THE ABSITE REVIEW

Steven M. Fiser

6th EDITION

Wolters Kluwer

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Sixth Edition

Steven M. Fiser, MD

Cardiac Surgery Specialists
Bon Secours Heart and Vascular Institute
Richmond, Virginia

Wolters Kluwer

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PREFACE TO THE FIRST EDITION

Each year, thousands of general surgery residents across the country express anxiety over preparation for the American Board of Surgery In-Training Examination (ABSITE), an exam designed to test residents on their knowledge of the many topics related to general surgery.

This exam is important to the future career of general surgery residents for several reasons. Academic centers and private practices searching for new general surgeons use ABSITE scores as part of the evaluation process. Fellowships in fields such as surgical oncology, trauma, and cardiothoracic surgery use these scores when evaluating potential fellows. Residents with high ABSITE results are looked upon favorably by general surgery program directors, as high scorers enhance program reputation, helping garner applications from the best medical students interested in surgery.

General surgery programs also use the ABSITE scores, with consideration of feedback on clinical performance, when evaluating residents for promotion through residency. Clearly, this examination is important to general surgery residents.

Much of the anxiety over the ABSITE stems from the issue that there are no dedicated outline-format review manuals available to assist in preparation. *The ABSITE Review* was developed to serve as a quick and thorough study guide for the ABSITE, such that it could be used independently of other material and would cover nearly all topics found on the exam. The outline format makes it easy to hit the essential points on each topic quickly and succinctly, without having to wade through the extraneous material found in most textbooks. As opposed to question-and-answer reviews, the format also promotes rapid memorization.

Although specifically designed for general surgery residents taking the ABSITE, the information contained in *The ABSITE Review* is also especially useful for certain other groups:

- General surgery residents preparing for their written American Board of Surgery certification examination
- Surgical residents going into another specialty who want a broad perspective of general surgery and surgical subspecialties (and who may also be required to take the ABSITE)
- Practicing surgeons preparing for their American Board of Surgery recertification examination

PREFACE TO THE SIXTH EDITION

The sixth edition of *The ABSITE Review* continues to target important material found in the ABSITE with new guidelines and information on infection, trauma care, breast cancer, humeral rejection, and a number of other topics. Like previous editions, *The ABSITE Review* provides a quick, easy review of important surgical topics while still providing sufficient explanation, so readers do not feel lost.

Again, I thank all of the residents who gave me feedback on the books or who I met at surgical meetings saying, "I used your books in residency and they were great." I am glad I could help out.

Thank you again and good luck on the ABSITE.

1 Cell Biology

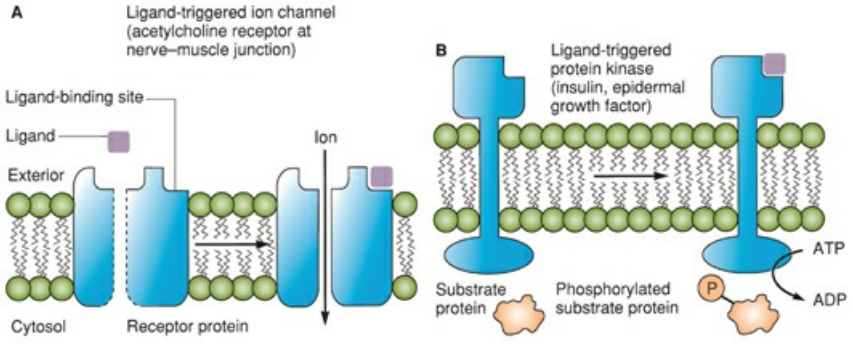
CELL MEMBRANE

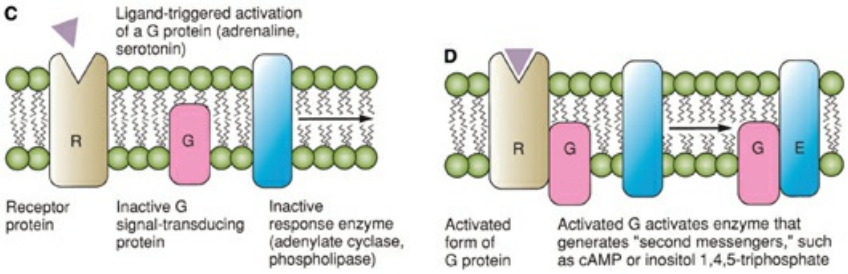
- A lipid bilayer that contains protein channels, enzymes, and receptors
- Cholesterol increases membrane fluidity
- Cells are negative inside compared to outside; based on Na/K ATPase (3 Na^+ out/2 K^+ in)
- The Na^+ gradient that is created is used for co-transport of glucose, proteins, and other molecules

Electrolyte Concentrations of Intracellular and Extracellular Fluid Compartments

	Extracellular Fluid (mEq/L)	Intracellular Fluid (mEq/L)
CATIONS		
Na^+	140	12
K^+	4	150
Ca^{2+}	5	10^{-7}
Mg^{2+}	2	7
ANIONS		
Cl^-	103	3
HCO_3^-	24	10
SO_4^{2-}	1	–
HPO_4^{3-}	2	116
Protein	16	40
Organic anions	5	–

- Desmosomes/hemidesmosomes – adhesion molecules (cell–cell and cell–extracellular matrix, respectively), which anchor cells
- Tight junctions – cell–cell occluding junctions; form an impermeable barrier (eg epithelium)
- Gap junctions – allow communication between cells (connexin subunits)
- G proteins (are GTPases) – intramembrane proteins; transduce signal from receptor to response enzyme
- Ligand-triggered protein kinase – receptor and response enzyme are a single transmembrane protein (eg receptor tyrosine kinase).





Types of cell surface receptors. *(A)* Ligand-activated ion channel; binding results in a conformational change, opening or activating the channel. *(B)* Ligand-activated protein kinase; binding activates the kinase domain, which phosphorylates substrate proteins. *(C and D)* Ligand activation of a G protein, which then activates an enzyme that generates second, or intracellular, messengers.

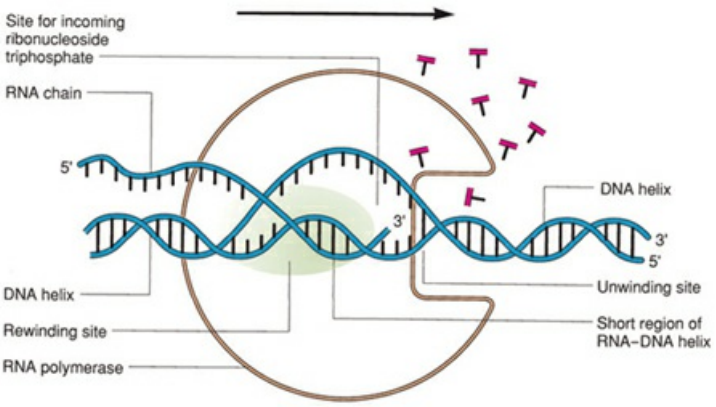
- ABO blood-type antigens – glycolipids on cell membrane
- HLA-type antigens – glycoproteins (Gp) on cell membrane
- Osmotic equilibrium – water will move from an area of low solute concentration to an area of high solute concentration and approach osmotic equilibrium

CELL CYCLE

- G1, S (protein synthesis, chromosomal duplication), G2, M (mitosis, nucleus divides)
- G1 most variable, determines cell cycle length
- Growth factors affect cell during G1
- Cells can also go to G0 (quiescent) from G1
- Mitosis
  - Prophase – centromere attachment, centriole and spindle formation, nucleus disappears
  - Metaphase – chromosome alignment
  - Anaphase – chromosomes pulled apart
  - Telophase – separate nucleus reforms around each set of chromosomes

NUCLEUS, TRANSCRIPTION, AND TRANSLATION

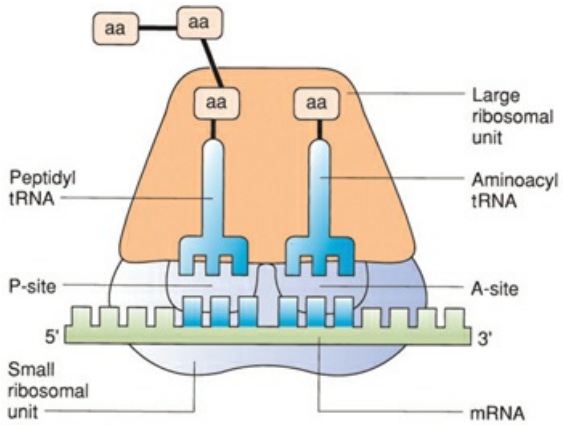
- Nucleus – double membrane, outer membrane continuous with rough endoplasmic reticulum
- Nucleolus – inside the nucleus, no membrane, ribosomes are made here
- Transcription – DNA strand is used as a template by RNA polymerase for synthesis of an mRNA strand



Transcription of DNA. RNA polymerase acts to unwind the DNA helix, catalyzes the formation of a transient RNA–DNA helix, and then releases the RNA as a single-strand copy while the DNA rewinds. In the process, the polymerase moves along the DNA from a start sequence to a stop sequence.

- Transcription factors – bind DNA and help the transcription of genes
  - Steroid hormone – binds receptor in cytoplasm, then enters nucleus and acts as transcription factor
  - Thyroid hormone – binds receptor in nucleus, then acts as a transcription factor
  - Other transcription factors – AP-1, NF-κB, STAT, NFAT
- Initiation factors – bind RNA polymerase and initiate transcription
- DNA polymerase chain reaction – uses oligonucleotides to amplify specific DNA sequences
- Purines – guanine, adenine
- Pyrimidines – cytosine, thymidine (only in DNA), uracil (only in RNA)
  - Guanine forms 3 hydrogen bonds with cytosine
  - Adenine forms 2 hydrogen bonds with either thymidine or uracil
- Translation – mRNA used as a template by ribosomes for the synthesis of protein

Ribosomes – have small and large subunits that read mRNA, then bind appropriate tRNAs that have amino acids, and eventually make proteins



Schematic view of the elongation phase of protein synthesis on a ribosome. As the ribosome moves along the mRNA, incoming aminoacyl–tRNA complexes bind to the A-site on the ribosome, after which a new peptide bond is formed with the nascent polypeptide chain previously attached to the peptide tRNA. The ribosome then moves, ejecting the now-empty tRNA and opening the A-site for the next aminoacyl–tRNA complex.

CELLULAR METABOLISM

- Glycolysis – 1 glucose molecule generates 2 ATP and 2 pyruvate molecules
- Mitochondria – 2 membranes, Krebs cycle on inner matrix, NADH/$FADH_2$ created
  - Krebs cycle (citric acid cycle) – the 2 pyruvate molecules (from the breakdown of 1 glucose) create NADH and $FADH_2$
  - NADH and $FADH_2$ enter the electron transport chain, leading to formation of a H^+ gradient and creation of ATP by ATP synthase
  - Overall, 1 molecule of glucose produces 36 ATP
  - Amino acids, ketones, and short-chain fatty acids can also enter the Krebs cycle to produce ATP
- Gluconeogenesis – mechanism by which lactic acid (Cori cycle) and amino acids (#1 alanine) are converted to glucose
  - Used in times of starvation or stress (basically the glycolysis pathway in reverse)
  - Fat and lipids are not available for gluconeogenesis because acetyl CoA (breakdown product of fat metabolism) cannot be converted back to pyruvate
- Cori cycle – mechanism in which the liver converts muscle lactate into new glucose; pyruvate plays a key role in this process

OTHER CELL ORGANELLES, ENZYMES, AND STRUCTURAL COMPONENTS

- White blood cells – contain nuclear material
- Red blood cells and platelets – do not contain nuclear material
- Rough endoplasmic reticulum – synthesizes proteins that are exported (increased in pancreatic acinar cells)
- Smooth endoplasmic reticulum – lipid/steroid synthesis, detoxifies drugs (increased in liver and adrenal cortex)
- Golgi apparatus – modifies proteins with carbohydrates; proteins are then transported to the cellular membrane, secreted, or targeted to lysosomes
- Lysosomes – have digestive enzymes that degrade engulfed particles and worn-out organelles
- Phagosomes – engulfed large particles; these fuse with lysosomes
- Endosomes – engulfed small particles; these fuse with lysosomes
- Major signaling pathways – phospholipase C, protein kinase A, and MAPK/ERK pathway
  - Utilize second messengers for signal transduction
- Phospholipase C – cleaves phospholipid phosphatidylinositol 4,5-bisphosphonate (PIP_2) into diacylglycerol (DAG) and inositol 1,4,5-triphosphate (IP_3)
  - IP_3 causes release of calcium from the smooth endoplasmic reticulum

Protein kinase C – activated by calcium and diacylglycerol (DAG); phosphorylates other enzymes and proteins

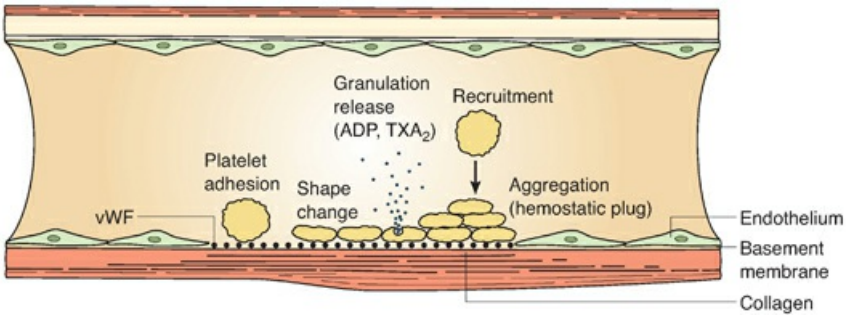
Protein kinase A – activated by cAMP; phosphorylates other enzymes and proteins

- MAPK/ERK – very complex pathway
- Myosin – thick filaments, uses ATP to slide along actin to cause muscle contraction
- Actin – thin filaments, interact with myosin above
- Intermediate filaments – keratin (hair/nails), desmin (muscle), vimentin (fibroblasts)

- Microtubules – form specialized cellular structures such as cilia, neuronal axons, and mitotic spindles; also involved in the transport of organelles in the cell (form a latticework inside the cell)
  - Centriole – a specialized microtubule involved in cell division (forms spindle fibers, which pull chromosome apart)

2 Hematology

INTRODUCTION



Primary hemostasis is achieved initially with a platelet aggregation as illustrated. Note that platelet adhesion, shape change, granule release followed by recruitment, and the hemostatic plug at the area of subendothelial collagen and collagen exposure are the initial events for thrombus formation.

NORMAL COAGULATION

Three initial responses to vascular injury: vascular vasoconstriction, platelet adhesion, and thrombin generation

Intrinsic pathway: exposed collagen + prekallikrein + HMW kininogen + factor XII

↓

activate XI

↓

activate IX, then add VIII

↓

activate X, then add V

↓

convert prothrombin (factor II) to thrombin

↓

thrombin then converts fibrinogen to fibrin

Extrinsic pathway: tissue factor (injured cells) + factor VII

↓

activate X, then add V

↓

convert prothrombin to thrombin

↓

thrombin then converts fibrinogen to fibrin

Prothrombin complex (for intrinsic and extrinsic pathways)

X, V, Ca, platelet factor 3, and prothrombin
Forms on platelets
Catalyzes the formation of thrombin

Factor X is the convergence point and is common for both paths
Tissue factor pathway inhibitor – inhibits factor X

Fibrin – links platelets together (binds GpIIb/IIIa molecules) to form platelet plug → hemostasis
XIII – helps crosslink fibrin

Thrombin
Key to coagulation
Converts fibrinogen to fibrin and fibrin split products
Activates factors V and VIII
Activates platelets

NORMAL ANTICOAGULATION

Antithrombin III (AT-III)
Key to anticoagulation
Binds and inhibits thrombin
Inhibits factors IX, X, and XI
Heparin activates AT-III (up to 1000× normal activity)
Protein C – vitamin K–dependent; degrades factors V and VIII; degrades fibrinogen
Protein S – vitamin K–dependent, protein C cofactor
Fibrinolysis
Tissue plasminogen activator – released from endothelium and converts plasminogen to plasmin
Plasmin – degrades factors V and VIII, fibrinogen, and fibrin → lose platelet plug
Alpha-2 antiplasmin – natural inhibitor of plasmin, released from endothelium

- Factor VII – shortest half-life
- Factors V and VIII – labile factors, activity lost in stored blood, activity not lost in FFP
- Factor VIII – only factor not synthesized in liver (synthesized in endothelium along with von Willebrand's Factor [vWF])
- Vitamin K–dependent factors – II, VII, IX, and X; proteins C and S
- Vitamin K – IV form takes 12 hours to have effect
- FFP – effect is immediate
- Factor II – prothrombin
- Normal half-life – RBCs: 120 days; platelets: 7 days; PMNs: 1–2 days
- Prostacyclin (PGI_2)
  - From endothelium
  - Decreases platelet aggregation and promotes vasodilation (antagonistic to TXA_2)
  - Increases cAMP in platelets

- Thromboxane (TXA_2)
  - From platelets
  - Increases platelet aggregation and promotes vasoconstriction
  - Triggers release of calcium in platelets → exposes GpIIb/IIIa receptor and causes platelet-to-platelet binding; platelet-to-collagen binding also occurs (GpIb receptor)

COAGULATION FACTORS

- Cryoprecipitate – contains highest concentration of vWF-VIII; used in von Willebrand's disease and hemophilia A (factor VIII deficiency), also has high levels of fibrinogen
- FFP (fresh frozen plasma) – has high levels of all coagulation factors, protein C, protein S, and AT-III
- DDAVP and conjugated estrogens – cause release of VIII and vWF from endothelium

COAGULATION MEASUREMENTS

- PT (prothrombin time) – measures II, V, VII, and X; fibrinogen; best for liver synthetic function
- PTT (partial thromboplastin time) – measures most factors *except VII and XIII (thus does not pick up factor VII deficiency)*; also measures fibrinogen
  - Want PTT 60–90 sec for routine anticoagulation
- ACT = activated clotting time
  - Want ACT 150–200 sec for routine anticoagulation, > 480 sec for cardiopulmonary bypass
- INR > 1.5 – relative contraindication to performing surgical procedures
- INR > 1.3 – relative contraindication to central line placement, percutaneous needle biopsies, and eye surgery

BLEEDING DISORDERS

- Incomplete hemostasis – most common cause of surgical bleeding
- von Willebrand's disease
  - *Most common congenital bleeding disorder*
  - MC Sx – epistaxis
  - Types I and II are autosomal dominant; type III is autosomal recessive
  - vWF links GpIb receptor on platelets to collagen
  - PT normal; PTT can be normal or abnormal
  - Have long bleeding time (ristocetin test)
  - Type I is most common (70% of cases) and often has only mild symptoms
  - Type III causes the most severe bleeding
  - Type I – reduced quantity of vWF
    - Tx: recombinant VIII:vWF, DDAVP, cryoprecipitate
  - Type II – defect in vWF molecule itself, vWF does not work well
    - Tx: recombinant VIII:vWF, cryoprecipitate, DDAVP
  - Type III – complete vWF deficiency (rare)
    - Tx: recombinant VIII:vWF; cryoprecipitate (highest concentration of vWF:VIII)
    - *DDAVP will not work for type III*
- Hemophilia A (VIII deficiency)

- Sex-linked recessive
- MC Sx – hemarthrosis
- Need levels 100% pre-op; keep at 80%–100% for 10–14 days after surgery
- Prolonged PTT and normal PT (follow PTT Q 8 hours after surgery)
- Factor VIII crosses placenta → newborns may not bleed at circumcision
- Hemophiliac joint bleeding – *do not aspirate*
  - Tx: ice, keep joint mobile with range of motion exercises, factor VIII concentrate or cryoprecipitate
- Hemophiliac epistaxis, intracerebral hemorrhage, or hematuria
  - Tx: recombinant factor VIII or cryoprecipitate

- Hemophilia B (IX deficiency) – Christmas disease
  - Sex-linked recessive
  - Need level 100% pre-op; keep at 30%–40% for 2–3 days after surgery
  - Prolonged PTT and normal PT
  - Tx: recombinant factor IX or FFP
- Factor VII deficiency – prolonged PT and normal PTT, bleeding tendency. Tx: recombinant factor VII concentrate or FFP
- Platelet disorders – cause bruising, epistaxis, petechiae, purpura
  - Acquired thrombocytopenia – can be caused by H_2 blockers, heparin
  - Glanzmann's thrombocytopenia – GpIIb/IIIa receptor deficiency on platelets (cannot bind to each other)
    - Fibrin normally links the GpIIb/IIIa receptors together
    - Tx: platelets
  - Bernard Soulier – GpIb receptor deficiency on platelets (cannot bind to collagen)
    - vWF normally links GpIb to collagen
    - Tx: platelets
  - Uremia (BUN > 60–80) – inhibits platelet function, mainly by inhibiting release of vWF
    - Tx: hemodialysis (1st line Tx), DDAVP (for acute reversal), cryoprecipitate (for moderate to severe bleeding)
- Heparin-induced thrombocytopenia (HIT)
  - Thrombocytopenia due to anti-heparin antibodies (IgG heparin-PF4 antibody) results in platelet destruction
  - Can also cause platelet aggregation and thrombosis (HITT; T = thrombosis)
  - Clinical signs: platelets < 100, a drop in platelets > 50% admission levels, or thrombosis while on heparin
  - Forms a white clot
  - Can occur with low doses of heparin
  - Dx: ELISA for heparin Ab's; serotonin release assay
  - Tx: *stop heparin*; start argatroban (direct thrombin inhibitor) to anticoagulate
  - *Avoid giving platelets (risk of thrombosis)*
- Disseminated intravascular coagulation (DIC)
  - Decreased platelets, low fibrinogen, high fibrin split products (high D-dimer)
  - Prolonged PT and prolonged PTT
  - Often initiated by tissue factor
  - Tx: need to treat the underlying cause (eg sepsis)
- ASA – stop 7 days before surgery; patients will have prolonged bleeding time

- Inhibits cyclooxygenase in platelets and decreases TXA_2
- Platelets lack DNA, so they cannot resynthesize cyclooxygenase

- Clopidogrel (Plavix) – stop 7 days before surgery; ADP receptor antagonist
  - Tx for bleeding: platelets
  - Coronary stent and need to stop Plavix for elective surgery – Tx: bridge with Integrilin (eptifibatide [GpIIb/IIIa inhibitor])
- Coumadin – stop 7 days before surgery, consider starting heparin while Coumadin wears off
  - Tx for bleeding: Vit K and FFP
- Platelets – want them > 50,000 before surgery, > 20,000 after surgery
- Prostate surgery – can release urokinase, activates plasminogen → thrombolysis
- Tx: **ε**-aminocaproic acid (Amicar; inhibits fibrinolysis)
- H and P – best way to predict bleeding risk
- Normal circumcision – does not rule out bleeding disorders; can still have clotting factors from mother
- Abnormal bleeding with tooth extraction or tonsillectomy – picks up 99% patients with bleeding disorder
- Epistaxis – common with vWF deficiency and platelet disorders
- Menorrhagia – common with bleeding disorders

HYPERCOAGULABILITY DISORDERS

- Present as venous or arterial thrombosis/emboli (eg DVT, PE, stroke)
- Factor V Leiden mutation – 30% of spontaneous venous thromboses
  - *Most common congenital hypercoagulability disorder*
  - Causes resistance to activated protein C; the defect is on factor V
  - Tx: heparin, warfarin
- Hyperhomocysteinemia – Tx: folic acid and B_{12}
- Prothrombin gene defect G20210 A – Tx: heparin, warfarin
- Protein C or S deficiency – Tx: heparin, warfarin
- Antithrombin III deficiency
  - *Heparin does not work in these patients*
  - Can develop after previous heparin exposure
  - Tx: recombinant AT-III concentrate or FFP (highest concentration of AT-III) followed by heparin, then warfarin
- Dysfibrinogenemia, dysplasminogenemia – Tx: heparin, warfarin
- Polycythemia vera – from bone marrow overproduction; can get thrombosis
  - Keep Hct < 48 and platelets < 400 before surgery
  - Tx: phlebotomy, ASA, hydroxyurea
- Anti-phospholipid antibody syndrome
  - Sx's: thrombosis; loss of pregnancy
  - Not all of these patients have SLE
  - Procoagulant (get prolonged PTT but are hypercoagulable)
  - Caused by antibodies to phospholipids including cardiolipin (mitochondria) and lupus anticoagulant (cell membrane)
  - Dx: prolonged PTT (not corrected with FFP), positive Russell viper venom time, false-positive RPR test for syphilis

- Tx: heparin, warfarin
- Acquired hypercoagulability – tobacco (most common factor causing acquired hypercoagulability), malignancy, inflammatory states, inflammatory bowel disease, infections, oral contraceptives, pregnancy, rheumatoid arthritis, post-op patients, myeloproliferative disorders
- Cardiopulmonary bypass – factor XII (Hageman factor) activated; results in consumptive coagulopathy
  - Tx: heparin to prevent
- Warfarin-induced skin necrosis
  - Occurs when placed on Coumadin without being heparinized first
  - Due to short half-life of proteins C and S, which are first to decrease in levels compared with the procoagulation factors; results in relative hyperthrombotic state
  - *Patients with relative protein C deficiency are especially susceptible*
  - Tx: heparin if it occurs; prevent by placing patient on heparin before starting warfarin
- Key elements in the development of venous thromboses (Virchow's triad) – stasis, endothelial injury, and hypercoagulability
- Key element in the development of arterial thrombosis – endothelial injury

DEEP VENOUS THROMBOSIS (DVT)

- Stasis, venous injury, and hypercoagulability (Virchow's triad) are risk factors
- The majority of adult surgery inpatients should receive DVT prophylaxis.
- Post-op DVT Tx:
  - 1st – warfarin for 6 months
  - 2nd – warfarin for 1 year
  - 3rd or significant PE – warfarin for lifetime
- IVC filters (some are removable) – indicated for patients with either:
  1. Contraindications to anticoagulation
  2. PE while on anticoagulation
  3. Free-floating IVC, ilio-femoral, or deep femoral DVT (controversial)
  4. Recent pulmonary embolectomy
     - Place IVC *below* the renal veins
     - PE with filter in place – likely arise from SVC (upper extremities), IVC above filter, or gonadal veins

PULMONARY EMBOLISM (PE)

- If clinical suspicion is high, do not wait on CT scan results, just give heparin bolus unless there is a contraindication
- If the patient is in shock despite massive inotropes and pressors, go to OR for open removal or angiography for suction catheter Tx; otherwise give heparin (thrombolytics have not shown an improvement in survival) or suction catheter–based intervention
- Most commonly from the ilio-femoral region

HEMATOLOGIC DRUGS

- Procoagulant agents (anti-fibrinolytics)
  - **ε**-Aminocaproic acid (Amicar)

    - Inhibits fibrinolysis by inhibiting plasmin
  - Used in DIC, persistent bleeding following cardiopulmonary bypass, *thrombolytic overdoses*
- Anticoagulation agents
  - Warfarin – prevents vitamin K–dependent decarboxylation of glutamic residues on vitamin K–dependent factors; need to follow INR level
  - Dabigatran (Pradaxa), apixaban (Eliquis), and rivaroxaban (Xarelto) – new oral anticoagulation agents that do not use INR levels; used for patients with atrial fibrillation not due to a heart valve problem and in patients with DVT or PE
    - Are direct thrombin inhibitors
    - Currently not reversible
  - Sequential compression devices – improve venous return but also induce fibrinolysis with compression (release of tPA [tissue plasminogen activator] from endothelium)
  - Heparin
    - Binds and activates anti-thrombin III (1000× more activity); increases neutralization of factors IIa (prothrombin) and Xa
    - Reversed with protamine (binds heparin)
    - Half-life of heparin is 60–90 minutes (want PTT 60–90 seconds)
    - Is cleared by the reticuloendothelial system (spleen; macrophages)
    - Long-term heparin – osteoporosis, alopecia
    - Heparin does not cross placental barrier (can be used in pregnancy) → warfarin does cross the placental barrier (not used in pregnancy)
    - Protamine – cross-reacts with NPH insulin or previous protamine exposure; 1% get protamine reaction (hypotension, bradycardia, and decreased heart function)
  - Low molecular weight heparin (eg enoxaparin) – lower risk of HIT compared to unfractionated heparin; binds and activates antithrombin III but increases neutralization of just factor Xa; *not* reversed with protamine
  - Argatroban – reversible direct thrombin inhibitor; metabolized in the liver, half-life is 50 minutes, often used in patients w/ HITT
  - Bivalirudin (Angiomax) – reversible direct thrombin inhibitor, metabolized by proteinase enzymes in the blood; half-life is 25 minutes
  - Hirudin (Hirulog; from leeches) – irreversible direct thrombin inhibitor; also the most potent direct inhibitor of thrombin; high risk for bleeding complications
  - Ancrod – Malayan pit viper venom; stimulates tPA release
- Thrombolytics – usually used for thrombosis; given with heparin
  - tPA (MC; tissue plasminogen activator), Streptokinase (has high antigenicity), and urokinase
  - All activate plasminogen
  - Need to follow fibrinogen levels – fibrinogen < 100 associated with increased risk and severity of bleeding
  - *Tx for thrombolytic overdose* – **ε**-*aminocaproic acid (Amicar)*

Contraindications to Thrombolytic Use (Urokinase, Streptokinase, tPA)

Degree	Contraindications
Absolute	Active internal bleeding; recent CVA or neurosurgery (<3 mo); intracranial pathology, recent GI bleeding

Major	Recent (<10 d) surgery, organ biopsy, or obstetric delivery; left heart thrombus; active peptic ulcer; recent major trauma; uncontrolled hypertension, recent eye surgery
Minor	Minor surgery; recent CPR; atrial fibrillation with mitral valve disease; bacterial endocarditis; hemostatic defects (ie renal or liver disease); diabetic hemorrhagic retinopathy; pregnancy

Modified. Data from NIH Consensus Development Conference. Thrombolytic therapy in treatment. *Ann Intern Med*. 1980;*93*:141.

3 Blood Products

INTRODUCTION

All blood products carry the risk of HIV and hepatitis except albumin and serum globulins (these are heat treated).
Donated blood is screened for HIV, HepB, HepC, HTLV, syphilis, and West Nile virus.
CMV-negative blood – use in low-birth-weight infants, bone marrow transplant patients, and other transplant patients
Type O blood – universal donor, contains no antigens
Type AB blood – contains both A and B antigens
Females of childbearing age should receive Rh-negative blood
Stored blood is low in 2,3-DPG → causes left shift (increased affinity for oxygen)
Type and crossmatch – determines ABO compatibility
Type and screen – determines ABO compatibility and looks for preformed Ab's to minor antigens
One unit of pRBCs should raise the Hgb by 1 (Hct 3–5)
One six-pack of platelets should raise platelet count by 50,000

HEMOLYSIS REACTIONS

- Acute hemolysis – from ABO incompatibility; antibody mediated (type II hypersensitivity)
  - Back pain, chills, tachycardia, fever, hemoglobinuria
  - Can lead to ATN, DIC, shock
  - Haptoglobin < 50 mg/dL (binds Hgb, then gets degraded), free hemoglobin > 5 g/dL, increase in unconjugated bilirubin
  - Tx: fluids, diuretics, HCO_3^-, pressors
  - In anesthetized patients, transfusion reactions may present as diffuse bleeding
- Delayed hemolysis (mild jaundice) – antibody-mediated against minor antigens from donor
  - Tx: observe if stable
- Nonimmune hemolysis – from squeezed blood
  - Tx: fluids and diuretics

OTHER REACTIONS

- Febrile nonhemolytic transfusion reaction – *most common transfusion reaction*
  - Usually recipient antibody reaction against donor WBCs (cytokine release)
  - Tx: discontinue transfusion if patient had previous transfusions or if it occurs soon after transfusion has begun
  - Use WBC filters for subsequent transfusions
- Urticaria (rash) – usually nonhemolytic
  - Usually recipient antibodies against donor plasma proteins (eg peanuts) or IgA in an IgA-deficient patient
  - Tx: histamine blockers (Benadryl), supportive

- Anaphylaxis – bronchospasm, hypotension, angioedema, urticaria
  - Usually recipient antibodies against donor IgA in an IgA-deficient recipient
  - Can be an airway emergency
  - Tx: epinephrine, fluids, pressors, steroids, histamine blockers (Benadryl)
- Transfusion-related acute lung injury (TRALI) – rare
  - Caused by donor antibodies to recipient's WBCs, clot in pulmonary capillaries
  - Leads to noncardiogenic pulmonary edema in < 6 hours (ARDS)
  - *MCC of death from transfusion reaction*

OTHER TRANSFUSION PROBLEMS

- Cold – poor clotting can be caused by cold products or cold body temperature (coagulopathy due to slowing of enzyme reactions); patient needs to be warm to clot correctly
- Dilutional thrombocytopenia and dilution of coagulation factors occurs with massive transfusion
- Hypocalcemia – can cause poor clotting; occurs with massive transfusion; Ca is required for the clotting cascade; hypocalcemia can also cause hypotension
- Citrate used in stored blood binds Ca after transfusion and causes hypocalcemia
- Most common bacterial contaminate – GNRs (usually *E. coli*)
- Most common blood product source of contamination – platelets (not refrigerated)
- Chagas' disease – can be transmitted with blood transfusion

4 Immunology

T CELLS (THYMUS) – CELL-MEDIATED IMMUNITY

- Helper T cells (CD4)
  - Release IL-2, which mainly causes maturation of cytotoxic T cells
  - Release IL-4, which mainly causes B-cell maturation into plasma cells
  - Release interferon-gamma which activates macrophages
  - Involved in delayed-type hypersensitivity (type IV; brings in inflammatory cells by chemokine secretion)
- Suppressor T cells (CD8) – regulate CD4 and CD8 cells
- Cytotoxic T cells (CD8) – recognize and attack non–self-antigens attached to MHC class I receptors (eg viral gene products); responsible for the majority of liver injury due to HepB
- Cell-mediated immunity does not require Ab's
- Effector cells in cell-mediated immunity – macrophages, cytotoxic T cells, natural killer cells
- Intradermal skin test (ie TB skin test) – used to test cell-mediated immunity; takes 2–3 days
- *Infections associated with defects in cell-mediated immunity – intracellular pathogens (TB, viruses)*

B CELLS (BONE) – ANTIBODY-MEDIATED IMMUNITY (HUMORAL)

- IL-4 from helper T cells stimulates B cells to become plasma cells (antibody secreting)
- 10% become memory B cells which can be reactivated
- IgG (as opposed to IgM) is secreted with reinfection

MHC CLASSES

- MHC class I (A, B, and C)
  - CD8 cell activation
  - Present on all nucleated cells
  - Single chain with 5 domains
  - *Target for cytotoxic T cells (bind T cell receptor)*
- MHC class II (DR, DP, and DQ)
  - CD4 cell activation
  - Present on antigen-presenting cells (APCs; eg dendrites [most important], monocytes)
  - 2 chains with 4 domains each
  - *APCs activate helper T cells (bind T cell receptor) when passing through lymph nodes.*
  - *Stimulates antibody formation after interaction with B cells*

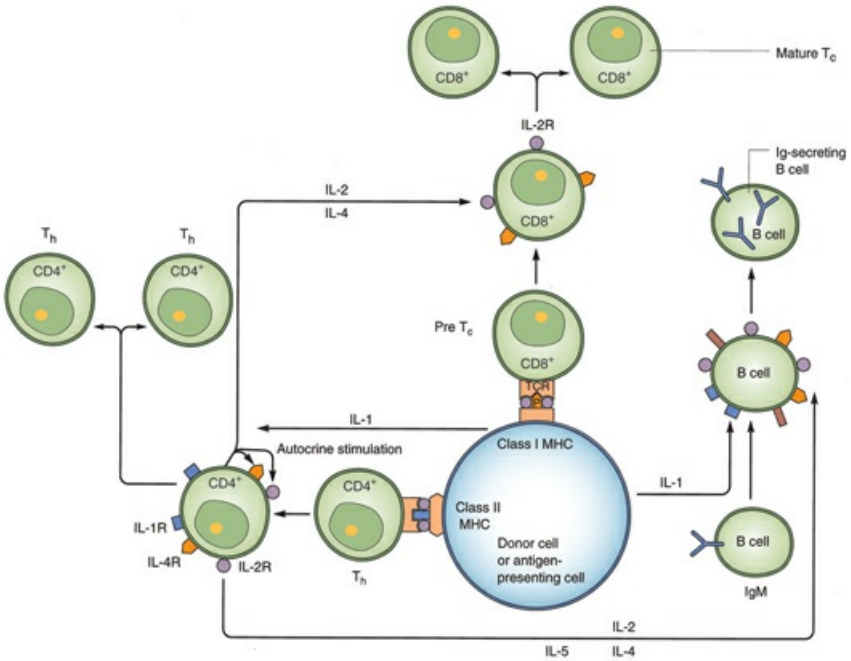
Viral infection – endogenous viral proteins produced, are bound to class I MHC, go to cell surface, and are recognized by CD8 cytotoxic T cells

Bacterial infection – endocytosis, proteins get bound to class II MHC molecules, go to cell surface, recognized by CD4 helper T cells → B cells which have already bound to the antigen

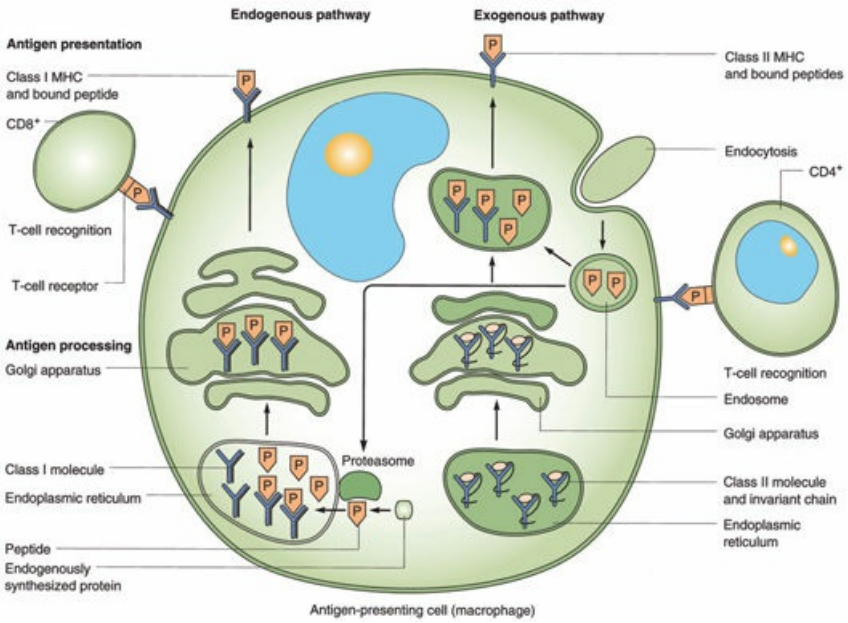
are then activated by the CD4 helper T cells; they then produce the antibody to that antigen and are transformed to plasma cells and memory B cells

NATURAL KILLER CELLS

- Not restricted by MHC, do not require previous exposure, do not require antigen presentation
- Not considered T or B cells
- *Recognize cells that lack self-MHC*
- Part of the body's natural immunosurveillance for cancer
- Also attack cells with bound Ab (have Fc receptor)



T-cell and B-cell activation. Two signals are required. First, alloantigen binds to antigen-specific receptors—the TCR (T cells) or surface IgM (B cells). The second, or costimulatory, signal is provided by IL-1 released by the antigen-presenting cell. CD4 helper T cells (T_h) release IL-2 and IL-4, which provide help for CD8 T cells (T_c) and for B-cell activation.



Antigen processing and presentation. Endogenously synthesized or intracellular proteins are degraded into peptides that are transported to the ER. These peptides bind to class I MHC molecules and are transported to the surface of the antigen-presenting cell. $CD8^+$ cells recognize the foreign peptide bound to class I MHC by way of the TCR complex. Exogenous antigen is endocytosed and broken down into peptide fragments in endosomes. Class II MHC molecules are transported to the endosome, bind the peptide, and are delivered to the surface of the antigen-presenting cell, where they are recognized by $CD4^+$ cells.

ANTIBODIES

- IgM – initial antibody secreted after exposure to antigen (primary immune response). It is the largest antibody, having 5 domains (10 binding sites); MC Ab in the spleen
- IgG – most abundant antibody in body. Responsible for secondary immune response. Can cross the placenta and provides protection in newborn period. MC Ab overall
- IgA – found in secretions, in Peyer's patches in gut, and in breast milk (additional source of immunity in newborn); helps prevent microbial adherence and invasion in gut
- IgD – membrane-bound receptor on B cells (serves as an antigen receptor)
- IgE – allergic reactions, parasite infections (type I hypersensitivity reactions, see below)
- IgM and IgG are opsonins
- IgM and IgG fix complement (requires 2 IgGs or 1 IgM)
- All Ab's have 2 antigen-binding sites except IgM (which has 10 antigen-binding sites)
- Variable region – antigen recognition
- Constant region – recognized by PMNs, macrophages, and natural killer cells
  - Fc fragment does not carry variable region
- Polyclonal antibodies have multiple binding sites to the antigen at multiple epitopes
- Monoclonal antibodies have only 1 binding site to the antigen at 1 epitope
- Basophils – major source of histamine in blood
- Mast cells – major source of histamine in tissue; main cell type for type I hypersensitivity
- Primary lymphoid organs – liver, bone, thymus
- Secondary lymphoid organs – spleen and lymph nodes
- Immunologic chimera – 2 different cell lines in one individual (eg bone marrow transplant

patients)

Hypersensitivity Reactions		
Type	Description	Examples
I	Immediate hypersensitivity reaction (allergic reaction; anaphylaxis) – IgE receptors on mast cells and basophils react with the antigen and cause release of histamine, serotonin, and bradykinin	Bee stings, peanuts, hay fever, Lymphazurin blue dye; Sx's – urticaria, hypotension, bronchoconstriction, angioedema; Tx: epinephrine, airway management
II	IgG or IgM reacts with cell-bound antigen	ABO blood incompatibility, hyperacute rejection, myasthenia gravis
III	Immune complex deposition	Serum sickness, SLE
IV	Delayed-type hypersensitivity – APCs present antigen to helper T cells, which then activate macrophages to destroy the antigen; only hypersensitivity reaction not to involve Ab's (cell-mediated immunity)	TB skin test (PPD), contact dermatitis Generally takes 2–3 days

IL-2

- Converts lymphocytes to lymphokine-activated killer (LAK) cells by enhancing their immune response to tumor
- Also converts lymphocytes into tumor-infiltrating lymphocytes (TILs)
- Has shown some success for melanoma

TETANUS

- Non–tetanus-prone wounds – give tetanus toxoid only if patient has received < 3 doses or tetanus status is unknown, or > 10 years since booster
- Tetanus-prone wounds (> 6 hours old; obvious contamination and devitalized tissue; crush, burn, frostbite, or missile injuries) – always give tetanus toxoid unless patient has had ≥ 3 doses and it has been < 5 years since last booster
- Tetanus immune globulin (given intramuscular near wound site) – give only with tetanus-prone wounds in patients who have not been immunized or if immunization status is unknown

5 Infection

INTRODUCTION

Malnutrition – most common immune deficiency; leads to infection

MICROFLORA

- Stomach – virtually sterile; some GPCs, some yeast
- Proximal small bowel – 10^5 bacteria, mostly GPCs
- Distal small bowel – 10^7 bacteria, GPCs, GPRs, GNRs
- Colon – 10^{11} bacteria, almost all anaerobes, some GNRs, GPCs
- Anaerobes (anaerobic bacteria)
  - Most common organisms in the GI tract
  - More common than aerobic bacteria in the colon (1,000:1)
  - Need low-oxygen environment (lack superoxide dismutase and catalase, making them vulnerable to oxygen radicals)
  - *Bacteroides fragilis* – most common anaerobe in the colon
- *Escherichia coli* – most common aerobic bacteria in the colon

FEVER

- MC fever source within 48 hours — Atelectasis
- MC fever source 48 hours – 5 days — Urinary tract infection
- MC fever source after 5 days — Wound infection
- Fever sources (sequentially over time) – atelectasis, urinary tract infection, pneumonia, DVT, wound infection, intra-abdominal abscess

GRAM-NEGATIVE SEPSIS

- *E. coli* most common
- Endotoxin (lipopolysaccharide lipid A) is released
- Endotoxin triggers the release of TNF-**α** (most potent stimulus; released from macrophages, triggers inflammation), activates complement, and activates coagulation cascade
- Early gram-negative sepsis – ↓ insulin, ↑ glucose (impaired utilization)
- Late gram-negative sepsis – ↑ insulin, ↑ glucose secondary to insulin resistance
- Hyperglycemia – often occurs just before the patient becomes clinically septic
- Optimal glucose level in a septic patient: 80–120 mg/dL

CLOSTRIDIUM DIFFICILE COLITIS (PSEUDOMEMBRANOUS COLITIS)

- Sx's: foul-smelling diarrhea; nursing home or ICU patients
- Dx: ELISA for toxin A; elevated WBCs (often in 30–40's)
- Tx: oral – vancomycin or Flagyl; IV – Flagyl; lactobacillus can also help

- Pregnancy – oral vancomycin (no systemic absorption)
- Fluid resuscitation; stop other antibiotics or change them
- Fulminant (eg severe sepsis, perforation) pseudomembranous colitis – Tx: total colectomy with ileostomy

ABSCESSES

- 90% of abdominal abscesses have anaerobes
- 80% of abdominal abscesses have both anaerobic and aerobic bacteria
- Abscesses are treated by drainage (usually percutaneous)
- Usually occur 7–10 days after operation
- Antibiotics for an abscess are needed in patients with diabetes, cellulitis, clinical signs of sepsis, fever, or who have bioprosthetic hardware (eg mechanical valves, hip replacements)

WOUND INFECTION (SURGICAL SITE INFECTION)

- Clean (hernia): 2%
- Clean contaminated (elective colon resection with prepped bowel): 3%–5%
- Contaminated (gunshot wound to colon with repair): 5%–10%
- Gross contamination (abscess): 30%
- Prophylactic antibiotics are given to prevent surgical site infections
  - Give antibiotics within 1 hour of incision
  - Stop within 24 hours of end operation time, except cardiac, which is stopped within 48 hours of end operation time
- *Staphylococcus aureus* – coagulase-positive
  - Most common organism overall in surgical site infections
- *Staphylococcus epidermidis* – coagulase-negative
- Exoslime released by staph species is an exopolysaccharide matrix
- *E. coli* – most common GNR in surgical wound infections
- *B. fragilis* – most common anaerobe in surgical wound infections
  - Recovery from tissue indicates necrosis or abscess (only grows in low redox state)
  - Also implies translocation from the gut
- $\geq 10^5$ bacteria needed for wound infection; less bacteria is needed if foreign body present
- Risk factors for wound infection: long operations, hematoma or seroma formation, advanced age, chronic disease (eg COPD, renal failure, liver failure, diabetes mellitus), malnutrition, immunosuppressive drugs
- Tx wound infection (erythema, warmth, tenderness) – antibiotics, may need to open wound if wound abscess is present (get U/S if not sure)
- Surgical infections within 48 hours of procedure
  - Injury to bowel with leak
  - Invasive soft tissue infection – *Clostridium perfringens* and beta-hemolytic strep can present within hours postoperatively (produce exotoxins)
- Most common infection in surgery patients – urinary tract infection
  - Biggest risk factor – urinary catheters; most commonly *E. coli (GNRs)*
  - Tx: remove urinary catheter, abx's
- Leading cause of infectious death after surgery – nosocomial pneumonia
  - Related to the length of ventilation; aspiration from duodenum thought to have a role

- Most common organisms in ICU pneumonia – #1 *S. aureus*, #2 *Pseudomonas*, #3 *E. Coli*
- GNRs #1 class of organisms in ICU pneumonia

LINE INFECTIONS

- #1 *S. epidermidis*, #2 *S. aureus*, #3 yeast
- Femoral lines at higher risk for infection compared to subclavian and intrajugular lines; subclavian lines have the lowest risk
- 50% line salvage rate with antibiotics (important for patients requiring long-term central access; 2 weeks of antibiotics); much less likely with yeast line infections
- Suspected line infection (temporary line) → move to new site or pull out the central line and place peripheral IVs if central line not needed

NECROTIZING SOFT TISSUE INFECTIONS

- Beta-hemolytic *Streptococcus* (group A), *C. perfringens*, or mixed organisms
- Usually occur in patients who are immunocompromised (eg diabetes mellitus, AIDS) or who have poor blood supply
- Can present very quickly after injury or surgical procedures (within hours)
- Pain out of proportion to skin findings (infection starts deep to the skin), mental status changes, WBCs > 20, thin gray drainage that is foul-smelling, can have skin blistering/necrosis, induration and edema, crepitus or soft tissue gas on x-ray, can be septic
- Necrotizing fasciitis – usually beta-hemolytic group A strep or MRSA
  - Overlying skin can look normal in the early stages (spreads along fascial planes)
  - Overlying skin progresses from pale red to purple with blister or bullae development
  - Thin, gray, foul-smelling drainage; crepitus
  - GPCs without PMNs
  - Beta-hemolytic group A strep and MRSA have exotoxin
  - Tx: early debridement, high-dose penicillin; may want broad spectrum if thought to be poly-organismal
- *C. perfringens* infections
  - Necrotic tissue decreases oxidation-redux potential, setting up environment for *C. perfringens*
  - *C. perfringens* has alpha toxin (major source of morbidity)
  - Pain out of proportion to exam; may not show skin cellulitis (is a deep infection)
  - Gram stain shows GPRs without WBCs
  - Myonecrosis and gas gangrene – common presentations
  - Can occur with farming injuries (dirty wounds)
  - Tx: early debridement, high-dose penicillin
- Fournier's gangrene
  - Severe infection in perineal and scrotal region
  - Risk factors – diabetes mellitus and immunocompromised state
  - Caused by mixed organisms (GPCs, GNRs, anaerobes)
  - Tx: early debridement; try to preserve testicles if possible; antibiotics

FUNGAL INFECTION

- Need fungal coverage for positive blood cultures, 2 sites other than blood, 1 site with severe

symptoms, endophthalmitis, or patients on prolonged bacterial antibiotics with failure to improve

- Actinomyces (not a true fungus) – pulmonary symptoms most common; can cause tortuous abscesses in cervical, thoracic, and abdominal areas; characteristic yellow sulfur granules on Gram stain
  - Tx: drainage and penicillin G
- Nocardia (not a true fungus) – pulmonary and CNS symptoms most common
  - Tx: drainage and sulfonamides (Bactrim)
- Candida – common inhabitant of the respiratory tract; MCC of fungemia
  - Tx: fluconazole (some *Candida* resistant), anidulafungin for severe infections
  - Candiduria – Tx: remove urinary catheter only (anti-fungal not necessary)
- Aspergillosis
  - Tx: voriconazole for severe infections
- Histoplasmosis – pulmonary symptoms usual; Mississippi and Ohio River valleys
  - Tx: liposomal amphotericin for severe infections
- Cryptococcus – CNS symptoms most common; usually in AIDS patients
  - Tx: liposomal amphotericin for severe infections
- Coccidioidomycosis – pulmonary symptoms; Southwest
  - Tx: liposomal amphotericin for severe infections
- Mucormycosis – extensive burns or widespread trauma patients at risk; area turns black
  - Tx: debridement; liposomal amphotericin

SPONTANEOUS BACTERIAL PERITONITIS (SBP; PRIMARY)

- Sx's: mental status changes, fever, abdominal pain in a cirrhotic patient
- Low protein (< 1 g/dL) in peritoneal fluid – risk factor
- Monobacterial (50% *E. coli*, 30% *Streptococcus*, 10% *Klebsiella*)
- Secondary to decreased host defenses (intrahepatic shunting, impaired bactericidal activity in ascites); not due to transmucosal migration
- Fluid cultures are negative in many cases
- Peritoneal fluid with PMNs > 250 or positive cultures are diagnostic
- Tx: ceftriaxone or other 3rd-generation cephalosporin
- Need to rule out intra-abdominal source (eg bowel perforation) if not getting better on antibiotics or if cultures are polymicrobial
- Liver transplantation not an option with active infection
- Weekly fluoroquinolones good for prophylaxis (norfloxacin; indicated after and episode of SBP)

SECONDARY BACTERIAL PERITONITIS

- Intra-abdominal source (implies perforated viscus)
- Polymicrobial – *B. fragilis*, *E. coli*, *Enterococcus* most common organisms
- Tx: usually need laparotomy to find source

HIV

- AIDS – loss of cell mediated immunity (decreased CD4 cells) leading to opportunistic infections

- RNA virus with reverse transcriptase
- Exposure risk
  - HIV blood transfusion 70%
  - Infant from positive mother 30%
  - Needle stick from positive patient 0.3%
  - Mucous membrane exposure 0.1%
  - Seroconversion occurs in 6–12 weeks
  - AZT (zidovudine, reverse transcriptase inhibitor) and ritonavir (protease inhibitor) can help decrease seroconversion after exposure
  - Antivirals should be given within 1–2 hours of exposure
- Opportunistic infections – most indication for laparotomy in HIV patients (CMV infection most common)
  - Neoplastic disease – 2nd most common reason for laparotomy (lymphoma most common)
- CMV colitis – most common intestinal manifestation of AIDS (can present with pain, bleeding, or perforation)
- Kaposi's sarcoma – MC neoplasm in AIDS patients (although surgery rarely needed)
- Lymphoma in HIV patients – stomach most common followed by rectum
  - MC malignancy requiring laparotomy
  - Mostly non-Hodgkin's (B cell)
  - Tx: chemotherapy usual; may need surgery with significant bleeding or perforation
- GI bleeds – lower GI bleeds are more common than upper GI bleeds in HIV patients
  - Upper GI bleeds – Kaposi's sarcoma, lymphoma
  - Lower GI bleeds – CMV, bacterial, HSV
- CD4 counts: 800–1,200 normal; 300–400 symptomatic disease; < 200 opportunistic infections

HEPATITIS C

- Now rarely transmitted with blood transfusion (0.0001%/unit)
- 1%–2% of population infected
- Fulminant hepatic failure rare
- Chronic infection in 60%; cirrhosis in 15%; hepatocellular carcinoma in 1%–5%
- MC indication for liver TXP
- Now curable with Sovaldi (sofosbuvir) in combination with ribavirin

CMV INFECTION

- Transmitted via leukocytes
- MC infection in TXP patients
- MC manifestation – febrile mononucleosis (sore throat, adenopathy)
- Most deadly form – CMV pneumonitis
- Dx: biopsy – shows characteristic cellular inclusion bodies; CMV serology
- Tx: ganciclovir; CMV immune globulin (Cytogam) indicated for severe infections or a CMV-negative patient receiving a CMV-positive organ

OTHER INFECTIONS

- Aspiration pneumonia – MC in the superior segment of the right lower lobe

- Strep pneumonia MC organism; also need to cover anaerobes
- Highest sensitivity test for osteomyelitis – MRI (avoid bone Bx)
- Brown recluse spider bites – Tx: oral dapsone initially; avoid early surgery; may need resection of area and skin graft for large ulcers later
- Acute septic arthritis – *Gonococcus*, staph, *H. influenzae*, strep
  - Tx: drainage, 3rd-generation cephalosporin and vancomycin until cultures show organism
- Diabetic foot infections – mixed staph, strep, GNRs, and anaerobes
  - Tx: broad-spectrum antibiotics (Unasyn, Zosyn)
- Cat/dog/human bites – polymicrobial infection usual (MC – *Strep pyogenes*)
  - *Eikenella* found only in human bites; can cause permanent joint injury
  - *Pasteurella multocida* found in cat and dog bites
  - Tx: broad-spectrum antibiotics (Augmentin)
- Impetigo, erysipelas, cellulitis, and folliculitis – staph (most common) and strep
- Furuncle – boil; usually *S. epidermidis* or *S. aureus.* Tx: drainage ± antibiotics
- Carbuncle – a multiloculated furuncle
- Peritoneal dialysis catheter infections
  - Sx's: cloudy fluid, abdominal pain, fever; usually monobacterial
  - *S. epidermidis* (#1), *S. aureus*, and *Pseudomonas* most common organisms
  - Fungal infections hard to treat
  - Tx: intraperitoneal vancomycin and gentamicin; increased dwell time and intraperitoneal heparin may help; IV antibiotics not as effective as intra-peritoneal
  - Removal of catheter for peritonitis that lasts for 4–5 days
  - Fecal peritonitis requires laparotomy to find perforation
  - Some say need removal of peritoneal dialysis catheter for all fungal, tuberculous, and *Pseudomonas* infections
- Sinusitis
  - Risk factors – nasoenteric tubes, intubation, patients with severe facial fractures
  - Usually polymicrobial
  - CT head shows air–fluid levels in the sinus
  - Tx: broad-spectrum antibiotics; rare to have to tap sinus percutaneously for systemic illness
- Prevention of nosocomial infections (hospital-acquired infections)
  - Hand washing – best prevention strategy
  - Highest risk patients – burn patients
  - If patient is on isolation, leave gloves and gown in the room
- Prevention of surgical site infections
  - Use clippers preoperatively instead of razors
  - Keep glucose 80–120
  - Keep PO_2 elevated (give 100% oxygen)
  - Keep patient warm (keep OR 70°F; warm air conduction [Bair Hugger] best for warming patients)
  - Chlorhexidine prep with iodine-impregnated drapes

6 Antibiotics

INTRODUCTION

- Antiseptic – kills and inhibits organisms on body
- Disinfectant – kills and inhibits organisms on inanimate objects
- Sterilization – all organisms killed
- Common antiseptics in surgery
  - Iodophors (Betadine) – good for GPCs and GNRs; poor for fungi
  - Chlorhexidine gluconate (Hibiclens) – good for GPCs, GNRs, and fungi

ANTIBIOTIC MECHANISM OF ACTION

- Inhibitors of cell wall synthesis – penicillins, cephalosporins, carbapenems, monobactams, vancomycin
- Inhibitors of the 30s ribosome and protein synthesis – tetracycline, aminoglycosides (tobramycin, gentamicin), linezolid
- Inhibitors of the 50s ribosome and protein synthesis – erythromycin, clindamycin, Synercid
- Inhibitor of DNA helicase (DNA gyrase) – quinolones
- Inhibitor of RNA polymerase – rifampin
- Produces oxygen radicals that breakup DNA – metronidazole (Flagyl)
- Sulfonamides – PABA analogue, inhibits purine synthesis
- Trimethoprim – inhibits dihydrofolate reductase, which inhibits purine synthesis
- Bacteriostatic antibiotics – tetracycline, clindamycin, erythromycin (all have reversible ribosomal binding), Bactrim
- Aminoglycosides – have irreversible binding to ribosome and are considered bactericidal

MECHANISM OF ANTIBIOTIC RESISTANCE

- PCN resistance – due to plasmids for beta-lactamase (eg *Staph aureus*)
- Transfer of plasmids – most common method of antibiotic resistance
- Methicillin-resistant *S. aureus* (MRSA) – resistance caused by a mutation of cell wall–binding protein
- Vancomycin-resistant *Enterococcus* (VRE) – resistance caused by a mutation in cell wall–binding protein
- Gentamicin resistance – resistance due to modifying enzymes leading to a decrease in active transport of gentamicin into the bacteria

APPROPRIATE DRUG LEVELS

- Vancomycin – peak 20–40 µg/mL; trough 5–10 µg/mL
- Gentamicin – peak 6–10 µg/mL; trough < 1 µg/mL
- Peak too high → decrease amount of each dose
- Trough too high → decrease frequency of doses (increase time interval between doses)

SPECIFIC ANTIBIOTICS

- Penicillin
  - GPCs – streptococci, syphilis, *Neisseria meningitides* (GPR), *Clostridium perfringens* (GPR), beta-hemolytic *Streptococcus*, anthrax
  - Not effective against *Staphylococcus* or *Enterococcus*
- Oxacillin, methicillin, and nafcillin
  - Anti-staph penicillins (staph only)
- Ampicillin and amoxicillin
  - Same as penicillin but also picks up enterococci
- Unasyn (ampicillin/sulbactam) and Augmentin (amoxicillin/clavulanic acid)
  - Broad spectrum – pick up GPCs (staph and strep), GNRs, ± anaerobic coverage
  - Effective for enterococci; not effective for *Pseudomonas*, *Acinetobacter*, or *Serratia*
  - Sulbactam and clavulanic acid are beta-lactamase inhibitors
- Ticarcillin and piperacillin (antipseudomonal penicillins)
  - GNRs – enterics, *Pseudomonas*, *Acinetobacter*, and *Serratia*
  - Side effects: inhibits platelets; high salt load
- Timentin (ticarcillin/clavulanic acid) and Zosyn (piperacillin/tazobactam)
  - Broad spectrum – pick up GPCs (staph and strep), GNRs, and anaerobes
  - Effective for enterococci; effective for *Pseudomonas*, *Acinetobacter*, and *Serratia*
  - Side effects: inhibits platelets; high salt load
  - Zosyn has QID dosing
- First-generation cephalosporins (cefazolin, cephalexin)
  - GPCs – staph and strep
  - Not effective for *Enterococcus*; does not penetrate CNS
  - Ancef (cefazolin) has the longest half-life → best for prophylaxis
- Second-generation cephalosporins (cefoxitin, cefotetan)
  - GPCs, GNRs, ± anaerobic coverage; lose some staph activity
  - Not effective for *Enterococcus*, *Pseudomonas*, *Acinetobacter*, or *Serratia*
  - Effective only for community-acquired GNRs
  - Cefotetan has longest half-life → best for prophylaxis
- Third-generation cephalosporins (ceftriaxone, cefepime)
  - GNRs mostly, ± anaerobic coverage
  - Not effective for *Enterococcus*; effective for *Pseudomonas*, *Acinetobacter*, and *Serratia*
  - Side effects: cholestatic jaundice, sludging in gallbladder (ceftriaxone)
- Monobactam (aztreonam)
  - GNRs; picks up *Pseudomonas*, *Acinetobacter*, and *Serratia*
- Carbapenems (meropenem, imipenem) – is given with cilastatin
  - Broad spectrum – GPCs, GNRs, and anaerobes
  - Not effective for MEP: MRSA, *Enterococcus*, and *Proteus*
  - Cilastatin – prevents renal hydrolysis of the drug and increases half-life
  - Side effects: seizures
- Bactrim (trimethoprim/sulfamethoxazole)
  - GNRs, ± GPCs
  - Not effective for *Enterococcus*, *Pseudomonas*, *Acinetobacter*, and *Serratia*
  - Side effects (numerous): teratogenic, allergic reactions, renal damage, Stevens–Johnson syndrome (erythema multiforme), hemolysis in G6PD-deficient patients

- Quinolones (ciprofloxacin, levofloxacin, norfloxacin)
  - Some GPCs, mostly GNRs
  - Not effective for *Enterococcus*; picks up *Pseudomonas*, *Acinetobacter*, and *Serratia*
  - 40% of MRSA sensitive; same efficacy PO and IV
  - Ciprofloxacin has BID dosing; levofloxacin has QD dosing
  - Side effects: tendon ruptures
- Aminoglycosides (gentamicin, tobramycin)
  - GNRs
  - Good for *Pseudomonas*, *Acinetobacter*, and *Serratia*; not effective for anaerobes (need O_2)
  - Resistance due to modifying enzymes leading to decreased active transport
  - Synergistic with ampicillin for *Enterococcus*
  - Beta-lactams (ampicillin, amoxicillin) facilitate aminoglycoside penetration
  - Side effects: reversible nephrotoxicity, irreversible ototoxicity
- Erythromycin (macrolides)
  - GPCs; best for community-acquired pneumonia and atypical pneumonias
  - Side effects: nausea (PO), cholestasis (IV)
  - Also binds motilin receptor and is prokinetic for bowel
- Vancomycin (glycopeptides)
  - GPCs, *Enterococcus*, *Clostridium difficile* (with PO intake), MRSA
  - Binds cell wall proteins
  - Resistance develops from a change in cell wall–binding protein
  - Side effects: HTN, Redman syndrome (histamine release), nephrotoxicity, ototoxicity
- Synercid (streptogramin – quinupristin-dalfopristin)
  - GPCs; includes MRSA, VRE
- Linezolid (oxazolidinones)
  - GPCs; includes MRSA, VRE
- Tetracycline
  - GPCs, GNRs, syphilis
  - Side effects: tooth discoloration in children
- Clindamycin
  - Anaerobes, some GPCs
  - Good for aspiration pneumonia
  - Can be used to treat *C. perfringens*
  - Side effects: pseudomembranous colitis
- Metronidazole (Flagyl)
  - Anaerobes
  - Side effects: disulfiram-like reaction, peripheral neuropathy (long-term use)
- Antifungal drugs
  - Amphotericin – binds ergosterols in wall and alters membrane permeability
    - Side effects: nephrotoxic, fever, hypokalemia, hypotension, anemia
    - Liposomal type has fewer side effects
  - Voriconazole – inhibits ergosterol synthesis (needed for cell wall)
  - Anidulafungin (Eraxis), micafungin, caspofungin – inhibit synthesis of cell wall glucan
  - Prolonged broad-spectrum antibiotics ± fever → anidulafungin (or other fungin drug)
  - Invasive aspergillosis → voriconazole
  - Candidemia → anidulafungin (or other fungin drug)

- Fungal sepsis other than candida and aspergillus → liposomal amphotericin
- Antituberculosis drugs
  - Isoniazid – inhibits mycolic acids (give with pyridoxine)
    - Side effects: hepatotoxicity, B_6 deficiency
  - Rifampin – inhibits RNA polymerase
    - Side effects: hepatotoxicity; GI symptoms; high rate of resistance
  - Pyrazinamide
    - Side effect: hepatotoxicity
  - Ethambutol
    - Side effect: retrobulbar neuritis
- Antiviral drugs
  - Acyclovir – inhibits viral DNA polymerase; used for HSV infections, EBV
  - Ganciclovir – inhibits viral DNA polymerase; used for CMV infections
    - Side effects: decreased bone marrow, CNS toxicity
- Broad-spectrum antibiotics can lead to superinfection
- Effective for *Enterococcus* – ampicillin/amoxicillin, vancomycin, Timentin/Zosyn
  - *Enterococcus is resistant to all cephalosporins*
- Effective for VRE (vancomycin-resistant *Enterococcus*) – Synercid, linezolid
- Effective for *Pseudomonas*, *Acinetobacter*, and *Serratia* – ticarcillin/piperacillin, Timentin/Zosyn, third-generation cephalosporins, aminoglycosides (gentamicin and tobramycin), meropenem/imipenem, or fluoroquinolones
- Effective for MRSA – vancomycin, Synercid, linezolid
- Double cover *Pseudomonas*
  - Has an alginate mucoid biolayer; can colonize tubes and lines

7 Medicines and Pharmacology

INTRODUCTION

- Sublingual and rectal drugs – do not pass through liver first (no first-pass metabolism); have higher bioavailability compared to oral drugs
- Skin absorption – based on lipid solubility through the epidermis
- CSF absorption – restricted to nonionized, lipid-soluble drugs
- Albumin – largely responsible for binding drugs (PCNs and warfarin 90% bound)
- Sulfonamides – will displace unconjugated bilirubin from albumin in newborns (avoid in newborns; can cause kernicterus [damages brain])
- Tetracycline and heavy metals – stored in bone
- 0 order kinetics – constant amount of drug is eliminated regardless of dose
- 1st order kinetics – drug eliminated proportional to dose
- Takes 5 half-lives for a drug to reach steady state
- Volume of distribution = amount of drug in the body divided by amount of drug in plasma or blood
  - Drugs with a high volume of distribution have higher concentrations in the extravascular compartment (eg fat tissue) compared with intravascular concentrations
- Bioavailability – fraction of unchanged drug reaching the systemic circulation
  - Assumed to be 100% for intravenous drugs, less for other routes (ie oral)
- ED_{50} – drug level at which desired effect occurs in 50% of patients
- LD_{50} – drug level at which death occurs in 50% of patients
- Tolerance – decline in potency with continued use
- Hyperactive – effect at an unusually low dose
- Tachyphylaxis – tolerance after only a few doses
- Potency – dose required for effect
- Efficacy – ability to achieve result without untoward effect
- Drug metabolism (hepatocyte smooth endoplasmic reticulum, P-450 system)
  - Phase I – demethylation, oxidation, reduction, hydrolysis reactions (mixed function oxidases, requires NADPH/oxygen)
  - Phase II – glucuronic acid (#1) and sulfates attached (forms water-soluble metabolite); usually inactive and ready for excretion. Biliary excreted drugs may become deconjugated in intestines with reabsorption, some in active form (termed entero-hepatic recirculation; eg cyclosporine)
  - Inhibitors of P-450 – cimetidine, isoniazid, ketoconazole, erythromycin, Cipro, Flagyl, allopurinol, verapamil, amiodarone, MAOIs, disulfiram
  - Inducers of P-450 – cruciform vegetables, ETOH, cigarette smoke, phenobarbital (barbiturates), Dilantin, theophylline, warfarin
- Kidney – most important organ for eliminating most drugs (glomerular filtration and tubular secretion); #2 biliary system
- Polar drugs (ionized) – water soluble; more likely to be eliminated in unaltered form

- Nonpolar drugs (non-ionized) – fat soluble; more likely metabolized before excretion
- Gout – caused by high uric acid in blood (negatively birefringent crystals); end product of purine metabolism; causes exquisite pain, swelling, and redness
  - Podagra – when it affects the big toe joint space (1st MTP joint); MC area affected (50% of cases)
  - Colchicine – anti-inflammatory; binds tubulin and inhibits migration (chemotaxis) of WBCs
  - Indomethacin – NSAID; inhibits prostaglandin synthesis (reversible cyclooxygenase inhibitor)
  - Allopurinol – xanthine oxidase inhibitor, blocks uric acid formation from xanthine
  - Probenecid – increases renal secretion of uric acid
- Lipid-lowering agents
  - Cholestyramine – binds bile acids in gut, forcing body to resynthesize bile acids from cholesterol, thereby lowering body cholesterol; can bind vitamin K and cause bleeding tendency
  - HMG-CoA reductase inhibitors (statin drugs) – can cause liver dysfunction, rhabdomyolysis
  - Niacin (inhibits cholesterol synthesis) – can cause flushing. Tx: ASA
- GI drugs
  - Metoclopramide (Reglan, prokinetic) – inhibits dopamine receptors; can be used to increase gastric and gut motility
  - Erythromycin (prokinetic) – binds and activates motilin receptor
  - Alvimopan (prokinetic) – antagonist to mu-opioid receptor; used for post-op ileus and to improve bowel recovery
  - Loperamide – slows gut motility; agonist to mu-opioid receptors
  - Lomotil (diphenoxylate/atropine) – slows gut; agonist to opioid receptors
  - Promethazine (Phenergan, antiemetic) – inhibits dopamine receptors; S/E: tardive dyskinesia (Tx: diphenhydramine [Benadryl])
  - Ondansetron (Zofran, antiemetic) – central-acting serotonin receptor inhibitor
  - Omeprazole – proton pump inhibitor; blocks H/K ATPase in stomach parietal cells
  - Cimetidine/ranitidine – histamine H_2 receptor blockers; decrease acid in stomach
  - Octreotide – long-acting somatostatin analogue; decreases gut secretions
- Cardiac drugs
  - Digoxin
    - Inhibits Na/K ATPase and increases myocardial calcium
    - Slows atrial-ventricular conduction
    - Also acts as an inotrope
    - Decreases blood flow to intestines – has been implicated in causing mesenteric ischemia
    - Hypokalemia increases sensitivity of heart to digitalis; can precipitate arrhythmias or AV block
    - Is not cleared with dialysis
    - Other side effects: visual changes (yellow hue), fatigue, arrhythmias
  - Amiodarone – good for acute atrial and ventricular arrhythmias
    - S/Es: pulmonary fibrosis w/ prolonged use; can also cause hypo- and hyperthyroidism
  - Magnesium – used to treat torsades de pointes (ventricular tachycardia)

- Adenosine – causes transient interruption of the AV node
- ACE inhibitors (angiotensin-converting enzyme inhibitors) – captopril
  - Best single agent shown to improve survival in patients with CHF
  - Can prevent CHF after myocardial infarction
  - Can prevent progression of renal dysfunction in patients with hypertension and DM
  - Can precipitate renal failure in patients with renal artery stenosis
- Beta-blockers – may prolong life in patients with severe LV failure
  - Reduce risk of MI and atrial fibrillation postoperatively
  - Best single agent shown to improve survival after myocardial infarction
- Atropine – acetylcholine antagonist; increases heart rate

- Metyrapone and aminoglutethimide – inhibit adrenal steroid synthesis
  - Used in patients with adrenocortical CA
- Leuprolide – analogue of GnRH and LHRH
  - Inhibits release of LH and FSH from pituitary when given continuously (paradoxic effect); used in patients with metastatic prostate CA
- Tamsulosin (Flomax) – alpha-adrenergic receptor antagonist used for BPH
- NSAIDs: nonselective COX inhibitors (indomethacin, ibuprofen)
  - Inhibit prostaglandin synthesis and lead to ↓ mucus and HCO_3^- secretion and ↑ acid production (mechanism of gastritis, ulcer formation, and GI bleeding)
  - Decreased prostaglandin synthesis also leads to constriction of renal afferent arterioles, leading to renal insufficiency
- NSAIDs: selective COX-2 inhibitors (celecoxib)
  - Only binds inducible cyclooxygenase 2
  - Fewer GI side effects compared to nonselective agents
  - Increased risk of cardiovascular events (stroke, myocardial infarction)
- Misoprostol – a PGE_1 derivative; a protective prostaglandin used to prevent peptic ulcer disease; consider use in patients on chronic NSAIDs
- Haldol – antipsychotic, inhibits dopamine receptors; can cause extrapyramidal manifestations (Tx: Benadryl)
- Furosemide (Lasix) – loop diuretic
  - Side effects (over-diuresis) – metabolic alkalosis, hypokalemia, ototoxicity
- Spironolactone – inhibits aldosterone
  - Side effects (over-diuresis) – metabolic acidosis, hyperkalemia
- Infliximab (Remicade) – antibody to TNF-alpha (given IV)
  - Used in inflammatory bowel disease
  - Most significant Cx is infection risk (TB reactivation or new infection)
  - CHF can also occur
  - Should not be used in patients with an active infection
- ASA poisoning – tinnitus, headaches, nausea, and vomiting
  - 1st – respiratory alkalosis
  - 2nd – metabolic acidosis
- Gadolinium – MC side effect: nausea
  - Do not use with renal insufficiency; can cause acute renal failure and nephrogenic systemic fibrosis
- Iodine contrast
  - MC side effect – nausea

    - MC side effect requiring medical Tx – dyspnea
- Tylenol overdose – Tx: *N*-acetylcysteine

8 Anesthesia

ANESTHESIA INDUCTION

- Results in loss of consciousness, lack of sensation, and anesthesia
- Can use inhalational (MC – sevoflurane) or intravenous agent (MC – propofol)

INHALATIONAL INDUCTION AGENTS

- MAC – minimum alveolar concentration = smallest concentration of inhalational agent at which 50% of patients will not move with incision
  - Small MAC → more lipid soluble = more potent
  - Speed of induction is inversely proportional to solubility
  - Nitrous oxide is fastest but has high MAC (low potency)
- Inhalational agents cause unconsciousness, amnesia, and some analgesia (pain relief)
- Blunt hypoxic drive
- Most have some myocardial depression, ↑ cerebral blood flow, and ↓ renal blood flow
- Nitrous oxide (NO_2) – fast, minimal myocardial depression; tremors at induction
  - Diffuses into closed spaces (avoid in patients with small bowel obstruction or pneumothorax)
- Halothane – slow onset/offset, highest degree of cardiac depression and arrhythmias; least pungent, which is good for children
  - Halothane hepatitis – fever, eosinophilia, jaundice, ↑ LFTs
- Sevoflurane – fast, less laryngospasm and less pungent; good for mask induction
- Isoflurane – good for neurosurgery (lowers brain O_2 consumption; no increase in ICP)
  - Pungent (not used for induction)
- Enflurane – can cause seizures
- MCC intra-op bradycardia – inhalational anesthesia (Tx: atropine)

INTRAVENOUS INDUCTION AGENTS

- Propofol – very rapid distribution and on/off; provides anesthesia and amnesia; sedative
  - Side effects: hypotension, respiratory depression, metabolic acidosis (avoid prolonged use in children)
  - Not an analgesic
  - Do not use in patients with egg allergy, pregnancy, or Parkinson's
  - Metabolized in liver and by plasma cholinesterases
- Ketamine – dissociation of thalamic/limbic systems; places patient in a cataleptic state (amnesia, analgesia)
  - No respiratory depression
  - Side effects: hallucinations, catecholamine release (↑ CO_2, tachycardia), ↑ airway secretions, and ↑ cerebral blood flow
  - *Contraindicated* in patients with head injury

- Good for children
- Etomidate – fewer hemodynamic changes; fast acting
  - Fewest cardiac side effects (good for patients with CHF or angina)
  - Not analgesic
  - Continuous infusions can lead to adrenocortical suppression
- Rapid sequence intubation – can be indicated for recent oral intake, GERD, delayed gastric emptying, pregnancy, bowel obstruction (pre-oxygenate, etomidate, succinylcholine typical sequence), cricoid pressure
- Dexmedetomidine (Precedex) – sedation agent for intubated patients (not an induction agent)
  - Provides anesthesia and analgesia without blunting hypoxic drive
  - Good for early extubation protocols (eg cardiac surgery)
  - Use not recommended for more than 24 hours
  - Is a CNS alpha-2 receptor agonist

MUSCLE RELAXANTS (PARALYTICS)

- Diaphragm – last muscle to go down and 1st muscle to recover from paralytics
- Neck muscles and face – 1st to go down and last to recover from paralytics
- Depolarizing agents – only one is succinylcholine; depolarizes neuromuscular junction
- Succinylcholine – fast, short acting; causes fasciculations, ↑ ICP; degraded by plasma pseudocholinesterases (can not be reversed); many side effects →
  - Malignant hyperthermia
    - Caused by a defect in calcium metabolism
    - Calcium released from sarcoplasmic reticulum causes muscle excitation – contraction syndrome (ryanodine receptor defect)
    - Side effects: 1st sign is ↑ end-tidal CO_2, then fever, tachycardia, rigidity, acidosis, hyperkalemia, rhabdomyolysis
    - Tx: dantrolene (10 mg/kg) inhibits Ca release and decouples excitation complex; cooling blankets, HCO_3, glucose, supportive care
  - Hyperkalemia – depolarization releases K
    - Do not use in patients with severe burns, neurologic injury, neuromuscular disorders, spinal cord injury, massive trauma, or acute renal failure (all have up-regulation of acetylcholine receptors which can release significant amounts of K)
  - Open-angle glaucoma can become closed-angle glaucoma
  - Atypical pseudocholinesterases – cause prolonged paralysis (Asians)
- Nondepolarizing agents
  - Inhibit neuromuscular junction by competing with acetylcholine
  - Can get prolongation of these agents with myasthenia gravis
  - Cis-atracurium – undergoes Hoffman elimination
    - Can be used in liver and renal failure (drug is broken down in the blood)
    - Histamine release (hypotension)
  - Rocuronium – fast, intermediate duration; hepatic metabolism
  - Pancuronium – slow acting, long-lasting; renal metabolism
    - Most common side effect – *tachycardia (no hypotension)*
  - Reversing drugs for nondepolarizing agents

- Neostigmine – blocks acetylcholinesterase, increasing acetylcholine
- Edrophonium – blocks acetylcholinesterase, increasing acetylcholine
- Atropine or glycopyrrolate should be given with neostigmine or edrophonium to counteract effects of generalized acetylcholine overdose

LOCAL ANESTHETICS

- Work by increasing action potential threshold, preventing Na influx
- Sensory block > motor block
- Can use 0.5 cc/kg of 1% lidocaine
- Maximum dosing
  - Lidocaine 4 mg/kg (7 mg/kg with epi)
  - Bupivacaine 2 mg/kg (3 mg/kg with epi)
- Can re-administer after 2 hours
- Infected tissues are hard to anesthetize secondary to acidosis
- Length of action – bupivacaine > lidocaine > procaine
- Side effects: perioral paresthesias (1st sign), tremors, seizures, tinnitus, arrhythmias (CNS symptoms occur before cardiac)
- Epinephrine allows higher doses to be used, stays locally
  - No epinephrine with arrhythmias, unstable angina, uncontrolled hypertension, poor collaterals (penis and ear), uteroplacental insufficiency
- Amides (all have an "i" in first part of the name) – lidocaine, bupivacaine, mepivacaine; rarely cause allergic reactions
- Esters – tetracaine, procaine, cocaine; ↑ allergic reactions due to PABA analogue

NARCOTICS (OPIOIDS)

- Morphine, fentanyl, Demerol (meperidine), codeine, hydromorphone (Dilaudid)
- Are all CNS mu-opioid receptor agonists
- Profound analgesia, respiratory depression (↓ CO_2 drive), no cardiac effects, blunt sympathetic response
- Metabolized by the liver and excreted via kidney
- Overdose of narcotics – Tx: Narcan (naloxone; works for all; mu-opioid receptor antagonist)
- Avoid use of narcotics (especially Demerol) in patients on MAOIs → can cause hyperpyrexic coma (serotonin release syndrome – fever, tachycardia, seizures, coma)
- Morphine – analgesia, euphoria, respiratory depression, miosis, constipation, histamine release (causes hypotension), ↓ cough
- Demerol – analgesia, euphoria, respiratory depression, miosis, tremors, fasciculations, convulsions
  - No histamine release
  - Can cause seizures (buildup of normeperidine analogues) – *avoid in patients with renal failure* and be careful with total amount given for other patients
- Methadone – simulates morphine, less euphoria; agonist to CNS mu-opioid receptor
- Fentanyl – fast acting; 80× strength of morphine (does not cross-react in patients with morphine allergy); no histamine release
- Sufentanil and remifentanil – very fast-acting narcotics with short half-lives
- Most potent narcotic – *sufentanil*

- Careful with combining opioids and benzodiazepines (synergistic effect)

BENZODIAZEPINES

- Anticonvulsant, amnesic, anxiolytic, respiratory depression; not analgesic; liver metabolism
- Agonist to the GABA receptor in the CNS (most prevalent inhibitory brain receptor)
- Versed (midazolam) – short acting; contraindicated in pregnancy, crosses placenta
- Valium (diazepam) – long acting
- Ativan (lorazepam) – long acting
- Overdose of these drugs – Tx: flumazenil (competitive inhibitor; may cause seizures and arrhythmias; contraindicated in patients with elevated ICP or status epilepticus)

EPIDURAL AND SPINAL ANESTHESIA

- Epidural anesthesia – allows analgesia by sympathetic denervation (sensory blockade); vasodilation
  - Has been shown to decrease respiratory Cx and cardiac events; no change in mortality
  - Morphine in epidural can cause respiratory depression (use Dilaudid to avoid this)
  - Lidocaine in epidural can cause decreased heart rate and blood pressure
  - Dilute concentrations allow sparing of motor function
  - Tx for acute hypotension and bradycardia: turn epidural down; fluids, phenylephrine, atropine
  - T-5 epidural can affect cardiac accelerator nerves
  - Epidural contraindicated with hypertrophic cardiomyopathy or cyanotic heart disease → sympathetic denervation causes decreased afterload, which worsens these conditions
  - Thoracotomy insertion level: T6–T9
  - Laparotomy insertion level: T8–T10
- Spinal anesthesia – injection into subarachnoid space, spread determined by baricity and patient position
  - Inject below L2 to avoid hitting the spinal cord
  - Can perform any surgery below the umbilicus with spinal anesthesia alone
  - Neurologic blockade is above motor blockade
  - Spinal contraindicated with hypertrophic cardiomyopathy, cyanotic heart disease
- Caudal block – through sacrum, good for pediatric hernias and perianal surgery
- Epidural and spinal complications – hypotension, headache, urinary retention (MC complication; need urinary catheter in these patients), abscess/hematoma formation, respiratory depression (with high spinal)
- Spinal headaches – caused by CSF leak after spinal/epidural; headache gets worse sitting up; Tx: rest, fluids, caffeine, analgesics; blood patch to site if it persists > 24 hours.

