The ABCs of Genetics

Self-Study Course, 2nd Edition

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The ABCs of Genetics

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The ABCs of Genetics
PREFACE

The desired and expected outcome of any pregnancy is the birth of a healthy, perfect baby. However, a small but significant number of babies are born with a congenital anomaly or a genetic disease. These babies’ parents experience a combination of grief, fear, sorrow, disappointment, and anger in response to the birth. The realization that the infant might have inherited the condition from one of the parents sometimes leads to feelings of guilt and tension within the family. The parents have many questions: “What caused it?” “What did we do?” “Is there a cure?” “Will it happen in future pregnancies?” The neonatal nurse who is prepared with a basic knowledge of genetics can anticipate the parents’ questions and concerns and, most important, can support the family during this difficult experience.

The age of first-time American mothers has risen steadily. American women are simply waiting longer to begin having families. In 2002 the average American woman having her first baby was 25.1 years old. In 1970 the average age was 21.4 years. The overall birth rates among women ages 35 to 39 (41 births per 1,000 women) and those ages 40 to 44 (8 per 1,000 women) were at the highest levels for those age groups in 3 decades. As women age, their risk of certain genetic disorders also increases (Centers for Disease Control and Prevention, National Center for Health Statistics, 2002).

The ABCs of Genetics outlines the basic principles of human genetics. It is intended to help the reader understand genetic inheritance patterns and the common neonatal conditions that have genetic underpinnings. Practice tests appear throughout to help the reader learn the concepts.
I. Basic Principles of Genetics

A. Definitions

1. Genetics: The science of human biologic variation
2. Deoxyribonucleic acid (DNA): A double-stranded nucleic acid built of nucleotides containing a phosphate group, a nitrogenous base (adenine, thymine, guanine, or cytosine), and the sugar deoxyribose (see Figure 1)
3. Mutation: A permanent, hereditary change in the sequence of the DNA
4. Chromosome: Structural unit composed of DNA on a framework of protein. Chromosomes carry genetic information. They are located in the cell nucleus and are visible in dividing cells as deeply stained, rod-shaped, or J-shaped structures. Each human cell has 23 pairs of chromosomes.
   a. Autosome: Nonsex chromosome; each human cell has 22 pairs of autosomes.
   b. Sex chromosome: Chromosome that contains the genes determining sex; each human cell has two sex chromosomes (i.e., one pair). Based on their appearance, the chromosomes of males are identified as XY and those of females as XX.
   c. Karyotype: The chromosome constitution of an individual. Also refers to a size-order chart of chromosomes in which the autosomes are numbered 1–22 on the basis of their overall length, except that chromosome 21 is slightly shorter than chromosome 22 (see Figure 2).
   d. Gene: A sequence of chromosomal DNA that can specify the sequence of amino acids in a particular polypeptide (protein sequence). The composition of genes is inherited from one’s parents and is referred to as the hereditary unit.
      (1) Allele: Alternate form of a gene found at the same locus (position) on homologous (the same or similar) chromosomes. Alleles segregate during meiosis, and an individual receives only one of each pair of alleles from each parent. Only two alleles can be present in any one individual.
      (2) Homozygous: Having two identical alleles for a particular gene
      (3) Heterozygous: Having two different alleles for a particular gene
      (4) Genotype: An individual’s genetic constitution; the alleles present at one locus
      (5) Phenotype: The observed biochemical, physiological, and morphological characteristics of an individual (e.g., blue eyes, fair skin), as determined by his or her genotype and the environment in which it is expressed
5. Pedigree: A standard chart that simultaneously displays family relationships and phenotypes. A pedigree is constructed of shapes connected by lines. Squares indicate...
males, circles indicate females, and diamonds indicate individuals of unspecified sex. Colored shapes indicate individuals who express the trait being evaluated, and half-filled shapes represent carriers. Vertical lines represent generations, horizontal lines connecting shapes at their centers represent parents, and shapes connected by vertical lines joined horizontally above them represent siblings (Lewis, 2008). Examples of pedigrees can be found in Figures 12–15.

B. History
1. 1860s: Gregor Mendel studied the transmission of seven traits in pea plants. He crossbred the plants and proposed the existence of homozygous and heterozygous alleles. His finding that alleles separate during meiosis was later called the law of segregation. Mendel’s second law, the law of independent assortment, states that a gene for one trait does not influence the transmission of a gene for another trait.
2. 1869: Miescher first isolated DNA, but it was not chemically characterized until the 1940s.
3. 1953: Watson and Crick proposed the double helical conformation of DNA.
4. 1956: Humans were discovered to have 46 chromosomes.
5. 1959: The first human chromosome abnormality was discovered (i.e., trisomy 21 in Down syndrome).
6. 1963: Population screening for a genetic disease (i.e., phenylketonuria) was introduced.
7. 1966: The first prenatal chromosomal analysis was performed.
8. 1972: Alpha-fetoprotein screening was introduced.
9. 1985: DNA was first used for genetic fingerprinting.
10. 1990: The Human Genome Project was launched. It is an international effort first to map and eventually to sequence all of the estimated 50,000–100,000 human genes.
11. 1997: Researchers at Scotland’s Roslin Institute reported cloning a sheep by transferring a cell nucleus from an adult ewe into an embryonic sheep cell. The result was a sheep named Dolly.
12. 1998: A human genetic map was produced, showing the chromosomal locations of markers from more than 30,000 human genes.
15. 2006: The Cancer Genome Atlas (TCGA) project was started.
16. 2006: Initiatives to establish the genetic and environmental causes of common diseases were launched (Lewis, 2008; National Human Genome Research Institute, 2007).

C. Cell division: Mitosis and meiosis
1. Mitosis (see Figure 3)
   a. One division
   b. Two daughter cells per cycle
   c. Daughter cells are genetically identical to each other and to the parent cell.
   d. The number of chromosomes in the daughter cells is the same as the number in the parent cell (2n [i.e., two daughter cells]).
   e. Occurs in somatic cells
   f. Occurs throughout the life cycle
   g. Used for growth, repair, and asexual reproduction
2. Meiosis (see Figure 4)
   a. Two divisions
   b. Four daughter cells per cycle
   c. Daughter cells are genetically different from one another and from the parent cell.
   d. The number of chromosomes in the daughter cells is half that of the parent cell (1n [i.e., one daughter cell]).
   e. In humans, meiosis is completed only after sexual maturity.
   f. Used for sexual reproduction, in which
new gene combinations arise (see Figure 5; Lewis, 2008)

II. Chromosome Disorders
A. Incidence
1. One in 150 live births
2. Chromosome disorders are the leading known cause of mental retardation and pregnancy loss. Chromosome abnormalities are seen in 50% of first trimester and 20% of second trimester miscarriages. Yet only 0.65% of newborns have abnormal chromosomes.
3. Chromosome abnormalities are an important cause of morbidity and mortality (Jorde, Carey, Bamshad, & White, 2003).
4. The chromosome disorders most commonly seen in the neonatal intensive care unit are outlined here.

B. Chromosome number abnormalities
1. The most frequent cause of all chromosome disorders is nondisjunction.
   a. Nondisjunction occurs when paired chromosomes fail to separate during cell division.
   b. If nondisjunction occurs in the sperm or the egg before fertilization, the resulting zygote has an abnormal chromosome makeup in all of its cells (i.e., trisomy or monosomy).

Figure 3. Mitosis

Figure 4. Meiosis
Diagrammatic representation of the process and its consequences. Two chromosome pairs and a single crossover in one chromosome pair, allowing for eight arrangements in the gametes, are shown. Meiosis I: 1 to 4, stages of prophase I; 5a and 5b, alternative arrangements of the chromosome pairs at metaphase I; 6a and 6b, anaphase I; 7a and 7b, telophase I; 8a1, 8a2, 8b1, 8b2, the four possible distributions of the parental chromosome pairs at the end of meiosis I. Meiosis II: 9al, 9a2, 9bl, 9b2, metaphase II; 10al, 10a2, 10b1, 10b2, anaphase II; 11a1, 11a2, 11b1, 11b2, the eight combinations of the genetic material possible in the gametes. From Genetics in Medicine (5th ed., p. 24–25), by M. W. Thompson, R. R. McInnes, and H. F. Willard, 1991, Philadelphia: W. B. Saunders. Copyright 1991 by W. B. Saunders. Reprinted with permission.
c. If nondisjunction occurs after fertilization, the zygote has cells with two or more different chromosome makeups, which will evolve into two or more cell lines within the same cell (i.e., mosaicism).

2. Nondisjunction is most commonly seen as trisomies, monosomies, or polyploidy.
   a. Trisomy: Three copies of one chromosome are present in one cell.
   b. Monosomy: One chromosome from a pair is missing.
   c. Polyploidy: The presence of any multiple of the basic haploid chromosome number (n) other than the diploid number (2n; e.g., 3n [69 chromosomes], 4n [92 chromosomes]). Most human polyploids die as embryos or fetuses, but occasionally an infant survives for a few days, with defects in nearly all organs (Lewis, 2008).

C. Chromosome structure abnormalities
   1. Deletion: A missing sequence of DNA or a missing part of a chromosome (see Figure 6)
   2. Duplication: An extra copy of a gene or DNA sequence, usually caused by misaligned pairing in meiosis
   3. Inversion: A part of a chromosome that has moved from its normal location; the normal sequence may be reversed.
   4. Nonreciprocal translocation: A piece that has broken off of one chromosome and become attached to another chromosome (e.g., in 97% of patients with chronic myeloid leukemia, the tip of chromosome 22 is attached to chromosome 9).
   5. Reciprocal translocation: Exchange of parts between two chromosomes. If the chromosome exchange does not break any genes, then the person is healthy and is called a translocation carrier. A common reciprocal translocation is between chromosomes 14 and 21 (Jorde et al., 2003).

