Rapid Review

"Study without thought is vain: thought without study is dangerous."
—Confucius

"It is better, of course, to know useless things than to know nothing."
—Lucius Annaeus Seneca

"For every complex problem there is an answer that is clear, simple, and wrong."
—H. L. Mencken

The following tables represent a collection of high-yield associations between diseases and their clinical findings, treatments, and key associations. They can be quickly reviewed in the days before the exam.

We have added a high-yield Pathophysiology of Important Diseases section for review of disease mechanisms and removed the Classic/Relevant Treatments section to accommodate the change in focus of the USMLE from pharmacology to pathophysiology.

▸ PATHOPHYSIOLOGY OF IMPORTANT DISEASES

CONDITION	MECHANISM	PAGE
Lesch-Nyhan syndrome	Absent HGPRT → ↑ de novo purine synthesis → ↑ uric acid production	35
β-thalassemia	Mutation at splice site or promoter sequences → retained intron in mRNA	38, 424
Lynch syndrome	Failure of mismatch repair during the S phase → microsatellite instability	37, 395
I-cell disease	N-acetylglucosaminyl-1-phosphotransferase defect → Golgi mediated mannose residues phosphorylation failure (↓ mannose-6-phosphate) → ↑ cellular debris in lysosomes	45
Osteogenesis imperfecta	Type 1 collagen defect due to inability to form triple helices; mutation in *COL1A1* and *COL1A2* genes	49
Menkes disease	Defective *ATP7A* protein → impaired copper absorption and transport → ↓ lysyl oxidase activity → ↓ collagen cross-linking	49
Marfan syndrome	*FBN1* mutation on chromosome 15 → defective fibrillin (normally forms sheath around elastin)	50
Prader-Willi syndrome	Uniparental disomy or imprinting leading to silencing of maternal gene. Disease expressed when paternal allele deleted or mutated	56
Angelman syndrome	Silenced paternal gene leading to mutation, lack of expression, or deletion of *UBE3A* on maternal chromosome 15	56
Cystic fibrosis	Autosomal recessive ΔF508 deletion in *CFTR* gene on chromosome 7 → impaired ATP-gated Cl^- channel (secretes Cl^- in lungs and GI tract and reabsorbs Cl^- in sweat glands)	58
Duchenne muscular dystrophy	Dystrophin gene frameshift mutations → loss of anchoring protein to ECM (dystrophin) → myonecrosis	59
Myotonic dystrophy	CTG trinucleotide repeat expansion in *DMPK* gene → abnormal expression of myotonin protein kinase → myotonia	59
Fragile X syndrome	CGG trinucleotide repeat in *FMR1* gene → hypermethylation → ↓ expression	60
Bitot spots in vitamin A deficiency	↓ differentiation of epithelial cells into specialized tissue → squamous metaplasia	64
Wernicke encephalopathy in alcoholic patient given glucose	Thiamine deficiency → impaired glucose breakdown → ATP depletion worsened by glucose infusion	64
Pellagra in malignant carcinoid syndrome	Tryptophan is diverted towards serotonin synthesis by tumor → B_3 deficiency (B_3 is derived from tryptophan)	65
Kwashiorkor	Protein malnutrition → ↓ oncotic pressure (→ edema), ↓ apolipoprotein synthesis (→ liver fatty change)	69
Lactic acidosis, fasting hypoglycemia, hepatic steatosis in alcoholism	↑ NADH/NAD^+ ratio due to ethanol metabolism	70
Aspirin-induced hyperthermia	↑ permeability of mitochondrial membrane → ↓ proton [H^+] gradient and ↑ O_2 consumption → uncoupling	76
Hereditary fructose intolerance	Aldolase B deficiency → Fructose-1-phosphate accumulates → ↓ available phosphate → inhibition of glycogenolysis and gluconeogenesis	78
Classic galactosemia	Galactose-1-phosphate uridyltransferase deficiency → accumulation of toxic substances (eg, galactitol in eyes)	78

CONDITION	MECHANISM	PAGE
Cataracts, retinopathy, peripheral neuropathy in DM	Lens, retina, Schwann cells lack sorbitol dehydrogenase → intracellular sorbitol accumulation → osmotic damage	79
Recurrent *Neisseria* bacteremia	Terminal complement deficiencies (C5–C9) → failure of MAC formation	105
Hereditary angioedema	C1 esterase inhibitor deficiency → unregulated activation of kallikrein → ↑ bradykinin	105
Paroxysmal nocturnal hemoglobinuria	*PIGA* gene mutation → ↓ GPI anchors for complement inhibitors (DAF/CD55, MIRL/CD59) → complement-mediated intravascular hemolysis	105
Type I hypersensitivity	Immediate (minutes): antigen cross links IgE on mast cells → degranulation → release of histamine and tryptase Late (hours): mast cells secrete chemokines (attract eosinophils) and leukotrienes → inflammation, tissue damage	110
Type II hypersensitivity	Antibodies bind to cell-surface antigens → cellular destruction, inflammation, cellular dysfunction	110
Type III hypersensitivity	Antigen-antibody complexes → activate complement → attracts neutrophils	111
Type IV hypersensitivity	T cell-mediated (no antibodies involved). $CD8^+$ directly kills target cells, $CD4^+$ releases cytokines	111
Acute hemolytic transfusion reaction	Type II hypersensitivity reaction against donor RBCs (usually ABO antigens)	112
X-linked (Bruton) agammaglobulinemia	Defect in *BTK* gene (tyrosine kinase) → no B-cell maturation → absent B cells in peripheral blood, ↓ Ig of all classes	114
DiGeorge syndrome	22q11 microdeletion → failure to develop 3rd and 4th branchial (pharyngeal) pouches	114
Hyper-IgM syndrome	Defective CD40L on Th cells → class switching defect	115
Leukocyte adhesion deficiency (type 1)	LFA-1 integrin (CD18) defect → impaired phagocyte migration and chemotaxis	115
Chédiak-Higashi syndrome	*LYST* mutation → microtubule dysfunction → phagosome-lysosome fusion defect	115
Chronic granulomatous disease	NADPH oxidase defect → ↓ ROS, ↓ respiratory burst in neutrophils	115
Candida infection in immunodeficiency	↓ granulocytes (systemic), ↓ T cells (local)	114, 116
Graft-versus-host disease	Type IV hypersensitivity reaction; HLA mismatch → donor T cells attack host cells	117
Recurrent *S aureus*, *Serratia*, *B cepacia* infections in CGD	Catalase ⊕ organisms degrade H_2O_2 before it can be converted to microbicidal products by the myeloperoxidase system	126
Hemolytic uremic syndrome	Shiga/Shiga-like toxins inactivate 60S ribosome → ↑ cytokine release	130, 432
Tetanus	Tetanospasmin prevents release of inhibitory neurotransmitters (GABA and glycine) from Renshaw cells	130
Botulism	Toxin (protease) cleaves SNARE → ↓ neurotransmitter (ACh) release at NMJ	130
Gas gangrene	Alpha toxin (phospholipase/lecithinase) degrades phospholipids → myonecrosis	131
Toxic shock syndrome, scarlet fever	TSST-1 and erythrogenic exotoxin A (scarlet) cross-link β region of TCR to MHC class II on APCs outside of antigen binding site → ↑↑ IL-1, IL-2, IFN-γ, TNF-α	131

CONDITION	MECHANISM	PAGE
Shock and DIC by gram ⊖ bacteria	Lipid A of LPS → macrophage activation (TLR4/CD14), complement activation, tissue factor activation	131
Prosthetic device infection by *S epidermidis*	Biofilm production	126, 133
Endocarditis 2° to *S sanguinis*	Dextrans (biofilm) production that bind to fibrin-platelet aggregates on damaged heart valves	126, 134
Pseudomembranous colitis 2° to *C difficile*	Toxins A and B damage enterocytes → watery diarrhea	136
Diphtheria	Exotoxin inhibits protein synthesis via ADP-ribosylation of EF-2	137
Virulence of *M tuberculosis*	Cord factor activates macrophages (promoting granuloma formation), induces release of TNF-α; sulfatides (surface glycolipids) inhibit phagolysosomal fusion	138
Tuberculoid leprosy	Th1 immune response → mild symptoms	139
No effective vaccine for *N gonorrhoeae*	Antigenic variation of pilus proteins	140
Cystitis and pyelonephritis by *E coli*	Fimbriae (P pili)	143
Pneumonia, neonatal meningitis by *E coli*	K capsule	143
Chlamydiae resistance to β-lactam antibiotics	Lack of classic peptidoglycan due to reduced muramic acid	146
Influenza pandemics	RNA segment reassortment → antigenic shift	166
Influenza epidemics	Mutations in hemagglutinin, neuraminidase → antigenic drift	166
CNS invasion by rabies	Binds to ACh receptors → retrograde transport (dynein)	169
HIV infection	Virus binds CD4 along with CCR5 on macrophages (early), or CXCR4 on T cells (late)	173
Granuloma	Macrophages present antigens to $CD4^+$ and secrete IL-12 → $CD4^+$ differentiation into Th1 which secrete IFN-γ → macrophage activation	213
Limitless replicative potential of cancer cells	Reactivation of telomerase → maintains and lengthens telomeres → prevention of chromosome shortening and aging	217
Tissue invasion by cancer	↓ E-cadherin function → ↓ intercellular junctions → basement membrane and ECM degradation by metalloproteinases → cell attachment to ECM proteins (laminin, fibronectin) → locomotion → vascular dissemination	217
Persistent truncus arteriosus	Failure of aorticopulmonary septum formation	302
D-transposition of great arteries	Failure of the aorticopulmonary septum to spiral	302
Tet spells in tetralogy of Fallot	Crying, fever, exercise → ↑ RV outflow obstruction → ↑ right-to-left flow across VSD; squatting → ↑ SVR → ↓ right-to-left shunt → ↓ cyanosis	302
Eisenmenger syndrome	Uncorrected left-to-right shunt → ↑ pulmonary blood flow → remodeling of vasculature → pulmonary hypertension → RVH → right to left shunting	303
Atherosclerosis	Endothelial cell dysfunction → macrophage and LDL accumulation → foam cell formation → fatty streaks → smooth muscle cell migration, extracellular matrix deposition → fibrous plaque → complex atheromas	305
Thoracic aortic aneurysm	Cystic medial degeneration	306
Myocardial infarction	Rupture of coronary artery atherosclerotic plaque → acute thrombosis	308