PERIOPERATIVE COMPLICATIONS

- Pre-op renal failure (#1) and CHF – associated with most postop hospital mortality
- Postop MI – may have no chest pain; can have hypotension, arrhythmias, ↑ filling pressures, oliguria, bradycardia; can happen intra-op or post-op (usually 2–3 days after surgery)
  - Dx – EKG and troponins (best test)
  - Initial Tx (BMOAN) – beta-blocker, morphine, oxygen, ASA, sublingual nitrates
  - ST elevation MI (STEMI) – emergently go to the cardiac cath lab for percutaneous

coronary intervention (PCI)

- Patients who need cardiology workup pre-op – aortic stenosis, angina, previous MI, shortness of breath, CHF, walks < 2 blocks due to shortness of breath or chest pain, FEV_1 < 70% predicted, severe valvular disease, PVCs > 5/min, high grade heart block, age > 70, DM, renal insufficiency, patients undergoing major vascular surgery (peripheral and aortic)

ASA Physical Status (PS) Classes

Class	Description
1	Healthy
2	Mild disease without limitation (controlled hypertension, obesity, diabetes mellitus, significant smoking history, older age)
3	Severe disease (angina, previous MI, poorly controlled hypertension, diabetes mellitus with complications, moderate COPD)
4	Severe constant threat to life (unstable angina, CHF, renal failure, liver failure, severe COPD)
5	Moribund (ruptured AAA, saddle pulmonary embolus)
6	Donor
E	Emergency

- Most aortic and peripheral vascular surgeries are considered high risk
- Carotid endarterectomy (CEA) is considered moderate risk surgery
- Biggest risk factors for postop MI: uncompensated CHF (#1, S3 gallop, JVD), recent MI, age > 70, DM, previous MI, unstable angina, Cr > 2, stroke/TIA
- Beta-blocker – most effective agent to prevent intra-op and post-op cardiovascular events
- Wait 6–8 weeks after MI before elective surgery

Cardiac Risk[a] Stratification for Noncardiac Surgical Procedures

High (cardiac risk > 5%) – emergent operations (especially in elderly); aortic, peripheral, and other major vascular surgery (*except* CEA); long procedure with large fluid shifts
Intermediate (cardiac risk < 5%) – CEA; head and neck surgery; intraperitoneal and intrathoracic surgery; orthopedic surgery; prostate surgery
Low[b] (cardiac risk < 1%) – endoscopic procedures; superficial procedures; cataract surgery; breast surgery

[a]Combined incidence of cardiac death and nonfatal myocardial infarction.

[b]Do not generally require further preoperative cardiac testing.

- Best determinant of esophageal vs. tracheal intubation – end-tidal CO_2 ($ETCO_2$)
- Intubated patient undergoing surgery with sudden transient rise in $ETCO_2$
  - Dx: most likely hypoventilation
  - Tx: ↑ tidal volume or ↑ respiratory rate
  - Could also be due to CO_2 embolus (would have associated hypotension, followed by a massive drop in $ETCO_2$)
  - Could also be due to malignant hyperthermia
- Intubated patient with sudden drop in $ETCO_2$ – likely became disconnected from the vent
  - Could also be due to pulmonary embolism or air embolism (patient would have hypotension)
- Air embolus
  - MC occurs with air sucking through a central line or central line site
  - CO_2 embolus can occur with laparoscopic procedures

- Sx's: sudden drop in $ETCO_2$, hypotension, tachycardia, mill wheel murmur (air lock prevents venous return)
- Tx: stop CO_2 insufflation if laparoscopic procedure
  - Trendelenburg (head down) and left lateral decubitus position (keeps air in right ventricle)
  - Hyperventilate with 100% oxygen (helps reabsorb air embolus faster)
  - Aspirate central line if present (try to remove air)
  - Pressors and inotropes
  - Prolonged CPR

- Endotracheal tube – should be placed 2 cm above the carina
- MC PACU complication – *nausea and vomiting*
- MCC post-op hypoxemia – atelectasis (alveolar hypoventilation)
- MCC post-op hypercarbia – poor minute ventilation (need to take bigger breaths or increase tidal volumes)
- Safest surgical setting – bipolar cautery (only affects area between circuit)
- Adequate pain control – 3/10 or less
  - Signs of inadequate pain control – tachycardia, diaphoresis, splinting, hypertension
- Visceral pain Tx: opioids
- Somatic pain Tx: NSAIDs and opioids
- Higher volume hospitals are associated with lower mortality for abdominal aortic aneurysm repair and for pancreatic resection

9 Fluids and Electrolytes

TOTAL BODY WATER

- Roughly ⅔ of the total body weight is water (men); infants have a little more body water, women have a little less
- ⅔ of water weight is intracellular (mostly muscle)
- ⅓ of water weight is extracellular
  - ⅔ of extracellular water is interstitial
  - ⅓ of extracellular water is in plasma
- Third space fluid is interstitial fluid
- Proteins – determine plasma/interstitial compartment oncotic pressures
- Na – determines intracellular/extracellular osmotic pressure
- Volume overload – most common cause is iatrogenic; first sign is weight gain
- Cellular catabolism – can release a significant amount of H_2O
- 0.9% normal saline: Na 154 and Cl 154; 3% normal saline: Na 513 and Cl 513
- Lactated Ringer's (LR; ionic composition of plasma): Na 130, K 4, Ca 2.7, Cl 109, lactate 28 (lactate is converted to HCO_3^- in the body)
- Plasma osmolarity: (2 × Na) + (glucose/18) + (BUN/2.8)
  - Normal: 280–295
- Water shifts from areas of low solute concentration (low osmolarity) to areas of high solute concentration (high osmolarity) to achieve osmotic equilibration

MAINTENANCE IV FLUIDS

- 4 cc/kg/h for 1st 10 kg
- 2 cc/kg/h for 2nd 10 kg
- 1 cc/kg/h for each kg after that
- IV maintenance fluids after major adult gastrointestinal surgery
  - During operation and 1st 24 hours, use LR
  - After 24 hours, switch to D5 ½ NS with 20 mEq K^+
    - 5% dextrose will stimulate insulin release, resulting in amino acid uptake and protein synthesis (also prevents protein catabolism)
    - D5 ½ NS @ 125/h provides 150 g glucose per day (525 kcal/day)
- During open abdominal operations, fluid loss is 0.5–1.0 L/h unless there are measurable blood losses
- Usually do not have to replace blood lost unless it is > 500 cc
- Best indicator of adequate volume replacement is urine output
- Urine output – should be kept at least 0.5 cc/kg/h; should not be replaced, usually a sign of normal postoperative diuresis
- Insensible fluid losses – 10 cc/kg/day; 75% skin (#1), 25% respiratory, pure water

FLUID RESUSCITATION (FOR SIGNIFICANT DEHYDRATION)

- Sweat loss (eg marathon runner) – Tx: normal saline
- Gastric fluid loss (eg gastric outlet obstruction) – Tx: normal saline
- Pancreas, biliary, or small bowel fluid loss – Tx: lactated ringers
- Large bowel (eg massive diarrhea) – Tx: lactated ringers
- GI fluid losses should generally be replaced cc/cc

GI FLUID SECRETION

Stomach	1–2 L/day
Biliary system	500–1,000 mL/day
Pancreas	500–1,000 mL/day
Duodenum	500–1,000 mL/day

GI ELECTROLYTE LOSSES

- Sweat – hypotonic (Na concentration 35–65)
- Saliva – K^+ (*highest concentration of K^+ in body*)
- Stomach – H^+ and Cl^-
- Pancreas – HCO_3^-
- Bile – HCO_3^-
- Small intestine – HCO_3^-, K^+
- Large intestine – K^+
- Dialysis can remove K, Ca, Mg, PO_4, urea, and creatinine
- Normal body K^+ requirement: 0.5–1.0 mEq/kg/day
- Normal body Na^+ requirement: 1–2 mEq/kg/day

POTASSIUM (NORMAL 3.5–5.0)

- Hyperkalemia – peaked T waves on EKG; often occurs with renal failure; Tx →
  - Calcium gluconate (1st drug to give; membrane stabilizer for heart)
  - Sodium bicarbonate (causes alkalosis, K enters cell in exchange for H)
  - 10 U insulin and 1 ampule of 50% dextrose (K driven into cells with glucose)
  - Kayexalate
  - Lasix
  - Albuterol
  - Dialysis if refractory
- Hypokalemia – T waves disappear (usually occurs in setting of <u>over-diuresis</u>)
  - Can also occur with diarrhea
  - May need to replace Mg^+ before you can correct K^+
- Pseudohyperkalemia – hemolysis of blood sample

SODIUM (NORMAL 135–145)

- Hypernatremia – usually from poor fluid intake; restlessness, irritability, seizures
  - If dehydrated, replace volume loss with D5 ½ normal saline
  - <u>If using D5 water, give slowly</u> to avoid brain swelling
- Hyponatremia – usually from fluid overload; headaches, nausea, vomiting, seizures

- Water restriction is first-line treatment for fluid overload hyponatremia, then diuresis
- Correct Na slowly to avoid central pontine myelinosis (no more than 1 mEq/h)
- Hyperglycemia (eg DKA) and hyperlipidemia (eg from acute pancreatitis) can cause pseudohyponatremia
- Hyponatremia can occur from isotonic fluid loss (usually from GI tract) compensated by water retention – treatment is isotonic fluids (lactated Ringer's if pH is normal/acidotic or normal saline if pH is alkalotic)

- Diabetes insipidus (↓ ADH) – ↑ urine output, ↓ urine specific gravity, ↑ serum Na, and ↑ serum osmolarity
  - Can occur with ETOH, head injury
  - Chronic – Tx: free water
  - Acute – Tx: DDAVP
- SIADH (↑ ADH) – ↓ urine output, concentrated urine, ↓ serum Na, and ↓ serum osmolarity
  - Can occur with head injury
  - Chronic – Tx: fluid restriction and diuresis (slowly)
  - Acute – Tx: conivaptan, tolvaptan

CALCIUM (NORMAL 8.5–10.0; NORMAL IONIZED CA 1.0–1.5)

- Hypercalcemia (Ca usually > 13 for symptoms) – causes lethargic state, N/V, hypotension
  - Breast cancer most common malignant cause
  - Hyperparathyroidism most common benign cause (also MCC overall)
  - MCC hypercalcemic crisis – undiagnosed hyperparathyroidism with stressor (eg surgery); as a group, hypercalcemia of malignancy is likely #1
  - No lactated Ringer's (contains Ca^{2+})
  - No thiazide diuretics (these retain Ca^{2+})
  - Tx: normal saline at 200–300 cc/h and Lasix
  - For malignant disease → calcitonin, alendronic acid (bisphosphonates; inhibit osteoclasts), dialysis
- Hypocalcemia (Ca usually < 8 or ionized Ca < 4 for symptoms) – perioral tingling and numbness (1st symptom), hyperreflexia, Chvostek's sign (tapping on face produces twitching), Trousseau's sign (carpopedal spasm), prolonged QT interval
  - Can occur after parathyroidectomy
  - May need to replace Mg^{+} before you can correct Ca
  - Protein adjustment for calcium – for every 1 g decrease in protein, add 0.8 to Ca
  - MCC – previous thyroidectomy (injured the parathyroid glands at surgery)

MAGNESIUM (NORMAL 2.0–2.7)

- Hypermagnesemia – causes lethargic state; usually occurs in renal failure patients taking magnesium containing products (laxatives, antacids)
  - Tx: calcium
- Hypomagnesemia – causes irritability, confusion, hyperreflexia, seizures; usually occurs with massive diuresis, chronic TPN without magnesium replacement, or ETOH abuse; signs similar to hypocalcemia

PHOSPHATE (NORMAL 2.5–4.5)

- Hyperphosphatemia – most often associated with renal failure
  - Tx: sevelamer hydrochloride (Renagel), low-phosphate diet (avoid dairy), dialysis
- Hypophosphatemia – most often associated with refeeding syndrome; usually from PO_4 shift from extracellular to intracellular
  - Sx's: failure to wean from the ventilator, muscle weakness
  - Tx: potassium phosphate

METABOLIC ACIDOSIS

- Anion gap = Na – (HCO_3 + Cl); Normal is < 10–15
- High anion gap acidosis – excessive production of fixed acids; "MUDPILES" = methanol, uremia, diabetic ketoacidosis, par-aldehydes, isoniazid, lactic acidosis, ethylene glycol, salicylates
- Normal anion gap acidosis – usually loss of Na/HCO_3^- (ileostomies, small bowel fistulas, lactulose), rapid infusion of HCO_3^--deficient fluids, primary hyperparathyroidism, mafenide acetate (Sulfamylon; inhibits carbonic anhydrase)
- Tx: underlying cause; keep pH > 7.20 with bicarbonate; severely ↓ pH can affect myocardial contractility
- Correction of acidosis can lead to hypokalemia

METABOLIC ALKALOSIS

- Usually a contraction alkalosis
- Nasogastric suction – results in hypochloremic, hypokalemic, metabolic alkalosis, and paradoxical aciduria →
  - Loss of Cl^- and H ion from stomach secondary to nasogastric tube (hypochloremia and alkalosis)
  - Loss of water causes kidney to reabsorb Na in exchange for K^+ (Na/K ATPase), thus losing K^+ (hypokalemia)
  - Na^+/H^- exchanger activated in an effort to reabsorb water along with K^+/H^- exchanger in an effort to reabsorb K^+ → results in paradoxical aciduria
  - Tx: normal saline (need to correct the Cl^- deficit)

Acid–Base Balance

Condition	pH (7.4)	CO_2 (40)	HCO_3 (24)
Respiratory acidosis	↓	↑	↑
Respiratory alkalosis	↑	↓	↓
Metabolic acidosis	↓	↓	↓
Metabolic alkalosis	↑	↑	↑

- Respiratory compensation (CO_2 regulation) for acidosis/alkalosis takes minutes
- Renal compensation (HCO_3^- regulation) for acidosis/alkalosis takes hours to days

ACUTE RENAL FAILURE

- FeNa = (urine Na/Cr)/(plasma Na/Cr) – fractional excretion of Na; *best test for azotemia*
- Prerenal – FeNa < 1%, urine Na < 20, BUN/Cr ratio > 20, urine osmolality > 500 mOsm

- 70% of renal mass must be damaged before ↑ Cr and BUN

- Contrast dyes – prehydration best prevents renal damage; HCO_3^- and *N*-acetylcysteine
- Myoglobin – converted to ferrihemate in acidic environment, which is toxic to renal cells; Tx: hydration, alkalinize urine

TUMOR LYSIS SYNDROME

- Release of purines and pyrimidines leads to ↑ PO_4, K, and uric acid, leads to ↓ Ca
- Can ↑ BUN and Cr (from renal damage; can lead to acute renal failure), EKG changes
- RFs – leukemias, lymphomas
- Tx: hydration *(best)*, rasburicase (converts uric acid in inactive metabolite allantoin), allopurinol (↓ uric acid production), diuretics, alkalinization of urine

VITAMIN D (CHOLECALCIFEROL)

- Made in skin (UV sunlight converts 7-dehydrocholesterol to cholecalciferol)
- Goes to liver for (25-OH), then kidney for (1-OH). This creates the active form of vitamin D
- Active form of vitamin D – increases calcium-binding protein, leading to increased intestinal Ca absorption

CHRONIC RENAL FAILURE

- ↑ K, Mg, PO_4, BUN, and creatinine
- ↓ Na and Ca
- ↓ Active vitamin D (↓ 1-OH hydroxylation) → ↓ Ca reabsorption from gut (↓ Ca-binding protein)
- Anemia – from low erythropoietin

Transferrin – transporter of iron
Ferritin – storage form of iron

10 Nutrition

INTRODUCTION

- Caloric need – approximately 20–25 calories/kg/day
- Calories:

Fat	9 calories/g
Protein	4 calories/g
Oral carbohydrates	4 calories/g
Dextrose	3.4 calories/g

- Nutritional requirements for average healthy adult male (70 kg)
  - 20% protein calories (1 g protein/kg/day; 20% should be essential amino acids)
  - 30% fat calories – important for essential fatty acids
  - 50% carbohydrate calories
  - 1,500–1,700 calories/day
- Trauma, surgery, or sepsis stress can increase kcal requirement 20%–40%
- Pregnancy increases kcal requirement 300 kcal/day
- Lactation increases kcal requirement 500 kcal/day
- Protein requirement also increases with above
- Burns
  - Calories: 25 kcal/kg/day + (30 kcal/day × % burn)
  - Protein: 1–1.5 g/kg/day + (3 g/day × % burn)
  - Don't exceed 3,000 kcal/day
- Much of energy expenditure is used for heat production
- Fever increases basal metabolic rate (10% for each degree above 38.0°C)
- If overweight and trying to calculate caloric need, use equation: weight = [(actual weight – ideal body weight) × 0.25] + IBW
- Harris–Benedict equation calculates basal energy expenditure based on weight, height, age, and gender
- Central line TPN – glucose based; maximum glucose administration –3 g/kg/h
- Peripheral line parenteral nutrition (PPN) – fat based
- Short-chain fatty acids (eg butyric acid) – fuel for colonocytes
- Glutamine – fuel for small bowel enterocytes
  - Most common amino acid in bloodstream and tissue
  - Most common amino acid released from muscle with catabolism
  - Releases NH_4 in kidney, thus helping with nitrogen excretion
  - Can be used for gluconeogenesis, as an energy source, or in the urea cycle
  - Enhances immune function by inhibiting small bowel mucosal breakdown and preventing bacterial translocation
- Primary fuel for most neoplastic cells – glutamine

PREOPERATIVE NUTRITIONAL ASSESSMENT

- Approximate half-lives

- Albumin – 18 days
- Transferrin – 8 days
- Prealbumin – 2 days

- Normal protein level: 6.0–8.5
- Normal albumin level: 3.5–5.5
- Normal pre-albumin level: 15–35
- Acute indicators of nutritional status – pre-albumin (#1), retinal binding protein, transferrin
- Ideal body weight (IBW)
  - Men = 106 lb + 6 lb for each inch over 5 ft
  - Women = 100 lb + 5 lb for each inch over 5 ft
- Preoperative signs of severe malnutrition
  - Acute weight loss > 20% in 3 months
  - Albumin < 3.0
  - Transferrin < 200
  - Anergy to skin antigens
- Low albumin (< 3.0) – strong risk factor for morbidity and mortality after surgery
- Pre-op nutrition is indicated *only* for patients with severe malnutrition undergoing major abdominal or thoracic procedures
- Early enteral feeding increases survival with sepsis and pancreatitis

RESPIRATORY QUOTIENT (RQ)

- Ratio of CO_2 produced to O_2 consumed – is a measurement of energy expenditure
- RQ > 1 = lipogenesis (overfeeding)
  - Tx: ↓ carbohydrates and caloric intake
  - High carbohydrate intake can lead to CO_2 buildup and ventilator problems
  - CO_2 is produced when excess carbohydrates are converted to fats
- RQ < 0.7 = ketosis and fat oxidation (starving)
  - Tx: ↑ carbohydrates and caloric intake
- Pure fat utilization – RQ = 0.7
- Pure protein utilization – RQ = 0.8
- Pure carbohydrate utilization – RQ = 1.0
- Balanced nutrition – RQ = 0.825

POSTOPERATIVE PHASES

- Diuresis phase – postoperative days 2–5
- Catabolic phase – postoperative days 0–3 (negative nitrogen balance)
- Anabolic phase – postoperative days 3–6 (positive nitrogen balance)

STARVATION OR MAJOR STRESS (SURGERY, TRAUMA, SYSTEMIC ILLNESS)

Metabolic Differences Between the Responses to Simple Starvation and to Injury

	Starvation	Injury
Basal metabolic rate	–	+ +
Presence of mediators (eg TNF-alpha, IL-1)	–	+ + +

Major fuel oxidized	Fat	Mixed (fat, protein)
Ketone body production	+ + +	±
Gluconeogenesis	+	+ + +
Protein metabolism	+	+ + +
Negative nitrogen balance	+	+ + +
Hepatic ureagenesis	+	+ + +
Muscle proteolysis	+	+ + +
Hepatic protein synthesis	+	+ + +

- The magnitude of metabolic response is proportional to the degree of injury

- Glycogen stores
  - Depleted after 24–36 hours of starvation (⅔ in skeletal muscle, ⅓ in liver) → body then switches to fat
  - Skeletal muscle lacks glucose-6-phosphatase (found only in liver)
  - Glucose-6-phosphate stays in muscle after breakdown from glycogen and is utilized there
  - The liver is the source of systemic glucose during stress times or starvation
- Gluconeogenesis precursors – amino acids (especially alanine, #1), lactate, pyruvate, glycerol; occurs in the liver
  - Alanine is the simplest amino acid precursor for gluconeogenesis
    - Is the primary substrate for gluconeogenesis
  - Alanine and phenylalanine – only amino acids to increase during times of stress
  - Late starvation – gluconeogenesis occurs in <u>kidney</u>
- Starvation
  - Protein-conserving mechanisms do <u>not</u> occur after trauma (or surgery) secondary to catecholamines and cortisol
  - Protein-conserving mechanisms do occur with starvation
  - Fat (ketones) is the main source of energy in starvation and in trauma; however, with trauma the energy source is more mixed (fat and protein)
  - Fat is the body's largest potential energy source
  - Most patients can tolerate a 15% weight loss without major complications
  - Patients can tolerate about 7 days without eating; if longer than that, place a Dobbhoff tube or start TPN
  - Try to feed gut to avoid bacterial translocation (bacterial overgrowth, increased permeability due to starved enterocytes, bacteremia) and TPN complications
  - PEG tube – consider when regular feeding not possible (eg CVA) or predicted to not occur for > 4 weeks
  - Tube feeds
    - Diarrhea – slow rate, add fiber, less-concentrated feeds
    - High gastric residuals – Tx: Reglan, erythromycin
    - Renal formulation – contains low concentrations of K, PO_4, and protein
  - Brain – utilizes <u>ketones</u> with progressive starvation (normally uses glucose)
  - Peripheral nerves, adrenal medulla, red blood cells, and white blood cells are all obligate glucose users
  - Refeeding syndrome
    - Occurs when feeding after prolonged starvation/malnutrition
    - ETOH abuse often present
    - Shift from fat to carbohydrate metabolism

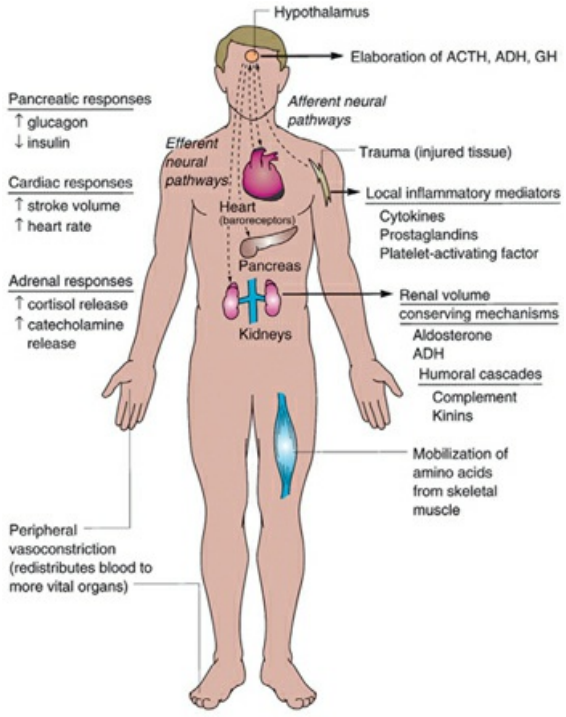
- Symptoms usually occur on day 4 following re-feeding
- Results in decreased K, Mg, and PO_4; causes cardiac dysfunction, profound weakness, encephalopathy, CHF, failure to wean from the ventilator
- Decreased ATP, the most significant problem
- Prevent this by starting to re-feed at a low rate (10–15 kcal/kg/day)

- Cachexia – anorexia, weight loss, wasting
  - Thought to be mediated by TNF-α
  - Glycogen breakdown, lipolysis, protein catabolism
- Kwashiorkor – protein deficiency
- Marasmus – starvation

- Major stress
  - Causes an increase in catecholamines, cortisol, and cytokines (eg TNF-alpha, IL-1)
  - Results in significant protein breakdown (negative nitrogen balance)
  - Hepatic urea formation occurs at high levels

NITROGEN BALANCE

- 6.25 g of protein contains 1 g of nitrogen
- N balance = (N in – N out) = ([protein/6.25] – [24-hour urine N + 4 g])
  - Positive N balance – more protein ingested than excreted (anabolism)
  - Negative N balance – more protein excreted than taken in (catabolism)
- Total protein synthesis for a healthy, normal 70-kg male is 250 g/day
- Liver
  - Responsible for amino acid production and breakdown
  - Majority of protein breakdown from skeletal muscle is glutamine (#1) and alanine
  - Urea production is used to get rid of ammonia (NH_3) from amino acid breakdown
- Urea cycle – glutamine is the primary NH_3 donor; reactions occur in the liver and urea is removed by the kidney; accounts for 90% of all N loss



Homeostatic adjustments initiated after injury.

FAT DIGESTION

- Triacylglycerides (TAGs), cholesterol, and lipids
  - Broken down by pancreatic lipase, cholesterol esterase, and phospholipase to micelles and free fatty acids
  - Micelles – aggregates of bile salts, long-chain free fatty acids, and monoacylglycerides
    - Enter enterocyte by fusing with membrane
    - Bile salts – increase absorption area for fats, helping form micelles
    - Cholesterol – used to synthesize bile salts
    - Fat-soluble vitamins (A, D, E, K) – absorbed in micelles
  - Medium- and short-chain fatty acids – enter enterocyte by simple diffusion
- Micelles and other fatty acids enter enterocytes
  - Chylomicrons are formed (90% TAGs, 10% phospholipids/proteins/cholesterol) which enter lymphatics (thoracic duct)
  - Long-chain fatty acids – enter lymphatics (terminal villous lacteals) along with chylomicrons
  - Medium- and short-chain fatty acids – enter portal system (same as amino acids and carbohydrates)
- Lipoprotein lipase – on endothelium in liver and adipose tissue; clears chylomicrons and TAGs from the blood, breaking them down to fatty acids and glycerol
- Free fatty acid–binding protein – on endothelium in the liver and adipose tissue; binds short- and medium-chain fatty acids
- Saturated fatty acids – used for fuel by cardiac and skeletal muscles
  - Fatty acids (ketones – acetoacetate, beta-hydroxybutyrate) – preferred source of energy for colonocytes, liver, heart, and skeletal muscle
- Unsaturated fatty acids – used as structural components for cells
- Hormone-sensitive lipase (HSL) – in fat cells; breaks down TAGs (storage form of fat) to fatty acids and glycerol, which are released into the bloodstream (HSL is sensitive to growth hormone, catecholamines, glucocorticoids)
- Essential fatty acids – linolenic, linoleic
  - Needed for prostaglandin synthesis (long-chain fatty acids)
  - Important for immune cells

CARBOHYDRATE DIGESTION

- Begins with salivary amylase, then pancreatic amylase and disaccharidases
- Glucose and galactose – absorbed by secondary active transport (Na gradient formed by ATPase); released into portal vein
- Fructose – facilitated diffusion; released into portal vein
- Sucrose = fructose + glucose
- Lactose = galactose + glucose
- Maltose = glucose + glucose
- Carbohydrates are the body's main energy source
- Glucose enters glycolysis or is stored as glycogen

PROTEIN DIGESTION

- Begins with stomach pepsin, then trypsin, chymotrypsin, and carboxypeptidase
- Trypsinogen released from pancreas and activated by enterokinase, which is released from the duodenum
  - Other pancreatic protein enzymes are then activated by trypsin
  - Trypsin can then also autoactivate other trypsinogen molecules
- Protein broken down to amino acids, dipeptides, and tripeptides by proteases
- Absorbed by secondary active transport; released as free amino acids into portal vein
- Amino acids are taken up by cells under the influence of insulin
- During stress, amino acids are shunted to the liver for gluconeogenesis
- Limit protein intake in patients with liver failure and renal failure to avoid ammonia and urea buildup (respectively) and possible worsening encephalopathy
- Branched-chain amino acids – leucine, isoleucine, valine ("LIV")
  - Metabolized in muscle
  - Possibly important source of protein in patients with liver failure
  - Are essential amino acids
- Essential amino acids – leucine, isoleucine, valine, histidine, lysine, methionine, phenylalanine, threonine, and tryptophan
- Non-essential amino acids – those that start with A, G, or C plus serine, tyrosine, and proline

CENTRAL VENOUS TPN (GENERAL COMPOSITION)

- 10% amino acid solution
- 25% dextrose solution
- Electrolytes (Na, Cl, K, Ca, Mg, PO4, acetate)
- Mineral and vitamins
- Makes 2–3 L solution, given at 100–150 cc/hr
- Lipids – given separately from TPN
  - 10% lipid solution contains 1.1 kcal/cc; 20% lipid solution contains 2 kcal/cc
- Acetate – buffer to increase pH of the solution
- Need to add Vit K separately
- ETOH abuse – add thiamine, folate, and multivitamin
- Long-term TPN Cx – cirrhosis
- Short-term TPN Cx – line issues (pneumothorax, infection)

Mineral and Vitamin Deficiencies

Deficiency	Effect
Chromium	Hyperglycemia, encephalopathy, neuropathy
Selenium	Cardiomyopathy, weakness
Copper	Pancytopenia
Zinc	Poor wound healing
Phosphate	Weakness (failure to wean off ventilator), encephalopathy, decreased phagocytosis
Thiamine (B_1)	Wernicke's encephalopathy, cardiomyopathy
Pyridoxine (B_6)	Sideroblastic anemia, glossitis, peripheral neuropathy
Cobalamin (B_{12})	Megaloblastic anemia, peripheral neuropathy, beefy tongue
Folate	Megaloblastic anemia, glossitis

Ascorbic acid (C)	Scurvy, poor wound healing
Niacin	Pellagra (diarrhea, dermatitis, dementia)
Essential fatty acids	Dermatitis, hair loss, thrombocytopenia
Vitamin A	Night blindness
Vitamin K	Coagulopathy
Vitamin D	Rickets, osteomalacia, osteoporosis
Vitamin E	Neuropathy

CORI CYCLE

- Glucose is utilized and converted to lactate in muscle
- Lactate then goes to the liver and is converted back to pyruvate and eventually glucose via gluconeogenesis
- Glucose is then transported back to muscle

METABOLIC SYNDROME (NEED 3)

- Obesity
- Insulin resistance (fasting glucose > 100)
- High TAGs (> 100)
- Low HDL (< 50)
- Hypertension (< 130/85)

11 Oncology

INTRODUCTION

- Cancer #2 cause of death in the United States
- MC CA in women – breast CA
- MC cause of CA-related death in women – lung CA
- MC CA in men – prostate CA
- MC cause of CA-related death in men – lung CA
- Most important prognostic indicator for lung CA and breast CA devoid of systemic metastases – nodal status
- Most important prognostic indicator for sarcoma devoid of systemic metastases – tumor grade
- PET (positron emission tomography) – used to identify metastases; detects fluorodeoxyglucose (FDG) molecules
  - False positives (5–10%) – inflammatory disease (eg histoplasmosis, TB, sarcoid)
  - False negatives (5–10%) – slow-growing tumors (carcinoid, bronchoalveolar lung CA)
  - Accuracy low in the head due to increased glucose uptake by the brain
  - Test may not work well in patients with diabetes (glucose competes) or hyper-insulinemia (insulin drives FDG into normal cells)
- Cytotoxic T cells need MHC complex to attack tumor
- Natural killer cells can independently attack tumor cells
- Tumor antigens are random unless viral-induced tumor
- Hyperplasia – increased number of cells
- Metaplasia – replacement of one tissue with another (GERD squamous epithelium in esophagus changed to columnar gastric tissue; eg Barrett's esophagus)
- Dysplasia – altered size, shape, and organization (eg Barrett's dysplasia)
- Core needle biopsy – gives architecture
- Fine-needle aspiration – gives cytology (just cells)

TUMOR MARKERS

- CEA – colon CA
- AFP – liver CA
- CA 19-9 – pancreatic CA
- CA 125 – ovarian CA
- Beta-HCG – testicular CA, choriocarcinoma
- PSA – prostate CA (thought to be the tumor marker with the highest sensitivity, although specificity is low)
- NSE – small cell lung CA, neuroblastoma
- BRCA I and II – breast CA
- Chromogranin A – carcinoid tumor
- Ret oncogene – thyroid medullary CA

- Half-lives – CEA: 18 days; PSA: 18 days; AFP: 5 days

ONCOGENESIS

- Cancer transformation:
  - Heritable alteration in genome *and;*
  - Loss of growth regulation
- Latency period – time between exposure and formation of clinically detectable tumor
  - Initiation – carcinogen acts with DNA
  - Promotion of cancer cells then occurs
  - Progression of cancer cells to clinically detectable tumor
- Neoplasms can arise from carcinogenesis (eg smoking), viruses (eg EBV), or immunodeficiency (eg HIV)
- Retroviruses contain oncogenes
  - Epstein-Barr virus – associated with Burkitt's lymphoma (8:14 translocation) and nasopharyngeal CA (c-myc)
- Proto-oncogenes are human genes with malignant potential

Malignancy	Associated Infectious Agent
Cervical cancer	*Human papillomavirus*
Gastric cancer	*Helicobacter pylori*
Hepatocellular carcinoma	Hepatitis B and hepatitis C viruses
Nasopharyngeal carcinoma	EBV
Burkitt's lymphoma	EBV
Various lymphomas	HIV

EBV, Epstein-Barr virus; HIV, human immunodeficiency virus.
(Modified from O'Connell C, Dickey VL. *Blueprints: Hematology and Oncology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2005, with permission.)

RADIATION THERAPY (XRT)

- M phase (mitosis) – most vulnerable stage of cell cycle for XRT
- Most damage done by formation of oxygen radicals → maximal effect with high oxygen levels
- Main target is DNA – oxygen radicals and XRT itself damage DNA and other molecules
- Higher-energy radiation has skin-preserving effect (maximal ionizing potential not reached until deeper structures)
- Fractionate XRT doses
  - Allows repair of normal cells
  - Allows re-oxygenation of tumor
  - Allows redistribution of tumor cells in cell cycle
- Very radiosensitive tumors (high mitotic rate) – seminomas, lymphomas
- Very radioresistant tumors (low mitotic rate) – epithelial, sarcomas
- Large tumors – less responsive to XRT due to lack of oxygen in the tumor
- XRT can be used for painful bony metastases
- Brachytherapy – source of radiation in or next to tumor (Au-198, I-128); delivers high, concentrated doses of radiation
- Gamma knife – cobalt XRT

CHEMOTHERAPY AGENTS

- Cell cycle–specific agents (5FU, methotrexate) – exhibit plateau in cell-killing ability
- Cell cycle–nonspecific agents – linear response to cell killing
- Tamoxifen (blocks estrogen receptor) – decreases short-term (5-year) risk of breast CA 45% (1% risk of blood clots, 0.1% risk of endometrial CA)
- Taxol promotes microtubule formation and stabilization that cannot be broken down; cells are ruptured; side effects – neuropathy
- Bleomycin and busulfan – can cause pulmonary fibrosis
- Cisplatin (platinum alkylating agent) – nephrotoxic, neurotoxic, ototoxic
- Carboplatin (platinum alkylating agent) – bone (myelo) suppression
- Vincristine (microtubule inhibitor) – peripheral neuropathy, neurotoxic
- Vinblastine (microtubule inhibitor) – bone (myelo) suppression
- Alkylating agents – transfer alkyl groups; form covalent bonds to DNA
  - Cyclophosphamide – acrolein is the active metabolite
    - Side effects: gonadal dysfunction, SIADH, hemorrhagic cystitis
    - Mesna can help with hemorrhagic cystitis
- Levamisole – anthelmintic drug thought to stimulate immune system against cancer
- Methotrexate – inhibits dihydrofolate reductase (DHFR), which inhibits purine and DNA synthesis
  - Side effects: renal toxicity, radiation recall
  - Leucovorin rescue (folinic acid) – reverses effects of methotrexate by re-supplying folate
- 5-Fluorouracil (5FU) – inhibits thymidylate synthetase, which inhibits purine and DNA synthesis
  - Leucovorin (folinic acid) – increases toxicity of 5FU
- Doxorubicin – DNA intercalator, O_2 radical formation
  - Heart toxicity secondary to O_2 radicals at total doses > 500 mg/m^2
- Etoposide (VP-16) – inhibits topoisomerase (which normally unwinds DNA)
- Least myelosuppression – bleomycin, vincristine, busulfan, cisplatin
- GCSF (granulocyte colony–stimulating factor) – used for neutrophil recovery after chemo; side effects – Sweet's syndrome (acute febrile neutropenic dermatitis)

MISCELLANEOUS

- Three main groups of CA – epithelial tumors (ectoderm), sarcomas (mesoderm), and adenocarcinoma (endoderm)
- Resection of a normal organ to prevent cancer
  - Breast – BRCA I or II with strong family history
  - Thyroid – RET proto-oncogene with family history thyroid CA
- Tumor suppressor genes (usually inhibit cell cycle or induce apoptosis)
  - Retinoblastoma (Rb1) – chromosome 13; involved in cell cycle regulation
  - p53 – chromosome 17; involved in cell cycle (normal gene induces cell cycle arrest and apoptosis; abnormal gene allows unrestrained cell growth)
  - APC – chromosome 5; involved with cell cycle regulation and movement
  - DCC – chromosome 18; involved in cell adhesion
  - bcl – involved in apoptosis (programmed cell death)
  - BRCA – involved in DNA damage/repair; also cell cycle regulation

- Proto-oncogenes
  - ras proto-oncogene – G protein defect (GTPase)
  - src proto-oncogene – tyrosine kinase defect
  - sis proto-oncogene – platelet-derived growth factor receptor defect
  - erb B proto-oncogene – epidermal growth factor receptor defect
  - myc (c-myc, n-myc, l-myc) proto-oncogenes – transcription factors
- Li–Fraumeni syndrome – defect in p53 gene → patients get childhood sarcomas, breast CA, brain tumors, leukemia, adrenal CA
- Colon CA
  - Genes involved in development include APC, p53, DCC, and K-ras
  - APC thought to be the initial step in the evolution of colorectal CA
  - Colon CA usually does not go to bone
- Carcinogens
  - Coal tar – larynx, skin, bronchial CA
  - Beta-naphthylamine – urinary tract CA (bladder CA)
  - Benzene – leukemia
  - Asbestos – mesothelioma
- Cancer spread
  - Suspicious supraclavicular nodes – neck, breast, lung, stomach (Virchow's node), pancreas
  - Suspicious axillary node – lymphoma (#1), breast, melanoma
  - Suspicious periumbilical node – pancreas (Sister Mary Joseph's node)
  - Ovarian metastases – stomach (Krukenberg tumor), colon
  - Bone metastases – breast (#1), prostate
  - Skin metastases – breast, melanoma
  - Small bowel metastases – melanoma (#1)
- Clinical trials
  - Phase I – is it safe and at what dose?
  - Phase II – is it effective?
  - Phase III – is it better than existing therapy?
  - Phase IV – implementation and marketing
- Types of therapy
  - Induction – initial treatment
  - Primary (neoadjuvant) – administration of an agent before another main Tx: eg chemo-XRT given 1st, followed by surgery
  - Adjuvant – combined with another modality; given after other therapy is used
  - Salvage – for tumors that fail to respond to initial chemotherapy
- Lymph nodes have poor barrier function → better to view them as signs of probable metastasis
- En bloc multiorgan resection can be attempted for some tumors (colon into uterus, adrenal into liver, gastric into spleen); aggressive local invasiveness is different from metastatic disease
- Palliative surgery – tumors of hollow viscus causing obstruction or bleeding (colon CA), breast CA with skin or chest wall involvement
- Sentinel lymph node biopsy – no role in patients with clinically palpable nodes; you need to go after and sample these nodes
- Colon metastases to the liver – 35% 5-year survival rate if successfully resected
- Prognostic indicators for survival after resection of hepatic colorectal metastases – disease-

free interval > 12 months, tumor number < 3, CEA < 200, size < 5 cm, negative nodes

- Most successfully cured metastases with surgery – germ cell tumor (#1 seminoma; 75% 5-YS)
- Ovarian CA – one of the few tumors for which surgical debulking improves chemotherapy (not seen in other tumors)
- Curable solid tumors with chemotherapy only – Hodgkin's and non-Hodgkin's lymphoma
- T-cell lymphomas – HTLV-1 (skin lesions), mycosis fungoides (Sézary cells)
- HIV-related malignancies – Kaposi's sarcoma, non-Hodgkin's lymphoma
- V-EGF (vascular epidermal growth factor) – causes angiogenesis; involved in tumor metastasis

12 Transplantation

TRANSPLANT IMMUNOLOGY

- HLA-A, B, and DR – most important in recipient/donor matching (human leukocyte antigens)
  - HLA-DR – most important overall (HLA = human leukocyte antigen)
  - HLA is the major histocompatibility complex (MHC) in humans
- Time on the list and HLA matching are the primary determinants of organ allocation in the U.S.
- ABO blood compatibility – generally required for all transplants (except liver)
  - Type O – universal donor
  - Type AB – universal recipient
- Cross-match – detects preformed recipient antibodies to the donor organ by mixing recipient serum with donor lymphocytes → if these antibodies are present, it is termed a positive cross-match and hyperacute rejection would likely occur with TXP
- Panel reactive antibody (PRA)
  - Technique identical to cross-match; detects preformed recipient antibodies using a panel of HLA typing cells
  - Get a percentage of cells that the recipient serum reacts with → a high PRA (> 50%) is often a contraindication to TXP (increased risk of hyper-acute rejection)
  - Transfusions, pregnancy, previous transplant, and autoimmune diseases can all increase PRA
- Mild rejection – pulse steroids
- Severe rejection – steroid and antibody therapy (ATG or thymoglobulin)
- Skin cancer – #1 malignancy following any transplant (squamous cell CA #1)
- Post-transplant lympho-proliferative disorder (PTLD) – next most common malignancy following transplant (Epstein-Barr virus related)
  - Sx's: small bowel obstruction, mass, adenopathy
  - RFs: cytolytic drugs
  - Tx: withdrawal of immunosuppression; rituximab (anti-CD20; decreases B cells); may need chemotherapy and XRT for aggressive tumor
- Risks of long-term immunosuppression – CA, cardiovascular disease, infection, osteopenia
- Donors with hepatitis or HIV can be matched with recipients having the same disease

DRUGS

- Mycophenolate (MMF, CellCept)
  - Inhibits de novo purine synthesis, which inhibits growth of T cells
  - Side effects: GI intolerance (#1, N/V/D), myelosuppression
  - Need to keep WBCs > 3
  - Used as maintenance therapy to prevent rejection
  - Azathioprine (Imuran) has similar action

- Steroids (prednisone, Solu-Medrol) – inhibit inflammatory cells (macrophages) and genes for cytokine synthesis (IL-2 most important); used for induction after TXP, maintenance, and acute rejection episodes
- Cyclosporin (CSA)
  - Binds cyclophilin protein; CSA-cyclophilin complex then inhibits calcineurin, which results in decreased cytokine synthesis (IL-2, IL-4, etc.); used for maintenance therapy
  - Side effects: nephrotoxicity, hepatotoxicity, tremors, seizures, hemolytic-uremic syndrome
  - Need to keep trough 200–300
  - Undergoes hepatic metabolism and biliary excretion (reabsorbed in the gut, get entero-hepatic recirculation)
- FK-506 (Prograf, tacrolimus)
  - Binds FK-binding protein; actions similar to CSA but more potent
  - Side effects: nephrotoxicity, more GI symptoms, mood changes, and diabetes than CSA, much less entero-hepatic recirculation compared to CSA
  - Less rejection episodes in Kidney TXP's w/ FK-506 compared to CSA
  - Need to keep trough 10–15
- Sirolimus (Rapamycin)
  - Binds FK-binding protein like FK-506 but inhibits mammalian target of rapamycin (mTOR); result is that it inhibits T and B cell response to IL-2
  - Used as maintenance therapy
  - Is not nephrotoxic (unlike CSA and tacrolimus)
  - Side effect – interstitial lung disease
- Anti-thymocyte globulin (ATG)
  - Equine (ATGAM) or rabbit (Thymoglobulin) polyclonal antibodies against T cell antigens (CD2, CD3, CD4)
  - Used for induction and acute rejection episodes
  - Is cytolytic (complement dependent)
  - Need to keep WBCs > 3
  - Side effects: cytokine release syndrome (fever, chills, pulmonary edema, shock) – steroids and Benadryl given before drug to try to prevent this; PTLD; myelosuppression

TYPES OF REJECTION

- Hyperacute rejection (occurs within minutes to hours)
  - Caused by preformed antibodies that should have been picked up by the cross-match (type II hypersensitivity reaction)
  - MCC – ABO incompatibility
  - Activates the complement cascade and thrombosis of vessels occurs
  - Tx: emergent re-transplant (or just removal of organ if kidney)
- Accelerated rejection (occurs < 1 week)
  - Caused by sensitized T cells to donor HLA
  - Tx: ↑ immunosuppression, pulse steroids, and possibly antibody Tx
- Acute cellular rejection (occurs after 1st week)
  - Caused by T cells (cytotoxic and helper T cells; cell-mediated) to HLA antigens
  - Tx: ↑ immunosuppression, pulse steroids, and possibly antibody Tx
- Acute humeral rejection (occurs after 1st week)
  - Caused by antibodies to donor antigens

- Tx: pulse steroids, antibody therapy, plasmapheresis
- Chronic rejection (occurs months to years after TXP)
  - Partially a type IV hypersensitivity reaction (sensitized T cells)
  - Antibody formation also plays a role
  - Leads to graft fibrosis
  - RF – increased number of acute rejection episodes
  - MCC – HLA incompatibility
  - Tx: ↑ immunosuppression – no really effective treatment; re-transplant

KIDNEY TRANSPLANTATION

- Can store kidney for 48 hours
- Need ABO type compatibility and cross-match
- UTI – can still use kidney
- Acute ↑ in creatinine (1.0–3.0) – can still use kidney
- HIV is not a contraindication
- Mortality primarily from stroke and MI
- Attach to iliac vessels
- Complications
  - Urine leaks (#1) – Tx: drainage and stenting best
  - Renal artery stenosis – diagnose with ultrasound (flow acceleration occurs at level of stenosis)
    - Tx: PTA with stent
  - Lymphocele – most common cause of external ureter compression
    - MC occurs 3 weeks after TXP (late decreased urine output with hydronephrosis and fluid collection)
    - Tx: 1st try percutaneous drainage; if that fails, then need peritoneal window (make hole in peritoneum, lymphatic fluid drains into peritoneum and is re-absorbed – 95% successful)
  - Postop oliguria – usually due to ATN (pathology shows hydrophobic changes [dilation and loss of tubules])
  - Postop diuresis – usually due to urea and glucose
  - New proteinuria – suggestive of renal vein thrombosis
  - Postop diabetes – side effect of CSA, FK, steroids
  - Viral infections – CMV – Tx: ganciclovir; HSV – Tx: acyclovir
  - Acute rejection – usually occurs in 1st 6 months; pathology shows tubulitis (vasculitis with more severe form)
  - Kidney rejection workup – usually for ↑ in Cr or poor urine output
    - Ultrasound with duplex (to rule out vascular problem and ureteral obstruction) and biopsy
    - Empiric decrease in CSA or FK (these can be nephrotoxic)
    - Empiric pulse steroids
    - Empiric fluid/Lasix challenge
  - Chronic rejection – usually do not see until after 1 year; no good treatment
  - 5-year graft survival overall – 70% (cadaveric 65%, living donors 75%)
  - Extends life by 15 years
  - MCC mortality – myocardial infarction

- Living kidney donors
  - Dual-collecting systems is not a contraindication
  - Most common complication – wound infection (1%)
  - Most common cause of death – fatal PE
  - The remaining kidney hypertrophies

LIVER TRANSPLANTATION

- Can store for 24 hours
- Contraindications to liver TXP – current ETOH abuse, acute ulcerative colitis
- Chronic hepatitis C – most common reason for liver TXP in adults
- MELD score uses creatinine, INR, and bilirubin to predict if patients with cirrhosis will benefit more from liver TXP than from medical therapy (MELD > 15 benefits from liver TXP)
- Criteria for urgent TXP – fulminant hepatic failure (encephalopathy – stupor, coma)
- Patients with hepatitis B antigenemia can be treated with HBIG (hepatitis B immunoglobulin) and lamivudine (protease inhibitor) after liver TXP to help prevent reinfection
- Hepatitis B – reinfection rate is reduced to 20% with the use of HBIG and lamivudine
- Hepatitis C – disease most likely to recur in the new liver allograft; reinfects essentially all grafts
- Hepatocellular CA – if no vascular invasion or metastases can still consider TXP (not if cholangiocarcinoma)
- Portal vein thrombosis – not a contraindication to TXP
- ETOH – 20% will start drinking again (recidivism)
- Macrosteatosis – extracellular fat globules in the liver allograft
  - Risk-factor for primary non-function – if 50% of cross-section is macrosteatatic in potential donor liver, there is a 50% chance of primary non-function
- Duct-to-duct anastomosis is performed
  - Hepaticojejunostomy in kids
- Right subhepatic, right, and left subdiaphragmatic drains are placed
- Biliary system (ducts, etc.) depends on hepatic artery blood supply
- Most common arterial anomaly – right hepatic coming off SMA
- Liver problems post-op – get liver duplex U/S with biopsy
- Complications
  - Bile leak (#1) – Tx: place drain, then ERCP with stent across leak
  - Primary nonfunction
    - 1st 24 hours – total bilirubin > 10, bile output < 20 cc/12 h, elevated PT and PTT; After 96 hours – mental status changes, ↑ LFTs, renal failure, respiratory failure
    - Usually requires re-transplantation
  - Hepatic artery stenosis – place stent
  - Early hepatic artery thrombosis
    - MC early vascular Cx
    - → LFTs, ↓ bile output, fulminant hepatic failure
    - Tx: MC will need emergent re-transplantation for ensuing fulminant hepatic failure (can try to stent or revise anastomosis)
  - Late hepatic artery thrombosis

    - Results in biliary strictures and abscesses (not fulminant hepatic failure)
  - Abscesses – most commonly from late (chronic) hepatic artery thrombosis
  - IVC stenosis/thrombosis (rare) – edema, ascites, renal insufficiency; Tx: thrombolytics, IVC stent
  - Portal vein thrombosis (rare): <u>early</u> – abdominal pain; <u>late</u> – UGI bleeding, ascites, may be asymptomatic; Tx – if <u>early</u>, re-op thrombectomy and revise anastomosis
  - Cholangitis – get PMNs around portal triad (<u>not</u> mixed infiltrate)
  - Acute rejection – T cell mediated against blood vessels
    - Clinical – fever, jaundice, ↓ bile output
    - Labs – leukocytosis, eosinophilia, ↑ LFTs, ↑ total bilirubin, and ↑ PT
    - Pathology – shows portal triad lymphocytosis, endotheliitis (mixed infiltrate), and bile duct injury
    - Usually occurs in 1st 2 months
    - Chronic rejection – after liver TXP; get disappearing bile ducts (antibody and cellular attack on bile ducts); gradually get bile duct obstruction with ↑ in alkaline phosphatase, portal fibrosis
- Retransplantation rate – 20%
- 5-year survival rate – 70%
- Living donor
  - For adult transplant – take right lobe
  - For child transplant – take left lateral lobe (segments 2 + 3)
  - Liver is regenerated 100% in 6–8 weeks

PANCREAS TRANSPLANTATION

- MC indication – DM w/ renal failure
- Need both donor celiac artery and SMA for arterial supply
- Need donor portal vein for venous drainage
- Attach to iliac vessels
- Most use enteric drainage for pancreatic duct. Take second portion of duodenum from donor along with ampulla of Vater and pancreas, then perform anastomosis of donor duodenum to recipient bowel
- Successful pancreas/kidney TXP results in stabilization of retinopathy, ↓ neuropathy, ↑ nerve conduction velocity, ↓ autonomic dysfunction (gastroparesis), ↓ orthostatic hypotension
  - *<u>No</u> reversal of vascular disease*
- Complications
  - Venous thrombosis (#1) – hard to treat
  - Rejection – hard to diagnose if patient does not also have a kidney transplant
    - Can see ↑ glucose or amylase; fever, leukocytosis

HEART TRANSPLANTATION

- Can store for 6 hours
- Need ABO compatibility and crossmatch
- For patients with life expectancy < 1 year
- Persistent pulmonary hypertension after heart transplantation

    - Associated with early mortality after heart TXP
    - Tx: inhaled nitric oxide, ECMO if severe
- Routine right ventricular biopsies (to check for rejection) are performed at set intervals
- Acute rejection – shows perivascular lymphocytic infiltrate with varying grades of myocyte inflammation and necrosis
- MCC early mortality – infection
- *Chronic allograft vasculopathy* (progressive diffuse coronary atherosclerosis) – MCC of late death and death overall following heart TXP
- Median: 10-year survival

LUNG TRANSPLANTATION

- Can store for 6 hours
- Need ABO compatibility and crossmatch
- For patients with life expectancy < 1 year
- #1 cause of early mortality – reperfusion injury (Tx: similar to ARDS)
- Indication for double-lung TXP – cystic fibrosis
- Exclusion criteria for using lungs – aspiration, moderate to large contusion, infiltrate, purulent sputum, PO_2 < 350 on 100% FiO_2 and PEEP 5
- Acute rejection – perivascular lymphocytosis
- Chronic rejection – *bronchiolitis obliterans*; MCC of late death and death overall following lung TXP
- Median: 5-year survival

OPPORTUNISTIC INFECTIONS

- Viral – CMV, HSV, VZV
- Protozoan – *Pneumocystis jiroveci* pneumonia (reason for Bactrim prophylaxis)
- Fungal – *Aspergillus*, *Candida*, *Cryptococcus*

Hierarchy for Permission for Organ Donation from Next of Kin – 1) Spouse, 2) adult son or daughter, 3) either parent, 4) adult brother or sister, 5) guardian, 6) any other person authorized to dispose of the body

13 Inflammation and Cytokines

INFLAMMATION PHASES

- Injury – leads to exposed collagen, platelet-activating factor release, and tissue factor release from endothelium
- Platelets bind collagen – release growth factors (platelet-derived growth factor [PDGF]); leads to PMN and macrophage recruitment
- Macrophages – *dominant role in wound healing*; release important growth factors (PDGF) and cytokines (IL-1 and TNF-α)

GROWTH AND ACTIVATING FACTORS

- PDGF
  - *Key growth factor in wound healing*
  - Chemotactic and activates inflammatory cells (PMNs and macrophages)
  - Chemotactic and activates fibroblasts → collagen and ECM proteins
  - Angiogenesis
  - Epithelialization
  - Chemotactic for smooth muscle cells
  - Has been shown to accelerate wound healing
- EGF (epidermal growth factor)
  - Chemotactic and activates fibroblasts
  - Angiogenesis
  - Epithelialization
- FGF (fibroblastic growth factor)
  - Chemotactic and activates fibroblasts → collagen and ECM proteins
  - Angiogenesis
  - Epithelialization
- PAF (platelet-activating factor) – is not stored, generated by phospholipase in endothelium; is a phospholipid
  - Chemotactic for inflammatory cells; ↑ adhesion molecules
  - Activates platelets
- Chemotactic factors
  - For inflammatory cells – PDGF, IL-8, LTB-4, C5a and C3a, PAF; TNF-alpha, IL-1
  - For fibroblasts – PDGF, EGF, FGF
- Angiogenesis factors – hypoxia (#1), PDGF, EGF, FGF, IL-8
- Epithelialization factors – PDGF, EGF, FGF
- PMNs – last 1–2 days in tissues (7 days in blood)
- Platelets – last 7–10 days
- Lymphocytes – involved in chronic inflammation (T cells) and antibody production (B cells)
- TXA_2 and PGI_2 – see Chapter 2 (Hematology)
- TGF-beta – immunosuppressive

TYPE I HYPERSENSITIVITY REACTIONS

- Mast cells – primary cell in type I hypersensitivity reactions
  - Main source of histamine in tissues
- Basophils
  - Main source of histamine in blood; not found in tissue
- Histamine – vasodilation, tissue edema, postcapillary leakage
  - Primary effector in type I hypersensitivity reactions (allergic reactions)
- Bradykinin – peripheral vasodilation, increased permeability, pain, pulmonary vasoconstriction, bronchoconstriction; involved in angioedema
  - Angiotensin-converting enzyme (ACE) – inactivates bradykinin; located in lung

NITRIC OXIDE (NO)

- Has arginine precursor (substrate for nitric oxide synthase)
- NO activates guanylate cyclase and increases cGMP, resulting in vascular smooth muscle dilation
- Is also called endothelium-derived relaxing factor
- Endothelin – causes vascular smooth muscle constriction (opposite effect of nitric oxide)

IMPORTANT CYTOKINES

- Main initial cytokine response to injury and infection is release of TNF-α and IL-1
- Initiates the inflammatory cascade
- Tumor necrosis factor-alpha (TNF-α)
  - Macrophages – largest producers of TNF
  - Increases adhesion molecules
  - Overall, a procoagulant
  - Causes cachexia in patients with cancer
  - Activates neutrophils and macrophages → more cytokine production, cell recruitment
  - High concentrations of TNF-α can cause systemic inflammatory response syndrome (SIRS), shock, and multisystem organ failure (MSOF)
- IL-1
  - Main source also macrophages; effects similar to TNF-α and synergizes TNF-α
  - Responsible for fever (PGE_2 mediated in hypothalamus)
    - Raises thermal set point, causing fever
    - NSAIDs decrease fever by reducing PGE_2 synthesis
  - Alveolar macrophages – cause fever with atelectasis by releasing IL-1
- IL-6 – increases hepatic acute phase proteins (C-reactive protein, amyloid A)
- IL-8 – PMN chemotaxis, angiogenesis
- IL-10 – decreases the inflammatory response

INTERFERONS

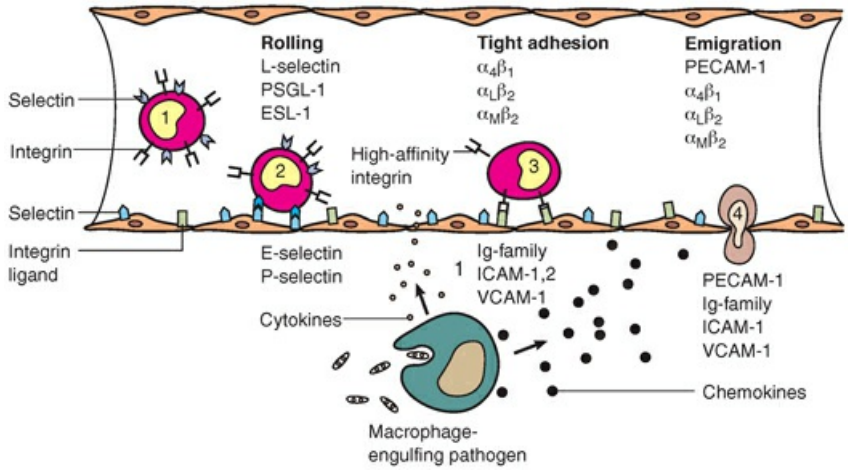
- Released by lymphocytes in response to viral infection or other stimulants
- Activate macrophages, natural killer cells, and cytotoxic T cells
- Inhibit viral replication

HEPATIC ACUTE PHASE RESPONSE PROTEINS

- IL-6 – most potent stimulus
- *Increased* – C-reactive protein (an opsonin, activates complement), amyloid A and P, fibrinogen, haptoglobin, ceruloplasmin, alpha-1 antitrypsin, and C3 (complement)
- *Decreased* – albumin, pre-albumin, and transferrin

CELL ADHESION MOLECULES

- Selectins – L-selectins, located on leukocytes, bind to E- (endothelial) and P- (platelets) selectins; rolling adhesion
- Beta-2 integrins (CD 11/18 molecules) – on leukocytes; bind ICAMs, etc., anchoring adhesion
- ICAM, VCAM, PECAM, ELAM – on endothelial cells, bind beta-2 integrin molecules located on leukocytes and platelets. These are also involved in transendothelial migration (diapedesis)



Leukocyte recruitment. (1) Circulating leukocytes express integrins in a low-affinity conformation. (2) Exposure to activated endothelium leads to rolling, which is mediated by L-selectin and P-selectin on the neutrophil and E-selectin on the endothelium. (3) Leukocyte exposure to cytokines released by macrophages phagocytosing pathogens induces a high-affinity integrin conformation. Tight leukocyte—endothelial adhesion involves integrin engagement with counter-ligand expressed on the endothelium. (4) Subsequent exposure to chemokines leads to diapedesis, which is further mediated by the family of β_1- and β_2-integrins.

COMPLEMENT

- Classic pathway (IgG or IgM) – antigen–antibody complex activates
  - Factors C1, C2, and C4 – found only in the classic pathway
- Alternative pathway – endotoxin, bacteria, other stimuli activate
  - Factors B, D, and P (properdin) – found only in the alternate pathway
- C3 – common to and is the convergence point for both pathways
- Mg – required for both pathways
- Anaphylatoxins – C3a, C4a, C5a; ↑ vascular permeability, bronchoconstriction; activate mast cells and basophils
- Membrane attack complex – C5b, C6b, C7b, C8b, C9b; causes cell lysis (usually bacteria)

by creating a hole in the cell membrane
- Opsonization (targets antigen for immune response) – C3b and C4b
- Chemotaxis for inflammatory cells – C3a and C5a

PROSTAGLANDINS

- Cyclooxygenase pathway (platelets and endothelium-derived)
- Produced from arachidonic precursors
- PGI_2 and PGE_2 – vasodilation, bronchodilation, ↑ permeability; inhibit platelets
- NSAIDs – inhibit cyclooxygenase (reversible)
- Aspirin – inhibits cyclooxygenase (irreversible), inhibits platelet adhesion by decreasing TXA_2
- Steroids – inhibit phospholipase, which converts phospholipids to arachidonic acid → inhibits inflammation

LEUKOTRIENES

- Lipoxygenase pathway (leukocyte-derived)
- Produced from arachidonic precursors
- LTC_4, LTD_4, LTE_4 – slow-reacting substances of anaphylaxis; bronchoconstriction, vasoconstriction followed by increased permeability (wheal and flare)
- LTB_4 – chemotactic for inflammatory cells

CATECHOLAMINES

- Peak 24–48 hours after injury
- Norepinephrine released from sympathetic postganglionic neurons
- Epinephrine and norepinephrine released from adrenal medulla (neural response to injury)

MISCELLANEOUS

- Neuroendocrine response to injury – afferent nerves from site of injury stimulate CRF, ACTH, ADH, growth hormone, epinephrine, and norepinephrine release
- Thyroid hormone – does ***not*** play a major role in injury or inflammation
- CXC chemokines – chemotaxis, angiogenesis, wound healing
  - IL-8 and platelet factor 4 are CXC chemokines
  - C = cysteine; X = another amino acid
- Oxidants generated in inflammation (oxidants/main producer oxidase):

Superoxide anion radical (O_2^-)	NADPH oxidase
Hydrogen peroxide (H_2O_2)	Xanthine oxidase

- Cellular defenses against oxidative species (oxidants/defense):

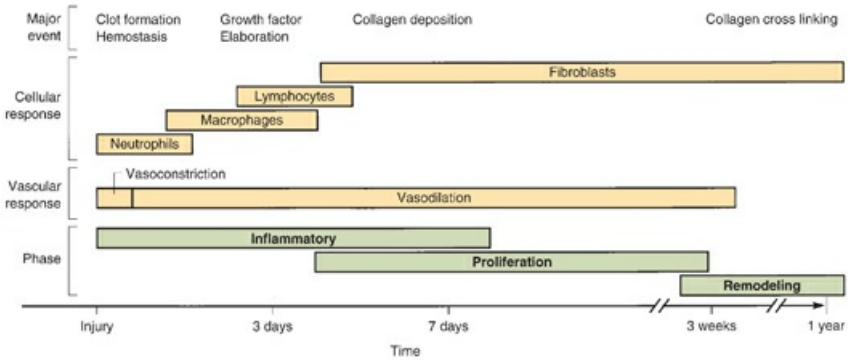
Superoxide anion radical	**Superoxide dismutase*
Hydrogen peroxide	*Glutathione peroxidase, catalase*

- Reperfusion injury – PMNs are the primary mediator
- Chronic granulomatous disease – NADPH-oxidase system enzyme defect in PMNs
  - Results in ↓ superoxide radical (O_2^-) formation
- Primary mechanism of injury for oxygen radicals – DNA damage
- Respiratory burst (macrophages and PMNs) – release of superoxide anion and hydrogen peroxide

14 Wound Healing

WOUND HEALING

- Inflammation (days 1–10) – PMNs, macrophages: TNF-alpha, IL-1, PDGF
- Proliferation (5 days–3 weeks) – fibroblasts (deposit collagen), neovascularization, granulation tissue formation; type III collagen replaced with type I; epithelialization (1–2 mm/day); PDGF, FGF, EGF
- Remodeling (3 weeks–1 year) – decreased vascularity
  - Net amount of collagen does not change with remodeling, although significant production and degradation occur
  - Collagen cross-linking occurs
- Peripheral nerves regenerate at 1 mm/day
- Order of cell arrival in wound
  - Platelets
  - PMNs
  - Macrophages
  - Lymphocytes (recent research shows arrival before fibroblasts)
  - Fibroblasts



Timeline of phases of wound healing with dominant cell types and major physiologic events.