D. Autosomal abnormalities
   1. Trisomy 21 (Down) syndrome
      a. Incidence
         (1) One in 660 live births; the most common chromosomal abnormality (Jones, 2006)
         (2) Relationship of maternal age to incidence (see Table 1)
      b. Genetic factors: Trisomy 21 (nondisjunction, usually during meiosis I) is present in 94% of infants born with Down syndrome; 14/21 unbalanced translocation, in 3.3%; and mosaicism, in 2.4%. Mosaic Down syndrome has the classic clinical features, except that the person may have normal intelligence.
      c. Clinical features
         (1) Hypotonia (80%)
         (2) Flattened facial profile (90%)
         (3) Poor moro reflex (85%)
         (4) Hyperflexibility of joints (80%)
         (5) Excess of skin on back of neck (80%)
         (6) Slanted palpebral fissures (80%)
         (7) Dysplasia of pelvis (70%)
(8) Anomalous auricles (60%)
(9) Congenital heart defects (40%)
(10) Transverse palmar crease (i.e., simian crease; 45%)
(11) Gastrointestinal anomalies such as duodenal atresia (12%)
(12) Small nose with low nasal bridge and tendency to have inner epicanthal folds
(13) Mental deficiency
(14) Brushfield spots (i.e., white speckling of the iris)
(15) Protrusion of the tongue
(16) High, arched palate
(17) Short fingers with incurved fifth finger
(18) Abnormal dermatoglyphics (i.e., ridged pattern of skin on fingers)

Table 1. Relationship of Mother’s Age to Incidence of Down Syndrome

<table>
<thead>
<tr>
<th>Maternal age (years)</th>
<th>Chance of Down syndrome</th>
<th>At 12 weeks</th>
<th>At birth</th>
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<tr>
<td>20</td>
<td>1 in 1070</td>
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<td>1 in 950</td>
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<td>1 in 310</td>
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<td>44</td>
<td>1 in 20</td>
<td>1 in 30</td>
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</tr>
</tbody>
</table>


d. Course and prognosis
(1) Short stature and mental retardation are always present (except in mosaic Down syndrome). Average IQ is less than 50, although social performance is often beyond that expected for mental age.
(2) Muscle tone tends to improve with age, whereas the rate of developmental progress slows with age.
(3) Males are always infertile, but females are not always so.
(4) Average life span is 49 years (Jones, 2006).

2. Trisomy 18 (Edward) syndrome (see Figures 7 & 8)

a. Incidence
(1) One in 6,000–8,000 live births; the second most common chromosomal abnormality
(2) Approximately 95% are aborted spontaneously.
(3) The female-to-male ratio is 3:1.
(4) Advanced maternal age is a factor.

b. Genetic factors: Complete trisomy, translocation, and mosaic forms

c. Clinical features (most common listed first)
(1) Severe mental deficiency
(2) Congenital heart defects (95%—usually severe defects)
(3) Clenched hands with overlapping of index finger over third finger and of fifth finger over fourth finger (50% or more)
(4) Severe hypotonia
(5) Prominent occiput (50% or more)
(6) Low-set, malformed auricles
(7) Narrow palatal arch (50% or more)
(8) Abnormal dermatoglyphics (50% or more)
(9) Single umbilical artery (50% or more)
(10) Short sternum (50% or more)
(11) Abnormal posture with flexion deformities of hips and limbs (50% or more)
(12) Microstomia (i.e., small mouth; 50% or more)
(13) Micrognathia (i.e., small jaw; 50% or more)
(14) Cryptorchidism (i.e., undescended testis; 50% or more)
(15) Growth deficiencies (50% or more)
(16) Syndactyly (i.e., webbing of the fingers; 10%–50%)
(17) Rocker bottom feet (10%–50%)
(18) Ptosis (i.e., drooping eyelid; 10%–50%)
(19) Gastrointestinal tract abnormalities such as omphalocele, malrotation of the intestine, and imperforate or malpositioned anus (10%–50%)
(20) Corneal opacities (<10%)
(21) Facial palsy (<10%)
(22) Renal abnormalities
(23) Various other organ malformations
d. Prognosis: 50% die within the first week and many of the remaining die in the next 12 months. Median age of survival is 14.5 days. Although rare, some older children smile, laugh, and interact with their families. There are at least 10 reports of affected children over the age of 10 (Chen, 2007; Jones, 2006).

3. Trisomy 13 (Patau) syndrome (see Figure 9)
a. One in 5,000 births
   (1) Risk of recurrence in future children is low.
   (2) Advanced maternal age is a factor.
b. Genetic factors: The extra chromosome usually arises from nondisjunction in maternal meiosis I; approximately 20% are caused by an unbalanced translocation.
c. Clinical features (most common are listed first)
   (1) Severe mental deficiency (100%)
   (2) Congenital heart defects (80%)
   (3) Cleft lip (60%–80%) and palate (50% or more)
(4) Holoprosencephaly-type deficit with varying degrees of incomplete development of forebrain and olfactory and optic nerves (50% or more)
(5) Microcephaly (i.e., abnormal smallness of the head) with sloping forehead and wide sagittal sutures and fontanels (50% or more)
(6) Microphthalmia (i.e., abnormal smallness of one or both eyeballs) and/or coloboma (i.e., a cleft of the iris that looks like a key; 50% or more)
(7) Apparent deafness (50% or more)
(8) Single umbilical artery (50% or more)
(9) Abnormal posturing of fingers (50% or more)
(10) Seizures (50% or more)
(11) Malformed ears (50% or more)
(12) Polydactyly (i.e., extra digits; 50% or more)
(13) Hyperconvex, narrow fingernails (50% or more)
(14) Skin defects of the posterior scalp (50% or more)
(15) Hemangiomas (i.e., a congenital anomaly in which a proliferation of vascular endothelium leads to a mass resembling neoplastic tissue; it can occur anywhere but is most frequently noticed in the skin and subcutaneous tissues; 50% or more)
(16) Bicornuate uterus in females (50% or more)
(17) Cryptorchidism and abnormal scrotum in males (50% or more)
(18) Severe hypotonia (<50%)
(19) Gastrointestinal tract defects (<50%)
(20) Micrognathia (<50%)
(21) Abnormal dermatoglyphics (<50%)
(22) Various other organ malformations
d. Prognosis: Median survival age is 7 days. Only one adult, 33 years of age, has been reported. Ninety-one percent die within first year (Best & Stallworth, 2006; Jones, 2006).

Figure 10. Newborn Infant with Cri du Chat Syndrome

PRACTICE QUESTIONS
1. The most common cause of trisomy 21 Down syndrome is
   a. nondisjunction
   b. translocation
   c. mosaicism
2. Name five common clinical features of infants with Down syndrome.
   a. ________________________________________
   b. ________________________________________
   c. ________________________________________
   d. ________________________________________
   e. ________________________________________
3. True or false? Infants with trisomy 13 or trisomy 18 syndrome usually die within the first year of life, although some live longer.
4. Clenched hands with overlapping fingers, abnormal posture with flexion deformities, a short sternum, and low-arch dermal ridge patterning on the fingertips are all associated with
   a. trisomy 18
   b. trisomy 13
5. Microcephaly, polydactyly, narrow hyperconvex fingernails, skin defects of the posterior scalp, and cleft lip and palate are all associated with
   a. trisomy 18
   b. trisomy 13
E. Sex chromosome abnormalities

1. Monosomy X (XO; Turner) syndrome (see Figure 11)
   a. Incidence
      (1) One in 2,500 live births
      (2) Usually occurs sporadically
      (3) The single most common abnormality in abortuses (18%)
   b. Genetic factors
      (1) Mosaicism in 25%; an isochromosome of the long arm of X in 17%; other structural abnormalities (i.e., ring X or short arm with deletion of one X) in a small percentage
      (2) The meiotic error usually is paternal.
      (3) The basis for the unusually high frequency of X or Y chromosome nondisjunction in paternal meiosis is unknown.
      (4) It is unclear why the karyotype is usually lethal in utero although it apparently is fully compatible with postnatal survival.
   c. Clinical features
      (1) Ovarian dysgenesis with hypoplasia to absence of germinal elements (>90%)
      (2) Broad shieldlike chest with widely spaced nipples (>80%)
      (3) Congenital lymphedema (i.e., puffy hands and feet; >80%)
      (4) Anomalous auricles (>80%)
      (5) Cubitus valgus (i.e., deviation of the extended forearm away from the midline of the body; >70%)
      (6) Excessive pigmented nevi (>50%)
      (7) Renal anomalies (>60%)
      (8) Webbed posterior neck (50%)
      (9) Low posterior hairline
      (10) Congenital heart disease: Bicuspid aortic valve (30%) and coarctation of the aorta (10%)
      (11) Underdeveloped secondary sex characteristics
      (12) Primary amenorrhea and infertility in females. However 10%–20% will have spontaneous menses, although it is usually transient; at least several 45X individuals have been fertile.
      (13) Intelligence and lifespan usually within normal limits
      (14) Some perceptual difficulties
      (15) Short stature
   d. Management: Growth hormone may help a child with Turner syndrome grow taller. Estrogen replacement therapy is often started when the girl is 13 or 14 years old. This helps induce the growth of breasts, pubic hair, and other sexual characteristics (Jones, 2006).

