PRINCIPLES OF GENETICS

Basic Principles

gene - a unit of inheritance that usually is directly responsible for one trait or character. Each individual has two genes for each trait, one comes from dad and the other from mom.

allele - alternate forms of a gene. Usually there are two alleles for every gene, sometimes there are more than two alleles present in population ï termed **multiple alleles**

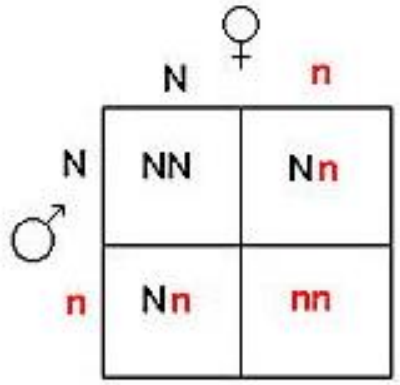
homozygous - when the two alleles are the same

heterozygous - when the two alleles are different

dominant - a trait (allele) that is expressed irregardless of the second allele

recessive - a trait that is only expressed when the second allele is the same (e.g. short plants are homozygous for the recessive allele)

- **Dominant –** always expressed
  - **Capital letters – N**
  - **Homozygous - NN**
  - **Heterozygous - Nn**
- **Recessive –** prevented by dominant
  - **Lower case letters – n**
  - **Homozygous - nn**



punnett square - probability diagram illustrating the possible offspring of a mating male genes on top of columns and female traits on side of rows

Dominant and Recessive

Autosomal Dominant - dominant gene on an autosome

Autosomal Recessive - recessive gene on an autosome

Sex-linked Dominant - dominant gene on a sex chromosome

Sex-linked Recessive ï recessive gene on a sex chromosome

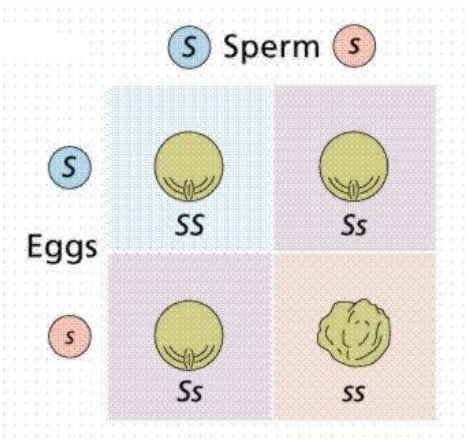
Genotype and Phenotype

phenotype - the physical expression of the genes for the trait by an individual

genotype - the gene makeup of an organism. Phenotype is the trait of an individual expresses while genotype is the two genes that cause that trait

Monohybrid Cross ï a cross involving only one trait.
(phenotype ratio ï 3:1 and genotype ratio 1:2:1)

hybrid ï an individual who has one dominant and one recessive gene for a trait



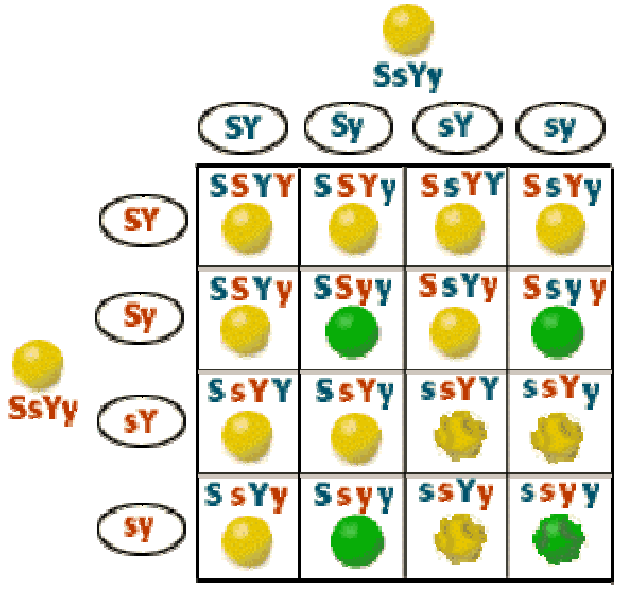
- **Hybrid – Ss X Ss**
- **One Trait – Smooth vs wrinkled**
- **Two gametes per parent**
- **S and s**
- **Punnett Square with 4 boxes – 4 offspring**

Genotype	**Phenotype**
SS or Ss	Round
ss	Wrinkled

Genotype frequency
1:2:1

Phenotype frequency
3:1

Dihybrid Cross ï a cross involving two traits.
(phenotype ratio-9:3:3:1 and
genotype ratio- 1:2:1:2:4:2:1:2:1)



Dihybrid – 2 traits
Gametes per parent = 4
Punnett Square – 16 boxes
Genotype ratio
1:2:1:2:4:2:1:2:1
Phenotype ratio
9:3:3:1

