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***Essentials of Medical Genetics for Nursing and Health Professionals: An Interprofessional Approach***

*Laura Gunder McClary*

Test Bank

## Chapter 1 – Introduction

1. A new patient comes to establish care at the family medicine clinic where you work. During your history taking, you create a diagram representing the familial relationships among the patient's relatives to analyze Mendelian inheritance of certain traits. What is this diagram called?
  - a. Karyotype
  - b. Genotype
  - c. Pedigree
  - d. Genome

Answer: C

Rationale: A diagram that represents relationships between family members is called a pedigree. Answer A is incorrect because a karyotype is the number and appearance of chromosomes within a cell. Answer B is incorrect because a genotype is the genetic makeup of a cell. Answer D is incorrect because a genome is the genetic material of an organism. Therefore, C is the correct answer choice.

2. You are counselling your patient with albinism, which is a homozygous recessive allele. She is worried about the chances of her future children being affected by this condition. Which of the following is a correct statement regarding your education of this patient?
  - a. More males than females are affected.
  - b. Affected individuals would not have affected offspring.
  - c. Affected individuals typically have affected parents.
  - d. Approximately 50% of siblings with the same parents are affected.

Answer: B

Rationale: Answer B is correct because her mating partner is likely homozygous for the normal (non-albino) allele, so her offspring would be heterozygous and therefore not affected. Answer A is incorrect because this is the description of an X-linked recessive condition; males are more affected because they only have one X chromosome and therefore require normal functioning of that chromosome. Answer C is incorrect because it contradicts the correct answer (B). Answer D is incorrect because all this patient's offspring are likely to be unaffected.

3. A karyotype halts mitosis in what stage?
  - a. Prophase
  - b. Metaphase
  - c. Anaphase
  - d. Telophase

Answer: B

Rationale: During a karyotype, mitosis is stopped in metaphase, just as the chromosomes are aligned and most condensed. Answer A is incorrect because the chromosomes are just beginning to condense. Answers C and D are incorrect because sister chromatids have separated and are being pulled apart. Thus, B is the only correct answer.

4. What genetic test often uses the metaphase arrangement of chromosomes to analyze the lengths and positions of their centromeres?
- Cytogenetics
  - Karyotyping
  - Probing
  - Fluorescence in situ hybridization (FISH)

Answer: B

Rationale: During a karyotype, mitosis is stopped in metaphase, just as the chromosomes are aligned and most condensed. Answer A is incorrect because cytogenetics is when light microscopy is used to analyze chromosomes. Answer C is incorrect because a probe is a small, fluorescent-dyed piece of nucleic acid that is similar to the gene being analyzed in fluorescence in situ hybridization (FISH). Answer D is incorrect because FISH is a diagnostic technique that uses fluorescence, or light emission, to analyze chromosomes with the use of a probe.

5. While counselling a couple regarding the likelihood that their child will inherit a certain genetic disorder, you explain that some genotypes do not always express their corresponding phenotype while other genotypes are always expressed. What concept are you explaining?
- Cytogenetics
  - Expressivity
  - Dominance
  - Penetrance

Answer: D

Rationale: Penetrance is the probability to which a genotype will be phenotypically expressed. Traits with full penetrance will be expressed in all patients of that genotype. With incomplete penetrance, the disease is not expressed in all patients of that genotype. Answer A is incorrect because cytogenetics is using light microscopy to study chromosomes. Answer B is incorrect because variable expressivity refers to differences in the clinical or phenotypical presentation of a disease. Answer C is incorrect because dominance is the ability of a trait to manifest itself in heterozygous carriers. Thus, answer D is the correct choice.

6. You are a graduate research student studying HIV and need to create large numbers of the viral DNA to use in experiments. What process will you use to replicate it exponentially?

- a. Polymerase chain reaction
- b. Chromosome painting
- c. Fluorescence in situ hybridization
- d. Karyotyping

Answer: A

Rationale: Polymerase chain reaction (PCR) is a technique used to amplify DNA exponentially. Answer B is incorrect because chromosome painting is when chromosomes are painted different colors to help identify pairs of homologous chromosomes. Answer C is incorrect because fluorescent in situ hybridization (FISH) is a diagnostic technique that uses fluorescence, or light emission, to analyze chromosomes with the use of a probe. Answer D is incorrect because a karyotype is the number and appearance of chromosomes within a cell. Therefore, answer A is the most appropriate choice.

7. You suspect your patient has an enzymatic defect. What type of testing is most appropriate at this time?
- a. Polymerase chain reaction
  - b. Biochemical analysis
  - c. Fluorescence in situ hybridization
  - d. Karyotyping

Answer: B

Rationale: Biochemical analysis is the most appropriate choice because it is used to detect the presence of proteins. Answer A is incorrect because Polymerase chain reaction (PCR) is a technique used to amplify DNA exponentially. Answer C is incorrect because fluorescent in situ hybridization (FISH) is a diagnostic technique that uses fluorescence, or light emission, to analyze chromosomes with the use of a probe. Answer D is incorrect because a karyotype is the number and appearance of chromosomes within a cell. Thus, answer choice B is the best answer.

8. A 6-year-old female presents to your pediatrics office with facial tenderness, cough, purulent rhinorrhea, and fever. A brief review of her history reveals frequent antibiotic use for recurrent lung infections. You recommend biochemical analysis to examine for an enzymatic defect in chloride and water transport, also known as:
- a. Phenylketonuria
  - b. Primary ciliary dyskinesia
  - c. Primary immunodeficiency
  - d. Cystic fibrosis

Answer: D

Rationale: Biochemical analysis is used for the detection of cystic fibrosis because it is used to detect the presence of proteins, namely enzymes. Answer A is incorrect because phenylketonuria (PKU) is an absence or deficit in phenylalanine hydroxylase, which

catabolizes phenylalanine. Answer B is incorrect because primary ciliary dyskinesia is a congenital condition where mucus clearance is impaired due to defective or absent cilia. Answer C is incorrect because primary immunodeficiency is a susceptibility to diseases due to poor antibody production. Thus, answer D is the correct choice.

9. The parents of a newborn baby girl were told that their neonate was screened for inborn errors of metabolism this morning. You educate the parents regarding what an inborn error of metabolism is and give examples, including phenylketonuria and
- Down Syndrome
  - Cystic fibrosis
  - Hemophilia
  - Familial Hypercholesterolemia

Answer: B

Rationale: Answer A, answer C, and answer D are not examples of inborn errors of metabolism. Only the only choice that is an inborn error of metabolism is cystic fibrosis. Therefore, answer B is the best answer.

10. A small piece of nucleic acid that is labeled with fluorescent dye used to identify specific mutated genes in fluorescence in situ hybridization (FISH) is called a:
- Probe
  - Homolog
  - Karyotype
  - Genome

Answer: A

Rationale: A probe matches a short part of the DNA being analyzed and is labeled with fluorescent dye to help potentially identify mutated genes. Answer B is incorrect because homologs are homologous chromosomes that pair up before separating during meiosis. Answer C is incorrect because a karyotype is the number and appearance of chromosomes within a cell. Answer D is incorrect because a genome is the genetic material of an organism. Thus, answer A is the best choice.

## Chapter 2 – Diagnostic Techniques in Medical Genetics

1. You create a pedigree for a client who reports several family members experiencing the same genetic disease. Which aspect of the pedigree indicates that the disorder has complete penetrance?
  - a. Two cousins have the same disorder.
  - b. Males and females are affected equally.
  - c. The disorder does not appear in one family.
  - d. The disorder appears in the female parents and male children.

Answer: B

Rationale: Penetrance is the proportion of organisms having a particular genotype that actually expresses the corresponding phenotype. If the phenotype is always expressed, penetrance is complete; otherwise, it is incomplete. One characteristic of complete penetrance is both males and females being equally affected by the disorder. Cousins having the same disorder or the disorder missing an entire family does not demonstrate complete penetrance. A disorder appearing in females and male children a characteristic of an x-linked genetic disorder.

2. A young adult client reports having several genetic disorders in the immediate family and wants to know the chances of having a child with a disorder. Which specimen should you consider collecting in anticipation of having a chromosomal analysis completed for this client?
  - a. Stool
  - b. Urine
  - c. Blood
  - d. Saliva

Answer: C

Rationale: Chromosomal analysis is done by growing human cells in tissue culture, chemically inhibiting mitosis, and staining, observing, photographing, sorting, and counting the chromosomes. Samples can be obtained from peripheral blood, amniotic fluid, trophoblastic cells from the chorionic villus, bone marrow, and cultured fibroblasts, usually obtained from a skin biopsy. Stool, urine, or saliva samples are not used to complete a chromosomal analysis.

3. A chromosomal analysis is being completed for a client with a questionable genetic disorder. Which technique is used to identify chromosomal abnormalities?
  - a. Treat with Giemsa stain
  - b. Grow the cells in a tissue culture
  - c. Use light microscopy to study the sample
  - d. Identify the order of the chromosome pairs

Answer: A

Rationale: Treating chromosomes with Giemsa stain causes the chromosomes to exhibit transverse bands or G-bands that are specific for each pair of homologs. These G-bands allow smaller segments of each chromosome arm to be identified in order to identify chromosomal abnormalities. Growing the cells in a tissue culture and using light microscopy to study the sample is the process used in chromosomal analysis, in which the chromosomes are routinely rearranged systematically in pairs from longest to shortest and numbered from 1 through 22 to represent the autosomes.

4. A blood sample from a client having genetic testing is being tested through fluorescence in situ hybridization (FISH). What will this type of testing reveal about the client?
- Detect risk for fertility issues
  - Validate the chromosomal pairs
  - Identify individual gene mutations
  - Predict if offspring will develop an abnormality

Answer: C

Rationale: Fluorescence in situ hybridization (FISH) makes it easier to visualize and map chromosomal and gene abnormalities. This technique does not identify the risk for fertility issues. It will not validate chromosomal pairs and does not predict if offspring will develop an abnormality.

5. A client is having genetic testing through fluorescence in situ hybridization (FISH). What is the purpose of the probe with this genetic test?
- Search for repeating DNA cycles
  - Identify the longest chromosomes
  - Validate the shortest chromosomes
  - Search for genes with the same sequence

Answer: D

Rationale: The probe is a short sequence of nucleic acid that matches a portion of the gene in question. The probe is then allowed to hybridize to suitably prepared cells or histological sections; hybrids are formed with complementary sequences of nucleic acids in a chromosome. Through rough nucleic acid hybridization, the degree of sequence identity can be determined and specific sequences located on specific chromosomes detected. A probe does not search for repeating DNA cycles. This laboratory test does not identify the longest or validate the shortest chromosomes.

6. You review data collected from a client during a health history. For which reason should cytogenetic testing be considered for this client?
- Experiences seasonal eczema
  - Older sibling spouse has twins

- c. Parents alive and both in their 70s
- d. Infertility with no physiologic cause

Answer: D

Rationale: There are specific situations in which cytogenetic testing is appropriate. One of these situations is infertility occurring without an obstetric or urogenital cause.

Cytogenetic testing would not be indicated for a seasonal allergic health problem. Having both parents alive in their 70s is not a reason for cytogenetic testing. An older sibling's spouse having twins does not indicate a genetic anomaly.

7. A client having genetic testing is asked to provide a strand of hair. How will this sample be used for DNA analysis?
- a. Treat with Giemsa stain
  - b. Create nucleic acid chains
  - c. Analyze under a microscope
  - d. Create a polymerase chain reaction

Answer: D

Rationale: In a DNA analysis, probes are used to identify specific genes that may be mutated in a certain hereditary disease. The probe may be a piece of the actual gene, a sequence close to the gene, or just a few nucleotides at the actual mutation. The closer the probe is to the actual mutation, the more accurate and the more useful the information. When even a minute amount of DNA from a patient such as a hair bulb is combined with the primers in a reaction mixture that replicates DNA—called polymerase chain reaction (PCR)—the region of DNA between the primers will be amplified exponentially after about a dozen cycles. Giemsa stain is used to identify chromosomal abnormalities. Fluorescence in situ hybridization (FISH) uses nucleic acid chains. DNA are not visible through microscopic analysis.

8. A client is scheduled for biochemical analysis to identify a genetic disorder. Which is the focus of this analysis?
- a. Genus of intestinal bacteria
  - b. Amount of subcutaneous tissue
  - c. Presence or absence of proteins
  - d. Levels of hormones required for development

Answer: C

Rationale: The primary goal of biochemical testing is to determine whether certain proteins are present or absent. Biochemical testing also identifies the proteins' characteristics and effectiveness in vitro. Biochemical analysis does not focus on intestinal bacteria, amount of subcutaneous tissue, or hormone levels.

9. A 3-month old baby is diagnosed with cystic fibrosis. On which body systems should you prepare teaching for the parents about this disorder?
- a. Respiratory and digestion
  - b. Musculoskeletal and renal
  - c. Cardiovascular and lymphatics
  - d. Neurologic and electrolyte balance

Answer: A

Rationale: Cystic fibrosis is caused by a gene that disrupts chloride and water transport, causing thick sticky mucus that blocks the airways in the lungs and pancreatic ducts. This leads to problems with breathing and digestion. Cystic fibrosis does not affect the musculoskeletal, renal, cardiovascular, lymphatic, neurologic, or electrolyte balance systems.

10. A client agrees to have genetic testing for a potential disorder. Which statement should you make so that the client understands the potential issues of having this kind of testing?
- a. "All of the test findings are confidential."
  - b. "Genetic testing costs the same as other diagnostic testing."
  - c. "Most genetic anomalies can be altered by lifestyle changes."
  - d. "You will not be denied health insurance, but your premiums may increase."

Answer: D

Rationale: There are no laws preventing insurance rate spikes that may follow genetic Testing. Insurance companies cannot deny people coverage, but they can raise premiums. A family member may inadvertently learn of a genetic disorder through an inheritance pattern, which is a violation of the Health Insurance Portability and Accountability Act (HIPAA). Genetic testing can be very expensive and is not always conclusive. Once a client has a positive diagnosis, it cannot be changed. Diet, exercise, and lifestyle modifications can do nothing to change one's genome.

## Chapter 3 – Prenatal Genetics

1. Which statement is correct concerning prenatal screening?
  - A. Chromosome analysis is the gold standard for prenatal screening
  - B. Prenatal screening includes Chorionic Villus Sampling
  - C. Prenatal screening includes Ultrasound \*
  - D. Prenatal screening is diagnostic
  - E. Residual risk is calculated during prenatal screening

Answer: C

Rationale: Prenatal screening includes ultrasound and is not a diagnostic testing method

2. Which of the following does not screen/test for ONTDs?
  - A. Chorionic Villus Sampling\*
  - B. Integrated Screen
  - C. Maternal Serum Screening
  - D. Sequential Screen
  - E. Quad Screen

Answer: A

Rationale: Chorionic Villus Sampling does not test for ONTDs therefore maternal serum alpha-fetoprotein is recommended for patients who have CVS.

3. Which of the following screening tests has the best detection rate for Down syndrome?
  - A. First trimester screen
  - B. First trimester screen with ultrasound
  - C. Integrated screen\*
  - D. Sequential screen
  - E. Quad Screen

Answer: C

Rationale: Integrated screen has the highest detection rates among the different maternal serum screens.

4. How is first trimester ultrasound used as a genetic screen?
  - A. Analyzes various analytes
  - B. Checking amniotic fluid volume

- C. Checking placental position
- D. Detecting large chromosome deletions or duplications
- E. Measuring nuchal translucency\*

Answer: E

Rationale: As a genetic screen, first trimester ultrasound measures the nuchal translucency.

5. Which of the following aneuploidies is not analyzed via FISH
- A. Klinefelter syndrome
  - B. Trisomy 13
  - C. Trisomy 18
  - D. Trisomy 21
  - E. Trisomy 23\*

Answer: E

Rationale: Trisomy 23 is not analyzed via FISH

6. ACOG guidelines recommend that all women, regardless of ethnicity, be offered carrier screening for?
- A. Cystic Fibrosis\*
  - B. Familial hyperinsulinism
  - C. Hereditary breast cancer
  - D. Huntington's disease
  - E. Maple syrup urine disease

Answer: A

Rationale: Cystic Fibrosis along with spinal muscular atrophy, sickle cell, and thalassemias are recommended carrier screening by ACOG

7. Which is not an analyte involved in Maternal Serum Screening?
- A. AFP
  - B. cfDNA\*
  - C. hCG
  - D. inhibin
  - E. uE3

Answer: B

Rationale: cfDNA is not an analyte tested in maternal serum screens. cfDNA evaluates fragments of DNA in the mother's blood that come from the placenta to provide a risk for different aneuploidy.

## Chapter 4 – Development and Teratogenesis

1. During organogenesis the cells of the ICM (intercellular mass) create the ectoderm, mesoderm, and endoderm. Which of the following organs and tissues are associated with development of the endoderm?
  - a. Bone, cartilage and blood
  - b. Brain, spinal cord and retina
  - c. Liver, pancreas, and blood vessels
  - d. Gallbladder, bladder, and respiratory system lining

Answer: D

Rationale: Gallbladder, Bladder and Respiratory Lining all line and all are formed from the endoderm. Bone, Cartilage, and Blood are all formed from the Mesoderm. Brain Spinal Cord are formed from the Ectoderm. The liver and pancreas are formed from the endoderm. However, the blood vessels are formed from the Mesoderm.

2. When is the most critical time period for development and also the most dangerous time to use teratogens?
  - a. Three weeks prior to conception- Four weeks after last menstrual period
  - b. Four weeks after last menstrual period- Fifteen weeks after last menstrual period
  - c. Fifteen weeks after last menstrual period- 25 weeks after last menstrual period
  - d. The three weeks prior to the delivery of the baby

Answer: B

Rationale: Four weeks after last menstrual period- Fifteen weeks after last menstrual period. The stage of embryonic development most susceptible to teratogenesis is during the formation of primordial organ systems. The critical period for teratogenic effects is between 3 and 16 weeks of gestation. During this time period the CNS is being developed.

3. Which of the following teratogens is most commonly known for stunted limb growth?
  - a. ACE Inhibitors
  - b. Thalidomide
  - c. Amphotericin
  - d. Isoretinoin

Answer: B

Rationale: A) This does not cause limb growth irregularities in pregnancy however it is a teratogen that can cause renal shutdown in the fetus.

- B) Thalidomide commonly causes limb abnormalities because it is used between weeks 4 and 10 of pregnancy as an anti-nausea medication during pregnancy during the critical period for limb formation.
  - C) Amphotericin is most commonly known to cause cell death and crosses the placenta but is in pregnancy category B due to few reported abnormalities.
  - D) This can cause CNS and ocular abnormalities
4. At time of delivery a 1-day-old female neonate on physical exam is found to have microcephaly and a diffuse spread red rash which of the following is highest on your differential diagnosis list?
- a. CMV
  - b. FAS
  - c. Rubella
  - d. Roseola'

Answer: A

Rationale: Rubella is a rash that is spread during fetal development through the mother's bloodstream so it can be present with microcephaly at birth. A and B are not associated with rashes. Roseola most commonly is known for a rash that affects infants between 6 months and 2 years of age. This is not a rash that is seen present at time of birth or 1 days old or associated with microcephaly.

5. What is the most common characteristic feature of a child whose mother ingested ethyl alcohol at some time during pregnancy and the child has FAS?
- a. Craniofacial abnormality and Behavior disturbances
  - b. Spinal Defects and Increased Birth Weight
  - c. Cardiac Defects and Stunted Limb Growth
  - d. Behavior disturbances and Seizure activity

Answer: A

Rationale: Increased birth weight is most likely due to gestational diabetes however spinal defects can occur with FAS. Cardiac Defects are common with FAS however Stunted Limb growth is most likely associated with Thalidomide use. Seizure activity is possible with FAS but not as common as craniofacial abnormalities

6. DES was taken during pregnancies to alleviate high risks however it caused some severe side effects for the fetus. Which of the following accurately describes the side effect of Diethylstilbesterol use during pregnancy?
- a. Microcephaly and Congenital Heart Defects

- b. Structural abnormalities of Vagina, Cervix and Gonads
- c. Absent Limbs or Stunted Limb growth
- d. Low Birth weight and Single Palmar crease

Answer: B

Rationale: Explanation DES was used for high risk pregnancies but was later had side effects reporting most commonly hypoplastic, T-shaped uterine cavity; cervical collars; hoods, septa, and coxcombs; and “withered” fallopian tubes. (Mcclary) Also male sexual organs were at higher risk for cancer. Microcephaly and Congenital Heart defects is common in cocaine and alcohol use during pregnancy but not the most common side effect with DES use. Absent Limbs or Stunted Limb growth is commonly seen in Thalidomide use during pregnancy. Low Birth weight and Single Palmar crease can be seen occasionally in Trisomy 23 also known as down syndrome and not likely in DES exposure.

7. During embryonic development it describes the time period and cells made up from time period of fertilization until the embryo gets implanted into the uterine wall. Which of the following is a correct description of cells and timeline of embryogenesis?
  - a. After fertilization the zygote undergoes rapid division is called a blastocyst
  - b. The ICM cells flatten and become a ring of cells termed a morula
  - c. Fluid accumulates inside the rapidly cleaved cells and creates a hollow sphere called a blastocyte
  - d. The group of cells that develop further to deliver fetal nutrients is called a trophoblast

Answer: C

Rationale: Fluid accumulates inside the rapidly cleaved cells and creates a hollow sphere called a blastocyte. A is incorrect because after fertilization the rapid exponential cellular division is called a morula not a blastocyte. B is incorrect because the Intracellular mass cells flatten and become a ring of cells known as a trophocyte. D is incorrect because the group of cells that further develop to deliver fetal nutrients is called a placenta not a trophocyte a flattened ring of cells that slowly develop into the placenta over time.