2. XXX (triple X) syndrome
   a. Incidence: One in 1,000 live births
   b. Genetic factors: Almost all cases result from errors in maternal meiosis, the majority in meiosis I. An increased maternal age effect has been seen for these females.
   c. Clinical features
      (1) Significant deficit in performance on intelligence tests; about 70% have serious learning problems.
      (2) Above average in stature, but not phe- notypically abnormal
      (3) Sexual development usually normal (Jones, 2006)

3. XXY (Klinefelter) syndrome
   a. Incidence: One in 500 live births; 50% of conceptions are lost prenatally.
   b. Genetic factors
      (1) Mosaic karyotypes in 15%; errors in paternal meiosis I in 50%; errors in maternal meiosis I in 33%; errors in
meiosis II or a postzygomatic meiotic error leading to mosaicism in 33%
(2) Affected individuals have a Barr body (i.e., one of the two X chromosomes is inactivated).
(3) There are several variants (i.e., XXY, XXXY, XXXXY). As a rule, the presence of each additional X chromosome causes a more abnormal phenotype.
c. Clinical features
(1) Although a wide range of IQs have been noted from well below to well above average, mean full-scale IQ is between 85 and 90 (Jones, 2006). Significant problems in expressive language, auditory processing abilities, and auditory memory
(2) Poor psychosocial development, insecurity, shyness, poor judgment; peer relationships are difficult.
(3) Tall and thin stature; long legs
(4) Occasional gynecomastia
(5) Physically normal genitalia until puberty, when hypogonadism (i.e., inadequate gonadal function caused by deficiencies in gametogenesis and/or the secretion of gonadal hormones) occurs
(6) Infertile; hypogenitalism (i.e., small testes and underdeveloped secondary sexual characteristics)
d. Treatment: Testosterone therapy may be prescribed beginning at the age of 11 or 12 years. This may help increase strength, improve appearance of muscles, grow body hair, improve mood and self-esteem, increase energy and sex drive, and improve concentration. Occasionally an infertility specialist may help a man to reproduce. Incidence of breast cancer is increased 20 times that of the normal male population (Jones, 2006).
4. XYY syndrome
a. Incidence: One in 840 live births
b. Genetic factors: Paternal nondisjunction at meiosis II, producing YY sperm
c. Clinical features
(1) IQ usually within normal limits but usually lower than siblings’; some poor motor coordination, speech delay, and learning disabilities (50%)
(2) Not dysmorphic but often large teeth, prominent glabella, and long ears
(3) Long at birth but tall stature is not evident until age 5 or 6 years.
(4) Increased risk of behavioral problems, hyperactivity, and temper tantrums; early reports suggested an increase in proportion of XYY individuals among institutionalized male juvenile delinquents. However, this does not seem to be a serious problem for these males in childhood or adolescence.
(5) Normal fertility (Jones, 2006)

**PRACTICE QUESTIONS**
1. Congenital lymphedema and widely spaced nipples are common in which of the following disorders?
   a. XO (Turner) syndrome
   b. XXY (Klinefelter) syndrome
   c. XYY
   d. XXX (triple X) syndrome
2. True or false? Females with Turner syndrome are infertile.
3. Hypogonadism and hypogenitalism are common in which disorder? ____________________________________________
4. An increased risk of behavioral problems is associated with which disorder? ____________________________________________

**III. Mendelian Single-Gene Disorders**

**A. Incidence**
One in 200 (Medline Plus, 2007)

**B. Autosomal dominant disorders**
1. Only one copy of the single abnormal gene is required (see **Figure 12**).
2. The trait appears in every generation, with no skipping of generations.
3. The trait is transmitted by an affected person to, on average, 50% of his or her offspring.

**Figure 12. Pedigree of Family with Huntington Disease**
4. Unaffected persons do not transmit the trait to their children.
5. Males and females are equally affected.
6. Mutations occur more frequently in the offspring of fathers who are more than 40 years old.
7. The genetic alteration appears in the phenotype in different ways (variable expressivity; Lewis, 2008).

C. Autosomal recessive disorders
1. The trait characteristically appears only in siblings, not in parents or other relatives (see Figure 13).
2. Two copies of the gene are required, one from each parent.
3. On average, 25% of the offspring of a couple are affected (i.e., the recurrence risk is 1 in 4 for each birth).
4. Males and females are equally affected.
5. The genetic alteration appears in the phenotype in the same way within a family (constant expressivity).
6. The chance of an autosomal recessive disorder is increased if both parents belong to the same family (Lewis, 2008).

D. X-linked dominant disorders
1. Affected males transmit the trait to all of their daughters and to none of their sons (see Figure 14).
2. Affected females who are heterozygous transmit the condition to half of their children of either sex. Affected females who are homozygous transmit the trait to all of their children.
3. In rare X-linked dominant disorders, twice as many females as males are affected; females are likely to express the trait in a milder form (Lewis, 2008).

E. X-linked recessive disorders
1. The trait occurs almost exclusively in males (see Figure 15).
2. The trait is passed from an affected man through all of his daughters and to half of his daughters’ sons.
3. The trait is never transmitted directly from father to son.
4. The trait can be transmitted through a series of female carriers; the affected males in a kindred are related to one another through females (Lewis, 2008).
F. **Common Mendelian single-gene disorders**

1. **Cystic fibrosis (CF)**
   a. Incidence: One in 2,500 live births. 1:25
      
      Caucasians is a heterozygote carrier of the CF gene.
   b. Genetic factor: Autosomal recessive.
      
      Majority with mutation in 508 position on chromosome 7.
   c. Defect: There is a protein abnormality that is responsible for chloride transport (CF transmembrane regulator) that leads to thick mucous in lumens of pancreas, lungs, intestines, biliary tract, and appendix.
   d. Clinical features
      
      (1) In the newborn
         - Meconium ileus
         - Intestinal atresia
         - Perforations and/or prolonged neonatal jaundice
      
      (2) In the infant
         - Failure to thrive
         - Chronic cough
         - Recurrent bronchiolitis, hyperinflation, persistent infiltrates, atelectasis
         - Chronic, foul-smelling diarrhea; abdominal distention
         - Persistent vomiting, especially with cough
         - Chronic hypochloremic metabolic alkalosis
   
   e. Diagnosis and clinical manifestation: Sweat test with sweat chloride concentration >60 mEq/L; not indicative of disease severity. Gene mutation analysis may be done.
   
   f. Treatment: Antibiotics, bronchodilators, corticosteroids, chest physiotherapy, pancreatic enzymes, and supplementation of fat-soluble vitamins. Gene therapy could eventually lead to a cure for this usually fatal disease (Bennett & Peckman, 2002; Jorde et al., 2003).
   
   g. Prognosis: For 80%, life expectancy of more than 30 years, if the person is compliant with treatment.

2. **Congenital myotonic dystrophy**
   a. Incidence: One in 7,500 live births
   b. Genetic factors: Autosomal dominant with anticipation (maternal effect) on the long arm of chromosome 19 for type I; a mother may show slight symptoms, but her children show increased disease severity. There may be a prenatal history of polyhydramnios and decreased fetal activity.
   c. Defect: In myotonic dystrophy type 1 (DM1) the gene is called a DMPK (dystrophia myotonica-protein kinase which codes for a myosin kinase expressed in skeletal muscle. In DM1 there is a triplet repeat of cytosine-thymine-guanine (CTG) in the DMPK gene. The average number of repeats in a healthy person is between 5 and 37. People affected with this have more than 50 and can have as many as 2,000 repeats.
   d. Clinical features
      
      (1) Poor sucking ability, difficulty swallowing
      
      (2) Generalized hypotonia
      
      (3) Facial diplegia (i.e., weakness on both sides of the face)
      
      (4) Clubfoot
      
      (5) Cataracts, ptosis
      
      (6) Mental retardation
      
      (7) Tent-shaped mouth
      
      (8) Gonadal insufficiency
      
      (9) Respiratory failure
   e. Diagnosis and clinical manifestations: Muscle biopsy, serum creatinine kinase, electromyography. Nerve conduction velocities are normal.
   f. Pathology: Abnormal central nervous system (CNS)
   g. Treatment: No specific treatment is available for the weakness; physical therapy and orthopedic measures as indicated.
   h. Prognosis: Many die in infancy; 25%–40% die from respiratory failure. Those who survive show delayed psychomotor development and more pronounced mental retardation than is expected for myotonic dystrophy.
Severe speech difficulties and dysarthria (i.e., difficulty in articulating words) are common (Jorde et al., 2003; Lopate, 2007).

3. Osteogenesis imperfecta (see Figure 16)
   a. Incidence: One in 5,000–10,000 live births
   b. Genetic factors: An estimated 90% are autosomal dominant with marked variability in expression.
   c. Clinical features
      (1) Type I
         (a) Postnatal onset of bone fragility—increased risk of fractures; 8% first fracture noted at birth, 23% in first year, 45% in preschool, and 17% during school years
         (b) Blue sclerae (35%)
         (c) Easy bruising (75%)
         (d) Triangular facial appearance (30%)
         (e) Hearing impairment, secondary to otosclerosis
         (f) Normal stature (usually)
         (h) Dentinogenesis imperfecta (i.e., a formation of both primary and permanent teeth characterized by translucent gray to yellow-brown color; the enamel fractures easily, leaving exposed dentin, which undergoes rapid attrition). Teeth are susceptible to caries, irregular placement, and late eruption.
         (i) Wormian bones in cranial sutures
         (j) Prognosis and mortality depend on degree of severity of kyphoscoliosis and number of fractures.
      (2) Type II
         (a) Minimal calvarial mineralization
         (b) Beaded ribs
         (c) Compressed femurs
         (d) Poorly mineralized, short, broad long bones with multiple fractures and callus formation
         (e) Platyspondylia (i.e., flatness of the bodies of the vertebrae)
         (f) Prognosis: Usually stillborn or die early in infancy due to respiratory failure
      (3) Type III
         (a) Autosomal dominant, in most cases the result of dominant mutations in one of the two genes. A rare autosomal recessive variety has been described.
         (b) Multiple prenatal bone fractures; newborn has “crumpled” or bowed bones, limb shortening, and limb deformities.
         (c) For a survivor of infancy, short stature and further deformities (i.e., kyphoscoliosis which can lead to respiratory compromise, pectus excavatum [i.e., a hollow at the lower part of the chest caused by a backward displacement of the xiphoid cartilage; funnel chest])
         (d) Deafness (commonly)
         (e) Blue sclerae (may be present in infancy and become normal in adulthood)
         (f) Prognosis: Severely and progressively deforming; high mortality rate in the perinatal period due to multiple fractures.
      (4) Type IV
         (a) Autosomal dominant
         (b) Normal to moderately short stature with significant bone deformity
         (c) Normal sclerae
         (d) Hearing loss may occur
         (e) Femoral bowing in the neonatal period that corrects itself with time
         (f) Dentinogenesis imperfecta
         (g) Prognosis and mortality depend on degree of severity of kyphoscoliosis and number of fractures.
      (5) Type V
         (a) Autosomal dominant inheritance not associated with collagen type I mutations
         (b) Moderate to severe tendency to fracture vertebrae and long bones
(c) Ligamentous laxity
(d) Blue sclerae and dentinogenesis are not features.
(e) Prognosis and mortality depend on degree of severity of kyphoscoliosis and number of fractures.