Trihybrid Cross

triple-het x triple-het cross

SsYyAa x SsYyAa

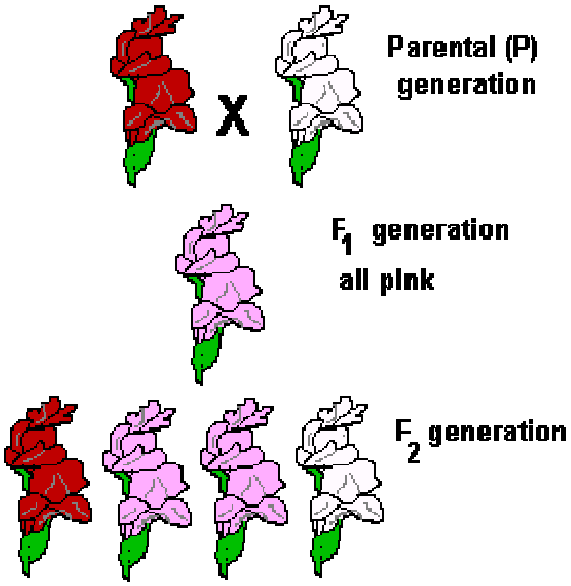
	SYA	SYa	SyA	Sya	sYA	sYa	syA	sya
SYA	SSYYAA	SSYYAa	SSYyAA	SSYyAa	SsYYAA	SsYYAa	SsYyAA	SsYyAa
SYa	SSYYaA	SSYYaa	SSYyaA	SSYyaa	SsYYaA	SsYYaa	SsYyAa	SsYyaa
SyA	SSyYAA	SSyYAa	SSyyAA	SSyyAa	SsyYAA	SsyYAa	SsyyAA	SsyyAa
Sya	SSyYaA	SSyYaa	SSyyaA	SSyyaa	SsyYaA	SsyYaa	SsyyaA	Ssyyaa
sYA	sSYYAA	sSYYAa	sSYyAA	sSYyAa	ssYYAA	ssYYAa	ssYyAA	ssYyAa
sYa	sSYYaA	sSYYaa	sSYyaA	sSYyaa	ssYYaA	ssYYaa	ssYyaA	ssYyaa
syA	sSyYAA	sSyYAa	sSyyAA	sSyyAa	ssyYAA	ssyYAa	ssyyAA	ssyyAa
sya	sSyYaA	sSyYaa	sSyyaA	sSyyaa	ssyYaA	ssyYaa	ssyyaA	ssyyaa

Phenotypes:
Out of 64 births.

- normal
- albinos
- anerythristic
- striped
- snow
- striped-albino
- striped-anery
- striped-snow

Incomplete Dominance

Incomplete dominance ï one allele (gene) is not completely dominant over another resulting in a blending of traits and where the phenotype of a hybrid displays a blending of the two alleles



Incomplete dominance ï

- **Hybrid** is a blend of two traits
- **Genotype frequency**
  1:2:1
- **Phenotype frequency**
  1:2:1
- **Examples:** Flowers, Animal fur

Co-dominance

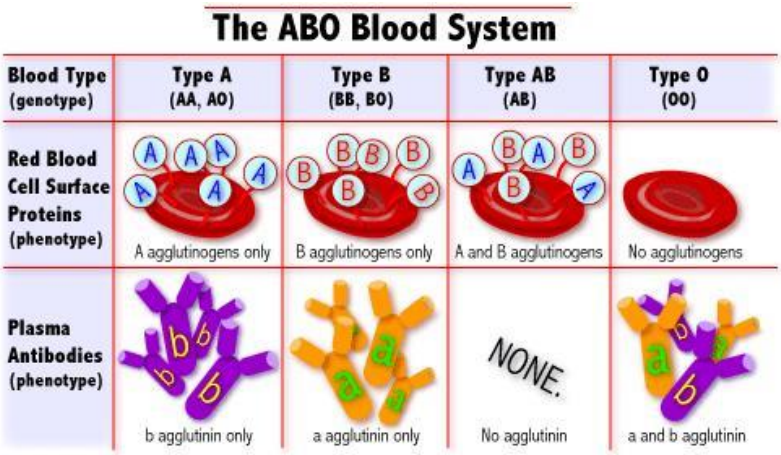
co-dominance ï both dominant alleles (genes) in an individual are expressed as in blood types

Blood types – A,B,O alleles

A and B genes are co-dominant and both dominant over the O gene which is recessive

Phenotypes	Genotype
A	I^AI^A or I^Ai
B	I^BI^B or I^Bi
AB	I^AI^B
O	ii

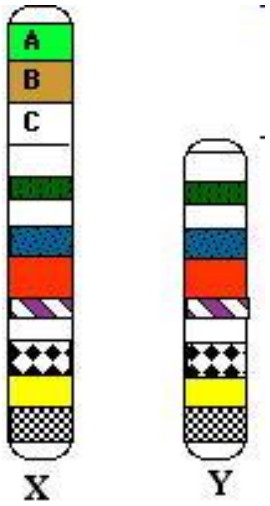
Blood Type	Genotype		Can Receive Blood From:
A	i^Ai i^Ai^A	AA AO	A or O
B	i^Bi i^Bi^B	BB BO	B or O
AB	i^Ai^B	AB	A, B, AB, O
O	ii	OO	O



Independent Assortment vs. Linkage

- **Independent Assortment** ï genes on different chromosomes separate independently during meiosis
- **Linkage –** genes on the same chromosome are inherited as a group
    - **Autosomal linkage –** on autosomes
    - **Sex-linked –** on sex chromosomes

Linkage – Sex Linkage



- **Linkage –** genes on the same chromosome inherited as a group
- **Sex-linkage –** genes on sex chromosomes (esp. X)
- **Y-chromosome shorter –** some genes from X missing
- X-linked traits more common in men
- Men get X-chromosome from mom
- Red-green colorblindness, hemophilia

sex-linkage – allele (gene) is located on a sex chromosome and it will be more common in one sex.

- It is usually on the x-chromosome and more common in males than in females.
- Barr bodies ï tightly coiled X chromosome in females ï inactive X chromosome.
- Calico cats ï usually on females. yellow and black alleles on X chromosome - female has 2 Xôs

Genetic Variations

Probability ï ratios or percents
Multiple Alleles – three or more alleles for a gene as blood type as skin color
Multifactorial Traits – more than 1 pair of genes plus environment
Pleiotrophy ï the action of an allele (gene) affects many parts of the body as sickle cell anemia
Variable expressivity ï an allele (gene) can be expressed differently in different people

Environmental influence on genes expression

- Gene function is influenced by environment as with identical twins
- Genes have blueprint for proteins or parts of proteins
- Proteins can be structural proteins (parts of body) or functional proteins (hormones/enzymes