CONDITION	MECHANISM	PAGE
Non–ST-segment elevation MI	Subendocardial infarcts (subendocardium vulnerable to ischemia)	308
ST-segment elevation MI	Transmural infarcts	308
Death within 0-24 hours post MI	Ventricular arrhythmia	309, 314
Death or shock within 3-14 days post MI	Macrophage-mediated ruptures: papillary muscle (2-7 days), interventricular septum (3-5 days), free wall (5-14 days)	309, 314
Wolff-Parkinson-White	Abnormal accessory pathway from atria to ventricle bypasses the AV node → ventricles begin to partially depolarize earlier → delta wave. Reentrant circuit → supraventricular tachycardia	311
Hypertrophic obstructive cardiomyopathy	Sarcomeric proteins gene mutations (myosin binding protein C and β-myosin heavy chain) → concentric hypertrophy (sarcomeres added in parallel). Death due to arrhythmia	315
Syncope, dyspnea in HOCM	Asymmetric septal hypertrophy, systolic anterior motion of mitral valve → outflow obstruction	315
Hypovolemic shock	↓ preload → ↓ CO	317
Cardiogenic shock	↓ CO due to left heart dysfunction	317
Distributive shock	↓ SVR (afterload)	317
Rheumatic fever	Antibodies against M protein cross react with self antigens; type II hypersensitivity reaction	319
Most common form of congenital adrenal hyperplasia	21-hydroxylase deficiency→ ↓ mineralocorticoids, ↓ cortisol, ↑ sex hormones, ↑ 17-hydroxyprogesterone	339
Heat intolerance, weight loss in hyperthyroidism	↑ Na^+-K^+ ATPase → ↑ basal metabolic rate → ↑ calorigenesis	344
Myxedema in hypothyroidism	↑ GAGs in interstitial space → ↑ osmotic pressure → ↑ water retention	344
Graves ophthalmopathy	Lymphocytic infiltration, fibroblast secretion of GAGs → ↑ osmotic muscle swelling, inflammation	346
1° hyperparathyroidism	Parathyroid adenoma or hyperplasia → ↑ PTH	349
2° hyperparathyroidism	↓ Ca^{2+} and/or ↑ PO_4^{3-} → parathyroid hyperplasia → ↑ PTH, ↑ ALP	349
Euvolemic hyponatremia in SIADH	↑ ADH → water retention → ↓ aldosterone, ↑ ANB, ↑ BNP → ↑ urinary Na^+ secretion	342
Small/large vessel disease in DM	Nonenzymatic glycation of proteins; small vessels → hyaline arteriosclerosis; large vessels → atherosclerosis	350
Diabetic ketoacidosis	↓ Insulin or ↑ insulin requirement → ↑ fat breakdown → ↑ free fatty acids → ↑ ketogenesis	351
Hyperosmolar hyperglycemic state	Hyperglycemia → ↑ serum osmolality, excessive osmotic diuresis	351
Zollinger-Ellison syndrome	Gastrin-secreting tumor (gastrinoma) of pancreas or duodenum → recurrent ulcers in duodenum/jejunum and malabsorption	357
Duodenal atresia	Failure to recanalize	366
Jejunal/ileal atresia	Disruption of SMA → ischemic necrosis of fetal intestine	366
Superior mesenteric artery syndrome	Diminished mesenteric fat → compression of transverse (third) portion of duodenum by SMA and aorta	370
Achalasia	Loss of postganglionic inhibitory neurons (contain NO and VIP) in myenteric plexus → failure of LES relaxation	383

CONDITION	MECHANISM	PAGE
Barrett esophagus	Chronic GERD → replacement (metaplasia) of nonkeratinized stratified squamous epithelium with intestinal epithelium (nonciliated columnar with goblet cells)	385
Acute gastritis 2° to NSAIDs	↓ PGE_2 → ↓ gastric protection	386
Celiac disease	Autoimmune-mediated intolerance of gliadin (found in wheat) → malabsorption (distal duodenum, proximal jejunum), steatorrhea	388
Fistula formation in Crohn	Transmural inflammation	389
Meckel diverticulum	Persistence of the vitelline (omphalomesenteric) duct	391
Hirschsprung disease	Loss of function mutation in *RET* → failure of neural crest migration → lack of ganglion cells/enteric nervous plexuses in distal colon	391
Adenoma-carcinoma sequence in colorectal cancer	Loss of *APC* (↓ intercellular adhesion, ↑ proliferation) → *KRAS* mutation (unregulated intracellular signaling) → loss of tumor suppressor genes (*TP53*, *DCC*)	395
Fibrosis in cirrhosis	Stellate cells	396
Reye syndrome	Aspirin ↓ β-oxidation by reversible inhibition of mitochondrial enzymes	398
Hepatic encephalopathy	Cirrhosis → portosystemic shunts → ↓ NH_3 metabolism	399
α_1-antitrypsin deficiency	Misfolded proteins aggregate in hepatocellular ER → cirrhosis. In lungs, ↓ α_1-antitrypsin → uninhibited elastase in alveoli → panacinar emphysema	400
Wilson disease	Mutated hepatocyte copper-transporting ATPase (*ATP7B* on chromosome 13) → ↓ copper incorporation into apoceruloplasmin, excretion into bile → ↓ serum ceruloplasmin, ↑ copper in tissues and urine	402
Hemochromatosis	*HFE* mutation on chromosome 6 → ↓ hepcidin production, ↑ intestinal absorption → iron overload (↑ ferritin,↑ iron, ↓ TIBC → ↑ transferrin saturation)	402
Gallstone ileus	Fistula between gallbladder and GI tract → stone enters GI lumen → obstructing ileocecal valve (narrowest point)	403
Acute cholangitis	Biliary tree obstruction → stasis/bacterial overgrowth	403
Acute pancreatitis	Autodigestion of pancreas by pancreatic enzymes	404
Rh hemolytic disease of the newborn	Rh ⊖ mother form antibodies (maternal anti-D IgG) against RBCs of Rh ⊕ fetus	411
Anemia in lead poisoning	Lead inhibits ferrochelatase and ALA dehydratase → ↓ heme synthesis, ↑ RBC protoporphyrin.	425
Anemia of chronic disease	Inflammation → ↑ hepcidin → ↓ release of iron from macrophages, ↓ iron absorption from gut	427
G6PD deficiency	Defect in G6PD → ↓ NADPH → ↓ reduced glutathione → ↑ RBC susceptibility to oxidant stress	428
Sickle cell anemia	Point mutation → substitution of glutamic acid with valine in β chain → low O_2, high altitude, acidosis precipitates sickling (deoxygenated HbS polymerizes) → anemia, vaso-occlusive disease	428
Bernard-Soulier syndrome	↓ GpIb → ↓ platelet-to-vWF adhesion	432
Glanzmann thrombasthenia	↓ GpIIb/IIIa → ↓ platelet-to-platelet aggregation, defective platelet plug formation	432
Thrombotic thrombocytopenic purpura	↓ *ADAMTS13* (a vWF metalloprotease) → ↓ degradation of vWF multimers → ↑ platelet adhesion and aggregation (microthrombi formation)	432

CONDITION	MECHANISM	PAGE
von Willebrand disease	↓ vWF → ↓ platelet-to-vWF adhesion, possibly ↑ PTT (vWF protects factor VIII)	433
Factor V Leiden	Mutant factor V (Arg506Gln) that is resistant to degradation by protein C	433
Axillary nerve injury	Fractured surgical neck or anterior dislocation of humerus → flattened deltoid	450
Radial nerve injury ("Saturday night palsy")	Compression of axilla (use of crutches), midshaft humerus fracture, repetitive pronation/supination of forearm (use of screwdriver) → wrist/finger drop, decreased grip strength	450
Median nerve injury (Ape's hand/Pope's blessing)	Proximal lesion: supracondylar fracture → loss of sensation over thenar eminence, dorsal and palmar aspect of lateral 3½ fingers Distal lesion: carpal tunnel syndrome	450
Ulnar nerve injury	Proximal lesion: fractured medial epicondyle → radial deviation of wrist on flexion Distal lesion: fractured hook of hamate (fall on outstretched hand) → ulnar claw on digital extension	450
Erb palsy (waiter's tip)	Traction/tear of C5-C6 roots during delivery on the neck of the infant, and due to trauma in adults	452
Klumpke palsy	Traction/tear of C8-T1 roots during delivery on the arm of the infant, and on trying to grab a branch in adults	452
Winged scapula	Injury to long thoracic nerve (C5-C7), like on axillary node dissection during mastectomy	452
Common peroneal nerve injury	Trauma on lateral aspect of leg or fracture of fibular neck → foot drop with steppage gait	457
Superior gluteal nerve injury	Iatrogenic injury during IM injection at gluteal region → Trendelenburg sign: lesion contralateral to side of hip that drops due to adductor weakness	457
Pudendal nerve injury	Injury during horseback riding or prolonged cycling; can be blocked during delivery at the ischial spine → ↓ sensation in perineal and genital area ± fecal/urinary incontinence	457
Radial head subluxation (nursemaid's elbow)	Due to sudden pull on arm (in children; head slips out of immature annular ligament)	466
Slipped capital femoral epiphysis	Obese young adolescent with hip/knee pain. Increased axial force on femoral head → epiphysis displaces relative to femoral neck like a scoop of ice cream slips off a cone	466
Achondroplasia	Constitutive activation of FGFR3 → ↓ chondrocyte proliferation → failure of endochondral ossification → short limbs	467
Osteoporosis	↑ osteoclast activity → ↓ bone mass secondary to 2° to ↓ estrogen levels, old age, and long term use of drugs like steroids	467
Osteopetrosis	Carbonic anhydrase II mutations → ↓ ability of osteoclasts to generate acidic environment → ↓ bone resorption leading to dense bones prone to fracture, pancytopenia (↓ marrow space)	468
Osteitis deformans (Paget disease)	↑ osteoclast activity followed by ↑ osteoblast activity → poor quality bone formed that is prone to fractures	468
Osteoarthritis	Mechanical degeneration of articular cartilage causing inflammation with inadequate repair and osteophyte formation	472
Rheumatoid arthritis	Autoimmune inflammation due to HLA-DR4 causing pannus formation → errodes articular cartilage and bone. Type III hypersensitivity reaction	111, 472

CONDITION	MECHANISM	PAGE
Sjogren syndrome	Autoimmune type IV hypersensitivity reaction leading to lymphocyte mediated damage of exocrine glands	474
Systemic lupus erythematosus	Predominantly a type III hypersensitivity reaction with decreased clearance of immune complexes. Hematologic manifestations are a type II hypersensitivity reaction	476
Blindness in giant cell (temporal) arteritis	Ophthalmic artery occlusion	478
Myasthenia gravis	Autoantibodies to postsynaptic nicotinic (ACh) receptors	480
Lambert-Eaton myasthenic syndrome	Autoantibodies to presynaptic calcium channels → ↓ ACh release	480
Albinism	Normal melanocyte number, ↓ melanin production	484
Vitiligo	Autoimmune destruction of melanocytes	484
Atopic dermatitis	Epidermal barrier dysfunction, genetic factors (ie, loss-of-function mutations in the filaggrin [*FLG*] gene), immune dysregulation, altered skin microbiome, environmental triggers of inflammation	485
Allergic contact dermatitis	Type IV hypersensitivity reaction. During the sensitization phase, Allergen activates Th1 cells → memory $CD4^+$ cells and $CD8^+$ form. Upon reexposure → $CD4^+$ cells release cytokines and $CD8^+$ cells kill targeted cells	485
Pemphigus vulgaris	Type II hypersensitivity reaction. IgG autoantibodies form against desmoglein 1 and 3 in desmosomes → separation of keratinocytes in stratum spinosum from stratum basale	489
Bullous pemphigoid	Type II hypersensitivity reaction. IgG autoantibodies against hemidesmosomes → separation of epidermis from dermis	489
Spina bifida occulta, meningocele, myelomeningocele, myeloschisis	Failure of caudal neuropore to fuse by 4th week of development	501
Anencephaly	Failure of rostral neuropore to close → no forebrain, open calvarium	501
Holoprosencephaly	Failure of the forebrain (prosencephalon) to divide into 2 cerebral hemispheres; developmental field defect typically occurring at weeks 3-4 of development; associated with *SHH* mutations	501
Lissencephaly	Failure of neuronal migration → smooth brain surface lacking sulci and gyri	501
Chiari I malformation	Downward displacement of cerebellar tonsils inferior to foramen magnum	502
Chiari II malformation	Herniation of cerebellum (vermis and tonsils) and medulla through foramen magnum → noncommunicating hydrocephalus	502
Dandy-Walker malformation	Agenesis of cerebellar vermis → cystic enlargement of 4th ventricle that fills the enlarged posterior fossa; associated with noncommunicating hydrocephalus and spina bifida	502
Syringomyelia	Fluid-filled, gliosis-lined cavity within spinal cord, associated with Chiari I malformation (low-lying cerebellar tonsils), less commonly with infections, tumors, trauma; damages crossing spinothalamic tract	502
Gerstmann syndrome	Lesion in the dominant parietal cortex → agraphia, acalculia, finger agnosia, left-right disorientation	524
Hemispatial neglect syndrome	Lesion in the nondominant parietal cortex → agnosia of contralateral side	524
Klüver-Bucy syndrome	Bilateral lesions in the amygdala; seen in HSV-1 encephalitis → disinhibition, including hyperphagia, hypersexuality, hyperorality	524

