

McCance: Pathophysiology, 6th Edition

Chapter 04: Genes and Genetic Diseases

Key Points – Print

SUMMARY REVIEW

DNA, RNA, and Proteins: Heredity at the Molecular Level

1. Genes, the basic units of inheritance, are composed of DNA and are located on the chromosomes.
2. DNA is composed of deoxyribose, a phosphate molecule, and four types of nitrogenous bases. The physical structure of DNA is a double helix.
3. The DNA bases code for amino acids, which in turn make up proteins. The amino acids are specified by triplet codons of nitrogenous bases.
4. DNA replication is based on complementary base pairing, in which a single strand of DNA serves as the template for attracting bases that form a new strand of DNA.
5. DNA polymerase is the primary enzyme involved in replication. It adds bases to the new DNA strand and performs “proofreading” functions.
6. A mutation is an inherited alteration of genetic material (i.e., DNA).
7. Substances that cause mutations are called mutagens.
8. The mutation rate in humans varies from locus to locus and ranges from 10^{-4} to 10^{-7} per gene per generation.
9. Transcription and translation, the two basic processes in which proteins are specified by DNA, both involve RNA. RNA is chemically similar to DNA, but it is single stranded, has a ribose sugar molecule, and has uracil rather than thymine as one of its four nitrogenous bases.
10. Transcription is the process by which DNA specifies a sequence of mRNA.
11. Much of the RNA sequence is spliced from the mRNA before the mRNA leaves the nucleus. The excised sequences are called introns, and those that remain to code for proteins are called exons.
12. Translation is the process by which RNA directs the synthesis of polypeptides. This process takes place in the ribosomes, which consist of proteins and rRNA.
13. During translation, mRNA interacts with tRNA, a molecule that has an attachment site for a specific amino acid.

Chromosomes

1. Human cells consist of diploid somatic cells (body cells) and haploid gametes (sperm and egg cells).

2. Humans have 23 pairs of chromosomes: 22 of these pairs are autosomes. The remaining pair consists of the sex chromosomes. Females have 2 homologous X chromosomes as their sex chromosomes; males have an X and a Y chromosome.
3. A karyotype is an ordered display of chromosomes arranged according to length and the location of the centromere.
4. Various types of stains can be used to make chromosome bands more visible.
5. About 1 in 150 live births has a major diagnosable chromosome abnormality. Chromosome abnormalities are the leading known cause of mental retardation and miscarriage.
6. Polyploidy is a condition in which a euploid cell has some multiple of the normal number of chromosomes. Humans have been observed to have triploidy (three copies of each chromosome) and tetraploidy (four copies of each chromosome); both conditions are lethal.
7. Somatic cells that do not have a multiple of 23 chromosomes are aneuploid. Aneuploidy is usually the result of nondisjunction.
8. Trisomy is a type of aneuploidy in which one chromosome is present in three copies in somatic cells. A partial trisomy is one in which only part of a chromosome is present in three copies.
9. Monosomy is a type of aneuploidy in which one chromosome is present in only one copy in somatic cells.
10. In general, monosomies cause more severe physical defects than do trisomies, illustrating the principle that the loss of chromosome material has more severe consequences than the duplication of chromosome material.
11. Down syndrome, a trisomy of chromosome 21, is the best-known disease caused by a chromosome aberration. It affects 1 in 800 live births and is much more likely to occur in women older than 35 years of age.
12. Most aneuploidies of the sex chromosomes have less severe consequences than those of the autosomes.
13. The most commonly observed sex chromosome aneuploidies are the 47,XXX karyotype, 45,X karyotype (Turner syndrome), 47,XXY karyotype (Klinefelter syndrome), and 47,XYY karyotype.
14. Abnormalities of chromosome structure include deletions, duplications, inversions, and translocations.

Elements of Formal Genetics

1. Mendelian traits are caused by single genes, each of which occupies a position, or locus, on a chromosome.
2. Alleles are different forms of genes located at the same locus on the chromosome.
3. At any given locus in a somatic cell, an individual has two genes, one from each parent. An individual may be homozygous or heterozygous for a locus.