Epistasis and Multifactorial Inheritance

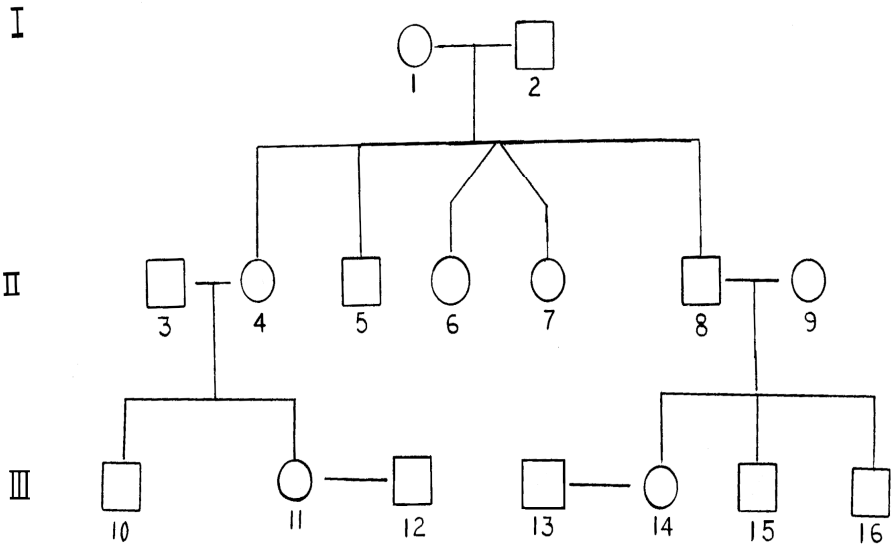
- **Epistasis -** the interaction between two or more genes to control a single phenotype so one pair of genes alters the expression of another pair of genes as albino
- **Multifactorial inheritance -** many factors (multifactorial) both genetic and environmental are involved in producing the trait or condition. Examples: height, weight, cleft palate, spina bifida

Pedigree Analysis

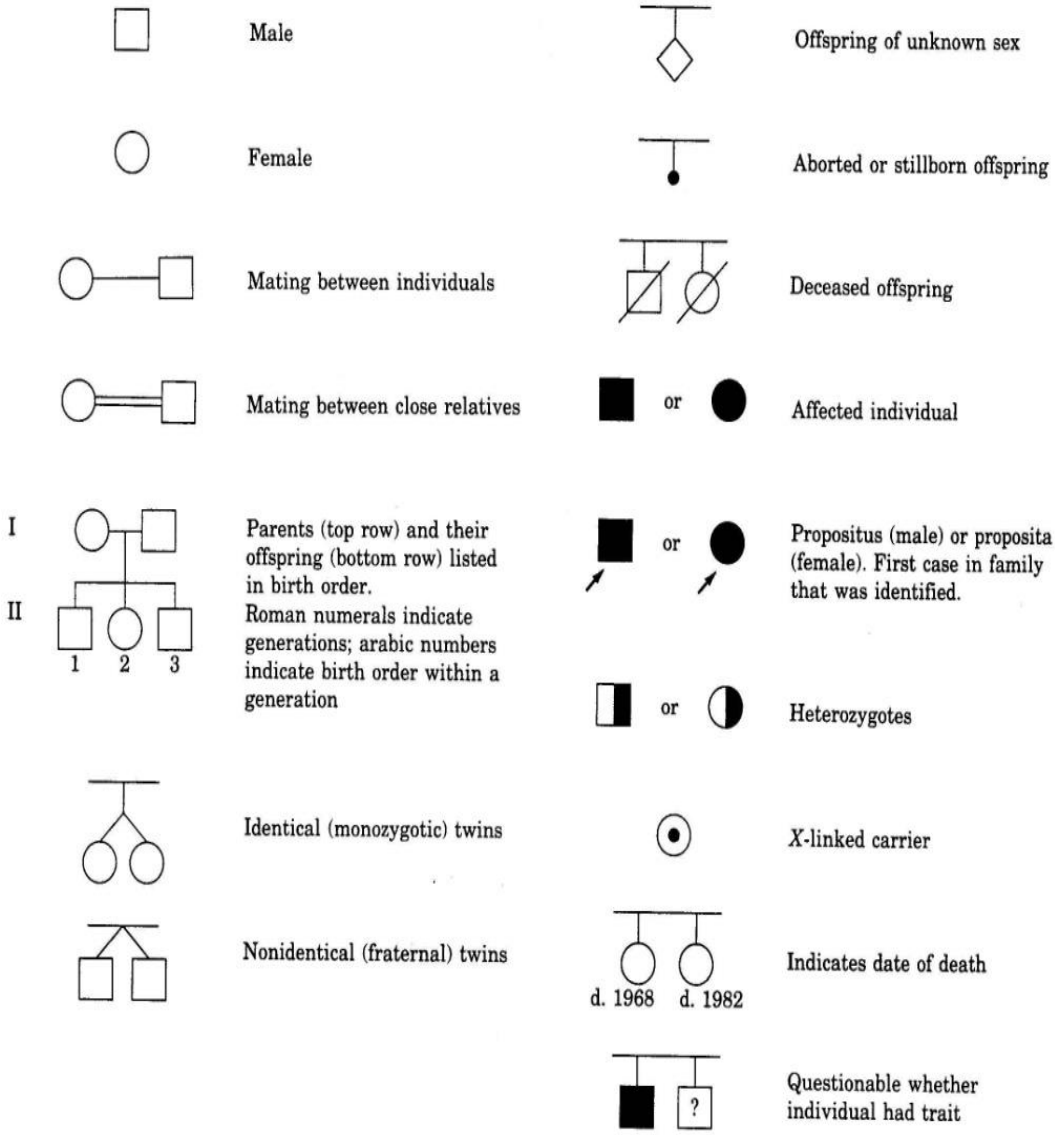
Pedigree is a family tree**.**

Squares are males and circles are females

Generations = I – Original Parents
II- F1 (children)
III – F2 (grandchildren)



Symbols Used in Pedigree Analysis

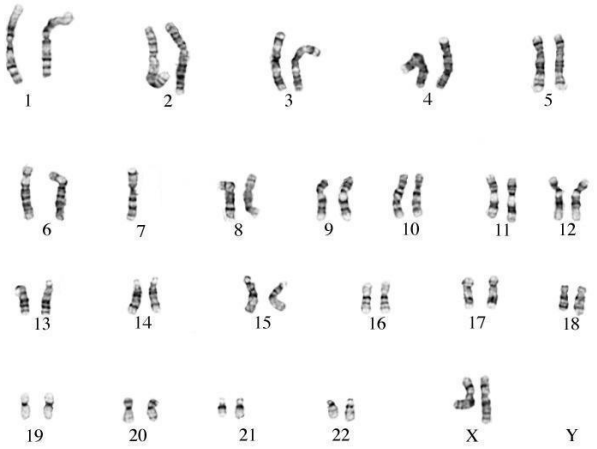


Karyotype Analysis - **karyotype** is print of human chromosomes

- **nondisjunction –** chromosomes do not separate during meiosis.
- Results in monosomy and trisomy

