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To my family and friends, for their love and encouragement; and to my parents, for being an example of everything I want to be.

—John

To my mother and my family.

—Dan
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Preface

Déjà Review™ USMLE Step 1 has been scrutinized and edited to produce a second edition that is even higher yield and easier to use than the first. Outstanding medical students who have recently taken Step 1 have revised the original text to ensure the material covered herein is complete and current. The authors, now with a combined 30 years of experience in the medical field, have also edited the manuscript to emphasize the relevant core concepts covered in the USMLE Step 1 examination. We are confident that our efforts have produced one of the most useful guides for Step 1 review available today.

The main objective of a medical student preparing for Step 1 of the United States Medical Licensing Examination (USMLE) is to commit a vast body of knowledge to memory. Having recently prepared for Step 1, we realize how daunting this task can be. We feel there are two main principles that will allow you to be successful in your preparations for Step 1: (1) repetition of key facts and (2) using review questions to gauge your comprehension and memory. The Déjà Review™ series is a unique resource that has been designed to allow you to review the essential facts and determine your level of knowledge on the subjects tested on Step 1. We also know, from experience, that building a solid foundation in the basic sciences will allow you to make a smooth transition into the clinical years of medical school.

ORGANIZATION

All concepts are presented in a question and answer format that covers the key facts on hundreds of commonly tested USM LE Step 1 topics. The material is divided into chapters organized by body systems. Special emphasis has been placed on the molecular and genetic basis of pathology, as this area has become increasingly emphasized in recent examinations. This question and answer format has several important advantages:

- It provides a rapid, straightforward way for you to assess your strengths and weaknesses.
- It allows you to efficiently review and commit to memory a large body of information.
- It offers a break from tedious, convoluted multiple-choice questions.
- The “Make the Diagnosis” section exposes you to the prototypic presentation of diseases classically tested on the USMLE Step 1.
• It serves as a quick, last-minute review of high-yield facts.

The compact, condensed design of the book is conducive to studying on the go, especially during any downtime throughout your day.

HOW TO USE THIS BOOK

This text has been sampled by a number of medical students who found it to be an essential part of their preparation for Step 1, in addition to their course examinations. Remember, this text is not intended to replace comprehensive textbooks, course packs, or lectures. It is simply intended to serve as a supplement to your studies during your first 2 years of medical school and throughout your preparation for Step 1. We encourage you to begin using this book early in your first year to reinforce topics covered in your course examinations. We also recommend having the book spiral bound to make it more portable and easier to use outside of the library or classroom. You may cover up the answers with the included bookmark and quiz yourself or even your classmates. For a greater challenge, try covering up the questions!

However you choose to study, we hope you find this resource helpful throughout your pre-clinical years and during your preparation for the USMLE Step 1. Best of luck!

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CHAPTER 1
Basic Principles

MOLECULAR BIOLOGY, BIOCHEMISTRY, AND GENETICS

DNA, Genes, and Chromosomes

Which nucleotide bases are purines and which are pyrimidines?
“CUT the PY”: Cytosine, Uracil, and Thymine = PYrimidines; “PURe As Gold”:
PURines = adenine and guanine

Which proteins make up the core of a nucleosome?
Histones: H2A, H2B, H3, and H4

Which proteins are associated with DNA between nucleosomes?
Histone H1

Name the type of mutations described below:
Type of mutation that does not result in a change in amino acid sequence
Silent
Type of mutation that results in a change in amino acid sequence
Missense
Type of mutation that results in a stop codon
Nonsense “NO sense”
Type of mutation that changes the reading frame
Frameshift
Type of mutation in which a portion of DNA is lost
Deletion
Type of mutation in which a single base is exchanged
Point

Name the type of cytogenetic disorders described below:
Failure of chromosomes to disjoin properly during cell division
Nondisjunction
Loss of a portion of a chromosome
Deletion
Two internal chromosomal breaks with inverted reincorporation of a portion of the chromosome
Inversion
Single breaks in two chromosomes resulting in the exchange of segments between chromosomes without loss of genetic material
Balanced reciprocal translocation
Single breaks in two acrocentric chromosomes resulting in one large chromosome and one small chromosome accompanied by the loss of some genetic information, hereditary form of Down syndrome
Robertsonian translocation
Mitotic error in early development leading to the development of two karyotypically distinct populations of cells in an organism
Mosaicism
What term is used to describe the AT-rich sequences in the genome where DNA replication begins?
Origin of replication

DNA Replication, Transcription, and Translation

Name the protein(s) involved in replication or DNA repair with the functions listed below:

Stabilize single-stranded DNA
Single-stranded DNA-binding proteins
Recognition of AT-rich sequences at the origin of replication and separation of DNA strands in bacteria (prokaryotes)
DnaA protein
Unwinding DNA double helix
DNA helicases
Prevention of supercoiling during replication
DNA topoisomerases
Placement of RNA primer at site where replication is initiated
Primase, and an RNA polymerase
Removal of RNA primers from DNA synthesized discontinuously
DNA polymerase I (specifically, the 5’-3’ exonuclease activity)
DNA chain elongation in prokaryotes
DNA polymerase III
Proofreading of newly synthesized DNA strand
DNA polymerase III (specifically, the 3’-5’ exonuclease activity)

Repair UV damage to DNA
UV-specific endonuclease, exonuclease, and DNA ligase

Removal of damaged bases from DNA
Apurinic or apyrimidinic endonuclease, exonuclease, and DNA ligase

What term is used to describe the DNA strand synthesized continuously toward the replication fork?
Leading strand

What term is used to describe the DNA strand synthesized discontinuously away from the replication fork?
Lagging strand

What are the three stop codons?
UGA, UAA, UAG (U Go Away, U Are Away, U Are Gone)

In which direction are DNA and RNA synthesized?
5’ → 3’

What is the start codon?
AUG

Name the type of RNA responsible for each of the following functions:
Largest RNA molecule
mRNA

Most abundant type of RNA
rRNA

Smallest RNA molecule
tRNA

Portion of RNA transcript encoding information for protein synthesis
Exons (“exons are expressed”)

Portion of RNA transcript that is found between sequences of RNA encoding information for protein synthesis
Introns

Type of RNA covalently bound to a single amino acid
tRNA

Name the term used to describe the region of genomic DNA where RNA polymerase and transcription factors bind to regulate transcription:
Promoter

Name the term used to describe the region of genomic DNA where transcription factors activators bind to enhance transcription:
Enhancer

Name the term to describe the region of genomic DNA where repressors bind.
Name the enzyme responsible for each of the following functions:

- Synthesis of rRNA
  RNA polymerase I
- Synthesis of mRNA
  RNA polymerase II
- Synthesis of tRNA
  RNA polymerase III

Name three major regulatory mechanisms of transcription in eukaryotes:

1. Regulation by transcription factors at the level of the promoter
2. Regulation by histones binding to specific genomic regions
3. Regulation of DNA structure (including methylation, gene rearrangement, and amplification)

What genetic structure regulates transcription in prokaryotes?

An operon

Name the elements of an operon responsible for each of the following functions:

- Region where proteins bind to enable transcription
  Promoter region
- Molecule that binds at the promoter
  Activator or repressor
- Sequence in DNA where regulatory protein bind
  Operator
- Molecule that binds the operator to regulate transcription
  Repressor

What are three modifications made to an RNA transcript before it leaves the nucleus?

1. 5’ Capping with 7-methylguanosine
2. 3’ Polyadenylation
3. Splicing of introns

Which small molecule provides the energy for charging a tRNA with its amino acid?

Adenosine triphosphate (ATP)

Which small molecule provides the energy for binding tRNA to the ribosome and for translocation?

Guanosine triphosphate (GTP)

Which molecules, central to the discipline of molecular biology, recognize and cleave specific sequences of a DNA molecule?

Restriction enzymes
Molecular Biology Techniques

Name the molecular biology techniques described below:

Method of separating molecules based on movement through a gel placed in an electric field
Gel electrophoresis

Technique for detecting specific DNA sequences using restriction enzymes and a radiolabeled DNA probe
Southern blot

Technique for detecting specific RNA sequences using restriction enzymes and a radiolabeled DNA probe
Northern blot

Technique for detecting specific protein sequences using radiolabeled antibodies
Western blot

A rapid technique for amplifying a specific DNA sequence in vitro
Polymerase chain reaction

Technique for detecting different alleles at a gene of interest using restriction enzymes
Restriction fragment length polymorphism analysis

Technique for detecting the presence of antigen or antibody using radiolabeled antibodies
Radioimmunoassay (RIA)

Technique for detecting the presence of antigen or antibody using antibodies linked to enzymes with detectable activity
Enzyme-linked immunosorbent assay (ELISA)

Inherited Diseases

Name inheritance patterns described below:

Twenty-five percent of offspring from two carrier parents affected
Autosomal recessive (AR)

Commonly cause defects in structural genes
Autosomal dominant (AD)

Commonly cause defects in enzymes
AR

Defect seen in multiple generations in both sexes
AD
Defects not typically seen in consecutive generations
AR
Disease is not observed in females.
X-linked (XL) recessive
Disease is transmitted by mother.
Mitochondrial inheritance
Half of male offspring from affected mother will manifest disease.
XL recessive
Disease manifestations commonly present after puberty.
AD
What are the conditions for a population to be in Hardy-Weinberg equilibrium?
1. No mutation at locus of interest
2. No selection for allele at locus of interest
3. Random mating
4. Closed population (no migration)
What are the two Hardy-Weinberg equations?
1. \[ p^2 + 2pq + q^2 = 1 \]
2. \[ p + q = 1 \] (p and q are separate alleles and pq is the heterozygote frequency)
Name the disease or condition associated with each of the following statements:
Lack of UV-specific endonuclease causing dry skin and malignant melanoma
Xeroderma pigmentosa
Lack of aldolase B causing hypoglycemia, jaundice, and cirrhosis
Fructose intolerance
Lack of fructokinase causing fructosmia and fructosuria
Essential fructosuria
Lack of galactose-1-phosphate uridyltransferase causing cataracts, hepatosplenomegaly (HSM), and mental retardation
Galactosemia
Deficiency of lactase causing bloating, flatulence, and diarrhea on consumption of dairy products
Lactose intolerance
Lactic acidosis and neurologic deficits in an alcoholic
Pyruvate dehydrogenase deficiency
Hemolytic anemia in patients of Mediterranean descent after eating fava beans or taking antimalarial medication
Glucose-6-phosphate dehydrogenase deficiency
Hemolytic anemia due to deficiency in glycolysis
Hexokinase, glucose-phosphate isomerase, aldolase, triose-phosphate isomerase, phosphate glycerate kinase, enolase, or pyruvate kinase deficiency

Inappropriate hepatocellular accumulation of glycogen caused by a deficiency of glucose-6-phosphatase, associated with severe fasting, hypoglycemia, lactic acidosis, hyperlipidemia, and impaired fructose metabolism

von Gierke disease/type I glycogen storage disease

Inappropriate accumulation of glycogen in the liver, heart, and muscle caused by a deficiency of lysosomal α-1,4-glucosidase, resulting in cardiomegaly

Pompe disease/type II glycogen storage disease

Inappropriate accumulation of glycogen in liver and heart due to deficiency of α-1,6-glucosidase, a debranching enzyme often leading to muscular hypotonia

Cori disease/type III glycogen storage disease

Inappropriate accumulation of glycogen in skeletal muscle fibers due to deficiency of glycogen phosphorylase, leading to myalgia and myoglobinuria with exercise

McArdle disease/type V glycogen storage disease

Defect in cystathionine synthase leading to the presence of homocysteine in the urine

Homocystinuria

Defect of renal tubular amino acid transporter for cysteine, ornithine, lysine, and arginine

Cystinuria

Inadequate catabolism of branched-chain amino acids (Ile, Val, and Leu) due to lack of α-ketoacid dehydrogenase leading to mental retardation

Maple syrup urine disease

Lack of phenylalanine hydroxylase (PAH) leading to a buildup of phenylalanine resulting in mental retardation, hypopigmentation, eczema, and a mousy odor

Phenylketonuria (can also get Phe buildup due to deficiency of tetrahydrobiopterin, BH4, cofactor of PAH)

Lack of homogentisic acid oxidase leading to a buildup of homogentisate, causing darkening of the urine and connective tissues

Alkaptonuria

Lack of tyrosinase leading to a lack of melanin

Albinism

Lack of adenosine deaminase inhibits DNA synthesis by causing the accumulation of metabolites in the purine salvage pathway; one of the causes of severe combined immunodeficiency syndrome

Adenosine deaminase deficiency
Lack of hypoxanthine-guanine phosphoryltransferase (HGPRTase) causing an overproduction of uric acid leading to neurologic deficits, hyperuricemia, and behavioral abnormalities, including self-mutilation

Lesch-Nyhan syndrome (Lacks Nucleotide Salvage)

Trisomy 21 → mental retardation, slanted palpebral fissures, hypertelorism, macroglossia, atrial septal defect (ASD), duodenal atresia, early-onset Alzheimer disease, and multiple visceral anomalies

Down syndrome

Expansion of unstable region of X chromosome (abnormal FMR1 gene with CGG expansion) leading to mental retardation, enlarged testes, and craniofacial anomalies

Fragile X syndrome

XL recessive deficiency of α-galactosidase A → buildup of ceramide trihexoside which causes pain in the extremities, ocular abnormalities, angiookeratomas, cardiovascular disease, and renal failure

Fabry disease

AR deficiency of galactosylceramide β-galactosidase leading to cerebral accumulation of galactocerebroside, which causes progressive neurologic degeneration

Krabbe disease (aka globoid cell leukodystrophy)

AR deficiency of β-glucocerebrosidase leading to the accumulation of glucocerebroside in the brain, bone marrow, liver, spleen → HSM, aseptic necrosis of femur, and neurologic dysfunction

Gaucher disease

AR deficiency of sphingomyelinase on Chromosome 11 leading to buildup of sphingomyelin and cholesterol in histiocytes of the liver, spleen, and lymphatic system, resulting in cortical atrophy, cherry red spot on macula, HSM

Niemann-Pick disease

AR deficiency of hexosaminidase A on Chromosome 18, leading to the accumulation of GM2 ganglioside within lysosomes resulting in neurologic degeneration and developmental delay, and cherry red spot on macula

Tay-Sachs disease

AR deficiency of arylsulfatase A, leading to an accumulation of cerebroside sulfate and dysfunction and demyelination of the central and peripheral nervous systems resulting in ataxia and dementia

Metachromatic leukodystrophy

XL recessive deficiency of iduronate sulfatase, leading to an accumulation of heparan and dermatan sulfate resulting in mental retardation, coarse facial features, and short stature

Hunter syndrome
AR deficiency of α-l-iduronidase, leading to the accumulation of partially degraded glycosaminoglycans within lysosomes resulting in dysmorphic, gargoylike facies, corneal clouding, HSM, and skeletal abnormalities
Hurler syndrome
AR deficiency of UDP-N-acetylglucosamine: N-acetylglucosaminyl-1-phosphotransferase, loss of protein tagging with mannose-6-phosphate, leading to defective trafficking of enzymes into lysosomes → developmental delay and coarse facial features
I-cell disease (mucolipidosis type II)

Name the genetic disease associated with each of the following clinical or pathologic findings:

- Cherry red spot of the macula
- Tay-Sachs disease and Niemann-Pick disease
- Cells containing “crinkled paper” cytoplasm and glycolipid-laden macrophages
- Gaucher disease
- Corneal clouding
- Hurler syndrome

Carbohydrate, Protein, and Lipid Metabolism

Name the major metabolic pathway regulated by the following enzymes:

- Isocitrate dehydrogenase
- Citric acid cycle
- Phosphofructokinase
- Glycolysis
- Fructose-1,6-bisphosphatase
- Gluconeogenesis
- Glycogen synthase
- Glycogen synthesis
- Glycogen phosphorylase
- Glycogenolysis
- Glucose-6-phosphate dehydrogenase
- Pentose phosphate pathway
- Acetyl-coenzyme A (CoA) carboxylase
- Lipogenesis
- Carnitine acyltransferase
- Lipolysis (β-oxidation)
- HMG-CoA reductase
Name the major activators and/or inhibitors for each of the following enzymes:

**Citrate synthase**
- Activator: no major activator
- Inhibitors: ATP, NADH, succinyl-CoA, and acyl-CoA derivatives of fatty acids

**Phosphofructokinase-1**
- Activator: AMP, fructose-2,6-bisphosphate (liver)
- Inhibitor: citrate, ATP, and cAMP

**Pyruvate dehydrogenase**
- Activator: CoA, nicotinamide adenine adenine (NAD), adenosine diphosphate (ADP), and pyruvate
- Inhibitor: acetyl-CoA, NADH, and ATP

**Pyruvate carboxylase**
- Activator: acetyl-CoA
- Inhibitor: ADP

**Fructose-1,6-bisphosphatase**
- Activator: cAMP
- Inhibitor: AMP and fructose-2,6-bisphosphate

**Glycogen synthase**
- Activator: glucose-6-phosphate
- Inhibitor: no major inhibitor

**Glycogen phosphorylase**
- Activators: cAMP and Ca$^{2+}$ (muscle)
- Inhibitors: glucose, glucose-6-phosphate, and ATP

**Glucose-6-phosphate dehydrogenase**
- Activator: NADP$^+$
- Inhibitor: NADPH

**Acetyl-CoA carboxylase**
- Activator: citrate
- Inhibitor: malonyl-CoA, palmitoyl-CoA, and cAMP

**Carnitine acyltransferase**
- Activator: no major activator
- Inhibitor: malonyl-CoA

**HMG-CoA reductase**
- Activator: no major activator
- Inhibitor: cholesterol and cAMP

Describe the effect of insulin on the following metabolic processes:
- Glycogen synthesis in muscle and liver
Increase
Gluconeogenesis in the liver
Decrease
Glycogenolysis in the liver
Decrease
Glucose uptake in muscle and adipose tissue
Increase
Triacylglycerol degradation
Decrease
Triacylglycerol synthesis
Increase
Protein synthesis
Increase

Describe the effect of glucagon on the following metabolic processes:
Glycogenolysis in the liver
Increase
Gluconeogenesis in the liver
Increase
β-Oxidation of fatty acids in the liver
Increase
Amino acid uptake by liver
Increase

Which small molecule accepts reducing equivalents and is typically involved in catabolic processes?
NAD⁺

Which small molecule donates reducing equivalents and is typically involved in anabolic processes?
Nicotinamide adenine dinucleotide phosphate (NADPH)

Name the cellular compartment (cytosol, mitochondria, or both) where each of the following processes occur:
Citric acid cycle
Mitochondria
Fatty acid oxidation
Mitochondria
Fatty acid synthesis
Cytosol
Gluconeogenesis
Both
Glycolysis
Cytosol
Heme synthesis
Both
Hexose monophosphate (HMP) shunt
Cytosol
Protein synthesis
Cytosol (rough ER)
Steroid synthesis
Cytosol (smooth ER)
Urea cycle
Both

Hexokinase or glucokinase?
Found in most tissues
Hexokinase
Found exclusively in the liver and β-islet cells
Glucokinase
High affinity for glucose
Hexokinase
Faster reaction velocity
Glucokinase
Inhibited by glucose-6-phosphate
Hexokinase

Name the molecule(s) that serve as the primary source of energy for the following organs:

Liver
Amino acids, lipids, glucose, fructose, and lactate
Central nervous system (CNS)
Glucose
Heart
Lipids, ketone bodies, lactate, and glucose
Adipose tissue
Glucose and lipids
Type I skeletal muscle fibers (slow twitch, “red”)
Lipids and ketone bodies
Type II skeletal muscle fibers (fast twitch, “white”)
Glucose

What are the four major enzymes that function in gluconeogenesis?
1. Pyruvate carboxylase
2. PEP carboxykinase
3. Fruuctose-1,6-bisphosphatase
4. Glucose-6-phosphatase (Pathway Produces Fresh Glucose)

**Name four important cellular processes that require reducing equivalents supplied primarily by the pentose phosphate pathway:**
1. Fatty acid and steroid biosynthesis
2. Glutathione-mediated reduction of H$_2$O$_2$
3. Cytochrome P-450 system
4. Respiratory burst in phagocytes

**Which molecule serves as donor of methyl groups in many metabolic processes?**
S-adenosylmethionine

**Name four biosynthetic pathways that require methyl group donation by S-adenosylmethionine:**
- Synthesis of
  1. Choline
  2. Creatine
  3. Epinephrine
  4. 7-Methylguanosine

**Which metabolic process is responsible for transferring reducing equivalents from RBCs and muscle tissue to the liver?**
Cori cycle

**Which two amino acids play key roles in the transport of nitrogen from the periphery to the liver?**
1. Alanine
2. Glutamine

**What are the cofactors for the pyruvate dehydrogenase complex?**
B$_1$, B$_2$, B$_3$, B$_5$, and lipoic acid

**Name the eight intermediates of the citric acid cycle:**
1. Citrate (Cindy)
2. Isocitrate (Is)
3. α-Ketoglutarate (Kinky)
4. Succinyl-CoA (So)
5. Succinate (She)
6. Fumarate (Fornicates)
7. Malate (More)
8. Oxaloacetate (Often)

**Name a toxin that directly blocks the flow of electrons through the electron transport chain:**
Cyanide is a by-product of the metabolism of what antihypertensive?
   Nitroprusside

Name a toxin that directly inhibits mitochondrial ATPase:
   Oligomycin

Name a toxin that uncouples oxidative phosphorylation by increasing the permeability of the inner mitochondrial membrane:
   2,4-Dinitrophenol (DNP)

What are the primary metabolic substrates released by the liver in the fed state and the fasting state?
   Very low-density lipoprotein (VLDL) (fed); glucose and ketone bodies (fasting)

Name the apolipoprotein or lipoprotein responsible for each of the following functions:
   Activates lecithin-cholesterol acyltransferase
      Apolipoprotein A-I
   Binds to low-density lipoprotein (LDL) receptor, mediates VLDL secretion
      Apolipoprotein B-100
   Delivery of cholesterol from the tissues to the liver
      High-density lipoprotein (HDL)
   Delivery of cholesterol produced by the liver to the tissues
      LDL
   Delivery of triglycerol absorbed in the small intestine to tissues
      Chylomicron
   Delivery of triglycerol produced by the liver to tissues
      VLDL
   Mediates chylomicron remnant uptake
      Apolipoprotein E
   Serves as a cofactor for lipoprotein lipase
      Apolipoprotein C-II

Which enzyme, found in the liver and bone marrow, catalyzes the rate-limiting step of heme synthesis?
   Aminolevulinate synthase

What are the major intermediates in the degradation of heme?
   Heme → biliverdin → bilirubin → bilirubin diglucuronide (conjugated bilirubin)

Conjugated bilirubin is excreted in which bodily fluid?
   Bile

Which compound produced by intestinal bacterial degradation of conjugated bilirubin gives urine its yellow color?
   Urobilinogen
Which common physical finding in severe liver disease results from the accumulation of bilirubin (hyperbilirubinemia)?

Jaundice

Name the essential amino acids:

“PriVaTe TIM HALL”: Phe, Val, Trp, Thr, Ile, Met, His, Arg, Leu, Lys

Which amino acids (AAs) are exclusively ketogenic?

Leu and Lys

Which AAs can be ketogenic or glucogenic?

Tyr, Ile, Phe, and Trp

Which AAs are exclusively glucogenic?

All the amino acids not listed in the above two items

Which AAs are negatively charged at physiologic pH (7.4)?

Asp, Glu (the two acidic AAs)

Which AAs are positively charged at physiologic pH (7.4)?

Arg, Lys (the two basic AAs), His also basic but weakly charged at pH 7.4

Which AA is used to carry ammonium from the muscles to the liver?

Alanine

Which small molecule, essential to the excretion of ammonium, is derived from the removal of ammonium from glutamine?

α-Ketoglutarate

What are the intermediates of the urea cycle?

1. Ornithine (Ordinarily)
2. Carbamoyl phosphate (Careless)
3. Citrulline (Crappers)
4. Aspartate (Are)
5. Arginosuccinate (Also)
6. Fumarate (Frivolous)
7. Arginine (About)
8. Urea (Urination)

What is the limiting reagent for hepatic ethanol (EtOH) catabolism?

NAD⁺

Which metabolic abnormality in chronic alcoholics results from depletion of NAD⁺ in the liver?

Hypoglycemia (due to inhibition of gluconeogenesis)

Depletion of NAD inhibits which two major metabolic processes?

1. The conversion of pyruvate to lactate
2. Oxaloacetate to malate

In what metabolic state does the liver commonly produce ketone bodies?
During starvation (or diabetic ketoacidosis)

**G Proteins**

What class of G protein is associated with the following cell surface receptors:
- $\alpha_1$
- Q
- $\alpha_2$
- I
- $\beta_1$
- S
- $\beta_2$
- S
- $M_1$
- Q
- $M_2$
- I
- $M_3$
- Q
- $M_4$
- S
- $D_1$
- S
- $D_2$
- I
- $H_1$
- Q
- $H_2$
- S
- $V_1$
- Q
- $V_2$
- S

Which two second messengers are increased by the activation of a $G_q$ protein?
1. IP3
2. Diacylglycerol (DAG)

Which enzyme is induced by the activation of a $G_q$ protein?
Protein kinase C

Which enzyme is induced by the activation of a $G_s$ protein?
Protein kinase A

Which second messenger is increased by the activation of a $G_s$ protein?
cAMP

Which enzyme is inhibited by the activation of a $G_i$ protein?
Protein kinase A

Which second messenger is decreased by the activation of a $G_i$ protein?
cAMP

Enzymes

What is the shape of the plot of reaction velocity against substrate concentration for enzymes following Michaelis-Menten kinetics?
Hyperbolic

For an enzyme following Michaelis-Menten kinetics, how does halving enzyme concentration affect $V_{\text{max}}$?
$V_{\text{max}}$ will be halved. ($V_{\text{max}}$ is directly proportional to enzyme concentration for all substrate concentrations.)

What is the shape of a plot of reaction velocity against substrate concentration for enzyme with a single allosteric regulator?
Sigmoid or “S” shaped

Name two important parameters of the cellular environment that directly affect enzyme kinetics:
1. pH
2. Temperature

The inverse of $V_{\text{max}}$ ((the maximum reaction velocity) for a given enzyme is represented by what point on a Lineweaver-Burk plot?
The $y$ intercept

The inverse of $K_m$ (the Michaelis-Menten constant) for a given enzyme is represented by what point on a Lineweaver-Burk plot?
The $x$ intercept

An enzyme with a small $K_m$ will have a high or low affinity for its substrate?
High affinity ($K_m = 1/2V_{\text{max}}$)

How does a competitive inhibitor affect $K_m$?
Increases

How does a noncompetitive inhibitor affect $K_m$?
How does a competitive inhibitor affect $V_m$?
No effect

How does a noncompetitive inhibitor affect $K_m$?
Decreases

Cell Cycle

Name the phase of the cell cycle associated with each of the following cellular events:

- Quiescence: $G_0$
- Centrosome duplication: S
- RNA, protein, organelle synthesis: $G_0$
- DNA, RNA, histone synthesis: S
- Release of E2F from Rb: $G_1/S$ transition
- Cyclin-dependent kinase (Cdk)-cyclin A and Cdk-cyclin B are active: $G_2/M$ transition
- Cdk-cyclin D and Cdk-cyclin E are active: $G_1/S$ transition
- Chromatin condensation, mitotic spindle formation: M: prophase
- Kinetochore assembly: M: prometaphase
- Centrosomes move to opposite poles: M: prophase
- Nuclear envelope and nucleolar disappearance: M: prometaphase
- Chromosome alignment at metaphase plate: M: metaphase
- Kinetochore separation: M: anaphase
- Nuclear envelope and nucleolar formation: M: telophase
Cytoplasmic division (cytokinesis)
M: cytokinesis
Most variable phase of cell cycle
G₁

Which two important molecules are involved in the G₁ to S checkpoint?
Rb, p53

What is the significance of p53?
Allows cell to detect DNA defects and repair them before proceeding with replication

Cell Membranes

What are the major categories of molecules that make up the cell membrane?
Cholesterol, phospholipids, sphingolipids, glycolipids, and proteins

Where in the cell membrane are glycoproteins found?
Exclusively in the noncytoplasmic side

What is the effect of increasing the cholesterol content of a cell membrane?
Membrane fluidity is decreased.

NUTRITION

Name the fat-soluble vitamins:
Vitamins A, D, E, and K

Where are these vitamins absorbed?
Ileum

What conditions cause fat-soluble vitamin deficiencies?
Malabsorption syndromes (eg, cystic fibrosis, celiac disease, ileal disease, ileal resection)

Why do toxicities occur more commonly with fat-soluble vitamins?
Fat-soluble vitamins can accumulate in fatty tissues; varying fat content with age leads to different thresholds of toxicity for children versus elderly.

Which prolonged dietary deficiency of protein and calories is characterized by retarded growth and cachexia in children?
Marasmus

Which disease, characterized by protein deficiency with adequate caloric intake, results in retarded growth, anemia, and severe edema?
Kwashiorkor
Name the vitamin(s) associated with each of the following statements:

**Composes NAD$^+$ and NADP$^+$**
Vitamin B$_3$ (niacin)

**Remains in the body with stores lasting up to 3 to 5 years**
Vitamin B$_{12}$ (cobalamin)

**Important in purine/pyrimidine synthesis**
Folate

**Important part of visual pigments and epithelial cell differentiation**
Vitamin A (retinol)

**Antioxidant that delays cataracts and atherosclerosis**
Vitamin E ($\alpha$-tocopherol)

**Component of CoA and fatty acid synthase**
Vitamin B$_5$ (pantothenate)

**Cofactors for pyruvate-dehydrogenase complex**
Vitamins B$_1$ (thiamine), B$_2$ (riboflavin), B$_3$ (niacin), and B$_5$ (pantothenic acid)

**Found only in animal products; Schilling test used to detect deficiency**
Vitamin B$_{12}$ (cobalamin)

**Cofactor for norepinephrine (NE) synthesis and collagen cross-linkage; ↑ Fe absorption**
Vitamin C (ascorbic acid)

**Cofactor in transamination reactions**
Vitamin B$_6$ (pyridoxine)

**Toxicity causes nausea, stupor, and hypercalcemia**
Vitamin D

**Important in methionine synthesis and isomerization of methylmalonyl-CoA**
Vitamin B$_{12}$ (cobalamin)

**Toxicity causes skin changes, arthralgias, and premature epiphyseal closure, the first sign of toxicity usually CNS changes from edema.**
Vitamin A (retinol)

**Catalyzes $\gamma$-carboxylation of coagulation factors, synthesized by GI flora**
Vitamin K

**The most toxic vitamin in overdose**
Vitamin D

**The most common vitamin deficiency in the United States**
Folate

Name the vitamin deficiency associated with each of the following findings:

**Wernicke-Korsakoff syndrome, beriberi**
Vitamin B$_1$ (thiamine); B$_1$ = Ber1Ber1
Rickets, osteomalacia, and hypocalcemic tetany
Vitamin D
Neonatal hemorrhage and ↑ prothrombin time (PT)
Vitamin K
Megaloblastic anemia with neurologic dysfunction
Vitamin B₁₂ (cobalamin)
Dermatitis, diarrhea, and dementia (pellagra)
Vitamin B₃ (niacin)
Deficiency caused by long-term raw egg ingestion
Biotin (avidin in egg whites binds biotin)
Megaloblastic anemia without neurologic dysfunction
Folate
Dry skin, dry eyes, and night blindness
Vitamin A (retinol)
Hemolysis (from RBC fragility) and ataxia
Vitamin E (α-tocopherol)
EEG abnormalities and peripheral neuropathy; caused by isoniazid (INH) and oral contraceptives
Vitamin B₆ (pyridoxine)
Cheilosis, corneal vascularization, and angular stomatitis
Vitamin B₂ (riboflavin)
Neural tube defects during pregnancy
Folate
Scurvy, hemorrhages, and impaired wound healing
Vitamin C (ascorbic acid)
Deficiency caused by *Diphyllobothrium latum* infection, sprue, pernicious anemia, and Crohn’s disease
Vitamin B₁₂ (cobalamin)

Name the trace element associated with each of the following statements:
Important in protein synthesis; deficiency causes acrodermatitis and ↑ sense of taste/smell
Zinc
Involved in hemoglobin synthesis; excess caused by ceruloplasmin deficiency
Copper
Cofactor for glutathione peroxidase; deficiency causes cardiomyopathy
Selenium
Involved in collagen cross-linkage; excess causes pulmonary fibrosis
Silicon
Involved in methionine metabolism; deficiency mimics vitamin B\textsubscript{12} deficiency
Cobalt (constituent of cobalamin)
Reduces insulin resistance, glucose tolerance factor
Chromium

**GENERAL EMBRYOLOGY**

**Name the embryonic structure described below:**
- **Consists of the inner cell mass which ultimately gives rise to the fetus**
  Embryoblast
- **Consists of the outer cell mass which ultimately gives rise to the placenta**
  Trophoblast
- **Derived from embryoblast; clefts form the amniotic cavity**
  Epiblast
- **Derived from embryoblast; ultimately forms the yolk sac**
  Hypoblast
- **Border between future mouth and pharynx; formed by both hypoblast and epiblast cells**
  Buccopharyngeal membrane
- **Produces β-human chorionic gonadotropin (hCG)**
  Syncytiotrophoblast
- **Forms the lining of the cytotrophoblast**
  Extraembryonic somatic mesoderm
- **Consists of the syncytiotrophoblast, cytotrophoblast, and extraembryonic somatic mesoderm**
  Chorion
- **Forms the covering of the yolk sac**
  Extraembryonic visceral mesoderm

**The following developmental milestones occur how long after contraception?**
- **Implantation**
  Within 1 week
- **Bilaminar disc**
  Within 2 weeks
- **Gastrulation**
  Within 3 weeks
- **Formation of the primitive streak and neural plate**
  Within 3 weeks
Organogenesis, peak of susceptibility to teratogens
Weeks 3 to 8
Limb formation
Week 4
Cardiac contractions begin
Week 4
Male and female genitals can be distinguished.
Week 10

Name the abnormality/abnormalities caused by the following teratogens:

Angiotensin-converting enzyme (ACE) inhibitors
Renal dysgenesis → oligohydramnios, pulmonary hypoplasia, and limb contractures

Tetracycline
Yellow teeth and enamel hypoplasia

Aminoglycosides
Eighth cranial nerve damage → deafness

Oral hypoglycemics
Neonatal hypoglycemia

Warfarin
Craniofacial (nasal hypoplasia) and CNS defects, stillbirth

Dilantin
Fetal hydantoin syndrome: craniofacial and limb defects, mental deficiencies

Valproic acid
Spina bifida

Lithium
Cardiac (Ebstein) anomaly

Isotretinoin
Craniofacial (small ears), CNS, cardiac, and thymus defects

Indomethacin
Constriction of ductus arteriosus

Diethylstilbestrol (DES)
Clear cell vaginal cancer and cervical/uterine malformations in female offspring

Thalidomide
Limb reduction defects

Alcohol
Fetal alcohol syndrome: craniofacial defects (absent philtrum, flattened nasal bridge, and microphthalmia), growth restriction, and brain, cardiac, and spinal defects

Tobacco
Growth restriction, prematurity, low birth weight

Radiation
Growth restriction, CNS defects, and leukemia

Name the embryonic layer that gives rise to each of the following tissues:

- Adrenal cortex
  - Mesoderm

- Anterior pituitary
  - Ectoderm (oral ectoderm/Rathke pouch)

- Aorticopulmonary septum
  - Ectoderm (neural crest)

- Autonomic nerves
  - Ectoderm (neural crest)

- Long bones and vertebrae
  - Mesoderm

- Facial bones
  - Ectoderm (neural crest)

- CNS neurons and astrocytes
  - Ectoderm (neural tube)

- Connective tissue
  - Mesoderm

- Epidermis
  - Ectoderm (surface ectoderm)

- Epithelial lining of the GI tract
  - Endoderm

- Myocardium
  - Mesoderm

- Kidneys
  - Mesoderm

- Lens of eye
  - Ectoderm (surface ectoderm)

- Liver parenchyma
  - Endoderm

- Mammary glands
  - Ectoderm (surface ectoderm)

- Melanocytes
  - Ectoderm (neural crest)

- Striated muscle
  - Mesoderm

- Nucleus pulposus
  - Mesoderm (notochord)

- Pancreas
Endoderm
**Parafollicular cells of the thyroid**
Ectoderm (neural crest)
**Retina**
Ectoderm (neural tube)
**Schwann cells**
Ectoderm (neural crest)
**Spleen**
Mesoderm
**Parathyroid**
Endoderm
**Posterior pituitary**
Ectoderm (neural tube)
**Thymus**
Endoderm
**Thyroid**
Endoderm
**Kidneys, ureters, and gonads**
Mesoderm

**BASIC PATHOLOGY**

Cellular Adaptations

Give the appropriate term for each of the following definitions:
Complete failure of cell production
Aplasia
Relative decrease in cell production
Hypoplasia
Increase in cell size
Hypertrophy
Replacement of one adult (differentiated) cell (epithelial or mesenchymal) type with another adult cell type
Metaplasia
Decrease in cell substance results in a decrease in cell size; may result in decreased tissue/organ size.
Atrophy
Increase of organ/tissue size due to an increase in the number of cells
Hyperplasia

**Cell Injury**

Name the mechanism of cell injury characterized by each of the following statements:

- **Mitochondrial dysfunction** → ↓ cellular ATP → failure of Na\(^+\)/K\(^+\) ATPase, failure of protein synthesis
- Ischemic/hypoxic cell injury
- **Dissociation of ribosomes and polysomes**
- ATP depletion
- **Causes lipid peroxidation of membranes**
- Reactive oxygen species (O\(_2\)-free radicals)
- Associated with ionizing radiation, UV light, and reperfusion after ischemic injury
- Reactive oxygen species (O\(_2\)-free radicals)
- **Prevented by enzymes such as glutathione peroxidase, catalase, and superoxide dismutase**
- Generation of reactive oxygen species (O\(_2\)-free radicals)

**Which molecules are released in response to mitochondrial damage?**
- Cytochrome c and H\(^+\)

Cytoskeletal abnormalities, ATP depletion, and cell swelling are associated with what key event in cell injury?
- Defective membrane permeability

**What is the effect of increased cytoplasmic calcium ions in a cell undergoing apoptosis or necrosis?**
- Activation of ATPase, endonuclease, phospholipase, and proteases

**Necrosis/Apoptosis**

Classify the following as features of apoptosis or necrosis:
- **Cellular blebbing and cell shrinkage**
- Apoptosis
- **Involves many contiguous cells**
- Necrosis
Physiologic, programmed cell removal
Apoptosis
Active form of cell death (requires energy consumption)
Apoptosis
**Gross, irreversible cellular injury**
Necrosis
Involves single cells or groups of cells
Apoptosis
Involution and shrinkage of affected cells and fragments
Apoptosis
**Marked inflammatory reaction**
Necrosis
Inhibited by \( bcl-2 \); facilitated by \( bax, p53 \)
Apoptosis

State the function of each of the following molecules during apoptosis:
- **Caspases (cysteine protease)**
  Protein cleavage
- **Endonucleases**
  DNA cleavage
- **Phosphatidylserine and thrombospondin**
  Cell surface molecules recognized by phagocytes
- **Tumor necrosis factor (TNF)-\( \alpha \) receptor and FAS (CD95)**
  Death receptors
- **Bcl-2 and Bcl-x**
  Major antiapoptotic proteins
- **Bad and Bax**
  Major proapoptotic proteins
- **Cytochrome \( c \)**
  Activation of procaspase 9
- **Apoptosis-activating factor-1 (Apaf-1)**
  Cytoplasmic receptor for cytochrome \( c \)
- **TNF-\( \alpha \)**
  Bindings of this ligand to its receptor induce association with a death domain.
- **Granzyme B**
  Activation of the caspase cascade (released by cytotoxic T cells)

Name the type of necrosis characterized by each of the following features:
- **Enzymatic degradation of tissue seen in abscesses**
- **Liquefactive necrosis**
- **Commonly seen in tuberculous granulomas**
Caseous necrosis
Fibrin-like, proteinaceous deposition in arterial walls
Fibrinoid necrosis
Lipase-induced autodigestion of adipose tissue → saponification
Fat necrosis
Interruption of blood supply to organs supplied by end arteries; architecture well preserved
Coagulative necrosis
Results from vascular occlusion; most commonly affects lower extremities or bowel
Gangrenous necrosis

Cell Changes/Accumulations

What type of cellular change is characterized by excess accumulation of intracellular triglycerides?
   Fatty change (steatosis)
What type of calcification is caused by hypercalcemia?
   Metastatic calcification
What type of calcification occurs in previously damaged tissues?
   Dystrophic calcification
Name four endogenous pigments that accumulate in cells:
   1. Melanin
   2. Bilirubin
   3. Hemosiderin
   4. Lipofuscin
Name four diseases associated with protein misfolding:
   1. Alzheimer disease
   2. α-1-Antitrypsin deficiency
   3. Cystic fibrosis
   4. Amyloidosis
Name the cellular pigment described below:
   Accumulates in jaundice
   Bilirubin
   Identified with Prussian blue dye; can result in organ damage or simple deposition
   Hemosiderin
   Yellowish, fat-soluble “wear-and-tear” pigment
Lipofuscin
Formed in the epidermis from tyrosine
Melanin

Inflammation

Which three classes of adhesion molecules are involved in inflammation?
1. Selectins (E, P, and L)
2. Immunoglobulin (Ig) family (intercellular adhesion molecule [ICAM], platelet cell adhesion molecule [PCAM])
3. Integrins

What are the five steps in the extravasation of inflammatory leukocytes?
1. Margination
2. Pavementing
3. Tumbling (rolling)
4. Adhesion
5. Transmigration

Which two groups of cell adhesion molecules pair mediate tumbling?
1. Selectins on endothelial cells
2. Sialylated glycoproteins (e.g., sialyl-Lewis-X) on leukocytes

Which two groups of cell adhesion molecules pair mediate leukocyte adhesion to endothelial cells?
1. ICAM and vascular cell adhesion molecule (VCAM) (Ig superfamily) on endothelial cells
2. Integrins on leukocytes

Which factors induce endothelial expression of P-selectin?
Platelet activation factor (PAF), histamine, and thrombin

Which factors induce endothelial expression of ICAM and VCAM?
Interleukin (IL)-1 and TNF

Name five chemotactic factors for neutrophils:
1. Bacterial products
2. C5a
3. LTB₄
4. Chemokines (IL-8)
5. Fibrin split (degradation) products

Name five functional responses of leukocytes following their activation:
1. Eicosanoid production
2. Cytokine secretion
3. Generation of reactive oxygen species
4. Degranulation
5. Altered cell adhesion molecule expression
6. Upregulation of receptors (toll-like, G protein-coupled, opsonin, cytokines)

**Name two receptors that function in binding and phagocytosis of bacteria:**
1. Mannose
2. Scavenger receptors

**What term is used to describe the process of coating substances (with Ig or C3b) to facilitate phagocytosis?**
Opsonization

**Which neutrophil intracellular microbicidal mechanism uses the HMP shunt to generate an oxidative burst?**
H$_2$O$_2$-myeloperoxidase (MPO)-halide system of bacterial killing

**Name two processes associated with impaired leukocyte adhesion:**
1. Recurrent bacterial infections
2. Altered wound healing

**Decide whether each of the following substances causes vasoconstriction or vasodilation:**

**Bradykinin**
Vasodilation

**Thromboxane (TXA)**
Vasoconstriction

**Prostacyclin (PGI$_2$)**
Vasodilation

**Leukotrienes (LTC$_4$, LTD$_4$, and LTE$_4$)**
Vasoconstriction

**Prostaglandins (PGD$_2$, PGE$_2$, and PGF$_2$)**
Vasodilation

**Remember:** most substances also cause analogous effects on bronchial tone.

**Name seven substances that increase vascular permeability:**
1. Histamine
2. Serotonin
3. C3a and C5a
4. Leukotrienes (LTC$_4$, LTD$_4$, and LTE$_4$)
5. Bradykinin
6. Nitric oxide (NO)
7. PAF (low concentration)
Which two enzymes stimulate the release of arachidonic acid from membrane phospholipids?
1. Phospholipase A₂
2. Phospholipase C

What are the two major pathways in arachidonic acid metabolism?
1. Cyclooxygenase (COX)
2. Lipoxygenase

What signaling molecules are produced by the COX pathway?
- TXA₂ (in platelets), PGI₂ (in endothelial cells), and other prostaglandins (in other tissues)

What are the two major enzymes involved in prostaglandin production?
1. COX-1
2. COX-2

Which cyclooxygenase enzyme serves in homeostatic functions?
COX-1

What products does the lipooxygenase pathway produce?
- HPETEs and leukotrienes

Which arachidonic acid metabolite is thought to sensitize nerve endings to pain mediators?
- PGE₂ (↓ PGE₂ → analgesic effects)

Name four acute-phase responses of inflammation.
1. Systemic effects (fever and leukocytosis)
2. Hepatic synthesis of acute-phase reactants (C-reactive protein [CRP] ferritin, complement, and prothrombin)
3. Synthesis of adhesion molecules
4. Neutrophil degranulation

Which substance links the kinin, coagulation, plasminogen, and complement systems?
- Factor XIIa (Hageman factor)

Which group of plasma proteins participates in immune-mediated lysis of cells?
- Complement system

Which substance produced by endothelial cells relaxes smooth muscle and inhibits platelet aggregation?
- Nitric oxide (NO)

Which factor is a pyrogen and causes fever?
- IL-1 → PGE₂

Name four possible outcomes of acute inflammation:
1. Complete resolution
2. Abscess/ulcer/fistula formation
3. Healing by fibrosis and scarring
4. Progression to chronic inflammation

**Which pattern of chronic inflammation is characterized by nodular collections of epithelioid histocytes and multinucleated giant cells?**
Granulomatous inflammation

**Name three etiologies of granulomatous inflammation:**
1. Infectious (*Mycobacterium tuberculosis*, *Histoplasma*, cat scratch disease, leprosy, syphilis)
2. Foreign bodies
3. Idiopathic (eg, sarcoidosis, Crohn’s disease)

**Tissue Repair**

**What are the four factors determining the size of a cell population?**
1. Proliferation
2. Cell death
3. Cell differentiation
4. Replacement by stem cells

**What are the three categories of cells based on their inherent proliferative activity?**
1. Permanent (cardiac myocytes, neurons)
2. Quiescent (hepatocytes, endothelial cells, lymphocytes)
3. Labile (epidermis, GI, and respiratory tract epithelial cells; bone marrow; hair follicles)

**Name five factors that mediate cellular proliferation during the process of tissue repair:**
1. Platelet-derived growth factor (PDGF)
2. Epidermal growth factor (EGF) and transforming growth factor-alpha (TGF-α)
3. Fibroblast growth factors (FGFs)
4. Hepatocyte growth factor
5. Vascular endothelial growth factor (VEGF)

**What highly vascular, newly formed connective tissue fills defects left by removal of cellular debris?**
Granulation tissue

**What are the four key components to the orderly formation of a scar?**
1. Angiogenesis and granulation tissue formation
2. Fibroblast emigration and proliferation
3. Deposition of extracellular matrix
4. Maturation and remodeling → scar
Name five factors that delay or impede tissue repair:
  1. Impaired circulation
  2. Persistent infection
  3. Retention of debris or foreign body
  4. Nutritional deficiency (e.g., protein and vitamin C)
  5. Metabolic disorders (e.g., diabetes mellitus)

Hemodynamic Dysfunction

Name five causes of edema:
  1. ↑ Hydrostatic pressure
  2. ↑ Capillary permeability
  3. ↓ Oncotic pressure
  4. ↑ Na⁺ retention (renal disorders or congestive heart failure [CHF])
  5. Lymphatic obstruction

Describe the contents of a transudate.
  Low-protein content (SG 1.012), few cells, and little protein

What type of fluid accumulation forms as a result of increased vascular permeability due to endothelial cell destruction?
  Exudate

What is the composition of exudate?
  High protein (SG > 1.020) ↑ inflammatory leukocytes, and ↑ protein

Name two organs commonly affected by chronic passive congestion and their related pathologic findings:
  1. Lungs: hemosiderin-laden macrophages or “heart-failure cells” (from left heart failure)
  2. Liver: nutmeg liver (from right heart failure)

Name the two types of infarcts and several examples of each:
  1. Anemic (white) infarcts: heart, spleen, and kidneys
  2. Hemorrhagic (red) infarcts: lungs, testes, and GI tract (occurs in areas with collateral circulation)

Thrombosis

What is Virchow triad?
  The three primary influences on thrombus formation:
  1. Endothelial injury
2. Stasis
3. Hypercoagulability

**Name the three components necessary for hemostasis:**
1. Vascular endothelium
2. Platelets
3. Coagulation cascade

**Name five factors that promote platelet aggregation:**
1. ADP
2. Thrombin
3. TXA₂
4. Collagen
5. Platelet-activating factor

**Which product of the COX pathway limits further platelet aggregation?**
\( \text{PGI}_2 \)

**Where are proteins C and S made?**
Endothelial cells

**Classify the following as features of the extrinsic or the intrinsic pathway:**
- Involves activation of factor VII
  Extrinsic pathway
- Clinically monitored by the PT
  Extrinsic pathway
- Initiated by activation of factor XII
  Intrinsic pathway
- Monitored by partial thromboplastin time (PTT)
  Intrinsic pathway

**Name the component(s) of the coagulation cascade associated with each of the following features:**
- **Vitamin K-dependent coagulation factors**
  Factors II, VII, IX, X, proteins C and S
- **Ion necessary for proper function of the coagulation cascade**
  Calcium
- **Factors inhibited by antithrombin III (AT III)**
  Thrombin, factors IX, X, XI, and XII
- **Complex that activates proteins C and S**
  Thrombomodulin-thrombin complex
- **The most important fibrinolytic protease**
  Plasmin
- **Converts plasminogen to plasmin**
Tissue plasminogen activator (t-PA), also urokinase plasminogen activator
Cleaved by activated protein C (APC) → inhibition of coagulation
Factors Va and VIIIa

Which molecule dramatically enhances the activity of AT III?
Heparin

What is the most frequent cause of hereditary thrombophilia?
Factor V (Leiden) mutation (2%-15% of white population)

Hereditary thrombophilia can also be caused by deficiency of what major antithrombotic proteins?
AT III, protein C, and protein S

How does the Leiden mutation confer hypercoagulability?
Renders mutant factor V resistant to cleavage by APC

Which prothrombotic disorder is characterized by autoantibodies that induce platelet activation?
Antiphospholipid antibody syndrome

Name the type of thrombus associated with each of the following:
Reddish-blue cast; usually in lower extremities
Venous thrombosis
Lines of Zahn
Arterial thrombus
Sterile vegetations of heart valves in patients with hypercoagulable states
Nonbacterial thrombotic endocarditis
Noninfective heart valve vegetations from circulating immune complexes
Verrucous (Libman-Sacks) endocarditis

Embolism

Name the type of embolism described by each of the following statements:
Venous thrombus that gains access to arterial circulation through a right-to-left shunt
Paradoxical embolus
Associated with decompression sickness
Air embolus
Occurs at parturition; can lead to disseminated intravascular coagulation (DIC) and death
Amniotic fluid embolus
Embolus obstructing the bifurcation of the pulmonary artery
Saddle embolus
Often arises from one wall of a heart chamber, especially in the context of atrial fibrillation
Mural thrombus → arterial emboli
**Important cause of death in immobilized, post-op patients**
Pulmonary embolus
**Occur after severe, multiple long bone fractures**
Fat emboli

**Shock**

**Name the type of shock described by each of the following statements:**
Associated with gram-negative endotoxemia
Septic shock
**Circulatory collapse from pump failure of left ventricle (LV)**
Cardiogenic shock
**IgE-mediated systemic vasodilation with ↑ vascular permeability**
Anaphylactic shock
**Caused by severe hemorrhage or fluid loss**
Hypovolemic shock
**Associated with severe trauma causing reactive peripheral vasodilation**
Neurogenic shock

**Which two mediators are associated with systemic vasodilation in septic shock?**
1. NO
2. PAF

**Name the characteristic manifestations of shock on each of the following organs:**
**Lungs**
Pulmonary edema
**Liver**
Steatosis and centrilobular necrosis
**Colon**
Patchy mucosal hemorrhages
**Adrenals**
Lipid depletion of cortex
**Kidneys**
Acute tubular necrosis
BASIC PHARMACOLOGY

Absorption/Distribution

In which part of the GI tract are most oral drugs absorbed?
Duodenum

Name three factors that influence absorption of drugs:
1. Chemical properties (active transport vs passive diffusion)
2. pH (percent of drug in the uncharged state determines rate of absorption)
3. Physical factors (blood flow, surface area, and contact time with absorptive surfaces)

What is first-pass metabolism?
Hepatic degradation/alteration of an oral drug after absorption, before it enters the general circulation

Complete the following formulas:
\[
\frac{\text{Rate of drug elimination}}{\text{plasma drug concentration}} = \text{Clearance (CL)}
\]
\[
\frac{\text{Amount of drug in body}}{\text{plasma drug concentration}} = \text{Volume of distribution (} V_d \text{)}
\]
\[
\frac{C_p \times V_d}{F} = \text{Loading dose (also defined as the amount of drug necessary to rapidly raise a desired plasma concentration of the drug)}
\]
\[
\frac{C_p \times CL}{F} = \text{Maintenance dose (also defined as the amount of drug necessary to maintain a desired plasma concentration of the drug)}
\]
\[
\frac{0.693 \times V_d}{CL} = C_p = \text{target plasma concentration, } F = \text{bioavailability}
\]
Half-life (\(t_{1/2}\))

If a patient were known to be a rapid metabolizer, would the loading dose or maintenance dose have to be adjusted to maintain a desired plasma concentration of the drug?
The loading dose would be unchanged; the maintenance dose would need to be increased.

How do dosage calculations change for patients with impaired renal/hepatic function?
Loading dose stays the same, maintenance dose decreases.
List four conditions that alter drug distribution:
1. Edematous state (e.g., CHF and nephrotic syndrome)
2. Pregnancy (↑ intravascular volume)
3. Obesity (accumulation of lipophilic agents in fat cells)
4. Hypoalbuminemia (no albumin to bind drugs →↑ availability)

Name the key mechanism of drug-drug interactions:
Drug displacement from albumin (combined administration of classes I and II drugs)

Metabolism/Elimination

Name four clinical situations that would result in increased drug half-life.
1. Prerenal state (↓ renal plasma flow)
2. Renal disease → decreased extraction ratio
3. Adding a second drug that displaces the first from albumin, thus ↑ $V_d$
4. ↓ Metabolism (hepatic insufficiency or drug interaction)

Classify each of the following statements as characteristic of phase I or phase II metabolism:
- Produces slightly polar, water-soluble metabolites
  Phase I
- Involves mixed-function oxidase (P-450)
  Phase I
- Involves conjugation reactions (acetylation, glucuronidation, and sulfation)
  Phase II
- Produces very polar, inactive metabolites that are excreted by the kidneys
  Phase II
- Reduction, oxidation, and hydrolysis
  Phase I
- Phase that may be compromised first in geriatric patients
  Phase I
- Phase that may be compromised in neonates
  Phase I

Classify each of the following statements as characteristic of first- or zero-order drug elimination:
- Constant fraction of drug eliminated per unit of time
  First-order elimination
- Constant amount of drug eliminated per unit of time
  Zero-order elimination
- Plasma concentration decreases linearly with time
Zero-order elimination
Plasma concentration decreases exponentially with time
First-order elimination
Elimination rate is independent of concentration
Zero-order elimination

Pharmacodynamics

What term describes the maximum effect a drug can produce?
Efficacy
What term describes the measure of the amount of drug needed to produce a given result?
Potency
What term describes the dose of a drug that produces the desired effect?
Effective dose (ED)
What term describes the dose of a drug that produces death?
Lethal dose (LD)
What term describes the measure of the safety of a drug?
Therapeutic index
How is therapeutic index calculated?
LD_{50}/ED_{50} (LD_{50} = dose lethal in 50% of the population, ED_{50} = dose effective in 50% of the population)
How does a competitive antagonist affect the dose-response curve?
Shifts it to the right (↑ ED_{50})
How does a noncompetitive antagonist affect the dose-response curve?
Shifts it downward (↓ maximal response)
How does a partial agonist differ from a full agonist?
Acts like an agonist when an agonist is not present; acts like an antagonist if an agonist is present

Drug Development

Name the phase of drug development described by each of the following statements:
Measures effect of the drug in patients with a disease
Phase II clinical testing
Measures whether the drug is safe in healthy volunteers
Phase I clinical testing
Postmarketing surveillance
Phase IV
Large, multicenter clinical trials to prove efficacy and safety
Phase III clinical trials

Toxicology

Name the antidote for each of the following toxins:

- **Iron**
  - Deferoxamine

- **Copper/gold/arsenic**
  - Penicillamine

- **Lead**
  - CaEDTA, succimer, dimercaprol (BAL in oil), and oral penicillamine

- **Arsenic/mercury**
  - Dimercaprol

- **Carbon monoxide**
  - 100% O_2 and hyperbaric O_2

- **Cyanide**
  - Nitrite, vitamin B_{12}, and thiosulfate

- **Methemoglobin**
  - Methylene blue

- **Methanol/ethylene glycol**
  - ETOH, fomepizole, and dialysis

- **Acetaminophen (Tylenol)**
  - N-acetylcysteine

- **Aspirin (salicylates)**
  - Alkalinize urine (promotes excretion) and dialysis

- **Opioids**
  - Naloxone (IV, IM, and SQ) or naltrexone (PO)

- **Benzodiazepines**
  - Flumazenil

- **Organophosphates, anticholinesterases**
  - Atropine and pralidoxime (PAM)

- **Heparin**
  - Protamine sulfate

- **Warfarin**
  - Vitamin K, fresh frozen plasma (FFP) for acute reversal
tPA
Aminocaproic acid

Digitalis
Antidig F\textsubscript{ab} fragments (first stop drug and stabilize K\textsuperscript{+}, Mg\textsuperscript{2+}, and lidocaine)

Cyclophosphamide
Mesna

P-450

Classify each of the following drugs as inhibitors or inducers of P-450:

Inducers: “Queen Barb takes Phen-phen and Refuses Greasy Carbs”
Inhibitors: “Inhibitors Stop Cyber-K ids from Eating Grapefruits”

Barbiturates
Inducer

INH
Inhibitor

Spironolactone
Inhibitor

Rifampin
Inducer

Cimetidine
Inhibitor

Ketoconazole
Inhibitor

Phenytoin and carbamazepine
Inducer

Quinidine
Inducer

Disulfiram
Inhibitor

Sulfonamides
Inhibitor

Steroids
Inhibitor

Macrolides (erythromycin)
Inhibitor

Chloramphenicol
Inhibitor
Griseofulvin
Inducer
Grapefruit
Inhibitor
Verapamil
Inhibitor
Chronic EtOH use
Inducer
Acute EtOH use
Inhibitor
CHAPTER 2
Immunology

IMMUNOLOGY BASICS

Cells of the Immune System

Name the type of immune cell that fits each description given below:

- **Major cells involved in innate immunity**
  - Monocytes, macrophages, neutrophils, natural killer (NK) cells

- **Cell-mediated immune response**
  - T lymphocyte

- **Humoral immunity**
  - B lymphocyte

- **Primary phagocytic cell in acute inflammation**
  - Neutrophil

- **Type of cell necessary for transplant rejection**
  - T lymphocyte

- **Contains myeloperoxidase and lysozyme**
  - Neutrophil

- **Major mediator of a type 1 hypersensitivity reaction**
  - Mast cell

- **Major mediator of the antiparasitic response**
  - Eosinophil

- **Granules contain histamine and heparin**
  - Basophils and mast cells

- **Major antigen-presenting cells in tissues**
  - Macrophages, dendritic cells, and B cells

- **Demonstrates a multilobed (“hypersegmented”) nucleus in vitamin B₁₂ or folate deficiency**
  - Neutrophil

- **Secretes interleukin (IL)-1 to promote T cell activity**
Macrophage
Expresses IgE receptors on its cell membrane to mediate the allergic response
Basophil
Expresses high levels of major histocompatibility complex (MHC) class II on its cell membrane
Macrophage
Macrophage precursor
Monocyte
Cell type increased in atopic asthma
Eosinophil
Recognizes antigen presented in the context of MHC class II molecules
T-helper cell
Antibody-producing cell with abundant rough endoplasmic reticulum
Plasma cell
Major source of IL-2 production
T-helper cell (specifically T_{H}1 cells)
Major cell of the humoral immune response
B lymphocyte

Immunoglobulins

Name the type of immunoglobulin (Ig) associated with the following features:
Most abundant type of Ig
IgG
First class of Ig produced in an immune response upon exposure to antigen
IgM
Able to fix complement
IgG and IgM
Found on the lining of mucous membranes and in secretions, including breast milk and saliva
IgA
Able to cross placenta
IgG
Type of Ig commonly occurring as a dimer
IgA
Type of Ig commonly occurring as a pentamer
IgM
Ig elevated in patients with asthma and allergies
IgE
- Responsible for long-term immunity

IgG
- Causes mast cells and basophils to release histamine when triggered by antigen

IgE
- Type of Ig found embedded in the cell membrane of developing B cells

IgD
- Total levels and concentration of this antibody can be estimated using radioimmunosorbent test (RIST) and radioallergosorbent test (RAST).

**What term is used to describe the portion of a molecule that serves as an antigenic determinant?**

Epitope

**What term is used to describe a small molecule that can serve as an antigenic determinant only if it is attached to a larger carrier molecule?**

Hapten

**What type of chemical bonds are critical in linking the heavy and light chains of Igs?**

Disulfide bonds

**Which products result when papain digests an Ig?**

- Two Fab fragments (each capable of binding antigen) and one Fc fragment

**Which products are produced following pepsin digestion of an Ig?**

- One F(ab’)2 fragment and one Fc fragment

**What term is used to describe the region in an antibody that determines antigen specificity?**

- The hypervariable region or complementarity determining region (CDR)

**Name five mechanisms by which antibody diversity is created:**

1. Mutations in the genes encoding the CDR region
2. Random VJ recombination in light chains
3. Random VDJ recombination in heavy chains
4. Random assembly of light and heavy chains
5. Imperfect recombination of VDJ genes

**T Cells**

**Name the T-lymphocyte cell surface protein associated with the following features:**

- Antigen-specific receptor on 95% of T cells
- αβ T-cell receptor (αβ TCR)
- Antigen-specific receptor on 5% (or less) of T cells
γδ T-cell receptor (γδ TCR)
Signal transduction protein always associated with TCR
CDS
T-cell marker expressed in immature T cells
CD2
Responds to MHC class II molecule expressed by antigen-presenting cells
CD4
Responds to MHC class I molecule expressed on all cells
CD8
Found specifically on T-helper cells
CD4
Found specifically on cytotoxic T cells
CD8
Cells with this surface marker ↓ in HIV/AIDS
CD4
Type of T cell that destroys virally infected cells
CD8

HLA Subtypes

Name the HLA haplotype(s) associated with the following diseases:
  Ankylosing spondylitis
  HLA-B27
  Type 1 diabetes mellitus
  HLA-DR3/DR4
  Multiple sclerosis
  HLA-DR2
  Rheumatoid arthritis
  HLA-DR4
  Screening for abacavir hypersensitivity
  HLA-B*5701

Cytokines

Name the cytokine described below:
  Endogenous pyrogen
  IL-1 (produced by macrophages)
Promotes IgA synthesis
IL-5
Induces IL-2 production by T cells
IL-1
High concentrations induce cell death in some tumors and cause cachexia.
Tumor necrosis factor (TNF)-α
Induces T- and B-cell activity during the initial stages of an immune response
IL-1
Induces production of IgE and IgG
IL-4 (produced by T-helper cells)
Induces differentiation of eosinophils and promotes growth in B cells
IL-5 (produced by T-helper cells)
Chemotactic factor for neutrophils
IL-8 (produced by monocytes and endothelial cells)
Secreted by activated T cells and induces maturation of bone marrow stem cells
IL-3
Inhibits production of interferon-gamma (IFN-γ) by T-helper cells
IL-10 (produced by T_H2 cells)
Inhibits production of IFN-γ
IL-4
Inhibits differentiation of T_H1 cells
IL-10
Stimulates T_H1 differentiation
IL-12 (produced by macrophages and B cells)
Activates T-helper, T-cytotoxic, natural killer, and B cells
IL-2 (produced by T-helper cells)
Promotes production of IFN-γ T-helper cells
IL-12
Low concentrations promote neutrophil activity and IL-2 receptor expression.
TNF-α
Inhibits growth and function of T and B cells and promotes collagen secretion
during tissue repair
Transforming growth factor-beta (TGF-β)

Gel and Coombs Hypersensitivity Reactions

Name the Gel and Coombs hypersensitivity reaction described below:
Mediated by IgE bound to mast cells and basophils
Type 1 (immediate or anaphylactic hypersensitivity)

Antibody-mediated cytotoxic reaction

Type 2 (cytotoxic reaction)

Occurs in response to environmental allergies

Type 1

Antigen-sensitized T cells release cytokines, which induce an inflammatory response up to 48 hours after initial contact with antigen.

Type 4 (delayed-type hypersensitivity)

Associated with the release of histamine, platelet-activating factor, leukotrienes, prostaglandins, and thromboxanes

Type 1

Binding of cytotoxic T cells or complement to Fc portion of antibody causes target cell lysis

Type 2

Immune complex deposition in tissues results in an inflammatory response

Type 3 (immune complex reaction)

Name the type of hypersensitivity reaction responsible for the following diseases or conditions:

- Arthus reaction
  Type 3
- Asthma
  Type 1
- Chronic transplant rejection
  Type 4
- Contact dermatitis, reaction to poison ivy
  Type 4
- Drug allergies
  Type 1
- Environmental allergies
  Type 1
- Erythroblastosis fetalis
  Type 2
- Goodpasture syndrome
  Type 2
- Graves disease
  Type 2
- Hemolytic anemia
  Type 2
- Immune complex-mediated glomerulonephritis
Type 3
Lambert-Eaton
Type 2
Myasthenia gravis
Type 2
Multiple sclerosis
Type 4
Pernicious anemia
Type 2
Purified protein derivative (PPD)/tuberculin skin test
Type 4
Rheumatic fever
Type 2
Rheumatoid arthritis
Type 3
Systemic anaphylaxis
Type 1
Serum sickness
Type 3
Systemic lupus erythematosus (SLE)
Type 3
Transfusion reaction due to ABO incompatibility
Type 2

Complement

Which class of bacteria is particularly susceptible to complement-mediated lysis?
Gram-negative organisms

Which antibody isotypes activate the classic pathway of the complement cascade?
IgG and IgM

Which molecules activate the alternative pathway of the complement cascade?
Aggregated IgA, endotoxin, and other components of the bacterial cell wall

Name the component(s) of the complement cascade responsible for the following functions:
Neutralization of viruses
Cl to C4
Opsonization
C3b
Neutrophil and macrophage chemotaxis
C5a

Synthesis of membrane attack complex (MAC)
C5b to C9

Formation of C3 convertase
C3b, Bb (alternative pathway) or C4b, C2b (classic pathway)

Name the disease or condition caused by a deficiency of the following complement components:
Cl esterase inhibitor
Hereditary angioedema
C3
Sinus and upper respiratory tract infections
C5b to C9
Recurrent Neisseria infections
Decay accelerating factor
Paroxysmal nocturnal hemoglobinuria

Transplant Rejection and MHC Molecules

For each of the following descriptions, name the type of transplant rejection:
Preformed antibodies in host react against graft antigens
Hyperacute rejection (minutes to hours)

Activation of previously sensitized T cells
Accelerated rejection (hours to days)

Involves T-cell activation, differentiation, and antibody production
Acute rejection (days to weeks)

Immune complex deposition combined with subacute cell cytotoxicity
Chronic rejection (months to years)

What are the four different classes of grafts?
1. Autograft (from self)
2. Syngeneic (from identical twin or clone)
3. Allograft (from same species)
4. Xenograft (from different species)

The activity of cytotoxic T cells against tumor or virally infected cells requires which cell surface receptor for antigen presentation?
MHC class I

The activity of cytotoxic T cells against pathogens phagocytosed by macrophages requires which cell surface receptor for antigen presentation?
Describe the disease associated with the following autoantibodies:

- **Antinuclear antibodies (ANA)**
  - SLE (sensitive but not specific for SLE)
- **Anti-acetylcholine esterase (ACh)**
  - Myasthenia gravis
- **Antibasement membrane**
  - Goodpasture disease
- **Anticentromere**
  - CREST syndrome (Calcinosis, Raynaud, Esophageal dysmotility, Sclerodactyly, Telangiectasias)
- **Anti-dsDNA**
  - SLE (highly specific for SLE)
- **Antiepithelial cell**
  - Pemphigus vulgaris
- **Antigliadin**
  - Celiac sprue
- **Antihistone**
  - Drug-induced lupus
- **Anti-IgG Fc (rheumatoid factor)**
  - Rheumatoid arthritis
- **Anti-Jo1**
  - Myositis
- **Antimicrosomal**
  - Hashimoto thyroiditis
- **Antimitochondrial**
  - Primary biliary cirrhosis
- **Antinuclear ribonucleoprotein (nRNP)**
  - Mixed connective tissue disease
- **Antiplatelet**
  - Idiopathic thrombocytopenic purpura
Anti-Scl-70 (DNA topoisomerase 1)  
Systemic sclerosis  
Anti-Smith  
SLE (highly specific for SLE)  
Anti-SS-A (Ro) and anti-SS-B (La)  
Sjögren syndrome  
Antithyroglobulin  
Hashimoto thyroiditis  
Anti-thyroid-stimulating hormone receptor (TSHr)  
Graves disease  
Anti-voltage-gated calcium channel  
Lambert-Eaton syndrome  
Cytoplasmic pattern of antineutrophil cytoplasmic antibodies (c-ANCA)  
Wegener granulomatosis  
Perinuclear pattern of antineutrophil cytoplasmic antibodies (p-ANCA)  
Microscopic PolyANgiitis, Polyarteritis Nodosa (PAN), and Churg-Strauss syndrome  

List the four types of nuclear antigens against which ANAs are directed:  
1. DNA  
2. Histones  
3. Nonhistone proteins  
4. Nucleolar antigens

Systemic Lupus Erythematosus

What pathologic finding is common to all tissues affected by SLE?  
Acute necrotizing vasculitis of small arteries and arterioles caused by immune complex deposition

Describe the effect of SLE on each of the following organs:  
Skin  
Malar rash, discoid rash, photosensitivity  
Joints  
Arthritis and arthralgias  
Brain  
Neuropsychiatric changes or seizures (2° to cerebral vasculitis), cognitive dysfunction  
Eyes  
Cotton-wool spots, retinal hemorrhages  
Heart  
Pericarditis, Libman-Sacks Endocarditis (SLE → LSE)
Lungs
Pleuritis, pulmonary fibrosis

Gastrointestinal (GI)
Oral and nasopharyngeal ulcers

Spleen
Splenomegaly and onion skinning of splenic vessels

Kidneys
Wire-loop glomerular lesions and mesangial immune complex deposits → glomerulonephritis

Hematology
Hemolytic anemia, leukopenia, thrombocytopenia, antiphospholipid antibody syndrome

Blood vessels
Raynaud phenomenon

Libman-Sacks endocarditis causes sterile vegetations to form on both sides of which cardiac valve?
Mitral valve

Name five medications capable of inducing a lupus-like syndrome:
1. Hydralazine
2. Isonicotinic acid (INH)
3. Phenytoin
4. Procainamide
5. Penicillamine

Name the disease related to SLE that is characterized by immune complex deposition at the dermal-epidermal junction:
Discoid lupus erythematosus

Immunodeficiencies

Name the immunodeficiency associated with the following clinical and pathologic features:
B-cell deficiency causing recurrent respiratory tract bacterial infections in boys >6 months of age
X-linked (XL) agammaglobulinemia
T-cell deficiency due to failure of development of the third and fourth pharyngeal pouches
Thymic aplasia (DiGeorge syndrome)
Defective B and T cells, most cases caused by XL recessive mutation in γ-chain of cytokine receptors or autosomal recessive (AR) mutation in adenosine deaminase
Severe combined immunodeficiency
AR disease characterized by IgA deficiency, cerebellar dysfunction, and conjunctival telangiectasias
Ataxia-telangiectasia
XL deficiency of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity, resulting in an impaired neutrophil respiratory burst and leading to increased bacterial and fungal infections
Chronic granulomatous disease
Recurrent bacterial infections early in life due to a defect in CD40 ligand that prevents B-cell class switching
Hyper-IgM syndrome
AR microtubule defect resulting in decreased phagocytosis, partial albinism, and neuropathy
Chediak-Higashi disease
AR syndrome characterized by failure of neutrophil chemotaxis-associated eczema, elevated IgE, noninf lamed staphylococcal abscesses
Job (hyper-IgE) syndrome
XL recessive disease characterized by recurrent infections, thrombocytopenia, eczema
Wiskott-Aldrich syndrome
Mutation of the Btk tyrosine kinase gene resulting in the underproduction of all classes of antibodies
XL agammaglobulinemia
Defect in the receptor for IL-7
Severe combined immunodeficiency
Associated with Staphylococcus aureus, Streptococcus pneumoniae, and Haemophilus influenzae respiratory infections and persistent Giardia lamblia infections
XL agammaglobulinemia
Associated with recurrent GI and pulmonary infections
Isolated IgA deficiency
Frequent viral and fungal infections in a patient with hypocalcemia due to low PTH levels
Thymic aplasia (DiGeorge syndrome)
Associated with tetany and congenital defects of the heart and aorta
Thymic aplasia (DiGeorge syndrome)
Small thymus devoid of lymphocytes, hypoplastic lymph nodes, and splenic white pulp
Severe combined immunodeficiency
↑ IgA, normal IgE, and ↓ IgM levels
Wiskott-Aldrich syndrome
Hypogammaglobulinemia commonly due to failure of T-cell-mediated B-cell maturation
Common variable immunodeficiency

Autoimmune Connective Tissue Disorders

Name the autoimmune disease of connective tissue associated with the following clinical and pathologic findings:

- Keratoconjunctivitis sicca or xerophthalmia, xerostomia, and evidence of other connective tissue disease
- Sjögren syndrome
- Autoimmune inflammatory disorder associated with malignancy; frequently caused muscle weakness
- Polymyositis
- Heliotrope rash
- Dermatomyositis
- Rapidly progressive diffuse fibrosis of skin and involved organs including the heart, GI tract, kidney, lung, muscle, and skin
- Diffuse scleroderma
- CREST syndrome of calcinosis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, telangiectasias
- Localized scleroderma
- ↑ Serum creatine kinase (CK) levels
- Polymyositis

What is the most common cause of death due to scleroderma?
Renal crisis (accounts for 50% of deaths related to scleroderma)

Which autoimmune disease of connective tissue lacks renal involvement?
Mixed connective tissue disease

Amyloidoses

Name the group of disorders characterized by extracellular deposition of protein in a β-pleated sheet conformation.