(6) Type VI
(a) Variability of expression from mild to moderate, pattern of inheritance is unknown.
(b) Usually mild, with postnatal onset-fractures first seen between 4 and 18 months.
(c) Sclerae white or faintly blue
(d) Dentinogenesis imperfecta is not a feature.
(e) Prognosis better

(7) Treatment for all: Directed toward prevention or correction of the symptoms. A team approach (i.e., pediatrician, orthopedist, nurse, and physical therapist) is often the most successful (Jones, 2006).

4. Infantile/childhood polycystic kidney disease
a. Incidence: One in 10,000–40,000 live births. Equally affects males and females and all racial and ethnic groups.
b. Genetics: Autosomal recessive; the ARP-KD gene (PKHD1) was localized to the short arm of chromosome 6.
c. Most commonly diagnosed on prenatal ultrasound findings
d. Clinical features
   (1) Potter facies with low-set flattened ears, short snubbed nose, deep eye creases, micrognathia, and possible clubfoot all as a result of oligohydramnios (i.e., insufficient amniotic fluid)
   (2) Large palpable bilateral renal masses, which may cause difficulty in delivery
   (3) Hypertension
   (4) Cardiac hypertrophy and congestive heart failure if hypertension poorly controlled
   (5) Hepatic involvement
   (6) Impaired renal function (70%–80%)
c. Prognosis: Determining the prognosis is difficult but with medical advances and surgical possibilities, such as dialysis and renal transplantation, morbidity and mortality have greatly improved (Verghese, Symons, Lederman, Hurh, & Baluarte, 2006).

5. Vitamin D-resistant rickets
a. Incidence: One in 20,000 live births
b. Genetic factor: X-linked dominant
c. Clinical features
   (1) Growth retardation
   (2) Childhood rickets
   (3) Reduced serum phosphate
d. Prognosis: Treatable with large doses of vitamin D (or its active metabolite calcitrol) and oral phosphate (Roth & Chan, 2007)

IV. Nonclassical Patterns of Single-Gene Inheritance
A. Principles
1. The general rule is that the patterns of inheritance and segregation ratios of single-gene disorders are in accordance with the principles of Mendelian inheritance.
2. Exceptions to Mendelian inheritance principles occur in human genetics and must be taken into account in clinical genetics. (Exceptions are revealed by close examination of certain unusual disorders and analysis of mutations in molecular detail; Lewis, 2008.)

B. Patterns
1. Mosaicism: The condition in which there are two or more cell lines derived from a single zygote that are different genetically because of postzygotic mutation or nondisjunction
2. Anticipation: The progressively earlier appearance and increased severity of a disease in successive generations
3. Imprinting: The differential expression of genetic material, at either a chromosomal or an allelic level, depending on whether the genetic material is inherited from the male or female parent
4. Mitochondrial DNA: The DNA in the circular chromosome of the mitochondria, which is inherited from the mother (Lewis, 2008)

PRACTICE QUESTIONS
1. What is the test to diagnose cystic fibrosis?
2. How is congenital myotonic dystrophy inherited?
3. What element in blood serum is reduced in vitamin D-resistant rickets?
4. What vitamin must infants with vitamin D-resistant rickets receive in large doses?
5. What disorder should be suspected when an infant presents with meconium ileus?
V. Multifactorial Disorders

A. Principles and patterns

1. Many congenital multifactorial disorders have a higher-than-average incidence in some families. These disorders do not follow the Mendelian laws of inheritance, probably because more than a single gene is involved; environmental influences may be instrumental in determining whether the disorder is expressed or not.

2. Although the disorder is obviously familial, there is no distinctive pattern of inheritance within a single family; counseling therefore is difficult.

3. The risk is sharply lower for second-degree than for first-degree relatives, but it declines less rapidly for more remote relatives.

4. The recurrence risk is higher when more than one family member is affected.

5. The more severe the malformation, the greater the recurrence risk (Lewis, 2008).

B. Common multifactorial disorders

1. Congenital heart defects (CHD)
   a. Incidence
      (1) Eight in 1,000
      (2) The risk for CHD increases if a parent or sibling has it but triples if two close relatives are affected.
      (3) Prenatal ultrasounds often identify structural malformations of the heart.
      (4) A high incidence among infants of diabetic mothers and infants born with chromosomal abnormalities
   b. Clinical features
      (1) Most affected infants present with a heart murmur, cardiac failure, cyanosis or hepatomegaly.
      (2) The infant may sweat and become breathless at feeding.
      (3) The infant may fail to thrive, especially if congestive heart failure is present.
      (4) Approximately 25% of infants with CHD have additional noncardiac anomalies.
   c. Management: Careful clinical examination includes taking blood pressure and echocardiography, which is the most useful diagnostic procedure. Oxygen saturations were maintained at higher and less variable levels during breastfeeding versus bottle feeding.
   d. Prognosis depends on the severity of the defect, which dictates the timing of surgery (Barbas & Kelleher, 2004; Geggel & Armsby, 2007).

2. Cleft lip (with or without cleft palate)
   a. Incidence
      (1) One in 1,000 live births
      (2) Higher incidence among Asian people
      (3) More common in males
   b. Clinical features
      (1) The least obvious type is the submucous cleft lip or palate, which is often associated with a bifid uvula.
      (2) Cleft lip and palate may be unilateral or bilateral.
   c. Associations
      (1) Feeding difficulties and orthodontic deformities are common.
      (2) Speech problems may occur with cleft palate, particularly after late closure.
      (3) Recurrent otitis media is common; deafness may arise related to regurgitation and sepsis in the nasopharynx.
   d. Prognosis: Surgery is performed in several stages.
      (1) Repair of the cleft lip to correct the cosmetic deformity is performed as soon as possible after birth.
      (2) Palate repair usually is performed later; within the first year of life, an excellent cosmetic result usually is achieved.
      (3) Multiple surgeries are required, depending on severity. If the initial deformity is severe, secondary repair of the lip or nose or pharyngoplasty may be required in later childhood (Tolarova & HeeSoo, 2006).

3. Pyloric stenosis (i.e., anomaly of the pylorus in which hypertrophy and hyperplasia of the smooth muscle narrows the antrum of the stomach so that it easily becomes obstructed)
   a. Incidence
      (1) 2–4 per 1,000 live births
      (2) Male to female predominance of 4:1, with 30% being firstborn
   b. Clinical features
      (1) Severe feeding problems with nonbilious projectile vomiting and dehydration, which can lead to hypochloremic metabolic alkalosis
      (2) In up to 60%–80% there will be a firm, nontender, and mobile hard pylorus that is 1–2 cm in diameter, described as an “olive”; may be present in the upper right quadrant at the lateral edge of the rectus abdominus muscle.
c. Diagnosis
   (1) Usually diagnosed in infants 3–12 weeks of age
   (2) Ultrasound is the imaging of choice with a sensitivity of 90%–99%.

d. Prognosis
   (1) Obstruction can be corrected surgically.
   (2) Complete recovery and catch-up growth if needed (Kass, Sinert, & Singh, 2006).

4. Neural tube defects (NTDs; i.e., malformations of the developing brain and spinal cord)
a. Incidence: Between 1 and 2 in 1,000 live births (Ellenbogen, 2006). Higher risk of all NTDs in infants of diabetic mothers with poor glycemic control (Dharan, Parviainen, Newcomb, & Poleshuck, 2006).

b. Types of lesions
   (1) Open: Neural tissue is either completely exposed or is covered with a thin transparent membrane. Open lesions arise during the process of neurulation that occurs at 17–30 days gestation.
   (2) Closed: Neural tissue is completely covered by skin or a thick opaque membrane.

c. Association of vertebral defects
   (1) Anencephaly: Absence of the forebrain and skull vault as well as secondary distortion of the face and ears. Most infants are stillborn, though a few survive for several hours or days (see Figure 17).
   (2) Rachischisis: A fatal condition in which the NTD extends the length of the spine (see Figure 18)
   (3) Encephalocele: Herniation of the meninges and brain through the skull. Prognosis depends on the amount of brain that has to be excised to close the skull defect (see Figure 19).
   (4) Spina bifida cystica
      (a) Myelomeningocele/meningomyelocele: The most common type of NTD; a cyst or sac containing portions of the spinal cord and meninges protrudes through an opening in the vertebrae.
      (b) Meningocele: Sac containing only the meninges; the spinal cord is usually in proper position.
   (5) Spina bifida occulta: The NTD is covered by a tuft of hair or layer of skin.

Figure 17. Infant with Anencephaly

Figure 18. An Anencephalic Fetus with Spinal Rachischisis

Figure 19. An Infant with a Large Occipital Encephalocele Associated with Microcephaly
One or two vertebrae usually are not properly fused, but the spinal cord and meninges are normal (see Figure 20).

d. Diagnosis
(1) Increased maternal serum α-fetoprotein levels at 16–18 weeks gestation (for open NTDs only)
(2) Increased acetylcholinesterase (i.e., the major cholinesterase in the fetal nervous system)
(3) High-resolution ultrasound

e. Prevention
(1) All women capable of becoming pregnant should consume 0.4 mg of folic acid per day.
(2) For women who have previously had an NTD-pregnancy, the Centers for Disease Control (2008) recommends increasing the intake of folic acid to 400 mg per day beginning at least 1 month before conception and continuing through the first trimester (American Academy of Pediatrics, 1999).

f. Prognosis
(1) For infants with myelomeningocele, the prognosis is related to the site of the lesion. Neurologic deficit is below the level of the lesion.
(2) For infants with thoracolumbar lesions, the risk of hydrocephalus is 96%; for those with sacral lesions, the risk is 60%.
(3) Infants with thoracolumbar lesions have a 35% mortality rate; 44% have an IQ greater than 80, and 71% are able to walk with braces and other supports.
(4) Infants with sacral lesions have no mortality risk; 100% have an IQ greater than 80; 83% can walk without the use of devices.
(5) Eighty percent of children born with spina bifida grow to adulthood.

g. Nursing responsibilities
(1) Prevent infection.
(a) Cover the protruding sac (whether open or closed) immediately with a nonadhesive sterile gauze dressing soaked with normal saline.
(b) Keep the infant prone.
(c) Place a diaper directly under the infant.
(d) Place a sterile piece of plastic above the anus to deflect feces away from the surgical site.
(2) Observe for symptoms of hydrocephalus: Rapidly enlarging head or increased head circumference, bulging fontanels, prominent forehead, shiny scalp, dilated scalp veins, irritability, vomiting, spasticity of the legs, and strabismus and nystagmus.
(3) Latex precautions—up to 50% may be sensitive to latex.
(4) Assess motor skills, skin, and urinary system (Ellenbogen, 2006).