8. What criteria must be met to have HELLP syndrome during pregnancy?
  - a. HTN, Elevated protein, Hemolysis, Elevated Liver Enzymes, and Low Platelets
  - b. Hemolysis, Ecchymosis, Lactate dehydrogenase deficiency and Low Platelets
  - c. High blood pressure, Elevated Protein, Seizure activity and Low Platelets
  - d. Hyperthermia, Elevated Proteins, and Low Platelets

Answer: A

Rationale: HELLP syndrome is related to preeclampsia HTN and elevated protein occurring after 20 weeks gestation-possibly 6 weeks postpartum. The Severity of HELLP is due to the components of hemolysis, elevated liver enzymes and low platelets along with preeclampsia. Lactate dehydrogenase deficiency does not correspond with this syndrome. Seizure activity corresponds with Eclampsia not preeclampsia or preeclampsia with HELLP syndrome. Hyperthermia does not correspond as a necessity for this syndrome

9. A 25-year-old Caucasian Female presents to the office and is going over her History she reports she does not remember her LMP and states she may be pregnant. She gives you a list of her Medications she is currently taking. Which of the following of her medications is a teratogen and needs to be discontinued?
- a. Griseofulvin
  - b. Phenergan
  - c. Acetaminophen
  - d. Hydrocortisone cream

Answer: A

- A) Rationale: Griseofulvin is known to cause many teratogenic defects one study recorded administered 125 milligram to pregnant rats and 75% more syndrome malformation and decreased survival rates were apparent in these pregnant rats (Beall) Two published cases of conjoined twins have been reported in patients taking Griseofulvin during the first trimester of pregnancy, therefore, Griseofulvin is contraindicated in women who are or may become pregnant during treatment. Phenergan has not displayed any teratogen effects. Acetaminophen is commonly recommended for pain due to its unlikelihood to harm the fetus. Hydrocortisone cream is an OTC that commonly recommended for pain due to its unlikelihood to harm the fetus

10. What is the most frequently documented pregnancy complication for cocaine users?
- a. Visual Defects
  - b. Placental Abruptio
  - c. Loss of Reproducibility
  - d. Low Birth weight

Answer: B

- A) Rationale: The most commonly documented complication is placental abruptio. Other documented complications include low birth weight, preterm labor, and preeclampsia. The reason being is that cocaine acts as a local vasoconstrictor and increases hypertension. Visual defects is incorrect because it is most frequently documented with FAS due to the craniofacial and cranial nerve formation changes directly associated with first trimester of development. Sterilization is not one of the most common defects caused

by vasoconstriction during cocaine use. However sterilization can be seen with use of DES. Low birth weight was recorded quite frequently with cocaine use however it is most commonly associated with Tobacco use during pregnancy.

## Chapter 5 – Genetic Counseling

1. What independent body now has control over accreditation of genetic counseling training programs?
  - a. National Society of Genetic Counselors (NSGC)
  - b. American College of Medical Genetics (ACMG)
  - c. American Board of Genetic Counseling (ABGC)
  - d. Accreditation Council for Genetic Counseling (ACGC)

Answer: D

Rationale: A is incorrect because NSGC was not an accrediting body. B is incorrect because ACMG originally had control in. C is incorrect because ABGC took over this responsibility from the ACMG in 1994. D is correct because ACGC split off on its own and took over the responsibility in 2012.

2. What are the four fundamental roles of genetic counseling?
  - a. Clinician, investigator, educator, and counselor
  - b. Doctor, nurse, educator, and counselor
  - c. Clinician, investigator, nurse, and educator
  - d. Doctor, nurse, investigator, and counselor

Answer: A

Rationale: B is incorrect because doctor and nurse are not specifically listed, but instead clinician and investigator are. C is incorrect because nurse is not specifically listed, but instead counselor is. D is incorrect because doctor and nurse are not specifically listed, but instead clinician and educator are.

3. What do all genetic counseling sessions begin with?
  - a. Bloodwork
  - b. Physical exam
  - c. Information gathering
  - d. Treatment plan

Answer: C

Rationale: A, B and D may be included in a session, but sessions always begin with information gathering.

4. What is coined with launching the genomic revolution?

- a. The Monkey Genome Project
- b. The Pig Genome Project
- c. The Rat Genome Project
- d. The Human Genome Project

Answer: D

Rationale: A is incorrect because testing is done on monkeys, but it is not what launched the genomic revolution. B is incorrect because testing is done on pigs, but it is not what launched the genomic revolution. C is incorrect because testing is done on rats, but it is not what launched the genomic revolution.

5. What does it mean for a variant identified on gene sequencing to be pathogenic?

- a. The variant will definitely cause disease
- b. There is strong evidence that the variant will cause disease
- c. The variant will definitely not cause disease
- d. There is strong evidence that the variant will not cause disease

Answer: B

Rationale: A and C cannot be made as definitive statements. D defines a benign variant. B is correct because strong evidence that a variant will cause a disease makes the variant pathogenic instead of likely pathogenic

6. What percent of early onset hearing loss has a genetic etiology?

- a. 0-10%
- b. 10-30%
- c. 30-50%

- d. >50%

Answer: D

Rationale: A genetic cause is to blame in over half of early onset hearing loss cases, so D is the only correct answer.

7. What type of inheritance pattern is most inherited cardiovascular disease?

- a. Autosomal dominant
- b. Autosomal recessive
- c. X-linked dominant
- d. X-linked recessive

Answer: A

Rationale: A is correct because you only need to get the abnormal gene from one parent in order for you to inherit the disease. C and D are not on the sex chromosomes.

8. What percent of pediatric epilepsy has a genetic cause?

- a. 5%
- b. 15%
- c. 40%
- d. 70%

Answer: C

Rationale: Epilepsy has a genetic cause 40% of the time, so C is the only correct option.

9. What percent of ALS, Alzheimer's disease, PD, and FTD are caused by single gene mutations?

- a. 0-5%
- b. 5-10%
- c. 10-15%
- d. 15-20%

Answer: B

Rationale: ALS, Alzheimer's disease, PD and FTD are only caused by a single gene mutation 5-10% of the time, so B is the only correct answer.

10. What originally protected people from health insurance discrimination based on genetic testing?

- a. Affordable Care Act
  - i. Incorrect- This act protects people from healthcare discrimination based on genetic testing, but it was not the first to do so.
- b. Genetic Information Non-discrimination Act
  - i. Correct- This act is what originally protected people from healthcare discrimination based on genetic testing.
- c. Human Genome Act
  - i. Incorrect- There is no Human Genome Act.
- d. Americans with Disabilities Act
  - i. Incorrect- This act prohibits discrimination based on genetic testing, but it does not specifically apply to insurance coverage.

Answer: B

Rationale: A is incorrect because the Affordable Care Act protects people from healthcare discrimination based on genetic testing, but it was not the first to do so. C is incorrect because there is no Human Genome Act. D is incorrect because the Americans with Disabilities Act prohibits discrimination based on genetic testing, but it does not specifically apply to insurance coverage. B is correct because the Genetic Information Non-Discrimination Act is what originally protected people from healthcare discrimination based on genetic testing.

## Chapter 6 – Neurodegenerative Diseases

1. What specific changes in the brain are noted in patients Alzheimer's Disease?
  - a. Loss of cholinergic neurons with formation of plaques and tangles
  - b. Protein deposits in nerve cells
  - c. Atrophy of the caudate nucleus
  - d. Chronically enlarged ventricles

Answer: A

Rationale: Protein deposits in nerve cells are more indicative of Lewy Body dementia. Atrophy of the caudate nucleus is more indicative of Huntington's disease. Chronically enlarged ventricles is more indicative of normal pressure hydrocephalus. Loss of cholinergic neurons with formation of plaques and tangles is noted in patients with Alzheimer's Disease.

2. Which of these is not a risk factor for Alzheimer's Disease?
  - a. Increased age
  - b. Male gender
  - c. Lower education level
  - d. Family history

Answer: B

Rationale: The risk of AD does increase with age, especially over age 60. Those with higher level of education tend to have lower rates of AD, although education level does not seem to affect the severity of the disease if diagnosed. There is a form of AD referred to as familial Alzheimer's Disease which tends to have early onset (before age 65) with mutations in chromosomes 1,14, or 21. It is inherited in an autosomal dominant pattern. AD is more common in females, making B the correct answer.

3. Which of the following does not help to slow the progression of Alzheimer's Disease?
  - a. NSAIDs
  - b. Moderate ethanol intake
  - c. Decreased caffeine intake
  - d. Strong social support

Answer: C

Rationale: NSAIDs, moderate ethanol intake and strong social support may all help slow the progression of AD; decreased caffeine intake is not one of the factors shown to slow disease progression.

4. How does Donepezil work to treat patients with Alzheimer's Disease?
  - a. It is an antagonist at the glutamate receptors, decreasing the amount of glutamate in the brain to decrease nerve degeneration
  - b. Inhibits acetylcholinesterase, thereby increasing the amount of available acetylcholine.
  - c. Dopamine receptor antagonist

- d. Inhibits acetylcholine

Answer: B

Rationale: A is false because this is the mechanism of action of memantine which is used to treat moderate to severe AD. Dopamine receptor antagonists include phenothiazines or haloperidol which can be used in the treatment of Huntington's Disease for relief of dyskinesia or behavioral symptoms, but not AD. AD involves the loss of cholinergic neurons so in the treatment we want to increase the amount of acetylcholine rather than decrease it. Therefore B is the only correct answer.

5. What populations are at risk for Huntington's Disease?
- a. Northwestern European
  - b. Ashkenazi Jews
  - c. African Americans
  - d. Asians

Answer: A

Rationale: Huntington's Disease primarily affects those of Northwestern European descent.

6. At what age do symptoms of Huntington's Disease typically begin to appear?
- a. 30-50 years old
  - b. 20-30 years old
  - c. Over age 50
  - d. Under age 20

Answer: A

Rationale: Symptoms typically appear between 30-50 years old and typically behavioral changes are noted first.

7. What is the most common form of dementia?
- a. Vascular dementia
  - b. Frontotemporal dementia
  - c. Lewy body dementia
  - d. Alzheimer's Disease

Answer: D

Rationale: Alzheimer's Disease is the most common form, accounting for approximately 65% of cases with the rest mostly attributed to vascular dementia.

8. Which of these is not a typical symptom of Huntington's Disease?
- a. Masked facies
  - b. Wide, prancing gait
  - c. Hesitant speech
  - d. Moodiness

Answer: A

Rationale: Wide, prancing gait, hesitant speech and moodiness are all typical symptoms of Huntington's Disease; only masked facies is not.

9. Which of these is true about the genetic basis of Huntington's Disease?
- a. Homozygotes and heterozygotes both express the disease with the same severity
  - b. Huntington's Disease is inherited in an autosomal recessive pattern
  - c. Huntington's Disease is only inherited and cannot occur sporadically
  - d. The sex of the parent from whom the HD allele is inherited does not influence the expression of the allele.

Answer: A

Rationale: Huntington's Disease is inherited in an autosomal dominant pattern and expresses complete dominance. It can occur either via inheritance or spontaneous mutation. Inheritance of the allele from the father results in clinical disease three years earlier than if the allele is inherited from the mother.

10. How can Alzheimer's Disease be definitively diagnosed?
- a. Post mortem autopsy
  - b. CT
  - c. MRI
  - d. Laboratory testing for the APOE e4 allele

Answer: A

Rationale: Post mortem autopsy is the only definitive way to diagnose Alzheimer's Disease by examining the brain tissue for plaques and tangles.

## Chapter 7 – Hereditary Breast and Ovarian Cancer Syndrome

1. Which of the following is not a major phenotypic feature of hereditary breast cancer and ovarian syndrome?
  - a. A Triple Negative Breast cancer diagnosis before the age of 70.
  - b. Increased incidence of family members with tumors in specific organs such as the ovaries, pancreas, or prostate.
  - c. A family member with more than one primary cancer (bilateral tumors) or a single individual diagnosed with both breast and ovarian cancer.
  - d. A breast cancer diagnosis before the age of 50.

Answer: A

Rationale: It is true that a triple negative breast cancer diagnosis is linked to Hereditary Breast and Ovarian Syndrome, however it is a greatest risk before the age of 60. Hereditary breast and ovarian cancer syndrome is linked to families with family members having ovarian, prostate, and pancreatic tumors; patients with multiple primary cancers and cancer diagnoses in both the breast and ovaries; and early onset breast cancer.

2. Which of the following is true of known genes that are linked to breast cancer?
  - a. BRCA 1 is found on Chromosome 17 and transmitted through an autosomal dominant pattern and is linked to male breast cancer, ovarian cancer, prostate cancer, and pancreatic cancer.
  - b. If a patient is BRCA gene positive they may never develop a cancer in their lifetime.
  - c. The inheritance of the BRCA gene always skips generation.
  - d. If a person is a BRCA gene carrier there is a 100% penetrance rate that the mutation will be passed on to their offspring.

Answer: B

Rationale: BRCA1 and BRCA 2 are germline mutations that begin the process of tumorigenesis. In order for a patient to develop a cancer, they must have a mutation in both copies of BRCA1 or BRCA2. If a patient never develops a second mutation, they will not develop a cancer. The BRCA 1 gene is located on chromosome 17 and transmitted in an autosomal dominant pattern. However, BRCA 2, found on chromosome 13, is transmitted autosomal dominant and is linked to male breast cancer, ovarian cancer, prostate cancer, and pancreatic cancer. Both BRCA 1 and BRCA2 are inherited in an autosomal dominant pattern. It can appear that the gene skipped a generation if a carrier does not have a second mutation. There is a 50:50 chance that BRCA gene carriers will pass on the mutation to their offspring.

3. What is the primary risk reducing recommendation for management of patients with a BRCA gene mutation?
  - a. Strict breast cancer and ovarian cancer surveillance for women and breast and prostate cancer screen in men.

- b. Intensive breast cancer screening.
- c. Bilateral mastectomy and adjuvant hormonal therapy with Tamoxifen or an aromatase inhibitor.
- d. A bilateral salpingo-oophorectomy between ages 35-40.

Answer: D

Rationale: They recommend a risk reducing bilateral salpingo-oophorectomy once childbearing is complete. This procedure has been linked to a significant reduction in ovarian cancer. Strict breast and ovarian cancer surveillance and breast and prostate cancer screen in men are not primary recommendations but can be offered to those who want to delay a surgical approach. Intensive breast cancer screening is offered to those with a BRCA mutation but is not a first recommendation. Bilateral mastectomy and adjuvant hormonal therapy is recommended to women who wish to not undergo as radical of procedure as a bilateral salpingo-oophorectomy. This is also not recommended in women diagnosed with ovarian cancer until 5 years after their ovarian diagnosis.

4. What type of Breast Cancer Screening is best for a woman with a BRCA gene mutation?
- a. Self breast exams starting at 18, annual clinical breast exams at age 25, an MRI for breast cancer screening annually beginning at age 25, and breast imaging every 6 months (mammogram or MRI) beginning at age 30.
  - b. Self breast exams starting at 18, annual clinical breast exams at age 20, an MRI for breast cancer screening annually beginning at age 30, and breast imaging annually (mammogram or MRI) beginning at age 40.
  - c. Self breast exams starting at 25, annual clinical breast exams at age 35, an MRI for breast cancer screening annually beginning at age 35, and breast imaging every 6 months (mammogram or MRI) beginning at age 40.
  - d. Self breast exams starting at 20, annual clinical breast exams at age 25, an MRI for breast cancer screening annually beginning at age 35, and breast imaging every 6 months (mammogram or MRI) beginning at age 40.

Answer: A

Rationale: Self breast exams should begin at 18, annual clinical breast exams at 25, an MRI for breast cancer screening annually beginning at age 25, and breast imaging every 6 months beginning at age 30.

5. What is an appropriate screening tool for men with men with both gynecomastia or parenchymal/glandular breast density and a BRCA gene mutation?
- a. Chemoprevention
  - b. Self breast exams with clinical breast exams beginning at age 35.
  - c. Mammogram annually in addition to CBE and SBE at age 35.
  - d. No extra testing should be offered.

Answer: C

Rationale: Chemoprevention is not a recommended option for men; this treatment is best used in women who choose not to undergo a prophylactic mastectomy.

6. What breast and ovarian cancer linked syndrome is associated with noncancerous growths known as hamartomas and malignancies such as breast, thyroid, colorectal, kidney and endometrial cancer?
- Li-Fraumeni Syndrome
  - Cowden Syndrome
  - Peuts-Jeghers Syndrome
  - Hereditary Nonpolyposis Colon Cancer

Answer: B

Rationale: Cowden Syndrome is also known as PTEN Hamartoma Tumor Syndrome. Women that suffer from this syndrome are at a 25%-50% lifetime risk for breast cancer. Li-Fraumeni Syndrome is associated with a germline mutation of the tumor suppressor tumor protein gene TP53 on chromosome 17. It is characterized by premenopausal breast cancer in combination with childhood sarcoma, brain tumors, leukemia, and adrenocortical carcinoma. Peuts-Jeghers Syndrome is a mutation in the STJ11 tumor suppressor gene. This syndrome is associated with dark freckling of the buccal mucosa/axillary/perioral area, hamartomas of the stomach and intestine, and increased risk for breast, ovarian, pancreatic, and gastrointestinal cancers. Hereditary Nonpolyposis Colon Cancer is associated with primary cancers of the colon, endometrium, ovaries, and the stomach.

7. What breast cancer linked syndrome often presents as lobular breast cancer in women and has a lifetime cancer risk 60%?
- Hereditary Diffuse Gastric Syndrome.
  - Peuts-Jeghers Syndrome
  - Cowden Syndrome
  - Hereditary Nonpolyposis Colon Cancer

Answer: A

Rationale: HDGS is a germline mutation in the cadherin-1 (CDH1) gene that presents as a lobular breast cancer. Peuts-Jeghers Syndrome is a mutation in the STJ11 tumor suppressor gene. This syndrome is associated with dark freckling of the buccal mucosa/axillary/perioral area, hamartomas of the stomach and intestine, and increased risk for breast, ovarian, pancreatic, and gastrointestinal cancers. Women that suffer from Cowden Syndrome are at a 25%-50% lifetime risk for breast cancer and most commonly have hamartomas in the GI tract. Hereditary Nonpolyposis Colon Cancer is associated with primary cancers of the colon, endometrium, ovaries, and the stomach.

8. Based on their risk profile for developing an ipsilateral or contralateral breast cancer, whom should practitioners refer for an ipsilateral mastectomy, a contralateral prophylactic mastectomy, and/or a prophylactic bilateral salpingo-oophorectomy?
- BRCA positive, postmenopausal patients with a previous cancer diagnosis
  - BRCA positive, premenopausal women with a previous cancer diagnosis.

- c. BRCA positive, postmenopausal patient with no personal history of breast cancer.
- d. BRCA positive, premenopausal patient with no personal history of breast cancer.

Answer: B

Rationale: BRCA positive, premenopausal women with a previous cancer diagnosis are at the greatest risk for developing a new contralateral cancer or new primary in the ipsilateral breast. Rationale: BRCA positive, premenopausal women with a previous cancer diagnosis are at the greatest risk for developing a new contralateral cancer or new primary in the ipsilateral breast. BRCA positive, pre-and-postmenopausal patients with no personal history of breast cancer are still at risk and may benefit from one or both of these surgical procedures, but they are not at as great of a risk. BRCA positive, postmenopausal patients with a previous cancer diagnosis will not see the same benefits as premenopausal women.

9. Which of the following will not cause a greater penetrance of the BRCA 1 or BRCA 2 gene mutation?
- a. Exposure to carcinogens such as tobacco and hormonal factors.
  - b. A common genetic mutation for BRCA1 or BRCA 2
  - c. A rare genetic mutation including Li-Fraumeni Syndrome, Lynch syndrome etc.
  - d. Radiation exposure at a young age in a BRCA positive male or female.

Answer: B

Rationale: A common genetic mutation for BRCA1 or BRCA 2 will not cause an increase of gene penetrance. Common gene mutations actually have a lower penetrance than a rare genetic mutation. Many environmental factors including hormones, radiation, and tobacco use are linked to increase cancer risk. Rare genetic mutations have a greater penetrance than a common gene mutation. Young women who are BRCA positive women are at a greater risk for developing a radiation induced cancer.

10. What is the term for an accumulation of random genetic changes in an isolated population as a result of its proliferation from only a few parent colonizers?
- a. De novo mutation
  - b. A Kindred
  - c. A germline mutation
  - d. The Founder Effect

Answer: D

Rationale: There are 3 mutations that occur at an increased rate in people of Ashkenazi Jewish ancestry and are believed to originate in this population. These genes have also been found in those in families originating from the Netherlands, Hungary, Iceland, Sweden, Italy, France, South Africa, Pakistan, Asia, French Canadians, Hispanics, and African Americans. This pattern represents the founder effect. A De Novo Mutation is defined as mutations that are not inherited, but rather appear first in the affected

individual. A kindred is defined as an aggregate of genetically related persons. An example of this is persons of Ashkenazi ancestry. A germline mutation is defined as a change in a gene in the body's reproductive cell (egg or sperm) that becomes incorporated into the DNA of every cell in the body of the offspring.

## Chapter 8 – Colorectal Cancer

1. John, a 27-year-old white male, with a PMHx of familial adenomatous polyposis (FAP) comes to the clinic because him and his wife are thinking about having children. He is concerned about passing FAP to his children because he knows that there is 50% chance of passing the condition to each of his children. He states that he had his colectomy when he was 16-years-old. What is true regarding the condition?
  - A. He cannot pass FAP to his children since he had his colon removed.
  - B. Since he had a colectomy, his chance of passing on FAP to his children reduced to 25%.
  - C. Since he had a colectomy, his chance of passing on FAP to his children increased to 75%
  - D. Even with a colectomy, he still has a 50% chance of passing FAP to each of his children.

Answer: D

Rationale: Individuals with FAP have a 50% chance of passing the condition to each of their children, even if the patient has had their own colon removed, and FAP can be passed on to offspring even after a colectomy.

