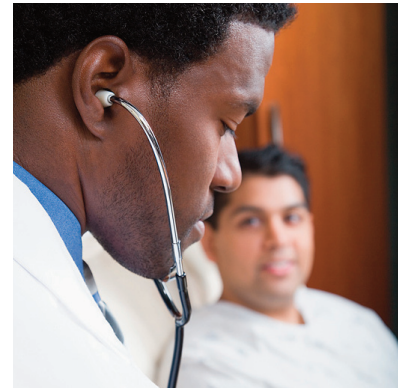




USMLE[®] Content Outline



A Joint Program of the Federation of State Medical Boards
of the United States, Inc., and the National Board of Medical Examiners[®]

This outline provides a common organization of content across all USMLE examinations. Each Step exam will emphasize certain parts of the outline, and no single examination will include questions on all topics in the outline. The examples listed within the outline are just examples. Questions may include diseases, symptoms, etc., that are not included in the outline. The USMLE program continually reviews its examinations to ensure their content is relevant to the practice of medicine. As practice guidelines evolve or are introduced, the content on USMLE is reviewed and modified as needed. At times, there is a change in emphasis on new content development that arises from our ongoing peer-review processes. For example, there has been an emphasis on new content developed assessing competencies related to geriatric medicine, and prescription drug use and abuse. USMLE has also focused recent efforts on the often unrecognized health care needs of recently returning servicemen and servicewomen (eg, traumatic brain injury and post-traumatic stress disorder), and the families of deployed servicemen and servicewomen. While many of the medical issues related to the health care of these special populations are not unique, certain medical illnesses or conditions are either more prevalent, have a different presentation, or are managed differently. Knowledge of foundational science and clinical science in these content areas will be assessed on the USMLE Step 1, Step 2 CK, and Step 3 examinations.

Examinees should refer to the test specifications for each examination for more information about which parts of the outline will be emphasized in the examination for which they are preparing. See the USMLE website (www.usmle.org) for more detail.

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General Principles of Foundational Science

Biochemistry and molecular biology

Gene expression: DNA structure, replication, exchange, and epigenetics (eg, imprinting, X-activation, DNA methylation)

Gene expression: transcription

Gene expression: translation, post-translational processing, modifications, and disposition of proteins (degradation), including protein/glycoprotein synthesis, intra-extracellular sorting, and processes/functions related to Golgi complex and rough endoplasmic reticulum

Structure and function of proteins and enzymes (eg, enzyme kinetics and structural/regulatory proteins)

Energy metabolism (eg, ATP generation, transport chain)

Biology of cells

Adaptive cell responses and cellular homeostasis (eg, hypertrophy)

Mechanisms of injury and necrosis, including pathologic processes (eg, liquefactive necrosis, free radical formation)

Apoptosis

Cell cycle and cell cycle regulation (eg, mitosis)

Mechanisms of dysregulation

cell biology of cancer (eg, role of p53, proto-oncogenes)

general principles of invasion and metastasis, including cancer staging

Cell/tissue structure, regulation, and function, including cytoskeleton, organelles, glycolipids, channels, gap junctions, extracellular matrix, and receptors

Human development and genetics

Principles of pedigree analysis
inheritance patterns

occurrence and recurrence risk determination

Population genetics: Hardy-Weinberg law, founder effects, mutation-selection equilibrium

Principles of gene therapy

Genetic testing and counseling

Genetic mechanisms (eg, penetrance, genetic heterogeneity)

Biology of tissue response to disease

Acute inflammatory responses (patterns of response)

acute inflammation and mediator systems (eg, histamine, prostaglandins, bradykinins, eosinophilic basic protein, nitric oxide)

vascular response to injury, including mediators

principles of cell adherence and migration (eg, ECAMs, selectins, leukocytic diapedesis, and rolling)

microbicidal mechanisms and tissue injury (eg, defensins)

clinical manifestations (eg, pain, fever, leukocytosis, leukemoid reaction, chills)

Chronic inflammatory responses (eg, tumor necrosis factor)

Reparative processes

wound healing, repair: thrombosis, granulation tissue, angiogenesis, fibrosis, scar/keloid formation

regenerative process

Pharmacodynamic and pharmacokinetic processes: general principles

Pharmacokinetics: absorption, distribution, metabolism, excretion, dosage intervals

Mechanisms of drug action, structure-activity relationships (eg, anticancer drugs)

Concentration and dose-effect relationships (eg, efficacy, potency), types of agonists (eg, full, partial, inverse) and antagonists and their actions
Individual factors altering pharmacokinetics and pharmacodynamics (eg, age, gender, disease, tolerance, compliance, body weight, metabolic proficiency, pharmacogenetics)
Mechanisms of drug adverse effects, overdose, toxicology
Mechanisms of drug interactions
Signal transduction, including structure/function of all components of signal transduction pathways such as receptors, ligands (eg, general principles of nitric oxide, autocrine and paracrine signaling)

Microbial biology

Microbial identification and classification, including principles, microorganism identification, and non-immunologic laboratory diagnosis

Bacteria

structure (eg, cell walls, composition, appendages, virulence factors, extracellular products, toxins, mechanism of action of toxins)
processes, replication, and genetics (eg, metabolism, growth, and regulation)
oncogenesis
antibacterial agents (eg, mechanisms of action on organism, toxicity to humans, and mechanisms of resistance)

Viruses

structure (eg, physical and chemical properties, virulence factors)
processes, replication, and genetics (eg, life cycles, location of virus in latent infection)
oncogenesis
antiviral agents (eg, mechanisms of action on virus, toxicity to humans, and mechanisms of resistance)

Fungi

structure (eg, cell wall, composition, appendages, virulence factors, extracellular products, toxins, mechanisms of action of toxins)
processes, replication, and genetics (eg, asexual vs. sexual, metabolism, growth)
antifungal agents (eg, mechanisms of action on fungus, toxicity to humans, and mechanisms of resistance)

Parasites

structure (eg, appendages, macroscopic features, and virulence factors)
processes, replication, and genetics (eg, life cycles, metabolism, and growth)
oncogenesis
antiparasitic agents (eg, mechanisms of action on parasite, toxicity to humans, and mechanisms of resistance)

Prions

Normal age-related findings and care of the well patient

Infancy and childhood (0-12 years)

Normal physical changes: linear growth, variations in linear growth, including constitutional delay; weight; head circumference; micturition, defecation, primary incontinence/bedwetting; normal physical examination; screening; sleep

Developmental stages: motor; speech; cognitive; psychosocial; anticipatory guidance

Lifestyle and routine preventive health care: nutrition; exercise (eg, benefits of exercise); preventive/travel medicine; risk factors and prevention (eg, guns, swimming, motor vehicles, car seats); routine vaccinations

Adolescence (13-17 years)

Normal physical changes: linear growth, variations in linear growth including constitutional delay; weight; puberty; normal physical examination; gynecomastia; autonomy/self-identity; sleep

Developmental stages: cognitive (eg, abstract thought); psychosocial (eg, autonomy, role confusion, sexual identity); anticipatory guidance

Lifestyle and routine preventive health care: nutrition; exercise (eg, benefits of exercise); preventive/travel medicine; risk factors and prevention (eg, risk-taking behavior, helmets, safe sex, motor vehicles, seat belts, distractions); routine vaccinations

Adulthood (18-64 years)

Normal physical changes: weight; normal physical examination; screening; sleep

Developmental stages: cognitive; intimacy vs isolation; anticipatory guidance

Lifestyle and routine preventive health care: nutrition; exercise (eg, benefits of exercise); preventive/travel medicine; risk factors and prevention; routine vaccinations

Senescence (65 years and older)

Normal physical changes, including normal physical exam for age: weight, height (spinal compression), skin, bruising; normal physical examination; response to temperature; micturition, defecation; sleep

Developmental stages: motor; cognitive (eg, benign senescent forgetfulness); psychosocial; integrity vs despair; retrospection; anticipatory guidance

Lifestyle and routine preventive health care: nutrition; exercise (eg, benefits of exercise); preventive/travel medicine; risk factors and prevention (eg, falls, general medical condition; polypharmacy, driving, caregiver stress); routine vaccinations

Immune System

Normal processes

Development of cells of the adaptive immune response, including positive and negative selection during immune development

Structure, production, and function

granulocytes, natural killer cells, macrophages, mast cells, dendritic cells, cell receptors (eg, complement receptors and toll-like receptors), cytokines, chemokines

T lymphocytes, including T-lymphocyte receptors, accessory molecules (eg, CD3, CD4, CD8, B7), cell activation and proliferation, cytotoxic T lymphocytes, and memory T lymphocytes

B lymphocytes and plasma cells, including B-lymphocyte receptors, immunoglobulins, cell activation and proliferation, including development of antibodies and memory B lymphocytes

host defense mechanisms, host barriers to infection, mucosal immunity (eg, gut-associated lymphoid tissue and bronchus-associated lymphoid tissue), anatomical locations of T and B lymphocytes

Cellular basis of the immune response and immunologic mediators

antigen processing and presentation in the context of MHC I and MHC II molecules (eg, TAP, beta-2 microglobulin), intracellular pathways, mechanisms by which MHC is expressed on the surface; including distribution of MHC I and MHC II on different cells, mechanisms of MHC I and MHC II deficiencies, and the genetics of MHC

regulation of the adaptive immune response (eg, peripheral tolerance, anergy, regulatory T lymphocytes, termination of immune response, and B-T

lymphocyte interactions)

activation, function, and molecular biology of complement (eg, anaphylatoxins)

functional and molecular biology of cytokines (eg, IL 1-15)

Basis of immunologic diagnostics (eg, antigen-antibody reactions used for diagnostic purposes, ELISA, immunoblotting, antigen-antibody changes over time, ABO typing)

Principles of immunologic protection

vaccine production and mechanisms of vaccine action

biologically active antibodies (eg, monoclonal antibodies, polyclonal antibodies including IVIG, VZIG, rabies immunoglobulin)

Effect of age on the function of components of the immune system

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Disorders associated with immunodeficiency

deficiency primarily of humoral immunity: common variable immunodeficiency; hyper IgM syndrome; hypogammaglobulinemia/agammaglobulinemia, X-linked (Bruton); selective immunodeficiency (eg, IgA, IgM, IgE)

deficiency/dysfunction primarily of cell-mediated immunity: adenosine deaminase deficiency; DiGeorge syndrome; severe combined immunodeficiency disease (SCID); Wiskott-Aldrich syndrome; granulomatosis; allergic reactions (insect bites)

complement deficiency: alternative pathway component deficiency (C2, C3b, C3bB, C36B6); classical pathway component deficiency (C1q, C1r, C1-C5); terminal component deficiency (C5b-C9; terminal complement complex); C1 esterase inhibitor deficiency, hereditary angioedema; mannose-binding lectin (MBL) deficiency; membrane attack complex deficiency

deficiency of phagocytic cells and natural killer cells: Chediak-Higashi disease; chronic granulomatous disease and other disorders of phagocytosis; leukocyte adhesion deficiency