5. Clubfoot (talipes equinovarus)
a. Incidence
(1) One in 1,000 live births
(2) Male-to-female ratio is 2:1.
(3) Bilateral involvement in 30%–50% of cases. Unilateral in 45% of cases; right foot more commonly affected (Jones, 2006).
(4) Increased incidence in siblings or parents (2% compared to 0.1% chance; University of Maryland Medical Center, 2008)

b. Clinical features: The affected foot is held in a flexed (equinus) and inverted (varus) position.

c. Prognosis
(1) Correction usually is attempted by splinting and casting (50% corrected nonoperatively). Ponseti reports an 89% success rate using his casting technique (including an Achilles tenotomy).
(2) If correction is difficult, surgical release of the contracted structures in the calf and ankle may be necessary. Satisfactory results are achieved in 75%–90% of instances with this operative treatment (appearance and function of the foot). The amount of
motion in the joints of the ankle and foot correlates with the degrees of satisfaction (Patel, 2007).

6. Hirschsprung disease (colonic aganglionosis)
   a. Incidence: One in 5,000 live births; 80% are males.
   b. Genetic factors
      (1) Usually multifactorial and generally sporadic though incidence of familial disease has been reported
      (2) Multiple loci appear to be involved including chromosomes 13q22, 21q22, and 10q.
      (3) Strongly associated with Down syndrome (5%–15%)
   c. Defect: Failure of complete cranial to caudal migration of neural crest cells at 8–10 weeks gestation
   d. Clinical features
      (1) Usually diagnosed within first 2 years of life
      (2) Neonates may fail to pass meconium within the first 48 hours of life or have repeated vomiting and abdominal distention.
      (3) Lack of peristalsis results in chronic constipation and signs of functional intestinal obstruction.
      (4) Emesis may be bile stained and, in severe cases, may have the odor or texture of feces.
      (5) At risk of acute bacterial enterocolitis, which can be fatal (20%–30%)
   e. Prognosis and treatment
      (1) Rectal biopsy confirms the absence of submucosal and myenteric ganglion cells. A short or long segment may be involved, starting with the rectum.
      (2) Most often, surgery is performed to remove the aganglionic bowel, performing a colostomy at the level of the normal bowel. However, prognosis is generally quite good. Only rarely is it necessary to maintain a permanent colostomy, but more frequent in children with Down syndrome (Neville & Cox, 2006).

7. Hypospadias
   a. Incidence: One in 300 male live births
   b. Clinical features
      (1) The urethral orifice is situated on the ventral aspect of the penis at a site proximal to the normal opening.
      (2) Hypospadias is often accompanied by a redundant dorsal hooded prepuce
VI. Teratogens

A. Definition

Agents that produce or increase the incidence of congenital malformations.

B. Drugs

1. Alcohol—most common teratogen exposure to fetus
   a. Consequences of prenatal alcohol exposure: Fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE). FAE describes the neurologic and cognitive problems associated with prenatal alcohol exposure without the facial and other physical characteristics of FAS. Some researchers believe that FAE is a mild form of FAS.
   b. Incidence: 1–3 per 1,000 live births
   c. Etiology
      (1) There is a 30%–45% chance that a child born to a mother who is alcoholic will be affected to some degree by prenatal exposure to alcohol.
      (2) Two mixed drinks per day appears to be the level at which damage occurs, but researchers are not yet certain of this.
      (3) Some women who drink only once or twice during a pregnancy give birth to an infant with full-blown FAS.
      (4) The earlier the period of exposure in utero the greater the likelihood of classic clinical features.
   d. Clinical features of FAS
      (1) Microcephaly
      (2) Short palpebral fissures
      (3) Epicanthic folds
      (4) Ptosis
      (5) Small midface
      (6) Short, upturned nose
      (7) Thin upper lip
      (8) Smooth philtrum
      (9) Misaligned or malformed teeth
      (10) Shortened linear growth
      (11) Weak sucking, increased irritability, fine motor disturbances
      (12) Hyperactivity in childhood
      (13) Mental deficiency (average IQ = 63)
   e. Diagnosis
      (1) Diagnosis is based on a positive history of maternal drinking and/or physical and neurologic signs.
   f. Prognosis
      (1) Teens and young adults are of short stature and have small heads.
      (2) The postchildhood mental effects of prenatal alcohol exposure are more severe than the physical vestiges. Many individuals remain at an early grade-school level, and they often lack social and communication skills (Chambers & Vaux, 2006).

2. Smoking
   a. Fetal weight decreases as the number of cigarettes smoked by the mother increases. Fetal weight is reduced by 5 percentile points per pack per day.
   b. The major effects of smoking during pregnancy include: Growth restriction (40% of intrauterine growth retardation cases in the United States), increased miscarriage rate, perinatal mortality and childhood effect such as SIDS (twice as common in infants of women who smoked), and asthma. Smoking alters the overall success rate of assisted reproductive technologies by 40%.
   c. Intervention—counseling and support groups are recommended. Bupropion (category B) is an antidepressant that can be considered for women during late pregnancy, especially if they have a combination of depression and smoking (Dharan et al., 2006).

3. Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs): Should not be used at any point during pregnancy. Effects include oligohydramnios, renal anomalies, neonatal renal failure, pulmonary hypoplasia, hypocalvaria, intrauterine growth retardation (IUGR), and death (Dharan et al., 2006).

4. Chemotherapeutic agents (i.e., aminopterin and methotrexate): Folic acid antagonist, which may cause IUGR, spontaneous abortion, stillbirth, neonatal death, craniofacial anomalies, neural tube defects, mental retardation, and skeletal anomalies (Lloyd, Carr, McElhatton, Hall, & Hughes, 1999).

5. Cocaine: Not actually a teratogen. Early belief that its use may cause limb reductions and other vascular anomalies has not been proven. Language skills may be affected. Possible spontaneous abortion, stillbirth, premature labor, abruptio placentae, fetal death, and reduced birthweight (Dharan et al., 2006).

6. Warfarin (Coumadin): Stillbirths, IUGR, deformities of the axial and appendicular skeleton, a hypoplastic nose, eye abnormalities, mental retardation, brachydactyly, and...
scoliosis (Scheinfeld, Allan, Davis, & Nazarian, 2008)

7. Isotretinoin (Accutane): Spontaneous abortion; deformities of the cranium, ears, face, limbs, and liver; hydrocephalus; microcephalus; heart defects without dysmorphology; craniofacial alterations; cleft palate; neural tube defects; cardiovascular malformations (conotruncal more common); thymic aplasia; psychological impairments; absent or defective ears; small jaw; and kidney alterations (Scheinfeld et al., 2008)

8. Phenytoin: Hand and foot defects include fingerlike thumbs, aplasia or hypoplasia of the distal phalanges, supernumerary phalangeal epiphyses, and clubfoot. Dermatoglyphic abnormalities include abnormal palmar creases and nail hypoplasia or aplasia. General defects include growth retardation, atypical facial appearance, hirsutism, and low hairlines. Facial problems include microcephaly, brachycephaly, midfacial hypoplasia, wide fontanels, metopic ridging, mild micrognathia, low-set deformed ears, blepharoptosis, mild hypertelorism, strabismus, short nose with a broad depressed nasal bridge and epicantal folds, cupid’s bow of the upper lip, and occasional cleft lip and palate. Torso abnormalities include short neck with mild webbing, widely spaced nipples, umbilical or inguinal hernia, and rib abnormalities. Congenital heart disease and intestinal malrotation may also be present. Increased risk of neonatal hemorrhage due to decreased vitamin K placental transfer (Scheinfeld et al., 2008).

9. Streptomycin: Damage to eighth cranial nerve, sensorineural hearing loss (Yun, Hamza, Berkowitz, & Khattak, 2007)

10. Tetracycline: Dental staining (i.e., permanent discoloration) and reduced skeletal bone growth (Scheinfeld et al., 2008)

11. Thalidomide: Bilateral limb reduction defects, malformed intestines, hearing defects, absent ears, and/or ocular and cardiac and renal anomalies and phocomelia (Scheinfeld et al., 2008)

12. Trimethadione: Fetal loss as high as 87%, malformed ears, cleft palate, cardiac defects, urogenital malformations, and skeletal abnormalities, delayed mental and physical developmental defects (Scheinfeld et al., 2008)

13. Valproic acid: Lumbosacral spina bifida with meningomyelocele of meningocele, often accompanied by midfacial hypoplasia, deficient orbital ridge, prominent forehead, congenital heart disease, and decreased postnatal growth (Scheinfeld et al., 2008)

C. Infections

1. Cytomegalovirus (CMV): Fetal death, mental deficiency, ocular (chorioretinitis) and cardiovascular anomalies, deafness, microcephaly, hydrocephaly, enlarged liver and spleen. Most common intrauterine infection worldwide. Ninety percent will be asymptomatic at birth (University of Michigan Health System, Women's Health Advisor, 2005).

2. Rubella: Fetal death, microcephaly, growth deficiency, mental deficiency including learning disabilities, speech and hearing problems including deafness, cataracts, heart defects, type I diabetes, and delayed skeletal development

3. Human immunodeficiency virus (HIV): 15%–30% of infants born to untreated HIV-positive mothers are HIV positive. Risk of transmission is greatly reduced if the mother is taking antiviral medications. Growth retardation, failure to thrive, and developmental delays are all possible.

4. Toxoplasmosis: Spontaneous abortion, stillbirth, prematurity, CNS abnormalities (i.e., microcephaly, intracranial calcification, hydrocephaly, seizures, mental retardation), ocular manifestations, generalized sepsis. More than 75% are asymptomatic. Sources include poorly cooked meat and cat feces. Prognosis: Poor outcome if delayed diagnosis, delayed treatment, or both.