Amyloidoses
Which stain is used to identify the presence of amyloid in tissue that exhibits apple green birefringence under polarized light?
  Congo red

Which molecular configuration is common to all forms of amyloid?
  Cross-β-pleated sheet

Name the effect of amyloidosis on each of the following organs:
  **Kidneys**
  Glomerular, peritubular, and vascular hyalinization
  **Spleen**
  Sago spleen (tapioca-like amyloid deposits in follicles) or lardaceous spleen (amyloid deposition in splenic pulp)
  **Liver**
  Hepatomegaly with amyloid deposition in the space of Disse
  **Heart**
  Restrictive cardiomyopathy
  **Tongue**
  Hypertrophy due to amyloid deposition
CHAPTER 3
Microbiology and Infectious Diseases

BACTERIOLOGY

Taxonomy

Name two genera of gram-positive cocci:
  1. Streptococcus
  2. Staphylococcus

Name four genera of gram-positive bacilli:
  1. Clostridium
  2. Listeria
  3. Bacillus
  4. Corynebacterium

Which of these gram-positive bacilli are spore forming?
  Clostridium and Bacillus

Which gram-positive cocci are catalase positive (+)?
  Staphylococcus

Which of these is also coagulase (+)?
  Staphylococcus aureus

Name the streptococci that typically show the following pattern of hemolysis:
  α (green/partial hemolysis) “almost hemolytic”
  Streptococcus pneumoniae and viridans group (eg, Streptococcus mutans)
  β (clear hemolysis) “better hemolysis”
  Group A (Streptococcus pyogenes) and group B (Streptococcus agalactiae)
  γ (no hemolysis)
  Group D (Enterococcus and Peptostreptococcus)

Laboratory Evaluation of Gram-Positive Bacteria
**How are *S. pneumoniae* and viridans streptococci differentiated in the laboratory?**

*Streptococcus pneumoniae* is bile soluble and optochin sensitive.

**How can capsulated *S. pneumoniae* bugs be detected in the laboratory?**

Quellung positive (capsule swells when antisera is added)

**What determines the Lancefield grouping of streptococci?**

C-carbohydrate in the bacterial cell wall

**How are groups A and B differentiated in the laboratory?**

Group A is bacitracin sensitive.

**How are spores from gram-positive rods killed?**

Autoclave (spores are resistant to heat and most chemicals)

**Name the gram-negative organisms associated with each of the following statements:**

**Three pathogenic gram-negative cocci**

1. *Neisseria meningitides*
2. *Neisseria gonorrhea*
3. *Moraxella catarrhalis*

**Six gram-negative coccobacilli**

1. *Haemophilus influenzae*
2. Pasteurella
3. Brucella
4. *Bordetella pertussis*
5. *Francisella*
6. *Legionella*

**Three clinically important gram-negative rods that are typically lactose fermenting**

1. *Enterobacter*
2. *Escherichia coli*
3. *Klebsiella* (all implicated in urinary tract infections [UTIs])

**Two obligate intracellular organisms**

1. *Chlamydia* (steals adenosine triphosphate [ATP] from host)
2. *Rickettsia* (lacks coenzyme A [CoA] and nicotinamide adenine [NAD] \(\rightarrow\) cannot produce own ATP)

**Four obligate aerobes**

1. *Nocardia*
2. *Pseudomonas*
3. *Mycobacterium tuberculosis*
4. *Bacillus*

**Three obligate anaerobes**

1. *Clostridium*
2. *Bacteroides*
3. *Actinomyces* (no catalase and/or superoxide dismutase → susceptible to oxidative damage)

How are the pathogenic *Neisseria* species differentiated in the laboratory?

*Neisseria meningitidis* ferments maltose.

How can *Pseudomonas* be rapidly differentiated from many lactose nonfermenters in the laboratory?

*Pseudomonas* is oxidase positive.

Provide culture requirements or conditions for each of the following bacteria:

- **Corynebacterium diphtheriae**
  - Tellurite agar or Loeffler media

- **Bordetella pertussis**
  - Bordet-Gengou potato blood agar

- **Neisseria gonorrhoea**
  - Thayer-Martin (VCN—vancomycin, colistin, and nystatin) and a selective medium

- **Legionella pneumophila**
  - Charcoal yeast agar with iron and L-cysteine

- **Mycoplasma pneumoniae**
  - Eaton agar

- **Mycobacterium tuberculosis**
  - Lowenstein-Jensen agar

- **Vibrio species**
  - Thiosulfate-Citrate-Bile Salts-Sucrose (TCBS) agar

- **Enterococcus**
  - 40% bile and 6.5% NaCl

- **Haemophilus influenzae**
  - Chocolate agar (contains factor V [NAD] and X [hematin])

- **Lactose-fermenters (*Klebsiella, Escherichia*, etc)**
  - MacConkey agar → pink colonies

- **Fungi**
  - Sabouraud agar

**Bacteriology Basics**

Which cell membrane structure is unique to gram-positive organisms?

Teichoic acid

Which molecule, unique to the bacterial cell wall, provides rigid support and resistance against osmotic pressure?

Peptidoglycan
Which heat-stable lipopolysaccharide (LPS) is found in the cell wall of gram-negative bacteria?

Endotoxin

Which is the only gram-positive organism with LPS-lipid A?

*Listeria monocytogenes*

Name five important systemic effects of endotoxin (particularly, lipid A):

1. ↑Interleukin (IL)-1 → fever
2. ↑ Tissue necrosis factor (TNF) → hemorrhagic tissue death
3. ↑ Nitric oxide → hypotension and shock
4. Activation of alternate complement pathway →↑ C3a (edema) and C5a (polymorphonuclear [PMN] chemotaxis)
5. Activation of factor XII → coagulation cascade → DIC

Which has a higher toxicity, endotoxins or exotoxins?

Exotoxins: fatal dose on the order of 1 μg (vs hundreds of micrograms for endotoxins)

Name the mechanism of DNA transfer characterized by the following statements:

DNA is taken up directly from the environment by competent cells
Transformation (can occur in eukaryotic cells, too)
Medically important natural transformers: HHSNG: “Here, Have Some New Genes”: *H. pylori, H. influenzae, S. pneumoniae, N. gonorrhoea*

Plasmid or chromosomal DNA transferred from one bacterium to another via cell-to-cell contact
Conjugation

DNA transferred by a virus from one cell to another; can be generalized or specialized
Transduction

DNA segments able to excise and reincorporate into different locations
Transposons

Name the bacterium whose exotoxin has the following effects:

Superantigen that induces IL-1 and IL-2 synthesis in toxic shock syndrome; also leads to food poisoning

*Staphylococcus aureus*

α-Toxin is a lecithinase → gas gangrene

*Clostridium perfringens*

Prevents the release of the neurotransmitter (NT) glycine from Renshaw cells in spinal cord → paralysis

*Clostridium tetani*

↑ Adenylate cyclase by adenosine diphosphate (ADP) ribosylation → whooping cough

*Bordetella pertussis*
Exotoxin encoded by β-prophage; α subunit → inactivates elongation factor 2 (EF-2) halting protein synthesis; β subunit → permits entry into cardiac and neural tissue

*Corynebacterium diphtherias*

Erythrogenic superantigen → rash in scarlet fever

*Streptococcus pyogenes*

Prevents release of acetylcholine (ACh) → central nervous system (CNS) paralysis; spores in canned food and honey, construction sites

*Clostridium botulinum*

Heat-stable toxin ↑ guanylate cyclase; heat-labile toxin ↑ adenylate cyclase by ADP ribosylation of G protein → watery diarrhea

*Escherichia coli*

Inactivates the 60S ribosome → kills intestinal cells

*Shigella dysenteriae*

Permanent ADP ribosylation of G protein → ↑ adenylate cyclase → ↑ Cl⁻ and H₂O₂ in gut → voluminous stools

*Vibrio cholerae*

Exotoxin A inhibits protein synthesis by blocking EF-2

*Pseudomonas*

Which virulence factor allows organisms to colonize mucosal surfaces?

IgA protease (eg, *S. pneumoniae* and *H. influenzae*)

Name the bacterial structure associated with each antigenic classification given below:

**K-antigen**
Capsule (related to virulence of the bacteria)

**K = Kapsule**

**O-antigen**
Outer portion of the polysaccharide of endotoxin

**O = Outer**

**H-antigen**
Flagella (seen in motile species)

Name the key virulence factor(s) associated with each of the following organisms:

**Group A streptococcus**
M-protein, streptokinase, and hyaluronidase

**Staphylococcus aureus**
Protein A (prevents complement fixation and phagocytosis), penicillinase, and hyaluronidase

**Streptococcus viridans**
Extracellular dextran → helps bind to heart valves

*Yersinia pestis*
F1 capsular antigen (antiphagocytic) and protease (degrades clots)

*Haemophilus influenzae*
Capsule: six types (a-f) and IgA protease

*Borrelia*
Antigenic variation

*Mycobacterium tuberculosis*
Mycosides (cord factor, wax D, and sulfatides)

**Infectious Diseases**

Name the organism(s) associated with each of the following characteristics:

- **Gram-positive rods with metachromatic granules**
  *Corynebacterium diphtheriae*

- **Three urease (+)**
  *Helicobacter pylori, Proteus, and Ureaplasma urealyticum*

- **Aerosol transmission from environmental water source (eg, air conditioner)**
  *Legionella pneumophila*

- **Contain mycolic acid in membranes**
  *Mycobacterium* and *Nocardia*

- **Peptidoglycan wall lacks muramic acid**
  *Chlamydiae*

- **Produces pyocyanin (blue-green) pigment**
  *Pseudomonas aeruginosa*

- **Produces yellow-gold pigment**
  *Staphylococcus aureus*

- **Produces reddish pigment**
  *Serratia marcescens*

- **Only bacterial membrane containing cholesterol**
  *Mycoplasma pneumoniae*

- **Filamentous, branching rods in a cervicofacial infection**
  *Actinomyces ismeli*

- **Two forms: elementary and reticulate bodies**
  *Chlamydiae*

- **Pleomorphic gram-negative rods in “school of fish” pattern**
  *Haemophilus ducreyi*

- **Clue cells on wet mount**
Gardnerella vaginalis
High liter of cold agglutinins (IgM)
Mycoplasma pneumoniae
Two fungi-like bacteria
Actinomyces israelii and Nocardia asteroides

Name the organism(s) associated with the following pathology:
Fitz-Hugh and Curtis syndrome
Chlamydia trachomatis or N. gonorrhea
Invades gastrointestinal (GI) mucosa → diarrhea; motile; can disseminate hematogenously
Salmonella
Infected dog or cat bites (or scratches)
Pasteurella multocida

Ghon complex
Mycobacterium tuberculosis (1° tuberculosis [TB]). Note: hilar nodes plus Ghon focus usually in lower lobe

Meningitis and pneumonia in neonates
Haemophilus influenzae
Atypical pneumonia with avian reservoir
Chlamydia psittaci
Gas gangrene in traumatic open wounds
Clostridium perfringens
Infected skin and superficial nerves
Mycobacterium leprae

Fibrocaseous cavitary lung lesion
Mycobacterium tuberculosis (2° TB). Note: usually at apex because ↑ affinity for ↑ O₂ environments

Mycobacterium causing disseminated disease in acquired immunodeficiency syndrome (AIDS) patients
Mycobacterium avium-intracellulare
Mycobacterium causing cervical lymphadenitis in kids
Mycobacterium scrofulaceum

For each of the following clinical findings, name the organism responsible and the drug(s) of choice:
Oral/facial abscesses with sulfur granules in sinus tracts
Actinomyces israelii——penicillin G (IV)
Currant jelly sputum
Klebsiella—first- or second-generation cephalosporins
Woolsorter’s disease
Bacillus anthracis—penicillin G or ciprofloxacin
Scarlet fever, impetigo, and pharyngitis
Streptococcus pyogenes—penicillin
Pontiac fever
Legionella pneumophila—macrolide (erythromycin and azithromycin)
Gram-positive coccus causing sepsis/meningitis in a newborn
Streptococcus agalactiae—ampicillin (Note: group B, think Babies)
Acute epiglottitis, meningitis, otitis, and pneumonia
Haemophilus influenzae—second-generation cephalosporins (treat meningitis with ceftriaxone, plus rifampin for contacts)
Gastritis and ~90% of duodenal ulcers
Helicobacter pylori—triple therapy
Waterhouse-Friderichsen syndrome
Neisseria meningitidis—ceftriaxone
Pneumonia in cystic fibrosis and burn patients
Pseudomonas cepacia—bactrim or ciprofloxacin
Bacterial vaginosis with discharge and fishy odor
Gardnerella vaginalis—metronidazole
Burn and wound infections with fruity odor
Pseudomonas aeruginosa—aminoglycoside plus antipseudomonal (eg, piperacillin and tazobactam)
Acute postinfectious glomerulonephritis
Streptococcus pyogenes—penicillin G
Pseudomembranous enterocolitis
Clostridium difficile—metronidazole or oral vancomycin
Atypical “walking” pneumonia in young adult
Mycoplasma pneumoniae—erythromycin or doxycycline
Urethritis/pelvic inflammatory disease (PID), neonatal conjunctivitis, and pneumonia
Chlamydia trachomatis types D to K—erythromycin eye drops in neonates, azithromycin for urethritis, pneumonia
Lyme disease
Borrelia burgdorferi—doxycycline
Malignant, vesicular papules covered with black eschar → bacteremia and even death
Bacillus anthracis—penicillin G or ciprofloxacin
Pneumonia, sepsis, otitis externa, UTIs, hot-tub folliculitis, osteomyelitis
Pseudomonas aeruginosa—aminoglycoside plus antipseudomonal piperacillin and tazobactam
Undulant fever, Bang disease
Brucella sp.—doxycycline plus gentamicin or rifampin (pasteurize milk to prevent)

Bubonic plague
Yersinia pestis—gentamicin

Rocky Mountain spotted fever
Rickettsia rickettsii—tetracycline/doxycycline

Trench fever (lasts 5 days; recurs in 5-day cycles)
Bartonella quintana—gentamicin/doxycycline

Tabes dorsalis, aortitis, and gummas
Treponema pallidum (3° syphilis)—penicillin G

Q fever (acute)
Coxiella burnetii—doxycycline

Weil disease
Leptospira interrogans—penicillin G

Yaws
Treponema pertenue—penicillin G

Pott disease
Mycobacterium tuberculosis (disseminated)—four-drug anti-tuberculous therapy, including rifampin plus isoniazid (INH)

Dental caries
Streptococcus mutans—amoxicillin or amoxicillin/clavulonic acid (prevention with topical fluoride/chlorhexidine)

Rheumatic fever
Streptococcus pyogenes—penicillin G

Scalded skin syndrome and toxic shock syndrome
Staphylococcus aureus—penicillin agent (vancomycin if methicillin-resistant S. aureus [MRSA])

Hansen disease
Mycobacterium leprae—dapsone plus clofazimine or rifampin

What is the differential for a rash affecting the palms and soles?
Rocky Mountain spotted fever, 2° syphilis, hand-foot-and-mouth disease (coxsackie A), and Kawasaki syndrome

Name the mode of transmission and reservoir(s) for each of the following bacteria:
Brucella sp.
Contact with animals or dairy products; cows

Francisella tularensis
Tick or deerfly bite; rabbits and deer

Pasteurella multocida
Animal bite/scratch; cats and dogs
**Borrelia burgdorferi**
Ixodes tick bite; lives on deer and mice

**Yersinia pestis**
Flea bite; rodents (e.g., prairie dogs)

**Rickettsia rickettsii**
Tick bite; dogs, rabbits, and rodents (endemic to eastern United States)

**Rickettsia prowazekii**
Human body louse; humans and flying squirrels

**Name the laboratory test described below:**

Dectects antirickettsial antibodies
Weil-Felix reaction (cross-reacts with proteus)

**Sensitive for treponemes**
Fluorescent treponemal antibody-absorption test (FTA-ABS) (+) (earliest and longest, used as confirmatory test for syphilis if RPR is reactive)

**Useful in screening for TB**
Purified protein derivative (PPD) test

**Name the screening test for syphilis and four biological false positives:**

VDRL test
1. Viruses (mononucleosis and hepatitis)
2. Drugs (narcotics)
3. Rheumatoid arthritis/fever
4. Leprosy and lupus

**Name the normal, dominant flora for each of the following locations:**

**Nose**
*Staphylococcus aureus*

**Oropharynx**
Group D streptococci (viridans)

**Dental plaques**
*Streptococcus mutans*

**Colon**
*Bacteroides fragilis > E. coli*

**Vagina**
*Lactobacillus;* colonized by *E. coli* and group B streptococcus

**Skin**
*Staphylococcus epidermidis*

**Name the nosocomial pathogen(s) associated with each of the following:**

**Urinary catheter**
*Escherichia coli* and *Proteus mirabilis*

**Respiratory therapy equipment, ventilators**
Pseudomonas aeruginosa
Wound infections
Staphylococcus aureus
Water aerosols
Legionella sp.

Tuberculosis

Decide whether each of the following statements is more closely associated with 1° or 2° TB:

Radiographic finding = Ghon complex; classically affects lower lobes
1°TB
Miliary TB
2°TB
Fibrocaceous cavitary lung lesion; classically affects apical lungs (↑ affinity for ↑ O₂ environment)
2°TB
Symptoms of cough/hemoptysis, fever, night sweats, and weight loss
2°TB

What type of hypersensitivity reaction is seen after infection with M. tuberculosis?
Type IV or delayed-type hypersensitivity (basis for PPD test)

What unique type of cell is seen in association with caseating granulomas in TB?
Langerhans giant cell

What is the mode of transmission of M. tuberculosis!
Respiratory droplets

What term describes the lymphatic and hematogenous spread of TB, causing numerous small foci of infection in extrapulmonary sites?
Miliary TB

Name five common sites of extrapulmonary TB:
1. CNS (tuberculous meningitis)
2. Vertebral bodies (Pott disease)
3. Psoas major muscle → abscess
4. GI tract (liver and cecum)
5. Cervical lymph nodes → scrofuloderma

What is an effective screening tool for latent TB?
PPD test

How is active TB infection diagnosed?
Clinical and radiologic signs of 2° TB and acid-fast bacilli in sputum
What is the management of PPD + latent TB?
Treatment with INH + pyridoxine (vitamin B₆) for 9 months

What is the treatment for active TB?
Respiratory isolation and initial four-drug therapy (**RIPE**: Rifampin, INH, Pyrizinamide, Ethambutol)

What is the major toxicity of most TB drugs?
Hepatotoxicity; INH → vitamin B₆ deficiency; ethambutol → optic neuritis

**ANTIBIOTICS**

Name the drug(s) whose mechanism of action is described below:
- Binds penicillin-binding proteins → inhibits transpeptidase → blocks cell wall synthesis; also releases autolytic enzymes (bactericidal)
- β-Lactam antibiotics (penicillin, cephalosporins, cephalomycins, carbapenems, and monobactams)
- Forms reactive cytotoxic metabolites inside cell
- Metronidazole
- Binds and inactivate β-lactamase → protects antibiotic
- β-Lactamase inhibitors
- **Inhibits 50S peptidyl transferase**
- Chloramphenicol
- Blocks entry of aa-tRNA to 30S ribosomal complex
- Tetracyclines
- Blocks transpeptidation of D-ala
- Inhibits dihydrofolate reductase
- Vancomycin
- **Inhibits dihydrofolate reductase**
- Trimethoprim (TMP)
- **Para-aminobenzoic acid (PABA) antimetabolites** → ↓ dihydropteroate synthase
- Sulfonamides
- **Binds to 30S subunit** → block formation of 70S initiation complex → misreading of mRNA
- Aminoglycosides
- **Binds to 50S subunit** → inhibit translocase
- Macrolides (erythromycin and azithromycin)
- **Blocks DNA topoisomerase (gyrase)**
- Quinolones (ciprofloxacin and levofloxacin)
- **Blocks 50S peptide bond formation**
Clindamycin
Inhibits DNA-dependent RNA polymerase
Rifampin
Interferes with mycolic acid synthesis
INH
Bind to bacterial/fungal cell membranes → disrupt osmotic properties
Polymyxins
PABA antagonist → blocks purine synthesis
Sulfones (dapsone and sulfoxone)

Name the antibacterial drug(s) associated with each of the following unique toxicities:

Kernicterus in infants
Sulfonamides and ceftriaxone
Interstitial nephritis
Penicillins
Disulfiram-like reactions
Metronidazole, second-generation cephalosporins
Photosensitivity rash
Doxycycline
Gray baby syndrome
Chloramphenicol
Megaloblastic anemia
IMP
Hemolytic anemia in G6PD-deficient patient
Sulfonamides, chloramphenicol, nitrofurantoin, and INH
Hepatotoxicity, vitamin B₆ deficiency, lupuslike syndrome
INH (Note: ↑ t₁/₂ in slow acetylators)
Pseudomembranous colitis
Clindamycin (most common)
Fanconi syndrome
Tetracycline (ingestion of expired drug)
Ototoxicity and nephrotoxicity
Aminoglycosides
Red, pruritic rash on torso with rapid IV infusion (red man syndrome)
Vancomycin
Reversible cholestatic hepatitis; ↑ GI motility
Erythromycin
Achilles tendonitis; cartilage damage in laboratory animals
Fluoroquinolones
Red-orange discoloration of bodily secretions
Rifampin
Discolors teeth; suppresses bone growth in kids
Tetracycline
Aplastic anemia (dose independent)
Chloramphenicol
Neurotoxicity and nephrotoxicity
Polymyxins

Name six uses for metronidazole:
1. Giardia
2. Entamoeba
3. Trichomonas
4. *Gardnerella vaginalis*
5. Anaerobes (*C. difficile*, bacteroides)
6. *Helicobacter pylori* (part of triple therapy)

Which drug is used as solo prophylaxis for TB?
INH

How do organisms develop resistance against vancomycin?
\[ \text{D-lac (or D-ser) replaces terminal D-ala in cell wall} \rightarrow \downarrow \text{affinity of vancomycin for cell wall} \]

**VIROLOGY**

**Taxonomy/Basics**

Name six medically important DNA viral families:

**HHAPPy:**
1. Hepadnaviridae
2. Herpesviridae
3. Adenoviridae
4. Poxviridae
5. Parvoviridae
6. Papovaviridae

Name two families of circular DNA viruses:
1. Papovaviridae
2. Hepadnaviridae
Name the only ssDNA viral genome:
  Parvovirus

Name the only DNA virus that replicates in the cytoplasm:
  Poxviridae (carries its own DNA-dependent RNA polymerase)

Name three naked DNA viruses:
  PAP:
  1. Parvo
  2. Adeno
  3. Papov

Name the only dsRNA viral genome:
  Reoviruses (e.g., rotavirus)

Name the family of the smallest RNA viruses:
  Picornaviruses

Name four families of naked RNA viruses:
  CRAP:
  1. Calicivirus
  2. Reovirus
  3. Astrovirus
  4. Picornavirus

Name two families of RNA viruses that do not replicate solely in the cytoplasm:
  1. Influenza viruses
  2. Retroviruses

Where do most enveloped viruses acquire their membranes?
  From plasma membrane (except herpesviruses—nuclear membrane)

Name four families of segmented viruses:
  BOAR (all RNA viruses)
  1. Bunyaviridae
  2. Orthomyxoviridae (influenza viruses)
  3. Arenaviridae
  4. Reoviridae

Name the only diploid viruses:
  Retroviruses

What types of nucleic acids do not require special enzymes to be infectious?
  Those with same structure as host nucleic acids (e.g., positive-stranded ssRNA and most naked dsDNA)

Name the type of viral genetic strategy described below:
  The virus contains its own genetic material but is coated with surface proteins from another virus, which determine its infectivity
  Phenotypic mixing
Occurs when viruses exchange segments of their genomes
Reassortment
Occurs when a nonmutated virus assists a mutated one by making a functional
gene product that serves both itself and the mutated virus
Complementation
Exchanging oligonucleotides by crossing-over within base sequences
Recombination

What type of antigenic change in the influenza virus causes epidemics?
Antigenic drift (minor changes from random mutation)

What type of antigenic change in the influenza virus causes pandemics?
Antigenic shift (reassortment of genome, including animal acquisition)
(Drifting is a Slow Process, Shifting is a Rapid Process)

For each of the following vaccines, state whether it is live attenuated or killed:

Sabin polio
Live attenuated

Salk polio
Killed (SalK = Killed)
May revert to virulence
Live attenuated (very rare)

For whom is it dangerous to receive live vaccines?
Immunocompromised hosts (ie, transplant recipients, AIDS patients, and pregnant
women)

Infectious Diseases

Name the virus(es) associated with each of the following statements:

Tzanck prep shows multinucleated giant cells
Herpes simplex virus (HSV)-1, HSV-2, and varicella-zoster virus (VZV)

Viral culture with buffy coat
Cytomegalovirus (CMV)

Transmitted by bat, raccoon, and skunk bites
Rabies virus

Transmitted by arthropods
Arboviruses

Cowdry type A inclusion bodies
Herpesviruses (HSV-1, CMV, and VZV)

Number 1 cause of diarrhea in kids 3 years old (y/o)
Rotavirus
Number 1 cause of viral pneumonia in infants 6 months
Respiratory syncytial virus (RSV)
Severe (but rare) sequelae include giant cell pneumonia and subacute sclerosing panencephalitis (SSPE)
Measles virus (rubeola)
**Councilman bodies in liver**
Yellow fever virus
**Reactivation of virus in brain of AIDS patient → demyelination, death**
JC virus → progressive multifocal leukoencephalopathy (PML)
**Bullet-shaped, helical nucleocapsid; travels up nerve axons to CNS in retrograde fashion**
Rabies virus
**Koplik spots**
Measles virus (rubeola)
**Dane particle**
Hepatitis B virus
**Atypical lymphocytes**
Epstein-Barr virus (EBV) and CMV
**Nosocomial infection associated with the newborn nursery**
CMV and RSV
**Negri bodies in neurons**
Rabies virus
**Incomplete RNA virus → requires envelope**
Hepatitis D virus
**Positive heterophile antibody test**
EBV
**Necrosis of large motor neurons in anterior horn spinal cord → flaccid paralysis**
Poliovirus

For each of the following clinical findings, name the associated virus:

**Shingles**
VZV

**Suboccipital lymphadenopathy**
Rubella virus

**Herpangina, hand-foot-and-mouth disease**
Coxsackie A virus

**Gingivostomatitis, keratitis, and temporal lobe encephalitis**
HSV-1

**Genital and neonatal infections**
HSV-2
Fever, hepatosplenomegaly pharyngitis, and posterior auricular lymphadenopathy; “kissing disease”
EBV (mononucleosis)
**Common cold**
Rhinoviruses (>100 serotypes; associated with 85% of cases)
**PML**
JC polyomavirus
**Chickenpox**
Varicella
**Small, pearly, umbilicated papular epidermal growths near genitals**
Molluscum contagiosum virus
**German measles and congenital infections**
Rubella virus
**Explosive gastroenteritis; recent epidemics on cruiseships and schools**
Norwalk virus
**Exanthem subitum (roseola)**
Human herpesvirus (HHV)-6
**Contains hemagglutinin and neuraminidase virulence factor; undergoes antigenic shift and responsible for pandemics**
Influenza A
**Fever, black vomitus, and jaundice; transmitted by *Aedes* mosquito**
Yellow fever virus
**Pericarditis, myocarditis, and pleurodynia**
Coxsackie B virus
**Acute viral hepatitis**
Hepatitis A and B
**Mononucleosis, congenital infection, and pneumonia**
CMV
**Subacute sclerosing panencephalitis (SSPE)**
Measles (rubeola) virus
**Intussusception from hyperplasia of Peyer patches**
Adenoviruses
**Kaposi sarcoma**
HHV-8
**Aseptic meningitis, orchitis, and parotitis**
Mumps virus
**Barking cough and laryngeal swelling**
Parainfluenza viruses (croup)
**Hepatitis from IV drug abuse or blood transfusion**
Hepatitis C virus
Hydrophobia, seizures, and fatal encephalitis
Rabies virus
**Cause of common and genital warts**
Human papillomavirus (HPV)
**Tropical spastic paresis**
Human T-cell leukemia/lymphoma virus (HTLV)
**Hepatitis with high mortality rate in pregnant women**
Hepatitis E virus
**Reye syndrome**
Influenza viruses (occurs with aspirin [ASA] ingestion)
**Epidemic keratoconjunctivitis; childhood URIs**
Adenoviruses
Cough, coryza, and conjunctivitis
Measles (rubeola) virus
**Erythema infectiosum (fifth disease); transient aplastic anemic crisis**
Parvovirus B19

Name the oncogenic virus associated with the following cancers:
- Burkitt lymphoma
  EBV
- Hepatocellular carcinoma
  Hepatitis B and C viruses
- Hairy cell leukemia
  HTLV-2
- Adult T-cell lymphoma
  HTLV-1
- Nasopharyngeal carcinoma
  EBV
- Kaposi sarcoma
  HHV-8
- Cervical, penile, and anal carcinoma
  HPV types: 16, 18, 31, 33, and 45

Name the family of viruses characterized by the following:
- Smallpox, molluscum contagiosum, and vaccinia
  Poxviridae
- Hantavirus and California encephalitis
  Bunyaviridae
- Marburg and Ebola hemorrhagic fever
  Filoviridae
Lassa fever and lymphocytic choriomeningitis
Arenaviridae

Human Immunodeficiency Virus

Which continent has the highest incidence (and prevalence) of AIDS?
   Africa

What are the three major routes of HIV transmission?
   1. Sexual contact
   2. Vertical (mother to newborn) transmission
   3. Parenteral

What is the most common mode of HIV transmission on a global basis?
   Heterosexual contact

What type of virus is HIV?
   Human retrovirus of the lentivirus family

What test is used to screen for HIV infection?
   Enzyme-linked immunosorbent assay (ELISA) looks for AB to viral proteins; ↑ sensitivity.

What test is used to confirm HIV(+) screening results?
   Western blot assay (high false negative within 2 months of infection); ↑ specificity

Which enzyme creates dsDNA from RNA for integration into host genome?
   Reverse transcriptase (RT)

What test is used to monitor the effects of antiretroviral therapy?
   HIV RT-polymerase chain reaction (RT-PCR) (measures viral load)

What is the strongest measure of disease progression in an HIV(+) patient?
   CD4\(^+\) T-cell count

Name two key glycoproteins on the surface of the HIV viral envelope:
   1. gp41 (fusion)
   2. gp120 (attachment) proteins; together = gp160

Name two key HIV viral core proteins:
   1. p24 (nucleocapsid)
   2. p17 (matrix protein)

Name three key HIV retroviral enzymes contained in the core:
   1. RT
   2. Integrase
   3. Protease (all encoded by pol gene)

Which viral antigen peaks within 2 months of infection, then rises again years later?
What are the two cell surface molecules to which gp120 must bind?
1. CD4
2. A chemokine receptor (CCR5 or CXCR4)

**HIV infects which three cell types?**
1. CD4\(^{+}\) T cells
2. Monocytes/macrophages
3. Dendritic cells

The induction of what cellular transcription factor during an immune response leads to activation of transcription of HIV proviral DNA?
Nuclear factor-kappa B (NF-KB)

**Protease inhibitors of HIV prevent cleavage of the protein product of what viral genes?**
*Gag* and *pol* genes

What are the three mechanisms by which HIV-infected CD4\(^{+}\) T cells are lost?
1. HIV cytopathic effect
2. Apoptosis
3. HIV-specific cytotoxic T-cell killing

What are the three stages of HIV infection?
1. Acute retroviral infection
2. Chronic phase
3. AIDS

What is the surrogate measure of viral load in an HIV\((+)^{+}\) patient?
HIV-1 RNA

What is the strongest measure of disease progression in AIDS?
CD4\(^{+}\) T-cell count

Which tissues are the major reservoirs of HIV-infected T cells and macrophages in patients?
1. Lymph nodes
2. Spleen
3. Tonsils

Which cell type in the brain is infected by HIV?
Microglial cells

List the major immune abnormalities in AIDS:
1. Decreased number of CD4\(^{+}\) T cells
2. Decreased T-cell function
3. Polyclonal activation of B cells
4. Altered macrophage function
What is the clinical picture of direct viral disease from HIV?
Constitutional symptoms (weight loss, fever, fatigue, and night sweats) and/or neurologic symptoms (encephalopathy with dementia and aseptic meningitis)

How is AIDS defined?
CD4+ 200 or AIDS-defining illness, regardless of CD4+ count

Name the common AIDS opportunistic organisms or infections/diseases associated with the following:

**Four fungal infections**
1. Candidiasis (GI tract)
2. Cryptococcosis (meningitis)
3. Histoplasmosis (disseminated)
4. Coccidioidomycosis (disseminated)

**Five bacterial infections**
1. *Mycobacterium tuberculosis* (lung/disseminated)
2. *Mycobacterium avium-intracellulare* (lung)
3. *Nocardia* (lung/CNS/disseminated)
4. *Salmonella* (disseminated)
5. Encapsulated organisms

**Four viral infections**
1. HSV
2. VZV (shingles)
3. CMV (retinitis or colitis)
4. JC virus (PML)

**Three protozoal infections**
1. *Pneumocystis* (lung or disseminated)
2. *Toxoplasma* (lung/CNS)
3. *Cryptosporidium* (GI)

State the typical CD4+ count associated with each of the following HIV complications:

**Opportunistic infections** are typically seen, especially *Pneumocystis jiroveci* pneumonia
200 cells/mL

*Mycobacterium avium* complex (MAC), CMV, and cryptosporidiosis
50 cells/mL

**Toxoplasmosis**
100 cells/mL

**TB becomes more common**
400 cells/mL

List four common neoplasms in patients with AIDS:
1. Kaposi sarcoma
2. Non-Hodgkin B-cell lymphoma
3. CNS lymphoma
4. Squamous cell carcinoma of the cervix or anus

What has been shown to minimize the risk of perinatal HIV transmission?
Zidovudine (AZT) given to pregnant women, cesarean delivery, and avoiding breast feeding

Prions

Which infectious agents lack both DNA and RNA?
Prions (made of proteins only)

What are symptoms of prion diseases?
Rapidly progressing dementia, psychiatric disturbances, and cerebellar symptoms (ataxia, myoclonis). All prion diseases are fatal.

Name four prion diseases:
1. Creutzfeldt-Jacob disease (rapidly progressive dementia)
2. Mad cow disease
3. Kuru
4. Fatal familial insomnia

What type of histopathologic change is seen in these diseases?
Spongiform encephalopathy

ANTIVIRAL AGENTS

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and uniquetoxicity (TOX) (if any):
   Acyclovir and valacyclovir
   MOA: guanosine analog; activated by herpes thymidine kinase → inhibits viral DNA polymerase
   IND: HSV (treatment and prophylaxis for oral, genital, and ocular herpes), VZV (chickenpox and shingles)
   TOX: neurotoxic (delirium and tremors) and nephrotoxic
   Ganciclovir
MOA: guanosine analog; activated by human thymidine kinase → inhibits CMV DNA polymerase
IND: CMV (retinitis, pneumonia, colitis), especially in immunocompromised people
TOX: bone marrow suppression, nephrotoxic, and ↓ spermatogenesis (toxicity → acyclovir because activated by human enzyme)

Foscarnet
MOA: pyrophosphate analog; inhibits viral DNA polymerase (no activation required)
IND: CMV, HSV (refractory infections)
TOX: reversible nephrotoxicity and anemia

Nucleoside RT inhibitors (zidovudine—azidothymidine [AZT], didanosine—ddl, zalcitabine—ddC, lamivudine-3TC, and stavudine—d4T)
MOA: nucleoside analogs; activated by phosphorylation → inhibits RT → prevents incorporation of viral genome into host DNA
IND: part of combination therapy for HIV
TOX: bone marrow suppression, peripheral neuropathy, pancreatitis (especially ddl), lactic acidosis, and macrocytic anemia (AZT)

Nonnucleoside RT inhibitors (nevirapine, delavirdine, and efavirenz)
MOA: binds directly to and inhibits HIV RT → prevents incorporation of viral genome into host DNA
IND: part of combination therapy for HIV
TOX: rash (including Steven-Johnson), ↑ liver enzymes, inhibits P-450, vivid dreams/CNS changes (with efavirenz)

Protease inhibitors (saquinavir, ritonavir, indinavir, nelfinavir, and amprenavir)
MOA: blocks protease enzyme → inhibits assembly of viral core and new viruses
IND: part of combination therapy for HIV
TOX: GI upset, insulin resistance, ↑ lipids, fat redistribution syndromes, interstitial nephritis, and thrombocytopenia (indinavir)

Amantadine and rimantadine
MOA: inhibits viral penetration and uncoating; releases dopamine (DA) from intact nerve terminals
IND: influenza A treatment/prophylaxis, Parkinson disease
TOX: CNS effects: confusion, ataxia, and slurred speech (less with rimantadine); teratogenesis

Zanamivir and oseltamivir
MOA: neuraminidase inhibitor → alters virion aggregation and release
IND: influenza A and B treatment and prophylaxis (oseltamivir)
TOX: bronchospasm in patients with asthma /COPD) (zanamivir)

Ribavirin
MOA: guanosine analog; activated by phosphorylation → inhibits inosine-5’-monophosphate (IMP) dehydrogenase
IND: RSV, hantavirus, and chronic hepatitis C
TOX: hemolysis (when given IV)

Interferon-α
MOA: human glycoproteins that interfere with ability of viruses to replicate (block protein synthesis and degrade mRNA)
IND: chronic hepatitis B and C, genital warts, Kaposi sarcoma, and hairy cell leukemia
TOX: bone marrow suppression

What constitutes highly active antiretroviral therapy (HAART)?
Two nucleoside RT inhibitors and a protease inhibitor or nonnucleoside RT inhibitor.
Note: no patient should ever be on monotherapy as resistance is invariable.

When is HAART typically initiated?
CD4⁺ 500 cells/mL or very high viral load

Which drug is used to prevent vertical transmission during pregnancy?
Zidovudine (AZT)

MYCOLOGY

Which four endemic mycoses can mimic TB?
1. Histoplasmosis
2. Coccidioidomycosis
3. Paracoccidioidomycosis
4. Blastomycosis

What is a dimorphic fungus?
Lives in two forms: cold = mold (37°C), heat = yeast

Name the fungus associated with each of the following statements:
“Spaghetti and meatball” appearance on KOH prep
Malassezia furfur
Contains cancer-causing aflatoxins
Aspergillus flavus
Dimorphic fungus living on rose thorns and splinters
Sporothrix schenckii
Urease (+), stains with India ink, and latex agglutination (+)
Cryptococcus neoformans
Organism found inside macrophages; spread in pigeon and bat droppings
Histoplasma capsulatum
Budding yeast, pseudohyphae; germ tubes at 37°C
*Candida albicans*
Wide angle (90°) branching of irregular nonseptated hyphae
*Mucor* and *Rhizopus* sp.
**Big, broad-based budding dimorphic fungus**
*Blastomycosis*
**B-B-B-B-B** (Big, Broad-Based Budding Blasto)
45° angle branching and septated hyphae; fruiting bodies
*Aspergillus* sp.
Narrow-based unequal budding yeasts with capsular halo
*Cryptococcus neoformans*
*Endemic to Ohio and Mississippi river valleys*
*Histoplasma capsulatum*
”Flying-saucer” appearance of silver stain
*Pneumocystis carinii* (also *P. jiroveci*)
”Captain’s wheel” appearance; endemic to rural Latin America
*Paracoccidioidomycosis*

For each of the following diseases, name the fungus/yeast responsible and the drug of choice:

**Rose gardener disease with ascending lymphangitis**
*Sporothrix schenckii*—potassium iodide
**Tinea nigra**
*Phaeoannellomyces werneckii*—topical salicylic acid
**Thrush in an immunocompromised patient**
*Candida albicans*—nystatin (swish and swallow) and amphotericin B if systemic infection

**San Joaquin (desert valley) fever; endemic to southwest United States, California**
*Coccidioides immitis*—fluconazole and amphotericin B

**Interstitial pneumonia of the immunocompromised**
*Pneumocystis carinii* (or *P. jiroveci*)—TMP-sulfamethoxazole (SMX) or pentamidine (prophylaxis when CD4+200 cells/mL)
**Tinea (pityriasis) versicolor**
*Malassezia furfur*—topical miconazole or selenium sulfide

**Meningitis from pigeon droppings**
*Cryptococcus neoformans*—amphotericin + flucytosine for 2 weeks followed by fluconazole
**Tinea cruris/capitis/corporis/unguium/pedis**
Trichophyton, Epidermophyton, or Microsporum sp.—topical miconazole, oral griseofulvin for capitis and unguium
Fungus ball in lungs or invasive disease
Aspergillus fumigatus—voriconazole

ANTIFUNGALS

Name the drug whose mechanism of action is described below:
Blocks ergosterol (unique to fungi) synthesis by inhibiting P-450
Azole family (ketoconazole, fluconazole, miconazole, voriconazole, and posaconazole)
Binds ergosterol → produces membrane pores
Amphotericin B and nystatin
Blocks ergosterol synthesis by blocking squalene epoxidase
Terbinafine
Interferes with microtubule formation → inhibits mitosis
Griseofulvin
Converted to 5-fluorouracil (5-FU) → blocks formation of purines
Flucytosine

Name the antifungal drug(s) associated with each of the following unique toxicities:
Rigors, acute febrile reaction, nephrotoxicity, and arrythmias
Amphotericin B—follow BUN/creatinine daily. Note: newer lipid formulations (ie, AmBisome less nephrotoxic)
Photosensitivity, mental confusion, bone marrow suppression, and induces P-450
Griseofulvin
Antiandrogenic effects, adrenal suppression, and liver dysfunction
Azole family (especially ketoconazole)
Bone marrow suppression and alopecia
Flucytosine

PARASITOLOGY

Protozoa
Name the protozoan associated with each of the following statements:

- Transmitted by Tsetse fly; shows antigenic variation
  - *Trypanosoma brucei* (gambiense and rhodesiense)
- Transmitted by *Anopheles* mosquito
  - *Plasmodium*
- Transmitted by Reduviid bug
  - *Trypanosoma cruzi*
- Transmitted by cysts in meat or cat feces
  - *Toxoplasma*
- Transmitted by sandfly
  - *Leishmania*
  - Obligate intracellular parasite; cysts on acid-fast stain
  - *Cryptosporidium*
  - Maltese “X” cross shape
  - *Babesia*
  - Pear-shaped, binucleate, flagellated trophozoite
  - *Giardia lamblia*
  - Blood smear shows trophozoites and schizonts
  - *Plasmodium*
  - Macrophages containing amastigotes
  - *Leishmania donovani*

For each of the following clinical findings, name the associated protozoan and the treatment:

- Megacolon, megaesophagus, and cardiomegaly (with apical atrophy)
  - *Trypanosoma cruzii* (Chagas disease)—nifurtimox
- Cyclic fever, headache, anemia, and splenomegaly
  - *Plasmodium*—chloroquine for erythrocyte forms and primaquine for latent forms
    - *(Plasmodium vivax and Plasmodium ovale)*
- Chloroquine-resistant malaria
  - *Plasmodium falciparum*—mefloquine or quinine and pyramethamine/sulfadoxine
- Bloody diarrhea with “flask-shaped” ulcers, liver abscesses, and trophozoites in stool
  - *Entamoeba histolytica*—metronidazole and iodoquinol
- Black fever or “kala-azar”
  - *Leishmania donovani*—sodium stibogluconate (pentavalent antimony)
- Severe, watery diarrhea in AIDS patient
  - *Cryptosporidium*—supportive (hydration, improve immune status)
- Flatulence, bloating, and foul-smelling diarrhea
  - *Giardia lamblia*—metronidazole
African sleeping sickness  
*Trypanosoma brucei (gambiense and rhodesiense)*—suramin (acutely) or melarsoprol (for CNS symptoms)  
Encephalitis with brain abscesses in immunocompromised host; congenital defects  
*Toxoplasma gondii*—pyrimethamine and sulfadoxine or clindamycin  
Vaginitis with foul-smelling, frothy discharge  
*Trichomonas vaginalis*—metronidazole  
Fever and hemolytic anemia after *Ixodes* tick bite  
*Babesia* sp.—quinine and clindamycin  

**Why are many Africans resistant to *P. vivax* infection?**  
They carry sickle cell trait and/or they lack antigens Duffy a and b on RBCs.  

**What causes the cyclic symptoms in malaria?**  
Immune response to burst RBCs that release merozoites

**Helminths**

For each of the following clinical findings, name the associated helminth and the treatment:  

Larvae penetrate skin of feet; GI infection → anemia  
*Ancylostoma duodenale* or *Necator americanus* (hookworms)—mebendazole or pyrantel pamoate  
Worms visibly crawling in conjunctiva; spread by deerfly  
*Loa loa*—diethylcarbamazine  
Fever, periorbital edema, and myositis after ingesting raw pork  
*Trichinella spiralis*—thiabendazole  
River blindness; spread by female blackflies  
*Onchocerca volvulus*—ivermectin (*rIVERmectin* for RIVER blindness)  
Elephantiasis from lymphatic blockage  
*Wuchereria bancrofti*—diethylcarbamazine  
Larvae penetrate skin → autoinfection; GI infection  
*Strongyloides stercoralis*—(threadworm)-thiabendazole or ivermectin  
Intestinal infection and anal pruritis; ↑ incidence in children; positive “tape test”  
*Enterobius vermicularis* (pinworms)—mebendazole or pyrantel pamoate  
Fluke associated with squamous cell carcinoma of the urinary tract  
*Schistosoma haematobium*—praziquantel  
Granulomatous hepatitis and chorioretinitis  
*Toxocara canis*—diethylcarbamazine
GI infection; competes for food → malnutrition in children; eggs visible in feces
*Ascaris lumbricoides*—mebendazole or pyrantel pamoate

**Inflammation and 2° bacterial infection of lungs from undercooked crab meat**
*Paragonimus westermani*—praziquantel

**Biliary tract inflammation from undercooked fish**
*Opisthorchis (Clonorchis) sinensis*—praziquantel

**Undercooked pork larval worm → mass lesions in brain; cysticercosis**
*Taenia solium*—praziquantel or niclosamide, albendazole for cysticercosis

**Hydatid liver cysts from eggs in dog feces → anaphylaxis if antigens released from cysts**
*Echinococcus granulosus*—albendazole, careful surgical removal of cysts (preinjected with ETOH)

**Fish tapeworm causing vitamin B\textsubscript{12} deficiency**
*Diphyllobothrium latum*—praziquantel

**Cercariae penetrate skin → granulomas and inflammation of liver and spleen; snails are hosts**
*Schistosoma* sp.—praziquantel

Which cell count is elevated during many helminth infections and can be detected by routine CBC?
*Eosinophils*

Which is the most common helminth infection in the United States?
*Enterobius vermicularis*

Name the antiparasitic drug(s) associated with each of the following unique toxicities:

**Cinchonism**
Quinine

**Hemolytic anemia in G6PD-deficient person**
Chloroquine, primaquine, quinine, and TMP-SMX

**Mazzotti reaction (pyrexia, hypotension, and respiratory distress caused by death of parasites)**
Diethylcarbamazine (with *Onchocerca*)
Name the structure(s) in the adult nervous system that arise from the following embryonic components:

- Alar plate
  - Sensory neurons
- Basal plate
  - Motor neurons
- Telencephalon
  - Cerebral hemispheres and lateral ventricles
- Diencephalon
  - Thalamus, optic nerves, and third ventricle
- Mesencephalon
  - Midbrain and aqueduct
- Metencephalon
  - Pons, cerebellum, and superior fourth ventricle
- Myelencephalon
  - Medulla and inferior fourth ventricle
- Neural crest cells
  - Peripheral sensory and autonomic nerves and sensory ganglia

What is the level of the conus medullaris in a newborn and in an adult?
- L2 or L3 (newborn), L1 (adult)

What are the divisions of the autonomic nervous system?
Sympathetic, parasympathetic

Where are the preganglionic cell bodies of the sympathetic nervous system?
   Intermediolateral horn of the spinal cord from T1 to L3

Where are the preganglionic cell bodies of the parasympathetic nervous system located?
   Brainstem (cranial nerve nuclei) and spinal cord from S2 to S4

Which is the primary neurotransmitter (NT) of both sympathetic and parasympathetic ganglia?
   Acetylcholine (ACh)

Which is the primary type of cholinergic receptor of both sympathetic and parasympathetic ganglia?
   Nicotinic

Which NT mediates the transmission of impulses from sympathetic neurons to effector organs?
   Norepinephrine (NE)

Which NT mediates the transmission of impulses from parasympathetic neurons to effector organs?
   ACh

Which NT mediates the transmission of impulses from somatic neurons to skeletal muscle?
   ACh

What types of receptors are present on the effector organs innervated by the sympathetic nervous system?
   $\alpha_1$, $\alpha_2$, $\beta_1$, and $\beta_2$

What type of receptor is present on the effector organs innervated by the parasympathetic nervous system?
   Muscarinic

What type of receptor is present on muscle innervated by the somatic nervous system?
   Nicotinic

Sympathetic Nervous System

Name the effect of the sympathetic nervous system on the following organ systems and the type of receptor which mediates each effect:
   **Eyes**
   Pupillary dilation ($\alpha_1$)
   **Salivary glands**
   Increased thick, viscous secretions
Bronchioles
Bronchodilation ($\beta_2$), ↑ secretions

**Heart**
Tachycardia ($\beta_1$), ↑ contractility ($\beta_1$), ↑ AV nodal conduction ($\beta_1$)

**Vascular smooth muscle**
Vasoconstriction of cutaneous mucous membrane and splanchnic vessels ($\alpha_1$); vasodilation in skeletal muscle ($\beta_2$)

**Gastrointestinal (GI) tract**
↓ Muscle motility and tone ($\beta_2$), contraction of sphincters ($\alpha_1$)

**Male sex organs**
Ejaculation ($\alpha_2$)

**Uterus**
Relaxation ($\beta_2$), contraction ($\alpha_1$)

**Bladder and ureters**
Relaxation of detrusor ($\beta_2$) contraction of trigone and sphincter ($\alpha_1$)

**Sweat glands**
↑ Secretions (muscarinic)

**Kidneys**
↑ Renin secretion

**Adipocytes**
↑ Lipolysis ($\beta_1$)

**Pancreas**
↓ Insulin secretion ($\alpha_2$), ↑ insulin secretion ($\beta_2$)

**Parasympathetic Nervous System**

What is the effect of the parasympathetic nervous system on the following organ systems:

**Eyes**
Pupillary constriction

**Bronchioles**
Bronchoconstriction

**Heart**
Bradycardia, ↓ contractility, ↓ AV nodal conduction

**GI tract**
↑ Motility, relaxation of sphincters

**Male sex organs**
Erection
Bladder and ureters
Contraction of detrusor, relaxation of sphincters and trigone

What type of cholinergic receptor mediates all of the effects on the organs above?
Muscarinic

Motor and Sensory Fibers?

What type of motor fiber innervates extrafusal muscle fibers?
A-alpha (A-α)

What type of motor fiber innervates intrafusal muscle fibers?
A-gamma (A-γ)

Name the function of each of the following types of sensory fibers:
Ia (A-α)
Proprioception, muscle spindles

Ib
Proprioception, Golgi tendon organs

II (A-β)
Touch, pressure, and vibration; secondary afferents of muscle spindles

III (A-δ)
Touch, pressure, fast pain, and temperature

IV (c)
Slow pain and temperature (unmyelinated)

What types of sensory fibers have the largest diameter and consequently the fastest conduction velocity?
Ia and Ib

What type of motor fibers have the largest diameter and consequently the fastest conduction velocity?
A-α

What type of sensory fibers have the smallest diameter and consequently the slowest conduction velocity?
C

What is the electrochemical effect of an inward Na⁺ current on a sensory fiber?
Depolarization

Name the function of each of the following components of a sensory pathway:
Sensory receptor
Translates environmental stimulus into an electrical impulse
First-order neuron
Carries impulse from sensory receptor into central nervous system (CNS)

Second-order neuron
Carries impulse from primary neuron to the thalamus

Third-order neuron
Carries impulse from second-order neuron to the cerebral cortex

Fourth-order neuron
Carries impulses from third-order neurons to appropriate somatosensory area of cerebral cortex

Name the type of mechanoreceptor described below:
- Onion-like subcutaneous receptors that respond to vibration and tapping
  Pacinian corpuscle
- Primary receptors of the dermal papillae that mediate two-point tactile discrimination
  Meissner corpuscle
- Encapsulated receptor that responds to pressure
  Ruffini corpuscle
- Disc-shaped touch receptor of the deep dermis
  Merkel tactile disc

Rods or cones?
- Sensitive to low-intensity light
  Rods
- Sensitive to high-intensity light
  Cones
- Receptor used primarily for night vision
  Rods
- Receptor used primarily for day vision
  Cones
- Present in fovea
  Cones
- High visual acuity
  Cones
- Receptor which adjusts to low light conditions most rapidly
  Cones
- Receptor capable of color vision
  Cones

Name the type of muscle sensor for each of the following functions:
- Detection of static and dynamic changes in muscle length
  Muscle spindles
Detection of muscle tension
Golgi tendon organs

Detection of vibration
Pacinian corpuscles

Detection of pain
Free nerve endings

What type of motoneuron is responsible for ensuring that a muscle will respond appropriately throughout contraction, despite changes in tension?
γ-Motoneurons

What type of muscle reflex, mediated by type Ia afferent fibers, causes muscle contraction in response to muscle stretch?
Stretch or myotatic reflex

What type of muscle reflex, mediated by type Ib afferent fibers, causes muscle relaxation in response to muscle contraction?
Golgi tendon reflex

What type of muscle reflex, mediated by types II, III, and IV afferent fibers, causes ipsilateral flexion and contralateral extension?
Flexor withdrawal reflex

What are the components of the afferent limb of a myotatic reflex arc?
Muscle spindle receptor → Ia fiber → dorsal root ganglion

What comprises the efferent limb of a myotatic reflex arc?
Ventral motor neuron

For each of the following muscle stretch reflexes, name the muscle group and spinal level tested:

Ankle jerk
Gastrocnemius (S1)

Knee jerk
Quadriceps (L2-L4)

Biceps jerk
Biceps (C5-C6)

Forearm jerk
Brachioradialis (C5-C6)

Triceps jerk
Triceps (C7-C8)

What type of posturing is caused by a transecting lesion above the level of the medulla but below the midbrain?
Decerebrate rigidity

What type of posturing is caused by a transecting lesion above the level of the red nucleus (midbrain)?
What are the three layers of the cerebellar cortex?
1. Granular layer (innermost)
2. Purkinje layer (middle)
3. Molecular layer (outermost)

Which is the major NT of cerebellar Purkinje cells?
γ-Aminobutyric acid (GABA).
Note: The output of Purkinje cells is always inhibitory.

Meninges

What are the three layers of the meninges?
“The meninges PAD the CNS”
1. P ia
2. A rachnoid
3. D ura

What meningeal space, which lies between the pia and arachnoid, contains the cerebrospinal fluid (CSF)?
Subarachnoid space

What structure produces CSF?
The choroid plexus of the lateral, third, and fourth ventricles

What structures reabsorb CSF into venous circulation?
The arachnoid granulations

Trace the flow of CSF from the choroid plexus into venous circulation.
Choroid plexus → lateral ventricles → interventricular foramina (of Monro) → third ventricle → cerebral aqueduct → fourth ventricle → lateral foramina (of Luschka) or median foramen (of Magendie) → subarachnoid space → arachnoid granulations → superior sagittal sinus

What are the three major functions of CSF?
1. To provide support and protection to the CNS
2. To remove metabolic waste products
3. To transport hormones and cytokines throughout the CSF and to the systemic circulation

Vasculature of the Central Nervous System

Name the blood vessel that supplies each of the following structures:
Anterior two-thirds of the spinal cord, the medullary pyramids, medial lemniscus, and root fibers of cranial nerve (CN) XII
Anterior spinal artery

Retina
Central artery of the retina (a branch of the ophthalmic artery)

Lateral geniculate body, globus pallidus, posterior limb of internal capsule
Anterior choroidal artery (an important branch of internal carotid artery)

Hypothalamus and ventral thalamus
Posterior communicating artery

Leg-foot area of motor and sensory cortices
Anterior cerebral artery (ACA)

Anterior putamen, caudate nucleus, and anteroinferior internal capsule
Medial striate arteries (branches of the ACA)

Broca (expressive) and Wernicke (receptive) speech areas, face and arm areas of motor cortices, frontal eye field
Middle cerebral artery (MCA)

Internal capsule, caudate nucleus, putamen, globus pallidus
Lateral striate arteries (branches of the MCA)

Nucleus ambiguus and the inferior surface of the cerebellum
Posterior inferior cerebellar artery

Caudal lateral pontine tegmentum (including portions of the nuclei of CN V, VII) and the inferior cerebellar surface
Anterior inferior cerebellar artery

Superior surface of cerebellum, cerebellar nuclei, and the cochlear nuclei
Superior cerebellar artery

Majority of midbrain, portions of the thalamus, lateral and medial geniculate bodies, occipital lobe, inferior aspect of the temporal lobes, and the hippocampus
Posterior cerebral artery (PCA)

Majority of the dura
Middle meningeal artery

Name the cerebral veins that drain directly into the superior sagittal sinus:
    Bridging veins

Name the cerebral vein that drains deep cerebral veins into the straight sinus:
    Vein of Galen

CN III, CN V₁, CN V₂, CN VI, postganglionic sympathetic fibers, and both internal carotid arteries all pass through which structure?
    Cavernous sinus
Axonal Transport

Name the cytoplasmic structure in the nerve cell body and dendrites that are involved in protein synthesis:
   Nissl substance

Name the type of axonal transport described below:
   Transport responsible for delivery of synthesized NTs away from the cell body
   Fast anterograde axonal transport
   Transport responsible for delivery of cytoskeletal and cytoplasmic components away from the cell body
   Slow anterograde transport
   Transport responsible for returning material to the cell body for degradation
   Fast retrograde transport
   Kinesin-dependent transport
   Fast anterograde axonal transport
   Dynein-dependent transport
   Fast retrograde transport
   Transport responsible for carrying nerve growth factor, viruses, and toxins to cell bodies
   Fast retrograde transport

Name the process of anterograde axonal and myelin degeneration accompanied by Schwann cell proliferation:
   Wallerian degeneration

Supporting Cells of the Nervous System

Name the type of cell described below:
   Primary supportive cell type of the CNS
   Astrocyte
   Myelin-producing cell type of the CNS
   Oligodendrocyte
   CNS scavenger cell type
   Microglia
   CSF-producing cell type
   Ependymal cell
   Myelin-producing cell type of the peripheral nervous system (PNS)
   Schwann cells
What type of intercellular connections are responsible for maintaining the integrity of the blood-brain barrier?
   Tight junctions

What proteins are commonly used to identify astrocytes?
   Glial fibrillary acidic protein (GFAP) and glutamine synthetase

Pigments and Inclusions

Name the process or disease associated with the following neuronal histopathologic findings:
   Lipofuscin granules
      Aging
   Depletion of neuromelanin in substantia nigra and Lewy bodies
      Parkinson disease
   Negri bodies
      Rabies
   Amyloid plaques and neurofibrillary tangles
      Alzheimer disease
   Cowdry type A inclusion bodies
      Herpes simplex encephalitis

Spinal Tracts

Name the spinal tract responsible for each of the following functions:
   Voluntary control of skeletal muscle
      Lateral corticospinal/pyramidal tract
   Sensation of pain and temperature
      Lateral spinothalamic tract
   Two-point discrimination and vibratory sensation
      Dorsal column-medial lemniscus tract
   Control of facial muscles
      Corticobulbar tract
   Coordination of muscle tone, posture, balance, and motor activity
      Dentothalamic tract

Describe the major difference between the innervation of the lower and upper facial muscles.
Corticobulbar fibers innervate the lower facial muscles unilaterally, while upper facial muscles are innervated bilaterally.

**Name the structure in the spinal cord composed of ascending fibers of the dorsal column-medial lemniscus pathway originating in the upper extremities:**

Cuneate fasciculus

**Name the structure in the spinal cord composed of ascending fibers of the dorsal column-medial lemniscus pathway originating in the lower extremities:**

Gracile fasciculus (medial to cuneate fasciculus)

**At what level of the brainstem do fibers of the dorsal column-medial lemniscus pathway cross?**

Caudal medulla

**What type of receptors provide input to the lateral spinothalamic tract?**

Free nerve endings

**At what level do fibers of the spinothalamic tract cross?**

At the same level or 1 to 2 levels above/below where they enter the spinal cord.

**Name the structure where fibers of the lateral spinothalamic tract cross the midline:**

Ventral white commissure/anterior commissure

**Where do fibers of the dorsal column-medial lemniscus pathway, the trigeminothalamic, and lateral spinothalamic tract all terminate?**

The sensory cortex (Brodmann areas 3, 1, and 2)

**What part of the cortex gives rise to the fibers of the lateral corticospinal and corticobulbar tracts?**

The motor, premotor, and sensory areas of the cortex (Brodmann areas 6, 4, and 3, 1, 2)

**Fibers of the lateral corticospinal tract pass through which limb of the internal capsule?**

Posterior limb

**Name the structure where fibers of the lateral corticospinal tract cross the midline:**

Medullary pyramids

**Classify each of the following clinical findings as upper motor neuron (UMN) or lower motor neuron (LMN) signs:**

- Spastic paresis: UMN
- Flaccid paralysis: LMN
- Babinski sign (upgoing toes): UMN
- Fasciculations and fibrillations: LMN
Cranial Nerves

Name the cranial foramen that each of the cranial nerves below pass through:

I
Cribiform plate

II
Optic canal

III, IV, V₁, VI
Superior orbital fissure. Note: all of these nerves pass through the cavernous sinus as well.

V₂
Foramen Rotundum

V₃
Foramen Ovale (for divisions of the trigeminal nerve think “Standing Room Only”)

VII, VIII
Internal acoustic meatus

IX, X, XI
Jugular foramen

XII
Hypoglossal canal

Name the function(s) for each cranial nerve listed below:

I: olfactory
Smell

II: optic
Vision

III: oculomotor
1. Eye movement
2. “Parasympathetic” ciliary and pupillary sphincter mm
Note: mm is used as the abbreviation for “muscles”.

IV: trochlear
Contraction of superior oblique muscle
\textbf{V_1: trigeminal—ophthalmic branch}  
Sensation from nose to forehead

\textbf{V_2: trigeminal—maxillary branch}  
Sensation from lateral nose, upper lip, superior buccal area

\textbf{V_3: trigeminal—mandibular branch}  
1. Sensation from areas of the lower face not covered by \textit{V}_1 and \textit{V}_2  
2. Movement of the \textbf{Muscles of Mastication (Masseter, temporalis, Medial, and lateral pterygoids)}, tensor veli palatini, and tensor tympani

\textbf{VI: abducens}  
Contraction of lateral rectus muscle

\textbf{VII: facial}  
1. Parasympathetic—lacrimal, submandibular, and sublingual glands  
2. \textit{Mm} of facial expression, stapedius, stylohyoid, and the posterior belly of the digastric muscle  
3. Taste—anterior two-thirds of tongue  
4. Sensation—skin of external ear

\textbf{VIII: vestibulocochlear}  
Hearing and sense of balance

\textbf{IX: glossopharyngeal}  
1. Parasympathetic—parotid gland  
2. Motor—stylopharyngeus \textit{mm}  
3. Taste—posterior one-third tongue  
4. Sensation—parotid gland, carotid body and sinus, pharynx, and middle ear  
5. Cutaneous sensation—external ear canal

\textbf{X: vagus}  
1. Parasympathetic—trachea, bronchi, heart, GI tract  
2. Contraction of laryngeal, pharyngeal, and esophageal striated \textit{mm}  
3. Taste—epiglottis and palate  
4. Sensation—trachea, GI tract  
5. Cutaneous sensation—external ear

\textbf{XI: accessory}  
Movement of sternocleidomastoid and trapezius muscles

\textbf{XII: hypoglossal}  
Contraction of muscles of tongue

\textbf{Which three cranial nerves are purely sensory nerves?}  
1. CN I  
2. CN II  
3. CN VIII
Which five cranial nerves are purely motor nerves?
1. CNIII
2. CNIV
3. CNVI
4. CNXI
5. CNXII

Which four cranial nerves have both motor and sensory components?
1. CNV
2. CNVII
3. CNIX
4. CNX

Which two cranial nerves are rostral to the midbrain?
1. CNI
2. CNII

Which two cranial nerve nuclei are located in the midbrain?
1. CNIII
2. CNIV

Which four cranial nerves have at least a portion of their nuclei in the pons?
1. CNV
2. CNVI
3. CNVII
4. CNVIII

Which seven cranial nerves have at least a portion of their nuclei in the medulla?
1. CN V
2. CN VI
3. CN VII
4. CNVIII
5. CN IX
6. CNX
7. CNXII

Name the only cranial nerve that crosses the midline and exits the brainstem posterior to the ventricular system:
CN IV—exits the brainstem posteriorly and crosses the midline after exiting the caudal midbrain

What nucleus serves as the origin of preganglionic parasympathetic fibers projecting to the ciliary ganglion?
Edinger-Westphal nucleus of CN III

What visceral sensory nucleus, located in the medulla, is a relay center for taste, sensory input from the carotid sinus, carotid body, and the vagus nerve?
What visceral motor nucleus, located in the medulla, is involved in coordinating swallowing and speech?  Nucleus aMbiguus

Which are the afferent and efferent limbs of the corneal reflex?  
   CN V₁ and CN VII

Which are the afferent and efferent limbs of the pupillary light reflex?  
   CN II and CN III

Which are the afferent and efferent limbs of the gag reflex?  
   CN IX and CN X

Name the site of a lesion, within the visual tract, capable of causing each of the following deficits:

   **Ipsilateral blindness**
   Transection of the optic nerve

   **Binasal hemianopia**
   Bilateral lateral compression of optic chiasm

   **Bitemporal hemianopia**
   Midsagittal transection or midline pressure on the optic chiasm (often caused by a pituitary tumor)

   **Right hemianopia without macular sparing**
   Transection of the left optic radiation

   **Right upper quadrantanopia**
   Transection of the lower division of the left optic radiation

   **Right lower quadrantanopia**
   Transection of the upper division of the left optic radiation

   **Right hemianopia with macular sparing**
   Destruction of the left visual cortex

What are five key structures of the pupillary light reflex pathway?

1. Ganglion cells of the retina
2. Pretectal nucleus of the midbrain
3. Edinger-Westphal nucleus
4. Ciliary ganglion
5. Postganglionic parasympathetic fibers of CN III

What are four key structures of the pupillary dilation pathway?

