Chapter 1. Cellular Adaptations, Cell Injury, and Cell Death

Cellular responses to stress and Noxious Stimuli
Adaptation vs Injury/Cell Death

Cellular Adaptations of Growth and Differentiation
Hyperplasia vs Hypertrophy vs Atrophy
*important to know how different organs undergo adaptations
Metaplasia
*important for Barret’s esophagus for patients with untreated reflux and can progress to adenocarcinoma of the esophagus

Cell Injury
Can be reversible and irreversible
*amorphous densities in mitochondria are indicative of severe mitochondrial damage which is irreversible
Causes of cell injury
Oxygen depravation, Physical agents, Chemical agents and drugs, Infectious agents, Immunologic reactions, Genetic derangements , Nutritional imbalances
Mechanisms of Cell Injury
Depletion of ATP
Mitochondrial Damage
Influx of Intracellular Calcium and Loss of Calcium Homeostasis
Accumulation of Oxygen-Derived Free Radicals (oxidative stress)
Defects in membrane permeability
Ischemia and hypoxic injury
Ischemia-reperfusion injury

Cell Death
Necrosis: *Be able to recognize coagulative, liquifactive, caseous, and fat necrosis microscopically
Apoptosis
Extrinsic (Death Receptor-Initiated) Pathway
Intrinsic (Mitochondrial) Pathway
*Be able to recognize difference between apoptosis (DNA ladder pattern) and necrosis (diffuse smearing of DNA) on gel electrophoresis
*Know p53 and its role in DNA Damage-Mediated Apoptosis

Intracellular Accumulations
Lipids; Steatosis (Fatty Change)
Proteins : *defective intracellular transport and secretion of critical proteins
Hyaline change
Glycogen: *Glycogen storage diseases
Pigments

Pathological Calcification
Dystrophic vs Metastatic Calcification

Cellular Aging: *telomeres
Chapter 2: Inflammation

Acute Inflammation

Stimuli for acute inflammation
- Infection, Trauma, Physical and Chemical Agents, Tissue Necrosis, Foreign bodies, Immune reactions

Vascular Changes
- Changes in Vascular Flow and Caliber (brief period of vasoconstriction then vasodilation)
- Increased Vascular Permeability

Cellular Events
- Leukocyte Adhesion and Transmigration
  - *Know role of selectins and Integrins; *One disease to know here is LAD, characterized by recurrent bacterial infections and impaired wound healing
- Chemotaxis
- Leukocyte Activation
- Phagocytosis

Chemical Mediators of Inflammation

Vasoactive Amines
- Histamine (found in basophils and platelets, and mast cells); Seratonin (platelets)

Plasma Proteins
- Complement system/Kinin system/Clotting system
  - *Importance of Factor XII (Hageman Factor) in linking the above 3 systems in addition to Fibrinolytic system

Arachidonic Acid Metabolites: Prostaglandins, Leukotrienes, and Lipoxins

Platelet-Activating Factor

Cytokines and Chemokines
- Cytokines (TNF and IL-1)
- Chemokines (mainly chemoattractants)

Nitric Oxide

Lysosomal granules

Oxygen-Derived Free Radical, know types of injury

Neuropeptides

Outcomes of Acute Inflammation

- Complete resolution
- Healing by connective tissue replacement (fibrosis)
- Progression to chronic inflammation

Chronic Inflammation

Causes

Morphologic Features
- *be able to recognize microscopic features of acute vs. chronic

Cells of Chronic Inflammation
- Macrophage, lymphocytes, eosinophils (immune reactions and parasitic Infections), Granulomas

Systemic Effects of Inflammation

Fever
- Acute phase proteins: *C-reactive protein, *Erythrocyte Sedimentation Rate
- Leukocytosis (left-shift)
- Sepsis
Chapter 3 Tissue Renewal and Repair

Repair by Healing, Scar Formation, and Fibrosis
- Angiogenesis
  - Regulation by growth factors and ECM proteins
- Scar Formation
  - Fibroblast migration and proliferation
  - ECM Deposition and Scar Formation
  - Tissue Remodeling

Cutaneous Wound Healing
- Healing by first intention (wounds with opposed edges)
- Healing by second intention (wounds with separated edges)
- Wound Strength
  - *after one week, strength is approx 10%

Overview of Repair Responses After Injury and Inflammation
- Regeneration
  - Ex: superficial skin wounds
- Healing
  - Ex: MI
- Fibrosis
  - Ex: Cirrhosis
Chapter 4 Hemodynamic Disorders, Thromboembolic Disease, and Shock

Edema
- Increased Hydrostatic Pressure
- Reduced Plasma Osmotic Pressure
- Lymphatic Obstruction
  - *filariasis
- Sodium and Water Retention
  - *Subcutaneous, Pulmonary (seen with LV failure), Brain

Hyperemia (active) and Congestion (Passive)
- *hemosiderin laden macrophages (heart failure cells)

Hemorrhage
- *introduce clinical disorders called hemorrhagic diatheses
  - hematoma vs. petechiae vs. purpura vs. ecchymoses

Hemostasis
- Normal hemostasis
  - Injury then arteriolar vasoconstriction
  - Exposure of thrombogenic subendothelial matrix allows platelets to adhere
    - And become activated
  - Recruitment of additional platelets leads to hemostatic plug
  - Tissue factor activates thrombin which activates fibrin, leading to
    - Secondary hemostasis
  - Counterregulatory mechanisms (i.e. TPA) limit the hemostatic plug to the
    - Site of injury

Endothelium
- Antithrombotic role in hemostasis
- Prothrombotic role in hemostasis
  - *von Willebrand Factor (vWF) deficiency

Platelets
- Adhesion
- Secretion
- Aggregation
  - ADP and Thromboxane A2 lead to build up of platelet aggregate
    - *Pharmacology correlation ex: Aspirin and Plavix

Coagulation Cascade
- Intrinsic Pathway
  - May be initiate by activation of factor XII
- Extrinsic Pathway
  - Activated by Tissue Factor

Thrombosis
- Pathogenesis *Virchow Triad
  - Endothelial injury
  - Stasis or turbulence of blood flow
  - Hypercoagulability
    - *antiphospholipid antibody syndrome
      - pts present with multiple thromboses and have false
        positive serologic tests for syphilis

Fate of a Thrombus
- Propagation
Embolization
Dissolution
Organization and recanalization
Disseminated Intravascular coagulation
  *not a primary disease but rather a potential complication of any condition associated with widespread activation of thrombin

**Embolism**
  - Pulmonary Thromboembolism
  - Systemic Thromboembolism
  - Fat Embolism
    *broken bone (often a femur on tests)
  - Air Embolism
    *decompression sickness
  - Amniotic Fluid Embolism

**Infarction**
  - Red (hemorrhagic) vs. White (anemic)
  - Dominant histologic characteristic is ischemic coagulative necrosis
  - In brain it is liquefactive

**Shock**
  - Cardiogenic shock
    - Myocardial pump failure
  - Hypovolemic
    - Loss of blood or plasma volume
  - Septic
    - Systemic microbial infection
  *Effects of Lipoploysaccharide (LPS)
    - initiates cytokine cascade (TNF, IL-1, IL-6, IL-8, NO, PAF)
    - at high levels syndrome of septic shock is seen
Chapter 5 Genetic Disorders

Mendelian Disorders
Transmission Patterns of Single Gene Disorders
Autosomal Dominant Disorders
*clinical features can be modified by reduced penetrance and variable expressivity
*commonly tested disorders:
  Marfan syndrome
  Huntington disease
  Familial hypercholesterolemia
Autosomal Recessive
*commonly tested disorders:
  Cystic fibrosis, PKU, Galactosemia, homocystinuria, Lysosomal storage diseases, alfa1-antitrypsin def,
  Wilson disease, Hemochromatosis, Glycogen storage Diseases, Sickle cell anemia, Thalassemias, CAH,
  Ehlers-Danlos syndrome, Alkaptonuria
X-linked recessive
  Duchenne muscular dystrophy, Hemophilia, G6PD, Wiskott-Aldrich syndrome, Lesch-Nyhan syndrome, Fragile-X syndrome

Biochemical and Molecular Basis of Mendelian disorders
Enzyme Defects
Defects in Receptors and transport systems
Alterations in Structure, Function, or Quantity of Nonenzyme proteins
Genetically determined adverse reactions to drugs

*Lysosomal Storage Diseases
  Tay-Sachs disease – microscopically, large neuron with lipid vacualation
  *PE hint is Cherry Red spot visible on macula
  Nieman Pick Disease
  Lysosomal accumulation of sphingomyelin
  Gaucher Disease
  Glucocerebrosides accumulate in phagocytic cells throughout bodies
    -Gaucher cells

*Glycogen Storage diseases
  Von Gierke’s disease – liver
  Pompe’s disease – heart
  McArdle’s disease – painful muscle cramps with strenuous exercise.

Cytogenetic disorders
  Trisomy 21, Trisomy 18 (Edward’s syndrome), Trisomy 13 (Patau Syndrome),
  DiGeorge Syndrome
  Klinefelter Syndrome, Turner Syndrome
Chapter 6: Diseases of Immunity

General Features

Innate immunity – epithelial barriers, phagocytic cells (PMNs, Macrophages), NK Cells, plasma proteins (complement system)
Adaptive immunity – consist of lymphocytes and their products (antibodies)
Cell mediated: defends against intracellular pathogens
Humoral immunity: protects against extracellular microbes and toxins

Cytokines: messenger molecules of the immune system

HLA and disease Association
*Inflammatory diseases: ankylosing spondylitis assoc with HLA-B27

Hypersensitivity reactions
Type 1 hypersensitivity – immediate immune response, releases vasoactive
Substances in an individual sensitized to antigen
Most are IgE mediated
*systemic anaphylaxis
Type 2 hypersensitivity – mediated by antibodies directed toward antigens present on cell surfaces or extracellular matrix
*transfusion reaction
Type 3 hypersensitivity – antigen-antibody complexes produce tissue damage mainly by causing inflammation at the sites of deposition
*serum sickness
Type 4 hypersensitivity – cell mediated immunity sensitized T lymphocytes are the cause of the cellular and tissue injury.
*TB classic example of delayed hypersensitivity
*graft rejection

Transplant rejection
Hyperacute rejection – minutes to hours
Acute rejection – days
Acute cellular rejection – initial months
Chronic rejection – 4-6 months

Autoimmune diseases
Systemic Lupus Erythematosus
Fundamental defect in SLE is a failure of the mechanisms that maintain self-tolerance
**antibodies to double stranded DNA and Smith antigen are virtually diagnostic of SLE
*recognize nuclear fluorescent patterns
*kidney is a frequent target of injury
Other organs affected
Skin, joints, CNS, Pericarditis, cardiovascular system (Libman-Sacks), spleen, lungs

Rheumatoid Arthritis
Sjogren Syndrome
*antibodies against Ro (SS-A) and La (SS-B)

Scleroderma
Diffuse scleroderma
Limited scleroderma
*CREST syndrome
Polyarteritis Nodosa – inflammation of the walls of the blood vessels
Immunologic deficiency syndromes

Primary immunodeficiencies
X-linked agammaglobulinemia of Bruton
Failure of B-cell precursors to mature into B-cells
*After 6 months, recurrent bacterial infections and certain viral inf
Common Variable immunodeficiency
Hypogammaglobulinemia, affects all antibody classes, but sometimes only IgG.
*effects both sexes in contrast Bruton’s syndrome; onset of symptoms is later
Isolated IgA deficiency
Low levels of both serum and secretory IgA