HIV/AIDS: HIV1 and HIV2; AIDS; AIDS complications (eg, neuropathy, dementia, renal insufficiency); immunology of AIDS; immune reconstitution syndrome (IRS); secondary infections; noninfectious complications

Immunologically mediated disorders

hypersensitivity reactions: type 1, 2, 3, including anaphylaxis; type 4; drug reactions; serum sickness

transplantation: rejection; graft-vs-host disease

Adverse effects of drugs on the immune system: Jarisch-Herxheimer reaction; drugs affecting the immune system (eg, prednisone, azathioprine, cyclosporine, methotrexate, monoclonal antibody drugs [eg, abciximab, adalimumab; bevacizumab, infliximab, omalizumab, rituximab]); vaccine adverse effects

Blood & Lymphoreticular System

Normal Processes

Embryonic development, fetal maturation, and perinatal changes

Organ structure and function

Cell/tissue structure and function

production and function of erythrocytes, including heme and hemoglobin synthesis;

hemoglobin O₂ and CO₂ transport, transport proteins, erythropoietin

production and function of platelets

production and function of coagulation and fibrinolytic factors; hemostasis

Repair, regeneration, and changes associated with stage of life

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Infectious and immunologic

infectious disorders

bacteria

viral: hemorrhagic fever (Ebola virus, Marburg virus); chikungunya; dengue fever

parasitic: malaria (*Plasmodium* spp); babesiosis (*Babesia* species)

primary infections of lymphoid tissue: lymphadenitis (viral, bacterial, fungal, parasitic); lymphangitis; buboes, bubonic plague (*Yersinia pestis*); cat scratch disease (*Bartonella henselae*)

immunologic and inflammatory disorders: cryoglobulinemia, essential mixed cryoglobulinemia; autoimmune hemolytic anemia; paroxysmal nocturnal hemoglobinuria; thrombotic thrombocytopenic purpura; hemolytic uremic syndrome

Neoplasms: leukemia, acute (ALL, AML); leukemia, chronic (CLL, CML); lymphomas, Hodgkin disease, non-Hodgkin lymphoma, Burkitt lymphoma, T-cell lymphoma; multiple myeloma, dysproteinemias, monoclonal gammopathy of unknown significance (MGUS); myelofibrosis; myelodysplastic syndrome, myelodysplasias; other immunoproliferative neoplasms (eg, Waldenstrom macroglobulinemia)

Anemia, cytopenias, and polycythemia anemias

decreased production: anemia of chronic disease

hemolysis: glucose-6-phosphate dehydrogenase deficiency; pyruvate kinase deficiency

disorders of hemoglobin, heme, or membrane: disorders of red cell membranes; hereditary spherocytosis, elliptocytosis; methemoglobinemia, congenital; sickle cell disease; sideroblastic anemia; thalassemias

other causes of anemia: blood loss, acute and chronic as a cause of anemia

cytopenias: aplastic anemia; leukopenia; neutropenia, cyclic neutropenia, agranulocytosis; pancytopenia; thrombocytopenia, quantitative; immune thrombocytopenic purpura (ITP)

cythemias: leukocytosis; polycythemia vera; secondary polycythemia

Coagulation disorders (hypocoagulable and hypercoagulable conditions)

hypocoagulable: disseminated intravascular coagulation; hemophilia, congenital factor VIII [hemophilia A] and IX [hemophilia B]; hypofibrinogenemia; von Willebrand disease; platelet dysfunction, qualitative

hypercoagulable: heparin-induced thrombocytopenia; other coagulopathies (eg, homocysteinemia, hypoplasminogenemia, antithrombin III, protein C/protein S deficiency, Factor V Leiden, anticardiolipin antibodies, lupus anticoagulant, prothrombin G20210A mutation)

reactions to blood components: ABO incompatibility/anaphylaxis; Rh incompatibility/anaphylaxis; hemolysis, delayed; transfusion reaction; transfusion contaminated with bacteria; transfusion-related acute lung injury (TRALI); anaphylactoid reaction (IgA deficiency)

Traumatic, mechanical, and vascular disorders: mechanical injury to erythrocytes (eg, cardiac valve hemolysis); disorders of the spleen; splenic rupture/laceration; splenic infarct; splenic abscess; effects/complications of splenectomy (eg, sepsis due to encapsulated bacteria); hypersplenism

Congenital disorders

Adverse effects of drugs on the hematologic and lymphoreticular systems: antiplatelet drugs, antithrombin drugs (eg, dabigatran); chemotherapeutic agents; inhibitors of coagulation factors; methemoglobinemia, acquired; propylthiouracil; tumor lysis syndrome; warfarin

Behavioral Health

Normal Processes

Psychodynamic and behavioral factors, related past experience (eg, transference, personality traits)

Adaptive behavioral responses to stress and illness (eg, coping mechanisms)

Maladaptive behavioral responses to stress and illness (eg, drug-seeking behavior, sleep deprivation)

Patient adherence: general adherence; adolescent adherence

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis,

Management, Risks, Prognosis

Psychotic disorders: brief psychotic disorder; delusional disorder; psychotic disorder due to a general medical condition; schizophrenia; schizoaffective disorder; substance-induced psychotic disorder

Anxiety disorders: acute stress disorder; anxiety due to a general medical condition; generalized anxiety disorder; hyperventilation syndrome; obsessive-compulsive disorder; panic disorder with and without agoraphobia; phobic disorders; anxiety disorder (social phobia); post-traumatic stress disorder; separation anxiety disorder; substance-induced anxiety disorder

Mood disorders: major depressive disorder with and without psychotic features, including seasonal affective disorder; major depressive disorder, postpartum, with and without psychotic features, including screening; cyclothymic disorder; dysthymic disorder; bipolar disorder, manic/depressed/mixed; premenstrual syndrome, premenstrual dysphoric disorder; mood disorder due to a general medical condition; substance-induced mood disorder (illegal or prescribed); suicidal ideation/attempt

Somatoform disorders: body dysmorphic disorder; conversion disorder, including psychogenic seizures; dissociative disorders; hypochondriasis; malingering; pain disorder; somatization disorder, somatoform disorder NOS

Factitious disorders: factitious disorder

Eating disorders and impulse control disorders: anorexia nervosa; binge-eating disorder; bulimia nervosa; eating disorder; disorders of impulse control (eg, gambling, shoplifting, pyromania, trichotillomania)

Disorders originating in infancy/childhood: attachment disorder; attention-deficit/hyperactivity disorder; developmental speech or language disorder; learning disability/dyslexia; mental retardation and developmental delay, undefined, including school problems, fetal alcohol syndrome; oppositional defiant disorder, conduct disturbance disorder, disruptive behavior disorder; pervasive developmental disorder, including autistic disorder, Asperger syndrome, Rett syndrome; psychoses with origin specific to childhood; elimination disorders (incontinence, encopresis); tic disorders/Tourette disorder

Personality disorders: antisocial personality disorder; avoidant personality disorder; borderline personality disorder; dependent personality disorder; histrionic personality disorder; narcissistic personality disorder; obsessive-compulsive personality disorder; paranoid personality disorder; schizoid personality disorder

Psychosocial disorders/behaviors: adjustment disorder; grief response/bereavement, normal

and abnormal; parent-child relational problems other than physical or emotional abuse; other psychosocial stress

Sexual and gender identity disorders: gender identity disorder; psychosexual dysfunction

Substance abuse disorders: alcohol abuse/intoxication/dependence/withdrawal; tobacco/nicotine abuse/dependence/withdrawal; cannabis abuse/intoxication/dependence; hallucinogen abuse/intoxication/dependence/withdrawal; inhalant abuse/intoxication/dependence/withdrawal; opioids, heroin, including prescription drugs, abuse/intoxication/dependence/withdrawal; sedatives, hypnotics, including benzodiazepines and barbiturates abuse/intoxication/dependence/withdrawal; stimulants, cocaine, methamphetamine abuse/intoxication/dependence/withdrawal; other drugs of abuse (eg, ecstasy, PCP, bath salts) abuse/intoxication/dependence/withdrawal; polysubstance abuse/intoxication/dependence/withdrawal

Adverse effects of drugs: steroid-induced psychosis; varenicline and suicide; drug-induced psychogenic polydipsia

Nervous System & Special Senses

Normal Processes

Embryonic development, fetal maturation, and perinatal changes, including neural tube derivatives, cerebral ventricles, and neural crest derivatives

Organ structure and function

spinal cord

gross anatomy and blood supply

spinal reflexes

brain stem (eg, cranial nerves and nuclei, reticular formation, anatomy and blood supply, control of eye movements)

brain

gross anatomy and blood supply

higher function: cognition, language, memory, executive function

hypothalamic function

limbic system and emotional behavior

circadian rhythms and sleep

sensory systems

general sensory modalities, including sharp, dull, temperature, vibratory, and proprioception

special sensory modalities, including vision, hearing, taste, olfaction, and balance

motor systems

brain and spinal cord (upper motoneuron)

basal ganglia and cerebellum

autonomic nervous system

peripheral nerves

Cell/tissue structure and function, including neuronal cellular and molecular biology

axonal transport

excitable properties of neurons, axons, and dendrites, including channels

synthesis, storage, release, reuptake, and degradation of neurotransmitters and neuromodulators

presynaptic and postsynaptic receptor interactions, trophic and growth factors

brain metabolism

glia, myelin

brain homeostasis: blood-brain barrier, cerebrospinal fluid formation and flow, choroid plexus

Repair, regeneration, and changes associated with stage of life

Abnormal Processes: Health and Health Maintenance, Screening,

Diagnosis, Management, Risks, Prognosis

Infectious, immunologic, and inflammatory disorders

infectious disorders: meningitis: bacterial (*Actinomyces israelii*; *Haemophilus influenzae*; *Listeria monocytogenes*; *Mycobacterium tuberculosis*; *Neisseria meningitidis*; *Staphylococcus aureus*, epidermidis; *Streptococcus agalactiae*; *Streptococcus pneumoniae*); viral (adenovirus, arboviruses, echovirus and coxsackie A & B viruses, polioviruses, herpes simplex virus, varicella zoster, human immunodeficiency virus, lymphocytic choriomeningitis virus, measles virus, mumps virus, St. Louis encephalitis virus, California encephalitis virus, Western equine encephalitis virus); fungal (*Blastomycosis dermatitidis*, *Cryptococcus neoformans/gattii*); spirochetal (*Borrelia burgdorferi*; *Leptospira*; *Treponema pallidum*, including neurosyphilis); protozoal/helminths (*Acanthamoeba*, *Naegleria fowleri*, *Strongyloides stercoralis*, *Angiostrongylus cantonensis*, *Baylisascaris procyonis*); encephalitis (herpesvirus [HSV-1], varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, mumps virus, enterovirus, West Nile virus, St. Louis encephalitis virus, rabies virus, Eastern and Western equine encephalitis virus, poliovirus, *Taenia*, *Toxoplasma gondii*); prion disease (eg, Creutzfeldt-Jakob disease); botulism (*Clostridium botulinum*), tetanus (*Clostridium tetani*); CNS disorders associated with AIDS (eg, progressive multifocal leukoencephalopathy)

immunologic and inflammatory disorders: myasthenia gravis, including thymoma; multiple sclerosis; transverse myelitis

