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with Answers

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PART I: GENERAL PRINCIPLES

General Principles

CHAPTER 1

BIOCHEMISTRY

TOPIC 1: MOLECULAR BIOLOGY I

1. The various features of the bases found in DNA or RNA are shown below. Complete the table by filling in the empty cells.

Base	Nucleoside	Nucleotide in Nucleic Acids
Adenine	Adenosine (deoxyadenosine)	dAMP, AMP
Guanine	*Guanosine (deoxyguanosine)*	dGMP, GMP
Cytosine	*Cytidine (deoxycytidine)*	dCMP, CMP
Uracil	Uridine (deoxyuridine)	*UMP*
Thymine	*Deoxythymidine*	*dTMP*

2. Two structural differences between DNA and RNA are:

   a) pyrimidine base b) ribose vs deoxyribose

3. A major assumption that must be made if a single strand of DNA or RNA sequence is shown and no orientation of the sequence is given is *5' to 3'*.

4. The difference between 10 nm and 30 nm chromatin is *the presence or absence of H1*.

5. In which intra-nuclear area (euchromatin, heterochromatin, or nucleolus) are the following RNAs synthesized?

   mRNA *euchromatin*

   tRNA *euchromatin*

   rRNA *nucleolus*

6. An oncologist is conducting a study of specific gene mutations that are hypothesized to increase the risk for developing breast cancer. Women who were shown to be positive for specific variations in the BRCA-1 and BRCA-2 gene sequence were further screened for sequence variations in other associated genes. Interestingly, the following gene sequence identified from exon 1 of the androgen receptor (AR) gene was found to have a high degree of heterogeneity between individuals with breast cancer: 5'-TTCATCATCATCATCATCATCATCATCC-3'. An increased length in this sequence was reportedly associated with increased incidence of breast cancer in BRCA-1 mutation carriers. During which phase of the cell cycle were these variations most likely generated?

   (A) G_0
   (B) G_1
   (C) G_2
   (D) M
   (E) S

7. In DNA replication in prokaryotes and eukaryotes, 5'-exonuclease performs the function of *removing the RNA primer* whereas the 3'-exonuclease performs the function of *proofreading activity*.

8. An important class of antimicrobials that is used to inhibit DNA replication in prokaryotes is *quinolones*, which inhibit the enzyme *Topoisomerase II (DNA gyrase)*.

9. *Telomeres* are the DNA sequences present at the ends of eukaryotic chromosomes. *Telomerase* is the enzyme present in eukaryotes, but not prokaryotes, which is involved in *maintaining the length of the chromosomes by completing the DNA synthesis at their ends.*

10. A drug targeted to inhibit telomerase would be useful to treat the *cancer* disease state.

11. For each cell type below, indicate the relative telomerase activity (high or low) found in each cell, and briefly discuss the biological ramifications of that level of telomerase activity for each cell.

    Embryonic cell:
    High. Allows embryonic cells to maintain telomere length and thus avoid cell senescence/death despite nearly continuous cell division, by maintaining chromosomal integrity.

    Normal adult cell:
    Low. Results in gradual decrease in telomere length during each cell division, ultimately leading to loss of chromosome integrity and to cell senescence/death → cause of aging.

    Tumor cell:
    High. Allows tumor cells to maintain telomere length and thus avoid cell senescence/death despite continuous cell division, by maintaining chromosomal integrity.

12. The various features of the DNA repair mechanism are shown below. Complete the table by filling in the empty cells.

DNA Repair	Example	Key Enzyme(s)	Clinical Relationship	Phase of Cell Cycle
Thymine dimer	UV radiation	*Excinuclease (excision endonuclease)*	*Xeroderma pigmentosum*	*G1*
Mismatch base	DNA replication errors	*Enzymes encoded by hMLH1 or hMSH2 genes*	HNPCC (Lynch syndrome)	G_2
Base excision	*Cytosine deamination*	Uracil glycosylase, AP endonuclease	None	*G1*

13. In RNA transcription, RNA polymerase first recognizes and binds to a region of DNA called promoter. Then the enzyme reads the strand of the double-stranded gene called the template strand in a 3' to 5' direction. The strand of the gene that is not read by RNA polymerase is called the coding strand.

14. An important antimicrobial that is used to inhibit transcription in prokaryotes is rifampin, which inhibits the enzyme RNA polymerase.
    The toxic substance in poisonous mushrooms that inhibits RNA transcription in eukaryotes is α-amanitin, which inhibits the enzyme RNA polymerase 2.
    Actinomycin D inhibits transcription in both prokaryotes and eukaryotes.

15. Two major similarities between DNA polymerase and RNA polymerase are:
    Both read the template strands in 3' to 5' direction
    Both synthesize nucleic acid in 5' to 3' direction
    Both require nucleoside triphosphates as substrates and add nucleoside monophosphates at the 3' end of the growing nucleic strand

16. Two major differences between DNA polymerase and RNA polymerase are:
    DNA polymerase requires a nucleic acid primer (RNA primer in cells) whereas RNA polymerase does not.
    DNA polymerase proofreads and corrects errors whereas RNA polymerase does not.

17. During replication, the DNA template sequence CTGTA would replicate to produce the sequence TACAG.

18. During transcription, the DNA template sequence CTGTA would transcribe to produce UACAG.

19. In systemic lupus erythematosus, autoantibodies are directed against which of the following?

    (A) 7-methyl-G cap of mRNA
    (B) Spliceosomes
    (C) Modified bases of tRNA
    (D) rRNA of the ribosome
    (E) Poly A tails of mRNA

20. Even though there are approximately 3 billion bases per haploid genome, only about 1.5% of the genome actually encodes for genes. Explain why chromosomal DNA is mostly non-coding DNA.

    Since the spontaneous mutation frequency of DNA is about 20 nucleotides per haploid genome, by probability these mutations would mostly occur in spacer DNA because there is so much more of it (98.5%) than in DNA encoding genes.

21. Even though improper splicing out of introns is the source of many diseases, what is the main advantage of introns in genes?

    "Alternative splicing" of the introns can generate more kinds of proteins than there are genes.

22. In prokaryotic ribosomes, the small subunit size is *30S* and the large subunit size is *50S* and together equal *70S*. In eukaryotic ribosomes, the small subunit size is *40S* and the large subunit size is *60S* and together equal *80S*.

23. tRNAs are the smallest of the RNAs and have a cloverleaf structure in which the amino acid is attached to the tRNA at the 3' end of the sequence *5'-CCA-3'*.

24. Describe a mechanism by which a gene in human cells could be expressed in 2 different forms, one that is translated on free ribosomes and remains in the cytoplasm, and a second form that is secreted from the cell. Assume that the mechanism is related to the expression steps for this gene and does not involve any alteration in the translation or secretory machinery of the cell.

Alternative splicing could occur such that one form has an exon corresponding to a signal peptide spliced in, and when this transcript was translated the signal peptide part of it would bind to SRP bringing this ribosome to the ER membrane, resulting in secretion of this form. In the other form of the transcript, this signal peptide-encoding exon would be skipped, so that this transcript would be translated on free ribosomes in the cytoplasm and the protein when finished translating would be in the cytoplasm.

25. Using the genetic code below, what is the amino acid sequence encoded by the following DNA sequence?

……..ATGTTTGCGAAACAG……

Met-Phe-Ala-Lys-Gln

First Position (5' End)	Second Position U	Second Position C	Second Position A	Second Position G	Third Position (3' End)
U	UUU, UUC: Phe; UUA, UUG: Leu	UCU, UCC, UCA, UCG: Ser	UAU, UAC: Tyr; UAA, UAG: Stop	UGU, UGC: Cys; UGA: Stop; UGG: Trp	U C A G
C	CUU, CUC, CUA, CUG: Leu	CCU, CCC, CCA, CCG: Pro	CAU, CAC: His; CAA, CAG: Gln	CGU, CGC, CGA, CGG: Arg	U C A G
A	AUU, AUC, AUA: Ile; AUG: Met	ACU, ACC, ACA, ACG: Thr	AAU, AAC: Asn; AAA, AAG: Lys	AGU, AGC: Ser; AGA, AGG: Arg	U C A G
G	GUU, GUC, GUA, GUG: Val	GCU, GCC, GCA, GCG: Ala	GAU, GAC: Asp; GAA, GAG: Glu	GGU, GGC, GGA, GGG: Gly	U C A G

26. DNA sequence surrounding the beginning of the 5'-exon of a gene is as shown below:

    ……..GG ATG TTT GCG TCG……

    Suppose a mutation resulted in the C (underlined) being converted to an (A) This kind of mutation is called *nonsense mutation*.

27. What would be the sequence of an anticodon that would bind to the codon transcribed from the trinucleotide CAG in the template strand of the gene?

    CAG

28. A summary of important antibiotics that inhibit translation in prokaryotes is shown below. List the site of action of the respective antibiotic and the consequence in translation.

Antibiotic	Site of Action and Consequence
Chloramphenicol	*Peptidyl transferase, preventing peptide bond formation*
Clindamycin	*Binds 50S large subunit, preventing translocation of ribosome*
Erythromycin	*Binds 50S large subunit, preventing translocation of ribosome*
Neomycin	*Binds 30S small subunit, preventing initiation of translation*
Tetracycline	*Binds 30S small subunit, preventing codon-anticodon pairing*

29. A 53-year-old man comes to his physician with complaints of strange movements and behavior changes for the past 2 months. His wife states that the patient has progressively become socially withdrawn, inattentive, uncharacteristically aggressive, and irritable. Physical examination shows irregular, sudden, jerky movements of both legs and arms that sometimes awaken the patient at night. Expansion of which of the following sequences is associated with this man's condition?

    (A) 5'-AAAAAAAAAAAA-3'

    (B) 5'-CAGCAGCAGCAG-3'

    (C) 5'-CAGGACCAGGAC-3'

    (D) 5'-GGGCCCGGGCCC-3'

    (E) 5'-GGGGGGGGGGGG-3'

30. Define the protein structures below and list an example.

Protein Structure	Definition	Example
Primary	*Sequence of amino acids*	*Ala-Pro-Lys-Arg-Glu*
Secondary	*Folding of peptide into stable structure*	*-Helix*
Tertiary	*Positioning of secondary structures to generate 3-dimensional shape*	*Globular protein*
Quaternary	*Interaction of multiple subunits*	*Hemoglobin with two α- and β-subunits*

31. What are 2 reasons why a protein misfolds?

Aging of a protein (half-life)

Lack of a required chaperone to assist in protein folding

32. Concisely explain how misfolded proteins are handled in the cytoplasm of cells.

Misfolded proteins are polyubiquitinated in enzyme-catalyzed, ATP required steps. The polyubiquitinated protein is handled by a cytoplasmic complex called the proteasome, which removes the ubiquitin peptides. The misfolded protein is engulfed within the proteasome and proteolyzes it to peptide fragments.

33. What determines whether a protein will be secreted or remain in the cytoplasm of a cell?

The presence of a stretch of 10-15 hydrophobic amino acids on the N-terminus of newly synthesized peptide undergoing translation will enable the Signal Recognition Particle (SRP) to bind and attach the complex to the surface of the endoplasmic reticulum. A channel will be opened and the peptide will enter the ER lumen to eventually be secreted.

34. N-glycosylation of proteins occurs in the *endoplasmic reticulum* (intracellular location) in the cell. An example of a protein that is N-glycosylated is *any blood clotting factor*. O-glycosylation of proteins occurs in the *Golgi apparatus* (intracellular location) in the cell. An example of a protein that is O-glycosylated is *any proteoglycan, like hyaluronic acid*.

35. List whether the respective protein modification is co-translational, post-translational, or both.

Modification	Co-Translational, Post-Translational, or Both?
Disulfide bond formation	*Post-translational*
Proteolysis	*Both*
Phosphorylation	*Post-translational*
Gamma-carboxylation	*Co-translational*
Prenylation	*Post-translational*
O-glycosylation	*Post-translational*
N-glycosylation	*Co-translational*

36. I-cell disease is most often due to a defect in the enzyme *Phosphotransferase*, which functions to *add phosphate onto C-6 of specific mannose residues following N-glycosylation*. The result of the catalytic function of the normal enzyme enables lysosomal enzymes to enter the lysosome of a cell. Another situation that could give rise to I-cell disease is a defect in *the receptor that recognizes the mannose-6-phosphate*.

37. Why do cells from patients with I-cell disease have inclusion bodies?

Without the mannose-6-phosphate on the enzymes, they will be secreted and the lysosomes will be empty. When the cell conducts endocytosis of molecules, the lysosomal contents will be unable to be digested properly and will accumulate.

38. While the collagen superfamily of proteins includes more than 25 collagen types, the most important types for the exam are shown below. Complete the table by filling in the blank cells.

Collagen Type	Characteristics	Tissue Distribution	Associated Diseases
I	*Bundles of fibers* *High tensile strength*	*Bone, skin, tendons*	*Osteogenesis imperfecta* *Ehler-Danlos (various)*
II	Thin fibrils; structural	*Cartilage* *Vitreous humor*	----------
III	Thin fibrils; pliable	*Blood vessels* *Granulation tissue*	*Ehlers-Danlos, type IV*
IV	Amorphous	*Basement membranes*	*Goodpasture syndrome* *Alport syndrome* *Epidermolysis bullosa*

39. Place the following steps in collagen synthesis in the proper sequential order.

__4__ Triple helix formation

__1__ Removal of the hydrophobic signal sequence

__7__ Oxidation by lysyl oxidase that requires O_2 and copper

__3__ Glycosylation of selected hydrolysines

__6__ Aggregation to form the fibril

__5__ Enzymatic removal of N- and C-terminal peptides

__2__ Enzymatic activity by 2 enzymes that require vitamin C

__8__ Secretion of the protein from the cell

40. The major organelles and macrostructures in a cell are shown below. Complete the table by filling in the empty cells.

Organelle and Macrostructure	Structural Features	Main Function(s)
Mitochondrion	*Double membrane*	*Many oxidation reactions* *Oxidative phosphorylation* *Ketone body synthesis*
Peroxisome	*Small Spherical*	*Catabolism of very long chain FA* *H2O2 metabolism* *Bile acid synthesis*
Smooth endoplasmic reticulum	*Network of single membrane organelles of various sizes*	*Detoxification of drugs* *Steroid synthesis* *Sequestration and release of Ca^{2+}*
Rough endoplasmic reticulum	*Network of single membrane organelles with ribosomes attached*	*Translation of proteins destined for secretion, membrane-bound or lysosomal*
Golgi apparatus	*Cluster of small membrane organelles*	*O-glycosylation* *Sorting of proteins destined for secretion, membrane, or lysosomal*
Nucleus	Double membrane compartment	*Replication* *Transcription*
Lysosome	*Small Spherical*	*Degradation of macromolecules*
Vacuole	Single membrane compartment	*Storage organelle*
Cilia	Microtubule protein	*Mucociliary clearance* *Motility of sperm*

41. Kinesin is the name of the ATPase motor molecule involved in anterograde transport on microtubules, and Dynein is involved in retrograde transport on microtubules. Vincristine and Colchicine are examples of drugs that inhibit microtubule assembly.

42. Chediak-Higashi Syndrome is the name of the genetic disease that involves a microtubule polymerization defect, impairing fusion of phagosomes and lysosomes. A key feature of this disease is partial albinism.

43. Kartagener syndrome is the name of the genetic disease that involves immotile cilia and infertility due to immotile spermatozoa.

TOPIC 2: MOLECULAR BIOLOGY II

1. Several major specific transcription factors are shown below. Complete the table by filling in the empty cells.

Name	Response Element	Function	Protein Class
Steroid receptors	*HRE*	Response to steroids	*Zinc finger*
CREB	*CRE*	*Response to cAMP*	*Leucine zipper*
PPARs	*PPRE*	*Regulates genes in lipid metabolism*	*Zinc finger*
NF = κB	κB elements	*Regulates genes in inflammation*	Re1 domains
Homeodomain proteins	----------	*Regulates genes in fetal development*	Helix-turn-helix

2. A child is brought to the university hospital with severe birth defects, including limb abnormalities, congenital deafness, and pigment abnormalities. Which of the following genes or DNA sequences is most likely mutated in this individual?

(A) CCAAT box within an enhancer

(B) PAX gene

(C) RAS gene

(D) Tyrosine hydroxylase gene

(E) UPE GC-rich sequence within an enhancer

3. Extracellular estrogen initiates a series of steps by a cell. These steps constitute a signaling pathway. List these steps (that is, how does estrogen give a signal to a cell?).

   1. *Entry into cell*
   2. *Binding E receptor*
   3. *Moving to nucleus*
   4. *Dimerization*
   5. *DNA binding*
   6. *Activating downstream target genes*

   Imagine that cells could be cultured in sodium chloride, potassium, calcium, and magnesium only. How would this impact estrogen signaling?

   Disrupt Zn^{+2} finger

   Post-menopausal women with breast cancer can often be successfully treated with estrogen or related compounds. In one such patient, a clinical response of several years ended when her cancer relapsed. List 3 possible explanations for how her tumor became resistant to estrogen therapy.

   1. *ER (estrogen receptor) unable to bind Estrogen*
   2. *ER unable to move to nucleus*
   3. *ER unable to dimerize*
   4. *ER unable to bind DNA because of zinc finger mutation*

4. The major differences between genomic and cDNA libraries are shown below. Complete the table by filling in the empty cells.

	Genomic Libraries	cDNA Libraries
Source of DNA	*Chromosomal DNA*	mRNA (cDNA)
Key enzymes to make library	*Restriction endonucleases* *DNA ligase*	*Reverse transcriptase* *DNA ligase*
Contains nonexpressed sequences of chromosomes	Yes	*No*
Cloned genes are complete sequences	Not necessarily	*Yes*
Cloned genes contain introns	*Yes*	*No*
Promoter and enhancer sequences present	Yes, but not necessarily in same clone	*No*
Gene can be expressed in cloning host	*No*	*Yes*
Gene can be used for gene therapy or transgenics	*No*	Yes

5. Cloning of a new eukaryotic gene was followed by insertion and ligation of the gene into an expression vector. The protein translated from this gene was then studied on a western blot and probed with ^{32}P-DNA, yielding a positive result. These findings eliminate which of the following substances as a candidate for the likely gene product?

(A) CREB

(B) Protein kinase A

(C) RNA polymerase

(D) PPAR

(E) Steroid receptor

6. Several types of commonly used blots are shown below. Complete the table by filling in the empty cells.

Name	Material Analyzed	Electrophoresis Required	Probe	Purpose
Southern	*DNA*	Yes	*^{32}P-DNA*	*Analyzing DNA fragments based on size*
Northern	*RNA*	*Yes*	*^{32}P-DNA*	*Analyzing RNA based on size*
Western	*Protein*	*Yes*	*^{125}I- or enzyme-linked antibody*	*Analyzing proteins based on size*
Dot	RNA, DNA, protein	*No*	Same as above	Detects RNA, DNA, or proteins

7. An HIV-positive woman who has been on combination therapy for 8 years goes to her physician with no complaints. Her blood work shows a steadily decreasing CD4 count. Physical examination reveals generalized lymphadenopathy, and she is diagnosed with cervical dysplasia. The physician wants to check her viral load before changing her treatment regimen. Which of the following tests should he use?

(A) ELISA for the p24 antibody

(B) HIV culture with antigen detection

(C) HIV DNA polymerase chain reaction (PCR)

(D) HIV reverse transcriptase-PCR

(E) Western blot for HIV-specific antibodies

TOPIC 3: MEDICAL GENETICS

1. Define the terms below.

	Definition
Gene	*Sequence of DNA encoding specific proteins or non-translated RNA*
Locus	*Physical location of a gene on a chromosome*
Allele	*Different variations of a particular gene*
Haploid	*One copy of each type of chromosome*
Somatic cell	*Non-ova or sperm cells*
Gametes	*Ova and sperm cells*
Polymorphism	*DNA sequence variations of a gene at a specific site in a chromosome*
Genotype	*Specific DNA sequence at a locus*
Phenotype	*Expression of a genotype with observable characteristics*
Loss of function mutation	*Mutation in a gene results in loss of protein activity*
Gain of function mutation	*Mutation in a gene results in gain of protein activity*
Recurrence risk	*Probability that offspring will express a genetic disease*
Punnett square	*A diagram used to predict the outcome of a particular cross*

2. If a pedigree shows that the disease trait has a vertical appearance and the disease is in every generation, the mode of inheritance is dominant or recessive (*circle one*).

3. If a pedigree shows that the disease trait has a horizontal appearance and the disease skips a generation, the mode of inheritance is dominant or recessive (*circle one*).

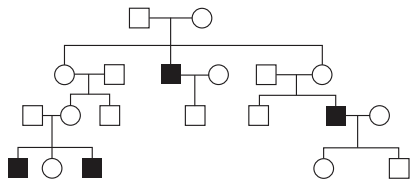
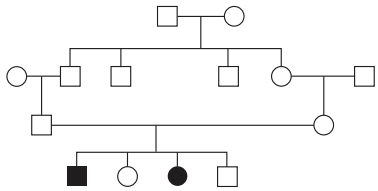
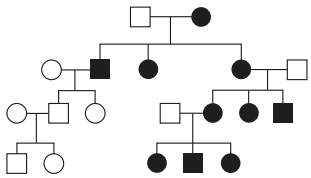
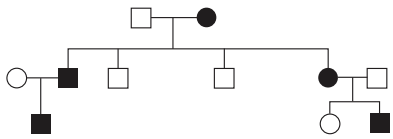
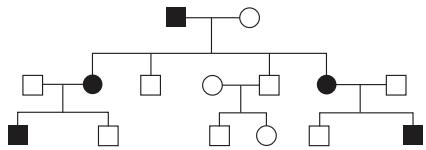
4. If a pedigree shows that the disease trait has male-to-male transmission, the mode of inheritance is autosomal or X-linked (*circle one*).

5. If a pedigree shows that the disease trait does not have male-to-male transmission, the mode of inheritance is autosomal or X-linked (*circle one*).

6. What is the main distinguishing characteristic of mitochondrial mode of inheritance?

   Transmission of trait is through the mother only since mitochondria come exclusively from the mother

7. For each of the pedigrees below, state the mode of inheritance:

	Mode of Inheritance
	*X-linked recessive*
	*Autosomal recessive*
	*Mitochondrial Inheritance*
	*Autosomal dominant*
	*X-linked dominant*

8. Listed below are factors that influence phenotypic expression in single gene disorders. Define the term and state a disease example of each.

Term	Definition	Disease Example
Environmental factors	*Degree of exposure to certain chemicals or radiation*	*Xeroderma pigmentosum*
Allelic heterogeneity	*Varied mutations located within a gene*	*Hemophilia A*
Incomplete penetrance	*Individuals with disease phenotype, but do not display disease phenotype*	*Retinoblastoma*
Variable expression	*Severity of disease varies from patient to patient, but display some pathology*	*Hemochromatosis*
Pleiotropy	*Single disease causing mutation affects multiple organ systems*	*Marfan syndrome*
Locus heterogeneity	*Same disease phenotype can be caused by mutations in different loci (locations)*	*Osteogenesis imperfecta*
Anticipation	*Increasing severity and earlier age of onset in succeeding generations*	*Huntington disease*
Imprinting	*Differential expression of a gene depending on parental origin*	*Prader-Willi*
Uniparental disomy	*Two copies of the same chromosome inherited from 1 parent*	*Prader-Willi*

9. The most common type of Prader-Willi syndrome involves a loss of genetic material on the *15q* chromosome, which was inherited from the *paternal* parent. The corresponding genetic material inherited from the other parent is transcriptionally inactive due to *imprinting*. The more rare type of Prader-Willi syndrome involves a child who inherits 2 copies of chromosome *15* from which parent? *mother*

10. The most common type of Angelman's syndrome involves a loss of genetic material on the *15q* chromosome, which was inherited from the *maternal* parent. The corresponding genetic material inherited from the other parent is transcriptionally inactive due to *imprinting*. The more rare type of Angelman's syndrome involves a child who inherits 2 copies of chromosome *15* from which parent? *father*

11. What is the definition of genotype frequency?

Measures the proportion of each genotype in a population

12. What is the definition of allele frequency?

Measures the proportion of chromosomes that contain a specific allele in a population

13. By convention, allele frequency is p + q = 1, where p is *the most common, normal allele* and q is *a minor, disease-producing allele*.

14. What is the definition of Hardy-Weinberg equilibrium and what is its formula?

Predicts allele and genotype frequencies in a non-evolving population.

$p^2 + 2pq + q^2 = 1$ where p^2 is the frequency of homozygous normal genotype, 2pq is the frequency of the heterozygous genotype and q^2 is the frequency of the homozygous mutant genotype.

15. If the prevalence of the autosomal recessive disease cystic fibrosis in a population of northern Europeans is 1/2500, what is the predicted carrier status of cystic fibrosis in that population?

Using $p^2 + 2pq + q^2 = 1$, q2 is given as 1/2500. Therefore the allele frequency is q = 1/50. 2pq is the carrier frequency. Since p is about equal 1, then 2 X 1 X q is the carrier frequency which = 2(1/50) = 1/25.

16. Define each of the following phrases related to population genetics.

	Definition
New mutation	*Disease caused by new mutation transmitted from unaffected parent to affected offspring*
Natural selection	*Increases/decreases frequency of alleles to promote survival or fitness*
Genetic drift	*Change in genetic composition of population due to chance or random events rather than natural selection*
Gene flow	*Exchange of genes/alleles from one population to another population*
Consanguinity	*Mating of individuals related to one another (second cousin or closer)*

17. Ploidy is the number of complete sets of chromosomes in a cell. Normally, the complete set of chromosomes in humans is known as *euploidy*. *Aneuploidy* is the condition in which the chromosome number in a cell is not the usual number. The normal human karyotypes contain *22* autosomes and one pair of sex chromosomes with the karyotype *46, XX* for females and *46, XY* for males.

18. Numerical chromosome abnormalities are generally caused by *nondisjunction* of sister chromatids during either meiosis 1 or meiosis 2.

19. List the disease that relates to each chromosome abnormality or state "lethal" where applicable.

Chromosomal Abnormality	Disease
45,X	*Turner's syndrome*
47,XX,+21	*Down's syndrome*
47,XY,+14	*Lethal*
47,XXY	*Klinefelter's syndrome*
47,XY,+18	*Edwards' syndrome*
45,XY	*Lethal; all monosomies of autosomes are incompatible with life*
47,XX,+13	*Patau's syndrome*

20. Concisely explain reciprocal translocation.

Exchange of genetic material between non-homologous chromosomes.

21. Concisely explain the consequence of reciprocal translocation during gametogenesis.

The offspring will carry the translocation in all cells and be known as a reciprocal translocation carrier. There will be no phenotype in that carrier since there is balanced alteration of genes (no loss or gain of genetic material). The consequence will be in that carrier's offspring which will typically result in pregnancy loss.

22. Concisely explain the consequence of reciprocal translocation in somatic cells.

Often no clinical consequence. But if the reciprocal translocation occurs at a site that fuses two genes, abnormal growth (CML, AML, Burkitt's lymphoma) may occur.

23. Concisely explain Robertsonian translocation.

Translocation between two of the five acrocentric chromosomes (13,14,15,21,22) in which there is a loss of the short p arms and subsequent fusion of the long q arms. No clinical consequence for the Robertsonian translocation carrier since the p arms contain no essential genetic material. However, it will be consequential in the offspring of the carrier.

24. Concisely explain any pathology associated with Robertsonian translocation.

4% of Down's syndrome results from Robertsonian translocation between chromosomes 14 and 21.

25. Microdeletions are the loss of some genetic material within a chromosome. List the disease that results from a microdeletion of the given chromosome and a hallmark of that disease.

Chromosome	Disease	Hallmark of Disease
5	*Cri-du-chat syndrome*	*High pitched, cat-like cry*
7	*Williams syndrome*	*Pathologies associated with deficiencies of elastin*
22	*DiGeorge syndrome*	*Thymic, parathyroid, and cardiac problems*

TOPIC 4: GENETIC DISEASES

1. Fill out the following table summarizing the common genetics diseases tested on the exam.

Name	Mode of Inheritance	Defective Gene	Pathologic Hallmark
Achondroplasia	*AD*	*Fibroblast GF receptor 3 gene*	*Dwarfism*
Polycystic kidney disease	*AD*	*PKD-1 gene*	*Enlarged kidney with cysts*
Familial adenomatous polyposis	*AD*	*APC gene*	*Colonic polyps and adenocarcinoma*
Familial hypercholesterolemia	*AD*	*LDL receptor gene*	*Significantly elevated LDL levels*
Hereditary hemorrhagic telangiectasia	*AD*	*(low yield)*	*Small vascular malformations in skin mucous membranes and several organs*
Hereditary spherocytosis	*AD*	*Ankyrin and spectrin genes (RBCs)*	*Auto-hemolytic due to sphere-shaped RBCs*
Huntington's disease	*AD*	*Huntingtin gene*	*Degeneration of GABA neurons of caudate nucleus*
Marfan syndrome	*AD*	*Fibrillin gene*	*Aortic and mitral valve insuficiency*
Multiple endocrine neoplasia syndromes	*AD*	*MEN I or IIA*	*Hyperplasia and tumors of endocrine glands*
Neurofibromatosis 1	*AD*	*NF-1*	*Multiple neurofibromas*
Neurofibromatosis 2	*AD*	*NF-2*	*Bilateral acoustic neuromas*
Tuberous sclerosis	*AD*	*(low yield)*	*Ash leaf spots on skin*
Von Hippel-Lindau disease	*AD*	*VHL tumor suppressor gene*	*Hemangioblastomas*
Albinism	*AR*	*Tyrosinase*	*Pale color urine*

Name	Mode of Inheritance	Defective Gene	Pathologic Hallmark
Cystic fibrosis	*AR*	*CFTR*	*Thick mucous plugs*
Phenylketonuria	*AR*	*Phenylalanine hydroxylase*	*Musty odor of urine*
Sickle cell anemia	*AR*	*β-globin*	*Rigid, sickle shape RBCs*
Tay-Sachs disease	*AR*	*Hexosaminidase A*	*Cherry red spot in macula*
Friedreich's ataxia	*AR*	*Frataxin*	*Gait ataxia*
Duchenne muscular dystrophy	*XR*	*Dystrophin*	*Severe muscular dystrophy*
G6PD deficiency	*XR*	*G6PD*	*Heinz bodies*
Hemophilia A	*XR*	*Factor VIII*	*Increased coagulation time*
Hemophilia B	*XR*	*Factor IX*	*Increased coagulation time*
Lesch-Nyhan syndrome	*XR*	*HGPRT*	*Severe hyperuricemia*
Fragile X syndrome	*XD*	*FMR-1*	*Mental Retardation* *(2nd most common cause)*
Hypophosphatemic rickets	*XD*	*PHEX*	*Excessive loss of phosphate in bone and urine*

TOPIC 5: SIGNAL TRANSDUCTION SYSTEMS AND VITAMINS

1. Define each of the 3 classes of hormones and provide an example.

Hormone Classification	Definition	Example
Autocrine	*Hormones that bind to receptors on a cell which produces them*	*Prostaglandins*
Paracrine	*Hormones that act on cells close to cell which produces them*	*Neurotransmitters*
Endocrine	*Hormones that bind to receptors on a target cell at a distant site*	*Glucagon*

2. Why is the regulation of metabolic pathways controlled by lipid-soluble hormones much slower (hours) compared to the regulation of metabolic pathways controlled by water-soluble hormones (min)?

All lipid-soluble hormones act at the genetic level to stimulate gene expression which takes hours to complete. Water-soluble hormones primarily (there are exceptions) act by stimulating phosphorylation/dephosphorylation or allosteric mechanism to affect an enzyme.

3. Why do water-soluble hormones require a second messenger to control a pathway whereas lipid-soluble hormones do not?

Water-soluble hormones cannot enter a cell to turn on/off a pathway and must transduce the signal to a second messenger. Lipid-soluble hormones do enter cells and do not require a second messenger.

4. The various features of signal transduction mediated by water-soluble hormones are shown below. Complete the table by filling in the empty cells.

Pathway	G-protein	Enzyme	Second Messenger	Protein Kinase	Hormone Example
cAMP	*Gs or Gi*	*Adenyl cyclase*	cAMP	*PKA*	*Glucagon* *Epinephrine (2)*
PIP2	*Gq*	Phospholipase C	*DAG, IP3, Ca^{2+}*	*PKC*	*Vasopressin* *Epinephrine (1)*
cGMP	none	*Guanyl cyclase*	cGMP	*PKG*	*NO, ANP*
Insulin; growth factors		----------	----------	*Tyrosine kinase*	*Insulin* *EGF* *PDGF*

5. Upon hormonal stimulation of trimeric G-proteins, which subunit binds GTP to function?

   Alpha

6. Growth factors function through binding to their receptors on the surface of specific cells causing activation of signaling cascades in the cell leading to cellular responses. A mutation in the ras gene resulting in constitutive activation of the protein can lead to the development of cancer. Concisely explain how this process occurs.

   Ras is a monomeric G-protein that normally does not bind GTP unless upstream SH2 proteins bind IRS-1 which binds hormone-stimulated receptor. The mutation in Ras may enable the Ras to bind GTP in absence of the preceding step being activated. Upon binding GTP, Ras is active resulting in downstream transcription steps becoming active. Genes involved in cell division are then expressed.

7. Explain the biochemical relationship of glycogen synthesis in muscle and blood glucose levels in diabetics.

   ↓insulin in diabetes → ↓GLUT4 in muscle PM → ↓Glc entry into muscle → ↓ Glycogen synthesis
   Therefore prolonged ↑ blood [Glc] after eating carbohydrates

8. The various features of water-soluble vitamins are shown below. Complete the table by filling in the empty cells.

Vitamin	Coenzyme Form	One Main Function	One Hallmark of Deficiency
Thiamine (B1)	*Thiamine pyrophosphate*	Decarboxylation	*Beri-Beri*
Riboflavin (B2)	FAD and FMN	Oxidation/reduction	*Cheilosis*
Niacin (B3)	*NAD(H) & NADP(H)*	*Oxidation/Reduction*	*Pellagra*
Pantothenic acid (B5)	Coenzyme A	*Carrier of FA*	Rare
Pyridoxine (B6)	*Pyridoxal phosphate*	Transamination	*Microcytic anemia*
Biotin (B7)	Biotinyl lysine	*Carboxylation*	Alopecia
Folic acid (B9)	*DHF & THF*	*1 carbon transfer*	Megaloblastic anemia
Cobalamin (B12)	Methylcobalamin or deoxyadenosylcobalamin	Methionine synthesis, odd-carbon fatty acid metabolism	*Megaloblastic anemia*
Ascorbic acid (C)	None; used as is	*Anti-oxidant*	*Scurvy*

9. Why do symptoms of pellagra sometimes appear after consumption of a diet consisting mostly of corn-based meals?

Corn lacks tryptophan, which can be used in cells to produce niacin. Normally, humans obtain niacin from the diet and from tryptophan. So the lack of tryptophan in corn would indicate that humans may be prone to pellegra.

10. Why do deficiencies of water-soluble vitamins usually manifest with erythrocyte, skin, or neuronal problems?

Water-soluble vitamins are needed to produce key coenzymes needed by rapidly growing cells to divide properly. These are the types of cells that would suffer if there is a lack of these vitamins.

11. How can megaloblastic anemia caused by vitamin B_{12} be differentiated from any other vitamin deficiency?

Methylmalonic acidemia or progressive peripheral neuropathy are other hallmarks of B12 problems.

12. Which vitamin deficiencies have cheilosis/stomatitis as a characteristic, and how are they distinguished from one another?

Riboflavin and pyridoxine vitamin deficiencies would have cheilosis/stomatitis as a characteristic. Riboflavin deficiency would also have magenta-colored or cracked tongue. Pyridoxine deficiency would also have sideroblastic anemia and microcytic anemia.

13. Which vitamin deficiencies have homocysteinemia as a characteristic? How are these vitamin deficiencies that have homocysteinemia distinguished from one another based on blood value information?

Vitamin B6: homocysteinemia + increased methionine
Folate: homocysteinemia + decreased methionine
Vitamin B12: homocysteinemia + decreased methionine + methylmalonic acidemia

14. Explain the difference between dry beriberi, wet beriberi, and Wernicke-Korsakoff syndrome.

Dry beri-beri: polyneuritis, muscle wasting
Wet beri-beri: high cardiac output, peripheral edema

Wernicke's: ataxia, nystagmus, ophthalmoplegia
Korsakoff's: psychosis, confabulation

15. What is sideroblastic anemia and how is it caused?

Sideroblastic anemia is the accumulation of iron in mitochondria. If there is a defect in heme synthesis, then iron will accumulate in mitochondria because this is location where iron is normally inserted into protoporphyrin by ferrochelatase.

16. The administration of which drugs can cause which water-soluble vitamins to become deficient?

Isoniazid therapy for TB treatment can interfere with vitamin B6 absorption and function.

17. Newborns undergoing phototherapy treatment are prone to deficiency of the water-soluble vitamin _*riboflavin*_. Explain in biochemical terms why frequent ingestion of raw eggs might cause a person to be prone to a deficiency of one of the water-soluble vitamins.

Egg whites have avidin, a protein which binds very tightly to biotin and prevents its absorption.

18. The various features of the fat-soluble vitamins are shown below. Complete the table by filling in the empty cells.

Vitamin	Active Form	One Main Function	One Hallmark of Deficiency	One Hallmark of Toxicity
Vitamin A	Retinol; retinoic acid cis-Retinal	*Gene expression* *Vision*	*Night Blindness*	*Teratogenic effects*
Vitamin D	*Calcitriol*	Increase blood calcium	*Rickets* *Osteomalacia*	*Hypercalcemia*
Vitamin K	Vitamin K as is	*Gamma-Carboxylation*	*Increased coagulation time*	Hemolytic anemia
Vitamin E	Vitamin E as is	*Anti-oxidant*	*Hemolysis and neuropathy*	Mild bleeding when administered warfarin

19. *Heparin* is a highly negatively charged substance which is an anti-coagulant and functions to activate anti-thrombin III.

20. In contrast to most water-soluble vitamins, why is a true deficiency of the fat-soluble vitamins rarely seen in normal adults?

Fat-soluble vitamins can be stored while water-soluble vitamins are not (except vitamin B_{12})

21. In the presence of warfarin, the K_m of vitamin K for its enzyme would be expected to (increase,) decrease, or be unchanged (*circle one*).

22. What are 2 reasons why newborns are prone to vitamin K deficiency?

Lack of bacterial flora to synthesize vitamin K
Vitamin K is not stored in fetal liver
Vitamin K does not easily cross the placental barrier

23. The primary event in photoreception is the light-dependent conversion of *11 cis-retinal* bound to rhodopsin to the *trans* isomer. This results in the dissociation of this isomer from rhodopsin. The consequence is a confirmation change which activates the *GTP→GDP* exchange activity of the α_t subunit of the protein called *Transducin*, which is then released, causing activation of the enzyme phosphodiesterase that cleaves *cGMP*.

TOPIC 6: OVERVIEW OF ENERGY AND CARBOHYDRATE METABOLISM

1. The various features of the major glucose transporters are shown below. Complete the table by filling in the empty cells.

Name	Tissues	Km Glucose	Functions
GLUT1	*Most tissues*	1 mM	*Basal uptake of Glc*
GLUT2	*Liver* *Pancreatic beta-cells*	15 mM	*Uptake and release of Glc liver and glucose sensor in beta-cell*
GLUT3	*Most tissues*	1 mM	*Basal uptake of Glc*
GLUT4	*Skeletal muscle* *Adipose tissue*	5 mM	*Insulin-stimulated Glc uptake; exercise in muscle*

2. Which of the following metabolites (letters A – I) correctly answers each of the statements below (1–5) concerning muscle energy metabolism?

   (A) Phosphocreatine
   (B) Creatinine
   (C) ADP
   (D) Glycogen
   (E) Phosphoenolpyruvate
   (F) Fructose 1,6-biphosphate
   (G) Lactic acid
   (H) Glucose
   (I) Fatty acids

   1. This material acts as an energy source during the first 3–5 seconds of strenuous activity in an anaerobic fast twitch fiber (type II). A
   2. This is the primary energy source for cardiac muscle. I
   3. This non-enzymatic reaction product is a useful indicator of kidney function. B
   4. This is the highest energy compound in the cell. E
   5. Metabolism of this energy source is linked to muscle contraction by Ca^{2+} regulation. D

3. A transporter has a Km for glucose of 15 mM and a Vmax of 12 mM glucose/sec/mg of transporter. If the glucose concentration in peripheral blood is 5 mM, the rate of glucose transport (in mM glucose/sec/mg of transporter) will be 3mmols/sec/mg.

4. A 24-year-old student represents his college in a marathon race. Energy required for him to run this distance at the fastest speed possible would be obtained from the 5 metabolic resources listed below.

   (1) Glycogenolysis

   (2) Gluconeogenesis

   (3) Creatine phosphate

   (4) Lipolysis

   (5) ATP stores

   Which of the following best represents the most probable sequence in which these energy stores are utilized?

   (A) 1-2-3-4-5

   (B) 4-1-3-2-5

   (C) 5-1-4-2-3

   (D) 5-2-3-1-4

   (E) 5-3-1-2-4

5. A 25-year-old man decides to pursue a strict workout regimen with an athletic trainer. The trainer recommends several dietary supplements, including carnitine, which would help him increase his muscle mass. In which situation would carnitine be most important to skeletal muscle during exercise?

   (A) Four attempts to bench press a 200-pound weight

   (B) Performing 45 pushups

   (C) Completing a 50-mile bicycle race

   (D) Jogging on the treadmill for 15 minutes

   (E) Running 2.5 miles

6. The oxidation of 1 mole of glucose by anaerobic glycolysis yields a net of:

   (A) 2 moles of pyruvate and 2 moles of ATP
   (B) 2 moles of pyruvate, 2 moles of NADH, and 2 moles of ATP
   (C) 2 moles of lactate and 2 moles of ATP
   (D) 2 moles of lactate, 2 moles of NADH, and 2 moles of ATP
   (E) 2 moles of lactate, 2 moles of NAD, and 2 moles of ATP

7. An Olympic runner participates in a 200-meter race. During the race, it is estimated that only 0.5 liter of oxygen will be consumed by the runner. However, more than 10 liters of oxygen would be consumed if the metabolism in this interval were entirely aerobic. The majority of ATP generated during this 200-meter race is derived from which of the following?

   (A) Lipolysis
   (B) Glycolysis
   (C) Glycogenesis to glucose
   (D) Creatine phosphate
   (E) ATP stores
   (F) β-oxidation of fatty acids
   (G) Krebs cycle
   (H) Oxidation phosphorylation

8. A genetic deficiency of glucose-6-phosphatase would be expected to produce which of the following laboratory values?

	Serum Glc	Serum Lactate	Serum Pyruvate
(A)	high	high	high
(B)	high	low	low
(C)	high	normal	normal
(D)	low	high	high
(E)	low	low	low
(F)	low	normal	normal

9. A man presents to the emergency department after ingesting an insecticide. His respiration rate is very low. Information from the Poison Control Center indicates that this particular insecticide binds to and completely inhibits cytochrome (C) Explain concisely whether the rate of CO_2 production in this patient would be increased, decreased, or remain the same.

   Would decrease because electrons would no longer flow through the ETC. NADH would not be regenerated adequately. Therefore, catabolic reactions would decrease, resulting in decreased CO2.

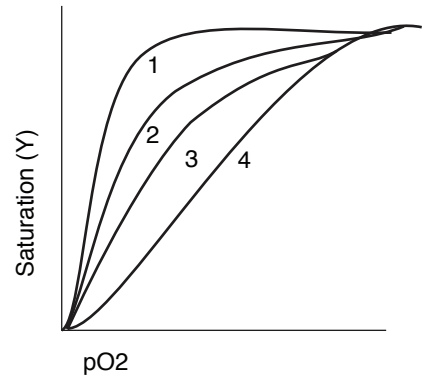
10. Explain how a person exposed to excessive amounts of CO could present with a fever.

    No fever. CO inhibits action of complex IV and therefore, the ETC would cease. No heat loss.

11. A 2-year-old girl has chronic anemia, jaundice, and a moderate increase in indirect bilirubin. Her spleen is slightly enlarged and her hemoglobin level is below normal. Hemoglobin electrophoresis shows the majority is normal adult type (AA), but an abnormally high percentage is saturated with 2,3-bisphosphoglycerate. Red blood cell morphology is normal, though red cell enzyme assays reveal a severe deficiency of a single enzyme, which is likely to be *Pyruvate kinase*. Explain in biochemical terms what Heinz bodies are and whether they would be likely to be seen in this patient.

    Heinz bodies are crosslinked Hb which precipitates caused by free radical (H_2O_2) oxidation and -SH groups. Patients would not have Heinz bodies since NADPH is being made properly. Nothing wrong with G6PD.

12. Several oxygen dissociation curves are shown in the graph below. Assuming that curve 3 corresponds to isolated hemoglobin placed in a solution containing physiological concentrations of CO_2 and 2,3-bisphosphoglycerate at pH 7.0, indicate (by number) which curve reflects the following changes in conditions.



(A) Decreased CO_2 concentration ___2___

(B) Increased 2,3-bisphosphoglycerate concentration ___4___

(C) Increased pH ___2___

(D) Dissociation of hemoglobin into subunits ___1___

13. Under normal conditions, the rate-controlling factor in mitochondrial electron transport is the availability of ___ADP___. Under severe exercise conditions, the rate-controlling factor in mitochondrial electron transport is the availability of ___oxygen___.

14. A medical student works on a farm during his summer break to earn extra money for tuition. His job is to spray tobacco plants with the chemical rotenone. He decides not to wear a mask. Consequently, he becomes sick and has convulsions, yet he recovers. Concisely explain whether the student would be expected to develop a fever during his illness.

Rotenone inhibits complex I and therefore electron flow ceases. No electron flow → no heat.

Concisely explain whether the student would have benefited from an I.V. solution of ATP during his convulsions.

ATP cannot enter cells (no transporter) → no benefit.

15. The various features of the major glycogen storage diseases are shown below. Complete the table by filling in the empty cells.

Name	Deficient Enzyme	Clinical Hallmark	Glycogen Structure
von Gierke	*Glc-6-phosphatase*	*Severe Hypoglycemia* *Hepatomegaly*	Normal
Pompe	*Lysosomal* *1,4-glucosidase*	*Cardiomegaly*	Glycogen-like material in inclusions
Cori	*Debranching* *Enzyme*	Mild hypoglycemia Hepatomegaly	*Single Glc residues at the branch points*
Andersen	*Branching enzyme*	Infantile hypotonia Cirrhosis	*Mostly linear glycogen*
McArdle	*Muscle* *Phosphorylase*	*Muscle weakness on exercise*	*Normal*
Hers	*Hepatic Phosphorylase*	*Mild hypoglycemia* *Hepatomegaly*	*Normal*

16. The sensitivity of Asians (particularly those from the Pacific Rim) to alcohol has an enzymatic basis. In Asians, the ingestion of ethanol results in rapid build-up of the intoxicant acetaldehyde; compared to non-Asians, their plasma concentration of acetaldehyde rises higher and remains elevated for a longer period of time. The first 2 steps in ethanol metabolism are: ethanol → acetaldehyde → acetate (each step requiring NAD+).

    - If the Vmax values of the 2 enzymes catalyzing the reactions are the same in Asians as in non-Asians, the Km of alcohol dehydrogenase of Asians must be higher/(lower)/the same (*circle one*) than that of non-Asians, and the Km of acetaldehyde dehydrogenase (converts acetaldehyde to acetate) of Asians should be (higher)/lower/the same (*circle one*) than that of non-Asians.

    - Conversely, if the Km values of the 2 enzymes are the same in Asians as in non-Asians, the Vmax of alcohol dehydrogenase of Asians must be (higher)/lower/the same (*circle one*) than that of non-Asians, and the Vmax of acetaldehyde dehydrogenase of Asians should be higher/(lower)/the same (*circle one*) than that of non-Asians.

TOPIC 7: LIPID METABOLISM

1. The various features of the major lipoproteins are shown below. Complete the table by filling in the empty cells.

Lipoprotein	Main Lipids	Main Proteins	Main Characteristics
Chylomicrons	TGs and cholesterol esters	*Apo B-48* *Apo C-II* *Apo E*	*Involved in the transport of dietary lipid from intestine to other organs*
Chylomicron remnants	*Cholesterol esters*	*Apo B-48* *Apo E*	*Involved in the transport of dietary lipid from intestine to other organs*
VLDL	*TGs and cholesterol*	*Apo B-100* *Apo C-II* *Apo E*	*Involved in the transport of liver lipids to other organs*
IDL	Cholesterol and cholesterol esters	*Apo B-100* *Apo E*	Intermediate particle in conversion of VLDL to LDL
LDL	*Cholesterol esters*	*Apo B-100*	*Delivers cholesterol to cells*
HDL	Relatively small amounts of cholesterol and cholesterol esters	*Apo A-1*	*Scavenges cholesterol* *Activates LCAT*

2. How is the metabolism of glucose by the hexose monophosphate shunt related to cholesterol synthesis?

HMS provides the NADPH required by HMG CoA reductase

3. Adipose cells manufacture triglycerides in the fed state and break triglycerides in the fasting state. In the fasting state, why are the triglycerides that are broken down not re-synthesized into triglycerides by adipose cells?

Glycerol 3 phosphate is required for the synthesis of TGs. In fasting, TGs are cleaved to 3FA and glycerol. Adipose cells contain no glycerol kinase. In adipose tissue, glycerol 3P is made by reduction of DHAP from glycolysis. But in fasting the entry of Glc (via GLUT4) and glycolysis are low.

4. Insulin is released after carbohydrate intake and is involved in recruiting glucose transporters to the surface of target cells. Describe 4 ways in which insulin biochemically acts to influence lipid metabolism after glucose uptake in adipocytes and in the liver.

A. *Increase glucokinase and PFK-2 in liver. Glc converts to Pyr to AcCoA. The AcCoA are the building blocks for FA synthesis*
B. *Decrease HSL in adipocytes, therefore TG will not be mobilized*
C. *Increase HMG CoA reductase levels at the gene level. More cholesterol will be made*
D. *Increase HMG CoA reductase by dephosphorylation mechanism to promote cholesterol synthesis.*

5. Which of the following items directly regulate the activity of acetyl-CoA carboxylase? More than one answer is possible.

(A) Acetyl-CoA
(B) ATP
(C) AMP
(D) Coenzyme A
(E) NADH
(F) Palmitate
(G) Citrate
(H) Phosphorylation by protein kinase A
(I) All of the above
(J) None of the above

6. Which of the following items would be found as an important component of VLDL? More than one answer is possible.

(A) Cholesterol
(B) Cholesterol ester
(C) LCAT
(D) Apo A
(E) Apo B48
(F) Apo C
(G) Apo E
(H) TG
(I) Free fatty acid
(J) Retinol
(K) Lipoprotein lipase
(L) Bile acid
(M) All of the above
(N) None of the above

7. Defects in lipoprotein lipase predispose people to pancreatitis. If lipoprotein lipase deficiency is diagnosed early, the ill effects can be controlled.

In the presence of lipoprotein lipase deficiency, chylomicrons and VLDL levels are greatly increased in the blood. From where do these lipoprotein complexes normally come? What therapeutic strategies would be suggested for controlling chylomicron and VLDL levels?

Chlyomicrons are produced by intestinal cells from dietary fat whereas VLDLs are assembled in liver synthesizing TG from glucose.

[Chylomicron] can be lowered by ↓ fat intake

[VLDL] can be lowered by eating frequent small meals (good glucose control)

Why are ascorbic acid and vitamin E particularly important with this condition?

Lipids are sensitive to free radical oxidation. The high concentration of lipids in blood of these patients makes this a particularly severe problem. Ascorbate and vitamin E are free radical scavengers and lessen the damage of lipids by oxidation.

Which of the following is true about lipoprotein lipase? More than one answer is possible.

(A) Present on the plasma membrane of adipocytes
(B) Present on the plasma membrane of endothelial cells that line adipocytes
(C) Activated by apo A
(D) Inhibited by heparin
(E) Involved in the conversion of LDL to IDL
(F) Activated by protein kinase A
(G) Synthesized by the liver

8. Concisely explain how the scavenger receptor in macrophages contributes to the process of atherosclerosis.

LDL→ oxidized LDL (cannot be taken up by LDL receptor)

Scavenger receptor B1 takes up oxidized LDL and is not down-regulated by cholesterol. Therefore macrophages get bloated and converted to foam cells which eventually die, spilling their cholesterol contents.

9. A 17-year-old girl consults her physician because of intermittent abdominal distress. The discomfort usually follows the ingestion of a large meal, often one containing greasy or fried foods, and is accompanied by a feeling of bloating. Analysis of her stool reveals a lot of triglycerides and very little fatty acid. A diagnosis of secretion defect in pancreatic juice is made. Concisely explain whether you would support this diagnosis and/or whether there is an alternative diagnosis.

Yes, the current diagnosis is possible since pancreatic juice has both pancreatic lipase and colipase that are needed to degrade TG. But problem could also be due to blockage of bile duct not allowing bile to be secreted for emulsification purposes.

10. The various features of the major hyperlipidemias are shown below. Complete the table by filling in the empty cells.

Type	Primary Defect	Accumulating Lipid in Blood	Accumulating Lipoprotein	Hallmarks
I	*LPL* *Apo C-II*	*TG*	*Chylomicrons* *VLDL*	*Red-orange eruptive xanthomas*
IIa	*LDL receptor*	*Cholesterol*	*LDL*	*Xanthomas of Achilles tendon;* *Corneal arcus*
III	*Apo E*	*Cholesterol*	*Chylomicrons* *VLDL*	Xanthomas; atherosclerosis
IV	*Overproduction of VLDL*	*TG*	*VLDL*	TG-induced pancreatitis

11. When large amounts of fatty acids are undergoing beta-oxidation in the liver in the fasting state, how is the simultaneous oxidation of glucose via glycolysis prevented?

Beta-oxidation of FA generates large amounts of ATP which inhibits PFK-1.

12. A 10-year-old boy goes hiking with his father and has a prolonged episode of nausea and diarrhea after drinking unfiltered water from a stream. He is unable to eat for 2 days. They begin the long hike back to their car, but after a few miles the boy experiences extreme muscle weakness and cramping. By the time they reach the car he can no longer walk on his own. A subsequent medical exam reveals a genetic deficiency as the cause of the boy's muscle weakness. Circle the one protein that is most likely to be the problem.

(A) Carnitine acyl transferase
(B) Glucose-6-phosphatase
(C) Muscle glycogen phosphorylase
(D) Debranching enzyme
(E) Glucose-6-phosphate dehydrogenase
(F) Branching enzyme
(G) Glucagon
(H) Glucagon receptor
(I) Hepatic glycogen phosphorylase

13. A 44-year-old alcoholic man is brought to the emergency department in a coma following a severe drinking episode. He is somewhat emaciated but has a protuberant abdomen. His urine is weakly positive for ketones by dipstick, but β-hydroxybutyrate levels in his blood and urine are very high. Blood glucose is 56 mg/dl. Biochemically explain why β-hydroxybutyrate is high in the urine but ketones are only slightly elevated.

↑$CH_3CH_2OH \rightarrow CH_3CHO \rightarrow CH_3COOH$
↑*NADH will reduce acetoacetate to* β*-OH butyrate*

14. Predict whether the following substances would lead to an increase, decrease, or no change in the serum level of free fatty acids if they were infused into a person.

    (A) Epinephrine ↑

    (B) Heparin ↑

    (C) Prostaglandin E ↓

    (D) cAMP no change

    (E) 10 mM glucose ↓ (↑insulin)

    (F) Ethanol ↑ (↑lipolytic hormones)

    (G) Methylxanthine ↑

    (H) Hormone-sensitive lipase no change

15. In the first several days of starvation, the primary source of energy (ATP) to sustain muscle function is derived from the metabolic pathway β-oxidation (KB-oxidation as well). Under conditions of severe starvation, the primary source of energy (ATP) to sustain red blood cell function is derived from the metabolic pathway glycolysis. Under conditions of severe starvation, the primary source of energy (ATP) to sustain liver function is derived from the specific metabolic pathway β-oxidation.

16. An unidentified 40-year-old man is brought to the emergency department in a coma. He is somewhat emaciated and has an enlarged abdomen. Laboratory tests indicate a metabolic acidosis with elevated blood lactate. His urine is weakly positive for ketones by dipstick, but β-hydroxybutyrate levels in his blood and urine are extremely high. Blood glucose is 60 mg/dL. What is the most likely diagnosis?

    (A) Alcoholic coma

    (B) Exercise-related hypoglycemia in a type 1 diabetic

    (C) Type 2 diabetes

    (D) Hypoglycemia associated with medium-chain acyl CoA dehydrogenase (MCAD) deficiency

    (E) Insulin overdose

17. The various features of the major sphingolipidoses are shown below. Complete the table by filling in the empty cells.

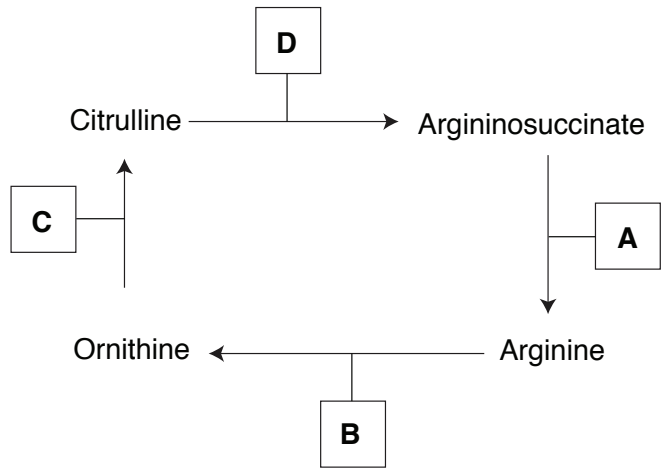
Name	Defective Enzyme	Accumulating Substrate	2 Major Hallmarks
Tay-Sachs	*Hexosaminidase A*	*GM2 ganglioside*	*Cherry red spot on macula* *Psychomotor retardation*
Gaucher's	*Glucocerebrosidase*	*Glucocerebroside*	*Crumpled paper inclusions* *Hapatosplenomegaly*
Niemann-Pick	*Sphingomyelinase*	*Sphingomeylin*	*Cherry red spot on macula* *Foamy macrophages*
Fabry's	*-Galactosidase*	Ceramide trihexoside	*Angiokeratomas* *Peripheral neuropathy*
Krabbe	*Galactocerebrosidase*	*Galactocerebroside*	Globoid cells Peripheral neuropathy
Metachromatic leukodystrophy	*Arylsulfatase A*	*Cerebroside sulfate*	Demyelination with ataxia Dementia

18. The various features of the 2 most important mucopolysaccharidoses are shown below. Complete the table by filling in the empty cells.