1. Paraventricular nucleus of the hypothalamus
2. Ciliospinal center of Budge at the level of T1 to T2
3. Superior cervical ganglion
4. Postganglionic sympathetic fibers traveling along the internal carotid artery and its branches to the eye
What part of the cortex is responsible for voluntary eye movements?
   Frontal eye field (Brodmann area 8)

What side will a patient’s eyes deviate toward if there is a lesion of the right frontal eye field?
   Right side (“Look toward the lesion of frontal eye fields”)

What structure connects the nucleus of CN VI and the nucleus of CN III?
   Medial longitudinal fasciculus (MLF)

What type of lesion will result in medial rectus palsy (inability to adduct the eye) on attempted lateral gaze but normal adduction on accommodation?
   Intranuclear ophthalmoplegia (a lesion of the MLF)

What classic idiopathic lesion is characterized by ptosis, miosis, and anhydrosis?
   Horner syndrome

Name the condition characterized by a pupil that will accommodate but cannot react to light:
   Argyll-Robertson pupil (associated with tertiary syphilis, lupus, and diabetes mellitus)

Name the condition caused by a lesion in the afferent fibers of the light reflex pathway:
   Marcus Gunn pupil

What are the primary sensory receptors of the auditory pathway?
   Inner hair cells of the organ of Corti

Where does the auditory pathway terminate?
   Bilateral input from both auditory tracts terminates in primary auditory cortex in superior temporal gyrus (Brodmann areas 41 and 42)

What type of cells are responsible for relaying auditory stimuli from the organ of Corti to the cochlear nuclei?
   Bipolar cells of the spiral or cochlear ganglion

What thalamic nucleus plays a key role in relay of impulses from the cochlear nuclei to higher cortical centers?
   Medial geniculate body of the thalamus

What pontine nucleus plays a key role in sound localization?
   Superior olivary nucleus

What are key structures of the hearing pathway?
   Cochlear → cochlear nucleus → decussating fibers in Trapezoid body → superior olivary nucleus → lateral lemniscus → inferior colliculi → medial geniculate nucleus → primary auditory cortex

Conduction deafness is caused by a lesion of which components of the auditory system?
   External auditory canal, tympanic membrane, or the middle ear
Sensorineural deafness is caused by a lesion of which components of the auditory system?

- Cochlea, cochlear nerve, or the cochlear nuclei

Patients with presbycusis have trouble hearing what types of sounds?

- High-frequency sounds

Which cells of the vestibular system respond to angular acceleration and deceleration?

- The hair cells of the three semicircular canals

What structures of the vestibular system respond to linear acceleration and deceleration?

- The hair cells of the utricle

What type of cells are responsible for relaying vestibular stimuli from the hair cells to the vestibular nuclei?

- Bipolar cells of the vestibular ganglion

What structures provide input to the vestibular nuclei?

- Hair cells of the semicircular canal, hair cells of the utricle, and the flocculonodular lobe of the cerebellum

What structures receive signals from the vestibular nuclei?

- The thalamus, spinal cord, cerebellum, and CNs III, IV, and VI

Cerebellum, Thalamus, Hypothalamus

What are the three primary functions of the cerebellum?

1. Maintenance of posture and equilibrium
2. Control of muscle tone
3. Coordination of voluntary muscle activity

What type of tremor may result from a cerebellar lesion?

- Intention tremor

A positive Romberg sign (loss of balance when the eyes are closed) suggests a lesion to which tract of the CNS?

- Dentothalamic tract (the main cerebellar pathway) or dorsal column (tabes dorsalis in neurosyphilis)

Name the thalamic nucleus/nuclei responsible for the relay of impulses for each modality listed below:

- **Vision**
  - Lateral geniculate nucleus (“Lateral to Look”)

- **Hearing**
  - Medial geniculate nucleus (“Medial for Music”)

Name the cerebellar lobule that normally receives input from the:

- **Central Vestibular Nucleus**
  - Flocculonodular lobe

- **Reticular Formation**
  - Paramedian lobule

- **Red Nucleus**
  - Ventrolateral lobe

- **Medial Lemniscus**
  - Medial lobe

- **Spinal Cord**
  - Lateral lobe

- **Spinal Nerve**
  - Lateral lobe

- **Cerebral Cortex**
  - Precentral gyrus

- **Hypothalamus**
  - Lateral lobe
Proprioception, pain, pressure, touch, vibration
Lateral portion of ventral posterior nucleus (VPL, “Posterior for Proprioception, Pain”)

Facial sensation
Medial portion of ventral posterior nucleus (VML)

Motor
Ventral anterior/lateral nuclei

Limbic function
Dorsomedial, anterior nuclei

Name the largest thalamic nucleus:
   Pulvinar

What is the function of the pulvinar?
   Integration of visual, auditory, and somesthetic input

Which portion of the internal capsule contains fibers of the corticobulbar tract?
   The genu

Which portion of the internal capsule contains fibers of the corticospinal, spinothalamic, visual, and auditory tracts?
   The posterior limb

Which arteries supply the posterior limb of the internal capsule?
   Perforating branches of the anterior choroidal artery and lenticulostriate arteries

Name the major hypothalamic nucleus (or nuclei) responsible for each function listed below:

   Regulation of the release of gonadotropic hormones
   Medial preoptic nucleus (which contains the sexually dimorphic nucleus)

   Regulation of circadian rhythms
   Suprachiasmatic nucleus

   Regulation of body temperature
   Anterior nucleus (lesion results in hyperthermia) and posterior nucleus (lesion results in poikilothermia)

   Regulation of water balance, synthesis of antidiuretic hormone, oxytocin, and corticotropin-releasing factor
   Paraventricular and supraoptic nuclei

   Regulation of appetite
   Ventromedial nucleus (lesion resulting from eating Very Much [hyperphagia, obesity]) and lateral hypothalamic nucleus (lesions cause anorexia and starvation)

   Regulation of hypothalamus
   Arcuate or infundibular nucleus

   Regulation of emotional expression
   Mammillary nucleus (a component of the limbic system)
What are the major structures of the Papez circuit?
Septal area, mammillary body, anteriornucleus of thalamus, cingulate gyrus, entorhinal cortex, and hippocampal formation

What is the most epileptogenic part of the cerebrum?
The hippocampus

What system within the CNS plays a central role in the initiation and coordination of somatic motor activity?
The striatal or extrapyramidal motor system

What are the major components of the striatal motor system?
Neocortex, basal ganglia (striatum [caudate + putamen], globus pallidus, subthalamic nucleus, substantia nigra), and thalamus

Neurotransmitters

Name the NT described below:
Major NT of the PNS
ACh
NT which is increased in the CNS of patients with schizophrenia
Dopamine
Major NT of the parasympathetic nervous system
ACh
NT believed to cause panic attacks when released suddenly by the locus coeruleus
NE
Major NT of the preganglionic sympathetic nervous system
ACh
NT highly concentrated in the substantia nigra that plays a key role in pain transmission
Substance P
Major NT of the postganglionic sympathetic neurons supplying sweat glands and certain blood vessels
ACh
NT which is depleted from the basal nucleus of Meynert in Alzheimer disease
ACh
NT which is depleted from the substantia nigra in patients with Parkinson disease
Dopamine
NT that causes renal vasodilation
Dopamine
Two NTs believed to be depleted in depression
1. NE
2. Serotonin

**Powerful analgesic NT found exclusively in the hypothalamus**
β-Endorphin

**Opiate peptides which play a role in pain suppression**
Enkephalins

**NT that regulates release of GH and TSH; markedly ↓ Alzheimer disease**
Somatostatin

**Major inhibitory NT of the cortex**
GABA

**Major inhibitory NT of the spinal cord**
Glycine

**Major excitatory NT of the brain**
Glutamate

**Gaseous, vasoactive NT involved in memory**
Nitrous oxide

**NT important in the initiation of sleep**
Melatonin

**NT which inhibits the reticular activating center, thereby increasing total sleep time**
ACh

Which two amino acids can serve as a precursor for the synthesis of catecholamines?
1. Phenylalanine
2. Tyrosine

**Cerebral Cortex**

What are the six layers of neocortex?
1. Layer I: molecular layer
2. Layer II: external granular layer
3. Layer III: external pyramidal layer
4. Layer IV: internal granular layer
5. Layer V: internal pyramidal layer
6. Layer VI: multiform layer

Name the site of a lesion, within the cortex, capable of causing each of the following deficits:

- Right-sided flaccid hemiparalysis
Left primary motor area (Brodmann area 4)

Left-sided pronator drift

Right primary motor area (Brodmann area 4)

Loss of abstract thought and self-restraint

Bilateral loss of frontal lobes anterior to the frontal eye fields

Slowed speech without any impairment of language comprehension

Broca speech area (Brodmann areas 44, 45; always in the dominant hemisphere, usually left)

Loss of right-sided tactile sensation and proprioception

Left somesthetic area (Brodmann areas 3, 1, 2)

Cortical deafness

Bilateral destruction of the auditory areas (Brodmann areas 41, 42); unilateral destruction of the auditory area causes a slight ↓ in hearing.

Inability to understand spoken language and verbalize coherent thoughts

Wernicke speech area (Brodmann area 22) in the dominant hemisphere, usually left

Ipsilateral anosmia (inability to smell)

Primary olfactory area (Brodmann area 34)

Alexia and agraphia (inability to read and write)

Angular gyrus (Brodmann area 39)

Loss of ability to transfer information from short-term to long-term memory

Bilateral destruction of the hippocampal cortex

Psychic blindness, hyperphagia, docility, and hypersexuality (Klüver-Bucy syndrome)

Bilateral destruction of the anterior temporal lobes (amygdala)

Loss of ability to recognize faces

Inferomedial right occipitotemporal area

Loss of vision in the right visual field with macular sparing

Destruction of the left primary visual area (Brodmann area 17)

Name the term used to describe a deficit in the ability to draw a geometric figure:

Construction apraxia

Name the term used to describe a “magnetic gait,” commonly seen in normal-pressure hydrocephalus:

Gait apraxia

What part of the nervous system is involved in maintaining wakefulness?

Reticular activating system and bilateral cortex
PATHOLOGY OF THE NERVOUS SYSTEM

Congenital Disorders

Name the type of neural tube defect with the following features:
- Failure of posterior vertebral arch closure (not evident on clinical examination)
  Spina bifida occulta
- Failure of posterior vertebral arch closure accompanied by herniation of the meninges
  Spina bifida cystica
- Herniation of the meninges outside of the spinal canal
  Meningocele
- Herniation of nervous tissue and meninges outside of the spinal canal
  Myelomeningocele
- Complete cerebral agenesis due to lack of closure of the anterior neuropore
  Anencephaly
- Diverticulum of malformed CNS tissue
  Encephalocele

What factor is used to screen pregnant mothers for neural tube defects?
- α-Fetoprotein

What is the most common cause of mental retardation?
- Fetal alcohol syndrome, often associated with cardiac and facial anomalies

What are two common chromosomal genetic causes of mental retardation?
- 1. Trisomy 21
- 2. Fragile X

Name the condition characterized by an excess of CSF in the cranial cavity:
- Hydrocephalus

What type of hydrocephalus is characterized by obstruction in the flow of CSF through the ventricular system and subarachnoid space?
- Noncommunicating hydrocephalus

What type of hydrocephalus is characterized by free flow of CSF but abnormal CSF absorption?
- Communicating hydrocephalus
What congenital malformation of the CNS is characterized by herniation of the cerebellar tonsils and medulla through the foramen magnum (which may result in obstruction of CSF circulation)?

Arnold-Chiari malformation (type 1)

What congenital malformation of the CNS is associated with syringomyelia (central cavitation of the spinal cord)?

Arnold-Chiari malformation (type 2)

What congenital malformation of the CNS is characterized by cystic dilation of fourth ventricle, agenesis of vermis, and associated with hydrocephalus?

Dandy-Walker malformation

What complication of premature babies usually results in hypoxic/ischemic injuries of brain?

Subependymal germinal matrix bleed

**Stroke**

Describe the artery that has been occluded in each of the following stroke syndromes:

**Paresis and sensory loss of contralateral lower extremity**

ACA

**Hemiparesis, contralateral hemisensory loss, homonymous hemianopsia, aphasia**

MCA supplying the dominant hemisphere, usually left hemisphere

**Loss of consciousness, hemisensory loss, homonymous hemianopsia with macular sparing**

PCA

**Amaurosis fugax**

Ophthalmic artery

**Vertigo, cranial nerve palsies, impaired level of consciousness, dysarthria**

Vertebrobasilar artery

**Sensory neglect and apraxia**

MCA supplying the nondominant hemisphere, usually right hemisphere

**Urinary incontinence, suck and grasp reflexes**

Middle or ACA supplying the frontal lobe

**Ipsilateral loss of pain and temperature for face, contralateral pain and temperature for body**

PICA—Wallenberg syndrome (lateral medulla)

What are the most frequent sites of thrombotic occlusion in the cerebral vasculature?

Carotid bifurcation, MCA, and basilar artery

What is the most frequent site of embolic occlusion in the cerebral vasculature?
Which cardiac arrhythmia is associated with embolic stroke?
   Atrial fibrillation
What type of stroke, associated with HTN, causes the formation of small, cystic, moon-shaped pits?
   Lacunar infarctions
Where do lacunar strokes usually occur?
   Basal ganglia, thalamus, internal capsule, white matter, pons, cerebellum
Name the term used to describe small aneurysms of the cerebral vasculature, caused by long-standing HTN, that may result in intracerebral hemorrhage:
   Charcot-Bouchard aneurysms
What are the most common locations for Charcot-Bouchard aneurysms?
   Thalamus and basal ganglia
Within the cerebral vasculature, what are the most common sites of berry aneurysm formation?
   At the bifurcations of the circle of Willis
What is the most common complication of berry aneurysms?
   Rupture causing subarachnoid hemorrhage
What are three disorders that predispose to the formation of berry aneurysms?
   1. Polycystic kidney disease
   2. Ehlers-Danlos syndrome
   3. Marfan syndrome
Which cranial nerve palsy is associated with internal carotid or posterior communicating artery aneurysms?
   CN III palsy causing papillary dilation
Name the term used to describe paroxysmal, self-limiting episodes of neurologic deficit, commonly including transient aphasia.
   Transient ischemic attack
Which syndrome is characterized by loss of all motor function except that of CN III and IV?
   Locked-in syndrome (usually a result of infarction or tumor at the base of the pons)

Seizures

Name the type of seizure associated with the following clinical findings:
   Loss of consciousness followed by loss of postural control, a tonic phase of muscle contraction and clonic limb jerking
   Tonic-clonic seizure
A child who appears to be daydreaming in class and is found to have a 3-second spike-and-wave pattern on EEG
Absence seizure
**Sudden, brief muscle contractions**
Myoclonic epilepsy
**Motor, sensory, visual, psychic, or autonomic phenomena with preserved level of consciousness**
Simple partial seizure
Seizure begins with behavioral arrest, which is followed by auditory or visual hallucination, automatisms, and finally by postictal confusion
Complex partial seizure
**What disorder is characterized by paroxysmal episodes of sharp, shooting facial pain in the distribution of one or more branches of CN V?**
Trigeminal neuralgia

**What is the drug of choice for trigeminal neuralgia?**
Carbamazepine

**What is the triad of cerebellar dysfunction?**
1. Loss of balance (disequilibrium)
2. Hypotonia
3. Loss of coordinated muscle activity (dyssynergia)

**Name the terms used to describe traumatic injury to the cortex at the site of impact and opposite the side of impact:**
- Coup injury (at the site of impact); contrecoup injury (opposite the site of impact)

**Intracranial Hemorrhage**

**Name the type of intracranial hemorrhage associated with the following features:**
- Bloody or xanthrochromic CSF on lumbar puncture
- Subarachnoid hemorrhage
- **Hematoma following the contour of a cerebral hemisphere on computed tomography (CT) scan**
- Subdural hematoma
- **Laceration of bridging cerebral veins**
- Subdural hematoma
- **Laceration of middle meningeal artery due to fracture of the temporal bone**
- Epidural hematoma
- **Lucid interval followed by rapid decline in mental status**
- Epidural hematoma
Most common type of intracranial hemorrhage resulting from trauma
Subdural hematoma
**Ruptured berry aneurysm or arteriovenous malformation**
Subarachnoid hemorrhage
**Seen in patients with long-standing, poorly controlled HTN**
Intraparenchymal hemorrhage
**Lens-shaped hematoma on CT scan**
Epidural hematoma
**Crescentic hematoma on CT scan**
Subdural hematoma
**Seen more commonly in alcoholics and the elderly**
Subdural hematoma

What is the most common cause of subarachnoid hemorrhage?
Trauma

**Meningitis/Encephalitis**

Name the type of meningitis associated with the following CSF findings:
- Greater than 1000 polymorphonuclear mononuclear leukocytes, ↓ glucose, increased protein
  - Bacterial meningitis
- Increased lymphocytes, minor elevation in protein, normal CSF pressure
  - Viral meningitis
- Increased lymphocytes, minor elevation in protein, elevated CSF pressure
  - Fungal meningitis

Perivascular cuffing, inclusion bodies, and glial nodules may be seen in what cerebral infection?
- Viral meningoencephalitis

Name the three most common bacteria causing neonatal meningitis:
1. Group B Streptococcus
2. *Escherichia coli*
3. Listeria

Name the parasite spread from cats to humans that causes periventricular calcifications and congenital disorders in offspring of infected mothers:
*Toxoplasma gondii*

Name the fungal meningitis most commonly associated with diabetics in DKA:
Mucormycosis
Bullet-shaped intracytoplasmic inclusions, Negri bodies are characteristic of which CNS viral infection?

   Rabies

Hemorrhagic necrosis of temporal lobes is most commonly associated with which viral encephalitis?

   HSV-1

Which infectious disease is characterized by neuronal vacuolization leading to small cysts in the gray matter of the brain without an associated inflammatory response?

   Spongiform encephalopathy

Which disease is characterized by progressive ataxia, dementia, and spongiform gray matter changes?

   Creutzfeldt-Jacob disease

**Demyelinating Disorders**

Name the demyelinating disorder associated with the following clinical and pathologic features:

   **Most common demyelinating disorder**
   Multiple sclerosis
   Associated with JC virus infection in AIDS patients
   Progressive multifocal leukoencephalopathy
   Periventricular calcification; spinal Multiple sclerosis lesions typically in the white matter of the cervical cord
   Multiple sclerosis
   Postviral autoimmune syndrome causing demyelination of peripheral nerves, especially motor fibers
   Guillain-Barré syndrome
   Triad of intention tremor, scanning speech, and nystagmus
   Multiple sclerosis
   May present with intranuclear ophthalmoplegia (MLF syndrome) or sudden visual loss due to optic neuritis
   Multiple sclerosis
   Ascending paralysis, facial diplegia, and autonomic dysfunction
   Guillain-Barré syndrome
   **Oligoclonal bands in the CSF**
   Multiple sclerosis
   **Albuminocytologic dissociation (↑ CSF protein with normal cell count)**
   Guillain-Barré syndrome
↑ CSF protein, normal glucose, ↑ lymphocytes
Multiple sclerosis

Leukodystrophies and Neurocutaneous Syndromes

Name the type of leukodystrophy associated with the following features:
  - Globoid bodies in white matter
    Krabbe disease
  - Deficiency of β-galactocerebrosidase
    Krabbe disease
  - Deficiency of arylsulfatase A
    Metachromatic leukodystrophy
  - Nervous tissue demonstrates loss of myelin and appears yellowish brown, build up of cerebroside in myelin sheath
    Metachromatic leukodystrophy
  - Peroxisomal deficiency, demyelination starts in occipital lobe and moves anteriorly
    Adrenoleukodystrophy (X-linked)

Name the type of neurocutaneous syndromes associated with the following features:
  - Cutaneous and plexiform neurofibromas, Lisch nodules on iris, cafe au lait spots, axillary freckling
    Neurofibromatosis (NF1)
  - Bilateral schwanomas, meningioma, ependyoma
    NF2
  - Capillary hemangiomas, hemagioblastomas in cerebellum and retina, increased incidence of renal cell carcinoma
    von Hippel-Lindau
  - Nasolabial subcutaneous angiofibroma, epilepsy, subependymal nodules, ungual fibroma, shagreen patch, ash leaf spots
    Tuberous sclerosis

What is the inheritance pattern of neurocutaneous syndromes?
  - Autosomal dominant (AD)

What is the inheritance pattern of leukodystrophies?
  - Autosomal recessive (AR)

Neurodegenerative Disorders
What are the two most common causes of dementia in the elderly?
Alzheimer dementia and multi-infarct dementia

Name the neurodegenerative disorder associated with the following clinical and pathologic features:

**Hirano bodies, neurofibrillary tangles, senile plaques (accumulations of β-amylloid protein)**
Alzheimer dementia

**Stepwise dementia in a patient with focal neurologic deficits**
Multi-infarct dementia

**Thiamine deficiency from alcohol abuse causing ophthalmoplegia, ataxia, nystagmus**
Wernicke encephalopathy

**Long-term alcohol abuse causing retrograde and anterograde amnesia, confabulation, and shrunken, petechial hemorrhage in mammillary bodies**
Korsakoff psychosis

** Progressive dementia with predominantly frontal and temporal gliosis and neuronal loss**
Pick disease

**Degeneration of the caudate nucleus**
Huntington disease

**Lewy bodies and depigmentation of the substantia nigra**
Parkinson disease

**Parkinsonian symptoms with autonomic dysfunction, including orthostatic hypotension**
Shy-Drager syndrome

**Resting tremor, cogwheel rigidity, akinesia, postural instability**
Parkinson disease

**Can be caused by MPTP use**
Parkinson disease

**Slowly progressive ataxia, dysarthria associated with kyphoscoliosis, diabetes, arrhythmias, and myocarditis due to triplet repeat GAA on chromosome 9**
Friedreich ataxia

**Autosomal dominant (AD) inheritance and anticipation (worsening of disease in future generations) due to increasing number of CAG repeats on chromosome 4**
Huntington disease

**UMN and LMN signs due to loss of myelinated fibers of the corticospinal tract**
Amyotrophic lateral sclerosis (ALS)

**Viral infection → inflammatory response in anterior horn of the spinal cord → LMN loss**
Poliomyelitis
Childhood ataxia associated with telangiectasias of the skin and conjunctiva associated with \textit{ATM} gene mutation
Ataxia-telangiectasia
Floppy baby (hypotonia) due to LMN degeneration, tongue fasciculation
Werdnig-Hoffman disease

Which protein gives rise to the amyloid fibrils of Alzheimer disease?
A-β

Which is the conformation of A-β protein in neuritic plaques?
β-Pleated sheet

The A-β protein is derived from processing of which larger molecule?
Amyloid precursor protein (APP)

Brain Tumors

Where are the majority of adults versus children CNS tumors found?
Supratentorial for adults, infratentorial for children

Name the brain tumor associated with each of the following clinical or pathologic findings:

Most common pediatric intracranial tumor
Juvenile pilocytic astrocytoma

Most common pituitary tumor
Pituitary adenoma

Most common pituitary adenoma
Prolactinoma

Most common pediatric supratentorial tumor
Craniopharyngioma

Most common primary brain tumor
Glioblastoma multiforme

Most common intracranial tumor
Metastases

Malignant pediatric tumor which metastasizes through CSF pathways
Medulloblastoma

Malignant pediatric tumor found exclusively in the posterior fossa
Medulloblastoma

Vascular tumor of cerebellum and retina in patients with von Hippel-Lindau syndrome
Hemangioblastoma
Abundant capillaries and vacuolated foam cells
Hemangioblastoma
Type of tumor that is found bilaterally in patients with neurofibromatosis II
Vestibular schwannoma
Tumor of the dorsal root that may grow in a dumbbell configuration through a vertebral foramen
Schwannoma
Tumor which originates from the vestibular division of CN VIII
Schwannoma
Tumor which grows in a mixture of Antoni A or Antoni B patterns
Schwannoma
Small round blue cell tumor
Medulloblastoma
Bipolar cells, Rosenthal fibers, and microcysts
Juvenile pilocytic astrocytoma
Verocay bodies
Schwannoma
Tumor derived from Rathke pouch
Craniopharyngioma
Two tumors often presenting with bitemporal hemianopia
Pituitary adenoma and craniopharyngioma
Tumor characterized by concentric whorls and calcified psammoma bodies
Meningioma
Tumor arising from ependymal lining of ventricular system
Ependymoma
Tumor commonly arising in the pineal region causing obstructive hydrocephalus by compromising the aqueduct of Sylvius
Germinoma
EBV positive B-cell tumor of the CNS in AIDS patients
CNS lymphoma
Tumor of the foramen of Monro causing obstructive hydrocephalus
Colloid cyst of the third ventricle
Benign tumor characterized by calcifications and cells with fried-egg appearance or perinuclear halos
Oligodendroma
Tumor characterized by highly malignant cells bordering necrotic areas
Glioblastoma multiforme
Benign tumor derived from arachnoid cap cells with well-delineated margins
Meningioma
Disorders of the Spinal Cord

Name a disease of the spinal cord associated with each of the following neurologic findings:

- Loss of all spinal modalities except tactile discrimination, vibratory sensation, and proprioception
  - Ventral spinal artery occlusion
- Impaired tactile discrimination, vibratory sensation, and proprioception
  - Tabes dorsalis
- Loss of pain and temperature sensation in a cape-like distribution and flaccid paralysis of the intrinsic muscles of the hand
  - Syringomyelia
- Impaired tactile discrimination, vibratory sensation and proprioception, UMN signs, and ataxia
  - Vitamin B₁₂ deficiency

Miscellaneous

What complication affecting the brainstem can be caused by rapid correction of hyponatremia?
- Central pontine myelinolysis

Describe how transtentorial herniation causes contralateral hemiparesis.
- Compresses the right crus cerebri → corticospinal and corticobulbar fibers are compromised (Kernohan notch)

Describe how transtentorial herniation causes pupillary dilation.
- Tension on CN III causes pupillary dilation.

Name a life-threatening complication of transforaminal or tonsillar herniation:
- Compression of the medullary respiratory center → respiratory insufficiency

What is the term used to describe brainstem hemorrhages caused by transtentorial and transforaminal herniation?
- Duret hemorrhages

What is the systemic response to increased intracranial pressure (Cushing triad)?
  1. HTN
  2. Bradycardia
  3. Irregular respirations

What is the most common reversible cause of dementia in the elderly?
- Normal pressure hydrocephalus
Normal pressure hydrocephalus is a common complication of what type of intracranial pathology?
- Subarachnoid hemorrhage

What is the triad of normal-pressure hydrocephalus?
1. Ataxic, magnetic gait (Wobbly)
2. Dementia and/or short-term memory loss (Weird)
3. Urinary incontinence (Wet)

What diuretic is commonly used to manage increased intracranial pressure?
- Mannitol (provides osmotic diuresis)

What is the protein change associated with prion diseases?
- Conformational change in PrPc (α-helix isoform) to PrPsc (β-pleated sheet isoform)

PHARMACOLOGY OF THE NERVOUS SYSTEM

Antiepileptics

For each of the following drugs, name:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects or important toxicity (TOX) (if any)

Carbamazepine
- MOA: Na\(^+\) channel blocker
- IND: Tonic-clonic, partial, and Jacksonian seizures
- TOX: ↑ LFT, agranulocytosis, a plastic anemia

Ethosuximide
- MOA: May block T-type Ca\(^{2+}\) channels in thalamus
- IND: Absence seizures
- TOX: GI upset, Stevens-Johnson syndrome

Diazepam
- MOA: Facilitates GABA action by ↑ frequency of Cl channel opening
- IND: Status epilepticus
- TOX: Sedation

Lamotrigine
- MOA: Blocks Na\(^+\) channels
- IND: Adjuvant antiepileptic agent
TOX: Life-threatening rash and Stevens-Johnson syndrome
Phenytoin
MOA: Na⁺ channel blocker
IND: Tonic-clonic, partial, and status
TOX: Nystagmus, ataxia, gingival hyperplasia, hirsutism, megaloblastic anemia, teratogenic
Phenobarbital
MOA: Facilitates GABA action by ↑ duration of Cl channel opening
IND: Tonic-clonic seizures
TOX: Induces P-450, drowsiness
Valproic acid
MOA: Unknown—may facilitate GABA action
IND: Myoclonic seizures
TOX: Hepatotoxicity, GI toxicity, inhibits P-450, thrombocytopenia

Name the drug(s) of choice for each of the following types of epilepsy:
- **Simple and complex partial**
  Phenytin, carbamazepine
- **Absence**
  Ethosuximide
- **Febrile**
  Phenobarbital
- **Myoclonic**
  Valproic acid, clonazepam
- **Status epilepticus**
  Phenytin, diazepam
- **Tonic-clonic**
  Phenytin, carbamazepine

Antiparkinsonian Agents

For each of the following drugs, name:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects or important toxicity (TOX) (if any)
   Amantidine
   MOA: May enhance dopamine release
   IND: Helpful for rigidity and bradykinesia
TOX: Acute psychosis (rare)
Benztropine
MOA: Antimuscarinic
IND: Adjuvant therapy
TOX: Similar to atropine

Bromocriptine
MOA: Dopamine receptor agonist
IND: Used with levodopa
TOX: Hypotension, confusion, hallucinations, nausea

Levodopa
MOA: Dopamine precursor converted to dopamine in CNS
IND: Combined with carbidopa, levodopa is the most efficacious regimen for Parkinson disease
TOX: Nausea, tachycardia, hypotension, hallucinations, dyskinesias

Carbidopa
MOA: Inhibition of dopamine decarboxylase →↑ levodopa availability in CNS
IND: Used with levodopa
TOX: spasms of the eyelid, irregular heartbeat, confusion, agitation, hallucinations

Selegiline
MOA: Inhibition of MAO b →↑ dopamine levels in CNS
IND: Used as adjuvant to levodopa
TOX: HTN

Anesthetics

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects or important toxicity (TOX) (if any)

Halothane
MOA: CNS depression
IND: Prototype general anesthetic; potent anesthetic but weak analgesic
TOX: Arrhythmias, ↓ cardiac output, hypotension, hepatotoxicity

Nitrous oxide
MOA: CNS depression
IND: Weak general anesthetic, strong analgesic
TOX: Anoxia, vitamin B₁₂ deficiency (with chronic use)

Thiopental
MOA: Prolongs inhibitory postsynaptic potentials by $\uparrow$ GABA levels (similar to phenobarbital)
IND: Surgical anesthesia
TOX: Laryngospasm
Benzodiazepines (diazepam, midazolam)
MOA: Facilitates GABA action by $\uparrow$ frequency of Cl$-$ channel opening
IND: Sedative, hypnotic, anxiolytic
TOX: Sedation
Ketamine
MOA: PCP analog
IND: General anesthetic
TOX: Postoperative hallucinations, amnesia, respiratory depression
Propofol
MOA: CNS depression
IND: General anesthetic—rapid onset and clearance
TOX: Cannot be given to patients with egg or soybean allergies
Local anesthetics (procaine, cocaine, tetracaine, lidocaine, bupivacaine)
MOA: Block Na$^+$ channels
IND: Anesthetic for minor procedures, spinal blocks
TOX: Arrhythmias, HTN; cardiotoxicity (bupivacaine), seizures
Succinylcholine
MOA: Depolarizing neuromuscular blocker
IND: Rapid sequence induction
TOX: Malignant hyperthermia when given with halogenated inhaled anesthetic; contraindicated in patients with glaucoma because of $\uparrow$ intraocular pressure (IOP)
Tubocurarine
MOA: Nondepolarizing neuromuscular blocker
IND: Adjuvant to general anesthesia
TOX: Hypotension

Why is epinephrine commonly combined with local anesthetics?
To prolong the duration of the anesthetic effect by causing local vasoconstriction

What types of fibers are affected most by local anesthetic agents?
Pain $>$ temperature $>$ touch $>$ pressure; small unmyelinated fibers most affected; large, myelinated fibers least affected

Which drug is used to reverse the effects of the nondepolarizing muscle blockers?
Neostigmine

Which drug is used to treat malignant hyperthermia?
Dantrolene
Analgesics

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and unique toxicity (TOX) (if any)

Acetaminophen
MOA: COX inhibitor
IND: Pain, fever (but not used as anti-inflammatory)
TOX: Overdose causes hepatic necrosis

Aspirin
MOA: Irreversible inhibition of COX-1 and COX-2
IND: Analgesic, antipyretic, anti-inflammatory, antiplatelet drug
TOX: GI ulcers, platelet dysfunction, hypersensitivity reactions, bronchoconstriction, tinnitus, Reye syndrome in children

Celecoxib
MOA: COX-2 inhibitor
IND: Osteoarthritis, rheumatoid arthritis
TOX: Similar to aspirin but less GI toxicity

Gabapentin
MOA: Structural analog of GABA
IND: Neuropathic pain
TOX: Sedation, movement disorders

Indomethacin
MOA: Reversible inhibition of COX-1 and COX-2
IND: Acute gout, neonatal patent ductus arteriosus
TOX: GI upset, headache

Meperidine
MOA: μ opioid receptor agonist
IND: Analgesic
TOX: Seizures; side effects similar to morphine

Morphine
MOA: μ opioid receptor agonist; opioid receptor binding activates G proteins and adenylyl cyclase.
IND: Analgesic, cough suppressant.
TOX: Constipation, emesis, sedation, respiratory depression, miosis, urinary retention.

Note: these symptoms are typical for heroin overdose.
Nalbuphine
MOA: Opioid mixed agonist-antagonist analgesic that activates κ and weakly blocks μ receptors
IND: Analgesic with less abuse potential

Naloxone
MOA: μ opioid receptor antagonist
IND: Used to reverse the effects of opioid agonists
TOX: CNS depression

What two types of opioid receptors mediate analgesia, respiratory depression, and physical dependence?
1. μ
2. δ

What type of opioid receptors mediate spinal analgesia and the sedative effects of opioids?
κ
CHAPTER 5
Cardiovascular

EMBRYOLOGY

What are the five dilatations of the primitive heart tube?
1. Truncus arteriosus
2. Bulbus cordis
3. Primitive ventricle
4. Primitive atrium
5. Sinus venosus

Name the structures in the mature heart that are derived from the following embryonic structures:

- **Truncus arteriosus**
  Ascending aorta and pulmonary trunk
- **Bulbus cordis**
  Smooth parts of left (aortic vestibule) and right (conus arteriosus) ventricle
- **Primitive ventricle**
  Trabeculated parts of left and right ventricle
- **Primitive atria**
  Trabeculated parts of left and right atria
- **Left horn of sinus venosus**
  Coronary sinus
- **Right horn of sinus venosus**
  Smooth part of right atrium (sinus venarum)
- **Transient common pulmonary vein**
  Smooth part of left atrium
- **Right common cardinal vein and right anterior cardinal vein**
  Superior vena cava

Which embryonic layer gives rise to most of the cardiovascular system?
Mesoderm

What structure divides the truncus arteriosus and bulbus cordis?
Aorticopulmonary septum
Name the structure between the atria that develops from the walls of the septum primum and septum secundum: 
  Foramen ovale

Name the three physiologic shunts in the fetal circulation and the structures they shunt between: 
  1. Foramen ovale (right to left atrium) 
  2. Ductus arteriosus (pulmonary artery to aortic arch) 
  3. Ductus venosus (umbilical vein to IVC)

**ANATOMY**

**What are the two anatomic divisions of the pericardium?**
  1. Serous pericardium (made of visceral epicardial layer and parietal layer) 
  2. Fibrous pericardium

Which nerve lies between the fibrous paricardium and mediastinal pleura? 
  Phrenic nerve (runs with pericardiophrenic vessels)

Name the chamber associated with each heart surface:
  - **Sternocostal surface**
    Right ventricle
  - **Posterior surface (base)**
    Left atrium
  - **Diaphragmatic surface**
    Right and left ventricles
  - **Pulmonary surface and apex**
    Left ventricle

Name the structures that compose each heart border: 
  - **Right border**
    Right atrium
  - **Left border**
    Left ventricle, left auricle
  - **Inferior border**
    Right ventricle
  - **Superior border**
    Right and left auricles, great vessels

Name the major artery that commonly supplies each of the following structures: 
  - **Right atrium and right ventricle**
    Right coronary artery (RCA)
Sinoatrial (SA) and atrioventricular (AV) nodes
RCA
Left atrium and left ventricle
Left coronary artery (LCA)
Interventricular septum
1. Anterior 2/3
2. Posterior 1/3
1. Left anterior descending (LAD)
2. Posterior interventricular artery

Which artery determines dominance of cardiac blood supply?
Posterior interventricular artery

What are the most common sites for coronary occlusion?
Left anterior descending (LAD) > RCA > circumflex

Trace the general pathway of venous drainage from myocardium.
Great, middle, and small cardiac veins → coronary sinus → right atrium

Trace the conduction pathway of a cardiac impulse.
SA node → AV node → bundle of His → right and left bundle branches → Purkinje fibers

Which nerve supplies parasympathetic input to heart?
Vagus nerve

Which syndrome is characterized by arm claudication, syncope, vertigo, nausea, and a supraclavicular bruit?
Subclavian steal syndrome (occlusion in subclavian artery proximal to take vertebral artery take-off → “stealing” of blood from vertebral artery to distal subclavian artery)

Describe the best location for auscultation of the following cardiac valves:

Tricuspid valve
Left sternal border, fifth intercostal space

Pulmonary valve
Left sternal border, second intercostal space

Mitral valve
Apex of heart, fifth intercostal space

Aortic valve
Right sternal border, second intercostal space

PHYSIOLOGY
Cardiac Electrophysiology

Name the electrical event in the heart associated with each feature of a normal electrocardiogram:
- **P wave**
  - Atrial depolarization
- **PR interval**
  - Atrial depolarization and conduction delay through AV node
- **QRS complex**
  - Depolarization of the ventricles
- **T wave**
  - Ventricular repolarization

**Which ion primarily dictates the resting membrane potential of a myocyte?**
- Potassium. Membrane has high K+ permeability through K+ channels.

**Which membrane protein maintains the ion gradient?**
- Sodium-potassium ATPase

**What is the effect of potassium efflux from a myocardial cell?**
- Hyperpolarization

**What is the effect of potassium influx into a myocardial cell?**
- Depolarization

Describe the electrochemical events that cause the following phases of the cardiac myocyte action potential:
- **Phase 0 (the upstroke)**
  - Influx of Na⁺ into cell
- **Phase 1 (initial repolarization)**
  - Efflux of K⁺ out of cell and ↓ Na⁺ influx
- **Phase 2 (the plateau)**
  - Influx of Ca²⁺ into cell, efflux of K⁺ out of cell
- **Phase 3 (repolarization)**
  - Efflux of K⁺ out of cell
- **Phase 4 (resting membrane potential)**
  - Equilibrium potential, balance between K⁺ leak current and Na⁺/K⁺ ATPase

**What unique electrochemical feature of SA node allows it to act as a pacemaker for the heart?**
- Phase 4 depolarization causing automaticity

**What ion and channel are responsible for automaticity?**
Describe the electrochemical events that cause the following phases of the SA nodal action potential:

Phase 0 (the upstroke)
Influx of Ca\(^{2+}\) into cell

Phase 3 (repolarization)
Efflux of K\(^{+}\) out of cell

Phase 4 (slow depolarization)
Increasing Na\(^{+}\) influx into cell

What phase 4 characteristic determines heart rate?
Slope which represents rate of depolarization

Name the component of the cardiac conduction system where phase 4 depolarization is fastest:
SA node

Name the component of the cardiac conduction system where phase 4 depolarization is slowest:
Bundle of His and Purkinje fibers

Define conduction velocity.
The rate at which an impulse spreads throughout cardiac tissue

What determines conduction velocity?
Rate of depolarization (phase 0 upstroke)

Where is conduction velocity fastest?
The Purkinje system

Where is conduction velocity slowest?
The AV node

What is the significance of the conduction delay at the AV node?
The delay in conduction allows for ventricular filling

Cardiac Contractility and Output

Describe the function of each myocardial cellular component:
Sarcomere
Contractile unit
Intercalated disks
Cell adhesion
Gap junction
Electrochemical communication between myocardial fibers
**Tubules**
Carry action potentials into the cell interior

**Sarcoplasmic reticulum**
Storage and release of calcium

**Which ion determines the magnitude of tension in a contracting myocardial cell?**
Amount of intracellular calcium

**Describe the effect of each of the following on contractility:**
- **Increased heart rate**
  Increased contractility
- **Catecholamines**
  Increased contractility
- **Digoxin**
  Increased contractility
- **Acetylcholine (ACh)**
  Decreased contractility

**What is the Frank-Starling relationship?**
The greater the end-diastolic volume (preload), the greater is the stroke volume.

**How does contractility affect cardiac output?**
Cardiac output increases as contractility increases.

**Name the four factors that determine myocardial oxygen consumption:**
1. Afterload
2. Size of heart (wall tension)
3. Contractility
4. Heart rate

**Provide formulas for each of the following:**
- **Stroke volume**
  End-diastolic volume − end-systolic volume =
- **Cardiac output**
  Stroke volume × heart rate =
- **Ejection fraction**
  Stroke volume/end-diastolic volume =
- **Stroke work**
  Aortic pressure × stroke volume
- **Cardiac output based on Fick principle**
  O$_2$ consumption/(arterial O$_2$ - venous O$_2$)
Heart Sounds

Name the event associated with each heart sound:

S1
Closure of the AV (tricuspid, mitral) valves

S2
Closure of semilunar (aortic, pulmonary) valves

S3
Flow of blood from atria into ventricles during diastole (often seen with large ventricular volumes, i.e., CHF; often benign in youth and trained athletes)

S4
Flow of blood from atria into ventricles during atrial systole (often present in patient with stiffened ventricle)

Maintenance of Blood Pressure

What is the site of highest resistance in the cardiovascular system?
Arterioles

Which vascular bed has the largest cross-sectional and surface areas?
Capillaries

Which vascular bed contains the largest volume of blood at any given time?
Veins

Define the following terms:

Systolic blood pressure
Highest arterial blood pressure during a cardiac cycle

Diastolic blood pressure
Lowest arterial blood pressure during a cardiac cycle

Pulse pressure
Difference between systolic and diastolic blood pressure

What is the most important determinant of pulse pressure?
Stroke volume

What is the effect of aging on pulse pressure?
Aging widens pulse pressure due to ↓ capacitance of blood vessels

How is left atrial pressure estimated clinically?
Pulmonary capillary wedge pressure

Where are the carotid baroreceptors located?
What is the function of the carotid baroreceptors?
Minute to minute regulation of blood pressure

Which nerve carries information from baroreceptors to the vasomotor center in the brainstem?
Cranial nerve IX

Describe the phases of the Valsalva maneuver and changes occurring with BP and heart rate.

Phase 1: forceful expiration against closed glottis (↑ BP with ↑ intrathoracic pressure, ↓ HR with baroreflex)
Phase 2: accommodation (↓ BP with reduced venous return, ↑ HR with baroreflex)
Phase 3: breathe in (↓ BP with ↓ intrathoracic pressure, ↑ HR with baroreflex)
Phase 4: recovery (↑ BP with normal venous return, marked ↓ HR with baroreflex overshoot)

Name two ways that the vasomotor center responds to decreased mean arterial pressure:
1. ↓ Parasympathetic output
2. ↑ Sympathetic output

Name the hormone(s) responsible for each of the following functions:
Long-term regulation of blood pressure
Renin-angiotensin-aldosterone system
Stimulation of aldosterone secretion and arterial vasoconstriction
Angiotensin II
Water retention and direct arteriolar vasoconstriction causing an increase in blood pressure
Vasopressin
Inhibition of renin release, stimulation of salt and water excretion, and vascular smooth muscle relaxation
Atrial natriuretic peptide

Name three stimuli for renin secretion:
1. ↓ Renal blood pressure
2. ↓ Na⁺ delivery to macula densa of JGA
3. ↑ Sympathetic tone

What is the effect of cerebral ischemia on blood pressure and heart rate?
Cushing reflex: blood pressure ↑ and heart rate ↓

What is the mechanism of increased blood pressure in cerebral ischemia?
Chemoreceptors in the vasomotor center stimulate increased sympathetic outflow

What is the mechanism of decreased heart rate in cerebral ischemia?
Baroreceptor reflex to increase in BP leads to increased parasympathetic outflow to heart

**Where are the carotid chemoreceptors located?**
Bifurcation of common carotid arteries and the aortic arch at carotid body

**What do chemoreceptors sense?**
Oxygen, CO₂, pH, and temperature

**What is the Starling equation?**
\[ J_v = K_f [(P_c - P_i) - (\pi_c - \pi_i)] \]

**Describe the effect of each of the following on capillary filtration:**
- **Increased capillary hydrostatic pressure**
  - Increased fluid filtration
- **Increased interstitial hydrostatic pressure**
  - Decreased fluid filtration
- **Increased capillary oncotic pressure**
  - Decreased fluid filtration
- **Increased interstitial oncotic pressure**
  - Increased fluid filtration

**Define autoregulation.**
The capacity of an organ to maintain constant blood flow despite changes in mean arterial pressure

**Define active hyperemia.**
The capacity of an organ to increase blood flow in response to metabolic demands

**Name the primary mechanism of blood flow regulation in the following tissues:**
- **Coronary arteries**
  - Local metabolic control
- **Cerebral vasculature**
  - Local metabolic control
- **Muscle**
  - Local metabolic control
- **Skin**
  - Sympathetic control
- **Pulmonary**
  - Local metabolic control

**Name five key metabolites which cause vasodilation:**
1. Lactate
2. K⁺
3. Adenosine
4. CO₂
5. H+
Name the primary vasoactive metabolite in the following tissues:

- **Coronary arteries**
  - O₂, adenosine
- **Cerebral vasculature**
  - CO₂ (most important), H⁺
- **Muscle**
  - Lactate, K⁺, adenosine
- **Pulmonary**
  - O₂

**CARDIOVASCULAR PATHOLOGY AND PATHOPHYSIOLOGY**

**Murmurs**

Name the valvular defect causing each murmur described below:

- **Harsh midsystolic murmur in the left second intercostal space at the left sternal border**
  - Pulmonic stenosis

- **Harsh midsystolic murmur in the right second intercostal space at the right sternal border, radiating to the neck (carotid arteries) and apex**
  - Aortic stenosis

- **Harsh midsystolic murmur at the left third and fourth interspaces radiating down the left sternal border; murmur louder with decreased preload (ie, on Valsalva); S₄ and biphasic apical impulse often present**
  - Hypertrophic cardiomyopathy

- **Blowing holosystolic murmur at apex radiating to the left axilla with increased apical impulse**
  - Mitral regurgitation

- **Blowing holosystolic murmur at the lower left sternal border radiating to the right of the sternum; may ↑ with inspiration**
  - Tricuspid regurgitation

- **Soft, late systolic murmur at the left sternal border or apex, accompanied by midsystolic click**
Mitral valve prolapse  
Harsh holosystolic murmur at the lower left sternal border, accompanied by a thrill  
Ventricular septal defect (VSD)  
Blowing, high-pitched diastolic murmur at the left second to fourth interspaces radiating to the apex  
Aortic regurgitation  
Low-pitched diastolic murmur at the apex that gets louder prior to $S_1$; an opening snap is often present just after $S_2$  
Mitral stenosis  
Systolic flow murmur at left upper sternal border; fixed splitting of $S_2$  
Atrial septal defect (ASD)  

What congenital valvular defect is associated with aortic stenosis?  
Bicuspid aortic valve  

What are two common manifestations of aortic stenosis?  
Angina and syncope  

Which disorder results from myxomatous degeneration of the mitral valve?  
Mitral valve prolapse  

Patients with mitral valve prolapse are at increased risk of which infection?  
Infective endocarditis  

Heart Failure  

What are the most common causes of left-sided heart failure?  
Ischemic heart disease, HTN, mitral and aortic valvular disease, myocardial disease (cardiomyopathy, myocarditis)  

Name four key mechanisms of compensation in congestive heart failure (CHF):  
1. Hypertrophy  
2. Ventricular compensation  
3. Blood volume expansion  
4. Tachycardia  

Name two major clinical signs/symptoms of left-sided heart failure:  
1. Pulmonary congestion  
2. Pulmonary edema causing dyspnea and orthopnea  

Name three consequences of suboptimal renal perfusion:  
1. RAA axis activation leading to salt and water retention  
2. Ischemic acute tubular necrosis (ATN)  
3. Prerenal azotemia
What is the consequence of impaired cerebral perfusion in CHF?
   Hypoxic encephalopathy

What is the most common cause of right-sided heart failure?
   Left-sided heart failure

Name two major pulmonary causes of right-sided heart failure:
   1. Interstitial fibrosis
   2. Pulmonary HTN

Name four key clinical signs of right-sided heart failure:
   1. Portal, systemic, peripheral congestion, and edema
   2. Hepatomegaly
   3. Congestive splenomegaly
   4. Renal congestion

Describe the phases of pathologic change in the liver that result from chronic right-sided heart failure.
   Nutmeg appearance → centrilobular necrosis → central hemorrhagic necrosis → cardiac sclerosis (cirrhosis)

What is the most common cause of acute right-sided heart failure in a patient with a deep venous thrombosis?
   Massive pulmonary embolus

What EKG findings may be seen with acute right-sided heart stress?
   S₁Q₃T₃: S wave in lead 1, Q wave in lead 3, T-wave inversion in lead 3

Ischemic Heart Disease

Name four important manifestations of ischemic heart disease:
   1. Angina
   2. Myocardial infarction (MI)
   3. Lethal arrhythmia causing sudden cardiac death
   4. Chronic CHF

What are the two major etiologies of myocardial ischemia?
   1. ↓ Coronary perfusion
   2. ↑ Myocardial O₂ demand

What conditions compound the consequences of impaired myocardial perfusion?
   Anemia, advanced lung disease, cigarette smoking, congenital heart disease

Name the type of angina:
   Pain precipitated by exertion, relieved by rest/vasodilators
   Stable angina
   Paroxysmal chest pain at rest in patient with or without coronary risk factors
Prinzmetal angina
Severe substernal pain/pressure at rest
Unstable angina

Describe the underlying pathology for each type of angina:

**Stable angina**
Greater than 75% occlusion of coronary artery

**Prinzmetal angina**
Coronary vasospasm

**Unstable angina**
Plaque disruption with resulting occlusive thrombosis within a coronary artery

Describe the associations between myocardial ischemia, injury, and infarction.
1. Ischemia—insufficient blood supply to the myocardium, occurs first
2. Injury—results when the ischemic process is prolonged
3. Infarction—describes necrosis or death of myocardial cells

Name the type of myocardial damage described below:

**Full-thickness infarction caused by complete occlusion of a coronary artery**
Transmural infarction

**Infarction of the inner half (or less) of the ventricular wall supplied by a partially occluded coronary artery**
Subendocardial infarction

**T-wave inversion on ECG**
Transmural ischemia

**ST depression on ECG**
Subendocardial injury

**ST elevation on ECG**
Transmural injury

**Q waves present on ECG**
Transmural infarction

What is the initial event in the development of a transmural infarction?
Acute plaque disruption

What are the most common symptoms of a myocardial infarct?
Crushing retrosternal chest pain or pressure, dyspnea, pain radiating into left arm or neck, diaphoresis, nausea

What type of necrosis is seen in myocardium within 24 hours of infarction?
Coagulative necrosis

What type of inflammatory cells are seen in the myocardium within 24 hours of infarction?
Neutrophils
What is the most common type of inflammatory cell seen in myocardium from the 2nd to 10th day after an infarction?

Macrophages

When is the risk of myocardial rupture greatest and why?

At 4 to 7 days. Tissue is weakest following phagocytosis of debris by macrophages and prior to growth of granulation tissue.

How many days does it take to form granulation tissue in a region of infarcted myocardium?

7 to 10 days

How many weeks does it take to form contracted scar tissue in a region of infarcted myocardium?

7 weeks

What is the diagnostic test of choice in a patient with suspected MI?

ECG

What two classic ECG changes are seen during an MI?

1. Q waves
2. ST elevation

When does CK-MB begin to rise, peak, and return to normal?

Rise: 3 to 8 hours
Peak: 10 to 24 hours
Return to normal: 2 to 3 days

When does troponin I begin to rise, peak, and return to normal?

Rise: 3 to 8 hours
Peak: 24 to 48 hours
Return to normal: 5 to 10 days

What are the advantages and disadvantages of the CK-MB serum cardiac marker?

Allows diagnosis of re-infarction as levels quickly return to normal; may be falsely elevated with skeletal muscle injury

What are the advantages of the Troponin test?

Very specific to cardiac injury; allows diagnosis of late presenting MI

What are the two most common complications of MI?

1. Cardiac arrhythmia
2. CHF

List five less common but severe complications of MI:

1. Cardiogenic shock
2. Ventricular aneurysm or rupture
3. Papillary muscle rupture
4. Mural thrombosis with resulting peripheral embolism
5. Dressler syndrome
Cardiomyopathy

How does the left ventricle respond to long-standing HTN?
  Concentric hypertrophy

What are the three types of cardiomyopathy?
  1. Dilated or congestive
  2. Hypertrophic
  3. Restrictive

What are the most common nongenetic etiologies of dilated cardiomyopathy?
  “ABCDE”
  Alcohol abuse
  Beriberi (thiamine deficiency)
  Coxsackie B myocarditis, Cocaine, Chagas disease
  Doxorubicin toxicity
  Pregnancy

Name the type of cardiomyopathy associated with the following clinical and pathologic features:

- 30% to 40% of cases are genetic
  Dilated

- 100% of cases are genetic
  Hypertrophic
  Associated with alcoholism and thiamine deficiency

- Dilated
  Associated with coxsackie virus B and with Trypanosoma cruzi

- Dilated
  Associated with doxorubicin

- Dilated
  Associated with eosinophilia
  Restrictive (Loeffler endocarditis)
  Associated with pregnancy

- Dilated
  Asymmetric septal hypertrophy, banana-shaped left ventricle without dilatation
  Hypertrophic
  Can be caused by sarcoidosis, amyloidosis, scleroderma, hereditary hemochromatosis, endocardial fibroelastosis, radiation-induced fibrosis

- Restrictive
  Cardiomyopathy most commonly caused by endomyocardial fibrosis

Restrictive
Causes sudden death in young, otherwise healthy athletes

Hypertrophic

Commonly inherited in an autosomal-dominant (AD) fashion

Hypertrophic

Four-chamber hypertrophy and dilation

Dilated

Left ventricular outflow obstruction

Hypertrophic

Myocyte tangles, disorientation

Hypertrophic

Symptoms relieved by squatting

Hypertrophic

Pericarditis and Cardiac Tumors

Name the type of pericarditis based on the following exudates descriptions:

Clear, straw colored, minimal inflammation, decreased fibrin
Serous pericarditis

Fibrin rich
Fibrinous pericarditis

Bloody
Hemorrhagic pericarditis

What are the most common etiologies of serous pericarditis?
Uremia, systemic lupus erythematosus (SLE), rheumatic fever

What are the most common etiologies of fibrinous pericarditis?
Uremia, SLE, rheumatic fever, coxsackie viral infection, MI, trauma

What are the most common etiologies of hemorrhagic pericarditis?
Trauma, malignancy, tuberculosis

What ECG and BP findings are seen in pericarditis?
ECG: diffuse ST elevations in all leads
BP: pulsus paradoxus

What is the most common cardiac tumor of adults?
Metastases (eg, melanoma)

What is the most common primary cardiac tumor of adults?
Left-sided atrial myxoma

What is the most common primary cardiac tumor in children?
Rhabdomyoma, commonly associated with tuberous sclerosis
Congenital Heart Disease

Name the congenital heart defect associated with each of the following statements:

Three most common causes of R->L shunting
1. Atrial septal defect (ASD)
2. VSD
3. Patent ductus arteriosus (PDA)

Two most common defects
1. VSD
2. PDA

Five defects causing cyanosis at birth
“5 T’s”:
1. Tetralogy of Fallot
2. Transposition of the great vessels
3. Truncus arteriosus
4. Total anomalous pulmonary venous return
5. Tricuspid atresia

Continuous machinery-like murmur
PDA

Pulmonic stenosis, right ventricular hypertrophy, overriding aorta, VSD (“PROVe”)

Tetralogy of Fallot

Boot-shaped cardiac silhouette
Tetralogy of Fallot

Defect causing lower body cyanosis
Preductal coarctation

Defect causing upper extremity HTN and diminished lower extremity pulses
Postductal coarctation (stenosis distal to the ductus arteriosus)

Associated with Turner syndrome
Coarctation of the aorta

Associated with Down syndrome
ASDs, VSDs, and AV valve abnormalities (due to endocardial cushion abnormalities)

Associated with Rubella
Patent ductus arteriosus

Associated with 22q11 syndrome
Truncus arteriosus, Tetralogy of Fallot

Common cyanotic congenital heart defect in children born to diabetic mothers
Transposition of the great vessels
Aorta arises from right ventricle and pulmonary trunk arises from left ventricle
Transposition of the great vessels
Valvular defect associated with increased risk of infective endocarditis and calcification
Bicuspid aortic valve

What is the consequence of leaving a left-to-right shunting untreated?
Right → left shunting

What type of infection are patients with VSD at an increased risk for?
Infective endocarditis

What drug is used to induce closure of a PDA?
Indomethacin

What drug is used to prevent closure of a PDA?
Prostaglandins

What is the most common genetic cause of congenital heart disease?
Trisomy 21

Cardiac Infectious Disorders

What type of infection is responsible for causing rheumatic fever?
Group A streptococcal pharyngitis

How does streptococcal pharyngitis cause rheumatic heart disease?
Antistreptococcal antibodies cross-react with a cardiac antigen

What serologic test is elevated in rheumatic heart disease:
Antistreptolysin antibodies (ASO)

Name the five major Jones criteria for rheumatic heart disease:
1. Joints: migratory polyarthritis
2. ♥ (o) = pancarditis
3. Nodules: subcutaneous nodules
4. Erythema marginatum
5. Sydenham chorea

Name five minor Jones criteria for rheumatic heart disease:
1. Fever
2. Arthralgia
3. Elevated ESR/CRP
4. Leukocytosis
5. Heart block on ECG
What term is used to describe the foci of pink collagen surrounded by lymphocytes and Anitschkow cells (macrophages) that are pathognomonic for rheumatic heart disease?

Aschoff bodies

Which valve is most commonly affected in rheumatic heart disease?

Mitral valve

What is the most commonly observed valvular deformity in rheumatic heart disease?

Fishmouth or buttonhole stenosis of the mitral valve

What are the three major categories of endocarditis?

1. Infective
2. Nonbacterial thrombotic or marantic
3. Libman-Sacks

What is the most common valve affected by bacterial endocarditis?

Mitral valve

What is the most common valve affected by bacterial endocarditis in IV drug users?

Tricuspid valve

Name the type of endocarditis described in each of the following vignettes:

- 25-year-old (y/o) IV drug user with rapid onset of high fever, rigors, malaise, and tricuspid regurgitation
  Acute infective endocarditis

- 60-y/o woman with mitral valve prolapse, who has recently undergone dental extraction, presents with low-grade fever and flu-like symptoms
  Subacute infective endocarditis

- 65-y/o man with metastatic colon cancer and new murmur consistent with mitral regurgitation
  Nonbacterial thrombotic endocarditis

- 30-y/o woman with SLE
  Libman-Sacks endocarditis

Which organism most often causes acute infective endocarditis?

*Staphylococcus aureus*

Which organism most often causes subacute infective endocarditis?

*Streptococcus viridians*

What are the clinical signs of bacterial endocarditis?

- Fever
- Roth spots
- Osler nodes
- Murmur
- Janeway lesions
- Anemia
Nail bed hemorrhages
Emboli

Define the following eponyms used to describe signs of bacterial endocarditis:

**Osler nodes**
Tender, raised lesions on finger and toe pads

**Janeway lesions**
Small, erythematous lesions on palms and soles

**Roth spots**
Erythematous spots with white centers on retina

What are some sequelae to bacterial endocarditis?
Valvular injury, renal injury (glomerulonephritis), septic emboli to brain, kidneys causing infarction or abscess

**Atherosclerosis**

What are the major risk factors for coronary heart disease?
Age (men > 45, women > 55 or with premature menopause)
Family history of premature heart attacks (MI or sudden cardiac death in men 55, women 65)
Cigarette smoking
Hypertension (HTN)
HDL 40, HDL > 60 negates one risk factor

What are the two main histopathologic components of an atheroma?
Superficial fibrous cap overlying a necrotic core

What are the components of the fibrous cap?
Smooth muscle cells, macrophages, foam cells, lymphocytes, collagen, and elastin.

What is the pathologic precursor to atheroma?
Fatty streak

What is the term for ulcerated, calcified, hemorrhagic atheromas that predispose to thrombosis?
Complicated plaques

What is the underlying pathologic basis for the initiation of atherosclerosis?
Endothelial injury

What may produce this endothelial injury?
Hypercholesterolema, mechanical injury, HTN, immune mechanisms, toxins, etc.

How are foam cells created?
Macrophages that ingest oxidized LDL that has accumulated in the vessel wall become foam cells.
Which lipids are most commonly found in an atheromatous plaque?
Cholesterol and cholesterol esters (LDL)

What is the function of smooth muscle cells in an atheroma?
Smooth muscle cells when activated by growth factors proliferate and migrate into intima. They then secrete extracellular matrix glycoproteins.

What are the major cell types associated with the formation of an atheroma?
Macrophages (foam cells), T lymphocytes (attracted to zone of injury), smooth muscle cells, and endothelial cells

What are the most common locations for atherosclerotic disease?
Abdominal aorta, coronary arteries, popliteal arteries, and carotid arteries

What are the four major clinical manifestations of atherosclerosis?
1. Arterial insufficiency (ie, stroke, MI, peripheral vascular disease, ischemic bowel disease)
2. Thrombus formation due to plaque rupture
3. Atheroembolism
4. Aneurysm, dissection, or rupture of a major vessel

Arteriolosclerosis

Name the type of arteriolosclerosis associated with the following clinical and pathologic features:
- Hyaline deposits causing thickening of arteriolar walls
- Hyaline arteriolosclerosis
- Onion skin arteriolar thickening
- Hyperplastic arteriolosclerosis
- Deposition of calcium in the medial coat of arteries of the lower extremities
- Monckeberg arteriosclerosis
- Pipestem arteries with ringlike calcifications
- Monckeberg arteriosclerosis
- Two types of arteriolosclerosis that occur in patients with long-term HTN
  1. Hyaline arteriolosclerosis
  2. Hyperplastic arteriolosclerosis

Hypertension

HTN is the most important risk factor in which two vascular diseases?
1. Coronary artery disease
What percentage of hypertensive patients have essential HTN?
90% to 95%

What are two common renal causes of secondary HTN?
1. Renal artery stenosis
2. Renal parenchymal disorders

What are some common endocrine causes of secondary HTN?
1. Pheochromocytoma
2. Conn syndrome (primary aldosteronism)
3. Hyperthyroidism
4. Oral contraceptive use
5. Cushing syndrome
6. Acromegaly

Name two common cardiac complications of long-standing HTN:
1. Left ventricular hypertrophy
2. Left-sided heart failure (a result of secondary to left ventricular hypertrophy)

Define hypertensive urgency and emergency.
Urgency: blood pressure > 200/120 without symptoms
Emergency: blood pressure > 200/120 with symptoms or evidence of end organ damage

List the possible effects of malignant HTN on each organ system below:
Heart
Acute LV failure, MI
Aorta
Dissection
Lungs
Pulmonary edema
Kidneys
Acute renal failure
Eyes
Papilledema, fundal hemorrhages, blurred vision
Brain
Headache, encephalopathy, seizure, hemorrhagic cerebrovascular accident (CVA)

What is the most common cause of death in patients with untreated HTN
Coronary artery disease

Aneurysms and Dissection
What is the most common site for atherosclerotic aneurysm?
Abdominal aorta, below renal arteries and above iliac bifurcation

What is the most common site for syphilitic aneurysm?
Thoracic aorta (often ascending)

What is the mechanism of syphilitic aneurysms?
Obliteration of the arteries supplying the aorta (endarteritis obliterans), leading to necrosis of the media

Name the type of aneurysm referred to in the following clinical vignettes:
55-y/o man, who is a smoker with HTN, diabetes, and coronary artery disease, is found to have a pulsatile midline abdominal mass.
Atherosclerotic, abdominal aortic aneurysm

35-y/o with a family history of polycystic kidney disease presents with the worst headache of his life.
Berry Aneurysm rupture leading to subarachnoid hemorrhage

40-y/o prostitute with angina and shortness of breath (SOB) is found to have wide pulse pressure and a high-pitched blowing diastolic murmur.
Syphilitic/luetic, dilation of aortic root leads to aortic regurgitation

What are the most common etiologies for the development of aortic dissection?
HTN and connective tissue disorders (such as Marfan syndrome)

Name two characteristic histopathologic findings in the aorta in a patient with Marfan syndrome:
1. Elastic tissue fragmentation
2. Cystic medial degeneration

What is the genetic defect in Marfan disease?
Defect in fibrillin-1 which forms a scaffold for elastic fibers.

What is the classic clinical presentation of aortic dissection?
Sudden onset of severe tearing pain radiating to the back and descending as the dissection progresses

What is the underlying mechanism in the development of varicose veins?
Venous dilation or deformation leading to venous valvular incompetence

State two complications of varicose veins:
1. Varicose ulceration
2. Stasis dermatitis

Vasculitides

Name the type of vasculitis associated with the following clinical and pathologic features:
**Presence of C-ANCA**
Wegener granulomatosis

**Presence of P-ANCA**
Microscopic PolyANgiitis, PolyArteritis Nodosa (PAN), and Churg-Strauss syndrome

**Most common vasculitis in the United States**
Temporal or giant cell arteritis

**Fibrous thickening of origins of the great vessels leading to absent pulses**
Takayasu arteritis

**Well-demarcated, segmental fibrinoid necrosis of the arterial wall and diffuse neutrophilic infiltrates in medium-sized arteries**
PAN

**Commonly affecting the coronary arteries and may result in coronary aneurysm**
Kawasaki disease

**Segmental inflammation/thrombosis of arteries and adjacent veins, nerves, and connective tissue; results in painful ischemic disease and associated with smoking**
Buerger disease (Thromboangiitis obliterans)

**Vascular and mesangial deposition of IgA complexes with abdominal pain, palpable purpura especially on buttocks, glomerulonephritis, and arthritis**
Henoch-Schonlein purpura

**Which vessels are most commonly involved in temporal arteritis?**
External carotid artery and its branches

**What is the triad of Wegener granulomatosis?**
1. Focal necrotizing vasculitis of upper airways and lungs
2. Necrotizing granulomas of upper and lower respiratory tract
3. Necrotizing glomerulitis

**What are the six clinical signs of acute arterial occlusion?**
“Six P’s”:
1. Pain
2. Pallor
3. Poikilothermia
4. Paresthesia
5. Paralysis
6. Pulselessness

**Name the type of vasculitis associated with each of the following clinical vignettes:**
**70-y/o white man with constitutional symptoms, headache, jaw claudication, acute onset of blindness; W/U: ↑ ESR**
Temporal (giant cell) arteritis

**30-y/o Korean woman with constitutional symptoms, arthritis; physical examination (PE): loss of carotid and radial pulses**
Takayasu arteritis
35-y/o hepatitis B positive man with fever, HTN; W/U: neutrophilia, P-ANCA ⊕ PAN

12-y/o girl recovering from a viral infection presents with exertional chest pain; PE: febrile, conjunctival injection, cervical lymphadenopathy, strawberry tongue, diffuse erythematous rash, edema of hands and feet

Kawasaki disease
40-y/o man with asthma; PE: palpable purpura, diffuse wheezes; CBC: eosinophilia; transbronchial biopsy: upper airway granulomas and elevated P-ANCA and ESR

Churg-Strauss syndrome
8-y/o boy presents with abdominal pain, hematuria, and recent history of URI; PE: palpable purpura, heme ⊕ stools; W/U: vascular biopsy shows perivascular granulocytes, IgA deposition

Henoch-Schonlein purpura
55-y/o man presents with chronic cough, rhinorrhea, ulcerations of nasal septum; W/U: RBC casts in urine and C-ANCA ⊕

Wegener granulomatosis
21-y/o woman smoker with pallor and cyanosis of fingertips after exposure to cold

Raynaud disease

Vascular Tumors

Name the vascular disorder associated with the following clinical or pathologic features:

Most common tumor of infancy
Port-wine stain birthmark

Cutaneous vascular tumor commonly seen in patients with end-stage liver disease (hyperestrinism)
Spider telangiectasia

AD condition is characterized by a localized dilation of venules and capillaries in skin and mucous membrane leading to epistaxis and GI bleeding
Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber) syndrome

AD condition is characterized by the presence of multiple cavernous hemangiomas of skin, liver, pancreas, and spleen and hemangioblastomas of cerebellum with ↑ risk of renal cell carcinoma
von Hippel-Lindau disease
Vascular tumor associated with thorium contrast material and polyvinyl chloride
Hemangiosarcoma
Vascular tumor commonly seen in men of eastern European descent and in those infected with HIV consisting of red or purple cutaneous plaques on the lower extremities
Kaposi sarcoma
Vascular tumor caused by human herpesvirus (HHV) 8 or HIV
Kaposi sarcoma
Syndrome is characterized by cyanosis and edema of upper extremities, head, and neck in a patient with bronchogenic carcinoma
Superior vena cava syndrome

PHARMACOLOGY

Antianginal Agents

What are the three classes of antianginal drugs?
1. Organic nitrates
2. β-Blockers
3. Calcium channel blockers

How do nitrates cause vasodilation?
Nitrates are metabolized to nitric oxide (NO) → NO causes ↑ in cyclic guanosine monophosphate (cGMP) in endothelial cells → vasodilation

Describe how nitrates reduce angina.
1. Vasodilation causes venous pooling, which reduces preload and consequently myocardial oxygen consumption.
2. Coronary vasodilation improves oxygen delivery to the myocardium.

What is the most common side effect of nitrates?
Headache

Describe how each of the following drugs reduces angina:
β-Blockers
By ↓ contractility and heart rate
Nifedipine
Coronary arteriaolar vasodilation
Verapamil
Decreased heart rate and contractility, slowed conduction (especially through AV node)

**What is the antianginal drug of choice for Prinzmetal angina?**
Diltiazem

**What antianginal drug is contraindicated in patients with asthma and COPD?**
β-Blockers

### Inotropic Support

**Name the only oral inotropic agent:**
Digoxin

**Describe the three-step mechanism by which digitalis potentiates myocardial contractility.**

1. Inhibition of Na\(^+/\)K\(^+\) ATPase.
2. Buildup of intracellular Na\(^+\).
3. High intracellular Na\(^+\) impairs Na\(^+\)-Ca\(^{2+}\) antiport, causing increased intracellular Ca\(^{2+}\).

**What is the unique side effect of digoxin on the heart?**
Dysrhythmia

**Which agent can be used to counteract the cardiac toxicity of digoxin? By what mechanism?**

K\(^+\) supplementation. Digoxin binds near K\(^+\) site on Na\(^+\)/K\(^+\) ATPase. When K\(^+\) is low, digoxin has better access and vice versa.