Neoplasms (cerebral, spinal, and peripheral): benign (meningioma, neurofibromatosis); malignant (glioblastoma multiforme, astrocytoma, medulloblastoma, primary CNS lymphoma); metastatic (eg, breast, lung, pancreatic, testicular, melanoma)

Cerebrovascular disease: arteriovenous malformations, ectatic cerebral vessels; transient ischemic attack; stroke, thrombotic: cerebral artery occlusion/cerebral infarction; stroke, embolic: cerebral embolism; stroke: intracerebral hemorrhage, including subarachnoid hemorrhage, traumatic intracranial hemorrhage; cerebral artery aneurysm; carotid artery stenosis/atherosclerosis/occlusion/dissection; vertebral artery deficiency/dissection; subclavian steal syndrome; vascular dementia; hypertensive encephalopathy; posterior reversible encephalopathy syndrome; venous sinus thrombosis

Disorders relating to the spine, spinal cord, and spinal nerve roots: cauda equina syndrome; spinal artery thrombosis/embolus/infarct; spinal cord compression; spinal cord transection, paraplegia and quadriplegia, acute and chronic effects (eg, autonomic dysreflexia); spinal stenosis (cervical, lumbar)

Cranial and peripheral nerve disorders

cranial nerve injury/disorders: cranial nerve injury; Bell palsy; anisocoria, miosis, mydriasis; internuclear ophthalmoplegia; nystagmus and other irregular eye movements; vestibular neuritis, labyrinthitis; ptosis of the eyelid; Horner syndrome

peripheral nerve/plexus injury/disorders: peripheral nerve injury, including brachial plexus; carpal/cubital/tarsal/peroneal tunnel syndrome; mononeuritis, Guillain-Barré syndrome; Miller Fisher syndrome; neuropathy (eg, Charcot-Marie-Tooth disease); herpes zoster

Neurologic pain syndromes: complex regional pain syndrome (reflex sympathetic dystrophy, causalgia); fibromyalgia; postherpetic neuralgia; phantom limb pain; thalamic pain syndrome; trigeminal neuralgia

Degenerative disorders/amnestic syndromes: Alzheimer disease; frontotemporal dementia, including Pick disease, progressive supranuclear palsy, Lewy body disease

Global cerebral dysfunction: altered states of consciousness; delirium; coma/brain death

Neuromuscular disorders: amyotrophic lateral sclerosis/spinal muscular atrophy; muscular dystrophy; muscle channelopathies

Movement disorders: acute dystonia; adult tic disease; essential tremor; Huntington disease; Parkinson disease, including Parkinson dementia

Metabolic disorders: adrenoleukodystrophy; metabolic encephalopathy

Paroxysmal disorders: headache, including migraine, mixed, tension, ice-pick, cluster, medication withdrawal, caffeine withdrawal; seizure disorders, including generalized tonic-clonic, partial, absence, febrile

Sleep disorders: cataplexy and narcolepsy; circadian rhythm disorders; insomnia, primary; sleep terror disorder and sleepwalking; REM sleep behavior disorder; restless legs syndrome

Traumatic and mechanical disorders and disorders of increased intracranial pressure: anoxic brain damage, cerebral hypoxia; epidural, subdural hematoma (cerebral and spinal); intraparenchymal hemorrhage, traumatic subarachnoid hemorrhage; cerebral edema; pseudotumor cerebri (idiopathic intracranial hypertension); torticollis/cervical dystonia; hydrocephalus, including normal-pressure; traumatic brain injury (concussion)/postconcussion syndrome (dementia pugilistica); traumatic brain syndrome

Congenital disorders: Friedreich ataxia; neural tube defects (eg, spina bifida, holoprosencephaly, anencephaly); microcephaly; Sturge-Weber syndrome; tuberous sclerosis, von Hippel-Lindau disease; hydrocephalus, obstructive (Arnold-Chiari)

Adverse effects of drugs on the nervous system: acute dystonic reaction; drug-induced meningitis (eg, NSAIDs, sulfa drugs); drug-induced neuropathy (eg, vincristine, isoniazid, metronidazole); extrapyramidal adverse effects (eg, akathisia, dystonia, drug-induced parkinsonism); neuroleptic malignant syndrome; poisoning by psychotropic agents, including antidepressants; serotonin syndrome; tardive dyskinesia

Disorders of the eye and eyelid

infectious and inflammatory disorders of the eye: blepharitis/eyelid inflammation; chalazion; chorioretinitis; conjunctivitis (adenovirus)/keratoconjunctivitis; dacryocystitis; endophthalmitis; hordeolum; iridocyclitis; optic neuritis; periorbital cellulitis; uveitis

neoplasms of the eye: melanoma; retinoblastoma

disorders of the eye and eyelid, structural: cataract; glaucoma; lacrimal system disorders; pterygium; refractive disorders (presbyopia, myopia, hyperopia, astigmatism)

disorders of the pupil, iris, muscles (extraocular): amblyopia; strabismus

disorders of the retina: hypertensive retinopathy; macular degeneration; papilledema; retinal detachment; retinitis pigmentosa; vascular disorders affecting the retina, including central retinal artery embolus, retinal hemorrhage, amaurosis fugax, embolus, carotid artery stenosis, central retinal vein occlusion; visual impairment/blindness, night blindness

traumatic and mechanical disorders: black eye; burn of the eye and adnexa; corneal

abrasion, ulcer; dislocated lens; foreign body in eye; hyphema; injury to optic nerve and pathways; laceration of the eye and eyelid; ocular open wounds; orbital fracture; subconjunctival hemorrhage

adverse effects of drugs on the eyes: ethambutol; hydroxychloroquine; prednisone

Disorders of the ear

infectious and inflammatory disorders of the ear: chondritis; mastoiditis; otitis, externa, media, interna, serous, suppurative, malignant otitis externa

neoplasms: acoustic neuroma, neurofibromatosis type 2; cholesteatoma

hearing loss/deafness: hearing loss, including noise induced; otosclerosis; tinnitus

disorders of balance and spatial orientation: Ménière disease; motion sickness; vertigo, including benign positional vertigo

traumatic and mechanical disorders: barotrauma; foreign body in ear; impacted cerumen; laceration, avulsion; perforation of tympanic membrane; eustachian tube disorders

adverse effects of drugs on the ear: antineoplastic agents, including cisplatin; aminoglycosides; furosemide; salicylates

Skin & Subcutaneous Tissue

Normal Processes

Embryonic development, fetal maturation, and neonatal changes

Organ structure and function, including barrier function, thermal regulation

Cell/tissue structure and function, eccrine function

Repair, regeneration, and changes associated with stage of life (eg, senile purpura, male pattern baldness, postmenopausal hair changes)

Skin defense mechanisms and normal flora

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis,

Management, Risks, Prognosis

Infectious, immunologic, and inflammatory disorders

infectious disorders and infestations

bacterial: cellulitis, erysipelas, impetigo, staphylococcal scalded skin syndrome; abscess, cutaneous, including septic abscess; anthrax (*Bacillus anthracis*); carbuncle; folliculitis; pilonidal cyst, infected; pyoderma gangrenosum; MSSA and MRSA skin infections; mycobacterial infections (eg, leprosy, draining sinus); scarlet fever (group A streptococcus)

viral: herpes simplex type 1 & type 2, herpes zoster, Ramsay-Hunt syndrome; molluscum contagiosum; hand-foot-and-mouth disease; herpangina; parvovirus; chickenpox, erythema infectiosum (fifth disease), rubella, measles, roseola (exanthema subitum); verrucae vulgaris

fungal (deep and superficial): candidiasis, skin; dermatophytosis, tinea corporis; dermatomycoses; diaper rash; onychomycosis

parasitic: cutaneous larva migrans; cutaneous leishmaniasis

infestations, nonvenomous bites, stings: scabies; lice; insect bites, including bed bugs

immunologic and inflammatory disorders

papulosquamous and eczematous dermatoses: psoriasis; lichen planus and lichenoid dermatoses; allergic/irritant contact dermatitis (eg, nickel); dermatoses caused by plants (poison ivy, poison oak)

vesiculobullous disorders: epidermolysis bullosa; dermatitis herpetiformis;

pemphigus; pemphigoid

urticaria, erythema, exanthema, and purpura: erythema nodosum; atopic dermatitis; pityriasis rosea; urticaria; Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis

autoimmune disorders: vitiligo

Neoplasms

benign neoplasms, cysts and other skin lesions: actinic keratoses; cysts, including epidermal; hemangiomas; lipoma; pigmented nevi; seborrheic keratosis; xanthomas

malignant neoplasms: basal cell carcinoma; squamous cell carcinoma; melanoma, including genital; Kaposi sarcoma; cutaneous T-cell lymphoma, mycosis fungoides

Adnexal disorders (hair and hair follicles, nails, sweat glands, sebaceous glands, oral mucous membranes)

disorders of the hair and hair follicles: alopecia; seborrhea capitis/seborrheic dermatitis; tinea barbae and capitis

disorders of the nails (including ingrowing nail)

disorders of sweat and sebaceous glands: acne vulgaris; hidradenitis suppurativa; hyperhidrosis; ichthyosis; rosacea

Oral disease: aphthous ulcers (stomatitis, canker sores); leukoplakia

Disorders of pigmentation: albinism; lentigo

Traumatic and mechanical disorders: animal bites (dogs, cats, etc); burns or wounds affecting the skin or subcutaneous tissue (eg, sunburn, other including blast injuries and burns); cauliflower ear; effects of ultraviolet light; keloids; tattoo; thermal injury, perniosis, frostbite; ulcers, decubitus

Congenital disorders: xeroderma pigmentosum; benign lesions in neonates, infants, children (eg, congenital nevi)

Adverse effects of drugs on skin and subcutaneous tissue: drug reactions, eruptions, including local reaction to vaccine