CONDITION	MECHANISM	PAGE
Parinaud syndrome (inability to move eyes up and down)	Lesion in the dorsal midbrain; often due to pineal gland tumors	524
Cerebral edema	Fluid accumulation in the brain parenchyma → ↑ ICP; may be cytotoxic (intracellular fluid accumulation due to osmotic shift; associated with early ischemia, hyperammonemia, SIADH) or vasogenic (extracellular fluid accumulation due to increased permeability of BBB; associated with late ischemia, trauma, hemorrhage, inflammation, tumors)	525
Aphasia	Stroke in dominant (usually left) hemisphere, in either the superior temporal gyrus of temporal lobe (Wernicke; receptive aphasia) or inferior frontal gyrus of frontal lobe (Broca; expressive aphasia)	526, 529
Locked-in syndrome (loss of horizontal, but not vertical, eye movements)	Stroke of the basilar artery	526
Lateral pontine syndrome	Stroke of the anterior inferior cerebellar artery	526
Lateral medullary (Wallenberg) syndrome	Stroke of the posterior inferior cerebellar artery	527
Medial medullary syndrome	Stroke of the anterior spinal artery	527
Neonatal intraventricular hemorrhage	Reduced glial fiber support and impaired autoregulation of BP in premature infants → bleeding into the ventricles, originating in the germinal matrix (a highly vascularized layer within the subventricular zone)	527
Epidural hematoma	Rupture of middle meningeal artery, often secondary to skull fracture involving the pterion	528
Subdural hematoma	Rupture of bridging veins; acute (traumatic, high-energy impact, sudden deceleration injury) or chronic (mild trauma, cerebral atrophy, ↑ age, chronic alcohol overuse, shaken baby syndrome)	528
Subarachnoid hemorrhage	Trauma, rupture of aneurysm (such as a saccular aneurysm), or arteriovenous malformation → bleeding	528
Intraparenchymal hemorrhage	Systemic hypertension (most often occur in the putamen of basal ganglia, thalamus, pons, and cerebellum), amyloid angiopathy, arteriovenous malformation, vasculitis, neoplasm, or secondary to reperfusion injury in ischemic stroke → bleeding	528
Phantom limb pain	Most commonly following amputation → reorganization of primary somatosensory cortex → sensation of pain in a limb that is no longer present	529
Diffuse axonal injury	Traumatic shearing of white matter tracts during rapid acceleration and/or deceleration of the brain (eg, motor vehicle accident) → multiple punctate hemorrhages involving white matter tracts → neurologic injury, often causing coma or persistent vegetative state	529
Conduction aphasia	Damage to the arcuate fasciculus	529
Global aphasia	Damage to both Broca (inferior frontal gyrus of frontal lobe) and Wernicke (superior temporal gyrus of temporal lobe) areas	529
Heat stroke	Inability of body to dissipate heat (eg, exertion) → CNS dysfunction (eg, confusion), rhabdomyolysis, acute kidney injury, ARDS, DIC	530
Migraine	Irritation of CN V, meninges, or blood vessels (release of vasoactive neuropeptides [eg, substance P, calcitonin gene-related peptide])	532
Parkinson disease	Loss of dopaminergic neurons of substantia nigra pars compacta	534

CONDITION	MECHANISM	PAGE
Huntington disease	Trinucleotide (CAG) repeat expansion in huntingtin (*HTT*) gene on chromosome 4 → toxic gain of function → atrophy of caudate and putamen with ex vacuo ventriculomegaly → ↑ dopamine, ↓ GABA, ↓ ACh in brain → neuronal death via glutamate excitotoxicity via NMDA receptor binding	534
Alzheimer disease	Widespread cortical atrophy, narrowing of gyri and widening of sulci; senile plaques in gray matter composed of beta-amyloid core (formed by cleavage of amyloid precursor protein); neurofibrillary tangles composed of intracellular, hyperphosphorylated tau protein; Hirano bodies (intracellular eosinophilic proteinaceous rods in hippocampus)	534
Frontotemporal dementia	Frontotemporal lobe degeneration → ↓ executive function and behavioral inhibition	534
Vascular dementia	Multiple arterial infarcts and/or chronic ischemia	535
HIV-associated dementia	Secondary to diffuse gray matter and subcortical atrophy	535
Idiopathic intracranial hypertension	Increased ICP, associated with dural venous sinus stenosis; impaired optic nerve axoplasmic flow → papilledema	536
Communicating hydrocephalus	Reduced CSF absorption by arachnoid granulations (eg, arachnoid scarring post-meningitis) → ↑ ICP, papilledema, herniation	536
Normal pressure hydrocephalus	Idiopathic, CSF pressure elevated only episodically, no ↑ subarachnoid space volume; expansion of ventricles distorts the fibers of the corona radiata	536
Noncommunicating hydrocephalus	Structural blockage of CSF circulation within ventricular system (eg, stenosis of aqueduct of Sylvius, colloid cyst blocking foramen of Monro, tumor)	536
Ex vacuo ventriculomegaly	Decreased brain tissue and neuronal atrophy → appearance of increased CSF on imaging	536
Multiple sclerosis	Autoimmune inflammation and demyelination of CNS (brain and spinal cord) → axonal damage	537
Osmotic demyelination syndrome	Rapid osmotic changes, most commonly iatrogenic correction of hyponatremia but also rapid shifts of other osmolytes (eg, glucose) → massive axonal demyelination in pontine white matter	538
Acute inflammatory demyelinating polyneuropathy (subtype of Guillain-Barré syndrome)	Autoimmune destruction of Schwann cells via inflammation and demyelination of motor and sensory fibers and peripheral nerves; likely facilitated by molecular mimicry and triggered by inoculations or stress	538
Charcot-Marie-Tooth disease	Defective production of proteins involved in the structure and function of peripheral nerves or the myelin sheath	538
Progressive multifocal leukoencephalopathy	Destruction of oligodendrocytes secondary to reactivation of latent JC virus infection → demyelination of CNS	538
Sturge-Weber syndrome	Somatic mosaicism of an activating mutation in one copy of the *GNAQ* gene → congenital anomaly of neural crest derivatives → capillary vascular malformation, ipsilateral leptomeningeal angioma with calcifications, episcleral hemangioma	539
Pituitary adenoma	Hyperplasia of only one type of endocrine cells found in pituitary (most commonly from lactotrophs, producing prolactin)	540
Spinal muscular atrophy	Congenital degeneration of anterior horns *SMN1* mutation → defective snRNP assembly → LMN apoptosis	544
Amyotrophic lateral sclerosis	Combined UMN and LMN degeneration; familial form associated with *SOD1* mutation	544

CONDITION	MECHANISM	PAGE
Tabes dorsalis	Degeneration/demyelination of dorsal columns and roots (in 3° syphilis) → progressive sensory ataxia (impaired proprioception → poor coordination)	544
Poliomyelitis	Poliovirus infection spreads from lymphoid tissue of oropharynx to small intestine and then to CNS via bloodstream → destruction of cells in anterior horn of spinal cord (LMN death)	544
Friedreich ataxia	Trinucleotide repeat disorder (GAA) on chromosome 9 in gene that encodes frataxin (iron-binding protein) → impairment in mitochondrial functioning → degeneration of lateral corticospinal tract, spinocerebellar tract, dorsal columns, and dorsal root ganglia	545
Noise-induced hearing loss	Damage to stereociliated cells in organ of Corti → loss of high-frequency hearing first; sudden extremely loud noises can lead to tympanic membrane rupture → hearing loss	548
Presbycusis	Destruction of hair cells at the cochlear base (preserved low-frequency hearing at apex) → aging-related progressive bilateral/symmetric sensorineural hearing loss (often of higher frequencies)	548
Cholesteatoma	Abnormal growth of keratinized squamous epithelium in middle ear; 1° acquired from tympanic membrane retraction pocket; 2° from tympanic membrane perforation	548
Ménière disease	Increased endolymph in inner ear → vertigo, sensorineural hearing loss, tinnitus and ear fullness	548
Hyperopia	Eye too short for refractive power of cornea and lens → light focused behind retina	549
Myopia	Eye too long for refractive power of cornea and lens → light focused in front of retina	549
Astigmatism	Abnormal curvature of cornea → different refractive power at different axes	549
Presbyopia	Aging-related impaired accommodation, likely due to primarily due to ↓ lens elasticity	550
Glaucoma	Optic neuropathy causing progressive vision loss (peripheral → central), usually accompanied by increased intraocular pressure	551
Open-angle glaucoma	Associated with increased resistance to aqueous humor drainage through trabecular meshwork	551
Angle-closure glaucoma	Anterior chamber angle is narrowed or closed; associated with anatomic abnormalities (eg, anteriorly displaced lens resting against central iris) → ↓ aqueous flow through pupil → ↑ pressure in posterior chamber → peripheral iris pushed against cornea → obstruction of drainage pathways by the iris	551
Diabetic retinopathy	Chronic hyperglycemia → ↑ permeability and occlusion of retinal vessels → microaneurysms, hemorrhages (nonproliferative); retinal neovascularization due to chronic hypoxia (proliferative)	552
Hypertensive retinopathy	Chronic hypertension → spasm, sclerosis, and fibrinoid necrosis of retinal vessels	552
Retinal artery occlusion	Blockage of central or branch retinal artery usually due to embolism (carotid artery atherosclerosis > cardiogenic); less commonly due to giant cell arteritis	552

CONDITION	MECHANISM	PAGE
Retinal vein occlusion	Primary thrombosis → central retinal vein occlusion; secondary thrombosis at arteriovenous crossings (sclerotic arteriole compresses adjacent venule causing turbulent blood flow) → branch retinal vein occlusion	552
Retinal detachment	Separation of neurosensory retina from underlying retinal pigment epithelium → loss of choroidal blood supply → hypoxia and degeneration of photoreceptors; due to retinal tears (rhegmatogenous) or tractional or exudative (fluid accumulation) (nonrhegmatogenous)	552
Retinitis pigmentosa	Progressive degeneration of photoreceptors and retinal pigment epithelium	552
Papilledema	↑ ICP (eg, secondary to mass effect) → impaired axoplasmic flow in optic nerve → optic disc swelling (usually bilateral)	552
Relative afferent pupillary defect	Unilateral or asymmetric lesions of afferent limb of pupillary reflex (eg, retina, optic nerve)	554
Horner syndrome	Lesions along the sympathetic chain: 1st neuron (pontine hemorrhage, lateral medullary syndrome, spinal cord lesion above T1 like Brown-Sequard syndrome or late-stage syringomyelia); 2nd neuron (stellate ganglion compression by Pancoast tumor); 3rd neuron (carotid dissection)	555
Cavernous sinus syndrome	Secondary to pituitary tumor mass effect, carotid-cavernous fistula, or cavernous sinus thrombosis related to infection (spreads due to lack of valves in dural venous sinuses)	557
Delirium	Usually secondary to illnesses (eg, CNS disease, infection, trauma, substance use, metabolic/electrolyte imbalance, hemorrhage, urinary/fecal retention), or medications (eg, anticholinergics)	575
Schizophrenia	Altered dopaminergic activity, ↑ serotonergic activity, ↓ dendritic branching	577
Distal RTA (type 1)	Inability of α-intercalated cells to secrete H^+ → no new HCO_3^- generated → metabolic acidosis	611
Proximal RTA (type 2)	Defective PCT HCO_3^- reabsorption → ↑ excretion of HCO_3^- in urine → metabolic acidosis	611
Hyperkalemic tubular acidosis (type 4)	Hypoaldosteronism/aldosterone resistance → ↑ K^+ → NH_3 synthesis in PCT → ↓ NH_4^+ excretion	611
Nephritic syndrome	Glomerular inflammation → GBM damage → loss of RBCs in urine → dysmorphic RBCs, hematuria; ↓ GFR → oliguria, azotemia, ↑ renin release, HTN	613
Nephrotic syndrome	Podocyte damage → impaired charge barrier → proteinuria; hypoalbuminemia → ↑ hepatic lipogenesis → hypercholesterolemia; antithrombin loss → hypercoagulability; IgG loss → infections	613
Nephritic-nephrotic syndrome	Severe GBM damage → loss of RBCs in urine + impaired charge barrier → hematuria + proteinuria	613
Infection-related glomerulonephritis	Type III hypersensitivity reaction with consumptive hypocomplementemia	614
Alport syndrome	Type IV collagen mutation (X-linked dominant) → irregular thinning and thickening and splitting of GBM → nephritic syndrome	615
Stress incontinence	Outlet incompetence (urethral hypermobility/intrinsic sphincter deficiency) → leak on ↑ intraabdominal pressure (eg, sneezing, lifting)	618
Urge incontinence	Detrusor overactivity → leak with urge to void	618
Overflow incontinence	Incomplete emptying (detrusor underactivity or outlet obstruction) → leak with overfilling	618