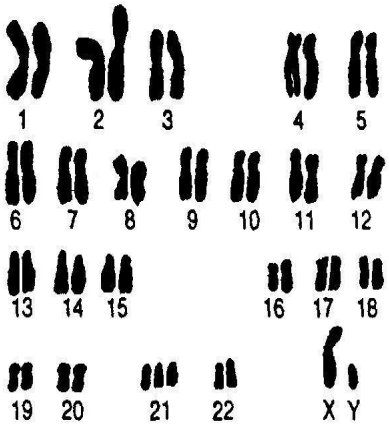
Karyotype Characteristics:

- The numbered chromosome pairs termed autosomes are arranged longest to shortest
- Chromosomes come in pairs
- The sex (X & Y) chromosomes are placed last with normal females having XX and normal males having XY
- If only X chromosomes are present, it will be female
- If X and Y chromosomes are present, it will be male
- Bent chromosomes are not abnormal. It is just the way they were photographed
- If an individual has an extra chromosome, it is termed **trisomy** and if a chromosome is missing, it is termed **monosomy**



Karyotype 1

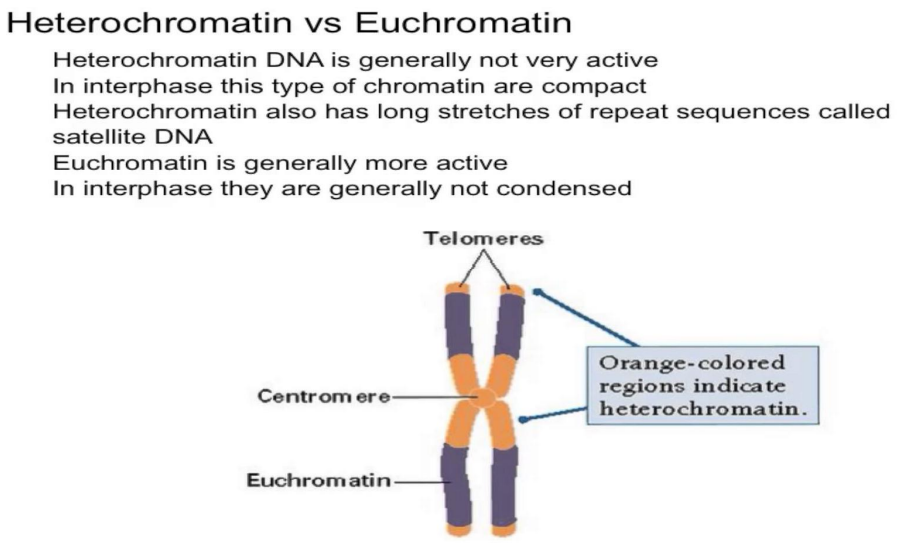
Male with Monosomy 7



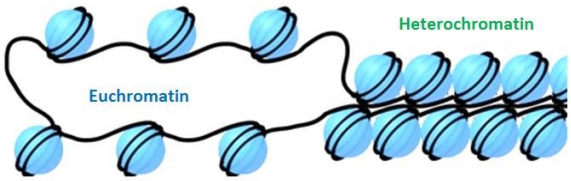
Karyotype 2

Female with Trisomy 21

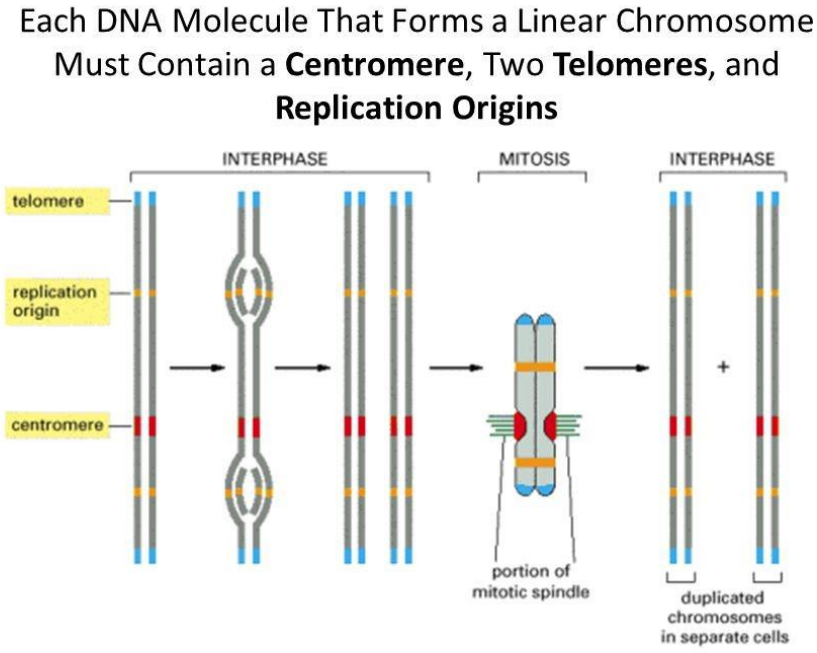
Regions of Chromosome for Replication



Difference between heterochromatin and euchromatin

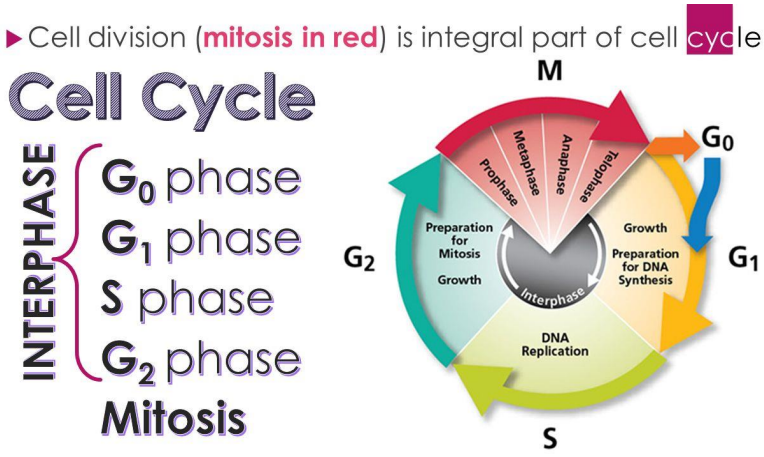


- **Heterochromatin** is a part of chromosome, a tightly packed form of DNA whereas **euchromatin** is an uncoiled form of chromatin.
- **Heterochromatin** has tighter DNA packing than **euchromatin**.
- **Heterochromatin** stains dark in interphase whereas **euchromatin** stains lightly with basic dyes but stains dark during mitosis, when it is in condensed state during each repetition of the cell cycle.
- **Heterochromatin** contains more number of DNA compare to **euchromatin**.