Musculoskeletal System

Normal processes

Embryonic development, fetal maturation, and perinatal changes

Organ structure and function

Cell/tissue structure and function

biology of bones, joints, tendons, skeletal muscle, cartilage

exercise and physical conditioning/deconditioning

Repair, regeneration, and changes associated with stage of life

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis,

Management, Risks, Prognosis

Infectious, inflammatory, and immunologic disorders

infectious disorders: gangrene, dry and wet, clostridial myonecrosis (*Clostridium perfringens*); discitis; myositis, infective; necrotizing fasciitis; osteomyelitis; septic arthritis; spondylitis, tuberculous

immunologic disorders: ankylosing spondylitis; dermatomyositis/polymyositis; juvenile idiopathic arthritis; rheumatoid arthritis, Felty syndrome; psoriatic arthropathy

inflammatory disorders: adhesive capsulitis of shoulder (frozen shoulder syndrome); ankylosis/spondylopathy (inflammatory); bursitis; fasciitis; osteochondritis,

osteochondritis dissecans; tendinitis, supraspinatus syndrome, enthesopathy of spine, elbow, ankle; temporomandibular joint disorders; fibrositis, myofascial pain syndrome; synovitis; tenosynovitis; myositis

Neoplasms: benign neoplasms (e.g., ganglion cyst); malignant neoplasms of bone (eg, osteosarcoma, sarcoma, leiomyosarcoma, rhabdosarcoma); metastases to bone, secondary malignant neoplasm of bone

Degenerative and metabolic disorders

degenerative/metabolic disorders of bone, tendon, and cartilage: chondromalacia; disc degeneration, herniated disc; Legg-Calvé-Perthes disease; Osgood-Schlatter disease; osteodystrophy; osteomalacia; osteonecrosis (avascular), bone infarct; osteoporosis; osteopenia; osteitis deformans (Paget disease of bone); pathologic fracture; spondylolisthesis/spondylosis (degenerative)

degenerative/metabolic disorders of joints: gout, gouty arthritis, pseudogout; joint effusion; osteoarthritis

degenerative/metabolic disorders of muscles, ligaments, fascia: Dupuytren contracture; muscle calcification and ossification; muscle wasting and diffuse atrophy; rhabdomyolysis

Traumatic and mechanical disorders: amputation and care of amputees; backache, including low back pain; blast injuries; contractures, hospital-acquired; contusions; dislocations; fractures; sprains, strains; kyphoscoliosis, scoliosis; rotator cuff syndrome; slipped capital femoral epiphysis; dislocation of hip

Congenital disorders: achondroplasia/dwarfism; disorders of limb development (HOX gene mutation, phocomelia); developmental dysplasia of the hip; dislocation of hip in infantile spinal muscular atrophy; genu valgum or varum; foot deformities (flat foot, valgus/varus deformities); osteogenesis imperfecta; McArdle disease; mitochondrial myopathies

Adverse effects of drugs on the musculoskeletal system: drug-induced myopathy (eg, steroids, statins, cocaine, AZT); malignant hyperthermia

Cardiovascular System

Normal Processes

Embryonic development, fetal maturation, and perinatal transitional changes

Organ structure and function

chambers, valves

cardiac cycle, mechanics, heart sounds, cardiac conduction

hemodynamics, including blood volume and systemic vascular resistance

circulation in specific vascular beds, including pulmonary and coronary

Cell/tissue structure and function

heart muscle, metabolism, oxygen consumption, biochemistry, and secretory function (eg, atrial natriuretic peptide)

endothelium and secretory function, vascular smooth muscle, microcirculation, and lymph flow

neural and hormonal regulation of the heart, blood vessels, and blood volume, including responses to change in posture, exercise, and tissue metabolism, and autonomic responses

Repair, regeneration, and changes associated with stage of life

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Infectious, immunologic, and inflammatory disorders

infectious disorders: infective endocarditis, myocarditis

immunologic and inflammatory disorders

Neoplasms: myxoma, metastases

Dysrhythmias: premature beats (PACs, PVCs); atrial flutter/fibrillation; multifocal atrial tachycardia; paroxysmal tachycardias; ventricular tachycardia/fibrillation; wide complex tachycardia; torsades des pointes; bradycardias; atrioventricular block (first-, second-, third-degree); conduction disorder (LBBB, RBBB); cardiac arrest; sick sinus syndrome; prolonged QT syndrome; Wolff-Parkinson-White syndrome; carotid sinus hypersensitivity; pacemaker dysfunction, including failure to sense, capture

Heart failure: chordae tendineae rupture; congestive heart failure; cor pulmonale; diastolic dysfunction; systolic dysfunction; mitral valve dysfunction; heart failure secondary to myocardial infarction; high-output heart failure, including thyrotoxicosis-induced, anemia-induced; tachycardia, induced; cardiogenic pulmonary edema

Ischemic heart disease: acute coronary syndrome, acute myocardial infarction; angina pectoris, stable and unstable/coronary artery disease/coronary insufficiency; coronary artery spasm

Diseases of the myocardium: cardiomyopathy, dilated, including alcoholic, viral, takotsubo; cardiomyopathy, obstructive hypertrophic; cardiomyopathy, familial dilated; cardiomyopathy, restrictive; hypertensive heart disease, left ventricular hypertrophy; complications of myocardial infarction; traumatic tamponade post-myocardial infarction; papillary muscle rupture/dysfunction; ventricular free wall rupture; myocarditis

Diseases of the pericardium: chronic constrictive pericardiopathy; pericardial effusion; pericardial tamponade; acute pericarditis; pericarditis, following myocardial infarction, surgery, trauma

Valvular heart disease: valve disorders, mitral/aortic/tricuspid/pulmonic; mitral valve prolapse; functional murmurs; rheumatic heart disease; complications of artificial valves

Hypotension: orthostatic hypotension

Hypertension: elevated blood pressure reading without diagnosis of hypertension; essential hypertension; malignant hypertension; secondary hypertension

Dyslipidemia: hypercholesterolemia; hyperlipidemia; hypertriglyceridemia; lipoproteins/lipoprotein lipase deficiency

Vascular disorders

disorders of the great vessels: aneurysm, aortic (abdominal/thoracic), dissection, ruptured; aneurysm, iliac, other peripheral vascular, ruptured; aortoiliac disease

peripheral arterial vascular disease: arterial embolus/thrombosis; arteriovenous fistula; atheroembolic disease; claudication; compartment syndrome; cholesterol emboli; hypertensive vascular disease; peripheral arterial disease; thromboangiitis obliterans

diseases of the veins: deep venous thrombosis, venous thromboembolism; phlebitis/thrombophlebitis; varicose veins; venous insufficiency; stasis ulcers, stasis dermatitis

Traumatic and mechanical disorders: ventricular puncture; myocardial contusion; lymphedema; myocardial rupture; traumatic aortic dissection

Congenital disorders, including disease in adults: anomalous left coronary artery; atrial septal defect; coarctation of the aorta; endocardial cushion defect; patent foramen ovale; patent ductus arteriosus; tetralogy of Fallot; transposition of the great vessels; ventricular septal defect

Adverse effects of drugs on the cardiovascular system: adriamycin; cocaine, amphetamine, PCP; ACE inhibitors, calcium channel blockers, alpha blockers, minoxidil

Respiratory System

Normal Processes

Embryonic development, fetal maturation, and perinatal changes

Organ structure and function

airways, including mechanics and regulation of breathing
lung parenchyma, including ventilation, perfusion, gas exchange
pleura
nasopharynx, sinuses

Cell/tissue structure and function, including surfactant formation, and alveolar structure

Repair, regeneration, and changes associated with stage of life

Pulmonary defense mechanisms and normal flora

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis,

Management, Risks, Prognosis

Infectious, immunologic, and inflammatory disorders

infectious, immunologic, and inflammatory disorders of the upper airways: acute upper respiratory infection; viral infections (adenovirus, coronaviruses, coxsackievirus, influenza virus, parainfluenza virus, rhinoviruses); sinusitis; nasopharyngitis; epiglottitis; croup; acute laryngitis; acute laryngotracheitis; tracheitis; pharyngitis; streptococcal throat infections; tonsillitis; peritonsillar abscess; rhinitis, allergic, chronic; ulcers of nasal cavity/sinuses

infectious, immunologic, and inflammatory disorders of the lower airways: hospital-acquired pneumonia; ventilator-associated pneumonia, community-acquired pneumonia, acute bronchiolitis; bronchiolitis obliterans with organizing pneumonia (BOOP); anthrax, pulmonary (Bacillus anthracis); aspiration pneumonia, pneumonitis; bronchitis, acute; bronchopneumonia; pneumonia (Bordetella pertussis, Burkholderia pseudomallei, Chlamydomphila pneumoniae, Coxiella burnetii, Francisella tularensis, Haemophilus influenzae, Klebsiella pneumoniae, Legionella, Moraxella catarrhalis, Mycoplasma pneumoniae, Pseudomonas aeruginosa, pulmonary tuberculosis, Streptococcus, MSSA, MRSA, other gram-negative bacteria); viral infection (eg, influenza A, B, adenovirus, H1N1, respiratory syncytial virus, parainfluenza virus); fungal infection (aspergillosis, including allergic bronchopulmonary aspergillosis and aspergilloma, histoplasmosis, coccidioidomycosis, Pneumocystis); lung abscess; viral infection (eg, influenza A, B, adenovirus, respiratory syncytial virus, parainfluenza virus, avian influenza virus); fungal infection (aspergillosis, including allergic bronchopulmonary aspergillosis and aspergilloma, histoplasmosis, coccidioidomycosis, Pneumocystis)

Neoplasms

benign neoplasms: upper airways (eg, vocal cord polyps, nasal polyps, juvenile papillomatosis); lungs and pleura (eg, solitary pulmonary nodule, bronchial carcinoid tumors)

malignant neoplasms

upper airways: lip, oral cavity, and pharynx; head and neck cancer; larynx; trachea

lower airways and pleura: malignant neoplasms of bronchus and/or lung (squamous

cell, adenocarcinoma, large cell, small cell); malignant neoplasms of pleura (mesothelioma); secondary malignant neoplasms of lung; secondary malignant neoplasms of pleura

metastatic neoplasms including pleural

Obstructive airway disease: asthma, reactive airway disease; bronchiectasis; chronic airway obstruction; chronic obstructive pulmonary disease (COPD), chronic bronchitis, emphysema

Pneumoconiosis/fibrosing/restrictive pulmonary disorders/interstitial lung disease:

pneumoconiosis; asbestosis; silicosis; silo-filler's lung, byssinosis, bagassosis, berylliosis; hypersensitivity pneumonitis; hypereosinophilic syndromes, Loeffler syndrome; interstitial pneumonia, usual (UIP), desquamative (DIP), nonspecific