**What are the unique neurotoxicities of digoxin?**
Headache, nausea, altered color perception, blurred vision, tinnitus

**For which arrhythmia is digoxin commonly used?**
Atrial fibrillation

**What is the β-agonist of choice for inotropic support in heart failure?**
Dobutamine

**Which antiarrhythmic is useful for abolishing torsades de pointes and digoxin toxicity?**
Mg\(^{2+}\)

**By which mechanism do β-agonists and phosphodiesterase inhibitors potentiate myocardial contractility?**
These agents increase cAMP which promotes increased intracellular Ca\(^{2+}\).
Antiarrhythmics

For each class of antiarrhythmic agent, state the mechanism of action. (Note: many of these agents have multiple mechanisms of action.):

IA
Na$^+$ channel blocker, some K$^+$ blockade

IB
Na$^+$ channel blocker

IC
Na$^+$ channel blocker

II
β$^+$ blockade

III
K$^+$ channel blocker

IV
Ca$^{2+}$ channel blocker

For each class of antiarrhythmic agent, describe how the myocyte action potential is affected:

IA
Slows phase 0 depolarization, slows phase 3 repolarization

IB
Shortens phase 3 repolarization

IC
Slows phase 0 depolarization

II
Suppresses phase 4 depolarization

III
Prolongs phase 3 depolarization

IV
Shortens duration of action potential

For each class of antiarrhythmic agent, name several commonly used agents:

IA
Quinidine, amiodarone, procainamide, disopyramide

IB
MeLT: Mexilitine, Lidocaine, Tocainamide

IC
For each subtype of class I antiarrhythmics, describe binding affinity for Na channels and the effect on APD

**IA**
Intermediate binding affinity to Na$^+$ channels, also blocks K$^+$ channels; prolongs AP duration

**IB**
Rapid rate of binding and release; shortens AP duration

**IC**
Tight binding and slow release; minimal change in AP duration

For each antiarrhythmic agent, name the unique toxicity/toxicities:

**Quinidine**
Cinchonism—headache, tinnitus, thrombocytopenia, torsades de pointes

**Procainamide**
Reversible drug-induced lupus

**Lidocaine**
CNS depression, cardiac depression, local anesthetic

**Flecainide**
Proarrhythmic

**Propranolol**
Sedation and fatigue, erectile dysfunction, exacerbation of asthma and COPD, masks effects of hypoglycemia

**Bretylium**
Severe postural hypotension

**Amiodarone**
Interstitial pulmonary fibrosis, thyroid dysfunction, hepatotoxicity, tremor, ataxia, neuropathy, bluish discoloration of skin, corneal deposits

What is the drug of choice for abolishing acute supraventricular tachycardia (SVT)?
Adenosine
Antihypertensives

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and unique toxicity (TOX) (if any)

β-Blockers

**MOA:** P-blockade ↓ cAMP
**IND:** intravenous agent for the short-term management of HTN
**TOX:** impotence, asthma, mask signs of hypoglycemia, CV effects (bradycardia, CHF, AV block), sedation

Prazosin, terazosin, doxazosin

**MOA:** α-blocker
**IND:** essential HTN, benign prostatic hypertrophy
**TOX:** first-dose hypotension

Phentolamine

**MOA:** reversible α-blocker
**IND:** diagnosis of pheochromocytoma

Phenoxybenzamine

**MOA:** irreversible α-blocker
**IND:** diagnosis of pheochromocytoma

Nifedipine

**MOA:** dihydropyridine Ca$^{2+}$ blockers, selective for vascular smooth muscle
**IND:** essential HTN
**TOX:** bradycardia, hypotension, metabolic acidosis

Diltiazem, verapamil

**MOA:** nondihydropyridine Ca$^{2+}$ blockers, verapimil is cardioselective, diltiazem has intermediate affinity for heart and vascular smooth muscle
**IND:** essential HTN
**TOX:** mild LFT abnormality, sexual dysfunction

Clonidine

**MOA:** centrally acting α$_2$-agonist that decreases sympathetic outflow
**IND:** mild-to-moderate HTN
**TOX:** dry mouth, rebound hypotension with sudden withdrawal

α-Methyldopa

**MOA:** converted to α-methyl norepinephrine (NE) to act centrally as an α-agonist and decrease sympathetic outflow
IND: pregnant patients with HTN
TOX: positive Coombs test, drowsiness

Hydralazine
MOA: causes arteriolar vasodilation by increasing cGMP in vascular smooth muscle
IND: essential HTN
TOX: drug-induced lupus, angina

Minoxidil
MOA: causes arteriolar vasodilation by causing K^+ channels to open on vascular smooth muscle hyperpolarizing the membrane and decreasing voltage-gated Ca^{2+} current
IND: HTN, alopecia
TOX: hypertrichosis, pericardial effusion

Nitroprusside
MOA: metabolism of nitroprusside releases NO which causes vasodilation via cGMP.
IND: malignant HTN.
TOX: cyanide toxicity (avoided if drug is mixed just prior to administration).

For each condition listed below, select the best antihypertensive agent(s):

Angina pectoris
β-Blockers, Ca^{2+} channel blockers

Diabetes
Angiotensin-converting enzyme inhibitors (ACEi), Ca^{2+} blockers, β-blockers

Hyperlipidemia
ACEi, Ca^{2+} blocker

SVT
β-Blockers

CHF
Diuretics, ACEi, β-blockers

History of MI
β-blockers, ACEi

Chronic renal failure
Diuretics, Ca^{2+} blockers

Anxiety
β-Blockers

Benign prostatic hyperplasia
α1-Selective antagonist

Pheochromocytoma
Phenoxybenzamine, phentolamine
Hypertrophic obstructive cardiomyopathy
Phenoxybenzamine, phentolamine

Asthma, COPD
Diuretics, Ca\(^{2+}\) blockers

Hyperthyroidism
β-Blockers

Moderate bradycardia
β-Blockers with intrinsic sympathomimetic activity: pindolol and acebutol

Pregnancy
α-Methyldopa

Migraine headaches
β-Blockers

For each condition listed below, list the antihypertensive agent that should be avoided:

CHF
Verapamil

Asthma, COPD
β-Blockers

What class of diuretics is especially useful in black and elderly patients?
Thiazide diuretics

What class of diuretics is useful in patients who have not responded to thiazides?
Loop diuretics

What class of antihypertensives is useful in patients who cannot tolerate the side effects of ACEi?
Angiotensin receptor blockers (ARBs)

What classes of antihypertensive agents are absolutely contraindicated in pregnant patients?
ACEi and ARBs

List three agents useful in the management of malignant HTN:
1. Sodium nitroprusside
2. Hydralazine
3. Labetalol

Lipid-Lowering Agents

Cholestyramine

**MOA:** bile acid-binding resin, \(↓\) bile acid stores, \(↑\) catabolism of plasma LDL

**IND:** adjuvant therapy for patients with familial hypercholesterolemia, \(↓\) LDL
**TOX:** constipation, GI discomfort, may interfere with intestinal absorption of other drugs, LFT changes, myalgias

**Statins**

**MOA:** hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors, rate-limiting step of XOL synthesis

**IND:** hypercholesterolemia: to ↓ LDL

**TOX:** hepatotoxicity, rhabdomyolysis

**Niacin**

**MOA:** reduces release of fatty acids from adipose; ↓ LDL synthesis in liver

**IND:** hypercholesterolemia: to ↑ HDL and ↓ LDL

**TOX:** flushing, pruritus (both reversible with aspirin), hepatotoxicity, GI upset, paresthesias

**Gemfibrozil, clofibrate**

**MOA:** stimulate lipoprotein lipase to increase catabolism of VLDL and triglycerides (↓ VLDL, ↓ TGs)

**IND:** hypercholesterolemia; dramatically ↓ TGs, ↑ HDL

**TOX:** myositis, hepatotoxicity

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**Autonomics**

**Direct cholinergic agonists**

**ACh**

**MOA:** physiologic cholinergic agonist

**IND:** no clinical use; ACh decreases heart rate, cardiac output, and blood pressure

**TOX** (for all direct cholinergic agonists):
1. Diarrhea
2. Diaphoresis
3. Miosis
4. Nausea
5. Urinary urgency

**Bethanechol**

**MOA:** binds primarily at muscarinic receptors; stimulates bowel and bladder smooth muscle contraction

**IND:** postoperative ileus and urinary retention

**Pilocarpine**

**MOA:** direct cholinergic agonist that activates ciliary muscle of the eye and pupillary sphincter

**IND:** glaucoma
Indirect cholinergic agonists (anticholinesterases)

Neostigmine, physostigmine
MOA: inhibitor of acetylcholinesterase → accumulation of ACh at synapses
IND: postoperative ileus, urinary retention, myasthenia gravis, reversal of neuromuscular blockade; atropine overdose (physostigmine)
TOX: generalized convulsions (rare)

Edrophonium, pyridostigmine
MOA: inhibitor of acetylcholinesterase
IND: diagnosis (edrophonium) and treatment (pyridostigmine) of myasthenia gravis

Echothiophate
MOA: irreversible inhibitor of acetylcholinesterase
IND: treatment of organophosphate overdose, galucoma

List the toxicities of acetylcholinesterase poisoning (caused by parathion or organophosphates):

“DUMBELS”
Diarrhea
Urination
Miosis
Bronchoconstriction
Excitation of skeletal muscles
Lacrimation
Sweating and Salivation

Atropine
MOA: nonselective muscarinic antagonist
IND: pupillary dilation, reduction of gastric acid secretion, reduction of GI motility, reduction of airway and salivatory secretions, organophosphate/cholinergic poisoning
TOX:”Dry as a bone, Red as a beet, Blind as a bat, Mad as a hatter, Hot as a hare.”
Dry as a bone: ↓ perspiration, lacrimation, salivation
Red as a beet: dry, red skin
Blind as a bat: blurry vision
Mad as a hatter: hallucinations, delirium
Hot as a hare: hyperthermia

Describe how atropine acts on the following organs or systems:

Eyes
Pupillary dilation (bella donna alkaloid), mydriasis, cycloplegia

Airways
Blocks bronchial secretion, bronchodilation

Salivary glands
Blocks salivary secretion
Heart
Bradycardia initially; tachycardia ultimately
Scopolamine
MOA: nonselective muscarinic antagonist
IND: motion sickness
Ipratropium
MOA: nonselective muscarinic antagonist
IND: bronchodilator used for asthma or COPD
Benztrapine
MOA: centrally acting antimuscarinic agent
IND: adjuvant therapy for Parkinson disease
Hexamethonium
MOA: competitive nicotinic ganglion blocker
IND: used for HTN in the past
Succinylcholine
MOA: depolarizing neuromuscular blocker (nicotinic antagonist)
IND: neuromuscular blockade during general anesthesia
TOX: malignant hyperthermia when combined with halogenated anesthetic agents in susceptible patients (treat with dantrolene)
Tubocurarine, atracurium, vecuronium
MOA: nondepolarizing neuromuscular blocker
IND: neuromuscular blockade during general anesthesia; atracurium and vecuronium are degraded in the plasma and therefore preferred in patients with renal failure
TOX: may cause histamine release resulting in bronchospasm, skin wheals, and hypotension
Pralidoxime
MOA: cholinesterase regenerator
IND: used for organophosphate poisoning

State the MOA for each of the following agents:
Hemicholinium
Inhibits reuptake of choline in cholinergic neurons (rate-limiting step in ACh synthesis)
Botulinum
Inhibits release of ACh in cholinergic neurons
Reserpine
Inhibits VMAT transporter of dopamine into storage vesicles in adrenergic neurons
Guanethidine
Inhibits release of NE from adrenergic neurons
Amphetamine
Stimulates release of NE from adrenergic neurons (indirect-acting amines)

Cocaine, tricyclic antidepressants
Inhibit reuptake of NE from synapse

**Direct adrenergic agonists**

**Epinephrine**

**MOA:** agonist at $\alpha_x$, $\alpha_2$, $\beta_1$, $\beta_2$ receptors

**IND:** acute, refractory asthma (bronchodilator), open angle glaucoma, anaphylactic shock, used with local anesthetic to ↑ duration of action (local vasoconstriction)

**TOX:** CNS disturbance, HTN, arrhythmia, pulmonary edema

**Describe the effect of epinephrine on each of the following organs or tissues:**

**Myocardium**
Positive inotropic and chronotropic effects ($\beta_1$)

**Blood vessels**
Overall ↑ blood pressure (vasoconstriction of cutaneous mucous membrane and visceral vasculature; vasodilation of liver and skeletal muscle vasculature) ($\alpha_1 > \beta_2$)

**Lungs**
Bronchodilation ($\beta_2$)

**Liver**
Increased glycogenolysis, increased insulin release ($\beta_2$)

**Adipose tissue**
Increased lipolysis ($\alpha_2$, $\beta_1$, $\beta_2$, $\beta_3$)

**Pupils**
Mydriasis ($\alpha_1$ radial dilator muscle contraction); accommodation for far vision ($\beta_2$ ciliary muscle relaxation)

**Skin**
Piloerection($\alpha_1$)

**Norepinephrine**

**MOA:** Selective adrenergic agonist. Strong $\alpha$-agonist that also stimulates $\beta_1$ receptors.
NE produces only minimal stimulation of $\beta_2$ receptors.

**IND:** Useful in maintaining blood pressure in shock.

**Compare the effects of NE and epinephrine (EPI) at the different adrenergic receptors.**

$\alpha_1$ EPI $\geq$ NE
$\alpha_2$ EPI $\geq$ NE
$\beta_1$ EPI = NE
$\beta_2$ EPI $>>$ NE *creates difference

**Phenylephrine**
MOA: direct adrenergic agonist; stimulates $\alpha_1 > \alpha_2$
IND: nasal decongestant
TOX: causes HTN

Clonidine
MOA: direct adrenergic agonist; stimulates $\alpha_2 > \alpha_1$
IND: HTN (especially in pregnant patients), nicotine, heroin, and cocaine withdrawal
TOX: rebound HTN, dry mouth, drowsiness

Isoproterenol
MOA: direct adrenergic agonist; stimulates $\beta_1$ and $\beta_2$ receptors equally
IND: Bronchodilator used in asthma

Dobutamine
MOA: direct adrenergic agonist; stimulates $\beta_1 > \beta_2$
IND: positive inotropic agent used to improve cardiac output in heart failure

Albuterol, terbutaline
MOA: direct adrenergic agonist; stimulates $\beta_2 > \beta_1$
IND: bronchodilator used in asthma; slows preterm labor by inhibiting uterine contraction (terbutaline)
TOX: tremor, tachycardia

Dopamine
MOA: direct adrenergic agonist; stimulates $D_1$ and $D_2$ receptors equally
IND: maintenance of blood pressure in shock

What is the toxicity of most adrenergic agonists?
1. CNS disturbance—fear, anxiety, tension, headache
2. HTN
3. Arrhythmias
4. Pulmonary edema

Indirect adrenergic agonists

Amphetamine
MOA: stimulates release of NE from adrenergic neurons
IND: attention deficit hyperactivity disorder, narcolepsy, appetite control
TOX: psychosis, anxiety

Tyramine
MOA: stimulates release of NE from adrenergic neurons
IND: no clinical indications; found in fermented foods
TOX: severe vasopressor effects in combination with MAOIs

Ephedrine
MOA: stimulates release of NE from synaptic vesicles in adrenergic neurons
IND: nasal decongestant, enhances athletic performance
TOX: causes HTN
Cocaine
MOA: inhibition of catecholamine reuptake
IND: local anesthetic
TOX: arrhythmias, MI, seizures

*Adrenergic antagonists*

**Phenoxybenzamine**
MOA: irreversible adrenergic antagonist; blocks $\alpha_1 > \alpha_2$
IND: HTN 2° to pheochromocytoma
TOX: nasal congestion, postural hypotension, compensatory tachycardia

**Phentolamine**
MOA: reversible adrenergic antagonist; blocks $\alpha_1$ and $\alpha_2$ receptors equally
IND: diagnosis of pheochromocytoma; management of intraoperative HTN

**Prazosin, terazosin**
MOA: adrenergic antagonist; selectively blocks $\alpha_1$ receptors
IND: treatment of HTN and benign prostatic hypertrophy
TOX: orthostatic hypotension

**Propranolol**
MOA: adrenergic antagonist, blocks both $P_1$ and $P_2$ receptors
IND: HTN, angina prophylaxis, antiarrhythmic, anxiety, thyroid storm, migraine prophylaxis
TOX: bronchoconstriction, arrhythmias, sexual dysfunction, CNS sedation, and fatigue

Describe the effect of propranolol on each of the following tissues:

**Heart**
Decreased cardiac output

**Blood vessels**
Reflex peripheral vasoconstriction

**Kidneys**
Increased $Na^+$ retention

**Lungs**
Bronchoconstriction

**Metoprolol, atenolol, esmolol**
MOA: adrenergic antagonist; selectively blocks $P_1$ receptors
IND: HTN, angina prophylaxis, MI, supraventricular tachycardia (esmolol)
TOX: Hypotension, bradycardia, hyperglycemia, ventricular dysrhythmias

List two β-blockers with intrinsic sympathomimetic activity:
1. Acebutolol
2. Pindolol

Which β-blocker also blocks α₁ receptors?
Labetalol

What are the six common side effects of β-blockers?
1. Bronchoconstriction/asthma attack
2. Arrhythmia
3. Sexual dysfunction
4. Fasting hypoglycemia, masking of hypoglycemic signs
5. CNS sedation, fatigue
6. Hypotension

Describe the effect of dopamine on each of the following organs or tissues:

Myocardium
Positive inotropic and chronotropic effects

Blood vessels
Vasoconstriction →↑ BP

Kidneys
Increases renal blood flow at low and moderate doses
CHAPTER 6
Pulmonary

EMBRYOLOGY

From what structure does the lung bud arise?
   Foregut

From which embryonic layer is the lining of the respiratory tract derived?
   Endoderm

From which embryonic layer is the muscle and connective tissue of the respiratory tract derived?
   Mesoderm

What is the consequence of incomplete separation of the lung bud from the esophagus?
   Tracheoesophageal fistula (TEF)

What is the most typical type of TEF?
   Esophageal atresia (ends in blind pouch)

What other constellation of developmental abnormalities should you look for with TEF?
   VATER syndrome: Vertebral, Anal, Tracheal, Esophageal, Radial/Renal

At what gestational age is a human capable of respiration?
   25 weeks

In what period do the majority of alveoli develop?
   Postpartum

What histology is typical of cells lining the conducting airway?
   Pseudocolumnar ciliated cells

Which cells produce surfactant?
   Type II pneumocytes

List the structures the diaphragm is derived from:
   “Several Parts Build Diaphragm”—Septum transversum, Pleuroperitoneal folds, Body wall, Dorsal mesentery of esophagus

Which disorder results from abnormal development of the diaphragm?
   Diaphragmatic or hiatal hernia

Where can pain from the diaphragm refer?
   To the shoulder
ANATOMY

Which nerve provides motor innervation to the diaphragm?
   Phrenic nerve (“C3, C4, C5 keep the diaphragm alive”)

Which muscles are involved in respiration?
   Diaphragm (most important), external intercostals, sternocleidomastoids, anterior and medial scalene

What area of the left lung is most similar to the right middle lobe?
   Lingula (technically part of the left upper lobe)

Which lobe does foreign body aspiration most commonly affect when supine?
   Superior segment of right lower lobe (because right main stem bronchus is wider, more vertical, and the superior segment ostium is posteriorly located)

The bifurcation of the trachea occurs at the level of which vertebral body?
   Intervertebral disk T4 to T5

What four structures make up a bronchopulmonary segment?
   1. Segmental bronchus
   2. Branch of the pulmonary artery
   3. Branch of the bronchial artery
   4. Tributaries of the pulmonary vein

Which syndrome can result from a malignant tumor in the region of the superior pulmonary sulcus?
   Pancoast syndrome (lower trunk brachial plexopathy and Horner syndrome)

PHYSIOLOGY

Lung Volumes and Capacities

Name the lung volume defined below:
   Expired volume with each normal breath
      Tidal volume (TV)
   Volume that can be inspired beyond the TV
      Inspiratory reserve volume (IRV)
   Volume that can be expired beyond the TV
      Expiratory reserve volume (ERV)
Volume that remains in the lungs after maximal expiration
Residual volume (RV)

Name the lung capacity defined below:
TV + IRV
Inspiratory capacity (IC)
ERV + RV
Functional residual capacity (FRC)
TV + IRV + ERV
Vital capacity (VC)

Volume which can be forcibly expired in 1 second after maximal inspiration
Forced expiratory volume (FEV\textsubscript{1})

Total volume which can be forcibly expired
Forced VC (FVC)
TV + IRV + ERV + RV
Total lung capacity (TLC)

What is the formula for minute ventilation?
TV \times \text{respiratory rate (breaths per minute)}

Lung Compliance and Resistance

What is the relationship between compliance and elasticity?
Compliance and elasticity are inversely related.

Name four common causes of decreased lung compliance:
1. Pulmonary fibrosis
2. Atelectasis
3. Acute respiratory distress syndrome
4. Neonatal respiratory distress syndrome

What is a common smoking-related cause of increased lung compliance?
Emphysema, normal aging lungs

What is the effect of surfactant on alveolar surface tension and lung compliance?
Surfactant decreases surface tension to allow small alveoli to stay open and increases compliance.

What is the law of Laplace?
Pressure = 2 \times \text{surface tension/radius}. The larger the radius of the vessel/airway, the more stable and less likely it is to collapse.

What is the relationship between airflow and resistance?
Airflow is inversely proportional to airway resistance.

What is the relationship between airway radius and resistance?
Resistance is inversely proportional to the fourth power of the radius (Poiseuille law).

For each factor below, state whether airway resistance will be increased or decreased:
- Bronchoconstriction
  Increased
- Parasympathetic stimulation
  Increased
- Sympathetic stimulation
  Decreased
- High lung volumes
  Decreased
- Low lung volumes
  Increased

Hemoglobin

For each of the factors below, determine whether the hemoglobin dissociation curve will be shifted to the left or to the right?
- Increased PCO₂
  Right
- Increased pH
  Left
- Decreased temperature
  Left
- Increased 2,3-bisphosphoglycerate (2,3-BPG) concentration
  Right
- Fetal hemoglobin
  Left
- carbon monoxide poisoning
  Left

Note: ↑ in any factor (except pH) results in right shift.

What is the mnemonic for right shift?
- CADET face RIGHT (C O₂, Acid/Altitude, D PG (2,3-D PG), E xercise, T emperature

Which quaternary conformation of Hb has the highest affinity for oxygen?
- The R (relaxed form)

How does hemoglobin’s affinity for O₂ compare to that of CO?
- The affinity of CO is 200 times as great as that of O₂.

What are the signs and symptoms of carbon monoxide toxicity?
Headache, nausea/vomiting, loss of consciousness, confusion

What are the three ways in which CO\textsubscript{2} is transported from the tissues to the lungs?

1. As HCO\textsubscript{3}\textsuperscript{-} in erythrocytes
2. Bound to hemoglobin (carbaminohemoglobin)
3. Dissolved in blood

Which enzyme catalyzes the conversion of CO\textsubscript{2} into HCO\textsubscript{3}\textsuperscript{-}?
Carbonic anhydrase

Which protein is the main buffer within erythrocytes?
Deoxyhemoglobin

**Acclimatization to High Altitude**

For each of the values below, determine how they are affected by high altitude *acutely*:

**Ventilation**
Increased

**PAO\textsubscript{2}, PaO\textsubscript{2}**
Decreased (due to decreased partial pressure of atmospheric O\textsubscript{2})

**PACO\textsubscript{2}, PacO\textsubscript{2}**
Decreased (due to hyperventilation)

**Systemic arterial pH**
Increased

**Hemoglobin saturation**
Decreased

**Hemoglobin concentration**
No change

For each of the values below, determine how they are affected by high altitude *chronically*:

**Ventilation**
Increased

**PAO\textsubscript{2}, PaO\textsubscript{2}**
Decreased (due to decreased partial pressure of atmospheric O\textsubscript{2})

**PACO\textsubscript{2}, PaCO\textsubscript{2}**
Decreased (due to hyperventilation)

**Systemic arterial pH**
Increased (but closer to normal due to renal excretion of bicarbonate)

**Hemoglobin saturation**
Decreased
Hemoglobin concentration
Increased (polycythemia due to increased erythropoietin production)

Lung Zones

Choose the zone or region of the lungs that fits each description below:
- Alveolar pressure > arterial pressure > venous pressure
  Zone 1
- Arterial pressure > alveolar pressure > venous pressure
  Zone 2
- Arterial pressure > venous pressure > alveolar pressure
  Zone 3
- V/Q ≈ 3 → wasted ventilation
  Apex
- V/Q ≈ 0.6 → wasted perfusion
  Base

What is the effect of hypoxia on pulmonary blood vessels?
  Vasoconstriction. Note: hypoxia causes vasodilation in all other vascular beds.

What is the quotient of V/Q in a lung where the pulmonary artery is completely occluded (shunt-unventilated blood)?
  0

What is the quotient of V/Q in complete airway obstruction (physiologic dead space)?
  ∞

Neurologic Regulation of Respiration

Describe the function of each of the following neural structures in the control of respiration:
- Medullary respiratory center
  Determines the rhythm of breathing by controlling inspiration and expiration
- Pontine apneustic center
  Stimulates inspiration
- Cerebral cortex
  Voluntary control of respiration
- Lung stretch receptors in bronchial smooth muscle
  Reflexive slowing of respiratory frequency (Hering-Breuer reflex)
- Irritant receptors in airway epithelial cells
Initiate coughing

**Juxtacapillary (J) receptors in alveolar walls**
Cause rapid shallow breathing in congestive heart failure

**Joint and muscle receptors**
Stimulate respiration at the initiation of exercise

**Medullary chemoreceptors**
Increase breathing rate in response to low pH

**Peripheral chemoreceptors in the carotid and aortic bodies**
Increase breathing rate in response to low arterial PO$_2$, low pH, and high PCO$_2$

### PATHOLOGY

**Pulmonary Edema, ARDS, and Neonatal RDS**

Which syndrome is characterized by diffuse alveolar damage, pulmonary edema, and respiratory failure?
- Adult respiratory distress syndrome (ARDS)

What type of material is seen in the alveoli of a patient in the acute phase of ARDS?
- Hyaline membranes formed by a fibrinous exudate and necrotic cellular debris

What are some of the causes of ARDS?
- Shock of any etiology, fat embolism, gram-negative sepsis, severe bacteria/viral infections, near-drowning, aspiration of GI contents, acute pancreatitis, heroin overdose, oxygen toxicity, cytotoxic drugs

What is the most common cause of respiratory failure in the newborn and also of death in premature infants 28 weeks gestational age?
- Neonatal respiratory distress syndrome (hyaline membrane disease)

What is the typical clinical presentation of neonatal respiratory distress syndrome?
- Preterm infants with initially normal respirations followed by cyanosis, tachypnea, and signs of respiratory distress

What is the pathogenesis of neonatal respiratory distress syndrome?
- Deficiency of pulmonary surfactant leading to increased surface tension

What type of cells produce pulmonary surfactant?
- Type II pneumocytes

What is the predominant chemical in pulmonary surfactant?
- Dipalmitoyl phosphatidylcholine (lecithin)

What is the diagnostic test of choice to judge fetal lung maturity?
Amniotic fluid lecithin: sphingomyelin ratio (a ratio of 2:1 implies adequate surfactant is present)

What are the three strongest risk factors for neonatal respiratory distress syndrome?
1. Prematurity
2. Maternal diabetes
3. Delivery by caesarean section

What is the classic pathologic finding in the alveoli of an infant with neonatal respiratory distress syndrome?
Intra-alveolar hyaline membranes

Infants surviving an initial bout of neonatal respiratory distress syndrome are at risk for which five complications?
1. Bronchopulmonary dysplasia (resulting in part from oxygen therapy)
2. Retinopathy of prematurity (resulting from oxygen therapy)
3. Patent ductus arteriosus
4. Intraventricular cerebral hemorrhage
5. Necrotizing enterocolitis

What medications can you give to prevent neonatal respiratory distress syndrome?
Glucocorticoids given to the mother can accelerate fetal lung maturation and reduce the risk of neonatal respiratory distress syndrome.

Pulmonary Embolism

What are the most common clinical presentations of PE?
Tachycardia, tachypnea, dyspnea, pleuritic chest pain, or hemoptysis

What is the etiology of 95% of pulmonary emboli?
Dislodged deep venous thromboses (DVT) from the deep veins of the thigh or pelvis

What factors favor the development of a DVT?
Virchow triad: (1) stasis, (2) hypercoagulability, (3) endothelial damage

How do you diagnose a PE radiographically?
V/Q scan or CT angiogram (1st line), pulmonary angiography (gold standard)

What type of tumors commonly cause a DVT by inducing a hypercoagulable state?
Adenocarcinomas

What is the most common genetic disease that predisposes to the development of DVT?
Factor V Leiden

What type of embolism can develop uniquely in a peripartum woman?
Amniotic fluid embolism

For what type of embolism is a patient with a long bone fracture at risk?
Fat emboli from bone marrow, pulmonary thromboembilsm due to trauma and stasis

**What type of infarction results from a PE?**
Hemorrhagic infarction (appears as wedge-shaped opacity on chest x-ray [CXR])

**What therapy is indicated for high-risk patients during the workup of PE and for patients diagnosed with PE?**
Full treatment doses of heparin (unfractionated or low molecular weight)

**What is used for long-term prophylaxis for patients at risk of developing DVT?**
Warfarin

**What is an alternative to warfarin for outpatient DVT prophylaxis?**
Subcutaneous heparin (low molecular weight or unfractionated)

**Obstructive Lung Disease**

**What are the most common disease categories causing pulmonary hypertension?**
1. Chronic obstructive pulmonary disease (COPD)
2. Left-sided heart disease
3. Recurrent PE
4. Autoimmune disorders

**How is the heart affected by long-standing pulmonary hypertension?**
Pulmonary hypertension causes right ventricular hypertrophy and dilatation.

**What is the reversal of a left-to-right shunt to a right-to-left shunt due to long-standing pulmonary hypertension?**
Eisenmenger syndrome

**What is the most common cause of COPD?**
Cigarette smoking

**What is the effect of COPD on hematocrit (Hct)?**
Chronic hypoxia leads →↑ Hct

**What is the effect of COPD on FEV$_1$/FVC?**
↓ FEV$_1$/FVC 0.8

**Name the obstructive pulmonary disorder described by the following pathologic features:**
Smooth muscle and goblet cell hyperplasia; mucus-plugged airways containing Curschmann spirals, eosinophils, and Charcot-Leyden crystals
Bronchial asthma
Hyperplasia of bronchial submucosal glands, hypersecretion of mucus, squamous metaplasia or dysplasia of bronchial epithelium
Chronic bronchitis
Permanent airway dilation and scarring; inflammation and necrosis of bronchial walls and alveolar fibrosis
Bronchiectasis
Alveolar enlargement due to alveolar wall destruction; ↓ lung elasticity
Pulmonary emphysema
Diagnosed clinically by productive cough for > 3 consecutive months for 2+ years
Chronic bronchitis

Name the chronic disorder characterized by increased airway reactivity, resulting in paroxysmal bronchial contraction:
Bronchial asthma

Name the two types of bronchial asthma:
1. Atopic or immune asthma
2. Nonatopic or nonimmune asthma

What type of hypersensitivity response is seen in atopic asthma?
Type I hypersensitivity response mediated by IgE and mast cells, eosinophils, and basophils

What other conditions are typically seen in association with atopic asthma?
Allergic rhinitis, eczema

Name several common triggers of atopic asthma:
Dust, pollen, food, and animal dander

Name several triggers of nonatopic asthma:
Respiratory tract infection, cold, chemical irritants, exercise

What are the two common presenting features of bronchial asthma?
1. Dyspnea
2. Wheezing

Which four conditions are commonly associated with bronchiectasis?
1. Bronchial obstruction from tumor or foreign body
2. Cystic fibrosis (CF)
3. Kartagener syndrome
4. Necrotizing pneumonia

What are the three common presenting features of bronchiectasis?
1. Abundant, copious, often foul-smelling sputum
2. Chronic cough
3. Hemoptysis

What are the components of an acinus of the lungs?
Alveoli, air ducts, respiratory bronchioles, terminal bronchioles

Name the type of emphysema described below:
Enlargement of bronchioles, typically in the upper lobes and apices (most often associated with smoking)
Centriacinar emphysema
Destruction and dilation of entire acinus, typically in the lower lobes; associated with (α₁-antitrypsin deficiency
Panacinar emphysema
Destruction of the distal acinus occurring typically near the pleura and areas of fibrosis that may cause pneumothorax
Paraseptal emphysema
Irregular involvement of the acinus that may be related to inflammatory processes of the lungs
Irregular emphysema

How does smoking cause emphysema?
Smoke particles recruit inflammatory cells, promote the release and enhance the activity of elastase, and inhibit the activity of α₁-antitrypsin.

What is the role of (α₁-antitrypsin deficiency in the development of emphysema?
The lack of this protease inhibitor results in the digestion of the elastin in alveolar walls by elastase.

What is the effect of emphysema on the anteroposterior diameter of the chest and the TLC?
Both are increased.

Restrictive Lung Disease

What general category of pulmonary disease is characterized by dyspnea, decreased lung volumes, and decreased compliance?
Restrictive lung disease

What is the effect of restrictive lung disease on FEV₁/FVC?
↓ FEV₁/FVC ≥ 0.8

What are the two categories of restrictive lung disease?
1. Pulmonary: interstitial lung disease or pneumonitis, resulting in poor lung expansion
2. Extrapulmonary: extrapulmonary disease associated with disorders of the chest wall, pleura, or respiratory muscles

What are the common causes of pulmonary restrictive lung disease?
Idiopathic, connective tissue disease, drug-related, sarcoidosis (all → poor lung expansion)

What are the common causes of extrapulmonary restrictive lung disease?
Neuromuscular disease (polio), obesity, pleural disease, and scoliosis (all → poor breathing mechanics)

Name the specific type of restrictive lung disease described below:

65-year-old (y/o) hay farmer with recent exposure to moldy hay presents with chronic dry cough, chest tightness; physical examination (PE): bilateral diffuse rales; bronchoscopy: interstitial inflammation; bronchoalveolar lavage: lymphocyte and mast cell predominance
Hypersensitivity pneumonitis

35-y/o man presents with intermittent hemoptysis and hematuria; W/U demonstrates alveolar hemorrhage and acute glomerulonephritis
Goodpasture syndrome

40-y/o with progressive hypoxemia and cor pulmonale; lung biopsy demonstrates chronic inflammation of the alveolar wall in a pattern consistent with honeycomb lung; bronchoalveolar lavage: mild eosinophilia
Idiopathic pulmonary fibrosis

58-y/o former shipbuilder presents with the insidious onset of dyspnea; transbronchial biopsy demonstrates interstitial pulmonary fibrosis, ferruginous bodies; chest CT scan demonstrates pleural effusion and dense pleural fibrocalcific plaques
Asbestosis

55-y/o miner (nonsmoker) presents with dyspnea and dry cough; pulmonary function tests (PFTs) show both obstructive and restrictive pattern; chest x-ray (CXR): hilar lymphadenopathy with eggshell calcifications
Silicosis

60-y/o male with 100 pack-year history of (h/o) smoking presents with pleuritic chest pain, hemoptysis, and dyspnea; PE: dullness to percussion and absent breath sounds in the right lower lung field
Pleural effusion (secondary to malignancy)

50-y/o former heavy smoker presents with multiple lung and rib lesions; biopsy: cells (similar to the Langerhans cells of the skin) containing tennis racket-shaped Birbeck granules
Eosinophilic granuloma

30-y/o black female presents with DOE, fever, arthralgia; PE: iritis, erythema nodosum; W/U: eosinophilia, ↑ serum ACE levels; PFT: restrictive pattern; CXR: bilateral hilar lymphadenopathy interstitial infiltrates; lymph node biopsy: noncaseating granulomas
Sarcoidosis

Which typically asymptomatic disorder causes visible black deposits in the lungs of coal workers?
Anthracosis

Which three medications are known to commonly cause interstitial lung disease?
Bleomycin, methotrexate, and amiodarone

Pulmonary Infections

What infection is characterized by fever > 39°C, chills, cough productive of blood-tinted, purulent sputum, pleuritic pain, hypoxia, and lobar infiltrate on CXR?
Acute pneumonia

What infection is characterized by fever 39°C, nonproductive cough, GI upset, and diffuse patchy infiltrates on CXR?
Atypical pneumonia

Name the most common organism(s) associated with the pulmonary infection described below:

Community-acquired acute pneumonia
*Streptococcus pneumoniae*

Commonly follow a viral respiratory infection
*Staphylococcus aureus* and *Haemophilus influenzae*

Interstitial pneumonia
*Mycoplasma pneumoniae* (most common), *Chlamydia pneumoniae*

Fungal pneumonia in an AIDS patient
*Pneumocystis jiroveci* (previously *Pneumocystis carinii*)

Typical pneumonia in neonate
*Streptococcus agalactiae* (group B streptococcus)

Typical pneumonia in an alcoholic after aspiration
*Klebsiella pneumoniae*

Atypical pneumonia in patient with positive cold agglutinin test
*Mycoplasma pneumoniae*

Atypical pneumonia in a neonate with trachoma
*Chlamydia trachomatis*

Atypical pneumonia in a dairy worker
*Coxiella burnetti*

Atypical pneumonia in a rabbit hunter
*Francisella tularensis*

Pneumonia in a bird owner with splenomegaly and bradycardia
*Chlamydia psittaci*

Hospitalized patient with lobar pneumonia
*Streptococcus pneumoniae* > *S. aureus*
Pneumonia in an IV drug user
Streptococcus pneumoniae, K. pneumoniae, and S. aureus

Pneumonia in a patient recovering from viral upper respiratory infection
Staphylococcus aureus, H. influenzae

Atypical pneumonia in a spelunker from the Ohio river valley
Histoplasma capsulatum

Atypical pneumonia in a patient from the southwestern United States
Coccidioides immitis

Associated with spread by inhalation of contaminated water droplets from air conditioners
Legionella pneumophila

Name the most common causative pathogen(s) of pneumonia for each age group below:

**Neonates**
Group B streptococci, *Escherichia coli, Listeria*

**Children (6 weeks-18 years)**
RSV and other viruses, *M. pneumoniae, C. pneumoniae, S. pneumoniae*

**Adults (18-40 years old)**
*Mycoplasma pneumoniae, C. pneumoniae, S. pneumoniae*

**Adults (45-65 years old)**
*Streptococcus pneumoniae, H. influenzae, anaerobes, viruses, M. pneumoniae*

**Adults (> 65 years old)**
*Streptococcus pneumoniae, viruses, anaerobes, H. influenzae, gram-negative rods*

Name four common complications of lobar pneumonia:
1. Abscess formation (especially *S. aureus* and anaerobes)
2. Empyema or spread of infection to the pleural cavity
3. Organization of exudate to form scar tissue
4. Sepsis

What type of pulmonary infection is characterized by localized suppurative necrosis of lung tissue?
Lung abscess

Name several bacterial pathogens capable of causing lung abscess:
*Staphylococcus aureus*, aerobic and anaerobic streptococci, gram-negative bacilli, and anaerobic oral flora

**Cystic Fibrosis**

What is the most common lethal genetic disease in Caucasians?
What is the mode of inheritance of CF?
Autosomal recessive (chromosome 7)

Which membrane protein is defective in CF?
The cystic fibrosis transmembrane conductance regulator (CFTR), a chloride channel protein

What is the function of CFTR?
Regulation of sodium, chloride, and bicarbonate transport across the plasma membrane

What is the most common genetic lesion causing CF?
Deletion of three nucleotides encoding phenylalanine 508 in the CFTR; AF508 prevents the normal expression of CFTR

Describe how the ΔF508 mutation prevents normal expression of CFTR:
Altered membrane folding precludes glycosylation and transport to the plasma membrane.

What is the end result of the ΔF508 mutation of the CFTR gene?
Complete loss of CFTR in the plasma membrane

How does a defect in the CFTR affect exocrine glands?
Altered CFTR activity causes the accumulation of hyperviscid mucus that blocks the secretions of exocrine glands.

What tests are used to diagnose CF in infants?
Sweat chloride test, measurement of nasal potential difference, genotyping (definitive)

How does CF typically present in an infant?
Failure to thrive, meconium ileus, mother complains child “tastes salty”

Describe the effect of CF on each of the following organs:

Lungs
Recurrent pulmonary infections, bronchiesctasis; ↑RV and TLC in chronic disease; ↓FEV₁/FVC in acute exacerbation; pulmonary hemorrhage may occur

Pancreas
Variable defects in pancreatic exocrine function; may cause pancreatic insufficiency and diabetes mellitus

Intestines
Mucus plugs → small bowel obstruction; meconium ileus in some infants

Liver
Plugging of bile cannaliculi → cirrhosis

Epididymis and ductus deferens
Bilateral absence of the vas deferens

Salivary glands
Ductal dilation; squamous metaplasia of ductal epithelium and glandular atrophy
Which organisms are commonly responsible for pulmonary infections in CF?
   *Pseudomonas aeruginosa, S. aureus, and Pseudomonas cepacia*

What is a common nutritional deficiency in CF?
   Deficiency of the fat-soluble vitamins (vitamins A, D, E, and K)

What type of heart disease is common in patients with CF?
   Cor pulmonale

Lung Cancer

What is the most common cause of cancer deaths in the United States for both men and women?
   Lung cancer

What is the most common type of malignant tumor in the lungs?
   Metastasis

What are the most common primary lung tumors?
   Adenocarcinoma is slightly more common than squamous cell carcinoma

Name the type(s) of primary lung cancer associated with the following features:

   **Central location**
   - Squamous cell and small (oat) cell carcinomas

   **Peripheral location**
   - Adenocarcinoma, large cell carcinoma, bronchioalveolar carcinoma

   **Dysplasia and carcinoma in situ precede development of this tumor**
   - Squamous cell carcinoma

   **Strongest link to smoking**
   - Squamous cell and small (oat) cell carcinomas

   **Least linked to smoking, frequently seen in nonsmoking women**
   - Bronchioalveolar carcinoma

   **Most aggressive tumor**
   - Small (oat) cell carcinoma

   **Associated with production of PTH-related peptide, hypercalcemia**
   - Squamous cell carcinoma

   **Associated with production of ADH (SIADH) and ACTH (Cushing syndrome)**
   - Small (oat) cell carcinoma

   **Carcinoembryonic antigen (CEA) positive**
   - Adenocarcinoma

   **Secretion of 5-hydroxytryptamine (5-HT, serotonin)**
   - Carcinoid

   **Oat-like, dark blue cells**
Small (oat) cell carcinoma
Tumor cells lining alveolar walls
Bronchioalveolar adenocarcinoma
Giant pleomorphic cells, poor prognosis, and high likelihood of cerebral metastasis
Large cell carcinoma
Tumor at apex of lung causes Horner syndrome or lower brachial plexopathy
Pancoast tumor
Rare pleural tumor is found in patients with a h/o exposure to asbestos
Malignant mesothelioma
Most common cancer in patients with h/o exposure to asbestos
Lung cancer

OTHER PATHOLOGY

Immotile cilia secondary to a dynein arm defect, associated with situs inversus, infertility, bronchiectasis
Kartagener syndrome
Causes stridor, toxic presentation, may be life threatening, thumbprint sign on x-ray, caused by *H. influenzae*
Acute epiglottitis
Causes stridor, nontoxic presentation, steeple sign on x-ray, caused by parainfluenza virus
Laryngotracheobronchitis, croup

PHARMACOLOGY

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and unique toxicity (TOX) (if any)

**Albuterol**

*MOA:* $\beta_2$-agonist $\rightarrow$ bronchodilator, short acting
*IND:* asthma
*TOX:* tachycardia, arrhythmias, tremor, hyperglycemia

**Inhaled corticosteroids** (beclomethasone, fluticasone, triamcinolone)
Cromolyn
MOA: anti-inflammatory; inhibits histamine release from mast cells
IND: prophylaxis for asthmatic attack
TOX: laryngeal edema (very rare)

Ipratropium
MOA: bronchodilator; cholinergic antagonist
IND: COPD.
TOX: Rare—minor systemic manifestations of anticholinergic effect

Leukotriene inhibitors (zileuton, zafirlukast, montelukast)
MOA: inhibits leukotriene synthesis (zileuton) or blocks leukotriene receptors (zafirlukast, montelukast)
IND: prophylaxis for asthmatic attack
TOX: elevation of liver enzymes

Theophylline
MOA: bronchodilator; exact mechanism unknown
IND: asthma
TOX: seizures and arrhythmias

What is the drug of choice for mild asthma?
Inhaled albuterol as needed

Which three classes of bronchodilators are useful in the management of asthma and COPD?
1. Anticholinergic agents (eg, ipratropium)
2. β-Agonists (eg, albuterol)
3. Theophylline (much less useful)

What is the drug of choice in an asthmatic requiring daily albuterol use?
Inhaled glucocorticoids

Describe how glucocorticoids act on airways to control asthma:
Glucocorticoids reduce inflammation and decrease the reactivity of airways to irritants such as cold, cigarette smoke, allergens, and exercise.

What type of therapy may be required in patients with daily asthma attacks?
Systemic steroid therapy; usually with oral prednisone or IV methylprednisolone

Name three agents used in the treatment of allergic rhinitis:
1. Antihistamines (eg, diphenhydramine, loratadine, terfenadine)
2. α-Agonist aerosols (eg, phenylephrine)
3. Corticosteroid nasal sprays (eg, beclomethasone, fluticasone, triamcinolone)

Which class of bronchodilators is useful in patients who cannot tolerate β-agonists?
Anticholinergic agents (eg, ipratropium)
CHAPTER 7
Gastroenterology

EMBRYOLOGY

What portion of the GI tract is derived from the embryonic foregut?
From the intra-abdominal esophagus → pancreas (distal to sphincter of Oddi)

What portion of the GI tract is derived from the embryonic midgut?
From the second part of the duodenum → proximal two-thirds of the colon (at the splenic flexure)

What portion of the GI tract is derived from the embryonic hindgut?
From the distal one-third of the colon → rectum (proximal to the pectinate line)

What GI structures are derived from the embryonic ectoderm?
Oropharynx (anterior two-thirds of tongue, lips, parotids, tooth enamel), anus, and rectum (distal to the pectinate line)

Name the embryonic layer supplied by the following arteries:
Celiac trunk
Foregut
Inferior mesenteric artery
Hindgut
Superior mesenteric artery
Midgut

What embryonic structure gives rise to the anterior two-thirds of the tongue?
First branchial arch

What embryonic structure gives rise to the posterior one-third of the tongue?
Third and fourth branchial arches

What disorder results from failure of fusion of the maxillary and medial nasal processes?
Cleft lip

What disorder results from failure of fusion of the nasal septum, lateral palatine processes, and/or median palatine process?
Cleft palate

What is Meckel diverticulum?
Persistence of the vitelline duct or yolk stalk that may contain ectopic tissue. **Remember: “The rule of 2’s”:** 2 in long, 2% of population, 2 ft from ileocecal valve, presents within 2 years of life, can contain 2 types of epithelia (gastric, pancreatic).

**What primordial embryonic structures give rise to the pancreas?**
- Ventral bud → pancreatic head, uncinate process, main duct
- Dorsal bud → everything else (body, tail, isthmus, accessory duct)

**What congenital defect is caused by abnormal fusion of the ventral and dorsal buds of the pancreas?**
- Annular pancreas (leads to ring around duodenum and obstruction)

**What congenital defect results from failure of migration of neural crest cells, causing an absence of parasympathetic ganglion cells in the distal colon?**
- Hirschsprung (congenital aganglionic) megacolon

**What congenital defect results from incomplete canalization of the bile ducts during development and presents shortly after birth with clay-colored stools and jaundice?**
- Biliary atresia

**ANATOMY**

**What are the four main layers of the wall of the digestive tract?**
- 1. Mucosa
- 2. Submucosa
- 3. Muscularis
- 4. Serosa

**Name the enteric plexus associated with the following descriptions:**
- Located between mucosa and inner layer of smooth muscle in GI tract wall
  - Submucosal (Meissner) plexus
- Located between inner (circular) and outer (longitudinal) layer of smooth muscle in GI tract wall
  - Myenteric (Auerbach) plexus
  - Coordinates motility along the entire gut wall
    - Myenteric plexus = Motility
  - Controls local secretions, absorption, and blood flow
    - Submucosal plexus = Secretions

**Name the lymphoid tissue found in lamina propria and submucosa of small intestine:**
- Peyer patches

**What is the major function of the Peyer patch?**
- Detect antigens → secrete IgA into lumen
In the liver, which zone of the portal acinus contains the highest O\textsubscript{2} concentration and nutrients?

Zone 1

Which zone of the portal acinus contains the lowest O\textsubscript{2} concentration and nutrients?

Zone 3

Name the three major branches of the abdominal aorta and their approximate vertebral level:

1. Celiac trunk (T12)
2. Superior mesenteric artery (L1)
3. Inferior mesenteric artery (L3)

What structure provides collateral venous drainage to the superior vena cava (SVC) when there is obstruction of the inferior vena cava (IVC)?

Azygous vein

Name the four key sites for portal-systemic shunt and the veins involved:

1. Esophagus (left gastric \rightarrow esophageal)
2. Umbilicus (paraumbilical \rightarrow superficial/inferior epigastric)
3. Rectum (superior rectal \rightarrow middle/inferior rectal)
4. Posterior abdominal wall (colic \rightarrow lumbar)

Which two vessels merge to form the portal vein?

Splenic (inferior mesenteric vein has already joined the splenic vein) and superior mesenteric veins

What important neural structure traverses the parotid gland?

Facial nerve (CN VII)

Which syndromes may result from reinnervation of the CN VII after Bell palsy or surgical severance of nerve?

Frey syndrome (sweating occurs along with salivation), crocodile tears syndrome (tearing occurs along with salivation)

What are the muscles of mastication?

Three open: masseter, temporalis, and medial pterygoid; one close: lateral pterygoid

What types of muscle are found in the esophagus?

Proximal one-third = skeletal; distal one-third = smooth; middle one-third = both

What is the function of the pylorus?

Acts as muscular sphincter to regulate movement of food out of the stomach and prevents reflux of duodenal contents

Which blood vessel lies posterior to the first part of the duodenum?

Gastroduodenal artery (a concern in cases of posterior perforation due to ulcers)

The common bile duct and main pancreatic duct empty into what portion of the duodenum?
Second (descending) part

The common bile duct and pancreatic duct drain into the duodenum through what structure?
   Hepatopancreatic ampulla (of Vater)

What structure controls the release of bile into the duodenum?
   Sphincter of Oddi

Which two ducts combine to form the common bile duct?
   1. Common hepatic
   2. Cystic duct

What structures make up the porta hepatis?
   Hepatic artery, portal vein, common bile duct

What structure keeps the cystic duct open at all times for bile to flow freely in both directions?
   Spiral valve (of Heister)

What is the “bare area” of the liver?
   A portion of the diaphragmatic surface of the liver that is devoid of peritoneum

What divides the left and right lobes of the liver?
   Interlobar fissure (an invisible line running from the gallbladder to the IVC)

What structure supports the duodenum at the duodenojejunal flexure?
   Suspensory ligament (of Treitz)

Name the intestinal structures (duodenum, ileum, jejunum, or colon) associated with each of the following characteristics:
   Long, finger-shaped villi
   Jejunum
   Intestinal glands (crypts) and 3 cm luminal diameter
   Ileum
   No villi, large crypts, and 6 to 9 cm luminal diameter
   Colon
   Large, numerous, plicae circularis
   Jejunum
   Accounts for the terminal three-fifths of the small intestine
   Ileum
   Contains fatty tags (appendices epiplloicae)
   Colon
   Contains prominent Peyer patches
   Ileum
   Contains long vasa recta
   Jejunum
What term is used to describe the three longitudinal bands of smooth muscle in the colon?
   Teniae coli

What is the name for the wall sacculations in the colon that are separated by the plicae semilunaries?
   Hastra

What anatomic feature divides the upper and lower anal canal?
   Pectinate line

What muscle holds the rectum in a 90° flexure?
   Puborectalis muscle

Describe the arterial supply, venous drainage, and innervation of internal hemorrhoids:
   Vasculature = superior rectal artery/vein (drains to portal circulation); visceral innervation → not painful

Describe the arterial supply, venous drainage, and innervation of external hemorrhoids:
   Vasculature = inferior rectal artery/vein (drains to systemic circulation via IVC); somatic innervation → painful

What type of muscle is found in the internal anal sphincter?
   Smooth muscle (under involuntary control via autonomic innervation)

What type of muscle is found in the external anal sphincter?
   Striated muscle (under voluntary control via the pudendal nerve)

What are the boundaries of Hesselbach triangle?
   Inferior epigastric artery, inguinal ligament, lateral border of rectus abdominus muscle

Name the types of hernia:
   Peritoneum protrudes through Hesselbach triangle, medial to the inferior epigastric artery
   Direct hernia
   Retroperitoneal structures to enter the thorax because of defective development of pleuroperitoneal membrane
   Diaphragmatic hernia
   Peritoneum protrudes through both the internal (deep) and external (superficial) inguinal rings
   Indirect hernia
   Stomach herniates upward through the esophageal hiatus of the diaphragm
   Hiatal hernia
   Occurs in infants as a result of failure of processus vaginalis to close
   Indirect hernia
Protrudes below the inguinal ligaments and lateral to the pubic tubercle; more common in females
Femoral hernia

**PHYSIOLOGY**

**Saliva**

Which three glands produce saliva?
1. Parotid
2. Submandibular
3. Sublingual

Name three important functions of saliva:
1. Protection of dental health by buffering oral bacterial acids
2. Digestion (starches by a-amylase); triglycerides (TGs) by lingual lipase
3. Lubrication of food with mucins

What determines the relative composition of salivary contents?
Flow rate

How is the regulation of saliva production unique?
It is stimulated by both parasympathetic and sympathetic activity.

**GI Hormones and Secretions**

Name the source of the following GI secretory products:
- **Intrinsic factor (IF)**
  Parietal cells (stomach)
- **Pepsinogen**
  Chief cells (stomach)
- **Histamine**
  Mast cells (stomach)
- **Gastric acid (H⁺)**
  Parietal cells (stomach)
- **Gastrin**
  Antral G cells and duodenum
Bicarbonate  
Surface mucosal cells (of stomach and duodenum)

Secretin  
S cells (duodenum)

Somatostatin  
D cells (duodenum)

Cholecystokinin (CCK)  
I cells (duodenum) and jejunum

Gastric inhibitory peptide (GIP)  
Duodenum and jejunum

For each of the following substances, state the factors that regulate its secretion:

Gastric acid (H\(^+\))
↑ By histamine, acetylcholine (ACh), gastrin; ↓ by prostaglandin, somatostatin, GIP

Pepsinogen
↑ By vagal stimulation (ACh) and low pH

Gastrin
↑ By small peptides and amino acids (AAs) (Phe and Trp = most potent), gastric distention, and vagus (via gastrin-releasing peptide[GRP]); ↓ by pH 3.0 and secretin

Bicarbonate in pancreatic secretions
↑ By secretin (potentiated by CCK and vagal input)

Secretin
Acid (H\(^+\) and fatty acids [FAs]) in the duodenum

Somatostatin
↑ By acid; ↓ by vagus

CCK
↑ By FAs, AAs, and small peptides

GIP
↑ By FAs, AAs, and oral glucose

List the most important functions of the following GI secretions:

IF
Binds vitamin B\(_{12}\) for uptake in terminal ileum

Gastric acid (H\(^+\))
Converts pepsinogen to pepsin and sterilizes chyme. Note: inadequate acid production →↑ risk of *Salmonella* infections

Pepsinogen
Digests protein

Gastrin
Secretion of IF, HCl, and pepsinogen; stimulates gastric motility and growth of gastric mucosa

**Bicarbonate**
Neutralizes acid → prevents autodigestion

**Secretin**
↑ Pancreatic HCO$_3^-$ secretion; ↓ gastric acid secretion

**Somatostatin**
↓ H$^+$ and pepsinogen secretion, ↓ pancreatic and SI secretions, ↓ gallbladder contraction, ↓ release of both insulin and glucagon

**CCK**
↑ Gallbladder contraction, ↑ pancreatic enzyme secretion, ↓ gastric emptying

**GIP**
↑ Insulin (especially in response to oral glucose); ↓ H$^+$ secretion

Which enzyme in the parietal cell catalyzes the production of H and HCO$_3^-$ from CO$_2$ and H$_2$O?
Carbonic anhydrase

How is H$^+$ secreted into the lumen of the stomach?
H$^+$/K$^+$ ATPase pumps H out of cells and Cl$^-$ diffuses concurrently to maintain electrical neutrality forming HCl.

Which chemical potentiates the actions of ACh and gastrin in stimulating secretion?
Histamine. (This is why H receptor blockers are so effective in treating ulcers.)

Which prototypical drug blocks the effects of histamine at the level of the parietal cell?
Cimetidine (an H receptor blocker)

Why does not atropine block vagally mediated gastrin secretion?
Vagal stimulation of acid production is independent of ACh. (It is mediated by GRP.)

Which GI hormone is released by the small intestine in response to fats, proteins, and carbohydrates?
GIP

**GI Motility**

What are the two main divisions of the enteric nervous system?
1. Extrinsic (parasympathetic and sympathetic nervous systems)
2. Intrinsic (enteric nervous systems)

Parasympathetic innervation of the GI tract occurs via which nerves and has what general effect?
Vagus and pelvic → usually stimulatory

Sympathetic innervation of the GI tract occurs via which nerves and has what general effect?
   Fibers originate in spinal cord and synapse in the celiac and superior mesenteric ganglia → usually inhibitory.

What term is used to describe the vasovagal reflex that accommodates for food entering the stomach?
   Receptive relaxation

What reflex mediates colonic motility in response to food in the stomach?
   Gastrocolic reflex

What are the two components of the gastrocolic reflex?
   1. Fast: mediated by the autonomic nervous system
   2. Slow: mediated by CCK and gastrin

What two centers of the brain are integral to vomiting?
   1. Chemoreceptor trigger zone (floor of the fourth ventricle)
   2. The vomiting center of the medulla

What pacemaker cells in the GI tract regulate the basal rate of gut contraction?
   Interstitial cells of Cajal (ICC)

What are the frequencies of ICC’s pacemaker activities?
   Stomach—3/min, duodenum—12/min, ileum—10/min, colon—3/min

Miscellaneous GI Physiology

What part of the pancreas is responsible for synthesizing and releasing zymogens?
   Secretory acinar cells

Which two chemicals stimulate the release of zymogens?
   1. ACh
   2. CCK

Which hormone acts on the pancreatic ductal cells to increase mucus and HCO₃⁻ secretion?
   Secretin

Name the pancreatic enzymes responsible for the following actions:
   Starch digestion
   α-Amylase (secreted in active form)

   Protein digestion
   Proteases (eg, trypsin, chymotrypsin, elastase, carboxypeptidases—secreted as proenzymes)
Fat digestion
Lipase, phospholipase A, colipase

Which enzyme catalyzes the conversion of trypsinogen into trypsin?
Enterokinase (a brush-border enzyme)

Why is the conversion of trypsin an important part of protein digestion?
Trypsin converts proenzymes to their active forms (including trypsinogen to form a positive-feedback loop)

What is the rate-limiting step in carbohydrate digestion?
Production of monosaccharides by oligosaccharide hydrolases (at brush border)

What are the five major components of bile?
1. Water (97%)
2. Bile salts
3. Phospholipids
4. Cholesterol
5. Bilirubin (BR)

What property of bile salts allows them to solubilize lipids into micelles for absorption?
They are amphipathic (contain both hydrophilic and hydrophobic regions).

Where is bile produced and stored?
It is produced continuously by hepatocytes and stored in gallbladder.

What is the role of intestinal bacteria in the synthesis of bile acids?
They convert primary (1°) bile acids to secondary (2°) bile acids.

Which membrane protein is essential for bile acids recirculation?
Na⁺-bile cotransporter in terminal ileum

Why does ileal resection result in steatorrhea?
Lack of bile acid recirculation → depletion of the bile acid pool → impaired fat absorption

What types of carbohydrates can be absorbed?
Monosaccharides only (eg, glucose, galactose, fructose)

By what mechanism are carbohydrates absorbed?
Glucose/galactose: Na⁺-dependent cotransport; fructose: facilitated diffusion

How are fats absorbed?
Lipase breaks triglycerides into glycerol and FAs. Short- and medium-chain FAs undergo passive diffusion; long-chain FAs form micelles with bile salts for passive diffusion.

What metabolites of protein can be absorbed by the GI tract and what type of transport molecules are involved in their absorption?
AAs, dipeptides, and tripeptides; Na⁺-dependent cotransporters
Nonneoplastic Disorders of the Upper GI Tract

Name the nonneoplastic disorder of the upper GI tract with the following pathologic and clinical features:

- Common vesicular circumoral lesion with eosinophilic intranuclear inclusions
  - Herpes labialis (usually herpes simplex virus [HSV]-1)
- Connective tissue disorder characterized by xerostomia, keratoconjunctivitis sicca, and autoantibodies to SS-A (Ro) and SS-B (La)
  - Sjögren syndrome
- Esophageal dysmotility caused by inability of the lower esophageal sphincter to relax (due to loss of ganglion cells in the myenteric plexus)
  - Achalasia
- Type of hiatal hernia in which the stomach and the cardioesophageal junction slide in and out of the thorax
  - Sliding (axial) hernia
- Pharyngeal outpouching involving >1 layer of the esophageal wall; results in food accumulation and chronic halitosis
  - Zenker (pharyngoesophageal) diverticulum
- Retching-induced laceration of gastroesophageal (GE) junction resulting in hematemesis and mediastinitis; ↑ incidence in alcoholics
  - Mallory-Weiss tear
- Complete rupture of the esophagus (all layers), often due to severe retching
  - Boerhaave syndrome
- May result from Chagas disease causing the loss of myenteric plexus in the esophagus
  - 2° achalasia
- Hyperplasia of gastric surface mucosal cells
  - Ménétrier disease
- Postvagotomy, unimpeded passage of hypertonic food to SI → distention and diarrhea
  - Dumping syndrome
Neoplastic Disorders of the Upper GI Tract

Name the neoplastic disorder of the upper GI tract described by each of the following statements:

- Most common salivary gland tumor; contains a mix of epithelial and mesenchymal elements
  - Pleomorphic adenoma (mixed tumor)
- Irregular white mucosal patches in the mouth of an AIDS patient as a result of Epstein-Barr virus (EBV)
  - Oral hairy leukoplakia
- Accounts for 95% of oral cancers
  - Squamous cell carcinoma
- Benign salivary tumor containing cystic spaces lined by double-layered eosinophilic epithelium (oncocyes) embedded in dense lymphoid tissue
  - Warthin tumor (papillary cystadenoma lymphomatosum)
- Most common esophageal carcinoma; usually in proximal two-thirds; associated with alcohol and tobacco use
  - Squamous cell carcinoma
- Intestinal metaplasia of squamous epithelium in distal esophagus in response to prolonged injury (often due to GERD)
  - Barrett esophagus
- Mucin-producing glandular tumor of the distal one-third of the esophagus
  - Adenocarcinoma
- Infiltrating carcinoma, causing extensive thickening of stomach wall; “leather-bottle stomach”
  - Linitis plastica (signet ring carcinoma)
- Gastric carcinoma that has metastasized to the ovary
  - Krukenberg tumor

Name six important risk factors for gastric carcinoma:

These ↑ your “CHANSE” for gastric cancer:
1. C hronic gastritis
2. H elicobacter pylori infection
3. A blood type
4. N itrosamines
5. S ex (men > 50 years old)
6. E ating habits (low-fiber diet)

Name six important risk factors for esophageal carcinoma:

“ABCDEF”
1. A chalasia
2. B arrett esophagus
3. C orrosive esophagitis
4. D iverticuli
5. E sophageal webs
6. F amilial

What is the name for metastatic spread of gastric cancer to the supraclavicular node?

Virchow node

Pediatric GI Disorders

Name the GI disorder commonly diagnosed in the pediatric population with the following findings:

- Difficulty with feeding starting from birth, excessive oral secretions, inability to pass NG tube, no gas in abdomen, early pneumonia
- Tracheoesophageal fistula
- Nonbilious projectile vomiting, abdominal “olive” in epigastric region
- Pyloric stenosis
- Bilious vomiting, “double bubble,” associated with Trisomy 21
- Duodenal atresia
- Commonly occurs at ileocecal junction, most common cause of small bowel obstruction in toddlers
- Intussusception
- Failure to pass meconium in the first 48 hours of birth, abdominal distention, associated with CF
- Meconium ileus

Gastritis

Name the type of gastritis associated with the following findings:

- Autoimmune disorder with autoantibodies to parietal cells and IF, achlorhydria, pernicious anemia, and aging
- Type A (fundal) chronic gastritis (Remember: the 5 A’s for type A)
- “Coffee-ground emesis” from mucosal inflammation
- Acute (erosive) gastritis
- *Helicobacter pylori* infection
- Type B (antral) chronic gastritis (B = bug)
Left shoulder pain
Perforation of ulcer → irritation of left diaphragm

Peptic Ulcer Disease

Name the type of peptic ulcer (gastric or duodenal) disease associated with each of the following findings:

- **Pain is greater with meals**
  - Gastric ulcer (pain is greater with meals) → weight loss

- **Pain decreases with meals**
  - Duodenal ulcer (pain decreases with meals) → weight gain

Almost 100% associated with *H. pylori* infection

- Duodenal ulcer
- **Due to ↓ mucosal protection against gastric acid**

- Gastric ulcer
- **Associated with nonsteroidal anti-inflammatory drug (NSAID) use**

- Duodenal ulcer
- **Hypertrophy of Brunner glands**

- Duodenal ulcer
- **Blood type O**

- Duodenal ulcer
- **Elevated gastrin levels**

- Duodenal ulcer
  - **Due to ↑ gastric acid secretion and/or ↓ mucosal protection**

Name four common complications of peptic ulcer disease:

1. Bleeding
2. Penetration
3. Perforation
4. Obstruction

Name a classic complication of posterior duodenal ulcers:

- Massive hemorrhage from erosion of the gastroduodenal artery

Malabsorption

Name the malabsorption syndrome associated with each of the following pathologic and clinical findings:
Gluten sensitivity
Celiac disease (nontropical sprue)
Brush-border enzyme deficiency resulting in bacterial digestion of unabsorbed disaccharide, causing osmotic diarrhea
Disaccharidase deficiency (#1 = lactase deficiency)
Steatorrhea, weight loss, hyperpigmentation, polyarthritis, fever, and lymphadenopathy in an older, white male; infectious etiology
Whipple disease (caused by *Tropheryma whippelii*)
Increased risk of T-cell lymphoma, GI, and breast malignancy
Celiac disease
Autosomal recessive (AR) defect in chylomicron assembly resulting in an absence of chylomicrons, very low-density lipoproteins (VLDLs), or low-density lipoprotein (LDL) in blood
Abetalipoproteinemia
Flat, proximal intestinal mucosa with marked villous atrophy; lymphocytes and plasma cells in lamina propria
Celiac disease
Distinctive periodic acid-Schiff (PAS)-positive macrophages in intestinal mucosa
Whipple disease
Associated with HLA-DQ2 and HLA-DQ8
Celiac disease
Gram-positive actinomycetes
Whipple disease
Acanthocytes (*burr* cells) in blood
Abetalipoproteinemia

Diverticular Disease

What is the most common cause of painless bleeding from the lower GI tract?
Diverticulosis

What is the prevalence of diverticulosis in the US population older than age 60?
~50%

What part of the colon is most frequently affected by diverticulosis?
Sigmoid colon

Name the disorder characterized by diverticular inflammation causing left lower quadrant (LLQ) pain, anorexia, nausea, and vomiting:
Diverticulitis

Name four complications of diverticulitis:
1. Perforation
2. Peritonitis
3. Abscess
4. Obstruction

What part of the GI tract is most commonly affected by ischemic bowel disease?
“Watershed” areas (splenic flexure, rectosigmoid junction)

Define intussusception.
Telescoping of the intestines resulting in intestinal obstruction

Define volvulus.
Complete twisting of the bowel around its mesenteric base

Where does volvulus most commonly occur?
Sigmoid colon (more common in elderly)

Name the inflammatory bowel disease which is often characterized by overgrowth of exotoxin-producing bacteria:
Pseudomembranous colitis

Which organism is responsible for pseudomembranous colitis?
*Clostridium difficile*

What disorder is characterized by nausea, vomiting, anorexia, leukocytosis, and pain at McBurney point?
Appendicitis

**Inflammatory Bowel Disease**

**Ulcerative colitis or Crohn’s disease?**
**Pancolitis with crypt abscesses**
Ulcerative colitis (UC)
**Fistulas and fissures**
Crohn’s disease Both
Associated with ankylosing spondylitis
Both
Associated with sclerosing cholangitis
UC
**Amyloidosis**
Crohn’s disease
**Can lead to toxic megacolon**
UC
**Longitudinal ulcers**
Crohn’s disease
Punched-out aphthous ulcers
Crohn’s disease
Increased risk of colorectal carcinoma
UC >>> Crohn’s disease
Skip lesions
Crohn’s disease
Can involve any portion of the GI tract (usually terminal ileum and colon)
Crohn’s disease
“String sign” on x-ray (due to bowel wall thickening)
Crohn’s disease
Associated with pyoderma gangreosum
Both
Transmural inflammation
Crohn’s disease
Noncaseating granulomas
Crohn’s disease
Cobblestone mucosa
Crohn’s disease

Neoplastic Disorders of the Lower GI Tract

What is the most common histologic type of GI lymphomas?
95% are B cell (MALT omas).
What is the most common tumor of the appendix?
Carcinoid tumor
What type of cells give rise to carcinoid tumors?
Neuroendocrine cells
What substances are secreted from carcinoid tumors?
Serotonin, histamine, and prostaglandins
Which carcinoid tumors tend to be more aggressive?
Ileal, gastric, and colonic
Metastases to which organ result in carcinoid syndrome?
Liver
Name five clinical findings of carcinoid syndrome:
1. Vasomotor dysfunction
2. GI hypermotility
3. Bronchoconstriction
4. Hepatomegaly
What laboratory test is used in the diagnosis of carcinoid syndrome?
5-Hydroxyindoleacetic acid (5-HIAA) in urine

Name the types of neoplastic polyp:
Usually benign and pedunculated; most common
Tubular adenoma (75%)
Highly malignant; sessile tumor > 1 cm with fingerlike projections
Villous adenoma
Shares features of both other types of polyps
Tubulovillous adenoma

Name five major risk factors for colon cancer:
1. Presence of colonic villous adenomas
2. Inflammatory bowel disease
3. Low-fiber, high animal fat diet
4. Age (> 60)
5. Positive family/personal history

How does colorectal carcinoma classically present?
Left side lesions → blood in stool; right side lesions → anemia (from occult blood loss)

Where is the most common site for colorectal cancer?
Sigmoid colon

Name the autosomal dominant (AD) polyposis syndrome associated with each of the following findings:
Colonic polyps, osteomas, and soft tissue tumors; associated with abnormal dentition
Gardner syndrome
Hundreds of colonic polyps; malignant potential ~100%
Familial adenomatous polyposis (FAP)
Colonic polyps and CNS tumors; malignant potential ~100%
Turcot syndrome
Defect in DNA repair → many colonic lesions (especially proximal); malignant potential ~50%
Hereditary nonpolyposis colorectal carcinoma (HNPCC)
Benign, hamartomas of GI tract; melanotic pigmentation of hand, mouth, and genitalia; no malignant potential (but ↑ risk of other tumors)
Peutz-Jeghers syndrome

What are the three tumor syndromes in which the APC gene is mutated?
1. FAP
2. Gardner syndrome
3. Turcot syndrome

Pancreatitis and Pancreatic Cancer

Name nine causes of acute pancreatitis:
“GET SMASHED”
1. Gallstones (major cause)
2. Ethanol (major cause)
3. Trauma
4. Steroids
5. Mumps
6. Autoimmune disorder
7. Scorpion sting
8. Hyperlipidemia
9. Drugs (especially ddl)
Other causes: ischemia, infections, pancreatic cancer, and peptic ulcer disease

Name seven possible sequelae of acute pancreatitis:
1. Progression to chronic pancreatitis
2. Abscess
3. Pseudocyst
4. Hypocalcemia
5. Focal fibrosis and diffuse fat necrosis
6. Acute respiratory distress syndrome (ARDS)
7. Disseminated intravascular coagulation (DIC)

Name four common laboratory abnormalities in acute pancreatitis:
1. ↑ Serum amylase (within 24 hours)
2. ↑ Serum lipase (72-96 hours)
3. Hypocalcemia
4. Glycosuria

Name five causes of chronic pancreatitis:
“ABCCD”
1. Alcoholism (#1 in adults)
2. Biliary tract disease
3. Cystic fibrosis (#1 in kids)
4. Ca^{2+} (hypercalcemia)
5. Divisum (pancreas divisum)

Most pancreatic tumors are found in what region of the pancreas?
Two-thirds of pancreatic tumors are found in the pancreatic head.