CONDITION	MECHANISM	PAGE
Prerenal azotemia	↓ RBF → ↓ GFR → ↑ reabsorption of Na^+/H_2O and urea	620
Intrinsic renal failure	Patchy necrosis → debris obstructing tubules and fluid backflow → ↓ GFR	620
Postrenal azotemia	Outflow obstruction (bilateral)	620
Adnexal torsion	Twisting of ovary/fallopian tube around infundibulopelvic ligament and ovarian ligament → venous/lymphatic blockage → arterial inflow continued → edema → blockade of arterial inflow → necrosis	643
Preeclampsia	Abnormal placental spiral arteries → endothelial dysfunction, vasoconstriction, ischemia → new-onset HTN with proteinuria	660
Supine hypotensive syndrome	Supine position → compressed abdominal aorta and IVC by gravid uterus → ↓ placental perfusion and ↓ venous return	661
Polycystic ovary syndrome	Hyperinsulinemia and/or insulin resistance → altered hypothalamic feedback response → ↑ LH:FSH, ↑ androgens, ↓ rate of follicular maturation → unruptured follicles (cysts) + anovulation	662
Functional hypothalamic amenorrhea	Severe caloric restriction, ↑ energy expenditure, and/or stress → altered pulsatile GnRH secretion → ↓ LH, FSH, estrogen	663
Varicocele	Dilated veins in pampiniform plexus due to ↑ venous pressure → enlarged scrotum	669
Methemoglobin	Oxidized Hb secondary to dapsone, local anesthetics, nitrites → Hb oxidization (Fe^{2+}) → ↓ O_2 binding but ↑ cyanide affinity → tissue hypoxia	688
Deep venous thrombosis	Stasis, hypercoagulability, endothelial damage (Virchow triad) → blood clot within deep vein	690
Sarcoidosis associated hypercalcemia	Noncaseating granulomas → ↑ macrophage activity → ↑ 1α-hydroxylase activity in macrophage → vitamin D activation → ↑ Ca^{2+}	695
Acute respiratory distress syndrome	Alveolar injury → inflammation → capillary endothelial damage and ↑ vessel permeability → leakage of protein-rich fluid into alveoli → intra-alveolar hyaline membranes and noncardiogenic pulmonary edema → ↓ compliance and V/Q mismatch → hypoxic vasoconstriction → ↑ pulmonary vascular resistance	697
Sleep apnea	Respiratory effort against airway obstruction (obstructive); impaired respiratory effort due to CNS injury/toxicity, CHF, opioids (central); obesity → hypoventilation → ↑ $PaCO_2$ during waking hours	697

▸ CLASSIC PRESENTATIONS

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Gout, intellectual disability, self-mutilating behavior in a boy	Lesch-Nyhan syndrome (HGPRT deficiency, X-linked recessive)	35
Situs inversus, chronic ear infections, sinusitis, bronchiectasis, infertility	Primary ciliary dyskinesia (Kartagener syndrome)	47
Blue sclera, multiple fractures, dental problems, conductive/mixed hearing loss	Osteogenesis imperfecta (type I collagen defect)	49
Elastic skin, hypermobility of joints, ↑ bleeding tendency	Ehlers-Danlos syndrome (type V collagen defect, type III collagen defect seen in vascular subtype of ED)	49

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Arachnodactyly, lens dislocation (upward and temporal), aortic dissection, hyperflexible joints	Marfan syndrome (fibrillin-1)	50
Arachnodactyly, pectus deformity, lens dislocation (downward)	Homocystinuria (autosomal recessive cystathionine synthase deficiency)	50
Café-au-lait spots (unilateral), polyostotic fibrous dysplasia, precocious puberty, multiple endocrine abnormalities	McCune-Albright syndrome (G_s-protein activating mutation)	55
Meconium ileus in neonate, recurrent pulmonary infections, nasal polyps, pancreatic insufficiency, infertility/subfertility, malabsorption/vitamin deficiencies	Cystic fibrosis (*CFTR* gene defect, chromosome 7, ΔF508)	58
Calf pseudohypertrophy	Muscular dystrophy (most commonly Duchenne, due to X-linked recessive frameshift mutation of dystrophin gene)	59
Child uses arms to stand up from squat	Duchenne muscular dystrophy (Gowers sign)	59
Slow, progressive muscle weakness in boys	Becker muscular dystrophy (X-linked non-frameshift deletions in dystrophin; less severe than Duchenne)	59
Infant with cleft lip/palate, microcephaly or holoprosencephaly, polydactyly, cutis aplasia	Patau syndrome (trisomy 13)	61
Infant with microcephaly, rocker-bottom feet, clenched hands, and structural heart defect	Edwards syndrome (trisomy 18)	61
Single palmar crease, flat facies, prominent epicanthal folds, congenital heart disease, intellectual disability	Down syndrome (trisomy 21)	61
Microcephaly, high-pitched cry, intellectual disability	Cri-du-chat (cry of the cat) syndrome	62
Confusion, ophthalmoplegia/nystagmus, ataxia	Wernicke encephalopathy (add confabulation/memory loss and personality changes for Korsakoff syndrome)	64
Dilated cardiomyopathy/high-output heart failure, edema, alcoholism or malnutrition	Wet beriberi (thiamine [vitamin B_1] deficiency)	64
Dermatitis, dementia, diarrhea	Pellagra (niacin [vitamin B_3] deficiency)	65
Burning feet syndrome, dermatitis, enteritis, alopecia	Pentothenic acid (vitamin B_5) deficiency	65
Megaloblastic anemia, subacute combined degeneration, paresthesias, cognitive changes	Cobalamin (vitamin B12) deficiency; malabsorption, decreased intrinsic factor, absent terminal ileum	67
Swollen gums, mucosal bleeding, poor wound healing, petechiae, corkscrew hairs, perifollicular hemorrhages	Scurvy (vitamin C deficiency: can't hydroxylate proline/lysine for collagen synthesis); tea and toast diet	67
Bowlegs (children), bone pain, and muscle weakness	Rickets (children), osteomalacia (adults); vitamin D deficiency	68
Hemorrhagic disease of newborn with aPTT, normal bleeding time	Vitamin K deficiency	69
Intellectual disability, musty body odor, hypopigmented skin, eczema	Phenylketonuria (tetrahydrobiopterin [BH_4] deficiency)	82
Bluish-black connective tissue, ear cartilage, sclerae; severe arthralgias; urine turns black on prolonged exposure to air	Alkaptonuria (homogentisate oxidase deficiency; ochronosis)	82

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Infant with hypoglycemia, hepatomegaly, cardiomyopathy	Cori disease (debranching enzyme deficiency) or von Gierke disease (glucose-6-phosphatase deficiency, more severe)	85
Chronic exercise intolerance with myalgia, fatigue, painful cramps, myoglobinuria	McArdle disease (skeletal muscle glycogen phosphorylase deficiency)	85
"Cherry-red spots" on macula	Tay-Sachs (ganglioside accumulation; no hepatosplenomegaly); Niemann-Pick disease (sphingomyelin accumulation; hepatosplenomegaly); central retinal artery occlusion	86, 552
Hepatosplenomegaly, pancytopenia, osteoporosis, avascular necrosis of femoral head, bone crises	Gaucher disease (glucocerebrosidase [β-glucosidase] deficiency)	86
Achilles tendon xanthoma, corneal arcus	Familial hypercholesterolemia (↓ LDL receptor signaling)	92
Male child, recurrent infections, no mature B cells	Bruton disease (X-linked agammaglobulinemia [*BTK* gene defect])	114
Anaphylaxis following blood transfusion, atopy, airway/GI infections, autoimmune disease	Selective IgA deficiency	114
Recurrent cold (noninflamed) abscesses, eczema, high serum IgE, ↑ eosinophils	Hyper-IgE syndrome (Job syndrome: neutrophil chemotaxis abnormality; *STAT3* mutation)	114
Late separation (>30 days) of umbilical cord, no pus, recurrent skin and mucosal bacterial infections	Leukocyte adhesion deficiency (type 1; defective LFA-1 [CD18] integrin)	115
Recurrent infections and granulomas with catalase ⊕ organisms	Chronic granulomatous disease (defect of NADPH oxidase)	115
Fever, vomiting, diarrhea, desquamating rash following prolonged use of nasal pack or tampon	Staphylococcal toxic shock syndrome	133
"Strawberry tongue"	Scarlet fever (sandpaper rash); Kawasaki disease (lymphadenopathy, high fever for 5 days)	134, 478
Colon cancer associated with infective endocarditis	*Streptococcus gallolyticus* (formerly *S bovis*)	135
Flaccid paralysis in newborn after ingestion of honey	*Clostridium botulinum* infection (floppy baby syndrome)	136
Abdominal pain, diarrhea, leukocytosis, recent antibiotic use	*Clostridioides difficile* infection	136
Tonsillar pseudomembrane with "bull's neck" appearance	*Corynebacterium diphtheria* infection	137
Back pain, fever, night sweats	Pott disease (vertebral TB)	138
Acute adrenal insufficiency, fever, bilateral adrenal hemorrhage	Waterhouse-Friderichsen syndrome (meningococcemia)	140, 353
Red "currant jelly" sputum in patients with alcohol overuse or diabetes	*Klebsiella pneumoniae* pneumonia	143
Fever, chills, headache, myalgia following antibiotic treatment for syphilis	Jarisch-Herxheimer reaction (due to host response to sudden release of bacterial antigens)	144
Large rash with bull's-eye appearance, flu-like symptoms	Erythema migrans from *Ixodes* tick bite (Lyme disease: *Borrelia*)	144
Ulcerated genital lesion	Nonpainful, indurated: chancre (1° syphilis, *Treponema pallidum*) Painful, with exudate: chancroid *(Haemophilus ducreyi)*	145, 180

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Smooth, moist, painless, wartlike white lesions on genitals	Condylomata lata (2° syphilis)	145
Pupil accommodates but doesn't react to light	Neurosyphilis Argyll Robertson pupil (3° [neuro] syphilis)	145
Dog or cat bite resulting in infection (cellulitis, osteomyelitis)	*Pasteurella multocida* (cellulitis at inoculation site)	147
Atypical "walking pneumonia" with x-ray looking worse than the patient	*Mycoplasma pneumoniae* infection	148
Rash on palms and soles	Coxsackie A infection, 2° syphilis, Rocky Mountain spotted fever	148
Black eschar on face of patient with diabetic ketoacidosis and/or neutropenia	*Mucor* or *Rhizopus* fungal infection	150
Chorioretinitis, hydrocephalus, intracranial calcifications, +/– blueberry muffin rash	Congenital toxoplasmosis	153, 181
Pruritus, serpiginous rash after walking barefoot, microcytic anemia	Hookworm (*Ancylostoma* spp, *Necator americanus*)	156
Child with fever later develops red rash on face that spreads to body	Erythema infectiosum/fifth disease ("slapped cheeks" appearance, caused by parvovirus B19)	161
Fever, cough, conjunctivitis, coryza, diffuse rash	Measles	167
Small, irregular red spots on buccal/lingual mucosa with blue-white centers	Koplik spots (measles [rubeola] virus)	167
Hyperdynamic pulses, wide pulse pressure, early diastolic murmur (decrescendo), head bobbing	Aortic regurgitation	296
Systolic ejection murmur (crescendo-decrescendo), narrow pulse pressure, pulsus parvus et tardus	Aortic stenosis	296
Continuous "machinelike" heart murmur	PDA (close with indomethacin; keep open with PGE analogs)	296
Chest pain on exertion	Angina (stable: with moderate exertion; unstable: with minimal exertion or at rest)	308
Chest pain with ST depressions on ECG	Angina (⊖ troponins) or NSTEMI (⊕ troponins)	308
Chest pain, pericardial effusion/friction rub, persistent fever following MI	Postcardiac injury syndrome (autoimmune-mediated post-MI fibrinous pericarditis, 2 weeks to several months after acute episode)	314
Distant heart sounds, distended neck veins, hypotension	Beck triad of cardiac tamponade	317
Painful, raised red/purple lesions on pads of fingers/toes	Osler nodes (infective endocarditis, immune complex deposition)	318
Painless erythematous lesions on palms and soles	Janeway lesions (infective endocarditis, septic emboli/microabscesses)	318
Splinter hemorrhages in fingernails	Infective endocarditis	318
Retinal hemorrhages with pale centers	Roth spots (infective endocarditis)	318
Telangiectasias, recurrent epistaxis, skin discoloration, arteriovenous malformations, GI bleeding, hematuria	Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)	320
Polyuria, polydipsia	Primary polydipsia, diabetes mellitus (types 1 and 2), diabetes insipidus (central, nephrogenic)	342, 350
No lactation postpartum, absent menstruation, cold intolerance	Sheehan syndrome (severe postpartum hemorrhage leading to pituitary infarction)	343