Hyper-IgM Syndrome
Pts make IgM antibodies but are deficient in their producing IgG, IgA, and IgE antibodies
*present with recurrent pyogenic infections
may get PCP pneumonia

DiGeorge Syndrome
*failure of development of the 3rd and 4th pharyngeal pouches
loss of thymus leads to loss of T-cell mediated immunity
Severe Combined Immunodeficiency Diseases
Defect in both humoral and cell mediated immunity
*without bone marrow transplantation, die within 1 year
Wiskott-Aldrich Syndrome; *immunodeficiency with thrombocytopenia and eczema

Acquired Immunodeficiency Syndrome (AIDS)
Epidemiology
Etiology
Structure of HIV
p24, 2 copies of RNA, and 3 viral enzymes: protease, reverse transcriptase, and integrase
Gag, pol, and env genes code for viral proteins
Pathogenesis of HIV infection and AIDS
Life cycle
CD4 is a high affinity receptor for HIV
CD4+ T cells, macrophages, dendritic cells
Also gp 120 must bind a coreceptor CCR5 or CXCR4
Mechanism of T cell immunodeficiency
Natural History of HIV Infection
See figure 6-50
Clinical Features
*PCP pneumonia
Candidiasis
Cryptococcosis
*Kaposi Sarcoma

Amyloidosis
Pathologi proteinaceous substance in a Beta pleated sheet which accumulates and
causes pressure atrophy
*Congo red staining produces apple green birefringence when observed by polarizing microscopy
Organs
Kidney: Nephritic syndrome and proteinuria
Spleen
Liver
Heart
Chapter 7 Neoplasia

Definition
Neoplasia means new growth
Genetic changes allow excessive, unregulated, and autonomous proliferation

Nomenclature
Benign tumors
Suffix –oma attached to cell of origin (rule of mesenchymal cell tumors)
Adenoma – benign epithelial tumors that form glandular patterns or
derived from glands without producing glandular pattern
Malignant tumors
Sarcomas – malignant tumors arising in mesenchymal tissues
Carcinomas – malignant tumors of epithelial origin
Adeno- vs. Squamous cell carcinomas

Differentiation
The extent to which neoplastic cells resemble normal cells
(well differentiated tumors are composed of cells that resemble mature normal cells of the tissue
of origin.)

Anaplasia
Lack of differentiation
(poorly differentiated tumors have primitive appearing unspecialized cells)

Characteristics
Pleomorphism
Cells and nuclei vary in size and shape
Abnormal nuclear morphology
Mitoses
Loss of polarity

Rates of Growth
Growth fraction
Proportion of cells within tumor that are in proliferative stage
*tumors with large growth fraction (fast growing) are more susceptible to chemotherapy
agents
*10^9 tumor cells is the smallest clinically detectible mass

Local invasion
Nearly all benign tumors grow as cohesive masses remaining localized to site of origin
Malignant tumors are poorly demarcated from surrounding tissues
Besides metastases, invasiveness is the most reliable feature that differentiates
Malignant from benign tumors

Metastasis
Unequivocally marks a tumor as malignant
Pathways of spread
Seeding of body cavities and surfaces
Lymphatic spread
Hematogenous spread

Epidemiology
Cancer incidence (Research most recent cancer statistics)
*Top three incidence
Men – Prostate, Lung, Colon and Rectum
Women – Breast, Lung, Colon and Rectum
*Top three cancer deaths
Men – Lung, Prostate = Colon and Rectum  
Women – Lung, Breast, and Colon and Rectum  

Geographic and environmental factors  
Age  
Genetic Predisposition to Cancer  
    Autosomal dominant Inherited Cancers  
    Retinoblastomas  
    FAP  
    Defective DNA repair syndromes  
    HNPCC  
    Xeroderma pigmentosum  
    Familial cancers  
    BRCA1, BRCA2  
Nonhereditary predisposing conditions  
    Chronic Inflammation and Cancer  
        Ex: increased GI cancer in Ulcerative Colitis  
Precancerous conditions  

Molecular Basis of Cancer  
    Nonlethal genetic damage lies at the heart of carcinogenesis  
    Tumor is formed by the clonal expansion of a single precursor cell that has incurred genetic damage  
Four classes of normal regulatory genes  
    Growth promoting protooncogenes  
    Growth inhibiting tumor suppressor genes  
    Genes that regulate apoptosis  
    Genes involved in DNA repair  
DNA repair genes affect cell proliferation or survival indirectly by influencing the ability of the organism to repair non-lethal damage in other genes  
Carcinogenesis is a mult-step process  
    Essential Alterations for Malignant Transformation- 7 Criteria for Malignancy  
        Self-sufficiency in growth signals  
        Insensitivity to growth inhibitory signals  
        Evasion of apoptosis  
        Defects in DNA repair  
        Limitless replicative potential  
        Sustained angiogenesis (VEGF)  
        Ability to invade and metastasize  
Normal Cell Cycle  
    Cyclin D and RB phosphorylation  
    Cell cycle progression beyond the G1/S restriction point  
    Cell Cycle Inhibitors (CDK inhibitors)  
    Cell cycle check points  
        G1/S (for DNA damage)  
    G2/M (for completion of DNA replication)  
Self-sufficiency in Growth Signals: Oncogenes  
    Protooncogenes, Oncogenes, and Oncoproteins  
*specifics covered in CMB  
Insensitivity to Growth Inhibitory Signals: Tumor Suppressor Genes  
    Retinoblastoma as a paradigm for the two-hit hypothesis of Oncogenesis  
*p53
Telomerase-maintains telomere length, essential for maintaining replicative potential

**Invasion and Metastasis**
- Invasion of ECM
  - Detachment of tumor cells from each other
  - Attachment to matrix components
  - Degradation of ECM
  - Migration of tumor cells

**Carcinogenic Agents and Their Cellular Interactions**
*know difference between initiators and promoters and some specific examples
- Radiation Carcinogenesis
  - UV Rays and Ionizing radiation
- Microbial Carcinogenesis
  *know which viruses are associated with specific cancers
  - ex: HPV and Cervical cancer
  - ex: EBV and nasopharyngeal carcinomas and Hodgkin lymphoma and African Burkitt lymphoma
  - Ex: Hepatitis B virus and hepatocellular carcinoma
  - Ex: HTLV1 and T-cell leukemia/Lymphoma

**Host Defense against tumors – Tumor Identity**
- Tumor antigens
- Antitumor Effector Mechanisms
  *Cytotoxic T lymphocytes, NK cells, Macrophages, antibodies
- Immune surveillance

**Clinical Features of Tumors**
- Effects of Tumors on the host
  - Local and hormonal effects
  - Cancer Cachexia
    - Thought to be due to Cytokine production
  - Paraneoplastic Syndromes
    *Table 7-12
- Grading and Staging of tumors
  - Grading based on differentiation and mitoses
  - Staging based on size and spread to lymph nodes, +/- mets

**Laboratory diagnosis of cancer**
- Histologic and cytologic methods
- Immunohistochemistry
- Molecular diagnosis
  *BCR-ABL dx CML
- Flow Cytometry
- Tumor Markers
  *Table 7-13
Chapter 8 Infectious Diseases

General Principles of Microbial Pathogenesis

New and Emerging Infectious disease (Table 8-1)

Agents of Bioterrorism

Categories of infectious agents
- Prions (CJD)
- Viruses
- Bacteriophages, Plasmids, Transposons
- Bacteria
- Chlamydiae, Rickettsiae, Mycoplasmas
- Fungi
- Protozoa
- Helminths
- Ectoparasites

Transmission and Dissemination of Microbes

Host Barriers to Infection
- Skin, GI tract, Resp tract, UG tract,

Spread and Dissemination of Microbes

Release of Microbes from the Body
- *fecal-oral route, resp route, sexual route

Sexually Transmitted infections
- *infection with one increases risk for additional

Infections in Immunosuppressed Hosts
- *CF patients commonly get respiratory infections with Pseudomonas, S. aureus, and B. cepacia
- *lack of splenic functions in SC pts make them susceptible to infection with encapsulated bacteria (S. pneumoniae)

Special Techniques for diagnosing infectious agents
- Stains, nucleic acid-based tests, PCR

Spectrum of inflammatory responses to infection
- Suppurative inflammation/Mononuclear and Granulomatous inflammation/Cytopathic-
- Cytoproliferative inflammation/Necrotizing inflammation/Necrotizing inflammation and scarring

Viral infections (specifics covered during Micro)
- Herpesvirus
  - HSV-1 and HSV-2 (glassy intranuclear inclusion bodies)
  - CMV (Owl’s eyes inclusion bodies)
  - VZV

Bacterial infections
- Gram positive bacterial infections
  - Staphylococcal infections (figure 8-18)
  - Streptococcal infections (erysipelas, pharyngitis, scarlet fever) *rheumatic fever
  - Diphtheria (dirty gray membrane)
    - *severe sequelae due to exotoxin
  - Listeriosis (meningitis in neonates, still births in pregnant women)
  - Anthrax (cutaneous vs. inhalational)
    - Toxin edema factor (EF) and lethal factor (LF)
  - Nocardia (stained with modified acid fast stains)
    - Branching filaments

Gram Negative Bacterial Infections
- Neisserial infections
N. meningitides (major cause of meningitides ages 5-19)
N. gonorrhoeae
   *suspect in young person with acute arthritis
Whooping cough
Bordetella pertussis
Pseudomonas infectious; *secretes exotoxin similar to diphtheria toxin
Plague - Yersinia pestis (flea bites)
Chancroid
Hemophilus ducreyi (painful lesion)
Mycobacteria
   TB (primary vs secondary/reactivation disease)
   Ghon complex – combo of parenchymal lung lesion and nodal involvement
MAC
   Leprosy (tuberculoid vs lepromatous)
Spirochetes
Syphillis (Treponema pallidum)
   Primary, secondary, tertiary
   Congenital
   Tests (VDRL, FTA-Abs)
Lyme Disease
   Borrelia burgdorferi *(transmitted by Ixodes deer ticks)
Anaerobic Bacteria
Abscesses
Clostridal infections
   C. perfringens, C. tetani, C. botulinum, C. Difficile (*recent antibiotic tx and C. diff)
Obligate intracellular bacteria
   C. trachomatis (most common STI in the world)
   Rickettsial infections (Typhus fever, Rocky Mountain Spotted fever)
Fungal Infections
   Yeasts
      Candidiasis (thrush, esophagitis, vaginitis, cutaneous, invasive)
      *microscopically – budding yeasts and pseudohyphae
      Cryptococcosis (opportunistic infections)
      Encapsulated yeast stains with mucicarmine
Molds
   Aspergillosis (fruiting bodies)
   Mucormycosis (diabetes is a predisposing risk factor)
      Microscopically – affinity for vessel walls, right angle branching
Parasitic infections
Protozoa
   Malaria; *heterozygotes for HbS are protected against malaria
   Leishmaniasis (sand flies)
   African Trypanosomiasis (sleeping sickness)
   Chagas Disease (cardiac damage from direct invasion of myocardial cells)
Metazoa
   Strongyloidiasis (fig 8-56)
   Tapeworms: Cysticercosis and Hydatid disease
   Trichinosis (ingestion of larvae in undercooked meat)
   Schistosomiasis (bladder)
   Lymphatic Filariasis (Wuchereria bancrofti); Elephantiasis
Chapter 9: Environmental and Nutritional Pathology