Name	Defective Enzyme	Accumulating Substrate	Major Hallmark
Hurler's	α-*L-iduronidase*	*Heparan sulfate* *Dermatan sulfate*	*Corneal Clouding*
Hunter's	*Iduronate sulfatase*	*Heparan sulfate* *Dermatan sulfate*	*No Corneal Clouding*

TOPIC 8: AMINO ACID METABOLISM

1. The diagram below shows the hepatic cycle that captures ammonia and detoxifies it. Boxes A through D represent substances or enzymes either entering or leaving the cycle. Which substance or enzyme best represents each of the boxes?



(A) *Fumarate*

(B) *Urea*

(C) *Ornithine transcarbamoylase*

(D) *Aspartate*

2. The definition of BUN is *The measurement of urea in blood*. A low BUN value would indicate that the organ *liver* is malfunctioning, whereas a high BUN indicates the organ *kidney* is malfunctioning.

3. How is carbamoyl phosphate synthetase I deficiency distinguished from ornithine carbamoyltransferase deficiency?

   Orotic aciduria would be indicative of OTC deficiency because its substrate carbamoyl phosphate would accumulate and spill into the cytoplasm and enter pyrimidine synthesis forming orotic acid.

4. Shown are the various features of the major genetic disorders associated with amino acids. Complete the table by filling in the empty cells.

Name	Amino acid(s) involved	Defective Protein	Coenzyme/ cofactors needed	Clinical Hallmarks
PKU	Phe	*Phe hydroxylase*	*Tetrahydrobiopterin*	*Mental retardation* *Microcephaly* *Musty odor*
Albinism	Tyr	*Tyrosinase*	copper	*Hypo-pigmentation*
Alcaptonuria	Tyr	*Hemogentisate oxidase*	iron	*Dark urine* *Ochronosis*
Maple Syrup Urine Disease	*Ile, Leu, Val*	*Branched chain ketoacid dehydrogenase*	*Thiamine-PP, lipoic acid, coenzyme A, FAD, NAD*	*Mental retardation* *Maple syrup odor of urine*
Isovaleric Aciduria	Leu	Isovaleryl CoA dehydrogenase	FAD	*Sweaty feet odor*
Cystinuria	*Cys (basic aa)*	*Basic amino acid transporter*	none	*Cystine crystals*
Hartnup Disease	*Trp (large aa)*	*Large neutral amino acid transporter*	none	*Pellagra-like symptoms*
Cystathioninuria	Met	*Cystathionase*	Pyridoxal-P	Benign
Homocystinuria	Met	*Cystathionine β-synthase*	*Pyridoxal-P*	*Deep vein thrombosis* *Dislocated lenses* *Stroke*

5. In catecholamine synthesis, tyrosine is converted to dopa by the enzyme _tyrosine hydroxylase_, which uses _THB_ as a coenzyme. Dopa is converted by the enzyme _DOPA decarboxylase_ to dopamine by using the coenzyme _pyridoxal-P_. Dopamine is converted to norepinephrine by the enzyme _dopamine b-hydroxylase_, which uses _vitamin C_ and _copper_ as coenzymes/cofactors. Norepinephrine is converted to _epinephrine_ by the enzyme phenylethanolamine N-methyltransferase using _S-adenosylmethionine_ as a substrate.

6. In the treatment of Parkinson's disease, why are carbidopa and levodopa often administered together?

   Parkinson's disease involves the loss of dopaminergic neurons in the substantia nigra. While dopamine cannot cross the blood brain barrier, levodopa does cross but is converted relatively quickly to dopamine prior to reaching the barrier. Carbidopa does not cross the barrier and increases the levodopa effect by inhibiting peripheral metabolism of levodopa.

7. _Pheochromocytoma_ is a tumor of the adrenal gland characterized by excessive synthesis of the catecholamines, resulting in hypertension and weight loss.

8. Lead affects heme synthesis by affecting the enzyme _ferrochelatase_, which is located in the _mitochondrial matrix_ of a cell (*be specific*). The effect of lead on the Km of the substrate for this enzyme is (increased)/decreased/unchanged (*circle one*), and the effect of lead on the Vmax of this enzyme is increased/(decreased)/unchanged (*circle one*). Lead poisoning results in an accumulation of a substance that can be used diagnostically and this substance is _Zn protoporphyrin IX_.

9. Briefly discuss the biochemical rationale for the most common treatment of lead poisoning.

   Chelators would bind to Pb and the lead chelator complex would eventually be eliminated in urine.

10. The decision to fortify a widely consumed food with an essential nutrient is often politically and medically controversial. For each of the following proposed fortifications, state 1 medical reason in favor of it and 1 medical reason against.

    Fortification of flour with iron:

    Pro: *Anemia due to deficiency of iron is a common problem*

    Con: *Hemochromatosis is a common problem*

    Fortification of flour with folate:

    Pro: *↑folate intake → ↓neural tube defects and ↓megaloblastic anemia*

    Con: *↑folate intake can mask anemias cause by B12 deficiency*

11. Bacterial gut flora produce a number of reactions that have a direct bearing on human metabolism. Concisely describe the action of the flora in the following types of metabolism (state "none" if flora have no action).

    a. Metabolism of a specific water-soluble vitamin

       They synthesize B12 and biotin

    b. Metabolism of a specific fat-soluble vitamin

       They synthesize vitamin K

    c. Bile acid metabolism

       They deconjugate glyco- and tauro- containing bile acids (remove glycine and taurine)

    d. Cholesterol digestion

       None

    e. Carbohydrate digestion

       Cellulose and other fibers are partially digested → bloating, flatulence

    f. Bilirubin metabolism

       They deconjugate bilirubin diglucuronide and they reduce bilirubin to urobilinogens

12. A 13-year-old boy playing baseball slid into home plate, sustaining a large bruise on his thigh. The bruise was initially dark red, but at the hospital where x-rays were found to be negative for fracture, the bruise turned dark blue-green. After a few days the parents bring the boy back for evaluation, concerned that the affected area is now yellow-orange. The physician reassures them and explains the events leading to the color change of the bruise in lay terms. Concisely explain the events in biochemical terms.

Heme (red) → Biliverdin (green) → Bilirubin (orange)

13. A 2-year-old girl is taken to a pediatric clinic because of persistent anemia and failure to thrive. Laboratory analysis reveals extremely low vitamin B6 levels. Would the anemia be expected to be pernicious, hemolytic, megaloblastic, or microcytic (*circle one*)? Concisely explain the biochemical relationship between the kind of anemia present and the vitamin B6 deficiency.

Vitamin B6 → pyridoxal-P coenzyme

The pyr-P is used by ALA synthase to convert ALA → heme. If defect in B6 → cannot make heme → decrease size of RBC

TOPIC 9: PURINES AND PYRIMIDINES

1. Several major enzymes involved in pyrimidine synthesis are shown below. List a drug that is used to inhibit the respective enzyme.

Enzyme	Drug
Ribonucleotide reductase	*Hydroxyurea*
Thymidylate synthase	*5-Fluorouracil*
Dihydrofolate reductase (in cancer cells)	*Methotrexate*
Dihydrofolate reductase (in microbial cells)	*Trimethoprim*
Dihydrofolate reductase (in parasitic cells)	*Pyrimethamine*

2. Patients with gout often develop inflammation in the joints. What is the enzyme that is deficient that contributes to gout?

Hypoxanthine-Guanine phosphoribosyl transferase (HGPRT)

A deficiency in this enzyme results in the immediate buildup of which 2 compounds?

Hypoxanthine and Guanine Specifically, what happens when these 2 compounds build up?

An increase in Hypoxanthine and Guanine results in conversion to xanthine and then urate. A build-up of urate results in the precipitation of sodium urate crystals in the joints and inflammation.

What therapy is typically used for the treatment for chronic gout and why?

Allopurinol

This compound acts as a noncompetitive, suicide inhibitor of the enzyme xanthine oxidase. This would prevent the conversion of hypoxanthine and guanine to xanthine and urate and reduce sodium urate crystal deposition.

CHAPTER 2

PHARMACOLOGY

TOPIC 1: PHARMACODYNAMICS AND PHARMACOKINETICS

1. What is the equation for volume of distribution?

   VD = Dose/C

2. Drugs with a low V_d are found in the _____*plasma*_____, whereas drugs with a high V_d are found in _____*tissues*_____.

3. A new drug is found experimentally to have an apparent V_d of 2000 L in a 70-kg adult. What is your interpretation of these data?

   The drug is sequestered in tissues

4. Would hemodialysis be an effective way to eliminate this drug on overdose?

   No, hemodialysis is most effective for drugs with a low Vd

5. For a drug that is not secreted or reabsorbed, how would you interpret a finding that this drug's clearance is <GFR? _____*= drug is being reabsorbed*_____

   is >GFR? _____*= drug is actively secreted*_____

6. For a drug with a t½ (half-life) of 3 hours given by constant IV infusion, how long will it take for this drug to reach 75% of steady state?

   Two t½s or 6 hours

7. Complete the table below to compare loading dose (LD) with maintenance dose (MD).

	LD or MD
Must know clearance to calculate	*MD*
Must know volume of distribution to calculate	*LD*
Usually administered as a single bolus	*LD*
Most useful in emergency situations	*LD*
Given to achieve steady-state plasma levels over time	*MD*

8. Identify the 3 drugs whose elimination represents a constant amount over time when given at high therapeutic or toxic levels.

   Phenytoin, ethanol, aspirin are all eliminated by zero order kinetics at high doses

9. Complete the diagram below for drugs that are weak acids or weak bases.

Weak Acid	R-COOH $\rightleftharpoons$ $R\text{-}COO^- + H^+$ (*crosses membrane*) (better cleared)
Weak Base	RNH_3^+ $\rightleftharpoons$ $RNH_2 + H^+$ (better cleared) (*crosses membrane*)

10. Drug #1 is a weak acid with a pK_a of 4. Drug #2 is a weak base with a pK_a of 8. When placed at the given pH, complete the following table.

	pH	Mostly Ionized (I) or Nonionized (N)	Easily Crosses Membranes? Yes (Y) or No (N)
Drug #1	7.4	*I*	*N*
Drug #2	7.4	*I*	*N*
Drug #1	2	*N*	*Y*
Drug #2	9	*N*	*Y*

11. Complete the table below using acetylation, glucuronidation, or oxidation.

Statement	Type of Metabolism
Reduced activity in neonates	*Glucuronidation*
Cytochrome P-450 metabolism	*Oxidation*
Genotypic variation may cause SLE	*Acetylation*
Metabolism of chloramphenicol	*Glucuronidation*
Metabolism of hydralazine	*Acetylation*

12. P-450 inducer or inhibitor?

	Inducer or Inhibitor
Phenytoin	*Inducer*
Erythromycin	*Inhibitor*
Grapefruit juice	*Inhibitor*
Phenobarbital	*Inducer*
Cimetidine	*Inhibitor*
Ritonavir	*Inhibitor*

13. When given to a patient already receiving a full agonist, what effect will a competitive antagonist have on potency?

    Decrease potency

    Effect on efficacy?

    No effect on efficacy

14. When given to a patient already receiving a full agonist, what effect will a noncompetitive antagonist have on potency?

    No effect on potency

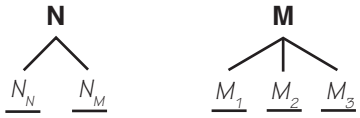
    Effect on efficacy?

    Decrease efficacy

15. The most dangerous drugs have a _____*lower*_____ TI, whereas safer drugs have a _____*higher*_____ TI.

TOPIC 2: SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEMS

1. Complete the flowchart below for nicotinic (N) and muscarinic (M) receptor types:



2. Identify the G-protein coupling for each receptor below using G_s, G_i, or G_q.

Receptor	G-protein
M_1	G_q
a_1	G_q
D_1	G_s
β_1	G_s
a_2	G_i
b_2	G_s
D_2	G_i
M_2	G_i
M_3	G_q

3. Identify the drug or drug class.

Statement	Drug
Blocks release of ACh	*Botulinum toxin*
Increases t½ of ACh	*ACh-ase inhibitors*
Destroys adrenergic nerve terminals	*Reserpine*
Promotes NE release from adrenergic nerves	*Amphetamines*
Stimulates negative feedback receptors on adrenergic nerves	*α_2 agonists*

4. Identify the primary use of each drug below.

Drug	Use
Bethanechol	*Ileus, urine retention*
Edrophonium	*Dx myasthenia gravis*
Dobutamine	*Acute CHF*
Esmolol	*Acute SVTs*
Pilocarpine	*Glaucoma, xerostomia*
Pyridostigmine	*Tx of myasthenia gravis*
Albuterol	*Asthma, COPD*
Tropicamide	*Dilated eye exams*

5. Identify the antidote for each drug.

Drug	Antidote
M agonist	*M antagonist (atropine)*
M antagonist	*ACh-ase inhibitor (physostigmine)*
Irreversible AChE inhibitor	*Atropine + pralidoxime (2-pam)*
β-blocker	*Glucagon*
Phenylephrine	α_1 *antagonist*

6. Match the drug with its action and corresponding receptor.

Drug	Action (Agonist, Antagonist)	Receptor(s)
Prazosin	Antagonist	α_1
Atenolol	Antagonist	β_1
Methacholine	Agonist	*M*
Albuterol	Agonist	β_2
Epinephrine	Agonist	$\alpha_1, \alpha_2, \beta_1, \beta_2$
Scopolamine	Antagonist	*M*
Phenoxybenzamine	Antagonist	α_1, α_2
Propranolol	Antagonist	β_1, β_2
Clonidine	Agonist	α_2

TOPIC 3: TOXICOLOGY AND ADVERSE EFFECTS OF MEDICATIONS

1. Complete the table below.

Drug or Poison	Antidote
Acetaminophen	*N*-acetyl cysteine
Aspirin	*Bicarbonate*
Iron	*Deferoxamine*
Methemoglobin	Methylene blue
Opioids	*Naloxone*
Methanol, Ethylene glycol	Fomepizole
Heparin	*Protamine*
Warfarin (rapid reversal)	*Fresh frozen plasma*
Benzodiazepines	Flumazenil

2. Complete the table below for the alcohols and their metabolism.

Alcohol	Aldehyde	Acid
Ethanol	*Acetaldehyde*	*Acetic Acid*
Ethylene glycol	*Glycoaldehyde*	*Glycolic, oxalic acid*
Methanol	*Formaldehyde*	*Formic Acid*

3. Match the alcohol with its side effect.

Alcohol	Side Effect
Methanol	Ocular damage
Ethylene glycol	Nephrotoxicity
Ethanol	Nausea, vomiting, headache

4. What enzyme is inhibited by the drug disulfiram?

   Acetaldehyde dehydrogenase

5. What substance accumulates as a result of drinking alcohol at the same time disulfiram is used?

   Acetaldehyde

CHAPTER 3

IMMUNOLOGY, HEMATOLOGY, AND ONCOLOGY

TOPIC 1: BLOOD CELLS AND LYMPHOID STRUCTURES

1. Fill in the table below for each of the white blood cells.

Cell Type	Identification (CD Marker and/or Description)		Function	
Neutrophil	*Multilobed nucleus, pink granules*		*Phagocytosis*	
Monocyte	*Horseshoe shaped nucleus, CD14*		*Phagocytosis*	
Macrophage	*CD14*		*Phagocytosis*	
Eosinophils	*Bilobed nucleus, pink (eosinophilic) granules*		*Killing Ab coated parasites*	
Basophil	*Bilobed nucleus, Purple (basophilic) granules*		*Type I HS reaction*	
Mast cell	*Small nucleus, purple granules*		*Type I HS reaction*	
Dendritic cell	*Long cytoplasmic arms*		*Antigen processing/presentation*	
Lymphocytes	**B cells**	**T cells**	**B cells**	**T cells**
	IgM and IgD, CD19, CD20, CD21	*CD3+CD4 or CD3+Cd8*	*Ab production*	*Cell mediated immunity*
Plasma cells	*IgG, or IgA or IgE and CD19, CD20 and CD21, eccentric nucleus*		*Secretion of antibodies*	

2. Fill in the table below for each description of the lymph node anatomy.

Description	Lymph Node Structure
Plasma cells and memory region	*Medulla*
T cell-rich region	*Paracortex*
B cell-rich region	*Cortex*
B cell activation occurs here	*Germinal center*
Antigens enter the lymph node	*Afferent lymphatic*
Activated and memory cells leave the lymph node	*Efferent lymphatic*

3. Name the site where naïve B cells and T cells enter the lymph nodes.
   High endothelial venules (HEV's)

4. Name the T cell-rich region of the spleen.
   Periarteriolar lymphoid sheath (PALS)

5. Name the B cell-rich region of the spleen.
   Marginal zones

6. A patient with asplenia would have an increased risk of infection from which types of organisms?
   encapsulated bacteria

7. List 3 signs of asplenia.
   Howell-Jolley Bodies, thrombocytosis, target cells

8. For each description below, list a "C" if it occurs or is found in the thymic cortex or an "M" if it occurs or is found in the thymic medulla.

Description	Region of Thymus
Immature T cells are found here	*C*
Mature T cells are found here	*M*
T cell selection occurs here	*C*

9. For the different stages of T cell development, place a "+," if the stage has a marker listed and a "–" if it does not.

Stage of Development	CD3	CD4	CD8	T Cell Receptor
Pre-thymic (pro-T cells)	–	–	–	–
Immature T cells found in the cortex	+	+	+	+
Mature T_H cells	+	+	–	+
Mature T_C cells	+	–	+	+

TOPIC 2: T CELL AND B CELL FUNCTION

1. Fill in the following table regarding MHC.

Description	MHC Class I	MHC Class II
Tissue distribution	*All nucleated cells*	*Antigen presenting cells*
Recognized by	*CD8+ T cells*	*CD4+ t cells*
Type of peptides bound within	*endogenous*	*Exogenous*
Where is antigen loaded?	*Endoplasmic reticulum*	*Cytoplasmic vesicle*

2. For each disease below, list the associated HLA type. Some diseases may be associated with more than one HLA type.

Disease	Associated HLA Type
Systemic lupus erythematosus	*DR2*
Goodpasture's disease	*DR2*
Ankylosing spondylitis	*B27*
Type 1 diabetes	*DR3 and DR4*
Multiple sclerosis	*DR2*
Rheumatoid arthritis	*DR4*
Hashimoto's thyroiditis	*DR3 and DR5*
Graves' disease	*B8*
Reactive arthritis	*B27*

3. Name the function of NK cells.

   Killing of tumors and viral infected cells

4. Describe 2 mechanisms for NK cell killing.

   ADCC (antibody mediated cellular cytotoxicity) and via activation of the KAR in absence of the KIR binding to class I MHC

5. List the cytokine that is important for differentiation from a Th0 to a Th1 cell. From a Th0 to a Th2 cell?

   IL-12, IL-4

6. Describe the function of the Th1 cells?

   Cell mediated immunity

   Of the Th2 cells?

   Humoral immunity

7. List signal 1 for CTL activation. *Class I MHC+TCR (CD8)*

   List signal 2 for CTL activation. *IL-2 from TH cell*

8. List signal 1 for plasma cell activation. *CD40+CD40L*

   List signal 2 for plasma cell activation. *Class switching*

9. Which Th1 cytokine inhibits Th2 cell development? *IFN-γ*

10. Which Th2 cytokine(s) inhibits Th1 cell development? *IL-4 and IL-10*

11. List the 5 heavy chain classes of antibodies. *IgM, IgG, IgD, IgA, IgE*

12. What is the function of the Fc region of the antibody molecule? Of the Fab region?

Fc region binds to cellular receptors leading to biologic effector functions (e.g. antibody mediated phagocytosis), The Fab region binds to antigens.

13. List 3 functions of antibodies.

Opsonization, Neutralization, Antibody-dependent cell-mediated cytotoxicity, complement activation.

14. Fill in the following table with a "+" if the antibody has that function or "–" if the antibody does not have that function.

Function	IgM	IgD	IgG	IgA	IgE
Complements activation	+	–	+	–	–
Opsonization	–	–	+	–	–
Antibody dependent cellular cytotoxicity (ADCC)	–	–	+	–	–
Crosses the placenta	–	–	+	–	–
Triggers mast cell granule release	–	–	–	–	+
Predominates in the primary immune response	+	–	–	–	–
Predominates in the secondary immune response	–	–	+	–	–

15. LPS is an example of a *thymic dependent* antigen that can produce only *IgM* (Ab class).

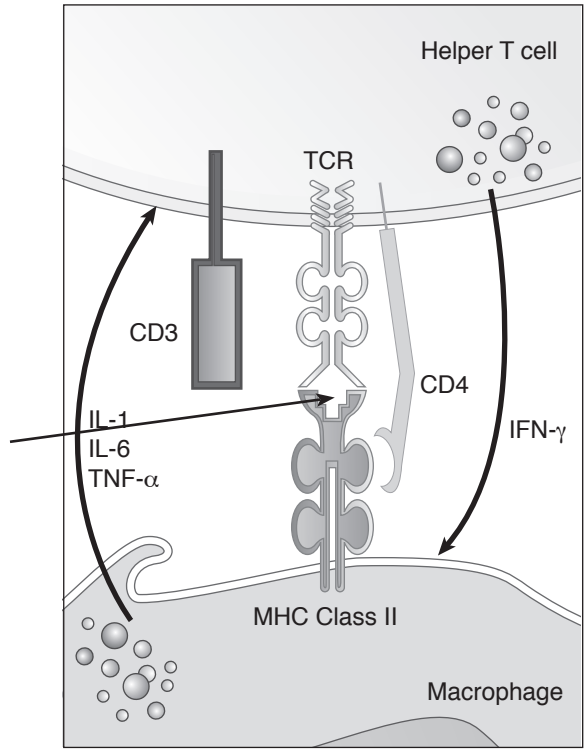
16. For each cytokine below, list the cell type that makes it and its major function. Note that while many cytokines have multiple roles, only the major function should be listed here.

Cytokine	Made by (Cell)	Major Function
IL-1	*macrophage*	*Pro-inflammatory*
IL-2	*TH1 cell*	*T cell proliferation*
IL-4	*TH2 cell*	*Class switching to IgG and E*
IL-5	*TH2 cell*	*Class switching to IgA*
IL-6	*macrophage*	*Pro-inflammatory*
IL-8	*macrophage*	*Chemotaxis*
IL-10	*TH2 cell*	*Inhibits TH1*
IFN-γ	*TH1 cell*	*Macrophage activation*
TNF-α	*macrophage*	*Pro-inflammatory*

17. For each CD marker listed, write the cell type on which it is expressed.

CD Marker	Cell Type
CD19	*B cells*
CD3	*T cells*
CD56	*NK cells*
CD21	*B cells*
CD16	*NK cells*
CD14	*Macrophages*
CD28	*Activated T cells*

18. Using the diagram below, draw where superantigens interact with the TCR and class II MHC.



19. For each example given, list whether it is an example of natural passive immunity "NP," natural active immunity "NA," artificial active immunity "AA" or artificial passive immunity "AP."

Example	Type of Immunity
Placental IgG	*NP*
Recovery from primary varicella zoster	*NA*
Anti-rabies immune globulin	*AP*
MMR vaccine	*AA*
Anti-venin after a snake bite	*AP*

TOPIC 3: IMMUNE HYPERSENSITIVITY

1. The cytokines essential in the development of toxic shock syndrome from activation of superantigens are:

   IL-1, IL-6, TNF-α and IFN-γ

2. The CD marker that binds to LPS is *CD14*.

3. Define antigenic variation.

   Changing surface antigens to avoid immune destruction

4. For each agent listed, write the antigen that undergoes antigenic variation.

   Salmonella: *flagella*

   Neisseria gonorhoeae: *pili*

   Influenza: *HA and NA*

5. Order the following events that occur in a type I hypersensitivity reaction by placing numbers 1 through 7 on the lines provided.

   (6) Allergen cross-links several IgE molecules on mast cells

   (3) B cells produce IgE

   (1) Exposure to allergen

   (7) Degranulation

   (4) IgE binds to mast cells via FcR

   (2) T_H2 mediated class switch to IgE

   (5) Re-exposure to allergen

6. Describe the mechanism of tissue destruction in a cytotoxic type II hypersensitivity reaction.

   Antibodies (IgG or IgM) bind to self tissues and activate complement. Complement activation recruits inflammatory cells that damage the tissue.

7. Describe the mechanism of tissue destruction in a type III hypersensitivity reaction.

   Circulating immune complexes (IgG or IgM) deposit in various tissues and activate complement. Complement activation recruits inflammatory cells that damage the tissue.

8. What is the name for a localized type III reaction?

   Arthus reaction

9. Describe the mechanism of a type IV hypersensitivity reaction.

   Macrophages take up the allergen and deliver it to a TH1 cell in the local draining lymph node. TH1 cells produce IFN-γ that activates macrophages. Macrophages will go back to the "source of the allergen" and damage tissue.

10. List the first antibody produced in response to an allergen.

    IgM

11. For each disease below, list the type of hypersensitivity reaction (type I, II, III, or IV).

Disease	Hypersensitivity Reaction
Post-streptococcal glomerulonephritis	*III*
Systemic lupus erythematosus	*III*
Allergic rhinitis	*I*
Hemolytic disease of the newborn	*II*
Transfusion reactions	*II*
Hashimoto's thyroiditis	*IV*
Serum sickness	*III*
Hay fever	*I*
Rheumatic fever	*II*
Multiple sclerosis	*IV*
PPD skin test	*IV*

12. For the autoimmune diseases listed, write in the autoantigen(s) associated with each disease.

Autoimmune Disease	Autoantigen(s)
Graves' disease	*TSH receptor*
Systemic lupus erythematosus	*DS DNA, histones, nucleosomes, etc.*
Rheumatoid arthritis	*IgM vs. Fc portion of IgG*
Scleroderma	*Centromere*
Celiac disease	*Gliadin, endomysal, transglutaminase*
Goodpasture's disease	*Type IV collagen (basement membranes)*
Pemphigus	*Desmoglian*
Hashimoto's thyroiditis	*Microsomal thyroglobulin, thyroid peroxidase*
Type 1 diabetes	*Glutamate decarboxylase*
Sjögren's disease	*SS-A, Ro, SS-B, La*
Wegener's granulomatosis	*c-ANCA*
Churg-Strauss syndrome	*p-ANCA*

TOPIC 4: IMMUNODEFICIENCY AND ORGAN TRANSPLANT

1. For the listed symptoms or lab values, fill in the corresponding immunodeficiency disease and if the disease is X-linked.

Symptoms	Immunodeficiency Disease	X-linked
↑ IgM, ↓ IgG, IgA, and IgE	*Hyper IgM*	*yes*
Recurrent GI and respiratory infections	*Selective IgA deficiency*	
No peripheral B cells, no Igs, recurrent bacterial infections	*Brutons agammaglobulinemia*	*yes*
Hypogammaglobulinemia that begins in late teens/early 20s	*Common variable agammaglobulinemia*	

2. List the major types of infections to which DiGeorge's syndrome patients are susceptible.
   Viruses and intracellular fungi

3. List the major types of infections to which patients with IL-12 receptor deficiency are susceptible.
   Disseminated mycobacteria.

4. The cytokine that is deficient in Job syndrome is called *IFN-γ*.

5. List 3 causes of severe combined immunodeficiency disease (SCID).
   IL-2 receptor deficiency (x-linked), ADA deficiency, recombinase deficiency

6. List the triad of symptoms observed in Wiskott-Aldrich syndrome.
   Thrombocytopenia, eczema, immunodeficiency

7. For each phagocytic immunodeficiency listed, name the mutation and the symptoms associated with each.

Disease	Mutation	Symptoms
Chronic granulomatous disease	*NADPH oxidase*	*Recurrent infections with catalase positive bacteria*
Leukocyte adhesion deficiency	*CD18 (integrin)*	*Omphalitis, gingivostomatitis, recurrent bacterial infections, NO PUS or ABSCESS*
Chédiak-Higashi syndrome	*Granule defect*	*Albinism, immune deficiency, increased incidence of lymphomas*

8. Define the following terms:

- Autograft *graft from one part of the body to a different part of the body on the same person.*
- Isograft *(syngeneic graft)-graft between identical twins*
- Allograft *graft between members of the same species (most common)*
- Xenograft *graft from outside of human species.*

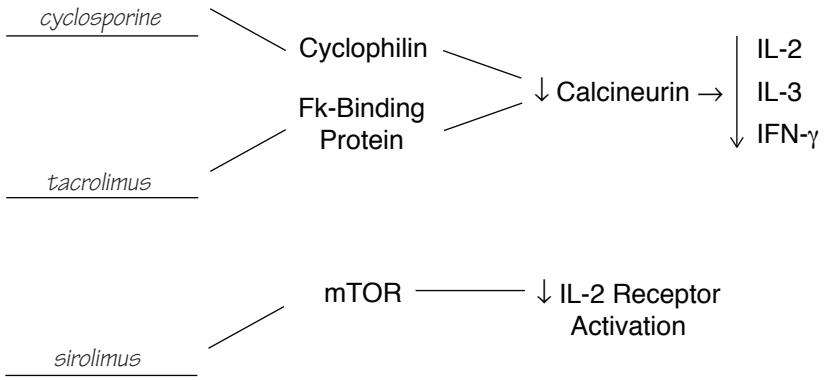
9. List the types of graft rejection from the fastest rejection to the slowest rejection.
hyperacute→acute (accelerated)→chronic

10. Define graft-versus-host disease.
This occurs when T cells from the donor marrow attack the graft recipient. Can only occur in BM transplants.

11. Major side effects for cyclosporine and tacrolimus drugs include _____*nephrotoxicity*_____.

12. Name the mechanism of action of sirolimus.
Inhibits B and T cell activation by inhibiting their response to IL-2

13. Complete the diagram below.



14. For each biologic agent listed, write the mechanism of action.

Monoclonal Antibody	MOA
Daclizumab	*Blocks IL-2 receptors*
Muromonab	*Blocks CD3*

15. For each recombinant cytokine listed in the table, list the major clinical uses.

Recombinant Cytokine	Clinical Uses
Aldesleukin	*Renal cell carcinoma, melanoma*
Erythropoietin	*Anemia*
IFN-α	*HBV, HCV*
IFN-β	*Multiple sclerosis*
IFN-γ	*CGD*
IL-11	*thrombocytopenia*

16. For each biologic drug listed, write in the mechanism of action.

Biologic	Mechanism of Action
Infliximab	*Binds TNF-α*
Adalimumab	*Binds TNF-α*
Abciximab	*Glycoprotein IIa/IIIb inhibitor*
Trastuzumab	*Binds HER2/neu*
Rituximab	*Binds CD20*

17. Match the antibody drug with its target.

Drug	Target
Trastuzumab	*Her2/neu (erb B_2)*
Daclizumab	IL-2 receptors
Abciximab	*GpIIb/IIIa Receptors*
Adalimumab or Infliximab	TNF-α

TOPIC 5: LYMPHOMA AND MULTIPLE MYELOMA

1. Would a patient with increased leukocytes and a left shift in peripheral blood most likely have a low, normal, or elevated leukocyte alkaline phosphatase?

   The patient probably has a leukemoid reaction, which characteristically has a low leukocyte alkaline phosphatase level.

2. Is Epstein-Barr virus more likely to be associated with Hodgkin's lymphoma or non-Hodgkin's lymphoma (NHL)? Which type of lymphoma is associated with HIV?

   Both HL and NHL are associated with EBV but only NHL is associated with HIV.

3. Is Hodgkin's lymphoma or NHL more likely to produce constitutional symptoms such as weight loss, fatigue, and night sweats?

   Hodgkin's

4. What immunohistochemical staining pattern is typical for a Reed-Sternberg cell?

   CD30/CD15 positivity is typical for Reed-Sternberg cells.

5. A lymph node biopsy showing areas of fibrosis with the intervening tissue containing a mixture of lymphocytes, histiocytes, scattered eosinophils, plasma cells, and lacunar-type Reed-Sternberg cells is most likely what type of lymphoma?

   Hodgkin's disease, nodular sclerosis type.

6. What characterizes stage 3 Hodgkin's lymphoma?

   More than one involved lymph node on both sides of the diaphragm

7. Complete the following table.

Disease	Translocation
Burkitt's lymphoma	*t(8;14), t(2; 8), t(8;22) (bring c-myc close to immunoglobulin locus)*
Mantle cell lymphoma	*t(11;14); Often CD5 positive*
Follicular lymphoma	*t(14;18); overexpression of bcl-2 leads to less apoptosis*

8. Adult T cell leukemia is associated with _____HTLV-1_____ virus.

9. Cells with unusual cerebriform nuclei found in peripheral blood are most likely to be of what leukocyte lineage?

   T cells; found in Sezary syndrome/mycosis fungoides

10. Multiple "punched out" lesions in the ribs and spine on x-ray studies suggest what hematologic malignancy?

    Multiple myeloma characteristically produces lytic bone lesions that may present with pathologic fracture.

11. What type of immunoglobulin chains tend to accumulate in kidney tubules of myeloma patients?

    Light chains (Bence-Jones proteins), especially kappa light chains

12. Would calcium levels be increased or decreased in multiple myeloma?

    There is hypercalcemia due to lytic bone lesions and production of osteoclast activating factor

13. Would rouleaux formation in the peripheral blood be more likely to suggest Hodgkin's disease, multiple myeloma, or follicular lymphoma?

    Multiple myeloma can cause rouleaux formation because of changes in plasma viscosity due to additional immunoglobulin protein in the blood.

14. What is the most likely diagnosis of a 65-year-old man who presents with priapism, is found to have an M-protein spike on serum protein electrophoresis, but does not have lytic lesions on x-ray?

Waldenstrom macroglobulinemia (IgM overproduction)

15. What is the most likely diagnosis in a 62-year-old asymptomatic woman with an M-protein spike on serum electrophoresis?

Monoclonal gammopathy of undetermined significance (MGUS)

TOPIC 6: LEUKEMIA AND MYELOPROLIFERATIVE DISORDERS

1. What is suggested by positive CD10 in a leukemic patient?

   CD10 (CALLA) in acute lymphocytic leukemia suggests a better prognosis.

2. Would warm autoimmune hemolytic anemia be more likely to be seen in acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myelogenous leukemia, or chronic myelogenous leukemia?

   Chronic lymphocytic leukemia (which can show "smudge cells" on smear)

3. A patient whose lymphocytes have long, wavy projections in the peripheral blood might now be potentially cured with which drug that acts as an apoptosis inhibitor?

   2-chloro-deoxyadenosine (2CdA) [Note: "apoptosis" should be "enzyme"]

4. What enzyme can be helpful in the diagnosis of hairy cell leukemia?

   Tartrate-resistant acid phosphatase (TRAP) is positive in hairy cell leukemia.

5. What translocation is associated with most types of acute myelogenous leukemia? With acute promyelocytic leukemia?

   AML, t(8;21); acute promyelocytic leukemia, t(15;17)

6. What can be used to treat the M3 (acute promyelocytic leukemia) subtype of AML?

   Vitamin A derivatives

7. Chronic myelogenous leukemia can be specifically targeted by which drug that targets the product of the translocation?

   Imatinib targets the bcr:abl translocation of t(9;22) Philadelphia chromosome.

8. Treatment of the M3 subtype of AML can cause what complication?

Numerous cytoplasmic Auer rods are characteristic of promyelocytic leukemia. Treatment of AML, including vitamin A treatment, can cause massive degranulation of the Auer rods leading to disseminated intravascular coagulation.

9. Complete the table below.

Disease	Translocation	Gene/Product Association	Cause of Disease
CML	*t(9;22)*	*bcr-abl fusion protein*	*Activation of tyrosine kinase*
Burkitt's lymphoma	*t(8;14)*	*c-myc activation*	*Transcriptional activation, proliferation*
Follicular lymphoma	*t(14;18)*	*bcl-2 overexpression responsive to vitamin A*	*Lack of normal apoptosis abnormal cellular differentiation*
AML-M3	*t(15;17)*	*Responsive to vitamin A*	*Abnormal cellular differentiation*
Ewing's sarcoma	*t(11;22)*	*EWS/FL1 fusion protein*	*Master regulator of disease formation*
Mantle cell lymphoma	*t(11;14)*	*cyclin D1 over-expression*	*Tumor cell growth*

10. Electron microscopy of a tumor shows tennis racquet-shaped cytoplasmic organelles. This is most likely a tumor of what cells?

Langerhans cells (skin dendritic cells with characteristic Birbeck granules)

11. What are 2 markers of Langerhans cell histiocytosis?

S-100 and CD1a

12. What 2 chronic myeloproliferative disorders are likely to evolve into myelofibrosis? What 2 are likely to evolve into acute leukemia?

Polycythemia vera and essential thrombocytosis can evolve into myelofibrosis. Essential thrombocytosis, polycythemia vera, and chronic myelogenous leukemia can all evolve into acute leukemia.

13. Teardrop cells in the peripheral blood suggest which myeloproliferative disorder?
Myelofibrosis

14. In polycythemia vera, are erythropoietin levels usually decreased or increased?
Decreased

15. Which 3 myeloproliferative disorders are associated with the JAK2 mutation?
Polycythemia vera, essential thrombocytosis, myelofibrosis

16. What is the term used when the liver and spleen produce red cells?
Myeloid metaplasia

17. Polycythemia vera can be associated with which diseases?
Renal cell carcinoma, hepatocellular carcinoma, Wilms tumor, and hydrocephalus

18. For each pathogen below, list the type(s) of associated cancer. As some agents may cause multiple types of cancer, list them all.

Pathogen	Cancer
HTLV	*T cell leukemia*
HBV/HCV	*Hepatocellular carcinoma*
EBV	*Burkitts lymphoma, nasopharyngeal carcinoma, hodgkins lymphoma*
HPV	*Cervical (and many others)*
HHV-8	*Kaposi's*
HIV	*Primary CNS lymphoma*
Helicobacter pylori	*Gastric adenocarcinoma*
Schistosoma haematobium	*Bladder cancer*

TOPIC 7: DNA REPLICATION AND REPAIR

1. In heterochromatin, genes are inactive due to _Cytosine methylation_. In euchromatin, genes are active due to _Histone acetylation_.

2. Circle the histone that is not in a nucleosome: (H1), H2A, H2B, H3, H4.

3. In the liver, where is the gene for factor VIII specifically located?

   Circle one: (euchromatin), heterochromatin, not present

   In the liver, where is the gene for β-globin specifically located?

   Circle one: euchromatin, (heterochromatin), not present

   In the erythrocyte, where is the gene for β-globin specifically located?

   Circle one: euchromatin, heterochromatin, (not present)

4. The key regulated enzyme of purine synthesis is _PRPP Amidotransferase_ and it is allosterically inhibited by the purine nucleotides _AMP_, _GMP_, and _IMP_. Pharmacologically, the enzyme is a target of the antineoplastic drug _6-mercaptopurine_. Why can this pharmacologic drug be used for the treatment of cancerous cells and yet not affect normal human cells?
   While the enzyme is present, it is inactive since most normal cells are in GO phase and not growing.

5. Carbamoyl phosphate synthetase II is located _cytoplasm_ of most cells and uses _CO_2_, _ATP_, and _glutamine_ as substrates to synthesize carbamoyl phosphate.

6. What are the 2 reactions catalyzed by UMP synthase?

   Transferring orotic acid onto ribose-P
   Decarboxylation of orotic acid portion on the ribose-P to UMP

7. Why does a deficiency of ornithine transcarbamylase in the urea cycle result in orotic aciduria?

   A deficiency of the enzyme results in the accumulation and spillage of carbamoyl phosphate out of the liver mitochondrion into the cytoplasm where it enters pyrimidine synthesis. Cells in GO phase do not need the extra orotic acid that then exits into blood and urine.

8. The enzyme that converts UMP to dUMP is _____*ribonucleotide reductase*_____, which can be inhibited by the drug _____*hydroxyurea*_____. The enzyme that converts dUMP to dTMP is _____*Thymidylate synthase*_____, which can be inhibited by the drug _____*5-fluorouracil*_____.

9. Dihydrofolate reductase converts _____*DHF*_____ to _____*THF*_____ and uses _____*NADPH*_____ as coenzyme. This enzyme in eukaryotes can be inhibited by the anticancer drug _____*methotrexate*_____ and in prokaryotes by _____*trimethoprim*_____ or _____*drug class sulfa*_____.

TOPIC 8: ANTINEOPLASTIC AND ANTIMETABOLITE DRUGS

1. For each antineoplastic drug, identify if it is cell-cycle specific (CCS) or non-cell cycle specific (NCSS). For each CCS drug, identify in which phase of the cell cycle the drug works.

Drug	CCS or NCSS	Cell Cycle Phase
Methotrexate	*CCS*	*S*
Doxorubicin	*NCCS*	
Vincristine	*CCS*	*M*
Cyclophosphamide	*NCCS*	
Cisplatin	*NCCS*	
6-Mercaptopurine	*CCS*	*S*
Bleomycin	*CCS*	*G_2*
Etoposide	*CCS*	*S/G_2*

2. Match the toxicity with the antineoplastic drug that may cause it.

Drug	Toxicity
Vincristine	Peripheral neuropathy
Doxorubicin	Dilated cardiomyopathy
Bleomycin	Pulmonary fibrosis
Cisplatin	Nephrotoxicity
Cyclophosphamide	Hemorrhagic cystitis

3. Match the cancer drug with its cellular target.

Drug	Target
Paclitaxel	*Tubulin*
Methotrexate	*DHFR*
5-Fluorouracil	*Thymidylate synthase*
Etoposide	*Topoisomerase II*
Cyclophosphamide	*DNA*
Hydroxyurea	*Ribonucleotide reductase*
Tamoxifen	*Estrogen receptors*

TOPIC 9: NONHEMOLYTIC ANEMIA AND PORPHYRIA

1. What transporter on the RBC excretes excess bicarbonate that accumulates in the RBC?

   Bicarbonate/chloride transporter

2. What is the average life span of a red blood cell?

   120 days

3. In an individual with type B blood, erythrocytes would have which antigens? What antibodies could be present in the serum?

   Type B erythrocytes have B antigen on their surface. The serum may have antibodies to A antigen.

4. What blood type is the universal donor? Universal recipient?

   Universal donor—type O; universal recipient –type AB

5. What is given to Rh– mothers prior to delivery to prevent formation of anti-Rh+ antibodies?

   RhoGAM (anti-Rh immunoglobulin)

6. Describe the structure of heme in basic terms.

   Fe^{2+} surrounded by a porphyrin ring.

7. What action does heme have on ALA synthase?

   Heme is a feedback inhibitor of ALA synthase.

8. What enzymes are inhibited by lead poisoning?

   Lead poisoning inhibits ALA dehydratase and ferrochelatase

9. Complete the mnemonic below for key facts about lead poisoning.

L

E

A
D > Enzyme inhibited by lead is: *ALA dehydratase*

P
A > Common symptom in heavy metal poisoning: *Pain in abdomen*

I

N – Symptom of lead poisoning: *Neuropathy*

T

E – Symptom of lead poisoning: *Encephalopathy*

A – Characteristic hematologic finding: *Anemia*

T – Treat with: _____

E – *EDTA*

R

S – *Succimer*

10. What enzyme is deficient in acute intermittent porphyria?
Porphobilinogen deaminase

11. How does acute intermittent porphyria present?
Abdominal pain, red urine, neuropathy, psychological disturbances

12. What enzyme is deficient in porphyria cutanea tarda?
    Uroporphyrinogen decarboxylase

13. What are the skin manifestations of porphyria cutanea tarda?
    Blistering rash after sun exposure

14. An anemia in which the mean corpuscular volume of the erythrocytes is 115 fL would be considered microcytic, normocytic, or macrocytic?
    Macrocytic

15. Would a peripheral smear that showed small, pale erythrocytes most likely be due to folate deficiency, iron deficiency, or vitamin B12 deficiency?
    Iron deficiency is one cause of microcytic anemia.

16. Hemoglobin H disease is caused by what genetic composition?
    Deletion of three of four alleles of the alpha-globin chain.

17. What is the result of deletion of 4 α chain genes?
    Hemoglobin Barts, hydrops fetalis

18. An asymptomatic patient suspected of having β-thalassemia minor should be tested for what form of hemoglobin?
    HbA_2

19. An X-linked defect in ALA synthase can cause what type of anemia?
    Sideroblastic anemia

20. Microcytic anemia due to lead poisoning can be treated with which drugs?
    EDTA, succimer, or dimercaprol

21. Macrocytic anemia related to vitamin B12 deficiency would most likely be caused by which diseases?
Pernicious anemia, D. latum infection, Crohn disease, and ileal resection.

22. How can folate deficiency be distinguished from B12 deficiency?
Methylmalonic acid is usually increased and neurologic symptoms are present in B12 deficiency

23. What processes can cause non-megaloblastic anemia?
Liver disease, alcoholism, and reticulocytosis.

TOPIC 10: HEMOLYTIC ANEMIA AND PATHOLOGIC RED BLOOD CELL FORMS

1. What is the difference between intravascular and intrinsic hemolysis? Between extravascular and extrinsic hemolysis?

   Intravascular refers to hemolysis occurring within a blood vessel and intrinsic refers to causes of hemolytic anemia due to factors in the erythrocyte. Extravascular refers to hemolysis occurring outside a blood vessel and extrinsic refers to hemolytic anemia due to factors outside the erythrocyte.

2. Would a patient with low haptoglobin, high LDH, and hemoglobinuria be most likely to have intravascular hemolysis or extravascular hemolysis?

   Intravascular hemolysis. Extravascular hemolysis would be characterized by high LDH and high unconjugated bilirubin.

3. Ankyrin and spectrin may be defective in which hemolytic anemia?

   Hereditary spherocytosis

4. Upon entry into a cell, glucose is phosphorylated to become glucose 6-phosphate. List the 3 separate metabolic pathways it can then enter and the purpose of each pathway.

   a. *Glycolysis to generate energy*

   b. *Glycogenesis for storage of glucose*

   c. *HMS for generating NADPH and ribose-P*

5. In glycolysis, the oxidation of glyceraldehyde 3-phosphate to 1,3-bisphosphoglycerate results in the conversion of NAD to NADH. The function of the NADH is to _____*generate ATP*_____.

6. In the hexose monophosphate shunt, the oxidation of glucose 6-phosphate by the enzyme G6PD results in the conversion of NADP to NADPH. In erythrocytes, what is the function of NADPH?

   Supply electrons to convert and replenish oxidized glutathione to reduced glutathione.

7. In which hemolytic anemia are Howell-Jolly bodies and osmotic fragility typical and erythrocytes more susceptible to oxidative stress secondary to low levels of glutathione?

   G6PD deficiency

8. What is the mode of inheritance of G6PD deficiency?

   X-linked recessive

9. What are some precipitating factors for hemolysis in G6PD deficiency?

   Sulfonamide drugs, fava beans, antimalarials (primaquine), anti-TB drugs

10. What is a Heinz body and how is it formed?

    A Heinz body is cross-linked, denatured, precipitated hemoglobin inside the RBC. Reactive oxygen species, especially H_2O_2, will oxidize the sulfhydryl groups on hemoglobin forming disulfide bridges among many hemoglobins.

11. Why are certain drugs such as sulfa drugs not administered to an individual with G6PD deficiency?

    Sulfa drugs, among others, can generate reactive oxygen species that can overwhelm the limited detoxification capacity of a patient's cells.

12. Why is an individual with G6PD deficiency expected to have hemolytic anemia?

    G6PD deficiency leads to an increase in reactive oxygen species (e.g. H2O2) that cause erythrocyte lysis.

13. What glycolytic enzyme deficiency can often lead to hemolytic anemia?

    Pyruvate kinase deficiency

14. Why is an individual with pyruvate kinase deficiency expected to have hemolytic anemia?

Pyruvate Kinase is a required step for glycolysis. One purpose of glycolysis is to generate ATP to power the active transport ion pumps. Without active ion transport membrane integrity is impaired, leading to cell lysis.

15. How is hemolytic anemia caused by G6PD deficiency distinguished from pyruvate kinase deficiency?

Heinz bodies are present in G6PD deficiency but not in PK deficiency.

16. What is the cause of sickle cell anemia?

Replacement of glutamic acid by valine in the beta chain, producing HbS

17. Which virus causes aplastic crises in sickle cell patients?

Parvovirus B19

18. What renal complication is characteristically associated with sickle cell anemia?

Renal papillary necrosis

19. What can be used in sickle cell disease to increase HbF?

Hydroxyurea

20. What is the biochemical defect in HbC disease?

Lysine replaces glutamic acid at position 6 of the hemoglobin chain.

21. Which CD marker is characteristically negative in paroxysmal nocturnal hemoglobinuria?

CD59 is negative.

22. Abnormality of which RBC membrane protein causes paroxysmal nocturnal hemoglobinuria?

GPI protein, which normally binds to decay accelerating factor (DAF)

23. In both the innate response and the adaptive response, formation of which complement factor leads to C5 production (that in turn leads to formation of the membrane attack complex)?

C3

24. C1 esterase inhibitor deficiency produces which disease? *Hereditary angioedema*

25. Which of the complement deficiencies are most strongly associated with anaphylactic shock?

C3a and C5a

26. Is warm agglutinin autoimmune hemolytic anemia mediated by IgM or IgG antibodies? Cold agglutinin hemolytic anemia?

IgG mediates warm agglutinin and IgM mediates cold agglutinin.

27. What is an autoimmune hemolytic anemia that develops when an Rh-negative mother creates antibodies against an Rh-positive fetus?

Erythroblastosis fetalis

28. What does the direct Coombs test look for?

Direct Coombs detects IgG on RBC surfaces

Indirect Coombs test?

indirect Coombs detects IgG in serum that binds to RBCs

29. Damage to RBCs during passage through narrowed vessels can produce what altered RBC form?

Schistocytes

30. What disease is suggested by a Maltese cross appearance in erythrocytes in a peripheral smear?

Babesiosis

31. Acanthocytes are found in what disease?

Liver disease

32. Basophilic stippling is seen in which diseases?

Thalassemias, anemia of chronic disease, iron deficiency, and lead poisoning (TAIL)

33. Bite cells are seen in what disease?

Glucose 6 phosphate deficiency

34. The mechanism underlying elliptocytosis is similar to the process underlying what other erythrocyte pathology?

Spherocytosis

35. Fragmented red blood cells are seen in which diseases?

Disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome.

36. Damage to a red cell by an artificial heart valve would produce what altered erythrocyte form?

Schistocyte

37. Teardrop cells typically signal the presence of what process?

Bone marrow infiltration, such as by myelofibrosis.

38. Target cells are found in which diseases?

Hemoglobin C disease, asplenia, liver disease, and the thalassemias.

39. Fill in the following table.

Disease	Serum Iron	Transferrin (TIBC)	Ferritin
Iron deficiency	*Low*	*High*	*Low*
Anemia of chronic disease	*Can be low*	*Very low*	*High*
Hemochromatosis	*High*	*Low*	*High*

TOPIC 11: THE NORMAL COAGULATION CASCADE AND PLATELET PLUG

1. What initiates the extrinsic coagulation pathway? Intrinsic coagulation pathway?

   Tissue thromboplastin initiates the extrinsic coagulation pathway. Surface contact, prekallikrein, and HMW-kininogen initiate the intrinsic coagulation pathway.

2. Fill in the following table about the kinin cascade.

Molecule	Function
HMWK	*Converts factor XII to XIIa*
Factor XIIa	*Converts prekallikrein into kallikrein*
Kallikrein	*Converts plasminogen into plasmin*
Bradykinin	*Induces vasodilation, permeability, and pain*
Plasmin	*Cleaves fibrin mesh and activates C3 to become C3a*
ACE	*Degrades bradykinin*

3. Which cofactors related to the clotting cascade require vitamin K for synthesis?

   Factors II, VII, IX, X, C, and S are all gamma-carboxylated by the vitamin K-requiring enzyme gamma-glutamyl carboxylase.

4. Warfarin inhibits what step in vitamin K-dependent synthesis of clotting factors?

   Recycling of vitamin K by vitamin K epoxide reductase and vitamin K reductase

5. After initiating therapy with warfarin, what clotting factor is the first one affected? Why?

   Factor VII, because it has the shortest t½ and therefore is the first to disappear.

6. The mutation causing factor V Leiden does what?
   The Leiden mutation in factor V makes the factor V resistant to inactivation by protein C.

7. What is the pathway of platelet production starting with a hematopoietic stem cell?
   Hematopoietic stem cell → promegakaryocyte → megakaryocyte → platelet

8. What do the platelet dense bodies contain?
   ADP, calcium, serotonin, histamine, epinephrine

9. Match the drug with its target.

Drug	Target
Aspirin	*TXA_2 (COX-1,2)*
Clopidogrel	*ADP receptors*
Warfarin	*Vitamin K epoxide reductase*
Heparin	*Antithrombin III*
Lepirudin	*Thrombin*

10. Fill in the following table.

Disease	Cause of Defective Platelet Formation
Bernard-Soulier syndrome	*Decreased Gp1b which causes impaired platelet-to-collagen aggregation*
Glanzmann thrombasthenia	*Decreased GpIIb/IIIa which causes impaired platelet-to-collagen aggregation*
Von Willebrand disease	*Autosomal dominant defect in quantity or quality of von Willebrand factor (vWF)*

TOPIC 12: COAGULATION AND PLATELET DISORDERS

1. Which factors are indirectly tested in the prothrombin time? Partial thromboplastin time?

   Prothrombin time (PT) tests for VII, X, V, prothrombin (II), and fibrinogen (I).
   Partial thromboplastin time (PTT) tests for XII, XI, IX, VIII, X, V, prothrombin (II), and fibrinogen (I)

2. Name 3 conditions that can cause a failure to clot related to low factor levels.

   Factor VIII deficiency, factor IX deficiency, and vitamin K deficiency

3. What effect on the PT and PTT do Bernard-Soulier syndrome and Glanzmann thrombasthenia have?

   None; these diseases are platelet disorders rather than clotting factor disorders.

4. What constitutes the characteristic pentad of TTP?

   Thrombocytopenic purpura, fever, renal failure, neurologic changes, microangiopathic hemolytic anemia

5. How does hemolytic-uremic syndrome (HUS) present differently from TTP?

   No fever or neurologic symptoms in HUS

6. What differences in the peripheral smear are seen between idiopathic thrombocytopenic purpura (ITP) and thrombotic thrombocytopenic purpura (TTP)?

   ITP shows deficient numbers of platelets with enlarged, immature platelets; TTP shows only a few platelets that are mostly normal and the red cells may show schistocytes and helmet cells.

7. Why does the PTT increase in von Willebrand disease?

   vWF stabilizes factor VIII, thereby increasing PTT.

8. What features are useful in diagnosis of disseminated intravascular coagulation?

Low platelets, low fibrinogen, increased PT, increased PTT, presence of fibrin degradation production products (increased D-dimer), and schistocytes.

9. Fill in the following table.

Condition	Causes of Excessive Thrombosis
Protein C or S	*Deficiency of these factors decreases the ability to inactivate factors V and VIII*
Factor V Leiden	*Mutant factor V cannot be degraded by protein C*
Prothrombin gene mutation	*Prothrombin gene mutation in the 3' untranslated region*
ATIII deficiency	*Deficiency of this potent inhibitor of the clotting cascade allows cascade to operate in an uncontrolled fashion*

10. In each clinical scenario below, identify the drug most likely to be used.

Scenario	Drug
Stable patient with PE	*Heparin or LMWH*
Emergency management of stroke	*Alteplase (tPA)*
Prophylaxis for TIAs	*Aspirin*
Alternative to aspirin post-MI	*Clopidogrel*
Pregnant patient needing anticoagulant	*Heparin or LMWH*
Patient with HIT needing anticoagulant	*Lepirudin*
Excessive bleeding following use of alteplase	*Aminocaproic Acid*
Rapid reversal of heparin	*Protamine sulfate*

CHAPTER 4

INFECTIOUS DISEASE

TOPIC 1: INTRODUCTION TO BACTERIOLOGY

1. For each of the following bacterial properties listed, fill in G+ if it is found only in Gram-positive bacteria, G– if it is found only in Gram-negative bacteria, or BOTH if it is found in BOTH.

Bacterial Property	G+, G–, or Both
Outer membrane	*G–*
LPS	*G–*
Thick peptidoglycan layer	*G+*
Thin peptidoglycan layer	*G–*
Cytoplasmic membrane	*BOTH*
Teichoic acid	*G+*
Stains pink in Gram stain	*G–*
Stains purple in Gram stain	*G+*

2. List the 4 types of antibiotics that target the cell wall:

penicillins

cephalosporins

vancomycin

carbapenems

3. Which bacterial genera have mycolic acid in the cell wall?
   Mycobacterium

4. Antibiotics would work best at which stage of the bacterial growth curve?
   log phase

5. A flask is inoculated to a density of 5×10^3 cells/ml. What is the density of cells in the culture after 70 minutes if the generation time is 20 minutes and the lag time is 10 minutes?
   $4x10^4$

6. Place an "X" under the genetic mechanism (transformation, transduction, etc) that utilizes or would be affected by the given requirement. Some rows may have multiple Xs.

Requirement	Hfr	Transduction	Conjugation	Transformation
Requires phage		x		
Majority of multi-drug resistant organisms arise from this			x	
Homologous recombination is required	x	x		x
Naked DNA is required				x
Cell-to-cell contact is required	x		x	
oriT is required for transfer of genetic information	x		x	
OriT + *tra* is required for transfer			x	

7. Define specialized transduction.

   Dependent on lysogenic phage that integrate into the bacterial genome at a specific site. An excision error is made as the phage begins to replicate lytically.

8. List the virulence factors acquired via specialized transduction.

   Shiga toxin, botulism toxin, S.pyogenes exotoxins, diphtheria toxin, cholera toxin, Salmonella O antigens, mnemonic COBED

9. Lipopolysaccharide (LPS) is also called ___*endotoxin*___; the toxic portion of the LPS is the ___*lipid A*___.

10. Exotoxins are ___*secreted*___ from bacterial cells. Many of these toxins are A-B toxins in which the A portion is the ___*active*___ portion of the toxin and the B portion is the ___*binds to the cell receptor*___.