2. A 26-year-old woman who was recently diagnosed with Hereditary Nonpolyposis Colorectal Cancer presents to the clinic worried about consequences of having this condition. What two types of cancers is she highest at risk for with HNPCC?
  - A. Colorectal cancer and endometrial cancer
  - B. Small bowel cancer and stomach cancer
  - C. Stomach cancer and bile duct cancer
  - D. Colorectal cancer and ovarian cancer

Answer: A

Rationale: The patient is highest at risk for colorectal and endometrial cancer. Individuals affected with HNPCC have a 60% - 80% risk of developing colorectal cancer in their lifetime and more than 40% risk of developing endometrial cancer in their lifetime. Although individuals with HNPCC are at risk for stomach, small bowel, bile duct cancer and ovarian cancer, these cancers are not as prominent as colorectal cancer and endometrial cancer for these patients.

3. 39-year-old white male presents to the clinic because he has a family history of colorectal cancer. Which of the following is a sign that he has to be cautious about?
  - A. Increase in caliber of stool
  - B. Hematochezia
  - C. Diarrhea due to an illness
  - D. Weight gain

Answer: B

Rationale: Hematochezia, blood in the stool, is a symptom of colorectal cancer that the patient should be cautious about. Persistent decrease in the size and caliber of stool is a sign associated with colorectal cancer, not increase in the size of caliber of stool. Diarrhea that is not the result of diet or illness is a sign associated with colorectal cancer. Weight loss is a sign associated with colorectal cancer, not weight gain.

4. Mutation in what genes causes familial adenomatous polyposis (FAP) and variant of familial adenomatous polyposis?
- A. APC and MYH
  - B. MLH1 and MSH2
  - C. PMS2 and APC
  - D. MSH6 and MYH

Answer: A

Rationale: FAP is an autosomal dominant condition caused by mutations in the APC tumor suppressor gene. Additionally, an autosomal recessive CRC syndrome, MUTYH-associated polyposis (MAP), a variant of FAP, has also been identified as another hereditary CRC. MLH1 and MSH2 mutations cause HNPCC, not FAP. A defect in one of several genes (MLH1, MSH2, MSH6, and PMS2) that are important in the detection and repair of DNA base-pair mismatches causes HNPCC.

5. An 18-year-old female presented with a positive HNPCC gene mutation who had relative that was diagnosed with HNPCC at the age of 30, 32 and 45. At what age should she start getting screened and with what test?
- A. At the age of 30, with a colonoscopy
  - B. At the age of 25, with a sigmoidoscopy
  - C. At the age of 25, with a colonoscopy
  - D. At the age of 30, with a sigmoidoscopy

Answer: C

Rationale: With a documented MMR gene mutation, affected relatives should be screened with colonoscopy every 1 to 2 years beginning at age 25 or at an age 5-10 years younger than the age at diagnosis of the youngest affected family member, whichever is first. Since this patient's youngest relative was diagnosed with HNPCC at the age of 30, she should start receiving screening at the age of 25. As stated earlier, these screenings should be done with a colonoscopy.

6. A 20-year-old male is diagnosed with FAP, what is the next recommendation?
- A. Complete proctocolectomy or colectomy
  - B. Partial proctocolectomy or colectomy
  - C. Complete proctectomy
  - D. Partial proctectomy

Answer: A

Rationale: Once FAP has been diagnosed, complete proctocolectomy or colectomy is recommended before the age of 20.

7. In what hereditary pattern is lynch syndrome most commonly inherited?
- A. Autosomal recessive
  - B. X-linked inheritance**
  - C. Autosomal dominant
  - D. Y-linked inheritance

Answer: C

Rationale: Lynch syndrome is an autosomal dominant condition that dramatically increases risk of many kinds of cancer, most commonly CRC.

8. Men and women at average risk for colorectal cancer should start getting screened at what age?
- A. Age 45
  - B. Age 50**
  - C. Age 60
  - D. Age 55

Answer: B

Rationale: Individuals with average risk for developing colorectal cancer should take the screening tests at the age of 50.

9. *Lynch syndrome occurs as a result of defect in one or several genes that are important in detection and repair of DNA base-pair mismatches. What is the phenotypic abnormality that results as a mutation in an allele of a mismatch repair (MMR) gene?*
- A. Chromosomal instability
  - B. Nucleotide instability
  - C. Macrosatellite instability
  - D. Microsatellite instability**

Answer: D

Rationale: The characteristic phenotypic DNA abnormality that results as a mutation in an allele of a mismatch repair (MMR) gene is microsatellite instability.

10. At what age should an individual with a family history of attenuated FAP begin getting screened for FAP? When should the screening be repeated?
- A. At age of 20 and repeated 1-3 years
  - B. At age of 15 and repeated 1-3 years**
  - C. At age of 15 and repeated 5-7 years
  - D. At age of 20 and repeated 5-7 years

Answer: B

Rationale: Individuals with a family history of attenuated FAP should begin getting screened for FAP at the age of 15 and it should be repeated every 1-3 years. This is because in a family with attenuated FAP, number of polyps and age of onset can vary greatly from one family member to another, so it is best to start screening early and repeat it frequent.

## Chapter 9 – Chronic Myelogenous Leukemia

1. A 52-year-old male presents to the office for his annual checkup. He complains of increasing fatigue and weight loss regardless of his diet, which he admits consists mainly of fast food and frozen dinners. Upon exam, pain is elicited when palpating the left upper quadrant and his spleen measures 12cm. You suspect the patient may have CML. What would be the typical CBC findings for this type of patient?
  - A. RBC greater than  $70 \times 10^6$
  - B. Neutrophils greater than 10,000
  - C. Platelets greater than 450,000
  - D. Lymphocytes greater than 6,000

Answer: B

Rationale: Neutrophils make up the majority of abnormal cells produced in CML patients. The number of RBC and the number of platelets are usually lower due to tumor burden. This type of leukemia only affects neutrophils, basophils and eosinophils.

2. Andrew is a 55-year-old Jewish male who was recently diagnosed with Chronic Myelogenous Leukemia. He has a past medical history of Hodgkins lymphoma as a teenager and a 30-pack year history of smoking. Which of the following factors most likely contributed to his new diagnosis of CML?
  - A. History of Hodgkins lymphoma
  - B. Ashkenazi Jewish decent
  - C. 30 pack year history of smoking
  - D. His age

Answer: A

Rationale: No connection has been made between his Jewish descent and CML, so this cannot contribute to his new diagnosis. His 30-pack year history of smoking may have contributed to his condition, but no clear connection has been made between smoking and CML. 55 is the average age at presentation, but not a significant predisposing factor. Ionizing radiation used to treat lymphoma is the only known predisposing factor of CML.

3. Which of the following is NOT a symptom of CML?
  - A. Easy bruising
  - B. Infection

- C. Nausea
- D. Abdominal pain

Answer: C

Rationale: Infection, easy bruising and abdominal pain are all symptoms of CML. Nausea is the only answer that is not.

4. What type of detection methods are used for patients where the Philadelphia chromosome is not identifiable by routine cytogenetic analysis?
- A. FISH
  - B. VDRL
  - C. Gel electrophoresis
  - D. ELISA

Answer: A

Rationale: VDRL is used to test for syphilis, not the Philadelphia Chromosome. Gel electrophoresis is used to detect DNA, RNA, and proteins, such as in patients with multiple myeloma. ELIAS is used to detect for antibodies such as HIV.

5. Which of the following is NOT a criteria of blast crisis?
- A. Night sweats
  - B. Fever
  - C. Fatigue
  - D. Splenomegaly

Answer: A

Rationale: Fever, fatigue, and splenomegaly are all criteria for blast crisis, plus at least 20% blasts in the blood count. Night sweats are a common symptom of CML, but not a criteria for blast crisis.

6. A 57 year old white male presents to your clinic with increasing fatigue for the past 2 years. You decide to order a CBC and peripheral blood smear. The CBC shows a decrease in RBC's and an unusually high number of WBC's. The blood smear shows 16% blasts. Based on these results you suspect CML. According to these results, which phase of CML if this patient experiencing?
- A. Chronic phase
  - B. Blastic phase
  - C. Acute phase
  - D. Accelerated phase

Answer: D

Rationale: In the accelerated phase, blasts are between 10-19%. In the chronic phase blasts are under 10% and in the blastic phase, blasts are 20% or higher. Acute phase is not an actual phase of CML.

7. What is the mechanism of action of Imatinib mesylate (Gleevec)?
- A. Inhibits the activity of the BCR/ABL oncogene to keep the number of blasts low
  - B. Recognizes the mutated cells, attaches to them, and induces apoptosis
  - C. Upregulating the activity of interferons to increase host defense mechanisms and protect healthy cells from invasion
  - D. A ribonucleotide reductase inhibitor which damages the DNA/RNA, preventing the cell to duplicate

Answer: A

Rationale: Imatinib mesylate inhibits the activity of BCR/ABL oncogene to keep the number of blasts low. IT does not directly produce apoptosis, so B cannot be correct, and the response in D is not how hydroxyurea works.

8. Which of the following is a proven curative treatment for Chronic Myelogenous Leukemia?
- A. Imatinib mesylate
  - B. Stem cell transplant
  - C. Hydroxyurea
  - D. Dasatinib

Answer: B

Rationale: Imatinib mesylate is typically tried first but is not a curative treatment. Hydroxyurea is used when CML is diagnosed but has not been confirmed as a curative treatment. Dasatinib is only used when Gleevec has failed. Stem cell transplant is the only proven curative treatment in this list.

9. Response to treatment with Imatinib mesylate is monitored by all of the following EXCEPT:
- A. Immunity response
  - B. Hematologic response
  - C. Cytogenetic response
  - D. Molecular response

Answer: A

Rationale: Hematologic response, cytogenetic response and molecular response are all monitored to check a patient's response to treatment with Imatinib mesylate. Immunity response is not a way of monitoring treatment.

10. What of the following is NOT a major side effect that may occur after allogeneic hematopoietic stem cell transplantation?
- A. Hemorrhage during surgery
  - B. The host succumbing to infection
  - C. Graft rejection
  - D. Graft-vs-host disease

Answer: A

Rationale: After allogeneic hematopoietic stem cell transplantation, graft rejection, graft-vs-host disease and the host succumbing to infection are all possible major side effects. Hemorrhage during surgery may occur, but it is not a major side effect.

## Chapter 10 – Hemophilia

1. Hemophilias are generally inherited in an X-linked pattern. How will this affect the offspring of a father with a normal gene and a carrier mother?
  - A. All sons will be affected and 50% of daughters will be carriers
  - B. No children will be affected but all will be carriers.
  - C. A 25% chance of having a son who is affected and a 25% chance of having a daughter who is a carrier, and 50% chance that a child (either boy or girl) does not have the gene at all.
  - D. 50% of sons are affected and all daughters are carriers.

Answer: C

Rationale: This couple has a 25% chance of having a son who is affected and a 25% chance of having a daughter who is a carrier, and 50% chance that a child (either boy or girl) does not have the gene at all.

2. Hemophilias are generally inherited in an X-linked pattern. How will this affect the offspring of an affected father and normal gene mother?
  - A. All sons will be affected and 50% of daughters will be carriers
  - B. No children will be affected but all will be carriers.
  - C. A 25% chance of having a son who is affected and a 25% chance of having a daughter who is a carrier, and 50% chance that a child (either boy or girl) does not have the gene at all.
  - D. All sons will be normal and all daughters are carriers.

Answer: D

Rationale: In the case of this couple, all sons will be normal and all daughters are carriers.

3. A 27-year-old man with a history of bleeding while brushing and flossing his teeth presents with a nosebleed. This episode is worse than ones he has experienced in the past. You suspect he may have this coagulopathy, the most common inherited bleeding disorder in the United States.
  - A. Von Willebrand disease
  - B. Hemophilia A
  - C. Hemophilia B
  - D. Hemophilia B Leyden

Answer: A

Rationale: Von Willebrand Disease is the most common inherited bleeding disorder in the United States.

4. A 27-year-old man with a history of bleeding while brushing and flossing his teeth presents with a nosebleed. This episode is worse than ones he has experienced in the past. Vital signs are stable, however, applying pressure has failed to control bleeding. What the next step in treatment?
- A. Platelets
  - B. Desmopressin
  - C. Cryoprecipitate
  - D. Fresh Frozen Plasma

Answer: B

Rationale: Since applying pressure failed to control the bleeding, Desmopression should be administered.

5. A 12-year-old boy with a history of bleeding while flossing his teeth presents with a nosebleed. He has had recurrent nosebleeds over the past 5 years. His parents deny a family history of bleeding disorders. You suspect von Willebrand disease. A decreased vWF along with what other lab findings confirms the diagnosis?
- A. Normal PT & bleeding time, prolonged aPTT
  - B. Normal aPTT & bleeding time, prolonged PT
  - C. Prolonged PT & aPTT, normal bleeding time
  - D. Normal PT & aPTT and prolonged bleeding time

Answer: D

Rationale: Decreased vWF along with normal PT & aPTT and prolonged bleeding time all confirm a diagnosis of von Willebrand disease.

6. A 43-year-old woman who has von Willebrand disease presents with a nosebleed that she can't control. She is currently menstruating and using intranasal DDAVP. Vital signs reveal tachycardia and a BP of 98/68. What treatment is indicated at this time?
- A. Platelets
  - B. vWF Factor containing Factor VIII concentrate
  - C. Fresh Frozen Plasma
  - D. IV Desmopressin

Answer: B

Rationale: vWF Factor containing Factor VIII concentrate should be administered at this time to help stop the bleeding.

7. What is the first line treatment for a patient who has Hemophilia B who presents with minor bleeding?

- A. Platelets
- B. Cryoprecipitate
- C. IX concentrate
- D. Desmopressin

Answer: C

Rationale: For a patient who has Hemophilia B and presents with minor bleeding, IX concentrate should be the first treatment administered.

8. The following pair matches coagulation factors with the correct pathway in the coagulation cascade:

- A. Factor VIII & IX- extrinsic
- B. Factor VIII & IX – intrinsic
- C. Factor VIII & IX - common
- D. Factor VII & IX – intrinsic

Answer: B

Rationale: Factor VIII & IX combine to make the correct pathway in the coagulation cascade.

9. This bleeding disease is most frequently inherited in an autosomal dominant pattern:

- A. Hemophilia A
- B. Von Willebrand disease
- C. Hemophilia B
- D. Hemophilia B Leyden

Answer: Von Willebrand Disease is most frequently inherited in an autosomal dominant pattern.

10. A patient who has a deficiency in Factor VIII has what disease?

- A. Hemophilia A
- B. Hemophilia B
- C. Hemophilia B Leyden
- D. Von Willebrand disease

Answer: A

Rationale: Patients with Hemophilia A will have a deficiency in Factor VIII.

## Chapter 11 – Sick Cell Disease

1. A 5-month-old African American boy presents to the ER for unexplained fever and swelling of his hands and feet. The mother states that 2 days ago when she was putting on his socks she noticed that his socks no longer fit, and he was extremely fussy and crying when touching both his feet. She states that at the end of day both of his feet had increased in size and appeared swollen. Yesterday morning while breastfeeding she noticed that his fingers appeared swollen and describes them as being “sausage like” and that he felt feverish. She measured his temperature that morning and it was 101.5 F, (temporal).

She denies any administration of medicine or antibiotics recently, or sick contacts. She states that their family just came back from a vacation in Colorado where they went skiing for the first time. Family history is negative except for a distant relative on the mother’s side having a disease she describes “where his RBCs were shaped differently and would make him sick in colder weather”. All newborn screening tests were negative.

You order a complete lab work-up and get back the CBC with differential results that show normocytic anemia, a low platelet count, target cells, and dehydrated cells also known as sickle cells. You suspect that your patient may have Sickle cell disease.

What test must you order is considered diagnostic for sickle cell disease?

- A. Solubility test
- B. Hemoglobin electrophoresis
- C. Bone marrow biopsy
- D. Flow cytometry

Answer: B

Rationale: The presence of large quantities of HbS using hemoglobin electrophoresis is considered diagnostic for sickle cell disease. Low platelet count, abdominal pain, nausea, and vomiting may also be present. This presentation occurs most frequently in young children with sickle cell disease and may include a febrile illness.

2. A 25-year-old African American male is in the hospital recovering from a cholecystectomy performed a day ago and is now complaining of priapism. He states that he noticed it around lunch time today and says that it has not gone down for the past couple hours. He mentions that he had a similar incident while visiting the Rocky Mountains on a skiing trip and went to the ER there and was told he had some kind of disease of the blood where his hemoglobin gene was defective.

You order a full lab-workup along with a solubility test to screen for HbS. CBC showed a normocytic anemia and solubility test was positive. The solubility test does not differentiate between sickle cell disease, sickle cell trait, and hemoglobin SC disease. You order a hemoglobin electrophoresis. The results of the electrophoresis will not be known for a couple days.

What lab results will show a notable differentiation between hemoglobin SS and hemoglobin SC disease?

- A. Hemoglobin levels
- B. Platelet count
- C. Hematocrit
- D. Iron levels

Answer: A

Rationale: Hemoglobin SC disease occurs in people who have one copy of the gene for sickle cell disease and one copy of the gene for **hemoglobin C disease**. Symptoms associated with HbSC disease are similar to sickle cell disease, but tend to be milder in some patients. A notable clinical differentiation between hemoglobin SS and hemoglobin SC disease is that SC patients tend to have higher hemoglobin levels (9-14 gm/dL) than SS patients (6.0 -9.0 gm/dL).

3. What is the leading cause of death among adult patients who suffer from sickle cell disease?
- A. Stroke
  - B. Myocardial infraction
  - C. Acute chest syndrome
  - D. Pulmonary hypertension

Answer: C

Rationale: The leading cause of death among adult patients with sickle cell disease is acute chest syndrome, although infection and fat emboli are also thought to play a role in bringing about this syndrome.

4. You just newly diagnosed a male patient with Sickle cell disease and are counseling them on the effects the disease can have on their body if they are not properly treated. Which of the following complications is this patient at risk for?
- A. Erectile dysfunction
  - B. Renal failure
  - C. Osteomyelitis
  - D. Ulcers in buccal mucosa

Answer: B

Rationale: Priapism is a frequent occurrence in males with sickle cell disease and may cause permanent tissue damage and impotence if not treated. Other problems associated with reduced blood supply include avascular necrosis of the femoral and/or humeral head, renal failure, cardiomyopathies, delayed growth, and superficial ulcers of the lower extremities.

5. A 30-year-old Caucasian male is at your office inquiring about what type of immunizations he will need regarding his trip to Africa next year for a missionary trip. The topic of Malaria comes up and he is concerned because he read that no antimalarial drug is 100% protective against being infected. Out of the following choices, what person would have a decreased risk of an infection by a malarial parasite?
- A. A person who uses insect repellent and long pants.
  - B. A person who sleeps in an insecticide-treated bed net.
  - C. A person who on electrophoresis shows Hemoglobin S.
  - D. A person taking Chloroquine weekly while in an endemic area.

Answer: C

Rationale: Normal adult hemoglobin is designated hemoglobin A (HbA), whereas adult sickle hemoglobin is designated as hemoglobin S (HbS). Hemoglobin S is correlated with lower rates of mortality among carriers who are of African and Mediterranean descent, because the HbS allele decreases the risk of infection by malarial parasites endemic in those areas.

6. A 2-day old female newborn recently underwent routine newborn screenings that are required for any infant born in the United States. You receive the results and notice that her screening test for Hemoglobin S was positive. By what age must the newborn be confirmed for having sickle cell disease or a significant hemoglobinopathy?
- A. 1 week of age
  - B. 1 month of age
  - C. 6 weeks of age
  - D. 6 months of age

Answer: C

Rationale: Any screening test that is positive for HbS or other significant hemoglobinopathies in a newborn must be confirmed by 6 weeks of age. The presence of large quantities of HbS using hemoglobin electrophoresis is considered diagnostic for sickle cell disease. Similarly, electrophoresis is used to confirm sickle cell trait by identifying the presence of HbS, albeit in lower quantities than are present in sickle cell disease.

7. Which of the following choices is a TRUE statement about the drug Hydroxyurea and its use in therapy for the sickle cell disease population?
- A. It improves red blood cell survival by inducing production of fetal hemoglobin (HbF) that is resistant to sickling.
  - B. It increases the white blood cell count and arrests inflammatory processes.
  - C. It metabolizes into nitrogen oxide, which acts as a vasodilator to help improve blood flow.

D. It is the only curative treatment available for sickle cell disease.

Answer: A

Rationale: Hydroxyurea is and has been the most commonly prescribed therapy for sickle cell disease since it was approved for use in this patient population in 1998. It works by multiple mechanisms. First, it improves red blood cell survival by inducing production of fetal hemoglobin (HbF) that is resistant to sickling. Second, it lowers the white blood cell count and arrests inflammatory processes. Third, it metabolizes into nitric oxide, which acts as a vasodilator to help improve blood flow and reduce the risk of stroke. The use of hydroxyurea has been shown to reduce the number of painful episodes, acute chest syndrome, and transfusions as well as to improve overall survival among persons with sickle cell disease. Allogeneic transplant is the only available curative treatment for sickle cell disease.

8. What is the only available curative treatment for Sickle cell disease?

- A. Hydroxyurea
- B. Red cell transfusions
- C. Allogeneic transplant
- D. Chemotherapy

Answer: C

Rationale: Allogeneic transplant is the only available curative treatment for sickle cell disease, but few patients have a suitable donor available. When a suitable donor is available, stem cell transplant has been reported to produce a disease-free survival rate as high as 85%, with the best outcomes reported in pediatric patients. Red cell transfusions of sickle negative and leukoreduced blood by simple or exchange transfusion can benefit patients in those indicated by decreasing their risk of stroke or recurrent CVA, pulmonary hypertension, and painful crises.