Nutrition and Disease
Nutritional Deficiencies
Protein-Energy Malnutrition
   Marasmus-severe reduction in caloric intake
   Kwashiorkor-marked protein deprivation (more severe than Marasmus)
Anorexia nervosa and Bulimia
   Amenorrhea is diagnostic of anorexia nervosa
Vitamin Deficiencies (Table 9-22)
   Vitamin A def. assoc. with night blindness, xeroophthalmia, blindness
   Vitamin D def. assoc. with rickets (children) and osteomalacia (adults)
   Vitamin E def. assoc. with spinocerebellar degeneration
   Vitamin K def assoc. with bleeding diatheses (cofactor for production of clotting factors)
   Thiamine def. assoc. with alcoholism and dry and wet beriberi, Wernicke syndrome, Korsakoff syndrome
   Riboflavin (B2) def. assoc. with cheilosis, glossitis, dermatitis, stomatitis, corneal vascularization
   Niacin def. assoc. with pellagra (dementia, dermatitis, diarrhea)
   Pyridoxine (B6) def. assoc. with glossitis, cheilosis, peripheral neuropathy
   Vitamin C def. assoc. with scurvy
   Folate def. assoc. with neural tube defects, megaloblastic anemia
Mineral Deficiencies (see Table 9-24)
   Iron- hypochromic microcytic anemia
   Zinc- acrodermatitis enteropathica, growth retardation, impaired wound healing, infertility
   Iodine-goiter, hypothyroidism
   Selenium-myopathy, rarely cardiomyopathy
   Copper- muscle weakness, neurologic defects, hypopigmentation, abnormal collagen cross-linking
   Fluoride- dental caries

Obesity
Know how to calculate BMI
Overweight is classified as BMI 25-30
Obesity is BMI >30
Chapter 10: Diseases of Infancy and Childhood

Congenital Anomalies

Definitions
- Malformations/Disruptions/Deformations/Sequence/Syndromes

Causes of Anomalies
- Genetic Causes
  - Karyotypic aberrations
  - Single gene mutations
  - *80-90% of spontaneous abortions are due to chromosomal abnormalities
- Environmental Causes (viruses, drugs/chemicals, radiation, maternal DM)

Pathogenesis of Congenital Anomalies
- Timing of Insult
  - *Weeks 3-8, organogenesis: susceptible to teratogens

Birth weight and gestational age

- Appropriate for gestational age (AGA) (birthweight b/t 10\textsuperscript{th} and 90\textsuperscript{th} percentile)
- Small for gestational age (SGA) (birthweight less than 10\textsuperscript{th} percentile)
- Large for gestational age (LGA) (birthweight greater than 90\textsuperscript{th} percentile)

Prematurity risk factors
- Preterm premature rupture of membranes (PPROM)
- Intrauterine infection

Complications of prematurity
- Hyaline membrane dz
- Necrotizing enterocolitis
- Sepsis
- Intraventricular Hemorrhage
- Developmental Delay

Perinatal Infections
- Transcervical (ascending)
- Transplacental (hematologic)

Neonatal Respiratory Distress Syndrome (RDS)
- AKA hyaline membrane dz
- Defect is a deficiency of surfactant
  - *Corticosteroids may be given to stimulate surfactant production in weeks 24-34.

Necrotizing Enterocolitis (NEC)
- Some postnatal insult (such as introduction of bacteria) may lead cascade of tissue destruction
- Sx: bloody stools, abdominal distension, circulatory collapse; *Pneumatosis intestinalis (gas in intestinal wall)

Fetal Hydrops
- Accumulation of edema fluid in fetus during intrauterine growth
  - See table 10-5 for causes (*Rh and ABO incompatibility show up on boards)
  - *Administration of Rhogam to Rh- mothers at 28 weeks and within 72 hours of birth

Inborn Errors of Metabolism (covered in detail in genetics course)
- PKU
  - Deficiency of phenylalanine hydroxylase
  - Severe mental retardation by age 6 mos. w/o diagnosis and avoidance of foods high in phenylalanine
  - *PKU is detected on routine newborn screening
Galactosemia
- Deficiency of either the enzyme GALT (common form) or galactokinase (rare form)
- Affects liver, eyes, brain
- Hepatomegaly due to fatty change
- *Cataracts develop within the first few weeks of life
- Sx: FTT, vomiting, diarrhea, jaundice in first week of life

Cystic Fibrosis
- Disorder of epithelial transport affecting fluid secretion, exocrine glands, and lining of resp, GI, and reproductive tracts
- Autosomal recessive defect in CFTR gene which regulates chloride channels
- Sx: range from mild to severe
  - Chronic sinopulmonary dz
  - GI: *meconium ileus
  - Male *congenital bilateral absence of vas deferens
  - Exocrine pancreatic insufficiency

SIDS
- 90% of all SIDS deaths occur in the first 6 mos. of life
- See table 10-8 for risk factors and postmortem findings

Tumors and Tumor-like Lesions of Infancy and Childhood

Benign Tumors and Tumor-like lesion
- Hemangiomas-*congenital capillary hemangiomas may regress spontaneously
- Lymphatic tumors
- Fibrous tumors
- Teratomas

Malignant Tumors
- *Most frequent childhood cancers arise in the hematopoietic system, nervous tissue, soft tissues, bone, and kidney
- Leukemia, ALL
- Neuroblastoma
  - Small, blue, round cells
  - Homer-Wright pseudorosettes
- Wilm’s tumor
  - Gross appearance is large, solitary, well-circumscribed mass
  - Triphasic microscopic appearance: blastemal, stromal, and epithelial components
- Hepatoblastoma
- Rhabdomyosarcoma
- Teratoma
- Ewing Sarcoma
- Posterior Fossa Tumors
- Juvenile Astrocytoma
- Medulloblastoma
- Ependymoma
Chapter 11: Blood Vessels

General Architecture of vessels
Basic Constituents
- Endothelial Cells/Smooth muscle cells
- ECM (including elastin, collagen, and glycosaminoglycans)

Three Concentric Layers
- Intima/Media/Adventitia (contains vasa vasorum in large and medium-sized vessels)

Classification
- Large or elastic arteries- aorta and pulmonary
- Medium or muscular – coronary and renal
- Small arteries and arterioles

Vascular Wall Cells and Their Response to Injury
- Endothelial Cells
- Vascular Smooth muscle cells (SMC)
- Vessel Development, Growth, and Remodeling
- Intimal Thickening – A response to vascular intimal injury
  - Vascular injury stimulate SMC growth
    - Migration of SMC to intima
    - SMC mitosis
    - Elaboration of ECM

Congenital Anomalies
- Berry aneurysms and AV fistulas

Arteriosclerosis (hardening of the arteries)
- Monckberg medial calcific sclerosis
- Arteriolosclerosis
- Atherosclerosis
  - Intimal lesions (atheromas) protrude into vascular lumens and weaken the media
    *causes 50% of all deaths in Western World

Natural History and Main Consequences (Fig 11-5)
- Foam cells, fatty streaks, atheromas (fig 11-7), fibroatheromas, and complicated lesions
- *distribution of atherosclerotic plaques
  - abd aorta > thoracic aorta
  - lesions more prominent around ostia of major branches
  - advanced lesion
    - rupture, ulceration, or erosion
    - hemorrhage
    - thrombosis
    - aneurismal dilation

Risk Factors
- Age, Sex, Genetics, Hyperlipidemia, HTN, Cigarettes, DM,

Pathogenesis
- Chronic endothelial injury, accumulation of lipoproteins, modification of lipoproteins by oxidation
- Adhesions of blood monocytes to endothelium, migration into intima and transformation into foam cells
- Platelet adhesion
- Release of factors that cause migration of SMCs from media into intima
- Proliferation of SMCs
- Accumulation of lipids
*possible role of infection with C. pneumoniae and CMV

**Hypertension**
Two forms of small blood vessel disease
- Hyaline arteriolosclerosis (hyaline thickening of the walls of arterioles)
- Hyperplastic arteriolosclerosis *onion skinning

**Aneurysms and Dissections**
- True aneurysm is bounded by arterial wall components
  - Ex: syphilitic and atherosclerotic
- False aneurysms
  - Breach in vascular wall leading to an extravascular hematoma that freely communicates with the intravascular space
  - Ex: post-MI rupture
- Abd Aortic Aneurysm (AAA)
- Syphilitic aneurysm
  - *obliterative endarteritis with plasma cells especially of thoracic aorta
- Aortic dissection
  - Blood between the laminar planes of the media
  - *Marfan syndrome

**The Vasculitides**
- Giant Cell (Temporal Arteritis)
  - Acute and chronic granulomatous inflammation of large to small arteries
  - *dx depends on biopsy
- Takayasu Arteritis (Pulseless disease)
  - Granulomatous vasculitis of medium and larger arteries
  - Ocular disturbances and weakening of UE pulses
- Polyarteritis Nodosa (PAN)
  - Necrotizing inflammation of medium to small arteries in any organ
  - Fibrinoid necrosis
- Kawasaki disease
  - Arteritis of coronaries in young children and infants
- Wegner Granulomatosis
  - Acute necrotizing granulomas of the URT, LRT, or both
  - Necrotizing or granulomatous vasculitis affecting small to medium vessels
  - Renal disease with focal crescentic glomerulitis
- Thromboangiitis Obliterans (Buerger disease)
  - Sharply segmental acute and chronic vasculitis of medium and small Arteries
- Infectious Arteritis
  - Aspergillus and mucormycosis

**Malignant Tumors**
- Angiosarcoma
  - Malignant endothelial neoplasm structure varies from highly differentiated to anaplasia
Chapter 12: The Heart

Heart Failure
Cardiac Hypertrophy
  Pressure Overload hypertrophy
    HTN or aortic stenosis
    Increased LV wall thickness
  Volume overload hypertrophy
    Characterized by ventricular dilation
    When compensatory mechanisms fail, heart failure results
Left Sided Heart Failure
  Caused by: ischemic heart disease, HTN, aortic and mitral valve disease
  *Heart failure cells – hemosiderin containing macrophages
  *leads to right heart failure
Right Sided Heart Failure
  *Cor Pulmonale secondary to disorders of lungs or pulmonary vasculature
  *nutmeg liver (passive congestion)

Congenital Heart Disease
Left to right shunts
  ASD, VSD, PDA, AVSD (*all have D)
Right to left shunts (early cyanosis)
  Tetralogy of Fallot (VSD, subpulmonary stenosis, overriding aorta, RVH)
    *Cause is anterosuperior displacement of infundibular septum
  Transposition of the Great Arteries
  Truncus Arteriousus
  Trucuspid Atresia
  Total Anomalous Venous Connection
Obstructive congenital anomalies
  Coarctation of aorta (*notching of undersurfaces of ribs on CXR)
  Pulmonary stenosis and atresia
  Aortic Stenosis and atresia