11. For each bacterial toxin listed, put an "X" in the column that reflects its mechanism of action.

Toxin	cAMP Inducer	Inhibition of Protein Synthesis
Anthrax	x	
Diphtheria		x
Cholera	x	
Shiga (Shiga-like)		x
Pertussis	x	
ETEC	x	
Pseudomonas exotoxin		x

TOPIC 2: INFECTIOUS DISEASES

1. Fill in the following table with the appropriate culture medium for the organisms listed.

Organism	Culture Media
Haemophilus influenzae	*Chocolate agar*
Gram-negative enteric	*MacConkey agar*
Fungi	*Sabouraud Dextrose agar*
Neisseria gonorrhoeae	*Thayer Martin*
Legionella pneumophila	*Buffered charcoal yeast extract*

2. For each case description below, list the top 3 bacterial causative agents.

   A 68-year-old male presents with a fever, shaking chills, and difficulty breathing. A right-sided lobar consolidation was noted on x-ray.

   Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus.

   A 50-year-old male presents with a dry cough, headache, and low-grade fever. An interstitial pattern is noted on x-ray.

   Mycoplasma pneumoniae, Chlamydophila pneumoniae, Legionella pneumophila

3. The treatment for streptococcal pharyngitis is _____*Penicillin*_____.

4. The treatment for pharyngitis caused by *Corynebacterium diphtheriae* is _____*Penicillin (erythromycin) + antitoxin*_____.

5. For each case description below, list the top 2 bacterial causative agents.

   A 4-year-old unvaccinated male develops difficulty swallowing, stridor, and drooling.
   Haemophilus influenzae and Streptococcus pneumoniae.

   A 28-year-old female develops sinus pressure and a purulent nasal discharge.
   Haemophilus influenzae and Streptococcus pneumoniae.

6. For each symptom or organism listed in the table below, place an "X" in the column that reflects whether it occurs during otitis media, otitis externa, or both.

Disease	Fever	Ear Pain	Bulging Tympanic Membrane	*Pseudomonas aeruginosa*	*Streptococcus pneumoniae* or *Haemophilus influenzae*	"Swimmer's Ear"
Otitis externa		x		x		x
Otitis media	x	x	x		x	

7. For each organism that causes gastroenteritis, place an "I" for invasive (generally bloody diarrhea), a "T" for toxin mediated (generally watery diarrhea), or a "B" for both.

Organism	Pathogenesis
Campylobacter jejuni	I
Salmonella	I
Shigella	B
Bacillus cereus	T
Clostridium botulinum	T
Vibrio cholerae	T
EHEC	T

8. What is the most common cause of both community-acquired and nosocomial urinary tract infection?
   Escherichia coli

9. A patient who develops kidney stones likely has a urinary tract infection with _____*Proteus*_____, which produces _____*urease*_____, which in turn raises the urine pH to cause the formation of the stones.

10. Name the most common causative agent of osteomyelitis.
    Staphylococcus aureus

11. List the most common causative agent of septic arthritis that affects a single joint.
    Neisseria gonorrhoeae

12. For the following evaluation of bacterial versus viral meningitis, put a ↑ if the lab values are increased, ↓ if the lab values are decreased, or N if the lab values stay normal.

CSF Findings	Bacterial Meningitis	Viral Meningitis
Glucose	↓	N
Lymphocytes	N	↑
PMNs	↑	N
Protein	↑	↑(may be slight)

13. List the top 3 causes of neonatal meningitis.
    Streptococcus agalactiae (group B Strep), Escherichia coli, Listeria monocytogenes

14. A college student presents with bacterial meningitis. What is the most likely cause? Is there a vaccine available?

Neisseria meningitidis, yes

15. For each organism associated with genital infections, indicate whether each presents with a discharge or lesion.

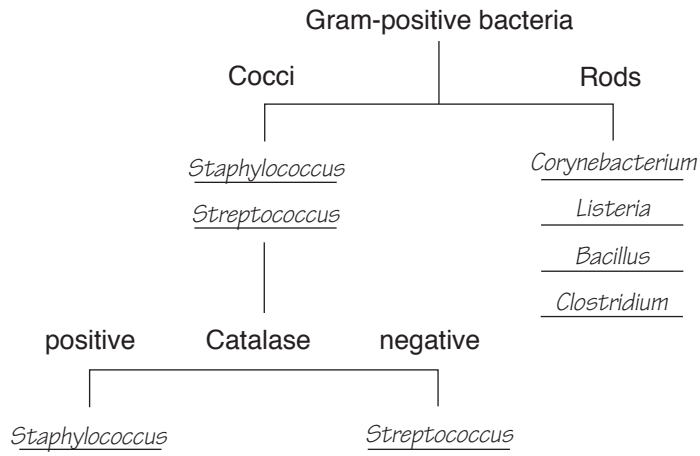
Organism	Discharge	Lesion
Neisseria gonorrhoeae	x	
Chlamydia trachomatis (D-K)	x	
Treponema pallidum		x
Bacterial vaginosis	x	
Trichomonas vaginalis	x	
Herpes simplex virus		x

16. Describe the discharge or lesion, as you indicated in the question above.

Organism	Discharge	Lesion
Neisseria gonorrhoeae	*purulent*	
Chlamydia trachomatis (D-K)	*purulent*	
Treponema pallidum		*Non-tender chancre*
Bacterial vaginosis	*Thin, watery, malodorous*	
Trichomonas vaginalis	*Frothy green, malodorous*	
Herpes simplex virus		*vesicular*

TOPIC 3: GRAM-POSITIVES

1. Complete the flow chart below for the Gram-positive bacteria. Genus designation is sufficient.



2. For the Gram-positive cocci listed below, place an α, β, or γ for the hemolytic pattern on blood agar.

Organism	Hemolytic Pattern on Blood Agar
Staphylococcus aureus	β
Staphylococcus epidermidis	γ
Staphylococcus saprophyticus	γ
Streptococcus pyogenes	β
Streptococcus agalactiae	β
Streptococcus pneumoniae	α
Streptococcus mutans	α
Streptococcus bovis	γ

3. List at least 5 genera or families that can cause infections in patients with chronic granulomatous disease.

Staphylococcus, Enterobacteriaceae, Pseudomonas, Aspergillus, Nocardia, Candida

What property do the above organisms have in common?

They are all catalase positive.

4. Protein A is made by *Staphylococcus aureus* and functions by binding to the *Fc* portion of the antibody to prevent *phagocytosis (or opsonization)*.

5. Identify the appropriate virulence factors for the staphylococcal diseases listed below.

Staphylococcal Diseases	
Gastroenteritis	*Enterotoxin*
Toxic shock syndrome	*Toxic shock syndrome toxin (TSST)*

6. A 58-year-old woman with an artificial heart valve would most likely get *endocarditis* from *Staphylococcus* *epidermidis*.

7. Fill in the appropriate type of hemolysis with the descriptions below.

Description	Hemolytic Pattern
Partial	α
Complete	β
No hemolysis	γ

8. List the 3 diseases for which *Streptococcus pneumoniae* is the most common cause.

   Community acquired pneumonia (lobar), otitis media, bacterial meningitis

9. Name the bacterial group that is associated with dental caries and endocarditis due to damaged heart valves.

   Streptococcus viridans

10. Name the major virulence factor for *Streptococcus pyogenes* that is anti-phagocytic?

    M protein

11. What are 2 important features of *Listeria monocytogenes*?

    Grows in the cold, facultative intracellular

12. Name the bacterium with a polypeptide instead of a polysaccharide capsule.

    Bacillus anthracis

13. Check off the Clostridium species that produce the described toxins. Some descriptions may be found in multiple organisms.

Toxin	*(C) botulinum*	*(C) tetani*	*(C) perfringens*	*(C) difficile*
Inhibits GABA, glycine		x		
Inhibits release of acetylcholine	x			
A-B toxin	x	x		
α toxin			x	
Enterotoxin			x	x

14. Identify whether the following descriptions are characteristic of *Nocardia* or *Actinomyces*. Some descriptions may apply to both organisms.

Description	*Nocardia*	*Actinomyces*
Endogenous infection		x
Exogenous infection	x	
Aerobic	x	
Anaerobic		x
Partially acid fast	x	
Gram-positive branching rods	x	x
Infections in immune-compromised patients	x	

TOPIC 4: GRAM-NEGATIVES

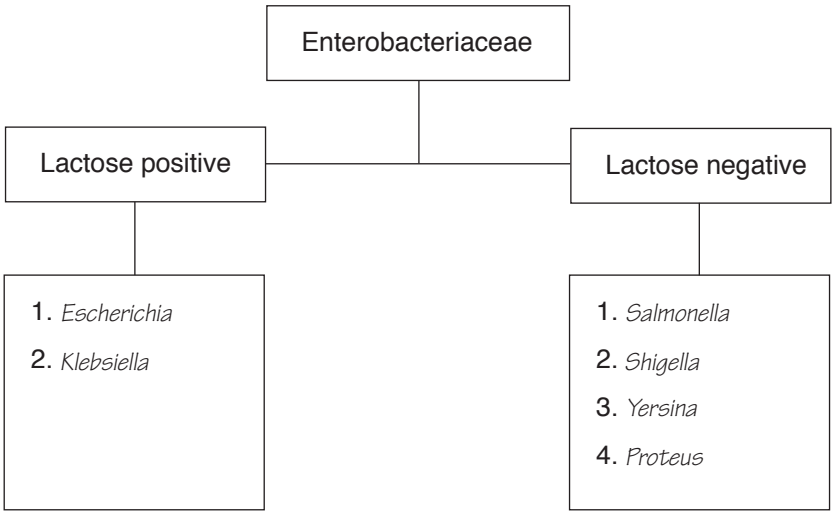
1. Fill in the table with an "M" for *Neisseria meningitidis*, a "G" for *Neisseria gonorrhoeae,* or a "B" for both.

Description	Causative Agent
Capsule	M
Ferments maltose	M
Ferments glucose	B
Grows on chocolate agar	B
Growth selected on Thayer-Martin agar	G
Commonly produces β-lactamases	G
Oxidase positive	B
Vaccine available	M
Antigenic variation	G

2. *Haemophilus influenzae* in grown on chocolate agar because it requires X and V factors.

3. List 3 diseases caused by *Haemophilus influenzae*.
   Meningitis, otitis media, epiglottitis

4. Fill in the flow chart with the following bacterial genera: *Escherichia, Klebsiella, Salmonella, Shigella*, *Yersinia*, and *Proteus*.



5. Lactose fermentation is detected on ___MacConkey___ agar and lactose positive bacteria appear ___pink___ on this agar.

6. Fill in the designation for the Enterobacteriaceae antigens from the descriptions in the table.

Description	Antigen Designation
Flagella	*H*
Capsule	*K*
Outer membrane	*O*

7. List the lab characteristics that would differentiate between *Salmonella* and *Shigella* in a patient with bloody diarrhea.

H_2S and motility

8. List the 2 lab characteristics that would be important in a patient with staghorn renal calculi.
   Urease, flagella (swarming)

9. Fill in the table below with the most important virulence factors for the organisms listed.

Organism	Most Important Virulence Factor
ETEC	*Exotoxin (enterotoxin)*
EHEC	*Exotoxin (enterotoxin)*
EUEC	*Pili*
(E) coli strains that cause meningitis	*capsule*

10. A patient from the southwestern United States who presents with a bubo is likely infected with _____*Yersinia pestis*_____, which exhibits _____*bipolar*_____ staining, whereas a child who presents with pseudo-appendicitis is likely infected with _____*Yersinia enterocolitica*_____, which can grow at 4° (C)

11. A patient with a duodenal ulcer is likely infected with _____*Helicobacter pylori*_____. The standard treatment for this is a multi-drug regiment involving _____*metronidazole, amoxicillin and a PPI*_____. This patient is also at risk for 2 types of cancer. List the two.
    Gastric adenocarcinoma and B-cell lymphoma (MALToma).

12. Fill in the table with a "W" for watery or a "B" for bloody depending on the type of diarrhea caused by the agent listed to the left.

Organism	Type of Diarrhea
Vibrio cholerae	*W*
Campylobacter jejuni	*B*
Vibrio parahaemolyticus	*W*
Vibrio vulnificus	*W*

13. Name the mode of transmission for *Legionella pneumophila*.

Inhalation of water aerosols

14. *Klebsiella pneumoniae* normally causes pneumonia in *alcoholics* patients, who tend to aspirate the organisms. The sputum would be described as *currant jelly*.

15. Fill in the blanks in the table below regarding *Pseudomonas aeruginosa*.

Properties (list at least 2)		
Distinguishing features	*Blue green pigment, strict aerobe*	
Important virulence factors	*Exotoxin, capsule*	
Diseases (list 2 for each category):		
Immune compromised	*Cellulitis (burn patients)*	*Pneumonia (CGD, neutropenia and CF)*
Otherwise healthy	*Hot tub folliculitis*	*Gasteroenteritis*
Treatment	*Antipseudomonal penicillin (ticaracillin or piperacillin*	*Aminoglycoside*

16. Fill in the table with an "A" if the listed organism is aerobic or "AN" if the listed organism is anaerobic.

Organism	**Oxygen Requirement**
Actinomyces	*AN*
Bacillus	*A*
Mycobacterium tuberculosis	*A*
Bacteroides	*AN*
Pseudomonas	*A*
Nocardia	*A*
Clostridium	*AN*

TOPIC 5: NON-GRAM STAINING ORGANISMS

1. Fill in the table below regarding *Mycobacterium tuberculosis*.

Property	*Mycobacterium tuberculosis*
Primary disease (list characteristic finding)	*Ghon complex*
Secondary disease (reactivation)	*Caseous necrosis*
Triad of symptoms	*Fever, night sweats, weight loss*

2. A giant cell found in a granulomatous lesion in a TB patient is which cell type?
   Macrophage

3. List 2 reasons a patient would test positive on a PPD test.
   Vaccine, exposure to TB

4. An AIDS patient with a CD4 T cell count of <50 cells/mm^3 is susceptible to which mycobacterial disease?
   Mycobacterium avium intracellulare (MAC)

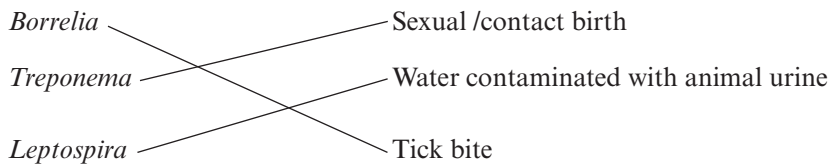
5. List the natural reservoir for *Mycobacterium leprae* in the United States.
   Armadillos

6. List the 2 types of diseases a patient can get when exposed to *Mycobacterium leprae*.
   Tuberculoid and lepromatous.

7. The diagnostic test for *Mycoplasma pneumoniae* is the _____*cold agglutinin reaction*_____.
   Beta-lactams don't work for treating this organism because it doesn't have _____*a cell wall*_____.

8. List the spirochetes in order of size.
   Borrelia, Leptospira and Treponema.

9. Draw a line from each organism to its correct mode of transmission.



10. Fill in the major symptoms for each listed stage of Lyme disease.

Stage of Disease	Major Symptoms
Primary	*Erythema chronicum migrans (bulls eye rash)*
Secondary	*CNS, carditis (A/V heart block)*
Tertiary	*Migratory polyarthritis*

11. For each symptom listed for the stages of syphilis, fill in a "1" if it occurs in primary, "2" if it occurs in secondary, "3" if it occurs in tertiary, or "C" if it occurs in congenital.

Symptom	Stage of Disease/Congenital
Gummas	*3*
Alopecia	*2*
Aortitis	*3*
Tabes dorsalis	*C*
Copper-colored rash	*2*
Chancre (painless)	*1*
Condylomata lata	*2*
Argyll Robertson pupils	*C*
Hutchinson teeth	*C*

12. The primary screening test for syphilis is the VDRL (non-specific) test, and the confirmatory test is the FTA-ABS.

13. Identify the animal associated with the infection produced by the organisms below.

Organism	Animal
Bartonella henselae	Cat
Brucella abortus	Cow
Francisella tularensis	Rabbit
Pasteurella multocida	Cat

14. A patient who develops a rash after a tick bite that spreads peripherally and moves centrally is likely infected with Rickettsia rickettsia.

15. A patient who develops a rash after a body louse infestation that spreads centrally and moves peripherally is likely infected with Rickettsia prowazekii.

16. Rickettsial diseases can be diagnosed by the Weil-Felix test, which takes advantage of a cross-reaction of rickettsial antigens with non-motile strains of Proteus.

17. The organisms in the genus *Chlamydia* are obligate intracellular because they can't make their own ATP. The infectious form of the organism is known as the elementary body, whereas the replicative form is known as the reticulate body.

18. A patient treated for *Chlamydia trachomatis* (serotypes D-K) should also be treated for Neisseria gonorrhoeae.

19. For each chlamydial disease listed in the table, put a "T" if it is caused by *(C) trachomatis*, a "PN" if it is caused by *(C) pneumophila,* or a "PS" if it is caused by *(C) psittaci.*

Disease	Chlamydia Species
Pelvic inflammatory disease	T
Trachoma	T
Parrot fever	PS
Lymphogranuloma venereum	T
Walking pneumonia	PN

20. For each disease caused by *Chlamydia trachomatis* listed in the table, fill in the appropriate serotypes that are responsible for the diseases.

Disease	Serotypes
Trachoma	A-C
Non-gonococcal urethritis	D-K
Neonatal conjunctivitis	D-K
Lymphogranuloma venereum	L1, L2 and L3

TOPIC 6: MYCOLOGY

1. Mammalian cells have *cholesterol* in the cell membrane, whereas fungi have *ergosterol* in the cell membranes.

2. List the 3 genera of fungi that appear in cutaneous fungal infections.
   Trichophyton, Epidermophyton and Microsporum

3. Cutaneous fungal infections are always monomorphic and in the *hyphal form*. A *KOH mount* is used to diagnose these types of infections.

4. Tinea versicolor is caused by *Malazzezeia furfur* and appears as *white patches* on the skin.
   A KOH mount would reveal a *spaghetti and meatballs pattern*.

5. For each organism listed below, fill in the geographic distribution and description of the yeast form.

Organism	Geography	Yeast Form
Sporothrix schenckii	N/A	*Cigar shaped yeast*
Histoplasma capsulatum	*Ohio/Mississippi river valley*	*Intracellular yeast*
Blastomyces dermatitidis	*East of Mississippi river*	*Broad based budding yeast*
Coccidioides immitis	*Desert southwest*	*Spherules*
Paracoccidioides brasiliensis	*Latin America*	*Ship steering wheel (captains wheel)*

6. For the different patient populations listed, write in the diseases that *Candida* can cause in each.

Patient Population	Diseases
AIDS	*Thrush, esophagitis*
Diabetic	*"yeast infections" (vulvovaginitis)*
IV drug users	*endocarditis*

7. Recurrent superficial *Candida* infections may suggest a defect in _____T cells_____, whereas recurrent systemic infections may suggest a defect in _____neutrophils_____.

8. *Aspergillus* infections can be diagnosed by finding _____septate_____ hyphae at _____45°_____ angles.

9. *Cryptococcus neoformans* is a monomorphic _____yeast_____ with a large _____capsule_____ that stains with India ink.

10. *Pneumocystis jiroveci* is most commonly found in which patient population? _____AIDS_____

11. *Mucor* infections can be diagnosed by finding _____non-septate (ribbon like)_____ hyphae at _____90°_____ angles.

TOPIC 7: PARASITOLOGY

1. Place an "X" under the property that corresponds to the organisms listed in the table.

Organism	Acid Fast	Found in Hikers	Liver Abscesses	Bloody Diarrhea	Malabsorption	Chronic Diarrhea in AIDS Patients
Giardia lamblia		X			X	
Entamoeba histolytica			X	X		
Cryptosporidium parvum	X					X

2. For each of the diseases/symptoms/findings caused by *Toxoplasma gondii*, place an "I" if it occurs in immuncompromised patients or a "C" if congenital.

Disease/Symptoms/Findings	Patient Population
Chorioretinitis	C
Encephalitis/ring-enhancing lesions	I
Brain abscess	I
Hydrocephalus	C

3. Fill in the insect vectors for the following parasites.

Parasite	Vector
Trypanosoma brucei	Tsetse fly
Trypanosoma cruzi	Reduviid bug
Leishmania	sandfly

4. Fill in the geography, RBC forms, and vector for the organisms listed in the table.

Organism	Geography	RBC Forms	Vector
Plasmodium falciparum	Africa	Ring forms	Mosquito
Babesia microti	Northeast US	Maltese cross	Tick

5. A patient with foul-smelling frothy green vaginal discharge would likely have motile trophozoites on a wet mount and an infection with Trichomonas vaginalis. Treatment for this patient is metronidazole.

6. Fill in the common names and major symptoms for the organisms listed in the table.

Organism	Common Name	Major Symptom
Diphyllobothrium latum	Fish tapeworm	Anemia
Echinococcus granulosus	Dog tapeworm	Hydatid cysts

7. Fill in the mode of transmission for each disease listed below caused by *Taenia solium.*

Disease	Mode of Transmission
Cysticercosis	Ingestion of eggs
Intestinal tapeworm	Ingestion of raw/undercooked pork

8. *Necator americanus* (or *Ancylostoma*) parasites are acquired via larval penetration of bare skin on feet. The symptoms of hookworm infections are usually anorexia, anemia and weight loss.

9. Fill in the appropriate parasite for each diagnostic stage listed in the table.

Diagnostic Stage (Egg)	Parasite
Tire-shaped egg	*Taneia*
Egg with flattened side, larvae inside	*Enterobius*
Football-shaped egg with bipolar plugs	*Trichuris*
Eggs with knobby coat	*Ascaris*

10. Fill in the mode of transmission for each of the parasites listed.

Parasite	Mode of Transmission
Trichinella spiralis	*Undercooked bear meat (wild game)*
Dracunculus medinensis	*Drinking infested water*
Loa loa	*Biting flies*
Wuchereria bancrofti	*Mosquito*
Toxocara canis	*Puppies, eating dirt*
Onchocerca volvulus	*Black fly*

11. For the following parasites, list their target site of infection:

Paragonimus westermani _____ *lung* _____

Clonorchis sinensis _____ *bile duct* _____

Schistosoma haematobium _____ *bladder* _____

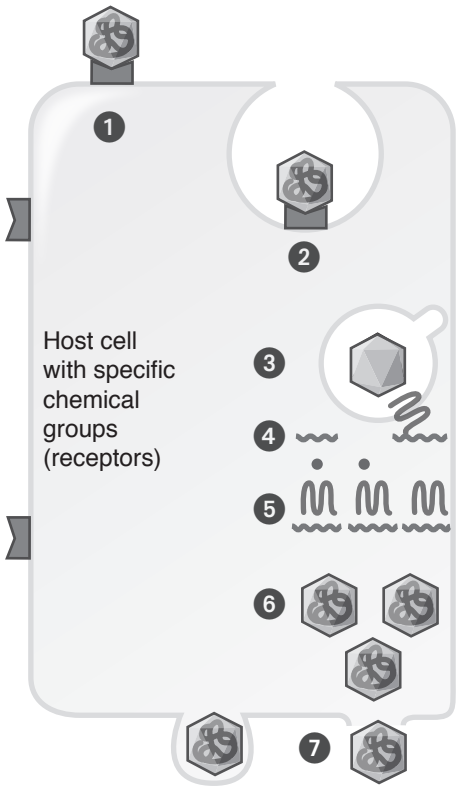
Schistosoma mansoni _____ *liver* _____

TOPIC 8: DNA VIRUSES

1. The viral envelope is typically derived from the *host cell membrane*, whereas herpes viruses utilize the *nuclear envelope* for their envelope.

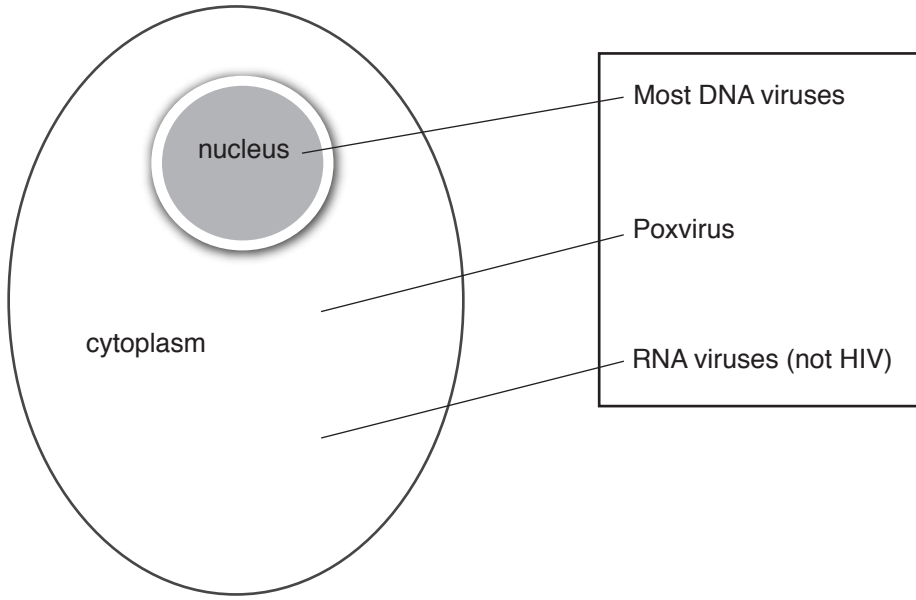
2. List the 2 types of common viral capsid symmetries.
   Helical, icosahedral

3. For each number listed, list the step in viral replication that is occurring.



1) *Attachment*
2) *Penetration*
3) *Uncoating*
4) *Macromolecular synthesis*
5) *Posttranslational modification of viral proteins*
6) *Assembly*
7) *Release*

4. Using the cell diagram below, draw lines to where each of the different viruses listed replicates.



5. Complete the following table regarding replication of viruses.

Virus Type (Genome)	Replicative Intermediate	Progeny Genome
DNA viruses	*none*	*DNA*
Positive stranded RNA	*Negative stranded RNA*	*Positive stranded RNA*
Negative stranded RNA	*Positive stranded RNA*	*Negative stranded RNA*

6. RNA viruses use an *RNA* dependent *RNA* polymerase.

   DNA viruses use a *DNA* dependent *DNA* polymerase.

   Retroviruses use an *RNA* dependent *DNA* polymerase.

7. For each infectious agent listed, add the type of viral infection: abortive, cytolytic, or persistent.

Virus	Type of Viral Infection
Poliovirus	*Cytolytic*
Adenovirus in hamsters	*Abortive*
HBV or HCV	*Persistent*
HSV-1 or HSV-2	*Persistent (latent)*

8. For each virus listed, put an "L" if the agent has a live vaccine, "K" if the agent has a killed vaccine, or "R" if the agent has a recombinant vaccine. Note that some agents have >1 vaccine available and can have >1 designation.

Virus	Vaccine Type
Measles, mumps, rubella	*L*
Hepatitis A virus	*K*
Influenza	*L,K*
Polio	*L,K*
Hepatitis B virus	*R*
Human papillomavirus	*R*
Varicella-zoster virus	*L*

9. The only ss DNA virus is ___*parvovirus*___. ALL others are ds.

10. The only DNA virus that replicates in the cytoplasm is ___*poxvirus*___; all others replicate in the nucleus.

11. Fill in the following categories for the herpesviruses listed.

Virus	Clinical Presentation of Primary Infection	Site of Latency	Clinical Presentation and Site of Reactivation
HSV-1	*gingivostomatitis*	*Trigeminal ganglia*	*Cold sores*
HSV-2	*Genital infection*	*Sacral ganglia*	*Genital infection*
VZV	*chickenpox*	*Dorsal root ganglia*	*Zoster (shingles)*
EBV	*Heterophile positive mononucleosis*	*B cells*	*Asymptomatic shedding*
CMV	*Heterophile negative mononucleosis*	*Mononuclear cells*	*Asymptomatic shedding*

12. Describe the heterophile antibody test and what it is used for.

Used for diagnosis of EBV, viral infection causes polyclonal activation of B cells resulting in heterophile antibodies that agglutinate sheep and cow rbc's.

13. For each disease listed, put "C" if it is caused by CMV, "E" if it is caused by EBV, or "B" if it can be caused by both.

Disease	Viral Cause
Mononucleosis in a teenager	*B*
Interstitial pneumonia in an immunocompromised patient	*C*
Retinitis in an AIDS patient	*C*
Burkitt lymphoma	*E*

14. Which of the following cases best describes roseola?

(A) A 10-year-old develops an asynchronous vesicular rash

(B) A 3-month-old develops a high fever for 3 days, the fever goes away, a lacy body rash appears

(C) A 14-year-old develops cough, coryza, conjunctivitis, and a maculopapular rash

15. Kaposi sarcoma is associated with what co-morbidity?

AIDS

16. For each characteristic listed, put a "B" if it is characteristic of HBV, a "C" if it is characteristic of HCV, or "both" if the characteristic applies to both viruses.

Characteristic	Virus
Uses reverse transcriptase in replication	*B*
DNA virus	*B*
RNA virus	*C*
More often causes chronic hepatitis	*C*
More often causes acute hepatitis	*B*
Cirrhosis/liver cancer	*BOTH*
Blood borne/sexually transmitted	*BOTH*

17. List at least 2 diseases caused by adenovirus.

Conjunctivitis, acute respiratory disease, hemorrhagic cystitis

18. List the 2 patient populations at high risk for severe infection with B19 virus.

Anemics, fetus

19. For each disease listed, provide the appropriate virus family.

Disease	Viral Family
Genital warts	*Papova*
Vaccinia	*Pox*
Molluscum contagiosum	*Pox*
Progressive multifocal leukoencephalopathy	*Papova*

20. For each viral family listed, put a "+" if the virus family is positive stranded or "–" if the virus family is negative stranded. Also, put an "X" if the viral family is segmented.

Viral Family	Genome Type + or – Stranded RNA	Segmented Genome
Retroviridae	+	
Orthomyxoviridae	–	X
Paramyxoviridae	–	
Reoviridae	–	X
Caliciviridae	+	
Picornaviridae	+	
Bunyaviridae	–	X
Togaviridae	+	
Rhabdoviridae	–	
Flaviviridae	+	
Arenaviridae	–	X

TOPIC 9: RNA VIRUSES

1. Name the mode of transmission for picornaviruses.
   Fecal oral

2. Name the mode of transmission for flaviviruses.
   Mosquito

3. Name the most common cause of pediatric gastroenteritis in the United States.
   Rotavirus

4. What is the function of the influenza hemagglutinin (HA) glycoprotein?
   Attachment

5. What is the function of the influenza neuraminidase (NA) glycoprotein?
   Cleaving nascent virus from the cell sialic acid

6. For each description regarding influenza viruses, put "shift" if it describes antigenic shift or "drift" if it describes antigenic drift.

Description	Antigenic Shift or Antigenic Drift
Influenza pandemics	*Shift*
Influenza epidemics	*Drift*
Random mutations in HA or NA	*Drift*
Complete viral assortment	*Shift*

7. Describe the rash caused by rubella virus in a child or adult.
   Maculopapular, begins on face and continues downward

8. The major concern about a primary infection with rubella virus during pregnancy is:
   Teratogen

9. List the 4 major viruses in the paramyxovirus family.
   Measles, mumps, RSV and parainfluenza

10. All paramyxoviruses have a _____*fusion*_____ protein in their viral envelope, which leads to the formation of _____*syncytia*_____ from cell:cell fusion.

11. The major symptom of infection with mumps virus in a child is _____*Bilateral parotitis*_____.

12. List 2 serious sequelae of infection with mumps.
    Orchitis, meningitis

13. List the top 3 animals associated with rabies transmission in the United States.
    Raccoons, bats, skunks

14. Describe the mechanism of spread of rabies virus from a bite wound on the leg to the brain.
    Retrograde transport from wound to ganglia to spinal cord to brain then back to highly innervated sites like salivary glands.

15. List 3 viral families associated with arboviral transmission.
    Bunyaviridae, Flaviviridae and Togavirudae

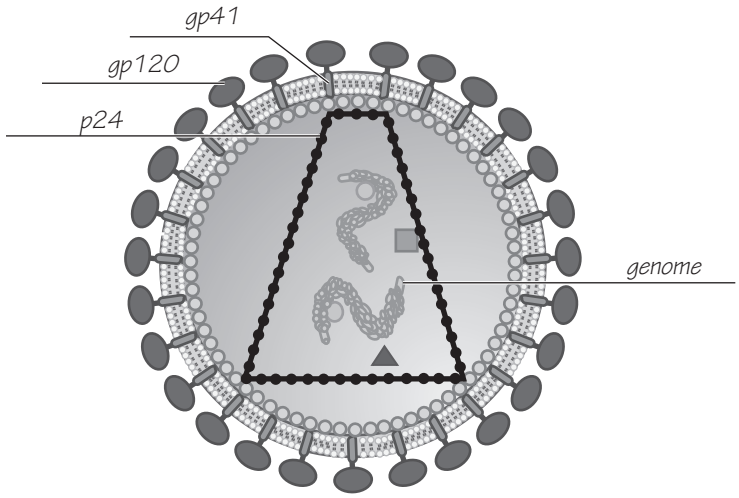
16. For each hepatitis virus, put an "X" where the listed trait applies to that virus.

Hepatitis Virus	Fecal–Oral Transmission	Blood borne/ Sexual Transmission	DNA Virus	RNA Virus	Associated with Chronicity
HAV	x			x	
HBV		x	x		x
HCV		x		x	x
HDV		x	x		
HEV	x			x	

17. For each description, write the HBV Ag or Ab that is appropriate.

- Provides immunity to HBV. HBsAb
- Important for screening recent infections. HBcAb
- If found in the blood past 6 months of first screening, indicative of a chronic infection with HBV. HBsAg
- If found indicates virus is easily transmitted. HBeAg

18. Label the following drawing of HIV virus for the following: gp41, gp120, p24, and genome.



19. List the screening and confirmatory tests for HIV.

ELISA, Western blot

20. List the progressive stages of HIV.

acute → asymptomatic → symptomatic → AIDS

21. List the HIV-associated neoplasms and virus associated with them (if applicable).

Kaposis sarcoma (HHV-8), cervical (HPV), non-hodgkins lymphoma (EBV), primary CNS lymphoma

22. Prions are what type of pathogen?

Infectious protein

23. How is Creutzfeldt-Jakob disease transmitted?

Ingestion of infected cow brains

24. List the agents that comprise the TORCHES.

Toxoplasma gondi, rubella, CMV, herpes, HIV and Treponema pallidum (syphilis)

TOPIC 10: ANTIBACTERIALS

1. Complete the diagram below for cell wall synthesis inhibitors.

2. Identify the generation of cephalosporin.

Drug	Generation
Cefaclor	2nd
Cefepime	4th
Ceftriaxone	3rd
Cefotaxime	3rd
Cephalexin	1st

3. Clavulanic acid is often combined with amoxicillin because _____.

Clavulanic acid is a β-lactamase inhibitor that prevents cleavage and inactivation of amoxicillin. This allows amoxicillin to effectively kill susceptible organisms producing β-lactamase

4. What type of bacteria are killed by vancomycin?

Only gram (+) organisms are killed by vancomycin. Its use is for serious gram (+) infections; such as those due to MRSA, enterococcus, and C. difficile

5. Match each drug listed with its ribosomal target.

Drug	Target
Chloramphenicol	*50s*
Doxycycline	*30s*
Gentamicin	*30s*
Clarithromycin	*50s*
Clindamycin	*50s*
Linezolid	*50s*

6. What antibiotic has its main use as a treatment for SIADH?

Demeclocycline

7. What 2 types of antibiotics are commonly used against atypical organisms such as chlamydia and mycoplasma?

Tetracyclines and macrolides

8. Add the antibiotic or antibiotic drug class most likely associated with the side effect listed.

Side Effect	Drug
Gray baby syndrome	*Chloramphenicol*
Ototoxicity	*Aminoglycosides*
Tooth discoloration	*Tetracyclines*
Red man syndrome	*Vancomycin*
Hemolytic anemia	*Sulfonamide*
Tendonitis	*Fluroquinolones*
Disulfiram reaction	*Metronidazole*

9. Using one of the following, classify each drug according to its mechanism.

CW = cell wall inhibitor
PSI = protein synthesis
AF = antifolate
DNA = DNA or nucleic acid synthesis inhibitor

Drug	Mechanism
Ciprofloxacin	*DNA*
TMP-SMX	*AF*
Penicillin G	*CW*
Azithromycin	*PSI*
Vancomycin	*CW*
Doxycycline	*PSI*
Metronidazole	*DNA*
Cefazolin	*CW*

10. Increased bacterial production of PABA may confer resistance to what type of antibiotic?

    Sulfonamides

11. Complete the mnemonic for a list of important TB drugs.

    R *Rifampin*

    E *Ethambutol*

    S *Streptomycin*

    P *Pyrazinamide*

    I *Isoniazid*

    r

    e

12. Bacterial conversion of the terminal d-alanine to d-lactate confers resistance to what drug?

    Vancomycin

TOPIC 11: OTHER ANTIBIOTICS

1. Match the antifungal drug or drug class with the listed target.

Drug	Target
Flucytosine	Thymidylate synthase
Griseofulvin	Microtubule formation
Amphotericin B	Ergosterol
Caspofungin	β-glucan synthesis
Azoles	Ergosterol synthesis
Terbinafine	Squalene epoxidase

2. What enzyme, present in influenza A and B, is targeted by oseltamivir?
   Neuraminidase

3. Activation of antiherpetic drugs such as acyclovir and ganciclovir require what viral enzyme?
   Thymidine kinase

4. What antiherpetic drug does not require the enzyme from the previous question?
   Foscarnet

5. Match each drug listed to the virus it targets. Use the last 4 letters of each drug name to help guide you.

Drug	Target
Oseltamivir	*Influenza*
Ganciclovir	*Herpes*
Ritonavir	*HIV*
Acyclovir	*Herpes*
Indinavir	*HIV*
Zanamivir	*Influenza*

6. Complete the table below for antiretroviral drugs.

Drug	Target
Zidovudine	*Reverse transcriptase*
Ritonavir	*Aspartate protease*
Enfuvirtide	Gp41
Efavirenz	*Reverse transcriptase*

7. For each sexually transmitted disease listed, identify the antimicrobial most likely to be used.

Disease/Cause	Drug
Chlamydia	*Doxycycline or azithromycin*
Trichomonas	*Metronidazole*
Gardnerella vaginosis	*Metronidazole*
Syphilis	*Penicillin G*
Gonorrhea	*Ceftriaxone*

CHAPTER 5

EPIDEMIOLOGY AND BIOSTATISTICS

TOPIC 1: EPIDEMIOLOGY

1. When comparing the actual cases to the number of potential cases in the determination of rate, the potential cases would be in the *Denominator* and the actual cases would be in the *Numerator*.

2. Rates are generally expressed per *100,000* (number) of persons with the exception of vital statistics, which are expressed per *1,000* (number) of persons.

3. Complete the following equation:
   Incidence rate = *(Number of new events in a specific period / Population at risk during the same time period) X 10^n*

4. What type of 'cases' should be excluded in the calculation of incidence rate?
   Cases that were diagnosed before the specified time period

5. What type of 'cases' should be excluded in the calculation of attack rate?
   Cases that were diagnosed before the specified time period

6. The attack rate is defined as *number of exposed people infected with a disease divided by the total number of exposed people.*.

7. Complete the following equation:

Prevalence rate = *(All cases of a disease at a given point in time/Total population at risk for that disease at a given point in time) X 10^n*

8. What is the difference between point prevalence and period prevalence?

Point prevalence describes the number of cases at a specific time whereas period prevalence describes the number of cases over a specified period or span of time

9. When incidence increases, then prevalence usually *increases*.

10. Prevalence = Incidence × *Duration*

11. Complete the following table with "no change," "increase," or "decrease."

What is the change to incidence and prevalence when:	Incidence	Prevalence
A new vaccine for a condition becomes available	*Decrease*	*Decrease*
Long-term survival rates for a disease are decreasing	*No change*	*Decrease*
A formerly effective medication is becoming ineffective due to widespread resistance	*No change*	*Increase*
Number of persons dying from a condition are increasing	*No change*	*Decrease*
A new effective treatment is available	*No change*	*Decrease*

12. Complete the table with the appropriate information on phases of a clinical trial.

	Phase I	Phase II	Phase III	Phase IV
Type of patients in sample	Healthy individuals (20 – 100)	Patients with disease (100-300)	Patients with disease (100s-1000s)	Patients with disease (1000s)
Data evaluated	- *Safety* - *Vital signs* - *Drug levels in the blood and plasma* - *Adverse Effects*	- *Dose response factors* - *Tolerability* - *Efficacy (limited)* - *Adverse Effects*	- *Continued Efficacy* - *Laboratory Data* - *Continued Safety* - *Adverse Effects*	- *Epidemiology* - *Safety and Efficacy* - *Common and Rare Adverse Effects*
Duration	1 – 30 days	Months	Months to years	*Years (continual)*

13. Cohort studies are observational studies in which subjects are classified as either having or not having a ___*risk factor*___ and then followed ___*forward*___ in time.

14. Data from cohort studies are usually analyzed by means of ___*relative risk and attributable risk*___ calculations to estimate the increase in incidence due to the presence of that risk factor.

15. Case-control studies identify individuals with disease, then go back in time to identify ___*risk factors*___ that might be associated with a given disease or condition.

16. Data from case-control studies are usually analyzed by means of ___*an odds-ratio*___.

17. Cross-sectional studies assess the ___*prevalence*___ of a disease in a given population and what factors are associated with having that disease.

18. In cross-sectional studies, association of identified factors with disease is usually assessed by using ___*chi-square analysis*___.

19. Crossover studies are clinical trials in which 2 comparison groups ___both___ receive the study drug and the comparative intervention but at ___different___ times.

20. A crossover study will begin with one study group receiving ___the investigated drug___, while a comparison (control) group receives ___a placebo or a comparative treatment___. Then, at some predetermined point, the first group is ___switched to the placebo or comparative treatment___, while the second group is ___given the drug being tested___.

21. Given the following 2 × 2 table, add TP (true positive), FP (false positive), FN (false negative), and TN (true negative).

	Disease Present		Disease Absent	
Screening Test Results Positive	*TP*	*180*	*FP*	*30*
Screening Test Results Negative	*FN*	*20*	*TN*	*170*

22. Based on the 2 × 2 table, what is the specificity for this test?
Specificity = TN / TN + FP = 170 / 170 + 30 = 85%

23. Based on the 2 × 2 table, what is the sensitivity for this test?
Sensitivity = TP / TP + FN = 180 / 180 + 20 = 90%

24. Based on the 2 × 2 table, what is the positive predictive value for this test?
Positive Predictive Value = TP / TP + FP = 180 / 180 + 30 = 86%

25. Based on the 2 × 2 table, what is the negative predictive value for this test?
Negative Predictive Value = TN / TN + FN = 170 / 170 + 20 = 89%

26. Explain what SNOUT means.
If a highly sensitive test is NEGATIVE then it will rule out the presence of the disease in question.

27. Explain what SPIN means.

If a highly specific test is POSITIVE then the patient has the disease.

28. A meta-analysis is a statistical way of combining the results of many studies to produce _____*an overall conclusion*_____.

29. A meta-analysis will increase _____*statistical power*_____.

30. A meta-analysis can be limited by what 2 factors?

Quality of individuals studied or bias in the study selection.

31. A meta-analysis will help to eliminate what kind of bias?

Confounding bias

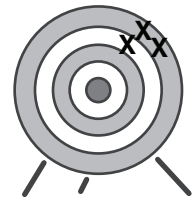
32. What is the difference between accuracy and precision?

Accuracy represents the true value of the attribute that is being measured AND precision is the ability of a test to consistently reproduce the same test result.

33. Is validity matched with accuracy or precision?

Accuracy

34. For the diagram below, what can be said with respect to accuracy and precision?



The 'shooter' is precise but NOT accurate since they are not getting all of the 'shots' in the center of the target but they are consistently 'grouping' the shots in one place.

35. What type of error reduces the accuracy in a test?

systematic error

36. What type of error reduces the precision in a test?

random error

37. For the table below, identify which patients have been exposed to the risk factor and which patients have not.

	Disease Present	Disease Absent
Risk Factor (+)	A	B
Risk Factor (–)	C	D

A & B = Exposed - - C and D = non-exposed

38. For the table above, how would the relative risk and attributable risk (cohort studies) be calculated?

Odds ratio = AD / BC *Relative Risk = A/(A+B) / C/(C+D)* *Attributable Risk = A/A+B – C/C+D*

39. Which of the following yields a p-value?

(A) Absolute risk reduction
(B) Attributable risk
(C) Number needed to treat
(D) Odds ratio
(E) Relative risk

40. NNT is the number of patients who need to be treated for _____1_____ patient to benefit.

41. Relative risk and attributable risk tell us that there are statistical differences, but they do not tell us _____why those differences exist_____.

42. The Hawthorne effect is what type of bias?

Measurement bias

43. The Pygmalion effect is what type of bias?

Experimenter expectancy bias

44. Recall bias is primarily seen in what types of research studies?

Retrospective OR Case control

45. Combining the results from multiple studies is a way to prevent what kind of bias?

(A) Confounding bias
(B) Design bias
(C) Late look bias
(D) Recall bias

46. To prevent design bias, researchers could do which of the following?

(A) Conformation
(B) Meta-analysis
(C) Random assignment
(D) Stratify by disease severity

47. A new screening test is developed that identifies a fatal disease earlier. Researchers soon report that patients with that particular disease are living longer. This is an example of _lead-time_ bias. This type of bias causes the reporting of _false estimate of survival rates_. How could researchers prevent this type of bias?

Use life expectancy to assess the benefit

TOPIC 2: BIOSTATISTICS

1. The null hypothesis is considered to be the _opposite_ of what a researcher is hoping to prove.

2. If a researcher wants to reject the null hypothesis, she must have a p-value of less than or equal to _0.05_.

3. If a researcher is able to obtain the desired p-value (in question 2), it means that _statistical significance_ has been achieved.

4. In the statistical testing of a hypothesis, the alternative hypothesis is _accepted_ if the null hypothesis is _rejected_.

5. In statistical hypothesis testing, researchers never do what to the null hypothesis?

   (A) Accept it
   (B) Fail to reject it
   (C) Reject it
   (D) Researchers can do all of the above

6. Researchers want to investigate the claim that the normal arterial pH is *not* between 7.35 and 7.45. The null hypothesis is _Normal arterial pH is between 7.35 to 7.45_. The alternative null hypothesis is _Normal arterial pH is NOT between 7.35 to 7.45_.

7. Define an alpha error.

   An alpha error or Type I error is rejecting the null hypothesis when it is really true.

8. If the p-value is 0.04, then the chance of committing a _type I_ error is _4 in 100_.

9. If a type II error is an error of omission, then a type I error is an error of ___commission___.

10. A research study is evaluating the effectiveness of a new powerful antimicrobial agent godzillacillin. When comparing godzillacillin to amoxicillin/clavulanic acid for the treatment of a specific infection, researchers achieve a p-value of 0.0001.

    Were researchers able to prove that godzillacillin is more effective than amoxicillin/clavulanic acid with absolute certainty? ___NO___ Why?

    Because there is still a 1/10,000 chance that a type I error has occurred.

11. The results of a landmark placebo-controlled, randomized clinical trial study are published.

    Which would be worse for the general population, the researchers committing a type 1 or type 2 error? ___type 1 error___ Why?

    If the researchers commit a type 1 error then they reject the null hypothesis when it should have been accepted; hence, the affected patient population would be taking a drug that is essentially no more effective than placebo and can potentially cause harmful side effects.

12. If researchers are able to obtain a p-value of 0.001 in a drug study, this p-value does not prove which of the following?

    (A) Clinical relevance
    (B) Statistical significance
    (C) Both A and B are proven with this p-value
    (D) Both A and B are not proven with this p-value

13. Power is directly related to a type ___II___ error and is most commonly increased when a researcher is able to increase ___the sample size___.

14. The most frequently occurring value in a set of observations is known as the ___Mode___.

15. What type of "skew" is occurring when the mean < median < mode? *Negative skew*

16. For the following set of numbers (3, 6, 6, 7, 9, 10, 12), what is the mean, median, and mode, respectively?

    Mean = 7.6, Median = 7, Mode = 6

17. In a normal distribution curve, what percent of cases are above 2 standard deviations below the mean? Provide your calculation.

    13.5% + 34% + 34% + 13.5 % + 2.4% + 0.15% = 97.55%

18. If 1.0 is not included in the confidence interval, then what are researchers able to assume?

    that the samples are different AND statistically significance

19. Complete the table below.

Variables			
Name of Statistical Test	**Interval**	**Nominal**	**Number of groups?**
Chi-square	0	2	Any number of groups
One-way ANOVA	*1*	*1*	2 or more groups
t-test	1	1	2 groups only
Pearson Correlation	*2*	*0*	*Is there a linear relationship?*

20. Prevention of a disease from occurring is an example of which of the following?

    (A) Primary prevention
    (B) Secondary prevention
    (C) Tertiary prevention
    (D) Treatment measure

21. Obtaining a PSA in an elderly male is an example of which of the following?

(A) Primary prevention
(B) Secondary prevention
(C) Tertiary prevention
(D) Treatment measure

22. The use of an antibiotic in a child with an ear infection is an example of which of the following?

(A) Primary prevention
(B) Secondary prevention
(C) Tertiary prevention
(D) Treatment measure

23. The use of abacavir + lamivudine + efavirenz in an HIV infected female is an example of which of the following?

(A) Primary prevention
(B) Secondary prevention
(C) Tertiary prevention
(D) Treatment measure

24. A 23-year-old sexually active female requiring her partner to wear a condom is an example of which of the following?

(A) Primary prevention
(B) Secondary prevention
(C) Tertiary prevention
(D) Treatment measure

25. If a patient has HIV, reporting to state and local authorities varies depending on _____*the individual state*_____. However, HIV is reportable _____*everywhere*_____.

26. Which of the following should be reported?

(A) AIDS
(B) Hepatitis A
(C) MMR
(D) All of the above

27. The leading causes of death in children ages 1–14 years are _injuries, cancer, homicide_.

28. Cancer, heart disease, and injuries are the leading causes of death in people of what age range?
Ages 25-64

29. Women attempt suicide _3_ times as often as men.

30. Suicides outnumber _homicides_ in the United States as a cause of death.

31. Approximately how many suicide attempts are there for every one that succeeds?

(A) 2–5
(B) 5–10
(C) 10–20
(D) 20–50
(E) 75–100

32. Medicare and Medicaid receive their funding from _the federal government_.

33. At what age are people eligible for Medicare?

(A) Any age
(B) >50 years
(C) >60 years
(D) >65 years

34. What are the criteria to be eligible for Medicaid?

Under the age of 65 and low Income

35. Medical residents receive their salaries from *Medicare and Medicaid funds*.

36. Salaries for medical residents across the United States are *uniform* because *they come from the same pool of funds*.

CHAPTER 6

BEHAVIORAL MEDICINE AND ETHICS

TOPIC 1: CHILD AND ADOLESCENT DEVELOPMENT

1. Complete the following table for the APGAR scoring system.

APGAR Scoring System			
Evaluation	**0 Points**	**1 Point**	**2 Points**
Heart rate	0	*< 100/min*	*> 100/min*
Respiration	None	Irregular, shallow gasps	*Crying*
Color	*Blue*	Pale, blue extremities	*Pink*
Tone	*None*	*Weak, passive*	Active
Reflex irritability	None	*Facial grimace*	*Active withdrawal*

2. Low birth weight is considered anything less than *2.5* kg.

3. APGAR stands for *Appearance, Pulse, Grimace, Activity, Respiration*.

4. A young girl should be able to copy a triangle at what age? *6 years*

5. An infant should be expected to change hands when playing with a toy at what age?
   6 months

6. At what age would a young boy be expected to turn a doorknob, imitate mannerisms, and parallel play? *2 years*

7. At what age would a child be expected to conform to peers, ask the meaning of words, and have a brain weight of approximately 75% of that of an adult? *5 years*

8. At what age would a child be expected to use approximately 900 words and stack 9 cubes?
   3 years

9. Describe the social development expectations for a 4-year-old boy.
   Imitation of adult roles, curiosity about sex, nightmares, monster fears, and imaginary fears

10. Complete the following table for the Tanner stages of development.

Tanner Stages of Development			
Stage	**Female Breast**	**Female and Male Pubic Hair**	**Male Genitalia**
1	Preadolescent	None	*Childhood size*
2	*Breast Bud*	*Sparse, long straight*	Enlargement of scrotum/testes
3	*Areolar diameter enlarges*	*Darker, curling, increased amount*	*Penis grows in length; testes continue to enlarge*
4	*Secondary mound; separation of contours*	Coarse, curly, adult type	*Penis grows in length/breadth, scrotum darkens, testes enlarge*
5	Mature female	*Adult; extends to thighs*	Adult shape/size

11. At what age would the pubic hair in a female or male be described as coarse and curly?
    11 to 13 years

12. What are the 3 major causes of sexual dysfunction in a man who is NOT diagnosed with erectile dysfunction?
    (A) Drugs
    (B) Disease
    (C) Psychological

13. What effect does stress have on cortisol levels, cholesterol levels, and immune function, respectively?
    Increased cortisol levels, increased cholesterol levels, and decreased immune function

14. BMI is a measure of weight adjusted for height, and is calculated as follows:
    weight in kg / height in meters squared

15. A BMI of 18.5 – 24.9 is considered to be normal.

16. A BMI of >30 is considered to be obese.

17. A BMI of 25 – 29.9 should be treated with diet and exercise.

TOPIC 2: GERIATRIC HEALTH AND GRIEF

1. Which of the following is decreased in the elderly?

   (A) Percentage body fat
   (B) Intelligence
   (C) Sexual interest
   (D) All of the above
   (E) None of the above

2. The sexually related changes that occur in men and women, respectively, are _slower erection/ejaculation, longer refractory period_ and _vaginal shortening, vaginal dryness, vaginal thinning_.

3. With respect to sleep patterns in the elderly, one would expect to see _decreased_ REM and slow-wave sleep and _increased_ latency and awakenings.

4. Men from the ages of _65-74_ have the highest suicide rate in the United States.

5. A physician would expect to see _an increased_ volume of distribution for highly lipid-soluble drugs in the elderly. Explain your answer.
   There is an increased percentage of fat in the elderly

6. Grief can last up to _12_ months and should be treated if it lasts more than _2_ months.

7. What are the 5 stages of grief according to Kubler-Ross?
   Denial, Anger, Bargaining, Depression and Acceptance

8. Do the 5 stages of grief in the Kubler-Ross model have to appear in a certain order to be classified as "normal" grief? No

9. Are antidepressants indicated for individuals experiencing normal grief? No

10. Crying, decreased libido, weight loss, and insomnia are common in which of the following?

(A) Depression
(B) Normal grief
(C) Prolonged grief
(D) All of the above
(E) None of the above

TOPIC 3: SLEEP AND SLEEP DISORDERS

1. The circadian rhythm is controlled by *suprachiasmatic nucleus of the hypothalamus*.

2. Beta waves would predominate on an EEG in what sleep stages? *Eyes open and REM sleep*

3. What is the main neurotransmitter in REM sleep? *acetylcholine*

4. Which of the following should be treated with amphetamine salts?

   (A) Depression
   (B) Enuresis
   (C) Narcolepsy
   (D) Sleep disorder in depressed patients
   (E) Sleep terror disorder

5. What is the difference between the sleep stages in night terrors and nightmares?

   Night terrors is stage 4 (late N3) and nightmares are in REM sleep

6. Fill in the blanks in the table below with "increase," "decrease," or "no change."

Sleep Patterns of Patients with Major Depression			
Slow wave sleep	**REM early in sleep cycle**	**REM latency**	**Total REM sleep**
Decreased	*Increased*	*Decreased*	*Increased*

7. What are the recommended treatment measures for sleep apnea syndromes?

   Weight loss, Continuous positive airway pressure (CPAP), Condition so not sleeping on back, and Surgery for severe cases

8. What increases the risk for sudden infant death syndrome?
   Sleeping on stomach, overstuffed beds/pillows, household smoking, fetal maternal exposure to smoking

9. What are the differences between the sleep stages for somnambulism and bruxism?
   Somnambulism is stage 4 (late N3) sleep AND bruxism is Stage 2 (N2) sleep

10. Which of the following is indicated for the treatment of chronic enuresis?

    (A) Amphetamine salts
    (B) Desmopressin
    (C) Diphenhydramine
    (D) Imipramine
    (E) Octreotide

TOPIC 4: INTRODUCTION TO PSYCHIATRIC DISORDERS

1. A 36-year-old female is diagnosed with generalized anxiety disorder. Her condition would be classified under which of the following Axes?

   (A) Axis I
   (B) Axis II
   (C) Axis III
   (D) Axis IV
   (E) Axis V

2. What are the primary Axis II disorders?

   Personality disorders and mental retardation

3. A patient with Down syndrome is described as being "trainable and would benefit from vocational training but needs adult supervision." What would be his expected IQ range? 35-49

4. Match the defense mechanism on the left with the appropriate definition or important association on the right.

(A)	Acting out	G	Attributing inner feelings to others
(B)	Altruism	K	The world is composed of polar opposites
(C)	Blocking	D	Substance abuse, reaction to death
(D)	Denial	C	Transient ability to remember
(E)	Isolation of affect	F	Unconscious, indirect hostility
(F)	Passive-aggressive	I	Enuresis, primitive behaviors
(G)	Projection	L	Forget and remember
(H)	Reaction formation	J	Moving an improper impulse into an acceptable channel
(I)	Regression	A	Affect covered up by excessive action or sensation
(J)	Sublimation	H	The unacceptable transformed into its opposite
(K)	Splitting	B	Guilt is alleviated by unsolicited generosity to others
(L)	Suppression	E	Facts without feelings

5. A 62-year-old woman is scheduled to have a colonoscopy and administered 10 mg of diazepam. This medication is likely to cause what type of amnesia?