5. Herpes simplex: Fetal death, mental deficiency, ocular anomalies, and microcephaly

6. Varicella-zoster (chicken pox): Growth deficiency, mental deficiency, ocular anomalies, microcephaly, hypoplastic limbs, neurogenic muscular atrophy, cutaneous defects, hypoplastic distal phalanges (Dharan et al., 2006)

D. Maternal disorders

1. Insulin-dependent diabetes mellitus: Transposition of great vessels, ventricular septal defect (VSD), cardiomyopathy, renal anomalies, NTDs including caudal regression, cleft lip or cleft palate, perinatal mortality. Large for gestational age (LGA; risk for birth trauma) or small for gestational age (SGA; if mother of baby has severe vascular effects)
VII. Newborn Screening Programs

A. Description

1. Most states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands now have their own mandatory newborn screening programs. In some states such as Wyoming and Maryland, the screening is not mandatory. Screening requirements vary from state to state as determined by the public health departments because the federal government has no set national standard.

2. The comprehensiveness of these programs varies, screening from 4 to 30 disorders. The average state program tests 4 to 10 disorders.

3. About half of the states are offering expanded screening with tandem mass spectrometry on every baby.

4. The purpose is to identify existing problems and to prevent secondary disabilities.

5. Nurses should not think of newborn screening as merely the “PKU test.”

6. An effective newborn screening program involves a carefully coordinated system for testing of all infants during the first few days of life, rapid retrieval of all infants who have positive tests, accurate diagnosis, initiation of appropriate treatment, and careful lifelong follow-up.

7. All of the states test for genetic disorders, but in different combinations. Illinois, for example, currently screens for six metabolic and genetic disorders: phenylketonuria (PKU), congenital hypothyroidism, galactosemia, congenital adrenal hyperplasia, biotinidase deficiency, and hemoglobinopathies (e.g., sickle cell disease). All of these disorders, except for congenital hypothyroidism, follow an autosomal recessive inheritance pattern. Other disorders commonly screened for in the United States include maple syrup urine disease, cystic fibrosis, tyrosinemia, homocystinuria, and toxoplasmosis (KidsHealth for Parents, n.d.).

B. Disorders screened for in Illinois

1. PKU
   a. Basic defect: Lack of enzyme needed to properly convert the amino acid phenylalanine to tyrosine
   b. Positive screening incidence: One in 10,000–25,000; most common among Caucasians
   c. Inheritance pattern: Autosomal recessive
   d. Symptoms: Vomiting, feeding difficulties, musty or mousy odor to sweat and urine, microcephaly, severe mental retardation, seizures, behavior disorders, decreased pigmentation, eczema, IUGR, congenital heart defects, vertebral anomalies, strabismus, and increased fetal wastage
   e. Criteria: Elevated phenylalanine level
   f. Treatment: Low-phenylalanine diet, possible tyrosine supplementation
   g. Follow-up needs
      (1) Lifelong dietary management
      (2) Careful management and preconception counseling and intervention for women who have given birth to a PKU-affected child, for the remainder of their reproductive years (Lewis, 2008)

2. Congenital hypothyroidism
   a. Basic defect: Absent or hypoplastic thyroid gland; dysfunctional thyroid gland
   b. Positive screening incidence: One in 3,600–5,000 Caucasians; rare in African Americans, more common in Hispanics
   c. Inheritance pattern: Autosomal recessive
   d. Symptoms: Large posterior fontanel, coarse facies and large protruding tongue, hoarse cry, poor weight gain, umbilical hernia, constipation, prolonged jaundice, hypothermia, absence of spontaneous activity, crying, feeding difficulties, abdominal distention, and mental retardation if not treated
   e. Criteria: Low T4, elevated thyroid-stimulating hormone
   f. Treatment: Replacement of l-thyroxine

PRACTICE QUESTIONS

1. Name five clinical features of fetal alcohol syndrome.
   a. ___________________________________________
   b. ___________________________________________
   c. ___________________________________________
   d. ___________________________________________
   e. ___________________________________________

2. Name four different drugs that can affect the fetus.
   a. ___________________________________________
   b. ___________________________________________
   c. ___________________________________________
   d. ___________________________________________

3. Name four different infections that can affect the fetus.
   a. ___________________________________________
   b. ___________________________________________
   c. ___________________________________________
   d. ___________________________________________
3. Galactosemia
   a. Basic defect: Absence or low activity of enzyme to convert galactose into glucose
   b. Positive screening incidence: One in 60,000–80,000 live births
   c. Inheritance pattern: Autosomal recessive
   d. Symptoms: Poor feeding, vomiting within first 2–3 days of life, possible neonatal death from severe dehydration, sepsis, or liver pathology; mental retardation, jaundice, blindness, cataracts, hypoglycemia, coagulation problems, depressed immunity, failure to thrive, and lethargy
   e. Criteria: Elevated galactose, low or absent fluorescence
   f. Treatment
      (1) Elimination of galactose and lactose from the diet
      (2) Use of soy formulas in infancy
   g. Follow-up needs
      (1) Early monitoring for speech and neurological problems
      (2) Parent education about hidden sources of lactose
      (3) Monitoring of females for secondary ovarian failure
      (4) Avoidance of medications with lactose fillers (Lewis, 2008)

4. Congenital adrenal hyperplasia
   a. Basic defect: Defect in the enzyme 21-hydroxylase
   b. Positive screening incidence: 1 in 12,000 Caucasians; 1 in 15,000 Jews; and 1 in 680 Yupik Eskimos
   c. Inheritance pattern: Autosomal recessive
   d. Symptoms: Hyponatremia, hypokalemia, hypoglycemia, and dehydration resulting in early death; ambiguous genitalia in females, progressive virilization in both sexes, and accelerated bone growth, which causes early fusion of the epiphyses of bone resulting in shortened stature
   e. Criteria: Elevated 17-hydroxy progesterone, abnormal electrolytes
   f. Treatment
      (1) Replacement of corticosteroids
      (2) Plastic surgery to correct ambiguous genitalia
   g. Follow-up needs
      (1) Maintenance of adequate level of corticosteroids; doses should be elevated or injectable doses should be given in times of stress.
      (2) Periodic bone age test to monitor adequacy of treatment
      (3) Regular pediatric endocrinology follow-up appointments (Lewis, 2008)

5. Biotinidase deficiency
   a. Basic defect: Low activity of the enzyme biotinidase; biotin deficiency
   b. Positive screening incidence: One in 70,000, rare in African Americans and Asians
   c. Inheritance pattern: Autosomal recessive
   d. Symptoms: Mental retardation, seizures, ataxia, skin rash, hearing loss, alopecia, optic nerve atrophy, metabolic acidosis resulting in coma, death
   e. Criteria: Deficient or absent activity of biotinidase on calorimetric assay
   f. Treatment: 10 mg biotin daily
   g. Follow-up needs
      (1) Monitoring of compliance
      (2) Periodic follow-up and evaluation (Lewis, 2008)

6. Sickle cell disease (i.e., sickle cell anemia, hemoglobin SS)
   a. Basic defect: A point mutation at the sixth position of the beta chain of the hemoglobin molecule that causes a change in the DNA code, substituting glutamate for valine in each beta chain that contains this mutation. This tiny alteration causes a distortion of the red blood cell shape. These cells eventually clog capillaries, causing the clinical symptoms.
   b. Positive screening incidence: One in 500 among African Americans; one in 1,000–1,400 Hispanic-American births; also well documented in all groups from southern Europe, the Mediterranean basin, the Middle East, or Asia
   c. Inheritance pattern: Autosomal recessive
   d. Symptoms: Fever, splenomegaly, and hyperbilirubinemia in neonate, infection, sequestration, anemia, mild painful episodes to severe organ damage, stroke shock, and sometimes death
   e. Criteria: Two abnormal genes for hemoglobin; normal hgb (A) can be distinguished from sickle hgb (S) by hemoglobin electrophoresis
6. Treatment (symptomatic)
   (1) Maximum fluids to prevent stagnation and clogging of cells
   (2) Acetaminophen drops for pain
   (3) Folic acid to stimulate new blood cell production
   (4) Placement of all identified infants on penicillin prophylaxis by 2 months of age
   (5) Timing of immunizations to reduce the risk of sickling
   (6) Avoidance of environmental causes of sickling (e.g., constricting clothing, drafts, sudden temperature changes)

g. Follow-up needs
   (1) Monitoring of compliance with treatment
   (2) Routine follow-up and evaluation (Lewis, 2008)

7. Maple syrup urine disease (not screened for in Illinois but done in other states)
   a. Basic defect: Autosomal recessive gene defect affecting branch-chain amino acids
   b. Positive screening incidence: 1 in 180,000 newborns in the United States and more common in children of Amish and Mennonite descent
   c. Symptoms: Little appetite, vomiting, dehydration, hypotonia, seizures, ketoacidosis, irritability, lethargy, and neurological decline. The urine can smell like maple syrup or sweet burnt sugar. If not treated early it can cause mental retardation, physical disability, and even death.
   d. Criteria: Caused by a deficiency of the metabolic enzyme branched-chain α-keto acid dehydrogenase (BCKDH), leading to a buildup of the branched-chain amino acids (leucine, isoleucine, and valine) and their toxic by-products in the blood and urine
   e. Treatment: Protein-free diet. During a flare-up, fluids, sugars, and fats are given intravenously. Following the special diet can provide a healthy, normal life.
   f. Follow-up needs: Careful monitoring of blood chemistry and a special diet often supervised by a dietician (Bodamer & Lee, 2006)

8. In addition to the above listed disorders, the state of Illinois includes the following disorders that have been demonstrated to be detectable by tandem mass spectrometry (Lewis, 2008):
   a. Amino acid disorders commonly screened for include tyrosinemia type I and homocystinuria (HCU).
   b. Urea cycle disorders include citrullinemia, argininosuccinic aciduria (ASA), and arginemia.
   c. Organic disorders include 2-methylbutyryl-CoA dehydrogenase deficiency (2MBCD), 3-methylcrotonyl-CoA carboxylase deficiency (3MCC), 3-hydroxy-3methylglutaryl-CoA lyase deficiency (HMG), glutaric aciduria type I (GA 1), propionic acidemia (PA), isovaleric acidemia (IVA), and methylmalonic acidemia (MMA).
   d. Fatty acid oxidation disorders include short chain acyl-CoA dehydrogenase deficiency (SCAD), medium chain acyl-CoA dehydrogenase deficiency (MCAD), long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD), very long chain acyl-CoA dehydrogenase deficiency (VL-CAD), carnitine palmitoyl transferase deficiency type II (CPT II), trifunctional protein deficiency (TFPD), glutaric aciduria type II (GAII) or multiple acyl-CoA dehydrogenase deficiency, and carnitine/acylcarnitine translocase deficiency (CACT; Bartoshesky & Dowshen, 2006; National Newborn Screening and Genetics Resource Center, 2007).