- *Macrophages are essential for wound healing (release of growth factors, cytokines, etc.)*
- Fibronectin – produced by fibroblasts; chemotactic for macrophages; anchors fibroblasts
- Provisional matrix – mostly fibronectin and hyaluronic acid
- Fibroblasts – replace fibronectin-fibrin with collagen
- Predominant cell type by day
  - Days 0–2 – PMNs
  - Days 3–4 – macrophages
  - Days 5 and on – fibroblasts
- Platelet plug – platelets and fibrin
- Accelerated wound healing – reopening a wound results in quicker healing the 2nd time (as healing cells are already present there)
- Epithelial integrity – most important factor in healing open wounds (secondary intention)

- Migration from hair follicles (#1 site), wound edges, and sweat glands
- Dependent on granulation tissue in wound
- Unepithelialized wounds leak serum and protein, promote bacteria

- Tensile strength – most important factor in healing closed incisions (primary intention)
  - Depends on collagen deposition and cross-linking of collagen
- Suture removal
  - Face – 1 week
  - Other areas – 2 weeks
- Delayed primary closure – thought to prevent wound infection; risk of abscess formation after closure
- Submucosa – strength layer of bowel
  - Weakest time point for small bowel anastomosis – 3–5 days
- Myofibroblasts (smooth muscle cell–fibroblast; communicate by gap junctions)
  - Involved in wound contraction and healing by secondary intention
  - Perineum has better wound contraction than leg

Collagen Subtypes

Type	Description
I	Most common type of collagen: skin, bone, and tendons Primary collagen in a healed wound
II	Cartilage
III	Increased in healing wound, also in blood vessels and skin
IV	Basement membranes
V	Widespread, particularly found in the cornea

- Alpha-ketoglutarate, vitamin C, oxygen, and iron are required for collagen synthesis; includes hydroxylation (prolyl hydroxylase) and subsequent cross-linking of proline residues in collagen
  - Collagen has proline every 3rd amino acid
  - Proline cross-linking improves wound tensile strength
- Scurvy – vitamin C deficiency
- Zinc – important for many enzyme reactions involved in wound healing
- Tensile strength never equal to pre-wound (80%)
  - Type III collagen – predominant collagen type synthesized during proliferation
  - Type I collagen – predominant collagen type synthesized during remodeling
  - Type III replaced by type I collagen by 3 weeks
    - At 8 weeks, wound reaches maximum tensile strength, which is 80% of its original strength
    - Maximum collagen accumulation at 3 weeks → after that the amount of collagen stays the same, but continued cross-linking improves strength
    - d-Penicillamine – inhibits collagen cross-linking
- Essentials for wound healing
  - Moist environment (avoid desiccation)
  - Oxygen delivery – optimize fluids, no smoking, pain control, arterial revascularization, supplemental oxygen
    - Want transcutaneous oxygen measurement (TCOM) > 25 mm Hg
  - Avoid edema – leg elevation

- Remove necrotic tissue
- Impediments to wound healing
  - Bacteria > $10^5/cm^2$ – ↓ oxygen content, collagen lysis, prolonged inflammation
  - Devitalized tissue and foreign bodies – retards granulation tissue formation and wound healing
  - Cytotoxic drugs – 5FU, methotrexate, cyclosporine, FK-506, etc. can impair wound healing in 1st 14 days after injury
  - Diabetes – can contribute to poor wound healing by impeding the early-phase inflammation response (hyperglycemia causes poor leukocyte chemotaxis)
  - Albumin < 3.0 – risk factor for poor wound healing
  - Steroids – prevent wound healing by inhibiting macrophages, PMNs, and collagen synthesis by fibroblasts; ↓ wound tensile strength as well
    - Vitamin A (25,000 IU qd) – counteracts effects of steroids on wound healing
  - Wound ischemia (hypoxia) – can be caused by fibrosis, pressure (sacral decubitus ulcer, pressure sores), poor arterial inflow (atherosclerosis), poor venous outflow (venous stasis), smoking, radiation, edema, vasculitis
- Diseases associated with abnormal wound healing
  - Osteogenesis imperfecta – type I collagen defect
  - Ehlers–Danlos syndrome – 10 types identified, all collagen disorders
  - Marfan's syndrome – fibrillin defect (connective tissue protein)
  - Epidermolysis bullosa – excessive fibroblasts. Tx: phenytoin
  - Scurvy – Vitamin C deficiency
  - Pyoderma gangrenosum – Tx: steroids
- Wound dehiscence – leakage of large amounts of pink "salmon-colored" fluid from wound; if left alone, can result in evisceration
  - Risk factors – deep wound infection (#1); poor nutrition, COPD, DM, coughers
  - Tx: place retention sutures
- Diabetic foot ulcers – usually at Charcot's joint (2nd MTP joint); secondary to neuropathy (can't feel feet, pressure from walking leads to ischemia); also on heel
- Leg ulcers – 90% due to venous insufficiency; Tx - Unna boot (elastic wrap)
- Scars – contain a lot of proteoglycans, hyaluronic acid, and water
  - Scar revisions – wait for 1 year to allow maturation; may improve with age
  - Infants heal with little or no scarring
- Cartilage – contains no blood vessels (get nutrients and oxygen by diffusion)
- Denervation – has no effect on wound healing
- Chemotherapy – has no effect on wound healing after 14 days
- Keloids – autosomal dominant; dark skinned
  - Collagen goes beyond original scar; from failure of collagen breakdown
  - Tx: intra-lesion steroid injection; silicone, pressure garments, XRT
- Hypertrophic scar tissue – dark skinned; flexor surfaces of upper torso
  - Collagen stays within confines of original scar
  - Often occurs in burns or wounds that take a long time to heal
  - Tx: steroid injection, silicone, pressure garments

PLATELET GRANULES

- Alpha granules

    - Platelet factor 4 – aggregation
    - Coagulation factors V and VIII
    - vWF
    - Fibrinogen
    - Beta-thrombomodulin – binds thrombin
    - Platelet-derived growth factor (PDGF) – chemoattractant
    - Transforming growth factor beta (TGF-beta) – modulates above responses
- Dense granules – contain adenosine, serotonin, and calcium
- Platelet aggregation factors – TXA_2, thrombin, platelet factor 4

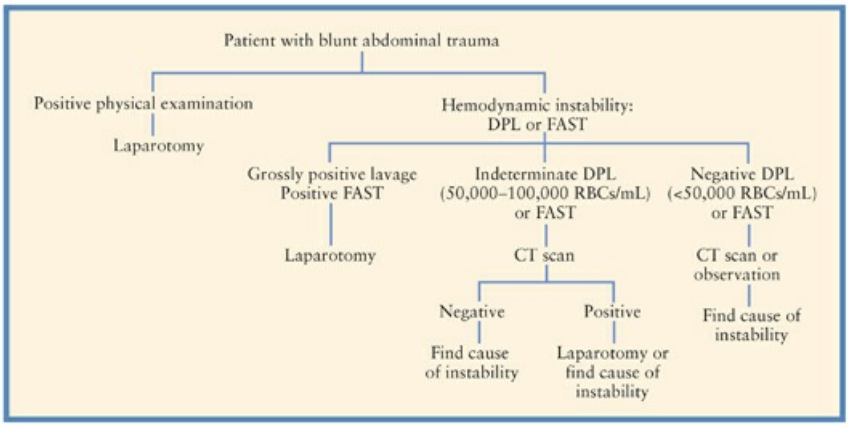
15 Trauma

TRAUMA STATISTICS/EARLY ISSUES

- 1st peak for trauma deaths (0–30 minutes) – deaths due to lacerations of heart, aorta, brain, brainstem, or spinal cord; cannot really save these patients; death is too quick
- 2nd peak for trauma deaths (30 minutes–4 hours) – deaths due to head injury (#1) and hemorrhage (#2); these patients can be saved with rapid assessment (golden hour)
- 3rd peak for trauma deaths (days to weeks) – deaths due to multisystem organ failure and sepsis
- Blunt injury – 80% of all trauma; liver most commonly injured (some texts say spleen)
  - Kinetic energy = ½ MV^2, where M = mass, V = velocity
  - Falls – age and body orientation biggest predictors of survival. LD_{50} is 4 stories
- Penetrating injury – small bowel most commonly injured (some texts say liver)
- Hemorrhage – most common cause of death in 1st hour
  - Blood pressure is usually OK until 30% of total blood volume is lost
  - Resuscitate with 2 L Lactated Ringers, then switch to blood
- Head injury – most common cause of death after reaching the ER alive
- Infection – most common cause of death in the long term
- Tongue – most common cause of upper airway obstruction → perform jaw thrust
- Seat belts – small bowel perforations, lumbar spine fractures, sternal fractures
- Saphenous vein at ankle – best cutdown site for venous access if large bore IV and central access not possible
- Intra-osseous proximal tibia cannulation – preferred alternative route in children < 6
- Hemorrhagic shock – SBP < 90, HR > 100; pale, shivering, cold, clammy, anxious, poor urine output (< 0.5 cc/kg/hr)
- Single patient with visible bleeding source – apply local pressure (gloved finger/hand) until definitive management
- Massive civilian casualties with visible bleeding sources – apply tourniquets until definitive management (health care provider can treat multiple patients)
- Acute traumatic coagulopathy/hemostatic resuscitation
  - Coagulopathy occurs in severely injured trauma patients *prior* to resuscitation and arriving at the hospital
    - Can result in massive transfusion; increases morbidity and mortality
    - Hemostatic resuscitation is indicated for patients receiving ≥ 4 units pRBCs in the *first hour or* ≥ 10 units pRBCs within 24 hours (approximate indications)
  - Hemostatic resuscitation – give RBCs:FFP:platelets in a ratio of 1:1:1
- Damage control surgery (for severely injured trauma patients)
  - Early control of bleeding (surgical and/or interventional) and contamination with *delay* in definitive surgery until patient is stabilized
  - Give blood products (hemostatic resuscitation) to ensure oxygenation and correct coagulopathy (*not give continued lactated Ringers*)

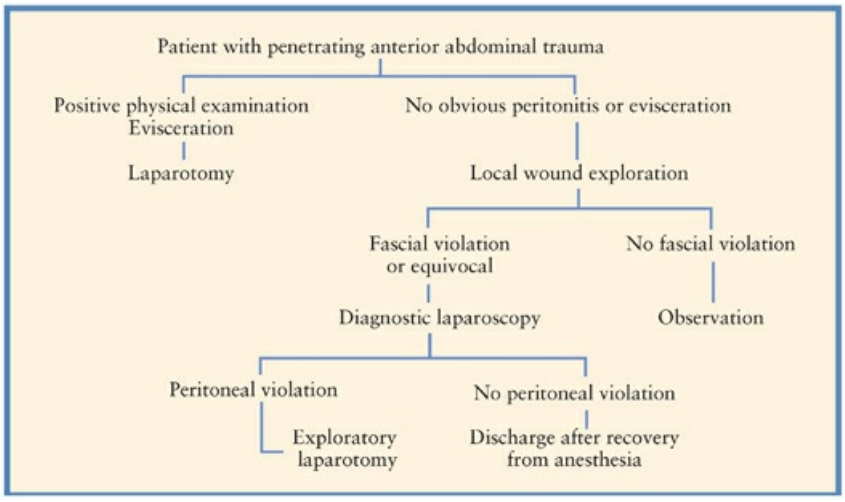
- *Limit crystalloid solutions* to avoid hemodilution (initial 2 L LR *only*)
- Allow permissive hypotension (SBP > 70) until hemorrhage controlled (after that want SBP > 90)
- Early correction of hypothermia/acidosis/hypocalcemia
- *Exceptions* – traumatic brain injury patients (want SBP > 90 initially)

- Prolonged abdominal surgery, multiple transfusions, now coagulopathic with hypothermia and acidosis – Tx: pack off bleeders, temporary abdominal closure, to ICU for resuscitation, warming, and correction of coagulopathy
- Diagnostic peritoneal lavage (DPL)
  - Used in hypotensive patients (SBP < 90) with blunt trauma
  - Positive if > 10 cc blood, > 100,000 RBCs/cc, food particles, bile, bacteria, > 500 WBC/cc
  - Need laparotomy if DPL is positive
  - DPL needs to be supraumbilical if pelvic fracture present
  - DPL misses – retroperitoneal bleeds, contained hematomas
- FAST scan (focused abdominal sonography for trauma)
  - Ultrasound scan used in lieu of DPL
  - Checks for blood in perihepatic fossa, perisplenic fossa, pelvis, and pericardium
  - Examiner dependent
  - Obesity can obstruct view
  - May not detect free fluid < 50–80 mL
  - Need laparotomy if FAST scan is positive
  - FAST scan misses – retroperitoneal bleeding, hollow viscous injury
- In hypotensive patients with a negative FAST scan (or negative DPL) you need to find the source of bleeding (pelvic fracture, chest, or extremity)
- Need a CT scan following blunt trauma in patients with abdominal pain, need for general anesthesia, closed head injury, intoxicants on board, paraplegia, distracting injury, or hematuria
  - Patients requiring DPL that turned out negative will need an abdominal CT scan
  - CT scan misses – hollow viscous injury, diaphragm injury
- Need exploratory laparotomy with peritonitis, evisceration, positive DPL, uncontrolled visceral hemorrhage, free air, diaphragm injury, intraperitoneal bladder injury, contrast extravasation from hollow viscus, specific renal, pancreas, biliary tract, and spleen and liver injuries



Diagnosis of blunt abdominal trauma.

- Penetrating abdominal injury (eg GSW) – requires exploratory laparotomy
  - Any entrance or exit wound below the nipple is considered to involve the abdomen
- Possible penetrating abdominal injuries (knife or low-velocity injuries) – local exploration in ED and observation if fascia not violated

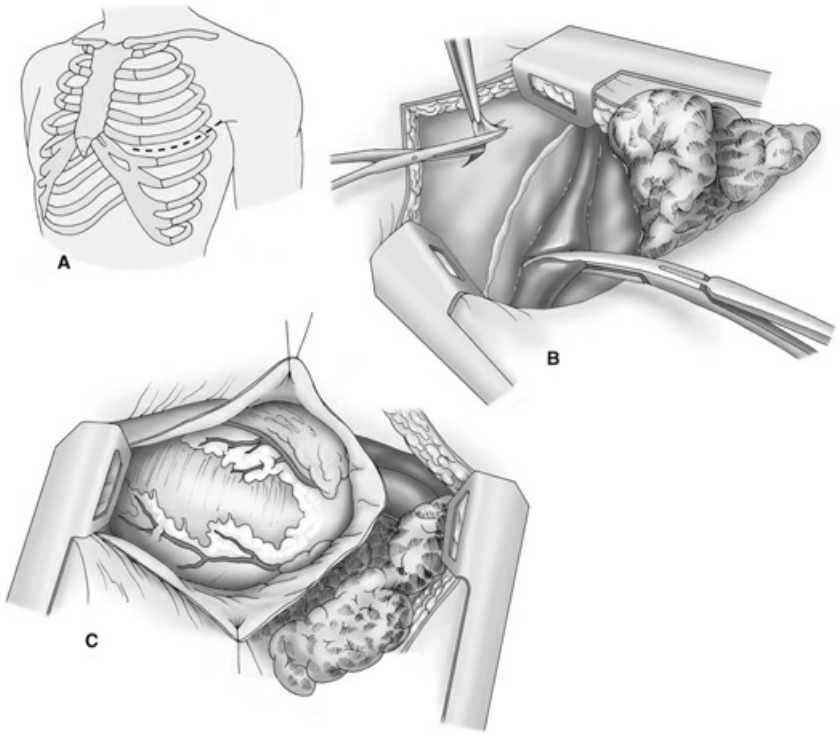


Diagnosis of low-velocity penetrating abdominal trauma.

- Abdominal compartment syndrome
  - Sx's – hypotension, distended abdomen, low urine output, increased airway pressures, prolonged transport time
  - Occurs after massive fluid resuscitation during the course of a prolonged laparotomy
  - Bladder pressure > 25–30 suggests compartment syndrome
  - IVC compression is the final common pathway for *decreased cardiac output*
  - Caused by swollen abdominal contents
  - Low cardiac output causes visceral and renal malperfusion (↓ urine output)
  - Upward displacement of diaphragm causes hypoxia
  - Tx: decompressive laparotomy
- Pneumatic antishock garment – controversial; use in patients with SBP < 50 and no thoracic injury. Release compartments one at a time after reaching ER
- ED thoracotomy
  - Blunt trauma – use only if pressure/pulse lost in ED (SBP < 60)
  - Penetrating trauma – use only if pressure/pulse lost on way to ED or in ED
  - Thoracotomy – open pericardium anterior to the phrenic nerve, cross-clamp the aorta, watch for the esophagus (anterior to the aorta)
- Catecholamines – peak 24–48 hours after injury
- ADH, ACTH, and glucagon – also ↑ after trauma (fight or flight response)
- Thyroid hormone not involved

BLOOD TRANSFUSION

- Type O blood (universal donor) – contains no A or B antigens; males can receive Rh-positive blood; females who are prepubescent or of childbearing age should receive Rh-negative blood
- Type-specific blood (nonscreened, non–cross-matched) – can be administered relatively safely, but there may be effects from antibodies to HLA minor antigens in the donated blood



A. Emergency department thoracotomies are performed through the fourth and fifth intercostal spaces using the anterolateral approach. B. If the thoracotomy is performed for abdominal injury, the descending thoracic aorta is clamped. If blood pressure improved to > 70 mm Hg, the patient is transported to the operating room for laparotomy. For patients in whom blood pressure does not reach 70 mm Hg, further treatment is futile. If the thoracotomy is performed for a cardiac injury, the pericardium is opened longitudinally and anterior to the phrenic nerve. C. The heart can then be rotated out of the pericardium for repair. (From Johnson JL, Moore EE. Thoracic trauma. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

HEAD INJURY

- Glasgow Coma Scale (GCS)
  - Motor
    - 6 – follows commands
    - 5 – localizes pain
    - 4 – withdraws from pain
    - 3 – flexion with pain (decorticate)
    - 2 – extension with pain (decerebrate)
    - 1 – no response
  - Verbal
    - 5 – oriented
    - 4 – confused
    - 3 – inappropriate words
    - 2 – incomprehensible sounds
    - 1 – no response
  - Eye opening
    - 4 – spontaneous opening

    - 3 – opens to command
    - 2 – opens to pain
    - 1 – no response
- GCS score – ≤ 14: head CT; ≤ 10: intubation; ≤ 8: ICP monitor
- Most important prognostic indicator – motor score

Indications for Head CT

- Suspected skull penetration by a foreign body
- Discharge of cerebrospinal fluid (CSF), blood, or both from the nose
- Hemotympanum or discharge of blood or CSF from the ear
- Head injury with alcohol or drug intoxication
- Altered state of consciousness at the time of examination
- Focal neurologic signs or symptoms
- Any situation precluding proper surveillance (eg going to the OR)
- Head injury plus additional trauma
- Loss of consciousness at any point

- Penetrating injury has worst survival of all head injuries
- Intubated patients get a score of 1T for verbal
- Neurologic damage in trauma can be caused by the initial blow, subsequent hematoma, and later brain swelling
- Epidural hematoma – most commonly due to arterial bleeding from the middle meningeal artery
    - Head CT – shows lenticular (lens-shaped) deformity
    - Patients often have loss of consciousness (LOC) → then lucid interval (awake) → then sudden deterioration (vomiting, restlessness, LOC)
    - Craniotomy for significant neurologic deterioration or shift > 5 mm
- Subdural hematoma – most commonly from tearing of venous plexus (bridging veins) that cross between the dura and arachnoid
    - Head CT – shows crescent-shaped deformity
    - Craniotomy for significant neurologic deterioration or shift > 5 mm
    - Chronic subdural hematomas – usually in elderly after minor fall or severe alcoholics; mental status deteriorates over days to weeks as hematoma forms
- Intracerebral hematoma – usually frontal or temporal
    - Can cause significant mass effect requiring operation
- Cerebral contusions – can be coup or contrecoup
- Traumatic intraventricular hemorrhage – need ventriculostomy if causing hydrocephalus
- Diffuse axonal injury – shows up better on MRI than CT scan
    - MRI – blurring of gray-white matter; multiple small punctate hemorrhages
    - Tx: supportive; may need craniectomy if refractory ICP elevation
    - Very poor prognosis
- Cerebral perfusion pressure (CPP = MAP – ICP)
    - CPP = mean arterial pressure (MAP) *minus* intracranial pressure (ICP)
    - Signs of elevated ICP – ↓ ventricular size, loss of sulci, loss of cisterns
    - Reduced CPP results in secondary traumatic brain injury
    - ICP monitors – indicated for GCS ≤ 8, suspected ↑ ICP, or patient with moderate to

severe head injury and inability to follow clinical exam (eg is intubated)
    - Supportive treatment for elevated ICP
        - Normal ICP is 10; > 20 needs treatment
        - Want CPP > 60 (give volume and pressors [eg phenylephrine] to improve MAP)
        - Sedation and paralysis (decrease brain activity and oxygen demand)
        - Raise head of bed (lowers ICP)
        - Relative hyperventilation for modest cerebral vasoconstriction (keep CO_2 30–35); do not want to over-hyperventilate and cause cerebral ischemia from too much vasoconstriction
        - Keep Na 140–150, serum Osm 295–310 – may need to use <u>hypertonic saline</u> at times (draws fluid out of brain)
        - Mannitol – load 1 g/kg, give 0.25 mg/kg q4h after that (draws fluid from brain)
        - Barbiturate coma – consider if above not working
        - Ventriculostomy w/ CSF drainage (keep ICP < 20)
        - Craniotomy decompression – if not able to get ICP down medically (can also perform Burr hole)
        - Fosphenytoin or Keppra – can be given prophylactically to prevent seizures with moderate to severe head injury
        - Peak ICP (max brain swelling) – occurs 48–72 hours after injury
        - Cushing's triad – bradycardia, HTN, low respiratory rate
        - Intermittent bradycardia is a sign of impending herniation
- Dilated pupil (blown pupil)
    - Possible ipsilateral temporal lobe pressure on CN III (oculomotor)
    - Blown pupil and patient stable – get head CT (patient may have baseline anisocoria)
    - Blown pupil and patient unstable – address hypotension before getting head CT (eg go to the OR for significant abdominal bleeding; angiography for significant pelvic bleeding); consider Burr hole if not able to make it to head CT for awhile
- Basal skull fractures
    - Raccoon eyes (peri-orbital ecchymosis) – anterior fossa fracture
    - Battle's sign (mastoid ecchymosis) – middle fossa fracture; can injure facial nerve (CN VII)
        - If acute facial nerve injury, need exploration and repair
        - If delayed, likely secondary to edema and exploration not needed
    - Can also have hemotympanum and CSF rhinorrhea/otorrhea with basal skull fractures
    - <u>*Avoid*</u> nasotracheal intubation in these patients
- Temporal skull fractures – can injure CN VII and VIII (vestibulocochlear nerve)
    - Most common site of facial nerve injury – *geniculate ganglion*
    - Temporal skull fractures most commonly associated with lateral skull or orbital blows
- Most skull fractures do <u>not</u> require surgical treatment
    - Operate if significantly depressed (> 1 cm), contaminated (open fracture), or persistent CSF leak not responding to conservative therapy (close dura)
- CSF leaks after skull fracture – treat expectantly; can use lumbar CSF drainage if persistent
- Coagulopathy with traumatic brain injury – due to release of tissue thromboplastin
- Head trauma and on Coumadin – repeat head CT in 8 hours (can have delayed bleeds)
- Hypovolemic shock cannot occur from intracranial bleeding alone – need to look for another source or the patient has neurogenic shock

SPINE TRAUMA

- The higher the spine injury, the greater the morbidity and mortality
- Screening for spine injury – CT scan
- Significant head injury – need to assess C-spine
- Best indication for steroids with spine injury – worsening deficit
- Cervical spine (MC spine injury)
  - C-1 burst (Jefferson fracture) – caused by axial loading
    - Tx: rigid collar
  - C-2 hangman's fracture – caused by distraction and extension
    - Tx: traction and halo
  - C-2 odontoid fracture
    - Type I – above base, stable
    - Type II – at base, unstable (will need fusion or halo)
    - Type III – extends into vertebral body (will need fusion or halo)
  - Facet fractures or dislocations – can cause cord injury; usually associated with hyperextension and rotation with ligamentous disruption
  - Dens = odontoid process
- Thoracolumbar spine
  - 3 columns of the thoracolumbar spine:
    - Anterior – anterior longitudinal ligament and anterior ½ of the vertebral body
    - Middle – posterior ½ of the vertebral body and posterior longitudinal ligament
    - Posterior – facet joints, lamina, spinous processes, interspinous ligament
  - If more than 1 column is disrupted, the spine is considered unstable
    - Compression (wedge) fractures usually involve the anterior column only and are considered stable (Tx: TLSO brace)
    - Burst fractures are considered unstable (anterior and middle; > 1 column) and require spinal fusion
  - Upright fall – at risk for calcaneus, lumbar, and wrist/forearm fractures
- Need MRI for neurologic deficits without bony injury to check for ligamentous injury
- MRI also indicated for prevertebral soft tissue swelling without bony injury
- Indications for emergent surgical spine decompression
  - Fracture or dislocation not reducible with distraction
  - Open fractures
  - Soft tissue or bony compression of the cord
  - Progressive neurologic dysfunction

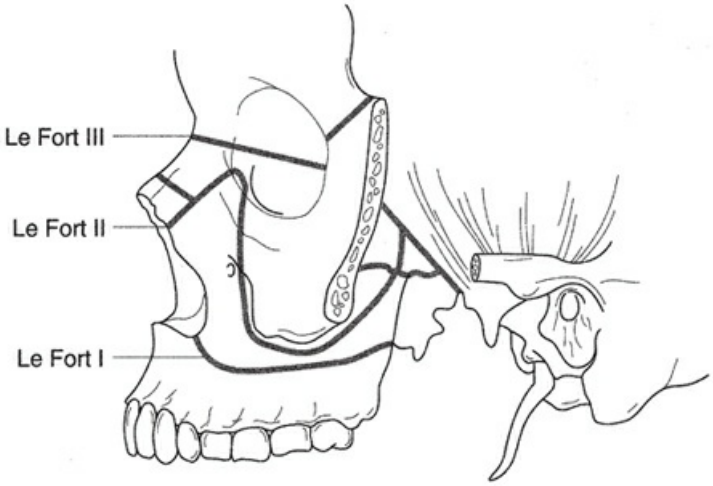
MAXILLOFACIAL TRAUMA

- Fracture of temporal bone is the most common cause of facial nerve injury (at the geniculate ganglion)
- Try to preserve skin and not trim edges with facial lacerations

Le Fort Classification of Facial Fractures

Type	Description	Treatment
I	Maxillary fracture straight across (–)	Reduction, stabilization, intramaxillary fixation (IMF) ± circumzygomatic and orbital rim suspension wires

II	Lateral to nasal bone, underneath eyes, diagonal toward maxilla (/ \)	Same as Le Fort I
III	Lateral orbital walls (- -)	Suspension wiring to stable frontal bone; may need external fixation



Le Fort classification system of maxillofacial fractures.

- Nasoethmoidal orbital fractures – 70% have a CSF leak (tau protein)
  - Conservative therapy for up to 2 weeks
  - Can try epidural catheter to ↓ CSF pressure and help it close CSF leak
  - May need surgical closure of dura to stop leak
- Nosebleeds
  - Anterior – packing
  - Posterior – can be hard to deal with; try balloon tamponade 1st
    - May need angioembolization of internal maxillary artery or ethmoidal artery
- Orbital blowout fractures – patients with impaired upward gaze or diplopia with upward vision need repair; perform restoration of orbital floor with bone fragments or bone graft
- Mandibular injury – malocclusion #1 indicator of injury
  - Diagnosis – fine-cut facial CT scans with reconstruction to assess injury
  - Most repaired with IMF (metal arch bars to upper and lower dental arches, 6–8 weeks) or open reduction and internal fixation (ORIF)
- Tripod fracture (zygomatic bone) – ORIF for cosmesis
- Patients w/ maxillofacial fractures are at high risk for cervical spine injuries
- Scalp lacerations – hair removal is generally <u>not</u> necessary

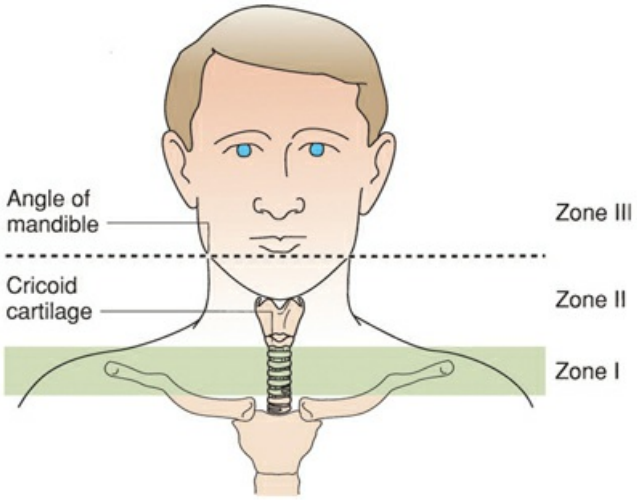
NECK TRAUMA

- Asymptomatic blunt – neck CT scan (include C-spine assessment)
- Asymptomatic penetrating – controversial; most common method below

Neck Zones

Zone	Asymptomatic Work-up
I	Clavicle to cricoid cartilage. *Need angiography, bronchoscopy, esophagoscopy, and water-soluble contrast swallow (followed by barium if negative)*; a pericardial window may be indicated. If surgery required, a median sternotomy is needed to reach these lesions
II	Cricoid to angle of mandible. *Need neck exploration in OR for all*

III	Angle of mandible to the base of skull. *Need angiography and laryngoscopy*. If surgery required, may need jaw subluxation/digastric and sternocleidomastoid muscle release/mastoid sinus resection to reach vascular injuries in this location



Zones of the neck. Zone I is the cricoid cartilage to the top of the clavicles. The important implication of a zone I injury is the greater potential for intrathoracic great vessel injury.

- Symptomatic blunt or penetrating neck trauma (Sx's – shock, bleeding, expanding hematoma, losing or lost airway, subcutaneous air, stridor, dysphagia, hemoptysis, neurologic deficit) → *all need exploration (use approaches listed above)*
- Esophageal injury
  - *Hardest neck injury to find*
  - Esophagoscopy and esophagogram – best combined modality (find essentially 95% of injuries when using both methods)
  - Contained injuries – can be observed
  - Noncontained injuries (ie can't repair):
    - If small injury and minimal contamination → primary closure
    - If extensive injury or contamination →
    - Neck esophageal injuries – just place drains (will heal)
    - Chest esophageal injuries – chest tubes to drain injury and place spit fistula in neck (will eventually need esophagectomy)
  - Always drain esophageal and hypopharyngeal repairs – 20% leak rate
  - Approach to esophageal injuries
    - Neck – left side
    - Upper ⅔ of thoracic esophagus – right thoracotomy (avoids aorta)
    - Lower ⅓ of thoracic esophagus – left thoracotomy (left-sided course)
- Laryngeal fracture and tracheal injuries
  - These are airway emergencies
  - Symptoms: crepitus, stridor, respiratory compromise
  - Need to secure airway emergently in ER (cricothyroidotomy usual)
  - Tx: primary repair, can use strap muscle for airway support; tracheostomy necessary for most to allow edema to subside and to check for stricture (need to convert cricothyroidotomy to tracheostomy)
- Thyroid gland injuries – control bleeding (suture ligate) and drain (not thyroidectomy)
- Recurrent laryngeal nerve injury – can try to repair or can reimplant in cricoarytenoid

muscle (Sx – hoarseness)

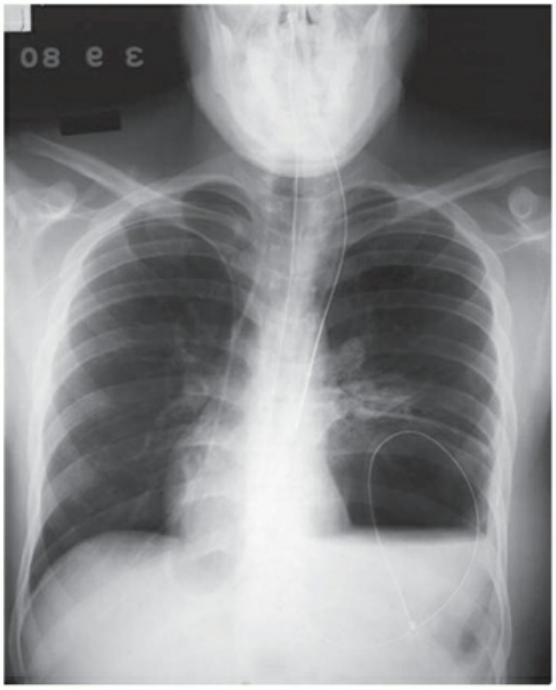
- Shotgun injures to neck – need angiogram and neck CT; esophagus/trachea evaluation
- Vertebral artery bleeds – can embolize or ligate without sequela in majority
- Common carotid bleeds – ligation will cause stroke in 20%
- Expanding neck hematoma – can compromise airway
- Cricothyroidotomy – indicated if usual intubation cannot be accomplished (eg severe maxillofacial trauma, airway foreign body, severe laryngospasm) and patient has impending loss of airway

CHEST TRAUMA

- Chest tube placement (for hemothorax)
  - > 1,000–1,500 cc after initial insertion, > 250 cc/h for 3 hours, > 2,500 cc/24 h, or bleeding with instability → all relative indications for thoracotomy in OR (anterolateral on side of injury; keep patient supine)
  - Need to drain all of the blood (in < 48 hours) to prevent fibrothorax, pulmonary entrapment, infected hemothorax, and empyema
  - Unresolved hemothorax after 2 well-placed chest tubes → thoracoscopic drainage
  - Most important RF for empyema – retained hemothorax
- Persistent pneumothorax despite 2 well-placed chest tubes – Dx: bronchoscopy (look for mucus plug or tracheobronchial injury)
- Multiple painful rib fractures – consider local nerve block and thoracic epidural to prevent splinting and hypoxia (especially in elderly; also prevents atelectasis and pneumonia)
- Sucking chest wound (open pneumothorax)
  - Needs to be at least ⅔ the diameter of the trachea to be significant
  - Cover wound with dressing that has tape on three sides → prevents development of tension pneumothorax while allowing lung to expand with inspiration
- Flail chest – ≥ 2 consecutive ribs broken at ≥ 2 sites → results in paradoxical motion
  - Underlying pulmonary contusion – biggest pulmonary impairment
- Pulmonary contusion – very sensitive to fluid overload; need judicious use of fluids/diuretics after resuscitation period to prevent further pulmonary dysfunction
  - Deteriorating blood gases and lung opacities can occur up to 48 hours after initial trauma
- Tracheobronchial injury
  - MC with blunt trauma
  - Sx's – large continuous air-leak; large pneumomediastinum, persistent pneumothorax, subcutaneous air
  - Patient may have worse oxygenation after chest tube placement
  - One of the very few indications in which clamping the chest tube may be indicated
  - Bronchus injuries are more common on the right
  - May need to mainstem intubate patient on unaffected side
  - Dx: bronchoscopy (90% are within 1 cm of the carina)
  - Tx: repair if large air leak and respiratory compromise, after 2 weeks of persistent air leak, if you can't get the lung up, or if the injury is > ⅓ the diameter of the trachea
  - Intubate with long, single-lumen tube to the unaffected side (*avoid* dual-lumen tube which can worsen injury)
  - Right thoracotomy for right mainstem, trachea, and proximal *left* mainstem injuries (avoids the aorta)

- Left thoracotomy for distal left mainstem injuries (rare injury)

- Esophageal injury – see section "Neck Trauma"; esophageal injuries are the hardest to Dx
- Diaphragm
  - Injuries are more likely to be found on left and to result from blunt trauma
  - CXR – see air–fluid level in chest from stomach herniation through hole (diagnosis can be made essentially with CXR)
  - Transabdominal approach if < 1 week
  - Chest approach if > 1 week (need to take down adhesions in the chest)
  - May need PTFE mesh (Gore-Tex)



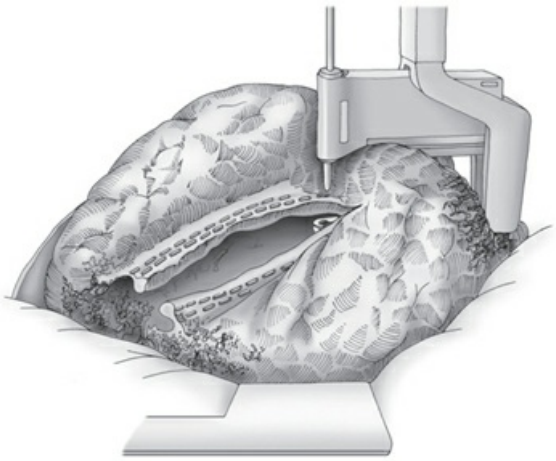
Chest roentgenogram demonstrating a nasogastric tube within the left chest. (From Thal ER, Friese RS. Traumatic rupture of the diaphragm. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

- Aortic transection
  - Signs – widened mediastinum, 1st or 2nd rib fractures, apical capping, loss of aortopulmonary window, loss of aortic contour, left hemothorax, trachea deviation to right, sternal fracture, scapular fracture
  - Tear is usually at the ligamentum arteriosum (just distal to left subclavian takeoff). Other areas include near the aortic valve and where the aorta traverses the diaphragm
  - Adventitial layer contains hematoma, although this can potentially rupture leading to exsanguination
  - CXR normal in 5% of patients with aortic tears – need aortic evaluation if significant mechanism (eg head on car crash > 45 mph, fall > 15 ft, other severe deceleration injuries)
  - Dx: CT angiogram of chest
  - Operative approach – place a covered stent endograft (majority repaired this way; distal transections only) or left thoracotomy and repair using partial left heart bypass
  - Important to treat other life-threatening injuries 1st → patient with positive DPL or other life-threatening injury needs to have that addressed before the aortic transection

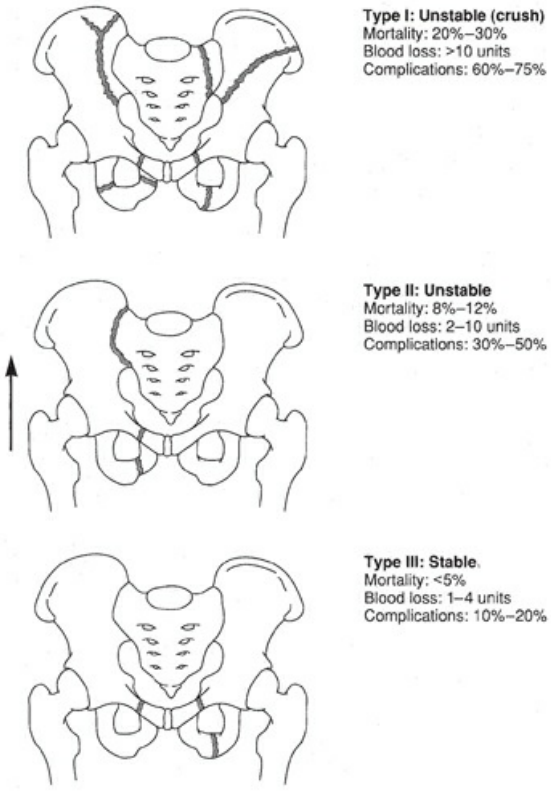
- Significant intracerebral hemorrhage is a contraindication to open repair
- Approach for specific injuries
  - Median sternotomy – for injuries to ascending aorta, innominate artery, proximal right subclavian artery, innominate vein, proximal left common carotid, proximal left subclavian artery (use trap-door incision through the left 2nd intercostal space)
  - Left thoracotomy – for injuries to distal left subclavian artery, descending aorta
  - Distal right subclavian artery – midclavicular incision, resection of medial clavicle
- Myocardial contusion – sternal fracture is a risk factor
  - V-tach and V-fib most common causes of death; risk highest in 1st 24 hours
  - Dx: EKG and troponins
  - Supra-ventricular tachycardia (SVT) – most common arrhythmia overall in these patients
  - Need telemonitoring for 24–48 hours
- Aspiration – may not produce CXR findings immediately
- Penetrating chest injury – start with a CXR if the patient is stable (place chest tube on side of injury for pneumothorax or hemothorax)
  - Penetrating "box" injuries – borders are clavicles, xiphoid process, nipples
  - Need pericardial window, bronchoscopy, esophagoscopy, barium swallow
  - Possible angiogram for high chest or low zone I neck injuries
  - Penetrating chest wound outside "box" without pneumothorax or hemothorax
    - Need chest tube if patient requires intubation
    - Otherwise follow patient's serial CXRs
  - Pericardial window – if you find blood, need median sternotomy to fix possible injury to heart or great vessels; place pericardial drain
  - Penetrating injuries anterior-medial to midaxillary line and below nipples
    - Need laparotomy or laparoscopy
    - May also need evaluation for penetrating "box" injury depending on the exact location
  - Some are using FAST scan of the pericardium instead of pericardial window for "box" injuries
- Traumatic causes of cardiogenic shock – cardiac tamponade, cardiac contusion, tension pneumothorax
- Tension pneumothorax (one way valve effect causes air entry and pressure build up)
  - Hypotension, ↑ airway pressures, ↓ breath sounds, bulging neck veins, tracheal shift
  - BP can worsen with intubation
  - Can see bulging diaphragm during laparotomy
  - Cardiac compromise secondary to ↓ venous return to the right atrium (IVC, SVC compression)
  - Tx: chest tube (needle decompression an option if chest tube not available)
- Sternal fractures – these patients are at high risk for cardiac contusion
- 1st and 2nd rib fractures – high risk for aortic transaction

PELVIC TRAUMA

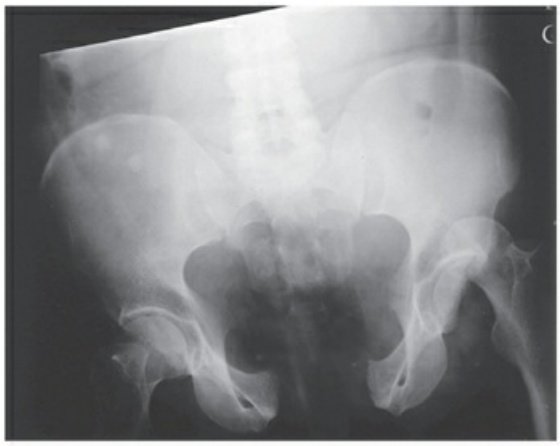
- Pelvic fractures can be a major source of blood loss.
- If hemodynamically unstable with pelvic fracture and negative DPL, negative CXR, and no other signs of blood loss or reasons for shock → stabilize pelvis (C-clamp, external fixator, or sheet) and go to angio for embolization



Pulmonary tractotomy. Dividing the pulmonary parenchyma between adjacent staple lines permits rapid direct access to injured vessels or bronchi along the tract of a penetrating injury. (From Johnson JL, Moore EE. Thoracic trauma. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)



Classification of pelvic fractures with relative stability, mortality rates, and blood loss indicated.



Wide pubic diastasis, characteristic of "open book" horizontally unstable pelvis (type B), with associated femoral head fracture and hip dislocation.

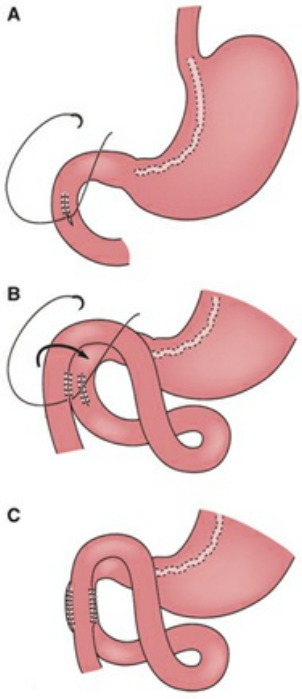
- These patients are at high risk for genitourinary and abdominal injuries
- Anterior pelvic fractures – more likely to have venous bleeding; MC source of bleeding (pelvic venous plexus); pelvic fixation will tamponade most pelvic venous bleeding
- Posterior pelvic fractures – more likely to have arterial bleeding
- May need colostomy for open pelvic fractures with rectal tears and perineal lacerations
- Pelvic fracture repair itself may need to be delayed until other associated injuries are repaired
- Intra-op penetrating injury pelvic hematomas – open (some suggest going to angiography for these)
- Intra-op blunt injury pelvic hematomas – leave; if expanding or patient unstable → stabilize pelvic fracture, pack pelvis if in OR, and go to angiography for embolization; if packs are placed intra-op, remove after 24–48 hours when patient is stable
- Severe pelvic trauma requires proctoscopy and retrograde cystourethrogram to look for injuries; also need vaginal exam in women
- Isolated anterior ring fracture with minimal sacral-iliac displacement – Tx: weight bearing as tolerated
- MC associated injury with pelvic fracture – head injury

DUODENAL TRAUMA

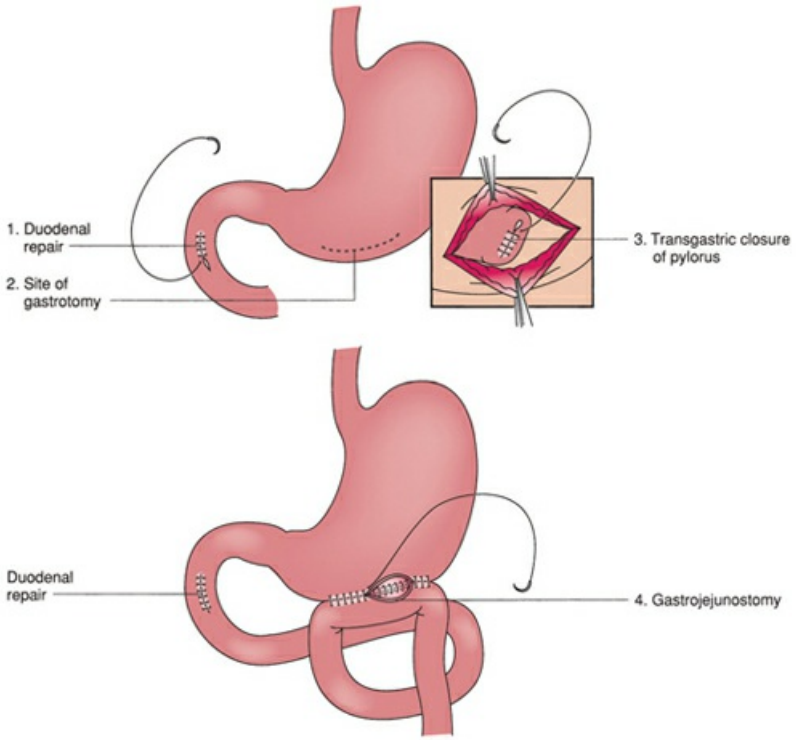
- Usually from blunt trauma (crush or deceleration injury)
- 2nd portion of the duodenum (descending portion, near ampulla of Vater) – most common area of injury
- Can also get tears near ligament of Treitz
- 80% of injuries requiring surgery can be treated with debridement and primary closure (or primary anastomosis); residual bowel circumference should be ≥ 50% normal
- Segmental resection with primary end-to-end closure possible with all segments *except* second portion of the duodenum
- 25% mortality in these patients because of associated shock
- Fistulas are the major source of morbidity
- Intra-op paraduodenal hematomas (≥ 2 cm considered significant; usually in third portion of duodenum overlying spine in blunt injury) – need to open for both blunt and penetrating injuries
- Paraduodenal hematomas on CT scan (or missed on initial CT scan)

- Can present with high small bowel obstruction (SBO) 12–72 hours after injury
- UGI study will show "stacked coins" or "coiled spring" appearance (make sure there is no extravasation of contrast)
- Tx: conservative (NGT and TPN) - cures 90% over 2–3 weeks (hematoma is reabsorbed)

- If at laparotomy and duodenal, biliary system, or pancreas injury suspected, perform Kocher maneuver and open lesser sac through the omentum; check for hematoma, bile, succus, and fat necrosis → if found, need formal inspection of the entire duodenum (also need to check for pancreatic/biliary system injury)
- Diagnosing suspected duodenal injury – abdominal CT with contrast initially. UGI contrast study best. CT scan may show bowel wall thickening, hematoma, free air, contrast leak, or retroperitoneal fluid/air
  - If CT scan is worrisome for injury but nondiagnostic, can repeat the CT in 8–12 hours to see if the finding is getting worse
  - Free intra-peritoneal air or contrast leak – Tx: go to the OR
- Tx: Try to get primary repair or anastomosis; may need to divert with pyloric exclusion and gastrojejunostomy to allow healing. Place a distal feeding jejunostomy and possibly a proximal draining jejunostomy tube that threads back to duodenal injury site. Place drains
  - If in 2nd portion of duodenum and can't get primary repair
    - Place jejunal serosal patch over hole; may need Whipple in future
    - Need pyloric exclusion and gastrojejunostomy
    - Consider feeding and draining jejunostomies; leave drains
    - Trauma Whipple is rarely if ever indicated (very high mortality)
  - Drains – remove when patient tolerating diet without an increase in drainage
  - Fistulas – often close with time; Tx: bowel rest, TPN, octreotide, conservative management for 4–6 weeks



Jejunal serosal patch.



Gastro-jejunostomy and pyloric exclusion for complex duodenal injury.

SMALL BOWEL TRAUMA

- Most common organ injured with penetrating injury (some texts say liver)
- These injuries can be hard to diagnose early if associated with blunt trauma
- Occult small bowel injuries
  - Abdominal CT scan showing intra-abdominal fluid not associated with a solid organ injury, bowel wall thickening, or a mesenteric hematoma is suggestive of injury
  - Need close observation and possibly repeat abdominal CT after 8–12 hours or so to make sure finding is not getting worse
  - Need to make sure patients with these nonconclusive findings can tolerate a diet before discharge
- Repair lacerations transversely → avoids stricture
- Large lacerations that are > 50% of the bowel circumference or results in lumen diameter < ⅓ normal → perform resection and reanastomosis
- Multiple close lacerations – just resect that segment
- Mesenteric hematomas – open if expanding or large (> 2 cm)

COLON TRAUMA (SIGMOID COLON CONSIDERED LEFT COLON HERE)

- Most associated with penetrating injury
- Right and transverse colon injuries Tx: 1) primary repair *or* 2) resection and anastomosis (for destructive injuries [ie > 50% circumference or associated with significant colon devascularization]); all are essentially treated like small bowel injuries
  - *No diversion needed for right and transverse colon injuries*
- Left colon – *perform primary repair without diversion for all injuries if < 50% circumference and not associated with colon devascularization (treats majority)*

- If left-sided colectomy is performed (ie for destructive lesions [> 50% circumference or colon devascularization]), *diverting ileostomy* is indicated for gross contamination (eg peritonitis), ≥ 6 hours has elapsed between injury and repair, significant comorbidities, *or* ≥ 6 units pRBCs have been given
- If patient is in shock and can't perform primary repair → just bring up end colostomy and leave Hartmann's pouch after resection (avoids left sided anastomosis in a sick patient and diverts stool)

- Paracolonic hematomas – open both blunt and penetrating

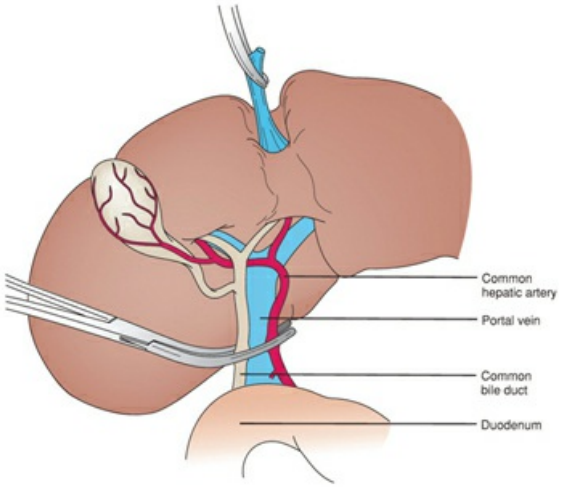
RECTAL TRAUMA

- Most associated with penetrating injury
- *Intra-peritoneal injuries*
  - *Perform primary repair without diversion for all injuries if nondestructive* (< 50% circumference and not associated with devascularization) – *treats majority*
  - If low anterior resection (LAR) is performed (ie for destructive lesions [> 50% circumference or for rectal devascularization]), *a diverting loop colostomy is always indicated (different than above);* if in shock, place end colostomy *only*
- *Extra-peritoneal injuries*
  - *High rectal* (proximal ⅓) – primary repair usual (laparotomy, mobilize rectum); if LAR needed, place diverting loop colostomy (follow LAR pathway above)
  - *Middle rectal* (middle ⅓) – often inaccessible due to location (too low for laparotomy, too high for transanal repair); if repair not easily feasible, there is extensive damage, or if you can't find it → *place end colostomy only (not APR);* this area will heal after 6–8 weeks, take down colostomy at that time
  - *Low rectal* (distal ⅓) – most repaired primarily with transanal approach; if repair not easily feasible, there is extensive damage, or if you can't find it → *place end colostomy only (not APR)*
- Presacral drains and rectal washout are generally not recommended

LIVER TRAUMA

- Most common organ injury with blunt abdominal trauma (some texts say spleen)
- Lobectomy rarely necessary
- Common hepatic artery – can be ligated with collaterals through gastroduodenal artery
- Pringle maneuver (clamping portal triad) does not stop bleeding from hepatic veins
- Damage control peri-hepatic packing – can pack severe penetrating liver injuries if patient becomes unstable in the OR and the injury is not easily fixed (eg retro-hepatic IVC injury). Go to the ICU and get the patient resuscitated and stabilized. Live to fight another day.
- Atriocaval shunt – for retrohepatic IVC injury, allows for control while performing repair
- Portal triad hematomas – need to be explored
- Contained subcapsular hematomas – leave alone
- Common bile duct injury (Kocher maneuver and dissect out portal triad)
  - < 50% of circumference – repair over stent
  - > 50% circumference or complex injury – go with choledochojejunostomy
  - May need intraoperative cholangiogram to define injury
  - 10% of duct anastomoses leak – place drains intra-op

- Portal vein injury – need to repair (lateral venorrhaphy)
  - May need to transect through the pancreas to get to the injury in the portal vein
  - Will need to perform distal pancreatectomy with that maneuver
  - Ligation of portal vein associated with 50% mortality



Pringle maneuver compression of the portal triad structures with a noncrushing vascular clamp for hepatic inflow control. If possible, clamp times should be limited to 15- to 20-minute intervals.

- Omental graft – can be placed in liver laceration to help with bleeding and prevent bile leaks
- Leave drains with liver injuries
- Unstable patients (SBP < 90 despite 2 L LR) with blunt liver injuries should go to the OR (may need angioembolization later)
- Nonoperative management of blunt liver injuries (only in stable patients)
  - If the patient becomes unstable (SBP < 90) or is a transient responder despite aggressive resuscitation including ≥ 4 units of pRBCs or requires ≥ 4 units of pRBCs to keep Hct > 25 → go to OR (if unstable) *or* angioembolization (if transient responder)
  - Active contrast extravasation (ie blush) or pseudoaneurysm on CT scan and patient is stable or transient responder → angioembolization
  - With nonoperative management requires bed rest for 5 days
  - The higher the injury grade, the more likely an intervention is needed (highest is grade VI – hepatic avulsion, likely not compatible with life)

SPLEEN TRAUMA

- Fully healed after 6 weeks
- Postsplenectomy sepsis greatest risk within 2 years of splenectomy
- Need vaccines to pneumococcus, meningococcus, and *H. influenzae* 2 weeks after splenectomy
- Threshold for splenectomy in children is high (unusual to have to remove spleen in children)
- Splenic salvage is associated with increased transfusions
- Subcapsular hematomas – leave alone
- Unstable patients (SBP < 90 despite 2 L LR) with blunt splenic injuries → go to OR
- Nonoperative management of blunt splenic injuries (only in stable patients)
  - If the patient becomes unstable (SBP < 90) or is a transient responder despite aggressive

resuscitation including ≥ 2 units of pRBCs or requires ≥ 2 units of pRBCs to keep Hct > 25 → go to OR (if unstable) *or* angioembolization (if transient responder)
- Active contrast extravasation (ie blush) or pseudoaneurysm on CT scan and patient is stable or transient responder → angioembolization
- With nonoperative management need bed rest for 5 days
- The higher the injury grade, the more likely an intervention will be needed (highest grade V – completely shattered spleen or complete hilar disruption that devascularizes spleen)

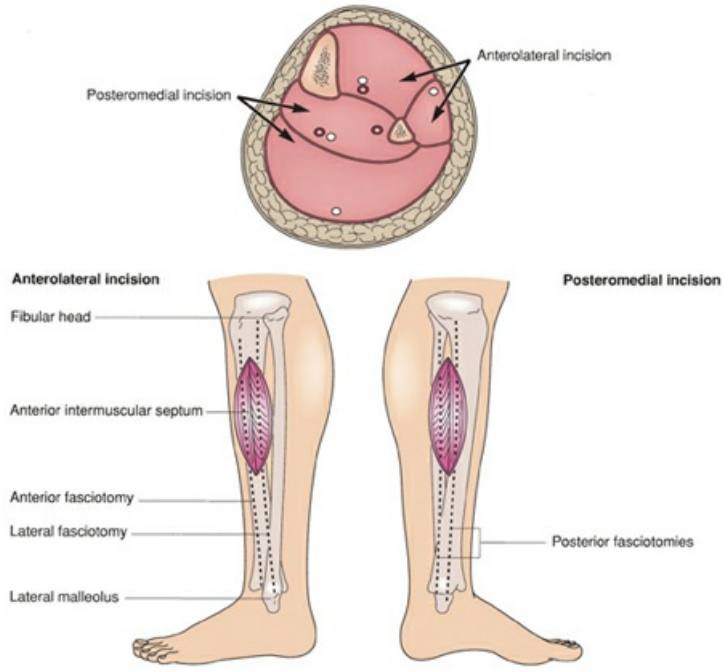
PANCREATIC TRAUMA

- Penetrating injury – accounts for 80% of all pancreatic injuries
- Blunt injury – can result in pancreatic duct fractures, usually perpendicular to the duct
- Edema or necrosis of peripancreatic fat usually indicative of injury
- Pancreatic contusion – leave if stable, place drains if in OR
- 80% of all injuries are treated with just drains
- Primary concern is figuring out if the pancreatic duct is involved
- Distal pancreatic duct injury – distal pancreatectomy, can take up to 80% of the gland
- Pancreatic head duct injury that is not reparable – place drains initially; delayed Whipple or possible ERCP w/ stent may eventually be necessary
- Whipple vs. distal pancreatectomy based on duct injury in relation to the SMV (superior mesenteric vein)
- Kocher maneuver helps evaluate the pancreas operatively
- Leave drains with pancreatic injury
- Pancreatic hematoma – both penetrating and blunt need to be opened
- Persistent or rising amylase may indicate missed pancreatic injury
- CT scans poor at diagnosing pancreatic injuries initially
  - Delayed signs – fluid, edema, necrosis
- ERCP good at finding duct injuries and may be able to treat with temporary stent

VASCULAR TRAUMA

- Vascular repair (or vascular shunt) performed *before* orthopedic repair
- Pulse deficit or distal ischemia with orthopedic injury → reduce fracture or dislocation 1st, then reassess pulse/ABIs (ankle brachial index)
- Major signs of extremity vascular injury (hard signs):
  - Active hemorrhage
  - Pulse deficit
  - Expanding or pulsatile hematoma
  - Distal ischemia
  - Bruit or thrill
    - → *Go to OR for exploration for any of above (may need angio in OR to define injury)*
- Minor signs of extremity vascular injury (soft signs):
  - History of hemorrhage
  - Large stable/nonpulsatile hematoma
  - ABI < 0.9
  - Unequal pulses
    - → *Get CT angio for any of above* (formal angiogram if vascular injury found)

- Saphenous vein graft – will be needed if segment > 2 cm missing
  - Use vein from the contralateral leg when fixing lower extremity arterial injuries
- Vein injuries that need repair – vena cava, femoral, popliteal, brachiocephalic, subclavian, and axillary
- Transection of single artery in the calf in an otherwise healthy patient → ligate
- Cover site of anastomosis with viable tissue and muscle
- Consider fasciotomy if ischemia > 4–6 hours (prevents compartment syndrome)
- Compartment syndrome – consider if compartment pressures are > 20 mm Hg or if clinical exam suggests elevated pressures (see Vascular chapter)
  - Pain with passive motion → paresthesia → anesthesia → paralysis → poikilothermia → pulselessness (late finding)
  - Most commonly occurs after supracondylar humeral fractures, tibial fractures, crush injuries, or other injuries that result in a disruption and then restoration of blood flow after 4–6 hours
  - Tx: fasciotomy



Surgical approach for four compartment fasciotomies through incisions on the medial and lateral aspects of the calf.

- IVC – primary repair if residual stenosis is < 50% the diameter of the IVC; otherwise place saphenous vein or synthetic patch
  - Bleeding of IVC best controlled with proximal and distal pressure, <u>not</u> clamps → can tear it
  - Repair posterior wall injury through the anterior wall (may need to cut through the anterior IVC to get to posterior IVC injuries)

ORTHOPAEDIC TRAUMA

- Can have > 2 L blood loss from a femur fracture
- Orthopaedic emergencies – pelvic fractures in unstable patients, spine injury with deficit,

open fractures, dislocations or fractures with vascular compromise, compartment syndrome

- Femoral neck fractures and hip dislocations – high risk for avascular necrosis
- Long bone fracture or dislocations with loss of pulse (or weak pulse) → immediate reduction of fracture or dislocation and reassessment of pulse:
  - If pulse does not return → go to OR for vascular bypass or repair (may need angiography in OR to define injury)
  - If pulse is weak → CT angio
  - Exception – *all knee dislocations* need to go for formal angiogram, unless pulse is absent, in which case you would just go to OR (may need angio in OR to define injury)
  - Upright falls are associated with calcaneus, lumbar, and distal forearm (radius/ulnar) fractures

Orthopaedic Trauma	Concomitant Nerve/Artery Injury
UPPER EXTREMITY	
Anterior shoulder dislocation	Axillary nerve
Posterior shoulder dislocation	Axillary artery
Proximal humerus Fx	Axillary nerve
Midshaft humerus Fx (or spiral humerus Fx)	Radial nerve
Distal (supracondylar) humerus Fx	Brachial artery
Elbow dislocation	Brachial artery
Distal radius Fx	Median nerve
LOWER EXTREMITY	
Anterior hip dislocation	Femoral artery
Posterior hip dislocation	Sciatic nerve
Distal (supracondylar) femur Fx	Popliteal artery
Posterior knee dislocation	Popliteal artery
Fibula neck Fx	Common peroneal nerve
OTHER FRACTURES	
Temporal or parietal bone Fx	Epidural hematoma; facial nerve
Maxillofacial Fx	Cervical spine Fx
Sternal Fx	Cardiac contusion
First or second rib Fx	Aortic transection
Scapula Fx	Pulmonary contusion, aortic transection
Rib Fx's (left, 8–12)	Spleen laceration
Rib Fx's (right, 8–12)	Liver laceration
Pelvic Fx	Bladder rupture, urethral transaction

RENAL TRAUMA

- MCC – blunt trauma (often associated with lower rib fractures)
- Hematuria is the best indicator of renal trauma
- All patients with hematuria need an abdominal CT scan
- IVP can be useful if going immediately to OR without abdominal CT scan → will identify presence of functional contralateral kidney, which could affect intraoperative decision making
- Left renal vein – can be ligated near IVC; has adrenal and gonadal vein collaterals; right renal vein does not have these collaterals
- Anterior → posterior renal hilum structures – vein, artery, pelvis (VAP)
- 95% of injuries are treated nonoperatively
- Not all urine extravasation injuries require operation
- Kidney cortical injuries – Tx: primary repair

- Indications for operation
  - Acutely – ongoing hemorrhage with instability
  - After acute phase – major collecting system disruption, non-resolving urine extravasation, severe hematuria
- With exploration, try to get control of the vascular hilum 1st
- Place drains intra-op, especially if collecting system is injured
- Methylene blue dye (given IV) can be used at the end of the case to check for leak
- When at exploration for another blunt injury or penetrating trauma:
  - Blunt renal injury with hematoma – leave unless pre-op CT/IVP shows no function or significant urine extravasation
  - Penetrating renal injury with hematoma – open unless pre-op CT/IVP shows good function without significant urine extravasation
- Trauma to flank and IVP (or CT scan) shows no uptake in stable patient – Tx: angiogram; can stent if flap present

BLADDER TRAUMA

- Hematuria best indicator of bladder trauma
- Blood at the meatus or scrotal/sacral hematoma – suspect bladder or urethral injury
- > 95% associated with pelvic fractures (blunt trauma)
- Signs and symptoms – meatal blood, sacral or scrotal hematoma
- Dx: cystogram (include post-void films)
- Extraperitoneal bladder rupture – cystogram shows starbursts
  - Tx: Foley 7–14 days
- Intraperitoneal bladder rupture – more likely in kids, cystogram shows leak
  - Tx: operation and repair of defect, followed by Foley drainage

URETERAL TRAUMA

- MCC – penetrating injury
- Hematuria unreliable → multiple shot IVP and retrograde urethrogram (RUG) best tests
- If large ureteral segment is missing (> 2 cm) and cannot perform reanastomosis:
  - Upper ⅓ injuries and middle ⅓ injuries that won't reach bladder (above pelvic brim)
    - Temporize with percutaneous nephrostomy (tie off both ends of the ureter); can go with ileal interposition or trans-ureteroureterostomy later
  - Lower ⅓ injuries – reimplant in the bladder; may need bladder hitch procedure
- If small ureteral segment is missing (< 2 cm):
  - Upper ⅓ injuries and middle ⅓ injuries – mobilize ends of ureter and perform primary repair over stent
  - Lower ⅓ injuries – re-implant in the bladder (easier anastomosis than primary repair)
- One-shot IVP does not evaluate the ureters sufficiently
- IV indigo carmine or IV methylene blue can be used to check for leaks
- Blood supply is medial in the upper ⅔ of the ureter and lateral in the lower ⅓ of the ureter
- Leave drains for all ureteral injuries

URETHRAL TRAUMA

- Hematuria or blood at meatus best signs; free-floating prostate gland; scrotal hematoma;

usually associated with pelvic fractures (blunt trauma)
- No Foley if this injury is suspected
- Retrograde urethrogram (RUG) best test
- Membranous portion at risk for transection
- Significant tears – Tx: suprapubic cystostomy and repair in 2–3 months *(safest method* – high stricture and impotence rate if repaired early)
- Small, partial tears – Tx: may get away with bridging urethral catheter across tear area and repair in 2–3 months
- Genital trauma – can get fracture in erectile bodies from vigorous sex
  - Need to repair the tunica albuginea and Buck's fascia
- Testicular trauma – get ultrasound to see if tunica albuginea is violated, then repair if necessary

PEDIATRIC TRAUMA

- Blood pressure is not a good indicator of blood loss in children – last thing to go
- Heart rate, respiratory rate, mental status, and clinical exam are best indicators of shock
- ↑ risk of hypothermia (↑ BSA compared with weight)
- ↑ risk of head injury

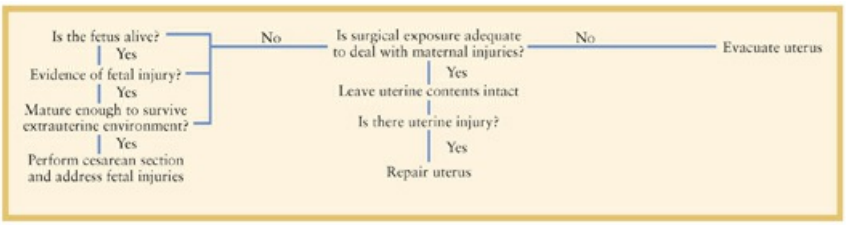
Normal Vital Signs by Age

Age Group	Pulse (beats/min)	SBP (mm Hg)	Respiratory Rate (breaths/min)
Infant (< 1 yr)	160	80	40
Preschool (< 5 yr)	140	90	30
Adolescent (> 10 yr)	120	100	20

TRAUMA DURING PREGNANCY

- At all costs, save the mother
- Pregnant patients can have up to a ⅓ total blood volume loss without signs
- Estimate pregnancy based on fundal height (20 cm = 20 wk = umbilicus). Place fetal monitor
- Try to avoid CT scan with early pregnancy. If life-threatening and needed, get CT scan.
- Ultrasound (FAST scan) may have a role in pregnant patients
- Check for vaginal discharge – blood, amnion; check for effacement, dilation, fetal station
- Fetal maturity – lecithin:sphingomyelin (LS) ratio > 2:1; positive phosphatidylcholine in amniotic fluid
- Placental abruption – > 50% results in almost 100% fetal death rate
  - > 50% of all traumatic placental abruptions result in fetal demise
  - Signs of abruption – uterine tenderness, contractions, fetal HR < 120
  - Can be caused by shock (most common mechanism) or mechanical forces
- Uterine rupture – more likely to occur in the posterior fundus
  - If occurs after delivery of child, aggressive resuscitation even in the face of shock leads to the best outcome. The uterus will eventually clamp down after delivery; just have to aggressively resuscitate until then (fluids, blood)
- Indications for C-section during exploratory laparotomy for trauma
  - Persistent maternal shock or severe injuries and pregnancy near term (> 34 weeks)

- Pregnancy a threat to the mother's life (hemorrhage, DIC)
- Mechanical limitation to life-threatening vessel injury
- Risk of fetal distress exceeds risk of immaturity
- Direct intra-uterine trauma



Assessment of the pregnant uterus during celiotomy.

Management of Hematomas

Hematoma (≥ 2 cm considered significant)	Penetrating Trauma	Blunt Trauma
Pelvic	Open	Leave
Paraduodenal	Open	Open
Portal triad	Open	Open
Retrohepatic	Leave if stable	Leave
Midline supramesocolic	Open	Open
Midline inframesocolic	Open	Open
Pericolonic	Open	Open
Perirenal	Open[a]	Leave[b]

[a]Unless preoperative CT scan or IVP shows no injury.

[a]Unless preoperative CT scan or IVP shows injury.

Zones of the Peritoneum

Zone	Location	Associated Injuries
1	Central retroperitoneum	Pancreaticoduodenal or major abdominal vascular injury (open hematomas in these areas for both penetrating and blunt trauma)
2	Flank or perinephric area	Injuries to the genitourinary tract or to the colon (ie with penetrating trauma; open hematomas if penetrating trauma; usually leave alone if blunt)
3	Pelvis	Pelvic fractures (usually leave these hematomas alone); may need angioembolization

OTHER

- Patients with penetrating injuries require a tetanus shot
- Drains – leave drains with pancreatic, liver, biliary system, urinary, and duodenal injuries
- Snakebites (symptoms depend on species) – shock, bradycardia, and arrhythmias can result; Tx: stabilize patient, anti-venin (different types for different species; eg rattlesnake, coral snake), tetanus shot
- Beestings – kill many more people in US than snake bites due to anaphylaxis; wheezing, rash, hypotension (vasomotor shock); Tx for anaphylaxis – epinephrine (EpiPen)
- Black widow spider bites – nausea, vomiting, muscle cramps; Tx – IV calcium gluconate, muscle relaxants
- Brown recluse spider bites – skin ulcer with necrotic center and surrounding erythema; Tx:

Dapsone; skin grafting may be needed but wait at least a week to see full extent of damage

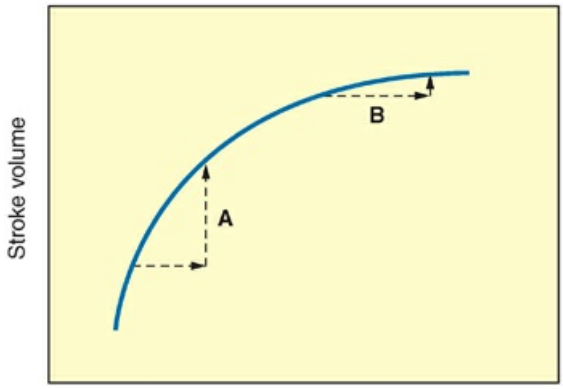
- Wild animal bites – need rabies prophylaxis unless the animal can be found, killed, and brain examined
- Human bites – can require extensive irrigation and debridement
- Hypothermia – best initial Tx: warm air conduction (Bair Hugger); also give warm IV fluids; do not stop CPR until warm and dead
- Electrical injuries – at risk for rhabdomyolysis and compartment syndrome
  - All need volume resuscitation
  - Other injuries – solid organ fracture, hollow viscous rupture, quadriplegia, cataracts
  - MCC of immediate death – cardiac arrest from ventricular fibrillation

16 Critical Care

CARDIOVASCULAR SYSTEM

Normal Values	
Parameter	Value
Cardiac output (CO) (L/min)	4–8
Cardiac index (CI) (L/min)	2.5–4
Systemic vascular resistance (SVR)	1,100 ± 300
Pulmonary capillary wedge pressure (PCWP)	11 ± 4
Central venous pressure (CVP)	7 ± 2
Pulmonary artery pressure (PAP)	25/10 ± 5
Mixed venous oxygen saturation (SvO2)	75 ± 5

- MAP = CO × SVR, CI = CO/BSA
- Kidney gets 25% of CO, brain gets 15%, heart gets 5%
- Cardiac performance (left ventricle) is determined by preload, afterload, contractility, and HR
- Preload – linearly related to left ventricular end-diastolic pressure (LVEDP) and filling pressure; wedge pressure measures preload



The concept of preload recruitable stroke volume is demonstrated. If the ventricle is on the steep part of the Starling curve *(A)*, then a given increase in preload will lead to a significant increase in stroke volume. By contrast, on the flatter part of the curve *(B)*, the stroke volume increases marginally if at all with the same increase in preload. Dynamic indices of preload-recruitable stroke volume are more accurate than static indices in identifying where on this curve the patient is at any point in time.

- Afterload – resistance against the ventricle contracting (SVR)
- Contractility – the force of contraction
- Stroke volume determined by LVEDV, contractility, and afterload
  - Stroke volume = LVEDV – LVESV
- Ejection fraction = stroke volume/LVEDV
- EDV (end-diastolic volume) – determined by preload and distensibility of the ventricle

- ESV (end-systolic volume) – determined by contractility and afterload
- Cardiac output increases with HR up to 120–150 beats/min, then starts to go down because of decreased diastolic filling time
- Atrial kick – accounts for 20% of LVEDV
- Anrep effect – automatic increase in contractility secondary to ↑ afterload
- Bowditch effect – automatic increase in contractility secondary to ↑ HR
- Arterial O_2 content (CaO_2) = Hgb × 1.34 × O_2 saturation + (PO_2 × 0.003)
- O_2 delivery = CO × arterial O_2 content (CaO_2) × 10
- O_2 consumption (VO_2) = CO × (CaO_2 – CvO_2); CvO_2 = venous O_2 content
  - Normal O_2 delivery-to-consumption ratio is 4:1. CO increases to keep this ratio constant.
  - O_2 consumption is usually supply independent (consumption does not change until low levels of delivery are reached)
- Causes of right shift of oxygen–Hgb dissociation curve (O_2 unloading) – ↑ CO_2 (Bohr effect) ↑ temperature, ↑ ATP production, ↑ 2,3-DPG production, or ↓ pH
  - Opposite above causes left shift (increased O_2 binding)
  - Normal p50 (O_2 at which 50% of O_2 receptors are saturated) = 27 mm Hg
- ↑ SvO_2 (saturation of venous blood, normally 75% ± 5%; used on some Swan–Ganz catheters) – occurs with ↑ shunting of blood or ↓ O_2 extraction (eg sepsis, cirrhosis, cyanide toxicity, hyperbaric O_2, hypothermia, paralysis, coma)
- ↓ SvO_2 – occurs with ↑ O_2 extraction (eg malignant hyperthermia) or ↓ O_2 delivery (eg ↓ O_2 saturation, ↓ CO, ↓ Hgb)
- Wedge – may be thrown off by pulmonary hypertension, mitral stenosis, mitral regurgitation, high PEEP, poor LV compliance
- Swan–Ganz catheter – should be placed in zone III (lower lung; has less respiratory influence on wedge pressure)
  - Hemoptysis after flushing Swan–Ganz catheter – increase PEEP, which will tamponade the pulmonary artery bleed, mainstem intubate non-affected side; can try to place Fogarty balloon down mainstem on affected side; may need thoracotomy and lobectomy
  - Absolute contraindications – right-sided mechanical valve (rare)
  - Relative contraindications – previous pneumonectomy, left bundle branch block, recent pacemaker, right-sided endocarditis
  - Approximate Swan–Ganz catheter distances to wedge – R SCV 45 cm, R IJ 50 cm, L SCV 55 cm, L IJ 60 cm
  - Pulmonary vascular resistance (PVR) can be measured only by using a Swan–Ganz catheter (ECHO does not measure PVR)
  - Wedge pressure measurements should be taken at end-expiration (for both ventilated and nonventilated patients)
- ↑ Ventricular wall tension (#1) and HR are the primary determinants of myocardial O_2 consumption → can lead to myocardial ischemia
- Unsaturated bronchial blood – empties into pulmonary veins; thus, LV blood is 5 mm Hg (PO_2) lower than pulmonary capillaries
- Alveolar–arterial gradient – is 10–15 mm Hg in a normal nonventilated patient
- Blood with the lowest venous saturation → coronary sinus blood (30%)

- Blood with highest venous saturation → renal veins (80%)

SHOCK

- Shock = inadequate tissue oxygenation (most basic definition)
  - Tachypnea and mental status changes occur with progressive shock
  - Blood shunted to the heart and brain
- Adrenal insufficiency
  - MCC – withdrawal of exogenous steroids
  - Acute – cardiovascular collapse; characteristically unresponsive to fluids and pressors; nausea and vomiting, abdominal pain, fever, lethargy, ↓ glucose, ↑ K
  - Dx: corticotropin stimulation test (ACTH given, cortisol measured)
  - Tx: Dexamethasone (give empirically if adrenal insufficiency is suspected; does not interfere with test)
  - Steroid potency
    - 1× – cortisone, hydrocortisone
    - 5× – prednisone, prednisolone, methylprednisolone
    - 30× – dexamethasone
- Neurogenic shock (vasogenic shock) – loss of sympathetic tone (↓ SVR)
  - Causes – high spine or head injury; anaphylactic reactions (eg bee stings)
  - Usually have ↓ HR, ↓ BP, pink and warm skin
  - Tx: give volume 1st, then phenylephrine after resuscitation
- Hemorrhagic shock – initial alteration is ↑ diastolic pressure
- Cardiogenic shock (eg massive MI, severe CHF exacerbation) – Tx: dobutamine, IABP
- Cardiac tamponade (causes a type of cardiogenic shock)
  - Mechanism of hypotension is decreased ventricular filling due to fluid in the pericardial sac around the heart
  - Beck's triad – hypotension, jugular venous distention, and muffled heart sounds
  - Echocardiogram shows impaired diastolic filling of right atrium initially (1st sign of cardiac tamponade)
  - Pericardiocentesis blood does not form clot
  - Tx: fluid resuscitation to temporize situation; need pericardial window or pericardiocentesis

Types of Shock

Shock	CVP and PCWP	CO	SVR
Hemorrhagic (hypovolemic)	↓	↓	↑
Septic (hyperdynamic)[a]	↓ (usually)	↑	↓
Cardiogenic (eg MI, cardiac tamponade)	↑	↓	↑
Neurogenic (eg head or spinal cord injury)	↓	↓	↓
Adrenal insufficiency	↓ (usually)	↓	↓

[a]Severe septic shock that leads to cardiac dysfunction can cause a hypodynamic state, leading to ↓ CO and ↑ SVRI.