**What is a common clinical presentation of a mass in the pancreatic head?**
- Painless jaundice causing malabsorption and Courvoisier (enlarged, palpable) gallbladder

**What is Trouseau syndrome?**
- Migratory thrombophlebitis associated with visceral cancer, commonly pancreatic adenocarcinoma

**What are the two most commonly mutated genes causing pancreatic adenocarcinoma?**
1. *K-ras* (> 90% mutated)
2. *p53* (60%-80% mutated)

**What is the prognosis for pancreatic adenocarcinoma?**
- Averages 6 months or less (very aggressive)

**Disorders of Bilirubin Metabolism**

**What type of hyperbilirubinemia results from cholestasis?**
- Conjugated

**Name the hereditary hyperbilirubinemia described in each of the following statements:**
- **Mildly ↓ UDP-glucuronyl transferase; asymptomatic; associated with stress in 6% of people**
  - Gilbert syndrome
- **AR defect causing ↓ canalicular excretion of BR conjugates → grossly black liver; asymptomatic**
  - Dubin-Johnson syndrome
- **AR absence UDP-glucuronyl transferase → ↑ unconjugated BR → jaundice, ker nicterus, early death**
  - Crigler-Najjar syndrome, type I
- **AR defect causing asymptomatic, conjugated bilirubinemia**
  - Rotor syndrome

**Liver Disorders**

**What three pathologic characteristics define cirrhosis?**
1. Fibrosis
2. Nodular regeneration of hepatocytes
3. Disruption of parenchymal architecture

**Name four common causes of micronodular cirrhosis:**
1. Chronic alcoholism (think of a micro brewery)
2. Hereditary hemochromatosis
3. 1° biliary cirrhosis
4. Wilson disease (hepatolenticular degeneration)

**Name four common causes of macronodular cirrhosis:**
1. Hepatitis B virus (HBV)
2. Hepatitis C virus (HCV)
3. α₁-Antitrypsin deficiency
4. Wilson disease

**List the effects of hepatic failure on the following body systems:**

**Eye**
Scleral icterus

**Neurologic**
Coma, hepatic encephalopathy (asterixis, hyperreflexia, behavioral changes)

**Systemic**
Peripheral edema, malnutrition

**Skin**
Jaundice, palmar erythema, spider angiomata, caput medusae

**Reproductive**
Testicular atrophy, gynecomastia, loss of pubic hair

**Hematopoietic**
Anemia, bleeding tendency (↓ coagulation factors), splenomegaly

**Renal**
Hepatorenal syndrome (ARF 2° to hypoperfusion)

**GI**
Fetor hepaticus, ascites, esophageal varices, hemorrhoids

**Name the liver disorder associated with each of the following findings:**

**Mallory bodies**
Alcoholic hepatitis

**Occlusion of IVC or hepatic veins with centrilobular congestion → congestive liver disease; associated with polycythemia, pregnancy, and hepatocellular carcinoma**
Budd-Chiari syndrome

**Obliteration of hepatic vein radicals following bone marrow transplant**
Veno-occlusive disease

**Copper deposition in liver, kidneys, brain, and cornea → asterixis, basal ganglia degeneration, dementia**
Wilson disease (hepatolenticular degeneration)
AST:ALT ratio > 1.5
Alcoholic hepatitis
Lymphoid aggregates and interface hepatitis
Chronic hepatitis
May be incidental finding in young woman taking oral contraceptives
Hepatic adenoma
Sinusoidal hepatic dilations from use of anabolic steroids
Peliosis hepatis
Hemolysis, elevated LFTs, and low platelets in a pregnant woman
HELLP syndrome (hepatic disease of pregnancy)
Elevated α-fetoprotein (AFP)
Hepatocellular carcinoma

Name the etiology of cirrhosis associated with each of the following findings:

- Panacinar emphysema
- α₁-Antitrypsin deficiency
- Decreased ceruloplasmin
- Wilson disease (hepatolenticular degeneration)
- Triad of bronze diabetes, skin pigmentation, and micronodular pigment cirrhosis
- Hemochromatosis
- Antimitochondrial antibodies
- Primary biliary cirrhosis
- Nutmeg liver
- Congestive heart failure
- Kayser-Fleischer rings
- Wilson disease (hepatolenticular degeneration)
- Micronodular fatty liver; portal hypertension, asterixis, jaundice, and gynecomastia
- Chronic alcohol abuse
- ↑ Ferritin, transferrin, and total iron; ↓ total iron-binding capacity (TIBC)

Hereditary hemochromatosis. Note: total body iron is sometimes high enough to trigger metal detectors.

Name the major risk factors for hepatocellular carcinoma:

“WATCH for ABC”
- Wilson disease
- α₁-AntiTrypsin
- Carcinogens (eg, aflatoxin B₁, polyvinyl chloride)
- Hemochromatosis
Alcoholic cirrhosis
Hepatitis B
Hepatitis C

Hepatocellular carcinoma tends to spread through which route?
Hematogenous

What is the most common type of malignancy in the liver?
Metastasis

Which primary tumors tend to metastasize to the liver?
Colon > Stomach > Pancreas > Breast > Lung (Remember: “Cancer Sometimes Penetrates Benign Liver!”)

Name the hepatobiliary disorder associated with the following:
Strawberry gallbladder
Cholesterolosis
Associated with Opisthorchis sinenis (liver fluke) infection in Asia
Cholangiocarcinoma
Tumor arising at the junction of the left and right hepatic ducts
Klatskin tumor
Inflammation of the bile duct; commonly due to Escherichia coli infection

Disorders of the Gallbladder

What is Courvoisier law?
An enlarged, palpable gallbladder with jaundice is likely the result of an underlying malignancy (often in head of the pancreas) and not from a stone in the common duct (because gallbladder is typically too scarred from infection).

What is Charcot triad?
Spiking fevers with chills, jaundice, and right upper quadrant (RUQ) pain (biliary colic); strongly suggests cholangitis

What are the risk factors for cholelithiasis?
4 F’s: Fertile, Fat, Forty-year-old Female

What is the most common type of gallstone?
Mixed stone (components of pigment and cholesterol stones)

Name six complications of cholelithiasis:
1. Biliary colic and common bile duct obstruction
2. Cholecystitis (acute or chronic)
3. Ascending cholangitis
4. Acute pancreatitis
5. Gallstone ileus
6. Malignancy (adenocarcinoma)

Viral Hepatitis

Name the hepatitis virus (viruses) associated with the following features:

- **Fecal-oral transmission**
  - Hepatitis A virus (HAV)
- **Water-borne transmission**
  - Hepatitis E virus (HEV)
- **Infection may lead to a carrier state**
  - HBV, HCV, and hepatitis D virus (HDV, delta agent)
- **Defective virus requiring HBsAg as its envelope**
  - HDV (delta agent)
- **Sexual, parenteral, and transplacental transmission**
  - HBV, HCV, HDV
- **DNA hepadnavirus**
  - HBV
- **High mortality rate in pregnant women**
  - HEV
- **Associated with IV drug use**
  - HCV
- **Long incubation (~3 months)**
  - HBV
- **Increased risk of hepatocellular carcinoma**
  - HBV, HCV
- **Immune globulin vaccine available**
  - HAV, HBV (and HDV)
- **Short incubation (~2 weeks)**
  - HAV

Name the hepatitis serologic marker described below:

- **Antigen found on surface of HBV; continued presence suggests carrier state**
  - HBsAg
- **Antigen associated with core of HBV**
  - HBcAg
- **Antigen in the HBV core that indicates transmissibility**
  - HBeAg
- **Antibody suggesting low HBV transmissibility**
HBeAb
Acts as a marker for HBV infection during the “window” period (acute phase)
IgM-HBcAb
Provides immunity to HBV
HBsAb

What is the “window” period of a hepatitis infection?
Period during acute infection when HBsAg has become undetectable, but HBsAb has not yet appeared

Infectious Diarrhea

Name six infectious causes of bloody diarrhea:
1. *Salmonella*
2. *Shigella*
3. *Campylobacter jejuni*
4. Enteroinvasive and enterohemorrhagic *E. coli*
5. *Yersinia enterocolitica*
6. *Entamoeba histolytica*

Name the diarrhea-causing organism associated with the following statements:
Most common cause of diarrhea in infants
Rotavirus
Ten to twelve loose, bloody, and mucous diarrhea stools per day due to ingestion of cysts
*Entamoeba histolytica*
Comma-shaped organisms causing rice-water stools
*Vibrio cholera*
Second to rotavirus as a cause of gastroenteritis in kids
Caliciviruses (Norwalk-like and Sapporo-like)
Bloody diarrhea; very low ID$_{50}$ (small numbers of organisms can cause disease); nonmotile
*Shigella*
Usually transmitted from pet feces
*Yersinia enterocolitica*
Motile; lactose nonfermenter; causes bloody diarrhea
*Salmonella*
Comma- or s-shaped organisms causing bloody diarrhea; grows at 42°C
*Campylobacter jejuni*
Watery diarrhea with extensive fluid loss in AIDS patient
Cryptosporidium
Foul-smelling diarrhea after returning from a camping trip
Giardia lamblia
Watery diarrhea caused by antibiotic-induced suppression of colonic flora
Clostridium difficile

Name the organism responsible for food poisoning from the following items:
- Reheated rice
  - Bacillus cereus
- Reheated meat dishes
  - Clostridium perfringens
- Improperly canned food
  - Clostridium botulinum
- Contaminated seafood or raw oysters
  - Vibrio parahaemolyticus and Vibrio vulnificus
- Meats, mayonnaise, custards
  - Staphylococcus aureus. Note: starts and ends quickly
- Undercooked beef products
  - Escherichia coli O157:H7
- Raw poultry, milk, eggs, and meat
  - Salmonella

PHARMACOLOGY

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and unique toxicity (TOX) (if any)

Omeprazole, pantoprazole, lansoprazole
- MOA: Irreversibly inhibits H⁺/K⁺-ATPase in parietal cells (proton pump inhibitor)
- IND: Peptic ulcer disease, Zollinger-Ellison syndrome, erosive esophagitis
- TOX: Liver toxicity, pancreatitis, agranulocytosis (rare)

Cimetidine, ranitidine, famotidine, nizatidine
- MOA: H₂ receptor antagonist in parietal cell
- IND: GE reflux disease
- TOX: Endocrine effects (gynecomastia—primarily caused by cimetidine, galactorrhea, ↓ sperm count), potent inhibitor of P-450, ↓ renal creatinine clearance

Misoprostol
MOA: PGE₁ analog →↑ secretion of gastric mucus and bicarbonate
IND: Prophylaxis for NSAID-induced peptic ulcer disease (PUD); maintenance of a patent ductus arteriosus (PDA)
TOX: Abortifacient

**Aluminum sucrose sulfate (sucralfate)**
MOA: Polymerizes in stomach → binds to injured tissue, forming a protective coating over ulcers (Note: requires an acidic environment)
IND: Peptic ulcer disease
TOX: Osteodystrophy, osteomalacia (mainly in pts with renal failure)

**Ondansetron, granisetron**
MOA: 5-HT₃ receptor antagonist
IND: Postoperative nausea/vomiting, chemotherapy-induced emesis
TOX: Headache, diarrhea

**Meclizine**
MOA: H₁ receptor antagonist
IND: Motion sickness
TOX: Teratogenic

**Loperamide, diphenoxylate**
MOA: Antimotility agents (meperidine analogs)
IND: Diarrhea
TOX: Toxic megacolon in kids (loperamide)

**Metoclopramide**
MOA: Stimulates ACh release →↑ upper GI motility
IND: Nausea, ileus
TOX: Sedation, diarrhea, and extrapyramidal symptoms (EPS) (especially in kids)

**Lactulose**
MOA: Osmotic laxative
IND: Hyperammonemia, colonic lavage precolonoscopy
TOX: Dehydration with overuse

**What is “triple therapy” for peptic ulcer disease?**
Proton pump inhibitor (PPI), bismuth salicylate, and two of the following antibiotics: metronidazole, amoxicillin, clarithromycin, or tetracycline

**What is the most important approach to healing peptic ulcers?**
Eradicating *H. pylori*

**How long does proton pump inhibition last?**
48 hours

**Name two uses for bismuth subsalicylate:**
1. *Helicobacter pylori* infection
2. Traveler diarrhea

What two weak bases that are used as antacids have minimal systemic absorption?
1. MgOH₂
2. AIOH₃ (combined to make milk of magnesia)

For each of the following antacids list the toxicity/toxicities:

- **Antacids**
  - Hypokalemia, alter absorption of other drugs
- **Sodium bicarbonate**
  - Systemic alkalinization
- **Aluminum hydroxide**
  - Constipation
- **Magnesium hydroxide**
  - Diarrhea

Name the therapy of choice for each of the following disorders:

- **Hereditary hemochromatosis**
  - Repeated phlebotomy and deferoxamine
- **Wilson disease**
  - Chelation therapy (with penicillamine)
- **Acute cholecystitis from gallstones**
  - Cholecystectomy
CHAPTER 8
Reproduction and Endocrinology

EMBRYOLOGY

During embryogenesis, when is male/female phenotypic differentiation complete?
By week 20

Which gene determines phenotypic differentiation?
*Sry* gene (encodes for a protein called testis-determining factor [TDF])

Which cells secrete Mullerian-inhibiting factor (MIF) during fetal development?
Sertoli cells

What factors are required to direct the indifferent embryo into a male phenotype?
TDF, MIF, testosterone, and dihydrotestosterone (DHT)

In what structure, within the testes, does spermatogenesis occur?
Seminiferous tubules

What molecule is the primary (1°) source of energy for sperm?
Fructose

Give the number of chromosomes and amount of DNA found in each of the following cell types:
- Spermatogonia
  46,2N
- 1° spermatocyte/oocyte
  46,4N
- Secondary (2°) spermatocyte/oocyte
  23,2N
- Spermatid/ovum
  23,1N

What stage is each cell type halted in and when is the stage finally completed?
- 1° oocyte
  Prophase I, just prior to ovulation
- 2° oocyte
  Metaphase II, at fertilization

Name the structure of the mature sperm associated with each of the following statements:
Derived from the Golgi apparatus
Acrosomal cap
Contains mitochondria
Middle piece (neck)
Derived from one of the centrioles
Flagellum (tail)

Name the congenital disorder that results from each of the following aberrations:
Complete lack of fusion of paramesonephric ducts
Double uterus with double vagina
Partial fusion of the paramesonephric ducts
Bicornate uterus
Testes fail to descend into the scrotum
Cryptorchidism (bilateral → sterility)
Patency of processus vaginalis
If small → hydrocele; if large → congenital inguinal hernia
Failure of urethral folds to close
Hypospadias (penile urethra opens on inferior/ventral side)
Faulty positioning of genital tubercle
Epispadias (penile urethra opens on superior/dorsal side)

Name the embryonic structure that gives rise to each of the following tissues:
Thyroid gland
Thyroid diverticulum
Thymus, inferior parathyroids
Third branchial pouch
Superior parathyroids and the parafollicular “C” cells
Fourth branchial pouch (fourth is superior to third)
Chromaffin cells of adrenal medulla
Neural crest cells
Adrenal cortex
Mesoderm

What is the most common site for ectopic thyroid tissue and why?
The tongue; during development, the thyroid migrates caudally from the level of the developing tongue.

Which syndrome is caused by a failure of the development of the third and fourth pharyngeal pouches?
DiGeorge syndrome

Describe the clinical features of DiGeorge syndrome:
“CATCH 22”
Cardiac abnormalities (eg, tetralogy of Fallot, interrupted aortic arch)
Abnormal facies
Thymic aplasia/hypoplasia and T-cell deficiency
Cleft palate
Hypocalcemia → tetany Chromosome 22q11

ANATOMY

Name the five types of endocrine cells found in the pars distalis of the anterior pituitary:

1. Somatotrophs (~50%)
2. Mammatrophs
3. Thyrotrophs
4. Corticotrophs
5. Gonadotrophs

Where is antidiuretic hormone (ADH) primarily produced?
Supraoptic nucleus of hypothalamus

Where is oxytocin primarily produced?
Paraventricular nucleus of hypothalamus

What part of the pituitary stores and releases ADH and oxytocin?
Neurohypophysis (posterior pituitary)

Where is the hypophyseal portal system located?
Adenohypophysis (in the pars tuberalis)

What is the 1° arterial supply to the gonads?
Testicular/ovarian arteries (directly from abdominal aorta branches)

What is the 1° venous drainage of the gonads?
Left testicular/ovarian vein → left renal vein; right testicular/ovarian vein → inferior vena cava (IVC)

Which lymph nodes filter lymph from the gonads?
Deep lumbar/para-aortic nodes

Which lymph nodes filter lymph from the scrotum?
Superficial inguinal nodes

What are the two pathways for venous drainage from the prostate gland?
1. Prostatic venous plexus → internal iliac veins → IVC
2. Prostatic venous plexus → vertebral venous plexus → cranial dural sinuses

Describe the type of innervation for each phase of the male sexual response cycle:
Erection
Parasympathetic nerves (Point)
Emission
Sympathetic nerves (Shoot)

Ejaculation
Visceral autonomic and somatic nerves

Name the structure(s) contained in the following uterine ligaments:
- Transverse cervical (cardinal) ligament
  Uterine vessels
- Suspensory ligament of ovaries
  Ovarian vessels, lymphatics, autonomic nerves
- Broad ligament
  Round ligaments of the uterus, ovarian ligament, ureters, uterine tubes, and uterine vessels

What is the anatomic relationship of the ureter and the uterine artery?
Ureter lies posterior and inferior to uterine artery. “Water (ureter) under the bridge (uterine artery)”

What is the normal position of the uterus?
Anteverted (uterus to cervix) and anteflexed (cervix to vagina)

What is the landmark for a pudendal nerve block?
Ischial spine

Name the part of the fallopian tube described below:
- Opens into the peritoneal cavity
  Infundibulum
- Site of fertilization
  Ampulla
- Opens into the uterine cavity
  Intramural
- Majority of the length of the tube
  Isthmus

Describe the venous drainage of the adrenal glands.
Right adrenal vein → IVC; left adrenal vein → left renal vein

What type of nerves synapse in the adrenal medulla?
Preganglionic sympathetic (through splanchnic nerves)

In the adrenal medulla, onto what cells do the preganglionic sympathetic nerves synapse?
Chromaffin cells → secrete catecholamines
Second Messengers

Name the second messenger mechanism used by each of the following hormones:

Hypothalamic hormones— gonadotropin-releasing hormone (GnRH), thyrotropin-releasing hormone (TRH), growth hormone-releasing hormone (GHRH), oxytocin, ADH (V₁ receptor)
Inositol triphosphate (IP₃)

Hypothalamic hormones— corticotropin-releasing hormone and ADH (V₂ receptor)
cAMP

Anterior pituitary hormones— luteinizing hormone (LH), follicle-stimulating hormone (FSH), adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH)
Cyclic adenosine monophosphate (cAMP)

Growth hormone (GH)
Tyrosine kinase activation

Insulin
Tyrosine kinase activation

Melanocyte-stimulating hormone (MSH)
cAMP

Angiotensin II
IP₃

Calcitonin
cAMP

Glucagon
cAMP

Parathyroid hormone (PTH)
cAMP

Insulin-like growth factor (IGF)-I
Tyrosine kinase activation

Atrial natriuretic peptide (ANP)
Cyclic guanosine monophosphate (cGMP)

Nitric oxide
Steroid Hormones

How do steroid hormones circulate in the body?
They are bound to specific globulin carrier proteins (which ↑ solubility and delivery to target organs).

How are the cellular effects of steroids mediated?
Steroids pass through the cell membrane, bind cytoplasmic receptors, and translocate to the nucleus where they influence gene expression.

Adrenal Glands

Name the three layers of the adrenal cortex and their major secretory products:
GFR (from outside to inside), ”the deeper you go, the sweeter it gets: salt, sugar, sex”
1. Zona Glomerulosa— mineralocorticoids
2. Zona Fasciculata—glucocorticoids
3. Zona Reticularis—androgens

How does the secretion of glucocorticoids vary throughout the day?
Highest before waking and lowest at midnight

By what mechanism does ACTH increase steroid hormone synthesis?
Stimulates cholesterol desmolase

What is the effect of glucocorticoids on ACTH and cortisol secretion?
Potent glucocorticoids inhibit ACTH and cortisol secretion (a negative feedback mechanism).

What test is used to evaluate the response of the hypothalamic-pituitary axis to glucocorticoids?
Dexamethasone suppression test

Name four general actions of cortisol:
1. Stimulates gluconeogenesis (↑ protein catabolism and lipolysis)
2. Anti-inflammatory effects (block arachidonic acid pathway)
3. Acute exposure enhances immune response; chronic exposure suppresses immune response (inhibits interleukin [ILJ-2 production)
4. Maintains vascular responsiveness to catecholamines

Name three specific actions of aldosterone:
1. ↑ Renal Na^+ reabsorption
Sex Hormones

What is the function of LH in male reproduction?
LH acts on Leydig cells → stimulates cholesterol desmolase → testosterone

What is the function of FSH in male reproduction?
FSH acts on Sertoli cells → spermatogenesis and secretion of inhibin (inhibits FSH)

How does testosterone regulate LH secretion?
Acts to ↓ release of GnRH from hypothalamus and to ↓ release of LH from adeno-hypophysis

Which enzyme is required to convert testosterone to its active form, DHT?
5-α-Reductase

Which enzyme catalyzes conversion of testosterone to estrogen?
Aromatase

Name three androgens (in order of decreasing potency) and where they are produced:
1. DHT (prostate, peripheral tissues)
2. Testosterone (testes, adrenals)
3. Androstenedione (adrenals)

Name five important functions of testosterone:
1. Sexual differentiation during development
2. 2° Sexual development, growth spurt, and fusion of epiphyseal plates
3. ↑ Libido
4. Anabolic effects
5. Spermatogenesis maintenance

What is the average age of menarche?
Between 11 and 14 years (in the United States)

How does GnRH release change during puberty?
Pulsatile release of GnRH begins and it upregulates its own receptors in the adeno-hypophysis.

What is the function of LH in female reproduction?
LH acts on theca cells → stimulates cholesterol desmolase → testosterone

What is the function of FSH in female reproduction?
FSH acts on granulosa cells → stimulates aromatase → estrogen

What happens to LH:FSH ratio during puberty?
LH >> FSH
Where is estrogen made?
Blood (via aromatase), ovaries (estradiol), placenta (estriol), and testes

What is the relative potency of the major estrogens?
Estradiol > estrone > estriol

Which estrogen is an indicator of fetal well-being?
Estriol (↑ 1000 × in pregnancy)

Where is progesterone produced?
Corpus luteum, adrenal cortex, placenta, and testes

Decide whether each of the following are characteristics of estrogen, progesterone, or both:

- Development of genitalia
  - Estrogen
- Growth of follicle
  - Estrogen
- Proliferation of endometrium
  - Estrogen
- Maintains endometrium
  - Progesterone
- Maintains pregnancy
  - Both
- Produces thick cervical mucus
  - Progesterone
- Hepatic synthesis of transport proteins
  - Estrogen
- ↓ Myometrial excitability
  - Progesterone
- Development of breasts
  - Both
- ↑ Body temperature
  - Progesterone
- Spiral artery development
  - Progesterone
- LH surge
  - Estrogen
- Typical female fat distribution
  - Estrogen
- Uterine smooth muscle relaxation (prevents contractions)
  - Progesterone
- Decrease → endometrial sloughing
What are the two main phases of the menstrual cycle and when do they occur?
1. Follicular phase (days 1-14)
2. Luteal phase (days 14-28)

Classify the following as characteristics of the follicular or luteal phase:
- **Graafian follicle matures**
  - Follicular phase
- **Corpus luteum develops causing the release of estrogen and progesterone**
  - Luteal phase (early)
- **Basal body temperature increases**
  - Luteal phase
- **Oocyte progresses from meiosis I to meiosis II**
  - Follicular phase
- **Endometrial glands grow → spiral arteries**
  - Luteal phase
- **FSH and LH levels suppressed**
  - Follicular phase
- **Endometrial proliferation**
  - Follicular phase
- **Progesterone peaks**
  - Luteal phase
- **Menses**
  - Follicular phase (early)

When does ovulation occur?
14 days before menses (regardless of cycle length)

What changes in cervical mucus occur during ovulation?
- Cervical mucus is thinnest and most penetrable during ovulation.

What endocrine change induces ovulation?
- Estradiol burst at end of follicular phase causes a positive feedback effect, resulting in a surge of LH.

Which hormone prevents lactation during pregnancy?
- High estrogen and progesterone block the effects of prolactin on the breast.

Where is hCG made and what is its function?
- Syncytiotrophoblast of placenta produces hCG to maintain corpus luteum so it can produce progesterone during the first trimester until placenta can produce progesterone during the second and third trimester.

Name three scenarios in which hCG is elevated:
1. Pregnancy (in urine 10 days after fertilization)
2. Hydatidiform moles
3. Choriocarcinoma

**hCG peaks at what gestational age?**
Gestational week 9

**What happens to estrogen and progesterone just prior to delivery?**
Both increase throughout; near term estrogen:progesterone ratio increases.

**What is the average age of menopause?**
51 (tends to occur earlier in smokers)

**Name four hormonal changes characteristic of menopause:**
1. ↓ Estrogen
2. ↑↑ FSH
3. ↑ LH
4. ↑ GnRH

**Name four clinical findings characteristic of menopause:**
Menopause wreaks "HAVOC" on your body
1. Hot flashes
2. Atrophy of Vagina
3. Osteoporosis
4. Coronary artery disease risk increases

**Anterior Pituitary**

**Name the hormones produced by the anterior pituitary:**
"FLAT PiG" plus melanotropin (MSH)
FSH
LH
ACTH
TSH
Prolactin
GH

**Name four compounds derived from proopiomelanocortin (POMC):**
1. ACTH
2. MSH
3. β-Lipotropin
4. β-Endorphin

**Which hormones share a common α-subunit?**
T.S.H. and TSH = The Sex
Hormones (LH, FSH, hCG) and TSH

**Which glycoprotein subunit determines hormone specificity?**
β-Subunit

**How is GH regulated?**

↑ By GHRH, sleep, stress, exercise, hypoglycemia, and puberty; ↓ by somatomedins, somatostatin, obesity, pregnancy, and hyperglycemia

**Name four direct actions of GH (somatotropin):**
1. ↓ Glucose uptake into cells (diabetogenic)
2. ↑ Lipolysis
3. ↑ Protein synthesis in muscle
4. ↑ Production of somatomedins (IGF)

**Name three effects of IGF on growth:**
1. ↑ Linear growth (pubertal growth spurt)
2. ↑ Lean body mass
3. ↑ Organ size

**Which clinical syndrome results from GH hypersecretion before puberty?**
Increased linear growth (gigantism)

**Which clinical syndrome results from GH hypersecretion after puberty?**
Acromegaly (may include glucose intolerance)

**Name four functions of prolactin:**
1. Stimulates milk production
2. Inhibits ovulation
3. Stimulates breast development (with estrogen)
4. Inhibits spermatogenesis

**How is prolactin regulated?**

↑ By estrogen (pregnancy), breastfeeding, sleep, stress, TRH, dopamine (DA) antagonists; ↓ by DA and DA agonists, somatostatin, and prolactin

**What are the effects of excess prolactin?**
Galactorrhea, ↓ libido, and failure to ovulate

**How does prolactin inhibit ovulation?**
Inhibits GnRH synthesis and release

**Posterior Pituitary**

**Which hormones are released from the posterior pituitary and what are their function?**
Oxytocin—milk ejection and uterine contraction; vasopressin (ADH)—↑ H₂O reabsorption in kidneys
How is the release of oxytocin regulated?
↑ By suckling, dilation of the cervix, and orgasm

How is the release of ADH regulated?
↑ By high serum osmolarity, volume contraction, pain, nausea, nicotine, opiates; ↓ by low serum osmolarity, ethyl alcohol, ANP, and α-agonists

Thyroid

Which cells are responsible for thyroid hormone synthesis?
Follicular cells

Thyroid hormones are synthesized from which two molecules?
1. Iodide (I⁻)
2. Tyrosine

Which enzyme catalyzes the oxidation of I⁻ to I₂?
Thyroid peroxidase

What is the relative proportion of T₄:T₃ released into the bloodstream?
T₄ = 90%, T₃ = 10%

Which thyroid hormone has the greatest biological activity?
T₃ >> T₄ (T₄ converted into T₃ by liver and kidneys)

Which protein produced by and used entirely within the thyroid is used to produce and store T₄ and T₃?
Thyroglobulin

Which carrier protein is necessary for delivery of thyroid hormone to the tissues?
Thyroxine-binding globulin (TBG)

How is thyroid hormone production regulated?
↑ By TRH and TSH; T₃ down-regulates TRH receptors in AP →↓ TSH

List four key functions of thyroid hormone:
Remember the 4 B’s of T₃
1. Brain maturation
2. Bone and cartilage growth (synergistic with GH)
3. β-Agonist effects (↑ cardiac output [CO], heart rate [HR], stroke volume [SV])
4. ↑ BMR (by ↑ Na⁺/K⁺ ATPase →↑ O₂ consumption)

Calcium Regulation

What is meant by a "negative Ca²⁺ balance?"
Intestinal Ca$^{2+}$ absorption is less than Ca$^{2+}$ excretion.

Which is the most important hormone in the regulation of Ca$^{2+}$ levels and where is it made?

PTH is synthesized and secreted by the chief cells of the parathyroid gland.

What is the major stimulus for PTH secretion?

↓ Serum Ca$^{2+}$ (also mildly ↓ Mg$^{2+}$)

Which hormone is stimulated in response to ↑ PTH levels and ↓ serum Ca$^{2+}$?

Vitamin D (1,25-(OH)$_2$-cholecalciferol is active form.)

Which enzyme in the kidney catalyzes the activation of vitamin D?

1α-Hydroxylase

What factors increase 1α-hydroxylase activity?

↓ Serum Ca$^{2+}$, ↑ PTH, ↓ serum phosphate

What clinical syndrome results from vitamin D deficiency?

Kids → rickets; adults → osteomalacia

Which hormone is released in response to ↑ serum Ca$^{2+}$ and where is it made?

Calcitonin is synthesized and secreted by the parafollicular ”C” cells of the thyroid gland.

What is the effect of calcitonin on bones?

Blocks PTH-mediated resorption of bones

List the effects of PTH on each of the following organs:

Kidneys

↓ Phosphate reabsorption (by ↑ urinary cAMP), ↑ Ca$^{2+}$ reabsorption in distal convoluted tubule of kidneys

Intestines

↑ Ca$^{2+}$ absorption (by stimulating 1α-hydroxylase to activate vitamin D)

Bone

↑ Resorption (brings Ca$^{2+}$ and phosphate into extracellular fluid [ECF])

List the effects of vitamin D on each of the following organs:

Kidneys

↑ Ca$^{2+}$ and phosphate reabsorption

Intestines

↑ Ca$^{2+}$ and phosphate absorption

Bone

↑ Resorption
Pancreas

Name the three major cell types in the pancreatic islets of Langerhans, their location, and function:

1. **Alpha** (outer rim) → glucagons
2. **Beta** (central rim of islet) → insulin
3. **Delta** (intermixed) → somatostatin (SS) and gastrin

List three major actions of glucagon on the liver and adipose tissue:

1. ↑ Glycogenolysis and gluconeogenesis
2. ↑ Lipolysis and ketoacid production
3. ↑ Urea production

List five major functions of insulin:

1. ↓ Blood glucose
2. ↑ Fat deposition (-lipolysis)
3. ↓ Blood amino acids
4. ↓ Blood K⁺
5. ↑ Protein synthesis

**What is the 2° structure of insulin?**
An α-chain and a (β-chain, joined by two disulfide bridges

**What is C-peptide and why is it important?**
A connecting peptide removed from proinsulin, packaged and secreted with insulin; serves as a useful monitor of (β-cell function and exogenous insulin administration

**What are some factors that ↑ insulin secretion?**
↑ Blood glucose (major), ↑ A As, ↑ FAs, GH, cortisol, glucagon, ACh

**How does glucose trigger insulin release?**
Binds to GLUT-2 receptor on (3-cells → closes K⁺ channels → cell depolarization → opens Ca²⁺ channels → insulin secretion

**Which drugs mimic the action of glucose on (β-islet cells?**
Sulfonylurea drugs

**What is the effect of starvation and obesity on insulin receptor expression?**
↑ In starvation; ↓ in obesity

PATHOLOGY
Male Reproductive System

Name the male genitourinary disease characterized by each of the following statements:

- Intractable, painful erection; associated with venous thrombosis, trazodone, and sickle cell disease
- Priapism
- Inflammation of the glans associated with poor hygiene
- Balanitis
- Bent penis due to acquired fibrous tissue formation
- Peyronie disease
- Twisting of the testicular vasculature; may be spontaneous or the result of trauma
- Torsion
- Collection of serous fluid in the tunica vaginalis
- Hydrocele
- Palpable, "bag of worms" dilation of multiple veins of the pampiniform venous plexus of the spermatic cord
- Varicocele
- Acute purulent urethritis caused by gram-negative diplococci
- Gonorrhea
- Fever, chills, and dysuria; tender, boggy prostate; > 10 WBCs per high-power field on examination of prostatic secretions
- Acute bacterial prostatitis

What are the possible sequelae of cryptorchidism?
- 5 to 10 × ↑ risk of germ cell tumors (GCTs), atrophy, sterility, and inguinal hernias

What is the treatment for cryptorchidism?
- Orchiopexy. Note: ↓ risk of sterility, but no ↓ risk of malignancy

What are the most common etiologies of orchitis?
- Mumps virus (1 week postparotiditis)

Name the most likely organism(s) responsible for epididymitis in the following groups:

- Pediatric patients
  - Gram-negative rods
- Sexually active, 35-year-old (y/o)
  - Neisseria gonorrhoeae, Chlamydia trachomatis
- Older men
  - Escherichia coli, Pseudomonas spp.
Name the penile neoplasm associated with each of the following:

- Human papillomavirus (HPV) types 6 and 11
  - Condyloma acuminata
- Single, grayish plaque on shaft/scrotum; associated with ↑ risk of visceral malignancy
  - Bowen disease
- Premalignant, multiple wart-like, reddish lesions with HPV type 16 viral sequence
  - Bowenoid papulosis
- HPV types 16, 18, 31, and 33
  - Squamous cell carcinoma of the penis
- Single erythematous plaque representing carcinoma in situ of the penis, often on glans
  - Erythroplasia of Queyrat

What category of testicular tumors accounts for ~95% of all cases and has a peak incidence of 15- to 34-y/o?

- GCTs

Name the testicular tumor associated with each of the following:

- Malignant, painless enlargement of testis; most common GCT, radiosensitive
  - Seminoma
- Malignant, chemosensitive GCT
  - Nonseminoma GCT
- Malignant, painful GCT that has peak incidence in childhood; ↑ α-fetoprotein (AFP)
  - Yolk sac tumor (endodermal sinus tumor)
- Malignant GCT made of 2+ embryonic layers and multiple tissue types; more common in kids
  - Teratoma
- Malignant, aggressive GCT with > 1 neoplastic pattern
  - Mixed GCT
- Benign, androgen-producing stromal tumor with intracytoplasmic Reinke crystals
  - Leydig cell tumor (interstitial)
- Malignant, hemorrhagic tumor arising from trophoblastic cells; ↑ β-hCG
  - Choriocarcinoma
- Most common testicular cancer in older men
  - Testicular lymphoma

Benign prostatic nodular hyperplasia or prostatic carcinoma?

- Commonly affects peripheral zone
Prostatic carcinoma
Caused by age-related increase in DHT, testosterone, and estrogen
Nodular hyperplasia
Associated with bladder distention and urinary tract infections (UTIs)
Nodular hyperplasia
Enlarged, firm, nodular prostate on digital rectal examination (DRE)
Prostatic carcinoma
Commonly presents with nocturia and hesitancy
Nodular hyperplasia
Primarily affects central zone Primarily affects corpora amylacea
Nodular hyperplasia
↑ Total prostate-specific antigen (PSA), with ↓ fraction of free PSA
Prostatic carcinoma
↑ Total PSA, with proportionate ↑ in fraction of free PSA
Nodular hyperplasia
Hypermethylation of which gene is commonly associated with prostatic carcinoma?
GSTP1
What do the following findings suggest in a patient with prostatic carcinoma?
↑ Prostatic acid phosphatase
Capsule of the prostate has been penetrated.
↑ Alkaline phosphatase
Osteoblastic lesions from bony metastasis

Female Reproductive Pathology

Name the gynecologic infectious disorder characterized by each of the following features:
Clue cells in pap smear; ⊕ “whiff test”
Bacterial vaginosis (eg, Gardnerella vaginitis)
Thick, white discharge with vulvovaginal pruritis; most common form of vaginitis
Candidiasis
Fever, vomiting, diarrhea with desquamating rash; caused by exotoxins from Staphylococcus aureus associated with tampon use
Toxic shock syndrome
Soft, painful ulcerative lesion caused by Haemophilus ducreyi
Chancroid
Firm, painless chancre caused by a spirochete Treponema pallidum
1° syphilis
Small papule/ulcer associated with lymphadenopathy and caused by *C. trachomatis* serotypes LI, L2, or L3
Lymphogranuloma venereum
**Donovan bodies on biopsy**
Granuloma inguinale
Most common STD; frequent cause of pelvic inflammatory disease (PID) (though often asymptomatic); associated with Reiter syndrome
Chlamydial cervicitis (types D-K)
Sexually transmitted infection often associated with extragenital manifestations (eg, proctitis, arthritis, and neonatal conjunctivitis)
Gonorrhea
STD resulting in benign venereal warts caused by HPV types 6 and 11
Condyloma acuminatum
Painful vesicles/ulcers; cytologic evidence of multinuclear giant cells with viral inclusions
Herpes genitalis (most often HSV type 2)
STD caused by flagellated protozoan; #2 cause of vaginitis
Trichomoniasis
Commonly caused by *C. trachomatis* or *N. gonorrhoeae*; findings may include cervical motion tenderness, salpingitis, endometritis, or tubo-ovarian abscess
PID—at ↑ risk for ectopic pregnancy and infertility

**Name the female reproductive disorder associated with each of the following features:**
- Triad of 2° amenorrhea, obesity, and hirsutism, ↑ testosterone, ↑ LH, ↓ FSH
- Polycystic ovary (Stein-Leventhal) syndrome
- Menstrual disorder associated with excessive bleeding during or between menstrual periods
  - Dysfunctional uterine bleeding
  - Cyclic pain and bleeding from proliferation of ectopic endometrial tissue
  - Endometriosis
  - Islands of endometrium found in the myometrium that may cause the uterus to grow to two to four times its normal size
  - Adenomyosis
  - **Chocolate cysts**
  - Endometriosis (in ovaries)

**Name the tumor of the vulva or vagina associated with each of the following statements:**
- Eczematous lesion; biopsy shows large cells in epidermis with marginal clearing
- Paget disease of vulva. **Note**: not always associated with underlying adenocarcinoma
Rare, malignant tumor of vagina associated with maternal use of diethylstilbestrol (DBS) during pregnancy
Clear cell adenocarcinoma
Associated with HPV types 16, 18, 31, 33, and 45; #1 malignancy of vulva; ↑ in older women
Squamous cell carcinoma of vulva
“Bunch of grapes” protruding from vagina; usually in girls 5-y/o, desmin positive
Sarcoma botryoides
Accounts for 95% of neoplasms of vagina; usually from extension of cervical cancer
Squamous cell carcinoma of vagina

Name the uterine tumor associated with each of the following statements:
Neoplastic changes in the endometrium occurring at squamocolumnar junction; associated with HPV infection
Cervical intraepithelial neoplasia (CIN)
Invasive carcinoma evolving from CIN
Squamous cell carcinoma of the cervix
Very common, benign, estrogen-sensitive smooth muscle tumor of the uterus; usually 20- to 40-y/o
Leiomyoma (fibroid)
Most common gynecologic malignancy; associated with prolonged estrogen exposure; usually 55- to 65-y/o
Endometrial carcinoma
Highly aggressive, bulky tumor with areas of necrosis; arises de novo; ↑ incidence in blacks
Leiomyosarcoma

What HPV types are commonly associated with a high risk of squamous cell carcinoma?
Types 16, 18, 31, 33

What are the HPV viral proteins associated with squamous cell carcinoma?
E6 and E7

What role do HPV viral proteins play in the development of invasive cervical carcinoma?
Proteins E6 and E7 bind to and inactivate gene products of p53 and Kb, respectively.

What are the distinguishing histopathologic features of carcinoma in situ (CIN 3)?
Atypical changes extending through entire thickness of the epithelium

Name four factors associated with increased risk for invasive cervical carcinoma:
1. Early sexual activity
2. Multiple sex partners
3. ↓ Socioeconomic status
4. Cigarette smoking

**What is the most effective screening tool for cervical cancer?**
Routine pap smears

**Name five factors that predispose to endometrial carcinoma:**
1. Nulliparity
2. Obesity
3. Diabetes
4. Unopposed estrogen exposure (eg, estrogen-producing tumors, hormone replacement therapy [HRT])
5. Tamoxifen

**How does endometrial carcinoma typically present?**
Postmenopausal vaginal bleeding

**Name the ovarian cyst associated with each of the following statements:**
- **Distention of unruptured graafian follicle; may be associated with ↑ estrogen endometrial hyperplasia**
  - Follicular cyst
- **Hemorrhage into persistent corpus luteum; menstrual irregularity**
  - Corpus luteum cyst
- **Due to gonadotropin stimulation; often bilateral/multiple; associated with choriocarcinoma and moles**
  - Theca-lutein cyst

**Name the ovarian tumor associated with each of the following statements:**
- **Malignant tumor of epithelial origin; two-thirds are bilateral; psammoma bodies**
  - Serous cystadenocarcinoma
- **Benign adenoma; frequently bilaterally; lined with fallopian tubelike epithelium**
  - Serous cystadenoma
- **Malignant GCT that is homologous to seminoma and may occur in childhood**
  - Dysgerminoma
- **Malignant tumor of epithelial origin; can rupture and cause pseudomyxoma peritonei**
  - Mucinous cystadenocarcinoma
- **Benign multilocular cyst lined by mucus-secreting epithelium**
  - Mucinous cystadenoma
- **Benign GCT with elements from multiple embryonic layers; most common GCT**
  - Mature teratoma (dermoid cyst)
- **Benign tumor; cells resembling bladder transitional epithelium**
  - Brenner tumor
- **GCT with Schiller-Duval bodies; ↑ AFP**
Yolk sac (endodermal sinus) tumor
GCT associated with struma ovarii (mature thyroid tissue)
Teratoma (monodermal)
Malignant, aggressive tumor arising from syncitiotrophoblastic cells; ↑ serum β-hCG
Choriocarcinoma
Stromal tumor associated with Meigs syndrome (ascites, hydrothorax)
Thecoma-fibroma
Benign, estrogen-secreting tumor; Call-Exner bodies
Granulosa-theca tumor
Stromal tumor secreting androgens and causing virilization
Sertoli-Leydig cell tumor
Metastatic tumor from gastric adenocarcinoma; signet ring cells
Krukenberg tumor

Most ovarian carcinomas are associated with an increase in what serologic marker?
CA-125

What two genes are associated with a predisposition to ovarian cancer?
1. BRCA1
2. HNPCC

What is the most common type of ovarian neoplasm in women older than 20 years?
Epithelial cell neoplasms (~75% of all ovarian cancers)

What is the most common type of ovarian neoplasm in women younger than 20 years?
Germ cell neoplasms

Breast Disorders

Name the breast disease associated with each of the following statements:
Benign, firm, painless, rubbery mass; most common tumor 25-y/o
Fibroadenoma
Inflammatory lesion caused by S. aureus; often occurs during nursing
Acute mastitis
”Blue-domed” cysts; usually bilateral; breast tenderness during menstruation
Fibrocytic change
Benign tumor of lactiferous ducts; most common cause of serous or bloody discharge in females 35-y/o
Intraductal papilloma
Large, malignant form of fibroadenoma
Cystosarcoma phyllodes
Invasive, malignant tumor; cells arranged in linear fashion; bloody discharge; often bilateral
Invasive lobular carcinoma
Malignant, firm mass with cells in glands; most common carcinoma of breast
Invasive ductal carcinoma
Eczematous lesion of nipple or areola containing large cells with marginal clearings
Paget disease of the breast
Name six risk factors for breast cancer:
   1. Age > 45-y/o
   2. Early menarche and late menopause (↑ span of reproductive period)
   3. Family history of (1° relative with history of [h/o]) premenopausal breast cancer
   4. Personal h/o breast cancer
   5. Inherited mutation (eg, HER-2/neu oncogene)
   6. Obesity and high animal fat diet
Note: risk is not increased by fibroadenoma or nonhyperplastic cysts.
Which disease is almost always associated with Paget disease of the breast?
   Ductal carcinoma in situ
In which quadrant of the breast are most cancers located?
   ~50% found in upper, outer quadrant
What is the significance of estrogen/progesterone receptors on breast cancer?
   Presence of estrogen and progesterone receptors reflects good prognosis (because tumor will likely respond to hormonal therapy).
What is the single most important prognostic factor in breast cancer?
   Lymph node involvement (metastatic spread)
What two tumor suppressor genes are associated with a genetic predisposition for breast cancer?
   1. BRCA1
   2. BRCA2
What is the general function of the BRCA1 and BRCA2 genes?
   DNA repair
Trastuzumab (Herceptin) treatment of breast cancers is directed at the protein product of which overexpressed gene?
   HER2/neu
Pregnancy
Name the disorder of pregnancy associated with each of the following statements:
An ovum without DNA → “honeycombed uterus” and “cluster of grapes” appearance; formed from intrauterine proliferation of trophoblasts and cystic swelling of chorionic villi; ↑ serum β-hCG
Hydatidiform mole

Tear in placental membranes → sudden peripartal respiratory distress → shock → death
Amniotic fluid embolism

Placental attachment directly to myometrium → impaired separation and massive bleeding at delivery
Placenta accreta

Placental attachment to the lower uterine segment, extending to or obstructing the inner cervical os; painless bleeding in any trimester
Placenta previa

Premature detachment of a normally situated placenta; painful bleeding often in third trimester
Abruptio placentae

Hydatidiform mole with 46, XX genotype and markedly elevated β-hCG; no embryo; paternal chromosomes
Complete mole

Hydatidiform mole with triploid genotype and ↑ β-hCG; fetal parts may be present; (2 sperm + 1 egg)
Incomplete mole

Malignant, aggressive tumor that may arise from mole, ectopic, or normal pregnancy
Gestational choriocarcinoma

Toxemia of pregnancy with triad of HTN, edema, and proteinurea
Preeclampsia

Association with preeclampsia; can lead to death by cerebral hemorrhage or ARDS
Hemolysis, Elevated LFTs,
Low Platelets (HELLP syndrome)

Preeclampsia plus convulsions; DIC may be present
Eclampsia

What are some causes of polyhydramnios (> 1.5-2 L of amniotic fluid)?
Maternal diabetes, esophageal/duodenal atresia, anencephaly, Down syndrome

What are some causes of oligohydramnios (0.5 L of amniotic fluid) and what sequence can result?
Genitourinary obstruction (esp. posterior urethral valves in boys), bilateral renal agenesis; can result in Potter syndrome/sequence
Name the six clinically important and dangerous infections of pregnancy:
“ToRCHeS”
1. Toxoplasma
2. Rubella
3. CMV
4. and 5. HSV and HIV
5. Syphilis

Pituitary Disorders

Name the pituitary disorder associated with each of the following statements:

Most common pituitary adenoma
Prolactinoma (prolactin-secreting adenoma)
Deficiency of GnRH → lack of 2° sexual characteristics; associated with anosmia
Kallmann syndrome
Polyuria, polydipsia, hypernatremia from ↓ ADH; associated with a pituitary or hypothalamic injury
Central/neurogenic diabetes insipidus
Panhypopituitarism 2° to brain tumor, ischemia, or trauma
Simmonds disease. Note: > 75% of cells must be destroyed before clinically evident.
Hypopituitarism caused by postpartum pituitary necrosis
Sheehan syndrome
Somatotrophic adenoma causing excess GH and IGF-1
Acromegaly (adults)/gigantism (kids)

Pituitary hypersecretion of ADH → hyponatremia, ↓ urine output, mental status changes
Syndrome of inappropriate antidiuretic hormone (SIADH)

What are the most important hormones to replace in Sheehan syndrome or pituitary apoplexy?
Cortisol and thyroid hormones

Name the endocrine/renal disorder associated with the following statements:

↓ sNa, ↑ Uosm with Uosm > Sosm
Syndrome of inappropriate ADH (SIADH)
High-normal sNa, ↑ Sosm, ↓ Uosm but no change in Uosm with H₂O deprivation test
Diabetes insipidus (DI)
Low-normal sNa, ↓ Uosm but ↑ Uosm toward normal w/H₂O deprivation test
Primary polydipsia
What are the two common presentations of a pituitary tumor?
1. Mass effect (bitemporal hemianopia, cranial nerve [CN] palsies)
2. Endocrine effects (amenorrhea, galactorrhea, hyperthyroidism, ↓ libido)

Thyroid

What are the symptoms and physical findings of hypothyroidism?
Cold intolerance, ↓ HR, hypertension, hypercholesterolemia, pericardial effusion, periorbital myxedema, hypoactive deep tendon reflexes, coarse, dry skin; hair loss, weight gain, constipation, amenorrhea, ↓ pitch of voice, depression

What are symptoms and physical findings of hyperthyroidism?
Heat intolerance, hypertension, ↑ CO, ↑ HR, palpitations, cardiomegaly (long-term), staring gaze, lid lag, ↑ sympathetic activity, fine tremor, warm, moist, and flushed skin; fine hair; Graves disease → pretibial myxedema, weight loss despite hyperphagia, ↑ motility, menstrual abnormalities, osteoporosis, anxiety

Name four laboratory findings common in hyperthyroidism:
1. ↓ TSH (in 1°)
2. ↑ free T4
3. ↑ total T4
4. ↑ T3 uptake

Name four laboratory findings common in hypothyroidism:
1. ↑ TSH (very sensitive for 1°)
2. ↓ free T4
3. ↓ total T4
4. ↓ T3 uptake

Name the thyroid disorder associated with each of the following statements:
Child with coarse facial features, short stature, mental retardation, and umbilical hernia
Congenital hypothyroidism (cretinism)
Goiter occurring with high frequency in iodine-deficient areas
Endemic goiter
Painless enlargement of thyroid of autoimmune etiology; Hürthle cells and germinal centers; hypothyroid
Hashimoto thyroiditis
Triad of diffuse thyroid hyperplasia, ophthalmopathy, dermopathy; hyperthyroid
Graves disease
Normal thyroid replaced by fibrous tissue; hypothyroid
Riedel thyroiditis
Postviral, painful inflammation of thyroid; associated with HLA-B35
Subacute (granulomatous, de Quervain) thyroiditis
Painless goiter that may occur in the postpartum period; lymphocytic infiltrates without germinal centers
Subacute lymphocytic (painless) thyroiditis
Thyroid-stimulating immunoglobulin (TSI) and TSH-receptor antibody (AB)
Graves disease
Thyroid peroxidase antibody
Hashimoto disease
Extreme thyroid enlargement (> 2 kg) causing mass effects; most patients euthyroid
Multinodular goiter
Most common thyroid carcinoma
Papillary carcinoma
Calcitonin-secreting tumor with amyloid deposits
Medullary carcinoma
Biopsy shows “Orphan Annie” nuclei, “fingerlike” projections, and psammoma bodies
Papillary carcinoma
Carcinoma presenting as a single nodule with uniform follicles
Follicular carcinoma
Aggressive carcinoma of older patients with pleomorphic cells; dismal prognosis
Anaplastic (undifferentiated) carcinoma
Carcinoma associated with Hashimoto thyroiditis
Lymphoma

What type of nodules is more likely to be benign: hot or cold?
Hot

Which gene is associated with medullary carcinoma of the thyroid?
\(RET\)

What is the function of the two genes associated with papillary carcinoma of the thyroid?
Tyrosine kinase receptors
1. \(RET\)
2. \(NTRK1\)

Name the multiple endocrine neoplasia (MEN) syndrome characterized by the following features:
Pheochromocytoma, thyroid medullary carcinoma, and parathyroid adenomas
MEN 2 (Sipple syndrome)
MEN 1 (Wermer syndrome)
Mutation of RET oncogene on chromosome I0q
MEN 2
Tumors in MEN 2 plus tall, thin habitus, prominent lips, and ganglioneuromas of
the tongue and eyelids
MEN 3 (MEN 2b)
Mutation of MEN 1 gene on chromosome 11 q
MEN1
Autosomal-dominant (AD) inheritance
All MEN syndromes

Parathyroid Disorders

Name the parathyroid disorder associated with each of the following statements:
Caused by chronic renal failure or ↓ vitamin D
2° hyperparathyroidism
Most commonly due to parathyroid adenomas
1° hyperparathyroidism
Etiologies include congenital gland absence, surgically induced, and autoimmune
destruction
Hypoparathyroidism
Due to autonomous hormone-secreting adenoma, often occurs after correction of
chronic renal failure
3° hyperparathyroidism
Autosomal-recessive (AR) end-organ resistance to PTH → short stature and
short third/fourth metacarpals
Pseudohypoparathyroidism

What four systems are primarily targeted by hyperparathyroidism?
1. Painful bones: osteitis fibrosa cystica, osteoporosis
2. Renal stones: nephrolithiasis, nephrocalcinosis
3. Abdominal groans: constipation, peptic ulcer disease (PUD), pancreatitis
4. Psychic moans: depression, lethargy, seizures

Up to 20% of parathyroid adenomas are commonly associated with altered activity of
which gene?
PRAD1
Adrenal Disorders

**Name the four etiologies for hypercorticism (Gushing syndrome):**
1. Exogenous glucocorticoids (most common overall)
2. Pituitary ACTH hypersecretion (eg, adenoma)
3. Hypersecretion of cortisol (eg, adrenal hyperplasia)
4. Paraneoplastic (ectopic) ACTH secretion from a tumor

**What is the most common cause of endogenous hypercortisolism?**
Cushing syndrome (pituitary adenoma)

**What finding specific to an ACTH-producing pituitary adenoma differentiates it from adrenal cortisol-producing and ectopic ACTH-producing tumors?**
↓Cortisol level after high-dose dexamethasone suppression test

**In most cases of congenital adrenal hyperplasia, deficiency in which enzyme is associated with defective conversion of progesterone to 11-deoxycorticosterone?**
21-Hydroxylase

**Name nine clinical findings of Gushing syndrome:**
1. Hyperglycemia (insulin resistance)
2. Virilization and menstrual irregularities in women
3. Moon facies
4. Truncal obesity
5. Buffalo hump
6. Skin changes (thinning, striae)
7. Osteoporosis
8. Immune suppression
9. Proximal muscle weakness

**Name the adrenal disorder associated with each of the following statements:**
- Aldosterone-secreting adenoma causing HTN and hypokalemic, metabolic alkalosis
  - Conn syndrome
  - (1° hyperaldosteronism)
- Endotoxin-mediated massive adrenal hemorrhage
  - Waterhouse-Friderichsen syndrome (*N. meningitidis*)
- Deficiency of aldosterone and cortisol due to adrenal atrophy or destruction
  - 1° chronic adrenocortical insufficiency (Addison disease)
- Hypothalamic pituitary axis (HPA) disturbance causing failure of ACTH secretion
  - 2° adrenocortical insufficiency
Bilateral hyperplasia of zona glomerulosa caused by stimulation of renin-angiotensin-aldosterone (RAA) system

2° hyperaldosteronism

Results from rapid steroid withdrawal or sudden ↑ in glucocorticoid requirements

1° acute adrenocortical insufficiency (adrenal crisis)

Chromaffin cell tumor usually in adults; results in episodic hyperadrenergic symptoms

Pheochromocytoma

Malignant, “small blue cell” tumor of medulla in kids associated with N-myc oncogene amplification

Neuroblastoma

How are 1° and 2° adrenocortical insufficiencies differentiated?

Hyperpigmentation is absent in 2° adrenocortical insufficiency (POMC is not increased).

Measurement of what substance can differentiate between 1° and 2° hyperaldosteronism?

Renin (↑ in 2° hyperaldosteronism)

What is the drug of choice for hyperaldosteronism?

Spironolactone (aldosterone antagonist)

What is the “rule of 10’s” for pheochromocytomas?

10% malignant
10% bilateral
10% extra-adrenal
10% pediatric
10% familial
10% calcified

Besides MEN, name three familial syndromes associated with pheochromocytomas:

1. Sturge-Weber syndrome
2. von Recklinghausen syndrome
3. von Hippel-Lindau syndrome

What substances are secreted from pheochromocytomas and how are they detected?

Epinephrine and norepinephrine; detected by ↑ urinary secretion of catecholamines and their metabolites (metanephrine, VMA, and so forth)

Adrenogenital Syndromes
Name the enzyme deficiency responsible for each of the following androgenital syndromes:

- ↓ Sex hormones, ↓ cortisol, ↑ mineralocorticoids; HTN, hypokalemia, phenotypic female without maturation
  17α-Hydroxylase deficiency
- ↓ Cortisol, aldosterone, and corticosterone; ↑ sex hormones; virilization, HTN
  llβ-Hydroxylase deficiency
- ↓ Cortisol, aldosterone, and corticosterone; ↑ sex hormones; virilization, hypertension, hyperkalemia, “salt wasting”
  21-Hydroxylase deficiency

What is the phenotypic result of androgen insensitivity syndrome (testicular feminization)?

“Hairless woman”; XY with undescended testes but female/ambiguous genitalia

List the three syndromes associated with 21-hydroxylase deficiency:

1. Salt-wasting adrenogenitalism
2. Simple virilization adrenogenitalism (ambiguity and adrenal hyperplasia)
3. Asymptomatic

Diabetes

Describe the acute presentation of type 1 diabetes mellitus (DM).

Polydipsia, polyuria, polyphagia, weight loss, and diabetic ketoacidosis (DKA) if extreme

What causes hyperglycemia in type 1 DM?

Lack of insulin from decreased β-cell mass

What is the proposed mechanism of islet cell destruction in type 1 DM?

Environmental triggering of autoimmunity to islet β-cells

What is the theorized cause of type 2 DM?

Obesity increases insulin resistance and causes derangement of β-cell insulin secretion.

What are three ways to diagnose DM?

1. Fasting serum glucose > 126 (100-126 = impaired fasting glucose)
2. Oral glucose tolerance test > 200 (148-200 = impaired glucose tolerance)
3. Symptoms + random glucose > 200

What is HbA1c and what is it used for?

Percent of glycosylated hemoglobin in blood; correlates with glycemic control over the last 90 to 120 days

Type 1 or type 2 DM?
Relatively common in the US population
Type 2
Younger average age of onset
Type 1
Strong, polygenic predisposition
Type 2
Associated with obesity
Type 2
Insulin treatment required from the time of diagnosis
Type 1
Associated with HLA-DR3 and -DR4
Type 1
May present with hyperosmolar coma
Type 2
May present initially as DKA
Type 1
Amyloid deposition in the islets
Type 2

What two cleavage products of proinsulin are stored in the granules of β-islet cells?
1. Insulin
2. C-peptide

Which membrane protein mediates glucose uptake by β-islet cells?
GLUT-2

Increased cytoplasmic concentration of which ion stimulates the secretion of insulin?
Calcium

By what mechanism is the cytoplasmic concentration of calcium increased in β-cells following uptake of glucose?
Decreased activation of adenosine triphosphate (ATP)-sensitive potassium channels leads to membrane depolarization, resulting in an influx of extracellular calcium via a voltage-dependent calcium channel.

Glucose uptake in which organ is independent of insulin?
The brain

What signal transduction pathway mediates the mitogenic effects of insulin binding?
MAP-kinase pathway

Activation of the PI-3K signal transduction pathway by insulin results in the translocation of what molecule to the surface of myocytes in order to transport glucose into myocytes?
GLUT-4
List four potential effects of advanced glycation end products (AGEs) in type 1 diabetes:

1. Cross-linking of collagen
2. Accumulation of extracellular matrix proteins resistant to proteolytic degradation
3. Generation of reactive oxygen species
4. NF-κB activation

What is the most common cause of death in diabetics?
Myocardial infarction (MI) due to accelerated atherosclerosis

What is the most common morphologic change in the microvasculature of a diabetic?
Diffuse thickening of the basement membrane

Describe the long-term effect(s) of DM on each of the following organ systems:

Cardiovascular (large vessels)
Atherosclerosis → cerebrovascular accident (CVA), MI, peripheral vascular disease (PVD)

Renal/urinary
Glomerular: glomerulosclerosis, proteinuria
Vascular: arteriosclerosis → HTN, chronic renal failure
Infectious: UTIs, pyelonephritis, necrotizing papillitis

Nervous
Motor and sensory peripheral neuropathy, autonomic degeneration

Eye
Retinopathy, cataract formation

Skin
Xanthomas, cutaneous infections, poor wound healing, fungal infections

Name four causes of 2° DM:
1. Pancreatic disease (eg, hemochromatosis, pancreatitis, pancreatic carcinoma)
2. Pregnancy (gestational diabetes)
3. Gushing syndrome
4. Other endocrine disorders (eg, acromegaly, glucagonoma, hyperthyroidism)

Pancreatic Endocrine Tumors

Name the islet cell tumor associated with each of the following statements:

Most common islet cell tumor
Insulinoma (β-cell tumor)

2° DM, necrolytic migratory erythema
Glucagonoma (α-cell tumor)

Associated with Zollinger-Ellison syndrome
Gastrinoma
Associated with watery diarrhea, hypokalemia, and achlorhydria (WDHA) syndrome
VIPoma
2° DM, cholelithiasis, steatorrhea
Somatostatinoma (δ-cell tumor)
Clinically characterized by Whipple triad
Insulinoma (β-cell tumor)

Name the clinical findings of Whipple triad:
Hypoglycemia, concurrent central nervous system (CNS) dysfunction, and reversal of symptoms with glucose

What is Zollinger-Ellison syndrome?
Hypersecretion of gastric HC1, recurrent PUD, and hypergastinemia

PHARMACOLOGY

Pituitary

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and uniquetoxicity (TOX) (if any)

Octreotide
MOA: somatostatin analog
IND: acromegaly, secretory diarrhea from VIPoma, carcinoid symptoms, high-output fistulas

Leuprolide
MOA: GnRH analog. Note: given pulsatile = agonist; given continuous = antagonist
IND: continuous → prostate cancer, endometriosis, uterine fibroids. Pulsatile → infertility
TOX: antiandrogenic effects, nausea, vomiting

Oxytocin
MOA: ↑ uterine contraction
IND: induce/reinforce labor; control uterine hemorrhage
TOX: uterine rupture, hypertensive crisis

Desmopressin
Thyroid and Parathyroid

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and uniquetoxicity (TOX) (if any)

Levothyroxine (T₄)
MOA: synthetic T₄ → converted to T₃
IND: hypothyroidism (maintenance replacement)
TOX: nervousness, palpitations, ↑ HR, heat intolerance

Propylthiouracil/methimazole
MOA: blocks thyroid peroxidase, propylthiouracil also ↓ peripheral conversion of T₄ → T₃
IND: hyperthyroidism (propylthiouracil okay in pregnancy)
TOX: rash, agranulocytosis (rare), +ANCA vasculitis, hepatotoxicity, lupuslike syndrome

Risedronate
MOA: bisphophonate (inhibits osteoclastic function)
IND: osteoporosis, Paget disease, metastatic bone cancer, hyperparathyroidism
TOX: GI upset, esophagits

Calcitonin
MOA: ↓ bone resorption, ↓ serum Ca²⁺ and phosphate
IND: acute hypercalcemia, Paget disease, osteoporosis

Which other drug is used to treat the symptoms of hyperthyroidism?
Propanolol (β-blocker)

Diabetes

Sulfonylureas (eg, tolbutamide, glyburide, chlorpropamide)
MOA: pancreas, closes K⁺ channels in (β-cell membrane → depolarization → ↑ Ca²⁺ influx → insulin release
IND: type 2 diabetes (not used in type 1 because it requires some residual (β-cell activity)
TOX: hypoglycemia, weight gain

Metformin (Glucophage)
MOA: liver, ↓ gluconeogenesis; ↑ glycolysis; ↓ postprandial glucose
IND: newly diagnosed diabetic (no islet cell function required)
TOX: potentially life-threatening lactic acidosis, ↓ vitamin B₁₂ absorption, contraindicated in renal insufficiency

Glitazones (eg, rosiglitazone, pioglitazone)
MOA: ↑ target cell response to insulin
IND: type 2 diabetes (monotherapy or combination)
TOX: hepatotoxicity (troglitazone), upper respiratory infection (URI), weight gain, edema, congestive heart failure, and anemia (rosiglitazone)

α-Glucosidase inhibitor (eg, acarbose)
MOA: inhibits α-glucosidase at brush border → ↑ glucose absorption
IND: type 2 diabetes
TOX: GI upset (flatulence, diarrhea)

Insulin
MOA: tyrosine kinase activity → ↑ glycogen and protein synthesis, triglyceride (TG) storage, and K⁺ uptake
IND: type 1 and refractory type 2 diabetes; life-threatening hyperkalemia
TOX: hypoglycemia and rare hypersensitivity reaction

For each of the following types of insulin, state the peak and duration of action:
Insulin lispro
Peak = 30 to 60 minutes; duration = 3 to 4 hours
NPH insulin
Peak = 8 to 12 hours; duration = 18 to 24 hours
Lente insulin
Peak = 8 to 12 hours; duration = 18 to 24 hours
Ulentalente insulin
Peak = 8 to 16 hours; duration = 18 to 28 hours
Insulin glargine
Peak = none (peakless); duration 20 to 24+ hours

Adrenal Gland

Describe the mechanism of action of corticosteroids:
Corticosteroids bind to cytoplasmic receptors, pass into the nucleus complexed with their receptors, and act as transcription factors for specific target genes.

**How do glucocorticoids affect arachidonic acid metabolism?**
Glucocorticoids inhibit phospholipase A2, blocking the release of arachidonic acid and ↓ production of prostaglandins and leukotrienes.