PRACTICE QUESTIONS

1. Name six common metabolic or genetic disorders for which newborn screening programs commonly test.
   a. __________________________________________
   b. __________________________________________
   c. __________________________________________
   d. __________________________________________
   e. __________________________________________
   f. __________________________________________

2. Five of the above disorders follow which pattern of inheritance?
   a. autosomal dominant
   b. autosomal recessive
   c. X-linked dominant
   d. X-linked recessive
   e. more than one pattern of inheritance

3. Which disorders can cause mental retardation if they are not appropriately treated? (Circle all correct answers.)
   a. phenylketonuria
   b. congenital hypothyroidism
   c. galactosemia
   d. congenital adrenal hyperplasia
   e. biotinidase deficiency
   f. sickle cell disease
VIII. Prenatal Testing and Diagnostic Procedures

A. Ultrasonography

1. Timing: Can be performed as early as 5 weeks gestation
2. Method and accuracy
   a. Ultrasound is high-frequency sound (i.e., greater than 20,000 kHz). Ultrasound wavelengths are emitted from a transducer in pulses that bounce off structures and return to the transducer. Return times are measured and used to determine the locations of structures.
   b. The sensitivity of ultrasonography is low; however, the routine use of screening can increase the frequency with which major malformations are detected before birth.
3. Use: Many fetal organ systems and anatomical lesions including some congenital heart defects, gastrointestinal, genitourinary, skeletal, and CNS abnormalities can be visualized by ultrasound between 16 and 20 weeks gestation. In addition to major structural abnormalities, second-trimester ultrasound can detect minor markers for aneuploidy such as renal pyelectasis, echogenic intracardiac focus, choroids plexus cysts, and overlapping fingers. Detection of these minor markers should prompt consultation with a genetic or maternal fetal medicine specialist.
4. Maternal risks: No physical risks to the mother
5. Fetal risks: No detected risks to the fetus (Cleary-Goldman & Malone, 2005; Singh & Singh, 2005)

B. Nuchal scan/First trimester screen

1. Timing: 11–13 weeks is when accuracy is best, but may be done between 10 and 14 weeks
2. Method, use, and accuracy
   a. Assesses the amount of fluid behind the neck of the fetus, nuchal translucency
   b. Compared to the second trimester screening (alpha-fetoprotein [AFP]) it has a better detection rate with fewer false positives. However, open fetal defects such as spina bifida are not tested.
   c. Babies at risk of Down syndrome tend to have a higher amount of fluid around the neck. Between 65% and 85% of fetuses with Down syndrome or trisomy 18 will have a large nuchal thickness. Abnormal findings allow for early careful evaluation of chromosomes and possible structural defects. The outcome of the nuchal scan may be combined with the results of simultaneous blood tests, primarily human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein A (PAPP-A). In pregnancies affected by Down syndrome, hCG may be increased and PAPP-A may be decreased. The overall detection rate for using the combined method is 85% (4.2% of these are advised to have an amniocentesis).
3. Maternal risks: No physical risks to the mother
4. Fetal risks: No detected risks to the fetus (Natarajan & Klein, 2006)

C. Chorionic villus sampling

1. Timing: Most commonly performed at 10–12 weeks gestation. Earliest prenatal diagnostic technique but does not include neural tube defects.
2. Method and accuracy
   a. A transcervical catheter or transabdominal needle is inserted through the vagina into the placenta, and tissue is aspirated.
   b. A karyotype is prepared directly from the collected cells and no culturing is needed, so results are ready in a couple of days.
   c. Studies have demonstrated a 99.6% diagnostic success rate.
3. Use: Detection of chromosomal abnormalities (e.g., Down syndrome) or specific Mendelian disorders (e.g., cystic fibrosis, muscular dystrophy). However, does not sample amniotic fluid so testing for inborn errors of metabolism is not possible.
4. Maternal risks
   a. Vaginal bleeding with transcervical approach
   b. Infection with both approaches
   c. Acute amniotic fluid leakage (rarely)
5. Fetal risks
   a. Fetal loss rate using transcervical approach: Added risk of miscarriage to the general population is 8 in 1,000; no significant increases in fetal loss during preterm labor or among small-for-date infants.
   b. In 1 in 1,000–3,000 it may stop development of the feet and/or hands; transverse limb defects associated when the procedure is done before 9 weeks of gestation.
   c. Rh sensitization (Lewis, 2008; Natarajan & Klein, 2006)

D. Amniocentesis

1. Timing: Usually performed at 14–18 weeks gestation; can also be done later
2. Method and accuracy
   a. Insertion of spinal needle into the uterus through the abdomen to aspirate 20–30 ml of amniotic fluid. Cells are cultured for 7 to 14 days and typically 20 cells are karyotyped. DNA FISH probes can detect chromosomes in 132 days if necessary.
   b. A false-positive rate of <0.5%
   c. Can detect approximately 1,000 of the more than 5,000 chromosomal and biochemical problems

3. Use: Detection of chromosome abnormalities (e.g., Down syndrome) and specific Mendelian disorders (e.g., cystic fibrosis, muscular dystrophy)

4. Maternal risks
   a. Vaginal bleeding
   b. Amniotic fluid leakage
   c. Infection

5. Fetal risks
   a. Fetal loss rate from mid-trimester amniocentesis: Approximately 0.3%–1%
   b. Needle puncture of the fetus
   c. Rh sensitization from fetal bleeding into maternal circulation
   d. Umbilical cord hematoma and occlusion
   e. Cardiac damage caused by fetal contact with needle
   f. Inflammation of fetal membranes
   g. Premature labor (Lewis, 2008; Natarajan & Klein, 2006)

E. Maternal serum AFP/Triple or quad screen (second trimester screen)
1. Timing: 16–20 weeks of pregnancy
2. Use: To detect neural tube defects or possible chromosomal abnormalities. High AFP may indicate abnormal development of the brain, spinal cord, or abdominal wall or that the woman is expecting twins. Low AFP can point to chromosomal disorders including Down syndrome, trisomy 13, and trisomy 18.
3. Method and accuracy
   a. Blood is drawn from the mother to check the AFP level, a protein secreted by the fetal liver and excreted in the mother’s blood.
   b. The “quad screen” additionally tests hCG (a hormone produced by the placenta), unconjugated estriol (a protein produced in the placenta and in the baby’s liver), and inhibin-A (a hormone produced by the placenta) as well, which makes the screen more accurate. Levels of hCG and inhibin-A are higher than normal when the fetus is at risk for Down syndrome. Lower levels of estriol may also indicate a higher risk for Down syndrome.
   c. The panel, along with maternal age, is a more sensitive (60%–91%) screen for fetal aneuploidy.
   d. The triple panel can detect 57%–67% of fetuses with Down syndrome in women younger than 35 years of age and can detect 87% in older women.
   e. Some research claims only a 5% false-positive rate, yet other research finds there is a >80% rate of positive tests. Of the positive test results, 90% of these infants will not have any anomalies.
4. Maternal and fetal risks: None, but false positive may lead to an amniocentesis, which does carry a 1%–2% rate of fetal loss (MedicineNet.com, 2005; Natarajan & Klein, 2006).

F. Preimplantation genetic testing
1. Timing: Used with in vitro fertilization (IVF) before implantation in the uterus at the 8 cell stage, in a fetus of parents with high risk of a known genetic disorder, and in women with repeated miscarriages due to a chromosomal translocation.
2. Method and accuracy
   a. Cells from embryos are analyzed for chromosomal, biochemical, or DNA abnormalities.
   b. There is very little DNA to work with, but amplification by polymerase chain reaction makes prenatal diagnosis possible.
3. Maternal risks: Related to IVF procedures of oocyte recovery and embryo transfer
4. Fetal risks: None known, but the technique is still new and experimental. Little is known about its technical and biological safety (Marik, 2005; Natarajan & Klein, 2006).

G. Percutaneous umbilical blood sampling
1. Timing: Performed at 18 weeks gestation or later
2. Method and accuracy: A needle is guided by high resolution ultrasound equipment to the placental origin of the umbilical cord, where fetal blood is aspirated. The accuracy of the results is increased by obtaining fetal blood from a direct source.
3. Use: Detection of chromosomal abnormalities (e.g., Down syndrome) or specific Mendelian disorders (e.g., cystic fibrosis, muscular dystrophy)
4. Maternal risks
   a. Bleeding in uterus and umbilical cord
   b. Infection
   c. Rupture of membranes
   d. Premature labor
5. Fetal risks
   a. Fetal loss rate: 1%–2%
   b. Bradycardia
   c. Fetal trauma
   d. Abruptio placentae (Natarajan & Klein, 2006)

PRACTICE QUESTIONS
1. At what gestational age can the following tests be performed?
   - ultrasonography
   - chorionic villus sampling
   - amniocentesis
2. Which method carries no risk to the mother or the fetus?
   - ultrasonography
   - chorionic villus sampling
   - amniocentesis
3. Which method carries a risk of limb defects?
   - ultrasonography
   - chorionic villus sampling
   - amniocentesis

