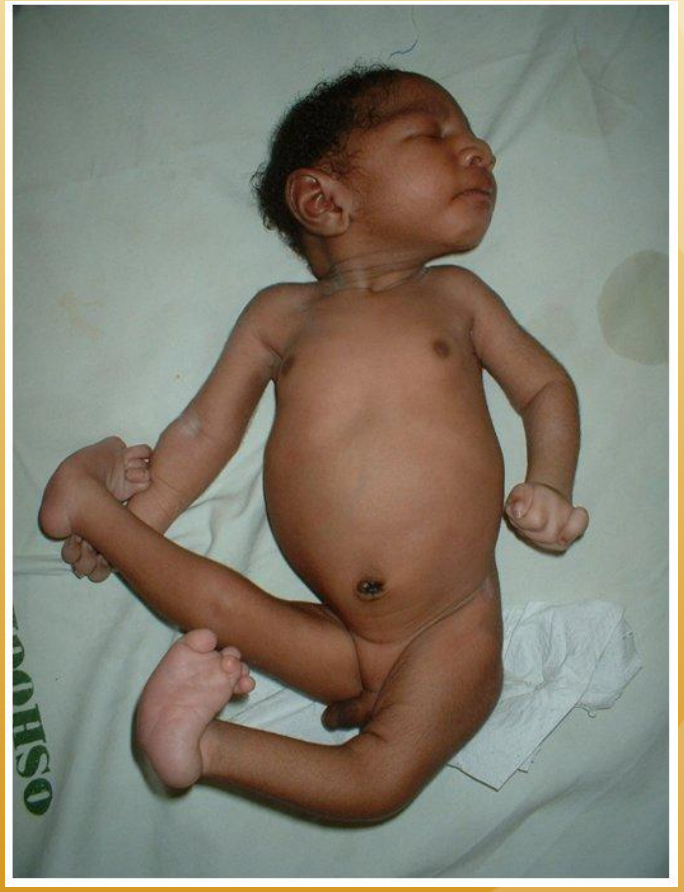
Down Syndrome—Trisomy 21

- Caused by an extra copy of chromosome #21
  - There are three copies of chromosome #21 in their somatic cells
- 0.15 percent of all live births
- Growth failure and delay in learning
- Big toes widely spaced; small chin; face is flat & broad; short neck
- Congenital heart disease
- Mean life expectancy is about 17 years and only 8 % survive past age 40



Edward's Syndrome
Trisomy 18

- Multiple defects
  - Mental and physical deficiencies
  - Facial abnormalities
    - Small head
    - Ear deformities
  - Extreme muscle tone
    - Spasticity and other damage
  - Clenched hands
  - Heart defects
  - Kidney malfunctions
- Low Survival Rate
  - Majority die before birth
  - Early Death
  - Death is typical by the age of 1



Patau Syndrome Trisomy 13

- Multiple defects
  - Mental and physical deficiencies
    - Large triangular nose; eye defects; extra fingers; low set ears
  - Wide variety of defects in organs
- Early death
  - ≈80% die within 1st year
  - Death is typical by the age of 3

Abnormalities in Chromosome Structure

Introduction I

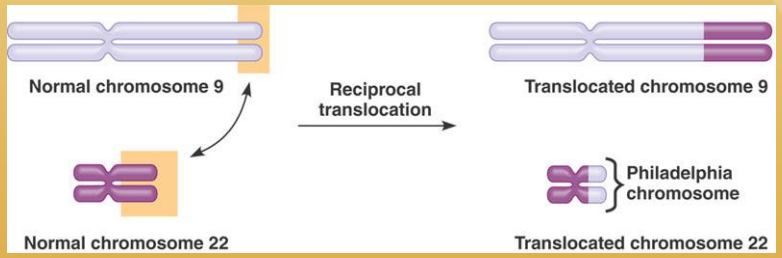
- The **changes in the shape of the chromosome** may be due to either of the following
  - Translocation
  - Deletions
  - Fragile sites