- **Heterochromatin** found in eukaryotes whereas **euchromatin** found in both eukaryotes and prokaryotes.
- **Heterochromatin** is genetically inactive and **euchromatin** is genetically active.
- **Heterochromatin** is late replicative whereas **euchromatin** is early replicative.



MITOSIS, MEIOSIS, ASEXUAL VS. SEXUAL REPRODUCTION

Cell Cycle – the life cycle of a cell



G_0 *Phase*– Cells that go into this phase when not actively reproducing as muscle or nerve cells

G_1 ***Phase*** **–** high rate of biosynthesis and growth

S *Phase* **–** DNA content doubles and chromosomes replicate

G_2 ***Phase*** **-** final preparations for Mitosis

M ***Phase*** **–** Mitosis and Cytokinesis

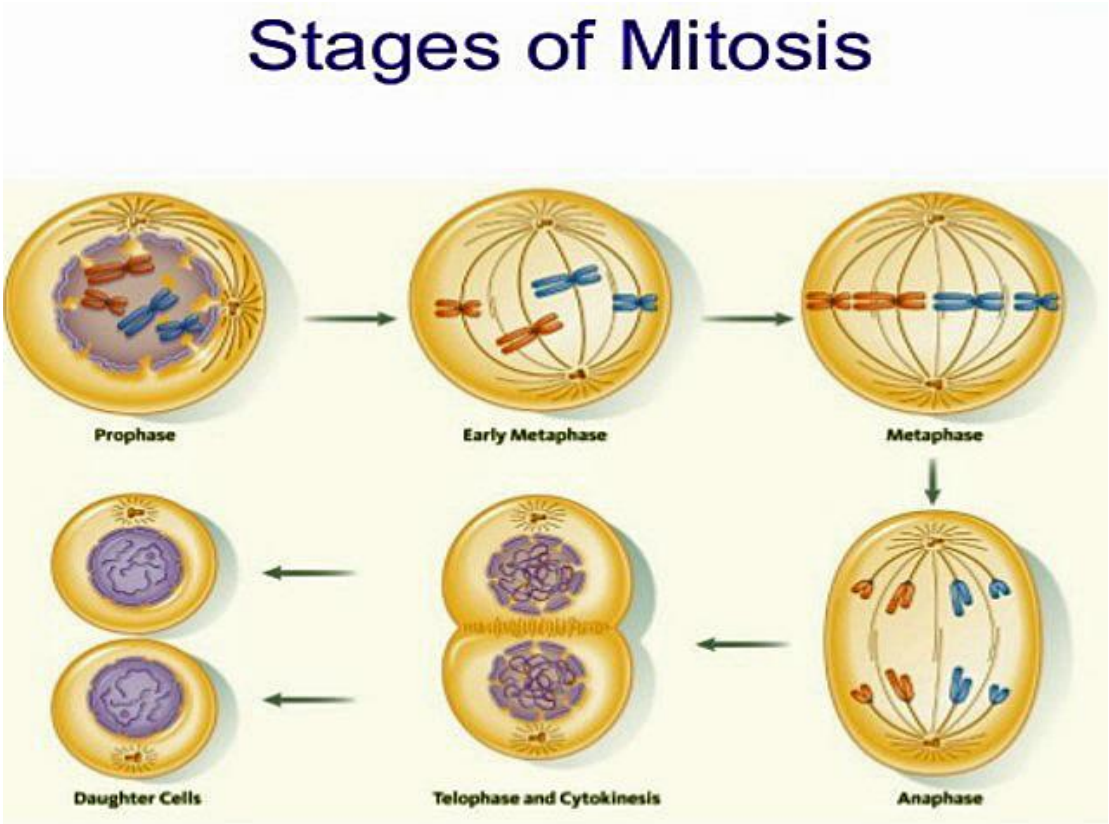
A. ***Prophase*** **–** chromatid pairs coil up, spindle forms, nuclear membrane dissolves, chromatid pairs attach to spindle fibers (microtubules),

B. ***Metaphase*** **–** chromatid pairs move to the equator, chromatid pairs align at the equator,

C. ***Anaphase*** **–** chromatids separate into individual chromosomes, chromosomes are pulled apart toward the equator by the spindle fibers (microtubules)

D. ***Telophase*** **-** chromosomes uncoil, spindle dissolves, nuclear membrane reforms

E. Cytokinesis **–** division of the cytoplasm to make two new cells



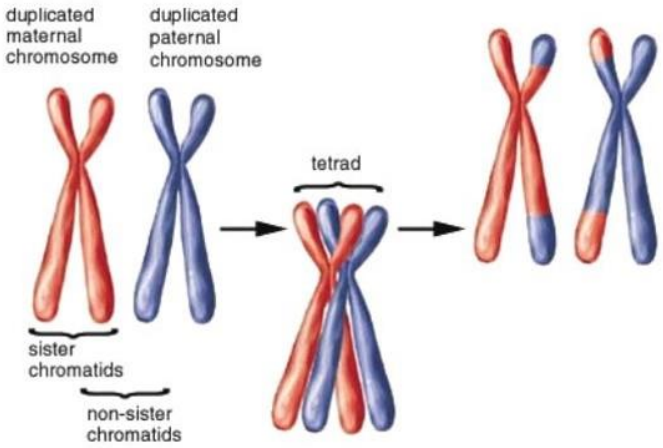
Mitosis vs Meiosis

Mitosis type of cell reproduction which produces two daughter cells that are genetically identical to the parent cell.