   (A) Anterograde amnesia
   (B) Dissociative amnesia
   (C) Korsakoff's amnesia
   (D) Retrograde amnesia

6. A patient with Korsakoff's amnesia is likely to be deficient in which of the following vitamins?

   (A) Vitamin B1
   (B) Vitamin B3
   (C) Vitamin B6
   (D) Vitamin B12
   (E) Vitamin K

7. Cognitive disorders are associated with significant changes in what?
   memory, attention, language and judgment

8. Label the following as delirium or dementia:

   (A) *Dementia* Insidious onset
   (B) *Delirium* Visual hallucinations more common
   (C) *Dementia* Associated with less sleep disruption
   (D) *Dementia* Attention span generally not decreased
   (E) *Delirium* Reversible condition
   (F) *Delirium* Duration is generally days to weeks
   (G) *Dementia* Remote memories seem as recent memories

9. Can patients with dementia develop delirium? *Yes*

10. Explain the relationship (if one exists) between illicit drug abuse and both delirium and dementia.

illicit drug abuse can acutely cause dementia and with chronic use can cause dementia (due to neurotoxicity of the drugs)

11. Fill in the missing neurotransmitter in the table below.

Disorder	Neurotransmitter Changes
Alzheimer's disease	Inc: *n/a* Dec: *ACh*
Anxiety	Inc: *NE* Dec: *GABA, 5-HT*
Depression	Inc: *n/a* Dec: *NE, 5-HT, Dopamine*
Huntington's disease	Inc: *Dopamine* Dec: *GABA, ACh*
Parkinson's disease	Inc: *5-HT, ACh* Dec: *Dopamine*
Schizophrenia	Inc: *Dopamine* Dec: *n/a*

TOPIC 5: CHILDHOOD AND PERVASIVE DISORDERS

1. Prolonged affection deprivation in an infant generally leads to all of the following *except*:

   (A) Anaclitic depression
   (B) Decreased muscle tone
   (C) Increased trust of other adults
   (D) Poor socialization skills
   (E) Weight loss
   (F) Affection deprivation leads to all of the above

2. All of the following must be reported to the proper authorities upon discovery by a physician *except*:

   (A) Child neglect
   (B) Physical abuse (child)
   (C) Physical abuse (spouse)
   (D) Sexual abuse (child)
   (E) All of the above must be reported by a physician

3. Antipsychotic medications are most commonly used in the treatment of which of the following?

   (A) ADHD
   (B) Conduct disorder
   (C) Oppositional defiant disorder
   (D) Separation anxiety disorder
   (E) Tourette's syndrome

4. Methylphenidate is most commonly used in the treatment of which of the following?

   (A) ADHD
   (B) Conduct disorder
   (C) Oppositional defiant disorder
   (D) Separation anxiety disorder
   (E) Tourette's syndrome

5. Continual pattern of defiant and hostile behavior toward authority figures is most commonly seen in patients with which of the following?

   (A) ADHD
   (B) Conduct disorder
   (C) Oppositional defiant disorder
   (D) Separation anxiety disorder
   (E) Tourette's syndrome

6. Motor and vocal tics are commonly seen in patients diagnosed with _____*Tourette's syndrome*_____.

7. Provide examples of the vocal and motor tics in patients diagnosed with the condition in question 6.

   snorting, sniffing, uncontrolled and often obscene vocalizations

8. Describe the treatment of autism.

   Behavioral shaping techniques + Medication: Only if accompanied by disruptive or harmful behavior

9. With respect to intelligence, what is the difference between patients with Asperger's syndrome and autism?

   Asperger's disorder patients have normal intelligence and 80% of autistic patients have IQ's below 70

10. Why is Rett's syndrome primarily seen in females?

    It is an X-linked disorder primarily seen in females because most affected males generally die in utero or shortly after birth

TOPIC 6: SCHIZOPHRENIA AND DISSOCIATIVE DISORDERS

1. Describe the difference between hallucinations and delusions.

   Hallucinations are imagined perceptions in the absence of external stimuli AND delusions are untrue beliefs despite the facts being presented

2. Which of the following hallucinations are most commonly seen in schizophrenia?

   (A) Auditory
   (B) Gustatory
   (C) Olfactory
   (D) Tactile
   (E) Visual
   (F) All of the above are commonly seen in schizophrenia

3. Which of the following hallucinations are most commonly seen in alcohol withdrawal?

   (A) Auditory
   (B) Gustatory
   (C) Olfactory
   (D) Tactile
   (E) Visual

4. What is believed to be the primary cause of schizophrenia?

   (A) Decreased acetylcholine
   (B) Decreased dopamine
   (C) Decreased serotonin
   (D) Increased acetylcholine
   (E) Increased dopamine
   (F) Increased serotonin

5. Negative symptoms of schizophrenia include:

   (A) Delusions
   (B) Disorganized or catatonic behavior
   (C) Disorganized speech
   (D) Hallucinations
   (E) Social withdrawal
   (F) All of the above are negative symptoms of schizophrenia

6. Delusions of persecution or grandeur are primarily associated with which of the following subtypes of schizophrenia?

   (A) Catatonic
   (B) Disorganized
   (C) Paranoid
   (D) Residual
   (E) Undifferentiated

7. What is the primary difference between high- and low-potency antipsychotics?

   High potency cause more EPS and less nonspecific side effect AND the low potency cause less EPS and more non-specific side effects

8. A patient experiencing repetitive movements of the lips, tongue, and limbs for the past 120 days is likely to be diagnosed with _____*Tardive dyskinesia*_____.

9. In addition to blocking the dopamine D2 receptors, olanzapine also acts as a _____*serotonin or 5HT2*_____ receptor antagonist.

10. Clozapine acts at the dopamine _____*D4*_____ receptor and is most commonly associated with the development of _____*agranulocytosis*_____ which requires _____*regular*_____ monitoring of _____*White blood cell counts*_____.

TOPIC 7: MOOD DISORDERS

1. A mood disorder is characterized by a disturbance in the person's mood and _loss of control_ over that mood.

2. A milder form of bipolar disorder is _cyclothymia_.

3. Complete the following table on the symptoms of mania. Keep in mind the DIG FAST mnemonic.

Symptom	Explanation
Distractibility	Inability to concentrate
Interest or irresponsibility	*Pleasure seeking without regard for consequences*
Grandiosity	Inflated self-esteem
Flight of ideas	*Racing thoughts*
Appetite or agitation	*Both dramatically increased*
Sleep	*Decreased need for sleep*
Talkativeness	Loud and pressured speech

4. A 28-year-old man is diagnosed with bipolar disorder in which manic symptoms predominate. Which of the following would be indicated as initial therapy?

   (A) Clozapine
   (B) Electroconvulsive therapy
   (C) Ethosuximide
   (D) Fluoxetine
   (E) Olanzapine

5. A non-pregnant woman with bipolar disorder is treated with lithium. Which of the following is most likely to occur as a direct result of her therapy?

   (A) Ebstein's anomaly

   (B) Hyperthyroidism

   (C) Nephrogenic diabetes insipidus

   (D) All of the above could occur in this patient as a direct result of lithium therapy

6. Is fluoxetine indicated for the treatment of both dysthymia and seasonal affective disorder?

   NO If not, then which condition should it be used to treat under what conditions?

   Seasonal affective disorder unresponsive to light therapy

7. According to the biogenic amine theory of depression, what 2 neurotransmitters are involved in major depression?

   norepinephrine and serotonin

8. Side effects of the tricyclic antidepressants are primarily mediated through

   muscarinic receptors and alpha-blockade.

9. If a patient is taking phenelzine and drinks a glass of red wine while eating aged cheese, which of the following is likely to occur?

   (A) Hypertensive crisis

   (B) Neuroleptic malignant syndrome

   (C) Pulmonary fibrosis

   (D) Serotonin syndrome

10. Describe serotonin syndrome.

    muscle rigidity, hyperthermia, myoclonus, ANS instability

11. Venlafaxine acts by what mechanism?

    Inhibits both serotonin and norepinephrine reuptake

12. A male patient taking trazodone should be concerned about which side effect?

    (A) Erectile dysfunction

    (B) Priapism

    (C) Seizures

    (D) All of the above

13. Electroconvulsive therapy is used in the treatment of depression in cases when
    good for suicidal patients and pregnant patients – It is only used for treatment of depression NOT prophylaxis.

TOPIC 8: ANXIETY DISORDERS

1. An anxiety disorder is characterized by excessive *fear or worry* and is associated with *physical* manifestations.

2. To make a diagnosis of generalized anxiety disorder, *3* out of 6 symptoms must be present. What are these possible symptoms?

   (A) *Restlessness or nervousness*
   (B) *Easy fatigability*
   (C) *Poor concentration*
   (D) *Irritability*
   (E) *Muscle tension*
   (F) *Sleep Disturbance*

3. Acute therapy for generalized anxiety disorder generally involves the use of *Benzodiazepines*. Long-term, first line therapy includes the use of *Buspirone, SSRIs, or SNRIs*.

4. Next to each drug below list its most common uses:

   (A) Alprazolam — *Anxiety, Panic, Phobias*
   (B) Chlordiazepoxide — *Alcohol detoxification*
   (C) Oxazepam — *Sleep disorder, anxiety*
   (D) Lorazepam — *Anxiety, preop sedation, status epilepticus (IV)*
   (E) Clonazepam — *Panic disorder, anxiety, seizures*

5. A patient with hepatic dysfunction should be prescribed one of 3 benzodiazepines. Name them:
   oxazepam, temazepam or lorazepam

6. Describe social anxiety disorder.

   Excessive fear of social and performance situations where the person is fearful of being embarrassed or negatively evaluated by others

7. Why should buspirone not be prescribed for acute anxiety?

   It takes 1-2 weeks to begin working so short-term benzodiazepine use is indicated initially

8. What is the most common phobia?

   Discrete performance anxiety OR Stage fright

9. List the 3 groups of symptoms seen in PTSD:

   (A) *Re-experiencing the event*

   (B) *Avoidant behavior*

   (C) *Hyperarousal*

10. The initial treatment for a 33-year-old woman with obsessive-compulsive disorder would be which of the following?

    (A) Fluoxetine
    (B) Lithium
    (C) Lorazepam
    (D) Olanzapine
    (E) Phenelzine

11. Symptoms of panic disorder generally peak in:

    (A) 3 minutes
    (B) 5 minutes
    (C) 10 minutes
    (D) 30 minutes
    (E) 1 hour
    (F) They are persistent and do not peak.

TOPIC 9: SOMATOFORM DISORDERS

1. Fill in the blanks in the table below with "unconscious" or "intentional."

Differentiating Somatoform Disorders from Factitious Disorders and Malingering			
	Malingering	Factitious	Somatoform
Symptom production	*Intentional*	*Intentional*	*Unconscious*
Motivation	*Intentional*	*Unconscious*	*Unconscious*

2. Somatization disorder is characterized by _____*multiple*_____ somatic symptoms that cannot be explained adequately based on _____*physical and laboratory examinations*_____.

3. Somatization disorders generally have _____*>4*_____ pain symptoms, _____*2*_____ GI symptoms, _____*1*_____ sexual symptom(s), and 1 _____*pseudoneurological*_____ symptom.

4. Conversion disorder generally occurs following _____*a severe stressor*_____.

5. A patient is diagnosed with hypochondriasis. In order to make this diagnosis, the associated "fear" with this condition should be present for how long?

   (A) 2–4 weeks

   (B) 4–12 weeks

   (C) 3–6 months

   (D) >6 months

6. Which of the following analgesics have been proven to be most effective for pain disorder?

   (A) Acetaminophen
   (B) Aspirin
   (C) Ibuprofen
   (D) Oxycodone
   (E) Analgesic therapy is ineffective in pain disorder

7. Which of the following drug classes have been shown to be most effective for body dysmorphic disorder?

   (A) Atypical antipsychotics
   (B) NSAIDs
   (C) SSRIs
   (D) Typical antipsychotics
   (E) Body dysmorphic disorder is unresponsive to drug therapy

8. What is the primary difference between Munchausen's syndrome and Munchausen's syndrome by proxy?

   In Munchausen's syndrome the patient inflicts 'sickness' on themselves and in Munchausen's syndrome by proxy, the patient inflicts 'sickness' on others and assumes the sick role by proxy

9. What is the primary motivation in malingering?

   secondary gain

TOPIC 10: PERSONALITY DISORDERS

1. What are the 5 basic dimensions of a personality?
   - (A) *Extraversion*
   - (B) *Agreeableness*
   - (C) *Conscientiousness*
   - (D) *Neuroticism*
   - (E) *Openness to experience*

2. It is believed that personality disorders may be differentiated by their *interactions* among the 5 dimensions rather than *differences on any single dimension*.

3. Fill in each personality disorder based on its "cluster."

Personality Disorder by Cluster		
Cluster A	**Cluster B**	**Cluster C**
Paranoid personality disorder	*Antisocial personality disorder*	*Avoidant personality disorder*
Schizoid personality disorder	*Borderline personality disorder*	*Dependent personality disorder*
Schizotypal personality disorder	*Histrionic personality disorder*	*Obsessive-compulsive personality disorder*
	Narcissistic personality disorder	

4. Match the personality disorder (PD) on the left with the correct phrase on the right.

(A)	Antisocial PD	D	Likely to end up as an abused spouse
(B)	Avoidant PD	G	Inflexible, orderly, rigid, perfectionist behavior
(C)	Borderline PD	A	Complete disregard for the rights of others
(D)	Dependent PD	F	Sense of entitlement and grandiosity
(E)	Histrionic PD	H	Defenses = projection
(F)	Narcissistic PD	B	Profound fear of rejection but desires relationships
(G)	Obsessive compulsive PD	I	Content in isolation and considered a loner
(H)	Paranoid PD	J	Associated with 'magical thinking'
(I)	Schizoid PD	C	Treated with mood stabilizers and anticonvulsants
(J)	Schizotypal PD	E	Defenses = regression, somatization, conversion and dissociation

TOPIC 11: EATING DISORDERS

1. Persons with eating disorders tend to have a distorted _____*body image*_____.

2. Binging and purging is seen in patients with which of the following?

   (A) Anorexia nervosa
   (B) Bulimia nervosa
   (C) Both conditions
   (D) Neither condition

3. Low body weight is primarily seen in patients with which of the following?

   (A) Anorexia nervosa
   (B) Bulimia nervosa
   (C) Both conditions
   (D) Neither condition

4. Electrolyte disturbances are primarily seen in patients with which of the following?

   (A) Anorexia nervosa
   (B) Bulimia nervosa
   (C) Both conditions
   (D) Neither condition

5. The forced vomiting seen in patients with bulimia nervosa tends to occur with what frequency?

   Several times a week to several times a day

6. Enamel erosion is primarily seen in patients with which of the following?

   (A) Anorexia nervosa
   (B) Bulimia nervosa
   (C) Both conditions
   (D) Neither condition

TOPIC 12: SEXUAL DISORDERS

1. What are the primary psychiatric disorders included in the differential for a sexual disorder?

   (A) *Alcoholism / Substance abuse*
   (B) *Depression / Bipolar disorder*
   (C) *Mental Retardation*
   (D) *Obsessive-compulsive disorder*
   (E) *Personality disorders*
   (F) *Posttraumatic stress disorder*
   (G) *Schizophrenia*

2. Match the sexual disorder on the left with the definition or association on the right:

(A)	Coprophilia	D	Sexual focus on shoes
(B)	Dyspareunia	G	Treatment with relaxation, Hegar dilators
(C)	Exhibitionism	F	Sexual pleasure derived from others' pain
(D)	Fetishism	A	Combining sex and defecation
(E)	Frotteurism	C	Desire to expose genitals to strangers
(F)	Sadism	B	Recurrent pain before, during, or after intercourse
(G)	Vaginismus	E	Act tends to occur in unknowing females on subways and buses
(H)	Voyeurism	H	Sexual pleasure derived from watching others having sex

3. What is the difference between hypoactive sexual disorder and sexual aversion?

   Hypoactive sexual disorder is a deficiency or absence of fantasies or desires but still have sexual contact; sexual aversion is a complete aversion to all sexual contact

4. What are the treatments of choice for secondary male erectile disorder?

   PDE5 inhibitors, prostaglandin analogs, devices, psychosexual therapy

TOPIC 13: SUBSTANCE ABUSE

1. Alcoholism is characterized by _____physiologic / physical_____ dependence and tolerance as well as symptoms of withdrawal when _____consumption is interrupted_____.

2. Wernicke-Korsakoff syndrome is associated with a triad of symptoms. These symptoms are _____ophthalmoplegia, confusion and ataxia_____. This condition is treated with _____Thiamine_____.

3. A 23-year-old man who overdoses on morphine should be treated with which of the following?

   (A) Buprenorphine
   (B) Flumazenil
   (C) Methadone
   (D) Naloxone

4. Benzodiazepines increase the _____frequency_____ of $GABA_A$ channel opening, and barbiturates increase the _____duration_____ of $GABA_A$ channel opening.

5. Which of the following exerts its mechanism of action by blocking the reuptake of dopamine, norepinephrine, and serotonin?

   (A) Cocaine
   (B) Lorazepam
   (C) Methylphenidate
   (D) Mescaline
   (E) Phencyclidine

6. What are the 6 basic stages of change in overcoming alcohol/drug addiction?

(A) Pre-contemplation

(B) Contemplation

(C) Determination

(D) Action

(E) Maintenance

(F) Relapse

7. Psychotherapy, drug counseling, and a 12-step program are likely to occur in which stage of overcoming alcohol/drug addiction?

(A) Action

(B) Contemplation

(C) Determination

(D) Maintenance

(E) Pre-contemplation

(F) Relapse

TOPIC 14: ETHICS

1. The ethical principles followed by physicians:

   (A) Are the same throughout the United States
   (B) Depend on the values of each individual physician
   (C) Vary depending on the health system in which the physician is practicing
   (D) Vary from state to state

2. The core ethical principle of "do no harm" is best described as which of the following?

   (A) Beneficence
   (B) Justice
   (C) Nonmaleficence
   (D) Patient autonomy

3. The ethical principle of justice can best be described as:

   To treat all patients fairly and equally

4. If a competent patient decides to go against the recommendations of the treating physician, whose preferences should always be honored?

   the patient's

5. Physicians have an ethical duty to act in the best interest of the patient. This ethical principle can best be described as which of the following?

   (A) Beneficence
   (B) Justice
   (C) Nonmaleficence
   (D) Patient autonomy

6. Informed consent requires that a patient *receives* and *understands* all the necessary information related to the procedure and/or treatment.

7. What are the 5 pieces of information that a patient must have in order for informed consent to be valid?

   (A) Nature of the procedure (What)

   (B) Purpose or rationale (Why)

   (C) Risks

   (D) Benefits

   (E) Alternatives

8. In informed consent, a patient must be given all the treatment alternatives, which must include the option for no intervention.

9. If a patient gives a written informed consent for a procedure, how can this consent be revoked?

   Informed consent can be revoked at any time, verbally and/or by signing off that informed consent has been withdrawn

10. Can a patient give informed consent verbally? Yes

11. Informed consent is a discussion of information where the patient voluntarily agrees to the care plan and must be free of coercion.

12. What are the 4 exceptions to informed consent?

    (A) Emergency situation where implied consent is assumed

    (B) Waiver by the patient

    (C) Patient is legally incompetent OR patient lacks decision-making capacity

    (D) Therapeutic privilege where the patient is unconscious, confused, physician deprives patient of autonomy in the interest of the patient's health

13. Children under the age of 18 are considered minors and legally incompetent.

14. Does pregnancy or giving birth in most cases emancipate a minor? No

15. Parental or guardian consent must be obtained unless the minor is *emancipated*. What are the 3 most common exceptions?

(A) *If older than the age of 13 and taking care of self*

(B) *Married*

(C) *Serving in the military*

16. Parental consent is not required for minors in which 5 situations?

(A) *Emergency Situations*

(B) *Prescribing contraceptives*

(C) *Treating STDs*

(D) *Medical care of pregnancy*

(E) *Treatment of drug addiction*

17. Regarding patient confidentiality, with whom is a physician permitted to discuss a patient's health-related issues without receiving patient permission?

(A) Health care professional directly related to the care of the patient

(B) Any physician

(C) Patient's family

(D) None of the above; patient must give permission

18. Is obtaining a consultation from another physician without patient permission a breach of patient confidentiality? *No*

19. If a physician receives a court subpoena, what should he do?

show up in court but do not divulge confidential information about the patient

20. What is the Tarasoff court decision?

A physician is required to directly inform and protect the potential victim from harm even if it involves a breach of patient confidentiality

21. Which of the following are exceptions to patient confidentiality?

    (A) Child abuse

    (B) Impaired automobile drivers

    (C) Patient is a threat to oneself or others

    (D) All of the above are correct

22. If a patient is a threat to others, the physician _MUST break_ patient confidentiality.

23. A 23-year-old man is distraught about his girlfriend having an affair. He tells the physician that he is going to kill his girlfriend and her lover. The physician calls and leaves a message on the girlfriend's cell phone. Did the physician sufficiently warn and protect the patient? _NO_ Explain your answer.

    According to the Tarasoff law, the physician should have immediately notified the police, try to detain the patient as well as make every possible effort to contact the girlfriend and her lover

24. A physician must determine if the patient is _legally_ and _psychologically_ competent to make _a specific healthcare-related decision_.

25. A 78-year-old man is about to undergo a surgical procedure. The patient's wife asks the physician to not tell the patient about the odds of success since she is worried that it will upset him. What should the physician do?

    (A) Tell the spouse that she/he will provide only the best case scenario to the husband.

    (B) Tell the spouse that she/he will not discuss the odds of success with the patient.

    (C) Tell the spouse that she/he needs to discuss all aspects of the procedure with the patient, including the odds of success.

26. What must occur for a surrogate to make a healthcare-related decision for a patient?

    (A) *Patient is incapacitated*

    (B) *Patient has not made an advance directive*

    (C) *An individual (surrogate) who knows what the patient would truly want if he/she were competent is identified*

27. Who is given first priority as a surrogate decision-maker?

(A) Adult children
(B) Adult siblings
(C) Parent
(D) Spouse

28. If a Health Care Power of Attorney (HCPOA) determines that a patient should not receive medical treatment for a condition that arose after the patient becomes incapacitated and the patient's spouse (who is not the HCPOA) wants the medical treatment administered, the physician should *follow the directive given by the HCPOA*.

29. A physician accused of malpractice could face which of the following?

(A) Civil lawsuit
(B) Criminal charges
(C) Both A and B

30. What are the 4 components of malpractice?

(A) *Physician had a duty to do something*
(B) *There was a breach of that duty (dereliction)*
(C) *Harm was done to the patient (damage)*
(D) *Breach of duty is what caused the harm (direct)*

31. What is the most common cause of a lawsuit? *Poor communication*

32. Competence is a:

(A) Legal issue
(B) Medical issue
(C) Both A and B

33. When surrogates make decisions for a patient, physicians should base their decisions using the "best interests standard, subjective standard, and substituted judgment" in which order?

Subjective standard, Substituted judgment and best interests standard

34. A 56-year-old man is deemed brain dead following a motor vehicle accident. The physician determines that there are no more treatment options but the family insists on further treatment. What should the physician do?

Treatment must stop since there is no treatment that can improve the patient's condition

35. A mentally competent quadriplegic patient asks the physician to remove his feeding tube. What should the physician do?

Remove the feeding tube

36. Immediately prior to a necessary surgical procedure, a physician learns that the patient does not have healthcare insurance. What should the physician do?

Perform the surgery

37. A 14-year-old girl comes to the physician requesting birth control. From whom should the physician obtain consent?

None is needed

38. A 12-year-old boy is in need of a life-saving surgical procedure following an accidental gunshot wound to the chest; however, the boy's parents indicate they do not want their son to have the surgery due to religious beliefs. What should the physician do?

Perform the surgery

39. A 12-year-old boy needs to have his left arm set and placed in a cast following a bicycle accident; however, the boy's parents indicate they do not want their son to undergo the procedure or have a cast on his arm due to religious beliefs. What should the physician do?

NOT perform the procedure or place the arm in a cast

40. A mentally ill patient is committed to the hospital. Which of the following statements is true?

(A) Patient can choose the treatments he wants to receive

(B) Patient can leave when he wants

(C) Patient can refuse treatment

(D) All of the above

Part II

Organ Systems

CHAPTER 1

NEUROSCIENCE

TOPIC 1: DEVELOPMENT OF THE NERVOUS SYSTEM AND ASSOCIATED PATHOLOGIES

1. What event in embryogenesis must occur just prior to neurulation?
   Gastrulation

2. What germ layer forms the cellular elements of both the CNS and PNS?
   Ectoderm

3. What mesoderm structure induces the formation of the neural plate?
   Notochord

4. What part of the neural tube closes first? On what day?
   Middle, day 23

5. What part of the neural tube closes second? On what day?
   Rostral, day 25

6. What part of the neural tube closes third and last? On what day?
   Caudal, day 27

7. What functional type of neurons develop in the alar plate? Basal plate?
   Alar- sensory neurons; Basal- Motor Neurons

8. What defect results if the rostral neuropore fails to close? If the caudal neuropore fails to close?
   Rostral- anencephaly. Caudal- Most severe form of Spina bifida

9. Name two proteins that will be elevated in an amniocentesis if the fetus has either neural tube defect? *AFP and AChE*

10. Which neural tube defect may also result in polyhydramnios? *Anencephaly*

11. Name the postnatal derivatives of the neural tube and the neural canal remnant that each contains.

Secondary Brain Vesicle	Postnatal Derivative	Neural Canal Remnant Inside?
Telencephalon (name 2)	*Cerebral Hemispheres; Most of Basal Ganglia*	*Lateral ventricles*
Diencephalon (name 4)	*Thalamus* *Hypothalamus* *Epithalamus (Pineal)* *Subthalamus*	*Third ventricle*
Mesencephalon	*Midbrain*	*Cerebral aqueduct*
Metencephalon	*Pons and Cerebellum*	*Fourth ventricle*
Myelencephalon	*Medulla*	*4th ventricle and central canal*
Spinal cord	*none*	*Central canal*

12. Match the defect with the description.

Choices:

- Anencephaly
- Spina bifida occulta
- Dandy Walker syndrome
- Myeloschisis
- Arnold Chiari type I
- Arnold Chiari type II
- Holoprosencephaly
- Meningomyelocele

Cause or Feature of Defect	Name of Defect
Incomplete separation of hemispheres; Single telencephalic ventricle	*Holoprosencephaly*
Rostral neuropore fails to close	*Anencephaly*
Associated with trisomy 13 (Patau syndrome)	*Holoprosencephaly*
Meninges line a lumbar cyst that contains the spinal cord	*Meningomyelocele*
Mildest and asymptomatic form of spina bifida	*Spina bifida occulta*
Downward herniation of cerebellar vermis	*Arnold Chiari Type II*
Failure of 4th ventricle foramina to open	*Dandy Walker syndrome*
Associated with meningomyelocele and lower limb weakness	*Arnold Chiari Type II*
Most severe form of spina bifida	*Myeloschisis*
Elevated levels of AFP and AChE in amniocentesis; polyhydramnios	*Anencephaly*
Tuft of hair present over area with missing spinous processes	*Spina bifida occulta*

TOPIC 2: CYTOLOGY OF THE NERVOUS SYSTEM AND ASSOCIATED PATHOLOGIES

1. Which part of a neuron lacks Nissl substance? *Axon*

2. Which elements of the neural cytoskeleton form neurofibrillary tangles in Alzheimer's disease?
   Microtubules

3. Glial cell matching.

   Choices:

   - Microglia
   - Astrocytes
   - Oligodendrocytes
   - Schwann cells

Feature	Glial Cell
Forms a single segment of myelin for a single axon	*Schwann cell*
Target of HIV-1 in the CNS	*Microglia*
Most numerous glial cell type in CNS	*Astrocyte*
Myelinates axons in tracts	*Oligodendrocyte*
Macrophages of CNS	*Microglia*
Remove K^+ and glutamate from extracellular space	*Astrocyte*
Derived from bone marrow monocytes	*Microglia*

4. What ATPase is necessary for anterograde axonal transport?
   For retrograde axonal transport?

   Anterograde: kinesin; Retrograde: dynein

5. Match the following conditions to a feature or cause:

Choices:

- Polio virus
- Rabies virus
- Tetanus toxin
- Herpes labialis (HSV-1)
- Herpes genitalis (HSV-2)
- Varicella zoster (chicken pox)
- Diabetic neuropathy

Feature	Condition
Affects Renshaw cells in spinal cord; muscle spasms	*Tetanus toxin*
Lies dormant in Trigeminal and dorsal root ganglia; causes Shingles	*Varicella zoster (Chicken pox)*
Lies dormant in sacral ganglia	*Herpes genitalis*
Lies dormant in Trigeminal ganglia only	*Herpes labialis*
Causes symmetrical loss of pain and Temperature in hands and feet	*Diabetic neuropathy*

6. Match the feature with the appropriate demyelinating condition.

Choices:

- Multiple sclerosis
- Guillain-Barré
- Central pontine myelinolysis
- Progressive multifocal leukoencephalopathy
- Disseminated encephalomyelinitis
- Metachromatic leukodystrophy
- Charcot-Marie-Tooth disease
- Krabbe disease

Feature	Condition
Deficient beta-galactosidase; presence of globoid cells	*Krabbe disease*
Common inherited neurologic sensorimotor disorder; gene mutation affects neuronal proteins; pes cavus	*Charcot-Marie-Tooth disease*
Sulfatase A deficiency; affects both PNS and CNS myelin	*Metachromatic Leukodystrophy*
Precipitated by *Campylobacter jejuni*; symmetrical ascending weakness, at risk for respiratory failure.	*Guillain Barre*
Overaggressive treatment for hyponatremia; causes "locked in" syndrome	*Central pontine myelinolysis*
CNS demyelination with no symmetry of sensory and motor deficits; optic neuritis	*Multiple sclerosis*
Symptoms similar to MS; autoimmune destruction of CNS myelin	*Disseminated Encephalomyelinitis*

7. What are the differences between the functions of an ependymal cell versus a tanycyte?

Ependymal cells line the ventricles in the adult brain. Some ependymal cells differentiate into choroid epithelial cells, forming part of the choroid plexus, which produces cerebrospinal fluid. Ependymal cells are ciliated and their ciliary action helps circulate CSF. Tanycytes are specialized ependymal cells that have basal cytoplasmic processes in contact with blood vessels; these processes may transport substances between a blood vessel and a ventricle.

8. List the 3 most common primary brain tumors.
   glioblastoma multiforme which is a grade IV astrocytoma, meningioma, schwannoma

9. Which axons have the capacity to regenerate if cut? What is their rate of regeneration?
   Only axons myelinated by Schwann cells, 1-3 mm per day

TOPIC 3: AUTONOMIC NERVOUS SYSTEM ORGANIZATION

1. Match a feature with a subdivision of the ANS.

   Choices:

   - Sympathetic
   - Parasympathetic
   - Both

Feature	ANS Choice
Preganglionic neurons are cholinergic	*BOTH*
Postganglionic neurons are derived from neural crest	*BOTH*
Target tissues contain muscarinic receptors	*BOTH*
Has ganglia in the form of chromaffin cells	*SYMPATHETIC*
Postganglionic neurons utilize norepinephrine as a neurotransmitter	*SYMPATHETIC*
Has preganglionic cell bodies in sacral spinal cord	*PARASYMPATHETIC*
Postganglionic neurons utilize ACh as a neurotransmitter	*BOTH*
A lesion of this system causes Horner's syndrome	*SYMPATHETIC*

TOPIC 4: THE VENTRICULAR SYSTEM AND ASSOCIATED PATHOLOGIES

1. How much CSF does the choroid plexus produce per day? *400 to 500mL produced daily*

2. How much space is in the ventricles and the subarachnoid space? *90 to 150 mL*

3. What disease might an individual with polymorphonuclear leukocytes in the CSF have?
   bacterial meningitis

4. What disease might an individual with elevated protein in the CSF have? *meningitis or a CNS tumor*

5. What disease might an individual with red blood cells in the CSF have? *subarachnoid hemorrhage*

6. What is the most common cause of a non-communicating hydrocephalus?
   Blockage of CSF flow through the ventricles

7. What is the most common cause of a communicating hydrocephalus?
   Drainage problem at arachnoid granulations

8. What are the 3 symptoms of normal pressure hydrocephalus?
   Dementia, Infantile bladder, Apraxic gait

9. What causes hydrocephalus ex vacuo?
   Loss of parenchymal mass secondary to cell death is filled with CSF

10. What 2 diseases most commonly cause hydrocephalus ex vacuo?
    Most commonly caused by loss of cortical neurons in Alzheimer's disease and or Caudate atrophy in Huntington's disease.

11. Name 3 lipid soluble compounds that cross the blood–brain barrier.
    heroin, ethanol, and nicotine

12. Name 2 vitamins that are transported across the blood–brain barrier.
    vitamins K and D

TOPIC 5: THE SPINAL CORD

1. How many pairs of spinal nerves are there? 31

2. What is the last tissue to be pierced by a spinal tap needle before it reaches the space containing the cauda equina? Arachnoid mater

3. What is the difference between a dorsal root and the dorsal horn?

   Dorsal root contains all sensory fibers that innervate muscle and cutaneous receptors in a single dermatome and myotome; all derived from neural crest. Dorsal horn contains sensory neurons derived from alar plate that mainly respond to incoming pain and temperature signals from the dorsal roots.

4. What is the difference between a ventral root and the ventral horn?

   Ventral root contains axons on CNS neurons in the ventral horn that innervate skeletal muscle and axons of autonomic neurons in the intermediate zone and lateral horn. Ventral horn contains cell bodies of skeletal motor neurons in ventral root including alpha and gamma motor neurons and interneurons including Renshaw cells.

5. What are the functions of the largest diameter, fastest conducting fibers of the dorsal roots?

   Ia Ib dorsal roots are proprioceptive; A-beta fibers are tactile.

6. What are the functions of the smallest diameter, slowest conducting fibers of the dorsal roots?

   A-delta and C fibers sense pain and temperature.

7. What are the functions of an alpha motor neuron?

   Alpha motoneurons innervate skeletal muscle at a neuromuscular junction.

   Of a gamma motor neuron?

   Gamma motoneurons innervate muscle fibers of the muscle spindle.

8. Name 2 functionally different neurons found in the intermediate zone of spinal cord gray matter.

The intermediate zone of the spinal cord runs from T1 to L2. It contains preganglionic sympathetic neuron cell bodies and Clarke's nucleus, which sends unconscious proprioception to the cerebellum

9. Name the 2 neurons that interact to cause a voluntary contraction of skeletal muscle.

The process of initiating a voluntary contraction of skeletal muscle begins with a neural signal that is generated in 1) upper motor neurons within the cerebral cortex. This signal travels caudally by way of the brainstem and spinal cord within upper motoneurons. Upper motorneurons synapse on 2) lower motoneurons (Alpha motor neurons) in the ventral horn of the cord. Lower motor neurons synapse on muscles.

10. Name the 2 neurons that provide efferent and afferent signals from skeletal muscle during reflex contraction of the skeletal muscle.

Ia dorsal root and lower motor neuron

11. Name a tendon in the upper limb and a tendon in the lower limb that can be utilized in a muscle stretch reflex.

Upper limb: biceps tendon, brachioradialis tendon, triceps tendon. / Lower limb: Patellar (Quadriceps) tendon, Achilles tendon

12. Match each feature below that is characteristic of an upper motor neuron (UMN) or a lower motor neuron (LMN).

Feature	UMN or LMN
Cell bodies are found in motor cortex	*UMN*
Are also known as alpha motor neurons	*LMN*
Axons cross at pyramidal decussation	*UMN*
All parts of this neuron are ipsilateral to the innervated muscle	*LMN*
Form the motor limb of a muscle stretch reflex	*LMN*
Has cell bodies in the ventral horn of the cord gray matter	*LMN*
Has a net inhibitory effect on muscle stretch reflexes	*UMN*
A lesion results in paralysis that is ipsilateral and at the level of the lesion	*LMN*
A lesion results in weakness with upgoing toes	*UMN*
A lesion may cause weakness that can be ipsilateral or contralateral and below the lesion	*UMN*
A lesion causes suppressed reflexes	*LMN*
Lesions may result in fasciculations and atrophy	*LMN*
A lesion may cause a clasp knife reflex	*UMN*
Lesions cause spastic weakness and a Babinski sign	*UMN*
Lesions may result in decerebrate or decorticate rigidity	*UMN*

13. How many neurons are needed to convey a sensory stimulus to conscious levels of cerebral cortex?

THREE

14. Where does the axon of a sensory neuron cross the midline?

Crosses in vicinity of its cell body

15. Fill in the table below with the correct components of each system.

Feature	Dorsal Column/Medial Lemniscal System	Anterolateral System
Sensory functions?	*Proprioception and touch*	*Pain and temperature*
Type of dorsal roots?	*Ia, Ib, A-beta*	*A-delta and C*
Axons of dorsal roots course in what tract(s)?	*Dorsal columns*	*Lissauer's tract*
Location of second neuron cell body?	*Ipsilateral Dorsal column nuclei in medulla*	*Ipsilateral Dorsal horn*
Axons of second neuron cross the midline of CNS in?	*Caudal medulla as internal arcuate fibers*	*All levels of cord in ventral white commissure*
Axons of second neuron course in what tract?	*Medial lemniscus*	*Spinothalamic tract*
Axons of second neuron synapse where?	*VPL thalamus*	*VPL thalamus*

16. What sensation is being tested by the Romberg test? *Unconscious proprioception*

    Which system? *Spinocerebellar pathways*

17. What is tested by a tuning fork? *Vibratory sense*

    Which system? *DC/ML*

18. Which specific tract carries vibratory sense from the lower limb through the cord? *Fasciculus gracilis*

19. Which specific tract carries vibratory sense from the upper limb through the cord? *Fasciculus cuneatus*

20. Which specific tract carries pain and temperature through the cord? *Spinothalamic tract*

21. What sensory information is carried by the dorsal spinocerebellar tract?

    Unconscious proprioception

    From where? *Clarke's nucleus from ipsilateral lower limb*

22. What sensory information is carried by the cuneocerebellar tract?

    Unconscious proprioception

    From where? *External cuneate nucleus from ipsilateral upper limb*

23. What chromosome contains a defective gene that encodes for Friedreich's ataxia?

    frataxin gene on chromosome 9

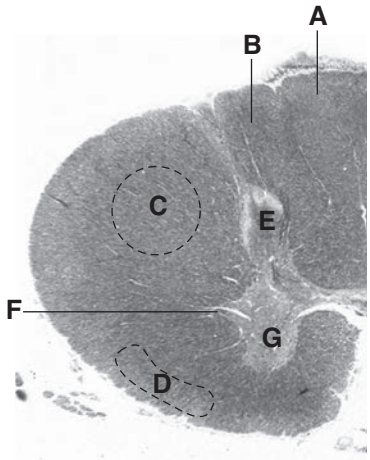
24. List 3 deficits in an infant born with Friedreich's ataxia.

    gait ataxia, dysarthria, hand clumsiness, loss of position sense, impaired vibratory sensation, and loss of tendon reflexes

25. Match a feature or symptom of a lesion with the tracts in the table below. More than one choice may be correct.

Symptom or Feature	Fasiciculus Gracilis	Fasiciculus Cuneatus	Spiniothalamic Tract	Lissauer's Tract
Loss of vibratory sense from ipsilateral lower limb	X			
Loss of pain and temperature from several dermatomes ipsilateral to a lesion				X
Loss of pain and temperature contralateral and below a lesion			X	
Has cell bodies in the ipsilateral dorsal horn			X	X
Axons cross in the cord			X	
Contains A-delta and C dorsal roots				X
Has neuron cell bodies in ipsilateral dorsal root ganglia (more than one answer)	X	X		

26. Identify points A–G of the spinal cord cross section below and fill in the table to describe the effects caused by a lesion at each location.



	Identify A–G	Lesions of A–G Result In	Deficit is Ipsi- or Contralateral to Lesion
A	*F. gracilis*	*Loss of vibratory sense in ipsi lower limb*	*Ipsilateral and below*
B	*F. cuneatus*	*Loss of vibratory sense in ipsi upper limb*	*Ipsilateral and below*
C	*Corticospinal tract*	*Spastic weakness ipsi and below the lesion*	*Ipsilateral and below*
D	*Spinothalamic tract*	*Loss of pain and temp contra and below the lesion*	*Contralateral and below*
E	*Dorsal horn*	*Loss of pain and temp ipsi and at the level of the lesion*	*Ipsilateral and at or just below*
F	*Lateral horn*	*Horner's syndrome if at T1*	*Ipsi ptosis, miosis and anhydrosis*
G	*Ventral horn*	*Flaccid paralysis ipsi and at the level of the lesion*	*Ipsilateral and at level of lesion*

27. For each symptom or feature below, place an "X" under the associated condition. Some may be found in more than one condition.

Symptom or Feature	Anterior Spinal Artery Occlusion	Amyotrophic Lateral Sclerosis	Poliomyelitis	Werdnig Hoffman Disease
Bilateral paralysis with suppressed reflexes			X	X
Bilateral spastic weakness in lower limbs; bilateral flaccid weakness in upper limbs		X		
Bilateral spastic weakness and bilateral loss of pain and temperature	X			
Bilateral flaccid weakness, hypotonia and tongue fasciculations				X

28. For each symptom or feature below, place an "X" under the associated condition. Some may be found in more than one condition.

Symptom or Feature	Brown Sequard Syndrome	Syringomyelia	Tabes dorsalis	Subacute Combined Degeneration
Altered vibratory sense in lower limbs, urine retention, pain, and Romberg sign			X	
Ipsilateral loss of vibratory sense, ipsilateral spastic weakness, contralateral loss of pain, and temperature	X			
Bilateral loss of pain and temperature initially; bilateral flaccid paralysis		X		
Bilateral loss of vibratory sense, bilateral spastic weakness				X

TOPIC 6: THE BRAINSTEM

1. Which cranial nerves arise from the midbrain? *CN III and IV*

2. Which cranial nerves arise from the pons? *CN V, VI, VII and VIII*

3. Which cranial nerves arise from the medulla? *CN IX, X and XII*

4. In the table below, indicate whether a tract lesion will cause ipsilateral or contralateral signs and symptoms.

Tract in Brainstem	Sign and Symptoms Ipsilateral and Below the Lesion	Sign and Symptoms Contralateral and Below the Lesion
Corticospinal tract		X
Medial lemniscus		X
Spinothalamic tract		X
Descending hypothalamic fibers	X	
Fasciculus gracilis	X	
Fasciculus cuneatus	X	

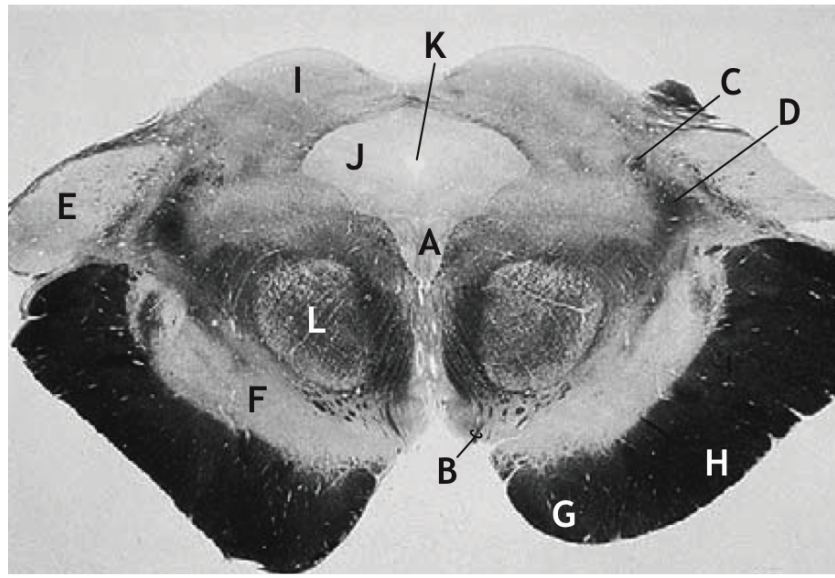
5. For each cranial nerve below, place an "X" under its function(s).

Cranial Nerve	Innervates Skeletal Muscle of Myotome Origin	Innervates Smooth Muscle, Glands, or Heart	Innervates Skeletal Muscle in a Pharyngeal Arch	Conveys Touch, Pain, or Tempera-ture	Conveys Taste	Inner-vates Chemo- or Baro-receptors
Oculomotor	X	X				
Trochlear	X					
Abducens	X					
Hypoglossal	X					
Trigeminal			X	X		
Facial		X	X	X	X	
Glossopha-ryngeal		X	X	X	X	X
Vagus		X	X	X	X	X
Accessory	X					

6. For each cranial nerve below, describe its general function, how it is tested, and the sign or symptoms present if lesioned.

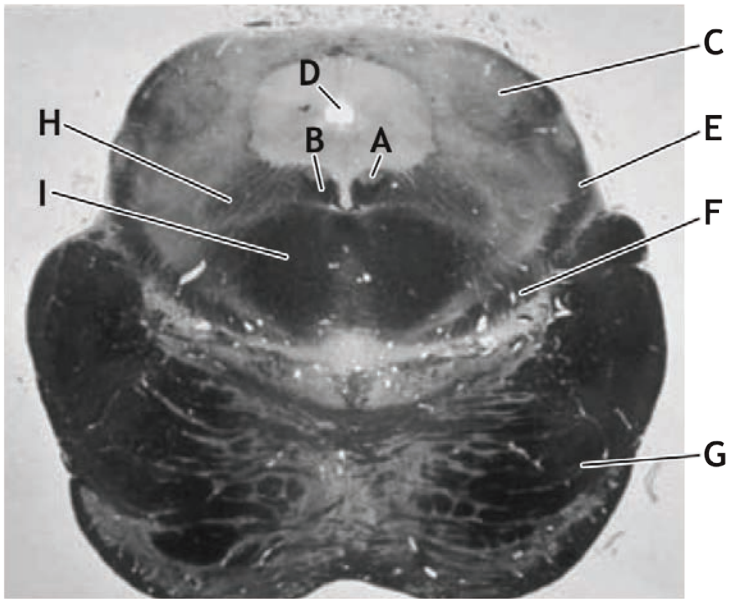
Cranial Nerve	Function(s)	Test	Sign or Symptoms if Lesioned
Oculomotor	*Adduct and elevate eye*	*Look in, look up*	*External strabismus*
Trochlear	*Depress adducted eye; intort*	*Look in then down*	*Adducted eye moved up, head tilts away from lesion side*
Abducens	*Abducts eye*	*Look out*	*Internal strabismus*
Trigeminal	*Facial sensation; chewing*	*touch and bite down*	*Altered/loss of facial sensation ipsilateral to the lesion, weakness in chewing*
Facial	*Facial muscles, anterior tongue taste, eye lacrimation, salivation, Stapedius muscle*	*Wrinkle forehead, Shut eye, smile*	*Cannot wrinkle forehead, shut eye, corner of mouth droops, eye is dry, numbness behind the ear, hyperacusis*
Glossopharyngeal	*Sensory limb of gag reflex, Stimulates parotid*	*Touch oropharyngeal mucosa stimulating gag relfex*	*Uvula does not move when oropharyngeal mucosa is touched*
Vagus	*Elevate palate, swallow, close larynx*	*Gag reflex*	*Uvula does not elevate on lesion side when oropharyngeal mucosa is touched*
Accessory	*Elevate shoulder, turn chin away from contracting muscle*	*Shrug shoulders against resistance*	*Shoulder droops on lesion side*
Optic	*Vision, causes both pupils to constrict in response to light*	*Light reflex*	*Marcus Gunn pupil; Pupil will not constrict on side of lesion and blurry vision*
Vestibulocochlear	*Hearing and balance*	*Weber and Rinne, Romberg*	*Hearing loss on side of lesion; Dizziness, nausea, vomiting vertigo, nystagums*
Olfactory	*Smell*	*Test for different odors*	*Dys- or anosmia*

7. Label points A–K.



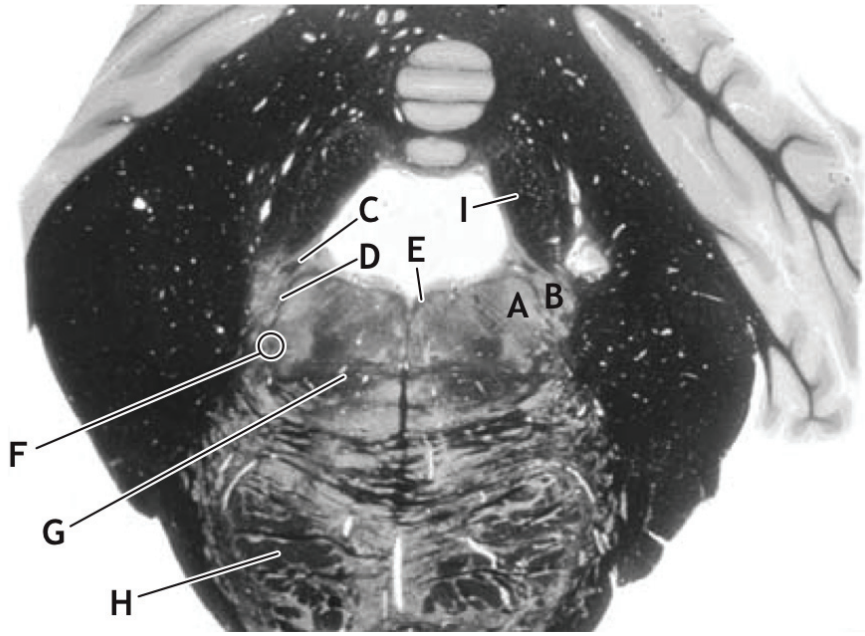
	Structure
A	*Oculomotor and Edinger- Westphal nuclei*
B	*CN III*
C	*Spinothalamic tract*
D	*Medial Lemniscus*
E	*Medial geniculate body*
F	*Substantia nigra*
G	*Corticobulbar fibers*
H	*Corticospinal fibers*
I	*Superior calculus*
J	*Periaqueductal gray*
K	*Cerebral aqueduct*

8. Label points A–H.



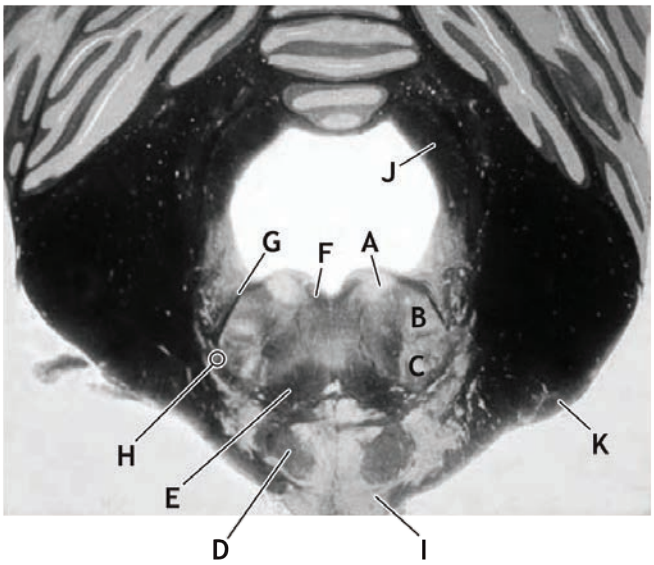
	Structure
A	*Trochlear nucleus*
B	*MLF*
C	*Inferior colliculus*
D	*Cerebral aqueduct*
E	*Spinothalamic tract and DHF (Descending hypothalamic fibers)*
F	*Medial Lemniscus*
G	*Corticospinal and corticobulbar fibers*
H	*Central tegmental tract*

9. Label points A–H.



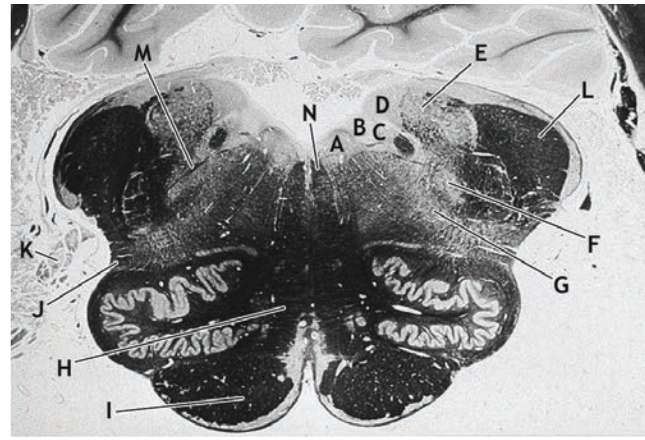
	Structure
A	*Motor V*
B	*Main sensory nucleus of V*
C	*Mesencephalic nucleus of V*
D	*CN V*
E	*MLF*
F	*Spinothalamic tract and DHF*
G	*Medial Lemniscus*
H	*Corticospinal and corticobulbar fibers*

10. Label points A–K.



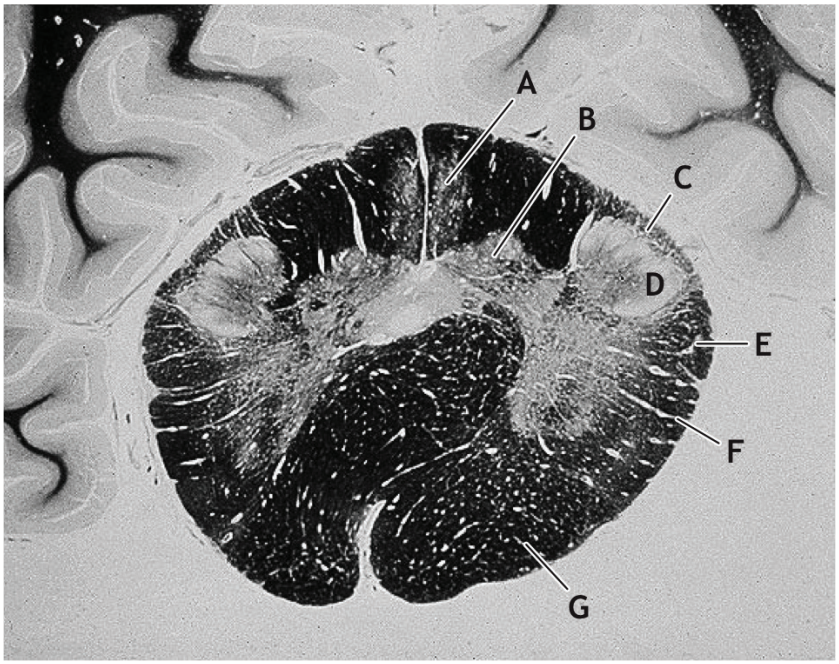
	Structure
A	*Abducens nucleus*
B	*Facial motor nucleus*
C	*Superior olivary nucleus*
D	*Corticospinal and corticobulbar fibers*
E	*Medial Lemniscus*
F	*MLF*
G	*Facial nerve*
H	*Spinothalamic tract and DHF*
I	*Pontine nuclei*
J	*Superior Cb Peduncle*
K	*Middle Cb Peduncle*

11. Label points A–N.



	Structure
A	*Hypoglossal nucleus*
B	*Dorsal motor nucleus of X*
C	*Solitary nucleus*
D	*Medial vestibular nucleus*
E	*Inferior vestibular nucleus*
F	*Spinal nucleus of V*
G	*Nucleus ambiguus*
H	*Medial lemniscus*
I	*Corticospinal and corticobulbar fibers*
J	*Spinothalamic tract and DHF*
K	*Roots of CN IX and X*
L	*Inferior Cb Peduncle*
M	*CN IX or X*
N	*MLF*

12. Label points A–G.



	Structure
A	*Nucleus Gracilis*
B	*Nucleus Cuneatus*
C	*Spinal Tract of V*
D	*Spinal nucleus of V*
E	*Spinothalamic tract and DHF*
F	*Dorsal spinocerebellar tract*
G	*Corticospinal and corticobulbar fibers*

13. Fill in the table below regarding trigeminal structures.

Trigeminal-related Structure	Function	Lesion Results In
Main sensory nucleus of V	*Touch from face, anterior tongue and oral mucosa*	*Loss of touch form ipsilateral face*
Motor nucleus of V	*Muscles of mastication*	*Jaw weakness*
Spinal nucleus of V	*Pain and temp from face, anterior tongue and oral mucosa*	*Loss of Pain and temp from ipsilateral face, anterior tongue and oral mucosa*
Mesencephalic nucleus of V	*Jaw proprioception*	*Weak jaw jerk reflex*
Ventral posterior medial nucleus of thalamus	*Contralateral Facial touch pain and temp and taste from ipsilateral tongue*	*Anesthesia of contralateral face and loss of taste from ipsilateral tongue*
Trigeminal ganglion	*All sensation from ipsilateral face, oral and nasal cavities and anterior tongue*	*Anesthesia of ipsilateral face and ipsilateral anterior tongue*

14. What is the most common deficit seen if all of the corticobulbar axons are lesioned on one side?
Lower face weakness

15. Name the three parts of the ear. *External, middle and inner*

Which ones are air-filled? Fluid-filled? *External and middle are air filled; inner is fluid filled*

16. What specialized fluid bathes the hairs of all inner ear hair cells? *Endolymph*

17. What are the frequency response characteristics of hair cells at the base of the cochlea? Apex of the cochlea?

Base- High frequency; Apex- Low frequency

18. Where are hair cells lost in someone who develops presbycusis? *Base of cochlea*

19. If bone conduction of sound is better than air conduction, where is the lesion?

Middle or external ear

20. If air conduction of sound is better than bone conduction, where is the lesion?

Inner ear or central pathways

21. What is the first site in the central auditory pathway where sound localization processing begins?

Superior olive

22. What does the Weber test determine?

Lateralizes hearing loss, does not determine cause

23. What does the Rinne test determine?

Presence of conductive hearing loss

24. Which vestibular system is stimulated when the head is turned horizontally to the right?

Right

25. Which direction do the eyes move in response to head turning?

Opposite the direction of head turning

26. If there is a lesion of the right vestibular nuclei, what is the direction of the fast or corrective phase of the vestibular evoked nystagmus?

Fast phase of nystagmus will be away from the lesion. To the left in this case.

27. What does COWS stand for with regard to caloric testing?

COWS – Cold Opposite, Warm Same is the normal response to caloric testing. With cold water calorics the eye slowly moves toward the cold water side and the fast phase of nystagmus is to the opposite side. With warm water calorics the eyes move to the opposite side and the fast phase of nystagmus is toward the same side as the water.