9. You are counseling a newly diagnosed sickle cell disease patient on the importance of avoiding certain activities because they might lead to precipitating a sickle cell crisis exacerbation. Which of the following scenarios listed below will most likely NOT lead to a sickle cell crisis?

- A. A person who undergoes an elective 6-hour Whipple procedure for pancreatic cancer.
- B. A person running a marathon in 95-degree weather and does not hydrate throughout the race.
- C. A person who indulges in a high purine, gluten, and dairy diet.
- D. A person traveling from Florida to Colorado and staying a week in the mountains.

Answer: C

Rationale: Patients should be counseled to avoid precipitating activities that might lead to sickle cell crisis, such as dehydration, **physical stress**, infection, change in altitude, and prolonged exposure to extreme temperatures of heat or cold.

10. A 55-year-old male with sickle cell disease, hyperlipidemia and hypertension is currently undergoing weekly red cell transfusions of sickle cell negative blood because of his high risk of stroke after experiencing a transient ischemic attack six months ago. It has been shown that transfusions can decrease a patient's risk of stroke or recurrent CVA. Conversely, repeated transfusions will result in iron overload, so iron and ferritin levels must be monitored closely. What test will provide the MOST accurate picture of total body iron burden in a patient undergoing multiple transfusions?
- A. Liver CT scan
  - B. Iron and Ferritin levels
  - C. Liver Biopsy
  - D. Transferrin and total iron-binding capacity

Answer: C

Rationale: Red cell transfusions of sickle negative and leukoreduced blood by simple or exchange transfusion can benefit patients in those indicated by decreasing their risk of stroke or recurrent CVA, pulmonary hypertension, and painful crises. Conversely, repeated transfusions will result in iron overload, so iron and ferritin levels must be monitored closely and reduced before iron accumulates and causes permanent organ damage. Liver biopsy with iron dry-weight quantitation or liver MRI will provide the most accurate picture of the total body iron burden

## Chapter 12 – Hemochromatosis

1. What type of inheritance is hereditary hemochromatosis?
  - A. Autosomal recessive
  - B. Autosomal dominant
  - C. X-linked recessive
  - D. X-linked dominant

Answer: A

Rationale: Hereditary hemochromatosis (type 1 HH) is an autosomal recessive disorder that is most commonly caused by a single mutation in the HFE gene.

2. Clinical evidence of HH presents at what age?
  - A. Younger than 10
  - B. Present at birth
  - C. 20s
  - D. 40 or older

Answer: D

Rationale: Because persons with HH absorb excess iron over a period of years, clinical evidence of disease does not typically present until the affected individual is 40 years of age or older. The average body stores approximately 4 grams of total iron in various forms.

3. Which of the following is not a permanent manifestation of HH?
  - A. Arthritis
  - B. Cardiomyopathy
  - C. Diabetes mellitus
  - D. Hypothyroidism

Answer: B

Rationale: Unless severe, cardiomyopathy is a reversible manifestation. Arthritis, Diabetes Mellitus and Hyperthyroidism are all permanent manifestations of HH.

4. The amount of stored iron in the body is estimated by
  - A. Serum ferritin levels
  - B. Serum iron levels
  - C. Total iron binding capacity
  - D. Transferrin saturation levels

Answer: A

Rationale: Serum iron identifies the amount of free iron that was recently absorbed from the diet, but before it has become bound to transferrin. Normal serum iron levels are often detected in HH due to storage of the majority of iron in other forms. The amount of stored iron in the body is estimated by the serum level of ferritin, the protein that stores iron. The TIBC is a measure of all proteins that are available to bind iron. It indirectly measures the amount of transferrin present, whereas transferrin saturation represents the portion of transferrin bound to iron.

5. Which lab values are correct for HH?

- A. Serum iron normal- increased, serum ferritin increased
- B. TIBC normal- increased, serum ferritin increased
- C. Serum iron decreased, serum ferritin decreased
- D. TIBC normal – decreased, serum transferrin saturation increased

Answer: A

Rationale: Serum ferritin levels increase progressively over time in individuals with HH. Elevated serum ferritin levels are sensitive predictors of disease, but are not specific to HH because any inflammatory process may elevate serum ferritin. Thus, this bio-marker is referred to as an **acute-phase reactant**. Serum ferritin tends to increase or decrease in the same direction as iron stores and provides a rough estimate of total body iron. When both transferrin saturation and serum ferritin are elevated, these findings have a higher combined sensitivity and specificity in supporting the diagnosis of HH than using either value alone.

6. Consumption of excessive amounts of which vitamin should be avoided in HH?

- A. C
- B. A
- C. B12
- D. D

Answer: C

Rationale: Consumption of excessive amounts of vitamin C should also be avoided—this water-soluble vitamin increases absorption of dietary iron.

7. What is the treatment of choice for HH in symptomatic as well as asymptomatic patients?

- A. Chelation
- B. Therapeutic phlebotomy
- C. Diet modification
- D. Liver transplant

Answer: B

Rationale: Therapeutic phlebotomy, which involves the removal of a portion of the affected individual's blood, is the treatment of choice for iron overload in symptomatic patients, as well as asymptomatic patients with a serum ferritin greater than 1000 µg/L or an elevated fasting transferrin saturation. This intervention is a simple, effective and inexpensive method to reduce the iron burden in patients with HH. Chelating agents are drugs that bind to iron and prevent its use or deposition in the body. These are rarely needed in patients with HH due to the efficacy of phlebotomy, but may be considered in special cases. Liver transplant is the only treatment for HH patients with end-stage liver disease. Historically, post-transplant survival in this patient population has been poor, but this has greatly improved in recent years. Dietary management should involve avoidance of iron-containing supplements and limited intake of foods that are high in iron, such as red meat. Consumption of excessive amounts of vitamin C should also be avoided—this water-soluble vitamin increases absorption of dietary iron. Patients with impaired hepatic function should avoid drinking alcohol because iron and alcohol have synergistic hepatotoxic effects.

8. Which of the following is not a frequently presenting symptom of HH?

- A. Abdominal pain
- B. Hyperpigmented skin
- C. Fatigue
- D. Arthralgias

Answer: B

Rationale: Hemochromatosis frequently presents with nonspecific symptoms such as abdominal pain, fatigue, and arthralgias. Factors that may raise clinical suspicion for advanced-stage iron overload include hepatomegaly, hepatic cirrhosis, hepatocellular carcinoma, diabetes mellitus, cardiomyopathy, hypogonadism, arthritis, and hyperpigmented skin.

9. Who is more likely to manifest symptoms of HH?

- A. Men
- B. Women
- C. Equal chance of manifesting symptoms
- D. Homosexuals

Answer: A

Rationale: Phenotypic expression of HH is found in both men and women, but is clinically expressed at a much greater frequency in men. The lower incidence of clinical expression in women is attributed to regular iron loss through the blood loss associated with menstruation.

10. Diagnosis is made by:

- A. HFE gene testing
- B. Liver biopsy
- C. Whole blood genetic testing
- D. Skin biopsy

Answer: A

Rationale: The wide availability of HFE gene testing has largely eliminated the need for liver biopsy. It identifies the C282Y and H63D mutations, and can determine if an individual is homozygous, heterozygous, or has normal HFE alleles. This testing is performed by **polymerase chain reaction (PCR)** using a whole blood sample, which makes it relatively affordable compared to other genetic tests. This technique is very useful for screening family members of an affected person

## Chapter 13 – Cystic Fibrosis

1. A patient recently diagnosed with CF comes into your office. The patient states that they have had difficulty breathing and have been feeling dizzy and light-headed. The patient is concerned that these symptoms are related to their CF. Which system is primarily affected by patients with Cystic Fibrosis?
  - A. Cardiovascular
  - B. Pulmonary/Respiratory
  - C. Nervous
  - D. Musculoskeletal

Answer: B

Rationale: The pulmonary/respiratory, digestive, and reproductive systems are typically most affected by Cystic Fibrosis. The most common cause of morbidity in CF is pulmonary disease; additionally, chronic pulmonary infections occur in most patients with CF.. An individual with CF produces thick mucous secretions that clog that airways, increasing the likelihood of infection and making it harder to breathe.

2. Among which population is CF the most common lethal inherited disorder?
  - A. Caucasians
  - B. Ashkenazi Jews
  - C. African-Americans
  - D. Asians

Answer: A

Rationale: The ACMG recommends that all Caucasians of non-Jewish descent and Ashkenazi Jews get screened, but CF is still the most common lethal inherited disorder among Caucasians in the U.S.

3. A 25 y/o patient with a history of Cystic Fibrosis comes in complaining of a productive cough, fever, chills, and shortness of breath. Upon physical exam, the patient has dullness to percussion, and increased tactile fremitus. Based on these findings, what are the two most common shapes you are likely see on gram stain and culture?
  - A. Gram + cocci in pairs and Gram + cocci in clusters
  - B. Gram + cocci in pairs and Gram – rods
  - C. Gram + cocci in clusters and Gram – rods
  - D. Gram - curved, helical “S” shaped organism

Answer: C

Rationale: *S. aureus* (Gram + cocci in clusters) and *P. aeruginosa* (Gram – rods) are the most common causes of pneumonia in patients with CF. Gram + cocci in pairs indicate an infection with *S. pneumo*, which is not the most likely organism to cause pneumonia in a patient with CF.

4. A 28 y/o male patient with a history of Cystic Fibrosis comes into your office with his wife. They are trying to conceive and are having difficulty. Which of the following information would you tell your patient?
- A. Tell the patient that most males with CF are infertile due to the absence of a vas deferens resulting in azoospermia.
  - B. Tell the patient that even though he has congenital absence of his vas deferens he is still fertile and they should consult a fertility specialist.
  - C. Tell the patient that most males with CF are infertile due to the absence of the seminal vesicle resulting in azoospermia.
  - D. Tell the patient that it is not him and probably his wife who is infertile and she needs to see a fertility specialist.

Answer: A

Rationale: Congenital absence of the vas deferens as well as other reproductive structures results in the absence of spermatozoa. While it is possible that his wife may be infertile, most males with CF are infertile due to the absence of this reproductive structure.

5. A woman who is a carrier for the CF gene marries a man who is also a carrier of the gene. They come in to see you because they are trying to get pregnant and want to know the likelihood of having an offspring with CF. What will you tell them?
- A. 75%
  - B. 33%
  - C. 100%
  - D. 25%

Answer: D

Rationale: CF is inherited in an autosomal recessive pattern. If both parents are carriers, the risk of inheriting the CFTR mutation and developing CF is 25%, or 1 in 4.

6. Which types of gene mutations represent a majority of CF mutations, ultimately leading to the wide variety of clinical phenotypes in patients with Cystic Fibrosis?
- A. Frameshift, splice site, missense
  - B. Missense, splice site, nonsense
  - C. Missense, splice site
  - D. Frameshift, splice site, nonsense

Answer: D

Rationale: Nonsense mutations, frameshift mutations, and splice site mutations, in addition to deletions of the CFTR gene result in complete absence of functioning of CFTR and make up a majority of the mutations.

7. The mother of a young boy with Cystic Fibrosis presents to your office. She would like to know if there is anything that can be done to improve the symptoms her son experiences as a result of his CF. Which of the following medications can help improve quality of life in patients with CF?
- A. Albuterol
  - B. Guanfenesisin
  - C. Ciprofloxacin
  - D. All of the above

Answer: D

Rationale: All of the above medications can be given to a patient with CF in order to improve quality of life. Albuterol is a bronchodilator which allows opening up of the airways in the lungs making it easier for the patient to breathe. Guanfenesisin is a decongestant which draws water into the bronchi thinning the mucous and lubricating the airway to help facilitate removal of the mucous, and antibiotics help kill bacteria that excess mucous harbors in the lungs preventing future lung infections.

8. Which of the following gene mutations are associated with CF?
- A. GFTR
  - B. CFTR and GFTR
  - C. CFTR
  - D. FTFR

Answer: C

Rationale: It is a mutation of the CFTR gene which results in absence of functional CFTR leading to CF mutations. There are no GTFR or FTFR gene mutations associated with CF.

9. Chloride channels are disrupted in patients with Cystic Fibrosis. What implications does this have on ion transport, water, and airway clearance?
- A. Defective chloride transport and enhanced sodium absorption lead to a net increase in water absorption, thinned airway surface liquids, and decreased ciliary clearance.
  - B. Defective chloride transport and enhanced sodium absorption lead to a net decrease in water absorption, thinned airway surface liquids, and decreased ciliary clearance.
  - C. Defective sodium transport and enhanced chloride absorption lead to a net increase in water absorption, thinned airway surface liquids, and decreased ciliary clearance.

D. Defective chloride transport and enhanced calcium absorption lead to a net decrease in water absorption, thinned airway surface liquids, and decreased ciliary clearance.

Answer: A

Rationale: Defective chloride transport and enhanced sodium absorption lead to a net increase in water absorption, thinned airway surface liquids, and decreased ciliary clearance.

10. Which aspect of the pathophysiology of CF is responsible for failure to thrive in patients with CF?

- A. Biliary cirrhosis
- B. Pancreatic fibrosis
- C. Cor pulmonale
- D. Meconium ileus

Answer: B

Rationale: Failure to thrive is a common finding in children with CF because of malabsorption related to pancreatic insufficiency, as well as increased caloric expenditure, and chronic infection. The endocrine pancreas becomes fibrotic reducing insulin secretion and islet cells. Biliary cirrhosis, Cor pulmonale, and Meconium ileus are not responsible for failure to thrive in patients with CF.

## Chapter 14 – Osteogenesis Imperfecta

The parents of a school-age child are concerned because the child experiences a fracture every 2 to 3 months for no apparent reason. Which should the nurse explain about genetic testing for osteogenesis imperfecta?

- a. It predicts the frequency of bone fractures.
- b. It checks for mutations in the genes that code for collagen proteins.
- c. It determines when the child will outgrow the frequency of fractures.
- d. It analyzes the order of chromosomes to determine if a gene is missing.

Answer: B

Rationale: Osteogenesis imperfecta (OI) is a group of genetic disorders that affects the development of bones. Specifically, mutations in the genes that are normally responsible for the coding of proteins for collagen type I are compromised, leading to the weakening of connective tissue, especially bones. Genetic testing for OI does not predict the frequency of bone fractures. OI is a genetic disorder that cannot be outgrown. Genetic testing for OI does not analyze the order of chromosomes to detect a missing gene.

2. You suspect that a client with a history of frequent fractures has undiagnosed dentinogenesis imperfecta. Which assessment finding supports your suspicion?
- a. Blue sclera
  - b. Progressive hearing loss
  - c. Brown teeth that are broken and worn down
  - d. Limbs that are short in relation to the body size

Answer: C

Rationale: Dentinogenesis imperfecta (DI) is characterized by discolored teeth, usually a gray or brown color, that easily degrade, break, or wear down. Individuals with type II osteogenesis imperfecta (OI) will have a blue or gray tint to the sclera and progressive hearing loss. Individuals with type VII OI have limbs that are short in relation to the body size.

3. A toddler with a history of fractures is brought to the emergency department for treatment of a broken leg. What should you prepare to rule out as a cause before considering the client has osteogenesis imperfecta (OI)?
- a. Muscular dystrophy
  - b. Battered child syndrome
  - c. Oppositional personality
  - d. Attention deficit disorder

Answer: B

Rationale: Although pathologic fractures are a feature of OI, other causes, such as nutritional deficiencies, malignancies, or even battered child syndrome, may also need to be ruled out at the time of diagnosis. Muscular dystrophy, oppositional personality, and attention deficit disorder are not identified as causes for fractures.

4. An adult client is diagnosed with osteogenesis imperfecta (OI) after having x-rays for spinal pain. Which finding was used to support the diagnosis of OI?
- Wormian bones
  - Popcorn deposits
  - Codfish vertebrae
  - Accordion femora

Answer: C

Rationale: One diagnostic feature of OI is “codfish” vertebrae. This is caused by repeated spinal compression fractures. Wormian bones are structural bones that are 6 mm by 4 mm in diameter or larger, in excess of ten in number, with a tendency to arrange in a mosaic pattern and are not associated with the spinal column. Popcorn deposits are found on the ends of long bones and are caused by the overabundance of mineral deposits. Accordion femora is a crumpling of a long bone.

5. A school-age child with a history of spontaneous fractures has coxa vera present on a recent hip x-ray. What should this finding indicate to you?
- Client has the mildest form of OI
  - Client has undiagnosed type VII osteogenesis imperfecta (OI)
  - Client has an associated hearing loss and change in teeth color
  - Client has nutritional deficiencies that can correct the x-ray finding

Answer: B

Rationale: Coxa vera, a deformed hip joint in which the neck of the femur is bent downward with the acute angle of the femur head less than 120 degrees causing a change in the hip socket, is a characteristic of type VII OI. Type I OI is the mildest form of the disorder. Hearing loss and change in teeth color are associated with types I, III, and IV OI.

6. A toddler being treated for a metastatic disease is brought for emergency treatment after experiencing a fractured arm. A sample of bone from a biopsy shows a fish scale appearance and the child’s alkaline phosphatase level is elevated. For which type of osteogenesis imperfecta (OI) will you plan care for this client?
- I
  - II
  - V

d. VI

Answer: D

Rationale: Type VI OI is extremely rare and is characterized by an elevated alkaline phosphatase level and a fish scale appearance of bone upon microscopic analysis. Types I, II, and V OI are not associated with an elevated alkaline phosphatase level and do not cause microscopic changes in the appearance of bone.

7. The parent of a child with osteogenesis imperfecta (OI) is upset because a dual energy x-ray absorptiometry (DEXA) scan did not show evidence of the disorder. What should you say in response to the parent's statement?
- "The scan wasn't completed correctly."
  - "The DEXA scan does not evaluate collagen."
  - "The disorder wasn't present at the time of the DEXA scan."
  - "The DEXA scan should have been repeated in 3 months to diagnose OI."

Answer: B

Rationale: OI is a disorder that affects the development of collagen, which is a part of bone. Although bone density may be detected through the use of a DEXA scan, bone density may appear to be normal because DEXA measures mineral content, as opposed to collagen content. The findings from the DEXA scan were not because the scan was completed incorrectly. The child had the disorder upon birth. The scan does not need to be repeated to diagnose OI.

8. A client diagnosed with type I osteogenesis imperfecta (OI) has no family history for the disorder. Which should you consider as a reason for the client to have this genetic disease?
- X-linked trait
  - Sporadic mutation
  - Autosomal recessive trait
  - Autosomal dominant trait

Answer: B

Rationale: Clients with OI type I who have no family history of the disorder were either previously misdiagnosed or developed the disorder through sporadic mutations. If the disorder was inherited through an X-linked, autosomal recessive, or autosomal dominant trait, someone in the client's family would have or had the disorder.

9. You learn that a client with type I osteogenesis imperfecta (OI) has no other family members with the disorder. Which type of genetic testing should you prepare the client to have completed?

- a. DNA analysis
- b. Biochemical analysis
- c. Chromosomal analysis
- d. Fluorescence in situ hybridization (FISH)

Answer: A

Rationale: Individuals who have inherited the disease through mutation must undergo DNA analysis to confirm the diagnosis. This is because these mutations actually code for the N-terminus of the helical region and do not result in the overmodified collagen, making it extremely difficult to pick up on gel electrophoresis. Instead, DNA sequencing must be implemented, requiring approximately 10,000 bases in each of the two genes. The process usually requires 100 polymerase chain reactions (PCRs), followed by an extensive screening for mutated strands. Testing for sporadic mutation of OI is not completed through biochemical analysis, chromosomal analysis, or the FISH process.

10. A school-age child with type I osteogenesis imperfecta (OI) is experiencing a spinal deformity because of repeated vertebral fractures. Which treatment should you expect this client to have to ensure mobility and function of the spinal cord?
- a. None
  - b. Bedrest
  - c. Exercise program
  - d. Intramedullary rodding

Answer: D

Rationale: No treatment exists to prevent or delay disease expression for any of the types of OI. The mainstay approach involves bracing the limbs, using orthotics to provide stabilization, promoting physical activity in appropriate environments, and providing physical and occupational therapy to maximize bone stability, improve mobility, and prevent deformities and contractures. The treatment of fractures will include intramedullary rodding as needed. Physical therapy is implemented after stabilization. The client will be treated, but bedrest is not identified as a treatment approach.

## Chapter 15 – Muscular Dystrophies

1. A mother presents to your pediatric office with her two-year-old son for his annual well-child exam. She states that her son did not begin walking until around the same time as her other children, at 16 months, however she has noticed that he often moves in a peculiar fashion. She states that when her son moves from sitting on the floor to standing, he awkwardly grasps and pulls on various body parts from the knees to hips until he is standing upright. What is the correct term to describe this movement and what does it suggest?
  - A. Gower's Sign, distal muscle weakness
  - B. Psoas Sign, proximal muscle weakness
  - C. Gower's Sign, proximal muscle weakness
  - D. Psoas Sign, distal muscle weakness

Answer: C

Rationale: Weakness in muscular dystrophy selectively affects the proximal before the distal limb muscles. It also affects the lower extremities before the upper extremities. The affected child often presents with difficulty running, jumping, and walking up steps. When arising from the floor, affected boys may also use hand support to push themselves to an upright position, an action termed "Gower's sign".

2. Which intracellular protein expressed in smooth, skeletal and cardiac muscle is entirely missing in Duchenne muscular dystrophy and reduced in Becker's muscular dystrophy?
  - A. Myostatin
  - B. Dystrophin
  - C. Myogenin
  - D. Casein

Answer: B

Rationale: Dystrophin is located on the cytoplasmic face of the plasma membrane of muscle fibers, functioning as a component of a large, tightly associated glycoprotein complex. In its absence, the glycoprotein complex is digested by proteases. Loss of these membrane proteins may initiate the degeneration of muscle fibers, resulting in muscle weakness. In Duchenne muscular dystrophy, dystrophin is missing, while in Becker's muscular dystrophy its presence is reduced, but not missing entirely.

