TERMS TO KNOW

- **Chromosome mutation/aberration**
  - Change in the total number of chromosomes
  - Rearrangement of genetic material within or among chromosomes

- **Gene mutation**
  - Addition, deletion, or rearrangement of individual genes

- **Aneuploidy**
  - Gain or loss of one or more chromosomes, but not a complete set
  - 1 chromosome = monosomy, 3 chromosomes = trisomy

- **Euploidy**
  - Complete haploid sets of chromosomes are present.
  - Example in humans: 23, 46, 69, etc. All multiples of 23

- **Polyploidy: a type of Euploidy**
  - More than 2 sets of chromosomes are present
  - 3 sets = triploid, 4 sets = tetraploid, 5 sets = pentaploid
DISJUNCTION VS. NONDISJUNCTION

After fertilization

First division nondisjunction

Haploid gamete

Trisomic
Trisomic
Monosomic
Monosomic

First meiotic division

Normal disjunction

Second meiotic division

Normal disjunction

Second division nondisjunction

Haploid gamete

Disomic (normal)
Disomic (normal)
Trisomic
Monosomic
Monosomy is evident in sex chromosomes for humans.

Monosomy for autosomes is not tolerated in humans or other animals.

Monosomy in autosomes may result in expression of lethal allele, therefore organism does not survive.

Trisomy of larger chromosomes is usually not tolerated; overload of information.

Trisomy of smaller chromosomes results in drastic phenotypic effects.

Most common human trisomic condition is Down Syndrome, Trisomy 21.
15 – 20% of ALL conceptions end in miscarriage.

30% of all miscarriages demonstrate some form of chromosomal abnormality.
- 70% of miscarriages are the result of trauma or maternal health issues.

90% of all chromosomal anomalies are terminated prior to birth through miscarriage.
- Only 10% survive to full gestation.
DOWN SYNDROME

- Trisomy 21, designated (47, 21+)
- 1 in every 800 live births
  - 4000 – 5000 births in US annually
  - 250,000 people living with this syndrome

- Syndrome classification:
  - Individuals do not present same phenotypes
  - 12-14 typical phenotypic characteristics
  - Most present 6-8 characteristics
DOWN SYNDROME

PHYSICAL CHARACTERISTICS

- EPICANTHIC FOLDS
- FLAT FACE
- ROUND HEAD
- SHORT STATURE
- LARGE, FURROWED TONGUE
- BROAD HANDS
- POOR MUSCLE TONE
- COGNITIVE, LEARNING
OTHER HUMAN TRISOMIC CONDITIONS

- Trisomy 8  Warkany syndrome 2
- Trisomy 9
- Trisomy 13  Patau syndrome
- Trisomy 18  Edwards syndrome
- Trisomy 22  Emanuel syndrome
WARKANY SYNDROME 2

- Trisomy of chromosome #8
- Usually lethal early in pregnancy leading to miscarriage.
- Severe mental retardation
- Expressionless face
- Musculoskeletal, visceral, and eye abnormalities.
Many do not survive after 20 days.

Those that do have:

- Malformations of skull, kidneys, heart, nervous system, and muscles.
- Severe mental retardation
- Expressionless face
- Musculoskeletal, visceral, and eye abnormalities.
PATAU SYNDROME

- Trisomy of chromosome #13
- Polydactyly
- Microcephaly
- Mental retardation
- Heart defects
- Cleft lip and palate
- Kidney malformations
- Facial deformities

DON'T LOOK THIS UP!
EDWARDS SYNDROME

- Trisomy of chromosome 18
- 2nd most common trisomic condition after Trisomy 21.
- Majority of fetuses die before birth.
- 1 in 6000 live births
- Most are female

- Microcephaly
- Intestines protrude out of body.
- Low-set, malformed ears
- Undeveloped fingers
- No radius in forearm.
- Clubfoot
Personal Story

Due to chromosomal breakage in one or more locations.

Results in loss of information.

- **Terminal deletion** is the loss of the end of a chromosome.
- **Intercalary deletion** is the loss within the interior of the chromosome.
- Centromere tends to stay in place.
- When synapsis occurs, a loop must occur in order for the homologs to match-up.
Deletion of small terminal portion of short arm chromosome #5.

Segmental deletion; sporadic loss of material in gametes.

46, 5p-

1 in 25,000 to 50,000 births

anatomic malformations
GI and cardiac problems
Characteristic cry
No clear explanation as to why some sites are more fragile than others.

Association between breakage and:
- Cancer development
- Mental retardation
- Current research on autism link
FRAGILE X SYNDROME

- AKA Martin-Bell Syndrome
- Leading hereditary cause of developmental disabilities
- 1 in 4000 males; 1 in 8000 females.
- Males affected more frequently than females
- Can follow X-linked dominant inheritance pattern
- normal structure
- broad forehead
- elongated face
- large prominent ears
- strabismus (crossed eyes)
- highly arched palate
- hyperextensible joints
- hand calluses (from self-abuse)
- pectus excavatum (indentation of chest)
- mitral valve prolapse (benign heart condition)
- enlarged testicles
- hypotonia (low muscle tone)
- soft, fleshy skin
- flat feet
- seizures (in about 10 percent)
FRAGILITY AND CANCER

- Gap or constriction of a chromosome
- Susceptible to breakage due to replication stress
- 120 fragile sites identified in human genome
- Present in nearly all humans
- Gene affected is thought to normally act as a tumor suppressor gene
- First identified in formation of lung cancer (FHIT gene)
- Other cancers:
  - Esophageal
  - Breast
  - Cervical
  - Liver
  - Kidney
  - Pancreatic
  - Colon
  - Stomach