Abnormalities in Chromosome Structure

Translocation

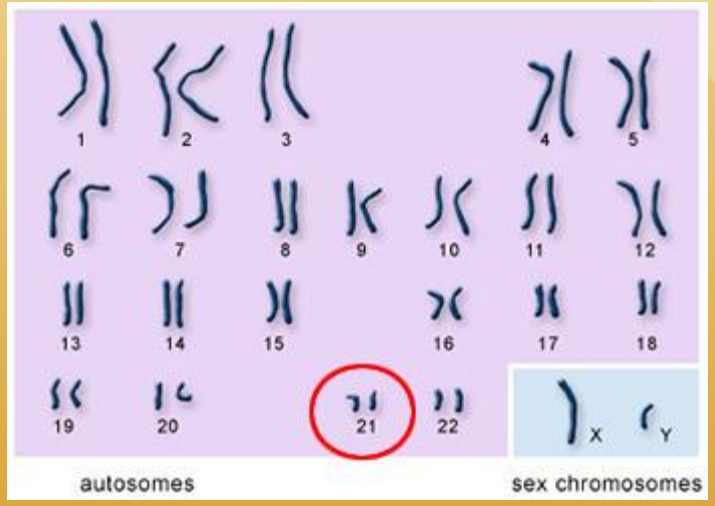
Translocation

1. A chromosome fragment breaking off and attaching to a non-homologous chromosome
   - Can result in deletion and/or duplication of genes
2. Reciporcal translocation
   - Two non-homologous pairs exchange genetic information



Translocation Down Syndrome

- 4% of Down Syndrome cases
- Individuals actually have 46 chromosomes
- One of copies of chromosome #14 has combined with chromosome #21
  - The large arm of chromosome #21 has been translocated to the large arm of another chromosome--usually chromosome #14



Abnormalities in Chromosome Structure

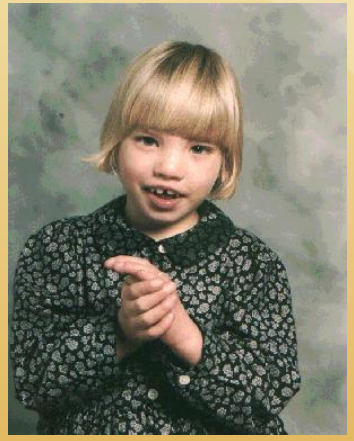
Deletion

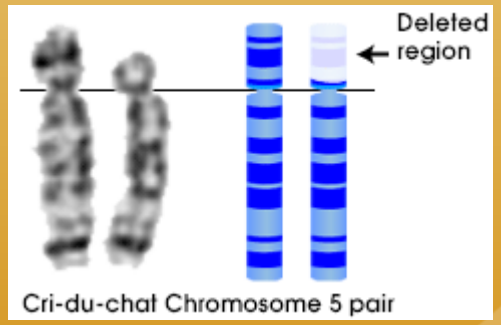
Deletion

- The loss of part of a chromosome
- The abnormal chromosome is known as a *deletion*
- Sometimes chromosomes break and fail to rejoin

Cri du Chat Syndrome (Cry of the Cat)

- Infants have a distinctive cry that sounds like a cat mewing
- Part of the short arm of chromosome #5 is deleted
  - Breakage point varies from case to case
- Infants normally have a small head with altered features
  - Moon face
- Infants normally survive childhood
- Exhibit severe mental retardation





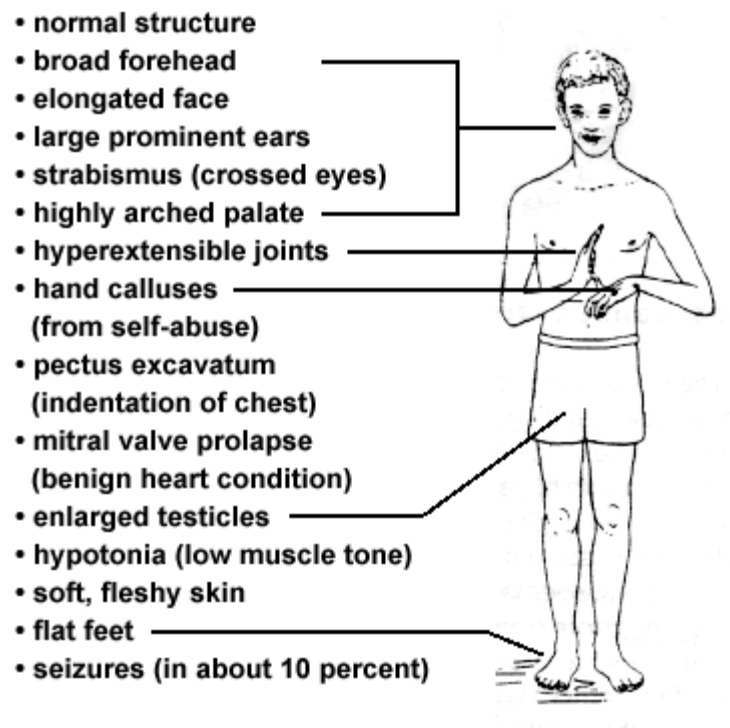
Abnormalities in Chromosome Structure

Fragile Sites

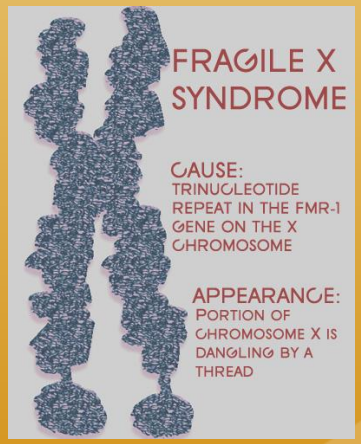
Fragile Sites

- Weak points at specific locations in chromatids
- Appears to be a place where part of a chromatid appears to be attached to the rest of the chromosome by a thin thread of DNA
  - Have been identified on the X chromosome and certain autosomes