3. A mother and father present with concerns regarding how their three-year-old son has been moving around the home. They state that when he is playing and chasing his seven-year-old sister, he often tires easily, walking on his tiptoes and moving in a waddling fashion, almost like a duck. They noticed it has been going on for the last 4-5 months and while they

assumed he would grow out of it, it has persisted. You explain that you would like to run preliminary testing, as his symptoms and age align with potential muscular dystrophy. You describe his gait pattern to the parents and label it as:

- A. Neuropathic gait
- B. Myopathic gait
- C. Choreiform gait
- D. Ataxic gait

Answer: B

Rationale: In muscular dystrophy, with bilateral weakness, you will have dropping of the pelvis on both sides during walking leading to a myopathic (or waddling gait).

Neuropathic gait is seen in patients with foot drop (weakness of foot dorsiflexion), the cause of this gait is due to an attempt to lift the leg high enough during walking so that the foot does not drag on the floor. In choreiform gait, the patient will display irregular, jerky, involuntary movements in all extremities. This type of gait is found in certain basal ganglia disorders including Sydenham's chorea, Huntington's disease and other forms of chorea, athetosis or dystonia. In an ataxic gait, caused by cerebellar disease, this gait is described as clumsy, staggering movements with a wide-based gait. The gait of acute alcohol intoxication will resemble the gait of cerebellar disease.

4. You are working as a hospitalist physician assistant, rounding on patients in the intensive care unit. Your shift has nearly ended when you enter the room of your final patient, a 21-year-old Caucasian male in moderate distress with a history of Duchenne muscular dystrophy. While you monitor his health from a global perspective, you recall that the most common cause of death in individuals with this condition is:
- A. Congestive Heart Failure
  - B. Renal failure
  - C. Respiratory Insufficiency
  - D. Myocardial Infarction

Answer: C

Rationale: Duchenne muscular dystrophy is characterized by progressive loss of muscle strength, eventually resulting in loss of ambulation, loss of respiratory muscle strength, and death from respiratory insufficiency. The majority of patients also develop cardiomyopathy. While death often results from cardiomyopathy and respiratory complications, the majority of patients die from respiratory insufficiency.

5. What is the suggested laboratory analysis of suspected muscular dystrophy and when do levels peak in adolescence?
- A. Creatine phosphokinase, peaks at age 6
  - B. Myoglobin, peaks at age 2

- C. Creatine phosphokinase, peaks at age 2
- D. Myoglobin, peaks at age 6

Answer: C

Rationale: Before clinical physical symptoms of Duchenne muscular dystrophy are apparent, the creatine phosphokinase concentrations are already elevated in newborn children. At age two, the levels have been shown to be at their highest, usually 10 to 20 times the upper limit of normal, at times even higher. These levels then progressively fall at a rate of about 25 percent per year, reaching normal CPK levels eventually as muscle is replaced by fat and fibrosis.

6. A concerned parent presents with her four-year-old son whom you recently diagnosed with Duchenne muscular dystrophy. She states that she has always planned on having a large family; however now she worries that the disease will also affect all of her future children and grandchildren. What type of inheritance pattern does this condition follow, in addition to often having de novo mutations?
- A. Autosomal dominant
  - B. Autosomal recessive
  - C. X-linked dominant
  - D. X-linked recessive

Answer: D

Rationale: With an X-linked recessive condition, the chance of passing on the changed (non-working) copy of the gene to a child is different for males and females. Males only have one copy of the X chromosome from their mother and one copy of the Y chromosome from their father. Therefore, if their X chromosome has a mutation of their dystrophin gene, they will have Duchenne muscular dystrophy. Females, however, have two copies of X chromosomes. Since females have two copies of this gene, if one copy does not work, they have a second “back-up” copy to produce the dystrophin protein. A woman who has a genetic change in one of her two copies is said to be “a carrier” of Duchenne muscular dystrophy. Carriers do not have Duchenne muscular dystrophy and most are unaware that they even carry this change in their genetic material unless they have a family history. In addition to following an x-linked recessive pattern, “de novo” mutations are also possible, meaning the disorder could arise in any individual, with no previous family history of muscular dystrophy.

7. A grandmother who has recently gained legal custody of her eleven-year-old grandson with Duchenne muscular dystrophy presents to your pediatric office. She admits that because she does not have a computer at home, she is unable to research the condition and is not familiar with the disease process. Today she requests information on the basic management of this

condition and questions how many years she has left with her grandson. You explain to her that while there are exceptions, the median age of survival is generally around:

- A. 30 years of age
- B. 10 years of age
- C. 18 years of age
- D. 6 years of age

Answer: C

Rationale: Patients with Duchenne muscular dystrophy are often confined to wheelchair by about age 12 years and die in their late teens or twenties from respiratory insufficiency or cardiomyopathy; only a few DMD patients survive beyond the third decade.

8. A 25-year-old Caucasian male presents to a cardiology office for a follow-up on his echocardiogram results. His history includes increased shortness of breath with activity over the last couple of years with no attributable cause, prompting the echocardiogram after an abnormal EKG. The echocardiogram revealed dilated cardiomyopathy with an ejection fraction of 37%. When questioned by the physician assistant about any other symptoms, he admits that he tends to bruise easily as he considers himself “clumsy”, often tripping over his own feet. He denies chest pain, numbness of his extremities or paresthesias, trouble with his vision or hearing. What associated condition is this patient most likely suffering from?
- A. Becker muscular dystrophy
  - B. Guillain Barre Syndrome
  - C. Duchenne muscular dystrophy
  - D. Multiple Sclerosis

Answer: A

Rationale: Although muscle involvement is less severe than in DMD, cardiac involvement in BMD is often more evident. In one report, for example, echocardiography revealed evidence of cardiac involvement in 60 to 70 percent of patients (mean age 18) with subclinical or benign BMD. It was suggested that, because patients with mild BMD are still able to perform strenuous exercise, the associated mechanical stress on the heart may be harmful for myocardial cells with abnormal dystrophin. Unlike Duchenne muscular dystrophy, individuals with Becker muscular dystrophy often live until mid to late adulthood. If cardiac aspects of this disease are well managed, they can often live a normal lifespan.

9. What is the gold standard for diagnosing Duchenne muscular dystrophy?
- A. Muscle Biopsy
  - B. Creatine Kinase
  - C. Immunostaining
  - D. Genetic Testing

Answer: D

Rationale: Molecular genetic testing is indicated for patients with an elevated serum CK level and clinical findings suggestive of a dystrophinopathy. The diagnosis is established if a disease-causing mutation of the dystrophin gene (DMD) is identified.

10. You are examining a six-year-old male patient recently diagnosed with Duchenne muscular dystrophy. As he is sitting on the exam table, you note an excessive lumbar curvature inward when viewed from the side. In the musculoskeletal portion of your physical exam, how do you document this finding?
- A. Hyperlordosis
  - B. Scoliosis
  - C. Kyphosis
  - D. Normal anatomical variant

Answer: A

Rationale: As the back muscles of young men with DMD become weaker, lordosis causes their bodies to lean forward, causing a curvature of the spine. DMD can also cause scoliosis, a lateral curvature of the spine, as well as kyphosis, an excessive outward curvature of the spine, however the clinical vignette describes a lordotic presentation.

## Chapter 16 – Familial Thoracic Aortic Aneurysms and Dissections

1. While examining a 20-year-old white male during a routine physical he reveals to you that his younger brother was recently diagnosed with a thoracic aortic aneurysm with dissection (TAAD). Which of the following is not an acceptable method to screen your patient for a possible TAAD?
  - A. MRI
  - B. Chest x-ray
  - C. CT
  - D. Echocardiogram

Answer: B

Rationale: Echocardiogram, CT and MRI are all appropriate screening methods to evaluate a first degree relative of a proband diagnosed with a thoracic aortic aneurysm and dissection (TAAD). Plain films (x-rays) are not a diagnostic imaging study of choice for TAAD, thus B is the correct answer. Abnormal chest x-ray findings should raise suspicion of TAAD. If an enlarged aortic knob or localized bulge, widened mediastinum, extension of the aortic shadow beyond a calcified wall, and longitudinal aortic enlargement, further diagnostic imaging should be performed. The loss of space between the aorta and the pulmonic artery on the PA view is also indicative but not diagnostic for an aneurysm or dissection.

2. After performing an annual screening echocardiogram on a patient with a known history of a thoracic aortic aneurysm (TAA) with a previous ascending aorta dimension of 3.0 cm the patient is now found to have an ascending aorta dimension of 4.4 cm. What is the appropriate management of this patient?
  - A. Continue annual screening
  - B. Increase screening frequency to every 6 months
  - C. Refer the patient for prophylactic surgical repair
  - D. Order a CT scan to confirm the echocardiogram findings

Answer: C

Rationale: Criteria for prophylactic repair includes dilation that increases at a rate of 1.0 cm annually or the presence of aortic regurgitation. Thus, C is the correct answer as the patients' ascending aorta dimension increased by 1.4 cm. Annual screening is only appropriate for patients with stable aortic dimensions with diameter increases of less than 0.5 cm. For aortic diameters that increase by more than 0.5 cm, but less than 1.0 cm more frequent screening is necessary. Both echocardiogram and CT are appropriate tests

to measure aortic diameter, and a confirmatory CT is unnecessary before proceeding to prophylactic surgical repair. Prophylactic repair is also recommended in patients with an ascending aorta diameter of 5.0 cm for patients with TAAD associated with TGFBR2 mutation and persons with a bicuspid aortic valve. For all other patients, the threshold for prophylactic repair is an ascending aortic diameter of 5.0 to 5.5 cm.

3. In addition to an annual screening echocardiogram of the ascending aorta, CT or MRI angiography of the entire aorta is recommended at what frequency for all first-degree relatives of individuals diagnosed with a thoracic aortic aneurysm/dissection (TAAD)?
- A. 2 to 3 years
  - B. 4 to 5 years
  - C. 6 to 7 years
  - D. 8 to 10 years

Answer: B

Rationale: CT or MRI angiography should be performed every 4 to 5 years to evaluate the entire aorta in addition to annual echocardiogram screening of the ascending aorta in all first-degree relatives of affected individuals, making B the correct answer. This routine surveillance should begin at 6 to 7 years of age. All previously undiagnosed individuals who are found to have abnormalities by this screening should have their first-degree relatives screened as well.

4. While discussing health maintenance with a patient whom you recently diagnosed with a thoracic aortic aneurysm (TAA), you advise them to avoid all the following except?
- A. Daily walking exercise
  - B. Weight lifting
  - C. Isometric yoga
  - D. Contact sports

Answer: A

Rationale: In patients with a diagnosed thoracic aortic aneurysm it is important to advise them to avoid activities that may contribute to accelerated dilatation, dissection or rupture. Weight lifting and isometric yoga both can increase intra-abdominal and intra-thoracic pressure, thus causing accelerated dilatation or dissection. Contact sports pose the threat of potential rupture or dissection following a blow to the thoracic cavity. Daily walking provides the individual with aerobic exercise, but does not pose a potential threat to additional dilation, dissection or rupture of a previously diagnosed TAA, thus A is the correct answer.

5. While managing the care of your 18-year-old patient with a thoracic aneurysm with dissection (TAAD), your patient reveals to you that his grandfather suffered from the same condition but was not diagnosed until the age of 63 when he first developed symptoms. What is the phenomenon in which one individual in a family may present with symptoms at a young age, whereas another individual may present at an elderly age?
- A. Penetrance
  - B. Genetic heterogeneity
  - C. Genocopy
  - D. Variable expressivity

Answer: D

Rationale: Variable expressivity is defined as a variation in disease symptoms among persons with the same mutation. In this case the variation refers to the age of onset of the symptoms, thus D is the correct answer. Penetrance refers to the proportion of individuals carrying a particular mutation who also express an associated, observable trait.

Genocopy refers to a genotype that determines a phenotype which closely resembles the phenotype determined by a different genotype. Genetic heterogeneity represents the production of the same or similar phenotypes by different genetic mechanisms; the character of a phenotype produced by mutation at more than one gene or by more than one genetic mechanism.

6. While examining a patient whom you suspect may have a thoracic aortic aneurysm (TAA) based on familial history, which of the following ocular abnormalities may you expect to find during your physical exam?
- A. Livedo reticularis
  - B. Retinitis pigmentosa
  - C. Iris floccule
  - D. Pinguecula

Answer: C

Rationale: Iris flocculi and livedo reticularis are both physical findings associated with individuals with familial TAAD although, livedo reticularis is not an ocular finding which makes C the correct answer. Livedo reticularis manifests as a purplish skin discoloration in a lacy pattern caused by constriction of deep dermal capillaries. Iris flocculi is seen when the central iris pigmented epithelial cysts undergo cycles of collapse and reformation resulting in wrinkled masses along the pupillary border. Retinitis pigmentosa is an inherited, degenerative eye disease that causes severe vision impairment due to the progressive degeneration of the rod photoreceptor cells in the retina and is not associated with aortic aneurysms or dissections. A pinguecula is seen as a yellow-white deposit on the conjunctiva adjacent to the junction between the cornea and sclera also unrelated to aortic aneurysms or dissections.

7. Which of the following is not part of the aortic dissection bundle questions included in the initial history for all patients complaining of chest pain?
- A. Does the patient have Loeys-Dietz syndrome or a family history of Loeys-Dietz syndrome?
  - B. Does the patient's family history have a history of aortic dissection?
  - C. Does the patient have Marfan syndrome or a family history of Marfan syndrome?
  - D. Do physical findings suggest the patient may have undiagnosed Marfan syndrome?

Answer: A

Rationale: When evaluating a patient of any age for a chief complaint of chest pain, it is strongly suggested that the aortic dissection bundle questions be included in the initial patient history. These questions can help identify patients risk for TAAD and could potentially add TAAD to the differential diagnosis. They include:

Does the patient's family history have a history of aortic dissection?

Does the patient have Marfan syndrome or a family history of Marfan syndrome?

Do the physical findings suggest the patient may have undiagnosed Marfan syndrome?

While Loeys-Dietz syndrome is caused by mutations in the TGFBR1 and TGFBR2 genes and can be characterized by aneurysms, arterial dissections, and tortuosities, it is not part of the aortic dissection bundle questions. Therefore, A is the correct answer.

8. A 22-year-old male presents to you with a chief complaint of chest pain. During your history and physical you review the aortic dissection bundle questions to which you gather a single "yes" answer. What is the appropriate next step in determining your diagnosis?
- A. Order an EKG
  - B. Order an emergent CT scan
  - C. Order a screening MRI within the next few days
  - D. Order a trans-thoracic echocardiogram

Answer: B

Rationale: When reviewing the aortic dissection bundle questions, a single "yes" answer indicates that dissection may be the cause of the patient's chest pain, and the diagnosis should be excluded by an emergent CT scan, MRI, or trans-esophageal echocardiogram. Thus, B is the correct answer. In the event of an TAAD, an EKG may show normal or nonspecific changes such as left ventricular hypertrophy. It may be helpful to compare EKG findings to previous baseline studies, but it is not an acceptable method to exclude TAAD from the differential diagnosis. In a patient presenting with chest pain and a positive answer to the aortic dissection bundle questions, it is inappropriate to wait a few

days before evaluating via MRI (or any imaging technique) for TAAD due to the severity of the potential consequences. While an echocardiogram could be used to detect TAAD, it must be a trans-esophageal echocardiogram, not a trans-thoracic echo.

9. Which of the following valvular conditions is seen in patients genetically predisposed to developing familial thoracic aortic aneurysms and dissections (TAAD)?
- A. Bicuspid aortic valve
  - B. Mitral valve prolapse
  - C. Tricuspid aortic valve
  - D. Aortic regurgitation

Answer: A

Rationale: Observations of families with TAAD have indicated that a minority of them have an incidence of a genetic bicuspid aortic valve. The presence of a bicuspid valve warrants further evaluation for possible TAAD via screenings. Thus, A is the correct answer. The aortic valve is normally a tricuspid semilunar valve. Mitral valve prolapse is often seen in patients with Marfan syndrome and while the potential for aortic aneurysms exists in these patients it is not indicative of familial TAAD. Aortic regurgitation is often a secondary symptom of a patient with a bicuspid aortic valve. This answer is incorrect, because it is a result of a bicuspid aortic valve and not in itself a genetic condition.

10. All genetic mutations resulting in familial thoracic aortic aneurysms and dissections (TAAD) appear to be inherited in an autosomal dominant manner. What is the risk that parents, siblings, and offspring of a proband will be affected?
- A. 25%
  - B. 50%
  - C. 75%
  - D. 100%

Answer: B

Rationale: In an autosomal dominant inheritance pattern, all offspring have a 50% chance of developing the phenotype, thus B is the correct answer. In an autosomal recessive inheritance pattern, each offspring of two carriers has a 25% chance of being affected, a 50% chance of being a carrier, and a 25% chance of inheriting neither mutant allele. Thus, two-thirds of all clinically unaffected offspring are carriers of the autosomal recessive phenotype. In an X-linked inheritance pattern heterozygous women transmit the mutant gene to 50% of their sons, who are affected, and to 50% of their daughters, who are heterozygotes.

## Chapter 17 – Familial Hypercholesterolemia

1. Which of the following best describes the result of a having a defective or absent cell surface receptor on low-density lipoprotein cholesterol (LDL-C)?
  - A. Unregulated synthesis leads to excess cholesterol in tissues
  - B. There is increased destruction of LDL-C receptors
  - C. Normal binding of LDL-C particles is inhibited
  - D. Severe atherosclerosis begins to develop in middle age

Answer: A

Rationale: When LDL receptors are absent or defective, unregulated synthesis of LDL-C occurs and excess cholesterol accumulates in the body and is deposited in tissues in abnormal amounts. Therefore, A is the correct answer.

2. Which of the following factors can initiate the development of atherosclerosis from plaques within blood vessel walls?
  - A. Alcohol use
  - B. Smoking
  - C. Hemorrhage
  - D. High sodium intake

Answer: B

Rationale: Lifestyle choices, including diet, exercise, and smoking, strongly influence the amount of cholesterol in the blood, which contributes to the development of atherosclerosis and increased plaque deposits on blood vessel walls.

3. A 35-year-old patient presents to the emergency department complaining of an episode of midsternal chest pain last evening that persisted for 2 hrs. He began to feel nauseous after dinner and went to bed early. He was awoken in the middle of the night with a “squeezing” feeling in his chest. He states the pain was a 6/10. He sat upright until the pain finally decreased. At present, the pain is 4/10. What other findings would support a diagnosis of familial hypercholesterolemia?
  - A. A history of cigarette smoking for 20 yrs
  - B. Abnormal electrocardiogram (EKG) findings
  - C. Presence of xanthelasmata under both eyelids
  - D. Reported 30 lb weight gain in 2 months

Answer: C

Rationale: Xanthelasmata occur when cholesterol deposits accumulate in the skin. They may also accumulate in the tendons and the peripheral border of the cornea, resulting in arcus corneus. These growths are a clear sign supporting a diagnosis of familial hypercholesterolemia.

4. At what age should screening for familial hypercholesterolemia begin in a family with a positive history for hypercholesterolemia?
- A. Screen once other comorbidities are present
  - B. All persons should be screened routinely at age 20 years
  - C. Screening should begin at age 2 years
  - D. Universal screening should begin at age 17 years

Answer: C

Rationale: For those with a positive family history, screening should begin at 2 years, as their risk is stratified using established cholesterol level criteria between the ages of 2 and 19.

5. Once the presence of hyperlipidemia has been confirmed, what would be the purpose of identifying the phenotype by using the Fredrickson classification?
- A. To identify which type of mutation is present
  - B. To assess the degree of atherosclerotic plaque deposition
  - C. To predict a person's long-term prognosis
  - D. To assist in determining the appropriate pharmacotherapy

Answer: D

Rationale: The Frederickson classification can assist in determining the appropriate pharmacotherapy for a patient with confirmed hyperlipidemia.

6. According to the US Department of Health and Human Services, what is the management goal for the LDL level in a patient with 2 or more risk factors for coronary heart disease (CHD)?
- A. Less than 80 mg/dL
  - B. Less than 100 mg/dL
  - C. Less than 130 mg/dL
  - D. Less than 160 mg/dL

Answer: C

Rationale: In patients with 2 or more risk factors for coronary heart disease, the management goal for the LDL level should be less than 130 mg/dL.

7. Which of the following agents is the most effective agent for lowering LDL-C?
- A. Cholesterol absorption inhibitors
  - B. Statins
  - C. Fibric acid derivatives
  - D. Bile-acid-binding resins

Answer: B

Rationale: Statins are generally well-tolerated and have been well documented to lower cholesterol by as much as 25-50% below baseline, so these agents are the most effective for lowering LDL-C. Cholesterol absorption inhibitors are frequently used in conjunction with statins to reach target goals but are not as effective on their own. Bile-acid binding resin only lowers LDL-C between 10% and 20% below baseline, and niacin's adverse effects typically contribute to decreased patient compliance.

8. An obese 32-year-old male has been diagnosed with familial hypercholesterolemia. Despite a 10 lb. weight loss and smoking cessation, his LDL-C remains elevated. He agrees to initiate statin therapy. In addition to monitoring his LDL-C level, what else should be monitored?
- A. His continued adherence to weight loss
  - B. His exercise tolerance
  - C. His level of cognitive function
  - D. His liver enzymes

Answer: D

Rationale: Statin treatment will cause an increase in liver enzymes (AST, ALT), so these enzyme levels should be monitored for any abnormal elevation during treatment. Patients should also be educated to report any muscle pain, as this is another effect of statin therapy.

9. What is the mechanism of action of statin drugs?
- A. They block intestinal absorption of cholesterol
  - B. They reduce the synthesis of triglycerides
  - C. They inhibit the enzyme implicated in cholesterol production
  - D. They bind the cholesterol in bile acids in the intestines

Answer: C

Rationale: Statin drugs inhibit the enzyme implicated in cholesterol production, resulting in as much as a 25-50% drop in LDL-C below baseline.