- Sepsis
  - Early sepsis triad – hyperventilation, confusion, hypotension
  - Early gram-negative sepsis – ↓ insulin, ↑ glucose (impaired utilization)
  - Late gram-negative sepsis – ↑ insulin, ↑ glucose (secondary to insulin resistance)

- Hyperglycemia – often occurs just before patient becomes clinically septic
- Tx: volume resuscitation and antibiotics initially; Levophed and vasopressin after that

- Neurohormonal response to hypovolemia
  - Rapid – epinephrine and norepinephrine release (adrenergic release; results in vasoconstriction and increased cardiac activity)
  - Sustained – renin (from kidney; renin-angiotensin pathway activated resulting in vasoconstriction and water resorption), ADH (from pituitary; reabsorption of water), and ACTH release (from pituitary; increases cortisol)

EMBOLI

- Fat emboli – petechia, hypoxia, and confusion (can also present similar to pulmonary embolism [PE])
  - Sudan red stain may show fat in sputum and urine
  - Most common with lower extremity (hip, femur) fractures/orthopaedic procedures
  - Can turn into ARDS with hypoxemia and bilateral patchy infiltrates on CXR
  - Tx: supportive (mechanical ventilation)
- Pulmonary emboli (PE) – chest pain and dyspnea; ↓ P_{O_2} and P_{CO_2}; respiratory alkalosis; ↑ HR and ↑ RR; anxiety and diaphoresis; hypotension and shock if massive
  - Intubated patients can present with decreased $ETCO_2$ and hypotension
  - MC EKG finding – tachycardia
  - Dx: CT angio
  - Most PEs arise from iliofemoral region
  - Tx: heparin, Coumadin; consider open (on cardiopulmonary bypass) or percutaneous (suction catheter) embolectomy if patient is in shock despite massive pressors and inotropes
- Air emboli – usually occurs when central vein is exposed to air (eg central line placement/removal, supraclavicular nodal biopsies)
  - Tx – CPR; place patient head down and roll to left (keeps air in RV and RA), then aspirate air out with central line or PA catheter to RA/RV
  - Prevention – use Trendelenburg when entering neck veins

INTRA-AORTIC BALLOON PUMP (IABP)

- Inflates on T wave (diastole); deflates on P wave (systole)
- Place tip of the catheter just distal to left subclavian (1–2 cm below the top of the arch)
- Used for cardiogenic shock (after CABG or MI), in patients with refractory angina awaiting revascularization, pre-op in high-risk patients, acute mitral regurgitation, and for ventricular septal ruptures
- Decreases afterload (deflation during ventricular systole)
- Improves diastolic BP (inflation during ventricular diastole), which improves diastolic coronary perfusion
- Absolute contraindications – aortic dissection, severe aortoiliac disease, aortic regurgitation
- Relative contraindications – vascular grafts, aortic aneurysms

RECEPTORS

- Alpha-1 – vascular smooth muscle constriction

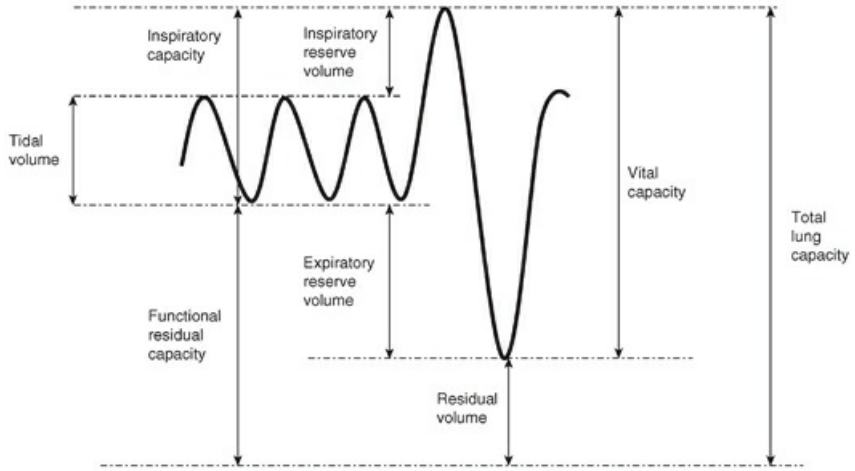
- Alpha-2 – venous smooth muscle constriction
- Beta-1 – myocardial contraction and rate
- Beta-2 – relaxes bronchial smooth muscle, relaxes vascular smooth muscle; increases renin
- Dopamine receptors – relax renal and splanchnic smooth muscle

CARDIOVASCULAR DRUGS

- Dopamine (2–5 µg/kg/min initially)
  - 2–5 µg/kg/min – dopamine receptors (renal)
  - 6–10 µg/kg/min – beta-adrenergic (heart contractility and heart rate)
  - >10 µg/kg/min – alpha-adrenergic (vasoconstriction and ↑ BP)
- Dobutamine (3 µg/kg/min initially)
  - Beta-1 (↑ contractility mostly, tachycardia with higher doses)
- Milrinone
  - Phosphodiesterase inhibitor (↑ cAMP)
  - Results in ↑ Ca flux and ↑ myocardial contractility
  - Also causes vascular smooth muscle relaxation and pulmonary vasodilation
  - Is not subject to receptor down-regulation (good for long-term Tx, eg chronic CHF)
- Phenylephrine (10 µg/min initially)
  - Alpha-1, vasoconstriction
- Norepinephrine (5 µg/min initially)
  - Alpha-1 and alpha-2; some beta-1
  - Potent splanchnic vasoconstrictor
- Epinephrine (1–2 µg/min initially)
  - Low dose – beta-1 and beta-2 (↑ contractility and vasodilation)
    - Can ↓ BP at low doses
  - High dose – alpha-1 and alpha-2 (vasoconstriction)
    - ↑ Cardiac ectopic pacer activity and myocardial O_2 demand
- Isoproterenol (1–2 µg/min initially)
  - Beta-1 and beta-2, ↑ HR and contractility, vasodilates
  - Side effects: extremely arrhythmogenic; ↑ heart metabolic demand (rarely used); may actually ↓ BP
- Vasopressin
  - V-1 receptors – arterial vasoconstriction
  - V-2 receptors (intrarenal) – water reabsorption at collecting ducts
  - V-2 receptors (extrarenal) – mediate release of factor VIII and von Willebrand factor (vWF)
- Nipride – arterial vasodilator
  - Cyanide toxicity at doses > 3 µg/kg/min for 72 hours; can check thiocyanate levels and signs of metabolic acidosis
  - Tx for cyanide toxicity – amyl nitrite, then sodium nitrite
- Nitroglycerin – predominately venodilation with ↓ myocardial wall tension from ↓ preload; moderate coronary vasodilator
- Hydralazine – α-blocker; lowers BP

PULMONARY SYSTEM

- Compliance – (change in volume)/(change in pressure)
  - High pulmonary compliance means lungs easy to ventilate (eg severe COPD)
  - Pulmonary compliance is *decreased* in patients with ARDS, fibrotic lung diseases, reperfusion injury, pulmonary edema, atelectasis
- Aging – ↓ FEV_1 and vital capacity, ↑ functional residual capacity (FRC)
- V/Q ratio (ventilation/perfusion ratio) – highest in upper lobes, lowest in lower lobes
- Ventilator
  - ↑ PEEP to improve oxygenation (alveoli recruitment) → improves FRC; can also ↑ F_IO_2
  - ↑ Rate or volume to ↓ CO_2 (improved ventilation)
  - Normal weaning parameters – negative inspiratory force (NIF) > 20, F_IO_2 ≤ 40%, PEEP 5 (physiologic), pressure support 5, RR < 24/min, HR < 120 beats/min, P_{O_2} > 60 mm Hg, P_{CO_2} < 50 mm Hg, pH 7.35–7.45, saturations > 93%, off pressors, follows commands, can protect airway
  - Pressure support – decreases the work of breathing (inspiratory pressure is held constant until minimum volume is achieved)
  - Keep F_IO_2 ≤ 60% – prevents O_2 radical toxicity to lungs
  - Barotrauma – high risk if plateaus > 30 and peaks > 50 → need to decrease TV; consider pressure control ventilation
  - PEEP – *improves FRC* and compliance by keeping alveoli open → best way to improve oxygenation
  - Excessive PEEP complications – ↓ right atrial filling (main reason for ↓ed CO), ↓ BP, ↓ renal blood flow (↑ed renin), ↓ urine output, ↑ wedge pressure, and ↑ pulmonary vascular resistance
  - High-frequency ventilation – used a lot in kids; tracheoesophageal fistula, bronchopleural fistula
- Pulmonary function measurements



Lung measurements: Tidal volume (TV) is the amount of gas moved during one normal inspiration and expiration. Functional residual capacity (FRC) represents the volume of gas left in the lung following normal expiration. Inspiratory capacity is the maximum volume of air, which can be inspired following a normal expiration. Inspiratory reserve volume is the additional amount of air, which can be inspired following normal inspiration. Expiratory reserve volume is the additional amount of air, which can be expired following normal expiration. Residual volume

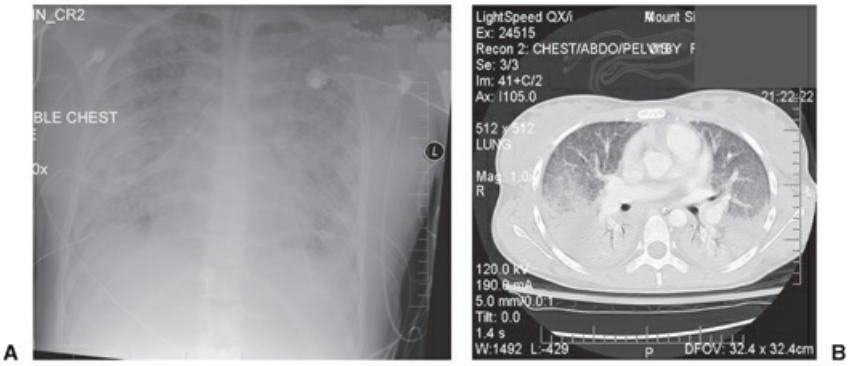
is the minimum lung volume possible, which is the air that remains in the lung following maximum expiration. Vital capacity is the maximum amount of air, which can be moved, maximum inspiration following maximum expiration. Total lung capacity is the total amount of volume present in the lung.

- Total lung capacity (TLC) – lung volume after maximal inspiration
  - TLC = FVC + RV
- Forced vital capacity (FVC) – maximal exhalation after maximal inhalation
- Residual volume (RV) – lung volume after maximal expiration (20% TLC)
- Tidal volume (TV) – volume of air with normal inspiration and expiration
- Functional residual capacity (FRC) – lung volume after normal exhalation
  - FRC = ERV + RV
  - Surgery (atelectasis), sepsis (ARDS), and trauma (contusion, atelectasis, ARDS) – all ↓ FRC
  - PEEP ↑s FRC
- Expiratory reserve volume (ERV) – volume of air that can be forcefully expired after normal expiration
- Inspiratory capacity – maximum air breathed in from FRC
- FEV_1 – forced expiratory volume in 1 second (after maximal inhalation)
- Minute ventilation = TV × RR
- Restrictive lung disease – ↓ TLC, ↓ RV, and ↓ FVC
  - FEV_1 can be normal or ↑
- Obstructive lung disease – ↑ TLC, ↑ RV, and ↓ FEV_1
  - FVC can be normal or ↓

- COPD – ↑ work of breathing due to prolonged expiratory phase
- Dead space
  - Part of lung that is ventilated but <u>not</u> perfused
  - Normally, dead space is the airway to level of the bronchiole (comprises 150 mL; conductive airways)
    - MCC of increased dead space (high V/Q ratio) – *excessive PEEP* (due to capillary compression); others – ↓ed CO (capillary collapse), PE, pulmonary hypertension
  - *Increased* dead space leads to *increased* P_{CO_2}
- Shunt (poor ventilation but good perfusion)
  - MCC of increased shunt (low V/Q ratio) – *atelectasis (alveolar hypoventilation)*; others – mucus plug, ARDS (alveoli filled with edema)
  - Shunt causes hypoxia (*decreased* P_{O_2})
- ARDS – inflammation of the lung parenchyma mediated primarily by PMNs; get ↑ proteinaceous material, ↑ A-a gradient, ↑ pulmonary shunt
  - Most common cause is pneumonia; other causes – sepsis, multi-trauma, severe burns, pancreatitis, aspiration, DIC
  - Can result in SIRS, shock, and MSOF
  - Tx: decrease barotrauma by allowing permissive hypercapnia (hypercarbia); lower tidal volume to keep plateau pressures < 30; PEEP 10–15; increase inspiratory time to improve oxygenation

Acute Respiratory Distress Syndrome (ARDS) Criteria

Acute onset
Bilateral pulmonary infiltrates
$PaO_2/FIO_2 \leq 300$
Absence of heart failure (wedge < 18 mm Hg)



Characteristic chest radiograph (A) and CT scan (B) in a patient with severe ARDS following multiple trauma. (From Cheadle WG, Branson R, Franklin GA. Pulmonary risk and ventilatory support. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

- Aspiration – pH < 2.5 and volume > 0.4 cc/kg is associated with ↑ degree of damage
  - Mendelson's syndrome – chemical pneumonitis from aspiration of gastric secretions
  - Most frequent site is superior segment of the right lower lobe (RLL)
- Atelectasis – collapse of alveoli resulting in reduced oxygenation; usually caused by poor inspiration postop
  - Most common cause of fever in first 48 hours after operation
  - Mediated by alveolar macrophages which release IL-1 (acts at the hypothalamus)
  - MCC of hypoxia early post-op
  - Sx's – fever, tachycardia, hypoxia
  - Increased in patients with COPD, upper abdominal surgery, obesity
  - Tx: incentive spirometer, pain control, ambulation
- Lots of things can throw off a pulse oximeter → nail polish, dark skin, low-flow states, ambient light, anemia, vital dyes
- Pulmonary vasodilation – PGE_1, prostacyclin (PGI_2), inhaled nitric oxide, sildenafil
- Pulmonary vasoconstriction – hypoxia (#1), acidosis, histamine, serotonin, TXA_2
- Alkalosis – pulmonary vasodilator
- Acidosis – pulmonary vasoconstrictor
- Pulmonary shunting (causes hypoxia) – occurs with nitroprusside (Nipride), nitroglycerin, and nifedipine

RENAL SYSTEM

- MCC of poor urine output early post-op – hypovolemia (Tx: give fluids)
- Hypotension intra-op – the most common cause of postoperative renal failure
- 70% of nephrons need to be damaged before renal dysfunction occurs
- Check serum and urine electrolytes; check urinary catheter for obstruction
- FeNa (fractional excretion of sodium) = (urine Na/Cr)/(plasma Na/Cr) → *best test for*

azotemia

Standard Measurements in the Diagnosis of Renal Failure		
Test	Prerenal	Parenchymal
Urine osmolarity (mOsm)	> 500	250–350
U/P osmolality	> 1.5	< 1.1
BUN:creatinine ratio	> 20	< 10
Urine sodium	< 20	> 40
FE_{Na}	< 1%	> 3%

FE_{Na}, fraction of excreted sodium; U/P, urine-to-plasma ratio.

- Oliguria
  - 1st – make sure patient is volume loaded (CVP 11–15 mm Hg)
  - 2nd – try diuretic trial → furosemide (Lasix)
  - 3rd – dialysis if needed
- Pre-renal oliguria/ARF – Tx: fluid volume
- Renal oliguria/ARF (eg acute tubular necrosis; ATN) – Tx: diuretic trial (try to make non-oliguric)
  - MCC of renal ATN – hypotension intra-op
- Post-renal oliguria/ARF (obstructive uropathy; eg ureteral obstruction, severe BPH)
  - Dx: U/S (shows hydronephrosis)
  - Tx: relieve obstruction
- Indications for dialysis – fluid overload, ↑ K, metabolic acidosis, uremic encephalopathy, uremic coagulopathy, poisoning
- Hemodialysis – rapid, can cause large volume shifts; Hct increases by about 5 for each liter taken off
- CVVH – slower, good for ill patients who cannot tolerate the volume shifts (septic shock, etc.); Hct increases by 5–8 for each liter taken off with dialysis
- Renin (released from kidney)
  - Released in response to ↓ pressure sensed by juxtaglomerular apparatus in kidney
  - Also released in response to ↑ Na concentrations sensed by the macula densa
  - Beta-adrenergic stimulation and hyperkalemia also cause release
  - Converts angiotensinogen (synthesized in the liver) to angiotensin I
  - Angiotensin-converting enzyme (lung) – converts angiotensin I to angiotensin II
  - Adrenal cortex – releases aldosterone in response to angiotensin II
  - Aldosterone acts at the distal convoluted tubule to reabsorb water by up-regulating the Na/K ATPase on the membrane (Na re-absorbed, K secreted)
  - Angiotensin II – also vasoconstricts as well as inhibits renin release
- Atrial natriuretic peptide (or factor)
  - Released from atrial wall with atrial distention (eg CHF)
  - Inhibits Na and water resorption in the collecting ducts
  - Also a vasodilator
- Antidiuretic hormone (ADH; vasopressin)
  - Released by posterior pituitary gland when osmolality is high
  - Acts on collecting ducts for water resorption
  - Also a vasoconstrictor
- Efferent limb of the kidney controls GFR

- Renal toxic drugs
  - NSAIDs – cause renal damage by inhibiting prostaglandin synthesis, resulting in renal arteriole vasoconstriction
  - Aminoglycosides – direct tubular injury
  - Myoglobin – direct tubular injury; Tx: hydration (best), alkalinize urine
  - Contrast dyes – direct tubular injury; Tx: pre-hydration before contrast exposure best for patients with elevated creatinine; HCO3-, *N*-acetylcysteine

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS)

- Mediated by massive IL-1 and TNF-alpha release
- Causes – shock, infection (MC – pneumonia), burns, multi-trauma, pancreatitis, ARDS
  - Endotoxin (lipopolysaccharide – lipid A) is the most potent stimulus for SIRS
  - Lipid A is a very potent stimulator of TNF release
- Mechanism – inflammatory response is activated systemically (TNF-alpha and IL-1 major components) and can lead to shock and eventually multi-organ dysfunction
  - Results in capillary leakage, microvascular thrombi, shock, and eventually end-organ dysfunction
- Need to Tx the underlying cause
- Sepsis = SIRS + infection
- Septic shock = sepsis + hypotension

Definitions of Systemic Inflammatory Response Syndrome (SIRS), Shock, and Multisystem Organ Dysfunction (MOD)

SIRS →	Shock →	MOD

SIRS

- Temperature > 38°C or < 36°C
- Heart rate > 90 beats/min
- Respiratory rate > 20/min or $PaCO_2$ < 32
- White blood count > 12,000/µL or < 4,000/µL

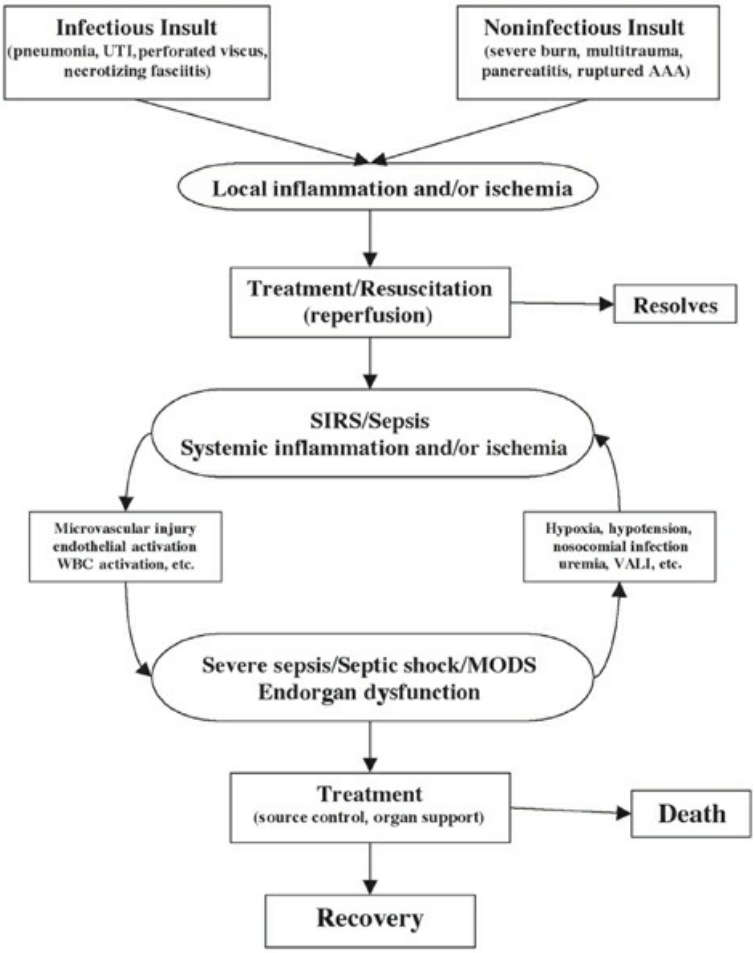
Shock

- Arterial hypotension despite adequate volume resuscitation (inadequate tissue oxygenation)

MOD

- Progressive but reversible dysfunction of 2 or more organs arising from an acute disruption of normal homeostasis

Modified from Awad SS, Gale SC. Multiple organ dysfunction syndrome: pathogenesis, management, and prevention. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.



Pathophysiology of multisystem organ dysfunctions (MODS). UTI, urinary tract infection; AAA, abnormal aortic aneurysm; SIRS, systemic inflammatory response syndrome; WBC, white blood count; VALI, ventilator-associated lung injury. (From Cheadle WG, Branson R, Franklin GA. Pulmonary risk and ventilatory support. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

BRAIN DEATH

- Precludes diagnosis – temperature < 32°C, BP < 90 mm Hg, drugs (eg phenobarbital, pentobarbital, ETOH), metabolic derangements (hyperglycemia, uremia), desaturation with apnea test
- Following must exist for 6–12 hours → unresponsive to pain, absent cold caloric oculovestibular reflexes, absent oculocephalic reflex (patient doesn't track), no spontaneous respirations, no corneal reflex, no gag reflex, fixed and dilated pupils, positive apnea test
- EEG – shows electrical silence; MRA – will show no blood flow to brain
- Apnea test – the patient is pre-oxygenated, a catheter delivering O_2 at 8 L/min is placed at the carina through the ET-tube and CO_2 should be normal before the start of the test
  - The patient is disconnected from ventilator for 10 minutes
  - A CO_2 > 60 mm Hg or increase in CO_2 by 20 mm Hg at the end of the test is a positive test for apnea (meets brain death criteria)
  - If BP drops (< 90 mm Hg), the patient desaturates (< 85% on pulse oximeter), or spontaneous breathing occurs, the test is terminated (negative test for apnea) → place back

on the ventilator (cannot declare brain death)
- *Can still have deep tendon reflexes with brain death*

OTHER CONDITIONS

- Carbon monoxide
  - Can falsely ↑ oxygen saturation reading on pulse oximeter
  - Binds hemoglobin directly (creates carboxyhemoglobin – HA, nausea, confusion, coma, death); CO has 250 × more affinity for Hgb than oxygen
  - Causes a left shift on the oxygen–Hgb dissociation curve
  - Can usually correct with 100% oxygen on ventilator (displaces carbon monoxide); rarely need hyperbaric O_2
  - Abnormal carboxyhemoglobin > 10%; in smokers > 20%
- Methemoglobinemia (from nitrites such as Hurricaine spray, fertilizers; nitrites bind Hgb) – O_2 saturation reads 85%
  - Tx: methylene blue
- Cyanide toxicity – disrupts the electron transport chain; can't utilize oxygen; get left to right shunt; Tx – amyl nitrite, then sodium nitrite; hydroxycobalamin
- Critical illness polyneuropathy – motor > sensory neuropathy; occurs with sepsis; can lead to failure to wean from ventilation
- Xanthine oxidase – in endothelial cells, forms toxic oxygen radicals with reperfusion, involved in reperfusion injury
  - Also involved in the metabolism of purines to uric acid
- Most important mediator of reperfusion injury – PMNs
- DKA – nausea and vomiting, thirst, polyuria, ↑ glucose, ↑ ketones, ↓ Na, ↑ K
  - Tx: normal saline and insulin initially
  - After treatment with insulin, hypokalemia can occur as K is driven back into cells along with glucose (Tx: potassium chloride)
- ETOH withdrawal – HTN, tachycardia, delirium, seizures after 48 hours
  - Tx: thiamine, folate, B_{12}, Mg, K, PRN lorazepam (Ativan)
- ICU (or hospital) psychosis – generally occurs after third postoperative day and is frequently preceded by lucid interval
  - Need to rule out metabolic (hypoglycemia, DKA, hypoxia, hypercarbia, electrolyte imbalances) and organic (MI, CVA) causes
- Atrial fibrillation – MCC of delayed discharge after cardiac surgery
- Magnesium – can be used to Tx ventricular fibrillation (torsades de pointes)

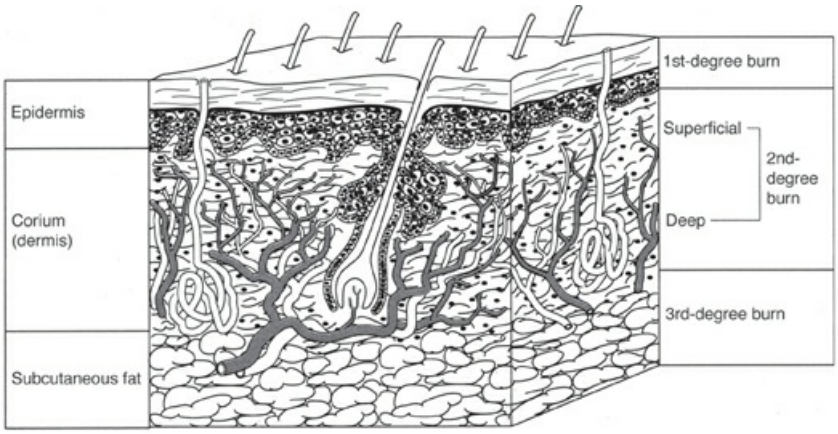
17 Burns

INTRODUCTION

Burn Classification

Degree	Description
1st	Sunburn (epidermis)
2nd	
Superficial dermis (papillary)	Painful to touch; blebs and blisters; hair follicles intact; blanches (do not need skin grafts)
Deep dermis (reticular)	Decreased sensation; *loss of hair follicles* (need skin grafts)
3rd	Leathery (charred parchment); down to subcutaneous fat
4th	Down to bone; adjacent adipose or muscle tissue

- 1st- and superficial 2nd-degree burns heal by epithelialization (primarily from hair follicles)
- Extremely deep burns, electrical burns, or compartment syndrome can cause rhabdomyolysis with myoglobinuria (Tx: hydration, alkalinize urine)



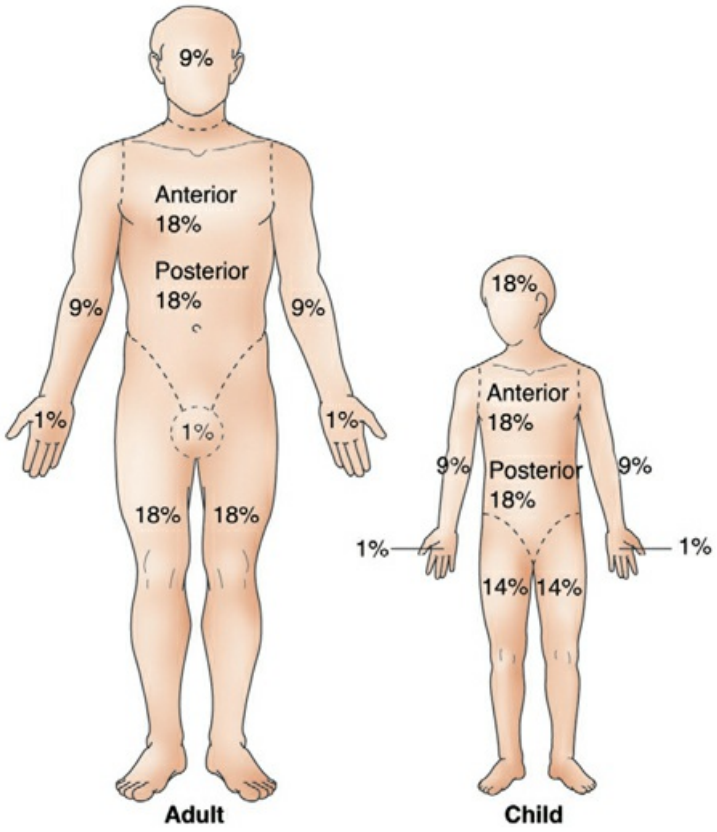
Schematic depiction of the skin.

ADMISSION CRITERIA[1]

- 2nd- and 3rd-degree burns > 10% BSA in patients aged < 10 or > 50 years
- 2nd- and 3rd-degree burns > 20% BSA in all other patients
- 2nd- and 3rd-degree burns to significant portions of hands, face, feet, genitalia, perineum, or skin overlying major joints
- 3rd-degree burns > 5% in any age group
- Electrical and chemical burns
- Concomitant inhalational injury, mechanical traumas, preexisting medical conditions
- Injuries in patients with special social, emotional, or long-term rehabilitation needs
- Suspected child abuse or neglect

BURN ASSESSMENT

- Deaths highest in children and elderly (trouble getting away)
- Scald burns – most common
- Flame burns – more likely to come to hospital and be admitted
- Assessing percentage of body surface burned (rule of 9s)
  - Head = 9, arms = 18, chest = 18, back = 18, legs = 36, perineum = 1
  - Can also use patient's palm to estimate injury (palm = 1%)
- Parkland formula
  - Use for burns ≥ 20% BSA (≥ 2nd degree; capped at 50% BSA) only – give 4 cc/kg × % burn in first 24 hours; give ½ the volume in the first 8 hours
  - Use lactated Ringer's solution (LR) in first 24 hours
    - Urine output best measure of resuscitation (> 0.5 cc/kg/h in adults, > 1 cc/kg/h in children, > 2 cc/kg/hr in infants < 6 months)
  - Parkland formula can grossly underestimate volume requirements with inhalational injury, ETOH, electrical injury, post-escharotomy
  - Important to use LR in first 24 hours
  - Colloid (albumin) in 1st 24 hours causes ↑ pulmonary/respiratory complications → can use colloid after 24 hours



Estimating burn size accurately is essential for care of the burn patient. The rule of nines provides a simple algorithm for calculating the burned surface area.

- Escharotomy indications (perform within 4–6 hours):
  - Circumferential deep burns (can cut off blood supply to the extremity)
  - Low temperature, weak pulse, ↓ capillary refill, ↓ pain sensation, or ↓ neurologic function in extremity

- Problems ventilating patient with significant chest torso burns
- May need fasciotomy if compartment syndrome suspected after escharotomy

- Risk factors for burn injuries – alcohol or drug use, age (very young/very old), smoking, low socioeconomic status, violence, epilepsy

CHILD ABUSE

- Accounts for 15% of burn injuries in children
- History and exam findings that suggest abuse:
  - History – delayed presentation for care, conflicting histories, previous injuries
  - Exam – sharply demarcated margins, uniform depth, absence of splash marks, stocking or glove patterns, flexor sparing, dorsal location on hands, very deep localized contact injury; scalding burns

LUNG AND AIRWAY INJURY

- Caused primarily by inhalation of carbonaceous materials and smoke, not heat
- Risk factors for injury – ETOH, trauma, closed space, rapid combustion, extremes of age, delayed extrication
- Signs and symptoms of possible injury – facial burns, wheezing, carbonaceous sputum (soot)
- Dx: fiberoptic bronchoscopy
- Indications for intubation – upper airway stridor or obstruction, worsening hypoxemia, massive volume resuscitation (can worsen symptoms)
- Pneumonia – most common infection in patients with > 30% BSA burns; also most common cause of death after > 30% BSA burns; inhalational injury #1 RF for pneumonia in burn patients

UNUSUAL BURNS

- Acid and alkali burns – copious water irrigation as soon as possible
  - Alkalis (Liquid Plumr, Drano) produce deeper burns than acid due to liquefaction necrosis
  - Acid burns (battery acid) produce coagulation necrosis
- Hydrofluoric acid burns – spread calcium on wound
- Powder burns – wipe away before irrigation
- Tar burns – cool, then wipe away with a lipophilic solvent (glycerol; eg adhesive remover)
- Electrical burns – need cardiac monitoring; injury is always deeper and worse than skin findings
  - Can cause rhabdomyolysis and compartment syndrome
  - Other complications – polyneuritis (demyelinization), quadriplegia, transverse myelitis, cataracts, liver necrosis, intestinal perforation, gallbladder perforation, pancreatic necrosis, posterior shoulder dislocations, vertebral body fractures
- Lightning – cardiopulmonary arrest secondary to ventricular fibrillation

1ST WEEK – EARLY EXCISION OF BURNED AREAS AND START NUTRITION

- Caloric need: 25 kcal/kg/day + (30 kcal × % burn)
  - Glucose – best source of nonprotein calories in patients with burns

- Burn wounds – use glucose in an obligatory fashion
- Place feeding tube in patients with significant BSA burns

- Protein need: 1 g/kg/day + (3 g × % burn)
  - Large burn wounds require a significant amount of protein for healing
- Excise burn wounds in < 72 hours (but not until after appropriate fluid resuscitation)
  - Used for deep 2nd-, 3rd-, and some 4th-degree burns
  - Viability is based on punctate bleeding (#1), color, and texture after removal (use dermatome)
  - Early excision and grafting (day 1 of burn) can be considered in stable patients with limited burns (< 20%) that are clearly 3rd degree (saves costs; minimizes pain, suffering, and complications)
- Wounds to face, palms, soles, and genitals are deferred for the 1st week
- For each burn wound excision – want < 1 L blood loss, < 20% of skin excised, and < 2 hours in OR
  - Patients can get extremely sick if too much time is spent in OR
- Skin grafts are contraindicated if culture is positive for beta-hemolytic strep or bacteria > 10^5
- Autografts (split-thickness [STSG] or full-thickness [FTSG]) – best
  - ↓ Infection, desiccation, protein loss, pain, water loss, heat loss, and RBC loss compared to dermal substitutes
  - Donor skin site is regenerated from hair follicles and skin edges on STSGs
  - Imbibition (osmotic) – blood supply to skin graft for days 0–3
  - Neovascularization – starts around day 3
  - Poorly vascularized beds are unlikely to support skin grafting → includes tendon, bone without periosteum, XRT areas
  - Split-thickness grafts are 0.12–0.15 mm (includes epidermis and part of dermis)
- Homografts (allografts; cadaveric skin) – not as good as autografts
  - Can be a good temporizing material; last 4 weeks
  - Allografts vascularize and are eventually rejected at which time they must be replaced
- Xenografts (porcine) – not as good as homografts; last 2 weeks; these do not vascularize
- Dermal substitutes – not as good as homografts or xenografts
- Meshed grafts – use for back, flank, trunk, arms, and legs
  - Reasons to delay autografting – infection, not enough skin donor sites, patient septic or unstable, do not want to create any more donor sites with concomitant blood loss
  - Most common reason for skin graft loss – seroma or hematoma formation under graft (prevents attachment)
    - Need to apply pressure dressing (cotton balls) to the skin graft to prevent seroma and hematoma buildup underneath the graft
  - STSGs are more likely to survive – graft not as thick so easier for imbibition and subsequent revascularization to occur
  - FTSGs have less wound contraction – good for areas such as the palms and back of hands
- Burn scar hypopigmentation and irregularities can be improved with dermabrasion thin split-thickness grafts

2ND TO 5TH WEEKS – SPECIALIZED AREAS ADDRESSED, ALLOGRAFT REPLACED WITH AUTOGRAFT

- Face – topical antibiotics for 1st week, FTSG for unhealed areas (nonmeshed)
- Hands
  - Superficial – ROM exercises; splint in extension if too much edema
  - Deep – immobilize in extension for 7 days after skin graft (need FTSG), then physical therapy. May need wire fixation of joints if unstable or open.
- Palms – try to preserve specialized palmar aponeurosis. Splint hand in extension for 7 days after FTSG
- Genitals – can use STSG (meshed)

BURN WOUND INFECTIONS

- The larger the burn, the greater the risk
- No role for prophylactic IV antibiotics
- Pseudomonas is most common organism in burn wound infection (some texts say staph but *Pseudomonas* is the classic answer), followed by *Staphylococcus*, *E. coli*, and *Enterobacter*
- More common in burns > 30% BSA
- Topical agents have decreased incidence of burn wound bacterial infections
- *Candida* infections have increased incidence secondary to topical antimicrobials
- Granulocyte chemotaxis and cell-mediated immunity are impaired in burn patients
- Silvadene (silver sulfadiazine) – can cause neutropenia and thrombocytopenia
  - Standard topical agent used for burns
  - Do not use in patients with sulfa allergy
  - Limited eschar penetration; can inhibit epithelialization
  - Ineffective against some *Pseudomonas*; effective for *Candida*
- Silver nitrate – can cause electrolyte imbalances (hyponatremia, hypochloremia, hypocalcemia, and hypokalemia)
  - Discoloration
  - Limited eschar penetration
  - Ineffective against some *Pseudomonas* species and GPCs
  - Can cause methemoglobinemia – contraindicated in patients with G6PD deficiency (causes hemolysis)
- Sulfamylon (mafenide sodium) – painful application
  - Can cause metabolic acidosis due to carbonic anhydrase inhibition (↓ renal conversion of $H_2CO_3 \rightarrow H_2O + CO_2$)
  - Good eschar penetration (good for deep burns); good for burns overlying cartilage
  - Broadest spectrum against *Pseudomonas* and GNRs
- Triple antibiotic ointment – good for burns near the eyes (Silvadene is irritating)
- Mupirocin – good for MRSA; very expensive
- Signs of burn wound infection – peripheral edema, 2nd- to 3rd-degree burn conversion, hemorrhage into scar, erythema gangrenosum, green fat, black skin around wound, rapid eschar separation, focal discoloration
- Burn wound sepsis – usually due to *Pseudomonas*
- HSV – most common viral infection in burn wounds
- $< 10^5$ organisms – not a burn wound infection
- Best way to detect burn wound infection (and differentiate from colonization) – biopsy of burn wound

- Tx of burn wound infection:
  - Burn wound excision with allograft placement (not autograft)
  - Systemic antibiotics
  - If just cellulitis around the wound, no excision and just give IV antibiotics

COMPLICATIONS AFTER BURNS

- Tetanus prophylaxis – required in patients with burn wounds
- Seizures – usually iatrogenic and related to Na concentration
- Peripheral neuropathy – secondary to small vessel injury and demyelination
- Ectopia – from contraction of burned adnexa. Tx: eyelid release
- Eyes – fluorescein staining to find injury. Tx: topical fluoroquinolone or gentamicin
- Corneal abrasion – Tx: topical antibiotics
- Symblepharon – eyelid stuck to conjunctiva. Tx: release with glass rod
- Heterotopic ossification of tendons – Tx: physical therapy; may need surgery
- Fractures – Tx: often need external fixation to allow for treatment of burns
- Curling's ulcer – gastric ulcer that occurs with burns
- Marjolin's ulcer – highly malignant squamous cell CA that arises in chronic (many years) non-healing burn wounds or unstable scars
- Hypertrophic scar
  - Usually occurs 3–4 months after injury secondary to ↑ neovascularity
  - More likely to be deep thermal injuries that take > 3 weeks to heal, heal by contraction and epithelial spread, or heal across flexor surfaces
  - Tx: steroid injection into lesion (best), silicone, compression; wait 1–2 years before scar modification surgery

RENAL ISSUES WITH SEVERE BURNS

- Hyperkalemia – from dead tissue and myonecrosis; avoid succinylcholine
- Myoglobinuria – from dead muscle; Tx: fluids; alkalinize urine
- Renal failure – from volume loss and myoglobinuria

FROSTBITE

- Tx: rapid re-warming in 40°C circulating water
- Tetanus shot, Silvadene; avoid early amputations

ERYTHEMA MULTIFORME AND VARIANTS

- Erythema multiforme – least severe form (self-limited, target lesions)
- Stevens–Johnson syndrome (more serious) – 10%–30% BSA
- Toxic epidermal necrolysis (TEN) – most severe form (> 30% BSA)
- Staph scalded skin syndrome (caused by *Staphylococcus aureus*)
- Skin epidermal–dermal separation seen in all
- Caused by a variety of drugs (penicillin [#1], Dilantin, Bactrim) and viruses
- Tx: fluid resuscitation and supportive; need to prevent wound desiccation with Telfa wraps; topical antibiotics; IV antibiotics if due to *Staphylococcus*; may need future skin grafts
- No steroids

[1]Modified from Feliciano DV, et al. *Trauma*. 3rd ed. Stamford, CT: Appleton & Lange; 1996:937.

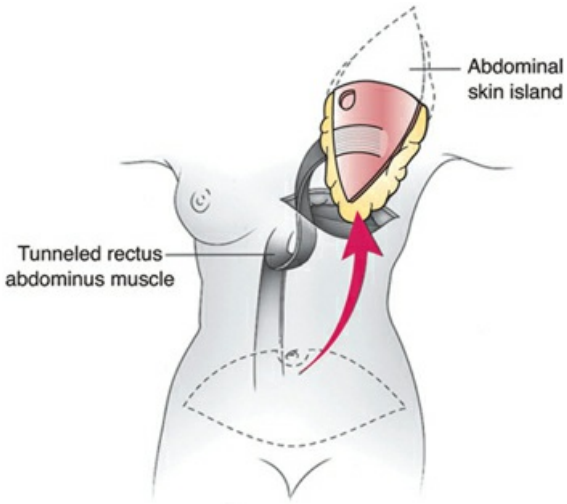
18 Plastics, Skin, and Soft Tissues

SKIN

- Epidermis – primarily cellular
  - Keratinocytes – main cell type in epidermis; originate from basal layer; provide mechanical barrier
  - Melanocytes – neuroectodermal origin (neural crest cells); in basal layer of epidermis
    - Have dendritic processes that transfer melanin to neighboring keratinocytes via melanosomes
    - Density of melanocytes is the same among races; difference is in melanin production
- Dermis – primarily structural proteins (collagen) for the epidermis
- Langerhans cells (dendritic cells)
  - Act as antigen-presenting cells (MHC class II)
  - Originate from bone marrow
  - Have a role in contact hypersensitivity reactions (type IV)
- Sensory nerves
  - Pacinian corpuscles – pressure
  - Ruffini's endings – warmth
  - Krause's end-bulbs – cold
  - Meissner's corpuscles – tactile sense
- Eccrine sweat glands – aqueous sweat (thermal regulation, usually hypotonic)
- Apocrine sweat glands – milky sweat
  - Highest concentration of glands in palms and soles; most sweat is the result of sympathetic nervous system via acetylcholine
- Lipid-soluble drugs – ↑ skin absorption
- Type I collagen – predominant type in skin; 70% of dermis; gives tensile strength
- Tension – resistance to stretching (collagen)
- Elasticity – ability to regain shape (branching proteins that can stretch to 2× normal length)
- Cushing's striae – decreased collagen results in loss of tensile strength and elasticity in the dermis; blood vessel dilation and neovascularization occur

FLAPS

- MCC of pedicled or anastomosed free flap necrosis – venous thrombosis
- Tissue expansion occurs by local recruitment, thinning of the dermis and epidermis, mitosis
- TRAM flaps
  - Complications – flap necrosis, ventral hernia, infection, abdominal wall weakness
  - Rely on superior epigastric vessels
  - Periumbilical muscle perforators most important determinant of TRAM flap viability



Transverse rectus abdominis myocutaneous (TRAM) flap reconstruction.

Pressure Sores		
Stage	Description	Treatment
I	Erythema and pain, no skin loss (epidermis)	Keep pressure off
II	Partial skin loss with yellow debris (into the dermis)	Local treatment, keep pressure off
III	Full-thickness skin loss, (subcutaneous fat exposure)	Sharp debridement; likely need myocutaneous flap
IV	Involves bony cortex, muscle, adipose tissue, tendon	Myocutaneous flaps (eg gluteal flap)

UV RADIATION

- Damages DNA and repair mechanisms
- Both a promoter and initiator
- Melanin single best factor for protecting skin from UV radiation
- UV-B – responsible for chronic sun damage
- Blistering sunburns in childhood place patient at higher risk for skin CA in later years

MELANOMA

- Most lethal skin CA – represents only 15% of skin CA but accounts for 65% of the deaths
- Risk factors for melanoma:
  - Dysplastic, atypical, or large congenital nevi – 10% lifetime risk for melanoma
  - Familial BK mole syndrome – almost 100% risk of melanoma
  - Xeroderma pigmentosum
  - Fair complexion, easy sunburn, intermittent sunburns, previous skin CA, previous XRT
  - 10% of melanomas familial
- Most common melanoma site on skin – back in men, legs in women
- Prognosis worse for men, ulcerated lesions, ocular and mucosal lesions
- Signs of melanoma (ABCDE) – asymmetry (angulations, indentation, notching, ulceration, bleeding), borders that are irregular, color change (darkening), diameter increase, elevation or evolving over time
- Originates from neural crest cells (melanocytes) in basal layer epidermis
- Blue color → most ominous
- Lung – most common location for distant melanoma metastases
- Most common metastasis to small bowel – melanoma

- Dx:
  - < 2 cm lesion – excisional biopsy (Tru-Cut core needle biopsy) unless cosmetically sensitive area – need resection with margins if pathology comes back as melanoma
  - > 2 cm lesions or cosmetically sensitive area – incisional biopsy (or punch biopsy), will need to resect with margins if pathology shows melanoma
  - Changes in a nevus – get biopsy
  - Stains for S-100 and HMB-45 proteins
- Types:
  - Melanoma in situ or thin lentigo maligna (ie Hutchinson's freckle) – just in the epidermis; 0.5-cm margins are appropriate here
  - Lentigo maligna melanoma – least aggressive, minimal invasion, radial growth 1st; presents as an elevated nodule
  - Superficial spreading (MC type) – intermediate malignancy; originates from nevus or sun-exposed areas
  - Acral lentiginous – very aggressive; palms/soles of African Americans; subungual (below fingernail)
  - Nodular – *most aggressive type*; most likely to have metastasized at time of Dx; deepest growth at time of Dx; vertical growth 1st; bluish-black with smooth borders; occurs *anywhere* on the body
- Staging – chest/abd/pelvic CT, LFTs, and LDH for all melanoma ≥ 1 mm; examine all possible draining lymph nodes
- Tx for all stages → 1) resection of primary tumor with appropriate margins (get down to muscle fascia) and; 2) management of lymph nodes

Recommended Surgical Margins for Melanoma Excision

Melanoma Thickness (mm)	Clinical Excision Margin (cm)
In situ	0.5
Thin (≤ 1.0)	1.0
Intermediate (1.1–2.0)	1.0–2.0
Thick (> 2.0)	2.0

Margins may need to be modified based on anatomic considerations but still require histologic confirmation of tumor-free margins. For clinically ill-defined lentigo maligna melanoma, wider margins may be required for histologic confirmation of tumor-free margins.

- Nodes
  - Always need to resect clinically positive nodes or if SLNBx is positive
  - You are trying to clear the tumor here, not stage (need formal lymphadenectomy, eg MRND)
  - Perform sentinel lymph node biopsy if nodes clinically negative and tumor ≥ 1 mm deep
  - Involved nodes usually nontender, round, hard, 1–2 cm
  - Need to include superficial parotidectomy for all scalp/face melanomas anterior to the ear and above the lip ≥ 1 mm deep including melanomas on the ear (20% metastasis rate to parotid)
- Axillary node melanoma with no other primary – Tx: complete axillary node dissection (remove Level I, II, and III nodes – unlike breast CA); primary lesion may have regressed or the melanoma primary is unpigmented
- Resection of metastases has provided some patients with long disease-free interval and is the

best chance for cure
- Isolated metastases (ie lung or liver) that can be resected with a low-risk procedure should probably undergo resection
- Dacarbazine first-line chemo for metastatic melanoma
- IL-2 and tumor vaccines (pembrolizumab) can be used for systemic disease
- No Mohs surgery for melanoma

BASAL CELL CARCINOMA

- Most common malignancy in United States; 4× more common than squamous cell skin CA
- 80% on head and neck
- Originates from epidermis – basal epithelial cells and hair follicles
- Pearly appearance, rolled borders, slow and indolent growth
- Pathology – peripheral palisading of nuclei and stromal retraction
- Rare metastases or nodal disease
- Regional adenectomy for rare clinically positive nodes
- Morpheaform type – most aggressive; has collagenase production
- Tx: 0.3–0.5-cm margins (or Mohs surgery)
  - XRT and chemotherapy – may be of limited benefit for inoperable disease, metastases or neuro/lymphatic/vessel invasion

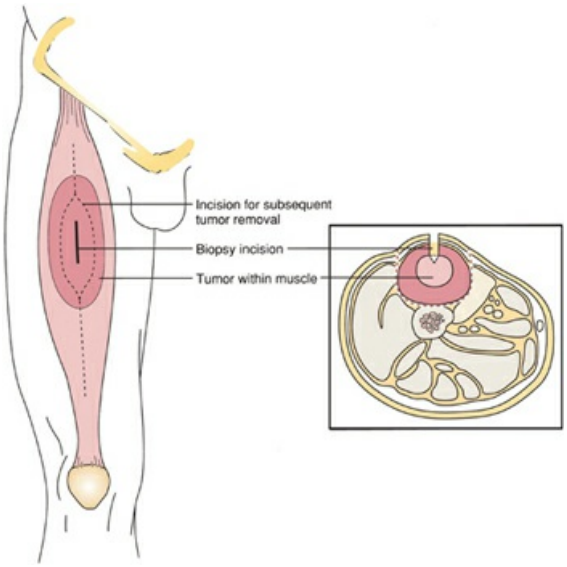
SQUAMOUS CELL CARCINOMA

- Overlying erythema, papulonodular with crust and ulceration; usually red-brown
- May have surrounding induration and satellite nodules
- Metastasizes more frequently than basal cell CA but less common than melanoma
- Can develop in post-XRT areas or in old burn scars
- Risk factors – actinic keratoses, xeroderma pigmentosum, Bowen's disease, atrophic epidermis, arsenics, hydrocarbons (coal tar), chlorophenols, HPV, immunosuppression, sun exposure, fair skin, previous XRT, previous skin CA
- Risk factors for metastasis – poorly differentiated, greater depth, recurrent lesions, immunosuppression
- Tx: 0.5–1.0-cm margins usual (2-cm margins for Marjolin's ulcers and penile/vulvar areas)
  - Can treat high risk with Mohs surgery (margin mapping using conservative slices; not used for melanoma) when trying to minimize area of resection (ie lesions on face)
  - Regional adenectomy for clinically positive nodes
  - XRT and chemotherapy – may be of limited benefit for inoperable disease, metastases or neuro/lymphatic/vessel invasion

SOFT TISSUE SARCOMA

- Most common soft tissue sarcomas – #1 malignant fibrous histiosarcoma, #2 liposarcoma
- 50% arise from extremities; 50% in children (arise from embryonic mesoderm)
- Most sarcomas are large, grow rapidly, and are painless
- Symptoms: asymptomatic mass (most common presentation), GI bleeding, bowel obstruction, neurologic deficit
- CXR – to R/O lung mets
- MRI *before* biopsy to R/O vascular, neuro, or bone invasion

- Core needle biopsy (best, 95% accurate); if that fails →
  - Excisional biopsy if mass < 4 cm
  - Longitudinal incisional biopsy for masses > 4 cm
  - Need to eventually resect biopsy skin site if biopsy shows sarcoma
  - Biopsy along the long axis plane of future incision for resection
- Hematogenous spread, not to lymphatics → metastasis to nodes is rare
  - Lung – most common site for metastasis
- Staging based on grade, not size
- Tumor grade is the most important prognostic factor (undifferentiated worse)
- Tx: Want at least 2–3 margins and at least 1 uninvolved fascial plane → try to perform limb-sparing operation
  - Place clips to mark site of likely recurrence → will XRT these later
  - Postop XRT – for high-grade tumors, close margins, or tumors > 5 cm
  - Chemotherapy is doxorubicin (Adriamycin) based
  - Tumors > 10 cm may benefit from preop chemo-XRT → may allow limb-sparing resection; 90% do not require an amputation
  - Isolated sarcoma metastases without other evidence of systemic disease can be resected and are the best chance for survival; otherwise can palliate with XRT
  - Midline incision favored for pelvic and retroperitoneal sarcomas
  - With resection, try to preserve motor nerves and retain or reconstruct vessels



Technique for biopsy of an extremity soft-tissue mass suspected of being a sarcoma. The incision should be oriented along the long axis of the extremity, at the point where the lesion is closest to the surface, and situated so that it can be readily excised along with the tumor if a diagnosis of sarcoma is made. There should be no raising of flaps or disturbance of tissue planes superficial to the tumor. The mass should not be enucleated within the pseudocapsule; rather, incisional biopsy leaving the bulk of the lesion undisturbed should be carried out. Before wound closure, hemostasis should be achieved to avoid a hematoma, which could disseminate tumor cells through normal tissue planes. Drains are not used routinely.

- Poor prognosis overall
  - Delay in diagnosis

- Difficulty with total resection
- Difficulty getting XRT to pelvic tumors
- Chemo and XRT have not changed survival
- 40% 5-year survival rate with complete resection

- Head and neck sarcomas – usually in the pediatric population (usually rhabdomyosarcoma)
  - Hard to get margins because of proximity to vital structures
  - Postop XRT for positive or close margins as negative margins may be impossible to obtain
- Retroperitoneal sarcomas – most commonly are leiomyosarcomas and liposarcomas
  - Especially poor prognosis due to delayed diagnosis and incomplete resection; also trouble getting XRT to the tumor due to proximity of vital structures
  - Ability to completely remove the tumor the most important prognostic factor
  - Need to rule-out lymphoma in this location (MC retroperitoneal tumor overall)
- Risk factors
  - Asbestos – mesothelioma
  - PVC and arsenic – angiosarcoma
  - Chronic lymphedema – lymphangiosarcoma
- Kaposi's sarcoma (KS) – vascular sarcoma
  - Oral and pharyngeal mucosa are the most common sites; bleeding, dysphagia
  - Associated with immunocompromised state; most common malignancy in AIDS
  - Rarely a cause of death in AIDS (very slow growing)
    - Tx: primary goal is palliation
    - AIDS Tx (HAART) shrinks AIDS-related KS – *best Tx*
    - Consider XRT or intra-lesional vinblastine for local disease
    - Interferon-alpha for disseminated disease
    - Surgery for severe intestinal hemorrhage
- Childhood rhabdomyosarcoma
  - #1 soft tissue sarcoma in kids
  - Head/neck, genitourinary, extremities, and trunk (poorest prognosis)
  - Embryonal subtype – most common
  - Alveolar subtype – worst prognosis
  - Rhabdomyosarcoma contains desmin
  - Botryoides tumor – vaginal rhabdomyosarcoma
  - Tx: surgery; doxorubicin-based chemotherapy
- Bone sarcomas
  - Most are metastatic at the time of diagnosis
  - Osteosarcoma
    - Increased incidence around the knee
    - Originates from metaphyseal cells
    - Usually in children
- Genetic syndromes for soft tissue tumors
  - Neurofibromatosis – CNS tumors, peripheral sheath tumors, pheochromocytoma
  - Li–Fraumeni syndrome – childhood rhabdomyosarcoma, many others
  - Hereditary retinoblastoma – also includes other sarcomas
  - Tuberous sclerosis – angiomyolipoma
  - Gardner's syndrome – familial adenomatous polyposis and intra-abdominal desmoids tumors

OTHER CONDITIONS

- Lip lacerations – important to line up vermillion border
- Xanthoma (cholesterol-rich) – yellow, contains histiocytes; benign
- Warts (verruca vulgaris) – viral origin, contagious, autoinoculable, can be painful
  - Tx: salicylic acid; liquid nitrogen
- Lipomas – common but rarely malignant; back, neck, between shoulders
  - Most common mesenchymal tumor
- Neuromas – can be associated with neurofibromatosis and von Recklinghausen's disease (café-au-lait spots, axillary freckling; peripheral nerve and CNS tumors)
- Keratoses
  - Actinic keratosis – premalignant in sun-damaged areas; need excisional biopsy if suspicious; Tx: diclofenac sodium; liquid nitrogen
  - Seborrheic keratosis – not premalignant; trunk on elderly; can be dark
  - Arsenical keratosis – associated with squamous cell carcinoma
- Merkel cell carcinoma – are neuroendocrine
  - Very aggressive malignant tumor with early regional and systemic spread
  - Red to purple papulonodule or indurated plaque
  - Have neuron-specific enolase (NSE), cytokeratin, and neurofilament protein
  - All patients get SLNBx or formal lymph node dissection
  - Need 2–3-cm margins
- Glomus cell tumor
  - Painful tumor composed of blood vessels and nerves
  - Benign; most common in the terminal aspect of the digit
  - Tx: tumor excision
- Desmoid tumors – benign but locally very invasive
  - Anterior abdominal wall (most common location) desmoids can occur during or following pregnancy; can also occur after trauma or surgery; occur in fascial planes
  - Intra-abdominal desmoids associated with Gardner's syndrome and retroperitoneal fibrosis; often encases bowel, making it hard to get en bloc resection
  - High risk of local recurrences; no distant spread
  - Tx: surgery if possible; chemotherapy (sulindac, tamoxifen) if vital structure involved or too much bowel would be taken (high risk of short bowel syndrome with surgery)
- Bowen's disease – SCCA in situ; 10% turn into invasive SCCA; associated with HPV
  - Tx: imiquimod, cautery ablation, topical 5-FU, *avoid wide local excision* if possible (high recurrence rate w/ HPV); regular biopsies to R/O CA
- Keratoacanthoma
  - Rapid growth, rolled edges, crater filled with keratin
  - Is not malignant but can be confused with SCCA
  - Involutes spontaneously over months
  - Always biopsy these to be sure
  - If small, excise; if large, biopsy and observe
- Hyperhidrosis – ↑ sweating, especially noticeable in the palms. Tx: thoracic sympathectomy if refractory to variety of antiperspirants
- Hidradenitis – infection of the apocrine sweat glands, usually in axilla and groin regions
  - Staph/strep most common organisms; avoid antiperspirants
  - Tx: antibiotics, improved hygiene 1st; may need surgery to remove skin and associated

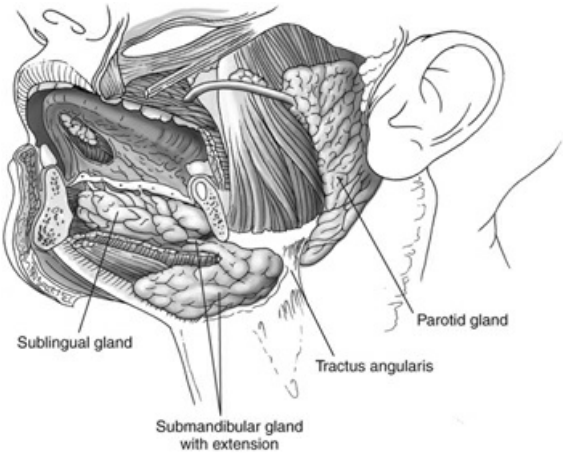
sweat glands (excise from skin to fascia)

- Benign cysts
  - Epidermal inclusion cyst – most common; have completely mature epidermis with creamy keratin material
  - Trichilemmal cyst – in scalp, no epidermis; contain keratin from hair follicles
  - Ganglion cyst – over joints, usually the wrist; filled with synovial fluid
    - Aspiration cures 50%; need to remove the check valve with surgery
  - Dermoid cyst – midline intra-abdominal and sacral lesions usual; need resection due to malignancy risk
  - Pilonidal cyst – congenital coccygeal sinus (at sacrococcygeal junction) with ingrown hair; gets infected and needs to be excised

19 Head and Neck

ANATOMY AND PHYSIOLOGY

- Anterior neck triangle – sternocleidomastoid muscle (SCM), sternal notch, inferior border of the digastric muscle; contains the carotid sheath
- Posterior neck triangle – posterior border of the SCM, trapezius muscle, and the clavicle; contains the accessory nerve (innervates SCM, trapezius, and platysma) and the brachial plexus
- Parotid glands – secrete mostly serous fluid
- Sublingual glands – secrete mostly mucin
- Submandibular glands – 50/50 serous/mucin
- In larynx, the false vocal cords are superior to the true vocal cords
- Trachea has U-shaped cartilage and a posterior portion that is membranous



Major salivary glands. The lateral view, illustrating the tractus angularis and submandibular gland with extension under the mylohyoid muscle and the sublingual gland. (From Byers RM. Operations involving the submandibular and sublingual salivary glands. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

- Vagus nerve – runs between internal jugular (IJ) vein and carotid artery
- Phrenic nerve – runs on top of the anterior scalene muscle
- Long thoracic nerve – runs posterior to the middle scalene muscle
- Trigeminal nerve – ophthalmic, maxillary, and mandibular branches
  - Gives sensation to most of face; mastication muscles
  - Marginal mandibular nerve comes off trigeminal nerve – gives fibers to the corner of the mouth
- Facial nerve – temporal, zygomatic, buccal, marginal mandibular, and cervical branches
  - Motor function to face
- Glossopharyngeal nerve – taste to posterior ⅓ tongue
  - Motor to stylopharyngeus

- Injury affects swallowing
- Hypoglossal nerve – motor to all of tongue except palatoglossus
  - Tongue deviates to the same side of a hypoglossal nerve injury
- Recurrent laryngeal nerve – innervates all of larynx except cricothyroid muscle
- Superior laryngeal nerve – innervates the cricothyroid muscle
- Frey's syndrome – occurs after parotidectomy; injury of auriculotemporal nerve that then cross-innervates with sympathetic fibers to sweat glands of skin
  - Symptom: gustatory sweating
- Thyrocervical trunk – "STAT": suprascapular artery, transverse cervical artery, ascending cervical artery, inferior thyroid artery
- External carotid artery – 1st branch is superior thyroid artery
- Trapezius flap – based on transverse cervical artery
- Pectoralis major flap – based on either the thoracoacromial artery or the internal mammary artery
- Torus palatini – congenital bony mass on upper palate of mouth. Tx: nothing
- Torus mandibular – similar to above but on lingual surface of mandible. Tx: nothing
- Modified radical neck dissection (MRND) – takes omohyoid, submandibular gland, sensory nerves C2–C5, cervical branch of facial nerve, and ipsilateral thyroid
  - No mortality difference compared with RND
- Radical neck dissection (RND) – same as MRND *plus* accessory nerve (CN XII), sternocleidomastoid, and internal jugular resection (rarely done anymore)
  - Most morbidity occurs from accessory nerve resection
- ENT chemotherapy – 5FU and cisplatin usual
- ENT tumors often present as an enlarged lymph node in the neck

ORAL CAVITY CANCER

- Most common cancer of the oral cavity, pharynx, and larynx – squamous cell CA
  - Biggest risk factors – tobacco and ETOH
  - Erythroplakia – considered more premalignant than leukoplakia
- Oral cavity includes mouth floor, anterior ⅓ tongue, gingiva, hard palate, anterior tonsillar pillars, and lips
- Lower lip – most common site for oral cavity CA (more common than upper lip due to sun exposure)
- Survival rate lowest for hard palate tumors – hard to resect
- Oral cavity CA increased in patients with Plummer–Vinson syndrome (glossitis, cervical dysphagia from esophageal web, spoon fingers, iron-deficiency anemia)
- Treatment
  - Wide resection (1 cm margins)
  - MRND for tumors > 4 cm, clinically positive nodes, or bone invasion
  - Postop XRT for advanced lesions (> 4 cm, positive margins, or nodal/bone involvement)
- Lip CA – may need flaps if more than ⅓ of the lip is removed
  - Lesions along the commissure are most aggressive
- Tongue CA – can still operate with jaw invasion (commando procedure)
- Verrucous ulcer – a well-differentiated SCCA; often found on the cheek; oral tobacco
  - Not aggressive, rare metastasis
  - Tx: full cheek resection ± flap; *no lymph node dissection*

- Cancer of maxillary sinus – Tx: maxillectomy
- Tonsillar CA – ETOH, tobacco, males; SCCA most common; asymptomatic until large; 80% have lymph node metastases at time of diagnosis
  - Tx: tonsillectomy best way to biopsy; wide resection with margins after that

PHARYNGEAL CANCER

- Nasopharyngeal SCCA – EBV; Chinese; presents with nose bleeding or obstruction
  - Goes to posterior cervical neck nodes
  - Tx: *XRT primary therapy* (*very sensitive*; give chemo-XRT for advanced disease – *no surgery*)
  - Children – lymphoma #1 tumor of nasopharynx. Tx: chemotherapy
  - Papilloma – most common benign neoplasm of nose/paranasal sinuses
- Oropharyngeal SCCA – neck mass, sore throat
  - Goes to posterior cervical neck nodes
  - Tx: XRT for tumors < 4 cm and no nodal or bone invasion
  - Combined surgery, MRND, and XRT for advanced tumors (> 4 cm, bone invasion or nodal invasion)
- Hypopharyngeal SCCA – hoarseness; early metastases
  - Goes to anterior cervical nodes
  - Tx: XRT for tumors < 4 cm and no nodal or bone invasion
  - Combined surgery, MRND, and XRT for advanced tumors (> 4 cm, bone invasion or nodal invasion)
- Nasopharyngeal angiofibroma – benign tumor
  - Presents in males < 20 years (obstruction or epistaxis)
  - Extremely vascular
  - Tx: angiography and embolization (usually internal maxillary artery), followed by resection

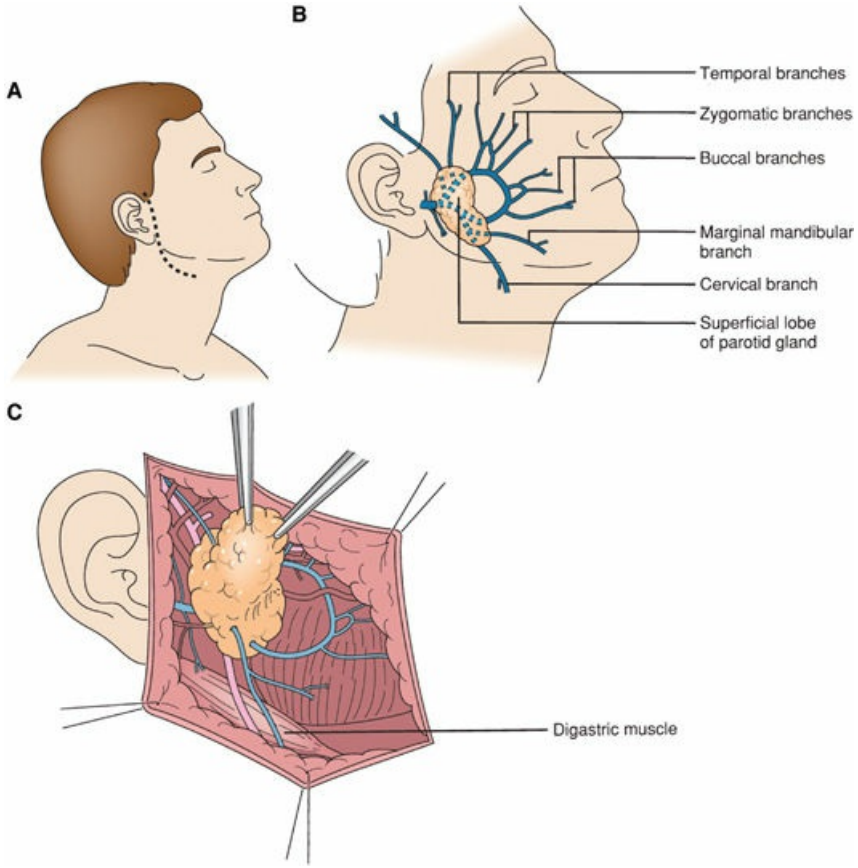
LARYNGEAL CANCER

- Hoarseness, aspiration, dyspnea, dysphagia
- Try to preserve larynx
- Tx: XRT (if vocal cord only) or chemo-XRT (if beyond vocal cord)
  - Spread XRT to ipsilateral neck nodes; bilateral neck nodes if the tumor crosses the midline
  - Surgery is not the primary Tx; try to preserve larynx
  - MRND needed if nodes clinically positive
  - Take ipsilateral thyroid lobe with MRND
- Papilloma – most common benign lesion of larynx

SALIVARY GLAND CANCERS

- Parotid, submandibular, sublingual, and minor salivary glands
- Submandibular or sublingual tumors – can present as a neck mass or swelling in the floor of the mouth
- Mass in large salivary gland → more likely mass is benign
- Mass in small salivary gland → more likely mass is malignant, although the parotid gland is the most frequent site for malignant tumor

- Pre-auricular masses are parotid tumors until proven otherwise
  - Dx: superficial parotidectomy (do not shell out; no enucleation)
  - No FNA unless in the deep parotid gland, is felt to be a metastasis from another site, or if the patient is a poor surgical risk
- Malignant tumors
  - Often present as a painful mass but can also present with facial nerve paralysis or lymphadenopathy (pain or facial nerve paralysis from a parotid mass is highly suggestive of malignancy)
  - Lymphatic drainage is to the intra-parotid and anterior cervical chain nodes
  - Most commonly metastasizes to the lung
  - Mucoepidermoid CA – #1 malignant tumor of the salivary glands
    - Wide range of aggressiveness
  - Adenoid cystic CA – #2 malignant tumor of the salivary glands
    - Long, indolent course; propensity to invade nerve roots
    - Very sensitive to XRT
  - Tx for both: resection of salivary gland (eg total parotidectomy), prophylactic MRND, and postop XRT
    - If in parotid, need to take whole lobe; try to preserve facial nerve
- Benign tumors
  - Often present as a painless mass
  - Pleomorphic adenoma (mixed tumor) – #1 tumor overall of the salivary glands
    - Malignant degeneration in 5%
    - Tx: superficial parotidectomy
    - If malignant degeneration, need total parotidectomy
  - Warthin's tumor – #2 benign tumor of the salivary glands
    - Males, bilateral in 10%
    - Tx: superficial parotidectomy
- Most common injured nerve with parotid surgery – greater auricular nerve (numbness over lower portion of ear)
- Most common injured nerve with submandibular gland resection – marginal mandibular nerve (branch of the facial nerve; get droop at the corner of the mouth)
- Most common salivary gland tumor in children – hemangiomas



Superficial parotidectomy. A. The standard Blair incision or the cosmetically superior facelift incision can be used. B. Branches of the facial nerve course between the superficial and deep lobes of the parotid. C. The main trunk of the facial nerve is identified 8 mm deep to the tympanomastoid suture line and at the same level as the digastric muscle.

EAR

- Pinna lacerations – need suture through involved cartilage
- Outer ear infections – early antibiotics to avoid cartilage necrosis
- Cauliflower ear – undrained hematomas that organize and calcify; need to be drained to avoid this
- Cholesteatoma – epidermal inclusion cyst of ear; slow growing but erode as they grow; present with conductive hearing loss and clear drainage from ear. Tx: surgical excision; can involve mastoid with possible need for mastoidectomy
- Chemodectomas – vascular tumor of middle ear (paraganglionoma). Tx: surgery ± XRT
- Acoustic neuroma – CN VIII (vestibulocochlear nerve) tinnitus, hearing loss, unsteadiness; can grow into cerebellar/pontine angle. Dx: MRI; Tx: craniotomy and resection; XRT is alternative to surgery
- Ear SCCA – 20% metastasize to parotid gland. Tx: resection and parotidectomy, MRND for positive nodes or large tumors
- Rhabdomyosarcoma – most common childhood aural malignancy (although rare) of the middle or external ear

NOSE

- Nasal fractures – set after swelling decreases

- Septal hematoma – need to drain to avoid infection and necrosis of septum
- CSF rhinorrhea – usually a cribriform plate fracture (CSF has tau protein)
  - Repair of facial fractures may help leak; may need contrast study to help find leak
  - Tx: conservative 2–3 weeks; try epidural catheter drainage of CSF; may need transethmoidal repair
- Epistaxis – 90% are anterior and can be controlled with packing; consider internal maxillary artery or ethmoid artery embolization for persistent posterior bleeding despite packing/balloon; can be life threatening in elderly patients with HTN

NECK AND JAW

- Radicular cyst – inflammatory cyst at the root of teeth; can cause bone erosion; lucent on X-ray; Tx local excision or curettage
- Ameloblastoma – slow-growing malignancy of odontogenic epithelium (outside portion of teeth); soap bubble appearance on X-ray. Tx: wide local excision
- Osteogenic sarcoma – poor prognosis. Tx: multimodality approach that includes surgery
- Maxillary jaw fractures – most treated with wire fixation
- TMJ dislocations – treated with closed reduction
- Lower lip numbness – inferior alveolar nerve damage (branch of mandibular nerve)
- Stensen's duct laceration – repair over catheter stent
  - Ligation can cause painful parotid atrophy and facial asymmetry
- Suppurative parotitis – usually in elderly patients; occurs with dehydration; staph most common organism
  - Tx: fluids, salivation, antibiotics; drainage if abscess develops or patient not improving; may need to remove salivary calculi if present
  - Can be life-threatening
- Sialoadenitis – acute inflammation of a salivary gland related to a stone in the duct; most calculi near orifice
  - 80% of the time affects the submandibular or sublingual glands
  - Recurrent sialoadenitis is due to ascending infection from the oral cavity
  - Tx: incise duct and remove stone
  - Gland excision may eventually be necessary for recurrent disease

ABSCESSES

- Peritonsillar abscess – older kids (> 10 years)
  - Symptoms: trismus, odynophagia; usually does not obstruct airway
  - Tx: needle aspiration 1st, then drainage through tonsillar bed if no relief in 24 hours (may need to intubate to drain; will self-drain with swallowing once opened)
- Retropharyngeal abscess – younger kids (< 10 years)
  - Symptoms: fever, odynophagia, drool; is an airway emergency
  - Can occur in elderly with Pott's disease
  - Tx: intubate the patient in a calm setting; drainage through posterior pharyngeal wall; will self-drain with swallowing once opened
- Parapharyngeal abscess – all age groups; occurs with dental infections, tonsillitis, pharyngitis
  - Morbidity comes from vascular invasion and mediastinal spread via prevertebral and retropharyngeal spaces

- Tx: drain through lateral neck to avoid damaging internal carotid and internal jugular veins; need to leave drain in
- Ludwig's angina – acute infection of the floor of the mouth, involves mylohyoid muscle
  - Most common cause is dental infection of the mandibular teeth
  - May rapidly spread to deeper structures and cause airway obstruction
  - Tx: airway control, surgical drainage (intra- or extra-oral), antibiotics

ASYMPTOMATIC HEAD AND NECK MASSES

- Neck mass workup
  - 1st – H and P, laryngoscopy, and *FNA (best test for Dx)*; can consider antibiotics for 2 weeks with re-evaluation if thought to be inflammatory
  - 2nd – if above nondiagnostic → panendoscopy (laryngoscopy, upper endoscopy, and bronchoscopy) with multiple random biopsies (looking for primary), neck and chest CT
  - 3rd – still cannot figure it out → perform excisional biopsy; need to be prepared for MRND
  - Adenocarcinoma in lymph node suggests breast, GI, or lung primary
  - Squamous cell CA in lymph node suggests lung or head/neck primary
- Posterior neck masses – if no obvious malignant epithelial tumor, considered to have lymphoma (Sx's – fever, night sweats; Tx – chemotherapy) until proved otherwise. Need FNA (core needle biopsy may be better if lymphoma suspected) or open biopsy
- Most common distant metastases for primary head and neck tumors → lung
- Epidermoid CA (SCCA variant) found in cervical node *without* known primary →
  - 1st – panendoscopy to look for primary; get random biopsies
  - 2nd – CT scan
  - 3rd – still cannot find primary → ipsilateral MRND, ipsilateral tonsillectomy (most common location for occult head/neck tumor), bilateral XRT (nodal region and potential primary sites)

OTHER CONDITIONS

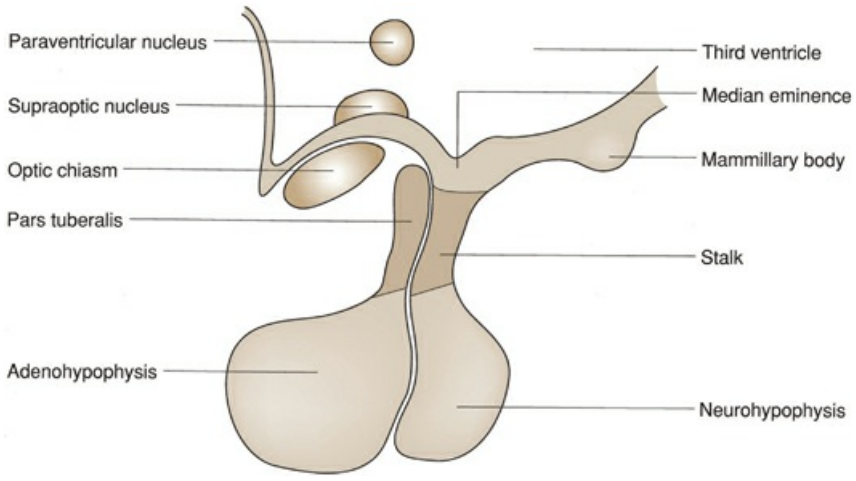
- Esophageal foreign body – dysphagia; most just below the cricopharyngeus (95%)
  - Dx and Tx: rigid EGD under anesthesia
  - Perforation risk increases with length of time in the esophagus
- Fever and pain after EGD for foreign body → Gastrografin followed by barium swallow to rule out perforation
- Laryngeal foreign body – coughing; emergent cricothyroidotomy as a last resort may be needed to secure airway
- Sleep apnea – associated with MIs, arrhythmias, and death
  - More common in obese and those with micrognathia/retrognathia → have snoring and excessive daytime somnolence; can get cor pulmonale (right heart failure)
  - Tx: CPAP, uvulopalatopharyngoplasty (best surgical solution), or permanent trach
- Prolonged intubation – can lead to subglottic stenosis, Tx: tracheal resection and reconstruction
- Tracheostomy – consider in patients who will require intubation for > 7–14 days
  - Decreases secretions, provides easier ventilation, decreases pneumonia risk
- Median rhomboid glossitis – failure of tongue fusion. Tx: none necessary

- Cleft lip (primary palate) – involves lip, alveolus, or both
  - Repair at 10 weeks, 10 lb, Hgb 10. Repair nasal deformities at same time
  - May be associated with poor feeding
- Cleft palate (secondary palate) – involves hard and soft palates; may affect speech and swallowing if not closed soon enough; may affect maxillofacial growth if closed too early → repair at 12 months
- Hemangioma – most common benign head and neck tumor in adults
- Mastoiditis – infection of the mastoid cells; can destroy bone
  - Rare; results as a complication of untreated acute supportive otitis media
  - Ear is pushed forward
  - Tx: antibiotics, tympanostomy tube; may need emergency mastoidectomy
- Epiglottitis
  - Rare since immunization against *H. influenzae* type B
  - Mainly in children aged 3–5
  - Symptoms: stridor, drooling, leaning forward position, high fever, throat pain, thumbprint sign on lateral neck film
  - Can cause airway obstruction
  - Tx: early control of the airway; antibiotics

20 Pituitary

ANATOMY AND PHYSIOLOGY

- Hypothalamus – releases TRH, CRH, GnRH, GHRH, and dopamine into median eminence; passes through neurohypophysis on way to adenohypophysis
- Dopamine – inhibits prolactin secretion
- Posterior pituitary (neurohypophysis)
  - ADH – supraoptic nuclei, regulated by osmolar receptors in hypothalamus
  - Oxytocin – paraventricular nuclei in hypothalamus
  - Neurohypophysis does not contain cell bodies
- Anterior pituitary (80% of gland, adenohypophysis)
  - Releases ACTH, TSH, GH, LH, FSH, and prolactin
  - Does not have its own direct blood supply; passes through neurohypophysis 1st (portal venous system)
- Bi-temporal hemianopia – pituitary mass compressing optic nerve (CN II) at chiasm
- Nonfunctional tumors – almost always macroadenomas; present with mass effect and decreased ACTH, TSH, GH, LH, FSH. Tx: transsphenoidal resection
- Contraindications to transsphenoidal approaches – suprasellar extension, massive lateral extension, dumbbell-shaped tumor
- Most pituitary tumors respond to bromocriptine (dopamine agonist)



Schematic diagram of the pituitary and floor of the third ventricle as seen in a midline sagittal view. Anterior is to the left.