**Select the most appropriate corticosteroid for each of the following clinical situations:**
- **Diagnosis of Gushing syndrome**
  - Dexamethasone
- **Autoimmune disorder**
  - Prednisone
- **Addison disease**
  - Hydrocortisone (+/- fludrocortisone)
- **Relief of inflammation**
  - Prednisone, cortisone
- **Asthma/allergies**
  - Beclomethasone or triamcinolone aerosol
- **Used to ↑ fetal lung maturity**
  - Betamethasone
- **Cancer chemotherapy**
  - Prednisone

**List the effect of glucocorticoids on each of the following systems:**
- **Metabolic**
  - ↑ Gluconeogenesis; net ↑ in fat deposition in prototypical areas
- **Muscle**
  - ↑ Muscle protein catabolism; myopathy → weakness
- **Bone**
  - ↑ Bone catabolism
- **Immune**
  - Inhibits cell-mediated immunity; ↑ PMNs; ↓ lymphocytes, basophils, eosinophils, and monocytes; ↓ leukocyte migration
- **Psych**
  - Behavioral changes, psychoses
- **GI**
  - ↓ Resistance to ulcers
- **Vascular**
  - ↓ Capillary permeability →↓ edema at sites of inflammation

**What is the consequence of abrupt discontinuation of corticosteroid use?**
- Acute adrenal insufficiency syndrome (potentially lethal)

**Name eight commonly observed effects of long-term corticosteroid use:**
1. Osteoporosis
2. HTN
3. Insulin resistance
4. Edema
5. Psychoses
6. Peptic ulcers
7. ↑ Susceptibility to infections
8. Cataracts

What classic toxicity is associated with excess corticosteroid use? 
latrogenic Gushing syndrome

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and uniquetoxicity (TOX) (if any)

**Spironolactone**
MOA: spironolactone binds estrogen receptors
IND: hirsutism (eg, in PCOS), prostate/breast cancer
TOX: gynecomastia, thrombocytopenia, hepatotoxicity

**Clomiphene**
MOA: blocks negative feedback → ↑ GnRH →↑ LH and FSH → ovulation
IND: infertility
TOX: ovarian enlargement, multiple births, hot flashes

**Tamoxifen**
MOA: competes for estrogen receptors → blocks binding to ER \(\oplus\) cells
IND: breast cancer
TOX: ↑ risk of endometrial carcinoma, hot flashes

**Finasteride**
MOA: 5α-reductase inhibitor →↓ DHT
IND: benign prostatic hyperplasia (BPH), hair loss
TOX: impotence, gynecomastia

**Flutamide**
MOA: competitive androgen receptor blocker
IND: prostatic carcinoma

**Mifepristone (RU486)**
MOA: competitive progesterone receptor blocker
IND: abortion
TOX: GI upset, metrorrhagia

**Dinoprostone**
MOA: PGE\(_2\) analog causes cervical dilation and uterine contraction
IND: induction of labor; abortion
Ritodrine, terbutaline
MOA: β₂-agonists relax the uterus
IND: preterm labor
TOX: maternal and fetal tachycardia, fluid retention, and hyperglycemia
Sildenafil, vardenafil
MOA: inhibits phosphodiesterase type 5 →↑ cGMP → smooth muscle relaxation of corpus cavernosum
IND: erectile dysfunction
TOX: hypotension if also taking a nitrate, priapism, headache, color vision changes

Name five benefits of oral contraceptives (OCPs):
1. ↓ Risk of ovarian and endometrial cancer
2. ↓ Genitourinary infections
3. Regulates menstrual cycle
4. Low failure rate (if taken appropriately)
5. ↓ Risk of ectopic pregnancy

Name five disadvantages of OCPs:
1. Requires daily pill ingestion
2. Not protective against STDs
3. ↑ Triglycerides
4. ↑ Risk of hepatic adenoma
5. Induces hypercoagulable state

Name four contraindications to OCPs:
1. Pregnancy
2. H/o thromboembolism or stroke
3. H/o breast cancer or endometrial cancer
4. Smoking (in women > 35-y/o)
CHAPTER 9
Renal and Genitourinary

EMBRYOLOGY

Name the structure(s) derived from each of the following:

Nephrogenic cord (three structures)
1. Pronephros
2. Mesonephros
3. Metanephros

Ureteric bud
C CUP ("see you pee"): Collecting tubules, Calyces, Ureter, Pelvis

Genital Ridge
Gonads

Reproductive structures from the mesonephric (Wolffian) duct
"SEED" (in males only): Seminal vesicles, Epididymis, Ejaculatory duct, Ductus deferens

Reproductive structures from the paramesonephric (Miillerian) duct
In women only: Fallopian tubes, uterus, superior portion of vagina

Metanephros
Definitive adult kidney

Name the embryologic tissue layer that following components of the genitourinary system develop from:

Kidneys (ie, nephrons)
Mesoderm (intermediate mesoderm)

Collecting tubules, calyces, pelvis, ureters
Mesoderm (intermediate mesoderm)

Bladder, urethra
Endoderm (cloaca)

Name the parts of the external genitalia in males and females derived from the following embryologic structures:

Genital tubercle
Males: glans penis; females: glans clitoris

Urogenital sinus
Males: corpus spongiosum, bulbourethral (Cowper) glands, prostate gland; females: vestibular bulbs, Bartholin and Skene glands

**Urogenital folds**
Males: ventral shaft of penis; females: labia minora

**Labioscrotal swelling**
Males: scrotum; females: labia majora

**Describe the following congenital disorders:**

**Exstrophy of the bladder**
Congenital defect in the anterior wall of the bladder and adjacent abdominal wall causing the bladder to be exposed at birth; associated with epispadias

**Horseshoe kidney**
Fusion of the lower (or upper) poles of kidneys → kidney fails to ascend → often mal-rotated and remains in pelvis

**Hypospadias**
Penile abnormality resulting in urethra opening on the ventral (inferior) side of penis; most common congenital penile abnormality

**Epispadias**
Penile abnormality resulting in urethral opening on the dorsal (superior) side of penis; associated with bladder exstrophy

**Renal agenesis**
Results from failure of the ureteric bud to form; associated with Potter syndrome

**Potter syndrome**
Renal agenesis → oligohydramnios → limb deformities and pulmonary hypoplasia

**What structure limits the ascent of a fused horseshoe kidney?**
Inferior mesenteric artery

**What substance secreted by the testes**

*Suppresses development of paramesonephric ducts in males?*
Müllerian-inhibiting substance

*Promotes development of the mesonephric ducts?*
Fetal androgens

**Describe the gonads and external genitalia of the following:**

**Female (XX) infant with congenital adrenal hyperplasia (CAH)**
Female gonads with masculinized genitalia

**Male (XY) infant with androgen-insensitivity syndrome**
Male gonads with female external genitalia, but no uterus or fallopian tubes
ANATOMY

Name the structures contained in the retroperitoneal space:
Ureters, kidneys, adrenals, pancreas, duodenum (2nd, 3rd, and 4th parts), ascending/descending colon, rectum, aorta, IVC

What is the approximate vertebral level of the kidneys?
T12 to L3 (The right kidney is slightly lower because of liver.)

Name the renal blood vessel that runs posterior to the superior mesenteric artery (SMA) and anterior to the aorta:
Left renal vein

What vessel does the left gonadal vein drain into?
Left renal vein

What important structures do the ureters pass under on their way to the bladder?
Females: uterine artery; males: ductus deferens; water (ureters) under the bridge (uterine artery, ductus deferens)

Which terminal vessels carry blood toward the glomerulus?
Afferent arterioles

What specialized cells are found between the afferent and efferent glomerular arterioles and have receptors for angiotensin II (AT II) and atrial natriuretic peptide (ANP)?
Lacis cells (extraglomerular mesangial cells)

What makes up the juxtaglomerular apparatus (JGA)?
JG cells, lacis cells, and the macula densa

What hormone do the JG cells secrete?
Renin

What anatomic feature makes stress incontinence more common in women?
External urethral sphincter does not completely surround female urethra.

Name the sensory and motor components of the micturition reflex:
Pelvic splanchnic nerves (parasympathetic S2-S4)

PHYSIOLOGY

What percentage of body weight is total body water (TBW)?
~60%

What proportion of TBW is accounted for by intracellular fluid (ICF) and extracellular fluid (ECF)?
Two-thirds ICF, one-third ECF (60 = 40 + 20. Rule: 40% body weight is ICF, 20% is ECF.)

Name the major cations and anions found in ICF:
Cations = K\(^+\), Mg\(^{2+}\); anions = proteins, organophosphates (eg, ADP, ATP)

Name the major cations and anions found in ECF:
Cations = Na\(^+\); anions = CF, HCO\(^-3\)

What are the relative proportions of plasma and interstitial fluid in ECF?
One-fourth plasma volume, three-fourths interstitial volume

What is considered normal ECF osmolality?
~290 mOsm

Clearance of what chemical can be used to measure glomerular filtration rate (GFR)?
Inulin (Inulin is freely filtered, but neither secreted nor reabsorbed.)

What is a useful clinical measure to estimate GFR?
Creatinine clearance

What is considered normal GFR?
~120 mL/min

Effective renal plasma flow (ERPF) can be measured by calculating the clearance of what substance?
Para-aminohippuric acid (PAH). PAH is filtered and secreted.

Complete the following calculations:
\[ U_xV/P_x \text{ (urine concentration X urine volume/plasma concentration)} = \]
Renal clearance (C\(_x\))
\[ \text{ERPF}/(1 - \text{hematocrit}) = \]
Renal blood flow (RBF)
\[ \text{GFR/RPF (renal plasma flow)} = \]
Filtration fraction (FF)
\[ \text{GFR} \times (\text{plasma}_x) = \]
Filtered load
\[ V_{urine \ flow} - (U_{osm} \ V/P_{osm}) = \]
Free water clearance

Define GFR using the Starling formula.
\[ K_f[(P_{GC} - P_{BS}) - (\pi_{GC} - \pi_{BS})], \text{ where } K_f = \text{filtration coefficient, GC = glomerular capillary, BS = Bowman space} \]

List the three components of the glomerular filtration barrier:
1. Fused basement membrane (negative charge barrier)
2. Fenestrated capillary endothelium (size barrier)
3. Epithelial or podocyte foot process layer

If C\(_x\) > GFR then there is net ...
tubular secretion of substance X

If $C_x$ tubular absorption of substance X

If $C_v = \text{GFR}$ then there is ...

no net tubular absorption or secretion of substance X

What proportion of total cardiac output does RBF account for?

~25%

How is RBF maintained at a constant level?

Autoregulation (via myogenic response to stretch and the activity of the JGA)

How do the following substances affect the renal arterioles, RPF, GFR, and FF?

Prostaglandins

Prostaglandins dilate afferent arterioles: ↑ RPF, ↑ GFR, thus FF stays constant

AT II

AT II constricts efferent arterioles: ↓ RPF, ↑ GFR, thus FF increases

What effect do the following have on RPF, GFR, and FF?

Afferent arteriole constriction

Decreased RPF and GFR, no change in FF

Efferent arteriole constriction

Decreased RPF, increased GFR, increased FF

Increased plasma protein concentration

No change in RPF, decreased GFR and FF

Decreased plasma protein concentration

No change in RPF, increased GFR and FF

What is the maximum plasma glucose concentration at which glucose will no longer be reabsorbed?

~200 to 250 mg/dL (Concentrations of > 250 mg/dL glucose will be lost in the urine.)

What is the transport maximum ($T_m$) for glucose?

At 350 mg/min, carriers are saturated ($T_m = \text{renal threshold/GFR}$).

What factors cause $K^+$ to shift out of cells?

- ↓ Insulin, (β-blockers, acidosis, digitalis, extreme exercise, cell lysis, hyperosmolarity

What factors cause $K^+$ to shift into cells?

- Insulin, (β-agonists, alkalosis

List four causes of decreased distal $K^+$ secretion:

1. Low-$K^+$ diet
2. Hypoaldosteronism
3. Acidosis
4. $K^+$-sparing diuretics
List six causes of increased distal K\(^+\) secretion:
1. High-K\(^+\) diet
2. Hyperaldosteronism
3. Alkalosis
4. Thiazide diuretics
5. Loop diuretics
6. Luminal anions

Describe a clinical scenario which might lead to each of the following physiologic changes:

**Isosmotic volume contraction**
Diarrhea

**Isosmotic volume expansion**
Isotonic fluid infusion (eg, normal saline IV)

**Hyperosmotic volume contraction (two scenarios)**
1. Profuse sweating
2. Diabetes insipidus

**Hyperosmotic volume expansion**
High NaCl intake, infusion of hypertonic saline

**Hypo-osmotic volume contraction**
Adrenal insufficiency (hypoaldosteronism)

**Hypo-osmotic volume expansion**
Syndrome of inappropriate antidiuretic hormone (SIADH)

**FUNCTIONAL REGIONS OF THE NEPHRON**

Name the part of the nephron where each of the following processes occur:

**Site of reabsorption of all glucose and amino acids, and the majority of bicarbonate, sodium, and water**
Proximal convoluted tubule (PCT)

**Site of active reabsorption K\(^+\), Na\(^+\), Cl\(^-\)**
Thick ascending loop of Henle

**Site of 50% of urea reabsorption**
PCT (passively)

**Site of active reabsorption of Na\(^+\), Cl\(^-\)**
Early distal convoluted tubule (DCT)

**Site of action of thiazide diuretics**
DCT
Site of action of K⁺-sparing diuretics
Collecting tubules

Sections that are impermeable to water
Thick ascending loop of Henle, collecting ducts (in absence of ADH)

Site where ammonia is excreted to act as a buffer for secreted H⁺ ions
PCT

Portion of the nephron which is impermeable to Na⁺ and passively reabsorbs water
Thin descending loop of Henle

Aldosterone-sensitive site where Na⁺ is exchanged for K⁺ or H⁺
Collecting tubules

Site of active Ca²⁺ reabsorption that is controlled by PTH
Early DCT

Site of action of loop diuretics
Thick ascending loop of Henle

Section where reabsorption of water is regulated by vasopressin (ADH)
Collecting tubules

Site of action of carbonic anhydrase inhibitors
PCT

Section which contains principal cells and intercalated cells
Collecting tubules

Site of 85% of all phosphate reabsorption (via cotransport)
PCT

ENDOCRINE FUNCTIONS OF THE KIDNEYS

List the four main endocrine functions of the kidneys:
1. PTH-mediated conversion of 25-OH vitamin D to 1, 25-OH vitamin D by 1α-hydroxylase
2. Secretion of renin by JG cells in response to arterial pressure changes and in response to Na⁺ and Cl⁻ delivery to the macula densa
3. Secretion of prostaglandins (to increase GFR by dilating afferent arteriole)
4. Secretion of erythropoietin in response to hypoxia by peritubular endothelial cells

Name the effect of each of the following on the kidneys:
ANP
↓ Na⁺ reabsorption, ↑ GFR
Aldosterone
↑ Na⁺ reabsorption, ↑ K⁺ secretion, ↑ H⁺ secretion in collecting tubule

Vasopressin (ADH)
↑ Na⁺/K⁺/2Cl⁻ transporters in thick ascending limb, ↑ water permeability in principal cells (via aquaporins), ↑ urea absorption in collecting duct

Where is angiotensin-converting enzyme (ACE) primarily found?
Lung capillaries

Briefly describe the renin-angiotensin-aldosterone cascade:
↓ BP (↓ stretch of cells in afferent arterioles) → secretion of renin → conversion of angiotensinogen to angiotensin I (AT I) → AT I converted to AT II by ACE

What is the function of AT II?
Increases intravascular volume and ↑ vascular tone → ↑ BP

Name six specific actions of AT II:
1. Causes potent vasoconstriction
2. Releases vasopressin and adrenocorticotropic hormone (ACTH) from the pituitary
3. Promotes release of aldosterone from adrenal cortex
4. Stimulates hypothalamus to increase thirst
5. Stimulates catecholamine release from the adrenal medulla
6. Increases Na⁺ and HCO₃⁻ reabsorption in proximal tubule

What cells in the kidneys produce and secrete erythropoietin?
Peritubular capillary cells

What stimulates erythropoietin production and release?
Hypoxia

PATHOLOGY

Polycystic Kidney Disease

Name the disease characterized by multiple 3 to 4 cm renal cysts, bilateral enlargement of the kidneys, and chronic renal failure in adults:
Autosomal dominant (adult) polycystic kidney disease (ADPKD)

What are the signs and symptoms of ADPKD?
Flank pain, hypertension, hematuria, and UTI

Which gene is most commonly associated with ADPKD?
PKD1 (85% of cases)
Name three extra renal manifestations of ADPKD:
1. Liver cysts (40%)
2. Berry aneurysms (10%-30%)
3. Mitral valve prolapse (25%)

What is the prognosis of patients with autosomal recessive polycystic kidney disease (ARPKD)?
   Poor; majority die in infancy or early childhood

What type of renal lesions are characteristic of ARPKD?
   Multiple cylindrical cysts found perpendicular to cortex in an enlarged kidney

Which of the cystic renal diseases is associated with an increased risk of renal cell carcinoma?
   Dialysis-associated cystic disease

Nephrotic and Nephritic Syndromes

What are the classic features of the following:
   **Nephrotic syndrome**
   Massive proteinuria (>3.5 g/d), hypoalbuminemia, hyperlipidemia, edema
   **Nephritic syndrome**
   Hypertension, azotemia, RBC casts, oliguria, hematuria

Glomerulonephropathies

What term describes the type of immune deposits found outside of the glomerular BM (GBM) but within the podocytes?
   Subepithelial

What term describes the type of immune deposits found outside the endothelium but inside the GBM?
   Subendothelial

Name the immunofluorescence pattern of deposition of immunoglobulins and/or complement associated with the following diseases:
   **Membranous glomerulonephritis (GN)**
   Granular or “starry-sky”
   **Goodpasture syndrome**
   Linear
   **IgA nephropathy (Berger disease)**
   Mesangial
Poststreptococcal
Granular or “starry-sky”

Name the electron microscopic (EM) appearance of the immunoglobulin and/or complement deposits in the following diseases:

Membranous GN
“Spike and dome” subepithelial deposits

Membranoproliferative GN (MPGN)
Subendothelial humps, “tram track”

Poststreptococcal GN
Subepithelial humps

Name the glomerulopathy most closely associated with each of the following statements:

X-linked syndrome of glomerulonephritis, lens dislocation, nerve deafness, and posterior cataracts
Alport syndrome

Nodular glomerulosclerosis, glomerular capillary basement membrane thickening

Diabetic glomerulosclerosis (Kimmelstiel-Wilson disease)

Commonly associated with HIV infection, heroin abuse, sickle cell disease, and obesity
Focal-segmental glomerulonephritis (FSGN)

Diffuse loss of foot processes of the visceral epithelial cells on EM, but normal appearance on light microscopy
Minimal change disease (lipoid nephrosis)

Apple green birefringence on Congo red stain
Amyloidosis

C-ANCA
Wegener granulomatosis

Most common cause of nephrotic syndrome in kids
Minimal change disease (lipoid nephrosis)

Electron dense deposits in the GBM proper and autoantibody to C3 nephritic factor

MPGN type II (aka dense deposit disease)

Crescents seen in glomeruli on light microscopy
Rapidly progressive glomerulonephritis (RPGN)

Most common cause of end-stage renal disease
Diabetic glomerulosclerosis

Basement membrane thickening and splitting (train tracks)

MPGN type I
Syndrome of hematuria and hemoptysis caused by anti-GBM antibodies
Goodpasture syndrome
Mesangial widening, recurrent hematuria, and proteinuria
Ig A nephropathy
Associated with hepatitis C
MPGN
Responds well to steroids
Minimal change disease (aka steroid responsive nephropathy)
X-linked recessive defect in collagen type IV
Alport syndrome
Asymptomatic familial hematuria
Thin membrane disease (GBM is only 50%-60% of normal thickness.)
“Wire loop lesions”
Systemic lupus erythematosus (SLE)— lupus nephropathy (diffuse proliferative pattern)
Henoch-Schönlein purpura
IgA nephropathy
Irregularly thick GBM with splitting of lamina densa seen on EM
Alport syndrome
Upper respiratory vasculitis and granulomas
Wegener granulomatosis

Renal Tubular Acidosis

Name the type of renal tubular acidosis (RTA) associated with the following statements:

- Decreased bicarbonate reabsorption
  Type II (proximal)
- Dysfunction of principal cells
  Type IV
- Decreased acidification and acid excretion
  Type I (distal)
- Hyperkalemia
  Type IV
- Nongap metabolic acidosis
  Types I, II, IV
- Fanconi syndrome
  Type II (proximal)
Aldosterone deficiency/resistance
Type IV
Most common RTA
Type IV

Acid-Base Disturbances

Name the simple acid/base disturbance and the associated compensatory response:

- \( \text{pH} > 7.4, \text{Pco}_2 > 40 \text{ mm Hg} \)
  - Metabolic alkalosis → hypoventilation

- \( \text{pH} 7.4, \text{Pco}_2 > 40 \text{ mm Hg} \)
  - Respiratory acidosis → renal \( \text{HCO}_3^- \) reabsorption

- \( \text{pH} > 7.4, \text{Pco}_2 40 \text{ mm Hg} \)
  - Respiratory alkalosis → renal \( \text{HCO}_3^- \) secretion

- \( \text{pH} 7.4, \text{Pco}_2 40 \text{ mm Hg} \)
  - Metabolic acidosis → hyperventilation

What is the formula for calculating anion gap?

\[ \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-) \]

What is a normal anion gap range?

- 8 to 12 mEq/L

List three common causes of nongap metabolic acidosis:

1. Diarrhea
2. Renal tubular acidosis
3. Hyperchloremia

Name the most common cause of respiratory acidosis:

- Hypoventilation (which can be caused by acute/chronic lung disease, sedatives, weakening of respiratory muscles)

List three common causes of respiratory alkalosis:

1. Hyperventilation
2. Early aspirin ingestion
3. Gram-negative sepsis

List five common causes of metabolic alkalosis:

1. Excessive vomiting
2. Diuretic abuse
3. Antacid use
4. Hyperaldosteronism
5. Gushing syndrome
List nine possible causes of anion gap metabolic acidosis:

“MUD FILERS”

1. Methanol
2. Uremia
3. Diabetic ketoacidosis
4. Paraldehyde
5. Isoniazid (INH) or Iron tablet overdose
6. Lactic acidosis
7. Ethylene glycol or Ethanol
8. Rhabdomyolysis (massive)
9. Salicylate toxicity

Acute Renal Failure

List the three main types of acute renal failure (ARF):

1. Prerenal
2. Intrinsic
3. Postrenal

List four common prerenal causes of ARF:

1. Hypovolemia
2. Decreased RBF (eg, decreased cardiac output, renal artery stenosis)
3. High peripheral vascular resistance
4. Drugs (eg, diuretics, NSAIDs)

List five common causes of intrinsic ARF:

1. Acute tubular necrosis (ischemic, nephrotoxic, sepsis)
2. Acute glomerulonephritis
3. Autoimmune vasculitis (eg, lupus, scleroderma)
4. Interstitial nephritis
5. Hemolytic uremic syndrome (children)

What is the general mechanism for the development of postrenal ARF?

Any outflow obstruction (benign prostatic hyperplasia [BPH], bladder-neck, stones, prior gynecologic surgery, bilateral ureteric). Note: postrenal ARF accounts for 5% of all causes of ARE

Name the type of ARF associated with each of the following:

Oliguria and Fe Na 1%
Prerenal

Oliguria and Fe Na > 1%
Intrinsic
Hyaline urine casts
Prerenal

Muddy brown/granular casts
Intrinsic (muddy brown casts are particularly associated with ATN)

Blood urea nitrogen (BUN): creatinine ratio > 20
Prerenal

Urine osmolality > 500 mOsm
Prerenal

List the effects of uremia on each of the following organs or systems:

Nervous system
Asterixis, confusion, seizures, coma

Cardiovascular system
Fibrinous pericarditis

Hematologic system
Coagulopathy, immunosuppression

Gastrointestinal system
Nausea, vomiting, gastritis

Skin
Pruritis

Endocrine system
Glucose intolerance

List six nonuremic complications of renal failure:
1. Metabolic acidosis
2. Hyperkalemia → arrhythmias
3. Na\(^+\) and H\(_2\)O excess → pulmonary edema and congestive heart failure (CHF)
4. Hypocalcemia → osteodystrophy (from failure to secrete active vitamin D)
5. Anemia (↓ EPO secretion)
6. Hypertension (from renin hypersecretion)

Which type of ATN often causes GBM rupture?
Ischemic

What substances cause direct injury to the proximal tubules?
Nephrotoxins: drugs (aminoglycosides), toxins, and massive amounts of myoglobin (typically in the setting of a crush injury or strenuous exercise)

Renal Infections
What infection commonly presents with flank pain, costovertebral angle tenderness, fever, dysuria, pyuria, bacteriuria?

Acute pyelonephritis

What are the two major causes of pyelonephritis?

1. Ascending infection
2. Hematogenous seeding

What are the most common organisms responsible for acute pyelonephritis?

*Escherichia coli* (most common), *Proteus, Klebsiella, Enterobacter, Pseudomonas.* (Think enteric gram-negative rods.)

What is the greatest risk factor for pyelonephritis?

Vesicoureteric reflux (or incompetence)

List five possible sequelae of acute pyelonephritis:

1. Abscess
2. Necrotizing papillitis
3. Renal scars
4. Perinephric abscess
5. Pyonephrosis

What condition is characterized by broad renal scarring, deformed calyces, progressive loss of renal parenchyma, and thyroidization of kidneys?

Chronic pyelonephritis

What finding on microscopic examination of urine is pathognomonic for pyelonephritis?

WBC casts

Tubulointerstitial Diseases

Name the tubulointerstitial disease associated with each of the following clinical scenarios:

- Abuse of phenacetin-containing compounds
  - Renal papillary necrosis
- Penicillin and NSAID use; associated with eosinophilia
  - Interstitial nephritis
- AR syndrome characterized by dysfunction of proximal tubules, leading to impaired reabsorption of amino acids, glucose, phosphate, and bicarbonate
  - Fanconi syndrome
- AR disease characterized by impaired tryptophan reabsorption; clinically resembles pellagra
  - Hartnup disease
AR syndrome characterized by impaired active chloride reabsorption in the loop of Henle; clinically mimics the actions of loop diuretics

Bartter syndrome

Name the five diseases associated with renal papillary necrosis:
1. Diabetes mellitus
2. Acute pyelonephritis
3. Analgesic nephropathy
4. Sickle cell disease
5. Urinary tract obstruction

Renal Vascular Disease

Name the renal vascular pathology associated with each of the following statements:

- Macroscopically, kidneys have a fine granular surface; hyaline arteriolosclerosis, interstitial fibrosis, glomerular sclerosis
- Benign nephrosclerosis
- Hyperplastic arteriolitis (onion skinning); presents with diastolic BP > 130, encephalopathy, proteinuria, hematuria, and papilledema
- Malignant nephrosclerosis
- Pediatric syndrome characterized by ARF, microangiopathic hemolytic anemia, thrombocytopenia, and hypertension
- Classic hemolytic-uremic syndrome (HUS)
- Syndrome characterized by ARF, microangiopathic hemolytic anemia, hypertension, fever, and mental status changes; associated with ADAMTS-13 defect
- Thrombotic thrombocytopenic purpura (TIP)

What is the most common cause of HUS?
*Escherichia coli*O157:H7 (75% of cases)

What three groups of patients are at increased risk of developing renal failure from benign nephrosclerosis?
1. African Americans
2. Diabetics
3. Patients with hypertension

What type of infarction typically occurs in the kidneys?
"White," due to end-organ type arterial supply of kidneys

What conditions are associated with diffuse cortical necrosis?
Obstetric catastrophes (eg, severe placental abruption) and septic shock

Name two major causes of renal artery stenosis (RAS):
1. Atherosclerosis (70%)
2. Fibromuscular dysplasia (30%)

What group of people are most likely to have secondary hypertension due to fibromuscular dysplasia-induced RAS?
Women in their 20’s and 30’s

**Urolithiasis**

Name the type of renal calculi associated with each of the following statements:

- **Radiopaque (two types)**
  1. Calcium stones
  2. Struvite stones

- **Staghorn calculi**
  Struvite (aka ammonium magnesium phosphate)

- **Infection with urease-positive bacteria**
  Struvite (think *Proteus*)

- **Most common type of calculus**
  Calcium

- **Gout (or any other hyperuricemic condition)**
  Uric acid stones

- **Elevated PTH**
  Calcium

- **Secondary to inherited defect of amino acid transporter**
  Cystine (due to cystinuria)

**What are the signs and symptoms associated with urinary stone disease?**

Renal colic (flank pain radiating to groin), hematuria, and pyelonephritis

**Renal and Urinary Tract Tumors**

**What must be ruled out in an older adult with hematuria?**

Urinary tract malignancies (renal and bladder)

Name the renal or urinary neoplasm associated with each of the following statements:

- **Large, palpable flank mass in a toddler**
  Wilms tumor (aka nephroblastoma) or neuroblastoma

- **Most common tumor of the renal pelvis**
  Transitional cell carcinoma

- **Benign tumor of kidney often associated with tuberous sclerosis**
  Angiomyolipoma
Most common renal malignancy
Renal cell carcinoma

Clear cells
Renal cell carcinoma

Associated with phenacetin abuse, cigarette smoking, cyclophosphamide, and aniline dyes
Transitional cell carcinoma
Large, benign tumor of kidney, composed of eosinophilic cells; arises from the intercalated cells of collecting duct

Oncocytoma
Secondary polycythemia
Renal cell carcinoma

Associated with Schistosoma haematobium
Squamous cell carcinoma of the bladder

Invades renal vein and sometimes IVC
Renal cell carcinoma

Painless hematuria in an older patient who smokes
Transitional cell carcinoma of the bladder

Classically manifests clinically with hematuria, flank pain, and a flank mass
Renal cell carcinoma

Which gene is most commonly altered in clear cell carcinomas?

VHL (von Hippel-Lindau) gene (mutated or hypermethylated)

Which gene is most commonly altered in papillary renal cell carcinomas?

MET

Which hormone is secreted by 5% to 10% of all renal cell carcinomas?

Erythropoeitin

Renal cell carcinomas (RCC) are associated with ectopic production of which other hormones?

ACTH, renin, parathyroid hormone receptor protein (PTHrp), prolactin

Why is RCC often refractory to chemotherapy?

Expression of P-glycoprotein, a marker of multidrug resistance

Name the syndrome characterized by Wilms tumor plus each of the following findings:

Gonadal dysgenesis, nephropathy associated with WT1 gene mutations
Denys-Drash syndrome

WT1 gene mutation, aniridia, GU malformations, and mental/motor retardation

WAGR complex

Organomegaly, hemihypertrophy, macroglossia, gigantism, neonatal hypoglycemia associated with the WT2 gene
Beckwith-Wiedemann syndrome

Name the most common genetic defect associated with each of the following:

**Transitional cell carcinoma**
Chromosome 9p and 9q alterations

**Renal cell carcinoma**
Alterations of chromosome 3 affecting the \textit{VHL} gene

**Wilms tumor**
Deletion of \textit{WT1} gene (tumor suppressor gene on 11p15.5)

**Beckwith-Wiedemann syndrome**
\textit{WT2} gene deletion (11p15.5)

What is the inheritance pattern of Beckwith-Wiedemann syndrome?
Genomic (paternal) imprinting

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**Urinary System**

Name the urinary disease associated with each of the following statements:

**Michaelis-Gutmann bodies**
Malakoplakia

**Fibrous masses over the sacrum and lower aorta that encroach on the ureters causing obstruction and hydrenephrosis**
Sclerosing retroperitonitis

**Disease characterized by chronic bacterial cystitis with yellow and gray plaques in the mucosa of the bladder**
Malakoplakia

How does chronic urinary outlet obstruction affect the bladder wall?
Chronic obstruction causes bladder wall hypertrophy

What are the common symptoms of lower urinary tract infection (cystitis)?
Dysuria, frequency, urgency

What is the most common source of bacteria that causes cystitis?
Colon (\textit{E. coli} = 80%)

Why are women at 10 times the risk of men for developing a urinary tract infection (UTI)?
The female urethra is shorter and more likely to be colonized with fecal flora.

List the most common UTI organisms:
“SEEKS PP”
\textit{Serratia marcescens}
Escherichia coli
Enterobacter cloacae
Which UTI-causing bacterium is frequently nosocomial, drug-resistant, and may produce a red pigment?

*Serratia marcescens*

Isomorphic red cells in the urine suggest bleeding from what portion of the urinary tract?

Lower urinary tract (ie, nonglomerular bleeding)

What type of trauma commonly causes extravasation of urine into the superficial perineal space?

Straddle injury (rupture of urethra below urogenital diaphragm)

Name the four types of urinary incontinence:

1. Stress
2. Urge
3. Overflow
4. Total

Name the type of voiding dysfunction or incontinence associated with the following characteristics:

A small urinary bladder and detrusor overactivity resulting in bladder wall thickening

Hypertonic neurogenic bladder

A large urinary bladder and detrusor areflexia that may result in overflow incontinence

Atonic neurogenic bladder

Small amounts of urine leakage associated with coughing, laughing, or straining

Stress incontinence

Leakage of urine associated with sudden, strong need to urinate

Urge incontinence

**PHARMACOLOGY—RENAL**

For each of the following drugs, provide the following:

1. The mechanism and location of action (MLOA)
2. Indication(s) (IND)
3. Significant side effects and uniqueness (TOX) (if any)
Furosemide, ethacrynic acid

**MLOA:** inhibitor of Na⁺/K⁺/2CF cotransporter in thick ascending loop of Henle

**IND:** diuresis, hypertension, CHF, and other edematous states (ascites, nephrotic syndrome, etc.)

**TOX:** “CHIA DOG”

- Calciuria
- Hypokalemic metabolic alkalosis
- Interstitial nephritis
- Allergy to sulfa
- Dehydration
- Ototoxicity
- Gout

**Spironolactone**

**MLOA:** competitive aldosterone receptor antagonist; acts in collecting duct (CD)

**IND:** diuresis, CHF

**TOX:** hyperkalemic metabolic acidosis, gynecomastia, antiandrogen effects

**Triamterene and amiloride**

**MLOA:** block Na⁺/K⁺ channels in collecting duct

**IND:** used in combination with other diuretics (especially loop and thiazide diuretics) for their K⁺-sparing properties

**TOX:** leg cramps (triame terene)

**Acetazolamide**

**MLOA:** carbonic anhydrase inhibitor (CAI) →↓ HCO₃⁻ reabsorption in PCT →↑ urine osmolarity

**IND:** diuresis, glaucoma

**TOX:** metabolic acidosis, ammonia toxicity, neuropathy. **Note:** sulfa allergy

**Mannitol**

**MLOA:** ↑ tubular fluid osmolarity →↑ urine flow; acts in PCT, thin descending limb, and CD

**IND:** diuresis, elevated intracranial pressure (ICP)

**TOX:** pulmonary edema, dehydration

**Thiazides—chlorothiazide, hydrochlorothiazide**

**MLOA:** inhibitor of NaCl reabsorption in early DCT →↑ urine osmolarity

**LOA:** DCT

**IND:** hypertension, CHF

**TOX:** may cause hyperglycemia, hyperlipidemia, hypercalcemia, and allergic response in patients sensitive to sulfa drugs

**ACE inhibitors—captopril, lisinopril, enalapril**
**MLOA:** inhibitor of ACE →↓ levels of AT II (→↑); prevents inactivation of bradykinin (potent vasodilator)

**IND:** hypertension, renal protective effects in diabetics, CHF

**TOX:** ”CAPTOPRIL”
- Cough
- Angioedema
- Proteinuria
- Taste changes
- Hypotension
- Pregnancy issues (fetal renal toxicity)
- Rash
- Increased renin and K⁺

Lowers AT II

**Contraindicated in bilateral RAS**

**Losartan**

**MLOA:** AT II receptor antagonist

**IND:** hypertension

**TOX:** dizziness, headache; teratogenic

**Demeclocycline**

**MLOA:** ADH antagonist in CD

**IND:** SIADH

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**Name the diuretic of choice in the following situations:**

**Diuresis in sulfa-allergic patient**

Ethacrynic acid

**Hypercalcemia**

Loop diuretics (eg, furosemide)

**Hyperaldosteronism**

Spironolactone

**Nephrogenic DI**

Thiazide diuretics (eg, chlorothiazide)

**Severe edematous states**

Loop diuretics (eg, furosemide)

**Elevated ICP**

Mannitol

**Altitude sickness**

Acetazolamide

**Calcium stones**

Thiazide diuretics (eg, chlorothiazide)
Used in shock to maintain RBF
Mannitol

**Which diuretics decrease blood pH?**
CAIs and K⁺-sparing diuretics

**Which diuretics increase blood pH?**
Loop and thiazide diuretics

**Which diuretics increase urinary Ca²⁺?**
Loop diuretics and spironolactone

**Which diuretics decrease urinary Ca²⁺?**
Thiazide diuretics and amiloride

**Which diuretics increase urinary NaCl?**
All classes
CHAPTER 10
Hematology and Oncology

EMBRYOLOGY

From what embryonic layer are angioblasts derived?
  Mesoderm
Name the site(s) of red blood cell (RBC) production during each of the following developmental phases:
  First trimester
  Yolk sac
  Second trimester
  Liver and spleen
  Third trimester
  Central and peripheral skeleton
  Postpartum
  Axial skeleton

PATHOLOGY

Coagulopathy

What is the most common inherited hypercoagulable state?
  Factor V Leiden
The factor V Leiden mutation inhibits factor V cleavage by which protein?
  Protein C
What is the effect of estrogen, endogenous or exogenous, on thrombosis?
  Estrogen induces a hypercoagulable state.
What clotting factors require vitamin K for their synthesis?
  Factors II, VII, IX, X, and proteins C and S
What common laboratory test is used to assess the intrinsic coagulation system?
Partial thromboplastin time (PTT)

**What common laboratory test is used to assess the extrinsic coagulation pathway?**
Prothrombin time (PT)

**What commonly used anticoagulant interferes with the extrinsic pathway?**
Warfarin. Remember: “WEPT“—Warfarin affects the Extrinsic pathway and is monitored by PT.

The use of the chelator, ethylene diamine tetra acetate (EDTA), as an anticoagulant, in tubes is designed to inactivate what factor in the blood?
Calcium

**What inhibitor of the coagulation cascade inactivates factors Va and VIIIa?**
Protein C

**What are the two major functions of von Willebrand factor?**
1. Transport of factor VIII
2. Linkage of platelets and collagen

**Dysfunction of what clotting component results in mucous membrane hemorrhage, petechiae, purpura, and prolonged bleeding time?**
Platelet abnormalities

**Dysfunction of what clotting component results in hemarthroses, purpura, and prolonged PT and/or PTT?**
Coagulation factor abnormalities

**Name the coagulopathy associated with the following clinical and pathologic features:**

- **Most common hereditary bleeding disorder**
  von Willebrand disease

- **Most common type of hemophilia**
  Hemophilia A (factor VIII deficiency)

- **Most common cause of acquired platelet dysfunction**
  Aspirin use

- **Autosomal dominant (AD) disorder causing increased bleeding time**
  von Willebrand disease

- **Autosomal recessive (AR) defect in platelet adhesion caused by lack of GpIIb/IX**
  Bernard-Soulier disease

- **AR defect in platelet aggregation caused by deficiency of GpIIb/GpIIIa, a membrane receptor responsible for binding fibrinogen**
  Glanzmann thrombasthenia

- **Common presentation includes hemarthroses and easy bruising, ↑ PTT, normal PT**
  Hemophilia (A and B)

- **Prolonged bleeding time with normal platelet count, normal PT, and ↑ PTT**
  von Willebrand disease
Prolonged PT, PTT, ↑ bleeding time, thrombocytopenia, presence of fibrin split products
Disseminated intravascular coagulation (DIC)
Normal PT, PTT, normal platelet count, ↑ bleeding time
Aspirin use
Syndrome characterized by antiplatelet antibodies (commonly anti-Ib-IX or IIb-IIIa), often post-viral infections
Idiopathic thrombocytopenia (ITP)
Syndrome characterized by thrombocytopenia, microangiopathic hemolytic anemia, fever, and neurologic symptoms
Thrombotic thrombocytopenic purpura (TTP)
Widespread hyaline microthrombi in arterioles and capillaries causing schistocytes and helmet cells
Microangiopathic hemolytic anemia
Splenomegaly, epistaxis, petechiae, generalized tender lymphadenopathy, serum antibodies (+)
SLE-autoimmune thrombocytopenia

Anemias

List five of the most common causes of microcytic anemia:
1. Iron deficiency
2. Lead poisoning
3. Chronic disease (sometimes normocytic)
4. Sideroblastic
5. Thalassemia

List four of the most common causes of normocytic anemia:
1. Sickle cell anemia
2. Aplastic anemia
3. Acute blood loss
4. Hemolytic anemia

List five of the most common causes of macrocytic anemia:
1. Liver disease
2. Vitamin B$_{12}$ deficiency
3. Folate deficiency
4. Alcoholism
5. Hypothyroidism

What is the primary site of iron absorption? Vitamin B$_{12}$? Folate?
What is the major cause of iron deficiency anemia in adults?
Menorrhagia or gastrointestinal (GI) bleeding (ie, colon cancer, ulcers)

What are two common clinical complaints in an anemic patient?
1. Dyspnea on exertion
2. Fatigue

Which amino acid substitution in the $\beta$-globin gene is most commonly seen in sickle cell anemia?
Glu6 → Val

What is the major type of hemoglobin in homozygous sickle cell anemia?
HbS

In sickle cell disease, what is the mechanism of ischemic necrosis of the bones, lungs, liver, brain, spleen, or penis?
↓ O$_2$ tension → abnormal RBCs sickle → microvascular occlusions

What is the major regulatory enzyme in heme biosynthesis?
Aminolevulinate (ALA) synthase

What two common enzyme deficiencies can cause hemolytic anemia?
1. Glucose-6-phosphate dehydrogenase (G6PD)
2. Pyruvate kinase

What hemolytic anemia is associated with exposure to oxidant stress?
G6PD deficiency

What two common RBC membrane defects can cause hemolytic anemia?
1. Hereditary spherocytosis
2. Paroxysmal nocturnal hematuria (PNH)

What common cause of atypical pneumonia is associated with cold autoimmune hemolytic anemia?
Mycoplasma pneumoniae

What type of anemia is caused by lack of intrinsic factor (IF) secretion by gastric parietal cells?
Pernicious anemia (vitamin B$_{12}$ deficiency)

What two autoimmune diseases of the GI tract can cause megaloblastic anemia?
1. Pernicious anemia (due to lack of IF production)
2. Crohn disease of the distal ileum (due to lack of IF-B$_{12}$ complex reabsorption)

What parasites are capable of causing megaloblastic anemia?
*Diphylllobothrium latum* (by depleting B$_{12}$) and *Giardia lamblia* (by depleting folate)

How does gastric resection cause megaloblastic anemia?
Parietal cells, which are responsible for IF production may be removed when the gastric fundus is resected.
What type of malignancy is associated with pernicious anemia?
   Gastric carcinoma

Name three medications capable of causing autoimmune hemolytic anemia:
   1. Penicillin
   2. Cephalosporins
   3. Quinidine

What types of malignancies are associated with autoimmune hemolytic anemia?
   Leukemias and lymphomas

What laboratory tests are seen in hemolytic anemia?
   ↑ Unconjugated bilirubin, ↑ urine urobilinogen, ↓ hemoglobin, hemoglobinuria, ↓ haptoglobin, hemosiderosis

Name two commonly used medications that can cause aplastic anemia:
   1. Nonsteroidal anti-inflammatory drugs (NSAIDs)
   2. Chloramphenicol

What happens to the total iron binding capacity (TIBC), serum iron concentration, and percent saturation of transferrin in each of the following diseases?
   Iron deficiency anemia
      ↑ TIBC, ↓ serum iron, ↓ % saturation
   Anemia of chronic disease
      ↓ TIBC, ↓ serum iron, normal saturation
   Iron overload
      Normal TIBC, ↑ serum iron, maximal saturation

Name the type(s) of anemia associated with the following clinical and pathologic features:
   Most common type of anemia
      Iron deficiency anemia
   Abnormal Schilling test
      Pernicious anemia
   ABO incompatibility, lymphoid neoplasm, Raynaud phenomena, anti-i antibodies
      Cold autoimmune hemolytic anemia
   Atrophic glossitis
      Pernicious anemia
   Autosplenectomy
      Sickle cell anemia
   Basophilic stipling of erythrocytes, blue-gray discoloration at gumline, wrist/foot drop
      Anemia from lead poisoning
   Celiac sprue
      Folate deficiency anemia (megaloblastic)
Chronic atrophic gastritis
  Pernicious anemia

**Colon cancer**
  Iron deficiency anemia (early) and anemia of chronic disease (late)

**Crescent-shaped erythrocytes and Howell-Jolly bodies**
  Sickle cell anemia

**Deficiency of α- or β-globin gene synthesis**
  Thalassemia

**Deficiency of decay accelerating factor**
  Paroxysmal nocturnal hemoglobinuria

**Demyelination of the dorsal and lateral tracts of the spinal cord**
  Pernicious anemia

**End-stage liver disease**
  Macrocytic anemia

**Helmet cells, burr cells, triangular cells**
  Microangiopathic anemia (2° to DIC, thrombotic thrombocytopenic purpura-hemolytic-uremic syndrome [TTPHUS], or mechanical heart valves)

**Hypersegmented polymorphonuclears (PMNs)**
  Vitamin B₁₂ or folate deficiency anemia

**Increased serum lactate dehydrogenase (LDH)**
  Hemolytic anemia

**Microcytosis, atrophic glossitis, esophageal webs (Plummer-Vinson syndrome)**
  Iron deficiency anemia

**Pancytopenia and fatty infiltration of bone marrow**
  Aplastic anemia

**Systemic lupus erythematosus (SLE), chronic lymphocytic leukemia (CLL), lymphomas, drugs; + direct Coombs test (due to IgG autoantibodies)**
  Warm autoimmune hemolytic anemia

**AD deficiency of spectrin, positive osmotic fragility test**
  Hereditary spherocytosis

**Reduced erythropoietin**
  Anemia of chronic disease

**Ringed sideroblasts**
  Sideroblastic anemia

**Susceptibility to infection by encapsulated organisms**
  Sickle cell anemia (from splenic autoinfarction)

**Transient normocytic anemia**
  Anemia of acute blood loss

What is the genetic defect in thalassemias?
Splicing defect, causing decreased α or β sub-chain production

Name the type of thalassemia responsible for each of the following findings:

- **β-Thalassemia** associated with growth retardation, frontal bossing, and hepatosplenomegaly (HSM) (from extramedullary hematopoesis), jaundice, and iron overload (2° to transfusions), and ↑ Hgb F
- **β-Thalassemia major** (β−/β−); **Note:** β-thalassemia minor (β+/β−), typically asymptomatic
- **α-Thalassemia** associated with mild microcytic anemia, usually asymptomatic
- **α-Thalassemia minor** (two alleles affected); **Note:** when only one allele involved (carrier state) → no anemia
- **α-Thalassemia** associated with pallor, splenomegaly, chronic hemolytic anemia, and intraerythrocytic inclusions
  - Hgb H disease (three alleles affected)
- **α-Thalassemia** associated with stillborn fetus
  - Hydrops fetalis (all four alleles affected)

**White Blood Cell (WBC) Neoplasms**

What are the two major categories of lymphoma?

1. Hodgkin disease (HD)
2. Non-Hodgkin lymphoma (NHL)

Name the general type of lymphoma (HD or NHL) associated with the following clinical and pathologic features:

- **Interleukin (IL)-5 secreting Reed Sternberg (RS) cells**
  - HD
- **Commonly arises from B cells**
  - NHL
- **Constitutional symptoms including Both fever, night sweats, weight loss**
  - Both
- **Mediastinal lymphadenopathy, contiguous spread**
  - HD
- **Many cases associated with Epstein-Barr virus (EBV)**
  - HD
- **Peripheral lymphadenopathy, noncontiguous spread**
  - NHL
- **Bimodal age distribution, but most common in young men**
  - HD
- **Peak incidence from 20 to 40 years of age**
NHL
Associated with immunosuppression including AIDS
NHL
Painful lymphadenopathy with alcohol consumption
HD

Name the type of HD associated with each of the following clinical and pathologic findings:

Most common type
Nodular sclerosis
Abundance of RS cells
Mixed cellularity
Lacunar cells and collagen banding
Nodular sclerosis
Commonly seen in older patients with HD
Mixed cellularity
Widely disseminated disease with poor prognosis
Lymphocyte depletion
More common in females
Nodular sclerosis
Abundance of lymphocytes
Lymphocyte predominance
Commonly seen in men 35 years presenting with cervical or axillary lymphadenopathy
Lymphocyte predominance
High proportion of RS cells relative to lymphocytes
Lymphocyte depletion

Name the type of NHL associated with each of the following clinical and pathologic findings:

Overexpression of cyclin D1
Mantle cell lymphoma
Starry-sky appearance on histopathology
Burkitt lymphoma
Clinically similar to CLL; characterized by nodules of small lymphocytes
Small cell lymphocytic lymphoma
Older adults with BCL2 gene mutations
Follicular lymphoma
Often appears at extranodal sites and can cause small bowel obstruction
Diffuse large cell lymphoma
Child presenting with enlarging mandibular mass
Burkitt lymphoma
Common in children who present with a mediastinal mass and a syndrome similar to that of acute lymphocytic leukemia (ALL)
Lymphoblastic lymphoma
**TdT+ lymphocytes**
Precursor B- or T-cell acute lymphoblastic leukemia/lymphoma
**Endemic in Africa and associated with EBV**
Burkitt lymphoma

Name the specific leukemia associated with the following age brackets:

- **0 to 14 years old**
  - ALL
- **15 to 39 years old**
  - AML
- **40 to 59 years old**
  - AML and CML
- **> 60 years old**
  - CLL

Name the specific leukemia associated with each of the following findings:

- **Very high white cell counts, often >200,000**
  - Chronic myelogenous leukemia (CML)
- **Isolated lymphocytosis**
  - CLL
- **TdT+ lymphoblasts**
  - ALL
- **Large, immature myeloblasts predominate**
  - Acute myelogenous leukemia (AML)
- **Neoplastic pre-T or pre-B lymphocytes, CD10 ©**
  - ALL
- **CD19/CD20 and CD5 © malignant cells**
  - CLL
- **Bone marrow is replaced with myeloblasts**
  - AML
- **Philadelphia chromosome t(9:22)**
  - CML
- **Auer rods**
  - AML (M3 > M2 > M1)
- **Low leukocytic alkaline phosphatase**
  - CML (also seen in paroxysmal nocturnal hematuria)
Associated with fatigue, thrombocytopenia, signs of anemia, frequent infections, leukemia cutis, and DIC
AML (M3)
Bone pain, fever, generalized lymphadenopathy, HSM, and signs of central nervous system (CNS) spread
ALL
Excellent prognosis if treated early
ALL
May progress to AML
CML
Most responsive to therapy
ALL
Associated with prior exposure to radiation
CML
Peripheral leukocytes containing tartarate-resistant acid phosphatase (TRAP) and cytoplasmic projections
Hairy cell leukemia (Remember: “TRAP the Hairy beast”)

Myeloproliferative Disorders

Name the four chronic myeloproliferative disorders:
1. CML
2. Polycythemia vera
3. Essential thrombocytosis
4. Myelofibrosis with myeloid metaplasia

Name the myeloproliferative disorder associated with each of the following clinical and pathologic findings:

- ↑ RBC mass and low/normal erythropoietin
  Polycythemia vera
- Tear drop deformity of erythrocytes, bone marrow hypercellularity
  Myelofibrosis with myeloid metaplasia
- Plethoric complexion, pruritus after showering, blurred vision, splenomegaly, and epistaxis
  Polycythemia vera
- Erythromelalgia (throbbing or burning of hands and feet)
  Essential thrombocytosis
- Basophilia
  Polycythemia vera
Widespread extramedullary hematopoiesis with megakaryocytic proliferation in the bone marrow
Myelofibrosis with myeloid metaplasia

**Hyperviscosity syndrome**
Polycythemia vera and essential thrombocytosis

**Peripheral thrombocytosis, bone marrow megakaryocytosis, and splenomegaly**
Essential thrombocytosis

**Name the plasma cell disorder associated with the following clinical and pathologic findings:**

- Bone pain, osteopenia, pathologic fractures, and “punched-out” lytic lesions on x-ray
  - Multiple myeloma
- **Russel bodies and “plymphocytes” (plasmacytoid lymphocytes)**
  - Waldenstrom macroglobulinemia
- **Bence-Jones proteinuria**
  - Multiple myeloma and Waldenstrom macroglobulinemia
- **Small M-spike on plasma electrophoresis in an otherwise healthy patient**
  - Monoclonal gammopathy of undetermined significance (MGUS)
- **Hypercalcemia; renal insufficiency**
  - Multiple myeloma
- **Hyperviscosity syndrome**
  - Waldenstrom macroglobulinemia
- **Large M-spike on plasma electrophoresis**
  - Multiple myeloma and Waldenstrom macroglobulinemia
- **Primary amyloidosis**
  - Multiple myeloma

**Peripheral Blood Smear**

**Name the condition associated with each of the following peripheral blood smear findings:**

- Defective PMN degranulation → accumulation of giant granules in PMNs and other leukocytes
  - Chediak-Higashi anomaly
- **Atypical lymphocytes**
  - Infectious mononucleosis
- **Large numbers of Auer rods (Faggot cells)**
  - AML (M3 subtype)
Basophilic stippling
Lead poisoning
Burr cells (echinocytes)
Burns, uremia
Dumbbell-shaped bilobed nuclei
Pelger-Huet anomaly
Giant platelets
Bernard-Soulier disease, May-Hegglin anomaly
Heinz bodies, bite cells
G6PD deficiency
Helmet cells, schistocytes
Microangiopathic hemolytic anemia (DIC, TTP, HUS)
Howell-Jolly bodies
Asplenia
Hypersegmented PMN nuclei
Megaloblastic anemia
Intracytoplasmic rings
Malaria, babesiosis
Lymphocytic cerebriform nuclei
Sézary syndrome
Nucleated erythrocytes
Hemolytic anemia
Rouleau formation
Multiple myeloma and Waldenstrom macroglobulinemia
Small platelets
Wiskott-Aldrich syndrome
Smudge cells
CLL
Spherocytes
Hereditary spherocytosis
Spur cells (acanthocytes)
Abetalipoproteinemia, liver disease
Target cells (codocytes)
Thalassemias, iron deficiency anemia, liver disease, sickle cell anemia
Teardrop cells (dacryocytes)
Myelofibrosis
Toxic granulations in leukocytes (Dohle bodies)
Sepsis
Chromosomal Translocations

Name the neoplasm associated with the following chromosomal translocations and genes/gene products:

- **t(11:14)** protooncogene under Ig promoter
  - Mantle cell lymphoma
- **t(11:22)** EWS (EWS-FLI1 fusion protein)
  - Ewing sarcoma
- **t(14:18)** BCL2
  - Follicular lymphoma
- **t(15:17)** (PML/RAR-β [retinoic acid receptor alpha])
  - AML (M3 subtype, treated with retinoic acid)
- **t(3:6)** VHL
  - von Hippel-Lindau syndrome (t[3:8] and t[3:11] are two common variants seen in VHL)
- **t(8:14)** c-myc and IgH
  - Burkitt lymphoma (t[8:22] and t[2:8] are two common variants seen in Burkitt lymphoma)
- **t(9:22)** bcr-abl fusion protein
  - CML (treated with imatinib)

Tumor Markers

Name the neoplasm associated with the following tumor markers:

- **α₁-AT**
  - Liver cancer, yolk-sac tumors
- **α-Fetoprotein (AFP)**
  - Germ cell tumors, hepatocellular carcinoma
- **Alkaline phosphatase**
  - Metastatic bone involvement, Paget disease
- **β-HCG**
  - Hydatiform moles, Choriocarcinoma, Gestational trophoblastic tumors
- **CA-125**
  - Ovarian cancers
- **Carcinoembryonic antigen (CEA)**
  - Colon, pancreatic, and other cancers of the GI tract
- **Prostate-specific antigen (PSA)**
Cancer Genetics

For each of the following tumor suppressor genes, state the function and the malignancy/malignancies they are associated with:

**APC**
*Function:* regulation of $\beta$-catenin in the Wnt/$\beta$-catenin signaling pathway—promotes cell adhesion and regulates cell proliferation  
*Associated malignancies:* familial adenomatosis polyposis (FAP) and many GI cancers

**BRCA1 and BRCA2**
*Function:* DNA repair and transcriptional regulation  
*Associated malignancies:* breast and ovarian cancers

**NF1 and NF2**
*Function:* regulates signal transduction through the ras pathway  
*Associated malignancies:* neurofibromas, schwannomas; (NF-2 also associated with meningioma)

**p16**
*Function:* regulates cell cycle by inhibiting cyclin-dependent kinases  
*Associated malignancies:* pancreatic and esophageal carcinomas and malignant melanoma

**p53**
*Function:* regulates cell death and proliferation in response to DNA damage  
*Associated malignancies:* most human cancers

**Rb**
*Function:* regulates transition from G1 to S in the cell cycle by sequestering E2Fs, a family of transcription factors  
*Associated malignancies:* retinoblastoma, osteosarcoma

**WT1**
*Function:* inhibits transcription of genes promoting cell proliferation  
*Associated malignancies:* Wilms tumor

For each of the following oncogenes, state the function and the malignancy/malignancies they are associated with:

**abl**
*Function:* promotes cell proliferation through tyrosine kinase activity
**BCL2**

**Function:** overexpression prolongs cell survival by inhibiting apoptosis

**Associated malignancies:** follicular and undifferentiated lymphomas

**cyclin D**

**Function:** promotes cell proliferation by stimulating the phosphorylation of pRb

**Associated malignancies:** lymphoma, breast, liver, and esophageal cancers

**CDK4**

**Function:** promotes cell proliferation by phosphorylating pRb

**Associated malignancies:** sarcoma, glioblastoma multiforme, malignant melanoma

**HER2/neu**

**Function:** amplification promotes cell proliferation by enhancing growth factor signal transduction

**Associated malignancies:** breast, ovarian, lung, stomach cancers

**myc**

**Function:** promotes cell proliferation by transcriptional activation of specific genes

**Associated malignancies:** Burkitt lymphoma, small cell carcinoma of the lung, neuroblastoma

**ras**

**Function:** signal transduction through the MAP kinase pathway

**Associated malignancies:** colon cancer and many other human cancers

**ret**

**Function:** receptor tyrosine kinase that promotes cell proliferation in response to growth factors

**Associated malignancies:** multiple endocrine neoplasia 2A and 2B; familial medullary thyroid carcinoma

**sis**

**Function:** β-chain of PDGF which promotes cell proliferation

**Associated malignancies:** astrocytomas, osteosarcomas

**Miscellaneous Oncology**

**Name the type of neoplasm associated with the following diseases:**

**Actinic keratosis**

Squamous cell carcinomas of skin

**AIDS**

Aggressive malignant lymphomas, Kaposi sarcoma, brain lymphomas

**Barrett esophagitis**
List the four major differences between benign and malignant neoplasms:
1. Differentiation and anaplasia
2. Rate of growth
3. Local invasion
4. Metastases (most important difference)

What are the three ways a tumor can spread?
1. Invasion of lymphatic system (eg, carcinoma of the breast)
2. Hematogenous (typical of sarcomas)
3. Seeding of body cavity (eg, ovarian cancer)

What four classes of genes are the primary targets for genetic mutation leading to cancer?
1. Protooncogenes (promote cellular growth)
2. Tumor suppressor genes (inhibit cellular growth)
3. Genes that regulate and mediate apoptosis
4. Genes that regulate and mediate DNA repair

What three genetic mechanisms can lead to the activation of protooncogenes?
1. Point mutations
2. Chromosomal rearrangements
What three chromosomal abnormalities are characteristic of tumor cells?
1. Amplification
2. Deletion
3. Translocation

What three factors influence tumor growth?
1. Doubling time of tumor cells
2. Cell proliferation
3. Cell death (apoptosis)

Name the six small, round, blue cell tumors of childhood:
1. Ewing sarcoma
2. Lymphoma
3. Neuroblastoma
4. Medulloblastoma
5. Rhabdomyosarcoma
6. Primitive neuroectodermal tumors

Chemical Carcinogens

What are the two steps in the process of chemical carcinogenesis?
1. Initiation: cells undergo irreversible genetic mutation.
2. Promotion: chemicals promote growth of initiated cells.

Name the neoplasm associated with each of the following chemical, viral, and microbial carcinogens and types of radiant energy:

**Aflatoxin**
Hepatocellular carcinoma

**Aniline dyes**
Bladder cancer

**Aromatic hydrocarbons**
Lung cancer (aromatic hydrocarbons found in cigarettes)

**Asbestos**
Malignant mesothelioma

**EBV**
Burkitt lymphoma, nasopharyngeal cancer, B-cell lymphoma in AIDS patients, some types of HD

**Estrogen**
Breast carcinoma and endometrial carcinoma

**Helicobacter pylori**
Gastric adenocarcinoma and marginal zone lymphoma (MALToma)

**Hepatitis B virus**
Hepatocellular carcinoma

**Human papilloma virus**
Cervical squamous cell carcinoma and genital warts

**Human T-cell lymphocytic virus-1 (HTLV-1)**
T-cell leukemia/lymphoma

**Ionizing radiation**
Nitrosamines
Myeloid leukemias and thyroid cancers

**Polyvinylchloride (PVC) assembly**
Hepatic hemangiosarcoma

**Ultraviolet radiation**
Skin cancers

*Schistosoma haematobium*
Squamous cell carcinoma of the urinary bladder

**Paraneoplastic Syndromes**

**Name the process of profound weight loss and weakness due to muscle and fat loss in a patient with an advanced neoplasm:**
Cancer cachexia

**Name the tumor associated with the following paraneoplastic syndromes:**

- **Acanthosis nigricans**
  Many types of visceral malignancies

- **Carcinoid syndrome**
  Carcinoid and neuroendocrine carcinomas of the bronchi or GI tract

- **Clubbing of fingers**
  Pulmonary or thoracic malignancies

- **Cushing syndrome**
  Adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma or a cortisol-secreting adrenal adenoma

- **DIC**
  AML (M3)

- **Hypercalcemia**
  Parathyroid hormone (PTH)-secreting squamous cell carcinoma of the lung

- **Lambert-Eaton myasthenic syndrome**
  Small cell carcinoma of the lung

- **Thrombophlebitis**
Pancreatic or lung adenocarcinoma
Syndrome of inappropriate antidiuretic hormone (SIADH)
Antidiuretic hormone (ADH)-secreting small cell carcinoma of the lung

PHARMACOLOGY

Medication for Anemia

Name the drug of choice for each of the following groups of anemic patients:
Adolescent girls with heavy periods and pregnant women
Iron
Patients on methotrexate who develop megaloblastic anemia
Folate
Elderly patients with atrophic gastritis who develop megaloblastic anemia
Cyanocobalamin (vitamin B$_{12}$)
Patients with anemia secondary to end-stage renal disease
Erythropoietin
Patients with extremely low WBC count and prone to infection
G-CSF, GM-CSF

Chemotherapeutic Agents

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and unique toxicity (TOX) (if any)
Methotrexate
MOA: folate analog that inhibits dihydrofolate reductase and, consequently, S phase of the cell cycle
IND: leukemia, lymphoma, carcinoma, sarcoma
TOX: myelosuppression (reversible with leucovorin)
5-Fluorouracil
MOA: inhibits pyrimidine synthesis which inhibits S phase progression
IND: colon cancer and other solid tumors
TOX: myelosuppression and phototoxicity
Cytarabine
**MOA:** inhibits pyrimidine synthesis which inhibits S phase progression
**IND:** acute leukemias
**TOX:** neurotoxicity

6-Mercaptopurine or 6-thioguanine
**MOA:** inhibits purine synthesis which inhibits S phase progression
**IND:** leukemia, lymphoma
**TOX:** myelosuppression, hepatotoxicity

Busulfan
**MOA:** DNA alkylating agent
**IND:** palliative role in CML treatment
**TOX:** pulmonary fibrosis, hyperpigmentation

Cyclophosphamide
**MOA:** DNA alkylating agent
**IND:** NHL, breast and ovarian carcinomas
**TOX:** hemorrhagic cystitis (prevented with mesna), myelosuppression

Nitrosureas (carmustine, lomustine, streptozocin)
**MOA:** DNA alkylating agent capable of crossing the blood-brain barrier
**IND:** brain tumors
**TOX:** CNS toxicity including dizziness and ataxia

Cisplatin
**MOA:** DNA alkylating agent
**IND:** testicular cancer, female reproductive tract cancers, bladder and testicular cancers
**TOX:** nephrotoxicity and acoustic nerve damage

Doxorubicin/adriamycin
**MOA:** intercalates into DNA and inhibits DNA replication
**IND:** Hodgkin disease, myeloma, sarcoma, solid tumors
**TOX:** cardiotoxicity, alopecia, myelosuppression

Bleomycin
**MOA:** intercalates into DNA and causes DNA strand breaks
**IND:** testicular cancer, lymphomas
**TOX:** pulmonary fibrosis, myelosuppression

Etoposide
**MOA:** inhibits topoisomerase, causing double-stranded breaks in DNA
**IND:** small cell carcinoma of lung, prostate cancer, testicular cancer
**TOX:** Bone marrow suppression, hypotension

Prednisone
**MOA:** may trigger apoptosis
IND: CLL, HD, lymphomas
TOX: cushingoid reaction, immunosuppression, cataracts, acne, osteoporosis, hypertension (HTN), peptic ulcers, hyperglycemia

Tamoxifen/raloxifene
MOA: estrogen receptor agonist/antagonist
IND: breast cancer
TOX: increased risk of endometrial cancer

Vinblastine/vincristine
MOA: binds tubulin to inhibit formation of the mitotic spindle
IND: HD, lymphoma, Wilms tumor, choriocarcinoma
TOX: vincristine: peripheral neuropathy and paralytic ileus; vinblastine: myelosuppression

Paclitaxel
MOA: binds tubulin to inhibit formation of the mitotic spindle
IND: ovarian and breast cancers
TOX: myelosuppression, hypersensitivity

Anticoagulants

What test is used to monitor anticoagulation in a patient treated with heparin?
PTT

What test is used to monitor anticoagulation in a patient treated with warfarin?
PT

Warfarin
MOA: causes synthesis of dysfunctional vitamin K-dependent clotting factors (II, VII, IX, X)
IND: chronic treatment and prophylaxis of DVT
TOX: hemorrhage, teratogenic, osteoporosis

Heparin
MOA: increases PTT by activating antithrombin III
IND: acute treatment of DVT, pulmonary embolus, angina, myocardial infarction (MI), ischemic stroke
TOX: hemorrhage, Heparin-Induced Thrombocytopenia Syndrome (HITS)

Low-molecular-weight heparin (LMWH) (eg, enoxaparin)
MOA: similar to heparin
IND: anticoagulation outside of the hospital, commonly for DVT
Thrombolitics (streptokinase, urokinase, tissue plasminogen activator, anistreplase)
**MOA:** facilitate the conversion of plasminogen to plasmin, which cleaves thrombin and fibrin clots  
**IND:** acute therapy for MI and ischemic stroke  
**TOX:** hemorrhage  

**Clopidogrel and ticlopidine**  
**MOA:** antiplatelet agent that blocks adenosine diphosphate (ADP) receptors to inhibit platelet aggregation  
**IND:** acute coronary syndrome, interventional cardiology procedures, transient ischemic attacks, and stroke  
**TOX:** hemorrhage, leukopenia, diarrhea  

**Eptifibatide and tirofiban**  
**MOA:** prevent platelet aggregation by blocking glycoprotein IIb/IIIa receptors  
**IND:** acute coronary syndromes  
**TOX:** hemorrhage
CHAPTER 11
Skin and Connective Tissues

EMBRYOLOGY/ANATOMY/HISTOLOGY

Name the embryonic structures that give rise to each of the following:

- Epidermis
- Ectoderm
- Melanocytes
- Neural crest cells

Name the layers of the epidermis:

- “Californians Like Girls in String Bikinis” (from surface → base)
  - Stratum Corneum
  - Stratum Lucidum (lacking in thin skin of face and genitalia)
  - Stratum Granulosum
  - Stratum Spinosum
  - Stratum Basalis

What epidermal dendritic cells are responsible for antigen presentation?

- Langerhans cells

Name the type of collagen described by the following statements:
- Found in Bone, tendons, skin, fascia, cornea, and dentin; replaces reticulin later in wound repair
  - Type I (Remember: bONE)
- Found in Cartilage, nucleus pulposus, and ocular vitreous body
  - Type II (Remember: carTWOlage)
- Found in skin, blood vessels, uterus, fetal tissues, and involved in early wound repair (granulation tissue)
  - Type III (Reticulin)
- Component of Basement membrane or basal lamina
  - Type IV (Remember: type IV, under the floor/basement membrane)
- Found at epiphyseal plates
  - Type X
- Accounts for ~90% of collagen in the body
  - Type I
Mnemonic for collagen types I to IV
    “Be Cool, Read Books”
Name the epithelial cell specialization described by the following statements:
    Allows adjacent cells to communicate via connexons
    Gap junction. Note: missing in cancer cells
    Connects cells to underlying extracellular matrix
    Hemidesmosomes
    Extends around entire perimeter; contains E-cadherin and actin filaments
    Zona adherens
    Prevents diffusion across intracellular space; extends around entire perimeter
    Zona occludens (tight junction)
    Small, discrete sites of attachment; contains desmoplakin and keratin
    Macula adherens (desmosome)
Helical array of polymerized dimmers of α and β tubulin
    Microtubules
How are the internal structures of cilia organized?
    9 + 2 arrangement of microtubules (9 doublets around 2 central microtubules)
Which enzyme causes bending of cilia and how does it work?
    Dynein is an adenosine triphosphatase (ATPase) that links the 9 doublets and causes bending by differential sliding.
Name the cytoskeletal elements that perform the following functions:
    Microvilli, muscular contraction, cytokinesis, adhering junction
    Actin and myosin
    Cilia, flagella, mitotic spindle, neurons, centrioles
    Microtubules
    Vimentin, desmin, cytokeratin, glial fibrillary acid protein, neurofilaments
    Intermediate filaments
Where are apocrine sweat glands found?
    Axilla, mons pubis, and anal regions

PATHOLOGY

Give the dermatologic term for each of the following descriptions:
    Flat, nonpalpable, circumscribed lesion 1 cm in diameter; different color than surrounding skin
    Macule
    A macule > 1 cm in diameter
Patch
Palpable, solid, elevated skin lesion Papule ≤5 mm in diameter
Papule
A papule > 5 mm in diameter
Plaque
Fluid-containing blister 0.5 cm in diameter
Vesicle
Fluid-containing blister > 0.5 cm in diameter
Bulla
Pus-filled, raised area
Pustule
Solid, round lesion; diameter = thickness, > 5 mm in diameter
Nodule

Name the dermatologic disorder characterized by the following descriptions:
Autosomal recessive (AR) defect in melanin synthesis → predisposition to multiple skin disorders
Albinism (oculocutaneous)
Acquired loss of epidermal melanocytes → depigmented white patches
Vitiligo
Masklike facial hyperpigmentation associated with pregnancy
Melasma
Tan-brown, evenly pigmented, localized overgrowth of melanin-forming cells of the skin present at birth with benign behavior and variable histology
Nevocellular nevus (mole)
Often multiple, atypical, irregularly pigmented lesions and on non-sun-exposed skin, that have the potential to transform into malignant melanoma
Dysplastic nevus
Eruption of comedones and pustules; ↑ during puberty and adolescence; associated with proliferation of Propionibacterium
Acne vulgaris
Umbilicated, pearly, dome-shaped papules typically occurring in the genitals; caused by poxvirus infection
Molluscum contagiosum
Benign papilloma caused by HPV infection, most commonly found on dorsum of hand; koilocytes are characteristic
Verruca vulgaris (common wart)
Common benign neoplasm of older adults; sharply demarcated, tan-brown plaques with a “pasted on” appearance
Seborrheic keratosis (senile keratosis)
Benign, flesh-colored, dome-shaped, > 1 cm nodule with central keratin-filled plug-craterlike that resembles squamous cell carcinoma; may resolve without treatment
Keratoacanthoma
Yellowish papules or nodules that tend to occur on the eyelids; associated with hypercholesterolemia
Xanthoma (on the eyelids = xanthelasma)
Accumulation of excessive dermal collagen that can occur following skin trauma; results in large, raised tumorlike scar
Keloid
Proliferation of Langerhans cells; electron microscopy (EM) shows Birbeck granules
Histiocytosis X
A T-cell lymphoproliferative disease arising in the skin; initially simulates eczema or other inflammatory dermatoses
Mycosis fungoides (cutaneous T-cell lymphoma)
Rough, scaling epidermal lesion, usually 1 cm, due to chronic sunlight exposure; may be a precursor for squamous cell carcinoma
Actinic keratosis
Thickened, hyperpigmented skin in the flexural areas; may be suggestive of visceral malignancy
Acanthosis nigricans
Capillary hemangioma appearing as a purple-red area on the face or neck
Port-wine stain

Name the inflammatory dermal lesion associated with each of the following findings:
Pruritic, inflammatory disorders due to infection, atopy, chemicals, UV light, or repeated trauma
Dermatitis
Characteristic “target” macule or papule; associated with infections, drugs, cancers, and autoimmune disease
Erythema multiforme
Silvery scaling plaques over the knees, Psoriasis elbows, and scalp
Psoriasis
“Saw toothing” of rete ridges
Lichen planus
Munro microabscesses in the stratum corneum
Psoriasis
Pruritic eruption commonly on flexor surfaces. Associated with asthma and allergic rhinitis
Atopic dermatitis (eczema)

**Wickham stria**

Lichen planus

*Purple, pruritic, polygonal, papules*

Lichen planus

**Characteristic rete elongation and parakeratosis**

Psoriasis

**Fever combined with erosions and hemorrhagic crusting of mucosal surfaces**

Stevens-Johnson syndrome

**Type IV hypersensitivity reaction following exposure to allergens such as poison ivy or poison oak**

Allergic contact dermatitis

**Sometimes associated with severe destructive rheumatoid arthritis-like lesions of the fingers**

Psoriasis (psoriatic arthritis)

Name the blistering dermal disease associated with each of the following descriptions:

Subepidermal bullae causing detachment of the entire thickness of the epidermis

Bullous pemphigoid

**Pruritic subepidermal blisters occurring in groups; eosinophils and IgA deposits at tips of dermal papillae; seen in patients with celiac disease**

Dermatitis herpetiformis

**Intraepidermal/suprabasal blisters that often rupture; may be fatal**

Pemphigus vulgaris

Immunofluorescence demonstrates linear deposition of complement and antibodies to hemidesmosome proteins BPAG1 and BPAG2

Bullous pemphigoid

**IgA and IgG antibodies to gluten**

Dermatitis herpetiformis

**Antibodies (Abs) to the desmosomal protein desmoglein 3 in the macula adherens**

Pemphigus vulgaris

Name the neurocutaneous syndrome characterized by each of the following features:

Port-wine stains of the face, ipsilateral glaucoma, retinal lesions, and hemangiomas of the meninges

Sturge-Weber syndrome

**Hypopigmented macules (ash-leaf spots), adenoma sebaceum, seizures, and mental retardation**

Tuberous sclerosis

**Multiple organ hemangioblastomas, cysts, and paragangliomas throughout the body**
von Hippel-Lindau disease
Café au lait spots, acoustic neuromas, and meningiomas
Neurofibromatosis

Which syndrome is characterized by mycosis fungoides, erythema, and scaling?
Sézary syndrome, cutaneous T-cell lymphoma

Connective Tissue Disorders

Name the connective tissue disorder characterized by each of the following descriptions:

- Immune complex deposition in almost any organ, characteristic butterfly malar rash, wire loop lesions in kidney, Libman-Sacks endocarditis, ANA, anti-dsDNA, anti-Smith antibodies
- Systemic lupus erythematosus
- Calcinosis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, telangiectasias; anticentromere antibodies
- CREST syndrome
- Autosomal dominant (AD) mutation in the fibrillin-1 gene (FBN1) on chromosome 15q
- Marfan syndrome
- Most common form is an AD defect in collagen type I synthesis; may be confused with child abuse
- Osteogenesis imperfecta
- Proximal muscle weakness, elevated serum creatine kinase, less often associated with malignancy
- Polymyositis
- Abnormal collagen synthesis causing bleeding tendency, hypermobile joints, and hyperextensible skin
- Ehlers-Danlos syndrome
- Blue sclera and brittle bones
- Osteogenesis imperfecta
- Proximal muscle weakness, heliotrope rash, more often associated with malignancy
- Dermatomyositis
- Antinuclear ribonucleoprotein (anti-nRNP) antibodies
- Mixed connective tissue disease
- Widespread visceral involvement; anti-Scl-70 antibodies
- Diffuse scleroderma
Triad of xerophthalmia (dry eyes), xerostomia (dry mouth), arthritis; anti-Ro, anti-La antibodies
Sjögren syndrome

Skin Cancer

Name the skin malignancy associated with each of the following statements:

- The most common skin malignancy
  Basal cell carcinoma
- Associated with excessive sunlight exposure; may arise from dysplastic nevus cells
  Malignant melanoma
- Actinic keratosis is a precursor lesion
  Squamous cell carcinoma
- Locally aggressive, ulcerating, and hemorrhagic; almost never metastases
  Basal cell carcinoma
- Occurs in sun-exposed areas and tends to involve the lower part of the face
  Squamous cell carcinoma
- Occurs in sun-exposed areas and tends to involve the upper part of the face
  Basal cell carcinoma
- Histopathology characterized by “keratin pearls”
  Squamous cell carcinoma
- Histopathology shows darkly staining cells with palisading nuclei
  Basal cell carcinoma
- Radial phase precedes vertical growth phase
  Malignant melanoma
- Associated with arsenic and radiation exposure
  Squamous cell carcinoma

What are the characteristics worrisome for malignant melanoma?