Respiratory failure/respiratory arrest and pulmonary vascular disorders: acute respiratory distress syndrome (ARDS); pulmonary hypertension; pulmonary vascular disorders, arteriovenous fistula; pulmonary edema, pulmonary cause and unspecified; pulmonary embolism; air and fat embolism; respiratory failure due to enteral feeding

Metabolic, regulatory, and structural disorders: disorders of gas exchange; hypoventilation; hypoxia; pulmonary alveolar proteinosis; ventilation-perfusion imbalance

Disorders of the pleura, mediastinum, and chest wall: chylothorax; costochondritis; empyema; hemothorax; mediastinitis; pleural effusion; pleuritis; pneumomediastinum; pneumothorax

Traumatic and mechanical disorders

upper airways: epistaxis; barotrauma, sinus; laryngeal/pharyngeal obstruction; tracheoesophageal fistula; tracheal stenosis; tracheomalacia; trauma (eg, tracheal injury); foreign body (nose, pharynx, larynx, trachea); traumatic/mechanical disorders of the nasal cavity/sinuses (eg, septal perforation)

lower airways and pleura: atelectasis; diaphragm/chest wall injury; drowning and near-drowning; foreign body, upper and lower respiratory tract; penetrating chest wounds; pulmonary contusion; sleep apnea, obstructive and central; hypoventilation syndrome, obesity-hypoventilation syndrome

Congenital disorders: bronchogenic cysts; congenital cysts; congenital diaphragmatic hernia; pulmonary sequestration; immotile cilia syndrome

Adverse effects of drugs on the respiratory system: bleomycin, amiodarone; adverse effects of 100% oxygen; tobacco, inhalants, cocaine

Gastrointestinal System

Normal Processes

Embryonic development, fetal maturation, and perinatal changes

Organ structure and function

anatomy of the alimentary canal, including mouth, pharynx, esophagus, stomach, small intestine, large intestine, anus, peritoneal cavity

liver and biliary system, including enterohepatic circulation

salivary glands and exocrine pancreas

gastrointestinal motility, including defecation digestion and absorption

Cell/tissue structure and function

endocrine and neural regulatory functions, including GI hormones (eg, gastrin)

salivary, gastrointestinal, pancreatic, hepatic secretory products, including enzymes, proteins, bile salts, and processes

synthetic and metabolic functions of hepatocytes

Repair, regeneration, and changes associated with stage of life

Gastrointestinal defense mechanisms and normal flora

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Infectious, immunologic, and inflammatory disorders

infectious disorders

bacterial: pseudomembranous colitis (*Clostridium difficile*); enteritis/enteric infections (includes gastroenteritis) (eg, *Staphylococcus aureus*, *Escherichia coli*, *Listeria monocytogenes*, *Yersinia enterocolitica*, *Campylobacter* species, *Vibrio cholerae*, *Salmonella* species, *Shigella* species, traveler's/infectious diarrhea); hepatic abscess, subhepatic abscess, subphrenic abscess; peritonitis, primary and secondary; Whipple disease

viral: infectious esophagitis (eg, CMV, herpes); hepatitis A, B, C, D, E; coxsackievirus enteritis/colitis; Echovirus enteritis/colitis; rotavirus enteritis; mumps; gingivostomatitis, herpetic

fungal: thrush

parasitic: *Cryptosporidium*, *Cyclospora*, *Entamoeba histolytica*, *Giardia*, *Isospora belli*, *Strongyloides stercoralis*

immunologic and inflammatory disorders: autoimmune hepatitis; celiac disease; eosinophilic esophagitis; granulomatous enteritis; inflammatory bowel disease, including Crohn disease, regional enteritis, microscopic colitis (collagenous and lymphocytic colitis), ulcerative colitis, toxic megacolon

Neoplasms

benign neoplasms, including polyps, cysts: stomach; small intestine; colon, rectum, and anus, including polyps

malignant neoplasms and pre-malignant conditions: oral cancer (eg, lips, mouth, tongue, salivary glands); esophageal, squamous and adenocarcinoma; Barrett esophagus; gastrinoma, Zollinger-Ellison syndrome; gastrointestinal carcinoid tumors; gastrointestinal stromal tumors; small intestine; stomach, adenocarcinoma, lymphoma, MALT; colon, rectum, anus; hereditary colon cancer syndromes, familial adenomatous polyposis (eg, Peutz-Jeghers syndrome, Gardner syndrome, Turcot syndrome,); MUTYH-associated polyposis; gallbladder, cholangiocarcinoma, adenocarcinoma of the ampulla of Vater; liver, including hepatoma; peritoneal cancer, including metastatic studding with cancer; pancreas

metastatic neoplasms

Signs, symptoms, and ill-defined disorders: upper gastrointestinal bleeding; lower gastrointestinal bleeding; constipation; diarrhea; hematochezia; bright red rectal bleeding; melena; nausea, vomiting, rumination

Disorders of the oral cavity, salivary glands, and esophagus

oral cavity and salivary glands: abscessed tooth; dental caries; malocclusion; disorders of the salivary glands (eg, stones, sialadenitis, parotitis); teething syndrome

esophagus: achalasia and cardiospasm; dysphagia; diverticulum (eg, Zenker); esophageal periapical abscess without sinus; esophagitis/esophageal reflux (GERD); esophagitis, pill; Mallory-Weiss syndrome; paraesophageal (hiatal) hernia; stricture and stenosis of esophagus

Disorders of the stomach, small intestine, colon, rectum, anus

stomach: dyspepsia/hyperacidity; gastric ulcer; gastritis; peptic ulcer; peptic ulcer perforation; gastroparesis

small intestine, colon: appendicitis; angiodysplasia; diverticula; duodenitis, duodenal ulcer, peptic ulcer; gastroenteritis and colitis (noninfectious); granulomatous enterocolitis; Hirschsprung disease; impaction of intestine; intestinal obstruction/stricture; intussusception; irritable colon/irritable bowel syndrome; ischemic bowel; necrotizing enterocolitis; paralytic ileus; volvulus; malnutrition and malabsorption, including lactose intolerance, short bowel syndrome

rectum and anus: abscess of anal and rectal regions; anal fissure; anal fistula; ulcer; fecal incontinence; hemorrhage (rectum, anus); proctitis; hemorrhoids; rectal prolapse

Disorders of the liver and biliary system, noninfectious

liver: cirrhosis; Dubin-Johnson, Rotor syndromes; end-stage liver disease, including indications for transplantation; Gilbert syndrome, Crigler-Najjar syndrome; hepatic coma/hepatic encephalopathy; hepatitis, noninfectious; hepatitis, fatty liver, alcoholic; hepatorenal syndrome; hepatopulmonary syndrome; jaundice; non-alcoholic fatty liver disease; portal hypertension/esophageal varices

biliary system: bile duct obstruction/cholestasis; cholangitis, including ascending; choledocholithiasis; cholelithiasis/cholecystitis; cholestasis due to parenteral nutrition; gallstone ileus; Mirizzi syndrome; primary biliary cirrhosis; primary sclerosing cholangitis

Disorders of the pancreas: pancreatitis, acute; pancreatitis, chronic; pancreatitis, hereditary; pancreatic cyst/pseudocyst; pancreatic duct obstruction; pancreatic insufficiency

Disorders of the peritoneal cavity: ascites

Traumatic and mechanical disorders: abdominal wall defects; adhesions, postsurgical; digestive system complications of surgery; post-gastric surgery syndromes (eg, blind loop syndrome, adhesions); duodenal tear; foreign body in digestive system; inguinal, femoral, and abdominal wall hernias; open wound, abdominal; perforation of hollow viscus and blunt trauma; perforation/rupture of esophagus (Boerhaave syndrome); umbilical hernia

Congenital disorders: annular pancreas; biliary atresia; cleft lip and palate; esophageal atresia; malrotation without volvulus; Meckel diverticulum; pyloric stenosis, gastric outlet obstruction; tracheoesophageal fistula

Adverse effects of drugs on the gastrointestinal system: drug-induced changes in motility (chronic laxative abuse, opioids); drug-induced gastritis, duodenitis, peptic ulcer disease (NSAIDs); drug-induced hepatitis (eg, acetaminophen, isoniazid); drug-induced pancreatitis (eg, thiazide diuretics)

Renal & Urinary System

Normal Processes

Embryonic development, fetal maturation, and perinatal changes

Organ structure and function

kidneys, ureters, bladder, urethra
glomerular filtration and hemodynamics
urine concentration and dilution
renal mechanisms in acid-base balance
renal mechanisms in body fluid homeostasis
micturition

Cell/tissue structure and function

renal metabolism and oxygen consumption

tubular reabsorption and secretion, including transport processes and proteins
hormones produced by or acting on the kidney (eg, renin, aldosterone, angiotensin II, vasopressin)

Repair, regeneration, and changes associated with stage of life

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Infectious, immunologic, and inflammatory disorders

infectious disorders

upper urinary tract: granulomatous pyelonephritis; perinephric abscess; pyelonephritis; pyonephrosis; renal abscess; renal tuberculosis

lower urinary tract and urinary tract infections of unspecified location: cystitis; urethritis, chlamydial and nonchlamydial

immunologic and inflammatory disorders

upper urinary tract

glomerular disorders: Alport syndrome; glomerular disease due to hepatitis B, C; glomerulonephritis, including poststreptococcal; IgA nephropathy; lupus nephritis; minimal change disease; nephrotic syndrome; thin basement membrane disease

tubular interstitial disease: acute tubular necrosis (ATN); acute interstitial nephritis; papillary necrosis; HIV nephropathy

lower urinary tract: interstitial cystitis

Neoplasms

benign neoplasms and cysts

malignant neoplasms: renal (eg, Wilms tumor/nephroblastoma, renal cell carcinoma, renal tumors associated with congenital/hereditary conditions); urinary bladder and collecting system

Signs, symptoms, and ill-defined disorders: dysuria; hematuria; oliguria, anuria; proteinuria

Metabolic and regulatory disorders: acute kidney injury; renal insufficiency; azotemia, uremic syndrome; chronic kidney disease, including end-stage renal disease; cystinuria; Fanconi syndrome; hypertensive renal disease (renal complications of hypertension); renal calculi, ureteral calculi, nephrolithiasis; renal tubular acidosis

Vascular disorders: renal artery stenosis (atherosclerosis, fibromuscular dysplasia, nephrosclerosis); renal vein thrombosis; renal infarction

Traumatic and mechanical disorders: bladder rupture; neurogenic bladder; obstructive uropathy; posterior urethral valves; renal laceration; renal vascular injury; ureteral laceration/avulsion/disruption; urethral diverticulum; urethral/ureteral obstruction/stricture/prolapse; urinary incontinence, including secondary enuresis; vesicoureteral reflux

Congenital disorders: double ureters/ureteral duplication/double collecting system; horseshoe kidney; hydronephrosis/reflux; renal agenesis, renal hypoplasia, renal dysplasia; single kidney