PROLACTINOMA

- Most common pituitary adenoma
- Mostly microadenomas
- Most patients do not need surgery. Prolactin is usually > 150 for symptoms to occur
- Symptoms: galactorrhea, irregular menses, ↓ libido, infertility
- If asymptomatic and a microadenoma (< 10 mm) – just follow with MRI

- If symptomatic or is a macroadenoma, need Tx
  - Bromocriptine (safe in pregnancy) or cabergoline (both are dopamine agonists)
  - Transsphenoidal resection for failure of medical management
  - Macroadenomas – transsphenoidal resection with hemorrhage, visual loss, wants pregnancy, CSF leak

ACROMEGALY (GROWTH HORMONE)

- Symptoms: HTN, DM, gigantism; can be life-threatening secondary to cardiac symptoms (valve dysfunction, cardiomyopathy)
- Usually macroadenomas
- Dx: elevated IGF-1 *(best test)* growth hormone > 10 in 90%; MRI
- Tx: transsphenoidal resection (first-line therapy); XRT, bromocriptine, octreotide, and pegvisomant (GH receptor antagonist) can be used as secondary therapies

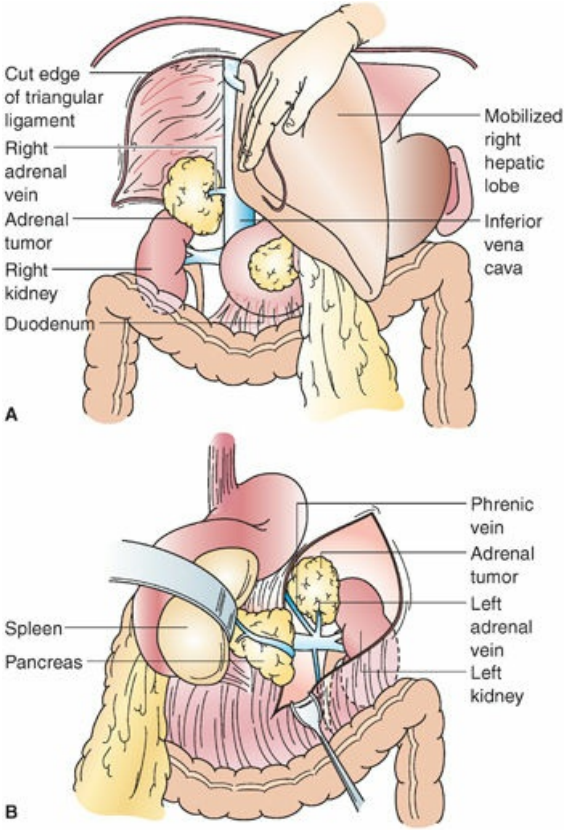
OTHER CONDITIONS

- Sheehan's syndrome
  - Post-partum trouble lactating – usually 1st sign
  - Can also have amenorrhea, adrenal insufficiency, and hypothyroidism
  - Due to anterior pituitary ischemia following hemorrhage and hypotensive episode during childbirth
  - Tx: corticosteroids and hormone replacement
- Pituitary apoplexy
  - Bleeding into a pituitary tumor with subsequent destruction of the gland
  - May have history of chronic headache, visual loss, or endocrine problems
  - Acute bleeding Sx's – severe headache, vision loss, stupor, hypotension
  - Tx: emergent corticosteroids; hormone replacement
- Craniopharyngioma – benign calcified cyst, remnants of Rathke's pouch; grows along pituitary stalk to suprasellar location (anterior pituitary)
  - Symptoms: most frequently presents with endocrine abnormalities, visual disturbances (bitemporal hemianopsia), headache, hydrocephalus
  - Tx: surgery to resect cyst
  - Diabetes insipidus – frequent complication postoperatively
- Bilateral pituitary masses – check pituitary axis hormones; if OK, probably metastases
- Nelson's syndrome
  - Occurs after bilateral adrenalectomy; ↑ CRH causes pituitary enlargement, resulting in amenorrhea and visual problems (bi-temporal hemianopia)
  - Also get hyperpigmentation from beta-MSH (melanocyte-stimulating hormone), a peptide byproduct of ACTH
  - Tx: steroids (prednisone)
- Waterhouse–Friderichsen syndrome – adrenal gland hemorrhage that occurs after meningococcal sepsis infection; can lead to adrenal insufficiency

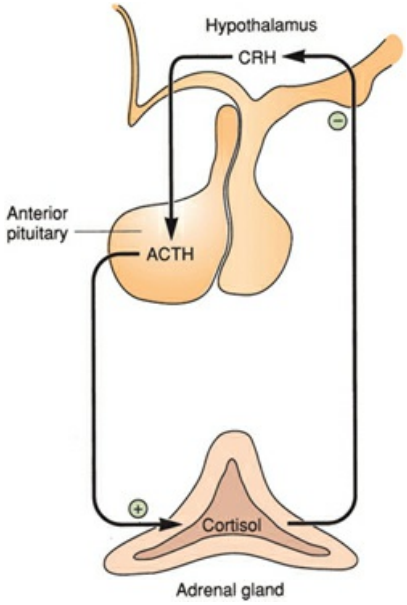
21 Adrenal

INTRODUCTION

- Vascular supply
  - Superior adrenal – inferior phrenic artery
  - Middle adrenal – aorta
  - Inferior adrenal – renal artery
  - Left adrenal vein goes to left renal vein
  - Right adrenal vein goes to inferior vena cava
- Made up of adrenal cortex and adrenal medulla
- No innervation to the cortex
- Medulla receives innervation from the sympathetic splanchnic nerves
- Lymphatics drain to subdiaphragmatic and renal lymph nodes
- Cortisol – increases vascular tone, gluconeogenesis, glycogenolysis, suppresses immune system



Anterior approach to right (A) and left (B) adrenalectomy. Note position of phrenic vein in relationship to the left adrenal vein and tumor.



Schematic of hypothalamic–pituitary–adrenal axis for cortisol. Regulatory feedback relationships are designated with arrows.

ASYMPTOMATIC ADRENAL MASS

- 1%–2% of abdominal CT scans show incidentaloma (5% are metastases)
- Benign adenomas are common
- Adrenals are also common sites for metastases
- Dx: check for functioning tumor ***before*** biopsy or surgery – urine metanephrines/VMA/catecholamines, urinary hydroxycorticosteroids, serum K with plasma renin and aldosterone levels
  - Consider CXR, colonoscopy, and mammogram to check for a primary tumor
- Surgery is indicated if mass has ominous CT scan characteristics (non-homogenous), is > 4–6 cm, is functioning, or is enlarging
- If going to follow an incidentaloma, need repeat imaging every 3 months for 1 year, then yearly
- Anterior approach for adrenal CA resection
- Common metastases to adrenal – lung CA (#1), breast CA, melanoma, renal CA
- Cancer history with asymptomatic adrenal mass – need biopsy
- Some isolated metastases to the adrenal gland can be resected with adrenalectomy

ADRENAL CORTEX

- From mesoderm – remember GFR = salt, sugar, sex steroids
  - Glomerulosa – aldosterone; fasciculata – glucocorticoids; reticularis – androgens/estrogens
- Cholesterol → progesterone → androgens/cortisol/aldosterone
- All zones have 21- and 11-beta hydroxylase
- Corticotropin-releasing hormone (CRH) is released from the hypothalamus and goes to anterior pituitary gland
- ACTH is released from the anterior pituitary gland and causes the release of cortisol
- Cortisol has a diurnal peak at 4–6 a.m.

- Cortisol – inotropic, chronotropic, and increases vascular resistance; proteolysis and gluconeogenesis; decreases inflammation
- Aldosterone stimulates renal sodium resorption and secretion of potassium and hydrogen ion
- Aldosterone secretion is stimulated by angiotensin II and hyperkalemia, and to some extent ACTH
- Excess estrogens and androgens by adrenals – almost always cancer
- Congenital adrenal hyperplasia (enzyme defect in cortisol synthesis)
  - 21-Hydroxylase deficiency (90%) – most common; precocious puberty in males, virilization in females
    - ↑ 17-OH progesterone leads to ↑ production of testosterone
    - Is salt wasting (↓ sodium and ↑ potassium) and causes hypotension
    - Tx: cortisol, genitoplasty
  - 11-Hydroxylase deficiency – precocious puberty in males, virilization in females
    - ↑ 11-Deoxycortisone
    - Is salt saving (deoxycortisone acts as a mineralocorticoid) and causes hypertension
    - Tx: cortisol, genitoplasty
- Hyperaldosteronism (Conn's syndrome)
  - Symptoms: HTN secondary to sodium retention without edema and hypokalemia; also have weakness, polydipsia, and polyuria
  - Primary disease (renin is low) – adenoma (85%) → #1 cause of primary hyperaldosteronism, hyperplasia (15%), ovarian tumors (rare), cancer (rare)
  - Secondary disease (renin is high) – more common than primary disease; CHF, renal artery stenosis, liver failure, diuretics, Bartter's syndrome (renin-secreting tumor)
  - Dx for primary hyperaldosteronism (1 and 2 below, best)
    1. Salt-load suppression test (best, urine aldosterone will <u>stay high</u>)
    2. Aldosterone:renin ratio > 20
    - Labs – ↓ serum K, ↑ serum Na, ↑ urine K, metabolic alkalosis
    - Plasma renin activity will be low
  - Localizing studies – CT scan initially; consider MRI, NP-59 scintigraphy (shows hyperfunctioning adrenal tissue; differentiates adenoma from hyperplasia; 90% accurate); adrenal venous sampling if others nondiagnostic
  - Pre-op need control of HTN and K replacement
  - Adenoma Tx – adrenalectomy
  - Hyperplasia Tx – ↑ morbidity with bilateral resection
    - Try medical therapy first (treats majority) for hyperplasia using <u>spironolactone</u> (inhibits aldosterone), <u>calcium channel blockers</u> (nifedipine), and <u>potassium</u>
    - If bilateral resection is performed (usually done for refractory hypokalemia), patient will need fludrocortisone postoperatively
- Hypocortisolism (adrenal insufficiency, Addison's disease)
  - #1 cause – withdrawal of exogenous steroids
  - #1 primary disease – autoimmune disease
  - Also caused by pituitary disease, adrenal infection/hemorrhage/metastasis/resection
  - Causes ↓ cortisol (ACTH will be high) and ↓ aldosterone
  - Dx: cosyntropin test (ACTH given, cortisol measured) – cortisol will remain low
  - Acute adrenal insufficiency – hypotension (refractory to fluids and pressors), fever, lethargy, abdominal pain, nausea and vomiting, ↓ glucose, ↑ K

    - Tx: dexamethasone, fluids, and give cosyntropin test (dexamethasone does not interfere with test)
  - Chronic adrenal insufficiency – hyperpigmentation, weakness, weight loss, GI symptoms, ↑ K, ↓ Na; Tx: corticosteroids
- Hypercortisolism (Cushing's syndrome)
  - Most commonly iatrogenic (exogenous steroids)
  - Sx's – moon face, acne, weight gain, buffalo hump, abdominal stria, DM, HTN, mental status changes
  - 1st – measure 24-hour urine cortisol (most sensitive test) and ACTH
    - If ACTH is low (and cortisol is high), patient has a cortisol secreting lesion (eg adrenal adenoma, adrenal hyperplasia)
    - If ACTH is high (and cortisol is high), patient has a pituitary adenoma or an ectopic source of ACTH (eg small cell lung CA) → go to 2nd below
  - 2nd – if ACTH is high, give high-dose dexamethasone suppression test
    - If urine cortisol is suppressed → pituitary adenoma
    - If urine cortisol is not suppressed → ectopic producer of ACTH (eg small cell lung CA)
  - NP-59 scintography can help localize tumors and differentiate adrenal adenomas from hyperplasia
  - Pituitary adenoma (Cushing's disease)
    - #1 non-iatrogenic cause of Cushing's syndrome → 80% of cases
    - Cortisol should be suppressed with either low- or high-dose dexamethasone suppression test
    - Mostly microadenomas
    - Dx: brain MRI
    - Tx: most tumors removed with transsphenoidal approach; unresectable or residual tumors treated with XRT
  - Ectopic ACTH
    - #2 non-iatrogenic cause of Cushing's syndrome
    - Most commonly from small cell lung CA
    - Cortisol is <u>not</u> suppressed with either low- or high-dose dexamethasone suppression test
    - Dx: chest and abdominal CT can help localize
    - Tx: resection of primary if possible; medical suppression for inoperable lesions
  - Adrenal adenoma
    - #3 non-iatrogenic cause of Cushing's syndrome
    - ↓ ACTH, unregulated steroid production
    - Dx: CT scan
    - Tx: adrenalectomy
  - Adrenal hyperplasia (macro or micro)
    - Tx: metyrapone (blocks cortisol synthesis) and aminoglutethimide; (inhibits steroid production); bilateral adrenalectomy if medical Tx fails
  - Adrenocortical carcinoma – rare cause of Cushing's syndrome (see below)
  - Bilateral adrenalectomy – consider in patients with ectopic ACTH from tumor that is unresectable (would need to be a slow growing tumor – rare) or ACTH from pituitary adenoma that cannot be found
  - Give steroids postop when operating for Cushing's syndrome (and mineralocorticoid

[fludrocortisone] if bilateral adrenalectomy)

- Adrenocortical carcinoma
  - Bimodal distribution (before age 5 and in the 5th decade); more common in females
  - 50% are functioning tumors – cortisol, aldosterone, sex steroids
  - Children display virilization 90% of the time (precocious puberty in boys, virilization in females); feminization in men; masculinization in women can occur
  - Symptoms: abdominal pain, weight loss, weakness
  - 80% have advanced disease at the time of diagnosis
  - Dx: CT scan findings usually suggests the diagnosis
  - Tx: radical adrenalectomy (take kidney); debulking helps symptoms, prolongs survival
    - Mitotane (adrenal-lytic) for residual, recurrent, or metastatic disease
- 20% 5-year survival rate

ADRENAL MEDULLA

- From ectoderm neural crest cells
- Catecholamine production: tyrosine → dopa → dopamine → norepinephrine → epinephrine
- Tyrosine hydroxylase – rate-limiting step (tyrosine to dopa)
- PNMT (phenylethanolamine *N*-methyltransferase) – enzyme converts norepinephrine → epinephrine
  - Enzyme is found only in the adrenal medulla (exclusive producers of epinephrine)
- Only adrenal pheochromocytomas will produce epinephrine
- MAO (monoamine oxidase) – breaks down catecholamines; converts norepinephrine to normetanephrine, epinephrine to metanephrine; VMA (vanillylmandelic acid) produced from these
- Extra-adrenal rests of neural crest tissue can exist, usually in the retroperitoneum, most notably in the organ of Zuckerkandl at the aortic bifurcation
- Pheochromocytoma (chromaffin cells)
  - Rare; usually slow growing; arise from sympathetic ganglia or ectopic neural crest cells
  - MC location – adrenal gland
  - 10% rule – malignant, bilateral, in children, familial, extra-adrenal
  - Can be associated with MEN IIa, MEN IIb, von Recklinghausen's disease, tuberous sclerosis, Sturge–Weber disease
  - Right-sided predominance
  - Extra-adrenal tumors are more likely malignant
  - Symptoms: HTN (frequently episodic), headache, diaphoresis, palpitations
  - Dx: urine metanephrines (24-hour urine; *best test*) and VMA
    - MIBG scan (norepinephrine analogue) – can help identify location if having trouble finding tumor with CT scan/MRI (best test for localization)
    - Clonidine suppression test – tumor doses not respond, keeps catecholamines ↑
    - No venography → can cause hypertensive crisis
  - Preoperatively: volume replacement and α-blocker first (phenoxybenzamine, prazosin → avoids hypertensive crisis); then β-blocker if patient has tachycardia or arrhythmias
    - Need to be careful with β-blocker and give after α-blocker → can precipitate hypertensive crisis (unopposed alpha stimulation, can lead to stroke), heart failure, and MI

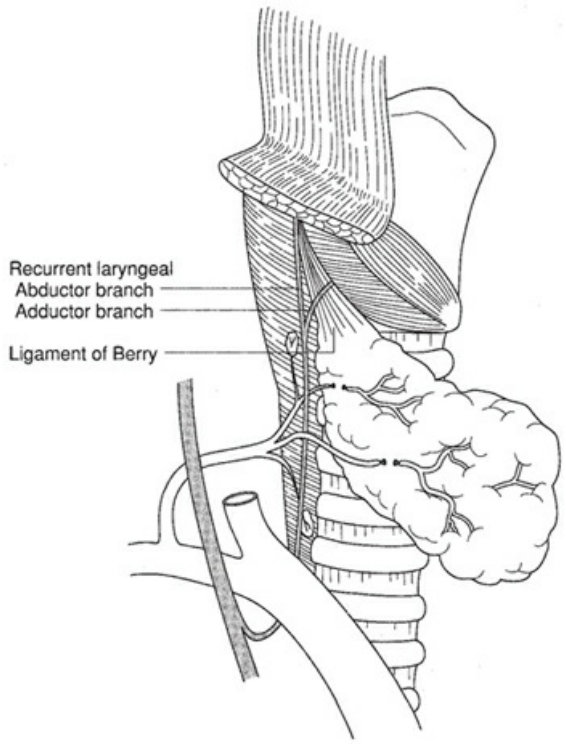
- Tx: adrenalectomy – ligate adrenal veins first to avoid spilling catecholamines during tumor manipulation
  - Debulking helps symptoms in patients with unresectable disease
  - Metyrosine – inhibits tyrosine hydroxylase causing ↓ synthesis of catecholamines (given pre-op or for unresectable disease)
  - Should have Nipride, Neo-Synephrine, and antiarrhythmic agents (eg amiodarone) ready during the time of surgery
- Postop conditions – persistent hypertension, hypotension, hypoglycemia, bronchospasm, arrhythmias, intracerebral hemorrhage, CHF, MI
- Other sites of pheochromocytomas – vertebral bodies, opposite adrenal gland, bladder, aortic bifurcation
- Most common site of extramedullary tissue – organ of Zuckerkandl (inferior aorta near bifurcation)
- Falsely elevated VMA – coffee, tea, fruits, vanilla, iodine contrast, labetalol, α- and β-blockers
- Extra-medullary tissue – responsible for medullary CA of thyroid and extra-adrenal pheochromocytoma

- Ganglioneuroma – rare, benign, asymptomatic tumor of neural crest origin in the adrenal medulla or sympathetic chain; Tx: resection

22 Thyroid

ANATOMY AND PHYSIOLOGY

- From the 1st and 2nd pharyngeal arches (not from pouches)
- Thyrotropin-releasing factor (TRF) – released from the hypothalamus; acts on the anterior pituitary gland and causes release of TSH
- Thyroid-stimulating hormone (TSH) – released from the anterior pituitary gland; acts on the thyroid gland to release T3 and T4 (through a mechanism that involves ↑ cAMP)
- TRF and TSH release are controlled by T3 and T4 through a negative feedback loop
- Superior thyroid artery – 1st branch off external carotid artery
- Inferior thyroid artery – off thyrocervical trunk; supplies ***both*** the inferior and superior parathyroids
  - Ligate close to thyroid to avoid injury to parathyroid glands with thyroidectomy
- Ima artery – occurs in 1%, arises from the innominate or aorta and goes to the isthmus
- Superior and middle thyroid veins – drain into internal jugular vein
- Inferior thyroid vein – drains into innominate vein
- Superior laryngeal nerve
  - Motor to cricothyroid muscle
  - Runs lateral to thyroid lobes
  - Tracks close to superior thyroid artery but is variable
  - MC injured nerve following thyroidectomy
  - Injury results in loss of projection and easy voice fatigability (opera singers)
- Recurrent laryngeal nerves (RLNs)
  - Motor to all of larynx except cricothyroid muscle
  - Controls vocal cords
  - Run posterior to thyroid lobes in the tracheoesophageal groove
  - Can track with inferior thyroid artery but are variable
  - Left RLN loops around aorta; right RLN loops around innominate artery
  - Injury results in hoarseness; bilateral injury can obstruct airway → need emergency tracheostomy
  - Non-recurrent laryngeal nerve – in 2%; more common on the right
  - Risk of injury is higher for a non-recurrent laryngeal nerve during thyroid surgery
- Ligament of Berry – posterior medial suspensory ligament close to RLNs; need careful dissection



The ligament of Berry and distal recurrent laryngeal nerves.

- Thyroglobulin – stores T3 and T4 in colloid
  - Plasma T4:T3 ratio is 15:1; T3 is the more active form (is tyrosine + iodine)
  - Most T3 is produced in periphery from T4 to T3 conversion by deiodinases
- Peroxidases link iodine and tyrosine together
- Deiodinases separate iodine from tyrosine
- Thyroxine-binding globulin – thyroid hormone transport; binds the majority of T3 and T4 in circulation
- TSH – most sensitive indicator of gland function
- Tubercles of Zuckerkandl – most lateral, posterior extension of thyroid tissue
  - Rotate medially to find RLNs
  - This portion is left behind with subtotal thyroidectomy because of proximity to RLNs
- Parafollicular C cells – produce calcitonin (lowers Ca)
- Thyroxine treatment – TSH levels should fall 50%; osteoporosis long-term side effect
- Post-thyroidectomy stridor – open neck and remove hematoma emergently → can result in airway compromise; can also be due to bilateral RLN injury → would need emergent tracheostomy

THYROID STORM

- Symptoms: ↑ HR, fever, numbness, irritability, vomiting, diarrhea, high-output cardiac failure (most common cause of death)
- Most common after surgery in patient with undiagnosed Graves' disease
- Can be precipitated by anxiety, excessive gland palpation, adrenergic stimulants
- Tx: **β**-blockers *(first drug to give)*, Lugol's solution (KI, most effective but takes while to work), cooling blankets, oxygen, glucose
  - Emergent thyroidectomy rarely indicated

- Wolff–Chaikoff effect – very effective for thyroid storm; patient given high doses of iodine (Lugol's solution, potassium iodide), which inhibits TSH action on thyroid and inhibits organic coupling of iodide, resulting in less T3 and T4 release

ASYMPTOMATIC THYROID NODULE

- 90% of thyroid nodules are benign; female predominance
- Get FNA *(best initial test)* and thyroid function tests
  - Determinant in 80% → follow appropriate treatment
    - Shows follicular cells → lobectomy (10% CA risk; see Thyroid CA section)
    - Shows thyroid CA → thyroidectomy or lobectomy and appropriate treatment (see Thyroid CA section)
    - Shows cyst fluid → drain fluid (send for cytology)
      - If it recurs or is bloody → lobectomy
    - Shows colloid tissue → most likely colloid goiter; low chance of malignancy (< 1%)
      - Tx: thyroxine; lobectomy if it enlarges
    - Shows normal thyroid tissue and TFTs are elevated → likely solitary toxic nodule
      - Tx: if asymptomatic can just monitor; methimazole and ^{131}I if symptomatic
  - Indeterminant in 20% → get radionuclide study
    - Hot nodule → Tx: if asymptomatic can monitor; methimazole and ^{131}I if symptomatic
    - Cold nodule → lobectomy (more likely malignant than hot nodule)
- Goiter
  - Any abnormal enlargement
  - Most identifiable cause is iodine deficiency; Tx: iodine replacement
  - MCC is U.S. – low-grade stimulation of the thyroid gland
  - Diffuse enlargement without evidence of functional abnormality = nontoxic colloid goiter
    - Unusual to have to operate unless goiter is causing airway compression or there is a suspicious nodule
    - Tx: thyroxine; need subtotal or total thyroidectomy for failure of medical Tx or if a suspicious nodule appears; subtotal has decreased risk of RLN injury
    - If the goiter is hyper-functioning (toxic goiter) – do not use thyroxine
- Substernal goiter
  - Usually secondary (vessels originate from superior and inferior thyroid arteries)
  - Primary substernal goiter – rare (vessels originate from innominate artery)
- Mediastinal thyroid tissue – most likely from acquired disease with inferior extensions of a normally placed gland (eg substernal goiter)

ABNORMALITIES OF THYROID DESCENT

- Pyramidal lobe – occurs in 10%, extends from the isthmus toward the thymus
- Lingual thyroid
  - Thyroid tissue that persists in foramen cecum at base of the tongue
  - Symptoms: dysphagia, dyspnea, dysphonia
  - 2% malignancy risk
  - Tx: thyroxine suppression; abolish with ^{131}I
    - Resection if worried about CA or if it does not shrink after medical therapy

- Is the only thyroid tissue in 70% of patients who have it
- Thyroglossal duct cyst
  - Midline cervical mass between the hyoid bone and the thyroid isthmus
  - May be all the thyroid tissue the patient has
  - Classically moves upward with swallowing
  - Susceptible to infection and may be premalignant; dysphonia
  - Tx: resection → need to take midportion or all of hyoid bone along with the thyroglossal duct cyst (Sistrunk procedure; lateral neck incision)

HYPERTHYROIDISM TREATMENT

- Thioamides – propylthiouracil (PTU) and methimazole
- Methimazole – *1st-line drug*
  - Not used in pregnancy
  - Inhibits peroxidases and prevents iodine–tyrosine coupling
  - Side effects: cretinism in newborns (crosses placenta), aplastic anemia, agranulocytosis (rare)
- PTU (thioamides) – not used 1st line anymore due to hepatotoxicity (especially in children)
  - Safe with pregnancy
  - Inhibits peroxidases and prevents iodine–tyrosine coupling
  - Side effects: aplastic anemia, agranulocytosis (rare)
- Radioactive iodine (^{131}I)
  - For patients who are poor surgical risks or unresponsive to methimazole
  - ^{131}I should not be used in children or during pregnancy → can traverse placenta
- Thyroidectomy
  - Good for cold nodules, toxic adenomas, Graves' disease not responsive to medical therapy, pregnant patients not controlled with PTU, multinodular goiters with compressive symptoms of suspicious nodule, and toxic multinodular goiters (^{131}I doesn't work well)
  - Best time to operate during pregnancy is 2nd trimester (↓ risk of teratogenic events and premature labor)
  - Subtotal thyroidectomy can leave patient euthyroid

CAUSES OF HYPERTHYROIDISM

- Graves' disease (toxic diffuse goiter)
  - MCC of hyperthyroidism
  - Women; exophthalmos, pretibial edema, atrial fibrillation, heat intolerance, thirst, ↑ appetite, weight loss, sweating, palpitations
  - Sx's found only in Graves' – exophthalmos, pretibial edema
  - Most common cause of hyperthyroidism (80%)
  - Caused by IgG antibodies to TSH receptor (long-acting thyroid stimulator [LATS], thyroid-stimulating immunoglobulin [TSI])
  - Dx: decreased TSH, increased T3 and T4; LATS level; ↑ ^{123}I uptake (thyroid scan) diffusely in thyrotoxic patient with goiter
  - Medical therapy usually manages hyperthyroidism (95% success rate)
  - Tx: thioamides (50% recurrence), ^{131}I (5% recurrence), or thyroidectomy if medical therapy fails; beta-blockers help symptoms only

- Unusual to have to operate on these patients (suspicious nodule most common reason)
  - Preop preparation: methimazole until euthyroid, β-blocker, Lugol's solution for 14 days to decrease friability and vascularity (start only after euthyroid)
  - Operation: bilateral subtotal (5% recurrence) or total thyroidectomy (need lifetime thyroxine replacement)
  - Indications for surgery: noncompliant patient, recurrence after medical therapy, children, pregnant women not controlled with PTU, or concomitant suspicious thyroid nodule (most common indication)
- Toxic multinodular goiter
  - Women; age > 50 years, usually nontoxic 1st
  - Symptoms: tachycardia, weight loss, insomnia, airway compromise; symptoms can be precipitated by contrast dyes
  - Caused by hyperplasia secondary to chronic low-grade TSH stimulation
  - Pathology shows colloid
  - Tx: Most consider *surgery (subtotal or total thyroidectomy) the* preferred initial Tx for toxic multinodular goiter, but a trial of ^{131}I should be considered, especially in the elderly and frail (generally doesn't work well due to non-homogenous uptake)
    - If compression or a suspicious nodule is present, need to go with surgery
- Single toxic nodule
  - Women; younger; usually > 3 cm to be symptomatic; function autonomously
  - Dx: thyroid scan (hot nodule) –20% of hot nodules eventually cause symptoms
  - Tx: thioamides and ^{131}I (95% effective); lobectomy if medical Tx ineffective
- Rare causes of hyperthyroidism – trophoblastic tumors, TSH-secreting pituitary tumors

CAUSES OF THYROIDITIS

- Hashimoto's disease
  - Most common cause of hypothyroidism in adults
  - Enlarged gland, painless, chronic thyroiditis
  - Women; history of childhood XRT
  - Can cause thyrotoxicosis in the acute early stage
  - Caused by both humeral and cell-mediated autoimmune disease (microsomal and thyroglobulin antibodies)
  - Goiter secondary to lack of organification of trapped iodide inside gland
  - Pathology shows a lymphocytic infiltrate
  - Tx: thyroxine *(first line)*; partial thyroidectomy if continues to grow despite thyroxine, if nodules appear, or if compression symptoms occur
  - Frequently, no surgery is necessary for Hashimoto's disease
- Bacterial thyroiditis (rare)
  - Usually secondary to contiguous spread
  - Bacterial upper respiratory tract infection (URI) usual precursor (staph/strep)
  - Normal thyroid function tests, fever, dysphagia, tenderness
  - Tx: antibiotics
    - May need lobectomy to rule out cancer in patients with unilateral swelling and tenderness
    - May need total thyroidectomy for persistent inflammation
- De Quervain's thyroiditis

- Can be associated with hyperthyroidism initially
- Viral URI precursor; tender thyroid, sore throat, mass, weakness, fatigue; women
- Elevated ESR
- Tx: steroids and ASA
  - May need lobectomy to rule out cancer in patients with unilateral swelling and tenderness
  - May need total thyroidectomy for persistent inflammation

- Riedel's fibrous struma (rare)
  - Woody, fibrous component that can involve adjacent strap muscles and carotid sheath
  - Can resemble thyroid CA or lymphoma (need biopsy)
  - Disease frequently results in hypothyroidism and compression symptoms
  - Associated with sclerosing cholangitis, fibrotic diseases, methysergide Tx, and retroperitoneal fibrosis
  - Tx: steroids and thyroxine
    - May need isthmectomy or tracheostomy for airway symptoms
    - If resection needed, watch for RLNs

THYROID CANCER

- Most common endocrine malignancy in the United States
- Thyroid CA generally does not affect thyroid function
- Follicular cells on FNA – 5%–10% chance of malignancy (unable to differentiate between follicular cell adenoma, follicular cell hyperplasia, and follicular cell CA on FNA)
- Worrisome for malignancy – solid, solitary, cold, slow growing, hard; male, age > 50, previous neck XRT, MEN IIa or IIb
- Sudden growth – could be hemorrhage into previously undetected nodule or malignancy
- Patients can also present with voice changes or dysphagia
- Follicular adenomas – colloid, embryonal, fetal → no increase in cancer risk
  - Still need lobectomy to prove it is an adenoma
- Papillary thyroid carcinoma
  - Most common (85%) thyroid CA
  - Least aggressive, slow growing, has the best prognosis; women, children
  - Risk factors: childhood XRT (very ↑ risk) → most common tumor following neck XRT
  - Older age (> 40–50 years) predicts a worse prognosis
  - Lymphatic spread 1st but is not prognostic → prognosis based on local invasion
  - Rare metastases (lung)
  - Children are more likely to be node positive (80%) than are adults (20%)
  - Large, firm nodules in children are worrisome
  - Many are multicentric
  - Pathology – psammoma bodies (calcium) and Orphan Annie nuclei
  - 95% 5-year survival rate; death secondary to local disease
- Follicular thyroid carcinoma
  - Hematogenous spread (bone most common) → 50% have metastatic disease at the time of presentation
  - More aggressive than thyroid papillary cell CA; older adults (50–60s), women
  - If FNA shows just follicular cells – have 10% chance of malignancy, need lobectomy
  - 70% 5-year survival rate; prognosis based on stage

- Surgery for papillary and follicular thyroid CA → start with lobectomy
  - Indications for <u>total</u> thyroidectomy:
    - Tumor > 1 cm
    - Extra-thyroidal disease (beyond thyroid capsule, clinically positive nodes, metastases)
    - Multi-centric or bilateral lesions
    - Previous XRT
  - Indications for MRND:
    - Extra-thyroidal disease
  - Indications for post-op ^{131}I (6 weeks after surgery, want TSH high for maximum uptake):
    - Tumor > 1 cm
    - Extra-thyroidal disease
    - *Need <u>total thyroidectomy for</u> ^{131}I to be effective*
  - Enlarged lateral neck lymph node that shows thyroid tissue (lateral aberrant thyroid tissue; ie papillary thyroid CA with lymphatic spread) → Tx: total thyroidectomy, MRND, and ^{131}I
  - Risk factors for thyroid CA <u>recurrence</u> or <u>metastases</u>: X-GAMES – previous XRT, high grade, age (< 20 or > 50), males, extrathyroidal disease, and size (> 1 cm)
- Medullary thyroid carcinoma
  - Can be associated with MEN IIa or IIb (RET proto-oncogene)
  - 80% are sporadic
  - Usually the 1st manifestation of MEN IIa and IIb (diarrhea)
  - Tumor arises from parafollicular C cells (which secrete calcitonin)
  - C-cell hyperplasia considered premalignant
  - Pathology – shows amyloid deposition
  - Calcitonin – can cause flushing and diarrhea
  - Need to screen for hyperparathyroidism and pheochromocytoma
  - Lymphatic spread – most have involved nodes at time of diagnosis
  - Early metastases to lung, liver, and bone
  - Worse prognosis – IIb and sporadic types
  - Tx: total thyroidectomy with central neck node dissection
    - MRND if patient has a palpable thyroid mass
    - Bilateral MRND if both lobes have tumor or if extrathyroidal disease present
    - Prophylactic thyroidectomy and central node dissection in MEN IIa (at age 6 years) or IIb (at age 2 years)
    - Liver and bone metastases prevent attempt at cure
    - XRT may be useful for unresectable local and distant metastatic disease
  - May be useful to monitor calcitonin levels for disease recurrence
  - More aggressive than follicular and papillary CA
  - 50% 5-year survival rate; prognosis based on presence of regional and distant metastases
- Hürthle cell carcinoma
  - Most are benign (80%; Hürthle cell adenoma); presents in older patients
  - Metastases go to bone and lung if malignant
  - Pathology shows Ashkenazi cells
  - Can <u>not</u> make the diagnosis of benign vs malignant on biopsy alone – need lobectomy
  - Tx: lobectomy; total thyroidectomy if malignant; MRND for clinically positive nodes
- Anaplastic thyroid cancer

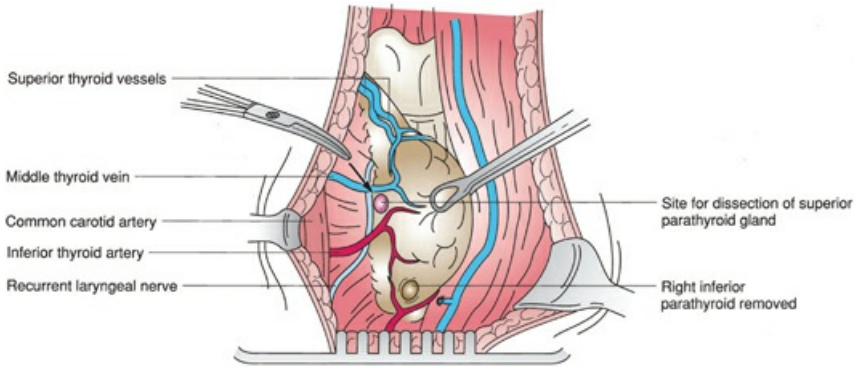
- Elderly patients with long-standing goiters
- Most aggressive thyroid CA
- Pathology shows vesicular appearance of nuclei
- Rapidly lethal (0% 5-year survival rate); usually beyond surgical management at diagnosis
- Tx: total thyroidectomy for the rare lesion that can be resected
- Can perform palliative thyroidectomy for compressive symptoms (or tracheostomy) or give palliative chemo-XRT

- XRT effective for papillary, follicular, medullary, and Hürthle cell thyroid CA
- ^{131}I effective for papillary and follicular thyroid CA *only*
  - Not used in children (CA risk), pregnancy (cretinism), or in lactating mothers (cretinism)
  - Can cure bone and lung metastases
  - Given 4–6 weeks after surgery when TSH levels are highest
  - Do not give thyroid replacement until after treatment with ^{131}I → would suppress TSH and uptake of ^{131}I
  - Indications (used only for papillary and follicular thyroid CA)
    - Recurrent CA
    - Primary inoperable tumors due to local invasion
    - Tumors that are > 1 cm or have extrathyroidal disease (extra-capsular invasion, nodal spread, or metastases)
  - Patients with papillary or follicular cell CA and metastases → need to perform total thyroidectomy to facilitate uptake of ^{131}I to the metastatic lesions (otherwise all gets absorbed by the thyroid gland)
  - ^{131}I Side effects (rare): sialoadenitis, GI symptoms, infertility, bone marrow suppression, parathyroid dysfunction, leukemia
- Thyroxine – can help suppress TSH and slow metastatic disease; administered only after ^{131}I therapy has finished

23 Parathyroid

ANATOMY AND PHYSIOLOGY

- Superior parathyroids – 4th pharyngeal pouch; associated with thyroid complex
  - Found lateral to recurrent laryngeal nerves (RLNs), posterior surface of superior portion of gland, above inferior thyroid artery
- Inferior parathyroids – 3rd pharyngeal pouch; associated with thymus
  - Found medial to RLNs, more anterior, below inferior thyroid artery
  - Inferior parathyroids have more variable location and are more likely to be ectopic
  - Occasionally are found in the tail of the thymus (most common ectopic site) and can migrate to the anterior mediastinum
  - Other ectopic sites – intra-thyroid, mediastinal, near tracheoesophageal groove
- 90% have all 4 glands
- Inferior thyroid artery – blood supply to *both* superior and inferior parathyroid glands



Lateral view of the right side of the neck after rotation of the thyroid lobe. The important anatomic landmarks are emphasized.

- PTH – *increases* serum Ca
  - ↑ kidney Ca reabsorption in the distal convoluted tubule, ↓ kidney PO_4 absorption
  - ↑ osteoclasts in bone to release Ca (and PO_4^-)
  - ↑ vitamin D production in kidney (↑ 1-OH hydroxylation) → ↑ Ca-binding protein in intestine → ↑ intestinal Ca reabsorption
- Vitamin D – ↑ intestinal Ca and PO_4 absorption by increasing calcium-binding protein
- Calcitonin – *decreases* serum Ca
  - ↓ bone Ca resorption (osteoclast inhibition)
  - ↑ urinary Ca and PO_4 excretion
- Normal Ca level: 8.5–10.5 (ionized 1.0–1.5)
- Normal PTH level: 10–60 pg/mL
- Normal PO_4 level: 2.5–5.0
- Normal Cl^- level: 98–107
- Most common cause of hypoparathyroidism is previous thyroid surgery

PRIMARY HYPERPARATHYROIDISM

- Women, older age
- Due to autonomously high PTH
- Dx: ↑ PTH and ↑ Ca; ↓ PO_4^-; Cl^- to PO_4^- ratio > 33; ↑ renal cAMP; HCO_3^- secreted in urine
- Can get hyperchloremic metabolic acidosis
- Osteitis fibrosa cystica (brown tumors) – bone lesions from Ca resorption; characteristic of hyperparathyroidism
- Most patients have no symptoms – ↑ Ca found on routine lab work for some other problem or on checkup
- Symptoms: muscle weakness, myalgia, nephrolithiasis, pancreatitis, ulcers, depression, bone pain, pathologic fractures, mental status changes, constipation, anorexia
- Hypertension can result from renal impairment

Diagnostic Workup for Primary Hyperparathyroidism

Take careful history, including records or medications, symptoms, prior head and neck radiotherapy, and other endocrinopathies in the patient and the patient's family.

Establish elevated calcium through 2 or 3 determinations.

Order a chest radiograph and search for bony metastases, sarcoidosis, and pulmonary tumors (ie looking for PTHrP source).

Order an excretory urogram and search for nephrolithiasis and, rarely, renal tumors.

Order a serum protein electrophoresis to rule out multiple myeloma.

Order a 24-hour urinary calcium determination (ie benign familial hypocalciuric hypercalcemia – would show low urine Ca).

Rule out multiple endocrine neoplasia (usually multiple endocrine neoplasia type I).

Check the absolute or relative elevation of the parathyroid hormone level.

From Smith SL, Van Heerden JA. Conventional parathyroidectomy for primary hyperparathyroidism. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.

- Indications for surgery:
  - Symptomatic disease
  - Asymptomatic disease with Ca > 13, ↓ Cr clearance, kidney stones, substantially ↓ bone mass (densitometry T score < –2.5), age < 50
- Single adenoma – occurs in 80% of patients
- Multiple adenomas – occur in 4% of patients
- Diffuse hyperplasia – occurs in 15%; patients with MEN I or IIa have 4-gland hyperplasia
- Parathyroid adenocarcinoma – very rare; can get very high Ca levels
- Treatment
  - Adenoma – resection; inspect other glands to rule out hyperplasia or multiple adenomas
  - Parathyroid hyperplasia
    - Do not biopsy all glands → risks hemorrhage and hypoparathyroidism
    - Tx: resect 3½ glands or total parathyroidectomy and autoimplantation (forearm or strap muscle)
  - Parathyroid CA → need radical parathyroidectomy (need to take ipsilateral thyroid lobe)
  - Pregnancy – surgery in 2nd trimester; ↑ risk of stillbirth if not resected
- Intraop frozen section → can confirm that the tissue taken was indeed parathyroid
- Intraop PTH levels → can help determine if the causative gland is removed (PTH should go to < ½ of the preop value in 10 minutes)
- Missing gland – check inferiorly in thymus tissue (most common ectopic location, can

remove tail of the thymus and see if PTH drops), near carotids, vertebral body, superior to pharynx, thyroid
    - Still cannot find gland – close and follow PTH; if PTH still ↑, get sestamibi scan to localize
- At reoperation for a missing gland, the most common location for the gland is normal anatomic position
- Hypocalcemia postop – from bone hunger or failure of parathyroid remnant/graft
    - Bone hunger – normal PTH, decreased HCO_3^-, ↑ urine cAMP
    - Aparathyroidism – decreased PTH, normal HCO_3^-, normal urine cAMP
    - Remember to give Ca post-op
- Persistent hyperparathyroidism (1%) – most commonly due to missed adenoma remaining in the neck
- Recurrent hyperparathyroidism – occurs after a period of hypocalcemia or normocalcemia
    - Can be due to new adenoma formation
    - Can be due to tumor implants at the original operation that have now grown
    - Need to consider recurrent parathyroid CA
- Reoperation associated with ↑ risk of RLN injury, permanent hypoparathyroidism
- Sestamibi scan
    - Will have preferential uptake by the overactive parathyroid gland
    - Good for picking up adenomas but not 4-gland hyperplasia
    - Best for trying to pick up ectopic glands

SECONDARY HYPERPARATHYROIDISM

- Seen in patients with renal failure
- ↑ PTH in response to low Ca (lose Ca with dialysis)
- Most do <u>not</u> need surgery (95%)
- Osteoporosis can occur
- Tx: Ca supplement, vitamin D, control diet PO_4, PO_4-binding gel (sevelamer chloride)
    - Cinacalcet – mimics Ca, inhibits PTH from the parathyroid glands
    - Surgery for bone pain (most common indication), fractures, or pruritus (80% get relief) despite medical Tx
    - Surgery involves total parathyroidectomy with autotransplantation or subtotal parathyroidectomy

TERTIARY HYPERPARATHYROIDISM

- Renal disease now corrected with transplant but still overproduces PTH
- Has similar lab values as primary hyperparathyroidism (hyperplasia)
- Tx: subtotal (3½ glands) or total parathyroidectomy with autoimplantation

FAMILIAL HYPERCALCEMIC HYPOCALCIURIA

- Patients have ↑ serum Ca and ↓ urine Ca (should be ↑ if hyperparathyroidism)
- Caused by defect in PTH receptor in distal convoluted tubule of the kidney that causes ↑ resorption of Ca
- Dx: Ca 9–11, have normal PTH, ↓ urine Ca

- Tx: nothing (Ca generally not that high in these patients); no parathyroidectomy

PSEUDOHYPOPARATHYROIDISM

- Because of defect in PTH receptor in the kidney, does not respond to PTH

PARATHYROID CANCER

- Rare cause of hypercalcemia
- ↑ Ca, PTH, and alkaline phosphatase (can have extremely high Ca levels)
- Lung most common location for metastases
- Tx: wide en bloc excision (parathyroidectomy and ipsilateral thyroidectomy)
- 50% 5-year survival rate
- Mortality is due to hypercalcemia
- Recurrence in 50%

MULTIPLE ENDOCRINE NEOPLASIA SYNDROMES

- Derived from APUD cells
- Neoplasms can develop synchronously or metachronously
- Autosomal dominant, 100% penetrance
- MEN I
  - Parathyroid hyperplasia
    - Usually the 1st part to become symptomatic; urinary symptoms
    - Tx: 4-gland resection with autotransplantation
  - Pancreatic islet cell tumors
    - Gastrinoma #1 – 50% multiple, 50% malignant; major morbidity of syndrome
  - Pituitary adenoma
    - Prolactinoma #1
  - Need to correct hyperparathyroidism 1st if simultaneous tumors
- MEN IIa
  - Parathyroid hyperplasia
  - Medullary CA of thyroid
    - Nearly all patients; diarrhea most common symptom; often bilateral
    - #1 cause of death in these patients
    - Usually 1st part to be symptomatic (diarrhea)
  - Pheochromocytoma
    - Often bilateral, nearly always benign
  - Need to correct pheochromocytoma 1st if simultaneous tumors
- MEN IIb
  - Medullary CA of thyroid
    - Nearly all patients; diarrhea most common symptoms; often bilateral
    - #1 cause of death in these patients
    - Usually 1st part to be symptomatic (diarrhea)
  - Pheochromocytoma
    - Often bilateral, nearly always benign
  - Mucosal neuromas
  - Marfan's habitus, musculoskeletal abnormalities

- Need to correct pheochromocytoma 1st if simultaneous tumors
- MEN I – MENIN gene
- MEN IIa and IIb – RET proto-oncogene

Disease Phenotypes Related to Mutation of the RET Proto-Oncogene

Phenotype	Genetic Defect	Clinical Features	Prevalence (%)
MEN 2A (60%)	Germline mutations in cysteine codons of extracellular and transmembrane domains of RET	Medullary thyroid carcinoma	100
		Pheochromocytoma	10–60
		Hyperparathyroidism	5–20
MEN 2B (5%)	Germline activating mutation in tyrosine kinase domain of RET	Medullary thyroid carcinoma	100
		Pheochromocytoma	50
		Marfanoid habitus	100
		Mucosal neuromas (gut) and ganglioneuromatosis	100
FMTC (35%)	Germline mutations in cysteine codons of extracellular or transmembrane domains of RET	Medullary thyroid carcinoma	100

FMTC, familial medullary thyroid carcinoma; MEN, multiple endocrine neoplasia.

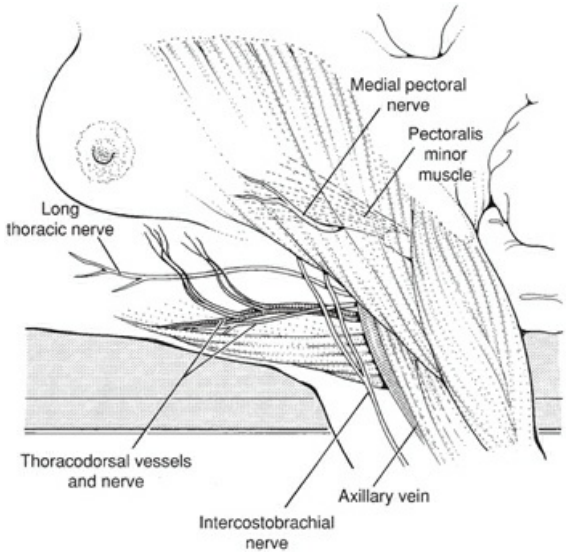
HYPERCALCEMIA

- Causes (90% from hyperparathyroidism or CA):
  - Malignancy
    - Hematologic (25%) – lytic bone lesions (eg multiple myeloma)
    - Nonhematologic (75%) – cancers that release PTHrP (eg squamous cell lung CA, breast CA)
  - Hyperparathyroidism
  - Hyperthyroidism
  - Familial hypercalcemic hypocalciuria
  - Immobilization
  - Granulomatous disease (sarcoidosis or tuberculosis)
  - Excess vitamin D
  - Milk–alkali syndrome (excessive intake of milk and calcium supplements)
  - Thiazide diuretics
- Mithramycin – inhibits osteoclasts (used with malignancies or failure of conventional treatment); has hematologic, liver, and renal side effects
- Hypercalcemic crisis – usually secondary to another surgery in patients with pre-existing hyperparathyroidism; Tx: fluids (normal saline) and furosemide (Lasix)
- Breast CA – releases PTHrP (rP = related peptide); can cause hypercalcemia
  - Squamous cell lung CA and other nonhematologic cancers can do this as well → this is <u>not</u> due to bone destruction
  - Associated with ↑ urinary cAMP (from action of PTHrP on kidney PTH receptors)
- Hematologic malignancies – these can cause bone destruction with ↑ Ca (urinary cAMP will be low)

24 Breast

ANATOMY AND PHYSIOLOGY

- Breast development
  - Breast formed from ectoderm milk streak
  - Estrogen – duct development (double layer of columnar cells)
  - Progesterone – lobular development
  - Prolactin – synergizes estrogen and progesterone
- Cyclic changes
  - Estrogen – ↑ breast swelling, growth of glandular tissue
  - Progesterone – ↑ maturation of glandular tissue; withdrawal causes menses
  - FSH, LH surge – cause ovum release
  - After menopause, lack of estrogen and progesterone results in atrophy of breast tissue
- Nerves
  - Long thoracic nerve – innervates serratus anterior; injury results in winged scapula
    - Lateral thoracic artery supplies serratus anterior
  - Thoracodorsal nerve – innervates latissimus dorsi; injury results in weak arm pull-ups and adduction
    - Thoracodorsal artery supplies latissimus dorsi
  - Medial pectoral nerve – innervates pectoralis major and pectoralis minor
  - Lateral pectoral nerve – pectoralis major only
  - Intercostobrachial nerve – lateral cutaneous branch of the 2nd intercostal nerve; provides sensation to medial arm and axilla; encountered just below axillary vein when performing axillary dissection
    - Can transect without serious consequences
    - Most common injured nerve with MRM or ALND
- Branches of internal thoracic artery, intercostal arteries, thoracoacromial artery, and lateral thoracic artery supply breast



Major neurovascular structures to be preserved in an axillary dissection.

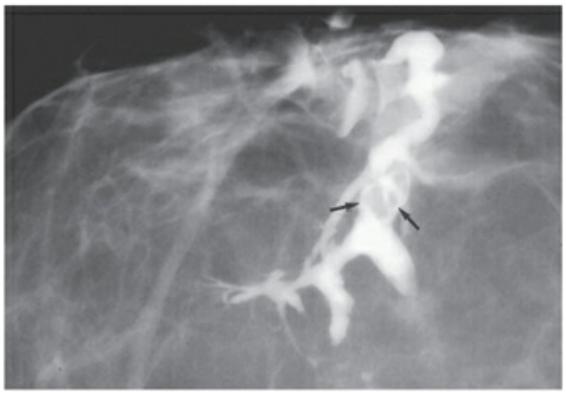
- Batson's plexus – valveless vein plexus that allows direct hematogenous metastasis of breast CA to spine
- Lymphatic drainage
  - 97% is to the axillary nodes
  - 2% is to the internal mammary nodes
  - Any quadrant can drain to the internal mammary nodes
  - Supraclavicular nodes – considered N3 disease
  - Primary axillary adenopathy – #1 is lymphoma
- Cooper's ligaments – suspensory ligaments; divide breast into segments
  - Breast CA involving these strands can dimple the skin

BENIGN BREAST DISEASE

- Abscesses – usually associated with breastfeeding. *Staphylococcus aureus* most common, strep
  - Tx: percutaneous or incision and drainage; discontinue breastfeeding; breast pump, antibiotics
  - Failure to resolve after 2 weeks – get excisional biopsy including the skin to rule out necrotic breast CA
  - Breast abscess in nonlactating women is breast CA until proven otherwise
- Infectious mastitis – most commonly associated with breastfeeding
  - *S. aureus* most common
  - In nonlactating women can be due to chronic inflammatory diseases (eg actinomyces) or autoimmune disease (eg SLE) → may need to rule out necrotic cancer (need incisional biopsy including the skin)
- Periductal mastitis (mammary duct ectasia or plasma cell mastitis)
  - Symptoms: noncyclical mastodynia, erythema, nipple retraction, creamy discharge from nipple; can have sterile or infected subareolar abscess
  - Risk factors – smoking, nipple piercings
  - Biopsy – dilated mammary ducts, inspissated secretions, marked periductal inflammation
  - Tx: if typical creamy discharge is present that is not bloody and not associated with nipple retraction, give antibiotics, reassure, and continue breastfeeding; if not or if it recurs,

need to rule out inflammatory CA (incisional biopsy including the skin)

- Galactocele – breast cysts filled with milk; occurs with breastfeeding
  - Tx: ranges from aspiration to incision and drainage
- Galactorrhea – can be caused by ↑ prolactin (pituitary prolactinoma), OCPs, TCAs, phenothiazines, metoclopramide, alpha-methyl dopa, reserpine
  - Is often associated with amenorrhea
- Gynecomastia – 2-cm pinch; can be associated with cimetidine, spironolactone, marijuana; idiopathic in most
  Tx: vast majority will regress; family reassurance and follow-up
- Neonatal breast enlargement – due to circulating maternal estrogens; will regress
- Accessory breast tissue (polythelia) – can present in axilla (most common location)
- Accessory nipples (polythelia) – can be found from axilla to groin (most common breast anomaly)
- Breast asymmetry – common
- Breast reduction – ability to lactate frequently compromised
- Poland's syndrome – hypoplasia of chest wall, amastia, hypoplastic shoulder, no pectoralis muscle
- Mastodynia – pain in breast; rarely represents breast CA
  - Dx: history and breast exam; bilateral mammogram
  - Tx: danazol, OCPs, NSAIDs, evening primrose oil, bromocriptine
  - Discontinue caffeine, nicotine, methylxanthines
  - Cyclic mastodynia – pain before menstrual period; most commonly from fibrocystic disease
  - Continuous mastodynia – continuous pain, most commonly represents acute or subacute infection; continuous mastodynia is more refractory to treatment than cyclic mastodynia
- Mondor's disease – superficial vein thrombophlebitis of breast; feels cordlike, can be painful
  - Associated with trauma and strenuous exercise
  - Usually occurs in lower outer quadrant
  - Tx: NSAIDs
- Fibrocystic disease
  - Lots of types: fibromatosis, sclerosing adenosis, apocrine metaplasia, duct adenosis, epithelial hyperplasia, ductal hyperplasia, and lobular hyperplasia
  - Symptoms: breast pain, nipple discharge (usually yellow to brown), lumpy breast tissue that varies with hormonal cycle
  - Dx: mammogram, U/S, and breast exam
  - Only cancer risk is <u>atypical</u> ductal or lobular hyperplasia –*need to resect these lesions*
    - Do not need to get negative margins with atypical hyperplasia; just remove all suspicious areas (ie calcifications) that appear on mammogram
- Intraductal papilloma
  - Most common cause of bloody nipple discharge
  - Are usually small, nonpalpable, and close to the nipple
  - These lesions are <u>not</u> premalignant → get contrast ductogram to find papilloma, then needle localization
  - Tx: subareolar resection of the involved duct and papilloma



Ductogram. A large defect *(arrow)* represents an intraductal papilloma.

- Fibroadenoma
  - Most common breast lesion in adolescents and young women; 10% multiple
  - Usually painless, slow growing, well circumscribed, firm, and rubbery
  - Often grows to several cm in size and then stops
  - Can change in size with menstrual cycle and can enlarge in pregnancy
  - Giant fibroadenomas can be > 5 cm (treatment is the same)
  - Prominent fibrous tissue compressing epithelial cells on pathology
  - Can have large, coarse calcifications (popcorn lesions) on mammography from degeneration
  - In patients < 40 years old:
    1. Mass needs to feel clinically benign (firm, rubbery, rolls, not fixed)
    2. Ultrasound or mammogram needs to be consistent with fibroadenoma
    3. Need FNA or core needle biopsy to show fibroadenoma
    - Need all 3 of the above to be able to observe, otherwise need excisional biopsy
    - If the fibroadenoma continues to enlarge, need excisional biopsy
    - Avoid resection of breast tissue in teenagers and younger children → can affect breast development
- In patients > 40 years old → excisional biopsy to ensure diagnosis (core needle biopsy if you are trying for 1-step surgery)

NIPPLE DISCHARGE

- Most nipple discharge is benign
- All need a history, breast exam, bilateral mammogram, and U/S
- Try to find the trigger point or mass on exam
- Green/yellow/brown discharge – usually due to fibrocystic disease; should have lumpy breast tissue consistent with fibrocystic disease
  - Tx: if cyclical and nonspontaneous, reassure patient
- Bloody discharge – most commonly intraductal papilloma; occasionally ductal CA
  - Tx: need ductogram and excision of that ductal area (wire-guided)
- Serous discharge – worrisome for cancer, especially if coming from only 1 duct or spontaneous
  - Tx: excisional biopsy of that ductal area
- Spontaneous discharge – no matter what the color or consistency is, this is worrisome for CA → all these patients need excisional biopsy of duct area causing the discharge

- Nonspontaneous discharge (occurs only with pressure, tight garments, exercise, etc.) – not as worrisome but may still need excisional biopsy (eg if bloody)
- May have to do a complete subareolar resection if the area above cannot be properly identified (no trigger point or mass felt)

DUCTAL CARCINOMA IN SITU (DCIS)

- Malignant cells of the ductal epithelium *without* invasion of basement membrane
- 50% get cancer if not resected (ipsilateral breast)
- 5% get cancer in contralateral breast
- Considered a premalignant lesion
- Usually not palpable and presents as a cluster of calcifications on mammography
- Can have solid, cribriform, papillary, and comedo patterns
  - Comedo pattern – most aggressive subtype; has necrotic areas
    - High risk for multicentricity, microinvasion, and recurrence
    - Tx: simple mastectomy
- ↑ recurrence risk with comedo type and lesions > 2.5 cm
- Tx: Lumpectomy and XRT; need 1 cm margins; *No ALND or SLNB*; possibly tamoxifen/raloxifene
  - Simple mastectomy if high grade (eg comedo type, multicentric, multifocal), if a large tumor not amenable to lumpectomy, or if not able to get good margins; *also need SLNBx* (last chance to sample the nodes)

LOBULAR CARCINOMA IN SITU (LCIS)

- Does not have basement membrane invasion
- 40% get cancer (either breast)
- Considered a marker for the development of breast CA, not premalignant itself
- Has no calcifications; is not palpable
- Primarily found in premenopausal women
- Patients who develop breast CA are more likely to develop a ductal CA (70%)
- Usually an incidental finding; multifocal disease is common
- 5% risk of having a synchronous breast CA at the time of diagnosis of LCIS (most likely ductal CA)
- Do not need negative margins (although you do need excisional biopsy of the suspicious area)
- Tx: nothing, tamoxifen/raloxifene, or bilateral subcutaneous mastectomy (no ALND)

Indications for Excisional Biopsy After Core Biopsy

Atypical ductal hyperplasia
Atypical lobular hyperplasia
Radial scar
Lobular carcinoma in situ
Columnar cell hyperplasia with atypia
Papillary lesions
Phyllodes tumor
Lack of concordance between appearance of mammographic lesion and histologic diagnosis

Nondiagnostic specimen (including absence of calcifications on specimen radiograph when biopsy is performed for calcifications)

BREAST CANCER

- Breast CA decreased in economically poor areas
- Japan has lowest rate of breast CA worldwide
- U.S. breast CA risk – 1 in 8 women (12%); 5% in women with no risk factors
- Breast CA in younger women (< 40) tends to be more aggressive
- Screening decreases mortality by 25%
- Untreated breast cancer – median survival 2–3 years
- 10% of breast CAs have negative mammogram and negative ultrasound
- Clinical features of breast CA – distortion of normal architecture; skin/nipple distortion or retraction; hard, tethered, indistinct borders
- Symptomatic breast mass workup
  - < 40 years old – need U/S and core needle Bx (CNBx; consider FNA)
    - Need mammogram in patients < 40 if clinical exam or U/S is indeterminate or suspicious for CA although in general want to avoid excess radiation in this group
  - > 40 years old – need bilateral mammograms, U/S, and CNBx
  - If CNBx or FNA is indeterminate, non-diagnostic, or non-concordant with exam findings/imaging studies → will need excisional biopsy
  - Clinically indeterminate or suspect solid masses will eventually need excisional biopsy unless CA diagnosis is made prior to that
  - Cyst fluid (send fluid for cytology) – if bloody, need cyst excisional biopsy; if clear and recurs, need cyst excisional biopsy; if complex cyst, need cyst excisional biopsy; if clear, does not recur, and cytology is negative – no further therapy
  - CNBx – gives architecture
  - FNA – gives cytology (just the cells)
  - CNBx and FNA can be performed with mammography or U/S guidance

Management of Breast Masses Based on FNA or CNBx

Diagnosis	Treatment
Malignant	Definitive therapy
Suspicious	Surgical biopsy
Atypia	Surgical biopsy
Nondiagnostic	Repeated FNA/CNBx or surgical biopsy
Benign	Possible observation – exam and imaging studies need to concordant with benign disease, otherwise need excisional biopsy (if age > 40, lean towards excisional biopsy)

- Mammography
  - Has 90% sensitivity/specificity
  - Sensitivity increases with age as the dense parenchymal tissue is replaced with fat
  - Mass needs to be ≥ 5 mm to be detected
  - Suggestive of CA – irregular borders; spiculated; multiple clustered, small, thin, linear, crushed-like and/or branching calcifications; ductal asymmetry, distortion of architecture

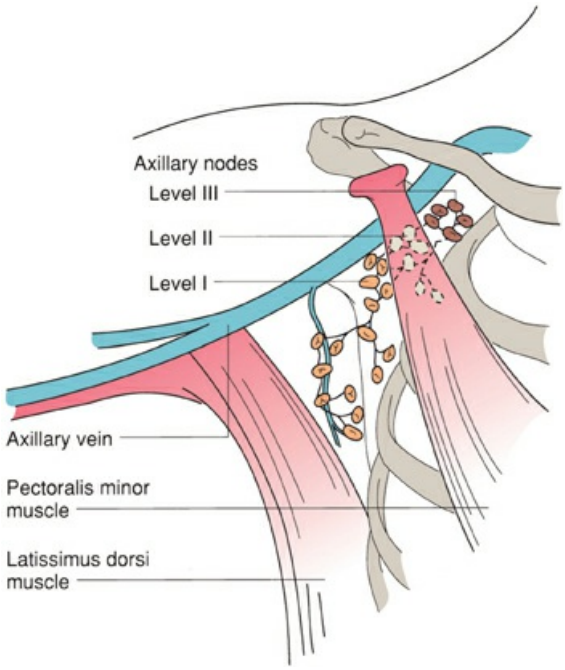
BI-RADS Classification of Mammographic Abnormalities

Category	Assessment	Recommendation
1	Negative	Routine screening
2	Benign finding	Routine screening
3	Probably benign finding	Short-interval follow-up mammogram (3–6 months)
4	Suspicious abnormality (eg indeterminate calcifications or architecture)	Definite probability of CA (4a – 15%, 4b – 35%, 4c – 80%); *get CNBx*
5	Highly suggestive of CA (suspicious calcifications or architecture)	High probability of CA (95%); *get CNBx*

BI-RADS, breast imaging, reporting, and data system.

- BI-RADS 4 lesion CNBx shows:
  - Malignancy → follow appropriate Tx
  - Non-diagnostic, indeterminate, or benign and non-concordant with mammogram → need needle localization excisional biopsy
  - Benign and concordant with mammogram → 6-month follow-up
- BI-RADS 5 lesion CNBx shows:
  - Malignancy → follow appropriate Tx
  - *Any other finding* (nondiagnostic, indeterminate, or benign) → all need needle localization excisional biopsy
- CNBx *without* excisional biopsy allows appropriate staging with SLNBx (mass is still present) and one-step surgery (avoids 2 surgeries) for patients diagnosed with breast CA

- Screening
  - Mammogram every 2–3 years after age 40, then yearly after 50
  - High-risk screening – mammogram 10 years before the youngest age of diagnosis of breast CA in first-degree relative
  - No mammography in patients < 40 unless high risk → hard to interpret because of dense parenchyma
  - Want to decrease radiation dose in young patients
  - Mammograms are not performed in patients < 20 (breast is too dense)
- Node levels
  - I – lateral to pectoralis minor muscle
  - II – beneath pectoralis minor muscle
  - III – medial to pectoralis minor muscle (extends to thoracic inlet)
  - Rotter's nodes – between the pectoralis major and pectoralis minor muscles
  - Need to take level I and II nodes (take level III nodes only if grossly involved)
  - Nodes are the most important prognostic staging factor. Other factors include tumor size, tumor grade, progesterone, and estrogen receptor status
    - Survival is directly related to the number of positive nodes
      - 0 nodes positive 75% 5-year survival
      - 1–3 nodes positive 60% 5-year survival
      - 4–10 nodes positive 40% 5-year survival



The axillary lymph nodes are divided into three levels by the pectoralis minor muscle. The level I nodes are inferior and lateral to the pectoralis minor, the level II nodes are below the axillary vein and behind the pectoralis minor, and the level III nodes are medial to the muscle against the chest wall.

- Bone – most common site for distant metastasis (can also go to lung, liver, brain)
- Takes approximately 5–7 years to go from single malignant cell to 1-cm tumor
- Central and subareolar tumors have increased risk of multicentricity
- Breast cancer risk
  - Greatly increased risk (relative risk > 4)
    - BRCA gene in patient with family history of breast CA
    - ≥ 2 primary relatives with bilateral or premenopausal breast CA
    - DCIS (ipsilateral breast at risk) and LCIS (both breasts have same high risk)
    - Fibrocystic disease with atypical hyperplasia
  - Moderately increased risk (relative risk 2–4) – prior breast cancer, radiation exposure, first-degree relative with breast cancer, age > 35 first birth
  - Lower increased risk (relative risk < 2) – early menarche, late menopause, nulliparity, proliferative benign disease, obesity, alcohol use, hormone replacement therapy
- BRCA I and II (+ family history of breast CA) and CA risk:
  - BRCA I:
    - Female breast CA 60% lifetime risk
    - Ovarian CA 40% lifetime risk
    - Male breast CA 1% lifetime risk
  - BRCA II:
    - Female breast CA 60% lifetime risk
    - Ovarian CA 10% lifetime risk
    - Male breast CA 10% lifetime risk
  - BRCA is the strongest RF for breast CA
  - Women with BRCA breast CA have the same prognosis stage for stage as non-BRCA

breast CA

TNM Definitions			
Tx	Primary tumor cannot be assessed		
T0	No evidence of primary tumor		
Tis	Carcinoma in situ, ductal, or lobular or Paget's disease of the nipple with no tumor		
T1	Tumor 2 cm or less in greatest dimension		
T2	Tumor more than 2 cm but not more than 5 cm in greatest dimension		
T3	Tumor more than 5 cm in greatest dimension		
T4	Tumor of any size with direct extension to the chest wall (not including pectoralis muscle), skin edema, skin ulceration, satellite skin nodules, or inflammatory carcinoma		
REGIONAL LYMPH NODES (PATHOLOGIC)			
Nx	Nodes cannot be assessed		
N0	No regional node metastases histologically, no additional examination for isolated tumor cells (ITCs)		
N1	Metastasis to one to three axillary nodes or in internal mammary (IM) nodes with microscopic disease detected by sentinel node biopsy, which is not clinically apparent		
N2	Metastases in four to nine axillary nodes or in clinically apparent IM nodes in the absence of axillary node metastasis		
N3	Metastases in 10 or more axillary nodes, or in infraclavicular nodes, or in IM nodes in the presence of one or more positive axillary nodes; or in more than three axillary nodes with IM metastases, or in supraclavicular nodes		
DISTANT METASTASES			
Mx	Distant metastasis cannot be assessed		
M0	No distant metastasis		
M1	Distant metastasis		
STAGE GROUPING			
Stage 0	Tis	N0	M0
Stage 1	TI	N0	M0
Stage IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

- BRCA screening – yearly mammogram and breast MRI starting at age 25
  - Yearly pelvic exam + U/S and CA-125 starting at age 25

- Consider total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) in BRCA families with history of breast CA
- Considerations for prophylactic mastectomy (vs careful follow-up +/– tamoxifen/raloxifene)
  - Family history + BRCA gene *or*
  - LCIS
  - Also need one of the following: high patient anxiety, poor patient access for follow-up exams and mammograms, difficult lesion to follow on exam or with mammograms, or patient preference for mastectomy
- Hormone receptors (estrogen/progesterone)
  - Positive receptors – better response to hormones, chemotherapy, surgery, and better overall prognosis
  - Receptor-positive tumors are more common in postmenopausal women
  - Progesterone receptor–positive tumors have better prognosis than estrogen receptor–positive tumors
  - Tumors that are both progesterone receptor and estrogen receptor positive have the best prognosis
  - 10% of breast CA is negative for both receptors
- HER2/neu receptor – worse prognosis stage for stage
  - Is a receptor tyrosine kinase
  - Trastuzumab (Herceptin) antibody blocks this receptor
- Male breast cancer
  - < 1% of all breast CAs; usually ductal
  - Poorer prognosis because of late presentation
  - Have ↑ pectoral muscle involvement
  - Associated with steroid use, previous XRT, family history, Klinefelter's syndrome
  - Tx: modified radical mastectomy (MRM)
- Ductal CA
  - 85% of all breast CA
  - Various subtypes
    - Medullary – smooth borders, ↑ lymphocytes, bizarre cells, more favorable prognosis
    - Tubular – small tubule formations, more favorable prognosis
    - Mucinous (colloid) – produces an abundance of mucin, more favorable prognosis
    - Cirrhotic – worse prognosis
  - Tx: MRM or BCT with postop XRT
- Lobular cancer
  - 10% of all breast CAs
  - Does not form calcifications; extensively infiltrative; ↑ bilateral, multifocal, and multicentric disease
  - Signet ring cells confer worse prognosis
  - Tx: MRM or BCT with postop XRT
- Inflammatory cancer
  - Considered T4 disease
  - Very aggressive → median survival of 36 months
  - Has dermal lymphatic invasion, which causes peau d'orange lymphedema appearance on breast; erythematous and warm
  - Dx: full thickness incisional breast biopsy including the skin

- Tx: neoadjuvant chemo, then MRM, then adjuvant chemo-XRT (most common method); BCT contraindicated here

- Surgical options (usually surgery first, followed by adjuvant Tx)
  - Subcutaneous mastectomy (simple mastectomy)
    - Leaves 1%–2% of breast tissue, preserves the nipple-areolar complex
    - Not indicated for breast CA treatment
    - Used for DCIS and LCIS

Contraindications to Breast-Conserving Therapy in Invasive Carcinoma

Absolute Contraindications to BCT

- Two or more primary tumors in separate quadrants of the breast
- Persistent positive margins after reasonable surgical attempts
- Pregnancy is an absolute contraindication to the use of breast irradiation. When cancer is diagnosed in the third trimester; it may be possible to perform breast-conserving surgery and treat the patient with irradiation after delivery
- A history of prior therapeutic irradiation to the breast region that would result in retreatment to an excessively high radiation dose
- Diffuse malignant-appearing microcalcifications

Relative Contraindications to BCT

- A history of scleroderma or active systemic lupus erythematosus
- Large tumor in a small breast that would result in cosmesis unacceptable to the patient

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- Breast-conserving therapy (BCT = lumpectomy, quadrectomy, etc. plus ALND or SLNB); combined with postop XRT; need 1-cm margin
- Modified radical mastectomy
  - Removes all breast tissue, including the nipple areolar complex
  - Includes axillary node dissection (level I and II nodes)
- SLNB
  - Fewer complications than ALND
  - Indicated only for malignant tumors > 1 cm
  - Not indicated in patients with clinically positive nodes; they need ALND
  - Accuracy best when primary tumor is present (finds the right lymphatic channels)
  - Well suited for small tumors with low risk of axillary metastases
  - Lymphazurin blue dye or radiotracer is injected directly into tumor area
  - Type I hypersensitivity reactions have been reported with Lymphazurin blue dye
  - Usually find 1–3 nodes; 95% of the time, the sentinel node is found
  - During SLNB – if no radiotracer or dye is found, need to do a formal ALND
  - Contraindications – multicentric disease, neoadjuvant therapy, clinically positive nodes, prior axillary surgery, inflammatory or locally advanced disease
- ALND – take level I and II nodes
- Complications of MRM – infection, flap necrosis, seromas
- Complications of ALND
  - Infection, lymphedema, lymphangiosarcoma
  - Axillary vein thrombosis – sudden, early, postop swelling
  - Lymphatic fibrosis – slow swelling over 18 months
  - Intercostal brachiocutaneous nerve injury – hyperesthesia of inner arm and lateral

chest wall; most commonly injured nerve after mastectomy; no significant sequelae
    - Drains – leave in until drainage < 40 cc/day
- Radiotherapy
  - Usually consists of 5,000 rad for BCT and XRT
  - Complications of XRT – edema, erythema, rib fractures, pneumonitis, ulceration, sarcoma, contralateral breast CA
  - Contraindications to XRT – pregnancy, scleroderma (results in severe fibrosis and necrosis), previous XRT and would exceed recommended dose, SLE (relative), active rheumatoid arthritis (relative)
  - Indications for XRT after mastectomy:
    - Advanced nodal disease – > 4 nodes, extracapsular nodal invasion, fixed axillary nodes (N2), or internal mammary nodes (N3)
    - Skin or chest wall involvement
    - Positive margins
    - T3 (> 5 cm) or T4 (eg inflammatory CA) tumor
  - BCT with XRT
    - Need to have negative margins (1 cm) following BCT before starting XRT
    - 10% chance of local recurrence, usually within 2 years of 1st operation, need to re-stage with recurrence
    - Need salvage MRM for local recurrence
- Chemotherapy
  - TAC (taxanes, Adriamycin, and cyclophosphamide) for 6–12 weeks
  - Positive nodes – everyone gets chemo *except* postmenopausal women with positive hormonal receptors → they can get hormonal therapy only with aromatase inhibitor (anastrozole)
  - > 1 cm and negative nodes – everyone gets chemo *except* patients with positive hormonal receptors → they can get hormonal therapy only with tamoxifen if they are premenopausal or aromatase inhibitor (anastrozole) if they are postmenopausal
  - < 1 cm *and* negative nodes – no chemo; hormonal therapy as above if positive hormonal receptors
  - After chemo, patients positive for hormonal receptors should receive appropriate hormonal therapy
  - Both chemotherapy and hormonal therapy have been shown to decrease recurrence and improve survival
  - Taxanes – docetaxel, paclitaxel
  - Tamoxifen – decreases risk of breast CA recurrence by 50%
    - Blocks estrogen and progesterone hormonal receptors
    - Side effects – 1% risk of blood clots; 0.1% risk of endometrial CA
    - Decreases risk of osteoporosis and fractures
  - Aromatase inhibitors – decreases risk of breast CA recurrence by 50%
    - Block conversion of testosterone to estrogen in the periphery
    - Side effects – fractures
    - Decreased risk of thromboembolic events and endometrial CA compared to tamoxifen
  - Trastuzumab (Herceptin) – decreases risk of breast CA recurrence by 50%
    - Should be given for HER2/neu receptor positive tumors either > 1 cm or if nodes are positive

    - Side effects – cardiac disease (heart failure)
- Almost all women with recurrence die of disease
- Increased recurrences and metastases occur with positive nodes, large tumors, negative receptors, unfavorable subtype
- Metastatic flare – pain, swelling, erythema in metastatic areas; XRT can help
    - XRT is good for bone or brain metastases
- Occult breast CA – breast CA that presents as axillary metastases with unknown primary; Tx: MRM (70% are found to have breast CA)
- Paget's disease
    - Scaly skin lesion on nipple; biopsy shows Paget's cells
    - Patients have DCIS or ductal CA in breast
    - Dx: full thickness incisional breast biopsy including the skin
    - Tx: need MRM if cancer present; otherwise simple mastectomy with SLNBx if DCIS is present (need to include the nipple-areolar complex with Paget's)
- Phyllodes tumor
    - 10% malignant (cystosarcoma phyllodes), based on mitoses per high-power field (> 5–10)
    - No nodal metastases, hematogenous spread if any (rare)
    - Resembles giant fibroadenoma; has stromal and epithelial elements (mesenchymal tissue)
    - Can often be large tumors
    - Tx: WLE with negative margins (1 cm); no ALND
- Stewart–Treves syndrome
    - Lymphangiosarcoma from chronic lymphedema following axillary dissection
    - Patients present with dark purple nodule or lesion on arm 5–10 years after surgery
- Pregnancy with mass
    - Tends to present late, leading to worse prognosis
    - Mammography and ultrasound do not work as well during pregnancy
    - Try to use ultrasound to avoid radiation
    - If cyst, drain it and send FNA for cytology
    - If solid, perform core needle biopsy or FNA
    - If core needle and FNA equivocal, need to go to excisional biopsy
    - Breast CA in pregnancy – no hormonal or radiation therapy at any time during the pregnancy; chemotherapy can be used after the 1st trimester

25 Thoracic

ANATOMY AND PHYSIOLOGY

- Azygous vein runs along the right side and dumps into superior vena cava
- Thoracic duct runs along the right side, crosses midline at T4–5, and dumps into left subclavian vein at junction with internal jugular vein
- Phrenic nerve – runs anterior to hilum
- Vagus nerve – runs posterior to hilum
- Right lung volume 55% (3 lobes: RUL, RML, and RLL)
- Left lung volume 45% (2 lobes: LUL and LLL and lingula)
- Quiet inspiration – diaphragm 80%, intercostals 20%
- Greatest change in dimension superior/inferior
- Accessory muscles – sternocleidomastoid muscle (SCM), levators, serratus posterior, scalenes
- Type I pneumocytes – gas exchange
- Type II pneumocytes – surfactant production (mainly phosphatidylcholine – keeps alveoli open)
- Pores of Kahn – direct air exchange between alveoli

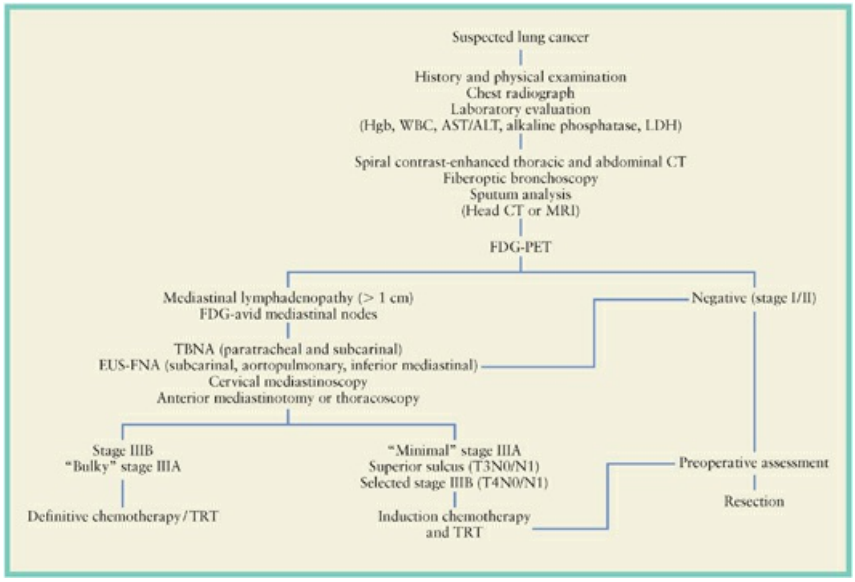
PULMONARY FUNCTION TESTS

- Need predicted postop FEV_1 > 0.8 (or > 40% of the predicted postop value)
  - If it is close → get qualitative V/Q scan to see contribution of that portion of lung to overall FEV_1 → if low, may still be able to resect
  - FEV_1 is the best predictor of pulmonary complications and being able to wean off the ventilator
- Need predicted postop DLCO > 10 mL/min/mm Hg CO (or > 40% of the predicted postop value)
  - Measures carbon monoxide diffusion and represents oxygen exchange capacity
  - This value depends on pulmonary capillary surface area, hemoglobin content, and alveolar architecture
- No resection if preop pCO_2 > 50 or pO_2 < 60 at rest
- No resection if preop VO_2 max < 10–12 mL/min/kg (maximum oxygen consumption)
- Persistent air leak – most common after segmentectomy/wedge
- Atelectasis – most common after lobectomy
  - MC complication following lung resection
  - Tx: incentive spirometer
- Arrhythmias – most common after pneumonectomy

LUNG CANCER

- Symptoms: can be asymptomatic with finding on routine CXR; cough, hemoptysis, atelectasis, PNA, pain, weight loss

- Most common cause of cancer-related death in the United States
- Nodal involvement has strongest influence on survival
  - Hilar nodal involvement does not preclude resection (N1)
- Brain – single most common site of metastasis
  - Can also go to supraclavicular nodes, other lung, bone, liver, and adrenals
- Recurrence usually appears as disseminated metastases
  - 80% of recurrences are within the 1st 3 years
- Lung CA overall 5-year survival rate 10%; 30% with resection for cure
- Stage I and II disease resectable; T3,N1,M0 (stage IIIa) possibly resectable
- Lobectomy or pneumonectomy most common procedure (need formal lung resection for lung CA); sample suspicious nodes
- Non–small cell carcinoma
  - 80% of lung CA
  - Squamous cell carcinoma usually more central
  - Adenocarcinoma usually more peripheral
  - Adenocarcinoma is the most common lung CA (not squamous)



Evaluation of the patient who presents with a pulmonary mass.