10. What effect does an increased fiber intake have upon cholesterol?

- A. Fiber increases HDL-C levels
- B. Fiber decreases cholesterol levels
- C. Fiber decreases triglycerides
- D. Fiber increases LDL-C levels

Answer: B

Rationale: Increased intake of dietary fiber decreases cholesterol levels by binding the fiber with cholesterol in bile acids and preventing the cholesterol from being absorbed in the gastrointestinal tract.

## Chapter 18 – Hereditary Cardiomyopathies

1. If the mother is heterozygous for the HCM trait and the father is homozygous recessive, going by the most common form of inheritance of the cardiomyopathy, what is the chance that their son will have HCM?
  - A. 100%
  - B. 75%
  - C. 50%
  - D. 25%
  - E. 0%

Answer: C

Rationale: Since the most common mode of inheritance is autosomal dominant, by doing a simple Punnett square will lead to half being heterozygous, and half being homozygous recessive

2. In which observable phased of ARVD/C does left ventricular involvement occur?
  - A. Phase 1
  - B. Phase 2
  - C. Phase 3
  - D. Phase 4
  - E. It can occur in any phase

Answer: E

Rationale: The four described phases of ARVD/C are: (1) concealed phase (no clinical manifestations of ARVD/C; (2) an overt electrical disorder (characterized by symptomatic arrhythmias); (3) right ventricular failure; and (4) a biventricular pump failure (resembles dilated cardiomyopathy). Left ventricle involvement can occur at any of the above stages

3. Which test would be the least useful for screening degree of cardiac involvement in hereditary cardiomyopathies?
  - A. 12-lead ECG
  - B. Cardiac enzymes
  - C. Exercise stress test
  - D. Echocardiogram
  - E. 24-hour Holter monitoring

Answer: B

Rationale: Screening recommendations for persons diagnosed with ARVD/C include: annual ECG, echocardiogram, holter monitoring, and cardiac MRI. Cardiovascular testing in HCM includes echocardiogram to measure degree of LVH, exercise testing to assess blood pressure response to exercise and ambulatory monitoring for significant ventricular ectopy. Cardiac enzymes will provide the least information for cardiomyopathies, it is mostly used to detect previous or current ischemia

4. One of the associated syndromes of cardiomyopathies includes \_\_\_\_\_ which is characterized by ST-segment abnormalities in leads V1-V3 and associated with ventricular fibrillation.
- A. Brugada syndrome
  - B. Woff-Parkinson-White syndrome
  - C. Torsades de Pointes
  - D. Right bundle branch block

Answer: A

Rationale: Brugada syndrome is definitively diagnosed when a Type 1 ST-segment elevation is observed in more than one right precordial lead (V1-V3) and in conjunction with one or more of the following: documented VF, polymorphic ventricular tachycardia (VT); a family history of SCD (<45 years old); coved-type ECGs in family members; inducibility of VT with programmed electrical stimulation (PES); syncope; or nocturnal agonal respiration

5. Which is NOT a symptom commonly seen with cardiomyopathies such as HCM and ARVD/C?
- A. Dyspnea
  - B. Palpitations
  - C. Peripheral edema
  - D. Fatigue
  - E. Syncope

Answer: C

Rationale: Structural and functional abnormalities associated with HCM produce a variety of symptoms with the most common being the following: fatigue, dyspnea, chest pain, palpitations, presyncope or syncope. The principle symptoms associated with ARVC are dizziness, palpitations, and syncope. However, as many as 40 percent of persons diagnosed with ARVC are asymptomatic. Peripheral edema is not a common symptom seen with HCM or ARVD/C. It is a common symptom seen with right-sided heart failure. In RV failure, the most common symptoms are ankle swelling and fatigue.

Sometimes patients feel a sensation of fullness in the abdomen or neck. Hepatic congestion can cause right upper quadrant abdominal discomfort, and stomach and intestinal congestion can cause anorexia and abdominal bloating. Less specific HF symptoms include cool peripheries, postural light-headedness, nocturia, and decreased daytime micturition

6. A diagnostic clue that a patient may have ARVD/C is the presence of a late diastolic, low frequency gallop sound resulting from a forceful atrial contraction. This extra heart sound is also known as \_\_\_\_
- A. Wide split S2
  - B. S3
  - C. S4
  - D. Pericardial rub

Answer: C

Rationale: The fourth heart sound is a low-pitched sound coincident with late diastolic filling of the ventricle due to atrial contraction and is the result of vibrations generated within the ventricle. It can be detected occasionally by inspection, commonly by palpation and auscultation, and it can be depicted graphically by phonocardiographic recording. The evaluation of a fourth heart sound arising from the left ventricle is most readily carried out with the patient in the left lateral recumbent position. Inspection and palpation are employed first to identify the apex impulse, where the fourth heart sound is usually most prominent. The third heart sound (S<sub>3</sub>) is a low-frequency, brief vibration occurring in early diastole at the end of the rapid diastolic filling period of the right or left ventricle. Pericardial rub is mostly seen with pericarditis. Pericardial friction rubs are characterized by: One systolic sound and two diastolic sounds (3 component rub) (systolic sound between S<sub>1</sub> and S<sub>2</sub>); One diastolic sound in early diastole and one at end diastole (2 component rub).

7. When people who inherit the mutation for cardiomyopathy don't develop the disease, it is known as
- A. Reduced penetrance
  - B. Recessive inheritance
  - C. Codominance
  - D. Polygenic inheritance

Answer: A

Rationale: Penetrance refers to the proportion of people with a particular genetic change (such as a mutation in a specific gene) who exhibit signs and symptoms of a genetic disorder. If some people with the mutation do not develop features of the disorder, the condition is said to have reduced (or incomplete) penetrance.

8. Which of the following is true regarding HCM and ARVD/C?
- A. LVH with aortic stenosis is a high indicator of the inheritable cardiomyopathies HCM and ARVD/C
  - B. They are sex-linked inherited
  - C. Pregnant women with HCM or ARVD/C do not need care by specialized obstetricians in high-risk pregnancies
  - D. There is no treatment to prevent or delay disease expression

Answer: D

Rationale: There's no treatment to prevent or delay disease expression, only treatment to prevent arrhythmias, syncopal episodes and sudden cardiac death. Mode of inheritance is autosomal dominance, and in rare cases autosomal recessive. Pregnant women SHOULD seek care by specialized obstetricians.

9. Fabry disease
- A. Affects alpha-galactosidase enzyme
  - B. Causes deposits of amyloid protein in the myocardium
  - C. Is an inherited glycogen storage disease
  - D. Is categorized as a pure restrictive cardiomyopathy

Answer: A

Rationale: Fabry disease is an x-linked inborn error. It leads to accumulation of globotriaosylceramide (Gb3) within lysosomes due to deficient activity of alpha-galactosidase. It's characterized by progressive hypertrophy of the cardiac muscle, with increasing interstitial and fibrotic changes. This is consistent with observations of relatively mild diastolic dysfunction in early stages of the disease and with the late appearance of signs and symptoms that might be observed in patients with restrictive cardiomyopathy

10. Which is NOT true regarding ARVD/C?
- A. It's the 2nd most common cause of sudden cardiac death
  - B. It is more common in those younger than 35

- C. Clinical presentation includes arrhythmias, palpitations, chest pain, syncope.
- D. Twelve genes are associated with it

Answer: D

Rationale: ARVD/C is associated with 8 genes: The eight genes in which pathogenic variants are known to cause ARVD/C are *TGFB3*, *RYR2*, *TMEM43*, *DSP*, *PKP2*, *DSG2*, *DSC2*, and *JUP*.

## Chapter 19 – Marfan Syndrome

1. What phenotypic features of Marfan syndrome are responsible for the major cause of morbidity and mortality associated with the syndrome?
  - A. Heart valve defects and weakening of the vessel wall of the aorta
  - B. Ocular disorders and an increased risk for retinal detachment
  - C. Skeletal abnormalities including arachnodactyly and dolichostenomelia
  - D. Pectus excavatum or pectus carinatum

Answer: A

Rationale: Heart valve defects and aortic aneurysms or aortic dissections due to stretching pose the worst threats to an individual with Marfan syndrome. Cardiovascular screening of individuals with Marfan syndrome should be done on a yearly basis and should include annual echocardiograms. Ocular disorders, skeletal abnormalities including arachnodactyly (long and slender fingers and toes in comparison to the palms of hands and soles of feet) and dolichostenomelia (an arm span that is more than the height of the individual) and pectus excavatum and carinatum are all phenotypic features of Marfan syndrome but are not the major cause of morbidity and mortality associated with Marfan syndrome.

2. The heritable form of Marfan syndrome is a result of:
  - A. Autosomal dominant pattern of inheritance on the fibrillin-1 gene on chromosome 15
  - B. Autosomal recessive pattern of inheritance on the fibrillin-1 gene on chromosome 15
  - C. Autosomal dominant pattern of inheritance on the NF1 gene on chromosome 15
  - D. De novo mutation of the fibrillin-1 gene on chromosome 15

Answer: A

Rationale: Marfan syndrome results from either an inherited mutation or a de novo mutation of the fibrillin-1 gene (FBN1) on chromosome 15. De novo mutations are found in people who do not have a positive family history and accounts for an estimated 25% of cases. The heritable form of Marfan syndrome is inherited by an autosomal dominant pattern where only one copy of the mutation is necessary to produce disease. An autosomal recessive pattern of inheritance would require two copies of the mutated gene to produce disease in an individual. The NF1 gene that is responsible for the condition of Neurofibromatosis is not to be confused with the FBN1 gene of Marfan syndrome. Therefore, answer choice A is the correct answer.

3. Marfan syndrome is phenotypically expressed in those with the disease through which of the following?
- A. Complete penetrance
  - B. Variable expressivity
  - C. Digenic inheritance
  - D. Sex-linked inheritance

Answer: B

Rationale: Variable expressivity is variation in disease symptoms among persons with the same mutation. Marfan syndrome has variable expression of symptoms by individual, therefore answer choice B is correct. Affected individuals can have a range of symptoms from mild expression to multiple or severe symptoms. Complete penetrance is observed in cases where the genotype status perfectly predicts the development of disease and can be reliably used for genetic counseling, although the genotype does not predict the age of onset or severity. An example of this is Huntington's disease. Digenic inheritance is an inheritance pattern in which mutations at two distinct loci are required for disease. Many of the diseases with reports of digenic inheritance exhibit classic autosomal recessive inheritance patterns. Sex-linked inheritance describes traits that are inherited on either the X or Y chromosome.

4. The management and treatment of individuals with Marfan syndrome should include:
- A. Cardiovascular surveillance with echocardiograms every 5 years
  - B. Use of a beta blocker to reduce blood pressure
  - C. Regular participation in contact sports, isometric exercises
  - D. Annual eye exams to preserve vision

Answer: D

Rationale: Cardiovascular surveillance with echocardiograms is recommended **annually** and even more frequently if aortic diameter is enlarged. Therefore, answer choice A is incorrect. Recent studies suggest that losartan, an angiotensin receptor blocker, might be helpful in prevention of some manifestations of Marfan syndrome including inhibiting aortic enlargement but this is not seen in other hypertension medication such as beta blockers which makes answer choice B incorrect. Answer choice C is incorrect because it is recommended that individuals with Marfan syndrome **avoid** and **not** participate in contact sports or isometric exercises because of the increased risks placed on the cardiovascular system. Answer choice D is correct. Individuals with Marfan syndrome are susceptible to ocular disorders and this puts them at an increased risk for retinal

detachment, cataracts and glaucoma. With annual eye exams it is hoped that vision can be preserved in Marfan syndrome patients.

5. A parent with Marfan syndrome carries what risk of having an affected child with the syndrome?
- A. 25%
  - B. 50%
  - C. 75%
  - D. 100%

Answer: B

Rationale: Marfan syndrome is inherited in an autosomal dominant pattern in 75% of those affected and 25% of those affected are from random de novo mutations. It is inherited in an autosomal dominant pattern and therefore only one gene is necessary of the FBN1 mutation. Autosomal dominant inheritance is observed by a dominant trait mapping to one of the autosomal (non-sex) chromosomes. An autosomal trait manifests equally in both males and females, and can be transmitted by either parent to approximately 50 percent of their offspring, making answer choice B correct. If an affected parent carries one copy of the gene they have a 50% possibility of passing that gene to their child.

6. Which of the following is criteria is diagnostic of Marfan syndrome?
- A. A family history of Marfan syndrome and pectus carinatum
  - B. A family history of Marfan syndrome and ectopia lentis
  - C. No family history of Marfan syndrome in an individual that meets aortic criterion with a  $Z > \text{or} = 2$  or aortic root dissection
  - D. No family history of Marfan syndrome and a causal FBN1 mutation

Answer: B

Rationale: Marfan syndrome in patients with a family history is diagnosed with by any one of the following criteria:

- Ectopia lentis
- Systemic score  $\geq 7$  points\*

- Aortic criterion (aortic diameter  $Z \geq 2$  above 20 years old,  $Z \geq 3$  below 20 years, or aortic root dissection)

\*Systemic score criteria: A systemic score  $\geq 7$  indicates major systemic involvement.

- Wrist **AND** thumb sign: 3 points (wrist **OR** thumb sign: 1 point)
- Pectus carinatum deformity: 2 (pectus excavatum or chest asymmetry: 1 point)
- Hindfoot deformity: 2 points (plain pes planus: 1 point)
- Pneumothorax: 2 points
- Dural ectasia: 2 points
- Protrusio acetabuli: 2 points
- Reduced upper segment/lower segment ratio **AND** increased arm span/height **AND** no severe scoliosis: 1 point
- Scoliosis or thoracolumbar kyphosis: 1 point
- Reduced elbow extension ( $\leq 170$  degrees with full extension): 1 point
- Facial features (at least three of the following five features: dolichocephaly [reduced cephalic index or head width/length ratio], enophthalmos, downslanting palpebral fissures, malar hypoplasia, retrognathia): 1 point.

- Skin striae: 1 point
- Myopia >3 diopters: 1 point
- Mitral valve prolapse (all types): 1 point

Marfan syndrome diagnosis in a patient without family history includes the following criteria:

- Aortic criterion (aortic diameter  $Z \geq 2$  or aortic root dissection) **and** ectopia lentis
- Aortic criterion (aortic diameter  $Z \geq 2$  or aortic root dissection) **and** a causal FBN1 mutation as defined above
- Aortic criterion (aortic diameter  $Z \geq 2$  or aortic root dissection) **and** a systemic score  $\geq 7$
- Ectopia lentis **and** a causal FBN1 mutation as defined above that has been identified in an individual with aortic aneurysm

7. Pregnancy requires special surveillance due to increased risk of what conditions in those with Marfan syndrome?
- A. Mitral valve prolapse
  - B. Scoliosis
  - C. Aortic dissection and rupture
  - D. Pneumothorax

Answer: C

Rationale: Although all of the answer choices are manifestations and pose risks to individuals with Marfan syndrome, **during pregnancy individuals are at an increased**

**risk of aortic dissection (answer choice C).** Answer choice A, Mitral valve prolapse is one of the leading causes of morbidity and mortality in affected individuals but is not the cause of increased surveillance during pregnancy. Answer choice B, scoliosis is a skeletal abnormality seen in Marfan syndrome that does not require special surveillance during pregnancy. Individuals with Marfan syndrome are at an increased risk for answer choice D, pneumothorax. They may experience spontaneous pneumothorax and are also advised not to scuba dive or breath against resistance which would exclude playing brass instruments.

8. Which of the following hobbies would be the best option for an individual with Marfan syndrome?
- A. Playing the trumpet
  - B. Scuba diving
  - C. Weight lifting
  - D. Playing the violin

Answer: D

Rationale: Answer choice D is the best option for an individual with Marfan syndrome. Playing a trumpet (answer choice A) is advised against due to possible pneumothorax because of the necessity of breathing against resistance. Answer choice B, scuba diving, is also advised against due to negative-pressure ventilation and associated increased risk of pneumothorax from barotrauma. Weight lifting (answer choice C) is an isometric exercise that is also cautioned against because of Valsava maneuver that can be associated with such exercises.

9. Which phenotypic features are consistent with Marfan syndrome?
- A. Epicanthic folds, Brushfield spots, flat facial profile, transverse palmar crease
  - B. Skin hyperextensibility, joint hypermobility, thoracolumbar scoliosis
  - C. Tall stature, arachnodactyly, elongated facies, scoliosis, pectus carinatum
  - D. Cleft palate, polydactyly, micro/anophthalmia

Answer: C

Rationale: Answer choice C is correct as it describes phenotypic features often seen in an individual with Marfan syndrome diagnosis. Answer choice A is incorrect because it describes phenotypic features of trisomy 21, Down's syndrome. Answer choice B is incorrect because it describes phenotypic features of an individual with Ehlers-Danlos syndrome. Answer choice D is incorrect because it describes phenotypic features of an individual with trisomy 13, Patau syndrome

10. Which of the following diagnostic criteria is true in individuals <20 years old with features of Marfan syndrome but do not meet diagnostic criteria?
- A. No additional clinical features will emerge after the age of 20 and therefore they should be considered as not having Marfan syndrome
  - B. If they have systemic findings that are consistent with Marfan syndrome but do not have cardiovascular involvement they should have annual echocardiograms due to potential risk of aortic disease
  - C. They should be considered to have Marfan syndrome if an FBN1 mutation is identified regardless of not being diagnosed by criteria
  - D. They should not have any further work-up or considerations and do not need to take any special precautions

Answer: B

Rationale: Additional clinical features may emerge in individuals under the age of 20. Therefore, special considerations to diagnostic criteria should be taken in trying to diagnose an individual who is under the age of 20. This makes answer choice A incorrect since it is important that features may emerge after the age of 20 and those who may not meet diagnostic criteria but do have some features should still be followed for emerging signs of the syndrome past the age of 20. Answer choice B is correct. It explains that although an individual does not have cardiovascular involvement at that particular time, they are still susceptible to involvement if they have Marfan syndrome. Answer choice C is incorrect because an FBN1 mutation alone is not diagnostic. Answer choice D is also incorrect because although someone does not meet diagnostic criteria at a particular point in time they may do so later and especially if there is familial history.

## Chapter 20 – Polycystic Kidney Disease

1. The majority of Polycystic kidney disease (PCKD) patients have what kind of genetic defect?
  - A. PKD3
  - B. PKD1
  - C. PKD2
  - D. PKD4

Answer: B

Rationale: 80 to 90% have the PKD1 genetic defect which encodes for the membrane protein polycystin-1.

2. A 30-year-old African American male patient is being evaluated for the possible diagnosis of Polycystic kidney disease. What are the most common renal sequelae associated with the disease?
  - A. Hypertension, fever, flank pain
  - B. Hematuria, renal insufficiency, palpable mass
  - C. Hypertension, flank pain, renal insufficiency
  - D. Renal insufficiency, hematuria, palpable mass

Answer: C

Rationale: Hypertension, flank pain, and renal insufficiency are the most common renal sequelae.

3. The most common cause of mortality in those with polycystic kidney disease is which one of the following?
  - A. Cardiovascular disease
  - B. Renal disease
  - C. Pulmonary complications
  - D. Infection

Answer: A

Rationale: Hypertension is the most common early manifestation. Long standing hypertension can lead to glomerular damage, kidney failure, aneurysms, cardiac valve disease and complications in pregnancy.

4. Patients with polycystic kidney disease have an increased risk of kidney stones. Most common calculi found in Autosomal dominant polycystic kidney disease (ADPKD) patients are what type?
- A. Uric Acid
  - B. Struvite
  - C. Cystine
  - D. Calcium Phosphate

Answer: A

Rationale: Most calculi in patients with ADPKD consist of uric acid with or without calcium oxalate, most likely due to decreased excretion of ammonia, acidic urinary pH, and decreased citrate concentration.

5. An ADPKD patient was concerned about the extra-renal manifestations that presents with polycystic kidney disease. Choose which is not one of the common extra-renal manifestations found in this disease.
- A. Liver
  - B. Pancreas
  - C. Seminal vesicles
  - D. Lungs

Answer: D

Rationale: Extra-renal manifestations may arise related to the liver, pancreas, seminal vesicles, arachnoid membrane, and spinal meninges.

6. What is the most common valvular disorder seen in 25% of affected individuals with Autosomal dominant polycystic kidney disease (ADPKD)?
- A. Aortic Stenosis
  - B. Mitral Valve Prolapse
  - C. Mitral Stenosis
  - D. Tricuspid Regurgitation

Answer: B

Rationale: The most common valvular disorder is mitral valve prolapse, which is observed in 25% of affected individuals.

7. By what means is the diagnosis of PCKD confirmed?
- A. Computed tomography (CT)
  - B. Magnetic Resonance (MRI)
  - C. Abdominal ultrasound
  - D. Molecular genetic testing

Answer: D

Rationale: Even though imaging is an invaluable tool, diagnosis of PCKD is confirmed by molecular genetic testing.

8. Which one of the following is not what makes ARPKD distinguishable from ADPKD?
- A. They have different gross configurations
  - B. They both have distinct microscopic pathology
  - C. ARPKD have other mutations besides PKD1 and PKD2
  - D. ARPKD patients do not have affected parents

Answer: C

Rationale: Autosomal recessive polycystic kidney disease is associated with bilateral renal cysts that have a different gross configuration as well as a distinct microscopic pathology from those observed in the autosomal dominant variant. Those persons affected with ARPKD do not have affected parents. Collectively, these features make ARPKD distinguishable from ADPKD.

9. What is the most common potentially lethal single-gene disorder in the United States?
- A. Autosomal dominant PCKD
  - B. Autosomal recessive PCKD
  - C. X-linked PCKD
  - D. Mitochondrial PCKD

Answer: A

Rationale: Inheritance of PCKD most commonly follows an autosomal dominant pattern, in which it is known as autosomal dominant polycystic kidney disease (ADPKD). This variant is the most common potentially lethal single-gene disorder in the United States, with a prevalence of 1 case in every 500 people.