28. For each finding listed below, indicate where the lesion would be located.

Ocular System Lesions; Feature	Frontal Eye Field	PPRF	MLF	CN III	CN IV
Cannot look away from side of lesion; right upper limb and right lower face weakness	X				
Cannot look toward side of lesion; complete facial weakness		X			
Cannot adduct an eye during attempted horizontal gaze; convergence is intact			X		
Cannot adduct an eye under any conditions				X	
Cannot abduct an eye					X
Dilated pupil, ptosis, external strabismus				X	
Internal strabismus					X

29. For each feature, indicate an associated syndrome. Each can be associated with more than one syndrome.

Features	Lateral Medullary Syndrome	Medial Medullary Syndrome	Lateral Pontine Syndrome	Medial Pontine Syndrome	Medial Midbrain Syndrome
Spastic weakness in contralateral limbs		*X*		*X*	*X*
Loss of vibratory sense in contralateral body and limbs		*X*		*X*	
Loss of pain and temperature in contralateral body and limbs	*X*		*X*		
Ptosis, miosis, anhydrosis	*X*		*X*		
Cranial nerve(s) affected (name them)	*CN IX and X, VIII*	*CN XII*	*CN VII and VIII*	*CN VI*	*CN III*
Analgesia of ipsilateral face	*X*		*X*		
Nystagmus	*X*		*X*		
Sensorineural hearing loss			*X*		
Blocked artery cause	*PICA*	*Ant Spinal*	*AICA*	*Paramedian branch of Basilar*	*Perf branch of PCA*

TOPIC 7: THE CEREBELLUM, BASAL GANGLIA, AND MOVEMENT DISORDERS

1. Compare and contrast the functions of the cerebellum and basal ganglia.

Feature	Basal Ganglia	Cerebellum
Initiates movement	X	
Coordinates movement		X
Utilizes GABA and glutamate as neurotransmitters	X	X
Lesions cause tremor at rest	X	
Lesions cause tremor with movement		X
Major output projects to VA/VL nuclei of thalamus	X	X
Modulates activity of upper motor neurons	X	X

2. Compare and contrast the functions of the cerebellar hemisphere and vermis.

Feature	Cerebellar Hemisphere	Cerebellar Vermis
Controls axial and proximal limb muscles		X
Control distal muscles	X	
Lesions cause dysmetria	X	
Lesions cause truncal ataxia		X
Lesions cause dysdiadochokinesis	X	
Lesions cause gait ataxia		X
Deficits are ipsilateral to lesion side	X	X

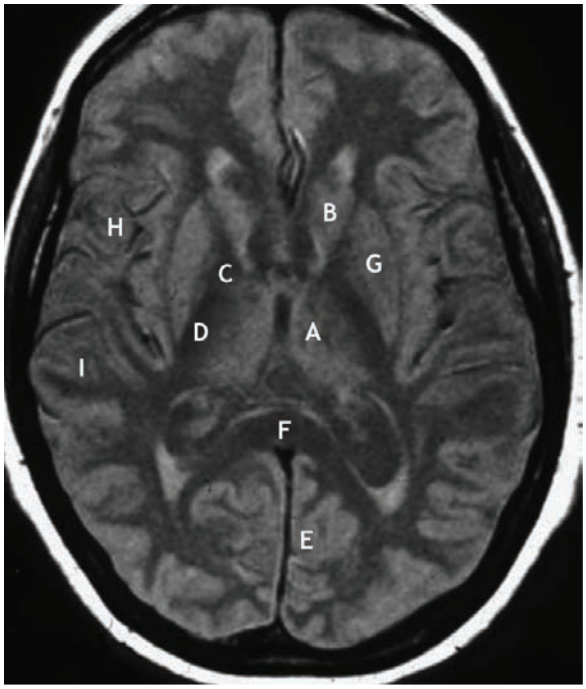
3. Compare and contrast the functions of the direct and indirect basal ganglia pathways.

Feature	Direct Basal Ganglia Pathway	Indirect Basal Ganglia Pathway
Initiates desired movement	X	
Suppresses unwanted movement		X
Uses two GABA neurons to disinhibit VA/VL thalamus	X	
Uses 2 GABA neurons to disinhibit the subthalamic nucleus		X
Driven by excitation from cortex	X	X
Functions enhanced by dopamine	X	
Functions enhanced by acetylcholine		X
Pathway begins with GABA neurons in the striatum	X	X

4. Compare and contrast the following conditions by placing an "X" next to each associated feature.

Features	Parkinson Disease	Huntington's Disease	Wilson's Disease	Hemiballismus
Loss of dopamine output from substantia nigra, pars compacta	X			
Atrophy of the caudate nucleus		X		
Autosomal dominance; unstable nucleotide repeat		X		
Kayser-Fleischer ring is pathognomonic			X	
Bradykinesia, masked facial expression, shuffling gait, pill rolling tremor	X			
Chorea and athetosis present		X		
Asterixis; wing beating tremor			X	
Caused by lacunar stroke of subthalamic nucleus				X
May be caused by MPTP by-product of heroin synthesis	X			
Lewy bodies are pathognomonic	X			
Results in involuntary flinging movements contralateral to lesion side				X

5. Label points A–I.



	Structure
A	*Thalamus*
B	*Head of caudate nucleus*
C	*Genu of internal capsule*
D	*Posterior limb of internal capsule*
E	*Visual cortex*
F	*Splenium of corpus callosum*
G	*Putamen*
H	*Brocas area (L hemisphere)*
I	*Wernicke's area*

TOPIC 8: THE EYE AND VISUAL PATHWAYS

1. Name the nerves and nuclei that form the circuit of the pupillary light reflex pathway.

   Optic nerve- pretectal nuclei - nucleus of Edinger Westphal - Ciliary ganglion – oculomotor nerve

2. What disease condition will result in a "blue sclera"?

   Osteogenesis Imperfecta

3. What is the cause of open angle versus closed angle glaucoma?

   Open- chronic painless decrease in drainage of aqueous humor through trabecular meshwork into Canal of Schlemm. Closed- drainage of aqueous humor is acutely blocked causing painful increase in intraocular pressure.

4. Complete the autonomic innervation of the eye in the table below.

Structure	Predominant Receptor	Receptor Innervation	Receptor Activation Causes	Receptor Blockage Causes
Pupillary sphincter	M3	CN III (ciliary ganglion)	*constriction*	Mydriasis
Pupillary dilator	*Alpha adrenergic*	Postgangionic sympathetics (SCG)	Dilation	Miosis
Ciliary muscle	*M3*	CN III (ciliary ganglion)	Contraction; lens gets rounder	Relaxation; lens gets flatter
Ciliary body	β-adrenergic	CN III (ciliary ganglion)	Increased secretion	Decreased secretion of aqueous humor

5. For each effect, place an "X" under the responsible class of drug.

Effects of Glaucoma Drugs	Beta-blockers (Timolol)	Cholinomimetics	Prostaglandin Analogue (Latanoprost)
Decrease synthesis of aqueous humor	X		
Increase outflow of aqueous humor		X	X

6. Review the common diseases of the eye in the table below.

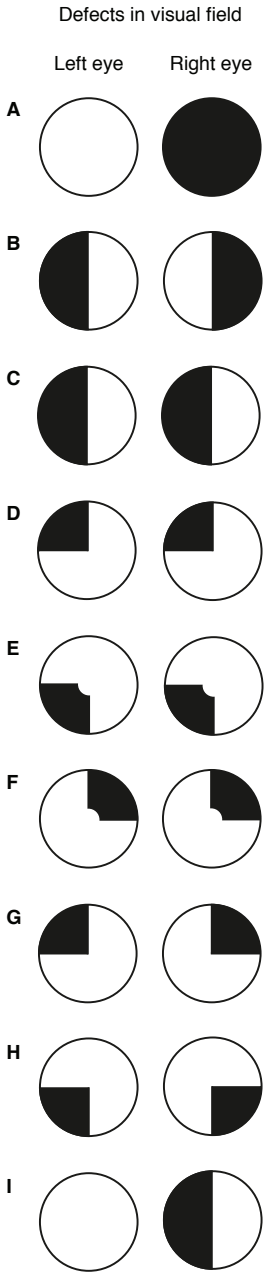
Structure	Myopia	Hyperopia	Astigmatism	Presbyopia	Cataracts
Eyeball too long; image focuses in front of retina	X				
Irregular curvature of cornea			X		
Loss of lens elasticity				X	
Eyeball too short; image focuses in back of retina		X			
Progressive opacification of lens					X

7. Match the findings with their cause by placing an "X" in the appropriate cell.

Feature	Argyll Robertson Pupil	Adie Pupil	Mydriasis with Ptosis	Miosis with Ptosis, Dry Face	Marcus Gunn Pupil
Caused by mass effect and uncal herniation			X		
Caused by degeneration of a ciliary ganglion		X			
Caused by demyelination of pretectal area	X				
Caused by a lesion of descending hypothalamic axons				X	
Caused by berry aneurysm compression			X		
Demonstrated by swinging flashlight test					X
Seen with multiple sclerosis	X				
Both pupils constrict in the near response but less briskly in response to light	X				

8. Match the cause or feature with a visual field deficit in A–I.

Caused by a right temporal lobe tumor	*D*
Caused by a blockage of the central artery of the retina	*A*
Caused by a lesion of the right optic tract	*C*
Caused by a medially expanding aneurysm of the right internal carotid artery	*I*
Caused by complete compression of the optic chiasm	*B*
Caused by a lesion of the cuneus gyrus	*E*
Seen in a patient with multiple sclerosis	*A*
Caused by compression by a small craniopharyngioma	*H*
Caused by a lesion to the left lingual gyrus	*F*
Caused by a lesion to Meyer's loop on the right	*D*
Caused by a complete blockage of the posterior cerebral artery (2 answers)	*E+F*



TOPIC 9: THE DIENCEPHALON

9. Name the 4 parts of the diencephalon.

Thalamus, Hypothalamus, Epithalamus, Subthalamus

10. What ventricle is surrounded by the diencephalon? *Third*

11. Match the functions and features to the thalamic nuclei below.

Function/ Feature	Ventral Postero-lateral	Ventral Postero-medial	Lateral Genicu-late	Medial Genicu-late	Ventral Anterior/ Ventral Lateral	Dorso-medial
Relays taste from solitary nucleus to cortex		X				
Gives rise to the visual radiations			X			
Projects to the temporal lobe				X		
Projects to motor cortex					X	
Degenerates in thiamine-deficient alcoholics						X
Relays body and limb somatosen-sory information to cortex	X					
Relays facial sensation to cortex		X				

12. Match the function or feature to the hypothalamic nuclei below.

Function/ Feature	Mammillary	Suprachi-asmatic	Supraoptic/ Paraventricular	Arcuate	Ventromedial
Receives direct retinal input for circadian rhythm		X			
Secretes releasing and inhibiting factors				X	
Releases ADH into posterior pituitary			X		
A satiety center					X
Neurons degenerate here in thiamine-deficient alcoholics	X				
Influences melatonin release by the pineal		X			

TOPIC 10: THE CEREBRAL CORTEX

1. What two lobes are separated by the central sulcus?

   Frontal and Parietal

2. What lies above and below the lateral fissure?

   Temporal below; Parietal and Frontal above

3. What part of the motor homunculus is represented on the lateral aspect of the precentral gyrus?

   Head, neck Upper limb and upper trunk

4. What is the dual arterial blood supply of the motor and the sensory homunculus?

   Middle cerebral and anterior cerebral

5. What is the difference between allocortex and neocortex?

   Allo- 3 layers; Neo- 6 layers

6. Match the feature with the correct intracranial bleed.

Features of Intracranial Bleeds	Intraventricular	Epidural	Subdural	Subarachnoid
Caused by tears in middle meningeal artery		X		
Lucid interval, uncal herniation		X		
Bleeding berry aneurysm, thunderclap headache, nuchal rigidity				X
Premature infant, bleeding in germinal matrix	X			
Head trauma lacerates cerebral veins that drain into dural sinuses; drowsiness and dementia			X	
Associated with Marfan syndrome, Ehlers-Danlos syndrome, and APKD				X

7. In the table below, match the lobe with the feature of a lesion.

Feature	Frontal Lobe	Parietal Lobe	Temporal Lobe	Occipital Lobe
Unilateral neglect (right side)		X		
Spastic weakness	X			
Bilateral hearing loss			X	
Homonymous hemianopsia with macular sparing				X
Facial numbness		X		
Loss of horizontal conjugate gaze	X			
Achromatopsia and prosopagnosia			X	
Loss of the ability to track moving objects		X		

8. Match the feature with the condition using an "X."

Feature	Motor Aphasia	Sensory Aphasia	Gerstmann Syndrome	Conduction Aphasia
Alexia and agraphia, finger agnosia, dyscalculia			X	
Speech reduced to single syllable words, frustrated by deficit	X			
Oral comprehension deficit, bilateral hearing loss, unaware of deficit		X		
Normal but paraphasic speech, comprehension intact, cannot name objects, frustrated by deficit				X

9. Name 2 locations of lesions that cause a disconnect syndrome.

Corpus callosum, arcuate fasciculus

10. What tracts pass through the posterior limb of the internal capsule?

Corticospinal, Thalamic somatosensory, Auditory, Visual radiations

11. What tract passes through the genu of the internal capsule?

Corticobulbar fibers

12. Match each feature with the white matter lesion site.

Feature	Arcuate Fasciculus	Genu of Internal Capsule	Posterior Limb of Internal Capsule	Corpus Callosum
Contralateral lower face weakness; no other CN deficits		X		
Contralateral limb and trunk anesthesia			X	
Cannot move left limb in response to command; no weakness				X
Normal but paraphasic speech, comprehension intact, cannot name objects, frustrated by deficit	X			
Cannot read but can write; other language functions intact				X

13. Match each feature with the limbic system lesions.

Sign, Symptom or Feature	Alzheimer's Disease	Kluver-Bucy Syndrome	Wernicke-Korsakoff Syndrome
Lesions result in one becoming placid with loss of sexual preference		X	
Lesions result in progressive anterograde amnesia for events in time	X		
Lesions result in retrograde amnesia with confabulations			X
Lesions caused by thiamine deficiency			X
Associated with gait ataxia and diplopia			X

14. Name a cortical neurotransmitter that is reduced in Alzheimer's dementia. Acetylecholine

15. What subcortical neuronal system projects directly to cortex without a thalamic relay?
Olfactory

TOPIC 11: CNS DISORDERS

1. With respect to the affected areas in the brain, what are the differences between Pick's disease and Alzheimer's disease?

   Pick's disease typically affects the frontal and/or anterolateral temporal lobes. Alzheimer's disease typically affects entorhinal cortex and hippocampal dysfunction.

2. Match the disease on the left with the histological-gross findings on the right.

(A) Alzheimer's disease	E	Kayser-Fleischer rings
(B) Creutzfeldt-Jakob disease	A	Neurofibrillary tangles
(C) Lewy body dementia	B	Spongiform cortex
(D) Pick's disease	D	Spherical tau protein aggregates
(E) Wilson's disease	C	Alpha-synuclein defect
	A	Senile plaques
	B	$PrP^{C} \rightarrow PrP^{SC}$ sheet
	D	Frontotemporal atrophy

3. What are the 4 A's of complex seizures?

   Aura, Alteration of consciousness, Automatisms, and Amnesia

4. Match the generalized seizure disorder on the left with the appropriate characteristic on the right.

(A) Absence	D	Epileptiform activity or focal, localizing activity on EEG
(B) Myoclonic	C	Seizure activity lasting 30 minutes
(C) Status epilepticus	B	Single or multiple myoclonic jerks
(D) Tonic-clonic	A	Generalized 3 Hz spike-and-wave on EEG
	A	Treated with ethosuximide
	D	Grand mal seizure
	A	Petit mal seizure

5. Fill in the blanks in the table below for commonly used anticonvulsants.

Drug	Mechanism	Notes
Benzodiazepines	*Increase frequency of GABAA (Cl^-) receptor opening*	Sedation, dependence, tolerance
Carbamazepine	Blocks axonal Na^+ channels in inactivated state	CNS depression, diplopia, ataxia, osteomalacia, megaloblastic and aplastic anemia, exfoliative dermatitis, dilutional hypernatremia (increased ADH secretion), cytochrome P450 inducer, hepatotoxicity, teratogenic
Ethosuximide	*Blocks T-type calcium channels in thalamic neurons*	GI distress, headache, lethargy, hematotoxicity, Stevens-Johnson syndrome
Felbamate	*Blocks Na+ channels and glutamate receptors*	*Aplastic anemia, hepatoxicity*
Gabapentin	GABA analogue	Sedation, ataxia
Lamotrigine	Blocks Na^+ channels and glutamate receptors	*Life-threatening rash, Stevens-Johnson syndrome*
Phenobarbital	*Increase duration of GABAA (Cl^-) receptor opening*	Induction of cytochrome P450, sedation, dependence, tolerance
Phenytoin	*Blocks Na+ channels*	Gingival hyperplasia, hirsutism, sedation, anemia, nystagmus, diplopia, ataxia, teratogenic (fetal hydantoin syndrome), P450 induction, zero-order kinetics
Topiramate	Believed to inhibit voltage-dependent sodium channels and enhance GABA activity	Sedation, dizziness, ataxia, anomia, renal stones, weight loss
Valproic acid	*Blocks Na+ channels, inhibits GABA transaminase*	GI distress, hepatotoxic (rare but can be fatal), inhibits drug metabolism, neural tube defects

6. Describe the clinical presentation for a patient with a cluster headache.

   Unilateral, rarely pulsatile, pre-orbital headache with a short duration (peaks minutes after onset, and lasts 30 minutes to 3 hours)

7. A patient with a classic migraine takes a medication that activates vascular serotonin 5-HT1 receptors. What medication did the patient receive?

   (A) Ergotamine

   (B) Fluoxetine

   (C) Propranolol

   (D) Sumatriptan

   (E) Verapamil

8. Cluster headaches can be differentiated from trigeminal neuralgia based on *duration*.

9. A patient is diagnosed with an autosomal dominant condition that is associated with the development of hamartomatous lesions that can affect every organ as well as ash leaf spots. What is the most likely diagnosis?

   (A) Neurofibromatosis

   (B) Sturge-Weber syndrome

   (C) Tuberous sclerosis

   (D) von Hippel-Lindau disease

10. Nevus flammeus in Sturge-Weber syndrome is generally present along a distribution of what cranial nerve?

    (A) I

    (B) II

    (C) III

    (D) IV

    (E) V

11. The etiology of neurofibromatosis type 1 can best be described as *Mutation of gene NF-1 (tumor suppressor) on chromosome 17*.

12. A patient is diagnosed with neurofibromatosis type 1. Which of the following would be an expected finding in this patient?

    (A) Ash leaf spots
    (B) Café-au-lait spots
    (C) Cavernous hemangiomas in skin, mucosa and organs
    (D) Cutaneous angiofibroma
    (E) Nevus flammeus

13. Von Hippel-Lindau disease is an autosomal *dominant* disorder caused by a mutation of *VHL tumor suppressor gene (chromosome 3p)*.

14. A patient is diagnosed with a prolactinoma. Recommended treatment options include *bromocriptine or, cabergoline and/or surgery*.

15. A patient with a somatotrope adenoma would most likely have which of the following features?

    (A) Amenorrhea
    (B) Galactorrhea
    (C) Short stature
    (D) Tall stature

16. Which of the following would be expected in a patient with hemangioblastoma?

    (A) Agranulocytosis
    (B) Leukocytosis
    (C) Pancytopenia
    (D) Polycythemia

17. Pathologic examination of a patient's tumor shows blue, small, round cells with Homer-Wright pseudorosettes. Which of the following is the most likely diagnosis?

(A) Craniopharyngioma
(B) Glioblastoma multiforme
(C) Medulloblastoma
(D) Meningioma
(E) Oligodendroglioma
(F) Pilocytic astrocytoma (grade 1)
(G) Schwannoma

18. During a procedure, a patient is administered a medication that causes the following: serum potassium 6.1 mEq/L, hypercarbia with acidosis, muscle rigidity, and temperature of 40°C (104°F). The most likely diagnosis is *Malignant hyperthermia*. The condition is most commonly caused by *succinylcholine and inhalation anesthetics*. It is treated with *dantrolene and supportive treatment measures*.

19. Following a procedure where a 48-year-old male was administered a general anesthetic, his hepatic enzymes become elevated. Which of the following agents was most likely administered to this patient?

(A) Enflurane
(B) Desflurane
(C) Halothane
(D) Isoflurane
(E) Methoxyflurane
(F) Nitrous Oxide

20. Would the effects of succinylcholine be reversed with neostigmine? *No* Why or why not?

Succinylcholine is a depolarizing skeletal muscle relaxant that is a non-competitive nicotinic agonist; however, neostigmine would reverse the effects of non-depolarizing agents (competitive nicotinic agonists), such as atracurium, vecuronium, rocuronium and mivacurium.

CHAPTER 2

MUSCULOSKELETAL AND CONNECTIVE TISSUE

TOPIC 1: DERMATOLOGY

1. Complete the following table.

Feature	Stratum Basale	Stratum Spinosum	Stratum Granulosum	Stratum Corneum	Stratum Lucidum
Contains stem cells	X				
Cells linked by desmosomes	X	X			
Attached to underlying basement membrane	X				
Contains melanocytes	X				
Found only in "thick" skin					X

2. Complete the following table.

Feature	Zonula Occludens	Zonula Adherens	Desmosome	Gap Junction	Hemi-Desmosome
Polarizes an epithelium	X				
Contains connexons				X	
Utilizes cadherins as adhesive molecules		X	X		
Linked to intracellular actin	X	X			
Utilizes claudins as adhesive molecules	X				
Utilizes desmoplakin to link to intermediate filaments			X		
Attaches the cell to the underlying ECM					X
Utilizes integrin adhesive molecules					X
Disrupted in pemphigus vulgaris			X		
Disrupted in bullous pemphigoid					X
Blocks paracellular diffusion	X				
Permits cell-to-cell communication				X	

3. Describe the size and appearance of a macule and a patch, and state which is bigger.

A macule is a flat skin discoloration less than 1 cm while a patch is a flat discoloration greater than 1 cm.

4. Describe the size and appearance of a plaque and a papule, and state which is bigger.

A papule is a raised skin lesion less than 1 cm while a plaque is a raised skin lesion more than 1 cm.

5. What is the difference between a vesicle and a wheal?

A vesicle is a small fluid filled blister that is less than 1 cm while a wheal is a localized area of edema that occurs transiently and never forms a distinct fluid collection.

6. A clear fluid containing a raised skin lesion larger than 1 cm is called _____*Bulla*_____.

7. An area of scar that becomes markedly hypertrophied is called _____*Keloid*_____.

8. Complete the following table.

Finding	Example of Condition
Crust	*Chickenpox, impetigo*
Hyperkeratosis	*Calluses*
Parakeratosis	*Psoriasis*
Acantholysis	*Pemphigus vulgaris*

9. Hyperkeratosis with retention of nuclei in stratum corneum is referred to as *Parakeratosis*.

10. Separation of the epidermal cells from one another is referred to as *Acantholysis*.

11. Name 2 skin diseases that can be caused by human papillomavirus.
Common warts and genital warts (condyloma acuminatum)

12. A nevus that contains atypical cells is called *Dysplastic nevus*.

13. What is the mechanism of formation of hives?
Mast cell degranulation with histamine release leading to formation of intensely pruritic wheals

14. Acanthosis with parakeratotic scaling, increased thickness of the stratum spinosum, and decreased thickness of the stratum granulosum are characteristic of which condition?
Psoriasis

15. What occurs when a psoriatic lesion is scraped?
Pinpoint bleeding – Auspitz sign

16. Which type of albinism is associated with an increased risk of cancer?
Oculocutaneous albinism

17. How does the extent of involvement of skin and subcutaneous tissues differ between cellulitis and necrotizing fasciitis?
Necrotizing fasciitis involves deeper layers, including fascia and muscle

18. The target of autoantibodies in pemphigus vulgaris is _Desmoglein in desmosomes_.

19. The target of autoantibodies in bullous pemphigoid is _Hemidesmosomes_.

20. Dermatitis herpetiformis is associated with what disease?

    Celiac disease

21. Name a very severe eruption similar to erythema multiforme.

    Stevens-Johnson syndrome (usually a drug reaction) and toxic epidermal necrolysis (Stevens-Johns like rash with involvement in greater than 30% of body surface area)

22. Acanthosis nigricans is associated with what systemic conditions?

    Hyperinsulinemia (most often in type II diabetics) and visceral malignancy

23. The painful nodules on the shins of patients with sarcoidosis are called _Erythema nodosum_.

24. What lesion commonly precedes development of a squamous cell carcinoma?

    Actinic keratosis

25. The whorled, densely eosinophilic protein and large cells in squamous cell carcinoma are called _Squamous pearls_.

26. A pearly papule lesion with rolled edges located on the upper face is likely to be _Basal cell carcinoma_.

27. A large, dark, multicolored skin lesion with irregular borders is likely to be _____Melanoma_____.

28. What marker can be used to assess tumor recurrence after resection of a melanoma?
S-100

TOPIC 2: ANATOMY AND PHYSIOLOGY OF MUSCLES AND LIGAMENTS

1. Name the calcium channel in the T tubule membrane.
   Dihydropyridine

2. Name the calcium channel in the sarcoplasmic reticulum membrane.
   Ryanodine

3. Do skeletal muscle cells have one or more than one nucleus? Where is the nucleus situated in the cell?
   More than one nucleus situated near periphery of cell

4. Complete the following table.

Feature	H Zone	A Band	I Band	Z Line
Changes length during sarcomere shortening	X		X	
Marks the end of each sarcomere				X
Band is found in 2 adjacent sarcomeres			X	
Band marks the length of the myosin filaments		X		
Band marks the center of the sarcomere	X			
Band does not change length when the sarcomere shortens		X		

5. Name the 4 key proteins involved in the physiology of skeletal muscle and briefly describe their functions.

Answer: 1) Myosin: Constitutes the A-band; myosin head binds actin and pulls it (power stroke). 2) Actin: Constitutes the I-band; will bind myosin. 3) Tropomyosin: Covers binding site on actin for myosin. 4) Troponin: Has a calcium binding site (troponin C) and will move tropomyosin to uncover the myosin binding site on actin when calcium binds to it.

6. Sketch the sequence of events that occurs in the neuromuscular junction when an action potential is evoked in an alpha-motor neuron.

Action potential depolarizes presynaptic membrane → Presynaptic voltage-gated Ca2+ channels open → Ca2+ entry causes release of acetylcholine (Ach) → Ach binds to the nicotinic receptor (ligand gated ion channel) on the sarcolemma of the muscle → depolarization of the muscle membrane (end plate potential—EPP) → action potential in skeletal muscle membrane.

7. The _____*Dihydropyridine (DHP)*_____ receptor is located on T tubules. It is a _____*voltage-gated*_____ Ca^{2+} channel that _____*blocks*_____ the ryanodine receptor, which is the _____*calcium channel*_____ on the sarcoplasmic reticulum (SR).

8. Sketch the sequence of events that occurs when an action potential travels down the T-tubule.

Depolarization causes a conformational shift in DHP (voltage-gated) → DHP block of ryanodine is removed → calcium enters cytosol → rise in cytosolic calcium opens more ryanodine channels (calcium induced calcium release).

9. Describe the 2 key roles that ATP plays with respect to the power stroke.

ATP: 1) Dissociates bound actin and myosin, 2) Provides the energy (cocks myosin head) for the power stroke.

10. What happens if a striated muscle cell is depleted of ATP?

Actin and myosin can't dissociate causing rigor mortis.

11. For the table below, place up or down arrows before each item to distinguish the important differences between slow twitch and fast twitch muscle fibers. Complete the final row to indicate what each is "best suited" for functionally.

Slow Twitch (Type I)	Fast Twitch (Type II)
↓ Myosin ATPase activity	↑ Myosin ATPase activity
↑ Aerobic capacity	↓ Aerobic capacity
↑ Mitochondrial content	↓ Mitochondrial content
↑ Myoglobin	↓ Myoglobin
Best for *Endurance, e.g., postural muscles*	Best for *Fast and/or powerful contractions, e.g. eyelids and sprinting*

12. What is meant by fiber grouping, and when does it typically occur?

Rather than being dispersed throughout the muscle, like fibers (Type I or II) will group together when a muscle reinnervates after being denervated.

13. Sketch the sequence of events that occurs to produce contraction of smooth muscle.

Depolarization or binding of an agonist → Cytosolic Ca^{2+} increases → Ca^{2+} binds calmodulin → Ca^{2+}-calmodulin stimulates myosin light chain kinase (MLCK) → MLCK phosphorylates myosin → myosin binds actin → smooth muscle contracts

14. Indicate what happens in smooth muscle on a cellular level if the cytosolic concentration of IP3, cAMP, or cGMP increases.

IP3 cause SR calcium release → contraction; cAMP results in phosphorylation of MLCK, thereby deactivating it → relaxation; cGMP dephosphorylates myosin → relaxation (mechanism of NO in smooth muscle).

15. Name 3 functions of the thenar and hypothenar eminence.

Abduction, flexion and opposition of thumb and pinkie respectively

16. What nerves innervate muscles in the thenar and hypothenar eminence?

Thenar- Median nerve (recurrent branch) Hypothenar- Ulnar nerve

17. What are the functional differences between the dorsal and palmar interosseous muscles?

Dorsals abduct (DAB) or allow finger spread
Palmars adduct (PAD) or bring fingers together

18. What functions do lumbrical muscles have at the MP joints? IP joints?

Lumbricals flex fingers at the MP joints and extend fingers at the IP joints

19. What two nerves innervate lumbricals?

Median nerve supplies the 1st and 2nd lumbricals
Ulnar nerve supplies the 3rd and 4th lumbricals

20. What condition occurs if lumbricals are denervated?

Digital clawing

21. The 4 SITS (rotator cuff) muscles are:

Supraspinatus, Infraspinatus, Teres minor, Subscapularis

22. Which SITS muscle is not a rotator?

Supraspinatus

23. Which SITS muscle abducts to 15 degrees?

Supraspinatus

24. Which SITS muscle takes over abduction above 15 degrees?

Deltoid

25. Which SITS muscles laterally rotate the arm at the shoulder?

Infraspinatus and teres minor

26. Which SITS muscle medially rotates the arm at the shoulder?

Subscapularis

27. Complete the following table.

Feature	Anterior Cruciate Ligament	Posterior Cruciate Ligament	Medial Collateral Ligament	Lateral Collateral Ligament	Medial Meniscus	Lateral Meniscus
Attaches to anterior tibial plateau	X					
Attaches to medial femoral condyle		X				
Tested by passive adduction of leg				X		
Tested while pulling the leg anteriorly while stabilizing the femur	X					
Injury causes a posterior drawer sign		X				
Attaches to the fibula				X		
Three injured components of the "unhappy triad"	X		X			X

28. What elbow ligament is stretched in "golfer's elbow"?

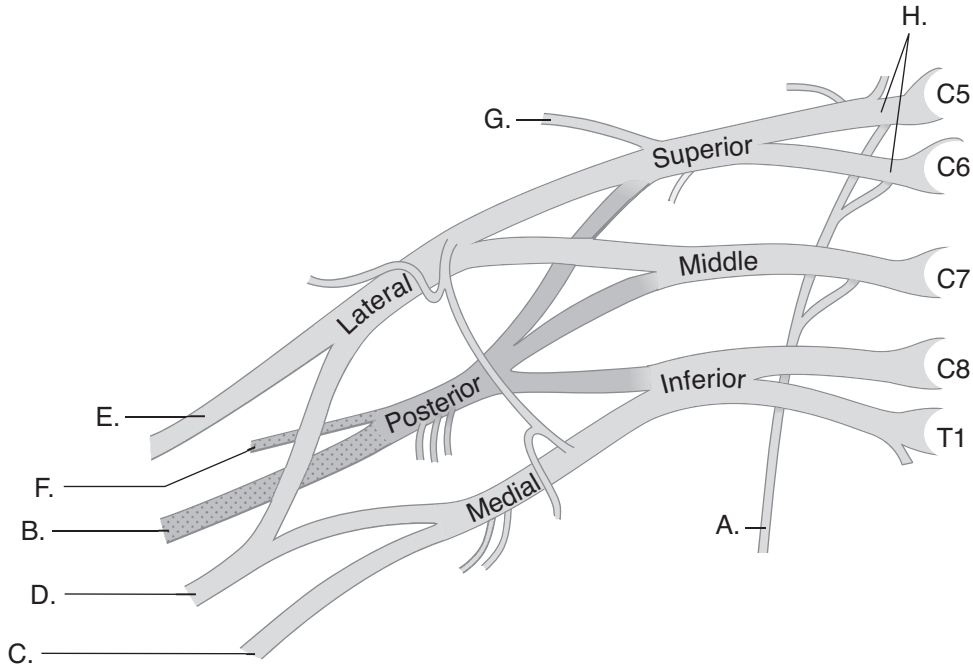
Medial collateral ligament

29. What elbow ligament is stretched in "tennis elbow"?

Lateral collateral ligament

TOPIC 3: INNERVATION OF THE EXTREMITIES

1. Label the main brachial plexus nerves.



	Identify
A	*Long thoracic nerve*
B	*Radial nerve*
C	*Ulnar nerve*
D	*Median nerve*
E	*Musculocutaneous nerve*
F	*Axillary nerve*
G	*Suprascapular nerve*
H	*C5 and C6 ventral rami*

2. What ventral rami form the brachial plexus roots?
   C5-T1

3. What cord segments are in the upper and lower trunks?
   Upper C5 and C6; Lower C8 and T1

4. What cord segments are in the musculocutaneous nerve and the axillary nerve?
   C5 and C6

5. What cord segments are in the ulnar nerve?
   C8 and T1

6. Shoulder dystocia injures what part of the plexus?
   Upper trunk

7. Name 2 causes of lower trunk compression.
   1. Cervical rib, 2. Pancoast neoplasm

8. Complete the following table.

Feature	Musculo-cutaneous Nerve	Median Nerve	Ulnar Nerve	Radial Nerve	Axillary Nerve
Lesioned by surgical neck humeral fracture					X
Lesioned by spiral groove fracture of humerus				X	
Compressed by misuse of crutch				X	
Lesioned by radius subluxation				X	
Lesioned by medial epicondylar humeral fracture			X		
Lesioned by supracondylar humeral fracture		X			
Stretched by humeral dislocation				X	X

9. Fill in the corresponding nerve dermatomes for each anatomic area.

	Corresponding Dermatome(s)
Axilla	T2
Medial forearm	T1
Lateral forearm	C6
Lateral palm	C7, C8
Medial palm	C8
Lateral part of dorsum of hand	C7

10. Complete the following table.

Feature	Musculo-cutaneous Nerve	Median Nerve	Ulnar Nerve	Radial Nerve	Axillary Nerve
Cord segments in?	*C5-C6*	*C6-T1*	*C8-T1*	*C5-C8*	*C5-C6*
Location of altered sensation if lesioned?	*Lateral forearm*	*Lateral palm; Lateral 3½ digits*	*Medial palm; medial 1½ digits*	*Lateral dorsum of hand*	*Arm over deltoid*
Motor weakness if lesioned?	*Elbow flexion and forearm supination*	*Forearm pronation, wrist flexion, flexion of radial digits and thumb*	*Wrist flexion; flexion of ulnar digits*	*Forearm extension; supination*	*Arm abduction and rotation*
Sign associated with motor deficit?	*none*	*Ape hand; hand of benediction*	*Ulnar claw*	*Wrist drop*	*none*

11. Complete the following table.

Feature	Upper Trunk	Lower Trunk	Long Thoracic Nerve
Cord segments in?	*C5 and C6*	*C8 and T1*	*C5, 6, 7*
Location of altered sensation if lesioned?	*Lateral arm and forearm*	*Medial hand, medial forearm*	*none*
Motor weakness if lesioned?	*Shoulder and arm muscles*	*Hand muscles*	*Serratus anterior*
Sign associated with motor deficit?	*Waiters tip*	*Complete claw hand and ape thumb*	*Winged scapula*

12. Complete the following table.

Feature	Obturator Nerve	Femoral Nerve	Tibial Nerve	Common Fibular Nerve
Cord segments in?	*L2, 3, 4*	*L2, 3, 4*	*L4-S3*	*L4-S2*
Location of altered sensation if lesioned?	*Medial thigh*	*Anterior thigh, medial leg*	*Posterior thigh, posterior leg, plantar foot*	*Lateral leg, dorsum of foot*
Motor weakness if lesioned?	*Abduction of hip*	*Hip flexion, Knee extension*	*Knee flexion, Foot plantar flexion, toe flexion*	*Foot eversion, Foot dorsiflexion, toe extension*
Sign associated with motor deficit?	*none*	*none*	*none*	*Foot drop*

13. Complete the following table.

Feature	Superficial Fibular Nerve	Deep Fibular Nerve	Superior Gluteal Nerve	Inferior Gluteal Nerve
Cord segments in?	*L4, L5, S1*	*L5, S1, S2*	*L4, L5, S1*	*L5, S1, S2*
Location of altered sensation if lesioned?	*Lateral leg, dorsum of foot*	*Webbed space between great and 2nd toe*		*Skin over gluteus maximus*
Motor weakness if lesioned?	*Weakness of eversion*	*Foot dorsiflexion, toe extension*	*Hip abduction*	*Hip extension from a fully flexed position*
Sign associated with motor deficit?	*none*	*Foot drop*	*Waddling gait*	*none*

14. What ligament is commonly torn in an inversion sprain?

Lateral collateral

15. Which other 2 bones may be fractured or avulsed by an inversion ankle sprain?

1. Fibular fracture; 2. 5th metatarsal avulsion

TOPIC 4: DISORDERS OF THE BONES

1. What is the molecular defect in achondroplasia?

   Fibroblast growth factor receptor (FGFR3) is constantly activated, leading to inhibition of chondrocyte proliferation.

2. Which bone disease is characterized by decreased bone mass, particularly in older adults?

   Osteoporosis

3. The decreased estrogen involved in the etiology of type 1 osteoporosis has what effect on RANK receptor expression?

   Decreased estrogen promotes increased RANK receptor expression, which leads to increased RANK ligand-receptor interaction and increased bone resorption.

4. What patient population develops type 2 osteoporosis?

   Adults of either sex older than age 70

5. What fractures are common among osteoporosis patients?

   Compression fracture of vertebrae, femoral neck fracture, hip fracture, and distal radius (Colles) fracture.

6. The main class of drugs used in the management of osteoporosis is the _____*bisphosphonates*_____. These drugs have a common ending to their names, which is _____*"-dronate"*_____.

7. A patient started on a drug in the class mentioned in the previous question is advised to remain upright for 30 minutes following drug administration to avoid what side effect?

   Esophageal irritation and esophagitis (heartburn)

8. Which genetic deficiency causes osteopetrosis?

Genetic deficiency of carbonic anhydrase II causes abnormal osteoclast function.

9. "Erlenmeyer flask" bones on x-ray suggest what disease?

Osteopetrosis

10. What is the likely cause of cranial nerve palsies in a patient with osteopetrosis?

Narrowing of skull foramina by bone overgrowth.

11. When considering osteomalacia and osteoporosis, which has defective bone mineralization, and which has reduced bone mass?

Osteomalacia has normal bone mass and defective bone mineralization; osteoporosis has reduced bone mass and normal bone mineralization.

12. What condition has normal osteoid matrix accumulation around trabeculae with absent mineralization?

Osteomalacia shows normal osteoid matrix accumulation around trabeculae with absent mineralization

13. How does vitamin D deficiency in an adult affect bone mineralization?

Vitamin D deficiency causes decreased calcium absorption, increased parathyroid hormone, and decreased serum phosphate.

14. What is craniotabes? Rachitic rosary?

Both cranial tabes and rachitic rosary are clinical manifestations of rickets in children. Craniotabes is softening and reduced mineralization of occipital and parietal bones of the skull, while rachitic rosary refers to an abnormal sternal area due to thickened costochondral junctions.

15. The abnormal bone architecture seen in Paget's disease is caused by *increases in both osteoblastic activity and osteoclastic activity*.

16. What is the suspected cause of Paget's disease?

Paramyxovirus is the suspected cause.

17. Serum studies on Paget's disease would be likely to show:

Normal serum calcium, normal serum phosphorus, normal parathyroid hormone levels, and increased alkaline phosphatase.

18. Name 3 significant complications of Paget's disease.

Arteriovenous malformations and shunting within the bone, high output cardiac failure, and osteogenic sarcoma.

19. What are the features of the triad of McCune-Albright syndrome?

The triad includes multiple unilateral bone lesions, other endocrine abnormalities such as precocious puberty, and café-au-lait spots of the skin.

20. Compare bone mass, bone mineralization, and laboratory studies for osteoporosis and osteopetrosis.

Both show normal bone mineralization and normal laboratory studies. Osteoporosis shows reduced bone mass and osteopetrosis shows increased bone mass.

21. Which disorder—osteomalacia or osteoporosis—would show hypocalcemia, hypophosphatemia, elevated parathyroid hormone, and alkaline phosphatase?

Osteomalacia

22. What lesion is characterized by brown tumors of the bone?

Osteitis fibrosa cystica

23. The combination of numerous colonic polyps and jaw osteoma suggests what syndrome?

Gardner's syndrome

24. The histology of osteoid osteoma is *interlacing trabeculae of woven bone, surrounded by osteoblasts*.

25. The histology of osteoblastoma most closely resembles the histology of what other tumor?

Osteoid osteoma

26. A radiographic study showing a "soap bubble" appearance of the distal femur suggests which tumor?

Giant cell tumor

27. Describe the histology of giant cell tumor of bone.

The tumor has a mixture of spindle shaped cells and multi-nucleated giant cells.

28. An osteochondroma that goes on to develop a malignancy would most likely develop which malignancy?

Chondrosarcoma

29. Enchondromas are characteristically located in what part of the bone?

Intramedullary space

30. What are some of the risk factors for osteosarcoma?

Paget's disease of bone, bone infarcts, history of bone irradiation, familial retinal blastoma

31. What is the characteristic translocation of Ewing's sarcoma?

11;22 translocation

32. When comparing the locations in bone where chondrosarcoma and Ewing sarcoma arise, what is one site that is different?

Chondrosarcoma can frequently involve spine while Ewing sarcoma usually does not.

33. Does lamellar or woven bone form an osteon?

Lamellar

34. Would you expect to find osteons in spongy or compact bone?

Compact

35. What is the difference between a Haversian canal and a canaliculi?

Haversian canal is in center of an osteon; Canaliculi are perpendicular to the Haversian canal and connect individual osteocyte lacunae.

36. Name two synonyms for spongy bone.

Trabecullar or cancellous

37. What type of bone formation utilizes a cartilaginous precursor?

Endochondral

TOPIC 5: ARTHRITIS

1. The polished, ivory-like appearance of bone in osteoarthritis is called *Eburnation*.

2. Distinguish between Heberden's nodes and Bouchard's nodes in osteoarthritis.

   Heberden's nodes are at the distal interphalangeal joint and Bouchard's nodes are at the proximal interphalangeal joint.

3. What would biopsy of a pannus from a joint involved with rheumatoid arthritis show?

   Hyperplasia and hypertrophy of the synovium

4. Contrast the timing of stiffness and pain in osteoarthritis and rheumatoid arthritis.

   Morning stiffness is characteristic of rheumatoid arthritis but pain often worsens during the day in osteoarthritis.

5. What term describes the cluster of rheumatoid arthritis, splenomegaly, and neutropenia?

   Felty's syndrome

6. What lung diseases can be part of the disease process of Felty's syndrome?

   Pleuritis and interstitial lung disease

7. Which laboratory studies are helpful in the diagnosis of rheumatoid arthritis?

   Rheumatoid factor, anti-CCP, HLA-DR4

8. What characteristic deformity of the metacarpophalangeal joints occurs in rheumatoid arthritis?

   Ulnar deviation

9. What characteristic lesions of the proximal interphalangeal joint are seen in rheumatoid arthritis?
Boutonniere deformity and swan neck deformity

10. What crystals are deposited in joints and other tissues in gout?
Monosodium urate crystals

11. What joint is classically affected in gout?
1st Metatarso-phalangeal joint.

12. Describe the appearance of gout crystals.
Needle-shaped, negatively birefringent crystals

13. Lesch-Nyhan syndrome patients develop gout because *a purine salvage pathway deficiency leads to use of an alternate pathway that degrades purines to uric acid, predisposing for developing gout an early age*.

14. Match the gout drugs and targets listed below.

Drug	Target
Colchicine	*Microtubules (tubulin)*
Allopurinol	Xanthine oxidase
Probenecid	*Uric acid reabsorption*
NSAIDs	COX-2

15. In pseudogout, what shape are the crystals, and what are their properties?

The calcium pyrophosphate crystals are rhomboid crystals that turn yellow under a perpendicular light and blue under a parallel light.

16. Name 3 important causes of infectious arthritis.

Staphylococcus aureus, Streptococcus, and Neisseria gonorrhoeae

17. Name 2 causes of chronic infectious arthritis.

Lyme disease and tuberculosis

18. Seronegative arthropathies are often associated with which HLA type?

HLA-B27 (HLA B-27 may also confer susceptibility to uveitis)

19. What condition often affects the fingers in psoriatic arthritis?

Dactylitis (sausage fingers)

20. What bones and joints are commonly affected in ankylosing spondylitis? What are their limitations? What characteristic appearance is seen on x-ray?

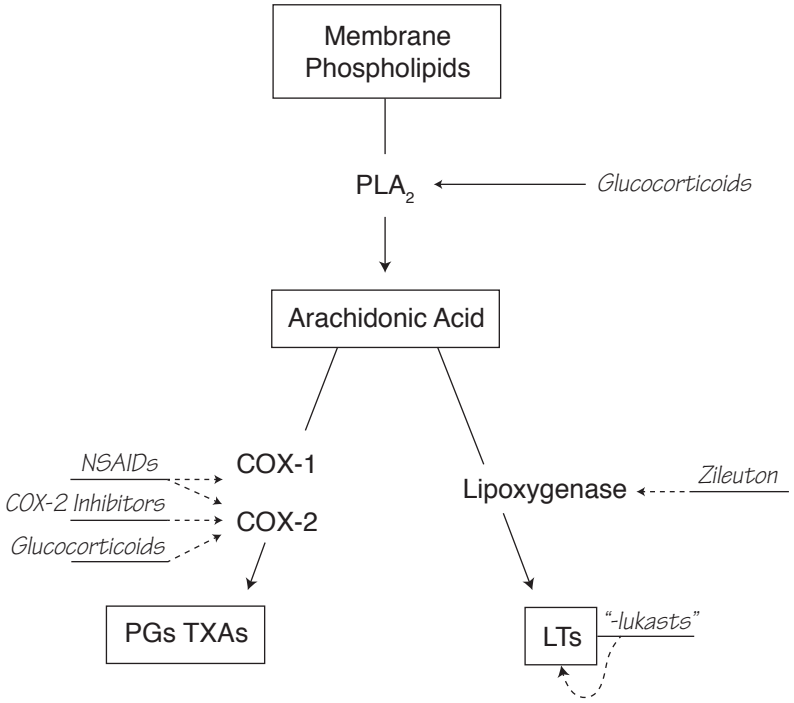
Spine and sacroiliac joints are primarily affected. Limited mobility in these joints causes patients to have a stiff back and difficulty bending forward. The disease produces a characteristic "bamboo spine" appearance on x-ray of the spine.

21. Reactive arthritis is considered to be an autoimmune reaction most commonly precipitated by exposure to _____*Campylobacter, Chlamydia*_____ pathogens.

22. What is the classic triad of reactive arthritis (Reiter syndrome)?

conjunctivitis, urethritis, and arthritis ("can't see, can't pee, can't climb a tree").

23. Identify the drugs in the following diagram.



24. Name the only NSAID that irreversibly inhibits cyclooxygenase.

Aspirin

25. Identify the drug with analgesic and antipyretic properties that lacks anti-inflammatory effects.

Acetaminophen

26. Patients taking 6-mercaptopurine would require what dosage adjustment if allopurinol were added to the regimen?

Decreased dose of 6-mercaptopurine

TOPIC 6: AUTOIMMUNE AND CONNECTIVE TISSUE DISEASES

1. What clinical triad is typical of Sjögren's syndrome?

   Xerophthalmia, xerostomia, and arthritis.

2. What autoantibodies are associated with Sjögren's syndrome?

   Anti-SSA (Ro) and anti-SSB (La).

3. What population does Sjögren's syndrome tend to affect?

   Females age 40-60

4. How does sicca syndrome differ from Sjögren's syndrome?

   Sicca syndrome is very similar to Sjogren's syndrome, but lacks the arthritic component.

5. Immune complex deposition onto heart valves in SLE can cause what condition?

   Nonbacterial verrucous (Libman-Sacks) endocarditis

6. The presence of which autoantibodies suggests the diagnosis of systemic lupus erythematosus?

   Anti-double-stranded DNA (anti-dsDNA), anti-Smith, anti-nuclear antibody, anti-phospholipid antibody.

7. Antiphospholipid antibodies target protein C and thrombin, producing a hypercoagulable state. Is the PTT prolonged, normal, or decreased?

   The PTT is prolonged. PTT does not correct after mixing with normal serum.

8. Name 3 hematologic disorders that lupus patients can develop.

   Thrombocytopenia, leukopenia, and anemia

9. Immune complex depositions in the kidney in lupus can cause what pattern on histology?

   Wire-loop glomerular lesion

10. The antiphospholipid antibodies of lupus can cause false-positive results in which tests?

    RPR and VDRL syphilis tests

11. Exposure to hydralazine and procainamide may induce formation of what antibody in patients with drug-induced SLE?

    Anti-histone body

12. What is the underlying pathology of sarcoidosis?

    Formation of non-caseating granulomas

13. What chest pathology is seen in sarcoidosis?

    Restrictive/interstitial lung disease and bilateral hilar adenopathy

14. What enzyme may be elevated in the blood of patients with sarcoidosis?

    Angiotensin converting enzyme (ACE)

15. A decrease in sensitivity of which test for tuberculosis is seen in sarcoidosis?

    PPD

16. What are characteristic histologic features of sarcoidosis?

    The non-caseating granulomas contain giant cells. Schaumann bodies and asteroid bodies may also be present.

17. Describe the muscular weakness usually seen in polymyalgia rheumatica. What is found on laboratory studies?

    The patients often think they have muscular weakness because they have pain and stiffness, but on testing they do not. Lab studies show normal creatine kinase.

18. Elevation of which lab test is generally characteristic of the myositis disorders?
Increased creatinine kinase

19. What histology is seen in polymyositis?
Endomysial inflammation within muscle fiber, mediated by CD8+ T cells.

20. What histology is seen in dermatomyositis?
Perivascular (perimysial) inflammation within muscle fibers

21. What can be seen on physical examination of patients with dermatomyositis?
Heliotrope rash, Gottron's papules on dorsal finger surface over joints

22. There is an increased risk for *malignancy* in dermatomyositis.

23. What autoantibody is specific for dermatomyositis?
Anti-Jo-1

24. In myasthenia gravis, what happens to muscle weakness with prolonged use?
Muscle weakness worsens with prolonged use.

25. What tumor is associated with myasthenia gravis?
Thymoma

26. What is the target of the autoantibodies of Lambert-Eaton syndrome?
Presynaptic calcium channels of the neuromuscular junction

27. What happens with repetitive nerve stimulation testing in Lambert-Eaton syndrome?
Progressive increase in action potential size occurs.

28. What autoantibody is associated with diffuse scleroderma?
Anti Scl-70 antibodies against topoisomerase 1

29. In CREST syndrome, CREST stands for:
Calcinosis, Raynaud's phenomena, Esophageal dysmotility, Sclerodactyly, and Telangiectasia

30. What autoantibodies are associated with CREST syndrome?
Anti-centromere antibodies

31. Identify the drugs that target tumor necrosis factor-alpha (TNF-α).

Recombinant TNF receptor = _____*Etarnecept*_____

TNF antibody drugs = _____*Infliximab and adalimumab*_____

CHAPTER 3

RESPIRATORY MEDICINE

TOPIC 1: RESPIRATORY ANATOMY

1. Name the vertebral body levels where the esophagus, aorta, and inferior vena cava pass through the diaphragm.

   Esophagus: T10
   Aorta: T12
   IVC: T8

2. Name 2 additional structures that also pass through the aortic hiatus.

   Tributaries of the azygous vein and thoracic duct

3. Name 2 additional structures that also pass through the esophageal hiatus.

   Vagal trunks

4. What are the 3 ventral rami that contribute to the phrenic nerves?

   C3, C4, C5 (keeps the diaphragm alive)

5. Name 2 muscles used in quiet breathing.

   Scalenes, External intercostals

6. Apart from the diaphragm, name 3 muscles used in labored inspiration.

   Scalenes, Sternocleidomastoid, External intercostals

7. Name 2 muscles used in labored expiration.

   Internal intercostals and abdominal wall muscles

8. What muscle is fatigued in a patient with paradoxical breathing?

   Diaphragm

9. What is the key physical sign observed during paradoxical breathing, and what does it indicate?

   Rather than expanding outward, the abdomen moves inward during inspiration. This indicates loss of diaphragmatic function (fatigued or paralyzed).

10. State the 2 major divisions of the respiratory system and the primary differences between them.

    Conducting and respiratory zones: The conducting zone represents the airways connecting terminal bronchioles to atmosphere. The conduction zone is anatomic dead space because no alveoli exist there.. The respiratory zone contains respiratory bronchioles, alveolar ducts, and alveoli. Gas exchange occurs in the respiratory zone because alveoli exist in this region.

11. What structures mark the beginning and the end of the anatomic dead space?

    Conduction part of respiratory system

12. Name the 3 components of the respiratory zone in the lung.

    1. Respiratory bronchioles, 2. Alveolar ducts, and 3. Alveoli

13. Name 2 structures which may compress the trachea.

    Aortic aneurysm and goiter.

14. Name 2 causes of carina displacement.

    Left atrial enlargement, e.g. CHF, and metastasis to carinal lymph nodes.

15. What is the arrangement of cartilage in the:

    a) Trachea?
    Incomplete rings

    b) Bronchi?
    Irregular plates

    c) Bronchioles?
    No cartilage

16. What key structural component in the trachea and main stem bronchi does not exist in bronchioles, and what is the functional implication of this?
    Bronchioles lack cartilage and thus can be compressed much more easily. This occurs during a forced expiration.

17. Which component of the respiratory tree contributes most to pulmonary resistance?
    Medium-sized smooth muscle of bronchi

18. Complete the following table.

Features	Right Lung	Left Lung
Number of lobes?	*3*	*2*
Horizontal lobe present?	*Yes*	*No*
Lingula present?	*No*	*Yes*
Relationship of pulmonary artery to main stem bronchus?	*Anterior*	*Superior (RALS)*

19. For each of the following positions, where will an aspirated foreign object tend to lodge?

Body Position	Location of Aspirated Object
Upright	*Posterior basal segment of R lung*
Supine	*Superior segment of R lower lobe*
Lying on the right	*R upper lobe*
Lying on the left	*Lingula*

20. Name 2 anatomic reasons why an aspirated foreign object tends to pass into the right main bronchus rather than the left.

R main bronchus is shorter, wider, and more vertical

21. How many bronchopulmonary segments are in the right and left lungs?

10 in right lung and 8-10 in left lung

22. Name 3 vascular components found in each segment.

Pulmonary artery, bronchial artery, and pulmonary veins. Lymphatics are intersegmental.

23. Name 2 main cell types found in the respiratory epithelium.

Type 1 and Type 2 Pneumocytes

24. Name 4 functions of a Clara cell.

Secrete surfactant precursor, detox airborne toxins, and serves as a stem cell
[Note to student: Question 24 should ask for 3, not 4 functions; this was an error not corrected in the printed Workbook.]

25. Complete the following table.

Features	Type 1 Pneumocyte	Type 2 Pneumocyte
Forms 97% of alveolar surface	X	
Secretes surfactant		X
A stem cell for alveolar epithelium		X
Part of blood-gas barrier	X	
Contains lamellar bodies in apical cytoplasm		X

TOPIC 2: RESPIRATORY MECHANICS AND PULMONARY CIRCULATION

1. A _Lecithin_ : _sphingomyelin_ ratio that is >2 indicates adequate lung maturity in a fetus. _Corticosteroids_ are given to the mother to stimulate lung maturity in the fetus.

2. _Histamine_ is a compound released from mast cells that causes bronchoconstriction. Another class of compounds that cause bronchoconstriction and are generated during the course of asthma and allergic reactions are the _leukotrienes (anaphylaxis)_.

3. Name and define the 4 lung volumes and lung capacities.

   Four lung volumes:
   1) Tidal volume: volume of air that enters or leaves the nose/mouth during quiet breathing.
   2) Inspiratory reserve volume: Volume of air that can be taken in starting at a normal tidal inspiration.
   3) Expiratory reserve volume: Volume of air that can be exhaled beginning at the end of a normal tidal expiration.
   4) Residual volume: volume of air remaining in the lungs after a maximal forced expiration.

   Four lung capacities (2 or more lung volumes added together):
   1) Inspiratory capacity: tidal + inspiratory reserve.
   2) Functional residual capacity (FRC): Expiratory reserve + residual volume (equilibrium for the respiratory system).
   3) Vital capacity: Inspiratory reserve + tidal + expiratory reserve (volume of air that can be exchanged with the environment).
   4) Total lung capacity (TLC): All lung volumes added together; total volume of the lungs.

4. _Dead space_ is a volume in the respiratory system that does not participate in gas exchange. _Anatomic dead space_ is a volume in the conducting zone. _Alveolar dead space_ are alveoli that are ventilated but not perfused, and _physiologic dead space_ is the sum of the two. In a normal individual, there is no _alveolar dead space_.

5. What is alveolar ventilation if a subject has a 600 ml tidal volume, 200 ml anatomic dead space, and a respiratory rate of 10 breaths/min?

   Alveolar ventilation (VA) = (Tidal volume – dead space) X respiratory rate. Thus, VA = (600 ml – 200 ml) X 10 breath/min = 4 L/min.

6. Breathing room air, at the end of a normal tidal inspiration, the PO_2 and PCO_2 in the conducting zone (anatomic dead space) are approximately _150_ mm Hg and _0_ mm Hg, respectively.