Fragile X Syndrome



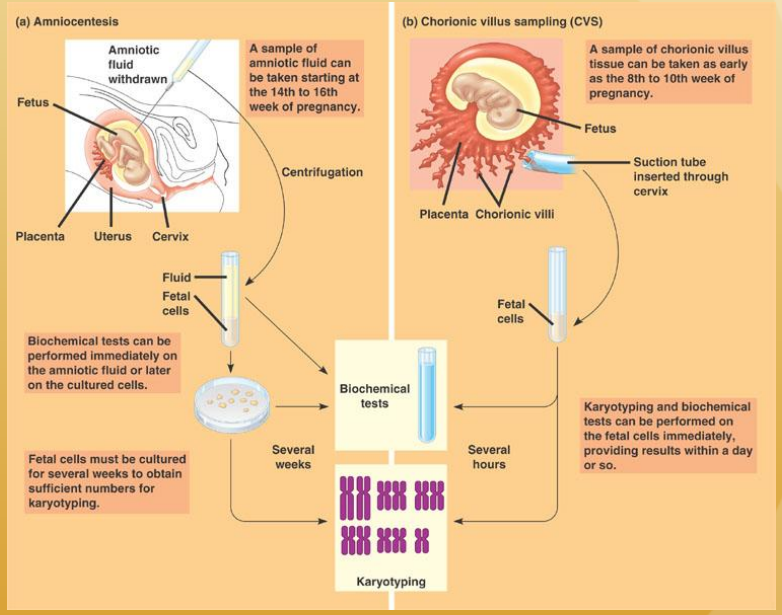
- Fragile site occurs near the tip of the X chromosome
  - Where nucleotide triplet CGG is repeated many more times than normal
- Most common cause of learning disabilities.



Genetic Screening & Pedigrees

Genetic Screening & Genetic Counseling

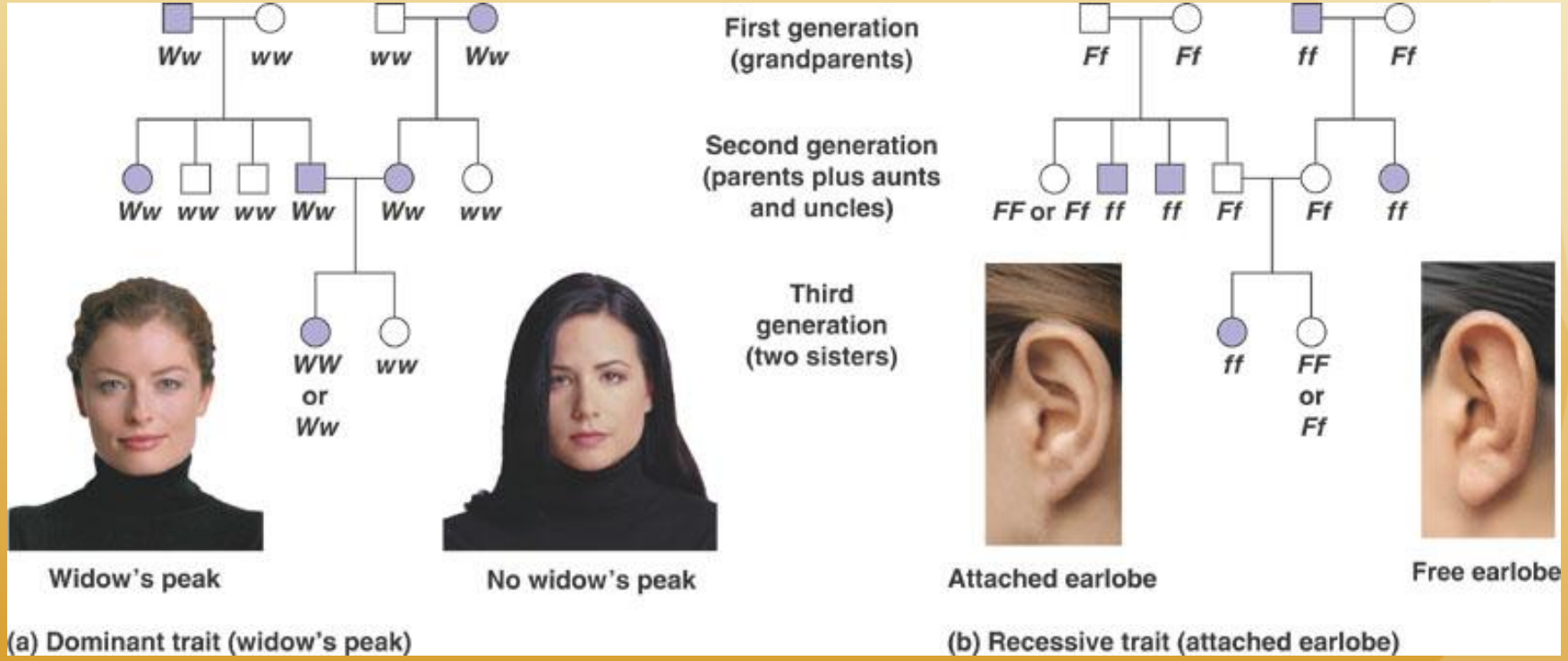
- Genetic Screening
  - Identifies individuals who might carry a serious genetic disease
    - Screening of newborns is the first step in preventative medicine
- Genetic Counseling
  - Provide couples, concerned about the risk of abnormality in their children, medical and genetic information