Adverse effects of drugs on the renal and urinary system: ACE inhibitors; aminoglycosides; amphotericin B; cisplatin; furosemide; gadolinium (nephrogenic systemic fibrosis); heroin; iodinated contrast dye; lithium; NSAIDs; penicillins; sulfa drugs; tenofovir; drug-induced urinary retention

Pregnancy, Childbirth, & the Puerperium

Normal Processes

Organ structure and function: pregnancy, including fertilization, implantation, development of embryo, labor and delivery, the puerperium, lactation, gestational uterus, placenta

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Prenatal care

preconception counseling and care: folate deficiency prevention; immunizations; nutritional assessment, including vitamins; Rh screening

prenatal risk assessment/prevention: adolescent pregnancy; antepartum fetal evaluation, including biophysical profile; genetic screening; α -fetoprotein; diabetes mellitus; neural tube defects; Rh isoimmunization

supervision of normal pregnancy: assessment of gestational age; iron deficiency prevention; nutrition, including weight management; surveillance, including ultrasonography and assessment of fetal growth; vitamin deficiency prevention; infections, maternal, fetal, newborn (focus on prevention and screening): cytomegalovirus, coxsackievirus, hepatitis B virus, herpes simplex viruses, HIV, influenza virus, parvovirus B19 virus, rubella virus, varicella-zoster virus, Chlamydia trachomatis, Treponema pallidum, Streptococcus agalactiae, Toxoplasma gondii, amnionitis; urinary tract infection

Obstetric complications: abortion, induced, septic, missed, spontaneous, threatened; acute fatty liver of pregnancy; anemia of pregnancy, sickle cell disease, thalassemia in pregnancy; antepartum hemorrhage, including third-trimester bleeding; cardiomyopathy of pregnancy; cervical incompetence, cervical shortening; cholestasis of pregnancy, intrahepatic; congenital abnormalities, maternal (eg, bicornuate uterus); ectopic pregnancy; fetal abnormality affecting management of mother (eg, hydrocephalus, spina bifida); gestational diabetes; intrauterine growth restriction; maternal mortality; multiple gestation; placental abnormalities (abruptio placentae, placenta previa, premature separation of placenta); polyhydramnios, oligohydramnios; preeclampsia, eclampsia, HELLP syndrome, gestational hypertension; prolonged pregnancy; Rh isoimmunization affecting management of mother; vomiting in pregnancy (morning sickness, hyperemesis gravidarum); trauma in pregnancy; infections complicating pregnancy

Labor and delivery: labor and delivery, uncomplicated; labor and delivery, complicated, including shoulder dystocia; cesarean delivery, including complications; cord compression, cord prolapse; fetal malpresentations (eg, breech); intrapartum fetal evaluation, including fetal heart tones; intrapartum prophylaxis (eg, HIV, Chlamydia, gonococcal prophylaxis); premature rupture of membranes; preterm (before 37 weeks' gestation) and postdates labor and delivery; threatened preterm labor

Puerperium, including complications: lactation problems; breast-feeding problems; lochia; postpartum cardiomyopathy; postpartum blues; postpartum hemorrhage; postpartum sepsis; retained placenta, products of conception (eg, placenta accreta); uterine atony

Newborn (birth to 4 weeks of age)

normal newborn

examination of liveborn at admission to hospital
screening, newborn

disorders of the newborn: screening, newborn; ABO incompatibility in newborn; hemolytic disease due to Rh incompatibility; birth asphyxia syndrome (liveborn neonate); birth trauma (eg, cord compression, brachial palsy, lacerations); drug

withdrawal syndrome in newborn; feeding problems in newborn; fetal growth and development abnormalities, including fetal growth restriction; gastrointestinal obstruction; hypocalcemia of newborn; infections, congenital or peripartum (cytomegalovirus, herpes simplex viruses, HIV, hepatitis B, rubella virus, parvovirus B19 virus, varicella zoster virus, Chlamydia trachomatis, Streptococcus agalactiae, Treponema pallidum, Toxoplasma gondii); intrapartum fetal distress/death including stillborn; jaundice, fetal/neonatal/perinatal; laryngomalacia; macrosomia (large for gestational age); meconium aspiration syndrome; neonatal acne; neonatal Candida infection (thrush); neonatal hypoglycemia; neonatal conjunctivitis and dacryocystitis; ophthalmic gonorrhoea; phenylketonuria; premature infant; post-term infant; pseudomembranous colitis of infancy; respiratory distress syndrome (hyaline membrane disease); respiratory problems after birth (eg, bronchopulmonary dysplasia, tracheomalacia; tracheoesophageal fistula in neonates); retinitis of prematurity; seizures in newborn; sudden infant death syndrome (SIDS), apparent life-threatening event (ALTE); tetanus neonatorum

Congenital disorders, neonatal: congenital malformations and anomalies; neonatal hydrocele

Adverse effects of drugs on pregnancy, childbirth, and the puerperium: alcohol, tobacco, and other drugs (ATOD); prenatal radiation exposure; teratology (eg, ACE inhibitors, SSRIs, warfarin, infections, toxins)

Systemic disorders affecting pregnancy, labor and delivery, and puerperium: appendicitis; asthma; carpal tunnel syndrome in pregnancy; cirrhosis; deep venous thrombosis (DVT); diabetes mellitus; heart failure, valvular heart disease; hypertension; myasthenia gravis; obesity; pancreatitis; psychiatric disorders; renal failure/renal disease, including SLE; seizure disorders; thyroid disorders, hypothyroidism, hyperthyroidism

Female Reproductive System & Breast

Normal Processes

Embryonic development, fetal maturation, and perinatal changes, gametogenesis

Organ structure and function

female structure, including breast

female function (eg, ovulation, menstrual cycle, puberty)

intercourse, sexual response

Cell/tissue structure and function: hypothalamic-pituitary-gonadal axis, sex steroids, and gestational hormones

Reproductive system defense mechanisms and normal flora

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis,

Management, Risks, Prognosis

Breast

infectious, immunologic, and inflammatory disorders: breast abscess; inflammatory disease of breast, fat necrosis; mastitis; nipple discharge

neoplasms

benign and undefined neoplasms: breast cyst, solitary; fibrocystic changes; fibroadenoma; hypertrophy of breast; intraductal papilloma

malignant neoplasms (including screening): breast cancer; intraductal carcinoma; Paget disease of breast; phyllodes tumors

Female reproductive system

infectious, immunologic, and inflammatory disorders: bacterial vaginosis, including during pregnancy; Bartholin gland abscess; cellulitis, pelvic; candidiasis of the vulva or vagina; lichen sclerosus; sexually transmitted infections and exposure; cervicitis and endocervicitis; chancroid (*Haemophilus ducreyi*); genital herpes; gonorrhea (*Neisseria gonorrhoeae*); human papillomavirus infection, genital/venereal/anal warts, condylomata acuminata; lymphogranuloma venereum (*Chlamydia trachomatis*), non-lymphogranuloma venereum; pelvic inflammatory disease; Fitz-Hugh–Curtis syndrome; salpingitis and oophoritis; syphilis (*Treponema pallidum*); trichomoniasis (*Trichomonas vaginalis*); urethritis; vaginitis; vulvovaginitis

Neoplasms of the cervix, ovary, uterus, vagina, and vulva

benign neoplasms and cysts: abnormal Pap smear; benign neoplasm of ovary; endocervical and endometrial polyps; leiomyomata uteri; ovarian cyst

malignant and precancerous neoplasms: cervical cancer; HPV causing cancer; cervical dysplasia, HPV causing dysplasia; endometrial hyperplasia; endometrial/uterine cancer; gestational trophoblastic disease (hydatidiform mole); ovarian cancer; vulvar dysplasia and cancer

Fertility and infertility: assisted reproductive techniques (ART); contraception (eg, oral contraceptives, IUD, vaginal cap, cervical sponge, diaphragm, implant, morning-after pill, male and female condoms); female infertility; gonadal dysgenesis 45,X (Turner syndrome); sterilization; tubal factors; infertility

Menopause: ovarian failure, premature menopause; perimenopause; premenopausal menorrhagia; postmenopausal atrophic vaginitis; postmenopausal bleeding; vasomotor symptoms

Menstrual and endocrine disorders: abnormal uterine bleeding, including perimenopausal; absence of menstruation (primary amenorrhea, secondary amenorrhea including undiagnosed pregnancy); anovulation; dysmenorrhea; endometriosis; hirsutism, virilization; mittelschmerz; pelvic pain; polycystic ovarian syndrome; postcoital bleeding; premenstrual syndrome

Sexual dysfunction: dyspareunia; orgasmic dysfunction; sexual desire/arousal syndrome; vaginismus

Traumatic and mechanical disorders: Asherman syndrome; chronic inversion of uterus; chronic pelvic pain syndrome; cystocele; imperforate hymen; injuries, wounds, and burns affecting the female reproductive system and injuries, wounds, burns, and blast injuries; ovarian torsion; pelvic relaxation; prolapse, vaginal walls, uterine, uterovaginal; rectocele; urethrocele

Congenital disorders: müllerian agenesis; uterus didelphys, bicornuate uterus; short cervix

Adverse effects of drugs on the female reproductive system and breast: antihistamines, H₂-receptor blockers; benzodiazepines; beta-adrenergic blockers; hormone replacement; opioids; spironolactone; selective serotonin reuptake inhibitors; tricyclic antidepressants

Male Reproductive System

Normal Processes

Embryonic development, fetal maturation, and neonatal changes, gametogenesis

Organ structure and function

structure, male genitalia and prostate

function, male genitalia and prostate (eg, spermatogenesis, puberty)

intercourse, orgasm, erection

Cell/tissue structure and function, including hypothalamic-pituitary-gonadal axis, sex steroids, and gestational hormones

Reproductive system defense mechanisms and normal flora

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Infectious, immunologic, and inflammatory disorders

infectious disorders: balanitis; epididymitis; orchitis; prostatitis; sexually transmitted infections and exposure; chancroid (*Haemophilus ducreyi*); genital herpes; gonorrhea (*Neisseria gonorrhoeae*); human papillomavirus infection, genital/venereal/anal warts, condylomata acuminata; lymphogranuloma venereum (*Chlamydia trachomatis*); syphilis (*Treponema pallidum*); trichomoniasis (*Trichomonas vaginalis*); urethritis, chlamydial and nonchlamydial, nongonococcal

immunologic and inflammatory disorders: autoimmune hypogonadism

Neoplasms: malignant neoplasms, penile, prostate, testicular, breast

Metabolic and regulatory disorders, including sexual dysfunction: erectile dysfunction, impotence; infertility, male factor; male sexual dysfunction; premature ejaculation