- ABCDE’s
- Asymmetry
- Border (irregular)
- Color
- Diameter
- Evolving

What is the most important prognostic factor in malignant melanoma?

- Depth of invasion

What clinical variant of malignant melanoma has the poorest prognosis?
Nodular melanoma

What clinical variant of malignant melanoma often appears on the hands and feet of dark-skinned people?
   Acral-lentiginous melanoma

Miscellaneous Skin Disorders

Name the dermatologic finding(s) associated with each of the following diseases:
   Gastric adenocarcinoma
   Acanthosis nigricans
   Addison disease
   Hyperpigmentation and striae
   Rheumatic fever
   Erythema marginatum
   Kawasaki syndrome
   Erythematos palms and soles; dry, red lips; desquamation of fingertips
   Insulin resistance, diabetes mellitus type 2
   Acanthosis nigricans
   Sézary syndrome
   Mycosis fungoides (lymphoma of the skin-simulating eczema)
   Severe chronic renal failure
   Uremic frost
   Bacterial endocarditis
   Osler nodes (tender, raised lesions on pads of fingers or toes) and Janeway lesions (small, erythematous lesions on palms or soles)
   Xeroderma pigmentosum
   Dry skin and melanoma
   Henoch-Schönlein purpura
   Purpuric lesions on extensor surfaces of arms, legs, buttock
   Hypothyroidism
   Cool, dry skin with coarse brittle hair
   Graves disease
   Warm, moist skin with fine hair; pretibial myxedema
   Graft-versus-host disease
   Maculopapular rash
   von Recklinghausen disease (NF-1)
   Multiple café au lait spots
   Familial hypercholesterolemia
Xanthomas
Systemic lupus erythematosus
Malar rash and photosensitivity
Pellagra
Dermatitis

Name the dermatologic finding(s) associated with each of the following infectious diseases:

**Anthrax**
Vesicular papules covered by black eschar

**Parvovirus B19**
Erythema infectiosum (*slapped cheek* appearance)

**Lyme disease**
Erythema chronicum migrans

**Primary syphilis**
Painless chancre

**Secondary syphilis**
Rash over palms and soles, condyloma latum

**Rocky Mountain spotted fever**
Rash over palms and soles (migrates centrally)

**Congenital cytomegalovirus**
Pinpoint petechial “blueberry muffin” rash

**HPV (in genital region)**
Condylomata acuminata

**Herpes simplex virus (type 1)**
Painful vesicles (at border of lips)

**Leprosy**
Hypopigmented, anesthetic skin patches
Name the peripheral nerve or region of the brachial plexus injured in each of the following scenarios:

- **Erb-Duchenne or Waiter’s tip palsy**
  - Upper trunk of the brachial plexus (C5, C6)

- **Klumpke injury due to sudden upward jerk of the arm; associated with Horner syndrome**
  - Lower trunk of the brachial plexus (C8, T1)

- **Claw hand (impaired wrist flexion and adduction)**
  - Ulnar nerve

- **Wrist drop**
  - Radial nerve

- **Vague pain in wrist with tingling, burning sensation in hand (carpal tunnel syndrome)**
  - Median nerve

- **Deltoid paralysis**
  - Axillary nerve

- **Winged scapula after mastectomy (paralyzed serratus anterior)**
  - Long thoracic nerve

- **Foot drop**
  - Common peroneal nerve

- **Loss of ability to plantarflex**
  - Tibial nerve

- **Anterior shoulder dislocation**
  - Axillary nerve

- **Positive distal tingling on percussion of anterior wrist (Tinel) and tingling on forced flexion (Phalen) tests**
  - Median nerve (at wrist)

- **Anterior hip dislocation resulting in loss of adduction of the thigh**
  - Obturator nerve
Loss of ability to rise from a seated position or climb stairs due to loss of gluteus maximus function
Inferior gluteal nerve
Positive Trendelenburg sign (when contralateral leg is raised, contralateral hip falls secondary to ipsilateral gluteus medius weakness)
Superior gluteal nerve
Posterior hip dislocation
Sciatic nerve

Name the fracture associated with the following statements:
Laceration of the deep brachial artery and/or radial nerve
Midshaft fracture of the humerus
Greatest risk of upper extremity compartment syndrome in children (Volkman contracture)
Supracondylar fracture of the humerus
Young person with fall on outstretched hand, tenderness in the anatomic snuff-box
Scaphoid fracture
Caused by closed fist striking a hard object
Boxer’s fracture or fracture of the fifth metacarpal
Elderly woman falling on an outstretched hand with the wrist extended
Colles fracture (fracture of the distal radius with dorsal displacement of hand)
Associated with foot drop due to injury of common peroneal nerve
Fracture of fibular neck
Lower extremity fracture caused by landing on foot from a large vertical drop
Calcaneal fracture (must check lumbar spine x-rays for associated fracture)

List the muscles that make up the hypothenar eminence:
Opponens digiti minimi, Abductor digiti minimi, Flexor digiti minimi (OAF)

List the muscles that make up the thenar eminence:
Opponens pollicis, Abductor pollicis brevis, Flexor pollicis brevis

What are the functions of the thenar and hypothenar muscles?
Oppose, Abduct, and Flex

What muscles ADduct at the metacarpophalangeal (MCP) joints?
Palmar interosseous muscles (PAD)

What muscles ABduct at the MCP joints?
Dorsal interosseous muscles (DAB)

What ligaments make up the borders of the anatomic snuffbox?
Extensor pollicis longus, extensor pollicis brevis, abductor pollicis longus

What artery passes through the anatomic snuffbox?
Radial artery
How can one test for radial or ulnar artery patency?
   Allen test (used before arterial blood sampling from the radial artery)

What structures are damaged by lateral impact to the knee/twisting injury?
   The terrible triad: anterior cruciate ligament (ACL), medial collateral ligament (MCL), and medial meniscus

What does a positive anterior drawer/Lachman sign suggest?
   Torn ACL

What does abnormal passive abduction (valgus instability) of the leg suggest?
   Torn MCL

What is the most common site for a clavicular fracture?
   Middle one-third

What is the term for increased pressure within a fascial compartment that causes damage to muscles and neurovascular structures?
   Compartment syndrome

What are the six P’s of compartment syndrome?
   1. Pain out of proportion/pain with passive stretch
   2. Parasthesias
   3. Paralysis
   4. Pallor
   5. Pulselessness
   6. Poikilothermia (cold)

What ligaments can be stretched or torn by inversion of the ankle?
   Anterior talofibular ligament (most common, “Always Tears First”), calcaneofibular (second most common), posterior talofibular ligament (least common)

What common carpal bone fracture can lead to avascular necrosis?
   Scaphoid fracture

What are the muscles of the rotator cuff?
   Supraspinatus, Infraspinatus, Teres minor, Subscapularis (SITS) muscles

What term is used to describe the syndrome of pain on extension of the wrist and fingers?
   Lateral epicondylitis (tennis elbow)

Name the syndrome characterized by sensory loss of the medial forearm and hand, disappearance of radial pulse on turning head away from affected side, with atrophy of thenar, hypothenar, and interosseous muscles:
   Thoracic outlet syndrome (often due to cervical accessory rib)

Fracture that presents with leg in abduction, external rotation, and appearing shorter than the contralateral leg
   Femoral neck fracture
Injury that presents with an internally rotated and adducted leg appearing shorter than the contralateral leg?
Posterior dislocation of the hip

PHYSIOLOGY

State the key cellular events in excitation-contraction coupling in skeletal muscle:
1. Action potentials cause depolarization of T tubules.
2. $\text{Ca}^{2+}$ release from sarcoplasmic reticulum.
3. $\text{Ca}^{2+}$ binds troponin C, causes conformational change.
4. Tropomyosin moves to expose actin-binding site.
5. Actin and myosin interact to generate contractile force.
6. $\text{Ca}^{2+}$ reuptake by sarcoplasmic reticulum.

How does $\text{Ca}^{2+}$ activate contraction in smooth muscle cells?
By binding to calmodulin, activating myosin light-chain kinase (MLCK)

Name the type(s) of muscle fiber associated with each of the following cellular or histologic features:

**Peripherally located nucleus**
Skeletal muscle fibers

**Centrally located nucleus**
Smooth and cardiac muscle fibers

**Distinct banding pattern**
Cardiac and skeletal muscle fibers; bands are appearance of sarcomeres

**Capacity to regenerate**
Smooth muscle fibers

**Z-lines**
Cardiac and skeletal muscle fibers; Z-lines are borders that separate sarcomeres

**Gap junctions**
Smooth muscle fibers

**Intercalated disks**
Cardiac muscle fibers

**Synapse with peripheral nerves**
Skeletal muscle fibers

**Inositol triphosphate (IP$_3$)-mediated calcium release**
Smooth muscle fibers

**$\text{Ca}^{2+}$-mediated calcium release**
Cardiac muscle fibers
Voltage-mediated, T-tubule-mediated calcium release
Skeletal muscle fibers
**Troponin is the major calcium-binding protein**
Cardiac and skeletal muscle fibers

Name the type of skeletal muscle fiber associated with each of the following features:

**Slow twitch**
Type 1—*one slow*

**Fast twitch**
Type 2

**Abundant lipid stores**
Type 1—*fat*

**Red color**
Type 1—*red*

**White color**
Type 2

**Primarily uses anaerobic metabolism, few mitochondria**
Type 2

**Primarily uses aerobic metabolism, many mitochondria**
Type 1—*ox*

**Abundant glycogen stores**
Type 2

**Generation of a sustained force**
Type 1

**Generation of a sudden movement**
Type 2

**Mnemonic for type 1 fibers**
*Remember:* “One Slow, Fat, Red Ox”

**MUSCULOSKELETAL AND CONNECTIVE TISSUE PATHOLOGY**

**Nonneoplastic Bone Disorders**

Name the bone disease associated with the following clinical and pathologic features:
AD disorder characterized by short limbs due to narrow epiphyseal plates, normal torso, enlarged head, frontal bossing, and bow legs
Achondroplasia, most common cause of dwarfism
A group of disorders characterized by abnormalities of type 1 collagen
Osteogenesis imperfecta
Inadequate proline and lysine hydroxylation of procollagen
Scurvy
Vitamin D deficiency → failure of bone mineralization
Rickets (children) or osteomalacia (adults)
Vitamin C deficiency → bone lesions, bleeding from gums and petechial hemorrhages
Scurvy
Associated with blue sclera and multiple fractures
Osteogenesis imperfecta
↑ Parathyroid hormone (PTH) → “Brown tumor” of bone (fibrosis, giant cells, osteoclasts hemorrhagic debris, and cyst formation)
Osteitis fibrosa cystica (von Recklinghausen disease of bone)
Slow paramyxovirus infection of osteoblasts and osteoclasts that results in multiple fractures and ↑ serum alkaline phosphatase
Paget disease of bone (osteitis deformans)
Marrow fibrosis, moth-eaten bones on x-ray (XR), and metastatic calcifications
Osteitis fibrosa cystica (von Recklinghausen disease of bone), caused by hyperparathyroidism
Multiple lytic lesions of spine and skull
Multiple myeloma
Progressive decrease in bone mass most pronounced in menopausal women
Osteoporosis
Hereditary disorder of increased bone density caused by defective osteoclast function and bone overgrowth
Osteopetrosis
Lateral curvature of spine, usually with rotational component; most common in adolescent females
Scoliosis
Subperiosteal hemorrhage, failure of epiphyseal cartilage replacement by osteoid, osteoporosis
Scurvy (vitamin C deficiency)
Delayed fontanelle closure, “Rachitic rosary” (thickening of costochondral junction), and Harrison groove
Rickets (vitamin D deficiency)
Marked cortical thinning and attenuation of bone trabeculae
Osteogenesis imperfecta
Poor calcification of bone leading to skeletal abnormalities, including bowing of legs, craniotabes, and pigeon breast deformity in children
Rickets
Mosaic pattern of lamellar bone, increased serum alkaline phosphatase
Paget disease of bone (osteitis deformans)
Bone infection → sequestrum and involucrum around the inflammatory focus
Pyogenic osteomyelitis
Infarction of osteocytes leading to joint pain and osteoarthritis
Avascular necrosis
Avascular necrosis of the head of the femur; typically presents with painless limp in obese adolescent
Legg-Calve-Perthés disease
Partial avulsion of tibial tuberosity; typically presents as knee pain in an active adolescent
Osgood-Schlatter disease
Bacterial infection of bone, causing an acute febrile illness and localized pain and inflammation at the site of infection
Pyogenic osteomyelitis
Granulomatous disease caused by spread of tuberculosis to spine
Pott disease
Vertebral compression fractures causing pain, kyphosis, and loss of height in the elderly
Osteoporosis
What is the most likely etiology of Paget disease?
Slow reaction to paramyxovirus infection of osteoblasts
What are the three phases of Paget disease of bone?
1. Osteolytic phase: bone reabsorption by large osteoclasts
2. Mixed phase: osteoblastic and osteoclastic activity results in mosaic pattern of bone
3. Burnt-out phase: osteoblastic activity predominates
Name six complications of Paget disease of bone:
1. High-output cardiac failure due to intraosseous atrioventricular (AV) shunting
2. Hearing loss
3. Leonitiasis ossea
4. Osteosarcoma
5. Osteoarthritis
6. Bone pain from fractures
Osteomyelitis

Name the most common organism(s) responsible for pyogenic osteomyelitis in each of the following patients:

- Otherwise healthy adult
  *Staphylococcus aureus*
- Intravenous drug user
  *Pseudomonas* spp.
- Sickle cell anemia patient
  *Salmonella*
- Newborn
  *Streptococci* spp. or *Escherichia coli*
- Child
  *Staphylococcus aureus*

Most common mechanism of seeding for adults
*Traumatic*

Most common mechanism of seeding for children
*Hematogenous*

Neoplasia of Bone

Name the bone tumor associated with the following clinical and pathologic findings:

Most common bone tumor
Metastatic tumors to bone

Most common primary bone tumor
Multiple myeloma

Most common benign tumor of bone
Osteochondroma or exostosis

Most common primary malignant tumor of bone
Osteosarcoma

Benign sessile tumor attached to the bone surface, usually affecting skull and facial bones
Osteoma

Benign tumor (2 cm) that is painful at night (due to excess PGE₂), relieved with aspirin and common in males 25 years old (y/o)
Osteoid osteoma
Malignant tumor typically occurring in the metaphyseal region prior to epiphyseal closure in patients 25 y/o
Osteosarcoma
Mushroom-shaped, laterally protruding tumor that may result from lateral displacement of the growth plate
Osteochondroma or exostosis
Benign tumor composed primarily of mature hyaline cartilage
Chondroma
Benign tumor composed of fibrous trabeculae of woven bone resembling Chinese characters
Fibrous dysplasia
Nodule of hyaline cartilage encased in reactive bone
Enchondroma
Malignant, painful, small round blue cell tumor of childhood occurring typically in the appendicular skeleton (may also affect ribs)
Ewing sarcoma/primitive neuroectodermal tumor (PNET)
Malignant tumor composed of multinucleated giant cells within a fibrous stroma, occurring in the epiphyses of long bones
Giant cell tumor of bone
Lacelike pattern of bone produced by tumor cells
Osteosarcoma
Homer-Wright pseudorosettes, onion skin appearance on x-ray
Ewing sarcoma/PNET
Malignant tumor of cartilage found in the central skeleton
Chondrosarcoma
Double bubble or soap bubble appearance on XR
Giant cell tumor of bone
Benign but painful bone tumor that appears as a radiolucent nidus surrounded by dense bone
Osteoid osteoma or osteoblastoma
Codman triangle on x-ray forms as tumor, causing periosteal elevation
Osteosarcoma
Onion skin appearance on x-ray
Ewing sarcoma

What is the most common genetic defect associated with Ewing sarcoma/PNET?
\[ t(11;22)(q24;q12) \] translocation (85%) associated with an \( EWS-FLI1 \) fusion gene product

Mutation of what gene increases the risk of osteosarcoma by 1000 X x?
\[ Rb \] gene
What malignancies are most likely to metastasize to bone?
  Breast, lung, thyroid, kidney, and prostate (BLT with a Kosher pickle)

What pediatric disease is characterized by the triad of skull lesions, diabetes insipidus, and exophthalmos?
  Hand-Schüller-Christian disease or histiocytosis X

What pediatric disease is characterized by polyostotic fibrous dysplasia, café au lait spots, precocious puberty, and other endocrine disorders?
  McCune-Albright syndrome

Arthritis

Name the arthritic joint disease associated with the following clinical and pathologic findings:
  Most common type of arthritis
    Osteoarthritis
  Most common type of infective arthritis and most common cause of arthritis in sexually active adults
    Gonococcal arthritis
  Anti-IgG Fc antibodies
    Rheumatoid arthritis (RA); anti-IgG Fc antibodies are called rheumatoid factor
  Subcutaneous rheumatoid nodules
    RA
  Heberden (DIP) and Bouchard (PIP) nodes
    Osteoarthritis
  PIP and MCP involvement
    RA (Note: RA almost never affects DIP)
  Most commonly affects great toe (podagra)
    Gout
    Presents as pain in weight-bearing joints after use, improves with rest
    Osteoarthritis
  Infrequent complication of psoriasis asymmetrically affecting DIP and PIP joints in the lower extremities
    Psoriatic arthritis
  Swan-neck and boutonniere deformity
    RA
  Chronic low back pain, rigidity, fixation of spine causing a condition referred to as bamboo spine
    Ankylosing spondylitis
Infection causing migratory polyarthritis and erythema chronicum migrans; may lead to pericarditis and aseptic meningitis

Lyme disease

Arthritic joint disease associated with inflammatory bowel disease

Arthritic joint disease associated with inflammatory bowel disease

Ankylosing spondylitis

Presents as morning stiffness improving with use, symmetric joint involvement, systemic symptoms

RA

Arthritis in the absence of systemic symptoms

Osteoarthritis

Extraskeletal manifestations of this arthritic disease include pulmonary fibrosis, aortic insufficiency, and cauda equina syndrome

Ankylosing spondylitis

Triad of conjunctivitis or anterior uveitis, urethritis, and arthritis

Reactive arthritis, previously known as Reiter syndrome (Remember: can’t see, can’t pee, can’t climb a tree)

Tophi (nodules of fibrous tissue) and crystals may be found on Achilles tendon or at external ear

Gout

Osteophyte formation at edge of articular surface and at sites of ligamentous attachment

Osteoarthritis

Filling of the joint space by granulation tissue (ie, a pannus)

RA

Frayed fragments of cartilage and osteophytes released into synovium forming “joint mice”

Osteoarthritis

Associated with hyperuricemia, thiazide diuretic use, and urate kidney stones

Gout

Eburnation of bone due to cartilage erosion

Osteoarthritis

Marginal erosion of subchondral bone

RA

Cystic changes in bones underlying affected joints

Osteoarthritis

Precipitation of urate crystals in joints resulting in an inflammatory response

Gout

Precipitation of calcium pyrophosphate dihydrate crystals in joints → inflammatory response
Pseudogout (aka calcium pyrophosphate deposition disease [CPPD])
Infective arthritis common in individuals with complement deficiencies; associated with ↑ susceptibility to meningitis
Gonococcal arthritis
Associated with deficiency of hypoxanthine guanine phosphoribosyl transferase (HGPRT)
Lesch-Nyhan syndrome (X-linked disease which may include gout as one of its manifestations)

**Positively birefringent, rhomboid-shaped crystals**
Pseudogout = Positively birefringent

**Negatively birefringent, needle-shaped crystals in synovial fluid**

Gout
Infective monoarticular arthritis typically causing knee pain and a pustular rash
Gonococcal arthritis
Infective polyarticular arthritis caused by *Borrelia burgdorferi*
Lyme disease
Monoarticular arthritis with gram-positive organisms on synovial fluid analysis
Nongonococcal septic arthritis
Stress, alcohol binge, or a large meal may precipitate an attack of this type of arthritis

**Gout**

**Treatment for acute gout attack**
Indomethacin (NSAID), Colchicine (use limited by GI side effects)

**Treatment for chronic gout**
Allopurinol (inhibits xanthine oxidase), probenecid (inhibits reabsorption of uric acid)

**Anticytokine therapy for RA is directed at which two cytokines?**
1. Interleukin (IL)-1
2. Tumor necrosis factor (TNF)

**What is the factor produced by activated T cells and fibroblasts that promotes bone destruction by osteoclasts?**
Receptor Activator of Nuclear Factor κ B Ligand (RANKL), also known as TNF-related activation-induced cytokine (TRANCE)

**What group of diseases is associated with high incidence (90%) in HLA-B27-positive patients?**
Seronegative spondyloarthropathies (ankylosing spondylitis, reactive arthritis, arthritis associated with inflammatory bowel disease [IBD])

**Name four extra-articular manifestations of RA:**
1. Pleural and pericardial effusions
2. Acute vasculitis
3. Inflammatory lesions of lungs, pleura, myocardium, pericardium, peripheral nerves, and eyes
4. Amyloidosis (in severe, long-term disease)

**What chemotactic factors are generated by urate crystal activation of complement?**
- C3a and C5a

**How is tissue injury mediated in gout?**
- Release of lysosomal enzymes from neutrophils

**Why are leukemia, multiple myeloma, and other neoplastic processes associated with gout?**
- High cell turnover releases uric acid and predisposes to an attack of gout.

**What is the renal complication of longstanding gout?**
- Urate nephropathy

**Which syndrome is characterized by cutaneous pigmentation, leg ulcerations, splenomegaly, neutropenia, and RA?**
- Felty syndrome

**What two bacteria most commonly cause nongonococcal septic arthritis?**
  - *Staphylococcus aureus* and *Streptococcus* spp.
LIFE CYCLE

Development

At what age is an average child expected to do each of the following:

- **Hold his/her head up**
  3 months

- **Sit up without support**
  6 months

- **Crawl**
  9 months

- **Walk**
  12 months

- **Ride a tricycle**
  36 months (tricycle at 3 years)

- **Display stranger anxiety**
  7 months

- **Use a pincer grasp**
  9 months (Remember: an upside-down pincer grasp forms the number “9”)

- **Say their first word**
  12 months (1 word at 1 year)

- **Use two-word combinations**
  24 months (2 words at 2 years)

- **Use three-word sentences**
  36 months (3 words at 3 years)

- **Understand object permanence**
  12 to 24 months

- **Toilet training**
  30 to 36 months
“No” phase, repeated temper tantrums
24 months (address tantrums by ignoring behavior)
Show abstract reasoning (formal operations)
Adolescence/puberty

At what age are the following reflexes considered normal:

- **Babinski**
  0 to 12 months
- **Palmar**
  0 to 2 months
- **Rooting**
  0 to 3 months

**Name the components of the Apgar score:**
APGAR (0, 1, or 2 in each category)
- Appearance/color (blue/pale, trunk pink, all pink)
- Pulse (0, 100, >100)
- Grimace (0, grimace, grimace + cough)
- Activity/muscle tone (limp, some, active)
- Respiratory effort (0, irregular, regular)

**Determine the Apgar score for these patients:**

- Newborn with a pink trunk, heart rate (HR) = 50, a grimace and cough when stimulated, strong muscle tone, and an irregular respiratory effort
  7
- A blue newborn, HR = 30, a grimace when stimulated, appears limp, and has no respiratory effort
  2

**What is the definition of low birth weight?**
Less than 2500 g

**Name four sequelae of low birth weight:**
1. Infections
2. Respiratory distress syndrome
3. Persistent fetal circulation
4. Necrotizing enterocolitis

**What term describes the act of a child reverting to a more primitive mode of behavior due to stress?**
Regression

**Name four long-term effects of depriving affection from infants:**
The 4 W’s:
1. Weak
2. Wordless
3. Wary
4. Wanting

What term describes depression in an infant due to sustained separation from the caregiver?
Anaclitic depression (results in impaired social, emotional, and physical development)

Name three findings that are suggestive of each type of abuse listed below:

**Physical child abuse**
1. Fractures at different stages of healing
2. Cigarette burns
3. Retinal hemorrhage/detachment (32% of kids 5 years old [y/o] are physically abused)

**Sexual child abuse**
1. Genital/anal trauma
2. STDs
3. UTIs (25% of kids 8 y/o are sexually abused)

**Elder abuse**
1. Evidence of depleted finances
2. Poor hygiene
3. Spiral fractures

**Aging**

Name the changes found in the elderly in each of the following categories:

**Psychiatric**
Depression and anxiety more common; ↑ suicide rate

**Sexual**
Men: slower erection/ejaculation, ↑ refractory period; women: vaginal shortening, thinning, and dryness

*Note:* sexual interest does not decrease.

**Sleep patterns**
↓ Rapid eye movement (REM), slow-wave sleep; ↑ sleep latency, awakenings

**Cognitive**
↓ Learning speed; intelligence stays the same

Name three conditions that would qualify normal bereavement as pathologic grief:
1. Prolonged grief (> 1 year)
2. Excessively intense grief (sleep disturbances, significant weight loss, suicidal ideations)
3. Grief that is delayed, inhibited, or denied
Name the Kübler-Ross stages of dying:
Denial, anger, bargaining, depression, acceptance. **Note:** one or more stages can occur at once and not necessarily in this order.

**PHYSIOLOGY**

**Sleep**

Name the sleep stage associated with each of the following descriptions:
- Light sleep, peacefulness, ↓ HR and BP
  Stage 1
- Deepest non-REM sleep; sleepwalking, bedwetting
  Stages 3 and 4
- Deeper sleep; EEG shows sleep spindles and K-complexes; occupies ~half of total sleep time in young adults
  Stage 2
- **Beta waves (↑ frequency, ↓ amplitude) only**
  Awake (eyes open) and alert REM
- **Beta, alpha, and theta waves → “sawtooth”**
  REM
- **Alpha waves**
  Awake (eyes closed)
- **Dreaming, loss of motor tone, ↑ brain O₂use, erections; occurs every 90 minutes**
  REM
- **Delta (slow) waves (↓ frequency, ↑ amplitude)**
  Stages 3 and 4

Name the sleep disorder described in each of the following statements:
- Abnormal behavior associated with sleep or sleep-wake transitions (eg, sleep terrors, enuresis, somnambulism)
  Parasomnia
- Disturbance in amount, quality, or timing of sleep (eg, insomnia, narcolepsy)
  Dyssomnia
- Nighttime respiratory effort against an impeded airway, resulting in 10-second lapses in breathing and chronic fatigue
  Obstructive sleep apnea

What is a useful drug for night terrors and sleepwalking?
Benzodiazepines (shortens stage 4 sleep)

Which drug treats enuresis in children by decreasing stage 4 sleep?
Imipramine

What is the main neurotransmitter involved in REM sleep?
Acetylcholine (ACh)

Name four physiologic changes that occur in REM sleep:
1. Increased and variable pulse
2. Increased and variable BP
3. Penile/clitoral tumescence
4. Rapid eye movements

Name four clinical findings of narcolepsy:
1. Sleep paralysis (brief paralysis upon awakening)
2. Hypnagogic (going to sleep) and hypnopompic (waking) hallucinations
3. ↓ REM latency (sleep episodes all start in REM)
4. Cataplexy (sudden loss of muscle tone, especially with extreme emotion)

How is narcolepsy treated?
Stimulants (eg, amphetamines), scheduled naps

What three sleep pattern changes are typical of depressed patients?
1. Reduced slow-wave sleep
2. ↓ REM latency
3. “Terminal insomnia” (early-morning awakenings)

Sexuality

Name the four stages of the sexual response cycle:
1. Excitement
2. Plateau
3. Orgasm
4. Resolution

Name three possible etiologies of sexual dysfunction:
1. Drugs (eg, selective serotonin reuptake inhibitors [SSRIs], ethanol [ETOH], anti-hypertensives)
2. Disease (eg, depression, diabetes, myocardial infarction [MI])
3. Psychologic (eg, aversion, hypoactive desire, premature ejaculation)

What disorder of sexual function is characterized by painful spasm of the outer one-third of the vagina during intercourse or pelvic examination?
Vaginismus

What is a paraphilia?
Unusual sexual activities or sexual desire for unusual objects (e.g., pedophilia, voyeurism, and so forth)

**Behavioral Neurochemistry**

For each of the following diseases, describe the associated neurotransmitter activity:

**Schizophrenia**
- ↑ Dopamine (DA) and 5-hydroxytryptamine (5-HT)

**Depression**
- ↓ Norepinephrine (NE) and 5-HT

**Anxiety**
- ↑ NE, ↓ γ-aminobutyric acid (GABA), and 5-HT

**Alzheimer dementia**
- ↓ ACh in Alzheimer dementia

**Parkinson disease**
- ↓ DA

**Huntington disease**
- ↓ GABA and ACh

**SUBSTANCE ABUSE**

What is the lifetime prevalence of substance abuse/dependence?
- 13%

How is “dependence” defined?
- Withdrawal occurs if substance is stopped and patient has tolerance to substance.

Excluding tobacco and caffeine, what is the most commonly abused substance?
- Alcohol

What is a short, useful alcoholism screening tool?
- “CAGE” questions
  - Have you felt the need to Cut down?
  - Have you ever felt Annoyed by criticism of your drinking?
  - Have you ever felt Guilty about drinking?
  - Have you ever had an Eye opener?

What is the major complication of alcohol withdrawal and when is it most likely to occur?
- Delirium tremens (DTs); peak occurrence is 2 to 7 days. **Note**: DTs are a medical emergency.
What is the mortality rate of DTs?

15% to 20%

Name three gastrointestinal (GI) complications of alcoholism:

1. GI bleeding (from ulcers, gastritis, esophageal varices, or Mallory-Weiss tears)
2. Pancreatitis
3. Liver disease

Which syndrome of anterograde amnesia, confabulations, ataxia, and nystagmus results from thiamine deficiency in chronic alcoholics?

Wernicke-Korsakoff syndrome—Remember: Wobbly-Konfabulations (associated with bilateral mammillary body necrosis)

What am I high on?

Central nervous system (CNS) and respiratory depression, euphoria, pinpoint pupils, nausea, and ↓ GI motility
Opioids; inspect for track marks along veins
Psychomotor agitation, dilated pupils, euphoria, ↑ HR and BP, prolonged wakefulness and attention, delusions, ↑ pain threshold
Amphetamines
All of the above, plus tactile hallucinations, angina, and sudden cardiac death
Cocaine
Belligerence, psychomotor agitation, nystagmus, ataxia, homicidality, psychosis, delirium, ↑ HR, and fever
Phencyclidine hydrochloride (PCP)
Delusions, visual hallucinations, postuse “flashbacks”
Lysergic acid diethylamide (LSD)
Euphoria, ↑ appetite, dry mouth, paranoid delusions, erythematous conjunctiva
Marijuana
Disinhibition, emotional lability, slurred speech, ataxia, blackouts, coma
Alcohol

What is the drug of choice for opioid overdose?

Naloxone and naltrexone (competitively inhibit opioid receptors)

Which drug is used for heroin detoxification?

Methadone (long-acting oral opioid)

PSYCHOLOGY

What are the three parts of Freud’s structural theory of the mind?

1. Id
2. Superego
3. Ego

Which of these parts is described by the following statements:

- Represents conscience and moral values
  Superego
- Controlled by primitive wishes and pleasures; represents instinctive sexual and aggressive drives
  Id
- Bridges unconscious mind and external world
  Ego

What Freudian term encompasses repressed sexual feelings of a child for the opposite-sex parent, plus a rivalry with the same-sex parent?
  Oedipus complex

What type of insight therapy, developed by Freud, may be useful for chronic personality problems?
  Psychoanalysis

What describes a scenario in which a patient’s unconscious feelings from past relationships are experienced in the present relationship with the physician?
  Transference reaction

What reaction occurs when the physician unconsciously reexperiences feelings about his/her parents (or other important persons) with the patient?
  Countertransference reaction

Name the four mature ego defense mechanisms:

1. Suppression
2. Altruism
3. Sublimation
4. Humor

Note: defense mechanisms are automatic and unconscious.

Name the type of learning that is described by each of the following statements:

- Reflexive response is elicited by a learned stimulus
  Classical conditioning
- Tendency of an organism to follow the first thing they see after birth
  Imprinting
- Behavior is eliminated when not reinforced
  Extinction
- Behavior is determined by its consequences
  Operant conditioning
- Unwanted behavior is paired with painful stimulus
  Aversive conditioning
Type of classical conditioning where the subject learns that it cannot escape a painful stimulus
Learned helplessness
In what type of reinforcement schedule is a reward presented after a random, unpredictable number of responses?
Variable ratio (slowest extinction when not rewarded); example = slot machine
In what type of reinforcement schedule is a reward presented after every response?
Continuous (rapid extinction when not rewarded); example = vending machine
Criteria for mental retardation begin below what IQ level?
Less than 70 (2 SD below the mean of 100)

PSYCHIATRY

Name the type of amnesia described below:
Inability to remember things that occurred before insult to CNS
Retrograde amnesia
Inability to remember things that occurred after a CNS injury → no new memory formation
Anterograde amnesia
Complication of electroconvulsive therapy (ECT)
Retrograde amnesia
Thiamine deficiency causing bilateral mammillary body necrosis; seen in alcoholics
Korsakoff (anterograde) amnesia

Delirium or dementia?
Waxing and waning level of consciousness
Delirium
Rapid onset; transient
Delirium
Characterized by memory loss
Dementia (think deMEMtia)
Associated with disturbances in sleep wake cycle
Delirium
Often irreversible
Dementia
Associated with changes in sensorium Delirium (hallucinations and illusions)
Delirium
Name four major causes of delirium:

“HIDE”:
1. Hypoxia
2. Infection (often UTIs)
3. Drugs
4. Electrolyte abnormalities

What is the most common etiology for dementia?
Dementia of Alzheimer type (DAT) = 70% to 80% of cases

Name some other etiologies for dementia:

“DEMENTIASS”
Degenerative diseases (Parkinson, Huntington)
Endocrine (thyroid, pituitary, parathyroid)
Metabolic (electrolytes, glucose, hepatorenal dysfunction, ETOH)
Exogenous (CO poisoning, drugs, heavy metals)
Neoplasia
Trauma
Infection (encephalitis, meningitis, cerebral abscess, syphilis, prion diseases, HIV, Lyme disease)
Affective disorders (depression may mimic dementia)
Stroke (multi-infarct dementia, ischemia, vasculitis). Note: vascular causes ~10% of dementias
Structure (normal-pressure hydrocephalus [NPH]).
Note: NPH is one of the few reversible causes of dementia.

Mood Disorders

Name the nine key features of major depressive disorder (MDD):

“SIG E CAPSS”
1. Sleep changes (insomnia/hypersomnia)
2. Inability to experience pleasure, Interest decreases
3. Guilt or feelings of worthlessness
4. Energy ↓ (fatigue)
5. Concentration ↓, indecisiveness increases
6. Appetite disturbance with weight change (> 5% body weight in 1 month)
7. Psychomotor changes (agitation or retardation)
8. Suicidal ideations
9. Sadness (depressed mood for most of day)

What features are required to make the diagnosis of MDD?
Two episodes (involving five of the above nine including # 1 or 2) of impaired functioning for 2 weeks, separated by 2 months

What is the suicide rate in MDD?
Approximately 15% to 30%

Name the risk factors for suicide:
“SAD PERSONS”
  Sex—male (women > attempts; men > actual suicides)
  Age (↓ 15-24 and the elderly)
  Depression
  Previous attempts = #1 risk factor
  Ethanol
  Rational thought
  Sickness
  Organized plan
  No spouse
  Social support lacking

What is the first-line pharmacotherapy for MDD?
SSRIs

Name two other alternate pharmacotherapies:
  1. Tricyclic antidepressants (TCAs)
  2. Monoamine oxidase inhibitors (MAOIs)

What is a safe, effective treatment for refractory MDD?
ECT

What is the distinctively abnormal, elevated, expansive mood that lasts > 1 week or is severely impairing (eg, requiring hospitalization)?
Manic episode

What are the seven key features of mania?
“DIG FAST” (at least three of the following for diagnosis):
  1. Distractibility
  2. Insomnia
  3. Grandiosity
  4. Flight of ideas or racing thoughts
  5. Psychomotor Agitation
  6. Speech that is pressured (hypverbal)
  7. Thoughtlessness (↑ pleasurable activities with ↑ consequences)

Name the following mood disorders:
  Chronic disorder > 2 years (alternating hypomania and mild depression); no period of euthymia > 2 months and no significant impairment
  Cyclothymia
Less severe features for several days that are *not* impairing; no psychotic features

**Hypomania**

**History of major depressive episodes and at least one hypomanic episode**

**Bipolar II disorder**

**Manic episodes that often alternate with depressive episodes**

**Bipolar I disorder**

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**Somatoform Disorders**

Name the somatoform disorder associated with each of the following descriptions:

- **Preoccupation with an imagined physical defect, causing significantly impaired social and occupational functioning**
  - Body dysmorphic disorder

- **Multiple, unrelated physical complaints leading to excessive medical attention seeking and severely impaired functioning**
  - Somatization disorder (requires four pain, two GI, one sexual/GU, and one pseudoneurologic complaints). **Note:** cannot be intentional or fake

- **Prolonged preoccupation with concerns of having a serious illness (despite negative medical work-ups) and exaggerated attention to bodily or mental sensations**
  - Hypochondriasis

- **Conscious simulation of physical or psychologic illness solely to receive attention from medical personnel**
  - Factitious disorder (Munchausen syndrome). **Note:** technically *not* a somatoform disorder because it is intentional

- **Intentionally simulating illness for personal gain (usually financial)**
  - Malingering. **Note:** also *not* a somatoform disorder; suspect in cases involving litigation

- **Sudden onset of motor/sensory neurologic disorder following traumatic emotional event**
  - Conversion disorder

Name the type of gain associated with each of the following descriptions:

- **Interpersonal or social advantages gained indirectly from illness**
  - Secondary gain

- **Benefits of illness on the patient’s internal psychic economy**
  - Primary gain

- **Advantage gained by the caretaker**
  - Tertiary gain

Name the type of anxiety disorder associated with each of the following:
Maladaptive reaction to environmental or psychologic stress that interferes with functioning and does not remit after the stress ends
Adjustment disorder
Marked, persistent fear of an object/situation that is excessive and unreasonable → stimulus is avoided; patient has insight (treat by exposure therapy)
Specific phobia
Occurs after a person is subjected to a traumatic event; lasts >1 month; may be debilitating
Posttraumatic stress disorder (PTSD)
Symptoms of PTSD that occur within 4 weeks of the stressor and last 4 weeks
Acute stress disorder
Moments of intense fear characterized by palpitations, choking sensation, GI upset, perspiration, chest pain, and chills
Panic disorder
Excessive worrying for the majority of days over the past 6 months that causes significant impairment
Generalized anxiety disorder
Recurrent, intrusive, senseless thoughts and impulses; plus the repetitive behaviors driven by the will to decrease the anxiety caused by them
Obsessive-compulsive disorder (OCD)

Name the dissociative disorder characterized by the following statements:
Two or more separate personalities in one individual; ↑ in women and sexually abused
Dissociative identity disorder (formerly multiple personality disorder)
A complete, often transient, inability to remember important personal information
Dissociative amnesia
Amnesia plus sudden wandering from home and taking on a different identity
Dissociative fugue

Psychoses

Give the appropriate term for each of the following psychotic symptoms:
False belief or wrong judgment held with conviction despite incontrovertible evidence to the contrary
Delusion
False perception of an actual external stimulus
Illusion
Thought disorder whereby ideas are not logically connected to those that occur before or after
Loose association
Misinterpreting others’ actions or environmental cues as being directed toward one’s self when, in fact, they are not
Ideas of reference
Subjective perception of an object or event when no such external stimulus exists
Hallucination

Name the psychotic disorder characterized by each of the following findings:
Two or more psychotic symptoms and disturbed behavior for > 6 months; results in impaired functioning
Schizophrenia
Psychotic symptoms lasting 1 to 6 months
Schizophreniform disorder
Psychotic symptoms lasting > 1 day, but 1 month (often with obvious precipitating psychosocial stressor)
Brief psychotic disorder
Fixed, nonbizarre delusional system; without other thought disorders or impaired functioning
Delusional disorder
Symptoms of major mood disorder as well as of schizophrenia (with psychotic features occurring before mood disturbance); chronic social and occupational impairment
Schizoaffective disorder
Clouded consciousness, predominantly visual hallucinations, often occurring in inpatient setting
Psychotic disorder due to a general medical condition
Adopting the delusional system of a psychotic person
Shared psychotic disorder (Folie-à-deux)

Name the five subtypes of schizophrenia:
1. Disorganized
2. Catatonic
3. Paranoid
4. Undifferentiated
5. Residual

Give two examples of positive symptoms of schizophrenia:
1. Hallucinations
2. Delusions

Positive symptoms respond best to what type of drugs?
Give four examples of negative symptoms that are characteristic of schizophrenia:

The 4 A’s:
1. Affect flat
2. Alogia
3. Anhedonia
4. Avolition

Negative symptoms respond best to what type of drugs?
Atypical antipsychotics. Note: worse prognosis if negative symptoms predominate

Childhood Disorders

Name the disorder of childhood described by each of the following statements:
Repetitive behaviors (in patient 18 y/o) that violate social norms; may exhibit physical aggression, cruelty to animals, vandalism, and robbery, along with truancy, cheating, and lying
Atypical antipsychotics. Note: worse actions)
Recurrent pattern of negativistic, hostile, and disobedient behavior toward authority figures; loss of temper and defiance (but not theft or lying)
Oppositional defiant disorder (predominantly words)
Developmentally inappropriate degrees of inattention, impulsiveness, and hyperactivity at home, in school, and in social situations
Attention deficit hyperactivity disorder (ADHD)
Pervasive developmental disorder (PDD) with stereotyped movements and non-progressive impairments in social interactions, communication, and behavior
Autism
Progressive syndrome of autism, dementia, ataxia, and purposeless hand movements; regression of development; mainly in girls
Rett syndrome
PDD with severe impairment in social skills and repetitive behaviors, leading to impaired social and occupational functioning but without significant delays in language development
Asperger disorder

Personality Disorders

List the three cluster A personality disorders:
“Weird”
1. Paranoid
2. Schizoid
3. Schizotypal

List the four cluster B personality disorders:
“Wild”
1. Histrionic
2. Borderline
3. Antisocial
4. Narcissistic

List the three cluster C personality disorders:
“Worried”
1. Avoidant
2. Obsessive-compulsive
3. Dependent

Name the personality disorder characterized by each of the following statements:
Socially inhibited, sensitive to rejection, feels inferior
Avoidant (C)
Peculiar appearance, interpersonal awkwardness, “magical” or odd thought patterns, no psychosis
Schizotypal (A)
Impulsive, unstable mood, chaotic relationships, feels empty and alone, self-mutilation, females >> males
Borderline (B)
Sense of entitlement, grandiosity, lacks empathy for others, insists on special treatment when ill
Narcissistic (B)
Suspicious and distrustful, uses projection as primary defense mechanism
Paranoid (A)
Lacks self-confidence, submissive, and clingy
Dependent (C)
Unable to maintain intimate relationships, extroverted, melodramatic, sexually provocative
Histrionic (B)
Disregards and violates rights of others, criminality, males > females; if 18 y/o = conduct disorder
Antisocial (B)
Lifelong pattern of voluntary social withdrawal, no psychosis, shows minimal emotions
PHARMACOLOGY—PSYCHOPHARMACOLOGY

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and unique toxicity (TOX) (if any)

Antidepressants

TCAs (imipramine, clomipramine, amitriptyline, desipramine, nortriptyline, doxepin, amoxapine)
MOA: prevents reuptake of NE and 5-HT
IND: depression, enuresis (imipramine), depression in elderly (nortriptyline), OCD (clomipramine), depression with psychotic features (amoxapine), neurologic pain
TOX: sedation (desipramine is least sedating), anticholinergic effects, lethal in overdose → respiratory depression, hyperpyrexia, and Tri-C’s: Cardiac arrhythmia, Convulsions, Coma

SSRIs (fluoxetine, paroxetine, sertraline, citalopram, fluvoxamine, escitalopram)
MOA: selectively blocks reuptake of 5-HT (usually requires 2-3 weeks to take effect)
IND: depression, premenstrual syndrome (fluoxetine), OCD (fluvoxamine)
TOX: agitation, insomnia, sexual dysfunction, “serotonin syndrome” with MAOIs (muscle rigidity, hyperthermia, cardiovascular collapse)

Bupropion
MOA: heterocyclic agent, mechanism not well known
IND: depression, smoking cessation
TOX: agitation, seizures, insomnia (↓ sexual side effects)

Trazodone
MOA: mainly inhibits serotonin reuptake
IND: depression
TOX: postural hypotension, sedation, priapism

Venlafaxine
MOA: inhibits 5-HT and NE reuptake
IND: depression, generalized anxiety disorder
TOX: stimulant effects, minimal effects on P-450

Mirtazapine
MOA: 5-HT₂ receptor antagonist and α₂-antagonist → ↑ NE and 5-HT release
IND: depression
TOX: sedation, ↑ appetite, ↑ cholesterol
MAOIs (TIP: T ranylcypromine, I socarboxazid, phenelzine)
MOA: nonselective MAOIs
IND: atypical depressions, anxiety disorders, pain disorders, eating disorder
TOX: hypertensive crisis with tyramine or meperidine ingestion, “serotonin syndrome” with SSRIs
Lithium
MOA: prevents generation of inositol triphosphate (IP₃) and diacylglycerol (DAG) ²° messenger systems
IND: bipolar disorder (prevents and treats acute mania)
TOX: hypothyroidism, nephrogenic DI, teratogenesis (Ebstein anomaly)
Carbamazepine
MOA: blocks sodium channels and inhibits action potentials
IND: bipolar disorder, mixed episodes, and rapid cycling form
TOX: hematologic SEs, elevated LFTs, teratogenesis (neural tube defects)
Valproic acid
MOA: increases CNS levels of GABA
IND: bipolar disorder, mixed manic episodes, and rapid cycling form
TOX: hepatotoxicity, thrombocytopenia, teratogenesis (neural tube defects)

Antipsychotics

What is the name for the stereotyped oral-facial movements that occur as a result of long-term antipsychotic use?
Tardive dyskinesia

Describe the chronology of extrapyramidal side effects from neuroleptic medications:
Rule of 4’s: 4 hours—acute dystonia, 4 days—akinesia, 4 weeks—akathesia, 4 months—tardive dyskinesia (usually irreversible)

What is the characteristic triad of neuroleptic malignant syndrome (NMS)?
Muscle rigidity, autonomic instability, and hyperpyrexia

What is the treatment for NMS?
Dantrolene and DA agonists

For each of the following drugs, provide:
1. The mechanism of action (MOA)
2. Indication(s) (IND)
3. Significant side effects and unique toxicity (TOX) (if any)
Typical antipsychotics—high potency (haloperidol, perphenazine, trifluoperazine)

**MOA:** block D\(_2\) DA receptors (less blockade of \(\alpha_2\), muscarinic, and histaminic receptors)

**IND:** schizophrenia, psychosis (especially positive symptoms)

**TOX:**↑ neurologic (eg, extrapyramidal) SEs, NMS, tardive dyskinesia, Parkinsonism, hyperprolactinemia

Typical antipsychotics—low potency (chlorpromazine, thioridazine)

**MOA:** block D\(_2\) DA receptors (more blockade of \(\alpha_2\), muscarinic, and histaminic receptors)

**IND:** schizophrenia, psychosis

**TOX:**↓ neurologic SEs, ↑ anticholinergic and endocrine SEs; cardiac conduction defects and retinal pigmentation (thioridazine), corneal and lenticular deposits (chlorpromazine)

Atypical antipsychotics (clozapine, risperidone, olanzapine, quetiapine)

**MOA:** block 5-HT\(_2\); block D\(_4\) and D\(_1\) > D\(_2\) receptors

**IND:** schizophrenia, psychosis (especially negative symptoms); OCD/anxiety disorder (olanzapine)

**TOX:**↓ anticholinergic and extrapyramidal symptoms (EPS); metabolic syndrome (hyperlipidemia, glucose intolerance), agranulocytosis (clozapine)

**MEDICAL ETHICS**

**What are four key components to informed consent?**

The patient must:

1. Understand the health implications of their diagnosis
2. Be informed of risks, benefits, and alternatives to treatment
3. Be aware of outcome if they do not give their consent
4. Have the right to withdraw consent at any time

**Name four exceptions to informed consent:**

1. Patient not legally competent to make decisions
2. In an emergency (implied consent)
3. Patient waives the right to informed consent
4. Therapeutic privilege—withholding info that would severely harm the patient or undermine decision-making capacity if revealed

**What are five situations in which parent/legal guardian consent is not required to treat a minor?**
1. Emergencies
2. STDs
3. Prescription of contraceptives
4. Treatment of ETOH/drug treatment
5. Care during pregnancy

What four criteria qualify a minor as emancipated?
1. Self-supporting
2. In the military
3. Being married
4. Having children that they support

What type of directive is based on the incapacitated patient’s prior statements and decisions?
Oral advance directive (substituted judgment standard)

What type of written advance directive gives instructions for the patient’s future health care should he/she become incompetent to make decisions?
Living will

What type of document allows the patient to designate a surrogate to make medical decisions in case the patient loses decision-making capacity?
Durable power of attorney

Name the ethical responsibility of the physician described by each of the following statements:
Requires physicians to “do no harm”
Nonmaleficence
Requires physicians to act in the best interests of the patient
Beneficence (may conflict with patient autonomy)
Demands respect for patient privacy and autonomy
Confidentiality

Name five exceptions to confidentiality:
1. Suspected child and/or elder abuse
2. Suicidal/homicidal patient
3. Impaired automobile driver
4. Specific infectious diseases—physician duty to report to public officials or individuals at risk
5. Tarasoff decision-law requiring physician to directly inform/protect potential victim from harm

What elements are required in order to prove a malpractice claim?
The “4 D’s”: must prove that the physician showed Dereliction (deviation from standard of care) of a Duty that caused Damages Directly to the patient

What is the legal standard of death?
Failure to meet cardiorespiratory criteria and irreversible cessation of all brain functions (including brainstem)

**BIOSTATISTICS**

For each description, name the proper term and the equation used to calculate the value described below:

- **Probability that a person without the disease will be correctly identified**  
  Specificity $\frac{TN}{TN + FP}$

- **Probability that a person who tests positive actually has the disease**  
  Positive predictive value $\frac{TP}{TP + FP}$

- **Probability that a person who has a disease will be correctly identified**  
  Sensitivity $\frac{TP}{TP + FN}$

- **Total number of cases in a population at any given time**  
  Prevalence $\frac{TP + FN}{\text{entire population}}$

- **Number of new cases that arise in a population over a given time interval**  
  Incidence $\frac{\text{Prevalence} \times \text{duration of disease}}{\text{approximately}}$

- **Used in case-control studies to approximate the relative risk if the disease prevalence is too high**  
  Odds ratio $\frac{TP \times TN}{FP \times FN}$

- **Used in cohort studies to compare incidence rate in exposed group to that in unexposed group**  
  Relative risk $\frac{(TP/[TP + FP])/(FN/[FN + TN])}{\text{approximately}}$

- **Probability that patient with a negative test actually has no disease**  
  Negative predictive value $\frac{TN}{FN + TN}$

**How are incidence and prevalence related?**  
Incidence $\times$ disease duration = prevalence  
Prevalence $>$ incidence for chronic diseases; prevalence $=$ incidence for acute diseases

**What quality is desirable for a screening tool?**  
High sensitivity (**SNOUT**—SeNsitivity rules OUT)

**What quality is desirable for a confirmatory test?**  
High specificity (**SPIN**—Specificity rules IN)

**Name four ways to reduce bias:**
1. Use of placebo  
2. Blinded studies (single, double)  
3. Crossover studies (each subject is own control)  
4. Randomization
Name the type of statistical distribution described below:
- Asymmetry with tail to the right
- Positive skew
- **Two peaks**
- Bimodal
- **Scores cluster in the high end**
- Negative skew
- **Bell-shaped**
- Normal (Gaussian)

What percent of the area under a normal curve falls within 1, 2, and 3 standard deviations (SD) of the mean?
- 68% (1 SD), 95% (2 SD), 99.7% (3 SD)

How is standard error of the mean (SEM) calculated?
\[
\sigma / \sqrt{n}
\]
square root of sample size

Name the term for each of the following descriptions:
- Refers to the reproducibility of a test
  Reliability
- Refers to the appropriateness of a test (whether the test measures what it is supposed to)
  Validity
- Absence of random variation in a test; consistency and reproducibility of a test
  Precision
- Closeness of a measurement to the truth
  Accuracy
- **Test that compares the difference between two means**
  t-test
- **Test that analyzes the variance of three or more variables**
  Analysis of variance (ANOVA)
- **Test that compares percentages or proportions**
  \( \chi^2 \) (chi-squared test)
- **Absolute value that indicates the strength of a relationship**
  \( r \) (always between -1 and 1)
- **Observational study where the sample is chosen based on presence/absence of risk factors**
  Cohort study (eg, prospective, historical)
- **Experimental study comparing benefits of two or more alternative treatments**
  Clinical trial
Observational study where the sample is chosen based on disease presence/absence
Case-control study (usually retrospective)
Assembling data from multiple studies to achieve great statistical power
Meta-analysis
Hypothesis postulating that there is no difference between groups
Null hypothesis ($H_0$)
Error of mistakenly rejecting $H_0$ (stating that there is a difference when there really is not)
Type I error ($\alpha$)
Error of failing to reject $H_0$ (stating there is no difference when there really is)
Type II error ($\beta$)
Probability of rejecting $H_0$ when it is in fact false
Power (1-$\beta$)
Probability of making an $\alpha$ error
$P$ value

**PUBLIC HEALTH/EPIDEMIOLOGY**

Name four reportable STDs:
1. Gonorrhea
2. Syphilis
3. Hepatitis B
4. Acquired immunodeficiency syndrome (AIDS) (nonreportable = HIV, chlamydia, genital herpes)

What is the leading cause of mortality in each of the following age groups:

1 y/o
Congenital anomalies
1 to 14 y/o
Unintentional injuries
15 to 24 y/o
Unintentional injuries (mostly car accidents)
25 to 64 y/o
Cancer (#1 lung, #2 breast/prostate, #3 colon)
65 years and older
Heart disease

What is 1° disease prevention?
Aims to prevent disease occurrence (eg, vaccination, education)

**What is 2° disease prevention?**
Early detection of disease; screening programs

**What is 3° disease prevention?**
Reduces disability resulting from disease (eg, physical therapy for stroke)

**What is the current definition of “obese”?**
BMI > 30, BMI > 25 is overweight

**Approximately what percentage of the US population is obese?**
~30%, > 50% overweight

**What is the divorce rate in the United States?**
~50%

**Name three risk factors for divorce:**
1. Teenage marriage
2. Mixed religions
3. Low SES. **Note:** peaks during second and third years

**What is the criterion to qualify for hospice care?**
Medically anticipated death within 6 months

**What federal program addresses health care needs of the elderly?**
MedicareE (Elderly)

**What federal and state program addresses health care needs of the underprivileged?**
Medicaid (Destitute)

**What 1996 law helps to protect rights to health coverage during events such as changing or losing jobs, pregnancy, moving, or divorce?**
Health insurance portability and accountability act (HIPAA)
CHAPTER 14
Make the Diagnosis

NUTRITION

1-year-old (y/o) impoverished child presents with lethargy and poor wound healing; physical examination (PE): low-grade fever, pallor, oral mucosal petechiae, and bleeding gums.
   Scurvy
50-y/o with history of (h/o) long-term treatment of psoriasis with methotrexate presents with nausea and fatigue; PE: within normal limits (WNL); workup (W/U): MCV > 100, hypersegmented neutrophils, and normal vitamin B12 levels.
   Folic acid deficiency
42-y/o alcoholic presents with ataxia and shortness of breath (SOB); PE: nystagmus, cardiomegaly with flow murmur, ↓ DTRs, ↓ peripheral sensation, and hepatomegaly.
   Beriberi
48-y/o Scandinavian woman presents with weakness, ataxia, and SOB; PE: ↓ balance and vibratory sensation in lower extremities; W/U: MCV > 100, hypersegmented PMNs, and positive Schilling test.
   Pernicious anemia

MICROBIOLOGY AND INFECTIOUS DISEASES

4-y/o with a superficial skin infection consisting of erythematous pustules with honey-colored scabs.
   Impetigo, most commonly due to Staphylococcus aureus
6-y/o child with poor hygiene presents with complaints of severe perianal itching that is worse at night; W/U: a “scotch tape test” reveals eggs visualized under the microscope.
   Pinworm infection
36-y/o man presents with flu-like symptoms since moving to a farm in Ohio 2 months ago; PE: fever and generalized lymphadenopathy; chest x-ray (CXR): bilateral hilar adenopathy.
   Histoplasmosis
Patient with recent h/o antibiotic use presents with fever, bloody diarrhea, and abdominal pain; PE: tender abdominal examination, guaiac + stool; complete blood count (CBC): leukocytosis; colonoscopy: tan nodules seen attached to erythematous bowel wall with superficial erosions.

Pseudomembranous colitis (Clostridium difficile colitis)

18-y/o student returns to clinic with a rash after being treated with ampicillin for fever and sore throat; PE: tonsilar exudates and enlarged posterior cervical lymph nodes; W/U: ↑ lymphocytes and ⊕⊕ heterophile antibody test.

Infectious mononucleosis due to Epstein Barr virus (EBV)

28-y/o with h/o treatment for 2° syphilis 5 hours ago with intramuscular (IM) penicillin presents with fever, chills, muscle pain (myalgias), and headache.

Jarisch-Herxheimer reaction

33-y/o northern European with h/o eating raw fish presents with shortness of breath and weakness; W/U: megaloblastic anemia, operculated eggs on stool examination.

Diphyllobothrium latum infection (with vitamin B₁₂ deficiency)

17-y/o swimmer presents with pain and discharge from the left ear; PE: movement of tragus is extremely painful; Gram stain shows gram-negative rods.

Otitis externa (most likely due to Pseudomonas aeruginosa)

10-y/o with sickle cell disease and recent h/o prodromal illness presents with sudden-onset pallor, fatigue, and tachycardia; CBC: pancytopenia with reticulocytes 1%.

Parvovirus B19 aplastic crisis

44-y/o parrot owner presents with fever, chills, headache, and cough; PE: Horder spots on abdomen and splenomegaly; CXR: bilateral, interstitial infiltrates.

Psittacosis

33-y/o epileptic with recent loss of consciousness presents with fever and cough with purulent, putrid sputum; W/U: Gram stain reveals mixed oral flora; CXR: consolidation of right lower lobe.

Aspiration pneumonia

50-y/o man presents with a fever of unknown origin. One month ago he had a dental procedure. He has a history of rheumatic heart disease; PE: significant for a heart murmur, splinter hemorrhages, Janeway lesions, Roth spots, and Osler nodes.

Subacute bacterial endocarditis due to Streptococcus viridans

9-y/o with recent viral prodromal illness presents to ER vomiting and lethargic after being given aspirin for fever; W/U: impaired liver function; computed tomography (CT): cerebral edema.

Reye syndrome

15-y/o new pet owner presents with painful axillary lumps and fever; PE: cervical lymphadenopathy.

Catscratch disease
2-month-old with maternal h/o rash and flu in first trimester presents with a rash and failure to attain milestones; PE: microcephaly, cataracts, jaundice, continuous machinery-like murmur at left upper sternal border, and hepatosplenomegaly (HSM).

Congenital rubella

8-y/o from Connecticut presents with fever, rash, headache, and joint pain after playing in the woods; PE: distinctive macule with surrounding 6 cm target-shaped lesion.

Lyme disease

35-y/o man with h/o urinary catheterization presents with fever, chills, dysuria, and perineal pain; PE: swollen, tender, hot prostate; urinalysis (UA): WBCs and culture ⊕ for *Escherichia coli*.

Acute bacterial prostatitis

38-y/o man with h/o asthma presents with recurrent fever, wheezing, and cough productive of brown mucous plugs; CBC: eosinophilia, high IgE titers; CXR: mucoid impaction of dilated central bronchi.

Allergic bronchopulmonary aspergillosis

6-y/o unvaccinated child presents with rhinorrhea, cough, conjunctivitis; PE: oral lesions are noted which are bluish with an erythematous border.

Measles

37-y/o man with a recent h/o upper respiratory infection (URI) presents with fever and severe chest pain; PE: friction rub and Kussmauls sign; W/U: ↑ ESR, normal cardiac enzymes, and diffuse ST elevations on ECG.

Acute pericarditis

4-y/o presents with barking cough, fever, and rhinorrhea; PE: respiratory distress and tachypnea; x-ray of soft tissues of neck reveals “steeple sign.”

Croup

18-y/o sexually active woman with h/o treatment for purulent vaginitis presents with a fever and tenderness, warmth, and swelling of her right knee.

Gonococcal arthritis

Newborn presents with rash and maternal h/o intrauterine growth retardation (IUGR) and flu during first trimester; PE: petechial rash, chorioretinitis, microcephaly, ↓ hearing, and HSM; W/U: ↓ platelets and periventricular calcifications on head CT.

Congenital cytomegalovirus (CMV)

25-y/o West Virginian man presents with fever, headache, myalgia, and a petechial rash that began peripherally but now involves his whole body, even his palms and soles; W/U: shows +OX19 and OX2 Weil-Felix reaction.

Rocky Mountain spotted fever
10-y/o presents with fevers and a pruritic rash spreading from the trunk to the arms; PE: vesicles of varying stages.

Varicella

29-y/o athlete presents with a red, pruritic skin eruption with an advancing peripheral, creeping border on the forearm; W/U shows septate hyphae in KOH scraping.

Tinea corporis (ringworm)

8-y/o presents with fever, photophobia, stiff neck, and headache; PE: Kernig and Brudzinski signs; lumbar puncture shows normal glucose and ↓ WBCs.

Viral meningitis

21-y/o presents with nausea, vomiting, bloating, and foul-smelling stools on returning from a camping trip; W/U: binucleate, flagellated trophozoites in stool.

Giardiasis

14-y/o adolescent boy with h/o recent travel to Mexico now presents with jaundice and dark yellow urine; PE: icterus and firm hepatomegaly; W/U: ↑ bilirubin (BR), ↑ LFTs with alanine transaminase (ALT) > aspartate transaminase (AST).

Hepatitis A infection

26-y/o sexually active, native Caribbean presents with painless, beefy-red ulcers of the genitalia and inguinal swelling; W/U: Donovan bodies on Giemsa-stained smear.

Granuloma inguinale

Patient presents with sudden onset of severe watery diarrhea, vomiting, and abdominal discomfort 4 hours after eating potato salad at a picnic; the symptoms resolve spontaneously within 24 hours.

Staphylococcus aureus-induced diarrhea

6-y/o with recent h/o sore throat presents with multiple joint pain and swelling, fever, and SOB; PE: erythema marginatum, subcutaneous nodules, and apical systolic murmur; W/U: ↑ ESR and CRP.

Acute rheumatic fever

25-y/o woman presents with malodorous vaginal discharge; W/U: visualization of the discharge under the microscope demonstrates multiple vaginal epithelial cells covered in bacteria.

Bacterial vaginosis due to Gardenella vaginalis

73-y/o presents with a painful, unilateral, vesicular rash in the distribution of the CN V₁; cornea shows diminished sensation and stains with fluorescein.

Herpes zoster ophthalmicus

29-y/o missionary with h/o travel to rural India presents with high fever and right upper quadrant (RUQ) pain; PE: severe hepatomegaly and dullness over right lower lung; abdominal CT: large, cavitating lesion in liver.

Amebic liver abscess
25-y/o sexually active man presents with dysuria, irritation, and cloudy discharge; W/U: a Gram stain of the discharge reveals neutrophils, but no organisms are visualized.

Nongonococcal urethritis, most likely due to *Chlamydia trachomatis*

31-y/o obese woman presents with pruritis in her skin fold beneath her pannus; PE: whitish curd-like concretions beneath the abdominal panniculus; W/U shows budding yeast on 10% KOH preparation.

Cutaneous candidiasis

**NEUROSCIENCE**

55-y/o man presents with lower extremity weakness and muscle atrophy; PE: positive Babinski reflex, upper extremity hyperreflexia, and spasticity.

Amyotrophic lateral sclerosis (ALS)

65-y/o presents with a gradual decline in memory and inability to complete activities of daily living; W/U: CT shows marked enlargement of ventricles and diffuse cortical atrophy.

Alzheimer disease

65-y/o woman with h/o spinal metastases from breast cancer presents with pain radiating down the back of her leg, saddle anesthesia, urinary retention; PE: absent ankle jerk reflexes; W/U: CT shows large bony fragment in lumbar spinal canal.

Cauda equina syndrome

65-y/o man with h/o carotid atherosclerosis presents with aphasia and right-sided weakness; PE: dense right-hemiparesis, positive Babinski on right; W/U: CT shows left middle cerebral artery (MCA) territory infarction and edema.

Left MCA cerebrovascular accident

20-y/o presents with nausea, vomiting, and headache 2 hours after being hit in the temple with a baseball; patient lost consciousness initially but recovered quickly; W/U: CT shows lens-shaped, right-sided hyperdense mass adjacent to temporal bone.

Epidural hematoma

40-y/o with h/o *Campylobacter* enteritis 1 week ago presents with ascending symmetric muscle weakness; CSF shows ↑ protein, normal cellularity (albuminocytologic dissociation).

Guillain-Barré syndrome

37-y/o man with family history (FH) of a father who died at 45 with worsening tremor and dementia presents with poor memory, depression, choreiform movements, and hypotonia; W/U: MRI demonstrates marked atrophy of the caudate nucleus.
Huntington disease
25-y/o with h/o bilateral temporal lobe contusions 1 week ago presents with a sudden increase in appetite, sexual desire, and hyperorality.

Klüver-Bucy syndrome
30-y/o woman with insidious onset of diplopia, scanning speech, paresthesias, and numbness of right upper extremity and urinary incontinence; W/U: MRI shows discrete areas of periventricular demyelination and CSF analysis is positive for oligoclonal bands.

Multiple sclerosis
65-y/o woman with h/o neurofibromatosis type 2 presents with headache, right-sided leg jerking, and worsening mental status; PE: papilledema and right-sided pronator drift; W/U: CT scan shows dural-based, enhancing, left-sided softball-sized tumor.

Meningioma
55-y/o with a h/o squamous cell carcinoma of the lung presents with nausea, vomiting, headache, and diplopia; PE: papilledema, left oculomotor palsy, right pronator drift; MRI: multiple round, hyperintense cortical and cerebellar lesions.

Metastases to brain
30-y/o woman presents with unilateral throbbing headache, nausea, photophobia, scotoma; similar symptoms occur monthly at the same time of her menstrual cycle.

Migraine
65-y/o with urinary incontinence, loss of short-term memory, and dementia; PE: wide based, magnetic gate; W/U: CT scan shows massively dilated ventricular system.

Normal pressure hydrocephalus
60-y/o presents with gradual onset of pill-rolling tremor; PE: masked facies, stooped posture, festinating gait, cogwheel muscle rigidity.

Parkinson disease
30-y/o presents with loss of libido, galactorrhea, and irregular menses; PE: bitemporal hemianopia; W/U: negative beta human chorionic gonadotropin (β-hCG).