IX. Implications for the Family
A. The parents’ response
   1. Immediate crisis event
      a. The birth represents the loss of a dream (i.e., the “perfect baby”).
      b. Emotions evoked can include anger, anxiety, feeling of being threatened.
      c. The child may be perceived as ugly and unlovable.
   2. Common defense mechanisms/the grief process
      a. Shock and disbelief: Parents subjectively feel that the diagnosis or event is not true or did not really happen. Stunned feelings, impaired judgment and functioning, and only short periods of concentration. A referral for a genetic consultation at this time should be deferred.
      b. Denial: Illustrated by parents’ search for a second opinion in the hope the original diagnosis was incorrect; the whole family is engaged in a wish-fulfilling fantasy. Allows parents to take in what they are capable of handling mentally, emotionally, and physically. Denial is often confused with disbelief, deferral, and dismissal. Disbelief occurs when parents cannot make sense of what they are being told. With deferral, parents accept the clinical findings but seem to ignore the clinical implications. Dismissal displaces the focus of the situation from the diagnosis to the “legitimacy of the purveyors.”
      c. Yearning and searching: Feelings of restlessness, anger, guilt, and ambiguity; a lot of how and why questions; intense feelings of anger toward caregivers, their partner, themselves, and God
      d. Disorientation and disorganization: Feelings of depression, guilt, and unfamiliarity. Defect or illness becomes a reality.
      e. Reorganization and resolution: Increased energy, increased decision-making abilities, and increased sense of self-confidence; a time of bringing reality into “focus”

B. Influential family characteristics
   1. Size, structure, and developmental stage of family
      a. The birth of a child with a defect may have a greater impact (i.e., be a more severe stressor) on a young, newly established family with few or no other children than on an established family.
      b. Families with a same-sex child close in age to the affected child may be at increased risk for poor coping.
      c. The sex of the affected child is relevant: The mother may have more difficulty coping with a severely affected daughter.
      d. Mothers and fathers cope in different ways.
   2. Relationship between parents
      a. In most families that successfully cope, both parents are present and have a mature relationship.
      b. Some studies have documented a divorce rate as high as 80% after the birth of an affected child.
c. If the parents’ relationship was satisfactory before the diagnosis of a genetic condition, the parents have the best chance of remaining together.

d. If the parents are not living together at the time of the birth, the parent with the baby will need more support from others to learn to value the baby and therefore to value himself or herself.

3. Availability of extended family members
   a. Absence of family members means the parents have fewer people to call on for help.
   
b. Presence of family members means parents have access to more help and support, if the relationships are positive.

4. Availability of coping and support resources
   a. Neighborhood community resources (e.g., friends, coworkers, employers who offer family medical leave)
   
b. State public health departments, public and private agencies (e.g., March of Dimes, Cystic Fibrosis Foundation), medical professionals, social workers, clergy, parents of other children with the same condition

5. Cultural, social, and religious influences
   a. Cultural beliefs associated with defects can result in social isolation or blaming of the parents.
   
b. Certain disorders are more socially acceptable than others.
      (1) Paralysis or skeletal deformities may elicit sympathy; uncontrolled movements and drooling in an older child or adult may cause disgust.
      (2) The reaction of others to craniofacial defects may cause social isolation of the family.
      (3) Defects with great family burden but no outward signs (e.g., PKU) may engender little support.
      (4) Having a child with ambiguous genitalia can have an impact on the parents’ sexual identity.
      (5) Conditions that are socially acceptable in children (e.g., developmental delay) are not considered acceptable in adults.
      (6) The degree of support given to parents who decide to terminate a pregnancy can vary depending on the disorder (e.g., more support if the disorder is trisomy 18, less support if it is cystic fibrosis).

   c. Religious beliefs
      (1) Negative influence: Curse on family, punishment for some wrongdoing
      (2) Positive influence: A special child as a gift from God

6. Lifestyle and family plans
   a. The family’s daily routine and future plans (i.e., career and educational plans, plans to have additional children, financial plans) may change.
   
b. The family’s response to the child may depend on the importance they assign to such traits as intellectual ability and beauty and on the degree to which the anomaly affects those traits.

7. Parents’ coping is affected by the characteristics of the disorder (i.e., age of onset, severity of the disease, frequency and types of treatment, necessity for surgery, hospitalization, and prognosis; Schwartz et al., 1993).

X. Nursing Considerations

A. Responsibilities of the nurse to the family
   1. Avoid stereotyping behaviors.
   2. Be present when the parents are informed of the infant’s diagnosis.
   3. Assess the present ability of the parents to cope with information or stressors; provide information in small amounts and easy-to-understand terms.
   4. Provide opportunities for parents to ask questions and understand information. Reinforce information in simple, truthful words; acknowledge that the baby has normal as well as abnormal traits.
   5. Be a positive role model in caring for the newborn; show that you value the infant and parents.
   6. Help parents become more comfortable in caring for their child; allow them to participate in the child’s care.
   7. Be sure parents recognize the infant’s strengths or positive qualities.
   8. Identify family strengths, supports, and limitations (e.g., financial stability, time constraints, need to care for other children, presence of grandparents).
9. Emphasize the normality of the parents’ feelings; inform parents that crying and feeling angry are normal, as are initial feelings of rejection of the child.

10. Talk with each parent independently to discover individual concerns and needs.

11. Inform parents of community resources.

12. Evaluate your own feelings about the birth defect.

13. Do not try to cheer parents by telling them, “Things could have been worse” (whether the defect is major or minor, parents feel it could not be worse).

14. Do not give information to parents unless you are absolutely confident it is accurate. Discuss information with specialists first.

15. Do not isolate the family because the child is “different.”

16. Remember that the family is going through an emotionally difficult time in which they greatly need your support (Schwartz et al., 1993).

B. Responsibilities of the nurse for discharge planning

1. Remember that discharge planning begins at admission.

2. Be aware that the state of crisis will continue at home.

3. Assess the supplies and equipment that will be needed and the compatibility of the home with the care of a technologically dependent infant (e.g., Is the electric wiring appropriate?).

4. Assess the ability of parents to care for their child (e.g., Are the parents developmentally delayed? Blind? Deaf? Teenagers?).

5. Consider how household responsibilities will change. Who will be the primary caregiver of the infant? Who will run errands? Who will care for the other children (e.g., relatives, friends, social support networks)? Consider loss of income if one parent must quit his or her job to provide care.

6. Examine the parental characteristics that may put a child with an anomaly at increased risk for abuse (i.e., history of abuse or neglect of other children; poor self-esteem or lack of identity; social isolation, exhaustion, or failure to form attachment to infant; poor problem-solving ability; adolescence; drug or alcohol abuse).

7. Coordinate discharge with social worker (e.g., for Medicaid application).

8. Refer the family for grief counseling, marital counseling (if necessary), and genetic counseling.

9. Refer the parents to family support groups or to other parents who have a child with the same condition.

10. When working with siblings, be honest and forthright. Children do not need all of the details but a simple explanation of what is happening may reduce a lot of anxiety and misconceptions.

11. Grandparents can be particularly challenged. Not only do they grieve for their grandchild but they feel the hurt of their son or daughter who is going through these difficult times (Schwartz et al., 1993).

C. The prolonged grief response

1. Genetic diseases are, unfortunately, forever.
   a. There is no cure for most genetic diseases, so their effects are chronic.
   b. Even after visible effects such as a cleft lip are repaired, the genetic material is still damaged.
   c. The genetic component affects others in the family through future offspring.
   d. The affected person’s self-identity is altered, and the effects on the family’s self-identity may last for generations.

2. Cyclical grieving describes the cyclical nature of the recurrence of the emotions with the grieving process. Here families typically move in and out of the “grief loop.”

3. Others experience chronic sorrow, always feeling sad. This can be described as a normal response to an abnormal situation (Clubb, 1991; Young, 1977).


BIBLIOGRAPHY

University of Colorado Health Sciences Center School of Nursing and School of Medicine Genetics Unit. (1988). Genetics applications: A health perspective. Lawrence, KS: Learner Managed Designs.
ANSWERS TO PRACTICE QUESTIONS

Page 11
1. a–nondisjunction
2. hypotonia; flattened facial profile; poor moro reflex; hyperflexibility of joints; excess of skin on back of neck; slanted palpebral fissures; dysplasia of pelvis; anomalous auricles; congenital heart defects; transverse palmar crease; gastrointestinal anomalies; small nose with low nasal bridge and tendency to have inner epicanthal folds; mental deficiency; Brushfield spots; protrusion of the tongue; high, arched palate; short fingers with incurved fifth finger; abnormal dermatoglyphics
3. true
4. a–trisomy 18
5. b–trisomy 13

Page 13
1. a–XO (Turner) syndrome
2. true
3. Klinefelter syndrome
4. XYY syndrome

Page 15
1. a–autosomal dominant trait
2. b–autosomal recessive
3. c–X-linked dominant & d–X-linked recessive

Page 17
1. sweat test
2. autosomal dominant
3. phosphate
4. vitamin D and oral phosphate
5. cystic fibrosis

Page 21
1. b–multifactorial
2. submucosal and myenteric ganglion cells
3. c–myelomeningocele
4. false
5. folic acid
6. increasing head circumference, bulging fontanels, prominent forehead, shiny scalp, dilated scalp veins, irritability, vomiting, spasticity of the legs, strabismus and nystagmus
7. covering the protruding sac
8. feeding problems with nonbilious projectile vomiting; firm, nontender, and mobile hard pylorus that is 1–2 cm in diameter in upper right quadrant

Page 24
1. microcephaly; short palpebral fissures; epicanthic folds; ptosis; small midface; short, upturned nose; thin upper lip; smooth philtrum; misaligned or malformed teeth; shortened linear growth; weak sucking, increased irritability, fine motor disturbances; hyperactivity in childhood; mental deficiency
2. angiotensin-converting enzyme inhibitors, chemotherapeutic agents, cocaine, warfarin, isotretinoin, phenytoin, streptomycin, tetracycline, thalidomide, trimethadione, valproic acid
3. CMV, rubella, HIV, toxoplasmosis, herpes simplex, varicella-zoster

Page 26
1. PKU, congenital hypothyroidism, galactosemia, congenital adrenal hyperplasia, biotinidase deficiency, sickle cell disease
2. b–autosomal recessive
3. a–phenylketonuria, b–congenital hypothyroidism, c–galactosemia & e–biotinidase deficiency

Page 29
1. 5 weeks, 10–12 weeks, 14–18 weeks
2. a–ultrasonography
3. b–chorionic villus sampling