TNM STAGING SYSTEM FOR LUNG CANCER

- T1: < 3 cm. T2: > 3 cm but > 2 cm away from carina. T3: invasion of chest wall, pericardium, diaphragm, or < 2 cm from carina. T4: mediastinum, esophagus, trachea, vertebra, heart, great vessels, malignant effusion (usually all indicate unresectability)
- N1: ipsilateral hilum nodes. N2: ipsilateral mediastinal, subcarinal, or aortopulmonary window (unresectable).
- N3: contralateral mediastinal or supraclavicular (unresectable)
- M1: distant metastasis

Stage	TNM Status
I	T1–2,N0,M0
IIa	T1,N1,M0
IIb	T2,N1,M0 or T3,N0,M0

IIIa	T1–3,N2,M0 or T3,N1,M0
IIIb	Any T4 or N3
IV	M1

- Small cell carcinoma
  - 20% of lung CA; neuroendocrine in origin
  - Usually unresectable at time of diagnosis (< 5% candidates for surgery)
  - Overall 5-year survival rate < 5% (very poor prognosis)
  - Stage T1,N0,M0 5-year survival rate – 50%
  - Most get just chemo-XRT
- Paraneoplastic syndromes
  - Squamous cell CA – PTH-related peptide
  - Small cell CA – ACTH and ADH
  - Small cell ACTH – most common paraneoplastic syndrome
- Mesothelioma
  - Most malignant lung tumor
  - Aggressive local invasion, nodal invasion, and distant metastases common at the time of diagnosis
  - Asbestos exposure
- Non–small cell CA chemotherapy (stage II or higher) – carboplatin, Taxol
- Small cell lung CA chemotherapy – cisplatin, etoposide
- XRT can be used for lung CA as well
- Chest and abdominal CT scan – single best test for clinical assessment of T and N status
- PET scan – best test for M status
- Mediastinoscopy
  - Use for centrally located tumors and patients with suspicious adenopathy (> 0.8 cm or subcarinal > 1.0 cm) on chest CT
  - Does not assess aorto-pulmonary (AP) window nodes (left lung drainage)
  - Assesses ipsilateral (N2) and contralateral (N3) mediastinal nodes
  - If mediastinal nodes are positive, tumor is *unresectable*
  - Looking into middle mediastinum with mediastinoscopy
    - Left-side structures – RLN, esophagus, aorta, main pulmonary artery (PA)
    - Right-side structures – azygous and SVC
    - Anterior structures – innominate vein, innominate artery, right PA
- Chamberlain procedure (anterior thoracotomy or parasternal mediastinotomy) – assesses enlarged AP window nodes; go through left 2nd rib cartilage
- Bronchoscopy – needed for centrally located tumors to check for airway invasion
- For lung CA, patients need to 1) be operable (eg have appropriate FEV_1 and DLCO values) and 2) be resectable (ie can't have N2, N3, or M disease)
- Pancoast tumor – tumor invades apex of chest wall and patients have Horner's syndrome (invasion of sympathetic chain → ptosis, miosis, anhidrosis) or ulnar nerve symptoms
- SVC syndrome (swelling of the head, neck, and upper extremities) – MCC is lung CA
  - Tx: emergent XRT if due to malignancy

- Coin lesion
  - Overall, 10% are malignant
  - MC lesion – granuloma
  - MC tumor – hamartoma
  - MC CA – lung adenocarcinoma
  - Age < 50 → < 5% malignant; age > 50 → > 50% malignant
  - No growth in 2 years, and smooth contour suggests benign disease
  - Noncalcified lesions – more likely CA
  - If suspicious, will need either guided biopsy (bronchoscopy guided for central lesions, CT guided for peripheral lesions) or VATS wedge resection
- Asbestos exposure increases lung CA risk 90×
- Bronchoalveolar CA – can look like pneumonia; grows along alveolar walls; multifocal
- Metastases to the lung – if isolated and not associated with any other systemic disease, may be resected for colon, renal cell CA, sarcoma, melanoma, ovarian, and endometrial CA

CARCINOIDS

- Neuroendocrine tumor, usually central
  - 5% have metastases at time of diagnosis; 50% have symptoms (cough, hemoptysis)
- Typical carcinoid – 90% 5-year survival
- Atypical carcinoid – 60% 5-year survival
- Tx: resection; treat like cancer; outcome closely linked to histology
- Recurrence increased with positive nodes or tumors > 3 cm

BRONCHIAL ADENOMAS

- Upper airway usual
- MC – carcinoid (90%)
- Others – mucoepidermoid adenoma, mucous gland adenoma, and adenoid cystic adenoma → *all are malignant tumors*
- Mucoepidermoid adenoma and mucous gland adenoma
  - Slow growth, no metastases
  - Tx: resection (1-cm margin)
- Adenoid cystic adenoma
  - From submucosal glands; spreads along perineural lymphatics, well beyond endoluminal component; *very XRT sensitive*
  - Slow growing; can get 10-year survival with incomplete resection
  - Tx: resection; if unresectable, XRT can provide good palliation

HAMARTOMAS

- Most common benign adult lung tumor
- Composed of fat, cartilage, and connective tissue
- Have calcifications and can appear as a popcorn lesion on chest CT
- Diagnosis can be made with CT
- Do not require resection
- Repeat chest CT in 6 months to confirm diagnosis

MEDIASTINAL TUMORS IN ADULTS

- Most are asymptomatic; can present with chest pain, cough, dyspnea
- MCC of mediastinal adenopathy – lymphoma
- Neurogenic tumors – most common mediastinal tumor in adults and children, usually in posterior mediastinum
- 50% of symptomatic mediastinal masses are malignant
- 90% of asymptomatic mediastinal masses are benign
- Location (adult)
  - Anterior (thymus) – most common site for mediastinal tumor; T's →
    - Thymoma (#1 anterior mediastinal mass in adults)
    - Thyroid CA and goiters
    - T-cell lymphoma
    - Teratoma (and other germ cell tumors)
    - Parathyroid adenomas
  - Middle (heart, trachea, ascending aorta)
    - Bronchiogenic cysts
    - Pericardial cysts
    - Enteric cysts
    - Lymphoma
  - Posterior (esophagus, descending aorta)
    - Enteric cysts
    - Neurogenic tumors
    - Lymphoma
- Thymoma
  - All thymomas require resection
  - Thymus too big or associated with refractory myasthenia gravis → resection
  - 50% of thymomas are malignant
  - 50% of patients with thymomas have symptoms
  - 50% of patients with thymomas have myasthenia gravis
  - 10% of patients with myasthenia gravis have thymomas
  - *Are rare in children*
- Myasthenia gravis – fatigue, weakness, diplopia, ptosis (ocular symptoms most common)
  - Antibodies to acetylcholine receptors
  - Tx: anticholinesterase inhibitors (neostigmine); steroids, plasmapheresis
  - 80% get improvement with thymectomy, including patients who do not have thymomas
- Germ cell tumors
  - If open biopsy is required, perform anterior thoracotomy (parasternal mediastinotomy [Chamberlain procedure])
  - Mediastinoscopy will not reach these lesions if they are in the anterior or posterior mediastinum
  - Teratoma – most common germ cell tumor in mediastinum
    - Can be benign or malignant
    - Tx: resection; possible chemotherapy
  - Seminoma – most common malignant germ cell tumor in mediastinum
    - 10% are beta-HCG positive; should not have AFP (alpha-fetoprotein)
    - Tx: *XRT (extremely sensitive);* chemotherapy reserved only for metastases or bulky nodal

disease; surgery for residual disease after that
    - Non-seminoma – 90% have elevated beta-HCG and AFP
        - Tx: *chemo (cisplatin, bleomycin, etoposide)*; surgery for residual disease
- Cysts
    - Bronchiogenic – usually posterior to carina. Tx: resection
    - Pericardial – usually at right costophrenic angle. Tx: can leave alone (benign)
- Neurogenic tumors – have pain, neurologic deficit. Tx: resection
    - 10% have intra-spinal involvement that requires simultaneous spinal surgery
    - Neurolemmoma (schwannoma) – most common
    - Paraganglioma – can produce catecholamines, associated with von Recklinghausen's disease
    - Can also get neuroblastomas and neurofibromas

TRACHEA

- MC benign tumors: adults – papilloma; children – hemangioma
- MC malignant – squamous cell carcinoma (adults), carcinoid (children)
- Most common late complication after tracheal surgery – granulation tissue formation
- Most common early complication after tracheal surgery – laryngeal edema
    - Tx: reintubation, racemic epinephrine, steroids
- Post-intubation stenosis – at stoma site with tracheostomy, at cuff site with ET tube
    - Serial dilatation, bronchoscopic resection, or laser ablation if minor
    - Tracheal resection with end-to-end anastomosis if severe or if it keeps recurring
- Tracheo-innominate artery fistula – occurs after tracheostomy, can have rapid exsanguination
    - Tx: place finger in tracheostomy hole and hold pressure → median sternotomy with ligation and resection of innominate artery (no graft, just ligate)
    - This complication is avoided by keeping tracheostomy between the 2nd and 3rd tracheal ring
- Tracheo-esophageal fistula
    - Usually occurs with prolonged intubation
    - Place large-volume cuff endotracheal tube below fistula
    - May need decompressing gastrostomy
    - Attempt repair after the patient is weaned from ventilator
    - Tx: tracheal resection, reanastomosis, close hole in esophagus, sternohyoid flap between esophagus and trachea

LUNG ABSCESS

- Necrotic area; most commonly associated with aspiration
- Most commonly in the superior segment of RLL
- MC organism – *staph aureus*
- Tx: *antibiotics alone (95% successful)*; CT-guided drainage if that fails
    - Surgery if above fails or cannot rule out cancer (> 6 cm, failure to resolve after 6 weeks)
- Chest CT can help differentiate empyema from lung abscess

EMPYEMA

- Usually secondary to pneumonia and subsequent parapneumonic effusion (staph, strep)
- Can also be due to esophageal, pulmonary, or mediastinal surgery
- Symptoms: pleuritic chest pain, fever, cough, SOB
- Pleural fluid often has WBCs > 500 cells/cc, bacteria, and a positive Gram stain
- Exudative phase (1st week) – Tx: chest tube, antibiotics
- Fibro-proliferative phase (2nd week) – Tx: chest tube, antibiotics; possible VATS (video-assisted thoracoscopic surgery) deloculation if lung doesn't re-expand
- Organized phase (3rd–4th week) – Tx: likely need decortication; fibrous peel occurs around lung (lung trapping)
  - Some are using intra-pleural tPA (tissue plasminogen activator) to try and dissolve the peel
  - May need Eloesser flap (open thoracic window – direct opening to external environment) in frail/elderly

CHYLOTHORAX

- Milky white fluid; has ↑ lymphocytes and TAGs (> 110 mL/μL); Sudan red stains fat
- Fluid is resistant to infection
- 50% secondary to trauma or iatrogenic injury
- 50% secondary to tumor (lymphoma most common, due to tumor burden in the lymphatics)
- Injury above T5–6 results in left-sided chylothorax
- Injury below T5–6 results in right-sided chylothorax
- Tx: 2–3 weeks of conservative therapy (chest tube, octreotide, low-fat diet or TPN)
  - If above fails and chylothorax secondary to trauma or iatrogenic injury, need ligation of thoracic duct on right side low in mediastinum (80% successful)
  - For malignant causes, need talc pleurodesis and possible chemo and/or XRT (less successful than above)

MASSIVE HEMOPTYSIS

- > 600 cc/24 h; bleeding usually from high-pressure bronchial arteries
- Most commonly secondary to infection, death is due to asphyxiation
- Tx: place bleeding side down; mainstem intubation to side opposite of bleeding to prevent drowning in blood; rigid bronchoscopy to identify site and possibly control bleeding; may need lobectomy or pneumonectomy to control; bronchial artery embolization if not suitable for surgery

SPONTANEOUS PNEUMOTHORAX

- Tall, healthy, thin, young males; more common on the right
- Recurrence risk after 1st pneumothorax is 20%, after 2nd pneumothorax is 60%, after 3rd pneumothorax is 80%
- Results from rupture of a bleb usually in the apex of the upper lobe of the lung
- Tx: chest tube
- Surgery for recurrence, air leak > 7 days, non-reexpansion (despite 2 chest tubes), high-risk profession (airline pilot, diver, mountain climber), patients who live in remote areas, tension PTX, hemothorax, bilateral PTX, previous pneumonectomy, large bleb on CT scan
- Surgery consists of thoracoscopy, apical blebectomy, and mechanical pleurodesis

OTHER CONDITIONS

- Malignant pericardial effusion: MCC – lung CA; Tx: pericardial window
- Malignant pleural effusion: MCC – lung CA; Tx: drainage and talc pleurodesis
- Tension pneumothorax – most likely to cause arrest after blunt trauma; impaired venous return
- Catamenial pneumothorax – occurs in temporal relation to menstruation
  - Caused by endometrial implants in the visceral lung pleura
- Residual hemothorax despite 2 good chest tubes → OR for thoracoscopic drainage
- Clotted hemothorax – surgical drainage if > 25% of lung, air–fluid levels, or signs of infection (fever, ↑ WBCs); surgery in 1st week to avoid peel; risk of empyema if not removed
- Broncholiths – usually secondary to infection
- Mediastinitis – usually occurs after cardiac surgery
- Whiteout on chest x-ray
  - Midline shift toward whiteout – most likely collapse → need bronchoscopy to remove plug
  - No shift – CT scan to figure it out
  - Midline shift away from whiteout – most likely effusion → place chest tube
- Bronchiectasis – acquired from infection, tumor, cystic fibrosis
  - Diffuse nature prevents surgery in most patients
- Tuberculosis – lung apices; get calcifications, caseating granulomas
  - Ghon complex → parenchymal lesion + enlarged hilar nodes
  - Tx: INH, rifampin, pyrazinamide
- Sarcoidosis – has non-caseating granulomas

Evaluation of Pleural Fluid

Test	Transudate	Exudate	Empyema
WBC	< 1,000	> 1,000	> 1,000 > 50,000 most specific
pH	7.45–7.55	≤ 7.45	< 7.30
Pleural fluid protein to serum ratio	< 0.5	> 0.5	> 0.5
Pleural fluid LDH to serum ratio	< 0.6	> 0.6	> 0.6

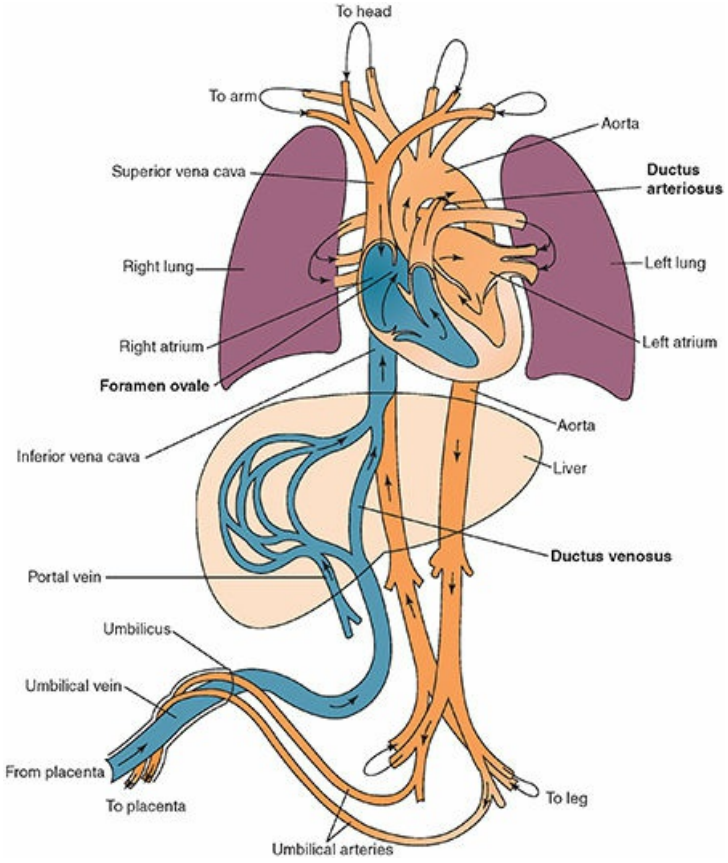
From Knight C, Paauw D. Respiratory tract infections. In: Shah SS, Hu KK, Crane HM, eds. *Blueprints Infectious Diseases*. Philadelphia, PA: Lippincott Williams & Wilkins; 2006, with permission.

- Recurrent pleural effusions can be treated with mechanical pleurodesis
  - Talc pleurodesis for malignant pleural effusions
- Airway fires – usually associated with the laser
  - Tx: stop gas flow, remove ET tube, re-intubate for 24 hours; bronchoscopy
- AVMs – connections between the pulmonary arteries and pulmonary veins; usually in lower lobes; can occur with Osler–Weber–Rendu disease
  - Symptoms: hemoptysis, SOB, neurologic events
  - Tx: embolization
- Chest wall tumors
  - Benign – osteochondroma most common
  - Malignant – chondrosarcoma most common

26 Cardiac

CONGENITAL HEART DISEASE

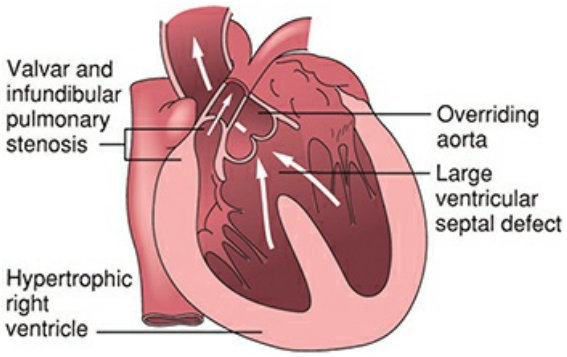
- R → L shunts cause cyanosis
  - Children squat to *increase* SVR and *decrease* R → L shunts
  - Cyanosis – can lead to polycythemia, strokes, brain abscess, endocarditis
  - Eisenmenger's syndrome: shift from L → R shunt to R → L shunt
    - Sign of increasing pulmonary vascular resistance (PVR) and pulmonary HTN; this condition is generally irreversible
- L → R shunts cause CHF – manifests as failure to thrive, ↑ HR, tachypnea, hepatomegaly, pulmonary edema; CHF in children – *hepatomegaly* 1st sign
- L → R shunts (CHF) – VSD, ASD, PDA
- R → L shunts (cyanosis) – tetralogy of Fallot
- Ductus arteriosus – connection between descending aorta and left pulmonary artery (PA); blood shunted away from lungs in utero
- Ductus venosum – connection between portal vein and IVC; blood shunted away from liver in utero
- Foramen ovale – shunts blood away from lungs
- Fetal circulation to placenta – 2 umbilical arteries
- Fetal circulation from placenta – 1 umbilical vein



Fetal circulation.

- Ventricular septal defect (VSD)
  - Most common congenital heart defect
  - L → R shunt
  - 80% close spontaneously (usually by age 6 months)
  - Large VSDs – usually cause symptoms after 4–6 weeks of life, as PVR ↓ and shunt ↑
  - Can get CHF (tachypnea, tachycardia) and failure to thrive
  - Medical Tx: diuretics and digoxin
  - Usual timing of repair:
    - Large VSDs (shunt > 2.5) – 1 year of age
    - Medium VSDs (shunt 2–2.5) – 5 years of age
    - *Failure to thrive – most common reason for earlier repair*
- Atrial septal defect (ASD)
  - L → R shunt
  - Ostium secundum – most common (80%); centrally located
  - Ostium primum (or atrioventricular canal defects or endocardial cushion defects); can have mitral valve and tricuspid valve problems; frequent in Down's syndrome
  - Usually symptomatic when shunt > 2 → CHF (SOB, recurrent respiratory infections)
  - Can get paradoxical emboli in adulthood
  - Medical Tx: diuretics and digoxin
  - Usual timing of repair – 1–2 years of age (age 3–6 months with canal defects)
- Tetralogy of Fallot (4 parts)
  - VSD, pulmonic stenosis, overriding aorta, right ventricular (RV) hypertrophy

- R → L shunt; child is small for age; clubbing; spells of cyanosis relieved by squatting
- Most common congenital heart defect that results in cyanosis
- Have decreased pulmonary perfusion
- Medical Tx: **β**-blocker
- Usual timing of repair – 3–6 months of age
- Repair: RV outflow tract obstruction (RVOT) removal, RVOT enlargement, and VSD repair



The four anatomic features of the tetralogy of Fallot. The primary morphologic abnormality, anterior and superior displacement of the infundibular septum, results in a malalignment ventricular septal defect, overriding of the aortic valve, and obstruction of the right ventricular outflow. Right ventricular hypertrophy is a secondary occurrence.

- Patent ductus arteriosus (PDA)
  - L → R shunt; bounding peripheral pulses, widened pulse pressure; machinelike murmur
  - Indomethacin – causes the PDA to close; rarely successful beyond neonatal period
  - Requires surgical ligation through left thoracotomy if it persists
- Aortic coarctation
  - Generally young patients with HTN in arms and low blood pressure in lower extremities
  - CXR – rib scalloping (erosion of large intercostal vessels into ribs)
  - Dx: CT angiogram
  - Tx: surgical resection
- Vascular ring
  - Difficulty swallowing, episodes of respiratory distress (stridor, crowing respirations), neck hyperextension
  - Trachea and esophagus are encircled by 2 aortic arches
  - Dx: barium swallow, bronchoscopy
  - Tx: surgery to divide the smaller of the 2 aortic arches

ADULT CARDIAC DISEASE

- Coronary artery disease
  - Most common cause of death in the United States
  - Risk factors – smoking, HTN, male gender, family history, hyperlipidemia, diabetes
  - Medical Tx: nitrates, smoking cessation, weight loss, statin drugs, ASA
  - Left main coronary artery branches into left anterior descending (LAD) and circumflex (Cx) arteries
  - Most atherosclerotic lesions are proximal

- Complications of myocardial infarction:
  - VSR (ventricular septal rupture) – hypotension, pansystolic murmur, usually occurs 3–7 days after MI; have a step-up in oxygen content between right atrium and pulmonary artery secondary to L → R shunt; Dx: echo; Tx: IABP to temporize, patch over septum
  - Papillary muscle rupture – get severe mitral regurgitation with hypotension and pulmonary edema; usually occurs 3–7 days after MI; Dx: echo; Tx: IABP to temporize, replace valve
- Drug-eluting stent – restenosis in 20% at 1 year
- Saphenous vein graft – 80% 5-year patency
- Internal mammary artery – off subclavian artery
  - Best conduit for CABG (> 95% 20-year patency when placed to LAD)
  - Collateralizes with superior epigastric artery
- CABG procedure
  - Potassium and cold solution cardioplegia – causes arrest of the heart in diastole; keeps the heart protected and still while grafts are placed
- Best indications for CABG (> 70% stenosis significant for most areas except left main disease)
  - Left main disease (> 50% stenosis considered significant)
  - 3-vessel disease (LAD, Cx, and right coronary artery)
  - 2-vessel disease involving the LAD
  - Lesions not amenable to stenting
- High mortality risk factors: *pre-op cardiogenic shock* (#1 risk factor), emergency operations, age, low EF

VALVE DISEASE

- Bioprosthetic tissue valves (do not require anticoagulation)
  - For patients who want pregnancy, have contraindication to anticoagulation, are older (> 65) and unlikely to require another valve in their lifetime, or have frequent falls
  - Tissue valves last 10–15 years – not as durable as mechanical valves
  - Because of rapid calcification in children and young patients, use of tissue valves is contraindicated in those populations
- Aortic stenosis (AS) – most from degenerative calcification; most common valve lesion
  - Cardinal symptoms:
    - Dyspnea on exertion – mean survival 5 years
    - Angina – mean survival 4 years
    - Syncope (*worst of the cardinal symptoms*) – mean survival 3 years
  - Indications for operation – when symptomatic (usually have a peak gradient > 50 mm Hg and a valve area < 1.0 cm^2)
- Mitral regurgitation (MR) – commonly caused by leaflet prolapse
  - Dyspnea, fatigue, pulmonary edema; can develop atrial fibrillation
  - Left ventricle becomes dilated
  - Ventricular function – key index of disease progression in patients with MR
  - Atrial fibrillation is common; in end-stage disease, pulmonary congestion occurs
  - Indications for operation – when symptomatic or if severe mitral regurgitation
- Mitral stenosis – rare now; most from rheumatic fever
  - Pulmonary edema and dyspnea; can get atrial fibrillation and hemoptysis as it progresses

- Indications for operation – when symptomatic (usually have valve area < 1 cm^2)
- Balloon commissurotomy to open valve often used as 1st procedure (not as invasive)

- Constrictive pericarditis
  - Dyspnea on exertion, hepatomegaly, ascites
  - Inflammation of the pericardium causes constriction of the heart
  - Square root sign on right heart catheterization (equalization of right atrial, right ventricular diastolic, pulmonary artery diastolic, wedge, and left ventricular diastolic pressures)
  - Tx: pericardiectomy

ENDOCARDITIS

- Fever, chills, sweats
- Aortic valve – most common site of prosthetic valve infections
- Mitral valve – most common site of native valve infections
- *Staphylococcus aureus* responsible for 50% of cases
- Most commonly left sided except in drug abusers (*Pseudomonas* most common organism for drug abusers)
- Medical therapy first – successful in 75%; sterilizes valve in 50%
- Indications for surgery – failure of antimicrobial therapy, severe valve failure, perivalvular abscesses, pericarditis

OTHER CARDIAC CONDITIONS

- Most common tumors of heart
  - Most common benign tumor – myxoma; 75% in LA
  - Most common malignant tumor – angiosarcoma
  - Most common metastatic tumor to the heart – lung CA
- Coming off cardiopulmonary bypass and aortic root vent blood is dark and aortic perfusion cannula blood is red
  - Tx: ventilate the lungs
- Coronary veins have the lowest oxygen tension of any tissue in the body due to high oxygen extraction by myocardium
- Superior vena cava (SVC) syndrome – swelling of the upper extremities and face
  - Most cases secondary to lung CA invading the SVC
  - These tumors are unresectable since the tumor has invaded the mediastinum
  - Tx: emergent XRT
- Mediastinal bleeding – > 500 cc for 1st hour or > 250 cc/h for 4 hours → need to re-explore after cardiac procedure
- Risk factors for mediastinitis – obesity, use of bilateral internal mammary arteries, diabetes
  - Tx: debridement with pectoralis flaps; can also use omentum
- Post-pericardiotomy syndrome – pericardial friction rub, fever, chest pain, SOB
  - EKG – diffuse ST-segment elevation in multiple leads
  - Tx: NSAIDs, steroids

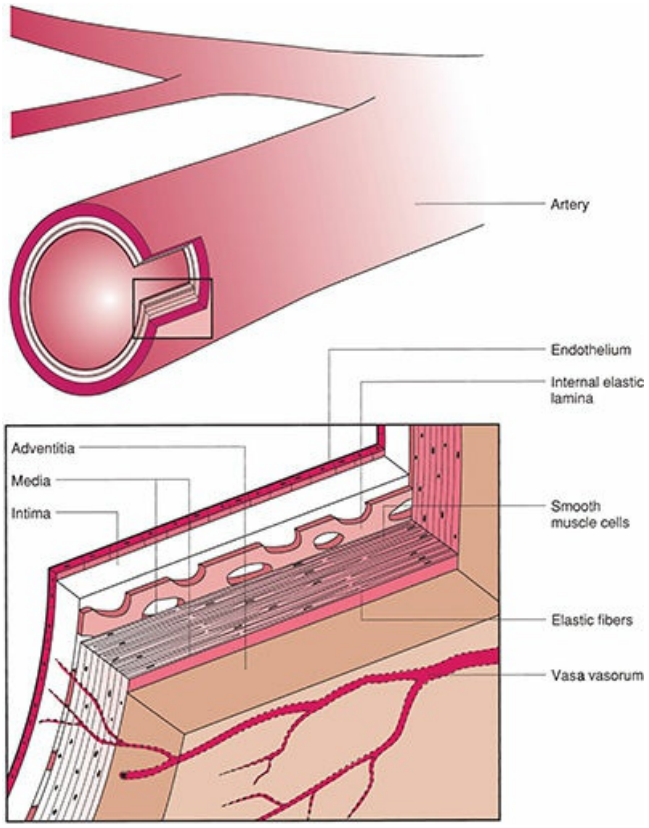
27 Vascular

INTRODUCTION

- Most common congenital hypercoagulable disorder – resistance to activated protein C (Leiden factor)
- Most common acquired hypercoagulable disorder – smoking

ATHEROSCLEROSIS STAGES

- 1st – foam cells → macrophages that have absorbed fat and lipids in the vessel wall
- 2nd – smooth muscle cell proliferation → caused by growth factors released from macrophages; results in wall injury
- 3rd – intimal disruption (from smooth muscle cell proliferation) → leads to exposure of collagen in vessel wall and eventual thrombus formation → fibrous plaques then form in these areas with underlying atheromas
- Risk factors: smoking, HTN, hypercholesterolemia, DM, hereditary factors

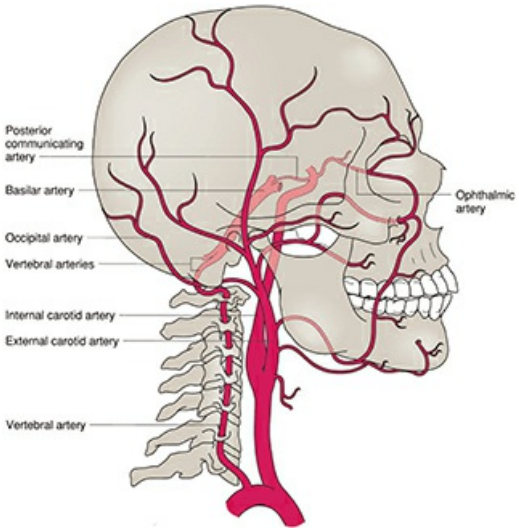


The artery wall is made of multiple layers (intima, media, and adventitia) that vary in composition depending on the artery.

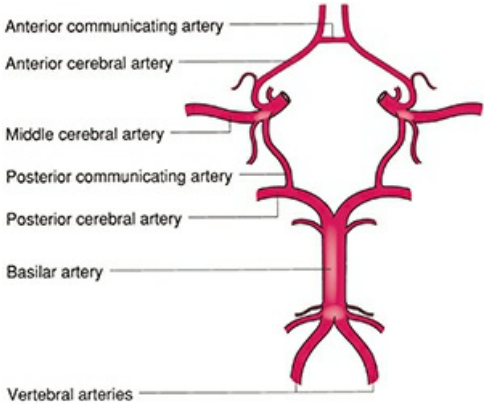
CEREBROVASCULAR DISEASE

- Stroke 3rd most common cause of death in the United States
- HTN – most important risk factor for stroke and cerebrovascular disease
- Carotids supply 85% of blood flow to brain
  - Carotid bifurcation – most common site of stenosis
- Normal internal carotid artery (ICA) has continuous forward flow
  - 1st branch of internal carotid artery – ophthalmic artery
- Normal external carotid artery (ECA) has triphasic flow (antegrade, retrograde, then antegrade again)
  - 1st branch of external carotid artery – superior thyroid artery
- Communication between the ICA and ECA occurs through the ophthalmic artery (off ICA) and internal maxillary artery (off ECA)
- Middle cerebral artery – most commonly diseased intracranial artery
- Cerebral ischemic events (eg stroke, TIA) – most commonly from arterial embolization from the ICA (not thrombosis)
  - Can also occur from a low-flow state through a severely stenotic lesion
  - Heart is the 2nd most common source of cerebral emboli
- Anterior cerebral artery events – mental status changes, release, slowing
- Middle cerebral artery events – contralateral motor and speech (if dominant side); contralateral facial droop
- Posterior cerebral artery events – vertigo, tinnitus, drop attacks, incoordination
- Amaurosis fugax – occlusion of the ophthalmic branch of the ICA (visual changes → shade coming down over eyes); visual changes are transient
  - See Hollenhorst plaques on ophthalmologic exam
- Carotid traumatic injury with major fixed deficit
  - If occluded, do not repair → can exacerbate injury with bleeding
  - If not occluded – repair with carotid stent or open procedure
- Carotid endarterectomy (CEA)
  - Repair indications: symptomatic > 50% stenosis, asymptomatic > 70% stenosis
  - Emergent CEA may be of benefit with fluctuating neurologic symptoms or crescendo/evolving TIAs
  - Repair the tightest side first if the patient has bilateral stenosis
  - Repair the dominant side first if the patient has equally tight carotid stenosis bilaterally
  - Removing the intima and part of the media with CEA
  - Most important technical concern – getting a good distal end point
  - Use a shunt if the back pressure is < 50 mm Hg or if the contralateral side is tight or occluded
  - Occluded ICA – do not repair (no benefit)
  - Facial vein – can routinely divide safely
  - Complications from repair
    - Vagus nerve injury – *most common cranial nerve injury with CEA* → secondary to vascular clamping during endarterectomy; patients get *hoarseness* (recurrent laryngeal nerve comes off vagus)
    - Hypoglossal nerve injury – tongue deviates to the side of injury → *speech and mastication difficulty*
    - Glossopharyngeal nerve injury – rare; occurs with really high carotid dissection → causes *difficulty swallowing*

- Ansa cervicalis – innervation to strap muscles; no serious deficits
- Mandibular branch of facial nerve – affects corner of mouth (smile); from the retractor at the angle of the jaw
- Acute event immediately after CEA → back to OR to check for flap or thrombosis
- Pseudoaneurysm – pulsatile, bleeding mass after CEA; Tx: drape and prep before intubation, intubate, then repair
- 20% have hypertension following CEA – caused by injury to carotid body; Tx: Nipride to avoid bleeding



The paired carotid and vertebral arteries supply blood to the brain. Extensive extracranial collaterals between the external carotid and vertebral systems allow for antegrade perfusion when a proximal occlusion develops in either vessel. Likewise, periorbital collaterals allow for retrograde flow through the ophthalmic artery to the internal carotid artery in the presence of a cervical internal carotid artery occlusion. Extensive side-to-side collaterals are found between the right and left external carotid arteries and right and left vertebral arteries.



The circle of Willis is a highly efficient intracranial collateral network; however, multiple important variations occur, and an incomplete circle producing an isolated hemisphere is not uncommon.

- Myocardial infarction – most common cause of non-stroke morbidity and mortality following CEA
- 15% restenosis rate after CEA

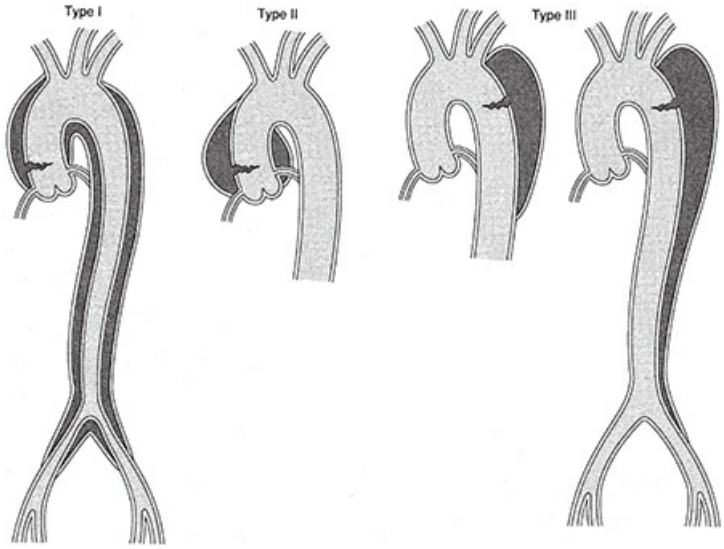
- Carotid stenting – for high-risk patients (eg patients with previous CEA and restenosis, multiple medical comorbidities, previous neck XRT)

- Vertebrobasilar artery disease
  - Anatomy: the two vertebral arteries arise from the subclavian arteries and combine to form a single basilar artery; the basilar then splits into two posterior cerebral arteries.
  - Usually need basilar artery or bilateral vertebral artery disease to have symptoms
  - Caused by atherosclerosis, spurs, bands; get vertebrobasilar insufficiency
  - Symptoms: diplopia, vertigo, tinnitus, drop attacks, incoordination
  - Tx: PTA with stent
- Carotid body tumors – present as a painless neck mass, usually near bifurcation, neural crest cells; are *extremely vascular*; can secrete catecholamines; Tx: resection

THORACIC AORTIC DISEASE

- Anatomy – aortic arch vessels include the innominate artery (which branches into the right subclavian and right common carotid arteries), the left common carotid artery, and the left subclavian artery
- Ascending aortic aneurysms
  - Often asymptomatic and picked up on routine CXR
  - Can get compression of vertebra (back pain), RLN (voice changes), bronchi (dyspnea or PNA), or esophagus (dysphagia)
  - Indications for repair: acutely symptomatic, ≥ 5.5 cm (with Marfan's > 5.0 cm), or rapid ↓ in size (> 0.5 cm/yr)
- Descending aortic aneurysms (also thoracoabdominal aneurysms)
  - Indications for repair
    - If endovascular repair possible – > 5.5 cm
    - If open repair needed – > 6.5 cm
  - Risk of mortality or paraplegia is less with endovascular repair (2%–3%) compared to open repair (20%)
  - Reimplant intercostal arteries below T8 to help prevent paraplegia with open repair
- Aortic dissections
  - Stanford classification – based on presence or absence of involvement of ascending aorta
    - Class A – any ascending aortic involvement
    - Class B – descending aortic involvement only
  - DeBakey classification – based on the site of tear and extent of dissection
    - Type I – ascending and descending
    - Type II – ascending only
    - Type III – descending only
  - Most dissections start in the ascending aorta
  - Can mimic myocardial infarction
  - Symptoms: tearing-like chest pain; can have unequal pulses (or BP) in upper extremities
  - 95% of patients have severe HTN at presentation
  - Other risk factors: Marfan's syndrome, previous aneurysm, atherosclerosis
  - CXR – usually normal; may have wide mediastinum
  - Dx: chest CT with contrast
  - Dissection occurs in medial layer of blood vessel wall
  - Aortic insufficiency occurs in 70%, caused by annular dilatation or when aortic valve cusp

is sheared off

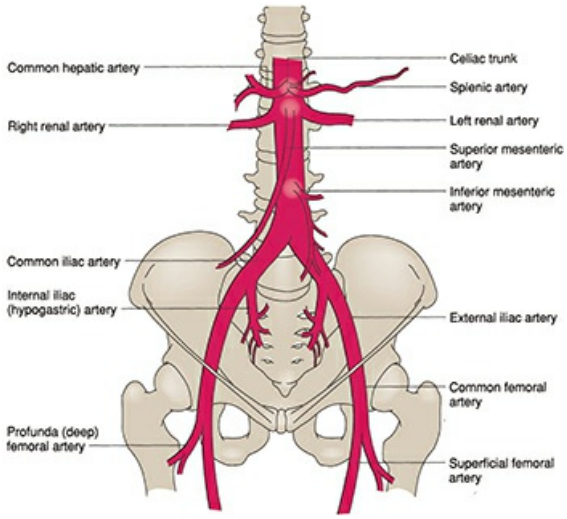


DeBakey classification of aortic dissection.

- Can also have occlusion of the coronary arteries and major aortic branches
- Death with ascending aortic dissections usually secondary to cardiac failure from aortic insufficiency, cardiac tamponade, or rupture
- Medical Tx initially → control BP with IV **β**-blockers (eg esmolol) and Nipride
- Tx:
  - Operate on *all ascending* aortic dissections – Tx: need open repair; graft is placed to eliminate flow to the false lumen (median sternotomy)
  - Only operate on descending aortic dissections with visceral or extremity ischemia or if contained rupture – Tx: endograft or open repair (left thoracotomy); can also just place fenestrations in the dissection flap to restore blood flow to viscera or extremity if ischemia is the problem
  - Follow these patients with lifetime serial scans (MRI to decrease radiation exposure); 30% eventually get aneurysm formation requiring surgery
- Postop complications for thoracic aortic surgery – MI, renal failure, paraplegia (descending thoracic aortic surgery)
- Paraplegia caused by spinal cord ischemia due to occlusion of intercostal arteries and artery of Adamkiewicz that occurs with descending thoracic aortic surgery

ABDOMINAL AORTIC DISEASE

- Abdominal aortic aneurysms (AAAs)
  - Normal aorta 2–3 cm
  - MCC – atherosclerosis (results in degeneration of the medial layer)
  - Risk factors: males, age, smoking, family history
  - Usually found incidentally
  - Can present with rupture, distal embolization, or compression of adjacent organs
  - Rupture
    - Leading cause of death without an operation
    - Symptoms: back or abdominal pain; can have profound hypotension



Anatomy of the abdominal aorta and iliac arteries.

- Dx: CT angio
- CT shows fluid in retroperitoneal space and extraluminal contrast with rupture
- Most likely to rupture on left posterolateral wall, 2–4 cm below renals
- More likely to rupture in presence of diastolic HTN or COPD (thought to be predictors of expansion)
- 50% mortality with rupture if patient reaches hospital alive

- Repair indications:
  - ≥ 5.5 cm for average male patient
  - ≥ 5.0 cm for women or those with high rupture risk (eg severe COPD, numerous relatives with rupture, poorly controlled HTN, eccentric shape)
  - Growth > 1.0 cm/yr
  - Symptomatic
  - Infected (mycotic)
  - EVAR *better* than open surgery for the elderly, for high-risk patients (ie multiple comorbidities), or those with "hostile" abdomens
  - For high-risk patients, delay in repair until 5.5 cm is warranted (non-symptomatic patients), especially if EVAR is not an option
- Technical aspects:
  - Reimplant inferior mesenteric artery (IMA) if backpressure < 40 mm Hg (ie poor backbleeding), previous colonic surgery, stenosis at the superior mesenteric artery, or flow to left colon appears inadequate
  - Ligate bleeding lumbar arteries
  - Usually use a straight tube Dacron graft for repair of AAAs
  - If performing an aorto-bifemoral repair instead of a straight tube graft, you should ensure flow to at least one internal iliac artery (hypogastric artery; should see back-bleeding) to avoid vasculogenic impotence
  - EVAR – has less peri-op mortality, ICU stay, and hospital stay; requires more reviews and late interventions; no change in late survival
- Complications
  - Major vein injury with proximal cross-clamp – retro-aortic left renal vein
  - Impotence in ⅓ secondary to disruption of autonomic nerves and blood flow to the

pelvis
- 5% mortality with elective repair
- #1 cause of acute death after surgery – MI
- #1 cause of late death after surgery – renal failure
- RFs for mortality – creatinine > 1.8 (#1), CHF, EKG ischemia, pulmonary dysfunction, older age, females
- Graft infection rate – 1% (*staph epidermidis* #1; *staph aureus*, *E. coli*)
- Pseudoaneurysm after graft placement – 1%
- Atherosclerotic occlusion – most common late complication after aortic graft placement
- Diarrhea (especially bloody) after AAA repair worrisome for ischemic colitis:
  - Inferior mesenteric artery (IMA) often sacrificed with AAA repair and can cause ischemia (most commonly the left colon)
  - Dx: endoscopy or abdominal CT; middle and distal rectum are spared from ischemia (middle and inferior rectal arteries are branches off internal iliac artery)
  - If patient has peritoneal signs, mucosa is black on endoscopy, or part of the colon looks dead on CT scan → take to OR for colectomy and colostomy placement

Ideal Criteria for Abdominal Aortic Aneurysm (AAA) Endovascular Repair

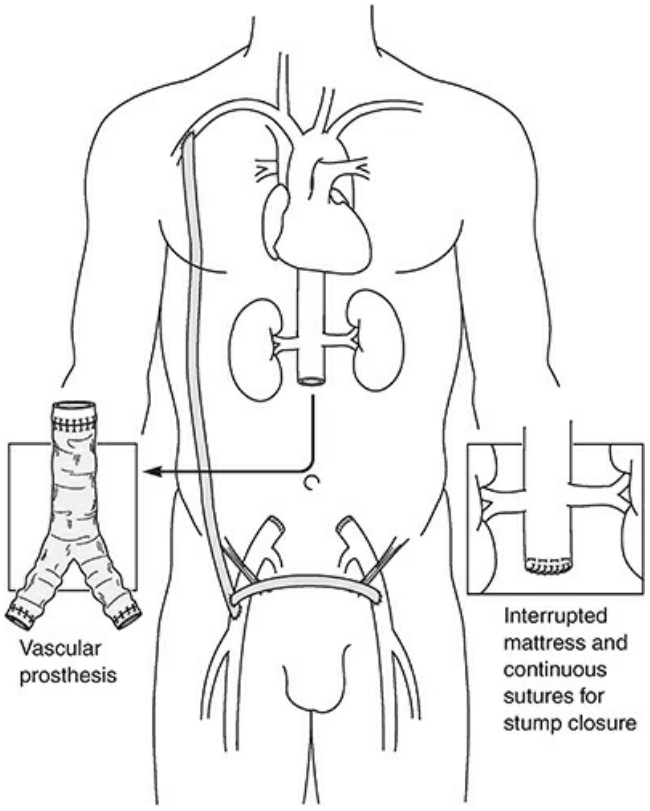
AAA Morphology	Criteria
Neck length	> 15 mm
Neck diameter	< 30 mm
Neck angulation	< 60 degrees
Common iliac artery length	> 10 mm
Common iliac artery diameter	8–18 mm
Other	Non-tortuous, noncalcified iliac arteries Lack of neck thrombus

Modified from Schermerhorn ML, Simosa HF. Type IV thoracoabdominal, infrarenal, and pararenal aortic aneurysms. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.

Endoleak Type	Failure Site	Tx
Type I	Proximal or distal graft attachment sites	Extension cuffs
Type II	Collaterals (eg patent lumbar, IMA, intercostals, accessory renal)	Observe most; percutaneous coil embolization if pressurizing aneurysm
Type III	Overlap sites when using multiple grafts or fabric tear	Secondary endograft to cover overlap site or tear
Type IV	Graft wall porosity or suture holes	Observe; can place nonporous stent if that fails
Type V (Endotension)	Expansion of aneurysm without evidence of leak	Repeat EVAR or open repair

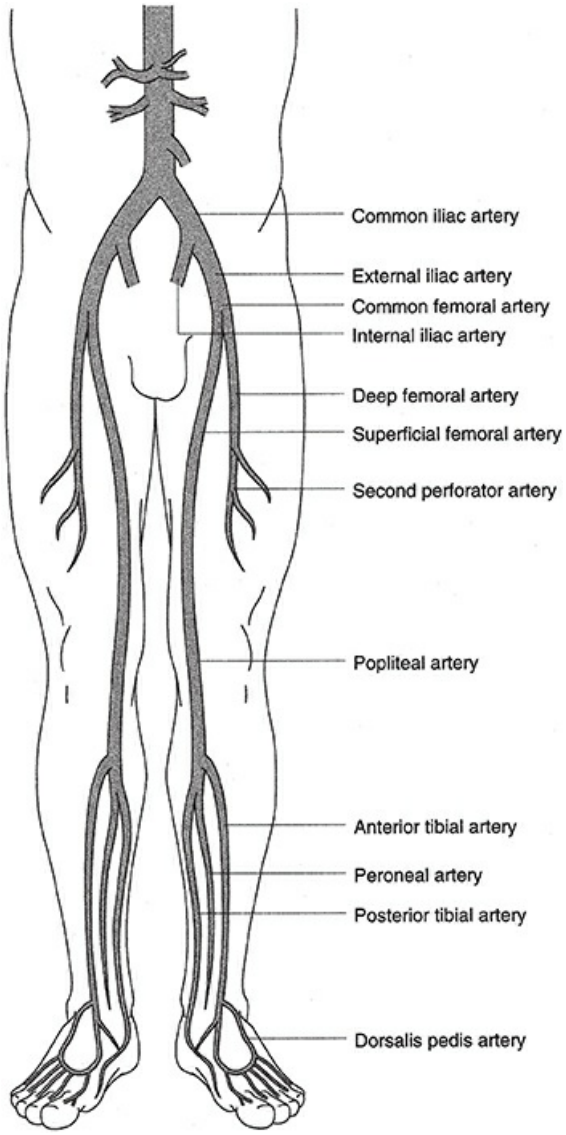
- Inflammatory aneurysms
  - Occurs in 10% of patients with AAA; males
  - Not secondary to infection – just an inflammatory process
  - Can get adhesions to the 3rd and 4th portions of the duodenum
  - Ureteral entrapment in 25%
  - Weight loss, ↑ ESR, thickened rim above calcifications on CT scan
  - May need to place preoperative ureteral stents to help avoid injury
  - Inflammatory process resolves after aortic graft placement

- Mycotic aneurysms
  - *Staphylococcus* #1, *Salmonella* #2
  - Bacteria infect atherosclerotic plaque, cause aneurysm
  - Pain, fevers, positive blood cultures in 50%
  - Periaortic fluid, gas, retroperitoneal soft tissue edema, lymphadenopathy
  - Usually need extra-anatomic bypass (axillary–femoral with femoral-to-femoral crossover) and resection of infrarenal abdominal aorta to clear infection
- Aortic graft infections
  - *Staphylococcus #1*, *E. coli* #2
  - See fluid, gas, thickening around graft
  - Blood cultures negative in many patients
  - Tx: bypass through non-contaminated field (eg axillary-femoral bypass with femoral-to-femoral crossover) and then resect the infected graft
  - More common with grafts going to the groin (eg aorto-bifemoral grafts)
- Aortoenteric fistula
  - Usually occurs > 6 months after abdominal aortic surgery
  - Herald bleed with hematemesis, then blood per rectum, then exsanguination
  - Graft erodes into 3rd or 4th portion of duodenum near proximal suture line
  - Tx: bypass through non-contaminated field (eg axillary-femoral bypass with femoral-to-femoral crossover), resect graft, and then close hole in the duodenum



Standard treatment for an infected aortic vascular prosthesis. An axillobifemoral bypass is performed first. This is followed a few days later by removal of the infected aortic prosthesis and careful oversewing of the aortic stump as illustrated.

PERIPHERAL ARTERIAL DISEASE (PAD)



Anatomy of the arterial circulation to the lower extremity.

- Leg compartments
  - Anterior – deep peroneal nerve (dorsiflexion, sensation between 1st and 2nd toes), anterior tibial artery
  - Lateral – superficial peroneal nerve (eversion, lateral foot sensation)
  - Deep posterior – tibial nerve (plantar flexion), posterior tibial artery, peroneal artery
  - Superficial posterior – sural nerve
- Signs/symptoms of PAD – extremity pain, pallor with dependent rubor, hair loss, shiny atrophic skin, slow capillary refill, ulcers (usually start in toe tips)
  - Most commonly due to atherosclerosis
- Statin drugs (lovastatin) – #1 preventive agent for atherosclerosis
- Homocystinuria can ↑ risk of atherosclerosis; Tx: folate and B_{12}
- Claudication (pain): medical therapy first → smoking cessation (#1), ASA, exercise until pain occurs to improve collaterals
- Symptoms occur one level below occlusion:
  - Buttock claudication – aortoiliac disease

- Mid-thigh claudication – external iliac
- Calf claudication – common femoral artery or proximal superficial femoral artery disease
- Foot claudication – distal superficial femoral artery or popliteal disease

- Lumbar stenosis can mimic claudication
- Diabetic neuropathy can mimic rest pain
- Leriche syndrome
  - No femoral pulses
  - Buttock or thigh claudication
  - Impotence (from ↓ flow in the internal iliacs)
  - Lesion at aortic bifurcation or above
  - Tx: aorto-bifemoral bypass graft
- Most common atherosclerotic occlusion in lower extremities – Hunter's canal (distal superficial femoral artery exits here); the sartorius muscle covers Hunter's canal
- Collateral circulation – forms from abnormal pressure gradients
  - Circumflex iliacs to subcostals
  - Circumflex femoral arteries to gluteal arteries
  - Geniculate arteries around the knee
- Postnatal angiogenesis – budding from preexisting vessels; angiogenin involved
- Ankle–brachial index (ABI)
  - < 0.9 – start to get claudication (typically occurs at same distance each time)
  - < 0.5 – start to get rest pain (usually calf and foot)
  - < 0.4 – ulcers (usually starts in toes)
  - < 0.3 – gangrene
  - ABIs can be very inaccurate in patients with diabetes secondary to incompressibility of vessels; often have to go off Doppler waveforms in these patients
  - In patients with claudication, the ABI in the extremity drops with walking (ie resting ABI may be 0.9 but can drop to < 0.6 with exercise, resulting in pain)
- Pulse volume recordings (PVRs) – used to find significant occlusion and at what level
- Arteriogram is indicated if PVRs suggest significant disease – can also at times treat the patient with percutaneous intervention; gold standard for vascular imaging
- Surgical indications for PAD – rest pain, ulceration or gangrene, lifestyle limitation, atheromatous embolization
  - PTFE (Gore-Tex) – *only* for bypasses above the knee (have reduced patency below knee); need to use saphenous vein for below the knee bypasses
  - Dacron – good for aorta and large vessels
  - Best predictor of long-term patency – vein quality
  - ASA after lower extremity bypass is the best treatment for patency and reducing cardiovascular events
  - Duplex U/S – best technique for graft surveillance
  - Aortoiliac occlusive disease – most get aorto-bifemoral repair
    - Need to ensure flow to at least 1 internal iliac artery (hypogastric artery; want to see good back-bleeding from at least 1 of the arteries, otherwise need a bypass to an internal iliac artery) when performing aorto-bifemoral repair to prevent vasculogenic impotence and pelvic ischemia
  - Isolated iliac lesions – PTA with stent 1st choice; if that fails, consider femoral-to-femoral crossover

- Femoropopliteal grafts
  - 75% 5-year patency
  - Improved patency rate with surgery for claudication as opposed to limb salvage
  - Popliteal artery exposure below knee – posterior muscle is gastrocnemius and anterior muscle is popliteus
- Femoral-distal grafts (peroneal, anterior tibial, or posterior tibial artery)
  - 50% 5-year patency; patency not influenced by level of distal anastomosis
  - Distal lesions more limb threatening because of lack of collaterals
  - Bypasses to distal vessels are usually used only for limb or tissue salvage (eg non-healing ulcer)
  - Bypassed vessel needs to have run-off below the ankle for this to be successful
- Synthetic grafts have decreased patency below the knee → need to use saphenous vein
- Extra-anatomic grafts can be used to avoid hostile conditions in the abdomen (multiple previous operations in a frail patient)
- Femoral-to-femoral crossover graft – doubles blood flow to donor artery; can get vascular steal in donor leg

- Swelling following lower extremity bypass:
  - Early – reperfusion injury and compartment syndrome (Tx: fasciotomies)
  - Late – DVT (Dx: U/S, Tx: heparin, Coumadin)
- Complications of reperfusion of ischemic tissue – compartment syndrome, lactic acidosis, hyperkalemia, myoglobinuria
- Technical problem – #1 cause of early failure of reversed saphenous vein grafts
- Vein atherosclerosis – #1 cause of late failure of reversed saphenous vein grafts
- Patients with heel ulceration to bone → Tx: amputation
- Dry gangrene – noninfectious; can allow to autoamputate if small or just toes
  - Large lesions should be amputated
  - See if patient has correctable vascular lesion
- Wet gangrene – infectious; remove infected necrotic material; keep moist; non-weight bearing; antibiotics
  - Can be a surgical emergency if extensive infection (eg swollen red toe with pus coming out and red streaks up leg) or systemic complications occur (eg septic) – *may need emergency amputation*
- Diabetic foot ulcer
  - Usually at the metatarsal heads (2nd MTP joint most common) or heel
  - Arises due to neuropathy; fails to heal due to diabetic microvascular disease
  - Can have osteomyelitis
  - Tx: non-weightbearing, debridement of metatarsal head (need to remove cartilage), antibiotics; assess need for revascularization
- Percutaneous transluminal angioplasty (PTA)
  - Excellent for common iliac artery stenosis
  - Best for short stenoses
  - Intima usually ruptured and media stretched, pushes the plaque out
  - Requires passage of wire first
- Compartment syndrome
  - Is caused by reperfusion injury to the extremity (mediated by PMNs; occurs with cessation of blood flow to extremity and reperfusion > 4–6 hours later)

- Reperfusion injury leads to swelling of the muscle compartments → raising compartment pressures, which can lead to ischemia
- Symptoms: pain with passive motion; extremity feels tight and swollen
- Most likely to occur in the anterior compartment of leg (get foot drop)
- Dx: often based on clinical suspicion; compartment pressure > 20–30 mm Hg abnormal
- Tx: fasciotomies (get all 4 compartments if in lower leg) → leave open 5–10 days
- Risk of superficial peroneal nerve injury with lateral incision
- Untreated compartment syndrome can lead to rhabdomyolysis

- Rhabdomyolysis
  - Muscle necrosis can lead to hyperkalemia, myoglobinemia, myoglobinuria, and renal failure
  - Tx: aggressive IVFs and alkalinization of urine; treatment of hyperkalemia
- Popliteal entrapment syndrome
  - Most present with mild intermittent claudication; can be bilateral
  - Men; *loss of pulses with plantar flexion*
  - Have medial deviation of artery around medial head of gastrocnemius muscle
  - Tx: resection of medial head of gastrocnemius muscle; may need arterial reconstruction
- Adventitial cystic disease
  - Men; popliteal fossa most common area
  - Ganglia originate from adjacent joint capsule or tendon sheath
  - Symptoms: intermittent claudication; changes in symptoms with knee flexion/extension
  - Dx: angiogram
  - Tx: resection of cyst; vein graft if the vessel is occluded
- Arterial autografts – radial artery grafts for CABG, IMA for CABG

AMPUTATIONS

- For gangrene, large non-healing ulcers, or unrelenting rest pain not amenable to surgery
- 50% mortality within 3 years for leg amputation
- BKA – 80% heal, 70% walk again, 5% mortality
- AKA – 90% heal, 30% walk again, 10% mortality
- Emergency amputation for systemic complications or extensive infection

ACUTE ARTERIAL EMBOLI

Clinical Distinctions Between Acute Arterial Embolism and Acute Arterial Thrombosis

Embolism	Thrombosis
Arrhythmia	No arrhythmia
No prior claudication or rest pain	History of claudication or rest pain
Normal contralateral pulses	Contralateral pulses absent
No physical findings of chronic limb ischemia	Physical findings of chronic limb ischemia

- Usually do not have collaterals, signs of chronic limb ischemia, or history of claudication with emboli
- Contralateral leg usually has no chronic signs of ischemia and pulses are usually normal
- Symptoms: pain, paresthesia, poikilothermia, paralysis
- Extremity ischemia evolution: pallor (white) → cyanosis (blue) → marbling

- Most common cause – *atrial fibrillation*, recent MI with left ventricular thrombus, myxoma, aorto-iliac disease
- *Common femoral artery* most common site of peripheral obstruction from emboli
- Tx: *embolectomy usual*; need to get pulses back; postop angiogram
  - Consider fasciotomy if ischemia > 4–6 hours
  - Aortoiliac emboli (loss of both femoral pulses) can be treated with bilateral femoral artery cutdowns and bilateral embolectomies
- Atheroma embolism – cholesterol clefts that can lodge in small arteries
  - Renals most common site of atheroma embolization
  - Blue toe syndrome – flaking atherosclerotic emboli off abdominal aorta or branches
    - Patients typically have good distal pulses
    - Aortoiliac disease most common source
  - Dx: chest/abdomen/pelvis CT scan (look for aneurysmal source) and ECHO (clot or myxoma in heart)
  - Tx: may need aneurysm repair or arterial exclusion with bypass

ACUTE ARTERIAL THROMBOSIS

- These patients usually do <u>not</u> have arrhythmias
- Do have a history of claudication and have signs of chronic limb ischemia and poor pulses in the contralateral leg
- Tx: <u>threatened limb</u> (loss of sensation or motor function) → give heparin and go to OR for *thrombectomy*; if <u>limb is not threatened</u> → angiography for *thrombolytics*
- Thrombosis of PTFE graft → thrombolytics and anticoagulation; if limb threatened → OR for thrombectomy

RENAL VASCULAR DISEASE

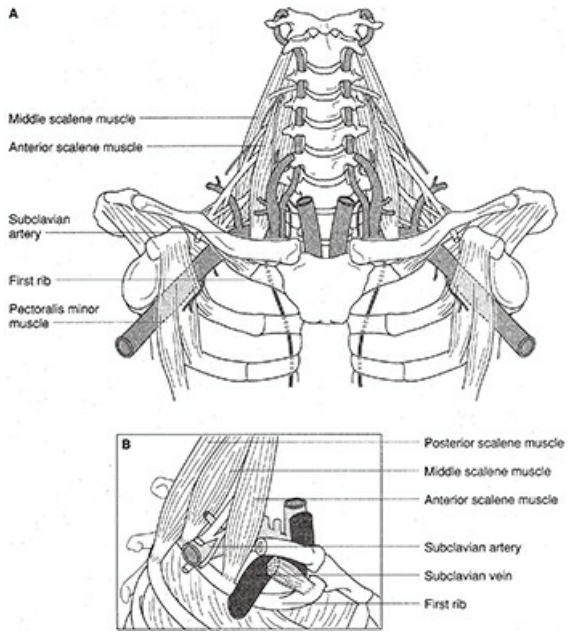
- Right renal artery runs posterior to IVC
- Accessory renal arteries in 25%
- Renovascular HTN (renal artery stenosis) – bruits, diastolic blood pressure > 115, HTN, in children or premenopausal women, HTN resistant to drug therapy
  - Renal atherosclerosis – left side, proximal ⅓, men
  - Fibromuscular dysplasia – right side, distal ⅓, women
  - Dx: CT angiogram
  - Tx: PTA *<u>without</u>* stent if due to FMD (percutaneous transluminal angioplasty); place stent if due to atherosclerotic disease
- Indications for nephrectomy with renal HTN → atrophic kidney < 6 cm with persistently high renin levels

UPPER EXTREMITY

- Occlusive disease – proximal lesions usually asymptomatic secondary to ↑ collaterals
  - Subclavian artery most common site of upper extremity stenosis
  - Tx: PTA with stent; common carotid to subclavian artery bypass if that fails
- Subclavian steal syndrome – proximal subclavian artery stenosis resulting in reversal of flow through ipsilateral vertebral artery into the subclavian artery
  - Dx – duplex U/S shows reversal of flow in the vertebral artery

- Operate for limb (claudication) or neurologic symptoms (usually vertebrobasilar – visual or equilibrium problems)
- Tx: PTA with stent to subclavian artery; common carotid to subclavian artery bypass if that fails

- Thoracic outlet syndrome (TOS)
  - Normal anatomy
    - Subclavian vein – passes over the 1st rib anterior to the anterior scalene muscle, then behind clavicle
    - Brachial plexus and subclavian artery – pass over the 1st rib posterior to the anterior scalene muscle and anterior to the middle scalene muscle
  - General symptoms: back, neck, and/or arm pain/weakness/tingling (often worse with palpation/manipulation)
  - Dx: cervical spine and chest MRI, duplex U/S (vascular etiology), electromyelogram (EMG; neurologic etiology)
  - Neurologic involvement – much more common than vascular
  - #1 anatomic abnormality – cervical rib
  - #1 cause of pain – brachial plexus irritation
  - Brachial plexus irritation
    - Usually have normal neurologic exam; tapping can reproduce symptoms (Tinsel's test)
    - Ulnar nerve distribution (C8–T1) most common (inferior portion of brachial plexus) → weakness of intrinsic muscles of hand, weak wrist flexion
    - Tx: cervical rib and 1st rib resection, divide anterior scalene muscle



The normal anatomy of the thoracic outlet in anteroposterior (*A*) and oblique (*B*) views. The brachial plexus and subclavian artery traverse the narrow triangle formed by the anterior and middle scalene muscles and the first rib. The subclavian vein lies anteriorly.