Ischemic heart disease
Role of:
  acute plaque change
  inflammation
  Coronary Thrombus
  Vasoconstriction
Angina Pectoris
  Stable/Prinzmetal/Unstable
Myocardial Infarction
  Transmural vs. subendocardial infarction
Pathogenesis
  Coronary arterial occlusion
  Myocardial Response
    Microscopic features
      24 hours – coagulative necrosis
      2-4 days – neutrophils
      5-10 days – macrophages and neutrophils
      7 weeks – contracted scar
  *rupture most common ~7 days
Infarct Modification by Reperfusion
Clinical features, *importance of laboratory markers
Consequences and Complication of MI
Contractile dysfunction, arrhythmias, myocardial rupture,
pericarditis, RV infarction, infarct extension, mural thrombus,
ventricular aneurysm, papillary muscle dysfunction, late heart failure

Valvular Heart Disease
Stenosis vs. insufficiency
Valvular degeneration caused by calcification
Calcific aortic stenosis
Congenital bicuspid aortic valve
Mitral annular calcification
Mitral valve prolapse
Intercordal ballooning
Complications include infective endocarditis, mitral insufficiency, stroke, arrhythmias
Rheumatic Fever and Rheumatic Heart Disease
*follows Group A Strep Pharyngitis, *Aschoff bodies
Pancarditis and fibrinous pericarditis
Infected Endocarditis
*frangible vegetations
Noninfective endocarditis
NBTE, Libman-Sacks disease

Cardiomyopathies
Dilated Cardiomyopathy; *assoc with myocarditis, alcoholism, and pregnancy
Hypertrophic Cardiomyopathy
*microscopic disarray, extreme hypertrophy, and characteristic branching of myocytes and
interstitial fibrosis
Restrictive cardiomyopathy
Idiopathic or associated with amyloidosis, radiation fibrosis, sarcoidosis, metastatic tumor
grossly: ventricles normal or slightly enlarged, cavities not dilated, myocardium is firm
microscopically: patchy or diffuse interstitial fibrosis
Myocarditis
*most common cause: Coxackieviruses A and B
Chagas disease

Pericardial disease
Effusion and hemopericardium - *cadiac tamponade is worst complication
Pericarditis
Acute
Serous pericarditis (noninfectious inflammations - lupus)
Fibrinous and Serofibrinous pericarditis (seen with MI)
Purulent or Suppurative Pericarditis (infectious)
Hemorrhagic pericarditis (malignancy or bacterial infection)
Caseous Pericarditis (TB until proven otherwise)
Chronic; Constrictive pericarditis
Rheumatoid heart disease

Tumors of the Heart
Primary
Myxoma (90% are in atria)
Lipoma, Papillary fibroelastoma, Rhabdomyoma, Sarcoma
Chapter 13: Red Blood Cell and Bleeding Disorders

Differentiation of Hematopoietic cells (fig 13-1)

Anemia

Blood loss

Hemolytic

Features

- Shortened RBC lifespan
- Increased erythropoietin levels
- Accumulation of products of hemoglobin catabolism

Intravascular (mechanical injury, complement fixation, infection)

* decreased serum haptoglobin

Extravascular (less deformable or RBC rendered foreign)

Hereditary Spherocytosis

* defect in spectrin makes cells less deformable and vulnerable to splenic destruction
* spherocytes: small, hyperchromic lacking central pallor
* treatment is splenectomy

G6PD deficiency

* abnormalities in the hexose monophosphate shunt or glutathione metabolism make RBC vulnerable to Oxidative injury
* antimalarials should be avoided

Heinz bodies (precipitated denatured Hb) and bite cells

Sickle Cell disease

Abnormal HbS polymerizes when deoxygenated
* autopsplenectomy and susceptible to encapsulated organism

Drepanocytes

Thalassemia Syndromes

Beta-thalassemias

* Extramedullary hematopoiesis and excessive iron absorption

see fig 13-14 and recognize “crew-cut” picture

Alpha-thalassemia

Hydrops fetalis

Paroxysmal Nocturnal Hemoglobinuria

Results from acquired mutations in phosphatidylinositol glycan A

Immunohemolytic anemia

* diagnosed with direct Coombs antiglobulin test

Warm Antibody Immunohemolytic anemia

Cold Agglutinin

Cold Hemolysin

Heomolytic anemia from RBC trauma

Microangiopathic hemolytic anemia

DIC, TTP, HUS

* helmet cells, burr cells

Anemias of Diminished Erythropoiesis

Megaloblastic anemia (impaired DNA synthesis)

Hypersegmented neutrophil

Pernicious anemia (vit B12 deficiency)

* Neurologic changes

Folate deficiency
Iron Deficiency anemia
*increased TIBC, decreased ferritin, decreased serum iron
hypochromic microcytic anemia
causes:
  dietary lack,
  impaired absorption
  increased requirements
  chronic blood loss
Anemia of chronic disease
*decreased TIBC, increased ferritin, decreased serum iron
inability to mobilize stored iron
Aplastic Anemia
  Marrow failure associated with pancytopenia
  Table 13-7 for causes
  Pure red cell aplasia

Polycythemia
  Polycythemia vera: neoplasms originating from myeloid stem cells

Bleeding disorders
*understand Bleeding time vs prothrombin time vs partial thromboplastin time
Bleeding disorders caused by vessel wall abnormalities
  Infections (Rickettsia and meningococcemia)
  Drug reactions
  Scurvy and Ehlers-Danlos syndrome
  HSP
  Hereditary hemorrhagic telangiectasia
  Amyloid infiltration of blood vessels
Bleeding related to thrombocytopenia
  Causes (see table 13-9)
    Decreased production of platelets
      Drug induced
      HIV
    Decreased platelet survival
      Immune Thrombocytopenic Purpura (ITP)
      Drug induced
      HIV
      TTP
      HUS
    Sequestration
    Dilutional
Defective platelet functions
Hemorrhagic diatheses
  Hemophilia A (Factor VIII Deficiency)
  Von Willebrand Disease
  Hemophilia B (Factor IX)
Disseminated Intravascular Coagulation
  2 major mechanisms
    release of tissue factor or thromboplastic substances into the
    circulation
    widespread injury to endothelial cells
    follows obstetric complications, malignant neoplasia, sepsis, and major trauma
Chapter 14: Diseases of WBC, Lymph Nodes, Splenic, and Thymus

Leukopenia

Neutropenia, Agranulocytosis
*drugs are responsible for the significant neutropenias (agranulocytoses)

Reactive (Inflammatory) Proliferations of WBC and Lymph Nodes

Leukocytosis
Acute Nonspecific lymphadenitis
Most often seen in cervical region due to microbial drainage
Chronic nonspecific lymphadenitis

Neoplastic Proliferations of White Cells

Etiological and Pathogenetic factors
Chromosomal translocations and oncogenes
Inherited genetic factors
Viruses
Environmental agents
Iatrogenic factors

Lymphoid neoplasms
ALL – 85% are pre B cell tumors often manifest in childhood
CLL – most common leukemia of adults in western world
*smudge cells
pts often asymptomatic
Follicular lymphoma
*hallmark is a 14;18 translocation
Diffuse Large B cell Lymphoma
*associated with Ebstein Barr Virus
Burkitt Lymphoma
*starry sky pattern
*tanslocation 8;14

Plasma cell neoplasms
Multiple myeloma
*sharply punched out lesions of skull
*Bence Jones proteinuria
Haldenstrom macroglobulinemia
Blood hyperviscosity due to high levels of IgM
Monoclonal Gammapathy of Uncertain Significance (MGUS)
Mantle Cell lymphoma
Marginal Zone Lymphomas. *Regression with treatment of H. pylori
Hairy Cell Leukemia

Peripheral T-cell and NK-Cell Neoplasms
Peripheral T-cell lymphoma, unspecified
Anaplastic Large Cell lymphoma
Adult T cell Leukemia/Lymphoma
Associated with HTLV-1
Mycosis fungoides/Sezary Syndrome
Marked predilection of the skin
Large Granular Lymphocytic Leukemia
Extranodal NK/Tcell lymphoma

Hodgkin Lymphoma
*Reed-Sternberg cells with background of nonneoplastic lymphocytes
Subtypes
- Nodular sclerosis (most common); Lacunar cells
- Mixed cellularity
- Lymphocyte rich
- Lymphocyte depletion
- Lymphocyte predominant
Understand staging in table 14-5

**Myeloid neoplasms**
Arise from hematopoietic cells of myeloid series (erythrocytes, granulocytes, monocytes, platelets)

**Acute Myelogenous Leukemia (AML)**
- Classification M0-M7
  - M2 AML with maturation t(8;21)
  - M3 acute promyelocytic leukemia t(15;17), *Treated with retinoic acid
  - *Auer rodes

**Myelodysplastic Syndromes**
- Ineffective hematopoiesis, cytopenia, and increased risk of transformation to AML

**Chronic Myeloproliferative Disorders**
- Increased production of terminally differentiated myeloid cells
- CML
  - *BCR-ABL t(9;22) Philidelphis chromosome
  - *Gleevec induces remission in >90% of pts
  - Polycythemia vera
    - Abnormal blood flow leads to major bleeding and thrombotic
    - Episodic, *intense pruritus
  - Essential thrombocytosis
    - Peripheral smear show abnormally large platelets
  - Primary myelofibrosis
    - Rapid development of obliterative marrow fibrosis

**Langerhans cell histiocytosis**
- Birbeck granules (tennis racket appearance)

**Spleen**
- Splenomegaly
- Hypersplenism
  - Anemia, leucopenia, thrombocytopenia, hyperplasia of marrow precursors
  - Correction of blood cytopenia by splenectomy
  - Nonspecific acute splenitis
  - Congestive splenomegaly
    - Caused by cirrhosis of the liver
  - Splenic infarcts
  - Neoplasms are rare except in tumors of the lymphohematopoietic system
  - Congenital anomalies
    - Complete absence, hypoplasia, accessory spleens
  - Rupture

**Thymus**
- Developmental disorders
  - Hypoplasia, Aplasia, cysts
- Thymic Hyperplasia
- Thymomas
  - Tumors of thymic epithelial cells; *associated with Myasthenia Gravis
Chapter 15: The Lung

Atelectasis
Resorption, Compression, Contraction

Acute Lung Injury
Pulmonary edema due to increased hydrostatic pressure or microvascular injury
Acute Respiratory Distress Syndrome (diffuse alveolar damage)
  Life threatening
  Diffuse damage to alveolar capillary walls
  *hyaline membranes (recognize microscopic appearance)
Acute Interstitial Pneumonia

Obstructive vs. Restrictive Lung Disease
  Obstructive
    Increased resistance to airflow
  Restrictive
    Reduced expansion of lung parenchyma with decreased TLC

Obstructive Pulmonary Diseases
  COPD: consists of emphysema and chronic bronchitis
  Emphysema
    Pathogenesis-protease/anti-protease imbalance and oxidant/anti-oxidant imbalance
    Types:
      Centroacinar
        *Associated with heavy smokers
        Respiratory Bronchioles affected, distal alveoli spared
      Panacinar
        *Associated with alpha1antitrypsin deficiency
        Acini are uniformly enlarged from resp. bronchiole to term. alveoli
      Paraseptal (distal)
      Irregular
      Bullous emphysema; *recognize gross appearance
  Chronic Bronchitis
    Defined clinically: *persistent productive cough for at least 3 mos. for at least 2 consecutive yrs
    Pathogenesis
      chronic irritation by ex. Tobacco smoke, silica dust, grain
      *hypersecretion of mucus
    *microscopically
      *increase in goblet cells
      clustering of pigmented macrophages
      inflammatory infiltration
      fibrosis of bronchiolar wall