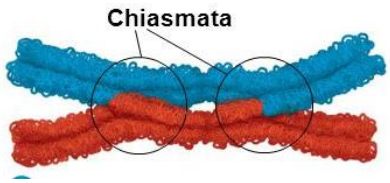
- ❖ **Growth and Asexual Reproduction**
- ❖ **One division – 2 diploid cells**
- ❖ **Genetically same as original**

- **Meiosis** type of cell reproduction which produces 4 cells which half the number of chromosomes as the original parent cell
  - ❖ **Gametes for Sexual Reproduction**
  - ❖ **2 divisions – 4 haploid cells**
- **Sexual Reproduction –** reproduction involving two parents ï male and female.
- **Asexual Reproduction –** reproduction involving only one parent. Offspring genetically the same as the parent.
- **Cloning –** asexual reproduction.

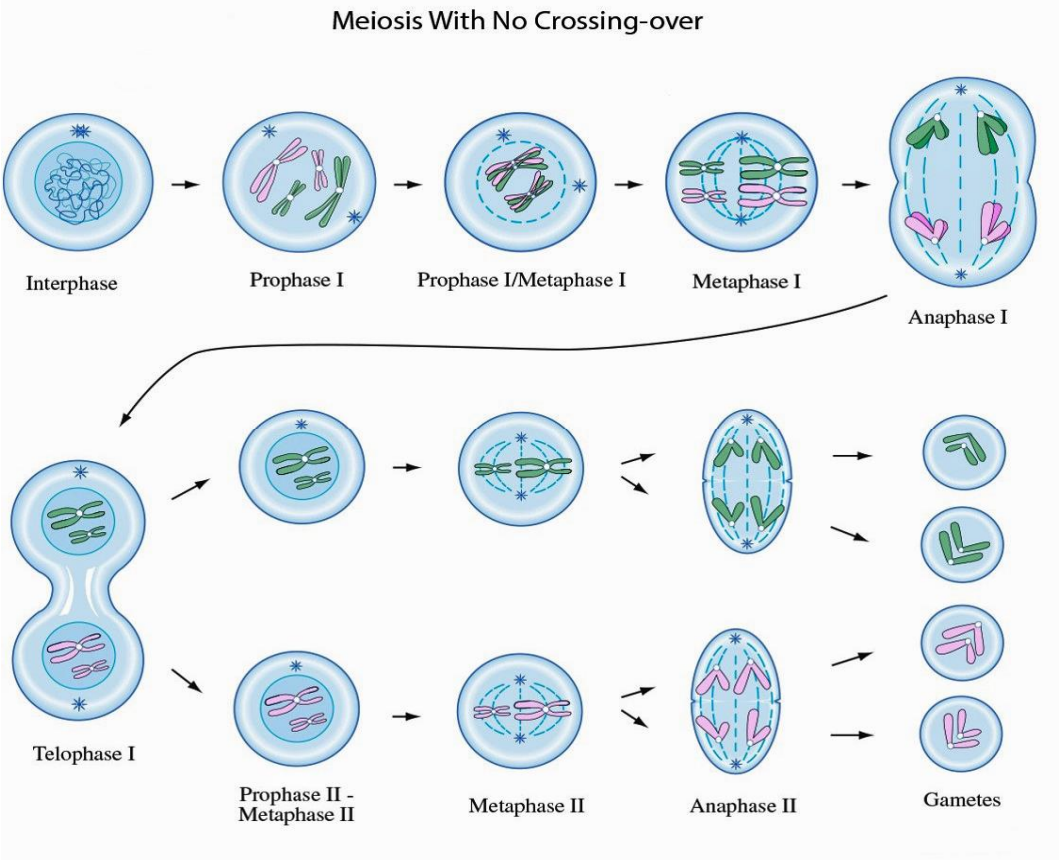
Stages of Meiosis I



- The first meiotic phase is **prophase 1**.
- As in mitosis, the nuclear membrane dissolves, chromosomes develop from the chromatin, and the centrosomes push apart, creating the spindle apparatus.
- The tight pairing of the homologous chromosomes is called **synapsis**
- These paired up chromosomesð two from each parentð are called **tetrads**.
- The point the points of contact, the physical link, between two (non-sister) chromatids belonging to homologous chromosomes is the **chiasmata**



- Homologous (similar) chromosomes from both parents pair up and **may** exchange DNA in a process known as **crossing over.** This results in genetic diversity.
- In **metaphase 1**, some of the spindle fibers attach to the chromosomes' centromeres.
- The fibers pull the tetrads into a vertical line along the center of the cell.
- **Anaphase 1** is when the tetrads are pulled apart from each other, with half the pairs going to one side of the cell and the other half going to the opposite side.
- It is important to understand that whole chromosomes are moving in this process, not chromatids, as is the case in mitosis.
- At some point between the end of anaphase 1 and the developments of **telophase 1**, cytokinesis begins splitting the cell into two daughter cells.
- In telophase 1, the spindle apparatus dissolves, and nuclear membranes develop around the chromosomes that are now found at opposite sides of the parent cell / new cells.