Traumatic and mechanical disorders: benign prostatic hyperplasia/hypertrophy; circumcision, including complications; epididymal cyst; hydrocele; injuries, wounds, and burns to male genitalia, including blast injuries; penile laceration, penile fracture, Peyronie disease; phimosis; scrotal laceration; spermatocele; testicular rupture/avulsion/laceration; torsion of testis; urethral laceration/disruption; varicocele

Congenital disorders of the male reproductive system: hypospadias; Klinefelter syndrome; undescended testicle

Adverse effects of drugs on the male reproductive system: alcohol; androgens, testosterone; antipsychotics, antidepressants including selective serotonin reuptake inhibitors; beta-adrenergic blockers; diuretic including thiazides; drug-induced priapism (eg, trazodone); finasteride, dutasteride; sildenafil, tadalafil, vardenafil; marijuana; nitric oxide reductase inhibitors

Endocrine System

Normal Processes

Embryonic development, fetal maturation, and perinatal changes

Organ structure and function

hypothalamus, posterior and anterior pituitary gland

thyroid gland

parathyroid gland

adrenal cortex, adrenal medulla

pancreatic islets

ovary and testis

adipose tissue

Cell/tissue/structure and function, including hormone synthesis, secretion, action, metabolism

peptide hormones

steroid hormones, including vitamin D

thyroid hormones

catecholamine hormones

renin-angiotensin system

Repair, regeneration, and changes associated with stage of life

Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis, Management, Risks, Prognosis

Diabetes mellitus and other disorders of the endocrine pancreas

diabetes mellitus: diabetes mellitus, type 1; diabetes mellitus, type 1.5; diabetes mellitus, type 2; diabetes mellitus, acute complications: hyperosmolar coma, hypoglycemic shock, ketoacidosis, including cerebral edema, associated electrolyte abnormalities; diabetes mellitus, chronic complications: gastrointestinal/gastroparesis, neurologic/neuropathy, ophthalmologic/retinopathy, peripheral vascular, renal/nephropathy, metabolic syndrome

hypoglycemia and islet cell disorders: hypoglycemia (secondary to insulinoma, surreptitious insulin use, sepsis, liver failure); hyperglycemia (secondary to glucagonoma); hyperinsulinism; islet cell tumors/insulinoma/somatostatinoma; pancreatic neuroendocrine tumors

Thyroid disorders: cyst, nodule; euthyroid sick syndrome; goiter (euthyroid-normal thyroid function with goiter); hypothyroidism; hyperthyroidism, including thyrotoxicosis and thyroid storm; thyroiditis, including Hashimoto; Graves disease; neoplasms (benign cysts and nodules, thyroid cancer including papillary, follicular, medullary, and anaplastic); thyroid deficiency from pituitary disorder; infertility due to thyroid disease; secondary hypothyroidism and hyperthyroidism

Parathyroid disorders: hyperparathyroidism; hypoparathyroidism; metabolic bone disease

Adrenal disorders: corticoadrenal insufficiency (Addison disease); adrenal insufficiency, secondary; hypocortisolism; Cushing disease, Cushing syndrome; hyperaldosteronism; neoplasms, benign and malignant (adrenal neuroblastoma, pheochromocytoma, adrenal carcinoma, adrenal adenoma, aldosteronoma, adrenal incidentaloma); delayed and precocious puberty; hypertensive endocrine disease

Pituitary disorders: acromegaly/gigantism; diabetes insipidus; galactorrhea not associated with childbirth; panhypopituitarism from any cause; pituitary apoplexy (eg, Sheehan syndrome); growth hormone deficiency; short stature; SIADH (inappropriate secretion of ADH [vasopressin]); neoplasm, benign and malignant (pituitary adenomas, craniopharyngioma, metastatic disease); prolactinoma and hyperprolactinemia, including infertility due to these disorders; hypogonadism, primary and secondary

Hypothalamic endocrine disorders

Multiple endocrine neoplasia (MEN1, MEN2)

Congenital disorders: disorders of sexual differentiation; congenital adrenal hyperplasia; androgen insensitivity/resistance syndrome; congenital hypothyroidism

Adverse effects of drugs on the endocrine system: drug, medicinal, and biologic substance effects; exogenous steroid suppression of adrenal glands, anabolic steroids

Multisystem Processes & Disorders

Normal Processes

Principles of nutrition

generation, expenditure, and storage of energy at the whole-body level
functions of nutrients (eg, essential, trans-fatty acids, cholesterol)

Electrolyte and water metabolism

electrolyte metabolism (calcium, potassium, phosphorus)
water metabolism

Intracellular accumulations (eg, pigments, fats, proteins, carbohydrates, minerals, inclusions, vacuoles, lysosomal/glycogen storage disease and structures related to

storage diseases, glycogen phosphorylase deficiency, Zellweger syndrome)
**Abnormal Processes: Health and Health Maintenance, Screening, Diagnosis,
Management, Risks, Prognosis**

Infectious, immunologic, and inflammatory disorders

infectious disorders

bacterial: brucellosis (*Brucella* spp); leptospirosis (*Leptospira interrogans*); Lyme disease (*Borrelia burgdorferi*); melioidosis (*Burkholderia pseudomallei*); miliary (disseminated) tuberculosis (*Mycobacterium tuberculosis*); tularemia (*Francisella tularensis*); toxic shock syndrome; Q fever (*Coxiella burnetii*); anaplasmosis and ehrlichiosis (*Anaplasma* and *Ehrlichia* species); rickettsiosis (Rocky Mountain spotted fever [*Rickettsia rickettsii*])

viral: infectious mononucleosis (Epstein-Barr virus); cytomegalovirus infection; yellow fever; human herpesvirus 8 (HHV-8)

fungal: blastomycosis (*Blastomyces dermatitidis*); candidiasis (*Candida albicans*); coccidioidomycosis (*Coccidioides immitis/posadasii*); histoplasmosis (*Histoplasma capsulatum*)

parasitic: schistosomiasis (*Schistosoma*); leishmaniasis (*Leishmania* spp), visceral (kala-azar); trypanosomiasis/Chagas disease, acute and chronic (*Trypanosoma*)

immunologic and inflammatory disorders: acute rheumatic fever; autoimmune arteritis/vasculitis; Behçet syndrome; Churg-Strauss syndrome; eosinophilic granuloma, histiocytosis, Langerhans cell histiocytosis; Goodpasture syndrome; Henoch-Schönlein purpura; Kawasaki disease; mixed connective tissue disease; polyangiitis; polyarteritis nodosa; polymyalgia rheumatica, temporal arteritis; Raynaud disease/Raynaud syndrome; reactive arthritis, formerly Reiter disease, including Reiter arthritis; scleroderma (systemic sclerosis); Sjögren syndrome; systemic lupus erythematosus; Takayasu arteritis; Wegener granulomatosis; familial Mediterranean fever; sarcoidosis, Lofgren syndrome

Neoplasms and related disorders

paraneoplastic syndromes: endocrine (eg, SIADH, Cushing syndrome, hypercalcemia of malignancy [PTHrP]); hematologic (polycythemia, nonbacterial thrombotic endocarditis); neurologic (myasthenic syndrome, paraneoplastic cerebellar degeneration, limbic encephalitis, pure sensory neuropathy); mucocutaneous (eg, acanthosis nigricans); musculoskeletal (eg, pulmonary osteoarthropathy, polymyositis); other (membranous glomerulonephritis)

inherited cancer syndromes: DNA repair abnormalities (eg, Fanconi anemia); Lynch syndrome (gastrointestinal and female reproductive)

Signs, symptoms, and ill-defined disorders: arthralgias; abdominal pain; chest pain; cough; dizziness, light-headedness, syncope, including breath-holding spells with syncope; dyspnea, shortness of breath; edema, anasarca; fatigue; fever of unknown origin; Gulf War syndrome; hemoptysis; joint pain; palpitations; pruritus; unexpected weight gain/weight loss

Nutrition

protein-calorie malnutrition (kwashiorkor, marasmus)

vitamin deficiencies and/or toxicities: vitamin A; vitamin B; vitamin B1, thiamine (eg, Wernicke-Korsakoff syndrome, beriberi); vitamin B3, niacin; vitamin B6, pyridoxine; vitamin B9, folic acid; vitamin B12, cobalamins (pernicious anemia); vitamin C (scurvy); vitamin D (rickets); vitamin E; vitamin K

mineral deficiencies and/or toxicities

obesity

enteral/parenteral nutrition (TPN)

Toxins and environmental extremes

physical and associated disorders

temperature (eg, hypothermia, hyperthermia, heat stroke)

radiation (eg, radon, uranium mining, imaging studies)

thermal injury, burns, electrocution, lightning

decreased atmospheric pressure, high-altitude sickness

increased water pressure

chemical including Gulf War illness/syndrome

gases, vapors, smoke inhalation

agricultural hazards (eg, pesticides, green tobacco poisoning, anhydrous ammonia,

Agent Orange)

volatile organic solvents

heavy metals

other chemical agents (eg, ethylene glycol, carbon tetrachloride, methanol; BPA)

principles of poisoning and therapy (eg, ASA, acetaminophen)

Venomous bites and stings: hymenoptera bites and stings; scorpion bites; snake bites; spider bites; jellyfish stings

Fluid, electrolyte, and acid-base balance disorders

fluid volume and electrolyte/ion disorders: fluid volume disorders; dehydration;

hypovolemia; volume overload; electrolyte disorders; hyponatremia, hypernatremia;

hypokalemia, hyperkalemia; hypocalcemia, hypercalcemia; hypophosphatemia,

hyperphosphatemia; hypomagnesemia

acid-base disorders: metabolic acidosis; metabolic alkalosis; respiratory acidosis;

respiratory alkalosis; mixed acid-base disturbances

Abuse

child, nonaccidental trauma/inflicted head trauma/factitious disorder by proxy intimate partner abuse, sexual, emotional, and physical including injuries (eg, rib fractures) related to abuse

elder abuse, sexual, emotional, and physical including injuries (eg, rib fractures) related to abuse

sexual assault

Multiple trauma (eg, prioritization, blast injury involving more than one organ system)

Shock, cardiogenic, hypovolemic, neurogenic, septic, sepsis, bacteremia, systemic inflammatory response syndrome (SIRS), refractory, multiorgan dysfunction syndrome: meningococemia