Asthma
  General
    Chronic inflammatory disorder of the airways
    Recurrent episodes of wheezing, breathlessness, cough
    Bronchoconstriction and airflow limitation
    Reversible (spontaneously or with treatment)
    Hypersensitivity/bronchospasm to a variety of stimuli
  Pathogenesis
    Genetic predisposition to type 1 hypersensitivity (“atopy”)
Types
   Atopic-most common type, begins in childhood
   Non-atopic-triggered by respiratory tract infections
   Drug-Induced-includes aspirin sensitive asthma
   Occupational-stimulated by fumes, dust, gases, and chemicals
Status Asthmaticus
Bronchiectasis
   General
   Permanent dilatation of bronchi and bronchioles resulting from chronic necrotizing infections
Pathogenesis/Association with: Infection and Obstruction
   CF
   Immunodeficiency states
   Kartagener’s Syndrome
   Tumor/foreign body obstruction
   RA, SLE
Clinical Course
   Causes severe, persistent cough, *foul-smelling, bloody sputum and dyspnea

Diffuse Interstitial (Infiltrative/Restrictive) Diseases
Fibrosing Diseases
   Idiopathic Pumonary Fibrosis
   Caused by repeated cycles of acute lung injury
Non-specific Interstitial Pneumonia
Cryptogenic Organzing Pneumonia
Pumonary Involvement in Collagen Vascular Diseases (RA, SLE)
Pneumoconioses
   *Most dangerous particles are 1-5 microns
   Coal
   Silica
   Asbestos; *Mesothelioma
Granulomatous Diseases
Sarcoidosis
   *bilateral hilar lymphadenopathy on CXR
   non-caseating granulomas
   subcutaneous skin nodules
Hypersensitivity Pneumonitis
   Immunologically-mediated response to an extrinsic antigen
   Involves immune-complex and delayed type hypersens. Rxns.

Diseases of Vascular Origin
PE, Hemorrhage, and infarction
   PE
   Often from deep femoral vein
   Risk factors
   Immobility, (recent surgery)
   Hypercoagulable, (OCPs, cancer, pregnancy)
Pulmonary HTN
   Causes:
   Chronic Obstructive or Interstitial lung dz
   Congenital or Acquired Heart dz
   Recurrent thromboemboli
   Autoimmune disorders
Diffuse pulmonary hemorrhage syndromes
  Goodpasture
    Rapidly progressive glomerulonephritis and a necrotizing hemorrhagic interstitial pneumonitis
    Anti-basement membrane antibodies
  Wegener Granulomatosis
    Capillaritis and scattered, poorly formed granulomas

Pulmonary infections
  Pneumonia (common causative organisms for each see Table 15-8)
    Community Acquired Pneumonia
      Lobar vs. bronchopneumonia
      Complications: Abscess formation, empyema, organization, dissemination
    Community Acquired Atypical (viral and mycoplasmal) pneumonias, SARS
    Nosocomial pneumonia - Must be in hospital minimum 48 hours
    Aspiration pneumonia
    Lung Abscess
    Chronic pneumonia
    Granulomatous disease of lung
      TB
      Histoplasmosis (Ohio and Mississippi river regions)
        *3-5 micron thin walled yeast
      Blastomycosis (Central and Southeastern US)
        *Broad based budding yeast 5-15 microns
      Coccidiodomycosis (Southwest and Far West US and Mexico)
        *nonbudding spherules 20-60 microns in diameter
    Pneumonia in the immunocompromised host: *P. carinii

Tumors
  Carcinomas
    Classification
      Squamous cell carcinoma (25-40%)
        Closely associated with smoking history
        Keratinization (squamous pearls)
        Intercellular bridges
        Located centrally
      Adenocarcinoma (25-40%)
        *Most common type in women and nonsmokers
        lesions are more peripheral, ex. Bronchioloalveolar CA
        grows along alveolar septa
      Small cell carcinoma (20-25%)
        Highly malignant
        Salt and pepper chromatin
        Major bronchi and periphery of the lung
        *incurable by surgical means
      Large cell carcinoma (10-15%)
        Know associations with paraneoplastic syndromes
    Neuroendocrine proliferations and tumors - Carcinoid tumors

Pleura
  Pleural Effusion - Inflammatory vs. Noninflammatory pleural effusions
  Pneumothorax
  Pleural Tumors - Malignant Mesothelioma
Chapter 16: Head and Neck

Tumors

Squamous cell carcinomas
   95% of cancers of the head and neck
   associated with cigarette, alcohol, and HPV
Nasopharyngeal carcinomas
   Associated with EBV infection
   *Common in southern China with adults
Carcinoma of the larynx
   Presents with hoarseness
Squamous papilloma and papillomatosis
   HPV 6 and 11

Neck

   Branchial Cyst
   Thyroglossal tact cyst
   Paraganglioma

Salivary glands

   Tumors
      Pleomorphic adenoma
      Warthin tumor
      Mucoepidermoid carcinoma
Chapter 17: The Gastrointestinal Tract

Esophagus

Congenital Anomalies
*Atresia and fistulas
Webs, rings, and stenosis
Lesions associated with motor dysfunction
Achalasia; *"bird beak” appearance on barium swallow
Hiatal hernia
Zenker Diverticula
Lacerations
Mallory-Weiss syndrome-longitudinal tear
Boerhave’s Syndrome-esophageal rupture *alcoholics
Esophageal Varices
Can rupture and cause hemorrhage
Esophagitis
GERD
Barrett Esophagus
Complication of long-standing GERD
Squamous to columnar metaplasia with intestinal goblet cells
*most important risk factor for adenocarcinoma of esophagus
Infectious and chemical
Alcohol, alkalis, HSV, CMV, Candida
Tumors
Malignant
*remain asymptomatic until large
Squamous cell carcinoma
most common esophageal cancer worldwide
in US squamous and adeno have comparable rates
Adenocarcinoma
*majority arise from Barret esophagus

Stomach

Congenital anomalies
Pyloric stenosis
*projectile vomiting in 2-3 week of life
Gastritis
Acute gastritis
Acute mucosal inflammatory process, usually transient
Associated with NSAIDs, excessive alcohol, smoking
Pathogenesis
Increased acid secretion with back diffusion
Decreased production of bicarb buffer
Reduced blood flow
Disruption of mucus layer
Chronic gastritis
Associated with
Chronic infection with H. pylori
*urea breath test
Autoimmune/Pernicious anemia
Intestinal metaplasia
Peptic Ulcer Disease
*sharply punched-out appearance
Zollinger-Ellison syndrome
Excess gastrin secretion by a tumor
Also associated with H. pylori

Tumors
Gastric carcinoma (table 17-5)
Second most common cancer in the world
Chronic infection with H. pylori increases risk
Types
Intestinal type
Diffuse type *signet-ring cells
Krukenberg tumor (metastatic to ovary)

Small and Large Intestine
Congenital anomalies
Malrotation, omphalocele, gastroschisis
Atresia and Stenosis
Meckel Diverticulum
*rule of 2s
heterotypic rests of gastric or pancreatic tissue
Hirschsprung disease
Failure of migration of neural-crest cells to anus
*failure to pass meconium in neonatal period

Enterocolitis
Diarrhea and dysentery
Infectious enterocolitis
Viral (Rotavirus)
Bacterial
Enterotoxins
*Bloodly/inflammatory stools
Shigella, Salmonella, Campylobacter, C. difficile
E. coli
*Cholera causes rice water stools

Parasitic
Nematodes
Ascaris lumbricoides, Strongyloides, Hookworm,
Enterobius vermicularis (pinworms)
Cestodes
*Diphyllobothrium latum, Taenia solium
Amebiasis
E. histolytica *flask shaped ulcers
Giardiasis
Giardia lamblia *treat with Flagyl

Necrotizing
Malabsorption Syndromes
Celiac Disease
*gluten sensitivity and loss of villi seen on biopsy
Tropical Sprue
Folate and vit. B12 deficiency are present
Lactase Deficiency
Inherited or acquired
Idiopathic Inflammatory Bowel Disease
Crohn Disease (lips to anus)
  Sharply delimited and *transmural involvement of the bowel wall
  *Non-caseating granulomas
  Fissuring with fistula formation
  *skip lesions, cobblestoning
Ulcerative Colitis
  *Limited to the colon
  *Affects only mucosa and submucosal layers
  *Involves rectum and extends continuously in a retrograde fashion
  pseudopolyps
Vascular Disorders
  Ischemic Bowel Dz
  Hemorrhoids
    Internal vs. External
Diverticular Dz
  Two causative factors
    Focal weakness in colonic wall
    Increased intraluminal pressure
Intestinal Obstruction
  Hernias
    Danger of incarceration
  Adhesions
  Intussusception
  Volvulus
Tumors
  Small intestine
    Tumors of small intestine are only 3-6% of GI tumors
    Most adenomas in ampulla of vater region
Adenocarcinoma
  Increased risk assoc. with Crohns, FAP, HNPCC, Peutz-Jeghers
Colon and Rectum
  Non-neoplastic Polyps (hyperplastic and hamartomatous)
  Adenoma
    Precursor lesion to invasive colo-rectal adenocarcinoma
    *recognize sessile vs. pedunculated
Familial Syndromes
  FAP-mutation of APC gene
    Risk of progression to adenocarcinoma is 100%
    Tx is colectomy
  HNPCC-mutation of DNA repair genes
Colorectal Carcinogenesis
  APC, K-ras, p53 mutations occur in sequence
Carcinoid tumors
  *appendix

Appendix
  Acute appendicitis
    Inflammatory response goes through to the serosa
Chapter 18: Liver and Biliary Tract

Patterns of Hepatic Injury
Degeneration and Intracellular Accumulation
- Ballooning Degeneration: swelling of damaged hepatocytes
- Microvesicular steatosis and macrovesicular steatosis
Necrosis and Apoptosis
- Centrilobular necrosis (seen with ischemic injury and drug/toxic reactions)
- Midzonal and periportal necrosis
Inflammation
- Hepatitis: injury associated with acute or chronic inflammatory cells
Regeneration
- Hepatocytes proliferate in response to tissue resection or cell death
Fibrosis
- Generally irreversible hepatic damage leading to cirrhosis

Hepatic Failure
- 80 to 90% of hepatic functional capacity must be eroded
Categories
- Massive hepatic necrosis
- Chronic liver disease
- Hepatic dysfunction without overt necrosis
Features
- Jaundice, hypoalbuminemia, hyperammonemia, *Fetor hepaticus, palmar erythema, spider angiomas, hypogonadism, gynecomastia
- Hepatic encephalopathy - *asterixis
- Hepato-renal syndrome

Cirrhosis
Causes: *alcohol abuse, *viral hepatitis, biliary disease, hemochromatosis, Wilson disease, alpha1 antitrypsin deficiency
Characteristics
- Bridging fibrous septae
- Parenchymal nodules
- Disruption of the architecture

Portal Hypertension
Types
- Prehepatic
  - Obstructive thrombosis and narrowing of the portal vein
- Intrahepatic
  - Cirrhosis
- Posthepatic
  - Right sided heart failure, constrictive pericarditis, hepatic vein outflow obstruction
Ascites
- Portosystemic shunts
- Splenomegaly

Jaundice and Cholestasis
Understand bilirubin metabolism
Pathophysiology of Jaundice
- Conjugated vs. Unconjugated
*Be able to determine pre-, intra-, or post-hepatic injury given lab values