10. Routine evaluation after initial diagnosis of PCKD includes all of the following except?
- A. Monitoring blood pressure
  - B. Evaluating renal function and structure
  - C. Monitoring lung function
  - D. Evaluating liver structure and blood lipids

Answer: C

Rationale: Routine evaluation after initial diagnosis of PCKD includes monitoring blood pressure, evaluating renal function and structure, evaluating liver structure, evaluating blood lipids, and screening for valvular and aortic disease.

## Chapter 21 – Rheumatologic Disorders

1. A pediatric patient with rhizomelia, macroencephaly, normal IQ, a flat nasal bridge and frontal bossing is diagnosed with achondrodysplasia. At what age will this patient's height fall to <5<sup>th</sup> percentile on the growth curve?
  - A. 4
  - B. 5
  - C. 6
  - D. 7

Answer: B

Rationale: *"These children are on the growth curve at birth, but by 5 months of age, their length has fallen to < 5th percentile. Note that children with achondroplasia have normal intellect and cognition."* (Genetics, Chapter 23- Rheumatologic Diseases, page 2, paragraph 4)

2. What is NOT considered Type I collagen
  - A. Skin
  - B. Bone
  - C. Sclera
  - D. Cornea

Answer: D

Rationale: "Type I collagen, which is responsible for skin, tendon, ligament, bone and sclera formation." (Genetics, Chapter 23- Rheumatologic Diseases, page 3, paragraph 2. Type II collagen is abundantly present in cartilage and vitreous humor of the cornea (Bacino, 2016). Therefore answer D is the only choice not created by Type I collagen and is the correct answer choice for the question.

3. An 8 year old Caucasian male presents to your office with complaints of bilateral upper arm pain x 1 month. The pain denies any recent trauma to the area. He states that the achy, localized pain is a 6/10 and is worse in the mornings. His mother has tried Ibuprofen to alleviate some symptoms but the pain often returns. There is no FHx of bone cancers. No signs of child neglect or abuse. Upon examination there is point tenderness along each humerus but no swelling or ecchymosis. The patient has full ROM and 4/5 strength

bilaterally in his upper extremities. X-ray reveals opacity and multiple hairline fractures in the humerus. The patient is referred to a rheumatologist. If this patient is found to have a mutation in the LRP5 gene, what region of the humerus would you expect the hairline fractures to be located?

- A. Epiphysis
- B. Epiphyseal Plate
- C. Metaphysis
- D. Diaphysis

Answer: C

Rationale: Patients with juvenile primary osteoporosis typically see fractures along the long bones of the arms and legs, especially where the new bone forms, so you would expect hairline fractures to be located in the metaphysis.

4. A 77 year old Black male presents to your office with hearing loss, headache, neck pain and bowing of the legs. He recalls that his late uncle had similar symptoms and was diagnosed with a bone disease late in his life but cannot recall the name. What is the most common cause of this patient's disease?
- A. TNFRSF11A mutation
  - B. SQSTM1 mutation
  - C. Measles virus
  - D. TREX1 mutation

Answer: B

Rationale: "Mutations in the SQSTM1 gene are the most common genetic cause of classic Paget disease of bone, accounting for 10 to 50 percent of familial cases and 5 to 30 percent of sporadic cases. Variations in the TNFRSF11B gene also appear to increase the risk of the classic form of the disorder, particularly in women. TNFRSF11A mutations cause the early-onset form of PDB. (Genetics, Chapter 23- Rheumatologic Diseases, page 4, paragraph 6). There is no single gene polymorphism that creates high risk for SLE, except for the rare TREX1 mutation or deficiencies of early components of complement (C1q, C2, C4). (Genetics, Chapter 23- Rheumatologic Diseases, page 7, paragraph 3). Therefore, answer B is the correct answer.

5. In addition to the classic "salt and pepper" appearance on x-ray of the skull, what other lab value is needed to diagnose Paget's Disease of the Bone?
- A. Elevated serum alkaline phosphatase
  - B. Low serum alkaline phosphatase

- C. Elevated serum calcium
- D. Low serum calcium

Answer: A

Rationale: “The diagnosis of PDB is made by finding an elevated serum alkaline phosphatase and characteristic radiographic findings. The classic “salt and pepper” appearance on plain radiographs is consistent with the osteoblast (salt) and osteoclast (pepper) dysregulation of bone.” (Genetics, Chapter 23- Rheumatologic Diseases, page 5, paragraph 1)

6. What is an effective first line treatment for a patient just diagnosed with Paget’s Disease of the Bone?
- A. DMARDs
  - B. Vitamin D
  - C. Calcitonin
  - D. NSAIDs

Answer: C

Rationale: Amino-biphosphonates and calcitonin are the most effective first-line treatments for patients just diagnosed with Paget’s disease of the bone.

7. A 69-year-old Hispanic female presents to the orthopedic clinic with bilateral osteoarthritic knee pain x 2 months. The patient states that the pain is worse when she is walking upstairs or standing up from her couch. In the past she has tried Tylenol and Cortisone injections to alleviate the pain but now she cannot find any relief. Plain film x-rays show the proximal tibia to be denser and more ivory than the rest of the bones. What is the name of this finding?
- A. Osteophytes
  - B. Eburnation
  - C. Subchondral cysts
  - D. Sclerosis

Answer: B

Rationale: The phenomenon known as eburnation is characterized not only by dense bone at the articular surface, but also by marked sclerosis of the subchondral cancellous bone and an ivory appearance of the epiphysis. Therefore, answer B is correct.

8. A 41-year-old Caucasian female presents to the office with a recent 10-pound weight loss, fatigue, and dry mouth. Upon further examination, the provider discovers that the patient has a low-grade fever and redness along the MCP joints bilaterally. When asked about joint pain, the patient reports that her PIP, MCP, and shoulders hurt bilaterally for about 2 hours each morning. What lab test should the provider order on this patient to make the diagnosis of Rheumatoid Arthritis?
- A. Antinuclear antibodies
  - B. anti-cyclic citrullinated peptide antibodies
  - C. rheumatoid factor antibodies
  - D. double stranded DNA antibodies

Answer: B

Rationale: ANA is non-specific for Rheumatoid Arthritis, a positive ANA helps diagnose patients with systemic lupus erythematosus and other autoimmune diseases (Bloch, 2016). RF is moderately specific for Rheumatoid Arthritis, but it may also indicate a diagnosis of systemic lupus erythematosus and primary Sjögren's syndrome. Anti-dsDNA and anti-ssDNA are highly specific for the diagnosis of SLE, not Rheumatoid Arthritis. Therefore, answer B is correct.

9. How long must a patient under 16 years of age have persistent synovitis in 1 or more joints to be diagnosed with Juvenile Idiopathic Arthritis?
- A. 4 weeks
  - B. 6 weeks
  - C. 6 months
  - D. 1 year

Answer: C

Rationale: A patient under 16 years of age must have persistent synovitis in 1 or more joints for at least 6 weeks or more to lead to a diagnosis of juvenile idiopathic arthritis.

10. What medication has been recognized to trigger Systemic Lupus Erythematosus?
- A. Methotrexate (Trexall)
  - B. Hydralazine (Apresoline)
  - C. Azathioprine (Imuran)
  - D. Hydroxychloroquine (Plaquenil)

Answer: B

Rationale: Hydralazine is among one of many triggers of lupus, alongside stress, hormonal therapies, sunlight and antecedent infections.

## Chapter 22 – Neurofibromatosis

1. A young adult client diagnosed with neurofibromatosis asks if the disorder is cancer. How should you respond to the client?
  - a. “No, it is a benign encapsulated tumor caused by a specific type of cell.”
  - b. “Unfortunately yes. Neurofibromatosis always produces cancerous tumors.”
  - c. “It depends on what the tissue sample reveals after the biopsy of the mass.”
  - d. “It may or may not be cancerous and depends upon how the tumor responds to treatment.”

Answer: A

Rationale: A neurofibroma is defined as a benign, encapsulated tumor resulting from proliferation of Schwann cells that are of ectodermal (neural crest) origin and that form a continuous envelope around each nerve fiber of peripheral nerves. The tumors are not cancerous. Determining if the tumor is cancerous is not dependent on the results of a biopsy or the response of the tumor to treatment.

2. The parent of a preschool-age child is upset because the child is developing brown spots over the lower legs. Which should you explain to the parent about this finding?
  - a. “These spots are harmless and should not cause any concern.”
  - b. “These are called café-au-lait spots. They are an indication of type 1 neurofibromatosis (NF-1).”
  - c. “These spots indicate an underlying bone cancer and must be biopsied immediately.”
  - d. “These spots indicate type 2 NF and indicate that a change in hearing will occur in a few years.”

Answer: B

Rationale: Type 1 NF manifests as tumors of the subcutaneous tissues and hyperpigmented skin lesions known as café-au-lait spots. The spots are not harmless and need to be identified. The spots do not indicate an underlying bone cancer. NF type 2 is characterized by the development of noncancerous tumors called schwannomas on the auditory and vestibular nerves that control hearing and balance. Although the tumors usually develop in late adolescence, some people do not develop problems until they are in their 40s and 50s.

3. You are concerned that a young adult client has underdiagnosed neurofibromatosis type 2. What did you assess to make this clinical decision?
  - a. Severe itching
  - b. Muscle wasting
  - c. High blood pressure
  - d. Freckles under the armpits

Answer: B

Rationale: Muscle wasting is a manifestation of NF type 2. Severe itching, high blood pressure, and freckles where the skin meet skin as under the arms are all manifestations of NF type 1.

4. Genetic testing shows the parents of a child with neurofibromatosis type 1 have no genetic evidence of the disorder. What should you say when the parents ask if any other future offspring will have the same disorder?
- “Unfortunately, all offspring will have the disorder.”
  - “There is a 50/50 chance that future offspring will have the disorder.”
  - “The disorder can be stopped if specific lifestyle actions are taken now.”
  - “Since neither of you are effected, the mutation occurred in utero and cannot be passed on to other offspring.”

Answer: D

Rationale: Approximately 50% of those affected by NF type 1 have a family history of the disorder. The other 50% appear to be the first members of their family to have the disorder. Should this occur, one parent either has the disorder but has mild symptoms or the disorder was caused by a mutation in the sperm or egg and will not pass it to other children. Since the parents were both tested as not having evidence of the disorder, these parents cannot pass the disorder to other offspring. All offspring will not have the disorder. There is not a 50/50 chance of offspring having the disorder. The disorder cannot be stopped by lifestyle actions.

5. A young adult diagnosed with neurofibromatosis type 2 asks what causes the disorder. What should you say in response?
- “The gene that suppresses tumors malfunctions after puberty.”
  - “The gene on chromosome 22 causes the formation of tumors.”
  - “There is no known reason for the development of the disorder.”
  - “The gene that suppresses the formation of tumors malfunctioned.”

Answer: B

Rationale: Type 2 NF is characterized by autosomal dominant inheritance and is caused by mutation in the NF-2 gene on chromosome 22 that encodes for merlin. Because merlin is also a tumor suppressor gene, the NF-related mutation disrupts this activity and leads to the formation of schwannomas. The gene that causes NF type2 causes tumor development in late adolescence and early adulthood. The disorder is caused by a mutation in the NF-2 gene on chromosome 22. NF type 1 is caused by a mutation in the NF-1 gene located on chromosome 17 that encodes for neurofibromin. The normal NF-1 gene is a tumor-suppressor gene that probably suppresses activity of the ras protein following stimulation by nerve growth factor or other agents. Loss of tumor suppression due to NF-1 mutation presumably permits uncontrolled ras activation, which leads to the formation of neurofibromas.

6. A school-age child has 2 café-au-lait spots that measure 0.6 cm in size located on the inner thigh. Which action should be taken in order to diagnose this client with neurofibromatosis (NF) type 2?
- Biopsy the areas
  - Reexamine the child in a year
  - Schedule for an immediate eye examination
  - Collect a skin scraping to have a chromosome analysis completed

Answer: B

Rationale: The presence of multiple café-au-lait spots strongly suggests, but does not prove, the diagnosis of NF-1. Because many features associated with NF-1 may not appear until late childhood or adolescence, it is often impossible to make a definitive diagnosis of NF-1 in a young child whose only manifestations are multiple café-au-lait spots. Even if the child is affected, it could take years before another feature of the disorder appears and confirms the diagnosis. Because of this, healthcare providers should reexamine these children for the appearance of new features on an annual basis. The areas are not biopsied. An immediate eye examination is not required for this form of NF. Skin scrapings are not collected for NF to have a chromosome analysis completed.

7. You are completing a physical assessment of a prepubescent client. For which reason should you mention the need for testing for neurofibromatosis type 1 (NF-1) with the healthcare provider?
- Bilateral hearing loss
  - Cataract development in the left eye
  - Hypertrichosis noted on the forearm above the elbow
  - Freckles along the bridge and nose, extending onto both cheeks

Answer: C

Rationale: One manifestation of NF-1 is hypertrichosis which is the growth of hair in excess of the normal. Bilateral hearing loss and cataract development in one eye are both manifestations of NF-2. Superficial freckles along the nose and cheeks are not manifestations of either type of NF.

8. The parents of a child with neurofibromatosis type 1 (NF-1) learn about the disorder. Which statement indicates that you need to provide more teaching to the parents?
- "There is no cure for the disorder."
  - "The spots can be removed which cures the disorder."
  - "The disorder is managed by detecting problems as they occur."
  - "Our child should be examined every year to check for problems."

Answer: B

Rationale: Because there is no cure for NF-1 or any medical or surgical treatment that

can reverse or prevent most related complications, medical management of NF-1 is limited to early detection of treatable complications. The café-au-lait spots cannot be removed in efforts to cure the disorder. The child should be examined annually to assess for new symptoms in order to implement early management.

9. A young adult client is demonstrating signs of neurofibromatosis type 2 (NF-2). Which diagnostic test should you anticipate being scheduled for this client?
- a. Spinal tap
  - b. Myelogram
  - c. MRI of the head
  - d. Cerebral angiogram

Answer: C

Rationale: In clients suspected of having NF-2, an MRI of the head is recommended in early adolescence. The value of such a scan in the absence of signs or symptoms of neurological impairment is not as clear, however, and different medical providers may make different recommendations. A spinal tap, myelogram, or cerebral angiogram are not identified as diagnostic tests for NF-2.

10. A client with neurofibromatosis type 1 (NF-1) is upset about having Lisch nodules. What should you explain about this finding?
- a. "They do not interfere with vision."
  - b. "You will need surgery to remove these nodules."
  - c. "They have no impact on the bones around your eyes."
  - d. "They have no effect on the development of an optic glioma on the future."

Answer: A

Rationale: The presence of Lisch nodules can help in establishing a diagnosis of NF-1. These nodules are not medically significant and do not interfere with vision, but complications relating to optic glioma or problems with the bones of the orbit may occur in people with NF-1. The client does not need surgery to remove the nodules.

## Chapter 23 – Familial Malignant Melanoma

1. Which statement about Malignant Melanoma is true?
  - A. MM occurs in Caucasian and Hispanic populations, but not African Americans
  - B. MM is the most common cancer among women between the ages of 25 through 29
  - C. The lifetime risk of MM has decreased
  - D. Sporadic MM is more aggressive than Familial MM

Answer: B

Rationale: Malignant Melanoma remains the most common cancer among women between the ages of 25 and 29, making B the correct answer. The lifetime risk of Malignant Melanoma has increased, the incidence rate of Malignant Melanoma among African Americans is 1 in 1,000, and Familial Malignant Melanoma is more aggressive than Sporadic Malignant Melanoma, most likely due to higher gene penetrance.

2. Which lesion is a well-documented (commonly seen) precursor to familial patterns of Malignant Melanoma?
  - A. Actinic Keratosis
  - B. Basal Cell Carcinoma
  - C. Atypical Nevi
  - D. Blue Nevi

Answer: C

Rationale: Most studies concur that AMS and DNS are associated with FAMMM syndrome and present in almost 15% of the general population.

3. A finding of how many nevi, and how many dysplastic nevi is significantly associated with family history of Malignant Melanoma?
  - A. >50 nevi, >5 dysplastic nevi
  - B. >80 nevi, >3 dysplastic nevi
  - C. >100 nevi, >6 dysplastic nevi
  - D. >120 nevi, >10 dysplastic nevi

Answer: C

Rationale: A finding of more than 100 nevi or six or more dysplastic nevi is significantly associated with a family history of MM.

4. Which statement is NOT true about family history as it relates to MM?
- A. Risk assessment by family history is the most reliable indicator of risk of MM
  - B. Patient with more than 2 family members with MM are more likely to develop MM themselves.
  - C. The greatest familial risk indicator is a parent affected by multiple primary melanomas
  - D. Familial melanoma is the most common form of Malignant Melanoma

Answer: D

Rationale: Sporadic MM is far more common (80%) than Familial MM (20%).

5. What is preferred method of biopsy for a suspected MM lesion?
- A. Shave biopsy
  - B. Cryotherapy
  - C. Punch biopsy
  - D. Excisional biopsy

Answer: D

Rationale: Excision biopsy is the recommended method for suspected malignant melanoma as it enables diagnosis, staging of the tumor, and determines future investigation, treatment, and prognosis. Other methods of biopsy, such as punch and shave, are not recommended as they do not allow complete histological staging.

6. What diameter size is suspicious for MM?
- A. >2 mm
  - B. >10 mm
  - C. >13 mm
  - D. >6 mm

Answer: D

Rationale: A diameter size of 6mm or greater is suspicious for MM, as indicated by the ABCDE Rule.

7. What are the approaches used in the initial staging of MM?
- A. Wide local excision, lymph node mapping, various imaging studies and laboratory assays
  - B. Punch biopsy, sentinel node biopsy, PET scan
  - C. MOHS surgery, removal of all lymph nodes in the area, genetic testing
  - D. Narrow local excision, lymph node mapping, various imaging studies and laboratory assays

Answer: A

Rationale: Approaches used in staging include wide local excision, lymph node mapping, various imaging studies, and laboratory assays. Other methods of biopsy, such as punch and shave, are not recommended as they do not allow complete histological staging.

8. Using the Clark scale, which level is used to classify MM that has spread into the subcutaneous tissue?
- A. I
  - B. II
  - C. IV
  - D. V

Answer: D

Rationale: Clark's levels are used to classify thin tumors in terms of how deep the cancer has spread into the skin. Tumors may be confined to the epidermis (Clark's level I), spread into different depths of the dermis (Clark's levels II, III, and IV), or spread into subcutaneous tissue (Clark's level V).

9. Which diagnostic test is used to detect smaller tumors all over the body that are not identifiable through other imaging studies?
- A. CT
  - B. PET
  - C. MRI
  - D. CXR

Answer: B

Rationale: The detection of smaller metastases requires a full-body positron emission tomography (PET) scan. This imaging procedure detects glucose uptake by cancer cells—such cells have a faster metabolic rate than noncancerous cells. It should be noted that PET scans are able to detect smaller tumors (micrometastases) that are not identifiable through other imaging studies, so B is the correct answer.

10. What is the first stage of MM where should you consider sentinel lymph node biopsy?
- A. I
  - B. II
  - C. III
  - D. IV

Answer: B

Rationale: Standard treatment of stage II melanoma comprises wide excision of skin around the tumor site. Sentinel lymph node biopsy is optional at this stage because deeper tumors have an increased risk of spreading to a lymph node. Treatment of stage I melanoma involves surgical removal of both the lesion and a margin of unaffected skin. The amount of unaffected skin removed depends on the thickness of the melanoma. No more than 2 cm of normal skin needs to be removed from all sides of stage I melanoma, as wider margins have not been found to improve overall survival. Stage III melanoma requires the same surgical treatment of the primary lesion as accorded to stage II melanoma, along with lymph node dissection. Stage IV melanoma has a very poor prognosis, given that melanoma cells have spread to distant areas of the body at this stage. Surgery may be performed to debulk the tumors and relieve symptoms depending on the location. Metastases that cannot be removed may be treated with regional radiation or adjuvant chemotherapy.

## Chapter 24 – Behavioral Medicine

1. During an interview with a 22-year-old male, he begins to share that over the last 2 weeks, he has felt that he has minimal feelings of happiness in his life; he is having trouble getting out of bed and there have been some days when he can't get out of bed to go to school. He states that he is not hungry anymore and all he does is sleep, though he's always tired and becomes easily angered. Based on this clients' description of symptoms, which of the following conditions would you further your assessment on?
  - A. Major depression disorder
  - B. Generalized anxiety disorder
  - C. Bipolar II disorder
  - D. Schizophrenia

Answer: A

Rationale: Defined by the Diagnosis and Statistical Manuel of Mental Disorders (DSM-5)m having five or more depressive symptoms during a 2-week period that represent a change in previous functioning. A depressive episode must include either depressed mood or anhedonia (loss of interest of pleasure). A depressive episode must include at least four of the following symptoms: Significant weight loss when not dieting, or weight gain (>5% total body weight in 1 month), or significant changes in appetite; Insomnia or hypersomnia every night; Psychomotor agitation or retardation (observable by others); Fatigue/loss of energy; Feelings of worthlessness or inappropriate/excessive guilt; Diminished ability to think/concentrate, or indecisiveness or Recurrent thoughts of death or suicide, suicidal ideation, or suicide attempt/planning.