4. An individual's genotype is his or her genetic makeup, and the phenotype reflects the interaction of genotype and environment.
5. At a heterozygous locus, a dominant gene's effects mask those of a recessive gene. The recessive gene is expressed only when it is present in two copies.

Transmission of Genetic Diseases

1. Genetic diseases caused by single genes usually follow autosomal dominant, autosomal recessive, or X-linked recessive modes of inheritance.
2. Pedigree charts are an important tool in the analysis of modes of inheritance.
3. Recurrence risks specify the probability that future offspring will inherit a genetic disease. For single-gene diseases, recurrence risks remain the same for each offspring, regardless of the number of affected or unaffected offspring.
4. The recurrence risk for autosomal dominant diseases is usually 50%.
5. Germline mosaicism can alter recurrence risks for genetic diseases because unaffected parents can produce multiple affected offspring. This situation occurs because the germline of one parent is affected by a mutation but the parent's somatic cells are unaffected.
6. Skipped generations are not seen in classic autosomal dominant pedigrees.
7. Males and females are equally likely to exhibit autosomal dominant diseases and to pass them on to their offspring.
8. A gene that is not always expressed phenotypically is said to have incomplete penetrance.
9. Penetrance may be age-dependent, as in Huntington disease and familial breast cancer.
10. Variable expressivity is a characteristic of many genetic diseases.
11. Evidence is increasing that the same DNA sequence can produce different phenotypes. Chemical modifications can alter the phenotype or expression of genes.
12. Epigenetics is the term used to describe modifications that affect phenotype without altering DNA sequencing.
13. Genomic imprinting, which may involve methylation, results in differing expressions of a disease gene, depending on which parent transmitted the gene.
14. Most commonly, parents of children with autosomal recessive diseases are both heterozygous carriers of the disease gene.
15. The recurrence risk for autosomal recessive diseases is 25%.
16. Males and females are equally likely to be affected by autosomal recessive diseases.
17. Consanguinity is often present in families with autosomal recessive diseases, and it becomes more prevalent with rarer recessive diseases.
18. Carrier detection tests for an increasing number of autosomal recessive diseases are available.
19. The frequency of genetic diseases approximately doubles in the offspring of first-cousin matings.

20. In each normal female somatic cell, one of the two X chromosomes is inactivated early in embryogenesis.
21. X inactivation is random, fixed, and incomplete (i.e., only part of the chromosome is actually inactivated). It may involve methylation.
22. Gender is determined embryonically by the presence of the *SRY* gene on the Y chromosome. Embryos that have a Y chromosome (and thus the *SRY* gene) become males, whereas those lacking the Y chromosome become females. When the Y chromosome lacks the *SRY* gene, an XY female can be produced. Similarly, an X chromosome that contains the *SRY* gene can produce an XX male.
23. X-linked genes are those that are located on the X chromosome. Nearly all known X-linked diseases are caused by X-linked recessive genes.
24. Males are hemizygous for genes on the X chromosome.
25. X-linked recessive diseases are seen much more often in males than in females because males need only one copy of the gene to express the disease.
25. Fathers cannot pass X-linked genes to their sons.
26. Skipped generations are often seen in X-linked recessive disease pedigrees because the gene can be transmitted through carrier females.
28. Recurrence risks for X-linked recessive diseases depend on the carrier and affected status of the mother and father.
29. A sex-limited trait is one that occurs in only one of the sexes.
30. A sex-influenced trait is one that occurs more often in one sex than in the other.

Linkage Analysis and Gene Mapping

1. During meiosis I, crossing over occurs and can cause recombinations of alleles located on the same chromosome.
2. The frequency of recombinations can be used to infer the map distance between loci on the same chromosome.
3. Loci that are on the same chromosome are syntenic.
4. A marker locus, when closely linked to a disease-gene locus, can be used to predict whether an individual will develop a genetic disease.
5. A more complete gene map will facilitate marker studies, studies of gene function and interaction, and gene therapy.