Neonatal
Hereditary hyperbilirubinemias
  *Crigler-Najjar syndrome, Gilbert syndrome, Dubin-Johnson syndrome

Cholestasis
  Obstructive and nonobstructive

**Infectious disorders**
Viral hepatitis (table 18-6)
*know transmission, Carrier state, Chronic hepatitis, hepatocellular CA
  Hepatitis A
  Hepatitis B
    *sequence of serologic markers
  Hepatitis C
    Persistent infection and chronic hepatitis are the hallmarks
  Hepatitis D, *requires presence of HBV
  Hepatitis E, *high mortality among pregnant women
Clinicopathologic syndromes
  Acute asymptomatic infection
  Acute symptomatic hepatitis
  Chronic hepatitis
  Fulminant hepatitis

**Autoimmune Hepatitis**
Absence of viral serologic markers
Presence of antismooth muscle antibodies
May present with other autoimmune diseases

**Drug and Toxin Induced Liver Disease**
Hepatic injury is predictable from overdoses of acetaminophen, CCl4, Amanita Phalloides
Alcoholic Liver Disease
  Hepatic steatosis; *fatty change is reversible with alcohol cessation
  Alcoholic hepatitis
    Hepatocyte swelling and necrosis
    Mallory bodies
    Neutrophillic reaction
    Fibrosis
  Cirrhosis (irreversible)
    Endstage resembles cirrhosis due to viral hepatitis

**Metabolic Liver Disease**
Nonalcoholic fatty liver disease (NAFL)
  Strong association with obesity and insulin resistance
Nonalcoholic steatohepatitis (NASH)
Hemochromatosis
  Micronodular cirrhosis, diabetes mellitus, skin pigmentation
    *HFE gene on Chromosome 6 (six syllable word)
Wilson Disease
  Accumulation of copper in liver, brain, and eye
    *Kayser-Fleischer rings
*treat with D-penicillamine

Alpha1 antitrypsin deficiency
Mutant polypeptide is abnormally folded and remains in ER

**Intrahepatic Biliary Tract Disease**

Secondary biliary cirrhosis
In adults caused by gallstones and malignancy
Children: biliary atresia, CF, choledochal cysts

Primary biliary cirrhosis
Non-suppurative, inflammatory destruction of medium sized intrahepatic ducts
*antimitochondrial antibodies
F>M

Primary sclerosing cholangitis
Associated with inflammatory bowel disease esp. UC
Increased risk for cholangiocarcinoma
M>F

**Hepatic Disease Associated with Pregnancy**

Preeclampsia and eclampsia
Acute fatty liver of pregnancy
Intrahepatic cholestasis

**Nodules and Tumors**

*most tumors in liver are metastatic, not primary
most common breast, lung, colon

Nodular hyperplasias
Focal nodular hyperplasia
Nodular regenerative hyperplasia

Benign neoplasms
Cavernous hemangiomas
Liver cell adenomas
*young women who use OCP, regress on discontinuance

Malignant tumors
Hepatocellular carcinoma
Associated with HBV and HCV
Cholangiocarcinoma
Hepatoblastoma
Angiosarcoma

**The Biliary Tract**

Disorders of the Gallbladder
Cholelithiasis; *80% are cholesterol stones, remainder are pigment stones
Cholecystitis
Acute cholecystitis; 90% caused by obstruction of the neck or cystic duct
Chronic cholecystitis

Disorders of the Extrahepatic Bile Ducts
Choledocholithiasis and ascending cholangitis
Biliary atresia
Choledochal cysts

Tumors
Carcinoma of the GallBladder
Carcinoma of the Extrahepatic bile ducts
Chapter 19 The Pancreas

Congenital Anomalies
- Agenesis
- Pancreas divisum
- *Annular pancreas
- Ectopic pancreas

Pancreatitis
- Acute
  - Reversible lesion ranging from edema and fat necrosis to parenchymal necrosis with severe hemorrhage
  - Causes: *biliary tract disease or alcoholism
  - Autodigestion
- Chronic
  - Irreversible destruction of exocrine parenchyma, fibrosis and destruction of endocrine parenchyma
  - Cause: long term alcohol abuse

Non-Neoplastic cysts
- Congenital cysts
- Pseudocysts (lack epithelial lining)

Neoplasms
- Cystic neoplasms
  - Serous cystadenomas
  - Mucinous cystic neoplasms
  - Intraductal papillary mucinous neoplasms
- Pancreatic carcinoma
  - *One of the highest mortality rates of any cancer
  - Smoking doubles risk
  - *Carcinomas of body and tail do not impinge on biliary tract and may be disseminated at time of discovery
  - *Migratory thrombophlebitis (Trousseau sign)
Chapter 20 The Kidney

Congenital Anomalies
- Agenesis of the kidney
- Hypoplasia
- Ectopic kidneys
  *Horseshoe kidneys- most common

Cystic Diseases of the Kidney
- Cystic renal dysplasia
- Autosomal Dominant (Adult) Polycystic Kidney Disease
  - Mutations of PKD1 account for 85% of cases
- Autosomal Recessive (Childhood) Polycystic Kidney Disease
  - Spongelike appearance
- Medullary Sponge Kidney
- Acquired (dialysis-associated) cystic disease
- Simple Cysts

Cystic Diseases of the Kidney
- Autosomal Dominant (Adult) Polycystic Kidney Disease
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Glomerular Diseases
- Nephritic Syndrome
  *Pts present with hematuria, red cell casts in the urine, azotemia, oliguria, HTN
  Acute Glomerulonephritis
  - Acute Proliferative (post-streptococcal, postinfectious)
    - Appears 1-4 weeks after strep throat or impetigo
    - Enlarged, hypercellular glomeruli
    - On IF microscopy, granular deposits of IgG, IgM and C3
    - On EM, electron dense “humps” on the epithelial side of the membrane
    - similar form of glomerulonephritis occurs in assoc. with other bacterial, viral, and parasitic infections
  - Rapidly Progressive (Crescentic) Glomerulonephritis
    *presence of crescents in the glomeruli
- Nephrotic Syndrome
  *Pts. Present with massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia
  Membranous Glomerulopathy-
    *most common cause of nephritic syndrome in adults
    Causes include: drugs, malignancy, SLE, infectious, other autoimmune d/o
    - Diffuse thickening of glomerular capillary wall
- Minimal Change Disease
  *most frequent cause of nephrotic syndrome in children
  *effacement of foot processes
- Focal Segmental Glomerulosclerosis
- Membranoproliferative Glomerulonephritis
- IgA Nephropathy (Berger Disease)
  *mesangial deposition of IgA
- Hereditary syndromes of isolated hematuria
  - Alport Syndrome
    - Thin Basement Membrane Disease (Benign familial hematuria)
- Chronic Glomerulonephritis
  - Thinned cortex and hyaline obliteration of glomeruli
- Glomerular lesions associated with systemic diseases
SLE
Henoch-Schonlein Purpura
Bacterial Endocarditis
Diabetic Glomerulosclerosis – papillary necrosis
Amyloidosis

**Diseases Affecting Tubules and Interstitium**
- Acute tubular necrosis
  - Pathogenesis (tubular injury and disturbances in blood flow)
- Tubulointerstitial nephritis
- Pyelonephritis and Urinary Tract Infection
- Acute Pyelonephritis
- Chronic pyelonephritis and Reflux nephropathy
- Tubulointerstitial nephritis induced by drugs and toxins

**Diseases of Blood Vessels**
- Benign nephrosclerosis
- Malignant hypertension and accelerated nephrosclerosis
  - Fibrinoid necrosis of arterioles and onion-skinning
- Renal Artery Stenosis
  - *surgical treatment is often successful
- Thrombotic microangiopathies (HUS and TTP)
- Sickle cell disease nephropathy
- Renal infarcts

**Urinary Tract Obstruction**
- Congenital anomalies
- Urinary calculi
  - Most are calcium containing
- BPH

**Tumors**
- Benign
- Malignant
  - Renal cell carcinoma
    - Clear cell, papillary, chromophobe
  - Urothelial carcinomas of the renal pelvis
Chapter 21: The Lower Urinary Tract and Male Genital System

Ureters

Congenital Anomalies
  Double ureters
  Ureteropelvic junction obstruction (*results in hydronephrosis)
  Diverticula
Tumors and tumor-like lesions
  Primary neoplasia is rare
  Benign tumors
    Fibroepithelial polyp
    Leiomyomas
  Malignant tumors
    Majority are transitional cell carcinomas

Obstructive Lesions
  Calculi
  Strictures
  Tumors
  Blood clots
  Neurogenic
  Pregnancy
  Endometriosis
  Sclerosing retroperitoneal fibrosis

Urinary bladder

Congenital anomalies
  Diverticula
  Exstrophy
  Vesicoureteral reflux
  Congenital fistulas
  Persistent urachus

Inflammations
  Acute and Chronic cystitis
    Common agents are *E.coli, Proteus, Klebsiella, Enterobacter
    Interstitial cystitis
      Inflammation and fibrosis of all layers of the bladder wall
  Malacoplakia
  Polypoid cystitis

Neoplasms
  Urothelial (transitional cell) carcinomas -*95% are this type
  Squamous cell carcinoma
  Adenocarcinoma (rare)
  Mesenchymal tumors
    Leiomyoma
    Sarcoma
  Secondary malignant involvement of bladder by direct extension

Urethra

Urethritis
  Gonococcal and Non-Gonococcal
  Component of *Reiter’s Syndrome
The Male Genital Tract

Penis
  Congenital Anomalies
    Hypospadias and Epispadias
    Phimosis
  Tumors
    Benign
      Condyloma acuminatum, type 6 and 11 HPV
    Malignant
      CIS
      Bowen dz
      Erythroplasia of Queyrat
      Invasive carcinoma, type 16 and 18 HPV

Testis and Epididymis
  Congenital Anomalies
  Cryptorchidism
  Inflammations
    Epididymitis and Orchitis
    Gonorrhea, Chlamydia, Mumps, TB, Syphilis
    Autoimmune (granulomatous) Orchitis
  Vascular Disturbances
    Torsion (twisting of spermatic cord)
  Testicular tumors
    *Germ cell tumors, know morphological differences and ages affected
      Seminomas, Embryonal Carcinoma, Yolk sac tumor, Choriocarcinoma, and Teratoma
    Sex-cord stromal tumors
      Leydig cell tumors and Sertoli cell tumors

Prostate
  Inflammations
    Acute and chronic bacterial prostatitis (E. coli), Chronic Abacterial Prostatitis, Granulomatous Prostatitis (BCG treatment)
  Benign Enlargement
    Nodular Hyperplasia (BPH)
  Tumors
    Adenocarcinoma
      Be able to distinguish microscopically from BPH
      *Gleason Grading system, TNM staging
      PSA
Chapter 22 The Female Genital Tract

Infections of the Female Genital tracts
Infections confined to the lower genital tract
HSV, Candida, Trichomonas vaginalis
Infections of lower and upper genital tract
PID *cervical motion tenderness, *Tubal ovarian abscess

Vulva
Bartholin cyst
Vulvar Vestibulitis
Non-neoplastic epithelial disorders
Lichen sclerosus
Neoplasms
Benign
Papillary hidradenoma
Condyloma acuminatum
Premalignant and malignant neoplasms
Carcinoma and vulvar intraepithelial neoplasia
Extramammary Paget disease
Malignant melanoma