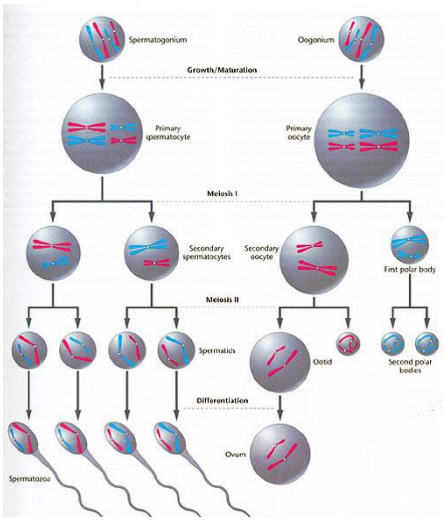


Stages of Meiosis II

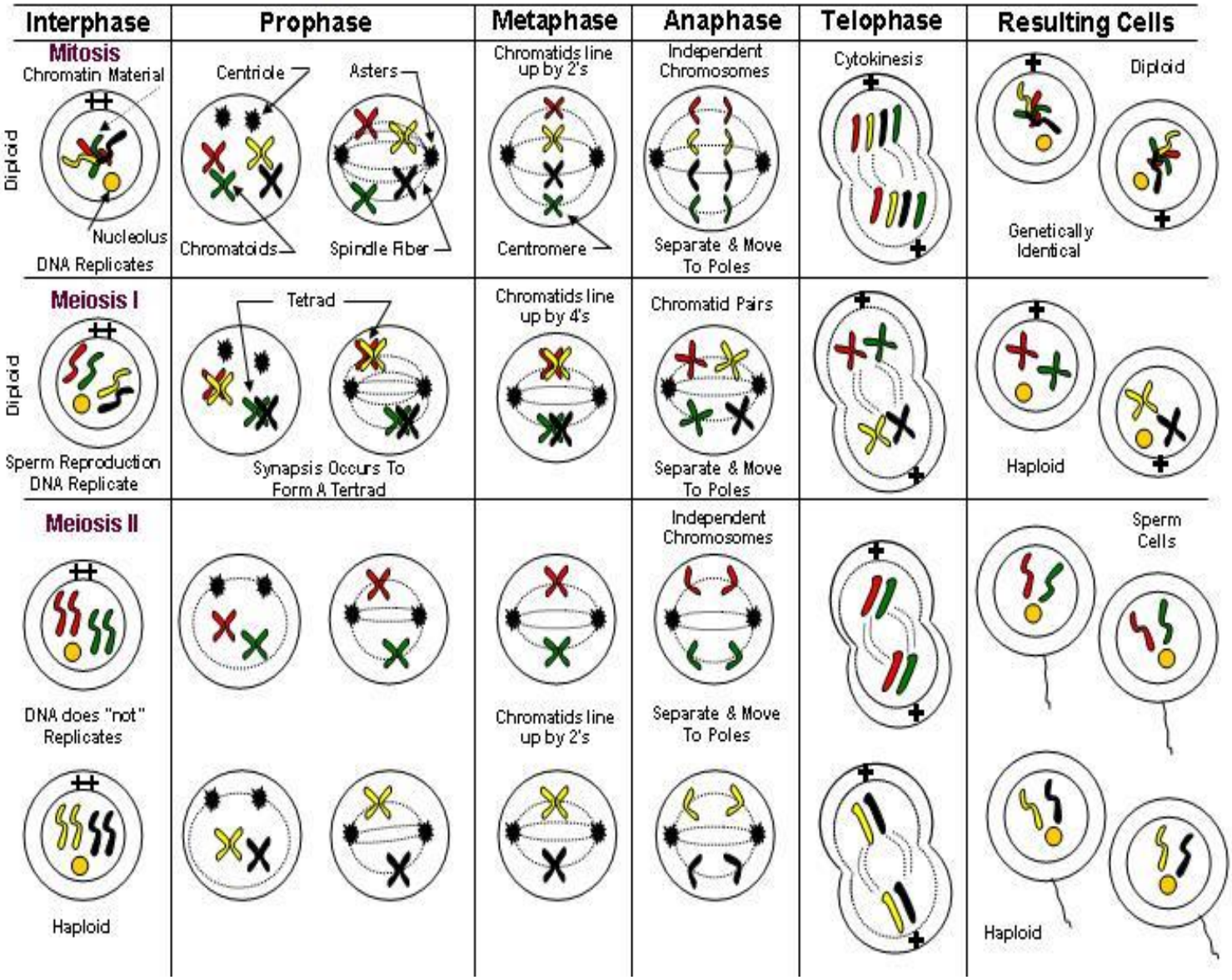
- In **prophase 2**, centrosomes form and push apart in the two new cells.
- A spindle apparatus develops, and the cells' nuclear membranes dissolve.
- Spindle fibers connect to chromosome centromeres in **metaphase 2** and line the chromosomes up along the cell equator.
- During **anaphase 2**, the chromosomes' centromeres break, and the spindle fibers pull the chromatids apart.
- The two split portions of the cells are officially known as "sister chromosomes" at this point.
- As in telophase 1, **telophase 2** is aided by cytokinesis, which splits both cells yet again, resulting in four haploid cells called gametes.
- Nuclear membranes develop in these cells, which again enter their own interphases.

Gamete Formation

- Spermogenesis ï 4 mature sperm cells from meiosis.
- Oogenesis ï 1 egg and 3 polar bodies



Comparison of Mitosis and Meiosis



Note: no crossing over is shown in meiosis.