Prolactinoma (prolactin-secreting pituitary adenoma)
45-y/o presents with the gradual onset of sharp pain radiating from his buttocks down his leg that began 2 weeks ago when he began to lift a heavy box; PE: positive straight leg raise test.

Sciatica from acute herniation of a lumbar disc
50-y/o with h/o polycystic kidney disease presents with “worst headache of life,” photophobia, nausea; PE: right eye deviated down and out; W/U: CSF is xanthrochromic.

Subarachnoid hemorrhage from ruptured berry aneurysm
32-y/o man with h/o Arnold-Chiari malformation presents with bilateral upper extremity muscle weakness; PE: loss of pain and temperature sensation, ↓ DTR in upper extremities and scoliosis; MRI shows central cavitation of the thoracic spinal cord.
Syringomyelia
75-y/o alcoholic man on warfarin for h/o atrial fibrillation presents with declining mental status, headache, and papilledema; CT shows crescenteric, hypodense, 2 cm fluid collection along convexity.

Chronic subdural hematoma
36-y/o woman with family h/o renal cell carcinoma presents with gait disturbance and blurred vision; PE: retinal hemangiomas, nystagmus, cerebellar ataxia, dysdiadochokinesia; MRI shows two cerebellar cystic lesions.

von Hippel-Lindau disease
A 50-y/o with h/o alcoholism presents with psychosis, ophthalmoplegia, and ataxia; MRI: mamillary body atrophy and diffuse cortical atrophy.

Wernicke encephalopathy

CARDIOVASCULAR

56-y/o woman presents with dyspnea on exertion (DOE); PE: loud S₁, delayed P₂, and a diastolic rumble; W/U: transesophageal echocardiogram shows mobile, pedunculated left atrial mass.

Atrial myxoma
60-y/o presents with chest pain relieved by sitting up and leaning forward; PE: pericardial friction rub; ECG: diffuse ST segment elevation; echocardiogram: pericardial effusion with thickening of the pericardium.

Acute pericarditis
65-y/o man presents with 1-week h/o fever, DOE, and orthopnea; PE: new, blowing holosystolic murmur at apex radiating into left axilla; W/U: blood cultures show *Viridans* spp. streptococci; echocardiogram: oscillating mass attached to mitral valve.

Acute infective endocarditis
60-y/o presents with dyspnea and palpitations; PE: 20 mm Hg decline in systolic BP with inspiration (pulsus paradoxicus), ↓ BP, jugular venous distention, diminished S₁ and S₂; echocardiogram: large pericardial effusion.

Tamponade
58-y/o man with Marfan syndrome presents with the abrupt onset of “tearing” chest pain radiating to the back; PE: ↓ BP, asymmetric pulses, declining mental status; CXR: widened mediastinum.

Aortic dissection
70-y/o diabetic with hypercholesterolemia presents with angina, syncope, DOE, and orthopnea; PE: diminished, slowly rising carotid pulses, crescendo-decrescendo systolic murmur at second interspace at the right upper sternal border.

Aortic stenosis

80-y/o diabetic with HTN and a h/o rheumatic heart disease presents with left-sided weakness; PE: pulses are irregularly irregular; ECG: absence of P waves and irregularly irregular QRS complexes.

Atrial fibrillation (leading to embolic stroke)

70-y/o with h/o coronary artery disease (CAD) presents with worsening DOE, orthopnea, and paroxysmal nocturnal dyspnea; PE: jugular venous distention, S₃ gallop, positive hepatojugular reflex, bibasilar rales, and peripheral edema; CXR: cardiomegaly, bilateral pleural effusions.

Congestive heart failure (CHF)

50-y/o alcoholic presents with worsening DOE, orthopnea, and paroxysmal nocturnal dyspnea; PE: laterally displaced apical impulse; ECG: four-chamber dilation, mitral and tricuspid regurgitation.

Alcoholic dilated cardiomyopathy

35-y/o man with FH of sudden cardiac death presents with DOE and syncope; PE: double apical impulse, S₄ gallop, holosystolic murmur at apex and axilla; ECG: left ventricular hypertrophy and mitral regurgitation.

Hypertrophic cardiomyopathy

40-y/o black man with a h/o HTN presents with chest pain, dyspnea, and severe headache; PE: BP = 210/130 mm Hg in all four extremities, flame-shaped retinal hemorrhages, papilledema; W/U: negative vanillylmandelic acid (VMA), urine catecholamines, and cardiac enzymes.

Malignant hypertension

35-y/o woman with a h/o rheumatic fever presents with worsening DOE and orthopnea; PE: loud S₁, opening snap and low-pitched diastolic murmur at the apex; CXR: left atrial enlargement.

Mitral stenosis

65-y/o man presents with substernal pressure for the past hour with radiation of the pain into the jaw and left arm, nausea, diaphoresis, and dyspnea; PE: S₄ gallop; W/U: ↑ serum troponin and CK-MB; ECG: ST segment elevation in leads aVL, V₁ to V₆.

Anterior myocardial infarction

PULMONARY
7-y/o with h/o environmental allergies presents in acute respiratory distress; PE: tachypnea, expiratory wheezes, intercostal retractions, accessory muscle usage during respiration; CXR: hyperinflation; CBC: eosinophilia.

Bronchial asthma

60-y/o with a 50 pack-year h/o smoking presents with fever and cough productive of thick sputum for the past 4 months; PE: cyanosis, crackles, wheezes; W/U: Hct = 48, WBC = 12,000; CXR: no infiltrates.

Chronic bronchitis

60-y/o with a 50 pack-year h/o smoking presents with DOE and dry cough, but no chest pain; PE: ↓ breath sounds, ↑ heart rate (HR), hyperresonant chest, distant S1 and S2; CXR: hyperlucent lung fields.

Emphysema

60-y/o with 50 pack-year h/o smoking presents with fatigue, DOE, hoarseness, anorexia; PE: miosis, ptosis, anhydrosis, dullness to percussion at right apex; CXR: large, hilar mass extending into the right superior pulmonary sulcus.

Pancoast tumor (most likely bronchogenic squamous cell carcinoma, causing Horner syndrome)

60-y/o 4 days s/p total knee replacement has a sudden onset of tachycardia, tachypnea, sharp chest pain, hypotension; W/U: arterial blood gas (ABG) shows respiratory alkalosis; ECG: sinus tachycardia; lower extremity venous duplex ultrasound (U/S): clot in right femoral vein.

Pulmonary embolism (most likely from DVT)

30-y/o black woman presents with DOE, fever, arthralgia; PE: iritis, erythema nodosum; W/U: eosinophilia, ↑ serum ACE levels; PFT: restrictive pattern; CXR: bilateral hilar lymphadenopathy, interstitial infiltrates; lymph node biopsy: noncaseating granulomas.

Sarcordosis

40-y/o white man presents with chronic rhinosinusitis, ear pain, cough, dyspnea; PE: ulcerations of nasal mucosa, perforation of nasal septum; W/U: ↑ C-ANCA; U/A: red cell casts; biopsy of nasal lesions: necrotizing vasculitis and granulomas.

Wegener granulomatosis

GASTROENTEROLOGY

20-y/o woman presents with bloody diarrhea and joint pain; PE: abdominal tenderness, guaiac ⊕ stool; laboratory values: ↑ ESR and CRP, HLA-B27 +; colonoscopy: granular, friable muscosa with pseudopolyps throughout the colon.
Ulcerative colitis (UC)  
28-y/o patient with h/o of UC presents with severe abdominal pain, distention, and high fever; PE: severe abdominal tenderness; CBC: leukocytosis; abdominal x-ray (AXR): dilated (> 6 cm) transverse colon.

Toxic megacolon  
cirrhotic patient presents with massive hematemesis; PE: jaundice, ↓ BP, ↑ HR, ascites; W/U: stems pancytopenia, ↑ ALT and AST; EGD: actively bleeding vessel with numerous cherry red spots.

Esophageal varices  
38-y/o man with recent h/o fatigue, excessive thirst, and impotence presents with hyperpigmentation of his skin; PE: cardiomegaly, HSM; W/U: ↑ glucose, ferritin, transferrin, and serum iron.

Hemochromatosis (hereditary)  
19-y/o woman with recent h/o behavioral disturbance presents with jaundice and resting tremor; PE: pigmented granules in cornea and HSM; W/U: ↓ serum ceruloplasmin.

Wilson disease  
29-y/o with h/o intermittent jaundice since receiving blood transfusion after motor vehicle accident (MVA) 2 years ago; PE: RUQ tenderness, hepatomegaly; W/U: negative HBV serology.

Hepatitis C infection  
31-y/o woman presents with 10-month h/o foul-smelling, greasy diarrhea; PE: pallor, hyperkeratosis, multiple ecchymoses, and abdominal distention; W/U: abnormal D-xylose test.

Celiac disease  
60-y/o white man presents with steatorrhea, weight loss, arthritis, and fever; small bowel biopsy shows PAS ⊕ macrophages and gram-positive bacilli.

Whipple disease  
19-y/o Jewish woman with h/o chronic abdominal pain presents with recurrent UTIs and pneumaturia; PE: diffuse abdominal pain; CT: enterovesical fistula; colonoscopy: skip lesions of linear ulcers and transverse fissures giving cobblestone appearance to mucosa.

Crohn’s disease  
21-y/o man presents with hematemesis after ingestion of aspirin and seven shots of whiskey; PE: diaphoretic, ↑ HR, epigastric tenderness; EGD: edematous, friable, reddened gastric mucosa.

Acute gastritis
Patient with h/o peptic ulcer disease (PUD) presents with melena; PE: ↑ HR, diaphoretic, diffuse abdominal pain; W/U: nasogastric tube (NGT) aspirate is bloody; EGD: visible bleeding vessel distal to the pylorus.

Bleeding duodenal ulcer
40-y/o obese, mother of four children presents with constant RUQ pain radiating to right scapula, N/V; PE: fever, tenderness, and respiratory pause induced by RUQ palpation, painful palpable gallbladder; W/U: ↑ WBC, ↑ ALP; U/S: thickened gall-bladder wall, pericholecystic fluid with gallstones present.

Acute cholecystitis
39-y/o man presents with dull, steady epigastric pain radiating to the back after an alcohol binge, N/V; PE: fever, ↑ BP, epigastric tenderness, guarding, and distention; W/U: ↑↑ amylase/lipase, ↑ WBC; AXR: ⊕⊕ sentinel loop and colon cutoff sign.

Acute pancreatitis
65-y/o black man with h/o smoking presents with anorexia, weight loss, pruritis, and painless jaundice; PE: palpable, nontender, distended gallbladder, migratory thrombophlebitis; W/U: ↑ direct BR, ALP, carcinoembryonic antigen (CEA), and CA 19-9.

Pancreatic adenocarcinoma
60-y/o black man with h/o gastroesophageal reflux disease (GERD) presents with weight loss and dysphagia; EGD: partially obstructing mass near GE junction.

Esophageal carcinoma
65-y/o presents with severe worsening left lower quadrant (LLQ) pain, N/V, and diarrhea; PE: fever, LLQ tenderness, local guarding, and rebound tenderness; W/U: ↑ WBC; abdominal CT: edematous colonic wall with localized fluid collection.

Diverticulitis
30-y/o woman presents with periumbilical pain which has now migrated to the RLQ followed by anorexia, N/V; PE: low-grade fever, local RLQ guarding, rebound tenderness, RLQ tenderness on LLQ palpation; W/U: β-hCG negative, ↑ WBC with left shift.

Appendicitis
55-y/o presents with colicky abdominal pain, small-caliber stools, and occasional melena; PE: cachexia, abdominal discomfort, guaiac ⊕ colonoscopy shows obstructing mass seen in ascending colon.

Right-sided colon carcinoma
80-y/o woman presents with halitosis, dysphagia, and regurgitation of undigested foods; W/U: barium swallow shows posterior midline pouch greater than 2 cm in diameter arising just above the cricopharyngeus muscle.

Zenker diverticulum
55-y/o Asian woman with h/o HBV presents with dull RUQ pain; PE: weight loss, painful hepatomegaly, ascites, jaundice; W/U: ↑ ALT/AST, ↑ α-fetoprotein; abdominal CT: mass seen in right lobe of liver.
Hepatocellular carcinoma

55-y/o with h/o choledocholithiasis presents with fever, chills, and RUQ pain; PE: jaundice; W/U: ↑ WBC, BR, and ALP; U/S: stone in common bile duct.

Cholangitis

43-y/o man presents with epigastric pain, diarrhea, and recurrent peptic ulcers; PE: epigastric tenderness; W/U: ↑ fasting gastrin levels, paradoxical ↑ in gastrin with secretin challenge; Octreotide scan: detects lesion in pancreas.
Zollinger-Ellison syndrome

72-y/o presents with recurrent, low-grade, painless hematochezia; PE: guaiac ⊕ stool; colonoscopy reveals slightly raised, discrete, scalloped lesion with visible draining vein in right colon.

Angiodysplasia

63-y/o Japanese man with h/o atrophic gastritis presents with weight loss, indigestion, epigastric pain, and vomiting; PE: supraclavicular lymph node; W/U: anemia, ⊕ fecal occult blood.

Gastric carcinoma

48-y/o with chronic watery diarrhea, hot flashes, and facial redness; PE: shows II/VI right-sided ejection murmur; W/U: ↑ 5-hydroxyindoleacetic acid (5-HIAA) in urine.
Carcinoid syndrome

40-y/o presents with dysphagia, regurgitation, and weight loss; W/U: barium swallow demonstrates dilated esophagus with distal narrowing (bird beak appearance).

Achalasia

16-y/o with strong FH of colorectal CA presents with rectal bleeding and abdominal pain; W/U: anemia; flexible sigmoidoscopy: > 100 adenomatous polyps visualized.

Familial adenomatous polyposis (FAP)

34-y/o bulimic presents with sudden-onset retrosternal pain after vigorous vomiting; upper GI series shows extravasation of contrast into mediastinum.

Boerhaave syndrome

44-y/o heavy smoker presents with heartburn and regurgitation that is worse when lying down and is relieved with antacids; upper GI series reveals mild hiatal hernia.
GERD

5-day-old infant presents with abdominal distention and failure to pass meconium until after a rectal examination; XR shows massively dilated colon.

Hirschsprung disease
39-y/o woman with h/o rheumatoid arthritis presents with fatigue and pruritus; PE: jaundice and HSM; W/U reveals ↑↑ ALP and γ-glutamyl transpeptidase (GGT) and presence of antimitochondrial antibodies.

Primary biliary cirrhosis

2-week-old first-born male infant presents with projectile vomiting and dehydration; PE: visible peristalsis and palpable knot in epigastrum.

Hypertrophic pyloric stenosis

50-y/o with long h/o retrosternal pain drinks and smokes despite undergoing treatment for GERD; biopsy of distal esophagus shows metaplasia.

Barrett's esophagus

34-y/o woman with factor V Leiden deficiency presents with abdominal distention and jaundice; PE: pitting pedal edema, markedly visible leg veins, HSM, and absent hepatojugular reflex; U/S shows obstruction of hepatic veins.

Budd-Chiari syndrome

7-month-old infant presents with vomiting and currant jelly-appearing stools; PE: right-sided, sausage-shaped, palpable mass in abdomen; barium enema (BE) shows telescoping of intestines.

Intussusception

REPRODUCTIVE/ENDOCRINE

31-y/o presents with loss of libido, galactorrhea, and irregular menses; PE: bitemporal hemianopia; W/U: negative β-hCG.

Prolactinoma

7-month-old with history of multiple infections turns cyanotic when aggravated; PE: abnormal facies, cleft palate, heart murmur; W/U: hypocalcemia, tetrology of Fallot.

DiGeorge syndrome (22q11)

Patient presents to clinic with polyuria and polydipsia; W/U: urine specific gravity 1.005, urine osmolality 200 mOsm/kg, hypernatremia.

Diabetes insipidus

30-y/o white woman presents with weight loss, tremor, and palpitations; PE: brisk DTRs, ophthalmopathy, pretibial myxedema; W/U: ↓ TSH, ↑ T4, ↑ T3 index.

Graves disease

40-y/o woman presents with fatigue, constipation, and weight loss; PE: puffy face, cold dry hands, coarse hair, and enlargement of thyroid gland; W/U: ↑ TSH, ↓ T3 and T4, ⊕ antimicrosomal and antithyroglobulin AB.

Hashimoto disease
32-y/o woman with h/o recurrent PUD presents with episodes of hypocalcemia and nephrolithiasis; W/U: fasting hypoglycemia, ↑ gastrin levels, and hypercalcemia.

Multiple endocrine neoplasia (MEN) 1

70-y/o presents with episodal hypertension, nephrolithiasis, and diarrhea; PE: ↑ BP, thyroid nodule; W/U: ↑ calcitonin levels, ↑ urinary catecholamines.

MEN 2

Female patient presents with bone pain, kidney stones, depression, and recurrent ulcers; W/U: hypercalcemia, hypophosphatemia, and hypercalciuria.

Hyperparathyroidism

35-y/o woman presents with weightgain, irregular menses, and HTN; PE: ↑ BP, weight in face and upper back, hirtuism, multiple ecchymoses; W/U: ↑ ACTH levels and suppression with high-dose dexamethasone suppression test.

Cushing disease

50-y/o woman presents with HTN, muscle weakness, and fatigue; W/U: hypokalemia, hypernatremia, and metabolic alkalosis.

Conn syndrome

30-y/o woman presents with progressive weakness, weight loss, N/V; PE: hyperpigmentation of skin, ↓ BP; W/U: hyperkalemia, hyponatremia, and eosinophilia.

Addison disease

40-y/o presents with episodes of HA, diaphoresis, palpitations, and tremor; PE: ↑ BP, ↑ HR; W/U: ↑ in urinary VMA and homovanillic acid.

Pheochromocytoma

17-y/o white adolescent with h/o diabetes mellitus (DM) presents with diffuse abdominal pain, N/V, and slight confusion; PE: ↓ BP, shallow, rapid breathing pattern; W/U: glucose = 300, hypokalemia, hypophosphatemia, and metabolic acidosis.

Diabetic ketoacidosis (DKA)-DM type 1

60-y/o diabetic obese patient found at home confused and disoriented; PE: ↓ BP, ↑ HR; W/U: glucose > 1000.

Hyperosmolar hyperglycemic non-ketotic (HHNK)-DM type 2

50-y/o woman presents with h/o weakness, blurred vision, and confusion several hours after meals, which improves with eating; W/U: ↑ fasting levels of insulin and hypoglycemia.

Insulinoma (with Whipple triad)

Newborn presents with ambiguous genitalia; PE: lethargy and ↓ BP; W/U: ↓ Na⁺, ↑ K⁺, ↓ 17 α-OH-progesterone, ↑ ACTH, and karyotype of 46, XX.

Congenital adrenal hyperplasia (21α-hydroxylase deficiency)
7-y/o girl presents with breast buds and monthly vaginal bleeding; PE: height and weight >> 95 percentile, full pubic and axillary hair; hand X-ray shows advanced bone age.

Precocious puberty
21-y/o woman presents with no h/o menarche; PE: normal breast tissue, no axillary or pubic hair, vagina ending in blind pouch, no palpable cervix or uterus; karyotype shows 46, XY.

Androgen insensitivity (testicular feminization) syndrome
45-y/o with recent h/o coarsening of facial features presents with headaches and states that his shoes no longer fit; PE: enlarged jaw, tongue, hands, and feet, and bitemporal hemianopia.

Acromegaly
65-y/o smoker with h/o lung cancer presents with fatigue and oliguria; W/U: ↓ Na⁺, ↓ serum osmolarity, ↑↑ urine osmolarity.

Syndrome of inappropriate antidiuretic hormone (SIADH)
22-y/o sexually active woman presents with dysuria, dyspareunia, vulvar pain for the past 3 days. PE: soft ulcer on labia majora, inguinal lymphadenopathy; W/U: culture grows Haemophilus ducreyi.

Chancroid
20-y/o sexually active woman presents with crampy abdominal pain and purulent vaginal discharge; PE: fever and adnexal tenderness; W/U: ↑ WBCs, ↑ ESR, and combined infection with C. trachomatis and Neisseria gonorrhoeae.

Pelvic inflammatory disease (PID)
18-y/o woman with 3 days of vaginal pruritus; PE: thick, white discharge; W/U: budding yeast on KOH preparation.

Vaginal candidiasis
28-y/o woman postpartum day 1 with excessive hemorrhage in labor becomes weak and loses consciousness. PE: hypotension; W/U: ↓ cortisol, ↓ TSH, ↓ fT₄, ↓ LH, ↓ FSH.

Sheehan syndrome (pituitary apoplexy)
31-y/o woman with h/o PID presents with sudden-onset nausea and LLQ pain; PE: ↓ BP, ↑ HR, rebound tenderness in LLQ; W/U shows ⊕ β-hCG and fluid in cul-de-sac on U/S.

Ruptured ectopic pregnancy
28-y/o man presents with gynecomastia and painless lump in his left testicle for 3 months; PE: firm 4 cm mass on left testis; W/U: ↑↑ serum hCG and AFP.

Testicular carcinoma
35-y/o man with sensation of heaviness in left scrotum; appears like a “bag of worms” on examination.
Varicocele
62-y/o obese nun with h/o menopause at age 57 presents with vaginal bleeding for the past 4 months; PE shows normal-sized uterus; Pap smear reveals abnormal endometrial cells.

Endometrial carcinoma
52-y/o obese patient presents with numbness in hands and feet; PE: ↑ BP and retinopathy; W/U: ↑ HbA1c and glycosuria.

DM type 2
55-y/o woman presents with an itching, scaling, oozing rash over her left nipple; PE: serosanguinous discharge and eczematous redness of left nipple with axillary lymphadenopathy.

Paget disease of the breast
4-y/o girl presents with a “bunch of grapes” protruding from her vagina. W/U: desmin positive.

Sarcoma botryoides
37-y/o woman presents with dysmenorrhea, dyspareunia, menorrhagia, and pain coinciding with her menstrual cycle; PE: nodularity of uterosacral ligaments and cul-de-sac.

Endometriosis
22-y/o woman with 6-month h/o amenorrhea presents for infertility evaluation; PE: obesity, hirsutism; W/U: ↑ LH:FSH ratio, ↑ testosterone, and enlarged ovaries on U/S.

Polycystic ovarian syndrome (Stein-Leventhal syndrome)
44-y/o with recent h/o thyroidectomy presents with muscle cramping; PE: circumoral numbness, positive Trousseau and Chvostek signs.

Hypoparathyroidism
23-y/o woman marathon runner presents with lack of menses for 5 months; PE shows no signs of pregnancy; W/U: negative β-hCG, normal prolactin and thyroid hormones.

Secondary amenorrhea
28-y/o black woman at 35 weeks gestation in her first pregnancy presents with swollen legs; PE: ↑ BP and pitting pedal edema; W/U: 3+ proteinuria.

Preeclampsia
2-y/o child presents with developmental delay; PE: macroglossia, short stature, and protuberant abdomen; W/U: ↑ TSH, ↓ T3 and T4.

Congenital hypothyroidism (cretinism)
51-y/o woman with 9-month h/o amenorrhea presents with fatigue and flushing of skin; PE: atrophic vaginal mucosa; W/U: ↑ FSH and LH.

Menopause
24-y/o woman presents with painless lump in her left breast; PE: small, firm, palpable, and freely mobile, rubbery mass in the upper-outer quadrant of the breast.

**Fibroadenoma**

19-y/o man is brought to you for failure of pubertal maturation; PE: anosmia, ↓ muscle mass, no axillary or pubic hair, and hypogonadism; W/U: ↓ LH and FSH.

**Kallmann syndrome**

9-y/o girl presents with muscle cramps; PE: rounded face with flat nasal bridge, abnormal dentition, positive Trousseau and Chvostek sign, and shortened third and fourth metacarpals.

**Albright hereditary osteodystrophy (pseudohypoparathyroidism)**

22-y/o pregnant woman at 27 weeks with painless vaginal bleeding that stopped after an hour. W/U: placenta overlying the cervical os on ultrasound.

**Placenta previa**

19-y/o woman with h/o recent hydatidiform mole presents with vaginal bleeding, nausea, and vomiting; PE: vascular growth at cervical os and enlarged uterus; W/U: ↑↑ β-hCG.

**Choriocarcinoma**

35-y/o man presents for sterility evaluation; PE: eunuchoid body habitus, small testicles, and gynecomastia; karyotype reveals 47, XXY.

**Klinefelter syndrome**

**RENAL AND GENITOURINARY**

Patient hospitalized for CHF is started on an aminoglycoside for a UTI and develops oliguria, N/V, and malaise; PE: ↑ BP and asterixis; serum electrolytes: ↑ creatinine (Cr), K⁺; UA: “muddy brown” casts, FeNa⁺ > 3%.

**Acute renal failure (drug-induced ATN)**

70-y/o black man with h/o of life-long DM presents with peripheral edema, SOB, and oliguria; PE: auscultatory rales, pitting edema, myoclonus, and uremic frost; serum electrolytes: ↑ Cr, hyperkalemia, hypocalcemia, hyperphosphatemia.

**Chronic renal failure**

Teenage female presents with fever, chills, and flank pain; PE: costovertebral angle (CVA) tenderness; UA: leukocyte esterase ⊕, 30 WBC/hpf with WBC casts.

**Pyelonephritis**

32-y/o man presents with pain and hematuria; PE: ↑ BP, palpable kidney, and mid-systolic ejection click; abdominal U/S: multiple cysts of renal parenchyma; cerebral angiogram: unruptured berry aneurysm.
Adult polycystic kidney disease

20-y/o man presents with significant blood loss following a trauma and begins to have decreased urine output. W/U: oliguria, FeNa 1%, and BUN:Cr > 20.

Acute renal failure—prerenal

12-y/o girl with recent h/o sore throat presents with low urine output and dark urine; PE: periorbital edema; W/U: hematuria, ↑ BUN and Cr, ↑ antistreptolysin O (ASO) titer.

Poststreptococcal glomerulonephritis

45-y/o Asian man with h/o hepatitis B presents with malaise, edema, and foamy urine; PE: anasarca; W/U: proteinuria (> 3.5 g/day), hyperlipiduria; hyperlipidemia and hypoproteinemia.

Membranous glomerulonephritis

Male infant is born with flattened facies, joint position abnormalities, and hypoplastic lungs. Oligohydramnios was noted prior to delivery.

Potter sequence—secondary to renal agenesis

80-y/o man presents with urinary hesitancy, nocturia, and weak urinary stream; PE: diffusely enlarged rubbery prostate; serum electrolytes: ↑ Cr, UA is WNL.

Benign prostatic hyperplasia (BPH)

68-y/o man, who is a smoker, presents with flank pain and hematuria; PE: fever, palpable kidney mass; W/U: hypercalcemia, polycythemia.

Renal cell carcinoma

20 y/o man presents with acute onset of left testicular pain and N/V; PE: swollen, tender testicle in transverse position, absent cremasteric reflex on left side; Doppler: no flow detected in left testicle.

Testicular torsion

65-y/o man, who is a smoker, presents with painless hematuria and occasional urinary urgency and frequency; PE: unremarkable; urine cytology positive for malignant cells.

Bladder—urothelial carcinoma

85-y/o man presents with back pain, weight loss, and weak urinary stream; PE: palpable firm nodule on digital rectal examination (DRE); W/U: ↑ PSA.

Prostate cancer

25-y/o Asian man presents with N/V and colicky right flank pain; PE: acute distress and CVA tenderness; W/U: hematuria and discrete radiopacities on abdominal XR.

Renal stones

45-y/o with documented h/o aortic atheromatous plaques presents with recent-onset, severe left flank pain, and hematuria; abdominal CT: wedge-shaped lesion in the left kidney.

Renal infarct
3-y/o boy presents with h/o flank mass found recently by his mother while bathing him; PE: palpable mass in left flank; abdominal CT: large mass growing out of left kidney.

Wilms tumor

55-y/o with long h/o DM presents with increasing fatigue and edema; PE: ↑ BP, retinopathy, and pitting edema; W/U: severe proteinuria and glycosuria.

Diabetic nephropathy (glomerulosclerosis)

21-y/o sexually active woman presents with frequency and dysuria; PE: suprapubic tenderness; W/U: E. coli-positive urine cultures.

Urinary tract infection (UTI)

25-y/o man presents with hemoptysis, dark urine, and fatigue; PE: bilateral crackles at lung bases; W/U: oliguria, hematuria, and anti-GBM antibodies.

Goodpasture syndrome

7-y/o presents in stupor after ingesting antifreeze; PE: Kussmaul respirations and mental status changes; W/U reveals anion gap of 21 mEq/L.

Metabolic acidosis (ethylene glycol toxicity)

6-y/o boy presents with hematuria and worsening vision; PE: corneal abnormalities, retinopathy, sensorineural hearing loss; W/U: hematuria with dysmorphic red cells.

Alport syndrome

3-y/o boy with h/o recent URI presents with facial edema; PE: ascitic fluid in abdomen and pedal edema; W/U reveals 4+ proteinuria and ↓ serum albumin.

Minimal change disease

HEMATOLOGY/ONCOLOGY

50-y/o with h/o bone marrow transplant for chronic myelogenous leukemia (CML) 3 weeks ago presents with severe pruritis, diarrhea, and jaundice; PE: violaceous rash on palms and soles; W/U: ↑ BR, ALT, and AST.

Graft-versus-host disease

1-y/o Greek child presents with pallor and delayed milestones; PE: skeletal abnormalities, splenomegaly; peripheral blood smear (PBS): hypochromic microcytic RBCs, target cells, fragmented RBCs; skull XR: “hair-on-end” appearance.

β-Thalassemia

10-y/o with a h/o recurrent chest pain presents with fever and bilateral leg pain; PE: febrile, multiple leg ulcers; PBS shows sickle-shaped erythrocytes; Hb electrophoresis shows HbS band.

Sickle cell anemia
60-y/o with headache, vertigo, blurry vision, pruritus, joint pain; PE: ↑ BP, plethoric splenomegaly; W/U: Hct = 60, mild leukocytosis, and hyperuricemia.

Polycythemia vera

4-y/o boy with a 1-week h/o fever, pallor, headache, and bone tenderness; PE: fever, HSM, and generalized, nontender lymphadenopathy; PBS reveals absolute lymphocytosis with abundant TdT+ lymphoblasts.

Acute lymphoblastic leukemia

27-y/o presents with 2-month h/o fatigue, oropharyngeal candidiasis, pseudomonal UTI, and epistaxis; PE: numerous petechiae and ecchymoses of skin, gingival mucosal bleeding, guaiac ⊕ stools; W/U: ↑ WBC; PBS shows >30% myeloblasts with Auer rods.

Acute myelocytic leukemia

17-y/o man presents with a 2-month h/o fever, night sweats, and weight loss; PE: nontender, cervical lymphadenopathy, and HSM; CBC: leukocytosis; CXR: bilateral hilar adenopathy; lymph node biopsy: Reed-Sternberg cells.

Hodgkin disease

60-y/o man presents with fatigue and anorexia; PE: generalized lymphadenopathy and HSM; W/U: WBC = 250,000, positive direct Coombs test; PBS: small, round lymphocytes predominate with occasional smudge cells.

Chronic lymphocytic leukemia

10-y/o African child presents with a 3-week h/o a rapidly enlarging, painless mandibular mass; CBC: mild anemia and leukopenia; cytogenetics reveal a t(8:14) translocation; excisional biopsy: “starry-sky” pattern.

Burkitt lymphoma

35-y/o presents with a 3-year h/o mild weight loss, anorexia, worsening DOE; PE: splenomegaly; CBC: mild anemia, WBC = 125,000; PBS: granulocytosis with 10% myeloblasts; cytogenetics reveal a t(9:22) translocation.

Chronic myelocytic leukemia

55-y/o with a recent h/o streptococcal pneumonia presents with bone pain and weight loss; W/U: mild anemia, hypercalcemia; PBS: ruleau formation; UA: Bence-Jones proteinuria; serum electrophoresis: M spike; XR: cranial “punched-out” lesions.

Multiple myeloma

18-y/o woman develops dyspnea and declining mental status 1 hour after a C-section complicated by excess blood loss; PE: mucosal bleeding, large clot in the vaginal vault; W/U: ↑ D-dimer, ↑ PT/PTT, ↓ antithrombin III, and thrombocytopenia.

Disseminated intravascular coagulation

7-y/o with h/o viral URI 1 week ago presents with epistaxis; PE: petechial hemorrhages of nasal mucosa and extremities; W/U: ↓ platelets, normal PT and PTT; bone marrow biopsy: ↑↑ megakaryocytes.
Idiopathic thrombocytopenic purpura
8-y/o with a h/o vomiting and diarrhea after eating a hamburger last week presents with fatigue, periorbital edema, and oliguria; PE: purpuric rash; CBC: ↓ platelets; PBS: burr cells, helmet cells; UA: RBC casts, proteinuria, hematuria.

Hemolytic uremic syndrome
8-y/o with a h/o environmental allergies presents with a painful rash on the legs, abdominal discomfort, joint pain; UA: hematuria and RBC casts; renal biopsy: glomerular mesangial IgA deposits.

Henoch-Schonlein purpura
8-y/o boy presents with a swollen painful knee; FH: maternal grandfather died from hemorrhage after a cholecystectomy; PE: cutaneous ecchymoses; W/U: gross blood in swollen knee joint, ↑ PTT, normal PT and platelet count, ↑ bleeding time.

Hemophilia A
2-y/o boy with a h/o recurrent epistaxis presents with the third episode of otitis media in 4 months; PE: eczematous dermatitis; W/U: thrombocytopenia, ↓ IgM, ↑ IgA.

Wiskott-Aldrich syndrome
Newborn develops jaundice rapidly during the first day of life; PE: HSM; W/U: severe anemia, ⊕ indirect Coombs test in both mother and newborn.

Rh incompatibility
16-y/o adolescent with a h/o menorrhagia presents with fatigue; PE: multiple cutaneous bruises; guaiac ⊕ stools; W/U: ↑ bleeding time, ↓ factor VIII, normal platelet count, PT, and PTT.

von Willebrand disease

SKIN AND CONNECTIVE TISSUES

30-y/o man with h/o recurrent sinusitis presents for sterility evaluation; PE: heart sounds are best heard over right side of chest.

Kartagener syndrome
9-y/o with h/o easy bruising and hyperextensible joints presents to the ER after dislocating his shoulder for the fifth time this year.

Ehlers-Danlos syndrome
5-y/o presents to the ER with his sixth bone fracture in the past 2 years; PE: bluish sclera and mild kyphosis; XR: fractures with evidence of osteopenia.

Osteogenesis imperfecta
8-y/o with a long h/o severe sunburns and photophobia presents to the dermatologist for evaluation of several lesions on the face that have recently changed color and size.
Xeroderma pigmentosum
6-y/o boy presents to the ophthalmology clinic with sudden ↓ visual acuity; PE: unusual body habitus, long and slender fingers, pectus excavatum, and superiorly dislocated lens.

Marfan syndrome
36-y/o with h/o celiac disease presents with clusters of erythematous vesicular lesions over the extensor surfaces of the extremities.

Dermatitis herpetiformis
5-y/o patient presents with honey-colored crusted lesions at the angle of his mouth; Gram stain of pus: gram-positive cocci in chains.

Impetigo
29-y/o HIV-positive patient presents with multiple painless pearly-white umbilicated nodules on the trunk and anogenital area.

Molluscum contagiosum
68-y/o fair-skinned farmer presents with large, telangiectatic, and ulcerated nodule on the bridge of the nose.

Basal cell carcinoma
11-y/o presents with bilateral wrist pain and a rash; PE: erythematous, reticular skin rash of the face and trunk with a “slapped-cheek appearance.”

Erythema infectiosum
43-y/o woman presents with difficulty swallowing; PE: bluish discoloration of the hands and shiny, tight skin over her face and fingers.

Progressive systemic sclerosis (scleroderma)
5-y/o Asian boy presents with fever and diffuse rash including the palms and soles; PE: cervical lymphadenopathy, conjunctival injection, and desquamation of his fingertips; echocardiogram reveals dilation of coronary arteries.

Kawasaki syndrome (mucocutaneous lymph node syndrome)
33-y/o patient presents with itchy, purple plaques over her wrists, forearms, and inner thigh; PE: Wickham striae.

Lichen planus
25-y/o woman with h/o Raynaud phenomenon presents with arthralgias and myositis; W/U reveals esophageal hypomotility and ↑ anti-nRNP titers.

Mixed connective tissue disease

MUSCULOSKELETAL
25-y/o man presents with morning stiffness, heel pain, and photophobia; PE: ↓ lumbar spine extension and lateral flexion, tenderness on lumbar spinous processes and iliac crests; W/U: HLA-B27 ⊕; XR: bamboo spine.

Ankylosing spondylitis

7-y/o girl presents with a limp, anorexia, and spiking fevers; PE: salmon-pink linear rash on trunk and extremities and swelling of bilateral hip, knee, elbow, and wrist joints; W/U: ↑ ESR.

Juvenile rheumatoid arthritis

50-y/o woman presents with long-standing h/o morning stiffness and diffuse joint pain; PE: boutonierre and swan neck deformities of fingers, shoulder tenderness, and ↓ range of motion (ROM), symmetric and bilateral knee swelling; W/U: RF positive.

Rheumatoid arthritis

25-y/o man with a h/o urethritis 2 weeks ago presents with unilateral knee pain, stiffness, and eye pain; PE: conjunctivitis, edema, and tenderness of left knee, mucoid urethral discharge; W/U: urethral swab ⊕ for *Chlamydia*.

Reiter syndrome

45-y/o woman presents with dry eyes and dry mouth, PE: parotid gland enlargement, bibasilar rales; W/U: ⊕ ANA, RF, SS-A/Ro titers.

Sjögren syndrome

70-y/o woman presents with pain in hands that is worse with activity, PE: Heberden and Bouchard nodes, bony enlargement at DIP and PIP joints, bilateral knee effusions; W/U: negative RF, normal ESR; hand XR: joint space narrowing, osteophytes.

Osteoarthritis

72-y/o woman presents with a 6-week h/o morning stiffness in neck and shoulders; PE: low-grade fever, tenderness to palpation, and decreased ROM in neck, shoulder, hip joints; W/U: ↓ ESR and CRP, but negative RF.

Polymyalgia rheumatica

50-y/o man presents with acute onset of sharp pain in the left great toe; PE: severe tenderness, swelling, and warmth of the left MTP joint; synovial fluid analysis shows negatively birefringent crystals.

Gout

25-y/o woman with a 1-week h/o pain in several joints presents with swelling, redness, and pain in her right knee; PE: pustular lesions on palms, right knee shows erythema, tenderness, and ↓ ROM; W/U: gram-negative diplococci in synovial fluid.

Gonococcal arthritis

28-y/o woman presents with difficulty keeping her eyelids open and holding her head up during the day; PE: weakness of facial muscles, deltoids; W/U: anti-ACh titer +; CXR: anterior mediastinal mass.

Myasthenia gravis (associated with thymoma)
20-y/o black woman presents with fatigue, arthralgias, Raynaud phenomenon, and pleuritic chest pain; PE: butterfly malar facial rash; W/U: ↓ platelets, proteinuria, and ⊕⊕ ANA, anti-dsDNA, and anti-Smith Abs.

Systemic lupus erythematosus (SLE)

20-y/o with a h/o developmental delay presents with facial weakness; PE: cataracts, marked weakness in muscles of hand, neck, and distal leg with sustained muscle contraction; genetic testing: CTG repeat expansion within DMPK gene.

Myotonic dystrophy

BEHAVIORAL SCIENCE

20-y/o woman presents with excessive anxiety about a variety of events for more than half of the days for the last 7 months.

Generalized anxiety disorder

8-y/o boy presents with a 5-month h/o regular bedwetting episodes; PE is unremarkable and fasting glucose is WNL.

Enuresis

28-y/o man who systematically checks each lock in his house every time before leaving, often causing him to be over an hour late for meetings.

Obsessive-compulsive disorder

29-y/o man presents with a 9-month h/o insatiable urges to rub himself against strangers, which he has regretably acted on several times.

Frotteurism

22-y/o woman college student who is 20% below her ideal body weight complains of not having any menstrual cycles and “feeling fat.”

Anorexia nervosa

26-y/o woman medical student is convinced for the past 9 months that she has SLE and despite numerous negative workups, she fears she will have to drop out of school.

Hypochondriasis

17-y/o woman presents with complaints of “feeling fat” and h/o eating dinner alone in her bedroom; PE shows normal height and weight, dental erosions, and scars on the back of her hand.

Bulimia

21-y/o woman with no h/o trauma presents to the ER because she cannot feel or move her legs; W/U is WNL; detailed history reveals that her boyfriend left her this morning.

Conversion disorder
43-y/o alcoholic with h/o confabulation and amnesia presents to ER after falling down; PE shows nystagmus and ataxic gait; W/U reveals macrocytic anemia.

Wernicke-Korsakoff syndrome

6-y/o presents with 8-month h/o hyperactivity, inattentiveness, and impulsivity both at school and at home; PE and W/U are WNL.

Attention deficit hyperactivity disorder (ADHD)

33-y/o woman presents to your office distressed after turning down a lucrative job offer because of the requirement to speak in front of people.

Social phobia

9-y/o boy with 2-year h/o involuntary tics is brought to your office because he has recently been shouting obscenities.

Tourette syndrome

33-y/o woman nurse presents with recent occurrences of hypoglycemia; PE reveals multiple crossed scars on abdomen; W/U shows insulin/C-peptide ratio > 1.0.

Factitious disorder (Munchausen syndrome)

33-y/o is referred to you for reports of random episode of shouting and screaming during the night; he has no recollection of the event and denies having nightmares.

Sleep terror disorder

16-y/o with h/o sudden-onset daytime sleep attacks with loss of muscle tone and audiovisual hallucinations while waking and falling asleep.

Narcolepsy

19-y/o with an 8-month h/o deteriorating grades and social withdrawal presents with auditory hallucinations; PE shows odd thinking patterns, tangential thoughts, and flattened effects.

Schizophrenia

24-y/o with h/o depression presents with ↓ need for sleep and auditory hallucinations; PE reveals easy distractibility and pressured speech; W/U shows normal TSH and negative toxicology screen.

Bipolar disorder—type 1 (manic episode)

48-y/o woman presents with recent h/o early morning waking, ↓ appetite, feelings of guilt, and loss of interest in her usual hobbies over the past 3 months; PE and laboratory results are WNL.

Major depressive disorder

68-y/o veteran presents with complaints of vivid flashbacks, hypervigilance, and difficulty falling asleep for the past several years; patient appears very anxious during the PE.

Posttraumatic stress disorder
6-month-old child presents with unyielding crying; PE reveals multiple bruises in different stages of healing and bilateral retinal hemorrhages; XR shows multiple, healing fractures along posterior ribs.

Shaken baby syndrome

43-y/o woman from Boston finds herself in Utah, but does not remember why she is there or how she got there; PE and W/U are WNL; detailed history reveals that her son suddenly died 1 week ago.

Dissociative fugue

3-y/o boy with h/o of poor cuddling presents with severely delayed language and social development; PE reveals below normal intelligence with unusual calculating abilities and repetitive behaviors.

Autism
APPENDIX

Abbreviations

AA
  amino acid
Ab
  antibody
ABG
  arterial-blood gas
ACE
  angiotensin-converting enzyme
ACEi
  ACE inhibitor
ACh
  acetylcholine
ACL
  anterior cruciate ligament
ACTH
  adrenocorticotropin hormone
AD
  autosomal dominant
ADH
  antidiuretic hormone
ADHD
  attention deficit hyperactivity disorder
ADP
  adenosine diphosphate
AFP
  α-fetoprotein
Ag
  antigen
AIDS
  acquired immunodeficiency syndrome
ALL
  acute lymphocytic leukemia
ALP
alkaline phosphatase
ALS
amyotrophic lateral sclerosis
ALT
alanine transaminase
AML
acute myelogenous leukemia
ANA
antinuclear antibody
ANOVA
analysis of variance
ANS
autonomic nervous system
AR
autosomal recessive
ARB
angiotensin receptor blocker
ARDS
acute respiratory distress syndrome
ASA
aspirin
ASD
atrial septal defect
ASO
antistreptolysin O
AST
aspartate transaminase
ATN
ischemic acute tubular necrosis
ATP
adenosine triphosphate
ATPase
adenosine triphosphatase
AV
atrioventricular
AXR
abdominal x-ray
AZT
azidothymidine
BAL
  British anti-Lewisite
BM
  basement membrane
BP
  blood pressure
BPG
  bisphosphoglycerate
BPH
  benign prostatic hyperplasia
BR
  bilirubin
BUN
  blood urea nitrogen
Bx
  biopsy
CA
  cancer/carcinoma
CAD
  coronary artery disease
cAMP
  cyclic adenosine monophosphate
cANCA
  cytoplasmic pattern of antineutrophil cytoplasmic antibodies
CBC
  complete blood count
CCK
  cholecystokinin
CEA
  carcinoembryonic antigen
CF
  cystic fibrosis
CFTR
  cystic fibrosis transmembrane regulator
cGMP
  cyclic guanosine monophosphate
CHF
  congestive heart failure
CIN
cervical intraepithelial neoplasia
CK  
serum creatine kinase
CLL  
chronic lymphocytic leukemia
CML  
chronic myelogenous leukemia
CMV  
cytomegalovirus
CN  
cranial nerve
CNS  
central nervous system
CO  
cardiac output
CoA  
coenzyme A
COMT  
catechol-O-methyltransferase
COPD  
chronic obstructive pulmonary disease
COX  
cyclooxygenase
$C_p$  
concentration in plasma
CPK  
creatine phosphokinase
Cr  
creatinine
CRP  
C-reactive protein
CSF  
cerebrospinal fluid
CT  
computed tomography
CV  
cardiovascular
CVA  
cerebrovascular accident or costovertebral angle
CXR
  chest x-ray
D or DA
dopamine
day(s)
d/o
disorder
DAG
diacylglycerol
DES
diethylstilbesterol
DHT
dihydrotestosterone
DI
diabetes insipidus
DIC
disseminated intravascular coagulation
DIP
distal interphalangeal joint
DKA
diabetic ketoacidosis
DM
diabetes mellitus
DNA
deoxxyribonucleic acid
DOE
dyspnea on exertion
DRE
digital rectal examination
ds
double stranded
DSM
diagnostic and statistical manual
DTR
deep tendon reflex
DTs
delerium tremens
DVT
deep venous thrombosis
E
epinephrine
EBV
Epstein-Barr virus
ECF
extracellular fluid
ECG
electrocardiogram
ECT
electroconvulsive therapy
EDV
end-diastolic volume
EEG
electroencephalogram
EF-2
elongation factor 2
EGD
esophagogastroduodenoscopy
ELISA
enzyme-linked immunosorbent assay
EM
electron microscopy
EOM
extraocular muscle
EPO
erythropoetin
EPS
extrapyramidal symptoms
ER
endoplasmic reticulum or emergency room
ESR
erthrocyte sedimentation rate
ESV
end-systolic volume
ETOH
ethanol
FAs
fatty acids
FAD
flavin adenine dinucleotide (oxidized)
FADH\textsubscript{2}
flavin adenine dinucleotide (reduced)
FAP
familial adenomatous polyposis
FEN\textsubscript{a}\textsuperscript{+}
fractional excretion of sodium
FFP
fresh frozen plasma
FH
family history
FSH
follicle-stimulating hormone
FN
false negatives
FP
false positives
FTA-ABS
fluorescent treponemal antibody-absorbed
Fx
fracture
G3P
glucose-3-phosphate
G6PD
glucose-6-phosphate dehydrogenase
GABA
γ-aminobutyric acid
GBM
glomerular basement membrane
GCT
germ cell tumor
GFR
glomerular filtration rate
GGT
γ-glutamyl transpeptidase
GH
growth hormone
GI
  gastrointestinal
G_i
  G protein, inhibitory
GMP
  guanosine monophosphate
GN
  glomerulonephritis
GnRH
  gonadotropin-releasing hormone
G_s
  G protein, stimulatory
GSE
  general somatic efferent
GTP
  guanosine triphosphate
GU
  genitourinary
GVE
  general visceral efferent
HA
  headache
Hb
  hemoglobin
HBV
  hepatitis B virus
hCG
  human chorionic gonadotropin
HDL
  high-density lipoprotein
HGPRT
  hypoxanthine guanine phosphoryltransferase
HHV
  human herpesvirus
HIV
  human immunodeficiency virus
HMG-CoA
  hydroxymethylglutaryl-CoA
indication(s)
INH
  isoniazid
IOP
  intraocular pressure
IP₃
  inositol triphosphate
IPV
  inactivated polio vaccine
IUGR
  intrauterine growth retardation
IV
  intravenous
IVC
  inferior vena cava
IVIG
  IV immunoglobulin
JG
  juxtaglomerular
JVD
  jugular venous distension
L
  left
LAD
  left anterior descending
LCA
  left coronary artery
LDH
  lactate dehydrogenase
LDL
  low-density lipoprotein
LES
  lower esophageal sphincter
LFT
  liver function test
LH
  leutinizing hormone
LLQ
  left lower quadrant
LLSB  left-lower sternal border
LMN  lower motor neuron
LP  lumbar puncture
LPS  lipopolysaccharide
LT  leukotriene
LUSB  left-upper sternal border
LUQ  left upper quadrant
LV  left ventricle
MAOI  monoamine oxidase inhibitor
MCA  middle cerebral artery
MCP  metacarpel phalangeal
MCL  medial collateral ligament
MCV  mean corpuscular volume
MEN  multiple endocrine neoplasia
MHC  major histocompatibility complex
MI  myocardial infarction
MLF  medial longitudinal fasciculus
mm  millimeters or muscles
MMR  measles, mumps, rubella
MOA  

mechanism of action
MPTP
1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
MRI
magnetic resonance imaging
MS
multiple sclerosis
MTP
metatarsal-phalangeal
MVA
motor vehicle accident
NAD
nicotinamide adenine dinucleotide (oxidized)
NADH
nicotinamide adenine dinucleotide (reduced)
NADP
nicotinamide adenine dinucleotide phosphate (oxidized)
NADPH
nicotinamide adenine dinucleotide phosphate (reduced)
NE
norepinephrine
NSAID
nonsteroidal anti-inflammatory drug
N/V
nausea/vomiting
OAA
oxaloacetic acid
OCP
oral contraceptive pills
OPV
oral polio vaccine
PABA
\textit{para}-aminobenzoic acid
PAF
platelet activity factor
PAH
\textit{para}-aminohippuric acid
PALS
periarterial lymphoid sheath
PAN  
  polyarteritis nodosa

P-ANCA  
  perinuclear pattern of antineutrophil cytoplasmic antibodies

PAS  
  periodic acid-Schiff (stain)

PBS  
  peripheral blood smear

PCAM  
  platelet cell adhesion molecule

PCI$_2$  
  prostacyclin I$_2$

PCL  
  posterior cruciate ligament

PCP  
  phencyclidine hydrochloride

PCR  
  polymerase chain reaction

PCWP  
  pulmonary capillary wedge pressure

PDA  
  patent ductus arteriosus

PDE  
  phosphodiesterase

PDGF  
  platelet-derived growth factor

PE  
  physical examination

PFK  
  phosphofructokinase

PFT  
  pulmonary function tests

PG  
  prostaglandin

PID  
  pelvic inflammatory disease

PIP  
  proximal interphalangeal
PIP<sub>2</sub>
- phosphatidylinositol-4,5-bisphosphonate

PK
- pyruvate kinase

PKU
- phenylketonuria

PMN
- polymorphonuclear

PNH
- paroxysmal nocturnal hemoglobinuria

PNS
- peripheral nervous system

PPI
- proton-pump inhibitor

PPRF
- parapontine reticular formation

PSA
- prostate-specific antigen

PT
- prothrombin time

PTH
- parathyroid hormone

PTT
- partial thromboplastin time

PVD
- peripheral vascular disease

R
- right

RA
- right atrium

RAA
- Renin angiotensin aldosterone

RBC
- red blood cell

RBF
- renal blood flow

RCA
- right coronary artery

REM
rapid eye movement
RER
rough endoplasmic reticulum
RF
rheumatoid factor
RLQ
right lower quadrant
ROM
range of motion
RPF
renal plasma flow
RPR
rapid plasma reagin
RR
respiratory rate
RSV
respiratory syncytial virus
RUQ
right upper quadrant
RV
right ventricle
RVH
right ventricular hypertrophy
s
second(s)
S1(2,3,4)1st
heart sound (2nd, 3rd, 4th)
SA
sinoatrial
SC
subcutaneous or sickle cell
SD
standard deviation
SEM
standard error of the mean
SES
socioeconomic status
SGOT
serum glutamic oxaloacetic transaminase
SGPT  
serum glutamic pyruvate transaminase

SLE  
systemic lupus erythematosus

SMX  
sulfamethoxazole

SOB  
shortness of breath

ss  
single stranded

SSA  
special somatic afferent

SSPE  
subacute sclerosing panencephalitis

SSRI  
selective serotonin reuptake inhibitor

STD  
sexually transmitted disease

SV  
stroke volume

SVA  
special visceral afferent

SVT  
supraventricular tachycardia

Sx  
symptom(s)

s/p  
status post

t\(_{1/2}\)  
half-life

T\(_{3}\)  
triiodothyronine

T\(_{4}\)  
thyroxine

TB  
tuberculosis

TBW  
total body water
TG  triglyceride
TIBC  total iron binding capacity
TMP  trimethoprim
TN  true negatives
TNF  tissue necrosis factor
TNM  tumor node metastasis
TOX  toxicity
TP  true positives
tPA  tissue plasminogen activator
TPR  total peripheral resistance
TRH  thyrotropin-releasing hormone
TSH  thyroid-stimulating hormone
TSS  toxic shock syndrome
TTP  thrombotic thrombocytopenic purpura
Tx  treatment/therapy
TXA  thromboxane
UA  urinalysis
UMN  upper motor neuron
UGI  upper GI
URI
upper respiratory infection
UTI
urinary tract infection
U/S
ultrasound
\( V_d \)
volume of distribution
VCAM
vascular cell adhesion molecule
VDRL
venereal disease research laboratory
Vfib
ventricular fibrillation
VHL
von Hippel-Lindau
VLDL
very low-density lipoprotein
VMA
vanillylmandelic acid
V/Q
ventilation/perfusion ratio
VSD
ventricular septal defect
vWF
von Willebrand factor
VZV
varicella-zoster virus
WBC
white blood cell
WNL
within normal limits
XL
x-linked
XR
x-ray
y/o
year-old
ZE
Zollinger-Ellison
5-FU
  5-fluorouracil
5-HIAA
  5-hydroxyindoleacetic acid
5-HT
  5-hydroxytryptamine (serotonin)

↑
  High or increases
↓
  Low or decreases
→
  Leads to or causes

1°/2°/3°
  primary/secondary/tertiary
~
  Approximately
⊕
  positive

>>> much greater than
much less than
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NE. See Norepinephrine
Necrosis
Negative predictive value
*Neisseria gonorrhea*
*Neisseria meningitides*
Nelfinavir
Neocortex
Neonatal respiratory distress syndrome (RDS)
Neoplasia of bone
Neoplastic disorders
Neoplastic polyp
Neostigmine
Nephron, functional regions of
Nephrosclerosis
Nephrotic and nephritic syndromes
Nervous system. See also Central nervous system disorders
  brain tumors
  congenital
demyelinating
encephalitis
intracranial hemorrhage
leukodystrophies
meningitis
miscellaneous
neurocutaneous syndromes
neurodegenerative
seizures
spinal cord
stroke
embryology
enteric
parasympathetic
pharmacology
  analgesics
  anesthetics
  antiepileptics
  antiparkinsonian agents
  sympathetic
Neuroblastoma
Neurocutaneous syndromes
Neurodegenerative disorders
Neurofibromatosis
Neurogenic shock
Neuroleptic malignant syndrome (NMS)
Neurotransmitters
Neutrophils
Nevirapine
Niacin
Niclosamide
Niemann-Pick disease
Nifedipine
Nifurtimox
Nitrate
Nitrates
Nitric oxide (NO)
Nitrofurantoin
Nitroprusside
Nitrosoureas
Nitrous oxide
Nizatidine
NMS. See Neuroleptic malignant syndrome
NO. See Nitric oxide
Nocardia
Nodule
Nondisjunction disorder
Nongonococcal septic arthritis
Non-Hodgkin lymphoma
Nonmaleficence
Nonneoplastic bone disorders
Nonneoplastic GI disorders
Nonnucleoside RT inhibitors
Nonsteroidal anti-inflammatory drugs (NSAIDS)
Norepinephrine (NE)
Northern blot
Nortriptyline
Norwalk virus
NSAIDS. See Nonsteroidal anti-inflammatory drugs
Nucleoside RT inhibitors
Null hypothesis
Nutmeg liver
Nutrition
Nystatin
Oat cell carcinoma
Obese
Obsessive-compulsive disorder (OCD)
Obstructive lung disease
Obstructive sleep apnea
OCD. See Obsessive-compulsive disorder
OCPs. See Oral contraceptives
Octreotide
Odds ratio
Oedipus complex
Olanzapine
Oligodendrocyte
Oligodendroma
Omeprazole
*Onchocerca volvulus*
Ondansetron
Operant conditioning
Operon
Opioids
*Opisthorchis sinensis*
Oppositional defiant disorder
Opsonization
Oral advance directive
Oral contraceptives (OCPs)
Oral hairy leukoplakia
Oral hypoglycemics
Organophosphates
Orthomyxoviridae
Oseltamivir
Osgood-Schlatter disease
Osler nodes
Osteitis fibrosa cystica
Osteoarthritis
Osteoblastoma
Osteochondroma
Osteogenesis imperfecta
Osteoma
Osteomalacia
Osteomyelitis
Osteopetrosis
Osteoporosis
Osteosarcoma
Otitis
Ovarian carcinoma
Ovarian cysts
Ovarian neoplasm
Ovarian tumors
Oxytocin

P

P value
Pacinian corpuscle
Paclitaxel
Paget disease
Palmar reflex
Pancoast syndrome
Pancreas
Pancreatic cancer
Pancreatic duct
Pancreatic endocrine tumors
Pancreatitis
Panic disorder
Pantoprazole
Pantothenate
Pantothenic acid
Papez circuit
Papillary carcinoma
Papovavirus
Papule
Paracoccidioidomycosis
Parainfluenza viruses
Peyer patches
Peyronie disease
p53
P–450
Pharmacodynamics
Pharmacology. See also specific drugs
  basic
  cardiovascular system
  endocrine system
  gastrointestinal system
  genitourinary system
  nervous system
  for psychiatric disorders
  respiratory system
Pharyngitis
Phencyclidine hydrochloride (PCP)
Phenelzine
Phenobarbital
Phenoxybenzamine
Phentolamine
Phenylalanine
Phenylephrine
Phenylketonuria
Phenytoin
Pheochromocytoma
Phobia
Phrenic nerve
Physical child abuse
Physiology
  cardiovascular system
  endocrine system
  gastrointestinal system
  genitourinary system
  musculoskeletal system
  reproductive system
  respiratory system
  sleep
Physostigmine
Pick disease
Picornaviruses
PID. See Pelvic inflammatory disease
Pigments
Pilocarpine
Pindolol
Pinworm infection
Pioglitazone
Piperacillin
Pituitary adenoma
Pituitary gland
Pituitary tumor
Placenta accreta
Placenta previa
Plaque
Platelet aggregation
Platelet cell adhesion molecule (PCAM)
Pleomorphic adenoma
Pleural effusion
*Pneumocystis*
Pneumonia
Poliomyelitis
Poliovirus
Polycystic kidney disease
Polycystic ovarian syndrome
Polycythemia vera
Polymyalgia rheumatica
Polymyositis
Polymyxins
Pontiac fever
Porta hepatis
Portal-systemic shunt
Port-wine stain birthmark
Posaconazole
Positive predictive value
Posterior pituitary
Posttraumatic stress disorder (PTSD)
Potassium iodide
Potency
Pott disease
Potter syndrome
Poxviridae
PPD test. See Purified protein derivative test
PR interval
Pralidoxime
Praziquantel
Prazosin
Precision
Precocious puberty
Prednisone
Preeclampsia
Pregnancy
Presbycusis
Prevalence
Priapism
Primaquine
Primary biliary cirrhosis
Prions
Probenecid
Procainamide
Procaine
Progesterone
Progressive multifocal leukoencephalopathy
Prolactin
Prolactinoma
Propafenone
Propofol
Propranolol
Propylthiouracil
Prostaglandins
Prostate cancer
Prostate gland
Prostatic carcinoma
Prostatitis
Protamine sulfate
Protease inhibitors
Protein(s)
digestion of
metabolism
Proteus
Protozoa
P-selectin
Pseudogout
Pseudohyperparathyroidism
Pseudohypoparathyroidism
Pseudomembranous colitis
Pseudomonas
Psittacosis
Psoriasis
Psychiatric disorders
  childhood
  mood
  personality
  psychopharmacology
  psychoses
  somatoform
Psychiatry
Psychoanalysis
Psychology
Psychopharmacology
Psychoses
PTH. See Parathyroid hormone
PTSD. See Posttraumatic stress disorder
Public health
Pulmonary edema
Pulmonary embolism
Pulmonary fibrosis
Pulmonary infections
Pulmonary thrombus
Pulmonic stenosis
Pulse pressure
Pulvinar
Pupillary dilation
Purified protein derivative (PPD) test
Purkinje system
Pustule
Pyelonephritis
Pyloric stenosis
Pylorus
Pyogenic osteomyelitis
Pyrantel pamoate
Pyridostigmine
Pyridoxine
Pyrimethamine
Pyruvate dehydrogenase deficiency

Q

Q fever
QRS complex
Quetiapine
Quinidine
Quinine
Quinolones

R

RA. See Rheumatoid arthritis
Rabies
Rabies virus
Radiation
Radioimmunoassay (RIA)
Raloxifene
Ranitidine
Rapidly progressive glomerulonephritis (RPGN)
RAS. See Renal artery stenosis
Raynaud disease
RBF. See Renal blood flow
RDS. See Neonatal respiratory distress syndrome (RDS)
Reactive arthritis
Reactive oxygen species
Reassortment
Receptive relaxation
Recombination
cystic fibrosis
lung cancer
neonatal RDS
obstructive lung disease
other pathology
pulmonary edema
pulmonary embolism
pulmonary infections
restrictive lung disease
embryology
pharmacology
physiology
Restriction fragment length polymorphism analysis
Restrictive cardiomyopathy
Restrictive lung disease
Retinol
Retrovirus
Rett syndrome
Reye syndrome
Rh incompatibility
Rheumatic fever
Rheumatic heart disease
Rheumatoid arthritis (RA)
Rhinoviruses
*Rhizopus* sp.
RIA. See Radioimmunoassay
Ribavirin
Riboflavin
Rickets
*Rickettsia*
Rifampin
Rimantadine
Risedronate
Risperidone
Ritodrine
Ritonavir
RNA
Rocky Mountain spotted fever
Rods
Rooting reflex
Rose gardener disease
Rosiglitazone
Rotavirus
Roth spots
Rotor syndrome
RPGN. See Rapidly progressive glomerulonephritis
RSV. See Respiratory syncytial virus
RTA. See Renal tubular acidosis
Rubella virus
Rubeola. See Measles virus
Ruffini corpuscle

S

SA node. See Sinoatrial node
Salicylates. See Aspirin
Salicylic acid
Saliva
Salivary glands
Salmonella
San Joaquin fever
Saquinavir
Sarcoidosis
Sarcoma botryoides
Scalded skin syndrome
Scar formation
Scarlet fever
Schistosoma
Schizoaffective disorder
Schizoid personality disorders
Schizophrenia
Schizophreniform disorder
Schizotypal personality disorders
Schwannoma
Sciatica
Scleroderma
Sclerosing retroperitonitis
Scoliosis
Screening tools
Scurvy
Second messengers
Secretin
Seizures
Selegiline
Selenium sulfide
SEM. See Standard error of the mean
Sensory fibers
Septic shock
Seronegative spondyloarthropathies
Serotonin
Sertraline
Severe combined immunodeficiency
Sex hormones
Sexual child abuse
Sexual response cycle
Sexuality
Sézary syndrome
Shaken baby syndrome
Shared psychotic disorder
Sheehan syndrome
Shigella dysenteriae
Shock
Shy-Drager syndrome
SIADH. See Syndrome of inappropriate antidiuretic hormone
Sildenafil
Silicosis
Simmonds disease
Sinoatrial (SA) node
Sjögren syndrome
Skeletal muscle
Skin
    anatomy
    disorders
    embryology
    histology
SLE. See Systemic lupus erythematosus
Sleep
Sleep terror disorder
Smooth muscle
SMX. See Sulfamethoxazole
Sodium bicarbonate
Sodium stibogluconate
Somatization disorder
Somatoform disorders
Somatostatin
Sotalol
Southern blot
Specificity
Sperm
Spherocytosis
Sphincter of Oddi
Spider telangiectasia
Spina bifida
Spinal cord disorders
Spinal tracts
Spiral valve
Spironolactone
Spleen
Spongiform encephalopathy
Squamous cell carcinoma
SSRIs
Standard error of the mean (SEM)
Staphylococcus aureus
Staphylococcus epidermidis
Starling equation
Statins
Statistical distributions
Stavudine (d4T)
STDs
Steatorrhea
Steroid hormones
Steroids
Stevens-Johnson syndrome
Stomach
Streptococcus sp.
  agalactiae
  pneumoniae
  pyogenes
  viridans
Stretch reflex
Striatal motor system
Stroke
Sturge-Weber syndrome
Subarachnoid space
Subdural hematoma
Subependymal germinal matrix bleed
Submucosal (Meissner) plexus
Suboptimal renal perfusion
Substance abuse
Substance P
Succimer
Succinylcholine
Suicide
Sulfadoxine
Sulfamethoxazole (SMX)
Sulfonamides
Sulfones
Sulfonylureas
Sulfoxone
Superego
Superior vena cava syndrome
Suramin
Surfactant
Sympathetic nervous system
Syncope
Syncytiotrophoblast
Syndrome of inappropriate antidiuretic hormone (SIADH)
Syphilis
Syringomyelia
Systemic lupus erythematosus (SLE)
Systemic sclerosis
Systolic blood pressure
T lymphocyte
Tabes dorsalis
*Taenia solium*
Takayasu arteritis
Tamoxifen
Tamponade
Tardive dyskinesia
Tay-Sachs disease
Tazobactam
TB. *See* Tuberculosis
TCAs
TEF. *See* Tracheoesophageal fistula
Teichoic acid
Temporal arteritis
*Teniae coli*
Teratogens
Terazosin
Terbinafine
Terbutaline
Terfenadine
Testes
Testicular tumors
Testosterone
Tetracaine
Tetracycline
Tetralogy of Fallot
Thalamus
Thalassemia
Thalidomide
T-helper cell
Thenar eminence
Theophylline
Therapeutic index
Thiabendazole
Thiamine
Thiazides
6-thioguanine
Thiopental
Thioridazine
Thiosulfate
Thoracic outlet syndrome
3TC. See Lamivudine
Thrombolytics
Thrombosis
Thrombotic thrombocytopenic purpura (TTP)
Thrash
Thymic aplasia (DiGeorge syndrome)
Thyroid gland
Thyroiditis
Ticlopidine
Tinea corporis
Tinea cruris/capitis/corporis/unguium/pedis
Tinea nigra
Tinea versicolor
Tirofiban
Tissue repair
TMP. See Trimethoprim
TMP-SMX
TNF. See Tumor necrosis factor
Tocainamide
Tolbutamide
Torsion
Tourette syndrome
Toxic megacolon
Toxic shock syndrome
Toxocara canis
Toxoplasma
tPA
Tracheoesophageal fistula (TEF)
Transference reaction
Transient ischemic attack
Transitional cell carcinoma
Transmural infarction
Transplant rejection
Tranylcypromine
Trastuzumab
Trazodone
Trench fever
Triamcinolone
Triamterene
Trichinella spiralis
Trichomonas vaginalis
Trichomoniasis
Trichophyton
Tricuspid regurgitation
Tricyclic antidepressants
Trifluoperazine
Trigeminal neuralgia
Trimethoprim (TMP)
Trisomy 21
Troponin test
Trousseau syndrome
Trypanosoma
Trypsin
t-test
TTP. See Thrombotic thrombocytopenic purpura
Tuberculosis (TB)
Tuberous sclerosis
Tubocurarine
Tubulointerstitial diseases
Tumor markers
Tumor necrosis factor (TNF)
Turcot syndrome
Tylenol. See Acetaminophen
Type I and II errors
Tyramine
Tyrosine

U

UC. See Ulcerative colitis
Ulcerative colitis (UC)
Undulant fever
Urea cycle
Urethritis
Urinary incontinence
Urinary system. See Genitourinary system
Urinary system disorders
Urinary tract infection (UTI)
Urinary tract tumors
Urobilinogen
Uroliothiasis
Urothelial carcinoma
Uterine ligaments
Uterus
UTI. See Urinary tract infection

V

Vaccines
Vaginismus
Vaginitis
Vagus nerve
Valacyclovir
Validity
Valproic acid
Valsalva maneuver
Vancomycin
Vardenafil
Variable ratio
Varicella-zoster virus (VZV)
Varicocele
Vascular cell adhesion molecule (VCAM)
Vascular tumors
Vasculitides
Vasoconstriction
Vasodilation
Vasopressin
VATER syndrome
VCAM. See Vascular cell adhesion molecule
Vecuronium
Venlafaxine
Veno-occlusive disease
Ventral spinal artery occlusion
Ventricular septal defect (VSD)
Verapamil
Verruca vulgaris
Vesicle
Vestibular schwannoma
Vestibular system
*Vibrio*
Vinblastine
Vincristine
Viral hepatitis
Virchow node
Viruses. See also specific viruses
antiviral agents and
infectious diseases
taxonomy
Vitamins
Vitiligo
Volume, lung
Volume of distribution
Volvulus
Von Hippel-Lindau disease
Von Recklinghausen disease
Von Recklinghausen disease of bone
Von Willebrand disease
Voriconazole
VSD. See Ventricular septal defect
VZV. See Varicella-zoster virus

W

Waiter’s tip palsy
Waldenstrom macroglobulinemia
Wallerian degeneration
Warfarin
Waterhouse-Friderichsen syndrome
WBC neoplasms. See White blood cell neoplasms
Wegener granulomatosis
Weil disease
Weil-Felix reaction
Werdnig-Hoffman disease
Wernicke encephalopathy
Wernicke-Korsakoff syndrome
Western blot
Whipple disease
White blood cell (WBC) neoplasms
Wilson disease
Wiskott-Aldrich syndrome
Woolsorter’s disease
Wuchereria bancrofti

X

Xanthoma
Xeroderma pigmentosa
XL agammaglobulinemia. See X-linked agammaglobulinemia
XL recessive disorders. See X-linked recessive disorders
X-linked (XL) agammaglobulinemia
X-linked (XL) recessive disorders

Y

Yaws
Yellow fever virus
Yersinia
Zafirlukast
Zalcitabine (ddC)
Zanamivir
Zenker diverticulum
Zidovudine (AZT)
Zileuton
Zollinger-Ellison syndrome