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Heat intolerance, weight loss, palpitations, fine tremor, hyperreflexia	Hyperthyroidism	344
Cold intolerance, weight gain, brittle hair, depressed mood, hyporeflexia	Hypothyroidism	344
Cutaneous/dermal edema due to deposition of mucopolysaccharides in connective tissue	Myxedema (caused by hypothyroidism or hyperthyroidism [Graves disease])	344
Facial muscle spasm upon tapping	Chvostek sign (hypocalcemia)	348
Carpal spasm upon inflation of BP cuff	Trousseau sign (hypocalcemia)	348
Rapid, deep, labored breathing/hyperventilation	Diabetic ketoacidosis (Kussmaul respirations)	351
Skin hyperpigmentation, orthostatic hypotension, fatigue, weakness, muscle aches, weight loss, GI disturbances	Chronic 1° adrenal insufficiency (Addison disease) → ↑ ACTH, ↑ MSH	353
Shock, altered mental status, vomiting, abdominal pain, weakness, fatigue in patient under glucocorticoid therapy	Acute adrenal insufficiency (adrenal crisis)	353
Pancreatic, pituitary, parathyroid tumors	MEN1 (autosomal dominant *MEN1* mutation)	356
Medullary thyroid carcinoma, parathyroid hyperplasia, pheochromocytoma	MEN2A (autosomal dominant *RET* mutation)	356
Medullary thyroid carcinoma, pheochromocytoma, mucosal neuromas, marfanoid habitus	MEN2B (autosomal dominant *RET* mutation)	356
Cutaneous flushing, diarrhea, bronchospasm, heart murmur	Carcinoid syndrome (↑ urinary 5-HIAA); indicates systemic dissemination (eg, post liver metastases)	357
Jaundice, palpable distended nontender gallbladder	Courvoisier sign (distal obstruction of biliary tree by pancreatic head malignancy)	375, 405
Vomiting blood following gastroesophageal lacerations, +/– abdominal/back pain	Mallory-Weiss syndrome (alcohol use disorder, bulimia nervosa)	384
Dysphagia (esophageal webs), glossitis, iron deficiency anemia	Plummer-Vinson syndrome (may progress to esophageal squamous cell carcinoma)	384
Enlarged, hard left supraclavicular node	Virchow node (metastasis from abdominal malignancy)	386
Hematemesis, melena	Upper GI bleeding (eg, peptic ulcer disease)	387
Hematochezia	Lower GI bleeding (eg, colonic diverticulosis)	387
Arthralgias, cardiac and neurological symptoms, diarrhea	Whipple disease (*Tropheryma whipplei*)	388
Severe RLQ pain with palpation of LLQ	Rovsing sign (acute appendicitis)	390
Severe RLQ pain with deep tenderness	McBurney sign (acute appendicitis)	390
Hamartomatous GI polyps, hyperpigmented macules on mouth, feet, hands, genitalia	Peutz-Jeghers syndrome (inherited, benign polyposis can cause bowel obstruction; ↑ breast/GI cancer risk)	394
Multiple colon polyps, osteomas/soft tissue tumors, impacted/supernumerary teeth	Gardner syndrome (subtype of FAP)	394
Severe jaundice in neonate	Crigler-Najjar syndrome (congenital unconjugated hyperbilirubinemia)	401
Golden brown rings around peripheral cornea	Wilson disease (Kayser-Fleischer rings due to copper accumulation)	402
Female, fat (obese), fertile (multiparity), forty, fair, feeds (TPN), fasting (rapid weight loss)	Cholelithiasis (gallstones)	403

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Bluish line on gingiva	Burton line (lead poisoning)	425
Short stature, café-au-lait spots, thumb/radial defects, ↑ incidence of tumors/leukemia, aplastic anemia	Fanconi anemia (genetic loss of DNA crosslink repair; often progresses to AML)	427
Red/pink urine in the morning, pancytopenia, venous thrombosis	Paroxysmal nocturnal hemoglobinuria	428
Painful blue fingers/toes, hemolytic anemia	Cold autoimmune hemolytic anemia (caused by *Mycoplasma pneumoniae*, infectious mononucleosis, CLL)	429
Petechiae, mucosal bleeding, prolonged bleeding time	Platelet disorders (eg, Glanzmann thrombasthenia, Bernard Soulier, HUS, TTP, ITP, uremic platelet dysfunction)	432
Low-grade fever, night sweats, weight loss	B symptoms of malignancy	434
Skin patches/plaques, Pautrier microabscesses, atypical T cells	Mycosis fungoides (cutaneous T-cell lymphoma) or Sézary syndrome (mycosis fungoides + malignant T cells in blood)	435
Neonate with arm paralysis following difficult birth, arm in "waiter's tip" position	Erb palsy (superior trunk [C5–C6] brachial plexus injury)	452
Anterior drawer sign ⊕	Anterior cruciate ligament injury	455
Bone pain, bone enlargement, long bone chalk-stick fractures	Osteitis deformans (Paget disease of bone, ↑ osteoblastic and osteoclastic activity)	468
Swollen, hard, painful finger joints in an elderly individual, pain worse with activity	Osteoarthritis (osteophytes on PIP [Bouchard nodes], DIP [Heberden nodes])	472
Sudden swollen/painful big toe joint, tophi	Gout/podagra (hyperuricemia)	473
Dry eyes, dry mouth, arthritis, parotid enlargement	Sjögren syndrome (autoimmune destruction of exocrine glands)	474
Urethritis, conjunctivitis, arthritis	Reactive arthritis associated with HLA-B27	475
"Butterfly" facial rash, arthritis, cytopenia, and fever in a female of reproductive age	Systemic lupus erythematosus	476
Cervical lymphadenopathy, desquamating rash, coronary aneurysms, red conjunctivae and tongue, hand-foot changes	Kawasaki disease (mucocutaneous lymph node syndrome, treat with IVIG and aspirin)	478
Palpable purpura on buttocks/legs, joint pain, abdominal pain, hematuria in a child	Immunoglobulin A vasculitis (Henoch-Schönlein purpura, affects skin and kidneys)	479
Painful fingers/toes changing color from white to blue to red with cold or stress	Raynaud phenomenon (vasospasm in extremities)	480
Dark purple skin/mouth nodules in a patient with AIDS	Kaposi sarcoma, associated with HHV-8	486
Pruritic, purple, polygonal planar papules and plaques (6 P's)	Lichen planus	491
Dorsiflexion of large toe with fanning of other toes upon plantar scrape	Babinski sign (UMN lesion)	523, 543
Ataxia, nystagmus, head tilting, fall towards injured side	Cerebellar lesion (hemispheric affects voluntary movement of extremities; vermis affects axial and proximal movement)	524

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Hyperphagia, hypersexuality, hyperorality	Klüver-Bucy syndrome (bilateral amygdala lesion; HSV-1 encephalitis)	524
Resting tremor, athetosis, chorea	Basal ganglia lesion (eg, Huntington disease, Parkinson disease)	524
Dysphagia, hoarseness, ↓ gag reflex, nystagmus, ipsilateral Horner syndrome	Lateral medullary (Wallenberg) syndrome (posterior inferior cerebellar artery lesion)	527
Lucid interval after traumatic brain injury	Epidural hematoma (middle meningeal artery rupture; branch of maxillary artery)	528
"Worst headache of my life"	Subarachnoid hemorrhage	528
Resting tremor, rigidity, akinesia, postural instability, shuffling gait, micrographia	Parkinson disease (loss of dopaminergic neurons in substantia nigra pars compacta)	534
Chorea, dementia, caudate degeneration, dementia	Huntington disease (autosomal dominant CAG repeat expansion)	534
Urinary incontinence, gait apraxia, cognitive dysfunction	Normal pressure hydrocephalus	536
Relapsing and remitting nystagmus, intention tremor, optic neuritis, scanning speech, bilateral internuclear ophthalmoplegia	Multiple sclerosis	537
Rapidly progressive, symmetric limb weakness and hyporeflexia that ascends following GI/upper respiratory infection	Guillain-Barré syndrome (acute inflammatory demyelinating polyneuropathy)	538
Café-au-lait spots, Lisch nodules (iris hamartoma), cutaneous neurofibromas, pheochromocytomas, optic gliomas	Neurofibromatosis type I	539
Bilateral vestibular schwannomas	Neurofibromatosis type II	539
Vascular birthmark (port-wine stain) of the face	Nevus flammeus (benign, but associated with Sturge-Weber syndrome)	539
Renal cell carcinoma (bilateral), hemangioblastomas, angiomatosis, pheochromocytoma	von Hippel-Lindau disease (deletion of *VHL* on chromosome 3p)	539
Hyperreflexia, hypertonia, Babinski sign present	UMN damage	543
Hyporeflexia, hypotonia, atrophy, fasciculations	LMN damage	543
Staggering gait, frequent falls, nystagmus, hammer toes, diabetes mellitus, hypertrophic cardiomyopathy	Friedreich ataxia	545
Unilateral facial drooping involving forehead	LMN facial nerve (CN VII) palsy; UMN lesions spare the forehead	546
Episodic vertigo, tinnitus, sensorineural hearing loss	Ménière disease	548
Ptosis, miosis, anhidrosis	Horner syndrome (sympathetic chain lesion)	555
Conjugate horizontal gaze palsy, horizontal diplopia	Internuclear ophthalmoplegia (damage to MLF; may be unilateral or bilateral)	558
"Waxing and waning" level of consciousness (acute onset), ↓ attention span, ↓ level of arousal	Delirium (usually 2° to other cause)	575
Polyuria, renal tubular acidosis type II, growth retardation, electrolyte imbalances, hypophosphatemic rickets	Fanconi syndrome (generalized reabsorption defect of the proximal convoluted tubule)	604, 611

CLINICAL PRESENTATION	DIAGNOSIS/DISEASE	PAGE
Periorbital and/or peripheral edema, proteinuria (> 3.5 g/day; frothy urine), hypoalbuminemia, hypercholesterolemia	Nephrotic syndrome	613
Hereditary nephritis, sensorineural hearing loss, retinopathy, anterior lenticonus	Alport syndrome (mutation in type IV collagen)	615
Wilms tumor, macroglossia, organomegaly, hemihyperplasia, omphalocele	Beckwith-Wiedemann syndrome (*WT2* mutation)	624
Streak ovaries, congenital heart disease, horseshoe kidney, cystic hygroma, short stature, webbed neck, lymphedema	Turner syndrome (45,XO)	655
Ovarian fibroma, ascites, pleural effusion	Meigs syndrome	665
Red, itchy, swollen rash of nipple/areola	Paget disease of the breast (sign of underlying neoplasm)	668
Fibrous plaques in tunica albuginea of penis with abnormal curvature	Peyronie disease (connective tissue disorder)	669
Pink complexion, dyspnea, hyperventilation	Emphysema ("pink puffer," centriacinar [tobacco smoking] or panacinar [α_1-antitrypsin deficiency])	692
Hypoxemia, polycythemia, hypercapnia	Chronic bronchitis (hypertrophy and hyperplasia of mucus-secreting glands, "blue bloater")	692
Bilateral hilar adenopathy, uveitis, arthropathy, skin changes	Sarcoidosis (noncaseating granulomas)	695