Genetic metabolic and developmental disorders

multifactorial: VATER syndrome, association syndromes

large genomic changes: Beckwith-Wiedemann syndrome; Down syndrome; Prader-Willi syndrome

enzymatic/metabolic: alpha-1 antitrypsin deficiency; porphyria; inborn errors of metabolism (eg, maple syrup urine disease, diseases involving urea cycle); storage diseases (eg, Fabry disease, Tay-Sachs disease, glycogen storage disease, mucopolysaccharidoses)

structural protein disorders: amyloidosis; Ehlers-Danlos syndrome; immotile cilia syndrome (Kartagener syndrome; primary ciliary dyskinesia); Marfan syndrome

intracellular/extracellular transport receptors: cystic fibrosis; hemochromatosis; Wilson disease

triplet repeat/RNA disorders: fragile X syndrome

Adverse effects of drugs on multisystem disorders: drug-induced electrolyte abnormalities and acid base-disorders (eg, albuterol, prednisone, diuretics, alcohol)

Biostatistics, Epidemiology/Population Health, & Interpretation of the Medical Literature

Epidemiology/population health

Measures of disease frequency: incidence/prevalence

Measures of health status: rates, crude and adjusted; reproductive rates (eg, maternal mortality, neonatal/infant/under-5 mortality); mortality, morbidity; standardization; life expectancy, health-adjusted life expectancy; population attributable risk (PAR), population attributable risk percent (PAR%); risk factors

Survival analysis interpretation (eg, Kaplan-Meier curve)

Composite health status indicators, measures of population impact: years of potential life lost; quality-adjusted life years; disability-adjusted life years; standardized mortality ratio

Population pyramids and impact of demographic changes

Disease surveillance and outbreak investigation: disease reporting; response to public health advisory, health promotion; recognition of clusters

Communicable disease transmission: attack rate; herd immunity; reportable diseases

Points of intervention: primary, tertiary; community level (eg, cigarette taxes, soda taxes, smoke-free cities, buildings: restaurants, public buildings); school policies; access, healthy food, transportation, clean air, safe environments

Study design, types and selection of studies (includes dependent/independent variables)

Descriptive studies (case report [one person]/case series [more than one])

Analytical studies: observational: community surveys; cross-sectional (individuals); ecological (populations); case control; retrospective and prospective cohort

Analytical studies: interventional: clinical trial (randomized controlled trial; double-blind; placebo-controlled; noninferiority/equivalence trials); community intervention

Systematic reviews and meta-analysis: potential uses; estimation of effect sizes; heterogeneity; publication bias; forest plots, funnel diagrams; risk of bias, bias risk scale

Obtaining and describing samples: matching, inclusion/exclusion criteria, selecting appropriate controls for studies, lack of controls, concealed allocation, randomization, stratification

Methods to handle noncompliance: loss to follow-up; intention-to-treat analysis

Qualitative analysis

Measures of association

Relative risk

Odds ratio, hazard ratio

Other measures of association: number needed to treat/harm; absolute risk (AR), absolute risk percent (AR%); population attributable risk (PAR), population attributable risk percent (PAR%)

Distributions of data: measures of central tendency; measures of variability; regression to mean; normal distribution; nominal measurement

Correlation and regression, uses and interpretation: correlation coefficients; multiple regression

Principles of testing and screening

Properties of a screening test: validity, accuracy, reliability; criteria for a screening test; confirmatory testing; appropriateness; lead-time bias, length bias; screening vs diagnostic tests

Sensitivity and specificity; predictive value, positive and negative

ROC curves

Probability: theory (independence, product, addition rules); decision trees; likelihood ratios (application of Bayes theorem); post-test, pretest

Study interpretation, drawing conclusions from data

Causation: hypothesis-generating vs hypothesis-driven testing; causal criteria, temporality, temporal sequence, dose-response relationship; reverse causality

Chance

null hypothesis, Type I error and alpha level (multiple comparisons, random error/chance)

sample size and Type II error, beta, power

selection and interpretation of basic tests of statistical significance: chi-square; confidence intervals; p-values; t-test

a priori vs. post hoc analysis: subgroup analysis; error rate; affect types

Interpretation of graphs/tables and text

Bias, confounding, and threats to validity (includes methods to address)

selection, sampling bias

information bias: recall; ascertainment, ecologic fallacy, lack of blinding; loss to follow up

confounding variables, Hawthorne effect (includes methods to address)

other threats to validity (eg, placebo effect)

Internal vs. external validity: generalizability (external validity); efficacy vs effectiveness

Statistical vs. clinical significance; clinical and surrogate outcome/end-point

Clinical decision making, interpretation and use of evidence-based data and

recommendations: application of study results to patient care and practice, including patient preferences and individualization of risk profiles; risk/benefit analysis; synthesis of concepts with real data

Research ethics

Informed consent for research

Privacy of patient data (HIPAA)

Roles of institutional review boards (IRBs)

Intervention analysis: interim analysis; stopping analysis; safety monitoring

Regulatory issues: drug development, phases of approval; appropriateness of placebo;

appropriateness of randomized clinical trial; components of studies; ethics; scheduling; off-label use

Other issues related to research ethics

Social Sciences

Communication and interpersonal skills, including health literacy and numeracy, cultural competence

Patient interviewing, consultation, and interactions with the family (patient-centered communication skills)

fostering the relationship (eg, expressing interest)

information gathering (eg, exploring patient's reaction to illness)

information provision (eg, providing information about working diagnosis)

making decisions (eg, eliciting patient's perspectives)

supporting emotions (eg, effective discussion with difficult patients)
enabling patient behaviors (eg, education and counseling)

Use of an interpreter

Medical ethics and jurisprudence, include issues related to death and dying and palliative care

Consent/informed consent to treatment, permission to treat (full disclosure, risks and benefits, placebos, alternative therapies, conflict of interest, and vulnerable populations)

Determination of medical decision-making capacity/informed refusal

Involuntary admission

Legal issues related to abuse (child, elder, and intimate partner)

child protective services, foster care, immunizations

legal requirements for reporting

Birth-related issues

Death and dying and palliative care

life support

advance directive, health care proxy, advance care planning

euthanasia and physician-assisted suicide

diagnosing death/determination of brain death

pronouncing death

organ donation

hospice

pain management, including ethical issues related to death and dying

information sharing, counseling families

psychosocial and spiritual counseling, fear and loneliness

Physician-patient relationship (boundaries, confidentiality including HIPAA, privacy, truth-telling, other principles of medical ethics, eg, autonomy, justice, beneficence)

Impaired physician, including duty to report impaired physician

Negligence/malpractice, including duty to report negligence and malpractice

Physician misconduct, including duty to report physician misconduct

Referrals

Cultural issues not otherwise coded

Systems-based practice (including health systems, public health, community, schools) and patient safety (including basic concepts and terminology)

Complexity/systems thinking

Characteristics of a complex system and factors leading to complexity: how complexity leads to error

Sociotechnical systems: systems engineering; complexity theory; microsystems

Health care/organizational behavior and culture: environmental factors, workplace design and process; staffing; overcommitment, space, people, time, scheduling; standardization, reducing variance, simplification, metrics; safety culture; integration of care across settings; overutilization of resources (imaging studies, antibiotics, opioids); economic factors

Quality improvement

Improvement science principles

Variation and standardization: variation in process, practice; checklists, guidelines, and clinical pathways

Reliability

Specific models of quality improvement: model for improvement: plan-do-study-act (PDSA), plan-do-check-act (PDCA); Lean, including recognition and types of waste; Six Sigma

Quality measurement

Structure, process, outcome, and balancing measures

Measurement tools: run and control charts

Development and application of system and individual quality measures: core measures; physician quality report system (PQRS); event reporting system

Strategies to improve quality

Role of leadership

Principles of change management in quality improvement: specific strategies

Attributes of high-quality health care

High-value/cost-conscious care: overutilization of resources, including diagnostic testing, medications

Equitable care: access

Patient-centered care

Timely care

Patient Safety

Patient safety principles

Epidemiology of medical error

Error categorization/definition: active vs latent errors; Swiss cheese model of error; preventable vs non-preventable; near miss events/safety hazards

Causes of error

Patient factors: understanding of medication use; health literacy; economic status; cultural factors (eg, religion); failure to make appointments; socioeconomic status

Physician factors: deficiency of knowledge; judgment errors; diagnostic errors; fatigue, sleep deprivation; bias – cognitive, availability, heuristic, anchoring, framing

Human factors (eg, cognitive, physical, environmental)

High reliability of organization (HRO) principles: change management and improvement science; conceptual models of improvement

Reporting and monitoring for errors: event reporting systems

Communication with patients after adverse events (disclosure/transparency)

Specific types of error

Transitions of care errors (eg, handoff communication including shift-to-shift, transfer, and discharge): handoffs and related communication; discontinuities; gaps; discharge; transfers

Medication errors

Ordering, transcribing, dispensing, administration (wrong quantity, wrong route, wrong drug)

Medication reconciliation

Mathematical error

Procedural errors

Universal protocol (time out); wrong patient; wrong site; wrong procedure

Retained foreign bodies

Injury to structures: paracentesis; bowel perforation; thoracentesis; pneumothorax; central venous/arterial line injuries; arterial puncture and bleeding and venous thrombosis; lumbar puncture bleeding; paralysis

Other errors: anesthesia-related errors; mathematical errors

Health care-associated infections: nosocomial infection – eg, surgical site, ventilator associated, catheter-related; handwashing procedures or inadequate number of handwashing stations; central line-associated blood stream infections; surgical site infections; catheter-associated urinary tract infections; ventilator-associated pneumonia

Documentation errors: electronic medical record (including voice-recognition software errors); record keeping; incorrect documentation (eg, wrong patient, wrong date, copying and pasting, pre-labeling)

Patient identification errors

Mislabeled: transfusion errors related to mislabeling

Verification/two identifiers: lack of dual validation, including verbal verification of lab results

Diagnostic errors: errors in diagnostic studies; misinterpretation

Monitoring errors

Cardiac monitoring/telemetry

Drug monitoring (warfarin, antibiotics)

Device-related errors

malfunction

programming error

incorrect use

Strategies to reduce error

Human factors engineering

Situational awareness

Hierarchy of effective interventions: forcing function; visual cues

Error analysis tools: error/near miss analysis; failure modes and effect analysis; morbidity and mortality review; root cause analysis

Safety behavior and culture at the individual level: hierarchy of health care, flattening hierarchy, speak up to power; afraid to report, fear; psychological safety; closed-loop communication

Teamwork: principles of highly effective teams; case management; physician teams, physician-physician communication; interprofessional/intraprofessional teams; strategies for communication among teams, including system-provider communication, physician-physician communication (eg, consultations), interprofessional communication, provider-patient communication

Health care policy and economics

Health care policy

Health care disparities: race/ethnicity; numeracy/literacy; socioeconomic status

Access to care: critical access systems or hospitals

Social justice

Health care economics/Health care financing

Types of insurance: Medicare, Medicaid, private insurance, self-pay

Navigating the insurance system: deductibles/co-pays; in-/out-of-network; preferred providers

Reimbursement issues affecting safety and quality: emergency services – EMTALA; pay-for-performance