**Chromosomal Abnormalities Notes 2019**

**Concept: Alterations of chromosome number or structure cause some genetic disorders**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ occurs when the members of a pair of homologous chromosomes do not separate properly during meiosis I, or sister chromatids don’t separate properly during meiosis II.

As a result of nondisjunction, one gamete receives two copies of the chromosome, whereas the other gamete receives none. If the faulty gametes engage in fertilization, the offspring will have an incorrect chromosome number. This is known as aneupoloidy.

-Errors in meiosis or damaging agents like radiation can cause portions of a chromosome to be lost or rearranged, resulting in the following mutations:

-A deletion occurs when a chromosomal fragment is lost, resulting in a chromosome with missing genes.

-A duplication occurs when a chromosomal segment is repeated

-An inversion occurs when a chromosomal fragment breaks off and reattaches to its original position but backward, so that the part of the fragment that was originally at the attachment point is not at the end of the chromosome.

-A translocation occurs when the deleted chromosome fragment joins a nonhomologous chromosome.

Nondisjunction

Problems with meiotic spindle cause errors in daughter cells

-homologous chromosomes do not separate properly during Meiosis 1

-sister chromatids fail to separate during Meiosis 2;

-too many or too few chromosomes

-Fertilized eggs that have received three copies of the chromosomes in question are said to be trisomic. Those that have received just one copy of a chromosome are said to be monosomic for the chromosomes.

-\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ is the condition of having more than two complete sets of chromosomes, forming in 3n or 4n individual. Rare in animals, this condition is fairly frequent in plants.

High frequency in humans

-most embryos are spontaneously aborted

-alterations are too disastrous

-developmental problems result from biochemical imbalance

-imbalance in regulatory molecules?

-hormones?

-transcription factors?

-Certain conditions are tolerated

-upset the balance less = \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-but characteristic set of symptoms = syndrome

Down Syndrome:

Trisomy 21: 3 copies of chromosome 21

-1 in 700 children born in U.S.

Chromosome 21 is the smallest human chromosome but still severe effects

Frequency of Down syndrome correlates with the age of the mother

Genetic Testing

Amniocentesis in 2nd trimester: take a sample of embryo cells. Stain & photograph chromosomes. Then analysis of karyotype

Human development more tolerant of wrong numbers in sex chromosome

But produces a variety of distinct syndromes in humans

\_\_\_\_\_\_\_\_ = Klinefelter’s syndrome male

XXX = Trisomy X female

XYY = Jacob’s syndrome male

XO = Turner syndrome female

Klinefelter’s syndrome

-XXY male; one in every 2000 live births and have male sex organs, but are sterile

-can have feminine characteristics including some breast development and lack of facial hair

-tall

-normal intelligence

Jacob’s syndrome male

 -XYY Males

-1 in 1000 live male births

-extra Y chromosome

-slightly taller than average

-more active

-normal intelligence, slight learning disabilities

-delayed emotional maturity

-normal sexual development

Trisomy X

 -XXX

 -1 in every 2000 live births and produces healthy females

-Why?

-Barr bodies

-all but one X chromosome is inactivated

Turner Syndrome

Monosomy X or X0

-occurrence: 1 in every 5000 births

-Has varied degree of effects

-webbed neck

-short stature

-sterile

Pedigree analysis

-Pedigree analysis reveals Mendelian patterns in human inheritance. The data mapped on a family tree

-Pedigree can help us understand the past & predict the future

-Thousands of genetic disorders are inherited as simple \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ traits

-from benign conditions to deadly diseases

-albinism

-cystic fibrosis

-Tay sachs

-sickle cell anemia

-PKU

Recessive diseases

The diseases are recessive because the allele codes for either a malfunctioning protein or no protein at all

Heterozygotes (Aa)

-carriers

-have a normal phenotype because one “normal” allele produces enough of the required protein

Cystic fibrosis (recessive)

 Primarily whites of European descent (strikes 1 in 2500 births)

-1 in 25 whites is a carrier (Aa)

-normal allele codes for a membrane protein that transports Cl- across cell membrane

-defective or absent channels limit transport of Cl- & H2O across cell membrane

-thicker & stickier mucus coats around cells

-mucus build-up in the pancreas, lungs, digestive tract & causes bacterial infections

-without treatment children die before 5;
-with treatment can live past their late 20s

Tay-Sachs (recessive)

Primarily Jews of eastern European (Ashkenazi) descent & Cajuns (Louisiana)

-strikes 1 in 3600 births: 100 times greater than incidence among non-Jews

-non-functional enzyme fails to breakdown lipids in brain cells

-fats collect in cells destroying their function

-symptoms begin few months after birth

-seizures, blindness & degeneration of muscle & mental performance

-child usually dies before 5ys

Sickle cell anemia (recessive)

Primarily Africans

-strikes 1 out of 400 African Americans

-high frequency

-caused by substitution of a single amino acid in hemoglobin

-when oxygen levels are low, sickle-cell hemoglobin crystallizes into long rods

-deforms red blood cells into sickle shape

-sickling creates pleiotropic effects = cascade of other symptoms

 -Substitution of one amino acid in polypeptide chain

Sickle cell phenotype

2 alleles are codominant

-both normal & mutant hemoglobins are synthesized in heterozygote (Aa)

-50% cells sickle; 50% cells normal

-carriers usually healthy

-sickle-cell disease triggered under blood oxygen stress such as exercise

Heterozygote advantage

Malaria

-single-celled eukaryote parasite spends part of its life cycle in red blood cells

In tropical Africa, where malaria is common:

-homozygous dominant individuals die of malaria

-homozygous recessive individuals die of sickle cell anemia

-heterozygote carriers are relatively free of both

-reproductive advantage

High frequency of sickle cell allele in African Americans is vestige of African roots

Huntington’s chorea (dominant)

-Dominant inheritance

-repeated mutation on end of chromosome 4

-mutation = CAG repeats

-glutamine amino acid repeats in protein

-one of 1st genes to be identified

-build up of “huntingtin” protein in brain causing cell death

-memory loss

-muscle tremors, jerky movements

-“chorea”

-starts at age 30-50

-early death

-10-20 years after start

Polydactyly (dominant)

-More fingers/toes/digits

Genetics and Culture

-Why do all cultures have a taboo against incest?

-laws or cultural taboos forbidding marriages between close relatives are fairly universal

-Fairly unlikely that 2 unrelated carriers of same rare harmful recessive allele will meet & mate

-but matings between close relatives increase risk

-“consanguineous” (same blood) matings

-individuals who share a recent common ancestor are more likely to carry same recessive alleles

**Concept: Some inheritance patterns are exceptions to standard Mendelian inheritance**

-In mammals, geneticists have identified traits that differ, depending on which parent passed along the allele for those traits. This phenomenon is called genomic \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. The phenotypic effect of a gene may depend on which allele is inherited from which parent.

-Genomic imprinting occurs during gamete formation and results in the silencing of a particular allele of certain genes. The offspring expresses only one allele of an imprinted gene, hence the exception to Mendelian inheritance. Over 60 imprinted genes have been identified, with hundred more suspected.

-Genes that are present in mitochondria and plastids are inherited only from the mother because the zygote’s cytoplasm comes only from the egg. You inherited your mitochondrial DNA only from your mother; your mother inherited her mitochondrial DNA only from her mother. Your mitochondrial DNA is your maternal grandmother’s!