Vagina
Premalignant and malignant neoplasms
Vaginal intraepithelial neoplasia and squamous cell carcinoma
Adenocarcinoma
*clear cell adenocarcinomas s/p DES treatment of mother
Embryonal Rhabdomyosarcoma

Cervix
Inflammations
Acute and chronic cervicitis
Endocervical polyps
Intraepithelial and invasive squamous neoplasia
Cervical intraepithelial neoplasia
*understand stages CIN I – III
*recognize koilocytosis
*recognize/interpret Pap Smears
Squamous cell carcinoma
Adenocarcinoma

Body of uterus and endometrium
Endometrial histology in the menstrual cycle; *recognize secretory vs. proliferative
Functional endometrial disorders (Dysfunctional Uterine Bleeding)
Anovulatory cycle
Inadequate luteal phase
Endometrial changes induced by oral contraceptives
Menopausal and postmenopausal changes
Inflammation
Chronic endometritis
*presence of plasma cells
Endometriosis and Adenomyosis
*chocolate cysts
Endometrial Polyps
  Associated with administration of Tamoxifen
Endometrial hyperplasia
  Simple non-atypical vs. complex atypical
Malignant Tumors of the endometrium
  Carcinoma of the endometrium
    Occurs in older women
    Risks: obesity, anovulatory cycles, DES, excess estrogen
Tumors of the myometrium
  Leiomyomas vs. Leiomyosarcoma

**Fallopian tubes**
Inflammations
  Suppurative salpingitis
    *Associated with PID, decreased fertility, risk of tubal pregnancy

**Ovaries**
Non-Neplastic and Functional Cysts
  Follicular and luteal cysts
  Polycystic ovaries
    *PCOD – anovulation, obesity, hirsutism
Ovarian tumors
  Risks: nulliparity, family history, BRCA1/2 mutations
  Major classifications (Table 22-3)
    Surface Epithelial-Stromal tumors
    Sex Cord stromal tumor
      Granulosa-theca cell tumors
      Fibroma-thecoma
      Sertoli-Leydig cell tumors
    Germ cell tumors
      Teratomas- mature are benign, immature are malignant

**Gestational and Placental disorders**
Disorders of Early pregnancy
  Spontaneous abortion
  Ectopic pregnancy
    *PID most impjt predisposing condition in 35-50% of pts
Disorders of late pregnancy
  Placental abnormalities and twin placentas
    Placenta acrreta, increta, percreta
  Twin placentas
    Dichorionic diamnionic, monochorionic diamnionic, and monochorionic monoamnionic
    Twin-twin transfusion
  Placental inflammations and infections
    *TORCH
    Toxemia of pregnancy (Preeclampsia and eclampsia)
    Intrauterine growth restriction
  Gestational trophoblastic disease
    Hydatidiform mole (complete and partial)
    Invasive mole
    Choriocarcinoma
    Malignant neoplasm of trophoblastic cells
Chapter 23 The Breast

Inflammations
- Acute mastitis
- Periductal mastitis
- Mammary duct ectasia
- Fat necrosis (*history of trauma)

Benign epithelial lesions
- Nonproliferative breast changes (fibrocystic changes)
  - Blue dome cysts, fibrosis, adenosis
  - *no increased risk of cancer
- Proliferative breast disease without atypia
  - Epithelial hyperplasia, sclerosing adenosis, complex sclerosing lesion,
    Papillomas; *mild increase in the risk of cancer
- Proliferative breast disease with atypia; *moderate increase in risk for cancer

Carcinoma of the breast

Risk factors
- Age, age at menarche, first live birth, first-degree relative, race

Etiology and pathogenesis
- Hereditary breast cancer (3% of all breast cancers)
  - *BRCA1 and BRCA2
- Sporadic breast cancer
  - Main risk factors are tied to hormone exposure

Classification of breast carcinoma
- Carcinoma in situ
  - Ductal carcinoma in situ (DCIS)
    - *presents as mammographic calcifications
    - Comedocarcinoma, noncomedo, *Paget disease
  - Lobular carcinoma in situ (LCIS)
- Invasive carcinoma
  - *presents as a palpable mass
- Invasive carcinoma, NST
- Invasive Lobular carcinoma
- Medullary carcinoma
- Mucinous carcinoma
- Tubular carcinoma
- Invasive papillary carcinoma

Major prognostic factors
- Invasive vs. in situ, distant metastases, axillary lymph node status, tumor size
- Inflammatory carcinoma
  - *Herceptin for HER2/neu expression, *Tamoxifen for estrogen receptor positive tumors

Stromal tumor
- Fibroadenoma
- Phyllodes tumor
- Sarcoma

The Male Breast
- Gynecomastia
  - Must be differentiated from carcinoma
    - Indicator of hyperestrinism (liver cirrhosis, functioning testicular tumor)
- Carcinoma (rare)
Chapter 24 The Endocrine System

Pituitary Gland

Pituitary adenomas and hyperpituitarism; *most arising from anterior lobe
  Prolactinomas (most frequent type)
    Women: amenorrhea and galactorrhea
  Growth hormone adenomas
    Gigantism prior to epiphyseal closure
    Acromegaly after closure of epiphyses
  Corticotroph cell adenomas
    ACTH over production (Cushing disease) and hyperpigmentation

Hypopituitarism
  Causes - tumors, surgery or radiation, apoplexy, *Sheehan syndrome, rathke cleft cyst, empty sella syndrome
Posterior pituitary syndromes
  Diabetes insipidus (know difference of central vs nephrogenic)
  SIADH

Hypothalamic suprasellar tumors (may produce hypo or hyper function)
  Gliomas
  Craniopharyngiomas (*remnants of Rathke’s pouch)

Thyroid gland

Hyperthyroidism
  Increased BMR, Tachycardia, Thyroid storm, Ocular changes (ophthalmopathy)
  *elevated T4 and decreased TSH

Hypothyroidism
  Causes
    Autoimmune most common
    Drugs (*Lithium)
      Elevated TSH, decreased T4
    Cretinism (childhood)
    Myxedema (older child or adult)

Thyroiditis
  Infectious thyroiditis
  Hashimoto thyroiditis
    Lymphocytes and Hurthle cells
    Anti-TSH receptor autoantibodies
  Subacute Thyroiditis (granulomatous, or DeQuervain )
    Usually follows viral infection
    Multinucleated gient cells
  Subacute lymphocytic thyroiditis
    Painless thyroiditis

Graves disease
  Triad of features
    Hyperthyroidis
    Infiltrative ophthalmopathy with exophthalmos
    Pretibial myxedema
  *Autoantibodies to TSH receptor
  *Recognize microscopic appearance (follicles lined by tall columnar epithelium

Diffuse and Multinodular goiter
  Enlargement of the thyroid or goiter is most common manifestation of thyroid dz
  Most often secondary to iodine deficiency
Diffuse nontoxic goiter- involves entire gland w/o producing nodularity
Multinodular goiter
  irregular enlargement of the gland, may be mistaken for neoplasm
  clinical features due to mass effects on midline structures

Neoplasms of the thyroid
Adenomas
  Discrete, solitary masses derived from follicular epithelium
  Usually not precancerous
  Called toxic adenomas if functional and producing thyrotoxicosis
  *solitary and encapsulated, cold nodules on scanning

Carcinomas
  Papillary carcinoma
    *Orphan Annie nuclei and psammoma bodies
  Follicular carcinoma
    Integrity of capsule used to distinguish b/t follicular adenomas and follicular carcinomas
  Medullary carcinoma
    Derived from parafollicular cells
    *acellular amyloid deposits are present
  Anaplastic carcinoma
    Mortality rate approaches 100%
    Compression and invasion sx are common

Congenital anomalies
  Thyroglossal duct or cyst

Parathyroid Glands
Hyperparathyroidism
  Primary hyperparathyroidism
    Causes hypercalcemia
    95% of cases caused by parathyroid adenoma
    Assoc. with MEN-1 and MEN-2
  Secondary hyperparathyroidism
    Most common cause is renal failure

Hypoparathyroidism
  Secondary to surgical removal during thyroidectomy
  Hypocalcemia and tetany (neuromuscular irritability)

Pseudohypoparathyroidism

The endocrine pancreas
Diabetes mellitus
  *Diagnosis
    random glucose >200 + sx
    fasting glucose >126 more than once
    OGTT >200 2 hrs after challenge

Classification
  Type 1 (lymphocytes on microscopy) vs. Type II (amyloid deposits)

Normal Insulin Physiology
  Regulation of Insulin Release
  Insulin action and insulin signaling pathways

Pathogenesis of type 1 diabetes mellitus (autoimmune)
  Mechanisms of Beta cell destruction
  Genetic susceptibility
  Environmental factors
Pathogenesis of type 2 DM
   Insulin resistance and link to obesity
   Beta cell dysfunction
Monogenic forms of diabetes- ex. MODY
Complications of diabetes
   Formation of Advanced Glycation End Products (HgA1C)
   Macrovascular dz
   Microangiopathy
   Diabetic Nephropathy (*Kimmelsteil-Wilson lesions)
   Retinopathy
   Neuropathy
Clinical features of DM
   Polyphagia, DKA (type 1 only), hyperglycemia, polyuria, polydipsia, diabetic coma
Pancreatic endocrine neoplasms
   Hyperinsulinism (insulinoma)
   Zollinger-ellison Syndroma (Gastrinomas)

Adrenal Glands
Hyperadrenalism
   Cushing syndrome
      Most cases result from exogenous glucocorticoid administration
      Figure 24-43
      *recognize clinical appearance of pts. with this dz.
   Primary hyperaldosteronism
      Sodium retention and potassium excretion
      *results in HTN and hypokalemia
      causes: adrenocortical neoplasm, adrenocortical hyperplasia
      features: suppression of the renin-angiotensin system
         decresed plasma rennin activity
   Secondary hyperaldosteronism
      Features:
         *Activation instead of suppression of renin-angiotensin sys.
         Increased levels of plasma renin
Adrenogenital syndromes
   Adrenal cortical neoplasms
      *Congenital adrenal hyperplasia (CAH)
         suspect in neonate with ambiguous genitalia
         21 hydroxylase deficiency
Adrenal insufficiency
   Primary acute adrenocortical insufficiency
      Causes: crisis, rapid withdrawal of steroids, failure to increase
         steroid dose in response to an acute stress, adrenal hemorrhage
Waterhouse-Friderichsen syndrome
   Associated with N. meningitides septicemia
   Hypotension leading to shock, DIC, purpura
Addison Disease
   Causes - Autoimmune adrenalitis, TB, AIDS, cancer
Secondary adrenocortical insufficiency
   Hyperpigmentation of primary addison’s disease is lacking b/c melanotropic hormone levels
   are low
Adrenocortical neoplasms
Adenomas vs. carcinomas
Adrenal medulla
Pheochromocytoma
  * surgically correctible form of HTN
  * rule of 10s
Neuroblastoma - Most common extracranial solid tumor of childhood
MEN
  Type 1 (Wermer syndrome) - 3 Ps
  Type 2A (Sipple syndrome)
  Type 2B
Pineal Gland - Pinealomas
Chapter 25 The Skin

Know macroscopic and microscopic terms

Disorders of Pigmentation and Melanocytes
  Vitiligo
  Freckle
  Melanocytic nevus
    Junctional
    Compound
    Dermal
  Dysplastic nevi
  Malignant Melanoma
    Radial vs. vertical growth

Benign Epithelial Tumors
  Seborrheic Keratoses
  Acanthosis Nigricans
    *cutaneous marker for associated benign and malignant conditions
  Fibroepithelial Polyp (skin tag)
  Epithelial cyst
  Adnexal (appendage) tumors
  Keratoacanthoma

Premalignant and Malignant Epidermal Tumors
  Actinic Keratosis
  Squamous Cell Carcinoma
  Basal Cell Carcinoma
    *most common
    pearly papules
    recognize microscopic appearance

Tumors of the Dermis
  Dermatofibroma
  Dermatofibrosarcoma protuberans
  Xanthomas

Tumors of Cellular Immigrants to the Skin
  Langerhans cell histiocytosis
  Mycosis Fungoides (cutaneous T-cell lymphoma)
    Pautrier microabscesses
  Mastocytosis
  Urticaria pigmentosa

Disorders of Epidermal Maturation
  Ichthyosis
    Fishlike scales

Acute Inflammatory Dermatoses
  Urticaria (hives)
  Acute Eczematous Dermatitis
  Erythema Multiforme
  Causes
    Infections such as herpes simplex
    Drugs (sulfonamides, PCN, hydantoins)
Malignancy
Collagen Vascular Dz (lupus, PAN)

**Chronic Inflammatory Dermatoses**

Psoriasis
*salmon colored plaque covered with silver scales, nail changes, affects elbows, knees, scalp commonly.

