

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 aberrations: 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)