▸ CLASSIC LABS/FINDINGS

LAB/DIAGNOSTIC FINDING	DIAGNOSIS/DISEASE	PAGE
Colonies of *Pseudomonas* in lungs ↑ Cl^- on sweat test, ↑ immunoreactive trypsinogen	Cystic fibrosis (autosomal recessive mutation in *CFTR* gene → fat-soluble vitamin deficiency and mucous plugs)	58
↓ AFP on second trimester screening	Down syndrome, Edwards syndrome	61
↑ β-hCG, ↓ PAPP-A on first trimester screening	Down syndrome	61
↑ serum homocysteine, ↑ methylmalonic acid, ↓ folate	Vitamin B_{12} deficiency	67
Anti-histone antibodies	Drug-induced lupus	113
↓ T cells, ↓ PTH, ↓ Ca^{2+}, absent thymic shadow on CXR	Thymic aplasia (22q11microdeletion: DiGeorge syndrome, velocardiofacial syndrome)	114
Recurrent infections, eczema, thrombocytopenia	Wiskott-Aldrich syndrome (*WAS* gene mutation)	115
Large granules in phagocytes, immunodeficiency	Chédiak-Higashi disease (*LYST* gene mutation: congenital failure of phagolysosome formation)	115
Optochin sensitivity	Sensitive: *S pneumoniae*; resistant: viridans streptococci (*S mutans*, *S sanguis*, *S mitis*)	132
Novobiocin response	Sensitive: *S epidermidis*; resistant: *S saprophyticus*	132
Bacitracin response	Sensitive: *S pyogenes* (group A); resistant: *S agalactiae* (group B)	132
Branching gram ⊕ rods with sulfur granules	*Actinomyces israelii*	137

LAB/DIAGNOSTIC FINDING	DIAGNOSIS/DISEASE	PAGE
Hilar lymphadenopathy, peripheral granulomatous lesion in middle or lower lung lobes (can calcify)	Ghon complex (1° TB: *Mycobacterium* bacilli)	138
"Thumb sign" on lateral neck x-ray	Epiglottitis (*Haemophilus influenzae*)	140
Bacteria-covered vaginal epithelial cells, ⊕ whiff test	"Clue cells" (*Gardnerella vaginalis*)	147
Ring-enhancing brain lesion on CT/MRI in AIDS	*Toxoplasma gondii* (multiple), CNS lymphoma (may be solitary)	153, 174
Dilated cardiomyopathy with apical atrophy, megacolon, megaesophagus	Chagas disease (*Trypanosoma cruzi*)	155
Atypical lymphocytes, heterophile antibodies	Infectious mononucleosis (EBV infection)	162
Narrowing of upper trachea and subglottis (Steeple sign) on x-ray	Croup (parainfluenza virus)	167
Eosinophilic inclusion bodies in cytoplasm of hippocampal and cerebellar neurons	Negri bodies of rabies	169
Concentrically laminated calcified spherules (psammoma bodies)	Meningiomas, papillary thyroid carcinoma, mesothelioma, papillary serous carcinoma of the endometrium and ovary	207
"Boot-shaped" heart on x-ray	Tetralogy of Fallot (due to RVH)	302
Rib notching (inferior surface, on x-ray)	Coarctation of the aorta	304
"Delta wave" on ECG, short PR interval, supraventricular tachycardia	Wolff-Parkinson-White syndrome (bundle of Kent bypasses AV node)	311
Electrical alternans (alternating amplitude on ECG)	Cardiac tamponade	317
Granuloma with giant cells after pharyngeal infection	Aschoff bodies (rheumatic fever)	319
Empty-appearing nuclei with central clearing of thyroid cells	"Orphan Annie" eyes nuclei (papillary carcinoma of the thyroid)	347
"Brown" tumor of bone	Hyperparathyroidism or osteitis fibrosa cystica (deposited hemosiderin from hemorrhage gives brown color)	349, 469
Hypertension, hypokalemia, metabolic alkalosis, ↑ aldosterone, ↓ renin	1° hyperaldosteronism (eg, Conn syndrome)	354
Mucin-filled cell with peripheral nucleus	"Signet ring" cells (diffuse gastric carcinoma)	386
Anti-transglutaminase/anti-deamidated gliadin/anti-endomysial antibodies	Celiac disease (diarrhea, weight loss)	388
Narrowing of bowel lumen on barium x-ray	"String sign" (Crohn disease)	389
"Lead pipe" appearance of colon on abdominal imaging	Ulcerative colitis (loss of haustra)	389
Thousands of polyps on colonoscopy after puberty	Familial adenomatous polyposis (autosomal dominant, mutation of APC gene)	394
"Apple core" lesion on barium enema x-ray	Colorectal cancer (usually left-sided)	395
"Nutmeg" appearance of liver	Chronic passive congestion of liver due to right heart failure, Budd-Chiari syndrome	397
Eosinophilic cytoplasmic inclusion of damaged keratin within hepatocyte	Mallory body (alcoholic hepatitis)	398
Triglyceride accumulation in liver cell vacuoles	Fatty liver disease (alcoholic or metabolic syndrome)	398
Anti-smooth muscle antibodies (ASMAs), anti-liver/kidney microsomal-1 (anti-LKM1) antibodies	Autoimmune hepatitis	399

LAB/DIAGNOSTIC FINDING	DIAGNOSIS/DISEASE	PAGE
Antimitochondrial antibodies (AMAs)	1° biliary cholangitis (female, cholestasis, portal hypertension)	402
Low serum ceruloplasmin	Wilson disease	402
Migratory thrombophlebitis (leading to migrating DVTs and vasculitis)	Trousseau syndrome (adenocarcinoma of pancreas)	405
Hypersegmented neutrophils	Megaloblastic anemia (vitamin B_{12} deficiency: neurologic symptoms; folate deficiency: no neurologic symptoms)	426
Basophilic nuclear remnants in RBCs	Howell-Jolly bodies (due to splenectomy or nonfunctional spleen)	422
Basophilic stippling of RBCs	Sideroblastic anemias, thalassemias	421
Hypochromic, microcytic anemia	Iron deficiency anemia, lead poisoning, thalassemia (fetal hemoglobin sometimes present), sideroblastic anemia	424, 425
"Hair on end" ("crew cut") appearance on x-ray	β-thalassemia, sickle cell anemia (marrow expansion)	425, 428
Anti-GpIIb/IIIa antibodies	Immune thrombocytopenia	432
High level of fibrin degradation products (D-dimers)	DVT, DIC	433, 690
Giant B cells with bilobed nucleus with prominent inclusions ("owl's eye")	Reed-Sternberg cells (Hodgkin lymphoma)	434
Sheets of medium-sized lymphoid cells with scattered pale, tingible body–laden macrophages ("starry sky" histology)	Burkitt lymphoma (t[8:14] c-*myc* activation, associated with EBV; "starry sky" made up of malignant cells)	435
Lytic ("punched-out") bone lesions on x-ray	Multiple myeloma	436
Monoclonal spike on serum protein electrophoresis	Multiple myeloma (usually IgG or IgA) Waldenström macroglobulinemia (IgM) Monoclonal gammopathy of undetermined significance	436
Stacks of RBCs	Rouleaux formation (high ESR, multiple myeloma)	436
Myeloperoxidase ⊕ cytoplasmic inclusions in myeloblasts, with ↑↑↑ circulating myeloblasts	Auer rods (APL)	437
WBCs that look "smudged"	CLL	437
"Tennis racket"-shaped cytoplasmic organelles (EM) in Langerhans cells	Birbeck granules (Langerhans cell histiocytosis)	439
"Soap bubble" in femur or tibia on x-ray	Giant cell tumor of bone (generally benign)	470
Raised periosteum (creating a "Codman triangle")	Aggressive bone lesion (eg, osteosarcoma, Ewing sarcoma)	471
"Onion skin" periosteal reaction	Ewing sarcoma (malignant small blue cell tumor)	471
IgM antibody that targets IgG Fc region, anti-cyclic citrullinated peptide antibodies	Rheumatoid arthritis (systemic inflammation, joint pannus, boutonniere and swan neck deformities)	472
Needle-shaped, ⊖ birefringent crystals	Gout (monosodium urate crystals)	473
↑ uric acid levels	Gout, Lesch-Nyhan syndrome, tumor lysis syndrome, loop and thiazide diuretics	473
Rhomboid crystals, ⊕ birefringent	Pseudogout (calcium pyrophosphate dihydrate crystals)	473

LAB/DIAGNOSTIC FINDING	DIAGNOSIS/DISEASE	PAGE
"Bamboo spine" on x-ray	Ankylosing spondylitis (chronic inflammatory arthritis: HLA-B27)	475
Antinuclear antibodies (ANAs: anti-Smith and anti-dsDNA)	SLE (type III hypersensitivity)	476
Antineutrophil cytoplasmic antibodies (ANCAs)	Microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis, and primary sclerosing cholangitis (MPO-ANCA/p-ANCA); granulomatosis with polyangiitis (PR3-ANCA/c-ANCA)	402, 479
Anticentromere antibodies	Limited scleroderma (CREST syndrome)	481
Anti-Scl-70 (anti-DNA topoisomerase-I) and anti-RNA polymerase III antibodies	Diffuse scleroderma	481
Anti-desmoglein (anti-desmosome) antibodies	Pemphigus vulgaris	489
Antihemidesmosome antibodies	Bullous pemphigoid	489
Keratin pearls on a skin biopsy	Squamous cell carcinoma	493
↑ AFP in maternal serum	Dating error, open neural tube defects.	501
Bloody or yellow CSF on lumbar puncture	Xanthochromia (due to subarachnoid hemorrhage)	528
Eosinophilic cytoplasmic inclusion in neuron	Lewy body (Parkinson disease and Lewy body dementia)	534
Extracellular amyloid deposition in gray matter of brain	Senile plaques (Alzheimer disease)	534
Loss of dopaminergic (pigmented) neurons in substantia nigra	Parkinson disease	534
Protein aggregates in neurons from hyperphosphorylation of tau protein	Neurofibrillary tangles (Alzheimer disease) and Pick bodies (frontotemporal dementia)	534
Pseudopalisading pleomorphic tumor cells on brain biopsy	Glioblastoma	540
Small blue cells surrounding central area of neuropil	Homer-Wright rosettes (neuroblastoma, medulloblastoma)	354, 542
RBC casts in urine	Glomerulonephritis, hypertensive emergency	612
WBC casts in urine	Acute pyelonephritis, transplant rejection, tubulointerstitial inflammation	612
Granular, "muddy-brown" casts in urine	Acute tubular necrosis (eg, ischemia or toxic injury)	612
"Waxy" casts with very low urine flow	End-stage renal disease/chronic kidney disease	612
"Lumpy bumpy" appearance of glomeruli on immunofluorescence	Infection-related glomerulonephritis (due to deposition of IgG, IgM, and C3)	614
Anti–glomerular basement membrane antibodies	Goodpasture syndrome (hematuria and hemoptysis)	614
Linear appearance of IgG deposition on glomerular and alveolar basement membranes	Goodpasture syndrome	614
Necrotizing vasculitis (lungs) and necrotizing glomerulonephritis	Granulomatosis with polyangiitis (PR3-ANCA/c-ANCA) and Goodpasture syndrome (anti–basement membrane antibodies)	614, 479
Cellular crescents in Bowman's space on light microscopy	Rapidly progressive (crescentic) glomerulonephritis	614
"Wire loop" glomerular capillary appearance on light microscopy	Diffuse proliferative glomerulonephritis (usually seen with lupus)	614