- Subclavian vein
  - Usually presents as effort-induced thrombosis of subclavian vein (Paget–von Schrötter disease; baseball pitchers) – acutely painful, swollen, blue limb
  - Venous thrombosis – much more common than arterial

- Dx: venography is the gold standard for diagnosis, but duplex U/S makes the diagnosis and is quicker to get
- 80% have associated thoracic outlet problem
- Tx: thrombolytics initially; repair at that admission (cervical rib and 1st rib resection, divide anterior scalene muscle)

- Subclavian artery
  - Compression usually secondary to anterior scalene hypertrophy (weight lifters); least common cause of TOS
  - Symptoms – hand pain from ischemia; thrombosis – cold, white hand
  - Absent radial pulse with head turned to ipsilateral side (Adson's test)
  - Dx: duplex U/S or angiogram (gold standard)
  - Tx: surgery → cervical rib and 1st rib resection, divide anterior scalene muscle; possible bypass graft if artery is too damaged or aneurysmal
- Motor function can remain in digits after prolonged hand ischemia because motor groups are in the proximal forearm

MESENTERIC ISCHEMIA

- Overall mortality 60%; usually involves the superior mesenteric artery (SMA)
- Findings on abdominal CT that suggest intestinal ischemia – vascular occlusion, bowel wall thickening, intramural gas, portal venous gas
- Most common causes of visceral ischemia:
  - Embolic occlusion – 50% (MC from heart)
  - Thrombotic occlusion – 25% (MC from atherosclerotic disease)
  - Nonocclusive mesenteric ischemia (NOMI) – 15% (MC from low cardiac output state)
  - Venous thrombosis – 5% (MC from hypercoagulable state)
- SMA embolism
  - Most commonly occurs near origin of SMA – heart #1 source (atrial fibrillation)
  - Pain out of proportion to exam; pain usually of sudden onset; hematochezia and peritoneal signs are late findings (followed by sepsis and acidosis)
  - May have a history of atrial fibrillation, endocarditis, recent MI, recent angiography
  - Dx: angiogram or abdominal CT with IV contrast
  - Tx: embolectomy, resect infarcted bowel if present
  - SMA exposure – divide ligament of Treitz, SMA is to the right of this near the base of the transverse colon mesentery
- SMA thrombosis
  - Often history of chronic problems (food fear, weight loss)
  - Symptoms: similar to embolism; may have developed some collaterals
  - Dx: angiogram or abdominal CT with IV contrast
  - Tx: thrombectomy (open thrombectomy or catheter directed thrombolytics); may need PTA with stent or open bypass after the vessel is opened for any residual stenosis; resection of infarcted bowel
- Mesenteric vein thrombosis
  - Usually short segments of intestine involved; bloody diarrhea, crampy abdominal pain
  - May have a history of vasculitis, hypercoagulable state, portal HTN
  - Dx: abdominal CT scan or angiogram with venous phase
  - Tx: heparin usual; resection of infarcted bowel if present

- Nonocclusive mesenteric ischemia (NOMI)
  - Spasm, low-flow states, hypovolemia, hemoconcentration, pressors → final common pathway is low cardiac output to visceral vessels
  - Risk factors: prolonged shock, CHF, prolonged cardiopulmonary bypass
  - Symptoms: bloody diarrhea, pain
  - Watershed areas (Griffith's – splenic flexure and Sudak's – upper rectum) most vulnerable
  - Tx: volume resuscitation; catheter-directed nitroglycerin can ↑ visceral blood flow; also need to ↑ cardiac output (dobutamine); resection of infarcted bowel if present
- Median arcuate ligament syndrome
  - Causes celiac artery compression
  - Bruit near epigastrium, chronic pain, weight loss, diarrhea
  - Tx: transect median arcuate ligament; may need arterial reconstruction
- Chronic mesenteric angina
  - Weight loss secondary to food fear (visceral angina 30 minutes after meals)
  - Get lateral visceral vessel aortography to see origins of celiac and SMA
  - Tx: PTA and stent; bypass if that fails
- Arc of Riolan is an important collateral between the SMA and IMA

VISCERAL AND PERIPHERAL ANEURYSMS

- Rupture – most common complication of aneurysms above inguinal ligament
- Emboli (MC) and thrombosis – most common complications of aneurysms below inguinal ligament
- Visceral artery aneurysms
  - Risk factors: medial fibrodysplasia, portal HTN, arterial disruption secondary to inflammatory disease (eg pancreatitis)
  - Repair all splanchnic artery aneurysms (> 2 cm) when diagnosed (50% risk for rupture) *except* splenic
    - Splenic artery aneurysm – most common visceral aneurysm (more common in women; 2% risk of rupture)
      - Repair splenic artery aneurysms if symptomatic, if patient is pregnant, if occurs in women of childbearing age, or is > 3–4 cm
      - High rate of pregnancy-related rupture – usually in 3rd trimester
  - Tx: covered stent (best); exclusion with bypass if that fails
  - Splenic artery aneurysms can just be ligated if open procedure is required (have good collaterals)
- Renal (> 1.5 cm) artery aneurysm – Tx: covered stent
- Iliac (> 3.0 cm) or femoral (> 2.5 cm) artery aneurysms – Tx: covered stent
- Popliteal artery aneurysm
  - Most common peripheral aneurysm
  - MCC – atherosclerosis
  - Rarely rupture
  - Leg exam reveals prominent popliteal pulses
  - ½ are bilateral
  - ½ have another aneurysm elsewhere (AAA, femoral, etc.)
  - Most likely to get emboli (MC) or thrombosis with limb ischemia
  - Can also get leg pain from compression of adjacent structures

- Dx: ultrasound
- Surgical indications: symptomatic, > 2 cm, or mycotic
- Tx: exclusion and bypass of all popliteal aneurysms; 25% have complication that requires amputation if not treated; *covered stent not recommended for these*

- Pseudoaneurysm
  - Collection of blood in continuity with the arterial system but not enclosed by all 3 layers of the arterial wall; most common location is the femoral artery
  - Can result from percutaneous interventions or from disruption of a suture line between graft and artery
  - If it occurs after percutaneous intervention → Tx: ultrasound-guided compression with thrombin injection (surgical repair if flow remains in the pseudoaneurysm after thrombin injection)
  - If it occurs at a suture line early after surgery → *need surgical repair*
  - Pseudoaneurysms that occur at suture lines late after surgery (months to years) → *suggests graft infection*

OTHER VASCULAR DISEASES

- Fibromuscular dysplasia
  - Young women; HTN if renals involved, headaches or stroke if carotids involved
  - Renal artery (renal artery stenosis) most commonly involved vessel, followed by carotid and iliac
  - String of beads appearance (stenotic regions followed by dilated areas)
  - Medial fibrodysplasia most common variant (85%)
  - Tx: PTA (*best*); bypass if that fails
- Buerger's disease
  - Young men, smokers
  - Severe rest pain with bilateral ulceration; gangrene of digits, especially fingers
  - Corkscrew collaterals on angiogram and severe distal disease; normal arterial tree proximal to popliteal and brachial vessels (is a small vessel disease)
  - Tx: stop smoking or will require continued amputations
- Cystic medial necrosis syndromes
  - Marfan's disease
    - Fibrillin defect (connective tissue elastic fibers); marfanoid habitus, retinal detachment, aortic root dilatation
- Immune arteritis
  - Temporal arteritis (large artery)
    - Women, age > 55, headache, fever, blurred vision (risk of blindness)
    - Temporal artery biopsy → giant cell arteritis, granulomas
    - Inflammation of large vessels (aorta and branches)
    - Long segments of smooth stenosis alternating with segments of larger diameter
    - Tx: steroids, bypass of large vessels if needed; no endarterectomy
- Radiation arteritis
  - Early – sloughing and thrombosis (obliterative endarteritis)
  - Late (1–10 years) – fibrosis, scar, stenosis
  - Late late (3–30 years) – advanced atherosclerosis
- Raynaud's disease – young women; *pallor* → *cyanosis* → *rubor*

- Tx: calcium channel blockers, warmth

VENOUS DISEASE

- Greater saphenous vein – joins femoral vein near groin; runs medially
- No clamps on IVC → will tear
- Left renal vein can be ligated near the IVC in emergencies because of collaterals (left gonadal vein, left adrenal vein); right renal vein does not have these collaterals
- Dialysis access grafts
  - Most common failure of A-V grafts for dialysis – venous obstruction secondary to *intimal hyperplasia*
  - Cimino – radial artery to cephalic vein; wait 6 weeks to use → allows vein to mature
  - Interposition graft (eg brachiocephalic loop graft) – wait 6 weeks to allow fibrous scar to form
- Acquired A-V fistula – usually secondary to trauma; can get peripheral arterial insufficiency, CHF, aneurysm, limb-length discrepancy
  - Dx: U/S
  - Most need repair → lateral venous suture; arterial side may need patch or bypass graft; try to place interposing tissue so it does not recur
- Varicose veins
  - Smoking, obesity, low activity
  - Tx: sclerotherapy
- Venous ulcers
  - Secondary to venous valve incompetence (90%)
  - Ulceration occurs above and posterior to medial malleoli
  - Ulcers < 3 cm often heal without surgery
  - Brawny edema – hemosiderin deposition
  - Tx: Unna boot (zinc oxide and calamine) compression wraps cure 90%
  - May need to ligate perforators or have vein stripping of greater saphenous vein (see below)
  - DVT is a contraindication to vein stripping
- Venous insufficiency
  - Aching, swelling, night cramps, brawny edema, venous ulcers
  - Edema – secondary to incompetent perforators and/or valves
  - Elevation brings relief
  - Dx: U/S
  - Tx: leg wraps, ambulation with avoidance of long standing, D/C smoking, weight loss
    - Greater saphenous vein stripping (for saphenofemoral valve incompetence) or removal of perforators (if just perforator valves are incompetent; stab avulsion technique) for severe symptoms or recurrent ulceration despite medical Tx
- Superficial thrombophlebitis – nonbacterial inflammation
  - Tx: NSAIDs, warm packs, ambulation, arm elevation, +/– antibiotics
- Suppurative thrombophlebitis – pus fills vein; fever, ↑ WBCs, erythema, fluctuance; usually associated with infection following a peripheral IV; *staph aureus* most common
  - Tx: resect entire vein for continued purulence or sepsis despite antibiotics
- Migrating thrombophlebitis – pancreatic CA
- Normal venous Doppler ultrasound – augmentation of flow with distal compression or release of proximal compression

- Sequential compression devices (SCDs) – help prevent blood clots by ↓ venous stasis and ↑ tPA release
- Deep venous thrombosis (DVT)
  - Most common in calf
  - Pain, tenderness, calf swelling
  - Left leg 2× more involved than right (longer left iliac vein compressed by right iliac artery)
  - Risk factors: Virchow's triad → venous stasis, hypercoagulability, venous wall injury
  - Calf DVT – minimal swelling
  - Femoral DVT – ankle and calf swelling
  - Iliofemoral DVT – leg swelling
  - DVT Tx: heparin, Coumadin
  - Phlegmasia alba dolens (painful, swollen white leg) – less severe than below
  - Phlegmasia cerulea dolens (painful, swollen blue leg) – more severe; can lead to gangrene; usually occurs with acute iliofemoral DVT
    - Tx: catheter-directed thrombolytics
    - Emergent thrombectomy if extremity threatened (ie loss of sensation or motor function)
    - 50% of these patients have a malignancy somewhere
- Venous thrombosis with central line – pull out central line if not needed, then heparin; can try to treat with systemic heparin or TPA down line if the access site is important
- Contraindications to vein stripping – DVT, venous outflow obstruction, pregnancy

LYMPHATICS

- Do not contain a basement membrane
- Not found in bone, muscle, tendon, cartilage, brain, or cornea
- Deep lymphatics have valves
- Lymphedema
  - Occurs when lymphatics are obstructed, too few in number, or nonfunctional
  - Is usually secondary lymphedema (MCC – previous ALND for breast CA)
  - Leads to woody edema secondary to fibrosis in subcutaneous tissue – toes, feet, ankle, leg
  - Cellulitis and lymphangitis secondary to minor trauma are big problems
  - Strep most common infection
  - Congenital lymphedema L > R
  - Tx: leg elevation, compression, antibiotics for infection
- Lymphangiosarcoma
  - Raised blue/red coloring; early metastases to lung
  - Stewart–Treves syndrome – lymphangiosarcoma associated with breast axillary dissection and chronic lymphedema
- Lymphocele following surgery
  - Usually after dissection in the groin (eg after femoral to popliteal bypass)
  - Leakage of clear fluid
  - Tx: percutaneous drainage (can try a couple of times); resection if that fails
  - Can inject isosulfan blue dye into foot to identify the lymphatic channels supplying the lymphocele if having trouble locating

28 Gastrointestinal Hormones

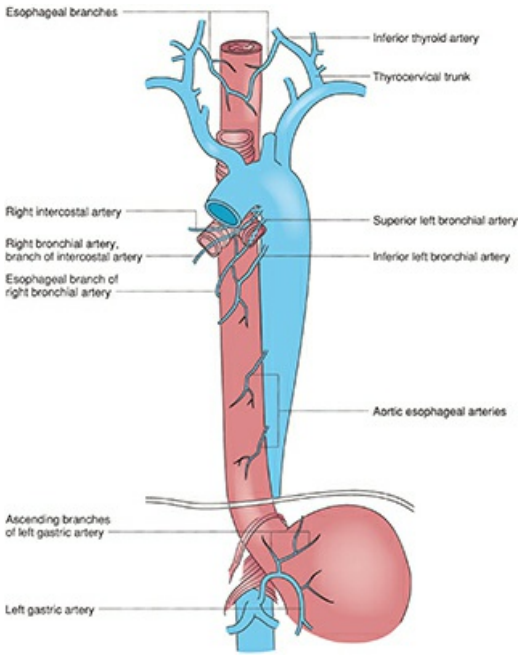
- Gastrin – produced by G cells in stomach antrum
  - Secretion stimulated by amino acids, vagal input (acetylcholine), calcium, ETOH, antral distention, pH > 3.0
  - Secretion inhibited by pH < 3.0, somatostatin, secretin, CCK
  - Target cells – parietal cells and chief cells
  - Response – ↑ HCl, intrinsic factor, and pepsinogen secretion (gastrin is the strongest stimulator for all)
  - Omeprazole blocks H/K ATPase of parietal cell (final pathway for H^+ release)
- Somatostatin – mainly produced by D (somatostatin) cells in stomach antrum
  - Secretion stimulated by acid in duodenum
  - Target cells – many; is the great inhibitor
  - Response – inhibits gastrin and HCl release (primary role); inhibits release of insulin, glucagon, secretin, CCK, and motilin; ↓ pancreatic and biliary output; slows gastric emptying
  - Octreotide (somatostatin analogue) – can be used to ↓ pancreatic fistula output
- CCK – produced by I cells of duodenum
  - Secretion stimulated by amino acids and fatty acid chains
  - Response – gallbladder contraction, relaxation of sphincter of Oddi, ↑ pancreatic enzyme secretion (acinar cells)
- Secretin – produced by S cells of duodenum
  - Secretion stimulated by fat, bile, pH < 4.0
  - Secretion inhibited by pH > 4.0, gastrin
  - Response – ↑ pancreatic HCO_3^- release (ductal cells), inhibits gastrin release (this is reversed in patients with gastrinoma), and inhibits HCl release
    - <u>High</u> pancreatic duct output – ↑ HCO_3^-, ↓ Cl^-
    - <u>Slow</u> pancreatic duct output – ↑ Cl^-, ↓ HCO_3^- (carbonic anhydrase in duct exchanges HCO_3^- for Cl^-)
- Vasoactive intestinal peptide – produced by cells in pancreas and gut
  - Secretion stimulated by fat, acetylcholine
  - Response – ↑ intestinal secretion (water and electrolytes) and motility
- Glucagon – mainly released by alpha cells of pancreas (starvation state)
  - Secretion stimulated by ↓ glucose, ↑ amino acids, acetylcholine
  - Secretion inhibited by ↑ glucose, ↑ insulin, somatostatin
  - Response – glycogenolysis, gluconeogenesis, ↓ gastric acid secretion, ↓ gastrointestinal motility, relaxes sphincter of Oddi, ↓ pancreatic secretion
- Insulin – released by beta cells of the pancreas (fed state)
  - Secretion stimulated by glucose, glucagons, CCK
  - Secretion inhibited by somatostatin
  - Response – cellular glucose uptake; promotes protein synthesis

- Pancreatic polypeptide – secreted by islet cells in pancreas
  - Secretion stimulated by food, vagal stimulation, other GI hormones
  - Response – ↓ pancreatic and gallbladder secretion
- Motilin – released by intestinal cells of gut
  - Primarily released from the duodenum
  - Primary target is the stomach antrum
  - Secretion stimulated by duodenal acid, food, vagus input
  - Secretion inhibited by gastrointestinal motility, relaxes sphincter of Oddi somatostatin, secretin, pancreatic polypeptide, duodenal fat
  - Response – ↑ intestinal motility (small bowel; phase III peristalsis) → erythromycin acts on this receptor
- Bombesin (gastrin-releasing peptide) – ↑ intestinal motor activity, ↑ pancreatic enzyme secretion, ↑ gastric acid secretion
- Peptide YY – released from terminal ileum following a fatty meal → inhibits acid secretion and stomach contraction; inhibits gallbladder contraction and pancreatic secretion
- Anorexia – mediated by hypothalamus
- Causes of B_{12} deficiency – gastric bypass (needs acidic environment to bind intrinsic factor), terminal ileum resection (is absorbed there)
- Bowel recovery
  - Small bowel 24 hours
  - Stomach 48 hours
  - Large bowel 3–5 days
- Peristalsis phases
  - I – resting
  - II – accelerating
  - III – peristalsis
  - IV – decelerating

29 Esophagus

ANATOMY AND PHYSIOLOGY

- Mucosa (squamous epithelium), submucosa, and muscularis propria (longitudinal muscle layer); *no serosa*
- Upper ⅓ esophagus – striated muscle
- Middle ⅓ and lower ⅓ esophagus – smooth muscle
- Thoracic esophagus – vessels directly off the aorta are the major blood supply

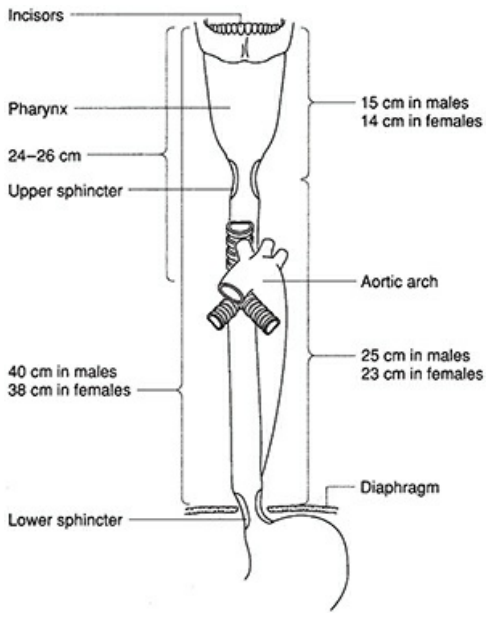


Arterial blood supply of the esophagus.

- Cervical esophagus – supplied by inferior thyroid artery
- Abdominal esophagus – supplied by left gastric and inferior phrenic arteries
- Venous drainage – hemi-azygous and azygous veins in chest
- Lymphatics – upper ⅔ drains cephalad, lower ⅓ caudad
- Right vagus nerve – travels on posterior portion of stomach as it exits chest; becomes celiac plexus; also has the criminal nerve of Grassi → can cause persistently high acid levels postoperatively if left undivided after vagotomy
- Left vagus nerve – travels on anterior portion of stomach; goes to liver and biliary tree
- Thoracic duct – travels from right to left at T4–5 as it ascends mediastinum; inserts into left subclavian vein
- Upper esophageal sphincter (UES; 15 cm from incisors) – is the cricopharyngeus muscle (circular muscle, prevents air swallowing); recurrent laryngeal nerve innervation
  - Normal UES pressure at rest: 60 mm Hg
  - Normal UES pressure with food bolus: 15 mm Hg

- Cricopharyngeus muscle – most common site of esophageal perforation (usually occurs with EGD); also most common site for esophageal foreign body
- Aspiration with brainstem stroke – failure of cricopharyngeus to relax

- Lower esophageal sphincter (40 cm from incisors) – relaxation mediated by inhibitory neurons; normally contracted at resting state (prevents reflux); is an anatomic zone of high pressure, not an anatomic sphincter (not visible on EGD)
  - Normal LES pressure at rest: 15 mm Hg
  - Normal LES pressure with food bolus: 0 mm Hg
- Anatomic areas of esophageal narrowing
  - Cricopharyngeus muscle
  - Compression by the left mainstem bronchus and aortic arch
  - Diaphragm
- Swallowing stages – CNS initiates swallow
  - Primary peristalsis – occurs with food bolus and swallow initiation
  - Secondary peristalsis – occurs with incomplete emptying and esophageal distention; propagating waves
  - Tertiary peristalsis – non-propagating, non-peristalsing (dysfunctional)
  - UES and LES are normally contracted between meals
- Swallowing mechanism – soft palate occludes nasopharynx, larynx rises and airway opening is blocked by epiglottis, cricopharyngeus relaxes, pharyngeal contraction moves food into esophagus; LES relaxes soon after initiation of swallow (vagus mediated)



Important clinical endoscopic measurements of the esophagus in adults.

- Surgical approach
  - Cervical esophagus – left
  - Upper ⅔ thoracic – right (avoids the aorta)
  - Lower ⅓ thoracic – left (left-sided course in this region)
- Hiccoughs
  - Causes – gastric distention, temperature changes, ETOH, tobacco
  - Reflex arc – vagus, phrenic, sympathetic chain T6–12

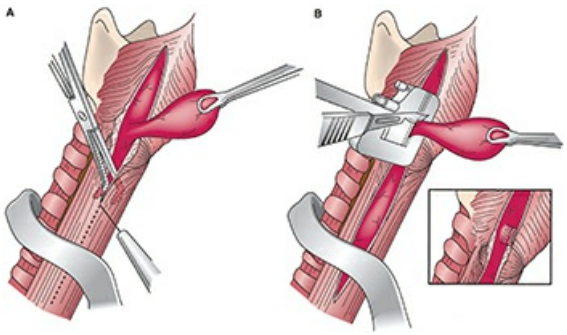
- Esophageal dysfunction
  - Primary – achalasia, diffuse esophageal spasm, nutcracker esophagus
  - Secondary – GERD (most common), scleroderma
- Endoscopy – best initial test for heartburn (can visualize esophagitis)
- Barium swallow – best initial test for dysphagia or odynophagia (better at picking up masses)
- Meat impaction – Dx and Tx: endoscopy
- Foreign body – Dx and Tx: endoscopy
- Perforation – Dx: Gastrografin swallow

PHARYNGOESOPHAGEAL DISORDERS

- Trouble in transferring food from mouth to esophagus
- Most commonly neuromuscular disease – myasthenia gravis, muscular dystrophy, stroke
- Liquids worse than solids
- Plummer–Vinson syndrome – can have upper esophageal web; Fe-deficient anemia. Tx: dilation, Fe; need to screen for oral CA

DIVERTICULA

- Zenker's diverticulum – caused by ↑ pressure during swallowing
  - Is a false diverticulum located posteriorly
  - Occurs between the pharyngeal constrictors and cricopharyngeus
  - Caused by failure of the cricopharyngeus to relax
  - Symptoms: upper esophageal dysphagia, choking, halitosis; regurgitation of non-digested food
  - Dx: barium swallow studies, manometry; risk for perforation with EGD and Zenker's
  - Tx: *cricopharyngeal myotomy* (key point); Zenker's itself can either be resected or suspended (removal of diverticula is not necessary)
    - Left cervical incision; leave drains in; esophagogram POD #1



Cricopharyngomyotomy and concomitant resection of a pharyngoesophageal diverticulum. *(A)* A cricopharyngomyotomy is performed. *(B)* After completion of the cricopharyngomyotomy, the base of the pouch is crossed with a TA-30 stapler and amputated.

- Traction diverticulum
  - Is a true diverticulum – usually lies lateral
  - Due to inflammation, granulomatous disease, tumor
  - Usually found in the mid-esophagus

- Symptoms: regurgitation of undigested food, dysphagia
- Tx: excision and primary closure if symptomatic, may need palliative therapy (ie XRT) if due to invasive CA; if asymptomatic, leave alone

- Epiphrenic diverticulum
  - Rare; associated with esophageal motility disorders (eg achalasia)
  - Most common in the distal 10 cm of the esophagus
  - Most are asymptomatic; can have dysphagia and regurgitation
  - Dx: esophagram and esophageal manometry
  - Tx: diverticulectomy and esophageal myotomy on the side opposite the diverticulectomy if symptomatic

ACHALASIA

- Dysphagia (worse for liquids), regurgitation, weight loss, respiratory symptoms
- Caused by lack of peristalsis and failure of LES to relax after food bolus
- Secondary to autoimmune destruction of neuronal ganglion cells in muscle wall
- Manometry – ↑ LES pressure, incomplete LES relaxation, no peristalsis
- Can get tortuous dilated esophagus and epiphrenic diverticula; bird's beak appearance
- Need EGD to rule out esophageal CA
- Tx: balloon dilatation of LES → effective in 80%; nitrates, calcium channel blocker
  - If medical Tx and dilation fail → Heller myotomy (left thoracotomy, myotomy of lower esophagus only; also need partial Nissen fundoplication)
- Can get esophageal CA late (squamous cell most common)
- *T. cruzi* can produce similar symptoms

DIFFUSE ESOPHAGEAL SPASM

- Dysphagia; may have psychiatric history
- Manometry – frequent strong non-peristaltic unorganized contractions, LES relaxes normally
- Tx: calcium channel blocker, trazodone; Heller myotomy if those fail (myotomy of upper and lower esophagus; right thoracotomy)
- Surgery usually less effective for diffuse esophageal spasm than for achalasia

NUTCRACKER ESOPHAGUS

- Chest pain (can be severe) +/– dysphagia
- Manometry – high-amplitude peristaltic contractions (> 180 mm Hg); LES relaxes normally
- Tx: calcium channel blocker, trazodone; Heller myotomy if those fail (myotomy of upper and lower esophagus; right thoracotomy)
- Surgery usually less effective for nutcracker than for achalasia

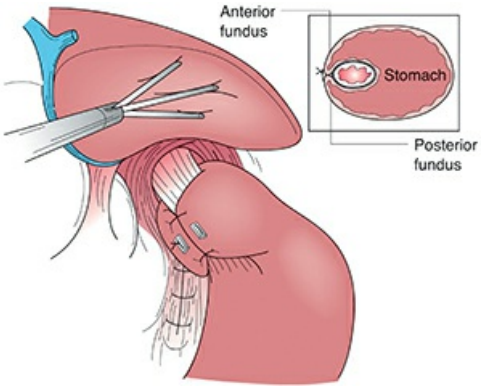
SCLERODERMA

- Heartburn, massive reflux, dysphagia
- Esophagus is the most common organ involved in scleroderma
- Fibrous replacement of esophageal smooth muscle

- Causes dysphagia and loss of LES tone with massive reflux and strictures
- Manometry – low LES pressure and aperistalsis
- Tx: PPI and Reglan; esophagectomy usual if severe

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

- Normal anatomic protection from GERD – need LES competence (most common defect in GERD), normal esophageal body, normal gastric reservoir
- GERD caused by ↑ acid exposure to esophagus from loss of gastroesophageal barrier
- Sx: heartburn (burning retrosternal chest pain) 30–60 minutes after meals; worse lying down, with tight clothing, or bending over
- Can also have asthma symptoms (cough), choking, aspiration
- Make sure patient does not have another cause for pain (check for unusual symptoms):
  - Dysphagia/odynophagia – need to worry about esophageal tumors (Dx: barium swallow)
  - Bloating – suggests aerophagia and delayed gastric emptying (Dx: gastric emptying study)
  - Epigastric pain – suggests peptic ulcer, gastric tumor (Dx: upper endoscopy)
- Most treated empirically with PPI (omeprazole, 99% effective)
- If long-standing, consider upper endoscopy to check for Barrett's esophagus
- Failure of PPI despite escalating doses (give it 3–4 weeks) → need diagnostic studies
- Dx: pH probe *(best test),* endoscopy, histology, manometry (resting LES < 6 mm Hg)
- Surgical indications: failure of medical Tx, avoidance lifetime meds, young patients, refractory complications (eg bleeding, esophagitis, stricture, ulcer)
- Tx: Nissen fundoplication → divide short gastrics, pull esophagus into abdomen, approximate crura, 270- (partial) or 360-degree gastric fundus wrap
  - Phrenoesophageal membrane is an extension of the transversalis fascia
  - Key maneuver for dissection is finding the right crura
  - Key maneuver for wrap is identification of the left crura
  - Complications – injury to spleen, diaphragm, esophagus, or pneumothorax
  - Belsey – approach is through the chest
  - Collis gastroplasty – when not enough esophagus exists to pull down into abdomen, can staple along stomach cardia and create a "new" esophagus (neo-esophagus)
  - Most common cause of dysphagia following Nissen – *wrap is too tight* (generally resolves on its own; give clears for 1st week; can dilate after 1 week)

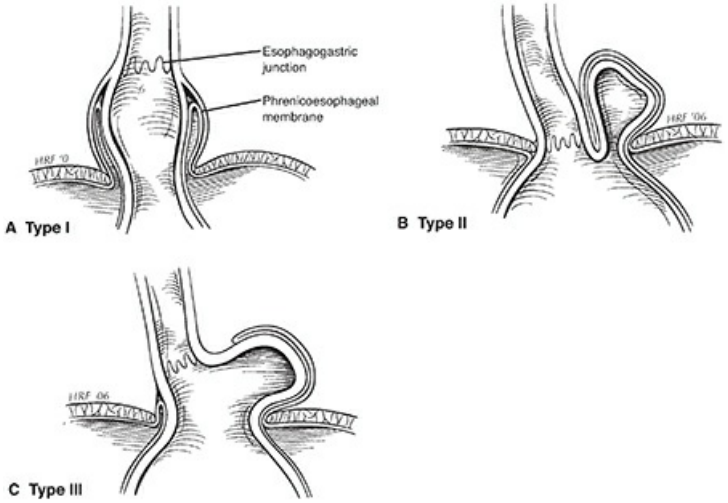


Fixation of the fundoplication. The fundoplication is sutured in place with a single U-stitch of 2-0 Prolene pledgeted on the outside. A 60-French mercury-weighted bougie is passed through the gastroesophageal junction prior to fixation of the wrap to assure a floppy fundoplication.

Inset illustrates the proper orientation of the fundic wrap.

HIATAL HERNIA

- Type I – sliding hernia from dilation of hiatus (most common); often associated with GERD; GE junction rises above the diaphragm
- Type II – paraesophageal; hole in the diaphragm alongside the esophagus, normal GE junction. Symptoms: chest pain, dysphagia, early satiety
- Type III – combined
- Type IV – entire stomach in the chest plus another organ (ie colon, spleen)
- With type II, still need Nissen as diaphragm repair can affect LES; also helps anchor stomach
- Paraesophageal hernia (type II–IV) – chest pain, retching without vomiting, can't pass NG tube; usually need repair → at risk for incarceration; may want to avoid repair in the elderly and frail if minimal symptoms



Classification of hiatal hernia. *(A)* Type 1, sliding. *(B)* Type II, pure paraesophageal. *(C)* Type III, mixed hernia. (From Critchlow J. Paraesophageal herniation. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

SCHATZKI'S RING

- Almost all patients have an associated sliding hiatal hernia
- Symptoms: dysphagia
- Found at the squamocolumnar junction
- Dx: barium esophagogram *(best)*
- Tx: dilatation of the ring and PPI usually sufficient;*do not resect*

BARRETT'S ESOPHAGUS

- Squamous metaplasia to columnar epithelium (raised, pink lesion)
- Occurs with long-standing exposure to gastric reflux (is acquired)
- Intestinal type columnar metaplasia is the only type predisposed to esophageal CA
  - Pathology shows goblet cells
  - CA risk is increased 50 times compared to general population (adenocarcinoma; relative

risk [RR] 50)

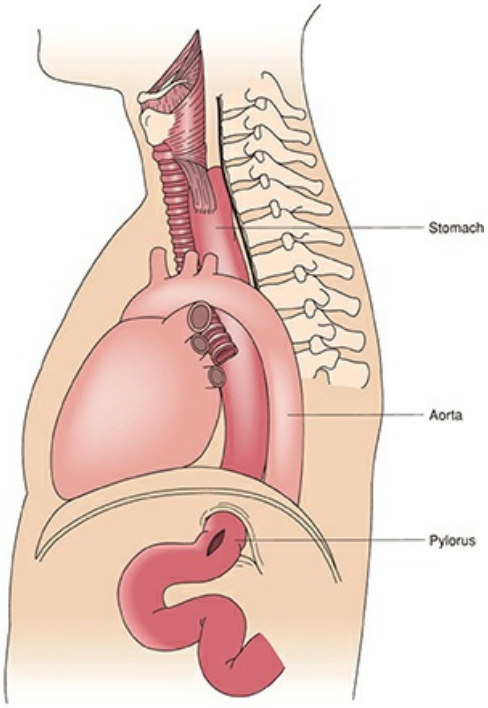
- High grade dysplasia (HGD) Barrett's esophagus (considered carcinoma in situ)
  - Needs to be confirmed by 2 experienced pathologists
  - Options:
    1. Esophagectomy *or*
    2. Endoscopic surveillance (3-month intervals; 4 quadrant Bx's at 1-cm intervals for entire length of HGD and Bx of any suspicious areas)
  - Some patients with HGD never develop CA (basis for option 2)
  - Cell types other than Barrett's (eg squamous cell CIS) – follow above as well
- Uncomplicated Barrett's (eg non-HGD) can be treated like GERD (ie PPI or Nissen) – Tx will decrease esophagitis and further metaplasia
  - Need annual follow-up EGD surveillance for lifetime, even after Nissen
  - *Barrett's CA risk is not reversed with PPI or fundoplication*

ESOPHAGEAL CANCER

- Esophageal tumors are almost always malignant; early invasion of nodes
- Spreads quickly along submucosal lymphatic channels
- Symptoms: dysphagia (especially solids), weight loss
- Risk factors: ETOH, tobacco, achalasia, caustic injury, nitrosamines
- Dx: esophagram (best test for dysphagia)
- Unresectability – hoarseness (RLN invasion), Horner's syndrome (brachial plexus invasion), phrenic nerve invasion, malignant pleural effusion, malignant fistula, invasion of another structure (eg airway invasion, vertebra, lung)
  - Chest and abdominal CT is the best single test for resectability
- Adenocarcinoma is the #1 esophageal cancer – not squamous
  - Adenocarcinoma – usually in lower ⅓ of esophagus; liver metastases most common; often have history of GERD
  - Squamous cell carcinoma – usually in upper ⅔ of esophagus; lung metastases most common; often have history of ETOH and smoking
- Nodal disease outside the area of resection (ie supraclavicular or celiac nodes – M1 disease) – contraindication to esophagectomy
- Most important prognostic factor in patient devoid of systemic metastases – nodal spread
- Pre-op chemo-XRT can downstage tumors and make them resectable (cisplatin and 5FU)
  - Indicated for T2 or greater tumors
- Esophagectomy – 5% mortality from surgery; curative in 20%
  - Need 6–8 cm margins
  - Right gastroepiploic artery – primary blood supply to stomach after replacing esophagus (have to divide left gastric and short gastrics)
  - Transhiatal approach – abdominal and neck incisions; bluntly dissect intrathoracic esophagus; may have → mortality from esophageal leaks with cervical anastomosis
  - Ivor Lewis – abdominal incision and right thoracotomy → exposes all of the intrathoracic esophagus; intrathoracic anastomosis
  - 3-Hole esophagectomy – abdominal, thoracic, and cervical incisions
  - Need pyloromyotomy with these procedures
  - Colonic interposition – may be choice in young patients when you want to preserve gastric function; 3 anastomoses required; blood supply depends on colon marginal vessels

- After esophagectomy → need contrast study on postop day 7 to rule out leak
- Postoperative strictures – most can be dilated
- Chylothorax – white to clear fluid; high in lymphocytes and TAGs
  - Tx: drainage, NPO, TPN, short-chain fatty acids; conservative Tx for 1–3 weeks
  - Thoracic duct ligation (right side, low in the mediastinum) if > 2 L/day or is refractory to medical Tx

- Post-op chemo – cisplatin and 5FU (indicated for node-positive disease)
- XRT – may help downstage tumors
- Malignant fistulas – most die within 3 months due to aspiration; Tx – esophageal stent for palliation



Final position of the mobilized stomach in the posterior mediastinum after transhiatal esophagectomy and cervical esophagogastric anastomosis. The gastric fundus has been suspended from the cervical prevertebral fascia, and an end-to-side cervical esophagogastrostomy has been performed. The pylorus is now located several centimeters below the level of the diaphragmatic hiatus.

LEIOMYOMA

- Most common benign esophageal tumor; located in muscularis propria
- Symptoms: dysphagia; usually in lower ⅔ of esophagus (smooth muscle cells)
- Dx: esophagram (tumor has smooth contour), endoscopic U/S (EUS), CT scan (need to rule out CA)
- Do not biopsy → can form scar and make subsequent resection difficult
- Tx: > 5 cm or symptomatic → excision (extra-mucosal enucleation; leave mucosa intact) via thoracotomy
- Leiomyosarcoma Tx: esophagectomy

ESOPHAGEAL POLYPS

- Symptoms: dysphagia, hematemesis
- 2nd most common benign tumor of the esophagus; usually in the cervical esophagus
- Small lesions can be resected with endoscopy; larger lesions require cervical incision

CAUSTIC ESOPHAGEAL INJURY

- No NG tube. Do not induce vomiting. Nothing to drink
- Alkali – causes deep liquefaction necrosis, especially liquid (eg Drano)
  - Worse injury than acid; also more likely to cause cancer
- Acid – causes coagulation necrosis; mostly causes gastric injury
- Chest and abdominal CT scan to look for free air and signs of perforation
- Endoscopy to assess lesion (best test)
  - Do not use with suspected perforation and do not go past a site of severe injury
- Serial exams and plain films required
- Degree of injury:
  - Primary burn – hyperemia
    - Tx: observation and conservative therapy
    - Conservative Tx: IVFs, spitting, antibiotics, oral intake after 3–4 days; may need future serial dilation for strictures (usually cervical)
    - Can also get shortening of esophagus with GERD (Tx: PPI)
  - Secondary burn – ulcerations, exudates, and sloughing
    - Tx: prolonged observation and conservative therapy as above; TPN
    - Indications for esophagectomy – sepsis, peritonitis, mediastinitis, free air, mediastinal or stomach wall air, crepitance, contrast extravasation, pneumothorax, large effusion
  - Tertiary burn – deep ulcers, charring, and lumen narrowing
    - Tx: as above; esophagectomy usually necessary
    - Alimentary tract not restored until after patient recovers from the caustic injury
- Caustic esophageal perforations require esophagectomy (are not repaired due to extensive damage)

PERFORATIONS

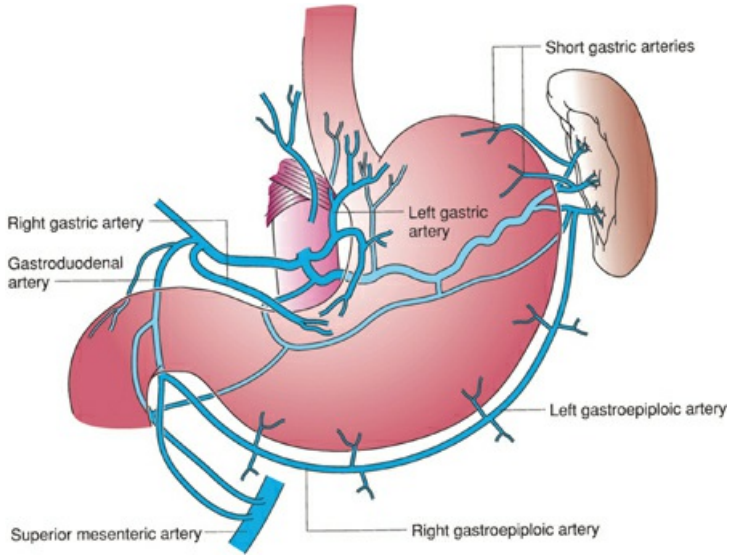
- Usually the result of EGD
- Cervical esophagus near cricopharyngeus muscle most common site
- Symptoms: pain, dysphagia, tachycardia, subcutaneous air in lower neck
- Dx: CXR initially (look for free air); Gastrografin swallow *(best test)* followed by barium swallow; *No EGD*
- Criteria for nonsurgical management – contained perforation by contrast, self-draining, no systemic effects
  - Conservative Tx: IVFs, NPO, spit, broad-spectrum antibiotics
- Non-contained perforations:
  - If quick to diagnose it (< 24 hours) and area has minimal contamination → primary repair with drains
    - Need longitudinal myotomy to see the full extent of injury
    - Consider muscle flaps (eg intercostal) to cover repair
  - If late to diagnose it (> 48 hours) or area has extensive contamination →
    - Neck – just place drains *(no esophagectomy)* → will eventually heal

    - Chest – need 1) resection (esophagectomy, cervical esophagostomy) or 2) exclusion and diversion (cervical esophagostomy, staple across distal esophagus, washout mediastinum, place chest tubes – late esophagectomy at time of gastric replacement)
    - Gastric replacement of esophagus late when patient fully recovers
  - Esophagectomy – may be needed for any perforation (contained or non-contained) in patients with severe intrinsic disease (eg burned out esophagus from achalasia, esophageal CA)
- Boerhaave's syndrome
  - Forceful vomiting followed by chest pain – perforation most likely to occur in the left lateral wall of esophagus, 3–5 cm above the GE junction
  - Hartmann's sign – mediastinal crunching on auscultation
  - Fever, leukocytosis, and sepsis occur as mediastinitis develops
  - *Highest mortality of all perforations* – early diagnosis and treatment improve survival
  - Dx: Gastrografin swallow *(best test)*
  - Tx: as above for esophageal perforations

30 Stomach

ANATOMY AND PHYSIOLOGY

- Stomach transit time 3–4 hours
- Peristalsis – occurs only in distal stomach (antrum)
- Gastroduodenal pain sensed through afferent sympathetic fibers T5–10
- Blood supply
  - Celiac trunk – left gastric, common hepatic artery, splenic artery
    - Left gastroepiploic and short gastric are branches of splenic artery
  - Greater curvature – right and left gastroepiploics, short gastrics
    - Right gastroepiploic is a branch of gastroduodenal artery
  - Lesser curvature – right and left gastrics
    - Right gastric is a branch off the proper hepatic artery *after* the GDA takeoff
  - Pylorus – gastroduodenal artery
- Mucosa – lined with simple columnar epithelium



Arterial blood supply of the stomach.

- Cardia glands – mucus secreting
- Fundus and body glands
  - Chief cells – pepsinogen (1st enzyme in proteolysis)
  - Parietal cells – release H^+ and intrinsic factor
  - Acetylcholine (vagus nerve), gastrin (from G cells in antrum), and histamine (from mast cells) cause H^+ release
  - Acetylcholine and gastrin activate *phospholipase* (PIP → DAG + IP_3 to ↑ Ca); Ca-calmodulin activates phosphorylase kinase →↑ H^+ release
  - Histamine activates *adenylate cyclase* → cAMP → activates protein kinase A → ↑ H^+

release
    - Phosphorylase kinase and protein kinase A phosphorylate H^+/K^+ ATPase to ↑ H^+ secretion and K^+ absorption
    - Omeprazole blocks H^+/K^+ ATPase in parietal cell membrane (final pathway for H^+ release)
    - Inhibitors of parietal cells – somatostatin, prostaglandins (PGE_1), secretin, CCK
    - Intrinsic factor – binds B_{12} and the complex is reabsorbed in the terminal ileum
- Antrum and pylorus glands
    - Mucus and HCO_3^- secreting glands – protect stomach
    - G cells release gastrin – reason why antrectomy is helpful for ulcer disease
        - *Inhibited* by H^+ in duodenum
        - *Stimulated* by amino acids, acetylcholine
    - D cells – secrete somatostatin; inhibit gastrin and acid release
- Brunner's glands – in duodenum; secrete alkaline mucus
- Somatostatin, CCK, and secretin – released with antral and duodenal acidification
- Rapid gastric emptying – previous surgery (#1), ulcers
- Delayed gastric emptying – diabetes, opiates, anticholinergics, hypothyroidism
- Trichobezoars (hair) – hard to pull out
    - Tx: EGD generally inadequate; likely need gastrostomy and removal
- Phytobezoars (fiber) – often in diabetics with poor gastric emptying
    - Tx: enzymes, EGD, diet changes
- Dieulafoy's ulcer – vascular malformation; can bleed
- Ménétrièr's disease – mucous cell hyperplasia, ↑ rugal folds

GASTRIC VOLVULUS

- Associated with type II (paraesophageal) hernia
- Nausea without vomiting; severe pain; usually organoaxial volvulus
- Tx: reduction and Nissen

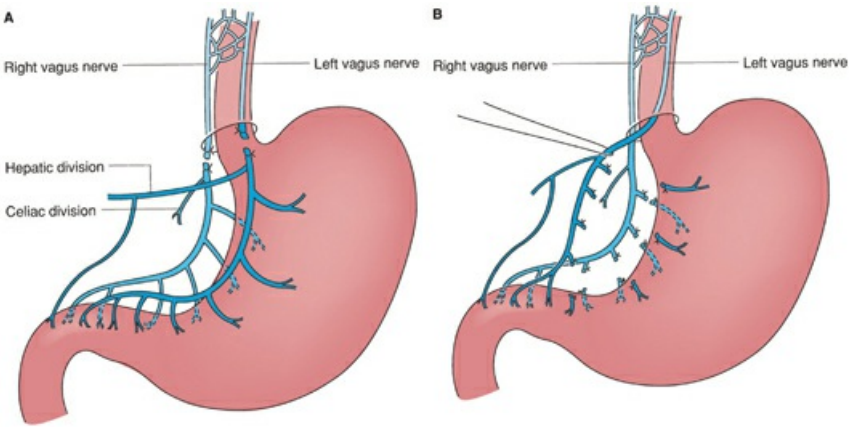
MALLORY–WEISS TEAR

- Secondary to forceful vomiting
- Presents as hematemesis following severe retching
- Bleeding often stops spontaneously
- Dx/Tx: EGD with hemo-clips; tear is usually on lesser curvature (near GE junction)
- If continued bleeding, may need gastrostomy and oversewing of the vessel

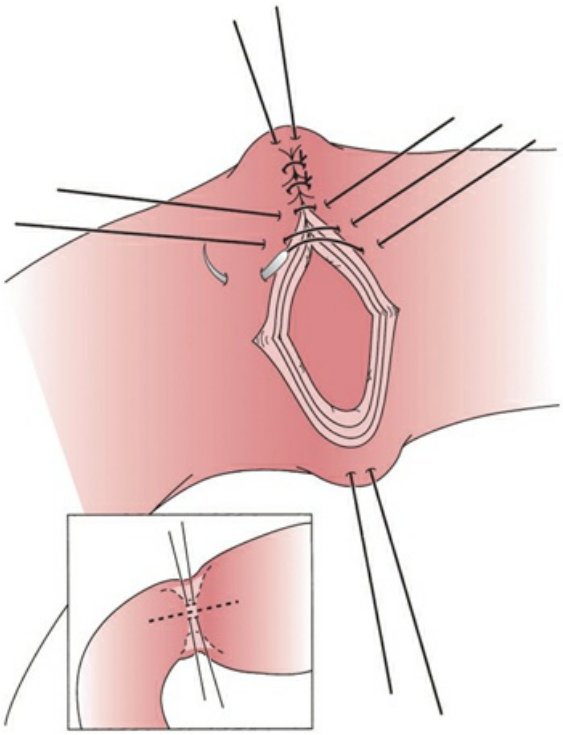
VAGOTOMIES

- Vagotomy – both truncal and proximal forms ↓ liquid emptying → vagally mediated receptive relaxation is removed (results in ↑ gastric pressure that accelerates liquid emptying)
- Truncal vagotomy – divides vagal trunks at level of esophagus; ↑ emptying of solids
- Proximal vagotomy (highly selective) – divides individual fibers, preserves "crow's foot"; normal emptying of solids
- Addition of pyloroplasty to truncal vagotomy results in ↓ solid emptying
- Other alterations caused by truncal vagotomy:

- Gastric effects – ↓ acid output by 90%, ↑ gastrin, gastrin cell hyperplasia
- Nongastric effects – ↓ exocrine pancreas function, ↓ postprandial bile flow, ↑ gallbladder volumes, ↓ release of vagally mediated hormones
- Diarrhea (40%) – most common problem following vagotomy
  - Caused by sustained MMCs (migrating motor complex) forcing bile acids into the colon
  - Tx: cholestyramine and loperamide



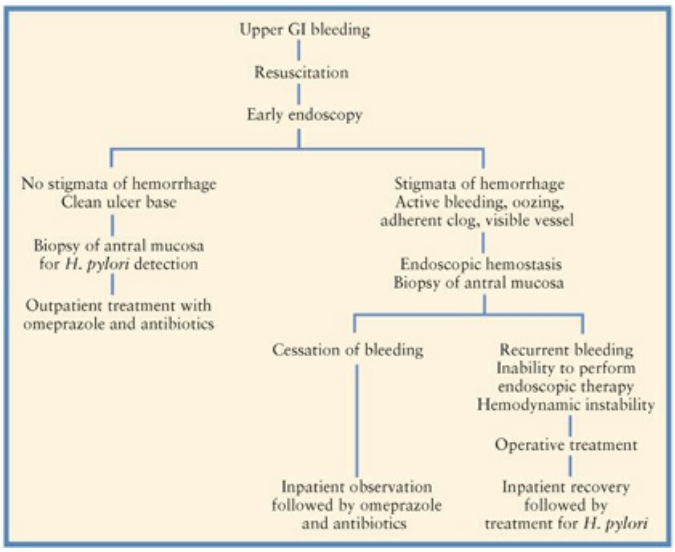
Truncal vagotomy and proximal gastric vagotomy. *(A)* With truncal vagotomy, both nerve trunks are divided at the level of the diaphragmatic hiatus. *(B)* Proximal gastric vagotomy involves division of the vagal fibers that supply the gastric fundus. Branches to the antropyloric region of the stomach are not transected, and the hepatic and celiac divisions of the vagus nerves remain intact.



Pyloroplasty formation. A Heineke–Mikulicz pyloroplasty involves a longitudinal incision of the pyloric sphincter followed by a transverse closure.

UPPER GASTROINTESTINAL BLEEDING (UGI BLEEDING)

- Symptoms – hematemesis; can also present with anemia, melena, or red blood per rectum
- Bleeding can be anywhere from the nose to the ligament of Treitz
- More common than lower GI bleeding
- Risk factors: previous UGI bleed, peptic ulcer disease, NSAID use, smoking, liver disease, esophageal varices, splenic vein thrombosis, sepsis, burn injuries, trauma, severe vomiting
- Dx/Tx: EGD (confirm bleeding is from ulcer); can potentially treat with hemo-clips, Epi injection, cautery



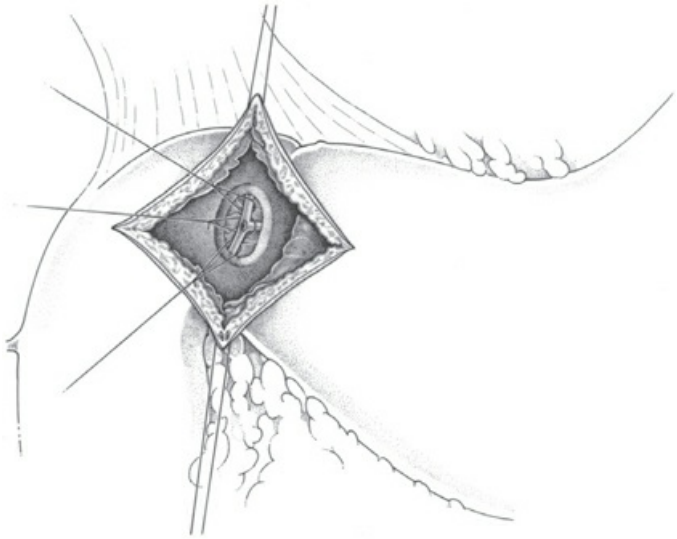
Treatment of bleeding ulceration.

- Slow bleeding and having trouble localizing source → tagged RBC scan
- Biggest risk factor for rebleeding at the time of EGD – #1 *spurting blood vessel* (60% chance of rebleed), #2 visible blood vessel (40% chance of rebleed), #3 diffuse oozing (30% chance of rebleed)
- Highest risk factor for mortality with non-variceal UGI bleed – *continued or re-bleeding*
- Patient with liver failure is likely bleeding from esophageal varices, <u>not</u> an ulcer → Tx: EGD with variceal bands or sclerotherapy; TIPS if that fails

DUODENAL ULCERS

- From ↑ acid production and ↓ defense
- Most common peptic ulcer; more common in men
- Usually in 1st part of the duodenum; usually anterior
  - Anterior ulcers <u>perforate</u>
  - Posterior ulcers <u>bleed</u> from <u>gastroduodenal artery</u>
- Symptoms: epigastric pain radiating to the back; abates with eating but recurs 30 minutes after
- Dx: endoscopy
- Dx of *H. pylori* – histiologic exam of antral biopsies
- Tx: proton pump inhibitor (PPI; omeprazole), triple therapy for *Helicobacter pylori* → bismuth salts, amoxicillin, and metronidazole/tetracycline (BAM or BAT)

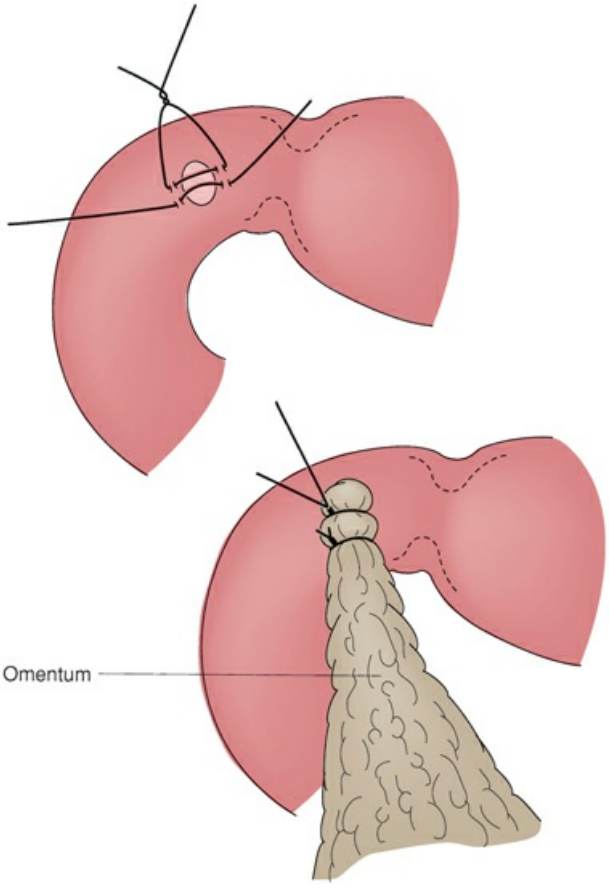
- Surgery for ulcers rarely indicated since PPIs
- Need to rule out gastrinoma in patients with complicated ulcer disease (Zollinger-Ellison syndrome – gastric acid hypersecretion, peptic ulcers, and gastrinoma)
- Surgical indications:
  - Perforation
  - Protracted bleeding despite EGD therapy
  - Obstruction
  - Intractability despite medical therapy
  - Inability to rule out cancer (ulcer remains despite treatment) → requires resection of ulcer
  - *If patient has been on a PPI, an acid-reducing surgical procedure is required in addition to above*
- Surgical options (acid-reducing surgery)
  - Proximal vagotomy – lowest rate of complications, no need for antral or pylorus procedure; 10%–15% ulcer recurrence; 0.1% mortality
  - Truncal vagotomy and pyloroplasty – 5%–10% ulcer recurrence, 1% mortality
  - Truncal vagotomy and antrectomy – 1%–2% ulcer recurrence (lowest rate of recurrence), 2% mortality
  - Reconstruction after antrectomy – Roux-en-Y gastro-jejunostomy (best)
  - *Less dumping syndrome and alkaline reflux gastritis* compared to Billroth I (gastro-duodenal anastomosis) and Billroth II (gastro-jejunal anastomosis)
- Bleeding
  - Most frequent complication of duodenal ulcers
  - Usually minor but can be life threatening
  - Major bleeding – > 6 units of blood in 24 hours or patient remains hypotensive despite transfusion
  - Tx: EGD 1st – hemoclips, cauterize, Epi injection
  - Surgery – duodenotomy and gastroduodenal artery (GDA) ligation
  - Avoid hitting common bile duct (posterior) with GDA ligation
  - If patient has been on a PPI, need acid-reducing surgery as well



Proper suture ligation of a bleeding ulcer arising from the gastroduodenal artery requires a 3-suture ligation. The proximal and distal branches of the gastroduodenal artery are transfixed. A third suture, U type in configuration, is necessary to transfix the transverse pancreatic branch of

the artery. (From Bailey RW, Martinez JM. Laparoscopic highly selective vagotomy. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

- Obstruction
  - PPI and serial dilation initial treatment of choice (IVFs and TPN up to 1 week; majority open up with conservative Tx)
  - Get metabolic alkalosis (hypochloremic, hypokalemic)
  - Surgical options – antrectomy and truncal vagotomy (best); include ulcer in resection if it's located proximal to ampulla of Vater
  - Need to Bx area of resection to rule out CA
- Perforation
  - 80% will have free air
  - Patients usually have sudden sharp epigastric pain; can have generalized peritonitis
  - Pain can radiate to the pericolic gutters with dependent drainage of gastric content
  - Tx: Graham patch (place omentum over the perforation)
    - Also need acid-reducing surgery if the patient has been on a PPI



Omental patching of perforated duodenal ulcer.

- Intractability
  - > 3 months without relief while on escalating doses of PPI
  - Based in EGD mucosal findings, <u>not</u> symptoms
  - Tx: acid-reducing surgery

GASTRIC ULCERS

- Older men; slow healing
- Risk factors: male, tobacco, ETOH, NSAIDs, *H. pylori*, uremia, stress (burns, sepsis, and trauma), steroids, chemotherapy
- 80% on lesser curvature of the stomach
- Hemorrhage is associated with higher mortality than duodenal ulcers
- Symptoms: epigastric pain radiating to the back; relieved with eating but recurs 30 minutes later; melena or guaiac-positive stools
- *Best test for H. pylori* – histiologic examination of biopsies from antrum
- CLO test (rapid urease test) – test for *H. pylori*, detects urease released from *H. pylori*
- Types:
  - Type I – lesser curve low along body of stomach; due to ↓ mucosal protection
  - Type II – 2 ulcers (lesser curve and duodenal); similar to duodenal ulcer with high acid secretion
  - Type III – pre-pyloric ulcer; similar to duodenal ulcer with high acid secretion
  - Type IV – lesser curve high along cardia of stomach; ↓ mucosal protection
  - Type V – ulcer associated with NSAIDs
- Tx: PPI and *H. pylori* Tx (vast majority heal)
- *Best test for H. pylori eradication* – urea breath test
- Surgical indications – perforation, bleeding not controlled with EGD, obstruction, cannot exclude malignancy, intractability (> 3 months without relief – based on mucosal findings)
- Surgery: truncal vagotomy and antrectomy best for complications; try to include the ulcer with resection (extended antrectomy) – need separate ulcer excision if that is not possible (gastric ulcers are resected at time of surgery due to high risk of gastric CA)
  - Omental patch and ligation of bleeding vessels are poor options for gastric ulcers due to high recurrence of symptoms and risk of gastric CA in the ulcer
- Cushing's ulcer – head trauma and gastric ulcer
- Curling's ulcer – burn patients and duodenal ulcer

STRESS GASTRITIS

- Occurs 3–10 days after event (eg multiple trauma, burns, complicated post-op)
- Lesions appear in fundus first; can progress to ulcers
- Tx: PPI
- EGD with cautery of specific bleeding point may be effective

CHRONIC GASTRITIS

- Type A (fundus) – associated with pernicious anemia, autoimmune disease
- Type B (antral) – associated with *H. pylori*
- Tx: PPI

GASTRIC ADENOCARCINOMA

- Pain unrelieved by eating, weight loss
- Antrum has 40% of gastric cancers
- Accounts for 50% of cancer-related deaths in Japan

- Dx: EGD
- Risk factors – adenomatous polyps, tobacco, previous gastric operations, intestinal metaplasia, atrophic gastritis, pernicious anemia, type A blood, nitrosamines
- Adenomatous polyps – 15% risk of cancer. Tx: endoscopic resection
- Krukenberg tumor – metastases to ovaries
- Virchow's nodes – metastases to supraclavicular node
- Intestinal-type gastric CA – ↑ in high-risk populations, older men; Japan; rare in United States; histology shows glands
  - Surgical Tx: try to perform subtotal gastrectomy (need 10-cm margins)
- Diffuse gastric cancer (linitis plastica) – in low-risk populations, women; most common type in the United States
  - Diffuse lymphatic invasion; no glands
  - Less favorable prognosis than intestinal-type gastric CA (overall 5-YS – 25%)
  - Surgical Tx: total gastrectomy because of diffuse nature of linitis plastica
- Chemotherapy (poor response): 5FU, doxorubicin, mitomycin C
- Metastatic disease outside area of resection → contraindication to resection unless performing surgery for palliation
- Palliation of gastric CA
  - Obstruction – proximal lesions can be stented; distal lesions can be bypassed with gastrojejunostomy
  - Low to moderate bleeding or pain – Tx: XRT
  - If these fail, consider palliative gastrectomy for obstruction or bleeding

GASTROINTESTINAL STROMAL TUMORS (GISTS)

- Most common benign gastric neoplasm, although can be malignant
- Symptoms: usually asymptomatic, but obstruction and bleeding can occur
- Hypoechoic on ultrasound; smooth edges
- Dx: biopsy – are C-KIT–positive
- Considered malignant if > 5 cm or > 5 mitoses/50 HPF (high-powered field)
- Tx: resection with 1-cm margins; *no nodal dissection*
- *Chemotherapy with* imatinib (Gleevec; tyrosine kinase inhibitor) if malignant

MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA (MALT LYMPHOMA)

- Related to *H. pylori* infection
- Usually regresses after treatment for *H. pylori*
- Stomach most common location
- Tx: *triple-therapy antibiotics for H. pylori* and surveillance; if MALT does not regress, need XRT

GASTRIC LYMPHOMAS

- Have ulcer symptoms; stomach is the most common location for extra-nodal lymphoma
- Usually non-Hodgkin's lymphoma (B cell)
- Dx: EGD with biopsy
- Chemotherapy and XRT are primary treatment modalities; surgery for complications

- Surgery possibly indicated only for stage I disease (tumor confined to stomach mucosa) and then only partial resection is indicated
- Overall 5-year survival rate > 50%

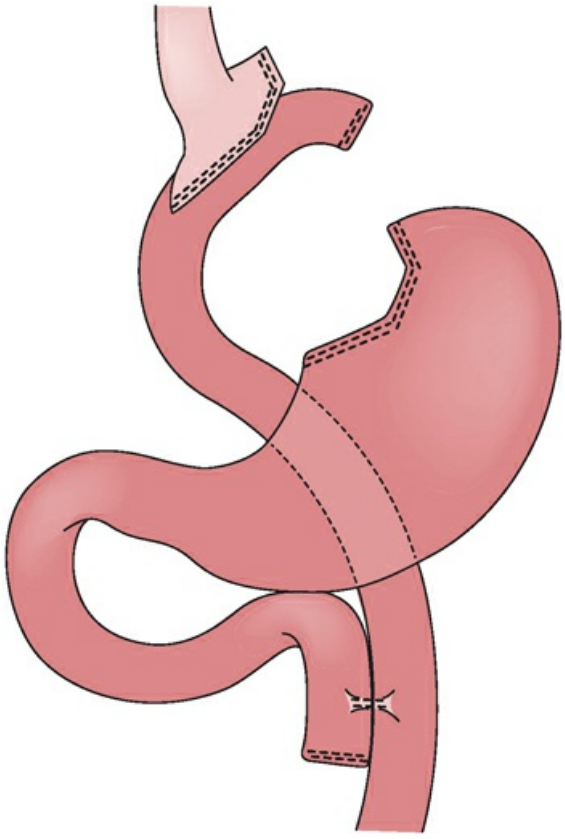
MORBID OBESITY

Criteria for Patient Selection for Bariatric Surgery (Need All 4)

- Body mass index > 40 kg/m^2 or body mass index > 35 kg/m^2 with coexisting comorbidities
- Failure of nonsurgical methods of weight reduction
- Psychological stability
- Absence of drug and alcohol abuse

- Central obesity – worse prognosis in general population
- Operative mortality is approximately 1%
- Gets better after surgery – diabetes, cholesterol, sleep apnea, HTN, urinary incontinence, GERD, venous stasis ulcers, pseudotumor cerebri (intracranial hypertension), joint pain, migraines, depression, polycystic ovarian syndrome, nonalcoholic fatty liver disease
- Does <u>not</u> get better – peripheral arterial disease
- Roux-en-Y gastric bypass
  - Better weight loss than just banding
  - Risk of marginal ulcers, leak, necrosis, B_{12} deficiency (intrinsic factor needs acidic environment to bind B_{12}), iron-deficiency anemia (bypasses duodenum where Fe absorbed), gallstones (from rapid weight loss)
  - Perform cholecystectomy during operation if stones present
  - UGI on postop day 2
  - 10% failure rate due to high-carbohydrate snacking
  - Leak
    - Ischemia – most common cause of leak
    - Signs of leak – ↑ RR, ↑ HR, fever, elevated WBCs; often do <u>not</u> have abdominal pain
    - Tx: early leak (not contained) → emergent re-op; late leak (weeks out from surgery, likely contained) → percutaneous drain, antibiotics
  - Marginal ulcers (on the jejunum) – develop in 10%. Tx: PPI
  - Stenosis – usually responds to serial dilation
  - Dilation of excluded stomach postop – hiccoughs, large stomach bubble
    - Dx: AXR; Tx: G-tube (gastrostomy tube)
  - Small bowel obstruction – nausea and vomiting, intermittent abdominal pain; AXR shows dilated small bowel; this is a *surgical emergency* in patients with gastric bypass due to the high risk of small bowel herniation, strangulation, infarction, and subsequent necrosis; Tx: emergent surgical exploration

Laparoscopic adjustable gastric band. (From Jones DB, Schneider BE. Surgical management of morbid obesity. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)



Laparoscopic proximal Roux-en-Y gastric bypass (retrocolic, retrogastric).

- Jejunoileal bypass
  - These operations are no longer done
  - Associated with liver cirrhosis, kidney stones, and osteoporosis (↓ Ca)

- Need to correct these patients and perform Roux-en-Y gastric bypass if ileojejunal bypasses are encountered

POSTGASTRECTOMY COMPLICATIONS

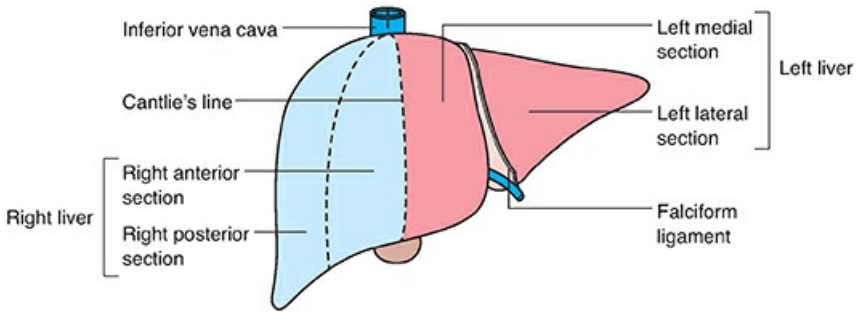
- Dumping syndrome
  - Can occur after gastrectomy or after vagotomy and pyloroplasty
  - Occurs from rapid entering of carbohydrates into the small bowel
  - 90% of cases resolve with medical therapy
  - 2 phases
    - Hyperosmotic load causes fluid shift into bowel (hypotension, diarrhea, dizziness)
    - Hypoglycemia from reactive ↑ in insulin and ↓ in glucose (2nd phase rarely occurs)
  - Can almost always be treated medically (and dietary changes)
  - Dx: gastric emptying study
  - Tx: small, low-fat, low-carbohydrate, high-protein meals; no liquids with meals, no lying down after meals; octreotide
  - Surgical options (rarely needed)
    - Conversion of Billroth I or Billroth II to Roux-en-Y gastrojejunostomy
    - Operations to ↑ gastric reservoir (jejunal pouch) or ↑ emptying time (reversed jejunal loop)
- Alkaline reflux gastritis
  - Postprandial epigastric pain associated with N/V; pain not relieved with vomiting
  - Dx: EGD – evidence of bile reflux into stomach, histologic evidence of gastritis
  - Tx: PPI, cholestyramine, metoclopramide
  - Surgical option: conversion of Billroth I or Billroth II to Roux-en-Y gastrojejunostomy with afferent limb 60 cm distal to gastrojejunostomy
- Chronic gastric atony
  - Delayed gastric emptying
  - Symptoms: nausea, vomiting, pain, early satiety
  - Dx: gastric emptying study
  - Tx: metoclopramide, prokinetics
  - Surgical option: near-total gastrectomy with Roux-en-Y
- Small gastric remnant (early satiety)
  - Actually want this for gastric bypass patients
  - Dx: UGI
  - Tx: small meals
  - Surgical option: jejunal pouch construction
- Blind-loop syndrome
  - With Billroth II or Roux-en-Y; caused by poor motility
  - Symptoms: pain, steatorrhea (bacterial deconjugation of bile), B_{12} deficiency (bacteria use it up), malabsorption
  - Caused by bacterial overgrowth (*E. coli*, GNRs) from stasis in afferent limb
  - Dx: EGD of afferent limb with aspirate and culture for organisms
  - Tx: tetracycline and Flagyl, metoclopramide to improve motility
  - Surgical option: re-anastomosis with shorter (40-cm) afferent limb
- Afferent-loop obstruction
  - With Billroth II or Roux-en-Y; caused by mechanical obstruction of afferent limb

    - Symptoms: RUQ pain; nonbilious vomiting, pain relieved with bilious emesis
    - Risk factors – long afferent limb with Billroth II or Roux-en-Y
    - Dx: CT scan – shows dilated afferent limb
    - Tx: balloon dilation may be possible
    - Surgical option: re-anastomosis with shorter (40-cm) afferent limb to relieve obstruction
- Efferent-loop obstruction
    - Symptoms of obstruction – nausea, vomiting, abdominal pain
    - Dx: CT scan, UGI
    - Tx: balloon dilation
    - Surgical option: find site of obstruction and relieve it
- Post-vagotomy diarrhea
    - Secondary to non-conjugated bile salts in the colon (osmotic diarrhea)
    - Caused by sustained postprandial organized MMCs
    - Tx: cholestyramine, loperamide
    - Surgical option: reversed interposition jejunal graft
- Duodenal stump blow-out (after gastrectomy) – Dx: CT scan; Tx: place lateral duodenostomy tube and drains; these patients can be really sick
- PEG complications – insertion into the liver or colon

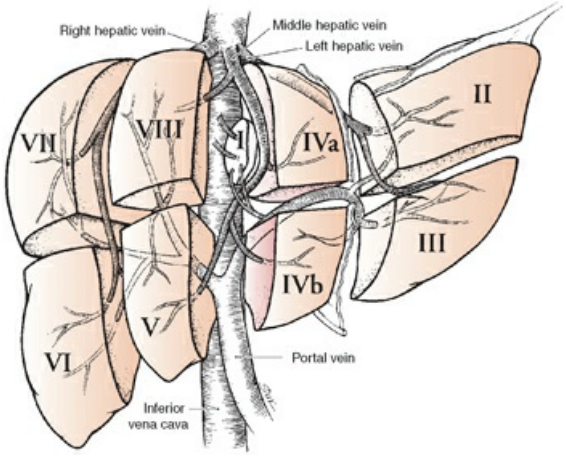
31 Liver

ANATOMY AND PHYSIOLOGY

- Hepatic artery variants
  - Right hepatic artery off superior mesenteric artery (#1 hepatic artery variant; 20%) courses behind pancreas, posterolateral to the common bile duct
  - Left hepatic artery off left gastric artery (about 20%) – found in gastrohepatic ligament medially
- Falciform ligament – separates medial and lateral segments of the left lobe; attaches liver to anterior abdominal wall; extends to umbilicus and carries remnant of the umbilical vein
- Ligamentum teres – carries the obliterated umbilical vein to the undersurface of the liver; extends from the falciform ligament
- Line drawn from the middle of the gallbladder fossa to IVC (portal fissure or Cantlie's line) separates the right and left liver lobes



Anatomic division of the liver into right and left halves by a line extending from the gallbladder fossa posteriorly to the inferior vena cava.

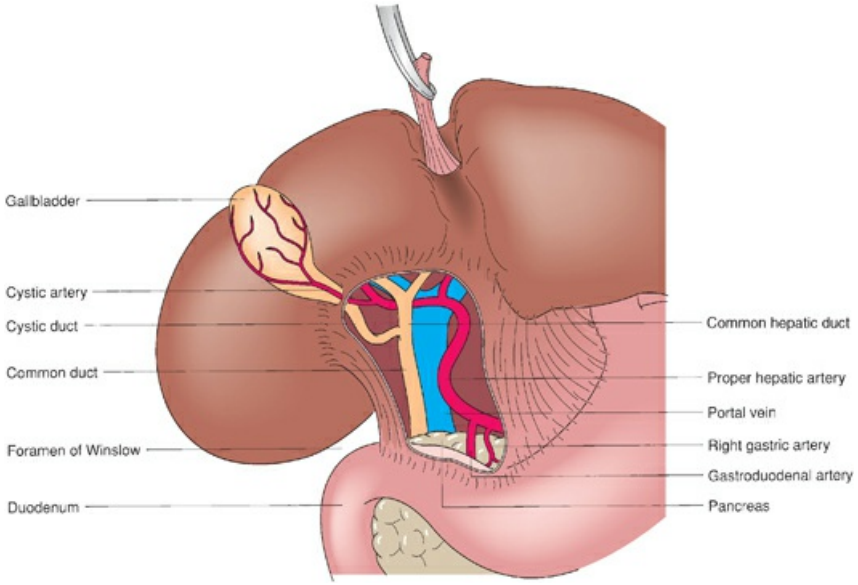


Couinaud's segmental anatomy of the liver. Segments II, III, and IV make up the left lobe and segments V, VI, VII, and VIII constitute the right lobe. Segment I is the caudate lobe.

- Segments
  - I – caudate

- II – superior left lateral segment
- III – inferior left lateral segment
- IV – left medial segment (quadrate lobe)
- V – inferior right anteromedial segment
- VI – inferior right posterolateral segment
- VII – superior right posterolateral segment
- VIII – superior right anteromedial segment

- Glisson's capsule – peritoneum that covers the liver
- Bare area – area on the posterior-superior surface of liver not covered by Glisson's capsule
- Triangular ligaments – lateral and medial extensions of the coronary ligament on the posterior surface of the liver; made up of peritoneum
- Portal triad enters segments IV and V
- Gallbladder lies under segments IV and V



Relationship of structures within the hepatoduodenal ligament.

- Kupffer cells – liver macrophages
- Portal triad – common bile duct (lateral), portal vein (posterior), and proper hepatic artery (medial); come together in the hepatoduodenal ligament (porta hepatis)
- Pringle maneuver – porta hepatis clamping; will not stop hepatic vein bleeding
- Foramen of Winslow (entrance to lesser sac)
  - Anterior – portal triad
  - Posterior – IVC
  - Inferior – duodenum
  - Superior – liver (caudate lobe)
- Portal vein
  - Forms from superior mesenteric vein joining splenic vein (no valves)
  - Inferior mesenteric vein – enters splenic vein
  - Portal veins – 2 in liver; ⅔ of hepatic blood flow
    - Left – goes to segments II, III, and IV
    - Right – goes to segments V, VI, VII, and VIII
- Arterial blood supply

- Right, left, and middle hepatic arteries (follows hepatic vein system below)
- Middle hepatic artery MC a branch off the left hepatic artery
- Most primary and secondary liver tumors are supplied by the hepatic artery

- Hepatic veins – 3 hepatic veins; drain into IVC
  - Left – II, III, and superior IV
  - Middle – V and inferior IV
  - Right – VI, VII, and VIII
  - Middle hepatic vein left hepatic vein in 80% before going into IVC; other 20% goes directly into IVC
  - Accessory right hepatic veins – drain medial aspect of right lobe directly to IVC
  - Inferior phrenic veins – also drain directly into the IVC
- Caudate lobe – receives separate right and left portal and arterial blood flow; drains directly into IVC via separate hepatic veins
- Alkaline phosphatase – normally located in canalicular membrane
- Nutrient uptake – occurs in sinusoidal membrane
- Ketones – usual energy source for liver; glucose is converted to glycogen and stored
  - Excess glucose converted to fat
- Urea – synthesized in the liver
- Not made in the liver – von Willebrand factor and factor VIII (endothelium)
- Liver stores large amount of fat-soluble vitamins
- B_{12} – the only water-soluble vitamin stored in the liver
- Bleeding and bile leak – most common problems with hepatic resection
- Hepatocytes most sensitive to ischemia – central lobular (acinar zone III)
- 75% of normal liver can be safely resected

BILIRUBIN

- A breakdown product of hemoglobin (Hgb → heme → biliverdin → bilirubin)
- Conjugated to glucuronic acid (glucuronyl transferase) in the liver → improves water solubility
- Conjugated bilirubin is actively secreted into bile
- Urobilinogen
  - Breakdown of conjugated bilirubin by bacteria in the terminal ileum occurs
  - Free bilirubin is reabsorbed, converted to urobilinogen, and eventually released in the urine as urobilin (yellow color)
  - Excess urobilinogen turns urine dark like cola

BILE

- Contains bile salts (85%), proteins, phospholipids (lecithin), cholesterol, and bilirubin
- Final bile composition determined by passive (Na/K ATPase) reabsorption of water in gallbladder
- Cholesterol – used to make bile salts/acids
- Bile salts are conjugated to taurine or glycine (improves water solubility)
  - Primary bile acids (salts) – cholic and chenodeoxycholic
  - Secondary bile acids (salts) – deoxycholic and lithocholic (dehydroxylated primary bile acids by bacteria in gut)

- Lecithin – main biliary phospholipid (emulsifies fat, solubilizes cholesterol)
- Bile solubilizes cholesterol and emulsifies fats in the intestine, forming micelles, which enter enterocytes by fusing with membrane

JAUNDICE

- Occurs when total bilirubin > 2.5; 1st evident under the tongue
- Maximum bilirubin is 30 unless patient had underlying renal disease, hemolysis, or bile duct–hepatic vein fistula
- Elevated un-conjugated bilirubin (indirect; usually with normal or mildly elevated conjugated bilirubin) – prehepatic causes (hemolysis); hepatic deficiencies of uptake or conjugation
- Elevated conjugated bilirubin (direct; accompanied by elevated un-conjugated bilirubin) – secretion defects into bile ducts (eg hepatitis); excretion defects into GI tract (obstructive jaundice; eg gallstones, cancer, benign stricture)
  - Hepatitis – very high transaminases, modest alkaline phosphatase
  - Obstructive jaundice – modest transaminases, very high alkaline phosphatase
- Syndromes
  - Gilbert's disease – abnormal conjugation; mild defect in glucuronyl transferase
  - Crigler–Najjar disease – inability to conjugate; severe deficiency of glucuronyl transferase; high unconjugated bilirubin → life-threatening disease
  - Physiologic jaundice of newborn – immature glucuronyl transferase; high unconjugated bilirubin
  - Rotor's syndrome – deficiency in storage ability; high conjugated bilirubin
  - Dubin–Johnson syndrome – deficiency in secretion ability; high conjugated bilirubin

VIRAL HEPATITIS

- All hepatitis viral agents can cause acute hepatitis (no surgery in setting of acute hepatitis)
- Fulminant hepatic failure can occur with hepatitis B, D, and E (very rare with A and C)
- Hepatitis B, C, and D can cause chronic hepatitis and hepatoma
- Hepatitis A (RNA) – serious consequences uncommon
- Hepatitis B (DNA) – MC hepatitis worldwide
  - Anti-HBc-IgM (c = core) is elevated in the first 6 months; IgG then takes over
  - Vaccination – have ↑ anti-HBs (s = surface) antibodies only
  - ↑ anti-HBc and ↑ anti-HBs antibodies and no HBs antigens (HBsAg) → patient had infection with recovery and subsequent immunity
- Hepatitis C (RNA) – can have long incubation period; currently most common viral hepatitis leading to liver TXP; Tx: Sovaldi (95% cure rate)
- Hepatitis D (RNA) – cofactor for hepatitis B (worsens prognosis)
- Hepatitis E (RNA) – fulminant hepatic failure in pregnancy, most often in 3rd trimester
- Hepatitis B + D has the highest overall mortality

LIVER FAILURE

- Most common cause of liver failure – cirrhosis (palpable liver, jaundice, ascites)
- Best indicator of synthetic function in patient with cirrhosis – prothrombin time (PT)
- Acute liver failure (fulminant hepatic failure) – 80% mortality

- Outcome determined by the course of encephalopathy
- Consider urgent liver TXP listing if King's College criteria are met

King's College Criteria of Poor Prognostic Indicators

Acetaminophen-Induced ALF
Arterial pH < 7.3 irrespective of coma grade
OR all of the following:
INR > 6.5, creatinine > 3.4 mg/dL (300 μmol/L), grade III/IV encephalopathy
Non–Acetaminophen-Induced ALF
INR > 6.5
OR any three of the following:
Age < 10 or > 40, drug toxicity or undetermined etiology, jaundice > 7 days before encephalopathy, INR > 3.5, bilirubin > 17 mg/dL (300 μmol/L)

ALF, acute liver failure; INR, international normalized ratio.

