Chapter 6

1. Principles of Inheritance
    a. Congenital disorders: present at birth, genetic/environmental causes mental retardation
    b. Congenital malformations: structural defects due to errors in fetal development, mostly genetic causes brain malformation
    c. Inherited genetic disorders that appear in later life are not considered congenital
2. Principles of Inheritance
    a. Gregor Mendel: first to notice that traits are transmitted in a predictable manner from parent to offspring
    b. Phenotype: observable physical/biochemical traits- eye color
    c. Genotype: unique genetic makeup, results from 23 maternal and 23 paternal chromosomes uniting at conception XX, XY
    d. Chromatids: two identical linear chromosome units which separate during meiosis
    e. Centromere: point at the center of X where 2 sister chromatids fuse
    f. Diploid: human chromosomes exist in homologous pairs with unique DNA sequences, one chromosome from each parent
        i. 23 pairs, 46 chromosomes
3. Principles of Inheritance
    a. Electron micrograph of chromosome: two sister chromatids attached at centromere
        i. P= short arm
        ii. Q= long arm
    b. Standard map of banding pattern of each of the 23 human chromosomes
        i. Alleles
4. Principles of Inheritance
    a. Chromosomes characterized by:
        i. Total size
        ii. X arm lengths
        iii. Specific band patterns when exposed to certain stains
5. 23 pairs of chromosomes:
    a. 22 homologous pairs: autosomes
    b. 1 hemizygous pair: sex chromosomes
        i. Female: XX, homologous, 1 X from each parent
        ii. Male: XY: heterogeneous, 1 maternal X and 1 paternal Y
6. Principles of Inheritance

a. Meiosis Replication of sex chromosome
b. Mitosis- replication of autosomes
c. Female puberty: mitosis 2, producing eggs
d. Two germ cells (egg and sperm), each with haploid number of chromosomes, combine to form new cell with complete 46 chromosomes
e. Requires two divisions of chromosome DNA

7. Principles of Inheritance
    a. Stages of Meiosis
        i. Duplicated sister chromatids closely contact their homologous pairs
        ii. Crossing over: parts of homologous pairs are precisely exchanged in order to mix maternal and paternal genes, results in new genetic combination
        iii. First cell division: 2-3 cross-over events, creates 2 diploid cells
        iv. Second cell division: sister chromatids pulled apart, creates 4 haploid cells
8. Principles of Inheritance
    a. Genetic Traits
        i. Genes coding for specific trait are found at specific loci on a chromosome and come in several forms called alleles
        ii. Each gene has 2 alleles, 1 from each parent, and can determine homozygous/heterozygous traits
    b. Types of alleles: dominant and recessive- must be homozygous to be expressive
    c. Types of traits
        i. Codominant: no clear dominant/recessive alleles, traits combine
        ii. Monogenic: interaction of single gene locus
        iii. Polygenic: interaction of multiple gene loci, heritable, unpredictable, affected by environmental factors
9. Principles of Inheritance
    a. DNA mutation and repair
        i. Mutation: rare, permanent change in DNA structure
        ii. Mutagens: radiation, chemicals, viruses, etc
        iii. Types of DNA damage:
            1. Single stranded break: easy repair (complementary strand still present)
            2. Double stranded break: permanent loss of genetic information at break point possible
        iv. Epstein-Barr Virus
            1. Cause lymphomas
            2. Nasal-pharyngeal carcinomas

10. Principles of Inheritance
    a. DNA mutation types
    b. Point mutation: single base pair substitution, results in affected codon to code an abnormal amino acid
    c. Frameshift mutation: addition/removal of 1 or more bases, change reading frame (all codons change downstream of mutation), dramatic change to amino acid sequence Everything shifted and changed, abnormal
        i. All amino acids will be different
11. Principles of Inheritance
    a. Genetic Disorders
        i. Apparent at birth or later in life
        ii. Inherited or acquired during fetal development
        iii. Classified as
            1. Mendelian single-gene disorders: DNA mutation coding for particular protein
            2. Chromosomal abberations: segment loss/gain/translocation
            3. Multifactorial/Polygenic disorders
            4. Non-Mendelian single-gene disorders: triple repeat mutations, mitochondrial gene mutations, genomic imprinting mutations
12. Mendelian Single-Gene Disorders
    a. Alteration or mutation of single gene
    b. Defective gene codes for abnormal enzymes and proteins
    c. Classification
        i. Location of defective gene: autosomal/sex chromosome
    d. Mode of transmission: dominant/recessive
    e. Pedigree charts: tool to determine pattern of inheritance
13. Chromosomal Abnormalities
    a. Abnormal number of chromosomes or altered chromosome structure due to errors in chromosome separation or crossing over during meiosis/mitosis
    b. Etiological factors: idiopathic, radiation/chemicals/viruses
    c. Risk factors: advanced maternal (downs syndrome) or paternal age (achondroplasia- dwarfism- torso is normal, slightly enlarged or normal head, very short limbs), abnormalities in parental chromosome structure
    d. Mutations- gametes (telomere) affected, easily damaged
    e. Risk starts at 30, by age 35 risk is 1 in 500
14. Chromosomal Abnormalities
    a. Aneuploidy (ploid= # of chromosomes)