7. At rest, the lungs have an _inward_ recoil, while the chest has an _outward_ recoil. When these forces are balanced, i.e., the same, the respiratory system is at _FRC (equilibrium of the respiratory system)_.

8. At low lung volumes, _compliance_ of the lungs is high, while _recoil_ is low. At high lung volumes, _compliance_ is low, while _recoil_ is high.

9. Name a disease that increases lung compliance, and name a disease that reduces lung compliance.
Emphysema (an obstructive disease); pulmonary fibrosis (also, sarcoidosis, asbestosis, pulmonary edema—restrictive diseases)

10. Low alveolar PO_2 causes _vasoconstriction (hypoxic vasoconstriction)_ of the arterioles perfusing hypoxic alveoli, thereby diverting blood flow away from the hypoxic region.

11. The rate of gas diffusion across the alveoli is directly related to the _surface area_ and _pressure gradient_, and inversely related to the _thickness (Fick's law of diffusion)_ of the barrier.

12. Define perfusion-limited gas exchange, and name the prototypical gas that exhibits this characteristic.
Perfusion-limited means the alveolar gas equilibrates with the gas in the blood. Nitrous oxide (N_2O) is the prototypical gas. O_2 and CO_2 are normally perfusion-limited. Thus, the blood leaving the alveolar capillary has the same PO_2 and PCO_2 as exists in the alveoli.

13. Define diffusion-limited gas exchange and give the prototypical gas that exhibits this characteristic.
Diffusion-limited means the gas does not equilibrate. The prototypical gas is carbon monoxide. Pathological states that reduce diffusion, i.e., restrictive lung disease, can create diffusion limitation for O_2.

14. Pulmonary vascular resistance is lowest at FRC.

15. State the 2 factors that determine O_2 delivery to tissues.

O_2 delivery = O_2 content of the blood times blood flow

TOPIC 3: NORMAL OXYGENATION

1. Write the equation used to estimate alveolar PO_2 (PAO_2).

   Answer: $PAO_2 = PIO_2 - (PACO_2/R)$: If breathing room air, then $P_IO_2 = 150$ mmHg. $PACO_2$ can be determined from the arterial CO_2 given on a blood gas or end-tidal PCO_2. R=0.8 unless stated otherwise.

2. Name the 4 endogenously produced factors that reduce hemoglobin's affinity for O_2.

   Increased H^+ (low pH), PCO_2, 2,3-DPG, and temperature

3. A patient has a normal arterial PO_2 and hemoglobin concentration, yet O_2 content is well below normal. What are the 2 most likely causes of this?

   Methemoglobin and carbon monoxide poisoning. Methemoglobin means the iron is in the 3^+ state, rather than the normal 2^+. In this condition, Hb does not bind O_2. Hb has a much higher affinity for carbon monoxide and thus carbon monoxide will displace O_2 from the Hb

4. Describe the "chloride shift" that occurs in the red blood cell at both the tissues and the lungs.

   CO_2 is primarily transported in the blood as bicarbonate. At the tissues, CO_2 is high, thus favoring the generation of bicarbonate in the red blood cell. This bicarbonate then moves into the plasma in exchange for chloride. At the lungs, CO_2 moves from the plasma into the alveolus causing bicarbonate to move into the red blood cell to regenerate CO_2. The bicarbonate movement into the cell occurs in exchange with chloride, which moves from inside the cell into the plasma. Bottom line: Chloride shifts into the red cell at the tissues and out of the red cell at the lungs.

TOPIC 4: HYPOXEMIA

1. What is the first step in determining the cause of hypoxemia? If the outcome is normal, what is the cause?

   Calculate the A-a gradient. If the A-a is normal then the cause is low alveolar PO_2 (hypoventilation or high altitude). Look at arterial PCO2 to distinguish: Increased in hypoventilation and decreased at high altitude.

2. What is the common characteristic for the hypoxemia caused by $\dot{V}_A/Q$ mismatch, diffusion impairment, and right-to-left shunts? What differentiates shunts from the other 2?

   All three show an elevated A-a gradient. Providing supplemental O2 corrects the hypoxemia associated with ventilation-perfusion mismatch and diffusion impairment, but typically fails to correct the hypoxemia caused by right-to-left shunts.

3. Fill in the following table with arrows to compare and contrast the apex (top) and base (bottom) of the lung in an upright individual.

	$\dot{V}A$	Q	$\dot{V}A/Q$	PAO_2	$PACO_2$
Apex	↓↓	↓↓↓	↑↑	↑	↓
Base	↑	↑↑	↓	↓	↑

4. Describe the immediate responses that occur when one ascends to high altitude.

   Because total pressure decreases as one ascends atmospheric PO_2 decreases. This will result in low arterial PO_2, which stimulates ventilation and reduces arterial PCO_2. The reduced arterial PCO_2 produces a respiratory alkalosis. In addition, the low alveolar PO_2 will cause hypoxic vascoconstriction in the pulmonary circulation, leading to a rise in pulmonary artery pressure.

5. Predict the physiologic compensations and problems that arise if a subject stays at high altitude for an extended period of time.

The kidneys will excrete bicarbonate to help resolve the alkalosis. The hypoxemia will stimulate the release of erythropoietin, resulting in red cell production and a relative polycythemia. This helps resolve the low O2 content of the blood. In addition, there is increased production of 2,3-BPG, resulting in a right shift of the oxyhemoglobin dissociation curve. However, this resultant polycythemia, in combination with the hypoxic vasoconstriction, will elevate pulmonary artery pressure, greatly increasing the likelihood of producing pulmonary hypertension. This can lead to cor pulmonale, which is right ventricular failure secondary to pulmonary hypertension.

6. Discuss the primary respiratory changes that occur with exercise.

Exercise produces a marked increase in ventilation. Pulmonary blood flow also rises, which increases diffusing capacity and improves the ventilation-perfusion matching in the apex. Arterial blood gases typically remain normal, although arterial PCO_2 will start to drop around the lactate threshold and continue to decline as the intensity increases. Blood pH can markedly decline as a result of this lactate release.

TOPIC 5: OBSTRUCTIVE LUNG DISEASE

1. Is a decrease in all lung volumes more characteristic of obstructive lung disease or restrictive lung disease?

   Restrictive lung disease

2. A decrease in *FEV1/FVC* is the most diagnostic marker indicating obstructive disease.

3. Fill in the following table to compare and contrast obstructive vs. restrictive lung disease.

	FEV_1/FVC	FVC	TLC	FRC	RV
Obstructive	*<<0.8*	↓ *(usually)*	↑↑	↑↑	↑↑
Restrictive	↑*/normal*	↓↓	↓↓	↓↓	↓

4. Measurement of mucous gland thickness divided by thickness of bronchial wall gives what index?

   Reid index

5. What enzyme is most responsible for the destruction of the interstitium of the lungs in emphysema?

   Elastase

6. Which form of emphysema is associated with alpha-1-antitrypsin deficiency? Chronic smoking?

   Panacinar; centriacinar

7. Name 2 conditions that predispose for bronchiectasis.

   Cystic fibrosis and Kartagener's syndrome

8. What test can be helpful in the diagnosis of asthma?

   Methacholine challenge test

TOPIC 6: RESTRICTIVE LUNG DISEASE

1. What is the main difference on pulmonary function testing between obstructive lung disease and restrictive lung disease?

   The FEV_1/FVC ratio is lower than normal in obstructive lung disease and is increased or normal in restrictive lung disease.

2. Name 4 or more examples of diseases that produce restrictive lung diseases.

   Adult respiratory distress syndrome, chest wall disorders, neonatal respiratory distress syndrome, pneumoconiosis, sarcoidosis, idiopathic pulmonary fibrosis, Goodpasture syndrome, Wegener's granulomatosis, eosinophilic granuloma, collagen-vascular diseases, hypersensitivity pneumonitis, and drug exposure.

3. What happens to angiotensin-converting enzyme in sarcoidosis?

   Total amount of enzyme increases

4. What histology is associated with sarcoidosis?

   Non-caseating granulomas

5. The decreased diffusion capacity in the lungs seen in idiopathic pulmonary fibrosis is due to what process?

   The decreased diffusion is related to infiltration of the interstitium with fibroblasts that deposit collagen.

6. Name 2 diseases that can cause both glomerulonephritis and pulmonary hemorrhage.

   Goodpasture syndrome and Wegener's granulomatosis

7. What is the origin of the malignant cell in eosinophilic granuloma?

   Langerhan's cells (dendritic cells of skin)

8. Name 3 drugs that are frequently implicated as causes of pulmonary fibrosis.
   Bleomycin, busulfan, and amiodarone

9. Hypersensitivity pneumonitis typically produces what pulmonary features?
   Interstitial nodular lesions and restrictive lung disease

10. Eggshell calcification of hilar lymph nodes is typical of what lung disease?
    Silicosis

11. A golden-brown body resembling a dumbbell in a microscopic sample from a lung biopsy would most likely be due to what disorder? What cancers are more likely in these patients?
    Asbestosis; mesothelioma and bronchogenic carcinoma

12. What process causes the pulmonary edema in adult respiratory distress syndrome?
    Injury to the alveoli and cells lining them leading to a non-cardiogenic pulmonary edema

13. Which experiences a greater pressure from the walls, a small alveolus or a large alveolus?
    Small alveoli experience greater pressure, and tend to collapse.

14. What is the principal component of surfactant?
    Dipalmitoylphosphatidylcholine

15. What value of the lecithin:sphingomyelin level indicates lung maturity?
    Ratio >2

16. What are some risk factors for neonatal respiratory distress syndrome?
    Prematurity, diabetes in the mother, and delivery through a caesarian section

17. What are some risk factors for adult respiratory distress syndrome?

Trauma, septic shock, severe pneumonia, pancreatitis, malignancy, uremia, and amniotic fluid embolism

18. Damage to what type of cells in the lung is most important in causing adult respiratory distress syndrome?

Alveolar pneumocytes and capillaries

19. What finding would typically be seen on chest x-ray in adult respiratory distress syndrome?

Bilateral "white-out"

TOPIC 7: PNEUMONIA AND ASSOCIATED PATHOGENS

1. What is the most common cause of lobar pneumonia?
   Streptococcus pneumoniae (Optochin-sensitive)

2. Bronchopneumonia tends to involve which lung structure(s)?
   Bronchioles and alveoli

3. What are common causes of bronchopneumonia?
   Staphylococcus aureus, Haemophilus influenza, Klebsiella, Streptococcus pyogenes

4. What are the common causes of interstitial pneumonia?
   Viruses (RSV, adenovirus, influenza), Mycoplasma, Legionella, Chlamydia

5. What important diseases are caused by *Streptococcus pneumoniae*?
   Lobar pneumonia, meningitis, otitis media, sinusitis

6. Patients with functional or true asplenia are at high risk for developing pneumonia with what organism?
   S.pneumoniae

7. What type of *Haemophilus influenzae* has a successful vaccine?
   Type B

8. What is the capsule of *H. influenzae* type B composed of?
   Polyribitol phosphate

9. List the growth requirements for *(H) influenzae*. What culture media are these grown in?
   X-heme and V-NAD+, chocolate agar

10. How is *Legionella pneumophila* transmitted?
    Through aerosolized water sources

11. List the clinical triad of legionnaires' disease.
    Pneumonia, diarrhea, and hyponatremia.

12. What is an unusual characteristic of *Legionella* pneumonia?
    Gastrointestinal symptoms

13. Name the agar that can allow for the growth of *Legionella*.
    Buffered charcoal yeast extract (BCYE)

14. Name the class of drugs commonly used to treat *Legionella*.
    Macrolides

15. List at least 2 risk factors for infections with *Pseudomonas aeruginosa*.
    Ventilator, cystic fibrosis and burns

16. List the mechanism of action of the *Pseudomonas* exotoxin.
    Inhibition of EF-2 via ADP ribosylation

17. What organism can notably cause both ventilator-associated pneumonia and swimmer's ear (external otitis)?
    Pseudomonas aeruginosa; external otitis can become malignant otitis externa in diabetics

18. What are the skin lesions that can occur in *Pseudomonas* sepsis?
    Ecthyma gangrenosum

19. Place an X by each characteristic or lab test that applies to *Pseudomonas aeruginosa*.

Oxidase negative	
Lactose fermenter	
Endotoxin	X
Exotoxin	X
Blue-green pigment	X
Catalase	X

20. Name 2 biochemical differences between Chlamydia and most bacteria.
Chlamydia cannot make their own ATP and there is no muramic acid in the cell walls.

21. Name the infectious form of Chlamydia.
Elementary body

22. Name the replicative form of Chlamydia.
Reticulate body

23. What diseases are caused by *Chlamydia trachomatis*?
Urethritis, reactive arthritis, conjunctivitis, pelvic inflammatory disease

24. What are 2 distinctive features about the structure of *Mycoplasma*?
Mycoplasma lack a cell wall and the bacterial membrane contains cholesterol.

25. Why can't *Mycoplasma* be treated with penicillins or cephalosporins?

No cell wall

26. What serologic test can be used to confirm *Mycoplasma* infection?

Cold agglutinins

TOPIC 8: FUNGAL RESPIRATORY INFECTIONS

1. Dimorphic fungi are a mold at (list temperature) 20°C

   Dimorphic fungi are a yeast at (list temperature) 37°C

2. Name the primary treatment for the systemic fungal infections.

   Amphotericin B

3. For each characteristic listed, write if it applies to *Histoplasma* (H), *Blastomyces* (B), *Paracoccidioides* (P), or *Coccidioides* (C).

Characteristic	Systemic mycoses
Latin America	P
Fungus flu	H
Broad-based budding yeast	B
Southwestern United States	C
Intracellular yeast in macrophages	H
Desert bumps	C
Ship's steering wheel	P
Spherule	C
Ohio-Mississippi River Valley	H
Bird or bat feces	H
East of the Mississippi	B
Dissemination to the skin	B

4. Name the causative agent of tinea versicolor: _____Malasezzia furfur_____. A KOH mount from a patient with tinea versicolor would reveal what types of structures? Draw or describe the structures.

   Round yeasts and short hyphae (spaghetti and meatballs)

5. For each tinea listed, write the location where each is found.

   - Tinea corporis _____body_____
   - Tinea cruris _____scrotum_____
   - Tinea unguinum _____nails_____
   - Tinea barbae _____beard_____
   - Tinea pedis _____feet_____

6. List the 3 genera associated with cutaneous fungal infections.

   Trichophyton, Epidermophyton, Microsporum

7. List the *Candida* morphologies observed at the following temperatures.

   - 20°C _____yeast_____
   - 37°C _____germ tubes (hyphae)_____

8. List at least 2 diseases associated with recurrent *Candida* infections.

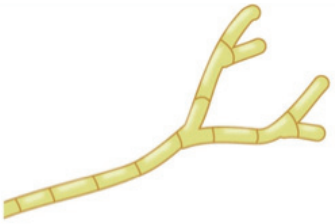
   Diabetes Mellitus, AIDS, Cancer, Obesity

9. List 3 disease states associated with *Aspergillus* infection.

   Allergic, Fungus ball, Invasive

10. Draw or describe the *Aspergillus* fungi.

    Septate hyphae at acute or 45°angles



11. List the natural environment(s) for *Cryptococcus neoformans*.
    Pigeons, soil associated with pigeon droppings

12. List the *Cryptococcus neoformans* morphologies observed at the following temperatures.
    20° *yeast*
    37° *yeast*

13. List the patients at risk for *Mucor* infections.
    Ketoacidotic diabetic patients and leukemic patients

14. Draw or describe the *Mucor* fungus.
    Non-septate hyphae with 90° angles.

15. *Pneumocystis jiroveci* is associated with diffuse pneumonia in what patient population?
    AIDS

16. Prophylaxis for *Pneumocystis* should begin at what CD4+ T cell count?
    <200

17. Name the causative agent of Rose Gardener's disease.
    Sporothrix schenkii

18. Describe the diagnostic yeast form of *Sporothrix*.
    Cigar shaped yeast

TOPIC 9: VIRAL RESPIRATORY INFECTIONS

1. Name 2 viral symmetries.
   Icosahedral, helical

2. Which type of viral capsid is always enveloped?
   Helical

3. Viral envelopes are derived from which cellular structure?
   Cell membrane

4. Reassortment of viral genomes can occur only with which types of viruses, in general?
   Segmented

5. What is the most important clinical example of viral reassortment?
   Influenza virus and genetic shift

6. Define complementation.
   2 viruses with defects in DIFFERENT genes infect the same cell and produce infectious progeny.

7. Define phenotypic mixing.
   Two different kinds of viruses (virus A and virus B) infect the same cell and the nucleic acid of virus A gets surrounded by the capsid of virus B. Because the capsid determines infectivity the new virus will have infectious properties of virus B but will infect a cell with the nucleic acid of virus A.

8. List the vaccine types in order of immunogenicity.
   Live>component>killed

9. List the vaccine type(s) that are safe to give to immunocompromised patients.
   Component, killed

10. Name the only DNA virus family that is single-stranded.
    Parvovirus (B19)

11. List the DNA viruses that have a circular genome.

Papillomaviruses, hepadnaviruses, and polyoma viruses

12. Name the only RNA virus family that is double-stranded.

Reoviridae

13. For each virus family listed, write "+" if the virus family is positive-stranded RNA or "–" if the virus family is negative-stranded RNA. Place an "S" in the box for each family that is segmented.

Virus Family	RNA Genome + or –
Reoviridae	–, S
Coronaviridae	+
Orthomyxoviridae	–, S
Paramyxoviridae	–
Retroviridae	+
Caliciviridae	+
Bunyaviridae	–, S
Arenaviridae	–, S
Herpesviridae	+
Rhabdoviridae	–
Filoviridae	–
Flaviviridae	+
Togaviridae	+
Picornaviridae	+

14. Name the only DNA virus that replicates in the cytoplasm.

Poxvirus

15. Name the RNA virus(s) that replicate in the nucleus.
    Influenza, retroviruses

16. Name the most common causative agent of the common cold.
    Rhinoviruses

17. List the 2 influenza viral proteins found in the viral envelope.
    Hemagglutinin and neuraminidase

18. List the functions of the above 2 molecules.
    - *HA-attachment*
    - *NA-cleaves viral progeny*

19. Name the pathology common to all paramyxoviruses. What specific viral protein is associated with this pathology?
    Syncytia (multinucleated cells); F protein

TOPIC 10: LUNG CANCER AND PLEURAL EFFUSIONS

1. Which organisms are likely to cause lung abscesses?

   Staphylococcus aureus, anaerobes, and Klebsiella

2. What are some of the causes of cavitary lesions of the lung?

   Necrotizing infections, abscesses, malignancy, necrotizing vasculitis (Wegener's granulomatosis), tuberculosis, fungal infections

3. Compare the protein content of transudative effusions with that of exudative effusions.

   Transudative effusions have a low protein content and exudative effusions have a high protein content.

4. What causes transudative effusions?

   Imbalance between hydrostatic and oncotic pressures

5. Bilateral obliteration of the costophrenic angles can be seen in what condition?

   Bilateral pleural effusions, likely in the setting of congestive heart failure.

6. Cirrhosis patients tend to accumulate extravascular fluid in what sites?

   Abdomen (ascites), dependent areas (e.g. pedal edema), and lungs (pleural effusion)

7. In what conditions can collagen vascular disease produce exudative effusions?

   Systemic lupus erythematosus, rheumatoid arthritis, and scleroderma

8. How do the laboratory studies on transudates and exudates differ?

   Compared to exudates, transudates have low cell counts, low protein content, and specific gravity below 1.012.

9. What is the most common cancer found in the lung?
   Metastatic cancer

10. Popcorn calcification in a coin lesion on chest x-ray would be more likely to be malignant or non-malignant?
    Non-malignant

11. What are some complications of lung cancer?
    Superior vena cava syndrome, Horner syndrome, paraneoplastic syndromes such as SIADH and hypercalcemia, recurrent laryngeal nerve involvement, pleural effusions

12. What would be likely to cause hypercalcemia in a patient with lung cancer?
    PTHrP (can be related to squamous cell carcinoma)

13. Keratin pearls and intracellular bridges in a biopsy from a lung nodule suggest what tumor histology?
    Squamous cell carcinoma

14. Hypertrophic osteoarthropathy would most likely be seen in which type of lung cancer?
    Adenocarcinoma

15. Biopsy of a lung mass demonstrates sheets of small blue cells, which suggests what tumor?
    Small cell carcinoma

16. What paraneoplastic syndromes are associated with small cell carcinoma?
    Cushing syndrome, SIADH, Lambert-Eaton myasthenic syndrome

17. From which cells does small cell carcinoma arise?
    Enterochromaffin (Kulchitsky) cells

18. A primary lung cancer with many pleomorphic giant cells on microscopy would most likely be what cancer?

Large cell carcinoma

19. What cardiac problems can carcinoid tumors cause?

Tricuspid stenosis, tricuspid insufficiency, pulmonic stenosis

20. What tumor might cause extensive involvement of the pleura and show many areas of calcification?

Mesothelioma

21. What does the presence of ptosis, miosis, anhidrosis, and hoarseness in a patient with cancer involving the lung suggest?

Pancoast tumor (associated with Horner syndrome)

22. A patient with a lung cancer who develops hyponatremia would most likely have what form of lung cancer?

Small cell carcinoma of the lungs

TOPIC 11: PULMONARY HYPERTENSION AND PULMONARY EMBOLISM

1. What pressures in the pulmonary artery define pulmonary hypertension?

   Pulmonary artery pressure > 25 mm Hg at rest or > 35 mm Hg during exercise

2. What is the histopathology of vessels in pulmonary hypertension?

   Medial hypertrophy and intimal fibrosis

3. What mutation is associated with primary pulmonary hypertension?

   Inactivating mutation of BMPR-2 – a serine/threonine receptor kinase

4. What are the cardiac complications of pulmonary hypertension?

   Right ventricular hypertrophy and right heart failure

5. Name 3 or more causes of secondary pulmonary hypertension.

   Left heart failure, mitral stenosis, tricuspid stenosis, recurrent thromboemboli, scleroderma, Eisenmenger syndrome, sleep apnea, lung transplant rejection

6. Central sleep apnea occurs because of cessation of signals from what brain site?

   Medullary center

7. How can obstructive sleep apnea cause pulmonary hypertension?

   By causing chronic hypoxic vasoconstriction in the lungs

8. When compared to normal sleep patterns, the sleep patterns in obstructive sleep apnea show which characteristics?

   Shorter induction of sleep (stage 1), shorter delta wave (stage 3 and 4 sleep), and shorter REM sleep

9. Which medications are useful for treatment of pulmonary hypertension?

   Prostaglandins, sildenafil, and bosentan (endothelin receptor antagonist)

10. What is the most important cause of fat emboli?

    Long bone fracture

11. What are typical presenting complaints for pulmonary embolism?

    Chest pain, tachypnea, and tachycardia

12. In the context of deep venous thrombosis, what term is used for the combination of stasis, hypercoagulability, and endothilial injury?

    Virchow's triad

13. What is a physical sign of deep venous thrombosis in the leg?

    Calf pain on dorsiflexion of the foot (Homan's sign)

CHAPTER 4

CARDIOLOGY

TOPIC 1: CARDIAC OUTPUT

1. In general, if an arteriole vasoconstricts, blood flow ___decreases___, pressure upstream from the site of the constriction ___increases___, while pressure downstream from the site of the constriction ___decreases___.

2. In general, if an arteriole vasodilates, blood flow ___increases___, pressure upstream from the site of the constriction ___decreases___, while pressure downstream from the site of the constriction ___increases___.

3. When considering whole body hemodynamics, MAP equals ___CO (cardiac output)___ times ___TPR (total peripheral resistance)___.

4. The velocity of blood is highest in the ___Aorta___ and lowest in ___capillaries___.

5. Fill in the table below for adrenergic receptors.

Receptor	G Protein	Signal Transduction	Vascular Effect	Heart Effect
α_1	G_q	↑ Phospholipase C → ↑ IP3, DAG, Ca^{2+}	Vasoconstriction	N/A
α_2	G_i	↓ AC → ↓ cAMP	Indirect vasodilation (CNS ↓SNS)	N/A
β_1	G_s	↑ AC → ↑ cAMP	N/A	↑ HR; ↑ contractility; ↑ conduction velocity; ↑ rate of relaxation
β_2	G_s	↑ AC → ↑ cAMP	Vasodilation	N/A

6. Cardiac output equals Heart rate (HR) times stroke volume (SV).

7. The following data were obtained from subject A:

   O_2 consumption = 300 mlO_2/min

   Hb concentration = 15 mg/dl

   Arterial O_2 saturation = 99%

   Mixed-venous O_2 saturation = 75%

   What is the cardiac output of subject A?

   *Use the Fick Principle to calculate: O_2 consumption = Q * (CaO_2 – CvO_2). Rearranging to solve for flow gives: Q = O_2 consumption/(CaO_2 – CvO_2). O_2 consumption is given (300 mlO_2/min) while arterial and mixed-venous must be determined from the data. CaO_2 = 15 (Hb concentration) * 1.34 * 99% (O_2 saturation) = 19.9 mlO_2/dl. CvO_2 = 15 (Hb concentration) * 1.34 * 75% (O_2 saturation) = 15.1 mlO_2/dl. Thus, Q (CO) = 300 mlO_2/min * 0.048 ml O_2/ml (converted to ml O_2/ ml from ml O_2/dl) = 6250 ml/min.*

8. Independent of heart rate (HR), list the 3 factors that influence ventricular output.

   Stroke volume (SV) is ventricular output per beat. It is influenced by: 1) contractility (directly related), 2) afterload (inversely related), and 3) preload (directly related—Frank-Starling mechanism).

9. Discuss the mechanisms by which β-1 receptor stimulation increases contractility of the heart. How is this process altered by the inotropic agents inamrinone and milrinone?

   Beta-1 activation increases contractility by increasing the amount of calcium in the cytoplasm. Beta-1 activation stimulates increasing cAMP production -> rise in cAMP increases calcium flux through sarcolemmal calcium channels -> increases calcium-induced calcium release from the sarcoplasmic reticulum (SR). In addition, the rise in cAMP stimulates sarcoplasmic/endoplasmic reticulum calcium ATPase (SERCA), which increases the amount of calcium in the SR. Increased calcium in the SR allows for more calcium release on subsequent contractions.

   Inamrinone and milrinone block phosphodiesterase -> increased cAMP and thus increased contractility by the mechanisms described above.

10. Discuss the mechanisms by which digoxin increases contractility of the heart.

    Digoxin blocks the sarcolemmal Na^+/K^+ ATPase -> increased cytosolic sodium -> inhibits sarcolemmal Na^+/Ca^{2+} antiporter that pumps Ca^{2+} out of the cell -> increased cytosolic calcium -> increased contractility. Additionally, the increase in cytosolic calcium is then pumped into the SR by SERCA, increasing the available pool of calcium during systole.

11. What is preload for the ventricle and how does it impact ventricular output?

    Preload for the ventricle is the volume of blood present in the heart before the 'load' from atrial blood enters the ventricle. End-diastolic volume is preload for the ventricle. This volume provides the stretch on sarcomeres just prior to contraction. If preload increases, then stroke volume (SV) increases. Similarly, If preload decreases, then SV decreases. Thus, SV is dependent upon the amount of blood available to be pumped. This is the Frank-Starling mechanism for the heart.

12. Stroke volume divided by end-diastolic volume gives _____*Ejection fraction (EF). Normal EF is ~ 0.6 or 60%*_____, which is a clinical marker of myocardial contractility.

13. List the 2 factors that directly determine mean systemic filling pressure. Also describe their relationship with venous return.

    1) Blood volume: venous return is directly related to blood volume. 2) Compliance (veins): venous return is inversely related to venous compliance. Recall that ventricular preload is determined by venous return.

14. Indicate what happens to venous return when arterioles vasoconstrict or vasodilate.

    Arteriolar dilation increases venous return while arteriolar vasoconstriction decreases venous return.

TOPIC 2: THE CARDIAC CYCLE

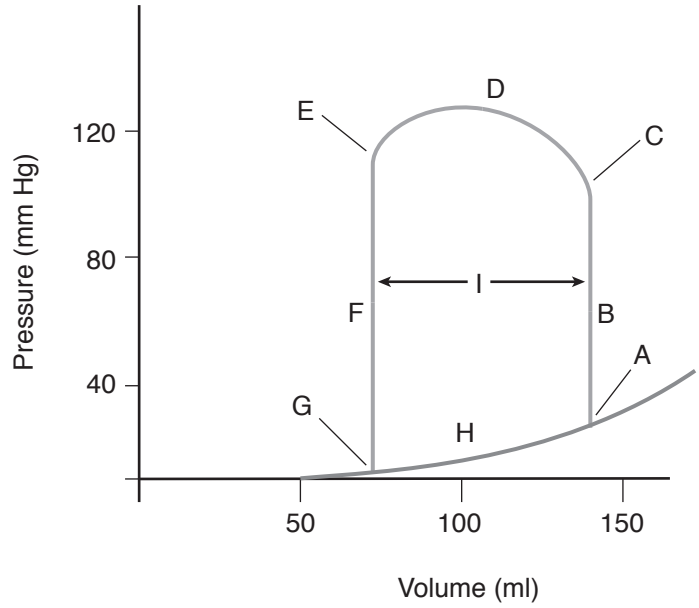
1. On a basic level, what are the 2 things the heart does during systole?

   Pressurizes; ejects

2. On a basic level, what are the 2 things the heart does during diastole?

   Depressurizes; refills

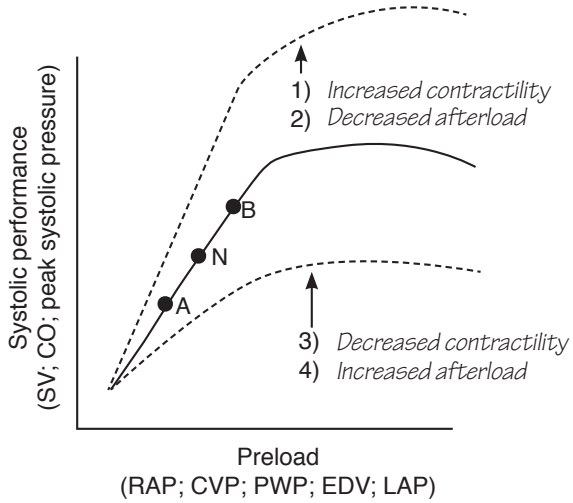
3. Indicate the event/phase/representation of the labeled parts of the left ventricular pressure-volume loop provided below.



A = mitral valve closes
B = isovolumetric contraction (pressurization)
C = aortic valve opens
D = ejection
E = aortic valve closes
F = isovolumetric relaxation (depressurization)
G = mitral valve opens
H = filling; I = stroke volume

4. Fill in the blanks using the pressure-volume loop depicted above. A change in volume at point ___A___ indicates a Frank-Starling alteration in function. A change in pressure at point ___C___ would indicate a change in ___Afterload___. The first heart sound (S1) occurs at point ___A___, while the second heart sound (S2) occurs at point ___E___.

5. Ventricular function can be shifted by 4 basic factors. Note them on the graph below.



6. Using the ventricular function curve above, indicate the shift (1/2, 3/4, N → B, or N → A, with N representing normal) that directly occurs (no compensation) in response to:

1) Hemorrhage N→A

2) Propranolol 3/4

3) Dobutamine 1/2

4) Standing upright N→A

5) Myocardial ischemia 3/4

6) Phenylephrine 3/4

7) Entering space (zero gravity) N→B

8) Lying down N→B

9) Prazosin 1/2

10) Cholera toxin 3/4 (volume loss from diarrhea).

7. Below is a depiction of a right atrial/venous pulse pressure trace. Indicate what occurs during each labeled portion, and note on the picture the valve problem causing the depicted alteration.

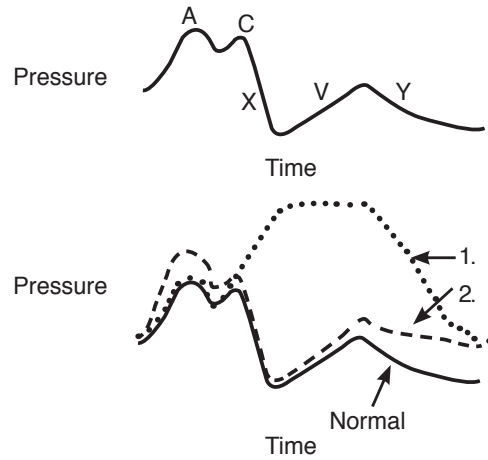
   (A) *A wave is atrial contraction*

   (C) *C wave is ventricular contraction*

   (X) *X-descent represents atrial relaxation*

   (V) *V wave is filling of the right atrium*

   (Y) *Y-descent is opening of the tricuspid valve and ventricular filling. 1) tricuspid regurgitation; 2) tricuspid stenosis*



8. Fill in the table below for the arterial baroreflex.

Arterial Blood Pressure	Baroreceptor Activity	Parasympathetic Activity	Sympathetic Activity	HR	TPR
Increase	↑	↑	↓	↓	↓
Decrease	↓	↓	↑	↑	↑

9. Discuss the long-term regulation of blood pressure.

   The long-term regulation of blood pressure involves the kidneys and RAAS (renin-angiotensin-aldosterone system). Reduced perfusion pressure or sympathetic activation to the kidney → renin release → increased level of angiotensin II → stimulates aldosterone → increased sodium reabsorption in the kidney → increased extracellular volume of fluid in a fixed space → increased blood pressure.

TOPIC 3: REGULATION OF BLOOD FLOW AND FLUID EXCHANGE

1. _Autoregulation_ is the maintenance of a relatively constant flow despite changes in pressure. _Metabolic_ and _myogenic_ mechanisms cause this effect.

2. Although the brain is a good autoregulator, an increase in _$PaCO_2$_ will vasodilate the cerebral circulation.

3. Considering the Fick principle related to O_2 consumption, what unique characteristic does the heart at rest have compared to the other organs?

   Oxygen extraction by the heart is near maximal at a resting HR.

4. Describe how the pulmonary circulation responds to low O_2 differently than systemic vessels.

   Pulmonary arterioles constrict in response to alveolar hypoxia. This is termed hypoxic vasoconstriction and it aids in ventilation-perfusion matching. Systemic arterioles dilate in response to local hypoxia.

5. Given the following variables, what is the net force for filtration and what direction is water moving?

   Pc = 32 mm Hg $\pi c = 30$
   Pif = –3 $\pi if = 2$

   Net filtration is 7 mmHg favoring filtration: (32 – -3) – (30 – 2) = 7

6. Hydrostatic pressure in the capillary is directly related to what 3 variables?

   1) Blood flow to the capillary, 2) venous pressure, and 3) blood volume

7. Compare and contrast transudative and exudative fluid flux.

   Transudative is protein free fluid flux across the capillary. Exudative is flux of fluid containing proteins and other large molecules into the interstitium.

8. Identify the agonist from the receptor(s) it stimulates.

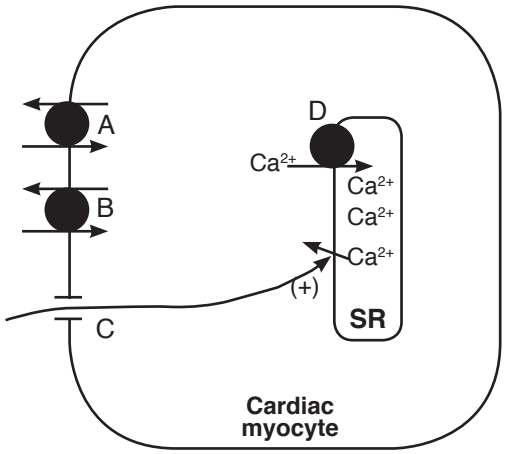
Drug	Receptor(s)
Norepinephrine	α_1, α_2, β_1
Phenylephrine	α_1
Isoproterenol	β_1, β_2
Epinephrine	α_1, α_2, β_1, β_2
Dopamine	D_1, β_1, α_1
Dobutamine	β_1

9. Use the Vaughan-Williams classification system to classify the drugs below.

Drug	Classification
Lidocaine	*Ib*
Amiodarone	*III*
Procainamide	*Ia*
Esmolol	*II*
Verapamil	*IV*
Sotalol	*III*
Quinidine	*Ia*

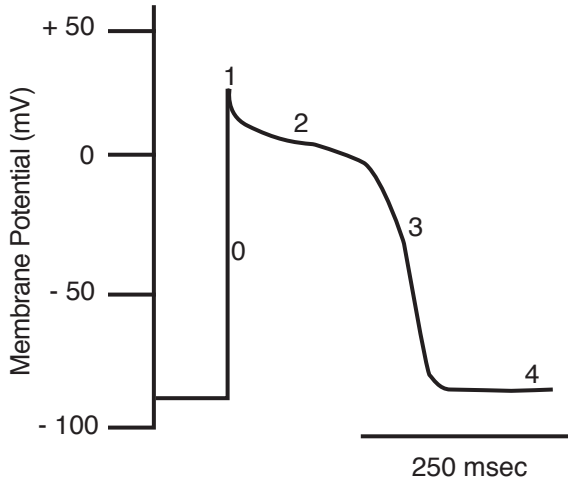
TOPIC 4: CARDIAC ELECTROPHYSIOLOGY

1. Name/indicate what is occurring at the 4 labeled points in the cardiac myocyte (A–D).



A is Na^+—K^+ ATPase (3 Na^+ out; 2 K^+ in); B is Na^+—Ca^{2+} exchanger (3 Na^+ in; 1 Ca^{2+} out); C is sarcolemmal voltage-gated Ca^{2+} channel (primarily L-type). Influx of Ca^{2+} via these channels causes Ca^{2+} release from the sarcoplasmic reticulum (SR). D is smooth endoplasmic reticulum calcium ATPase (SERCA), which pumps cytosolic calcium back into the SR and is primarily responsible for relaxation.

2. Name the ion that is primarily responsible for the voltage or voltage change at the 5 labeled points (0–4) on the cardiac action potential.

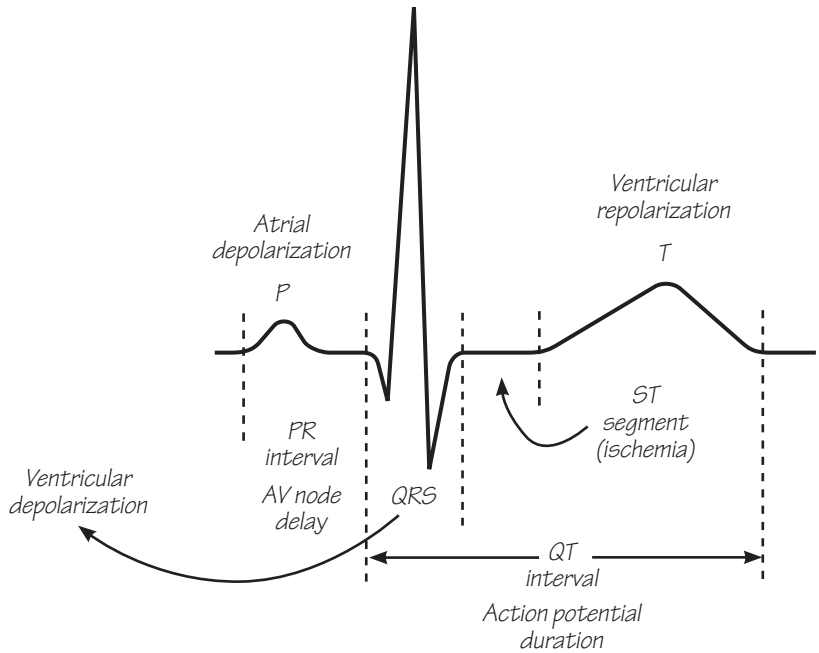


Phase 0: Upstroke of the action potential—Na^+; Phase 1: Transient repolarization—K^+; Phase 2: Plateau phase—Ca^{2+} in, K^+ out; Phase 3: Repolarization—K^+; Phase 4: Resting membrane potential, and there is a high K^+ permeability.

3. Discuss the ionic currents responsible for phase 4 (pacemaker potential) and phase 0 in the SA and AV node.

Phase 4 is mediated by an inward Na^+ current (funny current), an inward Ca^{2+} current, and a reduced K^+ permeability. Phase 0 is the upstroke of the action potential, but in SA/AV nodes, this is mediated by Ca^{2+}, not Na^+.

4. On the ECG trace below, label the various waves, intervals, and segments, as well as a brief explanation about how they are caused.



TOPIC 5: ARRHYTHMIAS

1. A long *QT interval* can lead to torsades de pointes.

2. What is a delta wave, and what arrhythmia does it indicate?

   A delta wave is slurred upstroke of the QRS complex with a concomitant shortened PR interval. A delta wave indicates Wolff-Parkinson-White syndrome

3. Define first-, second-, and third-degree heart blocks.

   First degree: Elongated PR interval (>200 msec); Second degree: Every QRS is preceded by a P wave, but not every P wave is followed by a QRS. Two types: 1) Mobitz type II (Wenckebach—progressive prolongation of the PR interval until a QRS is dropped and then repeats the pattern), 2) Mobitz type I (PR interval, when it occurs, is usually fixed); Third degree: Complete dissociation between P and QRS. Ventricle has its own pacemaker.

4. Prior to starting therapy with amiodarone, 3 organ function tests should be performed. List each test and the side effect for which you would monitor.

Test	Side Effect
Liver Function	*Liver Failure*
Pulmonary Function	*Pulmonary Fibrosis*
Thyroid Function	*Hypo- or Hyperthyroidism*

TOPIC 6: HEART SOUNDS

1. Fill in the chart below to indicate common causes for altered splitting of the second heart sound.

	Wide	Fixed	Paradoxical
Condition	1) *Right BB block* 2) *Pulmonic stenosis*	1) *Atrial-septal defect*	1) *Left BB block* 2) *Advanced aortic stenosis*

2. For valve stenosis, it is important to remember that ___*pressure*___ and ___*volume*___ upstream of the defective valve increase.

3. List the 4 valve pathologies that can create a systolic murmur.

   1) Aortic stenosis, 2) Pulmonic stenosis, 3) Mitral regurgitation, and 4) Tricuspid regurgitation

4. List the 4 valve pathologies that can create a diastolic murmur.

   1) Aortic regurgitation, 2) Pulmonic regurgitation, 3) Mitral stenosis, and 4) Pulmonic stenosis

5. An ejection "click" occurs in what valve pathology?

   Mitral valve prolapse

6. An opening "snap" occurs in what valve pathology?

   Mitral stenosis

TOPIC 7: HYPERTENSION

1. Name some long-term consequences of hypertension.

   Stroke, left ventricular hypertrophy, and retinopathy.

2. What is the most common cause of renal artery stenosis in an older patient? In a young female patient?

   Atherosclerosis is common in older patients and fibromuscular dysplasia is common in young female patients.

3. Decreased pressure in the renal afferent arteriole triggers secretion of what enzyme by the juxtaglomerular cells? What does this enzyme do?

   The juxtaglomerular cells secrete the enzyme renin → cleaves angiotensinogen to angiotensin-I → angiotensin-I is subsequently converted in the lung to angiotensin –II → acts on the zona glomerulosa to produce aldosterone.

4. Compared with a normal person, how do the number of peripheral arterioles change in a patient with primary hypertension? The arteriolar wall thickness? The total peripheral resistance?

   Patients with primary hypertension have decreased number of arterioles, increased arteriolar wall thickness, increased total peripheral resistance.

5. Hypertrophy of the wall of which cardiac chamber is most prominent in longstanding cases of hypertension?

   Concentric left ventricular hypertrophy is most characteristic of long-standing hypertension.

6. What are some other consequences of long-standing hypertension?

   renal failure, retinopathy, aortic dissection

7. What vessel changes characterize essential hypertension? Malignant hypertension?

   Essential hypertension produces hyaline thickening, malignant hypertension produces hyperplastic arteriosclerosis.

8. In hypertension, what does the term "onion-skinning" refer to?

   The term "onion-skinning" refers to a layering with luminal narrowing of the wall of an arteriole caused by proliferation of intima and muscular layers that is induced by malignant hypertension (which is associated with acute renal failure and in some cases, papilledema).

9. What types of material does the necrotic core contain in an advanced atherosclerotic plaque?

   Cell debris, cholesterol crystals, foam cells, and calcium

10. What are locations of 4 clinically important aneurysms?

    Berry aneurysms (circle of Willis), coronary artery aneurysms, ascending thoracic aneurysm (can dissect), abdominal aortic aneurysm

11. What type of degeneration in the aorta is occurring in cystic medial necrosis?

    Myxomatous degeneration

12. What finding on chest x-ray is most characteristic of aortic dissection?

    Widened mediastinum

13. A hypertensive patient with diabetes would benefit more from what type of drug?

    ACEI or ARB

14. Complete the table below on cardiovascular drugs.

Drug/Drug Class	Property
Thiazides	Diuretic, ↑LDLs
Verapamil, diltiazem	Antiarrhythmic CCBs
Methyldopa	α_2 agonist, (+) Coombs test
Phenoxybenzamine	Irreversible α-blocker
Spironolactone, eplerenone	Diuretic, ↓ cardiac remodeling
Verapamil	Most cardiodepressant CCB
α1-blockers	Useful in BPH and hypertension

TOPIC 8: LIPID METABOLISM

1. What is the function of bile?

   Facilitating the absorption of fats, cholesterol, and fat-soluble vitamins by forming micelles around dietary lipids.

2. Name the enterocyte enzyme responsible for breaking down the following dietary lipids at the brush border:

   (A) Triglycerides — *Pancreatic lipase*

   (B) Cholesterol esters — *Cholesterol esterase*

   (C) Phospholipids — *Phospholipase A2*

3. Which lipase enzyme catalyzes the breakdown of dietary triglycerides in the small intestine?

   Pancreatic lipase

4. Which lipase enzyme catalyzes the breakdown of triglycerides circulating in chylomicrons and VLDL?

   Lipoprotein lipase

5. Which lipase enzyme catalyzes the breakdown of triglycerides stored in adipocytes?

   Hormone-sensitive lipase

6. Which apoprotein mediates chylomicron secretion from intestinal enterocytes into lymphatic vessels?

   apoB-48

7. What lipids and what lipoproteins are elevated in the blood in familial lipoprotein lipase deficiency? Familial hypercholesterolemia? Hepatic overproduction of VLDL?

   Familial lipoprotein lipase - triglyceride and chylomicrons; familial hypercholesterolemia- cholesterol and LDL; hepatic overproduction of VLDL - VLDL and TG.

8. Which apoproteins are lacking in abetalipoproteinemia?

   ApoB-100 and ApoB-48

9. Identify the lipid-lowering drug corresponding to the mechanism of action:

   (A) Activates PPAR-α — *Fibrates*

   (B) Causes flushing and itching — *Niacin*

   (C) Absorption of vitamins A, D, E, K — *Bile Acid Sequestrants*

   (D) Cholesterol absorption in GI tract — *Ezetemibe*

   (E) Monitor LFTs and creatine kinase — *Statins*

TOPIC 9: ATHEROSCLEROSIS

1. Atherosclerosis is a disease of which vessels?

   Large and medium sized arteries

2. What 2 substances contribute to smooth muscle migration out of the media toward the intima in atherosclerosis?

   Platelet-derived growth factor (PDGF) and transforming growth factor (TGF)-beta

3. Where are berry aneurysms most commonly located?

   Circle of Willis

4. What is the difference between Stanford A and Stanford B dissections?

   Stanford A dissection involves the ascending and sometimes descending aorta while Stanford B dissection involves only the descending aorta; Stanford A dissection requires surgical intervention while Stanford B does not.

5. What can happen if a dissecting aneurysm spreads back toward the heart to involve the coronary arteries?

   Myocardial infarction

6. What are 3 risk factors for aortic dissection?

   Atherosclerosis, hypertension, Marfan syndrome (cystic medial necrosis)

7. What is Prinzmetal's angina?

   Angina in association with vasospasm

8. What are 4 clinical syndromes associated with ischemic heart disease?

   Angina, myocardial infarction, sudden cardiac death, chronic ischemic heart disease

TOPIC 10: ISCHEMIC HEART DISEASE

1. What is the first histologic sign of myocardial infarction (MI)?

   Contraction bands.

2. When does neutrophilic infiltration of myocardium peak in an MI?

   48-72 hours

3. When does maximal softening of the necrotic myocardium occur after an MI?

   5-10 days (day 7 is classic). Myocardial or papillary muscle rupture can occur.

4. Of troponin I, CK-MB, AST, and LDH, which has the most cardiac specificity?

   Troponin I

5. ECG showing ST elevations early on and Q waves later suggests what condition?

   Transmural myocardial infarction

6. ST segment changes and Q waves in the V4-V6 leads suggest which location for an MI?

   Anterolateral wall

7. Pump failure with resulting hypoperfusion of all organs causes what condition?

   Cardiogenic shock

8. Papillary muscle rupture would most likely occur how long after an MI?

   5-10 days post myocardial infarction

9. A ventricular aneurysm can occur several weeks to months after an MI. What complications can ventricular aneurysm predispose to?

   Mural thrombus (which can cause embolism or stroke) and arrhythmia

10. What condition causes a fibrinous pericarditis due to an autoimmune process?

    Dressler's syndrome or postmyocardial infarction syndrome occurs 2-10 weeks after MI

11. List the classes of drugs used in stable angina.

    Nitrates, β-blockers, calcium channel blockers

12. List the classes of drugs used in vasospastic angina.

    Nitrates and calcium channel blockers

13. What is the primary therapeutic strategy for prevention of stable angina?

    β-blocker (decrease myocardial oxygen consumption)

TOPIC 11: CONGESTIVE HEART FAILURE AND CARDIOMYOPATHIES

1. The cardiac remodeling that occurs during the development of dilated cardiomyopathy occurs by what process?

   Addition of sarcomeres in series within each myocyte

2. Name frequently abused substances that can cause a dilated cardiomyopathy.

   Alcohol and cocaine

3. Name 2 infectious causes of dilated cardiomyopathy.

   Coxsackie B virus, Chagas disease

4. Roughly what percentage of hypertrophic cardiomyopathy is thought to be genetically related?

   50%

5. What mechanism causes the S4 heart sound in hypertrophic cardiomyopathy?

   Decreased compliance leads to diastolic dysfunction which produces the S4 sound

6. Hemochromatosis and amyloidosis tend to cause what type of cardiomyopathy?

   Restrictive cardiomyopathy

7. Decreased renal blood flow in the setting of congestive heart failure can cause edema by what mechanism?

   Decreased renal blood flow → increased renin secretion → increased angiotensin II → increased aldosterone → increased sodium retention.

8. Central venous congestion of the liver produces what findings on intraoperative examination of the liver?

   Hepatomegaly with nutmeg liver

9. What name is used for decreased pulse strength during inspiration during tamponade?
   Pulsus paradoxus (Kussmaul's pulse)

10. Identify the cellular target of each inotrope.

Drug	Target
Digoxin	*Na^+/K^+ ATPase*
Dobutamine	*β_1 Receptors*
Inamrinone	*Phosphodiesterase III*

TOPIC 12: CONGENITAL HEART DISEASE

1. What specific germ layer forms the heart?

   Lateral plate mesoderm

2. Match each heart tube dilatation, from caudal to cranial, with its postnatal fate.

Heart Tube Dilatation	Fate
Sinus venosus right horn	*Smooth right atrium*
Sinus venosus left horn	*Coronary sinus*
Primitive atrium	*Trabeculated R and L atrium*
Primitive ventricle	*Trabeculated R and L ventricle*
Conus arteriosus	*Smooth parts of L and R ventricle (outflow)*
Truncus arteriosus	*Ascending aorta and pulmonary trunk*

3. What do cardinal veins form when they fuse?

   Superior vena cava

4. What septum divides the truncus arteriosus?

   Aorticopulmonary septum

5. If this septum does not develop in the form of a spiral, what condition develops?

   Transposition of the great vessels

6. Name the 2 parts of the interventricular septum.

   Muscular part, Membranous part (neural crest)

7. What structures fuse and close the atrioventricular canals?

   Endocardial cushions

8. Name 2 endocardial cushion defects.

   Ebstein's anomaly (displacement of septal leaflet of tricuspid valve), Tricuspid atresia

9. Which endocardial cushion defect is associated with maternal lithium use?

   Ebstein's anomaly

10. Which endocardial cushion defect results in a hypoplastic right side of the heart?

    Tricuspid atresia

11. Which endocardial cushion defect results in an "atrialized" right ventricle?

    Ebstein's anomaly

12. Name 3 congenital heart defects that might undergo an L-to-R shunt reversal and develop the Eisenmenger syndrome and late cyanosis.

    atrial septal defect, ventricular septal defect, patent ductus arteriosus

13. What is the underlying problem in Eisenmenger's syndrome?

    There is an uncorrected left-to-right shunt that may be related to an atrial septal defect, a ventricular septal defect, or a patent ductus arteriosus. The increased pressure on the right side of the heart leads to right sided hyprtrophy that eventually leads to reversal of the shunt to produce a R→L shunt

14. Name the 2 components of the interatrial septum.

    Septum primum and septum secundum

15. Which component fuses with the endocardial cushions?

    Septum primum

16. What foramina are found in each septum?

    Septum Primum: foramen primum at free edge; foramen secundum in upper part. Septum secundum: foramen ovale

17. What is a patient with a patent foramen ovale at risk for?

Clot from venous circulation passing directly into left atrium.

18. What is the most common atrial septal defect?

patent foramen secundum

19. Fill out the table according to when sites of fetal erythropoiesis begin producing red blood cells.

Fetal Erythropoiesis Sites	Timeline (Weeks)
Bone marrow	*After 28 weeks*
Liver	*6-30 weeks*
Yolk sac	*3-8 weeks*
Spleen	*6-30 weeks*

20. What is the difference in subunit composition of fetal versus adult hemoglobin?

Fetal: 2 alpha and 2 gamma chains. Adult: 2 alpha, 2 beta chains

21. Name 2 organs that fetal circulation is designed to divert oxygenated fetal blood away from.

Liver and lungs

22. Name the shunts that bypass each organ.

Ductus venosus bypasses liver; Ductus arteriosus bypasses lungs

23. What changes in levels of prostaglandins and oxygen tension promote closure of the ductus arteriosus?

Decrease in prostaglandins; increase in oxygen tension

24. List the 5 "T" titled cyanotic right-to-left shunts and 3 non-cyanotic left-to-right shunts.

Five Cyanotic R-L Shunts	Three Non-Cyanotic L-R Shunts
1. *Tetralogy of Fallot*	1. *VSD*
2. *Transposition of great vessels*	2. *ASD*
3. *Persistent truncus arteriosus*	3. *PDA*
4. *Tricuspid atresia*	
5. *Total anomalous pulmonary venous return*	

25. Failure of what mechanism causes persistent truncus arteriosus?

Incomplete development of AP septum

26. What 2 additional defects must be present with tricuspid atresia in order for the newborn to be viable?

ASD and VSD

27. Which of the 3 postnatal conditions that undergo the Eisenmenger syndrome results in a differential cyanosis?

PDA causes cyanosis in lower limbs only

28. Which part of the tetralogy of Fallot is the most important determinant of prognosis?

Severity of pulmonary stenosis is more important than the VSD, RVH or overriding aorta.

29. How does squatting aid an individual with Tetralogy of Fallot?

Squatting increases total peripheral resistance → increases blood flow to lungs

30. What are the 3 initial defects in tetralogy of Fallot? What pathology arising from the initial defects creates the 'boot-shaped' heart?

Pulmonary stenosis, Overriding aorta, VSD. Right ventricular hypertrophy creates the boot shape

31. In what population is transposition of the great vessels commonly seen?

Babies of diabetic mothers

32. What 3 additional defects must be present for a newborn with transposition of the great arteries to be viable?

ASD, VSD, PDA

33. Which form of a coarctation of the aorta is associated with Turner's syndrome?

Preductal or infantile

34. Which coarctation type will be associated with "rib notching?"

Postductal

35. Which coarctation type will show cyanosis in the lower limbs?

Infantile

36. Which coarctation type will show evidence of higher blood pressures in the upper limbs and lower blood pressures in the lower limbs?