Mutations

- Mutation ï any change in the DNA
- Gene mutation
- Chromosomal mutation
- Agents causing mutations ï radiation, chemicals, excess heat

Genetic Disorders

- **Causes of mutations –** chemicals, radiation, temperature, viruses
- **Nondisjunction** ï chromatids do not separate properly during meiosis. Individual formed from such gametes have extra or missing chromosomes. as Downôs Syndrome
- **Trinucleotide repeats –** sequences of 3 nucleotides is repeated, often several times in a gene when too many repeats are formed ï cause genetic disorders triplet nucleotides -repeated too often as Huntingtonôs
- **Defective genes** ï does not produce correct protein as sickle cell anemia (A & T traded places)
- **Genetic disorders and their causes** as nondisjunction (Downôs syndrome), trinucleotide repeats (fragile X and Huntingtonôs), defective genes (sickle cell anemia, hemophilia)
- **Human genetic disorders –** can be dominant, recessive, sex-linked, epistatic, variable expressed
- **Crossover frequency –** during meiosis, pieces trade places ï determining frequency

Examples of Human Genetic Disorders

Autosomal Dominant

- **Huntington Disease** - degenerative brain disorder which results in loss of both mental and physical abilities-- adult onset generally
- **Marfan Syndrome** - disorder of connective tissue affecting the heart, blood vessels, lungs, eyes, bones, and ligaments
- **syndactyly** ï webbing between toes and fingers
- **Polycystic Kidney Disease** - a disease which causes cysts to grow on a person's kidneys (and liver); the third leading cause of kidney failure in the United States
- **Brachdactyly** ï short fingers
- **Myotonic Dystrophy –** a disorder that causes muscle weakness and the inability of muscles to relax after use.
- **porphyria** - a group of disorders caused by a deficiency of an enzyme in the pathway for making heme (a component of hemoglobin)-- this causes a variety of symptoms: sensitivity to light, mental changes which border on insanity, itchy and blistering skin, dark colored urine, abdominal pain and cramping, and hairiness
- **achondroplasia** ï growth defect causing abnormal body proportions, the arms and legs are very short while the torso is normal in size.
- **chronic simple glaucoma** ï increased pressure inside the eyeball
- **hypercholesterolemia** -excessive levels of cholesterol in the blood stream
- **polydactyly** ï extra toes and fingers
- **Ehlers-Danlos Syndrome** - connective tissue disorders characterized by articular hypermobility (the ability to flex joints beyond the "normal" range), skin hyperelasticity (the ability to stretch the skin away from the body), and fragile skin and tissues (easy bruising and easily ruptured skin and blood vessels).
- **Neurofibromatosis** - trait characterized by cafe-au-lait ("coffee and milk" pigmented skin) spots and small tumor-like growths on or under the skin-- deformation of bones and curvature of the spine can also be symptoms

- **Nonsyndromic deafness –** hearing loss due to a defective gene. Most defects affect the structure of the inner ear
- **Congenital cataracts** ï clouding of the lens in the eye
- **Familial high cholesterol** ï high cholesterol levels

Autosomal Recessive

- **Tay-Sachs Disease** - a degenerative disorder causing death usually by age 5 ï Jewish heritage
- **sickle cell anemia** - disease causing the red blood cells in the body to have a sickle shape (not a round shape). These sickle shapes can block veins, arteries, and capillaries and cause blood flow to an area to be stopped for a while. This can have serious side effects such as tissue death and stroke.
- **Beta thalassenia *(Cooley's Anemia)*-** a defect in the beta chain of hemoglobin resulting in severe anemia
- **galactosemia –** individuals lack the enzyme that helps the body break down galactose.
- **albinism *(Oculocutaneous)*** - disorder characterized by absence of pigment in hair, skin, and eyes
- **agammaglobulinemia –** defect that causes the absence of the white blood cells (B cells) causing recurrent bacterial infections
- **phenylketonuria** - individuals with PKU cannot digest the amino acid phenylalanine (part of many proteins)-- levels of phenylalanine rise in the bloodstream and cause brain damage
- **cystic fibrosis** - A disease caused by defective chloride transport that leads to high levels of mucus in the lungs and pancreas, high sweat chloride levels, and other digestive and respiratory problems.

Sex-linked

X- dominant

- **ichthyosis simplex** (d) Ichthyosis is a form of severe dry skin that causes affected areas to look like fish scales
- **Hypertrichosis -** generalized hairiness covering the whole body

X- linked recessive

- **hemophilia** (r) - There is a defect in blood coagulation factor VIII which prevents blood clotting. This causes hemorrhage, easy bruising, and prolonged bleeding from wounds.
- **red-green colorblindness** (r) ï unable to distinguish between red and green
- **Duchenne's muscular dystrophy** (r) - a disease that begins to affect individuals between the ages 2 and 6. It causes muscle wasting and weakness. This can eventually affect all muscles of the body. Generally by age 10-12 affected individuals become confined to a wheelchair.
- **Anhidrotic Ectodermal Dysplasia -** a group of disorders characterized by the absence of sweat glands, abnormal teeth, and hypotrichosis (less hair than normal)
- **Fragile X Syndrome** - A disorder that causes various levels of mental impairment-- from learning disabilities to severe retardation, both combined with delayed speech and language development. caused by more than 200 repeats of the trinucleotide CGG. Karyotypes of individuals with Fragile X Syndrome appear to be missing a small piece of the X chromosome near the end.
- **Lesch-Nyhan Disease -** the absence of an enzyme HPRT (hypoxanthine-guanine phosphoribosyltransferase) causes an accumulation of uric acid in the urine and self-mutilative behavior

Y-linked

- **Hairy ears** - hair grows on the pinnae of the ears-- in some cases it is quite thick; in others it is only one
- or two long hairs

Nondisjunction

Autosomes:

- **Down's syndrome (trisomy 21**) - an extra copy of the 21st chromosome-- generally through
- non-disjunction but occasionally the extra copy of critical chromosome material can be as
- a result of translocation causing a combination of birth defects including some mental retardation
- and characteristic facial features
- **monosomy 21** ï a chromosome missing in pair 21.

Sex Chromosomes:

- **monosomy X (Turner's syndrome)**
- **trisomy X**
- **XXY (Klinefelter's syndrome)**
- **XYY**
- **XXXX or XXXY**

Multifactorial Inheritance (many genes + environment)

- **cleft palate and/or lip**
- **club foot**
- **congenital dislocation of the hip**
- **spina bifida (open spine)**
- **hydrocephalus (with spina bifida)**
- **pyloric stenosis**
- **diabetes mellitus** ï Type I diabetes - Individuals do not produce insulin and must take shots of insulin to control their blood glucose levels
- **Breast Cancer** - multi-factorial- two genes have recently been identified inherited in an autosomal dominant fashion that increase susceptibility to breast cancer. These genes are known as BRCA1 and BRCA2. They are responsible for a very small proportion of all cases, particularly those which affect women at a younger age.