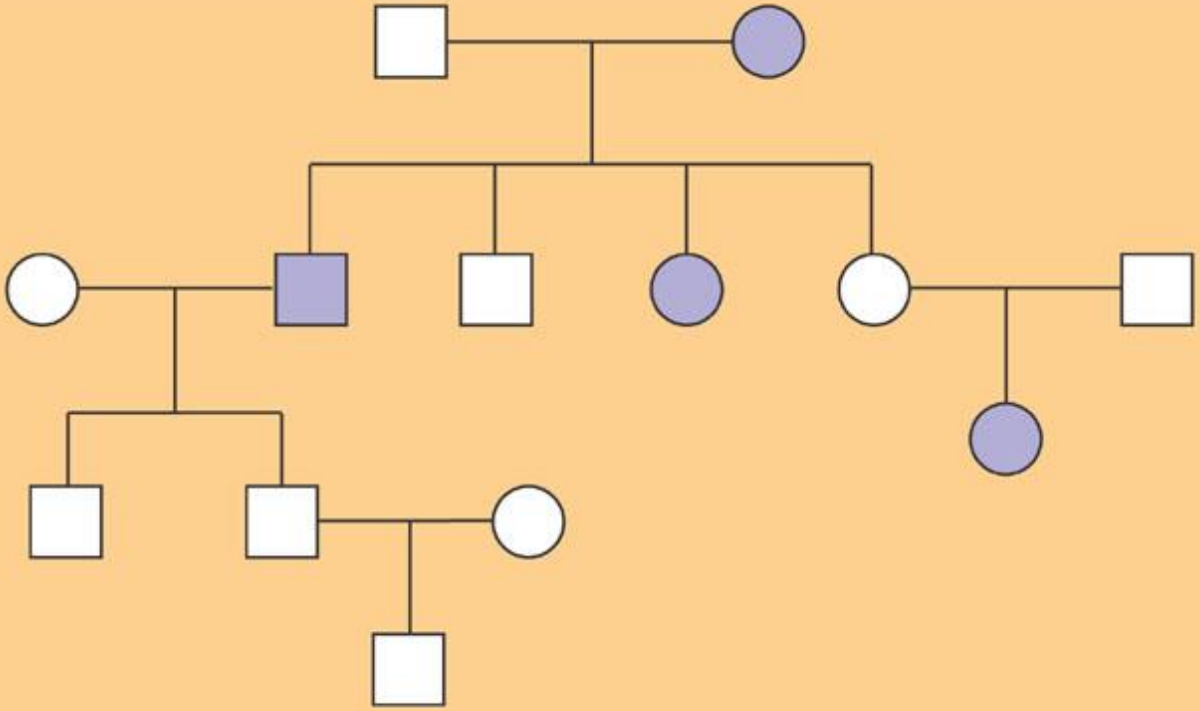
Pedigrees

- Definition
  - A family tree that shows the transmission of genetic traits within a family over several generations.
- Pedigree Analysis
  - Useful in detecting autosomal dominant mutations, autosomal recessive mutations, X linked recessive mutations and defects due to genomic imprinting
    - Genomic Imprinting
      - Expressions of a gene based on its parental origin

Pedigree Analysis



Pedigree Analysis



Homework

- Bioinformatics
- Proteomics
- Aminocentesis
- Chronic villus sampling (CVS)
- Preimplantation genetic diagnosis (PGD)
- Know how to discuss (argue for/against)
  - Genetic discrimination
  - The Human Genome Project