Postductal

37. Which coarctation type is associated with a bicuspid aortic valve?

Postductal

38. What structure in an adult corresponds to the ductus arteriosus in a fetus?

Ligamentum arteriosum

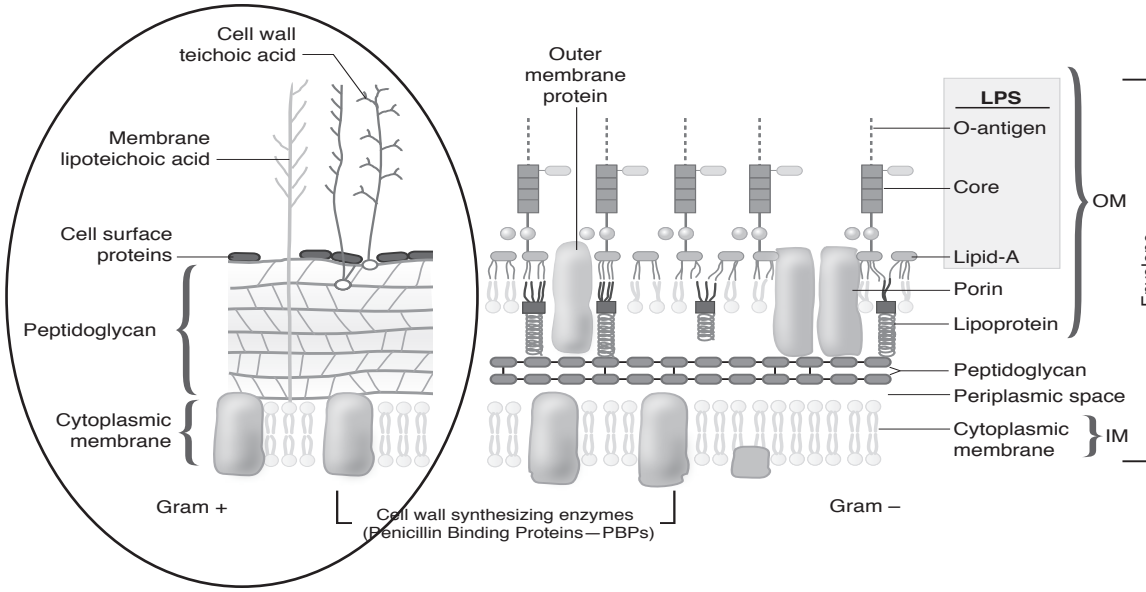
39. Match each congenital heart condition with a frequent association or cause. Condition choices may be used more than once:

(A) Tetralogy of Fallot
(B) ASD or VSD
(C) PDA
(D) Transposition of great vessels
(E) Preductal coarctation of aorta
(F) Truncus arteriosus
(G) Aortic insufficiency
(H) Endocardial cushion defect

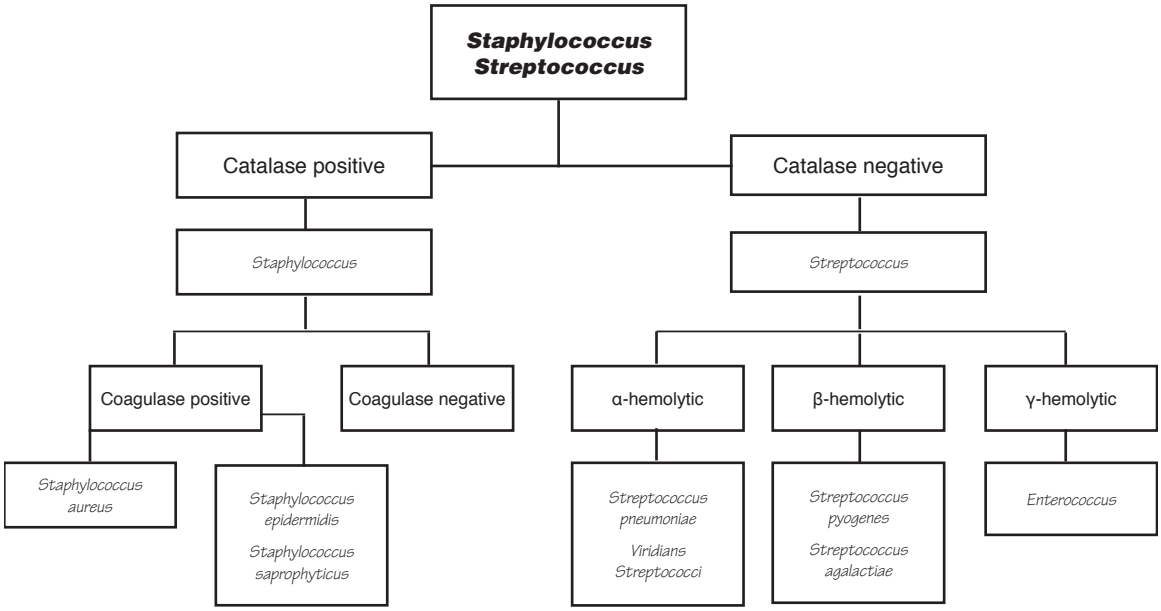
1. Down syndrome *H*
2. Marfan's syndrome *G*
3. Infant of diabetic mother *D*
4. 22q11 syndrome (DiGeorge) *F & A*
5. Congenital rubella *C*
6. Turner's syndrome *E*

TOPIC 13: INFECTION-RELATED HEART DISEASE

1. Circle the Gram-positive cell wall.



2. Fill in the flow chart with the Gram-positive cocci.



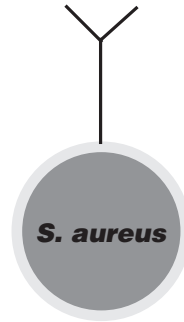
3. List the substrate for myeloperoxidase.

   H_2O_2

4. Discuss why patients with chronic granulomatous disease have frequent infections with catalase-positive bacteria.

   Patients with chronic granulomatous disease do not effectively convert H_2O_2 into hypochlorite. If a bacterium does not have catalase then H_2O_2 will be sufficient to kill the bacterium. A bacterium that makes catalase will break the H_2O_2 down to water and oxygen.

5. Describe the function of protein A produced by *Staphylococcus aureus.* A drawing is shown.



Protein A binds the Fc portion of the Ab molecule to prevent opsonization, and complement activation.

6. List the toxin made by *S. aureus* that is a superantigen (sAg).

Toxic shock syndrome toxin -1 (TSST-1)

7. Discuss the mechanism by which the sAg leads to shock.

The sAg binds to the TCR and MHC class II OUTSIDE of the peptide binding groove → overstimulates T cells → over activate macrophages → massive release of cytokines "cytokine storm" → shock.

8. List the major surface type that *Staphylococcus epidermidis* binds to.

surface of prosthetic devices

9. Discuss the mechanism by which viridans streptococci adhere to damaged heart valves.

Viridans Strep makes dextrans from the sugars we eat. Dextrans bind tightly to fibrin, which is found in fibrin clots on damaged valves.

10. Name the compound that enterococci can be selectively grown in.

NaCl (6%)

11. Name the drug of choice for enterococci infection.

Vancomycin

12. Name the drug of choice for vancomycin-resistant enterococci infection.
    Linezolid

13. Name the co-morbidity associated with endocarditis caused by *Streptococcus bovis*.
    Colon cancer

14. List at least 3 common symptoms of endocarditis.
    - *Fever*
    - *Roth spots*
    - *Janeway lesions*
    - *NEW murmur*
    - *Splinter hemorrhages*
    - *Oslers nodes*

15. *Staphylococcus aureus* typically causes what type of endocarditis? *Streptococcus viridans*?
    Staphylococcus aureus typically cause acute bacterial endocarditis (previously normal valve) while Streptococcus viridans causes subacute bacterial endocarditis (previously damaged valves).

16. What type of endocarditis is associated with pancreatic cancer?
    Marantic endocarditis (associated with thrombus formation)

17. For each characteristic listed, place an "A" if the characteristic is associated with acute endocarditis or an "S" if it is associated with subacute endocarditis.

Characteristic	Type of Endocarditis
Affects previously damaged heart valves	S
Affects normal valves	A
S. aureus is the most common causative agent	A
High virulence	A
Low virulence	S
Streptococcus viridans are common in this group	S

18. List the HACEK organisms.
    - *Haemophilus aphrophilus (Agggregatibacter)*
    - *Actinobacillus actinomycetemcomitans (Agggregatibacter)*
    - *Cardiobacterium hominus*
    - *Eikenella corrodens*
    - *Kingella kingae*

19. Where are the HACEK organisms normally found?
    Oral cavity

20. Name the valve most commonly associated with endocarditis.
    Mitral

21. Name the valve most commonly associated with endocarditis in an IV drug user.
    Tricuspid

22. List the autoimmune disease associated with Libman-Sacks endocarditis.
    SLE

23. Libman-Sacks endocarditis can involve sterile vegetations on both sides of which heart valves?
    Mitral and tricuspid

24. Name the stage of syphilis at which heart disease is usually detected.
    Tertiary

25. What valves are affected in rheumatic fever?
    Mitral

26. What is required for a diagnosis of rheumatic fever?
    Jones criteria (2 major or 2 minor and 1 major)

    The 5 major Jones criteria are: Migratory polyarthritis, pancarditis, subcutaneous nodules, skin rash (erythema marginatum), and Sydenham chorea. Note that the mitral valve is the most commonly affected valve.

TOPIC 14: VASCULITIS AND CARDIOVASCULAR TUMORS

1. What are some of the common causes of varicose veins?

   Prolonged standing or sitting, and pregnancy

2. The blanching and then cyanosis seen in Raynaud's disease is due to what process?

   Small artery vasospasm. Raynaud's phenomenon can be associated with SLE, scleroderma but Raynaud's disease does not have an associated underlying cause.

3. What 3 processes are typical of Wegener's granulomatosis?

   Small vessel vasculitis, involvement of the lung and upper airway, and glomerulonephritis.

4. C-ANCA are antibodies directed against what type of cells?

   Neutrophils

5. In C-ANCA, where does the antibody bind in the cell? How about in P-ANCA?

   C-ANCA binds to neutrophil cytoplasm, and P-ANCA binds to the perinuclear area.

6. Wegener's disease is associated with which form of ANCA?

   C-ANCA

7. How does microscopic polyangiitis differ from Wegener's disease?

   Microscopic polyangiitis lacks granulomas and is associated with p-ANCA. Churg-Strauss syndrome (granulomatous vasculitis with eosinophilia/asthma) is also p-ANCA positive.

8. What disease is characterized by congenital capillary malformations that may involve the face and leptomeninges?

   Sturge-Weber disease. May also have seizures and early-onset glaucoma.

9. Henoch-Schönlein purpura is linked to which virus?

   Parvovirus

10. The crescent formation seen in the rapidly progressive glomerulonephritis of Henoch-Schönlein purpura is most closely related to which type of immune complexes?

    IgA immune complexes. Note that complement levels are usually normal.

11. What is an alternate name for Buerger's disease? Name a risk factor.

    Thromboangiitis obliterans; smoking is the major risk factor

12. What is the most feared complication of Kawasaki disease?

    Coronary artery aneurysms

13. Which hepatitis virus is associated with polyarteritis nodosa? What can be seen on angiography?

    Hepatitis B. Imaging can show "beads on a string".

14. What is the most common site of involvement of Takayasu's arteritis?

    Aortic arch and major branches (sometimes called "pulseless disease"), more common in young Asian women, may cause visual problems.

15. Which cell is characteristically found in biopsies of temporal arteritis?

    Multinucleated giant cell

16. What musculoskeletal disease is often associated with temporal arteritis?

    Polymyalgia rheumatica

17. Temporal arteritis can by complicated by which ocular problem?

    Blindness due to involvement of the ophthalmic artery

18. What might cause a large, benign, pink-to-reddish, raised lesion seen on the cheek of a 1-year-old?

    Strawberry hemangioma. Usually regresses.

19. What lymphatic lesion of the neck is associated with Turner's syndrome?

    Cystic hygroma

20. In what organ are angiosarcomas most commonly seen?

    Liver

21. What are some risk factors for angiosarcoma?
Vinyl chloride, arsenic, Thorotrast; mastectomy

22. Myxomas tend to occur in which cardiac chamber? What do they cause there?
Left atrium; cause "ball-valve" obstruction

23. What histology is seen in a cardiac myxoma?
Stellate cells in a myxoid background

24. What is the most common primary cardiac tumor in children?
Rhabdomyoma

25. Cardiac rhabdomyoma is associated with what disorder?
Tuberous sclerosis

CHAPTER 5

GASTROENTEROLOGY

TOPIC 1: GASTROENTEROLOGY EMBRYOLOGY AND ASSOCIATED DISORDERS

1. What specific germ layer forms the epithelial lining of the gut tube?
   endoderm

2. What germ layer forms the rest of the wall of the gut tube?
   mesoderm

3. Fill in the component for each gut region.

	Foregut	Midgut	Hindgut
Parts?	*Pharynx to entrance of bile duct in duodenum; includes liver, pancreas and biliary apparatus*	*Entrance bile duct in duodenum to juncture between proximal 2/3 and distal 1/3 of transverse colon*	*Distal 1/3 of transverse colon to pectinate line of anal canal*
Parasympathetic innervation?	*vagus*	*vagus*	*Pelvic nerves S2,3,4*
Sympathetic innervation?	*Thoracic Splanchnics T5-T9 to ciliary ganglion*	*Thoracic splanchnics T9- T12 to Superior mesenteric ganglion*	*Lumbar Splanchnics L1- L2 to inferior mesenteric ganglion*
Referred pain site?	*Epigastric*	*Umbilical*	*Hypogastric*
Suspended by dorsal mesentery?	*Yes*	*Yes*	*Yes*
Suspended by ventral mesentery?	*Yes*	*No*	*No*
Amount of rotation and direction?	*90 degrees about long axis of gut tube*	*270 degrees counterclockwise about axis of SMA*	*None; separated by urorectal septum*
Physiological herniation?	*No*	*Yes*	*No*

4. Name 3 nerves that innervate the parietal peritoneum.

   Intercostal, Iliohypogastric, Ilioinguinal

5. Name 3 examples of a mesentery.

   Greater omentum, transverse mesocolon, gastrohepatic ligament

6. What structures pass between the 2 layers of a mesentery?

   Neurovascular bundles

7. Name 4 parts of the gut tube that are secondarily retroperitoneal (lost a mesentery during development).

   Midgut duodenum, ascending colon, descending colon, upper rectum

8. Name one part of the foregut, midgut, and hindgut that is suspended by a mesentery in postnatal life.

   Foregut: Liver, Midgut: Jejunum; Hindgut: Sigmoid colon

9. What 2 regions of the abdomen does the epiploic foramen connect?

   Great and lesser sac

10. What structures course in the anterior border of the epiploic foramen?

    Common bile duct, portal vein, proper hepatic artery

11. What 3 structures form the portal triad?

    Common bile duct, portal vein, proper hepatic artery

12. In 90% of cases the fistula in a tracheoesophageal fistula is located in what site?

    In the mid esophagus connecting the distal segment of the esophagus to the trachea

13. What is the cause of a tracheoesophageal fistula?

    Malformation of TE septum

14. Name 3 postnatal signs or symptoms of a tracheoesophageal fistula.

    Pneumonitis, cyanosis and gagging, inability to pass NG tube

15. What may be evident during pregnancy in which a fetus has a tracheoesophageal fistula?

    Polyhydramnios

16. What physical exam finding is characteristic of hypertrophic pyloric stenosis?

    Olive-like palpable mass at the right costal margin (history is classically projectile, nonbilious vomiting in first 2 weeks)

17. In an infant with hypertrophic pyloric stenosis, describe the nature of the vomiting and the sign evident at the right costal margin.

    non-bilious and a knot at costal margin

18. What is one complication of a congenital diaphragmatic hernia?

Left lung hyperplasia

19. What major anatomic problems can accompany congenital diaphragmatic hernia?

Intestinal malrotation and lung hypoplasia

20. What is the cause of duodenal atresia?

Failure of recanalization

21. For a child born with duodenal atresia, what condition might complicate the pregnancy, and what will be evident on the first day of life?

Polyhydramnios; bilious vomiting on first day of life

22. Duodenal atresia is associated with what syndrome?

Down's syndrome

23. What is thought to be the underlying cause of most small bowel atresias?

In utero vascular accidents

24. What 2 signs of small bowel atresias might be evident on x-ray?

Distended bowel proximal to atresia; absent or decreased air distal to atresia

25. At what fetal age does malrotation of the gut develop? What intestinal abnormality might develop in these patients?

Weeks 6-10; volvulus

26. Name 2 symptoms of volvulus.

Bilious vomiting; decreased stool output

27. At what site does gastroschisis usually develop? Are the viscera enclosed by amnion?

To the right of the umbilicus; no – Omphalocele has viscera enclosed with amnion

28. What is the cause of gastroschisis?

Defect in lateral body fold closure

29. At what site is the defect typically located?

R of umbilicus

30. What is the cause of an omphalocele?

Failure of midgut loop to return to abdominal cavity

31. Through what opening does the midgut protrude in an omphalocele?

Umbilical ring

32. Name 2 other congenital abnormalities that are frequently associated with an omphalocele. What membrane encloses the herniated midgut in this condition?

Congenital heart disease and chromosomal abnormalities; Amnion

33. What is the cause of Meckel's diverticulum?

Failure of vitelline duct to obliterate

34. Complete the following table.

	Meckel's Diverticulum Characteristics
Percentage of population affected?	*2%*
Distance from ileocecal valve?	*2 feet*
Length?	*2 cm*
Presentation age?	*About 2 years*

35. Name 2 complications associated with Meckel's diverticulum.

Rectal bleeding, bowel obstruction or intussusception

36. What is the relationship between Meckel's diverticulum and intussusception?

Meckel's diverticulum can be a "lead point" for intussusception

37. A vitelline fistula causes a patent connection between which 2 structures?

Intestinal lumen and umbilicus

38. What will drain through the vitelline fistula?

Meconium

39. What is the cause of Hirschsprung's disease? Name the most commonly affected area of the bowel.

Failure of neural crest to form myenteric plexus in wall of sigmoid colon or rectum

40. What techniques are used to diagnose Hirschsprung's disease? How does Hirschsprung's usually present in the neonatal period?

Barium enema and rectal biopsy; failure to pass meconium

41. In what mesentery does the liver and the biliary apparatus develop?

Ventral

42. What 2 remnants of this mesentery suspend the liver in postnatal life?

Lesser omentum and falciform ligament

43. Incomplete canalization of the lumen of biliary ducts leads to what condition?

Extrahepatic biliary atresia, causing hyperbilirubinemia and icterus

44. What is the nature of the stool and the urine in this condition?

Clay colored stool; dark urine

45. What components of the pancreas do the ventral and dorsal pancreatic buds form when they fuse?

Dorsal: neck, body and tail. Ventral: Head and uncinate process

46. What forms the main pancreatic duct?

Both dorsal and ventral pancreatic ducts

47. What is the name of the most common abnormality of the pancreas?

Pancreas divisum

48. What embryologic event causes pancreas divisum?

Failure of the accessory pancreatic duct and main pancreatic duct to fuse

49. How does annular pancreas cause polyhydramnios?

Annular pancreas can obstruct the duodenum prenatally, so that amniotic fluid cannot be swallowed and absorbed, leading to polyhydramnios.

50. What germ layer gives rise to the spleen?

Mesoderm

51. What 2 mesentery remnants suspend the spleen?

Splenorenal and gastrosplenic ligaments

52. From what artery does the splenic artery arise?

Celiac

TOPIC 2: GASTROENTEROLOGY ANATOMY, HISTOLOGY, AND PHYSIOLOGY

1. Name the 4 layers of the gut wall.

   mucosa, submucosa, muscularis externa, serosa

2. What are the 3 components of the mucosa?

   epithelium, lamina propria, muscularis mucosa

3. Complete the following table.

GI Intrinsic Innervation	Meissner's Plexus	Auerbach's Plexus
Location	*Submucosa*	*Between smooth muscle layers*
Function	*Gut secretion*	*Peristalsis*
Input source(s)	*Autonomic*	*Autonomic*
Parasympathetic effects	*Increase secretion*	*Increase peristalsis*
Sympathetic effects	*Inhibition*	*Inhibition*

4. Complete the following table.

Salivary Glands	Location	Composition and % of Saliva Volume
Parotid	*Lateral face on surface of masseter*	*All serous; 25% of saliva*
Submandibular	*Lower edge of mandible*	*Mixed serous and mucous; 77% of saliva*
Sublingual	*Base of tongue*	*Mixed serous and mucous; 5% of saliva*

5. Name the 4 main ionic components of saliva.

   lipase, amylase, lysozyme, defensins

6. Name 2 digestive enzymes found in saliva.

   lipase, amylase

7. What nerves control salivary secretions?

   parasympathetics

8. At what vertebral level does the esophagus traverse the diaphragm?

   T10

9. Name 4 narrow points along the length of the esophagus.

   Origin at pharynx, at aortic arch, at left main bronchus, esophageal haitus

10. What is the arrangement of smooth and skeletal muscle in the upper 1/3, middle 1/3, and lower 1/3 of the esophagus?

    Upper: skeletal, middle: skeletal and smooth, lower: smooth

11. What is characteristic of the epithelial lining of the esophagus?

    Non-keratinized stratified squamous

12. Name the 3 endogenous compounds that stimulate gastric acid secretion.

    Acetylcholine (Ach); gastrin; histamine

13. Discuss the stimuli and interaction of the 3 compounds named in the previous question.

    Acetylcholine (Ach)—Parasympathetic and enteric. Ach is released in response to the smell of food. In addition, distension of the stomach evokes a reflex (vago-vagal) release of Ach. Ach directly stimulates acid production and indirectly stimulates it by eliciting the release of both histamine and gastrin (distension activates vagus which stimulates the release of gastrin releasing peptide--GRP). Gastrin—release stimulated by GRP (vagally mediated) and high stomach pH (food entering the stomach increases pH). Histamine—release is stimulated by Ach and gastrin.

14. _____*Somatostatin*_____ is a hormone released from gastric and intestinal cells that inhibits gastrin release.

15. The pumping of H^+ into the lumen is an antiport H^+-ATPase. ___Potassium___ is the ion that antiports with H^+.

16. In addition to H^+, ___Potassium___ and ___chloride___ are secreted into the lumen of the stomach, thus making stomach secretions high in these electrolytes.

17. Discuss what is meant by "alkaline tide."

The alkaline tide refers to the rise in pH of the blood draining the stomach during high rates of acid secretion. The proton that is secreted into the lumen comes from the combination of CO2 and water. The bicarbonate that results from this reaction is then transported from the parietal cell into the blood in exchange for chloride.

18. Indicate the 2 mechanisms by which drugs inhibit acid secretion by parietal cells.

Proton pump inhibitors, i.e., omeprazole, block the H—K^+ antiporter on the luminal membrane. Histamine (H_2) receptor blockers, i.e., cimetidine, block histamine-induced acid secretion.

19. ___Bile salts___ and ___pancreatic lipases___ are required for complete fat digestion and absorption.

20. Name the 3 primary end products of carbohydrate digestion and the mechanism of absorption for each.

The three end products are glucose, galactose, and fructose. Digestion begins at the mouth with salivary amylase and continues in the small intestine with pancreatic amylase. Brush border enzymes breakdown disaccharides into the monosaccharides. Glucose and galactose are absorbed via a secondary active transport coupled to Na+. Fructose is absorbed via facilitated transport.

21. Protein digestion begins in the ___Stomach___ via the enzyme ___pepsin___.

22. ___CCK (cholecystokinin)___ stimulates the pancreas to release inactive proteases that will ultimately be converted to active proteases in the ___small intestine___.

23. Discuss the mechanism for the absorption of the end products of protein digestion.

Proteins are absorbed as amino acids, di- and tripeptides. These are absorbed in symport with either Na^+ or H^+ (secondary active transport).

24. The secretion of *Chloride* causes Na^+ and water to enter the lumen of the small intestine and is important for maintaining adequate hydration of the chyme.

25. Bicarbonate secretion begins in the *ileum*, which is also the site of bile salt and B12 absorption.

26. Fill in the table below for the key GI hormones.

Hormone	Source	Stimulus	Action
CCK	*Duodenum*	*Fats/AA*	*Pancreatic enzyme secretion; Gall bladder contraction; Relax sphincter of Oddi; ↓ gastric motility*
Gastrin	*Stomach; duodenum*	*GRP (second to vagal stimulation)*	*Stimulates acid secretion*
GIP	*Duodenum*	*Fats/AA/CHO*	*↓ gastric motility; ↑ insulin secretion*
Motilin	*Duodenum; jejunum*	*>2 hrs fasting*	*Migrating motility complex; Erythromycin is a motilin agonist*
Secretin	*Duodenum*	*Acid*	*Pancreatic bicarbonate secretion; ↓ gastric motility*

27. What are 2 types of diaphragmatic hernias seen in adults?

Sliding hiatal hernia and paraesophageal hernia

28. What type of inguinal hernia passes through Hesselbach's triangle, and what type passes outside of it?

Indirect hernia passes outside Hesselbach's triangle (lateral to inferior epigastric vessels) and direct inguinal hernia passes through Hesselbach's triangle (medial to inferior epigastrics).

TOPIC 3: GASTROINTESTINAL PATHOLOGY

1. Malignant salivary gland tumors are most common in what age group? Benign salivary tumors are most common in what age group?

   Malignant tumors are most common after age 60 and benign ones are most common after age 40.

2. What percentage of pleomorphic adenomas transform into carcinomas?

   Up to 10%

3. Where is a Zenker's diverticulum located?

   In the posterior pharynx above the cricopharyngeus muscle.

4. What are 2 risk factors for achalasia?

   Chagas disease and CREST syndrome

5. A "bird-beak" sign on a barium swallow study suggests what disease?

   Achalasia

6. What is the most appropriate name for a thin circumferential "ledge" made of mucosa and submucosa, located at the squamo-columnar junction proximal to the lower esophageal sphincter?

   Schatzki ring

7. Plummer-Vinson syndrome is related to deficiency of what nutrient?

   Iron

8. What is the difference between Mallory-Weiss syndrome and Boerhaave's syndrome?

   Boerhaave's syndrome is a complete rupture of the esophageal wall and Mallory-Weiss syndrome is characterized by linear lacerations at the gastroesophageal junction.

9. Mild non-bleeding esophageal varices can be treated with what medications?
   β-blockers

10. What medications are used to treat gastroesophageal reflux disease (GERD)?
    Proton pump inhibitors

11. For what condition is Barrett's metaplasia a risk factor?
    Esophageal adenocarcinoma

12. Squamous cell carcinoma most typically involves what part of the esophagus?
    Upper 2/3 of the esophagus (adenocarcinoma usually in distal third)

13. Ménétrier disease causes what histologic change?
    Diffuse hyperplasia of surface mucus-secreting cells and decrease of parietal cells

14. Blockade of what substance can be used to treat Ménétrier disease?
    Epidermal growth factor receptor

15. Zollinger-Ellison syndrome can be associated with what hereditary condition?
    MEN type I

16. What commonly used products are associated with acute gastritis?
    Aspirin and alcohol use

17. What are predisposing factors for gastric stress ulcers?
    Elevated intracranial pressure, severe sepsis, shock, burns or trauma, high incidence in ICU patients

18. What cells are thought to mediate parietal cell destruction in type A chronic gastritis?

    CD4 cells

19. Which bacteria are associated with type B gastritis?

    Helicobacter pylori

20. What are the major risk factors for peptic ulcers?

    Helicobacter infection and chronic NSAID and aspirin use.

21. Where in the duodenum are duodenal peptic ulcers typically located?

    Anterior wall of proximal duodenum

22. Where are gastric peptic ulcers typically located?

    Lesser curvature of antrum

23. Which blood group has an increased rate of gastric carcinoma?

    Blood type A

24. Signet-ring cells are characteristic of which type of gastric carcinoma?

    Diffuse type adenocarcinoma (linitis plastica)

25. What is the 5-year survival rate of gastric carcinoma?

    The 5-year survival rate is 20%.

26. What are some classic sites for metastasis of gastric cancer?

    Left supraclavicular (Virchow's) nodes, periumbilical area (Sister Mary Joseph's nodule), ovaries (Krukenberg tumor)

27. What are some of the risk factors for volvulus?

    Congenital gut rotation, redundant mesentery

28. A "target sign" on CT of the abdomen suggests which small intestinal disease?
Intussusception

29. What are the HLA types associated with celiac disease (gluten sensitivity)?
HLA-DQ2, DQ8

30. Name 2 important disease associations for celiac disease.
Dermatitis herpetiformis and small bowel lymphoma

31. What serologic tests can help diagnose celiac disease?
Antigliadin, antiendomysial, and antitransglutaminase antibodies (biopsy shows flatted villi)

32. Tropical sprue responds to what drug class?
Antibiotics, notably doxycycline/tetracycline + folic acid

33. What is the causative organism of Whipple disease?
Tropheryma whippelii

34. Are extraintestinal manifestations more common in ulcerative colitis or Crohn's disease?
Crohn's disease

35. A colon with rectal ulceration and pseudopolyp formation would be most likely to have ulcerative colitis or Crohn's disease?
Ulcerative colitis

36. Transmural inflammation, anal involvement, and skip lesions are characteristic of what type of inflammatory bowel disease?
Crohn's disease

37. Which type of inflammatory bowel disease confers a greater risk of cancer?

Ulcerative colitis

38. An acute exacerbation of ulcerative colitis that was unresponsive to 5-ASA derivatives might be treated by which type of drug?

Steroids

39. What colon areas are at increased risk for ischemic bowel disease?

Watershed areas, such as the splenic flexure of the colon.

40. Of what are hemorrhoids composed?

Dilated submucosal veins

41. What 2 conditions are risk factors for angiodysplasia?

Osler-Weber-Rendu syndrome and CREST syndrome

42. Melanosis coli is associated with use of what drug?

Laxative abuse

43. Pseudomembranous colitis is associated with overgrowth of what bacterium?

Clostridium difficile

44. Of what is the pseudomembrane of pseudomembranous colitis composed?

Neutrophils, mucin, fibrin, and necrotic cellular debris

45. What typically begins the process leading to appendicitis?

Obstruction of the appendiceal orifice by a fecalith

46. How does the pain of appendicitis change with time?

The initial pain is often periumbilical, while later pain localizes to the right iliac region.

47. What is the major risk factor for colonic diverticulosis?

Low-fiber diet

48. Adenomatous polyps can be subclassified in what ways?

Tubular versus villous; pedunculated versus sessile

49. Familial adenomatous polyposis is associated with what gene?

APC gene located at 5q21

50. In addition to colon cancer, what other tumors are associated with Gardner syndrome?

Osteomas, lipomas, fibromatosis, epidermal inclusion cysts

51. In addition to colon cancer, what other tumor is associated with Turcot syndrome?

Central nervous system tumors (particularly gliomas)

52. Lynch syndrome differs from other hereditary colon cancer syndromes by the absence of what?

Adenomatous polyps

53. Which polyposis syndrome does not cause colon cancers but is associated with an increased risk of developing cancers of lungs, pancreas, breast, and uterus?

Peutz-Jeghers syndrome

54. What dietary factors are risk factors for adenocarcinoma of the colon?

Low intake of fiber, fruits, and vegetables; high intake of red meat and animal fat

55. What configuration would colon cancer on the right side of the colon be most likely to have?

Right-sided cancers tend to be polypoid

On the left side of the colon?

Left-sided cancers tend to be ulcerated, napkin-ring tumors

56. A colon cancer that invades the muscularis propria with no known metastases to lymph nodes or other sites would have what TNM stage?

T2 NO MO

57. Metastatic adenocarcinoma of the colon is often treated with what agent?

5-fluorouracil

58. What are the most common locations for GI carcinoid tumors?

Appendix and terminal ileum

TOPIC 4: LIVER AND PANCREAS PATHOLOGY

1. What is final common pathway of most causes of acute pancreatitis?

   Activation of pancreatic zymogens with resulting autodigestion of the pancreas

2. Laboratory studies in a case of acute pancreatitis might show what findings?

   Increases in the following: amylase, lipase, leucocyte count, glucose, LDH, AST, and BUN; decreased calcium

3. What is the most accurate test for acute pancreatitis?

   CT scan

4. What are the most important risk factors for chronic pancreatitis?

   Long-standing alcohol abuse and bile stones

5. What finding is usually sought on x-ray and CT scan in the diagnosis of chronic pancreatitis?

   Calcification of the pancreas

6. Among pancreatic islet cell tumors, what clinical syndromes can be produced with insulinoma?

   hypoglycemia

   Gastrinoma?

   Zollinger-Ellison syndrome

   Glucagonoma?

   migratory necrolytic dermatitis and diabetes

   Somatostatinoma?

   diabetes, steatorrhea, and gallstones

   VIPoma?

   diarrhea, hypokalemia, and achlorhydria

7. What is the fourth most common cause of cancer death in the United States?

   Pancreatic cancer

8. Besides a mass, what can a CT scan demonstrate in pancreatic cancer that might be helpful in diagnosis?

   Dilation of bile and pancreatic ducts

9. List the 3 classes of conditions that cause jaundice due to an increase in indirect (unconjugated) bilirubin.

   Hemolysis; Physiologic (newborn); Hereditary (Gilbert and Crigler-Najjar syndromes)

10. List the 4 classes of conditions that cause jaundice due to an increase in direct (conjugated) bilirubin.

    Biliary tract obstruction; Biliary tract disease; Hereditary (Dubin-Johnson and Rotor syndromes); Liver disease (cirrhosis and hepatitis)

11. Jaundice due to hemolytic anemia can predispose to what type of gallstones?

    Pigment gallstones

12. Which of the hereditary hyperbilirubinemias produce conjugated hyperbilirubinemia?

    Dubin-Johnson syndrome and Rotor syndrome produce conjugated hyperbilirubinemias

    Unconjugated hyperbilirubinemia?

    Gilbert syndrome and Crigler-Najjar syndrome produce unconjugated bilirubinemia

13. What is the difference between micronodular and macronodular cirrhosis?

    Micronodular cirrhosis is cirrhosis with nodule size less than 3 mm, while macronodular cirrhosis has nodules greater than 3 mm.

14. What are some signs and symptoms of portal hypertension?

Ascites, esophageal varices, hemorrhoids, caput medusae, splenomegaly

Of liver failure?

Hepatic encephalopathy, spider angiomata, gynecomastia, hypoalbuminemia, decreased clotting

15. What is hepatorenal syndrome?

Renal failure developing secondary to liver disease

16. What histologic features characterize alcoholic hepatitis?

Hepatocyte swelling and necrosis, Mallory bodies

17. What percentage of alcoholics develop cirrhosis?

15%

18. Mutation of what gene is associated with Wilson disease?

ATP7b gene on 13q

19. What laboratory findings are used to diagnose Wilson disease?

Decreased ceruloplasmin in serum, increased copper in tissues, increased urinary copper excretion

20. What is the most common mutation of the HFE gene in hemochromatosis?

C282Y

21. What methods are used to diagnose hemochromatosis?

Liver biopsy with Prussian blue stain (in conjunction with elevated serum iron and ferritin levels)

22. What functions does alpha-1-antitrypsin have?

Alpha-1 antitrypsin inhibits neutrophil elastase, trypsin, chymotrypsin, and bacterial proteases.

23. What finding is characteristically seen in the liver in alpha-1-antitrypsin deficiency?

PAS positive, eosinophilic cytoplasmic globules within hepatocytes (especially in severe PiZZ genotype)

24. Most cases of Reye's syndrome occur in which patients?

Young children with varicella or influenza infection who are treated with aspirin

25. What clinical features are seen in Reye's syndrome?

Reye's syndrome patients develop hyperammonemia, cerebral edema, increased intracranial pressure, encephalopathy, and hepatic fatty change.

26. In the pathophysiology of non-alcoholic steatohepatitis, how is oxidative stress produced?

The oxidative stress is due to dysregulated cytokine production, lysosomal cathepsin release, mitochondrial dysfunction, and cellular apoptosis.

27. What laboratory studies can be used to detect non-alcoholic steatohepatitis?

Non-alcoholic steatohepatitis can cause increased transaminases and alkaline phosphatase.

28. What are examples of diseases that can lead to Budd-Chiari syndrome?

Polycythemia vera, pregnancy, oral contraceptive use, paroxysmal nocturnal hemoglobinuria, and hepatocellular carcinoma

29. What does the histology in Budd-Chiari syndrome show?
Centrilobular congestion and necrosis

30. Nutmeg pattern on gross examination of a liver suggests what disease process?
Chronic passive congestion of the liver

31. What is the most common primary tumor to affect liver?
Hemangioma

32. Hepatic adenoma is associated with use of what medication?
Oral contraception

33. What is seen histologically in hepatocellular adenoma?
Sheets of normal appearing hepatocytes without bile ducts or portal areas

34. Name some important risk factors for hepatocellular carcinoma.
Cirrhosis, hepatitis B and C, alcohol, exposure to aflatoxin B1

35. What is a useful serum tumor marker for hepatocellular carcinoma?
Alpha fetoprotein

36. Name 3 common primary cancers causing metastatic disease in the liver.
Colon, breast, and lung.

37. What are typical generalized symptoms of viral hepatitis?
Malaise, weakness, nausea, anorexia, and sometimes jaundice

38. What are some laboratory studies to diagnose hepatitis?

Elevation of ALT, AST, serologic confirmation of virus

39. What are the apoptotic hepatocytes seen in viral hepatitis called?

Councilman bodies

40. What type of virus causes hepatitis A? How is it transmitted?

Picornavirus; fecal-oral

41. What serum studies are helpful in demonstrating hepatitis B as the cause of a patient's hepatitis?

HBsAg, HBeAg, anti-HBc IgM, HBV DNA, and anti-HBs IgG

42. What does the presence of the IgG form of HBcAb suggest?

Chronic hepatitis B infection

43. What stage of hepatitis B infection would a patient have with the following profile?

Positive HBsAg, HBeAg, HBV-DNA, HBcAb IgM, and HBcAb IgG

Negative HBsAb IgG

Chronic infection

44. What medications can be used to treat chronic hepatitis C?

Interferon + Ribavirin + Boseprevir/Telaprevir

45. Hepatitis D virus replicates only in liver cells infected with what other virus?

Hepatitis B virus

46. In what patient population is hepatitis E virus particularly dangerous?

Pregnancy

47. Which 2 hepatitis viruses cause acute but not chronic hepatitis?

A and E

CHAPTER 6

ENDOCRINOLOGY

TOPIC 1: THE HYPOTHALAMIC-PITUITARY AXIS

1. Name the secretory product of each of the following hypothalamic nuclei.

Hypothalamic Nucleus	Secretory Product?
Supraoptic	*ADH*
Paraventricular	*Oxytocin*
Arcuate	*Releasing and inhibiting factors*
Preoptic	*Gonadotropin releasing factors*

2. Fill in the table below.

Hypothalamus	Anterior Pituitary Cell	Anterior Pituitary Hormone
GnRH (stimulates)	*Gonadotrophs*	*FSH; LH*
CRH (stimulates)	Corticotrophs	*ACTH*
TRH (stimulates)	*Thyrotrophs*	TSH
Dopamine (inhibits)	*Lactotrophs*	*Prolactin*
GHRH (stimulates)	*Somatotrophs*	GH
Somatostatin (inhibits)	*Somatotrophs*	GH

3. With the exception of _____TRH_____, all of the hypothalamic hormones are secreted in a _____pulsatile_____ fashion.

4. Elevated levels of the hypothalamic hormone _____TRH_____ can stimulate prolactin release. Name 4 non-hypothalamic agents that can stimulate prolactin release.

   1) serotonin, 2) acetylcholine, 3) opiates, and 4) estrogen, particularly estriol

5. What two specific subsets of ectoderm give rise to the anterior versus the posterior pituitary?

   Anterior: Oral ectoderm / Posterior: Neuroectoderm

6. Name two secretory products of the posterior pituitary.

   ADH and Oxytocin

7. Name the tumor that may develop from a remnant of Rathke's pouch.

   Craniopharyngioma

8. A 28-year-old female is still unable to lactate 2 days following parturition. Examination of her records shows a difficult labor with severe postpartum hemorrhaging. This patient likely suffers from _____Sheehan syndrome_____ and is unable to lactate because there is insufficient _____prolactin_____. What other hormones are likely low in this patient?

   Sheehan syndrome is ischemic damage to the anterior pituitary and can lead to panhypopituitarism. TSH and ACTH are often reduced and, if the disease is severe enough, FSH, LH, and GH will fall.

9. What is the typical cause of Sheehan syndrome?

   Severe postpartum hemorrhage in the setting of pituitary enlargement during pregnancy. Characterized by hypopituitarism (anterior pituitary function lost)

10. In diabetes insipidus, what symptoms and lab changes result from a decrease in the production of ADH or a decrease in responsiveness to ADH?

Decreased ADH activity leads to an inability to concentrate urine and reabsorb free water in response to decreased blood volume or increased plasma osmolarity, resulting in hypotonic polyuria, dehydration, polydipsia, and hypernatremia.

11. Central diabetes insipidus can be due to dysfunction in what areas of the hypothalamus?

Hypothalamic osmoreceptors, supraoptic or paraventricular nuclei, and supraoptico-hypophyseal tract

12. Nephrogenic diabetes insipidus can be due to mutation of what gene?

Inherited mutation of the aquaporin gene leads to the resistance of collecting duct epithelial cells to ADH stimulation.

13. What role does vasopressin administration play in the water deprivation test?

Vasopressin administration differentiates between central and nephrogenic diabetes insipidus.

14. Desmopressin is used in what form of diabetes insipidus? How about hydrochlorothiazide?

Desmopressin is used in central diabetes insipidus and hydrochlorothiazide is used in nephrogenic diabetes insipidus.

15. Name 4 conditions that can cause SIADH.

1) Small cell carcinoma, 2) head trauma, 3) CNS disorders, and 4) pulmonary disease

16. When compared to diabetes insipidus, SIADH shows what changes in urine osmolarity and ECF osmolarity?

Urine osmolarity is increased in SIADH and decreased in diabetes insipidus; ECF osmolarity is increased in diabetes insipidus and decreased in SIADH.

17. What complication can be caused by overaggressive correction of serum osmolarity in SIADH?

Central pontine myelinolysis

18. Fill in the table below to compare and contrast alterations in water homeostasis.

	Diabetes Insipidus	Syndrome of Inappropriate ADH (SIADH)	Dehydration	Primary Polydipsia
Urine flow	↑	↓	↓	↑
Urine osmolality	↓	↑	↑	↓
Plasma osmolality	↑	↓	↑	↓
Extracellular volume	↓	↑	↓	↑
Intracellular volume	↓	↑	↓	↑

19. Which 2 of the conditions in the previous question are often associated with hyponatremia?

SIADH, primary polydipsia

20. The most common type of microadenoma of the pituitary results in the hypersecretion of _____*Prolactin*_____. This can result in infertility because of the inhibition of _____*GnRH (prolactin inhibits)*_____. This is often treated with a _____*dopamine*_____ agonist, such as _____*bromocriptine*_____ and _____*cabergoline*_____.

21. Name 2 other high-yield conditions caused by hypersecreting pituitary adenomas.

Cushing's disease (elevated ACTH); Acromegaly (elevated GH)

22. List the direct catabolic effects of growth hormone.

Decreased tissue uptake of glucose; increased circulating free fatty acids by stimulating hormone sensitive lipase

23. List the direct and indirect anabolic effects of growth hormone.

GH promotes amino acid uptake and stimulates protein synthesis in a variety of tissues. GH stimulates the release of somatomedins, the most well-known being insulin-like growth factor (IGF), which stimulates growth of bones.

24. _____Laron_____ syndrome is a condition in which tissue production of somatomedins in response to growth hormone is lacking. Patients with the syndrome exhibit elevated circulating GH, but low levels of IGF-I.

25. What is the most common cause of acromegaly?
Growth hormone secreting pituitary adenomas

26. What drug can be used to suppress residual disease in acromegaly following surgery?
Octreotide

TOPIC 2: THE THYROID

1. Sketch the sequence of hormones related to thyroid hormone regulation and include negative feedback in this description.

   TRH (hypothalamus) → TSH (anterior pituitary) → T4/T3 from thyroid gland, T4 providing negative feedback on TRH and TSH.

2. Indicate the key effects of thyroid hormone for the items in the first column.

	T3/T4 Actions
Basal metabolic rate	*Stimulates: Long-term regulator of Na+--K+ ATPase; increases body temperature*
Nerves	*Necessary for normal myelination (cretinism in newborns lacking)*
Bone	*Permissive and needed for normal growth*
Beta-receptors	*Permissive: Recall beta receptor function; 1) heart (↑ HR and contractility), 2) Glycogenolysis, 3) Lipolysis*
Cholesterol	*Promotes clearance*
Muscle protein	*Catabolic when in excess*
Growth hormone	*Permissive for secretion*
Gut motility	*Increases*

3. Indicate the key clinical signs seen in hypo- and hyperthyroidism for the following categories.

	Hypo	Hyper
Basal metabolic rate	↓; *Cold intolerance; weight gain; low appetite*	↑; *heat intolerance; weight loss; increased appetite*
Nerves	*Cretinism in newborn; lethargy; change in mental status*	*Tremor; nervousness;* ↑ *deep tendon reflex*
Bone	*Minimal to none in adult*	*Minimal to none in adult*
Beta-receptors	↓ *Cardiac performance; bradycardia*	↑ *cardiac performance; tachycardia; arrhythmias (atrial fibrillation); sweating*
Cholesterol	↑ *plasma levels*	↓ *plasma levels*
Muscle protein	*Minimal*	*Excessive breakdown*
Growth hormone	*Minimal*	*Minimal*
Gut motility	*Constipation*	*Diarrhea*
Other	*Myxedma;* ↑ *Prolactin because of elevated TRH can lead to amenorrhea in females and infertility in both sexes (prolactin* ↓ *GnRH)*	*Exophthalmos if Graves'; pre-tibial myxedema*

4. Why is hyperprolactinemia seen in some cases of hypothyroidism?

The hyperprolactinemia is secondary to increased TRH.

5. Name some of the clinical features of myxedema crisis.

Hypotension, hypothermia, generalized non-pitting edema, hypoventilation, bradycardia, and ileus

6. List the 4 causes of hypothyroidism and indicate the most common cause.

1) Hashimoto's thyroiditis (most common—autoimmune destruction of thyroid gland as antibodies to peroxidase and thyroglobulin are produced), 2) subacute thyroiditis (self-limiting often following a "flu-like" illness), 3) Riedel thyroiditis (chronic inflammation of thyroid—hard, painless goiter), and 4) Congenital (results in cretinism)

7. Which HLA serotype is associated with Hashimoto's thyroiditis?

HLA-DR5 antigen serotype

8. What autoantibodies are associated with Hashimoto's thyroiditis?

anti-thyroid peroxidase and anti-thyroglobulin

9. Symptoms of hyperthyroidism may precede hypothyroidism in what diseases?

   Hashimoto's thyroiditis and giant cell thyroiditis (De Quervain's).

10. Biopsy of a thyroid gland damaged by giant cell thyroiditis (de Quervain's thyroiditis) would most likely show what feature?

    Granulomatous inflammation

11. In which form of thyroiditis does dense fibrosis replace the thyroid gland?

    Riedel's thyroiditis

12. What long-term effect does hyperthyroidism have on muscle?

    Hyperthyroidism can cause protein-wasting and subsequent muscle weakness.

13. Name 4 conditions that can cause hyperthyroidism.

    Graves' disease, toxic multinodular goiter, thyroid adenoma, TSH-secreting pituitary adenoma

14. Besides hyperthyroidism, what 2 conditions are characteristic of Graves' disease?

    Pretibial myxedema, exophthalmos

15. Graves' disease usually involves what type of autoantibodies?

    TSH receptor antibodies that stimulate the TSH receptor.

16. In toxic multinodular goiter, what causes the focal hyperfunctioning of follicular cells?

    Mutation of the TSH receptor

17. Benign, monoclonal tumors that form "cold nodules" on radioactive iodine uptake are typically what type of lesion?

    Thyroid adenomas

18. Radiation therapy predisposes for what thyroid lesion?

    Papillary carcinoma

19. What are characteristic histologic features of papillary thyroid carcinoma?
Psammoma bodies (spherical, laminated calcified structures), "Orphan Annie" nuclei

20. Which form of thyroid tumor has a particular propensity for metastasis via hematogenous spread to the bones or lungs?
Follicular carcinoma

21. Which thyroid tumor produces amyloid? What cell gives rise to this tumor?
Medullary carcinoma; parafollicular "C" cells

22. Which types of MEN are associated with medullary thyroid carcinoma?
MEN 2A and 2B

23. Where does the thyroglossal duct originate and what is its postnatal remnant called?
Midline endoderm of posterior tongue (oropharynx). Remnant is foramen cecum

24. What is the most common location of ectopic thyroid tissue?
Tongue

25. Name two other ventral outgrowths of foregut endoderm.
Trachea, Liver

26. Where would a thyroglossal cyst most likely be found?
Midline of anterior neck

TOPIC 3: THE PARATHYROIDS AND CALCIUM HOMEOSTASIS

1. Fill in the embryonic origins of the glandular tissue.

Glandular Tissue	Pharyngeal Pouch Origin?	Migrates To?
Superior parathyroid	*4*	*Behind thyroid*
Inferior parathyroid	*3*	*Behind thyroid*
Parafollicular "C" cells	*4*	*Into thyroid*

2. Indicate the stimulus for the release of parathyroid hormone (PTH), and describe its actions on peripheral tissue.

PTH is stimulated by low free calcium in the blood. It acts on bone, to cause resorption and subsequent release of calcium and phosphate. It acts on the kidney, causing 1) increase in distal tubule calcium reabsorption, 2) decrease in phosphate reabsorption in the proximal tubule, and 3) stimulation of the 1-alpha hydroxylase enzyme, the rate limiting step in the formation of active vitamin D.

3. Indicate the 2 sources for active vitamin D (calcitriol) and its primary physiologic effect.

Calcitriol can be obtained in the diet or synthesized from cholesterol in the skin in the presence of UV light. It undergoes a 25-hydoxylation step in the liver and becomes active following the 1-hydroxylation step that occurs in the kidneys (this step stimulated by PTH). Vitamin D enhances calcium and phosphate absorption in the GI tract by inducing the synthesis of a calcium binding protein (calbindin) in intestinal cells. It also enhances PTH's action on calcium reabsorption in the distal tubule.

4. Fill in the table below.

Signs/Symptoms	Disease	Plasma Ca^{2+} & Pi
↑ QT interval; spasms; ↓ urine Pi; ↓ plasma PTH	*Primary hypo PTH (DiGeorge's is one cause)*	↓ & ↑
↑ QT interval; spasms; ↓ urine Pi; ↑ plasma PTH	Pseudo-hypoparathyroidism	↓ & ↑
↓ QT interval; ↓ neuronal excitability; ↑ urine Pi	*Primary hyper PTH*	↑ & ↑
↑ QT interval; spasms; ↓ urine Pi; ↑ plasma PTH	Renal failure	↓ & ↑
↑ QT interval; spasms; ↑ urine Pi; ↑ plasma PTH	*Secondary hyper PTH (Vitamin D deficiency; malabsorption syndromes)*	↓ and ↓

5. What is the most common cause of hypoparathyroidism?

   Iatrogenic hypoparathyroidism secondary to the surgical removal of parathyroid glands, as can occur during thyroidectomy.

6. List 3 or more signs and symptoms of hypoparathyroidism.

   Hypocalcemia, psychiatric disturbances, prolonged QT interval on EKG, muscular spasms and tetany (Chvostek sign -twitching of ipsilateral facial muscles induced by tapping; Trousseau sign -induction of muscular contractions by inflating BP cuff)

7. What causes pseudohypoparathyroidism?

   Target tissue resistance, particularly in the kidneys, to parathyroid hormone

8. What chromosome defect causes DiGeorge's syndrome?

   Deletion on chromosome 22 at q11.2 (associated with hypocalcemia and tetany, T-cell deficiency leading to recurrent infections with viral and fungal organisms, and possible cardiac defects)

9. A serum chloride-to-phosphate ratio greater than what number suggests hyperparathyroidism?

   33, assuming that the patient is not taking thiazide diuretics

10. By what mechanism does chronic kidney disease cause secondary hyperparathyroidism?

    In chronic kidney disease there is no conversion of vitamin D to active form → there is no excretion of PO4 → formation of insoluble CaPO4 → hypocalcemia → increased secretion of PTH by parathyroid glands.

TOPIC 4: THE ADRENALS: STEROIDS AND CATECHOLAMINES

1. Fill in the functions and regulators of the regions of the adrenal gland.

Glandular Region	Product(s)?	Regulated By?
Zona glomerulosa	*Aldosterone*	*Renin-angiotensin system*
Zona fasciculata	*Cortisol and Androgens*	*Adrenocorticotropic hormone*
Zona reticularis	*Androgens*	*Adrenocorticotropic hormone*
Medulla	*Catecholamines (epinephrine)*	*Acetylcholine from sympathetic nerves*

2. Where does the left and right adrenal vein drain?

   L into L renal vein; R into IVC

3. Where does the left and right gonadal vein drain?

   L into L renal vein; R into IVC

4. Fill in the table below for the important distinctions related to enzyme deficiencies in adrenal steroid synthesis. In all cases, cortisol is reduced, resulting in elevated ACTH and adrenal hyperplasia.

Enzyme Deficiency	DOC	ALDO	Androgens	Renin	BP	Plasma K+
21-OH	↓	↓	↑	↑	↓	↑
11β-OH	↑	↓	↑	↓	↑	↓
17α-OH	↑	↓	↓	↓	↑	↓

DOC = 11-deoxycorticosterone; ALDO = aldosterone

If one remembers the basic function of mineralcorticoids (aldo being the primary one normally, DOC the key one in these conditions) and the basic synthetic pathway, then most of the arrows fall into place. BP goes the same direction as the mineralcorticoids, while renin and K+ go in the opposite direction.

5. 21-hydroxylase deficiency produces what changes in functional steroid hormones?

   Decreased cortisol, decreased mineralocorticoids, increased sex hormones

6. What adrenal enzyme deficiency accounts for 7% of adrenal enzyme deficiencies and causes increased androgens with virilization of female fetuses?

   11β-hydroxylase deficiency

7. Is there hypertension or hypotension in 21-hydroxylase deficiency?

   Hypotension *in 21-hydroxylase deficiency (decreased aldosterone).*

   In 11β-hydroxylase deficiency?

   Hypertension *in 11β-hydroxylase deficiency (increased 11-deoxycorticosterone).*

8. For the following, indicate the effects of cortisol.

   a. Carbohydrates: *Promotes glycogenolysis and gluconeogenesis to increase plasma glucose.*

   b. Fats: *Promotes lipolysis.*

   c. Proteins: *Causes protein degradation (AA can serve as substrates for gluconeogenesis).*

   d. Bone: *Promotes bone breakdown.*

   e. Phospholipase A2: *Inhibits.*

   f. IL-2 production: *Decreases*

9. Discuss the important permissive actions of cortisol and include any enzymes that may be involved.

   1) *Glucagon: Permissive for key enzymes in gluconeogenesis. These include, phosphoenolpyruvate caboxykinase (PEPCK), fructose 1,6—bisphosphatase, and glucose-6 phosphatase (G6P).*
   2) *Alpha-receptors: Normal function of alpha-receptors is dependent upon adequate levels of cortisol. Alpha-receptors are on vascular smooth muscle and needed for maintenance of arterial blood pressure.*
   3) *Beta-receptors: Similar to alpha, normal beta-receptor function requires adequate cortisol. Recall that beta-receptors are on the heart and enhance cardiac performance and they mediate the metabolic effects of epinephrine (lipolysis and increased blood glucose).*

10. Diagram the hypothalamic-pituitary-adrenal (HPA) axis.

    CRH (hypothalamus) → POMC (anterior pituitary) → ACTH (fragment of POMC) → cortisol (zona fasciculata). Highest secretion is in the early morning and stress stimulates.

11. Fill in the table below for the important hormonal alterations seen with adrenal cortex or HPA axis alterations.

Condition	Cortisol	ACTH	DEX Suppression?	Pigmentation?
Addison's disease	↓	↑	*N/A*	*Yes*
Secondary hypocortisolism	↓	↓	*N/A*	*No*
Primary hypercortisolism	↑	↓	*No*	*No*
Cushing's disease	↑	↑	*High dose*	*No*
Ectopic ACTH	↑	↑↑	*No*	*Yes*

DEX = dexamethasone

12. What is the most common cause of Cushing's syndrome?

Cortisol administration

13. "Buffalo hump" suggests what medical condition?

Cushing's syndrome (other features: moon facies, hyperglycemia, hypertension, poor wound healing, osteoporosis, cutaneous striae, and others)

14. Cushing's disease is related to what type of tumor?

Pituitary adenoma (can usually be suppressed by high dose dexamethasone, while ectopic ACTH production-related Cushing's syndrome will not be suppressed)

15. What are the typical etiologies of primary hypocortisolism (Addison's disease)?

Autoimmune disease (most common in U.S.), tuberculosis, neoplasms

16. What process would most likely cause an acute onset of adrenal insufficiency?

Bilateral adrenal hemorrhage

17. What parts of the adrenal glands atrophy in secondary hypocortisolism?

Zona fasciculata and zona reticularis (zona glomerulosa is not affected so aldosterone levels are normal)

18. Fill in the table below for the important alterations associated with changes in aldosterone.

Condition	ALDO	Renin	BP	Plasma K+	Acid-Base	Edema?
Addison's	↓	↑	↓	↑	*Acidotic*	*No*
Conn's	↑	↓	↑	↓	*Alkalotic*	*No*
Secondary hyper: renal artery stenosis	↑	↑	↑	↓	*Alkalotic*	*No*
Secondary hyper: CHF, cirrhosis; nephrotic	↑	↑	↓	↓	*Alkalotic*	*Yes*

19. What is the most common cause of primary hyperaldosteronism (Conn's syndrome)?
Aldosterone-secreting adrenal cortical adenoma

20. How does renal artery stenosis cause secondary hyperaldosteronism?
*The stenosis causes a decrease in renal blood flow with resultant excessive secretion of renin, which leads to **activation** of the renin-angiotensin system (renin is **decreased** in **primary** hyperaldosteronism) and an appropriate increase in aldosterone.*

21. Which species of bacteria is most likely to cause Waterhouse-Friderichsen syndrome?
Neisseria meningitidis (bilateral adrenal hemorrhage)

22. What substances are pheochromocytomas likely to secrete?
Catecholamines, such as epinephrine, norepinephrine, and occasionally, dopamine

23. Which urinary compounds are most important in the diagnosis of pheochromocytoma?
Catecholamines and vanillylmandelic acid (VMA)

24. In general, the MEN syndromes are characterized by what problems? Which types are associated with pheochromocytoma?

Hyperplasia and tumors of endocrine organs. Pheochromocytomas are common in MEN 2A and 2B (and also neurofibromatosis type 1).

25. MEN1 is caused by a loss of function mutation for the gene encoding what protein?

The MEN 1 gene encodes the nuclear protein menin.

26. What are the 3 Ps of MEN1?

Neoplasms of the Pancreas, Pituitary, and Parathyroid

27. A pancreatic VIPoma seen in an MEN1 patient would likely produce what symptoms?

The secreted vasoactive intestinal peptide can cause watery diarrhea with hypokalemia and achlorhydria

28. Mutation of the RET proto-oncogene can be seen in which forms of MEN?

MEN 2A and 2B

29. Which form of thyroid cancer is associated with MEN2?

Medullary carcinoma of the thyroid

30. What is the most common extracranial malignancy of childhood?

Neuroblastoma

31. What oncogene is amplified in neuroblastoma?

N-myc

32. An abdominal neuroblastoma most likely arose from what site?

Adrenal gland

33. What is Kerner-Morrison syndrome?

Kerner-Morrison syndrome refers to high levels of vasoactive intestinal peptide associated with neuroblastoma, producing intractable secretory diarrhea, hypovolemia, and hypokalemia.

34. Carcinoid syndrome is caused by secretion of what substance?

Serotonin

35. What urinary substance is characteristically increased in carcinoid syndrome?

5-HIAA

TOPIC 5: THE PANCREAS AND DIABETES

1. For the following islet cells, list the product and percentage of endocrine pancreas that each makes up.

Islet Cell	Product?	% of Islet Cells?
Alpha	*Glucagon*	*20%*
Beta	*Insulin*	*60-75%*
Delta	*Somatostatin*	*5%*

2. What are the signal transduction pathways for insulin and glucagon?

   Insulin—tyrosine kinase; Glucagon—G_s—cAMP

3. Sketch the steps involved in the secretion of insulin, and indicate the compound that is co-released with it.

   Glucose entry into cell → rise in cellular ATP → closing of ATP-sensitive K+ channels → depolarization → Ca^{2+} entry → fusion of vesicle containing insulin and c-peptide → release of insulin and c-peptide into the blood.