Seborrheic Dermatitis

Lichen Planus
*“pruritic, purple, polygonal papules”

Discoid Lupus

**Blistering (Bullous) Diseases**

Pemphigus
Autoimmune d/o results from loss of integrity of normal intercellular attachments within the epidermis and mucosal epithelium
*recognize pattern on direct immunoflurescence

Bullous Pemphigoid
*linear zone of immunoglobulin deposition caused by antibodies directed against proteins at the dermal-epidermal junction
blisters are tense

Dermatitis Herpetiformis
*granular deposits of IgA localized in the tips of the dermal papillae

**Disorders of Epidermal Appendages**

Acne

Panniculitis

Erythema Nodosum
Erythema Induratum

**Infection and Infestation**

Verrucae (warts)
Molluscum contagiosum
Impetigo
*honey colored crusted lesions

Superficial Fungal Infections
Tinea capitis, pedis, cruris, versicolor
Chapter 26: Bones, Joints, and Soft Tissue Tumors

Bone

Bone Diseases
- Osteogenesis Imperfecta
  - *blue sclerae
- Osteoporosis
  - Senile and post menopausal
- Paget Disease
- Rickets and Osteomalacia (Vit D deficiency)
- Hyperparathyroidism
  - *osteitis fibrosa cystica

Bone Infections
- Pyogenic osteomyelitis
  - *Staph. aureus responsible for 80-90%
- Tuberculous osteomyelitis
  - Pott disease in the spine

Bone Tumors (Know age groups affected and common presenting locations)
- Tumors of bone formation
  - Osteoma
  - Osteoid osteoma and osteoblastoma
  - Osteosarcoma
- Cartilage-forming tumors
  - Osteochondroma
  - Chondroma
  - Chondroblastoma
  - Chondrosarcoma
- Miscellaneous tumors
  - Ewing sarcoma and Primitive Neuroectodermal Tumor (PNET)
  - Small round cell tumors of bone and soft tissue
  - Giant cell tumor
  - Metastatic tumors are most common form of skeletal malignancy

Joints - Arthritis
- Osteoarthritis
  - Progressive erosion of articular cartilage
- Rheumatoid arthritis (RA)
  - Inflammatory synovitis ; *pannus
- Juvenile Rheumatorid Arthritis (JRA)
- Seronegative spondyloarthropathies
  - Ankylosing spondyloarthritis
  - Reactive arthritis
  - Psoriatic arthritis
- Infectious arthritis
  - Suppurative, TB, Lyme, Viral
- Gout and gouty arthritis
  - Urate crystals
- Pseudogout
Soft Tissue Tumors
  Fatty tumors, fibrous tumors
  Lipoma
  Liposarcoma
  Fibrosarcoma
  Tumors of skeletal muscle
    Rhabdomyosarcoma
      Most common soft tissue sarcoma of childhood and adolescence
      Embryonal
      Alveolar
      Pleomorphic
  Tumors of Smooth Muscle
    Leiomyoma
    Leiomyosarcoma
Chapter 27 Peripheral Nerve and Skeletal Muscles
Material covered in Rheumatology and Neurology of ICM II
Chapter 28: The Central Nervous System

Cellular Pathology of the Central Nervous System
Reactions of neurons to injury
  Acute neuronal injury (red neuron)
    Hypoxic/ischemic insult, eosinophilia of the cytoplasm
  Subacute and chronic neuronal injury (degeneration)
    ALS
    Axonal reaction (regeneration of the axons)
    Neuronal inclusions
      Lipofuscin, negri bodies with rabies, CMV
      Neuro-fibrillary tangles (AD) and Lewy bodies (PD)
Reactions of astrocytes to injury
  Gliosis (hypertrophy and hyperplasia)
  Cellular swelling
  Rosenthal fibers
    *cerebellar pilocytic astrocytoma
  Corpora amylacea
  Glial cytoplasmic inclusions

Cerebral edema
  Vasogenic edema
  Cytotoxic edema

Raised intracranial pressure and herniation
  Subfalcine (cingulate) herniation
  Transtentorial (uncinate, medial temporal) herniation
    *Duret hemorrhages
  Tonsillar herniation

Hydrocephalus

Malformations and Developmental Diseases
  Neural tube defects
    Anencephaly

Encephalocele

Spinal bifida
  Meningomyelocele vs. meningocele
  Forebrain anomalies
  Posterior fossa anomalies
    Arnold-Chiari malformation
    Dandy-Walker malformation
  Syringomyelia and Hydromyelia

Perinatal brain injury
  Cerebral palsy
  Intraparenchymal hemorrhage
    Premature infants

Trauma
  Parenchymal injuries
    Concussion, Contusion (Coup vs. contrecoup), Laceration
Traumatic vascular injury
   Epidural hematoma
      Associated with rupture of meningeal artery
      *pt may remain lucid for several hours
      *lens shaped
   Subdural hematoma
      Damage to bridging veins
      *crescent shaped
      *infants, elderly, alcoholics

Cerebrovascular Diseases
Hypoxia, Ischemia, and Infarction
   Global Cerebral Ischemia
   Hypotension, hypoperfusion, and low flow states
      *border zone (watershed) infarcts
   Focal Cerebral Ischemia
      Infarctions from Obstruction of local blood supply
      Hemorrhagic (red) vs. nonhemorrhagic (white)
Intracranial Hemorrhage
   Intracerebral hemorrhage
      *HTN most common underlying cause
   Subarachnoid hemorrhage and ruptured saccular aneurysms
      *berry aneurysm most common type
   Vascular malformations
      AV, cavernous hemangiomas, telangiectasias, venous angiomas
Hypertensive cerebrovascular disease
   Lacunar infarcts
   Slit hemorrhages
   Hypertensive encephalopathy

Infections
Acute Meningitis
   Acute Pyogenic (bacterial) meningitis
      *neonates – E. coli, GBBS
      *adolescents/adults – N. meningitidis
      *elderly – Strep. Pneumoniae, Listeria monocytogenes
      *CSF – increased WBC (PMNs), incr protein, decreased glucose
   Acute Aseptic (Viral) Meningitis
      *CSF – increased WBC (lymphocytes), moderate protein
elevation, normal glucose
   Acute focal suppurative infections
      Brain abscess
      Subdural empyema
Chronic bacterial meningoencephalitis
   TB, Neurosyphilis (*Tabes dorsalis), Lyme Disease
Viral meningoencephalitis
   Arthropod borne viral encephalitis
      Eastern and Western equine, St. Louis, West Nile
   HSV, Varicella-Zoster Virus, CMV, Poliomyelitis, Rabies, HIV, progressive multifocal
      Leukoencephalopathy (JC), *Subacute sclerosing Panencephalitis (rare sequelae of Measles)
   Fungal Meningoencephalitis
      Cryptococcus, Coccidioides, Histoplasma, Blastomyces
Cerebral toxoplasmosis most commonly AIDS pts

**Transmissible Spongiform Encephalopathies (Prion Diseases)**
- Creutzfeldt-Jakob disease

**Demyelinating Diseases**
- Multiple Sclerosis (MS)
  - Plaques
  - *CSF – oligoclonal bands*
  - Central pontine myelinolysis
  - *rapid correction of hyponatremia*

**Degenerative Diseases**
- Affecting the Cerebral cortex
  - Alzheimer Disease
    - Senile plaques, neurofibrillary tangles, and amyloid angiopathy
    - Most common cause of dementia in elderly
  - Pick Disease
  - Vascular Dementia
- Affecting Basal Ganglia and Brainstem
  - Parkinsonism
  - Parkinson Disease
    - Lewy bodies in Substantia Nigra
  - Multiple System Atrophy
  - Huntington Disease
    - *Autosomal dominant*
- Spinocerebellar degenerations
  - Spinocerebellar ataxias
    - Friedreich Ataxia, Ataxia-Telangiectasia
- Affecting motor neurons
  - Amyotrophic Lateral Sclerosis (ALS)

**Genetic Metabolic Diseases**
- Neuronal storage diseases, Leukodystrophies, Mitochondrial encephalomyopathy

**Toxic and Acquired Metabolic Disease**
- Vitamin Deficiencies
  - Thiamine
    - Beriberi
    - Wernicke encephalopathy
    - Korsakoff syndrome
    - *associated with chronic alcoholism*
  - Vitamin B12

**Tumors**
- Gliomas
  - Astrocytoma
  - Oligodendrogliomas
  - Ependymomas
    - Perivascular pseudorosettes
- Neuronal tumors
  - Ganglion cell tumors
  - Cerebral neuroblastomas
  - Poorly differentiated neoplasms
Medulloblastoma
   Homer Wright rosettes
Meningiomas; *psammoma bodies
Peripheral Nerve sheath tumors
   Schwannoma
      Antoni A and Antoni B patterns
      Associated with NF 2
Neurofibroma
Familial tumor syndromes
   Neurofibromatosis Type 1 (NF1)
      *Lisch nodules and café au lait spots
   Neurofibromatosis Type 2 (NF2)
   Tuberous Sclerosis
      *ash-leaf patches, and shagreen patches
Von Hippel-Lindau Disease
   *propensity to develop renal cell carcinoma

Chapter 29: The Eye
Not focused heavily in this class or on boards
Laboratory Evaluation

Hematology
  RBC indices
  CBC with differential
  Indices of iron deficiency anemia, anemia of chronic disease
  Indices of hemolytic anemia (intravascular, extravascular)
  Indices of B12, folic acid deficiency
  Coagulation, Hemostasis
    Bleeding time
    PT
    PTT

Renal
  Indices of acute and chronic renal failure

Acid Base
  Interpretation of blood gasses, CO2, pH, etc.

Cardiology
  Enzymes for diagnosis of myocardial infarction

Lung
  Blood gasses

Liver
  Indices of hepatitis
  Indices of biliary disease
  Interpretation of bilirubin, urobilinogen

Blood typing

Transplant reactions

GI
  H. pylori diagnosis
  Gastric acidity (Zollinger Ellison)

Endocrine
  Hormone levels

CSF evaluation

Tumor markers