2. When assessing a patient who states that for the last 6 months they have difficulty controlling their feelings of worrying, are easily fatigued with difficulty concentrating, poor sleep and highly irritable. The patient states that these episodes occur during various normal activities of daily living; denies any substance abuse; taking any prescribed medications or having been diagnosed with psychiatric disorder. The health care provider should consider treating this individual for which of the following conditions?
  - A. Hypomania
  - B. Bipolar I
  - C. Generalized anxiety disorder
  - D. Substance abuse

Answer: C

Rationale: As defined by the DMS-5, having excessive anxiety/worry on more days than not for at least 6 months, often about multiple events or activities. The patient will have difficulty controlling this worry, often about multiple events or activities, causing significant clinical distress or impairment. Symptoms present more often than not for at least 6 months and three or more must be present [restlessness/feeling on edge; being easily fatigued; difficulty concentrating or mind going blank; irritability; muscle tension or sleep disturbance.

3. The DSM-5 diagnostic criteria for a manic episode can include three of any of the following symptoms, except:
- A. Distractibility
  - B. Increase in goal-directed activity and/or psychomotor agitation
  - C. Increased need for sleep
  - D. Inflated self-esteem/grandiosity

Answer: C

Rationale: Distractibility, increased in goal-directed activity and/or psychomotor agitation and inflated self-esteem/grandiosity are all symptoms that can present in a manic episode. Decreased, not increased, need for sleep can also present in manic episodes.

4. Which of the following criteria does not apply when diagnosing a substance abuse disorder, provided the substance is being used under medical supervision?
- A. Tolerance for the substance
  - B. Craving/strong desire for the substance
  - C. Using the substance to avoid withdrawal
  - D. A + C

Answer: D

Rationale: When a substance is being used by a patient under medical supervision, tolerance for the substance and using the substance to avoid withdrawal cannot be used as criteria to indicate substance abuse disorder.

5. All of the following genes have been found to be associated with alcohol abuse, except:
- A. ALDH2

- B. DDC
- C. DRD4
- D. MADA

Answer: B

Rationale: DDC has not been found to be involved in alcohol abuse hereditarily.

6. Although generalized anxiety disorder has the smallest overlap in terms of affected genes and substance abuse, the three implicated genes involved are associated with what kind of substance abuse:
- A. Opiate abuse
  - B. Alcohol abuse
  - C. Cocaine abuse
  - D. Nicotine abuse

Answer: A

Rationale: For generalized anxiety disorder, all three implicated genes for susceptibility to substance abuse are associated with opiate abuse. This may be due to the calming tendencies of opiates.

7. All of these genes, all associated with major mood disorders, are only implicated in major depression, except:
- A. GRIK1
  - B. NTRK2
  - C. VMAT2
  - D. HTR2B

Answer: C

Rationale: VMAT2 can be implicated in either major depression or bipolar disorder.

8. Because patients with major mood disorders are at high risk for developing substance abuse disorders, what steps should be taken to monitor these patients?
- A. Ensure proper screening for preexisting substance abuse conditions or history
  - B. Be diligent when prescribing highly addictive substances
  - C. Educate these patients on their risks for developing substance abuse disorders

D. All of the above

Answer: D

Rationale: All of these steps are essential for monitoring these patients, and care providers should follow them closely to make sure they do not develop a concurrent substance abuse disorder.

9. Major mood disorders affect what segment of the American population?
- A. Between 10% and 30%
  - B. Between 30% and 60%
  - C. Between 40% and 70%
  - D. Between 20% and 50%

Answer: B

Rationale: Between 30% and 60% of all Americans are affected by major mood disorders.

10. True or false: The pathways implicated in both substance abuse and major mood disorders predominantly involve the serotonin and dopamine pathways in the brain.

Answer: True

## Chapter 25 – Pharmacogenomics

1. You are aware of a research study being conducted in your organization where genetic testing is being completed on each client before medications are prescribed. What should you expect the results of this testing to accomplish?
  - a. Multiple uses for the same medication
  - b. Reduced cost to manufacture medications
  - c. Less use of medications to treat health problems
  - d. More accurate methods of determining drug dosages

Answer: D

Rationale: One benefit of pharmacogenomics is a more accurate method of determining drug dosages. Pharmacogenomics is not used to identify multiple uses for the same medication, reduce the cost to manufacture medications, or reduce the use of medications to treat health problems.

2. Through genetic testing, a client learns of having a natural variation in a chromosome and gene. How should this finding affect the client's metabolism of medications?
  - a. It will have no effect.
  - b. Most medications will be metabolized as intended.
  - c. There is a limited number of medications that the client can metabolize.
  - d. The metabolism of medications will depend upon enzymes, transporters, or targets.

Answer: D

Rationale: The client has a polymorphism, which is a natural variation in a gene, DNA sequence, or chromosome that has no adverse effects on the person but will cause differences in drug response because of the genes encoding drug-metabolizing enzymes, drug transporters, or drug targets. The polymorphism will affect drug metabolism. There is no way to predict that medications will be metabolized as intended or the number of medications that the client can metabolize is limited.

3. A client with the CYP gene is identified as being a poor metabolizer. What dose should you expect when a cardiovascular drug is prescribed for this client?
  - a. The usual dose
  - b. Lower than normal
  - c. Higher than normal
  - d. Three times the normal dose

Answer: B

Rationale: The CYP enzymes include approximately 57 liver enzymes that metabolize more than 30 classes of drugs, including antidepressants, antiepileptics, and cardiovascular drugs. Based on variations in the associated CYP gene, clients can be

separated into poor, normal, and ultrarapid drug metabolizers. When a client who is a poor metabolizer of a particular drug is given a standard dose, the drug will be processed more slowly than expected, resulting in increased levels of the drug in the person's bloodstream. This can increase the risk for side effects and toxicity. The usual dose may cause side effects and toxicity. A higher than normal dose or a dose that is three times the normal dose will definitely cause side effects and toxicity.

4. A client taking isoniazid as part of treatment for tuberculosis is not demonstrating any improvement in the infection. What should you suspect is occurring with this client?
- The client is deficient in the TPMT enzyme.
  - The client is a slow accelerator because of the CYP gene.
  - The client is a fast accelerator because of N-acetyltransferase.
  - The client is lacking the enzyme UDP-glucuronosyltransferase.

Answer: C

Rationale: N-acetyltransferase is a liver enzyme that activates some drugs and deactivates others. A client who is a fast accelerator of this enzyme may not respond to isoniazid. The TPMT enzyme is used to metabolize azathioprine and other thiopurine medications. The CYP gene plays a role in the metabolism of antidepressants, antiepileptics, and cardiovascular drugs. UDP-glucuronosyltransferase is involved in the metabolism of irinotecan.

5. A client is prescribed a thiopurine medication to treat inflammatory bowel disease. Which laboratory value should indicate to you that the client has sufficient TPMT to metabolize this medication?
- Low platelet count
  - Elevated platelet count
  - Low red blood cell count
  - Normal red blood cell count

Answer: D

Rationale: A client who has low or limited amounts of TPMT to metabolize a thiopurine medication will demonstrate severe hematopoietic toxicity which affects red blood cell and platelet levels. The client with sufficient TPMP will not demonstrate hematopoietic toxicity and will have a normal red blood cell count.

6. A client is receiving irinotecan as treatment for metastatic colorectal cancer. Which symptom should indicate to you that the client has a UDP- glucuronosyltransferase deficiency?
- Muscle cramps
  - Severe diarrhea
  - Rapid respirations
  - Low blood pressure

Answer: B

Rationale: UDP-glucuronosyltransferase is involved in the metabolism of irinotecan, a chemotherapeutic drug that is used in the treatment of metastatic colorectal cancer. Variations in the gene that codes for this enzyme can influence the client's ability to break down the major active metabolite in irinotecan. The inability to degrade the metabolite can lead to increased blood concentrations and increased risk of experiencing severe diarrhea. Muscle cramps, rapid respirations, and low blood pressure are not symptoms that indicate a deficiency of UDP-glucuronosyltransferase.

7. A client needs to be prescribed warfarin. Which gene helps determine the dose and effectiveness of this medication?
- CYP2C9
  - CYP2D6
  - UGT1A1
  - CYP2C19

Answer: A

Rationale: The CYP2C9 genotype has been shown to incrementally improve prediction of warfarin dose maintenance. More than 30 medications are metabolized by CYP2D6, including analgesics, antidepressants, and antiemetics. The UGT1A1 gene produces the enzyme UDP-glucuronosyltransferase. CYP2C19 is not identified as impacting the metabolism of warfarin.

8. A client is deficient in the CYP2D6 enzyme. Which medication classification should you question before giving to this client?
- Antibiotic
  - Antiemetic
  - Antiepileptic
  - Antihypertensive

Answer: B

Rationale: More than 30 medications are metabolized by the CYP2D6 enzyme, including analgesics, antidepressants, and antiemetics. Antibiotics, antiepileptics, and antihypertensives are not medications that need the enzyme CYP2D6 for metabolism.

9. A client is found to have an increased level of the VKORC1 enzyme. How should you expect the client's dose of warfarin to be affected?
- No effect
  - Need a lower dose
  - Need a higher dose
  - Need to identify a different anticoagulant

Answer: C

Rationale: Warfarin acts by inhibiting vitamin K epoxide reductase complex subunit 1 (VKORC1). If the client has a higher level of the VKORC1 enzyme, the amount of warfarin dose should be increased to overcome the resistance to vitamin K. If the warfarin dose is unchanged or lower, it will take longer for effective anticoagulation to occur. There is no need to identify a different anticoagulant; the dose just needs to be adjusted upward.

10. A pharmaceutical company is implementing a drug program that is based upon extensive genomic testing conducted on one ethnic group. How will this affect some of your clients?
- This program will have no effect on any of the clients.
  - The clients within the ethnic group will have better outcomes.
  - The clients within the ethnic group will pay less for these medications.
  - This program may give the perception of a stigma based upon ethnicity.

Answer: D

Rationale: The future of pharmacogenomics will most likely focus on the development of drugs that work well with certain population groups; however, any program will need to be carefully implemented to avoid a perception of stigma based on ethnicity. Assuming that an individual's race can be used as a genetic profile can be a potential problem. There is no evidence that all clients within the ethnic group will have better outcomes. Individually targeted drug therapy is very attractive and is likely to be very expensive, regardless of testing on a specific ethnic group.

## Chapter 26 – Gene Therapy

1. Which of the following is not a purpose of gene therapy?
  - A. Delete an abnormal gene
  - B. Turning on or off a gene
  - C. Repair an abnormal gene
  - D. Exchange an abnormal gene with a normal gene

Answer: A

Rationale: Gene therapy is not being used to delete an abnormal gene. Answer B is incorrect, regulation of a gene is a purpose of gene therapy. Answer C is incorrect, repairing an abnormal gene by reversing the mutation is a purpose of gene therapy. Answer D is incorrect, exchanging an abnormal gene with a normal gene is a purpose of gene therapy. Answer A is correct.

2. The process of donated DNA entering the target cell to begin expression through a virus is known as?
  - A. Transduction
  - B. Conjugation
  - C. Transformation
  - D. Recombination

Answer: A

Rationale: Transduction is the process in which DNA is transferred to another cell which enables the target cell to begin expression. Answer B is incorrect, conjugation is the transfer of all or some of the donor's DNA into the target cell through mating. Answer C is incorrect, transformation is the process in which the target cell uptakes extracellular DNA and incorporates it. Answer D is incorrect, recombination is the mixing of the donor and recipient's genome to form a new genome. Answer A is correct.

3. Which of the following denotes a mutation that results in a nonfunctional or missing gene?
  - A. Gain of function
  - B. Loss of function
  - C. Missense mutation

D. Nonsense mutation

Answer: B

Rationale: Loss of function mutations result in a decrease of or complete absence of a gene. Answer A is incorrect because gain of function mutations result in a new gene function or increased gene activity. Answer C is incorrect because missense mutations are due to the exchange of a nucleotide in a gene; this results in a code for a different amino acid which eventually alters the protein product, possibly rendering the protein nonfunctional. Answer D is incorrect because nonsense mutations occur when a nucleotide is exchanged and the codon sequence is changed to a “stop” codon, prematurely stopping the construction of a protein. Answer B is correct.

4. A vector is a means to deliver a normal gene to a target cell. Which is an example of a commonly used vector for gene therapy?
- A. Pseudomonas
  - B. Candida
  - C. Herpes simplex
  - D. Giardia

Answer: C

Rationale: Vectors deliver a therapeutic gene to cells where it can then be integrated and alter the cell's gene expression; most vectors are viruses. Answer A is incorrect because Pseudomonas is a type of bacteria. Answer B is incorrect because Candida is a type of yeast. Answer D is incorrect because Giardia is a type of parasite. Answer C is correct.

5. What is a potential drawback of using retroviruses to deliver gene therapy?
- A. Tumor formation
  - B. Suppressed immune system
  - C. Recurrent fever
  - D. Erythema multiforme

Answer: A

Rationale: Retroviruses can activate proto-oncogenes while integrating in host's DNA, leading to tumor formation. Answer B is incorrect because although gene therapy can lead to a viral infection, it is not known to cause a suppressed immune system. Answer C is incorrect because gene therapy has not been linked to recurrent fevers. Answer D is

incorrect because erythema multiforme is not an associated risk of gene therapy. Answer A is correct.

6. A 5-year-old white male presents to the ER with shortness of breath. He has a history of recurrent respiratory infections and pancreatitis. A CXR reveals hyperinflation and peribronchial thickening. He has an abnormal sweat chloride test. What gene is most likely affected?
- A. CFTR
  - B. AAT
  - C. FGFR3
  - D. JAK3

Answer: A

Rationale: The patient has cystic fibrosis. Cystic fibrosis is caused by a mutation in the CFTR gene (cystic fibrosis transmembrane conductance regulator). Answer B is incorrect because a mutation in AAT (alpha-1 antitrypsin) is not actually a gene but a protein associated with emphysema. Answer C is incorrect because a mutation of FGFR3 (fibroblast growth factor receptor 3) results in achondroplasia which is a common cause of dwarfism. Answer D is incorrect because a mutation in JAK3 is responsible for severe combined immunodeficiency (SCID). Answer A is correct.

7. A 58-year-old white male is concerned about his recent 20-pound weight loss and recurrent fevers at night. On exam, he has splenomegaly. His CBC shows a WBC count of 95,000 with 20% blasts. Upon chromosomal analysis, it was determined that there is a translocation of chromosomes 9 and 22. He was diagnosed with chronic myelogenous leukemia. What gene is associated with this disease?
- A. BRCA 2
  - B. BCR/ABL
  - C. BRCA 1
  - D. P53

Answer: B

Rationale: The patient described has chronic myelogenous leukemia and the gene associated with this disease is bcr/abl. Answer A is incorrect, BRCA2 is linked to breast cancer, ovarian cancer, prostate cancer, pancreatic cancer, and melanoma. Answer C is incorrect, BRCA1 is linked to breast cancer, ovarian cancer, prostate cancer, pancreatic cancer, and colon cancer. Answer D is incorrect because p53 is a tumor suppressor gene related to Li-Fraumeni syndrome. Answer B is correct.

8. Which of the following can prevent an abnormal mRNA strand from translating a harmful protein, such as oncogenes?
- A. Vector
  - B. Liposome
  - C. Ribozyme
  - D. Oligonucleotide

Answer: D

Rationale: Oligonucleotides are being used to prevent oncogenes in colorectal and pancreatic cancer, from being expressed. Answer A is incorrect because vectors are the means in which DNA is delivered to target cells. Answer B is incorrect because liposomes are non-viral vectors that can deliver DNA by endocytosis. Answer C is incorrect because ribozymes can down regulate the production of an abnormal gene. Answer D is correct.

9. Which of the following is an example of a vector that can enter non-dividing cells through pores in its membrane?
- A. Herpes simplex virus
  - B. Parvovirus
  - C. Adenovirus
  - D. Human immunodeficiency virus

Answer: D

Rationale: The type of vector described is a lentivirus. An example of a lentivirus is HIV. Answer A is incorrect because herpes simplex viruses are neurotropic viruses that can infect neurons, but not through pores. Answer B is incorrect because Parvovirus is considered a parvoviridae virus and works by integrating genes at specific sites on chromosomes. Answer C is incorrect because adenoviruses can infect various cells but are not become integrated into the target's cells genome, but do not use pores. Answer D is correct.

10. What allows the production of viral copies when retroviruses are used as a vector targeting dividing somatic cells?
- A. Transduction
  - B. Packaging cells
  - C. Viral invasion

#### D. Modification

Answer: B

Rationale: When retroviruses are modified, they lose the ability to replicate by themselves. Packaging cells provide the necessary genes retroviruses need for replication. Answer A is incorrect because transduction is the process in which DNA is transferred to another cell which enables the target cell to begin expression. Answer C is incorrect because modified retroviruses are incapable of replicating by themselves so viral invasion would not lead to viral copies. Answer D is incorrect because modification reduces retroviruses ability to replicate.

## Chapter 27 – Ethical, Legal, and Social Issues

1. Which of the following should be included in genetic pretest education?
  - A. Limitation in available genetic test and interventions.
  - B. Implications of the test results for the patient and family members.
  - C. Limitations of confidentiality and possible discrimination.
  - D. All of the above.

Answer: D

Rationale: Patients should be made aware of limitations in available genetic testing and interventions, confidentiality and possible discrimination, and the implications of test results for themselves and their family members. Informed consent is crucial when preparing for genetic testing with patients.

2. As a primary care provider, before ordering genetic testing, it is important to do which of the following?
  - A. Obtain consent from state health department.
  - B. Obtain detailed family history and confirm the diagnosis.
  - C. Establish a wide differential to ensure sensitivity.
  - D. Primary care providers should not order genetic testing.

Answer: B

Rationale: Obtaining a detailed family history to confirm the diagnosis is the most important step for primary care providers to take prior to ordering genetic testing.

3. A 36-year-old female reported to your office with concerns of a family history of breast cancer. After proper counseling and investigation, the patient agreed to have genetic testing performed. Today her results have been sent to your office and show that she is possibly at a higher risk for breast cancer. How should you share the results with your patient?
  - A. Electronic communication (email, text message, facsimile).
  - B. Phone conversation with a medical assistant present to witness and document.
  - C. Written document mailed to the primary address provided by patient.
  - D. In person during a follow up visit.

Answer: D

Rationale: Results of genetic testing should always be shared in person during a follow up visit with the patient.

4. Genetic testing for mutations that may influence disease susceptibility is best suited for what patient population?
- A. All patients with signs and symptoms suggestive of disease.
  - B. All family members regardless of environmental risk.
  - C. Relatively few patients with known high-risk factors.
  - D. Only patient currently receiving treatment for suspected disease.

Answer: C

Rationale: Patients who are known to be at high risk, such as patients with a living member that has been diagnosed with a disease, are best suited for genetic testing for mutations that may influence disease susceptibility.

5. Which of the following is not considered a benefit of genetic testing?
- A. Provides opportunity for discrimination.
  - B. Provides opportunities for increased surveillance.
  - C. Provides knowledge that may affect future decisions.
  - D. Provide opportunities for early intervention.

Answer: A

Rationale: Genetic testing provides opportunities for increased surveillance, early intervention, and provides patients with opportunities to make lifestyle changes that can affect future decisions, but genetic testing should never be used as a chance to discriminate against a patient in any way.

6. During a follow up visit, while providing post-test counseling, your patient asked “Do these negative results guarantee I will not develop this disease?” What is the best response?
- A. The results represent a high level of accuracy.
  - B. The results represent a high level of precision.
  - C. The results represent only a probability.
  - D. The results represent only family members risk, and not the risk of the individual being tested.

Answer: C

Rationale: Patients should be educated that despite having negative test results, they are still at risk for developing certain diseases, just as others in the general population without known mutations. Both positive and negative genetic tests do not offer any guarantees of developing or not developing a disease.

7. A 16-year-old male presents to your office with his mother for a second opinion. He states that after having several occurrences of rectal bleeding, his primary care provider ordered a colonoscopy. The colonoscopy revealed no polyps. At a follow-up visit the primary care provider ordered genetic screening for familial adenomatous polyposis (FAP), which showed no mutation in APC gene. Which of the following statements best represent the patient's risk of developing FAP?
- A. Patient has no risk of developing FAP now or in the future.
  - B. The patient is at no risk however his sons should be screened at an early age.
  - C. The risk for developing FAP is the same any other male without known family history or known APC mutations.
  - D. The patient will likely develop FAP and should have genetic testing annually.

Answer: C

Rationale: Although this patient has no mutation in the APC gene, his risk for developing FAP remains the same as any other male with no known family history or known APC mutations. These findings do not indicate that he has no risk of developing FAP.

8. What is the primary problem with state legislation meant to protect the rights of patients undergoing genetic testing?
- A. Regulation has become so strict, it prevents adequate screening
  - B. The legal definition of “genetic information” is limited and provides legal loopholes.
  - C. The legal definition of testing is strictly defined and limits the number of tests available.
  - D. The increased policy regulation has significantly increased the cost of genetic testing.

Answer: B

Rationale: Steps have been taken by the federal statute to offer more clarity in the legal definition of “genetic information,” but its ambiguity can still result in legal loopholes.

9. A 44-year-old female received genetic testing that revealed a positive BRCA2 mutation. The patient's sister received a phone call two months later from her employer stating that due to a family member's recent lab results, she would be ineligible for promotion. Which of the following laws have been violated?
- A. GINA (Genetic Information Nondiscrimination Act)
  - B. HIPAA (Healthcare Insurance Probability and Accountability Act)
  - C. ADA (Americans with Disabilities Act)
  - D. A and B

Answer: D

Rationale: Both GINA and HIPAA prohibit employers from making promotion decisions based on genetic information from their employees.

10. The Genetic Information Nondiscrimination Act (GINA) does not offer protection in which of the following?
- A. Life insurance policy
  - B. Disability insurance policies
  - C. Long-term care policies
  - D. All the above

Answer: D

Rationale: The Genetic Information Nondiscrimination Act prohibits health insurers and health plan administrators from requesting and using genetic information to influence decisions on coverage, rates and preexisting conditions. GINA also prohibits employers from using genetic information to influence hiring, firing, and promotion decisions for individuals, but GINA does not offer protection for life insurance, disability insurance, or long-term care policies.