4. Fill in the table below for the important metabolic actions of insulin and glucagon.

Hormone	Gly-S	Gly-P	Glu-neo	G6P	Plasma Glucose	HSL	ACC	Protein Synthesis
Insulin	↑	↓	↓	↓	↓	↓	↑	↑
Glucagon	↓	↑	↑	↑	↑	↑	↓	*No role*

Gly-S = glycogen synthase; Gly-P = glycogen phosphorylase; Glu-neo = gluconeogenesis; G6P = glucose-6 phosphatase; HSL = hormone sensitive lipase; ACC = acetyl CoA carboxylase

5. Insulin increases the number of _____GLUT-4_____ transporters on skeletal muscle and adipose tissue. It also promotes the entry of the ion _____K^+_____ into cells.

6. What is the leading cause of nontraumatic lower limb amputation?
   Diabetes mellitus

7. Which HLA types are associated with type 1 diabetes mellitus?
   HLA types DR3, DR4, and DQ

8. What is the pathogenesis of diabetes mellitus type 2?
   Reduced tissue sensitivity to insulin due to decreased receptor number

9. What substances create a diabetogenic effect in gestational diabetes?
   Human placental lactogen, placental insulinase, cortisol, and progesterone

10. What are some renal complications of diabetes?
    Mesangial expansion, thickening of the glomerular basement membrane, glomerular sclerosis (including nodular glomerulosclerosis = Kimmelstiel-Wilson disease)

11. What problems can be seen with diabetic retinopathy?
    Microaneurysm, retinal hemorrhage, neovascularization, vitreous humor fibrosis, and retinal detachment

12. The neuropathy of diabetes mellitus is related to the increased intracellular concentration in neurons of what sugars or molecules closely related to sugars?
    Sorbitol and fructose

13. What is the most common acute, life-threatening complication of type 1 diabetes mellitus?

Diabetic ketoacidosis

14. Which serum ketones rise during diabetic ketoacidosis?

Acetoacetate, acetone, and hydroxybutyrate

15. What are some common precipitating factors for diabetic ketoacidosis?

Infections, surgery, trauma, pregnancy, lack of insulin therapy

16. What characterizes the HONK state?

HyperOsmolar NonKetotic coma is a state of severe hyperglycemia without ketosis (also increased serum osmolarity and prerenal azotemia)

17. How is diabetic hyperosmolar nonketotic state treated?

IV insulin, IV fluids, and electrolyte replacement

18. What are the current diagnostic criteria for diabetes?

Fasting glucose >126 mg/dL on at least 2 occasions, positive glucose tolerance test

19. How is hemoglobin A1c produced in the diabetic patient?

The glycosylated hemoglobin is produced by non-enzymatic condensation of glucose with free amino groups on globin.

20. With type 2 diabetics, how much weight loss is needed to improve insulin sensitivity and reduce postprandial hyperglycemia?

4-7% of body weight.

21. What condition would most likely be present in a diabetic patient who presented with diaphoresis, tremor, tachycardia, hunger, and altered mental status?

Hypoglycemia

CHAPTER 7

NEPHROLOGY

TOPIC 1: RENAL ANATOMY AND PHYSIOLOGY

1. Name the 3 stages of embryonic kidney development and indicate which stage will form the definitive human kidney.

   Pronephros, Mesonephros, Metanephros. Metanephros forms the definitive human kidney.

2. When the mesonephric kidney degenerates, what does the cranial end of the mesonephric duct form in males?

   Male internal reproductive structures such as the ductus deferens, ejaculatory duct and seminal gland.

3. What structure begins the formation of the definitive human kidney?

   Ureteric bud

4. Where does the definitive human kidney initially develop?

   Pelvis

5. The embryonic origin of the bladder and urethra is _____Urogenital sinus_____.

6. Name 3 malformations evident in a stillborn infant that succumbed from bilateral renal agenesis (Potter sequence).

   Clubbed feet, bilateral pulmonary hypoplasia, facial abnormalities

7. What vessel blocks the ascent of a horseshoe kidney?

   Inferior mesenteric artery

8. In a newborn with a patent urachus, there will be abnormal drainage of urine from _____From the umbilicus_____.

9. The 3 main anatomic regions of the kidney are _____Cortex, Medulla, Hilum_____.

10. Which nephrons have short loops of Henle and which nephrons have long ones?

    Short: Cortical / Long: Juxtamedullary

11. Name the 3 structures, in order, through which urine will pass to reach the ureter, beginning at the apex of a renal pyramid.

    Minor calyx, Major calyx, Renal pelvis

12. If Potter sequence develops from renal agenesis, what features are seen?

    In Potter sequence, bilateral (fatal) renal agenesis causes oligohydramnios, which in turn leads to clubbed feet, pulmonary hypoplasia, and craniofacial abnormalities, including flattened nose, low-set ears, and recessed chin.

13. Failure of the allantois to obliterate embryologically can cause what problem?

    Drainage of urine through the patent urachus can lead to leakage of urine out the umbilicus.

14. Name and briefly describe the 4 basic renal processes.

1) Filtration: Water/solute movement from glomerular capillary into Bowman's space. 2) Secretion: Solute movement from peritubular capillaries or tubular cells into the lumen of the nephron. 3) Reabsorption: Water/solute movement from the lumen of the nephron into the peritubular capillaries. 4) Excretion: Water/solute loss in the urine

15. About _____60%_____ of the body mass is water and its distribution is about _____one-third_____ extracellular and _____two-thirds_____ intracellular.

16. Four grams of inulin is infused into a patient, and the plasma concentration of inulin is 250 mg/ml after steady state has been achieved. What compartment is measured, and what is the volume of this compartment?

Inulin easily crosses the capillary membrane but not the cell membrane, thus, it is a marker for extracellular volume. Use the V=A/C equation in which V=volume, A=amount, and C=concentration. Thus, V=4 g/250 mg/ml=16 L.

17. Complete the table below to denote the body compartment that each tracer measures.

Tracer	Plasma	Extracellular	Total
^{125}I-albumin; Evan's blue dye; ^{51}Cr red blood cell	*Yes*	*No*	*No*
Inulin; mannitol; 22Na^{+}; sucrose	*No*	*Yes*	*No*
Heavy water; tritiated water; urea; antipyrine	*No*	*No*	*Yes*

18. Under normal circumstances, _____Plasma proteins (large molecular weight)_____ and _____lipid soluble_____ compounds are not filtered at the glomerular capillary.

19. Define glomerular filtration rate (GFR) and indicate the force producing it.

GFR is the rate at which fluid is filtered into Bowman's space. GFR is directly related to pressure in the glomerular capillary (P_{GC}).

20. Write the equation for filtration fraction and indicate the variable it influences (directly related).

Filtration fraction (FF)=GFR/RPF, where RPF=renal plasma flow. Oncotic pressure in the peritubular capillaries is directly related to FF. Remember, oncotic pressure in the peritubular capillaries influences reabsorption.

21. Using arrows, fill in the table below to indicate the effect sympathetic stimulation and angiotensin II have on renal function.

	RPF	P_{GC}	P_{PC}	GRF	FF	π_{PC}
Sympathetics (both but afferent > efferent)	↓↓	↓	↓↓	↓	↑	↑
Angiotensin II (efferent > afferent)	↓	↑	↓	↑	↑	↑

RPF = renal plasma flow; P_{GC} = pressure glomerular capillary; P_{PC} = pressure peritubular capillary; GFR = glomerular filtration rate; FF = filtration fraction; π_{PC} = oncotic pressure in the peritubular capillary

22. What is the important role of prostaglandins in the regulation of renal blood flow? Which over-the-counter compounds block prostaglandin production?

Prostaglandins help maintain dilation of the afferent arteriole. This is most prominent when constrictor actions are evoked, i.e., activation of the sympathetic nervous system. NSAID's are common over the counter medications that block prostaglandin production and thus can influence renal blood flow, particularly in times of stress.

23. Write the equation for clearance. The clearance of which compound is a measure of GFR? Why is this compound a measure of GFR?

Clearance = $U_X * V/P_X$, where U_X is the urine concentration of the solute, V is urine flow, and P_X is the plasma concentration of the solute. Clearance of inulin gives GFR because it is neither secreted nor reabsorbed.

24. Plasma creatinine is used as a marker of renal function because _____.

Plasma creatinine is a rough marker of GFR. It is freely filtered but not reabsorbed. There is a small secretion of creatinine. In the normal situation creatinine is released from muscle at a steady rate. Because creatinine is not reabsorbed, its elimination is inversely correlated to GFR. The correlation is not linear, thus GFR typically falls considerably before one sees a significant rise in plasma creatinine.

25. The clearance of *PAH* is a measure of effective renal plasma flow, and it is utilized for this measurement because if the plasma concentration is low enough, all of it is *secreted*.

26. Compound X is infused into a patient until it reaches a steady-state plasma concentration of 100 mg/dl. Once steady state is reached, the urine concentration of X is 2 mg/ml and urine flow is 1 ml/min. Inulin clearance is 100 ml/min. Given this, is there net secretion or reabsorption of X? What is the rate of this reabsorption or secretion, and is the clearance of X greater than, equal to, or less than GFR?

*Filtered load = GFR * P_X = 100 ml/min * 1 mg/ml [NOTE: clearance of inulin is GFR] = 100 mg/min. Rate of excretion = U_X * V = 2 mg/ml * 1 ml/min = 2 mg/min. Because the filtered load of X is greater than the rate of excretion, X is reabsorbed. The rate of reabsorption = filtered load minus rate of excretion = 100 mg/min – 2 mg/min = 98 mg/min. Clearance of X = (2 mg/ml * 1 ml/min)/ 1 mg/ml = 2 ml/min. Its clearance is therefore well below GFR. Any substance that is reabsorbed will have a clearance less than GFR, while any substance that is secreted will have a clearance that is greater than GFR.*

TOPIC 2: ELECTROLYTES AND ACID-BASE DISORDERS

1. For the following solutes, indicate if the proximal tubule transport is: simple diffusion (SD), secondary active transport—symport (2^{o} sym), secondary active transport—antiport (2^{o} anti), or primary active transport (1^{o}), and indicate if this transport is across the luminal (L) or basolateral (BL) membrane.

Glucose	*2°SYM; L*	AA	*2°SYM; L*	Ketones	*2°SYM; L*
Na^+–H^+	*2°ANTI; L*	Na^+–K^+	*1°ANTI; BL*	Na^+–Pi	*2°SYM; L*

AA = amino acids; Pi = phosphate

2. Discuss the steps involved in bicarbonate reabsorption across the luminal membrane of the proximal tubule.

Bicarbonate is freely filtered at the glomerular capillary. In the lumen of the nephron it combines with H^+ to form CO_2 and H_2O and this reaction is catalyzed by carbonic anhydrase (CA). Some of the H^+ for this reaction comes into the lumen via the Na^+--H^+ antiporter. The CO_2 produced then diffuses across the luminal membrane where the H^+ and bicarbonate are reformed in the cell, again catalyzed by CA. The bicarbonate then exits the basolateral membrane to enter the blood, thus completing its reabsorption.

3. Describe the effect on proximal tubular reabsorption of bicarbonate in the following conditions:

Acidosis — *Acidosis will increase the available pool of H^+ and thus will increase H^+ secretion into the lumen. This will increase bicarbonate reabsorption.*

Alkalosis — *Alkalosis will decrease the available pool of H^+, thus decreasing H^+ secretion and bicarbonate reabsorption.*

Administration of a carbonic anhydrase inhibitor

A CA inhibitor will reduce conversion of bicarbonate into CO_2 in the lumen, decreasing bicarbonate reabsorption. In addition, it will decrease the cellular generation of H^+ from CO_2 and water, thus reducing Na^+ reabsorption because of diminished availability of H^+ in the cell.

4. Discuss the renal consequences that occur when plasma glucose rises.

*Under normal circumstances, all filtered glucose is reabsorbed in the proximal tubule. However, as plasma glucose rises, the filtered load of glucose (GFR * P_G) increases and the renal transporters for glucose become saturated. At this point, glucosuria occurs. If plasma glucose continues to rise, then ultimately all of the transporters for glucose become saturated. Failure to reabsorb all of the filtered glucose will cause an osmotic diuresis, hence the reason diabetics exhibit polyuria if glucose control is compromised.*

5. Indicate the tubular fluid-to-plasma concentration ratio (TF/P) (normal = 1) for the following solutes at the end of the proximal tubule. Write 1, >1, <1, or 0.

	Glucose	Bicarbonate	Na^+	K^+	Cl-	Creatinine	Inulin
TF/P	*0*	*<1*	*1*	*1*	*>1*	*>>>1*	*>>1*

6. The descending limb of the loop of Henle is permeable to _____Water_____ and relatively impermeable to _____solute_____.

7. Indicate the predominant transporter in the ascending thick limb of the loop of Henle (ATL) and the class of drugs that inhibit it.

   Na^+--K^+--$2Cl^-$ and it is blocked by loop diuretics.

8. The back diffusion of _____K^+_____ from cells in ATL into the lumen drives the reabsorption of _____Ca^{2+}_____ and _____Mg^{2+}_____ in this region of the nephron.

9. The transporter in the distal tubule transports what 2 ions, and what class of drugs blocks this transporter?

   The distal tubule has a Na^+--Cl^- symporter that is blocked by thiazide diuretics.

10. Discuss the reabsorption of Ca^{2+} in the distal tubule, what regulates it, and how it is impacted by thiazide diuretics.

    The luminal membrane of the distal tubule contains Ca^{2+} channels that allow Ca^{2+} to follow its electrochemical gradient into the cell and thus be reabsorbed. This channel is regulated by parathyroid hormone (peptide hormone working through Gs—cAMP). PTH enhances Ca2+ reabsorption at this site. Thiazide diuretics increase Ca^{2+} reabsorption in the distal tubule.

11. _____Aldosterone_____ is a steroid hormone secreted from the adrenal cortex. It works on principal cells of nephron to increase _____Na^+_____ reabsorption and _____K^+_____ secretion.

12. What are the 2 mechanisms of action of aldosterone on principal cells of the collecting duct?

    Increases luminal Na^+ channels and enhances the activity of the basolateral Na^+—K^+ ATPase.

13. Intercalated cells of the collecting duct play an important role in ___Acid-base___ regulation. They secrete ___H^+___ into the lumen, which in turn binds to ___phosphate___ and/or ___ammonia___ and is thus eliminated from the body. This process generates ___new bicarbonate___. Aldosterone stimulates ___H^+___ secretion in these cells; thus an excess of aldosterone causes an ___alkalemia (alkalosis)___.

14. Principal cells contain receptors for the peptide hormone ___ADH (AVP);___. This hormone causes insertion of ___aquaporins (water channels)___ in the luminal membrane.

15. Describe what stimulates the release of atrial natriuretic peptide (ANP) and indicate its effects on the kidney.

    ANP is released by stretch of the atria. ANP increases GFR and reduces both sodium and water reabsorption. Thus, it causes a natriuresis and a diuresis, countering the actions of aldosterone and ADH.

16. List the 3 stimuli for renin release and the effects of renin.

    1) Decreased perfusion pressure to the kidney, 2) stimulation of sympathetic nerves innervating the kidney (beta-1), and 3) reduced delivery of Na+ to the macula densa.

    Effects of renin:

    Renin is an enzyme that converts angiotensinogen into angiotensin I, which is the rate-limiting step in the synthesis of angiotensin II.

17. List 4 important actions of angiotensin II.

    (1) *Vasoconstriction of peripheral arterioles*

    (2) *Release of aldosterone*

    (3) *Constriction of the efferent arteriole of the kidney*

    (4) *Thirst (hypothalamus)*

18. List the 2 stimuli for the release of anti-diuretic hormone (ADH; also called arginine vasopressin, AVP).

1) Increased plasma osmolarity, and 2) decreased arterial blood volume/pressure

19. Most of the body stores of K^+ are located in the *Intracellular* compartment.

20. Indicate whether the following conditions promote K^+ to shift into or out of cells.

Acidosis *out*

Alkalosis *in*

Lysis of cells *out*

Beta-2 agonists *in*

Insulin *in*

Exercise *out*

21. List 5 factors/conditions that increase K^+ secretion in the kidney.

(1) *Increased tubular flow*

(2) *Aldosterone*

(3) *Hyperkalemia*

(4) *Alkalosis (acute and chronic)*

(5) *Chronic metabolic acidosis (via aldosterone)*

22. Fill in the table below.

Acid/Base Disturbance	pH	Bicarbonate
Respiratory acidosis	↓	↑
Metabolic acidosis	↓	↓
Respiratory alkalosis	↑	↓
Metabolic alkalosis	↑	↑

23. Fill in the table below.

Acid-Base Disturbance	Computation/Data Used to Diagnose the Condition
Acute (uncompensated) respiratory acidosis	*Expected bicarbonate: 0.1 mEq/L * ↑ in PCO_2*
Chronic (compensated) respiratory acidosis	Expected bicarbonate: 0.35 mEq/L * ↑ in PCO_2
Metabolic acidosis	*Expected arterial PCO_2: Winter's equation = (1.5 * bicarbonate) + 8: Patient's PCO_2 should be ±2 of this computed value.*
Acute (uncompensated) respiratory alkalosis	Expected bicarbonate: 0.2 mEq/L * ↓ in PCO_2
Chronic (compensated) respiratory alkalosis	*Expected bicarbonate: 0.5 mEq/L * ↓ in PCO_2*
Metabolic alkalosis	*Expected arterial PCO_2: ↑ in bicarbonate * 0.7; Patient's PCO_2 should be ±2 of this computed value.*
Mixed disturbance	*Bicarbonate and PCO_2 go in opposite directions*
Normal blood values	pH = 7.4; bicarbonate = 24 mEq/L; PCO_2 = 40 mmHg

24. What is the normal anion gap and how is it calculated?

Plasma anion gap = Na^+ - (Cl^- + bicarbonate) and normal is 12±2.

25. List the agents that cause an increased anion gap metabolic acidosis.

"MUDPILES": Methanol; Uremia (kidney failure); Diabetes; Paraldehyde/Phenformin; Iron; Lactic acid; Ethylene glycol; Salicylates (mixed with respiratory alkalosis)

26. Complete the following table for renal tubular acidosis (RTA).

	RTA Type I	RTA Type II	RTA Type IV
Fundamental dysfunction	↓ *H+ secretion in distal nephron*	↓ *PT bicarbonate reabsorption*	↓ *Aldosterone*
Urine pH	↑	*Variable: depends on distal bicarb reabsorption*	↓
Plasma K^+	*Usually* ↓	*Usually* ↓	↑
Associated conditions	*Hypercalcemia*	*Fanconi's; Multiple myeloma; CA inhibitors; Lupus; hepatitis**	*Diabetes M; HIV; Lupus; adrenal disease; NSAIDS; ARB's; Aldo blockers**

TOPIC 3: NEPHRITIC AND NEPHROTIC SYNDROMES

1. What types of acellular and cellular casts can be present in urine?

   Acellular casts include hyaline, granular, fatty, and waxy casts. Cellular casts include red blood cell, white blood cell, and epithelial cell casts.

2. Hyaline casts are composed of what protein?

   Tamm-Horsfall mucoprotein, which is secreted from tubular epithelial cells.

3. Breakdown of cellular casts produces what type of cast as the next step?

   Granular casts

4. A patient with nephrotic syndrome would be most likely to have *Fatty casts* casts in the urine.

5. Red blood cell casts suggest damage to what renal structure?

   Glomeruli

6. Name 3 diseases that might be suggested by white blood cell casts.

   Tubulointerstitial inflammation, acute pyelonephritis, and graft rejection in transplanted kidneys

7. Which features are characteristic of nephritic syndrome? Nephrotic syndrome?

   Nephritic syndrome shows hematuria, hypertension, azotemia, oliguria, and proteinuria less that 3.5 g/day. Nephrotic syndrome has proteinuria greater than 3.5 g/day, hypoalbuminemia, generalized edema, hyperlipidemia, and lipiduria.

8. Which bacteria are particularly likely to cause acute postinfectious glomerulonephritis?

   β-hemolytic, group A streptococci

9. What characteristic feature is seen on electron microscopy of glomeruli in acute poststreptococcal glomerulonephritis? Immunofluorescence?

   Hump-shaped, subepithelial immune complex deposition; granular deposits of IgG, IgM, and C3

10. Is the prognosis for acute poststreptococcal glomerulonephritis better for children or for adults?

    95% of children, but only 60% of adults, recover completely.

11. The autoantibody of Goodpasture's syndrome is directed against what substance?

The Goodpasture autoantibody is directed against the non-collagenous component of type IV collagen found in the glomerular basement membrane and the pulmonary alveolar basement membrane.

12. On immunofluorescence, what pattern is seen in Goodpasture's syndrome?

Immunoflorescence characteristically shows a smooth, linear pattern of IgG and C3 deposition in glomerular basement membrane.

13. What is the outcome of most cases of rapidly progressive glomerulonephritis?

Most patients develop renal failure.

14. Rapidly progressive glomerulonephritis may occur in association with what diseases?

Goodpasture's syndrome, other forms of glomerulonephritis, and vasculitides such as Wegener's granulomatosis

15. What findings are seen on light microscopy in rapidly progressive glomerulonephritis?

Glomerular hypercellularity and crescents within Bowman's capsule

16. What medications are used to treat patients with rapidly progressive glomerulonephritis?

Steroids and cyclophosphamide

17. The most common cause of glomerulonephritis worldwide is _____*IgA nephropathy*_____.

18. What is seen on immunofluorescence of IgA nephropathy?

Mesangial IgA and C3 deposits

19. Membranoproliferative glomerulonephritis can occur secondary to what diseases?

SLE, endocarditis, hepatitis B and C, HIV, and chronic lymphocytic leukemia

20. Silver stain of a renal biopsy from a patient with membranoproliferative glomerulonephritis would likely show what distinctive feature?

Basement membrane splitting, also called "tram-tracking".

21. If a person with membranoproliferative glomerulonephritis undergoes renal transplantation, what typically happens to the transplant?

There is a high frequency of recurrence of the membranoproliferative glomerulonephritis in the kidney.

22. What genetic mutation is associated with Alport syndrome?

COL4A5 mutation leads to defective type IV collagen production.

23. When used in nephrotic syndrome, ACE inhibitors can help to control what disease manifestations?

Proteinuria and blood pressure control

24. Name several risk factors for membranous glomerulonephritis.

Drugs (penicillamine), infections (hepatitis B & C, syphilis), systemic disease (SLE, diabetes), carcinomas (lung, colon)

25. Light microscopy of silver-stained sections from a renal biopsy with membranous glomerulonephritis would show what distinctive feature?

Basement membrane projections that look like spikes

26. What is the probable range of outcomes of membranous glomerulonephritis?

One-third show spontaneous remission, one third have persistent proteinuria with preserved renal function, and one-third progress to end-stage renal disease.

27. The most common cause of nephrotic syndrome in children is _____*Minimal change disease*_____.

28. The most characteristic feature on electron microscopy of minimal change disease is _____*Podocyte foot process effacement*_____.

29. In the United States, focal segmental glomerulosclerosis is most prevalent in what patient population?

African Americans

30. Light microscopy of focal segmental glomerulosclerosis shows variable features with what range of appearance?

Focal segmental glomerular collapse to global capillary collapse, sclerosis, and hyalinization

31. What are typical glomerular pathologies seen in diabetic renal disease?

Nodular glomerulosclerosis, hyaline arteriosclerosis, and microangiopathy

32. Accumulation of amyloid deposits in glomeruli can produce what clinical syndrome?

Nephrotic syndrome

TOPIC 4: STONES, CANCERS, AND HEREDITARY DISORDERS

1. What features characterize the urine cytology in acute tubular necrosis?
   Muddy brown granular casts and epithelial casts

2. What are the most common etiologies of acute tubular necrosis?
   Ischemic and nephrotoxic causes are the most common causes of acute tubular necrosis.

3. What are the most important organisms to cause pyelonephritis?
   E. coli, Proteus, Klebsiella, and Enterobacter

4. Urinalysis in pyelonephritis would be most likely to show what features?
   Pyuria and WBC casts.

5. What processes can cause tubulointerstitial nephritis?
   Medications, infections, acute pyelonephritis, SLE, lead poisoning, and multiple myeloma

6. What is the mechanism by which drugs can cause interstitial nephritis?
   The drugs act as haptens, inducing a hypersensitivity reaction

7. What is the most common cause of chronic drug-induced interstitial nephritis?
   NSAID use

8. What processes can cause urate nephropathy?
   Gout, lead poisoning, and chemotherapy for leukemia and lymphoma

9. The damage to the kidney in renal papillary necrosis is localized to which areas?
   Inner medulla and papillae

10. Why are fluids given in renal papillary necrosis?
    To establish adequate hydration to ameliorate ischemia

11. The mechanism that causes diffuse cortical necrosis is: *A combination of vasospasm and disseminated intravascular coagulation*.

12. Which bacterial species characteristically cause magnesium-ammonium phosphate stones?

    Proteus

13. Vitamin C abuse predisposes to what type of renal stones?

    Calcium stones (cancer and hyperparathyroidism also predispose to stone formation)

14. Cystine stones are related to a metabolic disorder involving what biochemical process?

    An autosomal recessive amino acid transport disorder that causes cystinuria

15. What are the 2 most common presentations for nephrolithiasis?

    Renal colic and acute renal failure

16. A renal hamartoma composed of fat, smooth muscle, and blood vessels would most likely be associated with what disease?

    The tumor is an angiomyolipoma, and this type of tumor is associated with tuberous sclerosis.

17. Some risk factors for renal cell carcinoma are:

    Cigarette smoking, chronic analgesic use, asbestos, chronic renal failure, acquired cystic disease, Von Hippel-Lindau disease

18. Renal cell carcinoma often reaches the heart by invading what structure?

    Renal cell carcinoma tends to invade the renal vein, in which it will grow and shed tumor that can extend to the vena cava and the heart.

19. Renal cell carcinomas can secrete a variety of hormones leading to what symptoms?

    Polycythemia (erythropoietin), hypertension (renin), Cushing syndrome (corticosteroids), hypercalcemia (parathyroid hormone), and feminization or masculinization (gonadotropins)

20. What are the components of the WAGR syndrome?

    Wilms tumor, aniridia, genital anomalies, and mental retardation

21. What 3 elements are seen in the histology of Wilms tumor?
Metanephric blastema, epithelial elements, and stromal elements

22. The long-term survival of Wilms tumor patients can be how high?
While prognosis is variable, the long-term survival rates are up to 90%.

23. What are the risk factors for transitional carcinoma?
Cigarette smoking, aniline dye exposure, and phenacetin or cyclophosphamide exposure

24. The cysts of autosomal recessive polycystic kidney disease form in what structures?
The cysts are cortical and medullary cysts of the collecting ducts

25. Which genes are associated with adult (autosomal dominant) polycystic kidney disease?
PKD1 gene on chromosome 16 and PKD2 gene on chromosome 4

26. What vascular disease is associated with autosomal dominant polycystic kidney disease?
Berry aneurysms of the Circle of Willis

27. Acquired polycystic kidney disease is seen in what patient population?
Dialysis patients

28. What processes can lead to pre-renal failure?
Hypotensive states, structural lesions, and drug effects

29. What cardiac condition can be caused by renal failure?
Pericarditis

30. The impaired regulation of acid-base balance seen in renal failure is due to what process?
Decreased ability to excrete fixed-acid end products of metabolism

31. What endocrine functions of the kidney are disrupted by renal failure?
Activation of vitamin D, erythropoietin production

32. What is the underlying mechanism of pre-renal failure?

Decreased perfusion of the kidneys due to hypovolemia, dehydration, or congestive heart failure.

33. List some examples of acute intra-renal failure.

Glomerulonephritis, interstitial nephritis, ischemia, rhabdomyolysis, and sepsis

34. What are the 2 most common causes of chronic renal failure?

Uncontrolled hypertension and diabetes

35. The hyperkalemia of chronic renal failure is initially compensated for by increased secretion of what hormone?

Aldosterone

TOPIC 5: DIURETICS

1. For each description below, identify the type of diuretic as CAI (carbonic anhydrase inhibitor), loop, thiazide, or K^+-sparing.

Property	Diuretic
Causes hyperlipidemia	*Thiazide*
Blocks Na^+K^+ $2Cl^-$ pump	*Loop*
Used in acute mountain sickness	*CAI*
Hyperkalemic acidosis on overdose	*K^+-sparing*
Causes ototoxicity	*Loop*
Causes bicarbonaturia	*CAI*
Used in female hirsutism	*K^+-sparing (spironolactone)*
Blocks NA^+Cl^- pump	*Thiazide*

2. Identify whether each property below is for an ACEI, ARB, or both.

Property	Drug
Chronic cough	*ACEI*
↑ renin	*Both*
↑ angiotensin II	*ARB*
↑ angiotensin I	*ACEI*
Hyperkalemia	*Both*
Angioedema	*ACEI*
Teratogenic	*Both*
↓ aldosterone	*Both*

CHAPTER 8

REPRODUCTIVE MEDICINE

TOPIC 1: GAMETOGENESIS

1. When does spermatogenesis begin?

   puberty

2. Similar to the cerebral circulation, the testes have a *Blood-testes barrier* barrier. Why is this important?

   This protects against drugs and autoimmune dysregulation of the testes.

3. What cells form the blood-testis barrier? What germ cell is not protected by the barrier?

   Tight junctions between Sertoli cells; spermatogonia are not protected.

4. Diagram the basic sequence of spermatogenesis indicating whether each cell is diploid or haploid.

   Spermatogonia (2n) → primary spermatocytes (2n) → secondary spermatocytes (2n) → spermatids (1n) → spermatozoa (1n)

5. Diagram the basic sequence of folliculogenesis indicating whether each cell is diploid or haploid.

   Primordial follicle (2n) → primary follicle (2n) → mature (graafian) follicle (2n) → ovulation of secondary oocyte (2n) → fertilization (1n)

6. Fill in the number of chromosomes (e.g., 23 or 46) and the complement of DNA (1N, 2N, 4N) in the nucleus of germ cells in the table below.

	Karyotype
Spermatogonia	*46 single stranded chromosomes , 2n*
Primary spermatocytes	*46 double stranded chromosomes, 4n*
Secondary spermatocytes	*23 double stranded chromosomes, 2n*
Spermatids	*23 single stranded chromosomes, 1n*
Spermatozoa	*23 single stranded chromosomes, 1n*

7. *Dynein* is the ATPase protein associated with microtubules of the flagella and is necessary for normal motility.

8. What is the acrosome of the sperm derived from? *Golgi apparatus*

9. What is defective in sperm in Kartagener's syndrome? *Ciliary dynein*

10. What is a normal sperm count? *20 -40 million/mL*

11. How many days are required for sperm maturation? *75 days*

12. Where in the male does sperm mature? *Epididymis*

13. Which presumptive gametes develop closest to the basement membrane of a seminiferous tubule?
Spermatogonia

14. Sketch the hypothalamic-pituitary-gonadal axis in men. Indicate the cells influenced by the pituitary hormones and what each cell secretes to provide negative feedback regulation.

GnRH (hypothalamus—pulsatile secretion) → FSH & LH (anterior pituitary) → LH acts on Leydig cells to secrete testosterone, while FSH acts on Sertoli cells, which secrete inhibin for feedback regulation (primarily on FSH).

15. Name 2 pituitary hormones that would be elevated in the event of castration.

LH and FSH

16. Sketch the hypothalamic-pituitary-gonadal axis in women. Indicate the cells influenced by the pituitary hormones and what each cell secretes to provide negative feedback regulation.

GnRH (hypothalamus—pulsatile secretion) → FSH & LH (anterior pituitary) → LH acts on theca cells to secrete testosterone, while FSH acts on granulosa cells, which secrete inhibin for feedback regulation (primarily on FSH).

17. In a woman, when does the first secondary oocyte appear? *puberty*

18. In women, when does follicular atresia begin? *In utero*

19. What stage of gametogenesis are all oocytes in at birth? *Arrested in prophase of M1*

20. How many secondary oocytes are produced from a single primary oocyte? *1*

21. At what arrested stage of gametogenesis is an ovulated oocyte? *Secondary oocyte arrested in metaphase*

22. What event immediately precedes the completion of meiosis II in women?

Fertilization

23. _FSH_ stimulates the enzyme _aromatase_, which converts androgens into estrogens. This occurs in both the _Granulosa_ and _Sertoli_ cells.

24. What is the dominant hormone of the follicular phase, what cells secrete it, and what are the changes it evokes in the endometrium?

Granulosa cells secrete 17β-estradiol, which elicits growth of the endometrium (proliferative state).

25. What is the dominant hormone of the luteal phase, what secretes it, and what are the changes it evokes in the endometrium?

The corpus luteum secretes progesterone, which increases the vascularization and secretory capability of the endometrium (secretory phase of endometrium).

26. Near mid-cycle, estradiol exerts a _Positive_ feedback on the anterior pituitary, which induces a surge in _LH_ and _FSH_, resulting in ovulation.

27. A 23-year-old woman is being evaluated for infertility. Her BMI is 32 and plasma glucose 160 mg/dL. Hirsutism is noted. She indicates a lack of a regular menstrual cycle. This patient likely has _polycystic ovarian_ syndrome. Her anterior pituitary hormones show an elevated _LH_ and a reduced _FSH_.

28. Describe the hormonal changes and some key alterations experienced by women undergoing menopause.

Loss of follicular development results in a significant drop in estrogen resulting in elevated levels of FSH and LH. Females often experience hot flashes, vaginal drying, nights sweats, and osteoporosis.

29. What are some possible causes of anovulation?

Menopause, premature ovarian failure, PCOS, Asherman syndrome, hyperprolactinemia, thyroid disease, eating disorders, excessive exercise, and Cushing's syndrome

30. Estrogen treatment for some of the symptoms of menopause often includes giving *Progesterone* to reduce the risk of *uterine* cancer.

31. Indicate the source of maternal hormones in the first, second, and third trimesters, and include the source of these hormones.

First trimester: Estrogen and progesterone are secreted by the corpus luteum which remains viable because of human chorionic gonadotropin (hCG). In the second and third trimester, the placenta takes over the secretion progresterone. Estrogens, particularly estriol, are produced by aromatization (placenta expresses aromatase) of adrenogens supplied by the fetal adrenal gland and liver. The placenta also secretes human placental lactogen (hPL), which acts similarly to growth hormone, resulting in elevated maternal blood glucose and free fatty acids. Estriol stimulates the release of prolactin from the anterior pituitary.

TOPIC 2: FERTILIZATION AND EMBRYOGENESIS

1. What cell is formed at fertilization?
   zygote

2. What is occurring during capacitation?
   Uterine fluid removes glycoproteins covering the head of sperm

3. What must a capacitated sperm pierce for fertilization to occur?
   Zona pellucida

4. On what day does implantation typically occur?
   Day 6

5. Name 2 risk factors for a tubal ectopic pregnancy.
   Pelvic inflammatory disease; endometriosis

6. Name 3 signs of a patient with an ectopic tubal pregnancy.
   Vaginal bleeding, abdominal pain, fluid within abdomen

7. Name the 2 components of the blastocyst.
   Embryoblast and trophoblast

8. What cells produce human chorionic gonadotropin (hCG), and what is its function?
   Syncytiotrophoblast cells; maintain progesterone output of corpus luteum

9. What 2 cell layers make up the embryonic disk in week 2?
   Epiblast and hypoblast

10. What cells come in direct contact with fetal blood in the placenta?
    Syncytiotrophoblast cells

11. What is specifically detected in the urine in a pregnancy test?
Beta hCG

12. What might lower than normal levels of hCG indicate?
Spontaneous abortion or ectopic implantation

13. What might higher than normal levels of hCG indicate?
Multiple pregnancies or molar pregnancies

14. What germ layers are present in the embryo by week 3?
Ectoderm, mesoderm, endoderm

15. What is the name of the process that establishes the 3 germ layers?
Gastrulation

16. Name the 3 germ layers.
Ectoderm, Mesoderm, Endoderm

17. What does a sacrococcygeal teratoma develop from?
Remnants of primitive streak

18. In the list below, name the germ layer origin of the following structures: E for ectoderm, M for mesoderm, or EN for endoderm.

    (A) Spleen *M*
    (B) Urinary epithelium *EN*
    (C) Anterior pituitary *E*
    (D) Thymus *EN*
    (E) Heart *M*
    (F) Notochord *M*
    (G) Tracheal epithelium *EN*
    (H) Connective tissue *M*
    (I) Inner ear *E*
    (J) Liver parenchyma *EN*
    (K) Lung epithelium *EN*
    (L) Neural tube *E*
    (M) Submandibular glands *EN*
    (N) Auditory tube *EN*
    (O) Kidneys *M*
    (P) Lower vagina *EN*
    (Q) Thyroid epithelium *EN*

19. Name 2 organ systems that develop in week 4.

    Nervous, Cardiovascular

TOPIC 3: PREGNANCY

1. What is the most common cause of a spontaneous abortion in the first trimester?

   Chromosomal abnormality

2. What medication is used to treat stable ectopic pregnancies?

   Methotrexate

3. Spontaneous abortions in the second trimester can be due to what processes?

   Trisomies, maternal/fetal infections, maternal anatomic abnormalities

4. What is a common placental cause of painless vaginal bleeding? Painful vaginal bleeding?

   Painless = placenta previa; painful = placental abruption

5. What term is used when the umbilical cord runs over the inner cervical os?

   Vasa previa (can cause significant bleeding and possible fetal demise)

6. The presence of what condition distinguishes eclampsia from preeclampsia?

   Seizures (or coma)

7. What does the mnemonic in HELLP syndrome stand for?

   Hemolysis, Elevated Liver enzymes, Low Platelets

8. A pregnant woman who develops preeclampsia at less than 20 weeks would be most likely to have what form of pregnancy?

   Molar pregnancy

9. What are potential causes of polyhydramnios? Oligohydramnios?

   Polyhydramnios: Idiopathic etiology, esophageal atresia, neural tube defects, fetal polyuria, and maternal diabetes.

10. Describe the milk let-down reflex.

    Suckling of the breasts activates sensory afferent neurons that inhibit dopamine release from the hypothalamus, which in turn increases the secretion of prolactin. Prolactin stimulates milk production in the breasts. In addition, oxytocin is released from the posterior pituitary to contract the myoepithelial cells of the breast causing the ejection of milk.

TOPIC 4: NORMAL AND ABNORMAL DEVELOPMENT I

1. List the 4 hormones/factors required for normal sexual differentiation in men and their basic action.

   Sex determining region of Y (SRY) initiates the production of 1) testes determining factor (TDF), which promotes formation of the testes. The testes secrete 2) testosterone, which causes growth and differentiation of the Wolffian ducts into male internal genitalia. The testes also release 3) Mullerian-inhibitory factor (MIF), which causes regression of the Mullerian ducts. Finally, 4) 5-alpha reductase converts testosterone into dihydrotestosterone, which is needed for differentiation of the male external genitalia.

2. _____*Androgen insensitivity*_____ syndrome is a condition in which a genetic male exhibits the sexual external phenotype of a female at birth.

3. Where are the testes found in androgen insensitivity syndrome? What would be the findings on pelvic examination?

   Testes are found within the labia majora; no uterus or uterine tubes, vagina ending in blind pouch

4. An abnormal opening of the urethra on the dorsal side of the penis is called _____*Epispadias*_____.

5. Uterine didelphys is due to a failure of fusion of what structures?

   Paramesonephric ducts (Mullerian ducts)

6. Precocious puberty is defined to be the appearance of secondary sex characteristics before what age in girls?

   Age 8 in girls

   In boys?

   Age 9 in boys

7. What are possible causes of central precocious puberty?

   Idiopathic processes that cause early initiation of pulsatile GnRH release; CNS abnormalities such as tumor, inflammation, and trauma; and congenital hypothalamic hamartomas.

8. Besides the congenital adrenal hyperplasias, what other conditions can cause peripheral precocious puberty?

   Gonadal tumors, adrenal tumors, McCune-Albright syndrome, and hypothyroidism

9. What bone disease is associated with McCune-Albright syndrome?

   Polyostotic fibrous dysplasia (also see unilateral café-au-lait spots)

TOPIC 5: NORMAL AND ABNORMAL DEVELOPMENT II

1. What are 3 main categories of delayed puberty?

   Hypergonadotropic hypogonadism, hypogonadotropic hypogonadism, and constitutional delay

2. What changes in hormone levels are seen in hypergonadotropic hypogonadism?

   Low sex steroids and high LH/FSH

3. Turner syndrome patients have an increased risk for what ovarian tumor?

   Gonadoblastoma

4. What is the most common genetic composition for mixed gonadal dysgenesis?

   Mosaic 45, X/46, XY

5. What hormonal changes are seen in Klinefelter's syndrome?

   Decreased inhibin, decreased testosterone, increased LH/FSH, and increased estrogen

6. Patients with 47, XYY have a 1-2% risk of what psychiatric disorder?

   Antisocial personality disorder

7. What hormonal changes are seen in androgen insensitivity syndrome?

   Increased testosterone, increased estrogen, and increased LH

8. What conditions can cause hypogonadotropic hypogonadism?

   Idiopathic causes, Kallmann syndrome, congenital hypopituitarism, and eating disorders

9. What is Mayer-Rokitansky-Küster-Hauser syndrome?

   Complete/partial absence of upper 1/3 of vagina, uterus or cervix; sometimes with absence of kidney

10. What endocrine changes are seen in polycystic ovary syndrome?

Increased LH, hyperandrogenism, amenorrhea or oligomenorrhea, and insulin resistance

11. Considering the more common congenital adrenal hyperplasias, which have increased sex hormones? Decreased?

21-hydroxylase deficiency and 11 β-hydroxylase deficiency have increased sex hormones accompanied by masculinization and amenorrhea. 17 α-hydroxylase deficiency has decreased sex hormones and decreased DHT.

12. 5-α-reductase deficiency impairs the body's ability to convert _____*testosterone*_____ to _____*dihydrotestosterone (DHT)*_____.

TOPIC 6: ANATOMY AND PHYSIOLOGY

1. Name the 3 anatomic positions of the uterus in the pelvis.
   Anteverted, mid position, retroverted

2. Name the 3 parts of the uterine tube.
   Fundus, body, cervix

3. What kind of epithelium lines the uterine tube? *Ciliated columnar*

4. What 3 ligaments hold the uterus in place in the pelvis?
   Broad, Round and Uterosacral ligaments

5. What vessels course in the suspensory ligaments of the ovary? *Ovarian*

6. Into what vein do the right and the left ovarian veins drain? *R- IVC L- L renal vein*

7. What structures are contained in the broad ligament? *Uterine blood supply*

8. What structures are contained in the cardinal ligaments?
   Ureter, Uterine artery and vein

9. What embryonic structure becomes the round ligament?
   Remnant of the gubernaculum that travels through the inguinal canal

10. What different types of epithelium line the endocervix and the ectocervix?
    Endocervix- columnar; ectocervix- squamous

11. What is the name of the cervical zone where cervical cancers commonly develop?

Transformation zone where active metaplasia occurs

12. What muscle forms the pelvic floor?

Pelvic diaphragm; Levator ani and coccygeus muscles

13. What diaphragm is found in the perineum?

Urogenital

14. Name distinct structures that drain into the periaortic nodes, the hypogastric nodes, and the inguinal lymph nodes.

Gonads drain to pariaortic nodes, uterus and upper third of vagina drain to hypogastric nodes. Vulva, scrotum and lower one third of vagina drain to inguinal nodes.

15. Fill in the nerves involved in male sexual reflexes and their actions.

Event	Nerves Involved	Actions
Erection	*Pelvic splanchnic*	NO release and vascular engorgement
Emission	*Lumbar splanchnic*	Delivery of sperm and seminal fluid to prostatic urethra; secretion of lubricating glands
Ejaculation	*Pudendal*	Climax; contraction of bulbospongiosus to expel sperm and seminal fluid through urethra

16. Name a systemic cause of erectile dysfunction.

Medication side effects or systemic disease such as diabetes

17. Name 2 types of medications that could cause erectile dysfunction.

Antihypertensives, CNS depressants, Antidepressants and H2-receptor antagonists

18. What is the mechanism of action of sildenafil?

Inhibits breakdown of cGMP → increases vasodilation.

TOPIC 7: FEMALE TRACT PATHOLOGY I

1. What virus is associated with vulvar intraepithelial neoplasia?

   Human papilloma virus (HPV)

2. What is the most common form of invasive vulvar carcinoma? What are the less common forms?

   Squamous cell carcinoma is the most common form of invasive vulvar cancer; melanoma, basal cell carcinoma, and adenocarcinoma can also occur.

3. What important difference is present between Paget's disease of the breast and Paget's disease of the vulva?

   Paget's disease of the breast is often associated with an underlying tumor, while Paget's disease of the vulva is not typically associated with an underlying tumor.

4. Vaginal squamous cell carcinoma typically occurs in what part of the vagina?

   Vaginal squamous cell carcinoma typically involves the upper 1/3 of the vagina.

5. Clear cell adenocarcinoma of the vagina was historically associated with *in utero* exposure to what drug?

   Diethylstilbestrol (DES)

6. A polypoid grape-like soft tissue mass protruding from the vagina of a young girl is most likely what tumor?

   Embryonal rhabdomyosarcoma (may express desmin and show cross-striations due to muscle cell origin)

7. Which 2 types of HPV are particularly likely to cause cervical cancer?

   Types 16 and 18 (31 and 33 to a lesser extent)

8. What is the progression in development of invasive cervical squamous cell carcinoma?

   Cervical intraepithelial neoplasia to carcinoma in situ to invasive squamous cell carcinoma

9. What term is used for a cervical squamous cell with a perinuclear halo?

   koilocyte

10. Lymphatic spread from cervical cancer occurs to which nodes?

    Pelvic and perioaortic nodes

11. What conditions can cause increased risk of endometrial carcinoma related to increased estrogen exposure?

    Early menarche, late menopause, nulliparity, obesity, chronic anovulation, estrogen producing tumor, hormone replacement therapy

12. Endometrial carcinoma is also associated with what polyposis syndrome?

    Lynch syndrome (HNPCC)

13. How is endometrial hyperplasia classified?

    Most associated → least associated: complex hyperplasia with atypia → simple hyperplasia with atypia → complex hyperplasia → simple hyperplasia.

14. What is the most common tumor of the uterus? What is the associated histology?

    Leiomyoma; whorled pattern of smooth muscle bundles

15. At what site would a leiomyoma that causes menorrhagia most likely be located?

    Submucosal

16. What term would be used to describe a uterine sarcoma that contains bone and cartilage?

    Heterologous (homologous contain only uterine tissues)

17. What are common sites of endometriosis?

    Serosal surface of tubes or ovaries and pelvic peritoneum (posterior cul-de-sac)

18. What process would most likely cause a small patch of blue discoloration on the serosal surface of the pelvic cavity?

Endometriosis

19. Chocolate cysts of the ovaries are indicative of what condition?

Endometrial tissue in the ovaries (endometriomas)

20. High levels of what hormone can be generated by gestational trophoblastic disease?

β-*hCG*

21. From which parent does the genetic material of a complete mole derive from?

Just the sperm (usually 46,XX, minority 46,XY)

22. What is the risk of choriocarcinoma developing from a complete mole?

2%

23. What karyotypes do partial moles have?

69, XXX; 69, XXY; 69, XYY (fertilization by two sperm)

24. How common is fallopian tube carcinoma?

Less than 1% of gynecologic cancers

TOPIC 8: FEMALE TRACT PATHOLOGY II

1. What type of cyst would produce a deeply yellow, thick wall on cross-section of an ovary?

   Corpus luteum cyst

2. How are ovarian cancers classified?

   Epithelial tumors, germ cell tumors, gonadal stromal tumors, non-specific mesenchymal tumors, and metastases to the ovaries

3. What is the most common malignant ovarian tumor?

   Cystadenocarcinoma

4. What is a serum marker that can be used to monitor recurrence or response to therapy with cystadenocarcinoma?

   CA-125 (also can be positive with other epithelial neoplasms)

5. What tumor types are classified as germ cell tumors?

   Dysgerminoma, gonadoblastoma, endodermal sinus tumor, embryonal carcinoma, choriocarcinoma, and teratoma

6. What ovarian tumor is similar to male seminoma?

   Dysgerminoma (can sometimes produce hCG)

7. Gonadal dysgenesis and Turner's syndrome are associated with an increased risk for which ovarian tumor?

   Gonadoblastoma

8. Elevation of what serum marker is characteristic of yolk sac tumors (endodermal sinus tumors)?

   α-fetoprotein

9. What characteristic histologic feature is found in yolk sac tumors?

   Schiller-Duvall bodies (papillary structures around central blood vessels)

10. Elevations of what 2 serum markers are characteristic of embryonal carcinoma?
    α-fetoprotein and β-hCG

11. Choriocarcinoma arises from which 2 types of cells?
    Cytotrophoblasts and syncytiotrophoblasts

12. Which type of teratoma is usually benign in a female?
    Mature cystic teratoma

13. Struma ovarii is a monodermal teratoma of the ovary that produces what type of tissue?
    Thyroid tissue – may produce hyperthyroidism

14. What are the gonadal stromal tumors?
    Granulosa cell, theca cell, Sertoli cell, and Leydig cell tumors

15. "Coffee-bean"–shaped secretory spaces suggest which gonadal stromal tumor?
    The structures are Call-Exner bodies, and they are a feature of granulosa cell tumors.

16. Sertoli–Leydig cell tumors can produce what hormones?
    Androgens that can cause virilization

17. A Krukenberg tumor is a metastatic tumor to the ovary most commonly from what source?
    Stomach (rarely from the breast)

TOPIC 9: BREAST ANATOMY AND PATHOLOGY

1. What is the embryonic germ layer origin of breast tissue? *Ectoderm*

2. At puberty, what causes glandular proliferation of breast tissue? *Estrogen*

3. What kind of ducts drain into the area of the nipple? *Lactiferous ducts*

4. What does the breast produce immediately postpartum? *Colostrum*

5. Which bacteria commonly cause acute mastitis?
   Staphylococcus aureus and Streptococcus

6. Mammary duct ectasia most frequently occurs in what patient population?
   Multiparous women in 5th decade

7. Fat necrosis can cause calcifications in the breast that suggest what disease process?
   Breast cancer

8. What are some benign breast diseases?
   Fibrocystic disease, fibroadenomas, phyllodes tumors, papillomas

9. What is the most common breast disorder in premenopausal women?
   Fibrocystic disease

10. What would papillary proliferation of ductal epithelium seen in fibrocystic disease be called?
    Epithelial hyperplasia; some types have increased risk of cancer

11. What is the most commonly diagnosed breast mass in young women?
    Fibroadenoma

12. Is cystosarcoma phyllodes a benign or a malignant tumor?
    Mostly benign, but some behave malignantly

13. Clear, unilateral spontaneous nipple discharge from a single duct suggests what benign breast disease?
    Intraductal papilloma

14. What are some important breast cancer risk factors?
    Nulliparity or first child after age 34, early menarche, late menopause, obesity, and family history of breast cancer

15. Distinguish between BRCA1 and BRCA2.
    BRCA1 mutation has a nearly 100% increased lifetime risk of breast cancer and also has an increased risk of ovarian cancer; BRCA2 has increased risk of breast cancer (but not 100%) and does not increase the risk of ovarian cancer.

16. Which quadrant of the breast has the highest frequency of breast cancer?
    Upper outer quadrant

17. When a breast mass becomes "fixed," what does this suggest about where it has spread?
    If the mass becomes "fixed", it has typically spread to the thoracic fascia.

18. What type of mass does invasive lobular carcinoma usually produce?
    Does not typically form a mass or lump. May be described as a thickening or fullness of the breast.

19. What part of the breast does Paget's disease usually involve?
    Nipple and areola, with malignant "halo cells" underlying the epidermal lesion

20. A breast duct containing a duct epithelial proliferation with cheesy necrotic tissue is likely to be what? _____*Comedocarcinoma*_____

21. A breast cancer with sheets of large, pleomorphic cells showing lymphocytic infiltration would most likely be what type? _____*Medullary carcinoma*_____

22. What does a "peau d'orange" appearance of a breast suggest?

    Peau d'orange is French for 'orange skin' and is named because the skin of the breast resembles that of an orange peel. The condition is suggestive of underlying dermal lymphatic invasion by carcinoma – inflammatory carcinoma

23. What medication is an estrogen-receptor antagonist that is useful in breast cancer therapy?

    Tamoxifen

TOPIC 10: MALE TRACT PATHOLOGY

1. What term is used when the prepuce cannot be retracted over the glans penis?
   Phimosis

2. Squamous cell carcinoma of the penis in men is most likely to be related to what viruses?
   HPV 16 and 18

3. What is the most common cause of acute prostatitis? *E. coli*

4. What type of drug can relax the smooth muscle in the prostate and bladder neck to partially compensate for poor urine flow in patients with benign prostatic hyperplasia?
   Alpha-adrenergic antagonists, e.g., tamsulosin

5. In what part of the prostate do most prostatic carcinomas arise? *Peripheral zone*

6. Are prostate metastases to bone usually blastic or lytic? *Blastic*

7. A football player who experiences sudden, excruciating testicular pain on one side after being tackled might have what condition? *Testicular torsion*

8. What causes hydrocele?
   Hydrocele is most commonly caused by a slight patency of the processus vaginalis

9. Dilations of the testicular vein tributaries in the pampiniform plexus can produce what condition?
   Varicocele

10. Which testicular tumor is unusual in that it contains cells derived from ectoderm, mesoderm, and endoderm?
    Teratoma

11. What tumor marker is useful in seminoma?
    Placental alkaline phosphatase

12. What percentage of embryonal carcinomas of the testes have metastasized at the time of diagnosis?
    30%

13. What extratesticular manifestation may be caused by choriocarcinoma of the testes?
    Gynecomastia

14. In what male patient population is yolk sac tumor seen?
    Children and infants

15. When teratoma in testes is compared to teratoma in ovaries, which is more commonly malignant?
    Teratoma is more often malignant in males.

16. What is the most common testicular cancer in elderly men?
    Lymphoma

17. What percentage of pre-pubertal boys experience gynecomastia?
    70% (Usually transient)

TOPIC 11: SEX HORMONE PHARMACOLOGY

1. The key difference between tamoxifen and raloxifene occurs on what organ?

   Endometrium and tamoxifen increase the risk of endometrial cancer; raloxifene does not

2. What drug is used to stimulate ovulation in the treatment of infertility?

   Clomiphene

3. List the drug that matches the description below.

Property	Drug
Relax uterus	β_2 *agonist (terbutaline)*
Aromatase inhibitor	*Anastrazole*
5-α-reductase inhibitor	*Finasteride*
Blocks testosterone receptors	*Flutamide*
GnRH analog	*Leuprolide*
PGE_1 analog for erectile dysfunction	*Alprostadil*

TOPIC 12: SEXUALLY TRANSMITTED INFECTIONS

1. Add the symptoms, site of latency, and treatment for HSV-1 and HSV-2.

Virus	Symptoms	Site of Latency	Treatment
HSV-1	*Vesicular lesions in the oral mucosa*	*Dorsal root ganglia*	*Acyclovir*
HSV-2	*Vesicular lesions on the genitals*	*Sacral ganglia*	*Acyclovir*

2. Name the diagnostic cell forms found in herpesvirus infections.

   Giant multinucleated cells.

3. Visible cauliflower lesions due to HPV are most commonly due to which 2 viral serotypes?

   6,11

4. Genital cancers, including cervical cancer, are most commonly due to which 2 (or 4) serotypes? List 2 if possible.

   16, 18 (31,33)

5. List the causative agent, Gram stain reaction, and shape of syphilis.

   Treponema pallidum, gram negative spirochete

6. List at least 1 symptom for each stage of syphilis.

Stage of Syphilis	Symptom(s)
Primary	*Chancre*
Secondary	*Copper colored rash, condylomata lata, alopecia*
Latent	*Tabes dorsalis, gummas, aortic dissection*

7. List the screening and confirmatory tests for syphilis.

   Non-treponemal antibody tests (RPR, VDRL, etc) and FTA-ABS fluorescent treponemal antibody adsorbed

8. Place an "X" next to each symptom that occurs in congenital syphilis. If you can, list the congenital diseases with which the other symptoms are observed.

Symptoms	Congenital Syphilis
Cataracts	*Rubella*
Saddle nose	*X*
Snuffles	*X*
Blueberry muffin baby (thrombocytic purpura)	*CMV*
PDA	*B19*
8th cranial nerve damage	*X*
Hydrops fetalis	*B19*

9. For each of the following statements, place a "T" if the statement applies to gonorrhea or "F" if the statement does not apply to gonorrhea.

   - Causes urethritis in men *T*
   - Does not lead to infertility in women *F*
   - Is usually asymptomatic in women *T*
   - Can cause Fitz-Hugh-Curtis syndrome *T*
   - Causes an ulcerative lesion on the genitals *F*
   - Gram-negative diplococci on urethral Gram stain *T*

10. Name the special culture media used to isolate *Neisseria gonorrhoeae*.

    Thayer-Martin

    Name the treatment for *Neisseria gonorrhoeae*. *Ceftriaxone*

11. Fill in the blank with a > or <.

    Chlamydia trachomatis serotypes D–K are ___>___ common than *Neisseria gonorrhoeae*.

    Name the treatment for *Chlamydia trachomatis* serotypes D–K. ___doxycycline or azithromycin___

12. List the differential diagnosis for bacterial vaginosis. (list 3)

    - *Trichomonas vaginalis*
    - *Gardnerella vaginalis*
    - *Candida albicans*

13. Name the treatment for vaginitis. ___Metronidazole or tinidazole___

14. List the Gram reaction and shape for *Haemophilus ducreyi*. ___Gram negative coccobacilli___

    Discuss the diagnosis of *(H) ducreyi*.

    diagnosis of exclusion, exclude HSV-2 and syphilis

15. List the serotypes of *Chlamydia trachomatis* that are associated with LGV.

    L1, L2, and L3