LAB/DIAGNOSTIC FINDING	DIAGNOSIS/DISEASE	PAGE
"Tram-track" appearance of capillary loops of glomerular basement membranes on light microscopy	Membranoproliferative glomerulonephritis	615
"Spikes" on basement membrane, "domelike" subepithelial deposits	Membranous nephropathy (nephrotic syndrome)	616
Effacement of podocyte foot processes on electron microscopy	Minimal change disease (child with nephrotic syndrome)	616
Eosinophilic nodular hyaline deposits in glomeruli	Kimmelstiel-Wilson nodules (diabetic glomerulonephropathy)	616
Thyroidlike appearance of kidney	Chronic pyelonephritis	619
hCG elevated	Multifetal gestation, hydatidiform moles, choriocarcinomas, Down syndrome	652
Dysplastic squamous cervical cells with "raisinoid" nuclei and perinuclear halo	Koilocytes (HPV infection: predisposes to cervical cancer)	663
Sheets of uniform "fried egg" cells, ↑ hCG, ↑ LDH	Dysgerminoma	664
Schiller-Duval bodies (resemble glomeruli), ↑AFP	Yolk sac tumor	664
Disarrayed granulosa cells arranged around collections of eosinophilic fluid	Call-Exner bodies (granulosa cell tumor of the ovary)	665
"Chocolate cyst" in ovary	Endometriosis	666
Mammary gland ("blue domed") simple cyst	Fibrocystic change of the breast	667
Eosinophilic cytoplasmic inclusions in Leydig cells	Reinke crystals (Leydig cell tumor)	671
Interdigitating layers of pink and red in arterial thrombi	Lines of Zahn (layers of platelets and RBCs seen only in thrombi formed before death)	691
Eosinophilic, hexagonal, double-pointed crystals in bronchial secretions	Charcot-Leyden crystals (asthma)	693
Whorled mucus plugs formed from shed bronchial epithelium	Curschmann spirals (asthma)	693
"Honeycomb" appearance of the lung on CXR or CT	Idiopathic pulmonary fibrosis	694
Golden-brown fusiform rods resembling dumbbells in alveolar sputum, visualized with Prussian blue stain	Asbestos (ferruginous) bodies	696
Bronchogenic apical lung tumor on imaging	Pancoast (superior sulcus) tumor (can compress cervical sympathetic chain and cause Horner syndrome)	704

▸ KEY ASSOCIATIONS

DISEASE/FINDING	MOST COMMON/IMPORTANT ASSOCIATIONS	PAGE
Mitochondrial inheritance	Disease occurs in all offspring of affected females (maternal inheritance pattern), heteroplasmy	55, 57
Intellectual disability	Down syndrome (sporadic), fragile X syndrome (inherited)	60, 61
Vitamin deficiency (USA)	Folate (pregnant women are at high risk; body stores only 3- to 4-month supply)	66

DISEASE/FINDING	MOST COMMON/IMPORTANT ASSOCIATIONS	PAGE
Lysosomal storage disease	Gaucher disease	86
HLA-DR3	DM type 1, SLE, Graves disease, Hashimoto thyroiditis, Addison disease	98
HLA-DR4	Rheumatoid arthritis, DM type 1, Addison disease	98
Bacteria associated with gastritis, peptic ulcer disease, and gastric malignancies (eg, adenocarcinoma, MALToma)	*H pylori*	144
Opportunistic respiratory infection in AIDS	*Pneumocystis jirovecii*	151
Viral encephalitis affecting temporal lobe	HSV-1	162
Viral infection 2° to blood transfusion	Hepatitis C	171
Food poisoning (exotoxin-mediated)	*S aureus*, *B cereus*	175
Healthcare-associated pneumonia	*S aureus*, *Pseudomonas*, other enteric gram ⊖ rods	176
Bacterial meningitis (0–6 months old)	Group B streptococcus, *E coli*, *Listeria*	177
Bacterial meningitis (> 6 months old)	*S pneumoniae*	177
Osteomyelitis	*S aureus* (most common overall)	177
Osteomyelitis in sickle cell disease	*Salmonella*, *S aureus*	177
Osteomyelitis with injection drug use	*S aureus*, *Pseudomonas*, *Candida*	177
UTI	*E coli*, *Staphylococcus saprophyticus*	179
Bacterial STI	*C trachomatis (D-K)*	180
Pelvic inflammatory disease	*C trachomatis* (subacute), *N gonorrhoeae* (acute)	182
Metastases to bone	Prostate, breast >> lung > kidney, colon	219
Metastases to liver	Colon > breast >> pancreas, lung, prostate	219
Metastases to brain	Lung > breast >> melanoma > colon, prostate	219
S3 heart sound	↑ ventricular filling pressure (eg, MR, AR, HF, thyrotoxicosis), common in dilated ventricles	292
S4 heart sound	Stiff/hypertrophic ventricle (aortic stenosis, restrictive cardiomyopathy)	292
Holosystolic murmur	VSD, tricuspid regurgitation, mitral regurgitation	296
Ejection click	Aortic stenosis	296
Mitral stenosis	Rheumatic heart disease (late and highly specific sequelae of rheumatic fever)	296
Opening snap	Mitral stenosis	296
Heart murmur, congenital	Mitral valve prolapse	296
Cyanotic heart disease (early)	Tetralogy of Fallot (most common), D-transposition of great arteries, persistent truncus arteriosus, total anomalous pulmonary venous return, tricuspid atresia	302
Congenital heart disease (left-to-right shunts)	VSD > ASD > PDA	303
Late cyanotic shunt (uncorrected left to right becomes right to left)	Eisenmenger syndrome (caused by VSD, ASD, PDA)	303
2° hypertension	Renal/renovascular diseases (eg, fibromuscular dysplasia), atherosclerotic renal artery stenosis, 1° hyperaldosteronism, or obstructive sleep apnea	304

DISEASE/FINDING	MOST COMMON/IMPORTANT ASSOCIATIONS	PAGE
Sites of atherosclerosis	Abdominal aorta > coronary artery > popliteal artery > carotid artery > circle of Willis	305
Aortic aneurysm, thoracic	Marfan syndrome (cystic medial degeneration), 3° syphilis (obliterative endarteritis of vasa vasorum)	306
Aortic aneurysm, abdominal	Atherosclerosis, tobacco use	306
Aortic dissection	Hypertension (most important risk factor)	307
Irregularly irregular rhythm on ECG with no discrete P waves	Atrial fibrillation (associated with high risk of emboli)	311
Right heart failure due to a pulmonary cause	Cor pulmonale	316
Heart valve in infective endocarditis	Mitral > aortic, tricuspid (injection drug use)	318
Infective endocarditis presentation associated with bacterium	*S aureus* (acute, injection drug use, tricuspid valve), viridans streptococci (subacute, dental procedure), *S gallolyticus* (colon cancer), gram ⊖ (HACEK), culture ⊖ (*Coxiella*, *Bartonella*)	318
Cardiac tumor (adults)	Metastasis, myxoma (90% in left atrium; "ball valve")	320
Cardiac 1° tumor (children)	Rhabdomyoma (associated with tuberous sclerosis)	320
Congenital adrenal hyperplasia	21-hydroxylase deficiency	339
Hypopituitarism	Pituitary adenoma (undersecretion due to mass effect)	343
Congenital hypothyroidism	Thyroid dysgenesis/dyshormonogenesis, iodine deficiency	345
Thyroid cancer	Papillary carcinoma (*RET/PTC* rearrangements, *BRAF* mutations, childhood irradiation)	347
Hypoparathyroidism	Accidental excision during thyroidectomy	348
1° hyperparathyroidism	Adenomas, hyperplasia	349
2° hyperparathyroidism	Hypocalcemia of chronic kidney disease	349
Cushing syndrome	▪ Exogenous glucocorticoids ▪ Adrenocortical adenoma (secretes excess cortisol) ▪ ACTH-secreting pituitary adenoma (Cushing disease) ▪ Paraneoplastic (due to ACTH secretion by tumors)	352
Cushing disease	↓ ACTH and cortisol in high-dose dexamethasone suppression tests, and ↑ ACTH and cortisol in CRH stimulation test	352
1° hyperaldosteronism	Bilateral adrenal hyperplasia or adenoma (Conn syndrome)	354
Tumor of the adrenal medulla (children)	Neuroblastoma (malignant)	354
Tumor of the adrenal medulla (adults)	Pheochromocytoma (usually benign)	355
Refractory peptic ulcers and high gastrin levels	Zollinger-Ellison syndrome (due to gastrin-secreting tumor of the duodenum or pancreas), associated with MEN1	357
Esophageal cancer	Squamous cell carcinoma (worldwide); adenocarcinoma (US)	385
Acute gastric ulcer associated with CNS injury	Cushing ulcer (↑ vagal stimulation → ↑ ACh → ↑ H^+ production)	386
Acute gastric ulcer associated with severe burns	Curling ulcer (hypovolemia → mucosal ischemia)	386

DISEASE/FINDING	MOST COMMON/IMPORTANT ASSOCIATIONS	PAGE
Chronic atrophic gastritis	↑ risk of gastric cancers, pernicious anemia (if autoimmune)	386
Bilateral ovarian metastases from gastric carcinoma	Krukenberg tumor (mucin-secreting signet ring cells)	386
Alternating areas of transmural inflammation and normal colon	Skip lesions (Crohn disease)	389
Site of diverticulosis	Sigmoid colon	390
False pharyngoesophageal diverticulum	Zenker diverticulum	391
Hepatocellular carcinoma	HBV (+/– cirrhosis), other causes of cirrhosis (HCV, alcoholic liver disease), specific carcinogens (eg, aflatoxins)	399
Inherited conjugated hyperbilirubinemia secondary to hepatocyte inability to secrete conjugated bilirubin in bile	Dubin-Johnson syndrome (black liver), Rotor syndrome (uncolored liver)	401
Inherited benign unconjugated hyperbilirubinemia	Gilbert syndrome	401
Inherited ATP7B mutation (copper buildup in liver, brain, cornea [Kayser-Fleischer rings], kidneys)	Wilson disease	402
Multiple blood transfusions or hereditary *HFE* mutation (can result in heart failure, "bronze diabetes," and ↑ risk of hepatocellular carcinoma)	Hemochromatosis	402
Pancreatitis (acute)	Gallstones, alcohol	404
Pancreatitis (chronic)	Alcohol (adults), cystic fibrosis (children)	404
Microcytic anemia	Iron deficiency, thalassemias, lead poisoning, sideroblastic anemia	424, 425
Autosplenectomy (fibrosis and shrinkage), Howell-Jolly bodies	Sickle cell anemia (hemoglobin S)	428
Inherited platelet disorder with GpIb deficiency	Bernard-Soulier syndrome (↓ platelet-to-vWF adhesion)	432
Inherited platelet disorder with GpIIb/IIIa deficiency	Glanzmann thrombasthenia (↓ platelet-to-platelet aggregation and defective platelet plug formation)	432
Hereditary thrombophilia commonly associated with recurrent pregnancy loss	Factor V Leiden (mutant factor V that is resistant to degradation)	434
Hereditary thrombophilia	Leiden (also associated with recurrent pregnancy loss)	433
DIC	Heat stroke, snake bite, sepsis, trauma, obstetric complications, acute pancreatitis, malignancy, nephrotic syndrome, transfusion	433
Common malignancy associated with noninfectious fever and bimodal age distribution	Hodgkin lymphoma	434
Type of Hodgkin lymphoma (most common)	Nodular sclerosis	434
t(14;18)	Follicular lymphoma (*BCL-2* activation, anti-apoptotic oncogene)	435, 439
t(8;14)	Burkitt lymphoma (c-*myc* fusion, transcription factor oncogene)	435, 439
Type of non-Hodgkin lymphoma (most common in adults)	Diffuse large B-cell lymphoma	435

DISEASE/FINDING	MOST COMMON/IMPORTANT ASSOCIATIONS	PAGE
Age ranges for patient with ALL/CLL/AML/CML	ALL: child, CLL: adult > 60, AML: adult ~ 65, CML: adult 45–85	437
t(9;22)	Philadelphia chromosome, CML (*BCR-ABL* oncogene, tyrosine kinase activation), more rarely associated with ALL	437, 439
Vertebral compression fracture	Osteoporosis	467
HLA-B27	Psoriatic arthritis, ankylosing spondylitis, IBD-associated arthritis, reactive arthritis	475
Death in SLE	Renal disease (most common), infections, cardiovascular disease (accelerated CAD)	476
Giant cell arteritis	Risk of ipsilateral blindness due to occlusion of ophthalmic artery; polymyalgia rheumatica	478
Recurrent inflammation/thrombosis of medium-vessels in extremities	Buerger disease (strongly associated with tobacco smoking, Raynaud phenomenon)	478
Benign vascular tumor of infancy	Infantile hemangioma (grows rapidly then involutes starting at age 1)	486
Herald patch (followed by scaly erythematous plaques in a "Christmas tree" distribution)	Pityriasis rosea	491
Actinic keratosis	Precursor to squamous cell carcinoma	493
Cerebellar tonsillar herniation	Chiari I malformation (associated with spinal cord cavitations [eg, syringomyelia])	502
Bilateral mamillary body lesions with thiamine deficiency	Wernicke-Korsakoff syndrome	524
Epidural hematoma	Rupture of middle meningeal artery (trauma; biconvex/lentiform-shaped)	528
Subdural hematoma	Rupture of bridging veins (crescent-shaped)	528
Dementia	Alzheimer disease, vascular dementia (multiple infarcts)	534, 535
Demyelinating disease in young women	Multiple sclerosis	537
Brain tumor (adults)	Metastasis, glioblastoma (malignant), meningioma, hemangioblastoma	540
Galactorrhea, amenorrhea	Prolactinoma	540
Brain tumor (children)	Overall: pilocytic astrocytoma (benign) Infratentorial: medulloblastoma (most common malignant) Supratentorial: craniopharyngioma (malignant)	542
Combined UMN and LMN degeneration	Amyotrophic lateral sclerosis	544
Degeneration of dorsal column fibers	Tabes dorsalis (3° syphilis), subacute combined degeneration (dorsal columns, lateral corticospinal, spinocerebellar tracts affected)	544
Nephrotic syndrome (children)	Minimal change disease	616
Kidney stones (radiolucent)	Uric acid	617
Kidney stones (radiopaque)	Calcium (most common), struvite (ammonium), cystine (faintly radiopaque)	617

DISEASE/FINDING	MOST COMMON/IMPORTANT ASSOCIATIONS	PAGE
Renal malignancy (in males)	Renal cell carcinoma: associated with tobacco smoking and VHL (clear cell subtype); paraneoplastic syndromes (EPO, renin, PTHrP, ACTH)	623
1° amenorrhea	Turner syndrome (45,XO or 45,XO/46,XX mosaic)	655
Hypogonadotropic hypogonadism with anosmia	Kallmann syndrome (neuron migration failure)	656
Clear cell adenocarcinoma of the vagina	DES exposure in utero	662
Ovarian tumor (benign, bilateral)	Serous cystadenoma	664
Ovarian tumor (malignant)	Serous carcinoma	664
Benign tumor of myometrium	Leiomyoma (estrogen sensitive, not precancerous)	666
Gynecologic malignancy (most common)	Endometrial carcinoma (most common in resource-rich countries); cervical cancer (most common worldwide)	663–666
Breast mass	Fibrocystic change (in premenopausal females); carcinoma (in postmenopausal females)	667, 668
Breast tumor (benign, young woman)	Fibroadenoma	667
Breast cancer	Invasive ductal carcinoma	668
Testicular tumor	Seminoma (malignant, radiosensitive), ↑ PLAP	670, 671
Bladder outlet obstruction in men	BPH	672
Hypercoagulability, endothelial damage, blood stasis	Virchow triad (↑ risk of thrombosis)	690
Pulmonary hypertension	Idiopathic, left heart disease, lung diseases/hypoxia, chronic thromboembolism, multifactorial	698
SIADH	Small cell carcinoma of the lung	703

▸ EQUATION REVIEW

TOPIC	EQUATION	PAGE
Volume of distribution	$V_d = \frac{\text{amount of drug in the body}}{\text{plasma drug concentration}}$	229
Half-life	$t_{½} = \frac{0.7 \times V_d}{CL}$	229
Drug clearance	$CL = \frac{\text{rate of elimination of drug}}{\text{plasma drug concentration}} = V_d \times K_e$ (elimination constant)	229
Loading dose	$LD = \frac{C_p \times V_d}{F}$	229
Maintenance dose	$\text{Maintenance dose} = \frac{C_p \times CL \times \tau}{F}$	229
Therapeutic index	TI = median toxic dose/median effective dose = TD_{50}/ED_{50}	233
Odds ratio (for case-control studies)	$OR = \frac{a/c}{b/d} = \frac{ad}{bc}$	258

TOPIC	EQUATION	PAGE
Relative risk	$RR = \frac{a/(a+b)}{c/(c+d)}$	258
Attributable risk	$AR = \frac{a}{a+b} - \frac{c}{c+d}$	258
Relative risk reduction	$RRR = (ARC - ART)/ARC$	258
Absolute risk reduction	$ARR = \frac{c}{c+d} - \frac{a}{a+b}$	258
Number needed to treat	$NNT = 1/ARR$	258
Number needed to harm	$NNH = 1/AR$	258
Likelihood ratio +	LR+ = sensitivity/(1 – specificity) = TP rate/FP rate	259
Likelihood ratio –	LR– = (1 – sensitivity)/specificity = FN rate/TN rate	259
Sensitivity	Sensitivity = TP / (TP + FN)	260
Specificity	Specificity = TN / (TN + FP)	260
Positive predictive value	PPV = TP / (TP + FP)	260
Negative predictive value	NPV = TN / (TN + FN)	260
Cardiac output	$CO = \frac{\text{rate of } O_2 \text{ consumption}}{(\text{arterial } O_2 \text{ content} - \text{venous } O_2 \text{ content})}$ CO = stroke volume × heart rate	290
Mean arterial pressure	MAP = CO × total peripheral resistance (TPR) MAP (at resting HR) = ⅔ DBP + ⅓ SBP = DBP + ⅓ PP	290
Stroke volume	SV = EDV – ESV	290
Ejection fraction	$EF = \frac{SV}{EDV} = \frac{EDV - ESV}{EDV}$	290
Resistance	$\text{Resistance} = \frac{\text{driving pressure } (\Delta P)}{\text{flow } (Q)} = \frac{8\eta \text{ (viscosity)} \times \text{length}}{\pi r^4}$	291
Capillary fluid exchange	J_v = net fluid flow = $K_f[(P_c - P_i) - \sigma(\pi_c - \pi_i)]$	301
Reticulocyte production index	$RPI = \%\text{ reticulocytes} \times \left(\frac{\text{actual Hct}}{\text{normal Hct}}\right) / \text{maturation time}$	423
Renal clearance	$C_x = (U_x V)/P_x$	600
Glomerular filtration rate	$C_{inulin} = GFR = U_{inulin} \times V/P_{inulin}$ $= K_f[(P_{GC} - P_{BS}) - (\pi_{GC} - \pi_{BS})]$	600
Effective renal plasma flow	$eRPF = U_{PAH} \times \frac{V}{P_{PAH}} = C_{PAH}$	600
Filtration fraction	$FF = \frac{GFR}{RPF}$	601
Fractional excretion of sodium	$Fe_{Na^+} = V \times U_{Na} / GFR \times P_{Na} = P_{Cr} \times U_{Na} / U_{Cr} \times P_{Na}$	602

TOPIC	EQUATION	PAGE
Henderson-Hasselbalch equation (for extracellular pH)	$pH = 6.1 + \log \frac{[HCO_3^-]}{0.03\ P_{CO_2}}$	609
Winters formula	$P_{CO_2} = 1.5\ [HCO_3^-] + 8 \pm 2$	609
Anion gap	$Na^+ - (Cl^- + HCO_3^-)$	610
Physiologic dead space	$V_D = V_T \times \frac{P_{aCO_2} - P_{ECO_2}}{P_{aCO_2}}$	682
Pulmonary vascular resistance	$PVR = \frac{P_{pulm\ artery} - P_{L\ atrium}}{\text{Cardiac output}}$	684
Alveolar gas equation	$P_{AO_2} = P_{IO_2} - \frac{P_{aCO_2}}{RQ} = 150\ mm\ Hg^a - P_{aCO_2} / 0.8$	685

▸ EASILY CONFUSED MEDICATIONS

DRUG	CLINICAL USE/MECHANISM OF ACTION
Amiloride	K^+-sparing diuretic
Amiodarone	K^+ channel blocker (class III antiarrhythmic)
Amlodipine	Dihydropyridine Ca^{2+} channel blocker
Benztropine	Parkinson disease (cholinergic antagonist)
Bromocriptine	Parkinson disease (dopamine agonist; rarely used)
Buspirone	Generalized anxiety disorder (partial 5-HT_{1A}-receptor agonist)
Bupropion	Depression, smoking cessation (NE-DA reuptake inhibitor)
Cimetidine	Gastritis, peptic ulcer (H_2-receptor antagonist)
Cetirizine	Allergy (2nd-generation antihistamine)
Chloramphenicol	Antibiotic (blocks 50S subunit)
Chlordiazepoxide	Long-acting benzodiazepine
Chlorpromazine	Typical antipsychotic
Chlorpropamide	1st-generation sulfonylurea
Chlorpheniramine	1st-generation antihistamine
Chlorthalidone	Thiazide diuretic
Clozapine	Atypical antipsychotic
Clomipramine	Tricyclic antidepressant
Clomiphene	Infertility due to anovulation (selective estrogen receptor modulator in hypothalamus)
Clonidine	Hypertensive urgency, ADHD (α_2-agonist)
Doxepin	Tricyclic antidepressant
Doxazosin	BPH, HTN (α_1-antagonist)
Eplerenone	K^+-sparing diuretic

DRUG	CLINICAL USE/MECHANISM OF ACTION
Propafenone	Na^+ channel blocker (class Ic antiarrhythmic)
Fluoxetine	Depression (selective serotonin reuptake inhibitor)
Fluphenazine	Typical antipsychotic
Mifepristone	Pregnancy termination (progesterone receptor antagonist)
Misoprostol	Used with mifepristone for pregnancy termination (PGE_1-synthetic analog)
Naloxone	Opioid receptor antagonist (treats toxicity)
Naltrexone	Opioid receptor antagonist (prevents relapse)
Nitroprusside	Hypertensive emergency (↑ cGMP/NO)
Nitroglycerin	Antianginal (↑ cGMP/NO)
Omeprazole	Proton pump inhibitor (inhibits H^+/K^+-ATPase in parietal cells)
Ketoconazole	Antifungal (inhibits fungal sterol synthesis)
Aripiprazole	Atypical antipsychotic (D_2 partial agonist)
Anastrozole	ER ⊕ breast cancer in postmenopausal women (aromatase inhibitor)
Rifaximin	Hepatic encephalopathy (↓ ammoniagenic bacteria)
Rifampin	Antituberculous drug/antimicrobial (inhibits DNA-dependent RNA polymerase)
Sertraline	Depression, PTSD (selective serotonin reuptake inhibitor)
Selegiline	Parkinson disease (MAO-B inhibitor)
Trazodone	Insomnia (blocks 5-HT_2, α_1-adrenergic, and H_1 receptors); also weakly inhibits 5-HT reuptake
Tramadol	Chronic pain (weak opioid agonist)
Varenicline	Smoking cessation (nicotinic ACh receptor partial agonist)
Venlafaxine	Serotonin-norepinephrine reuptake inhibitor