- Hepatic encephalopathy
  - Liver failure leads to inability to metabolize → get buildup of ammonia, mercantanes, and false neurotransmitters
  - Causes other than liver failure for encephalopathy – GI bleeding, infection (spontaneous bacterial peritonitis [SBP]), electrolyte imbalances, drugs
  - May need to embolize previous therapeutic shunts or other major collaterals
  - Tx: lactulose – cathartic that gets rid of bacteria in the gut and acidifies colon (preventing NH_3 uptake by converting it to ammonium), titrate to 2–3 stools/day
    - Limit protein intake (< 70 g/day)
    - Branched-chain amino acids – metabolized by skeletal muscle, may be of some value
    - No antibiotics unless for a specific infection
    - Neomycin (gets rid of ammonia-producing bacteria from gut)
- Cirrhosis mechanism – hepatocyte destruction → fibrosis and scarring of liver → ↑ hepatic pressure → portal venous congestion → lymphatic overload → leakage of splanchnic and hepatic lymph into peritoneum → ascites
- Paracentesis for ascites – replace with albumin (1 g for every 100 cc removed)
- Ascites – from hepatic/splanchnic lymph
  - Tx: water restriction (1–1.5 L/d), ↓ NaCl (1–2 g/d), diuretics (spironolactone counteracts hyperaldosteronism seen with liver failure), paracentesis, TIPS if refractory, prophylactic antibiotics to prevent SBP (norfloxacin; used if previous SBP or current UGI bleed)
- Aldosterone is elevated with liver failure – secondary to impaired hepatic metabolism
- Hepatorenal syndrome – progressive renal failure; same lab findings as prerenal azotemia; usually a sign of end-stage liver disease; kidneys are normal but not perfused well
  - Volume challenge does not work (unlike prerenal azotemia)
  - Tx: stop diuretics, give volume; midodrine and octreotide; no good therapy other than liver TXP
- Neurological changes – asterixis; sign that liver failure is progressing
- Postpartum liver failure with ascites – hepatic vein thrombosis (from ovarian vein source); has an infectious component (pelvic thrombophlebitis)
  - Dx: SMA arteriogram with venous phase contrast
  - Tx: heparin and antibiotics

SPONTANEOUS BACTERIAL PERITONITIS (PRIMARY BACTERIAL PERITONITIS)

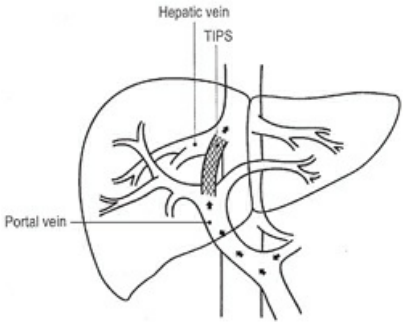
- Patient with ascites
- Fever, abdominal pain, PMNs > 250 in fluid, positive cultures
- *E. coli* (#1), pneumococci, streptococci
- Most commonly mono-organism; if not, need to worry about bowel perforation
- Risk factors – prior SBP, UGI bleed (variceal hemorrhage), low-protein ascites, childhood nephrotic syndrome
- Tx: 3rd-generation cephalosporins; patients usually respond within 48 hours

ESOPHAGEAL VARICES

- Bleed by rupture
- Tx: banding and sclerotherapy (95% effective)
  - Vasopressin (splanchnic artery constriction) and octreotide (↓ portal pressure by ↓ blood flow) can be used to temporize
  - Patients with history of CAD should receive NTG while on vasopressin
  - Sengstaken–Blakemore esophageal tube – has a balloon used to control variceal bleeding; risk of rupture of the esophagus (hardly used anymore)
- Propranolol – good for patients with asymptomatic varices or with previous variceal bleed to help prevent re-bleeding; no good role acutely
- Can get later strictures from sclerotherapy; usually easily managed with dilatation
- TIPS is needed for refractory variceal bleeding

PORTAL HYPERTENSION

- Pre-sinusoidal obstruction – schistosomiasis, portal vein thrombosis (50% of portal hypertension cases in children)
- Sinusoidal obstruction – cirrhosis
- Post-sinusoidal obstruction – Budd–Chiari syndrome (hepatic vein occlusive disease), constrictive pericarditis, CHF
- Measurement of portal vein pressure – get hepatic venous wedge pressure
- Portal vein pressure > 10–12 mm Hg considered significant
- Coronary veins act as collaterals between the portal vein and the systemic venous system of the lower esophagus (azygous vein)
- Portal HTN leads to esophageal variceal hemorrhage, ascites, splenomegaly, and hepatic encephalopathy
- Shunts can decompress portal system
- TIPS – used for protracted bleeding, progression of coagulopathy, visceral hypoperfusion, or refractory ascites
  - Allows antegrade flow from portal vein to the IVC
  - Complication of TIPS – *development of encephalopathy*



Transjugular intrahepatic portosystemic shunt (TIPS). A catheter is passed into the hepatic vein via the jugular vein. A needle, inserted through the catheter, is passed from the hepatic vein through the liver tissue into a major portal vein branch. The liver tract is dilated with an angioplasty balloon catheter, and the tract is kept open after deployment of an expandable metal stent. (From Krige JEJ, Bornman PC. Endoscopic therapy in the management of esophageal varices: injection sclerotherapy and variceal ligation. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

- Splenorenal shunt – low rate of encephalopathy; need to ligate left adrenal vein, left gonadal vein, inferior mesenteric vein, coronary vein, and pancreatic branches of splenic vein; *do not need splenectomy*
  - Used only for Child's A cirrhotics who present just with bleeding (rarely used anymore)
  - Contraindicated in patients with refractory ascites, as splenorenal shunts can worsen ascites
- Child's B or C with indication for shunt → TIPS
- Child's A that just has bleeding as symptom → consider splenorenal shunt (more durable); otherwise TIPS
- Child-Pugh Score correlates with mortality after open shunt placement

Child-Pugh Score	1 Point	2 Points	3 Points
Albumin	> 3.5	3–3.5	< 3.0
Bilirubin	< 2.5	2.5–4	> 4
Encephalopathy	None	Minimal	Severe
Ascites	None	Treatable with meds	Refractory
INR	< 1.7	1.7–2.3	> 2.3

- Child's A (5–6 pts) — 2% mortality with shunt
- Child's B (7–9 pts) — 10% mortality with shunt
- Child's C (10 pts or greater) — 50% mortality with shunt

- MELD score (model for end-stage liver disease) – uses INR, creatinine, and total bilirubin to grade liver failure; often preferred compared to Child's
- Portal HTN in children
  - Usually from extra-hepatic portal vein thrombosis
  - Most common cause of massive hematemesis in children

BUDD–CHIARI SYNDROME

- Occlusion of hepatic veins or IVC

- RUQ pain, hepatosplenomegaly, ascites, fulminant hepatic failure, variceal bleeding
- RF – polycythemia vera
- Dx: angiogram with venous phase, CT angiogram; liver biopsy shows sinusoidal dilatation, congestion, centrilobular congestion
- Tx: porta-caval shunt (needs to connect to the IVC above the obstruction); can try catheter-directed tPA if acute

SPLENIC VEIN THROMBOSIS

- Can lead to isolated gastric varices without elevation of pressure in the rest of the portal system
- These gastric varices can bleed
- Splenic vein thrombosis is most often caused by pancreatitis
- Tx: splenectomy if symptomatic

PORTAL VEIN THROMBOSIS

- Usually extra-hepatic
- RF – hypercoagulable states
- Get ascites *without* liver failure
- Can get esophageal varices (MCC of massive hematemesis in children)
- Tx: heparin indicated if acute thrombosis (avoid if UGI bleeding present); may eventually need a shunt

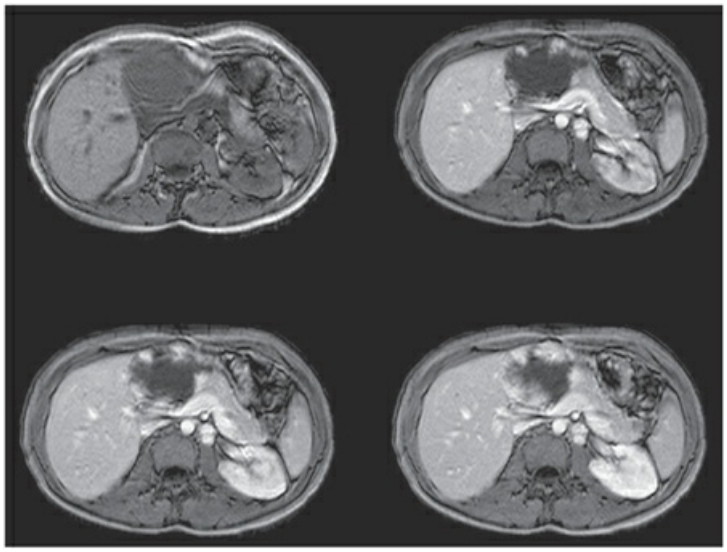
LIVER ABSCESSES

- Amebic
  - ↑ LFTs; ↑ in right lobe of liver, usually single
  - Primary infection occurs in the colon → amebic colitis
  - Risk factors – travel to Mexico, ETOH; fecal–oral transmission
  - Diagnosis – serology for *Entamoeba histolytica* (90% have infection)
  - Symptoms: fever, chills, RUQ pain, ↑ WBCs, jaundice, hepatomegaly
  - Reaches liver via portal vein
  - Cultures of abscess often sterile → protozoa exist only in peripheral rim
  - Can usually diagnose based on CT characteristics
  - Tx: Flagyl; aspiration *only* if refractory; surgery *only* if free rupture
- *Echinococcus*
  - Forms cyst (hydatid cyst)
  - Positive Casoni skin test, positive serology
  - Sheep – carriers; dogs – human exposure; ↑ in right lobe of the liver
  - *Do not aspirate → can leak out and cause anaphylactic shock*
  - Abdominal CT shows ectocyst (calcified) and endocyst (double-walled cyst)
  - Pre-op ERCP for jaundice, ↑ LFTs, or cholangitis to check for communication with the biliary system
  - Tx: pre-op albendazole (2 weeks) and surgical removal (intra-op can inject cyst with alcohol to kill organisms, then aspirate out); need to get all of cyst wall
  - Do not spill cyst contents – can cause anaphylactic shock
- Schistosomiasis

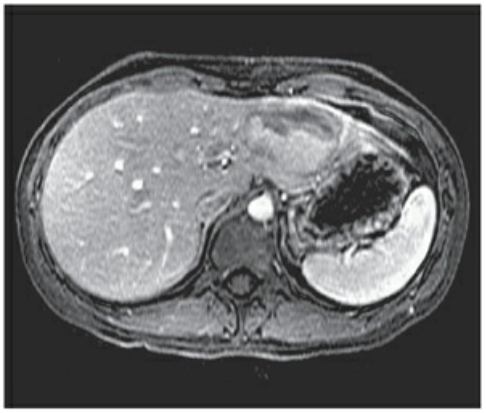
- Maculopapular rash, ↑ eosinophils
- Contact through the skin; acquired in water
- Can cause variceal bleeding
- Tx: praziquantel and control of variceal bleeding

- Pyogenic abscess
  - Account for 80% of all abscesses; can be multiple
  - Symptoms: fever, chills, weight loss, RUQ pain, ↑ LFTs, ↑ WBCs, sepsis
  - ↑ in right lobe; 15% mortality with sepsis
  - GNRs – #1 organism (*E. coli*)
  - Most commonly secondary to contiguous infection from biliary tract (eg cholangitis)
  - Can occur following bacteremia from other types of infections (eg diverticulitis, appendicitis)
  - Dx: aspiration
  - Tx: CT-guided drainage and antibiotics; surgical drainage for unstable condition and continued signs of sepsis

BENIGN LIVER TUMORS

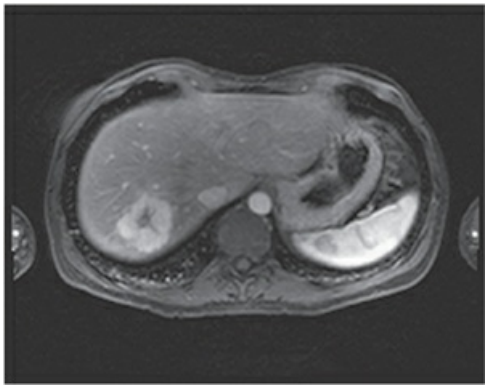


Magnetic resonance imaging of a hepatic hemangioma, demonstrating hypointensity on unenhanced images (*upper left*) and peripheral nodular enhancement with centripetal progression of enhancement on contrast-enhanced images (*upper right, lower left, lower right*).



Magnetic resonance imaging of a hepatic adenoma consuming much of segments II and III, with

intratumoral hemorrhage.



Gadolinium-enhanced magnetic resonance imaging of the liver, revealing a mass consistent with focal nodular hyperplasia.

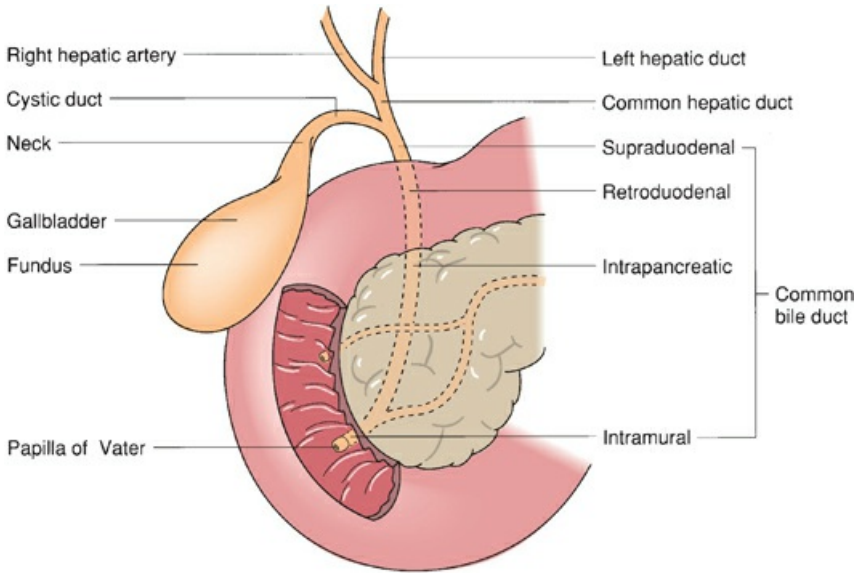
- Hepatic adenomas
  - Women, steroid use, OCPs
  - 80% are symptomatic; 50% risk of significant bleeding (rupture)
  - Can become malignant (5%)
  - More common in right lobe
  - Symptoms: pain, ↑ LFTs, ↓ BP (from rupture), palpable mass
  - Dx: no Kupffer cells in adenomas, thus no uptake on sulfur colloid scan (cold)
  - Tx:
    - Asymptomatic and < 4 cm – stop OCPs; if regression, no further therapy is needed; if no regression, patient needs resection of the tumor
    - Symptomatic or > 4 cm – tumor resection for bleeding and malignancy risk; embolization if multiple and unresectable
- Focal nodular hyperplasia
  - Has central stellate scar (diagnostic)
  - No malignancy risk; very unlikely to rupture
  - Dx: abdominal CT; has Kupffer cells, so will take up sulfur colloid on liver scan
  - Tx: conservative therapy *(no resection)*
- Hemangiomas
  - Most common benign hepatic tumor
  - Rupture rare; most asymptomatic; more common in women
  - *Avoid biopsy* → risk of hemorrhage
  - Dx: MRI and CT scan show peripheral to central enhancement
    - Appears as a *very hypervascular lesion (very bright)*
    - Tagged RBC scan *(best test)*
  - Tx: conservative unless symptomatic, then surgery ± pre-op embolization; steroids (possible XRT) for unresectable disease
  - Rare complications of hemangioma – consumptive coagulopathy (Kasabach–Merritt syndrome) and CHF; these complications are usually seen in children
- Solitary cysts
  - Congenital; women, right lobe; walls have a characteristic blue hue
  - Complications from these cysts are rare; most can be left alone

MALIGNANT LIVER TUMORS

- Metastases:primary ratio is 20:1
- Hepatocellular CA (hepatoma)
  - Most common cancer worldwide
  - Symptoms – RUQ discomfort and weight loss
  - Risk factors – HepB (#1 cause worldwide), HepC, ETOH, hemochromatosis, alpha-1-antitrypsin deficiency, primary sclerosing cholangitis, aflatoxins, hepatic adenoma, steroids, pesticides
  - Fibrolamellar type (adolescents and young adults) – best prognosis
  - Diffuse nodular type – worst prognosis
  - AFP level correlates with tumor size
  - 30% 5-year survival rate with resection
  - Few hepatic tumors are resectable secondary to cirrhosis, portohepatic lymph node involvement, or metastases (only 15% resectable)
  - Need 1-cm margin
  - Tumor recurrence most likely occur in the liver after resection
- Hepatic sarcoma
  - Risk factors – PVC, Thorotrast, arsenic → rapidly fatal
- Isolated colon CA metastases to liver – can resect if you leave enough liver for the patient to survive; 35% 5-year survival rate after resection for cure
- Primary liver tumors – generally hypervascular
- Metastatic liver tumors – generally hypovascular

32 Biliary System

ANATOMY AND PHYSIOLOGY



Anatomic divisions of the common bile duct.

- Gallbladder lies beneath segments IV and V
- Cystic artery branches off right hepatic artery
  - Is found in the triangle of Calot (cystic duct [lateral], common hepatic duct [medial], liver [superior])
- Right hepatic (lateral) and retroduodenal branches of the gastroduodenal artery (medial) supply the hepatic and common bile duct (9- and 3-o'clock positions when performing endoscopic retrograde cholangiopancreatography [ERCP]); considered longitudinal blood supply
- Cystic veins drain into the right branch of the portal vein
- Lymphatics are on the right side of the common bile duct
- Parasympathetic fibers come from left (anterior) trunk of the vagus
- Sympathetic fibers from T7–10 (splanchnic and celiac ganglions)
- Gallbladder has no submucosa; mucosa is columnar epithelium
- Common bile duct and common hepatic duct do not have peristalsis
- Gallbladder normally fills by contraction of sphincter of Oddi at the ampulla of Vater
  - Morphine – contracts the sphincter of Oddi
  - Glucagon – relaxes the sphincter of Oddi
- Normal sizes: common bile duct (CBD) < 8 mm (< 10 mm after cholecystectomy), gallbladder wall < 4 mm, pancreatic duct < 4 mm
- After cholecystectomy, total bile salt pools ↓
- Highest concentration of CCK and secretin cells are in the duodenum
- Rokitansky–Aschoff sinuses – epithelial invaginations in the gallbladder wall; formed from ↑

gallbladder pressure

- Ducts of Luschka – biliary ducts that can leak after a cholecystectomy; lie in the gallbladder fossa
- Bile excretion regulation
  - ↑ bile excretion – CCK, secretin, and vagal input
  - ↓ bile excretion – somatostatin, sympathetic stimulation
  - Gallbladder contraction – CCK causes constant, steady, tonic contraction
- Essential functions of bile:
  - Fat-soluble vitamin absorption
  - Essential fat absorption
  - Bilirubin and cholesterol excretion
- Gallbladder – forms concentrated bile by active resorption of NaCl (ATPase) and passive resorption of water
  - Active resorption of conjugated bile salts occurs in the terminal ileum (50%)
  - Passive resorption of nonconjugated bile salts can occur in the small intestine (45%) and colon (5%)
  - Postprandial gallbladder emptying is maximum at 2 hours (80%)
  - Bile secreted by hepatocytes (80%) and bile canalicular cells (20%)
  - Color of bile is mostly due to conjugated bilirubin
  - Stercobilin – breakdown product of conjugated bilirubin in gut; gives stool brown color
  - Urobilinogen – conjugated bilirubin is broken down in the gut and reabsorbed; gets converted to urobilinogen and eventually urobilin, which is released in the urine (yellow color)

	Na (mEq/L)	Cl (mEq/L)	Bile Salts (mEq/dL)	Cholesterol (mEq/dL)
Hepatic bile	140–170	50–120	1–50	50–150
Gallbladder bile	225–350	1–10	250–350	300–700

CHOLESTEROL AND BILE ACID SYNTHESIS

- HMG CoA → (HMG CoA reductase) → cholesterol → (7-alpha-hydroxylase) → bile salts (acids)
- HMG CoA reductase – rate-limiting step in cholesterol synthesis

GALLSTONES

- Occur in 10% of the population; vast majority are asymptomatic
- Only 10% of gallstones are radiopaque
- Nonpigmented stones
  - Cholesterol stones – caused by stasis, calcium nucleation, and ↑ water reabsorption from gallbladder
  - Also caused by ↓ lecithin and bile salts
  - Found almost exclusively in the gallbladder
  - Most common type of stone found in the United States (75%)
- Pigmented stones – most common worldwide
  - Calcium bilirubinate stones – caused by solubilization of unconjugated bilirubin with precipitation

- Dissolution agents (monooctanoin) do not work on pigmented stones
- Black stones
  - Can be caused by hemolytic disorders, cirrhosis, chronic TPN
  - Factors for development – ↑ bilirubin load, ↓ hepatic function, and bile stasis → get calcium bilirubinate stones
  - Almost always form in gallbladder
  - Tx: cholecystectomy if symptomatic
- Brown stones (primary CBD stones, formed in ducts, Asians)
  - Infection causing deconjugation of bilirubin
  - *E. coli* most common – produces beta-glucuronidase, which deconjugates bilirubin with formation of calcium bilirubinate
  - Need to check for ampullary stenosis, duodenal diverticula, abnormal sphincter of Oddi
  - Most commonly form in the bile ducts (are *primary common bile duct stones*)
  - Tx: almost all patients with primary stones need a biliary drainage procedure – sphincteroplasty (90% successful)
- Cholesterol stones and black stones found in the CBD are considered *secondary common bile duct stones*

CHOLECYSTITIS

- Due to obstruction of the cystic duct by a gallstone
- Results in gallbladder wall distention and wall inflammation
- Symptoms: RUQ pain (constant), referred pain to the right shoulder and scapula, nausea and vomiting, loss of appetite
  - Attacks frequently occur after a fatty meal; pain is persistent (unlike biliary colic)
- Murphy's sign – patient resists deep inspiration with deep palpation to the RUQ secondary to pain
- Alkaline phosphatase and WBCs are frequently elevated
- Suppurative cholecystitis associated with frank purulence in the gallbladder → can be associated with sepsis and shock
- Most common organisms in cholecystitis – *E. coli (#1)*, *Klebsiella*, *Enterococcus*
- Stone risk factors – age > 40, female, obesity, pregnancy, rapid weight loss, vagotomy, TPN (pigmented stones), ileal resection
- Ultrasound – 95% sensitive for picking up stones → hyperechoic focus, posterior shadowing, movement of focus with changes in position
  - Best initial evaluation test for jaundice or RUQ pain
  - Findings suggestive of acute cholecystitis – gallstones, gallbladder wall thickening (> 4 mm), pericholecystic fluid
  - Dilated CBD (> 8 mm) suggests CBD stone and obstruction
- HIDA scan – technetium taken up by liver and excreted in the biliary tract
- CCK-CS test (cholecystokinin cholescintigraphy)
  - *Most sensitive test for cholecystitis* (also uses HIDA above)
  - Indications for cholecystectomy after CCK-CS test:
    - If gallbladder not seen (the cystic duct likely has a stone in it; chronic cholecystitis)
    - Takes > 60 minutes to empty (biliary dyskinesia)
    - Ejection fraction < 40% (biliary dyskinesia)
- Indications for emergent ERCP (signs that a common bile duct stone is present) – jaundice,

cholangitis, dilated CBD *without* gallstone pancreatitis, or U/S shows stone in CBD

- Indications for pre-op ERCP (any of following needs to be persistently high for > 24 hours to justify pre-op ERCP) – AST or ALT (> 200) *without* gallstone pancreatitis or bilirubin (> 5)
  - < 5% of patients undergoing cholecystectomy will have a retained CBD stone → 95% of these are cleared with ERCP
- Tx for cholecystitis – cholecystectomy; cholecystostomy tube can be placed in patients who are very ill and cannot tolerate surgery
- ERCP – best treatment for late common bile duct stone
  - Sphincterotomy allows for removal of stone
  - Risks: bleeding, pancreatitis, perforation
- Biliary colic – transient cystic duct obstruction caused by passage of a gallstone
  - Resolves within 4–6 hours
  - If U/S shows gallstones, elective cholecystectomy is indicated
- Air in the biliary system most commonly occurs with previous ERCP and sphincterotomy
  - Can also occur with cholangitis or erosion of the biliary system into the duodenum (ie gallstone ileus)
- Bacterial infection of bile – dissemination from portal system is the most common route (not retrograde through sphincter of Oddi)
- Highest incidence of positive bile cultures occurs with postoperative strictures (usually *E. coli*, often polymicrobial)
- Pregnancy and cholecystitis – NPO and antibiotics (cefoxitin) treat 95%

ACALCULOUS CHOLECYSTITIS

- Thickened wall, RUQ pain, ↑ WBCs, no stones
- Occurs most commonly after severe burns, prolonged TPN, trauma, or major surgery
- Primary pathology is bile stasis (narcotics, fasting), leading to distention and ischemia
- Also have ↑ viscosity secondary to dehydration, ileus, transfusions
- Ultrasound shows sludge, gallbladder wall thickening, pericholecystic fluid, and *no stones*
- HIDA scan is positive
- Tx: cholecystectomy; percutaneous drainage if patient too unstable

EMPHYSEMATOUS GALLBLADDER DISEASE

- Gas in the gallbladder wall – can see on plain film
- ↑ in diabetics; usually secondary to *Clostridium perfringens*
- Symptoms: severe, rapid-onset abdominal pain, nausea, vomiting, and sepsis
- Perforation more common in these patients
- Tx: emergent cholecystectomy; percutaneous drainage if patient is too unstable

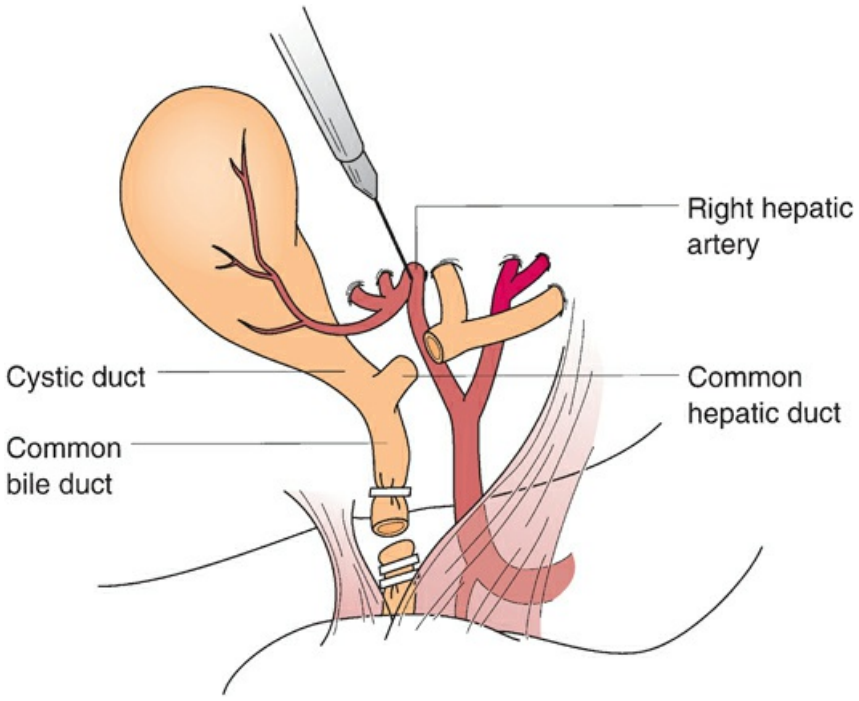
GALLSTONE ILEUS

- Fistula between gallbladder and duodenum that releases stone, causing small bowel obstruction; elderly
  - Can see pneumobilia (air in the biliary system) on plain film
- Terminal ileum – most common site of obstruction
- Tx: remove stone through enterotomy proximal to obstruction

- Perform cholecystectomy and fistula resection if patient can tolerate it (if old and frail, just leave the fistula)

COMMON BILE DUCT INJURIES

- Most commonly occur after laparoscopic cholecystectomy
- MCC – excess cephalad retraction of the gallbladder fundus
- Intraoperative CBD injury – if < 50% the circumference of the common bile duct, can probably perform primary repair; in all other cases, will likely need hepaticojejunostomy (or choledochojejunostomy); *do not try to attach to duodenum – won't reach*
- Persistent nausea and vomiting or jaundice following laparoscopic cholecystectomy → get U/S to look for fluid collection
  - If fluid collection is present, may be bile leak → percutaneous drain into the collection
    - If fluid is bilious, get ERCP → sphincterotomy and stent if due to cystic duct remnant leak, small injuries to the hepatic or common bile duct, or a leak from a duct of Luschka
    - Larger lesions (ie complete duct transection) will require hepaticojejunostomy or choledochojejunostomy (see below for timing)
  - If fluid collection not present and the hepatic ducts are dilated, likely have a completely transected common bile duct (PTC tube initially, then hepaticojejunostomy or choledochojejunostomy)
    - For lesions that cause early symptoms (≤ 7 days) – hepaticojejunostomy
    - For lesions that cause late symptoms (> 7 days) – hepaticojejunostomy 6–8 weeks after injury (tissue too friable for surgery after 7 days)
- Sepsis following laparoscopic cholecystectomy → fluid resuscitation and stabilize
  - May be due to complete transection of the CBD and cholangitis → get U/S to look for dilated intrahepatic ducts or fluid collections (pathway same as above)
- Anastomotic leaks following transplantation or hepaticojejunostomy → usually handled with percutaneous drainage of fluid collection followed by ERCP with temporary stent (leak will heal)



Classic laparoscopic bile duct injury. The common bile duct is mistaken for the cystic duct and transected. A variable extent of the extrahepatic biliary tree is resected with the gallbladder. The right hepatic artery, in background, is also often injured.

BILE DUCT STRICTURES

- Ischemia following laparoscopic cholecystectomy – most important cause of late postoperative biliary strictures
- Other causes – chronic pancreatitis, gallbladder CA, bile duct CA
- Symptoms: jaundice, sepsis, cholangitis
- Bile duct strictures without a history of pancreatitis or biliary surgery is CA until proven otherwise
- Dx: MRCP (magnetic resonance cholangiopancreatography) defines anatomy, looks for mass → if CA not ruled out with MRCP, need ERCP with brush biopsies
- Tx: if due to ischemia or chronic pancreatitis → *choledochojejunostomy* (best long-term solution)
  - If due to CA, follow appropriate workup

HEMOBILIA

- Fistula between bile duct and hepatic arterial system (most commonly)
- Patients classically present with UGI bleed, jaundice, and RUQ pain
- Most commonly occurs with percutaneous instrumentation (MC, eg PTC tube) or trauma to liver
- Dx: angiogram; EGD will show blood coming out of the ampulla of Vater
- Tx: angioembolization; operation if that fails

GALLBLADDER ADENOCARCINOMA

- Rare although most common CA of the biliary tract
- Four times more common than bile duct CA; most have stones (#1 risk factor)
- Liver – most common site of metastasis
- Porcelain gallbladder – risk of gallbladder CA (15%) → these patients need cholecystectomy
- Dx: MRCP
- 1st spreads to segments IV and V; 1st nodes are the cystic duct nodes (right side)
- Symptoms: jaundice 1st (bile duct invasion with obstruction) then RUQ pain
- Tx: if muscle <u>not</u> involved – cholecystectomy sufficient
  - If in muscle but not beyond – need wedge resection of segments IVb and V
  - If beyond muscle and still resectable – need formal resection of segments IVb and V
- High incidence of tumor implants in trocar sites when discovered after laparoscopic cholecystectomy (laparoscopic approach *contraindicated* for gallbladder CA)
- Overall 5-year survival – 5%

BILE DUCT CANCER (CHOLANGIOCARCINOMA)

- Occurs in elderly; males
- Risk factors: *C. sinensis* infection, ulcerative colitis, choledochal cysts, primary sclerosing cholangitis, chronic bile duct infection

- Symptoms: early – painless jaundice; late – weight loss, pruritus
- Persistent ↑ in bilirubin and alkaline phosphatase
- Dx: MRCP (defines anatomy, looks for mass)
- Invades contiguous structures early
- Discovery of a focal bile duct stenosis in patients without a history of biliary surgery or pancreatitis is highly suggestive of bile duct CA
- Tx (consider surgery if no distant metastases and tumor is resectable):
  - Upper ⅓ (Klatskin tumors)
    - Most common type, worst prognosis, usually unresectable
    - Tx: can try lobectomy and stenting of contralateral bile duct if localized to either the right or left lobe
  - Middle ⅓ – hepaticojejunostomy
  - Lower ⅓ – Whipple
- Palliative stenting for unresectable disease
- Overall 5-year survival rate – 20%

CHOLEDOCHAL CYSTS

- Female gender; Asians; 90% are extrahepatic; 15% CA risk (cholangiocarcinoma)
- Older patients have episodic pain, fever, jaundice, cholangitis
- Infants can have symptoms similar to biliary atresia
- Most are type I – fusiform or saccular dilatation of extrahepatic ducts (very dilated)
- Caused by abnormal reflux of pancreatic enzymes during uterine development
- Tx: cyst excision with hepaticojejunostomy and cholecystectomy usual
- Type IV cysts are partially intrahepatic, and type V (Caroli's disease) are totally intrahepatic → will need partial liver resection or liver TXP

PRIMARY SCLEROSING CHOLANGITIS

- Men in 4th–5th decade
- Can be associated with ulcerative colitis, pancreatitis, diabetes
- Symptoms: jaundice, fatigue, pruritus (from bile acids), weight loss, RUQ pain
- Get multiple strictures throughout the hepatic ducts
- Leads to portal HTN and hepatic failure (progressive fibrosis of intrahepatic and extrahepatic ducts)
- Does not get better after colon resection for ulcerative colitis
- Complications – cirrhosis, cholangiocarcinoma
- Tx: liver TXP needed long term for most; PTC tube drainage, choledochojejunostomy or balloon dilatation of dominant strictures may provide some symptomatic relief
  - Cholestyramine – can ↓ pruritus symptoms (↓ bile acids)
  - UDCA (ursodeoxycholic acid) – can ↓ symptoms (↓ bile acids) and improve liver enzymes

PRIMARY BILIARY CIRRHOSIS

- Women; medium-sized hepatic ducts
- Cholestasis → cirrhosis → portal hypertension
- Symptoms: jaundice, fatigue, pruritus, xanthomas
- Have antimitochondrial antibodies

- Tx: liver TXP; UDCA and cholestyramine for symptoms

CHOLANGITIS

- Usually caused by obstruction of the bile duct (most commonly due to gallstones)
- Can also be caused by indwelling tubes (eg PTC tube)
- Charcot's triad – RUQ pain, fever, jaundice
- Reynolds' pentad – Charcot's triad plus mental status changes and shock (suggests sepsis)
- *E. coli* (#1) and *Klebsiella* – most common organisms
- Colovenous reflux occurs at > 200 mm Hg pressure → systemic bacteremia
- Dx: ↑ AST/ALT, bilirubin, alkaline phosphatase, and WBCs
  - U/S – dilated CBD (> 8 mm, > 10 mm after cholecystectomy) if due to obstruction of the biliary system
- Stricture and hepatic abscess are late complications of cholangitis
- Renal failure – #1 serious complication; related to sepsis
- Other causes – biliary strictures, neoplasm, choledochal cysts, duodenal diverticula
- Tx: *fluid resuscitation and antibiotics initially*
  - Emergent ERCP with sphincterotomy and stone extraction; if ERCP fails, place PTC tube to decompress the biliary system
  - Generally needs cholecystectomy prior to discharge (prevents further episodes)
  - If the patient has cholangitis due to infected PTC tube, change the PTC tube
- Mortality: 5%–10%

SHOCK FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY

- Early (1st 24 hours) – hemorrhagic shock from clip that fell off cystic artery
- Late (after 1st 24 hours) – septic shock from accidental clip on CBD with subsequent cholangitis

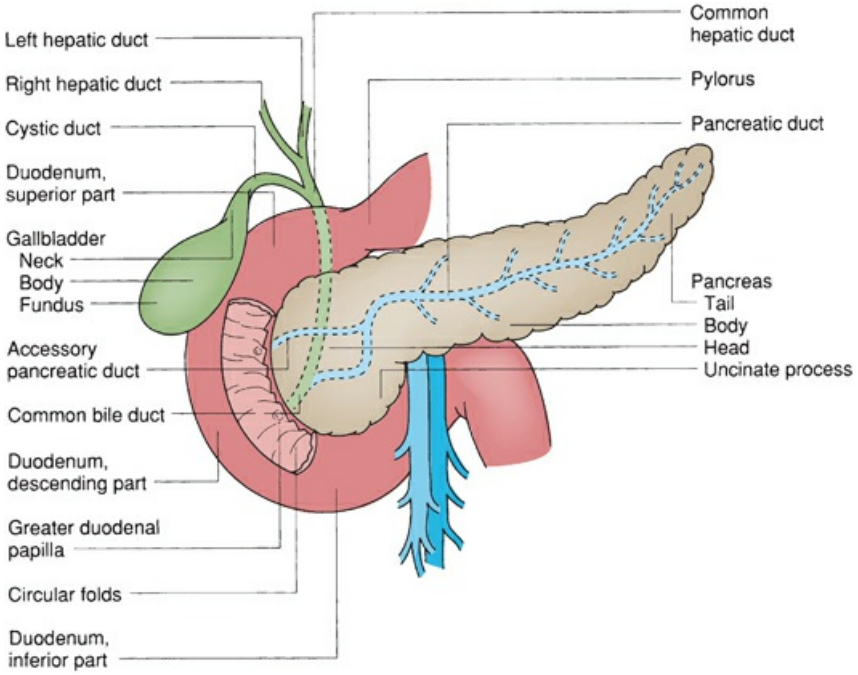
OTHER CONDITIONS

- Adenomyomatosis – thickened nodule of mucosa and muscle associated with Rokitansky–Aschoff sinus
  - Not premalignant; does not cause stones, can cause RUQ pain
  - Tx: cholecystectomy
- Granular cell myoblastoma – benign neuroectoderm tumor of gallbladder
  - Can occur in biliary tract with signs of cholecystitis
  - Tx: cholecystectomy
- Cholesterolosis – speckled cholesterol deposits on the gallbladder wall
- Gallbladder polyps – if > 1 cm, need to worry about malignancy
  - Polyps in patients > 60 years more likely malignant
  - Tx: cholecystectomy
- Delta bilirubin – bound to albumin covalently, half-life of 18 days; may take a while to clear after long-standing jaundice
- Mirizzi syndrome – compression of the common hepatic duct by 1) a stone in the gallbladder infundibulum or 2) inflammation arising from the gallbladder or cystic duct extending to the contiguous hepatic duct, causing common hepatic duct stricture; Tx: cholecystectomy; may need hepaticojejunostomy for hepatic duct stricture

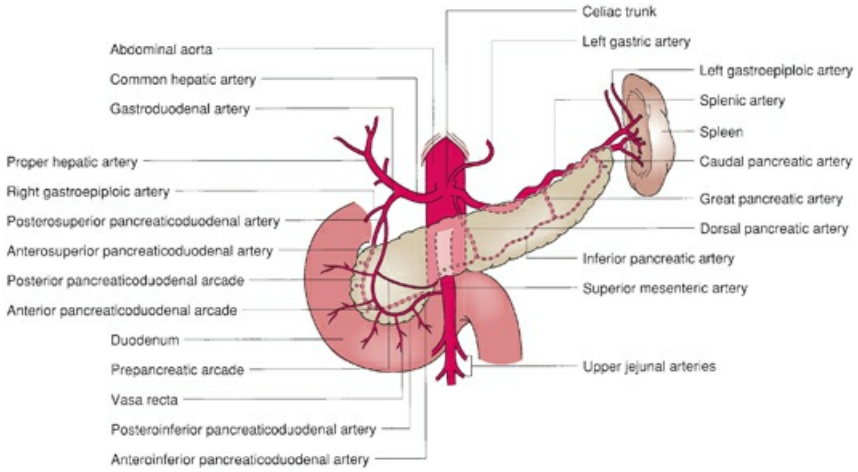
- Ceftriaxone – can cause gallbladder sludging and cholestatic jaundice
- Indications for asymptomatic cholecystectomy – in patients undergoing liver TXP or gastric bypass procedure (if stones are present)

33 Pancreas

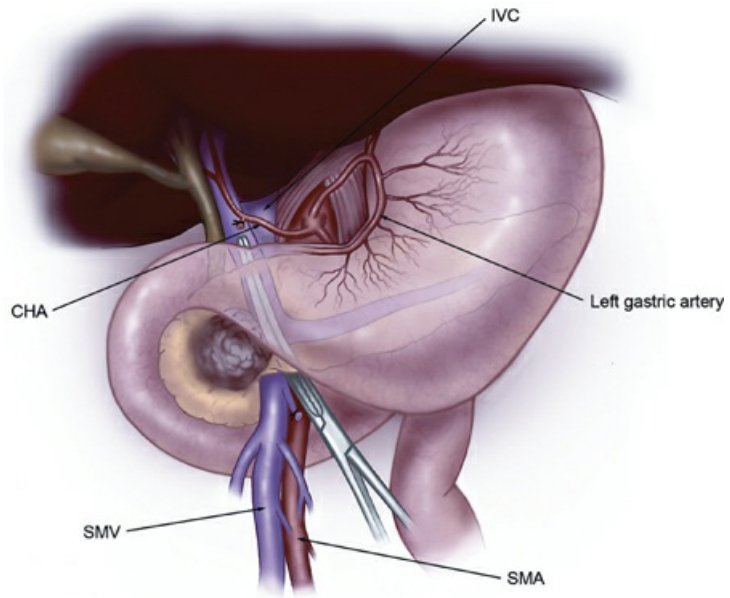
ANATOMY AND PHYSIOLOGY



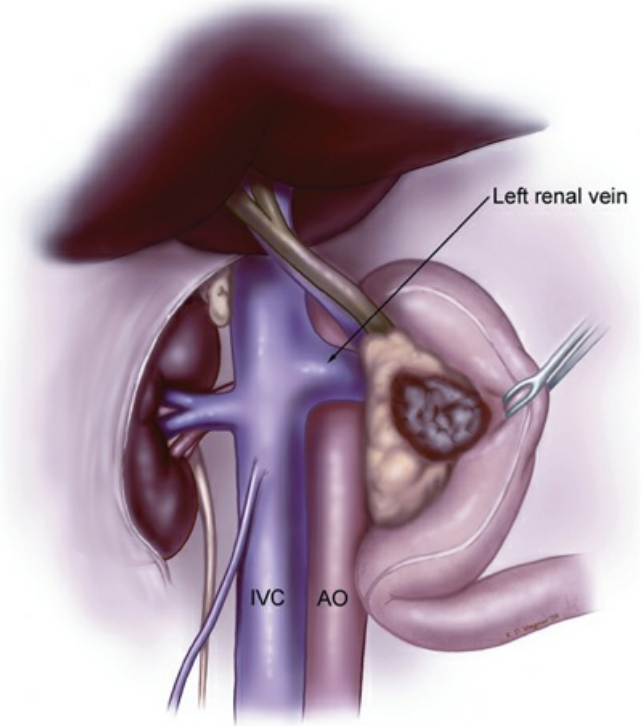
Relation of the pancreas to the duodenum and extrahepatic biliary system.



Arterial supply to the pancreas.



Relationship between the superior mesenteric vein and superior mesenteric artery. (Modified from Evans DB, Lee JE, Tamm EP, et al. Pancreaticoduodenectomy [Whipple operation] and total pancreatectomy for cancer. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)



Kocher maneuver and relationship between the aorta and inferior vena cava. (Modified from Evans DB, Lee JE, Tamm EP, et al. Pancreaticoduodenectomy [Whipple operation] and total pancreatectomy for cancer. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

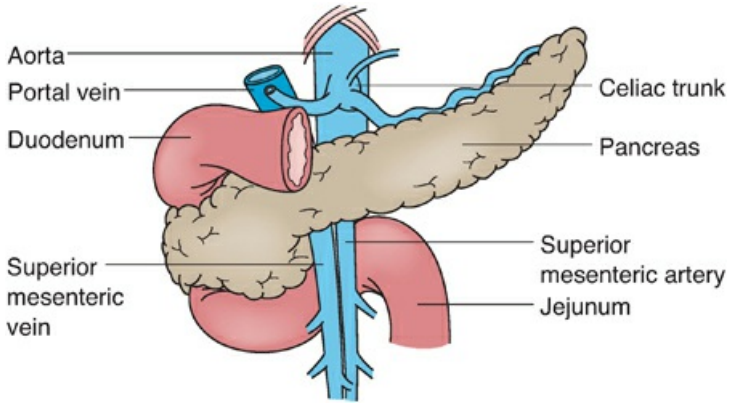
- Head (including uncinate), neck, body, and tail
- Uncinate process – rests on aorta, behind SMV
- SMV and SMA – lay behind neck of pancreas

- Portal vein – forms behind the neck (SMV and splenic vein)
- Blood supply
  - Head – superior (off GDA) and inferior (off SMA) pancreaticoduodenal arteries (anterior and posterior branches for each)
  - Body – great, inferior, and dorsal pancreatic arteries (all off splenic artery)
  - Tail – splenic, gastroepiploic, and caudal pancreatic arteries
- Venous drainage into the portal system
- Lymphatics – celiac and SMA nodes
- Ductal cells – secrete HCO_3^- solution (have carbonic anhydrase)
- Acinar cells – secrete digestive enzymes
- Exocrine function of the pancreas – amylase, lipase, trypsinogen, chymotrypsinogen, carboxypeptidase; HCO_3^-
  - Amylase – only pancreatic enzyme secreted in active form; hydrolyzes alpha 1–4 linkages of glucose chains
- Endocrine function of the pancreas (islet cells)
  - Alpha cells – glucagon
  - Beta cells (at center of islets) – insulin
  - Delta cells – somatostatin
  - PP or F cells – pancreatic polypeptide
  - Islet cells – also produce vasoactive intestinal peptide (VIP), serotonin
- Islet cells receive majority of blood supply related to size
  - After islets, blood goes to acinar cells
- Enterokinase – released by the duodenum, activates trypsinogen to trypsin
  - Trypsin activates other pancreatic enzymes including trypsinogen
- Hormonal control of pancreatic excretion
  - Secretin – ↑ HCO_3^- mostly
  - CCK – ↑ pancreatic enzymes mostly
  - Acetylcholine – ↑ HCO^- and enzymes
  - Somatostatin and glucagons – ↓ exocrine function
  - CCK and secretin – most released by cells in the duodenum
- Ventral pancreatic bud
  - Connected to duct of Wirsung; migrates posteriorly, to the right, and clockwise to fuse with the dorsal bud
  - Forms uncinate and inferior portion of the head
- Dorsal pancreatic bud – body, tail, and superior aspect of the pancreatic head; has duct of Santorini
- Duct of Wirsung – major pancreatic duct that merges with CBD before entering duodenum
- Duct of Santorini – small accessory pancreatic duct that drains directly into duodenum
- Sphincter of Oddi – CCK and glucagon relax the sphincter

ANNULAR PANCREAS

- 2nd portion of duodenum trapped in pancreatic band; can see double bubble on abdominal x-ray; get duodenal obstruction (N/V, abdominal pain)
- Associated with Down syndrome; forms from the ventral pancreatic bud from failure of clockwise rotation

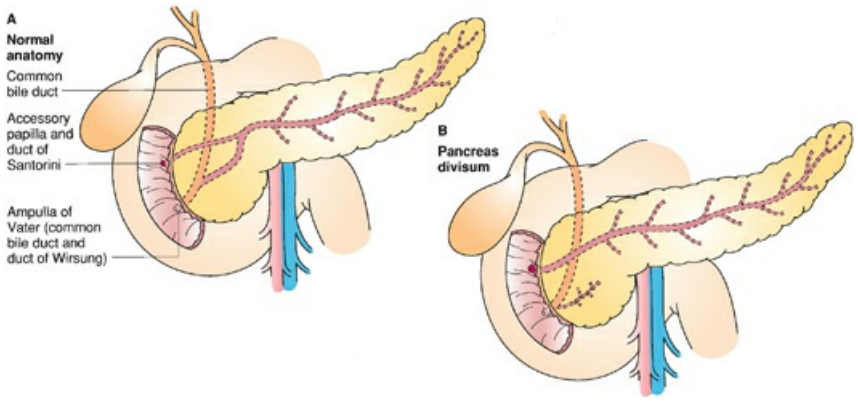
- Tx: duodenojejunostomy or duodenoduodenostomy; possible sphincteroplasty
  - Pancreas not resected



Annular pancreas.

PANCREAS DIVISUM

- Failed fusion of the pancreatic ducts; can result in pancreatitis from duct of Santorini (accessory duct) stenosis
- Most are asymptomatic; some get pancreatitis
- Dx: ERCP – minor papilla will show long and large duct of Santorini; major papilla will show short duct of Wirsung
- Tx: ERCP with sphincteroplasty; open sphincteroplasty if that fails



(A) Normal pancreatic ductal anatomy. *(B)* Pancreas divisum. There is no communication between the duct of Wirsung and the duct of Santorini. The duct of Wirsung is short or absent. Most of the pancreas is drained by the duct of Santorini through the accessory papilla. This anatomy is found in about 10% to 15% of normal individuals.

HETEROTOPIC PANCREAS

- Most commonly found in duodenum
- Usually asymptomatic
- Surgical resection if symptomatic

ACUTE PANCREATITIS

- Gallstones and ETOH most common etiologies in the United States

- Other etiologies – ERCP, trauma, hyperlipidemia, hypercalcemia, viral infection, medications (azathioprine, furosemide, steroids, cimetidine)
- Gallstones – can obstruct the ampulla of Vater, causing impaired extrusion of zymogen granules and activation of degradation enzymes → leads to pancreatic auto-digestion
- ETOH – can cause auto-activation of pancreatic enzymes while still in the pancreas

- Symptoms: epigastric pain radiating to the back; nausea, vomiting, anorexia
  - Can also get jaundice, left pleural effusion, ascites, or sentinel loop (dilated small bowel near the pancreas as a result of the inflammation)
- Mortality rate 10%; hemorrhagic pancreatitis mortality 50%
- MCC death – sepsis
- Pancreatitis without obvious cause → need to worry about malignancy
- Ranson's criteria
  - On admission → age > 55, WBC > 16, glucose > 200, AST > 250, LDH > 350
  - After 48 hours: Hct ↓ 10%, BUN ↑ of 5, Ca < 8, PaO_2 < 60, base deficit > 4, fluid sequestration > 6 L
  - 8 Ranson criteria met → mortality rate near 100%
- Labs: ↑ amylase, lipase, and WBCs
- Ultrasound – needed to check for gallstones and possible CBD dilatation
- Abdominal CT – to check for complications (necrotic pancreas will <u>not</u> uptake contrast)
- Tx: NPO, NG tube, and aggressive fluid resuscitation
  - ERCP is usually not needed in patients with gallstone pancreatitis (the stone usually passes on its own)
  - Antibiotics for stones, severe pancreatitis, failure to improve, or suspected infection
  - TPN may be necessary during recovery period
  - Patients with gallstone pancreatitis should undergo cholecystectomy when recovered from pancreatitis (same hospital admission)
  - Morphine should be avoided as it can contract the sphincter of Oddi and worsen attack
- Bleeding (hemorrhagic pancreatitis)
  - Grey Turner sign – flank ecchymosis
  - Cullen's sign – periumbilical ecchymosis
  - Fox's sign – inguinal ecchymosis
- 15% get pancreatic necrosis – leave sterile necrosis <u>alone</u>
  - Infected necrosis (fever, sepsis, positive blood cultures; may need to sample necrotic pancreatic fluid with CT-guided aspiration to get diagnosis) Tx: need *surgical debridement*
  - Pancreatic abscesses → Tx: need *surgical debridement*
  - CT-guided drainage of infected pancreatic necrosis or pancreatic abscess is generally <u>not</u> effective
  - Gas in necrotic pancreas = infected necrosis or abscess (need open debridement)
- Infection – leading cause of death with pancreatitis; usually GNRs
- Surgery only for infected pancreatitis or pancreatic abscess
- Obesity – most important risk factor for necrotizing pancreatitis
- ARDS – related to release of phospholipases
- Coagulopathy – related to release of proteases
- Pancreatic fat necrosis – related to release of phospholipases
- Mild ↑ amylase and lipase can be seen with cholecystitis, perforated ulcer, sialoadenitis, small bowel obstruction (SBO), and intestinal infarction

PANCREATIC PSEUDOCYSTS

- Most common in patients with chronic pancreatitis; can also occur after acute pancreatitis or pancreatic trauma (generally presenting around 6 weeks after the initial event)
  - Cysts not associated with pancreatitis – need to R/O CA (eg mucinous cystadenocarcinoma)
- Symptoms: vague abdominal discomfort, early satiety, weight loss, bowel obstruction from compression
- Often occurs in the head of the pancreas; is a non-epithelialized sac of pancreatic fluid
- Most resolve spontaneously (especially if < 5 cm)
- Fluid has high amylase
- Tx: *expectant management for 3 months* – (*most resolve on their own*; also allows pseudocyst to mature if cystogastrostomy is required)
  - May need to place these patients on TPN if unable to eat
  - *Surgery only for* continued symptoms (Tx: cystogastrostomy, open or percutaneous) or pseudocysts that are growing (Tx: resection to rule out CA)
- Complications of pancreatic pseudocyst – infection of cyst, portal or splenic vein thrombosis
- Incidental cysts not associated with pancreatitis should be *resected* (worry about intraductal papillary-mucinous neoplasms [IPMNs] or mucinous cystadenocarcinoma) *unless* the cyst is purely serous and non-complex
- Non-complex, purely serous cystadenomas have an extremely low malignancy risk (< 1%) and can be followed

PANCREATIC FISTULAS

- Most close spontaneously (especially if low output < 200 cc/day)
- Are usually associated with pancreatic surgery
- Tx: allow drainage, NPO, TPN, octreotide
  - If failure to resolve with medical management, can try ERCP, sphincterotomy, and pancreatic stent placement (fistula will usually close, then remove stent)
  - Unusual to have to operate on these patients

PANCREATITIS-ASSOCIATED PLEURAL EFFUSION (OR ASCITES)

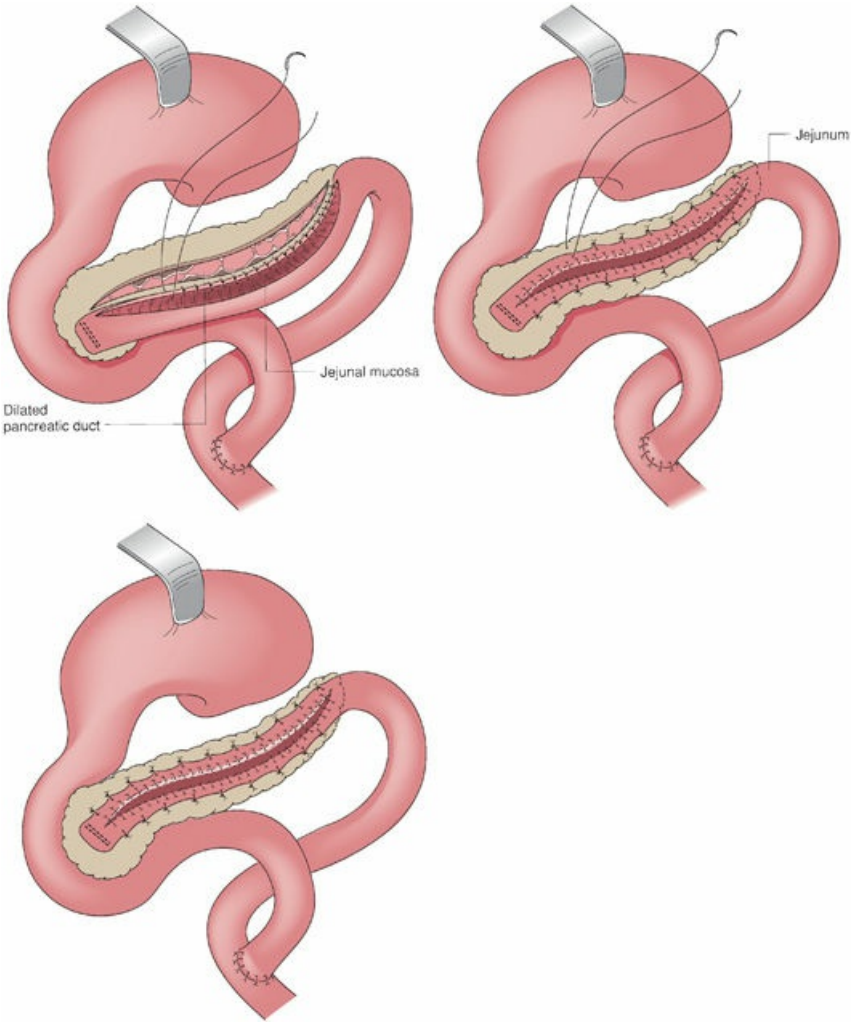
- Caused by retroperitoneal leakage of pancreatic fluid from the pancreatic duct or a pseudocyst (is not a pancreatic–pleural fistula); majority close on their own
- Tx: thoracentesis (or paracentesis) followed by conservative Tx (NPO, TPN, and octreotide)
  - Amylase will be elevated in the fluid (> 1,000)

CHRONIC PANCREATITIS

- Corresponds to irreversible parenchymal fibrosis
- ETOH most common cause; idiopathic 2nd most common
- Pain most common problem; anorexia, weight loss, malabsorption, steatorrhea
- Endocrine function usually preserved (Islet cell preserved); exocrine function decreased
- Can cause malabsorption of fat-soluble vitamins (Tx: pancrelipase; decreases steatorrhea)
- Dx: abdominal CT will show shrunken pancreas with calcifications

- Ultrasound – shows pancreatic ducts > 4 mm, cysts, and atrophy
- ERCP – very sensitive at diagnosing chronic pancreatitis
- Advanced disease – chain of lakes → alternating segments of dilation and stenosis in pancreatic duct

- Tx: supportive, including pain control and nutritional support (pancrelipase)
- Surgical indications – pain that interferes with quality of life, nutrition abnormalities, addiction to narcotics, failure to rule out CA, biliary obstruction
- Surgical options
  - Puestow procedure – lateral pancreaticojejunostomy, for enlarged ducts > 8 mm (most patients improve) → open along main pancreatic duct and drain into jejunum
  - Distal pancreatic resection – for normal or small ducts and only distal portion of the gland is affected
  - Whipple – for normal or small ducts with isolated pancreatic head disease
  - Beger-Frey (duodenal preserving head "core-out") – for normal or small ducts with isolated pancreatic head enlargement
  - Bilateral thoracoscopic splanchnicectomy or celiac ganglionectomy may be used for pain control



Lateral pancreaticojejunostomy.

- Common bile duct (CBD) stricture – causes CBD dilation; Dx: MRCP; Tx:

hepaticojejunostomy or choledochojejunostomy for pain, jaundice, progressive cirrhosis, or cholangitis (make sure the stricture is not pancreatic CA)

- Splenic vein thrombosis – chronic pancreatitis most common cause
  - Can get bleeding from isolated gastric varices that form as collaterals
  - Tx: splenectomy for isolated bleeding gastric varices

PANCREATIC INSUFFICIENCY

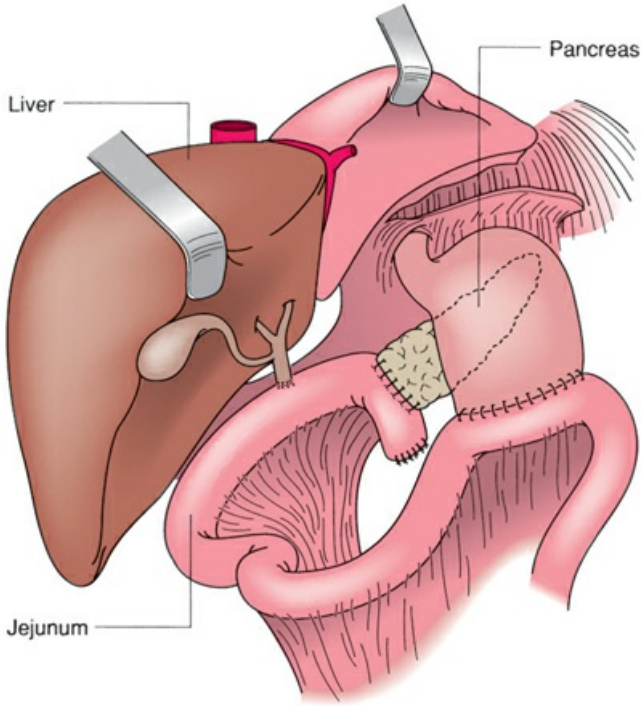
- Usually the result of long-standing pancreatitis or occurs after total pancreatectomy (over 90% of the function must be lost)
- Generally refers to exocrine function
- Symptoms: malabsorption and steatorrhea
- Dx: fecal fat testing
- Tx: high-carbohydrate, high-protein, low-fat diet; add pancreatic enzymes (Pancrease)

JAUNDICE WORKUP

- Ultrasound 1st
  - Positive CBD stones, no mass → ERCP (allows extraction of stones)
  - No CBD stones, no mass → MRCP
  - Positive mass → MRCP

PANCREATIC ADENOCARCINOMA

- Male predominance; usually 6th–7th decades of life
- Symptoms: weight loss (most common symptom), jaundice, pain (epigastric or back)
- 5-year survival rate with resection – 20%
- Risk factors – tobacco #1
- CA 19-9 – serum marker for pancreatic CA
- 95% have p16 mutation (tumor suppressor, binds cyclin complexes)
- Lymphatic spread 1st
- 70% are in the head
  - 50% invade portal vein, SMV, or retroperitoneum at time of diagnosis (unresectable disease)
  - Metastases to peritoneum, omentum, or liver – indicate unresectable disease
  - Metastases to celiac or SMA nodal system (nodal systems outside area of resection) – indicate unresectable disease
  - Most cures in patients with pancreatic head disease
- 90% are ductal adenocarcinoma
  - Others (more favorable prognosis) – papillary or mucinous cyst-adenocarcinoma



Reconstruction after standard pancreaticoduodenectomy (Whipple; the gallbladder is usually resected with the procedure).

- Labs: typically show ↑ conjugated bilirubin and alkaline phosphatase
- These patients usually do not get pancreatitis
- Patients with a resectable mass (and no signs of metastatic disease) in the pancreas do not need a biopsy because you are taking it out regardless. If the patient appears to have metastatic disease, a biopsy (CT guided or endoscopic U/S) is warranted to direct therapy
- MRCP good at differentiating dilated ducts secondary to chronic pancreatitis versus CA
  - Signs of CA on MRCP – duct with irregular narrowing, displacement, destruction; can also detect vessel involvement
- Abdominal CT – may show the lesion and double-duct sign for pancreatic head tumors (dilation of both the pancreatic duct and CBD)
- For unresectable disease, consider palliation with biliary stents (for biliary obstruction), duodenal stents (for duodenal obstruction), and celiac plexus ablation (for pain)
- Complications from Whipple – delayed gastric emptying #1 (Tx – metoclopramide), fistula (Tx: conservative therapy), leak (place drains and Tx like a fistula), marginal ulceration (Tx: PPI)
- Bleeding after Whipple or other pancreatic surgery – go to angio for *embolization* (the tissue planes are very friable early after surgery, and bleeding is hard to control operatively)
- Chemo-XRT usual postop (gemcitabine)
- Prognosis for non-metastatic disease related to nodal invasion and ability to get a clear margin

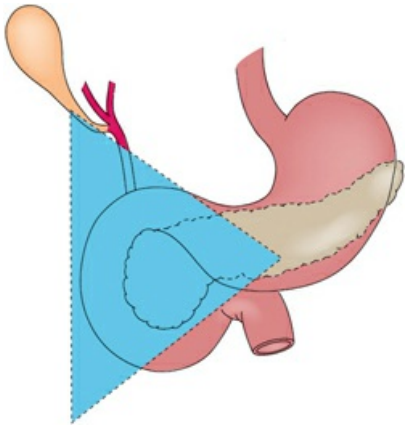
NON-FUNCTIONAL ENDOCRINE TUMORS

- Represent ⅓ of pancreatic endocrine neoplasms
- 90% of the nonfunctional tumors are malignant
- Tend to have a more indolent and protracted course compared with pancreatic adenocarcinoma

- Resect these lesions: metastatic disease precludes resection
- 5FU and streptozocin may be effective
- Liver metastases most common

FUNCTIONAL ENDOCRINE PANCREATIC TUMORS

- Represents ⅔ of pancreatic endocrine neoplasms
- Octreotide – effective for symptoms with insulinoma, glucagonoma, gastrinoma, and VIPoma
- Most common in pancreatic head – gastrinoma, somatostatinoma
- All tumors can respond to debulking
- Liver metastatic spread – 1st for all
- Insulinoma
  - Most common islet cell tumor of the pancreas
  - Symptoms: Whipple's triad – fasting hypoglycemia (< 50), symptoms of hypoglycemia (palpitations, ↑ HR, and diaphoresis), and relief with glucose
  - 90% are benign and evenly distributed throughout pancreas
  - Dx: insulin to glucose ratio > 0.4 after fasting; ↑ C peptide and proinsulin (→ if not elevated, suspect Munchausen's syndrome)
  - Tx: enucleate if < 2 cm; formal resection if > 2 cm
    - For metastatic disease → 5-FU and streptozocin; octreotide
    - Diazoxide for symptoms
- Gastrinoma (Zollinger–Ellison syndrome [ZES])
  - Most common pancreatic islet cell tumor in MEN-1 patients
  - 50% malignant and 50% multiple
  - 75% spontaneous and 25% MEN-1
  - Majority in gastrinoma triangle – common bile duct, neck of pancreas, third portion of the duodenum
  - Symptoms: refractory or complicated peptic ulcer disease (despite aggressive PPI and *H. pylori* eradication therapy) and diarrhea (improved with PPI)
  - Can have multiple ulcers or ulcers that extend beyond 1st portion of the duodenum



Most gastrinomas are found within the gastrinoma triangle.

  - Serum gastrin usually > 200 (1,000s is diagnostic)
  - Stomach basal acid output > 15 mEq/hour
  - Secretin stimulation test – ZES patients: ↑ gastrin (> 200); normal patients: ↓ gastrin

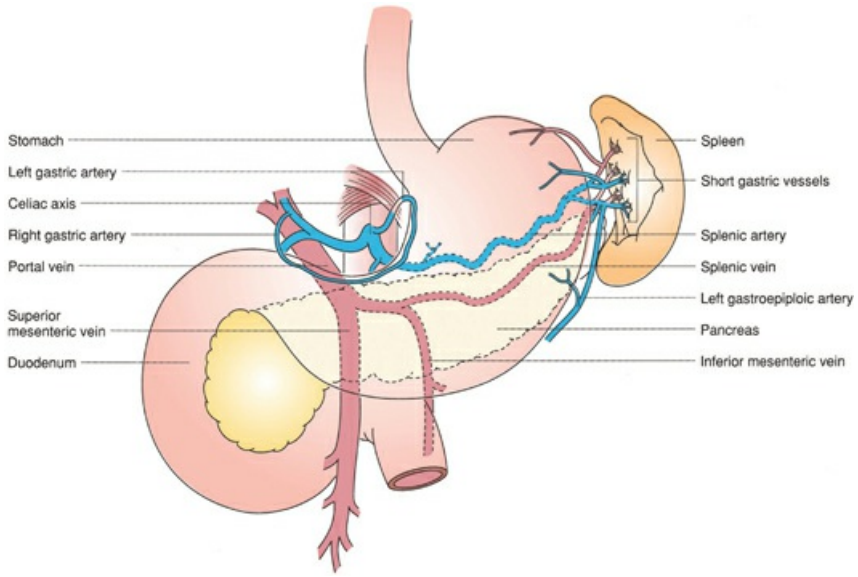
- Octreotide scan – single best study for localizing tumor
- Tx: enucleation if < 2 cm; formal resection if > 2 cm
  - Malignant disease → excise suspicious nodes
  - Cannot find tumor → perform duodenostomy and look inside duodenum for tumor (15% of microgastrinomas there)
  - Duodenal tumor – resection with primary closure; may need Whipple if extensive; be sure to check pancreas for primary
  - Debulking – can improve symptoms; PPI helps palliate metastatic disease

- Glucagonoma
  - Symptoms: diabetes, stomatitis, dermatitis (rash – necrolytic migratory erythema), weight loss
  - Diagnosis: fasting glucagon level
  - Most malignant; most in distal pancreas
  - Zinc, amino acids, or fatty acids may treat skin rash
- VIPoma (Verner–Morrison syndrome)
  - Symptoms: watery diarrhea, hypokalemia, and achlorhydria (WDHA)
  - Hypokalemia from diarrhea
  - Dx: exclude other causes of diarrhea; ↑ VIP levels
  - Most malignant; most in distal pancreas, 10% extrapancreatic (retroperitoneal, thorax)
- Somatostatinoma
  - Very rare
  - Symptoms: diabetes, gallstones, steatorrhea
  - Diagnosis: fasting somatostatin level
  - Most malignant; most in head of pancreas
  - Perform cholecystectomy with resection

34 Spleen

ANATOMY AND PHYSIOLOGY

- Short gastrics and splenic artery are end arteries
- Splenic vein is posterior and inferior to the splenic artery
- Spleen serves as an antigen-processing center for macrophages
- Is the largest producer of IgM (most common antibody in the spleen)
- 85% red pulp – acts as a filter for aged or damaged RBCs
  - Pitting – removal of abnormalities in RBC membrane
    - Howell–Jolly bodies – nuclear remnants
    - Heinz bodies – hemoglobin
  - Culling – removal of less deformable RBCs
- 15% white pulp – immunologic function; contains lymphocytes and macrophages
  - Major site of bacterial clearance that lacks preexisting antibodies
  - Site of removal of poorly opsonized bacteria, particles, and cellular debris
  - Antigen processing occurs with interaction between dendritic cells/macrophages and helper T cells



The arterial blood flow to the spleen is derived from the splenic artery, the left gastroepiploic artery, and the short gastric arteries (vasa brevia). The venous drainage into this portal vein is also shown.

- Tuftsin – an opsonin; facilitates phagocytosis → produced in spleen
- Properdin – activates alternate complement pathway → produced in spleen
- Hematopoiesis – occurs in spleen before birth and in conditions such as myeloid dysplasia
- Spleen serves as a reservoir for platelets
- Accessory spleen (20%) – most commonly found at *splenic hilum*
- Indication for splenectomy – idiopathic thrombocytopenic purpura (ITP) far greater than

for thrombotic thrombocytopenic purpura (TTP)
- ITP most common nontraumatic condition requiring splenectomy

IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)

- This can occur from many etiologies – drugs, viruses, etc.
- Caused by anti-platelet antibodies (IgG) – bind platelets; results in decreased platelets
- Petechiae, gingival bleeding, bruising, soft tissue ecchymosis
- Spleen is normal
- In children < 10 years, ITP usually resolves spontaneously (avoid splenectomy in children)
- Tx: *steroids* (primary therapy); gammaglobulin if steroid resistant
- Splenectomy indicated for those who fail steroids removes IgG production and source of phagocytosis; 80% respond after splenectomy
- Give platelets after ligation of the splenic artery

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

- Associated with medical reactions, infections, inflammation, autoimmune disease
- Loss of platelet inhibition – leads to thrombosis and infarction, profound thrombocytopenia
- Purpura, fever, mental status changes, renal dysfunction, hematuria, hemolytic anemia
- 80% respond to medical therapy
- Tx: *plasmapheresis* (primary); immunosuppression
- Death most commonly due to intracerebral hemorrhage or acute renal failure
- Splenectomy *rarely* indicated

POST-SPLENECTOMY SEPSIS SYNDROME (PSSS)

- 0.1% risk after splenectomy; ↑ risk in children
- *S. pneumoniae* (#1), *H. influenzae*, *N. meningitidis* – most common
- Secondary to specific lack of immunity (immunoglobulin, IgM) to capsulated bacteria
- Highest in patients with splenectomy for hemolytic disorders or malignancy
- Children also have ↑ risk of mortality after developing PSSS
- Try to wait until at least 5 years old before performing splenectomy → allows antibody formation; child can get fully immunized
- Most episodes occur within 2 years of splenectomy
- Children < 10 years should be given prophylactic antibiotics for 6 months (daily Augmentin)
- Vaccines needed *before* splenectomy – *Pneumococcus*, *Meningococcus*, *H. influenzae*
- Give vaccines at least 14 days before elective surgery or 14 days after emergency surgery
- Inform parents to take child to the ED for any signs of infection so IV antibiotics can be started

Definition of Hypersplenism

Decrease in circulating cell count of erythrocytes and/or platelets and/or leukocytes

and

Normal compensatory hematopoietic responses present in bone marrow

and

Correction of cytopenia by splenectomy

with or without

HEMOLYTIC ANEMIAS: MEMBRANE PROTEIN DEFECTS

- Spherocytosis
  - Most common congenital hemolytic anemia requiring splenectomy
  - Spectrin deficit (membrane protein) deforms RBCs and leads to splenic sequestration (hypersplenism)
  - Causes pigmented stones, anemia, reticulocytosis, jaundice, splenomegaly
  - Try to perform splenectomy after age 5; give immunizations first
  - Tx: splenectomy and cholecystectomy
  - Splenectomy curative
- Elliptocytosis
  - Symptoms and mechanism similar to spherocytosis; less common
  - Spectrin and protein 4.1 deficit (membrane protein)

HEMOLYTIC ANEMIAS: NON–MEMBRANE PROTEIN DEFECTS

- Pyruvate kinase deficiency
  - Results in congenital hemolytic anemia
  - Causes altered glucose metabolism; RBC survival enhanced by splenectomy
  - Is the most common congenital hemolytic anemia not involving a membrane protein that requires splenectomy
- G6PD deficiency
  - Precipitated by infection, certain drugs, fava beans
  - Splenectomy usually not required
- Warm antibody–type acquired immune hemolytic anemia
  - MC autoimmune hemolytic disease
  - Indication for splenectomy if refractory
- Sickle cell anemia – HgbA replaced with HgbS
  - Spleen usually autoinfarcts and splenectomy not required
- Beta thalassemia
  - Most common thalassemia; due to persistent HgbF
  - Major – both chains affected; minor – 1 chain, asymptomatic
  - Symptoms: pallor, retarded body growth, head enlargement
  - Splenectomy (if patient has splenomegaly) may ↓ hemolysis and symptoms
  - Most die in teens secondary to hemosiderosis
  - Medical Tx: blood transfusions and iron chelators (deferoxamine, deferiprone)

HODGKIN'S DISEASE

- A – asymptomatic
- B – symptomatic (night sweats, fever, weight loss) → unfavorable prognosis
- Stage I – 1 area or 2 contiguous areas on the same side of diaphragm
- Stage II – 2 non-contiguous areas on the same side of diaphragm
- Stage III – involved on each side of diaphragm
- Stage IV – liver, bone, lung, or any other non-lymphoid tissue except spleen
- See Reed–Sternberg cells

- Lymphocyte predominant – best prognosis
- Lymphocyte depleted – worst prognosis
- Nodular sclerosing – most common
- Lymphoma workup – need 1) core needle biopsy of lymph node, 2) bone marrow biopsy, and 3) gallium MRI or PET scan of the liver and spleen
- Tx: chemo
- MCC of chylous ascites – *lymphoma*

NON-HODGKIN'S LYMPHOMA

- Worse prognosis than Hodgkin's; 90% are B-cell lymphomas
- Generally systemic disease by the time the diagnosis is made
- Tx: chemo

OTHER CONDITIONS

- Hairy cell leukemia – Tx: rarely need splenectomy
- Spontaneous splenic rupture – mononucleosis, malaria, sepsis, sarcoid, leukemia, polycythemia vera
- Splenosis – splenic implants; usually related to trauma
- Hyposplenism – see Howell–Jolly bodies
- Pancreatitis – most common cause of splenic artery or splenic vein thrombosis
- Postsplenectomy changes – ↑ RBCs, ↑ WBCs, ↑ platelets; if platelets > 1×10^6, give ASA
- Hemangioma – #1 splenic tumor overall; #1 benign splenic tumor; Tx: splenectomy if symptomatic
- Non-Hodgkin's lymphoma – #1 malignant splenic tumor; MCC of splenomegaly
- Angiosarcoma – #1 malignant non-blood cell splenic tumor
- Splenic cysts – surgery if symptomatic or > 10 cm
- Sarcoidosis of spleen – anemia, ↓ platelets; Tx: splenectomy for symptomatic splenomegaly
- Felty's syndrome – rheumatoid arthritis, hepatomegaly, splenomegaly, and pancytopenia
  - Tx: methotrexate; treatment for RA usually helps
  - Splenectomy for symptomatic splenomegaly
- Splenic abscess – Tx: splenectomy usual (bleeding risk with percutaneous drainage; usually *Streptococcus*)
- Echinococcal splenic cyst – Tx: splenectomy
- Dermoid cyst – splenectomy

Results of Splenectomy/Hyposplenic Condition

ERYTHROCYTES

- Howell–Jolly bodies (nuclear fragments)
- Heinz bodies (hemoglobin deposits)
- Pappenheimer bodies (iron deposits)
- Target cellsSpur cells (acanthocytes)

PLATELETS

- Transient thrombocytosis

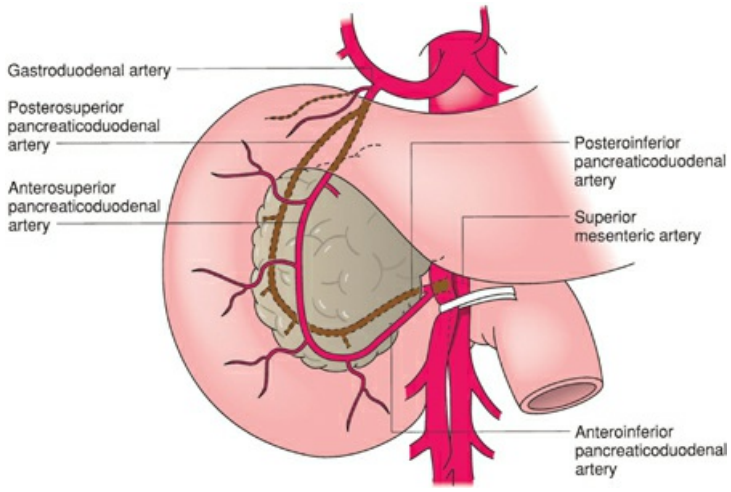
LEUKOCYTES

- Transient leukocytosis
- Persistent lymphocytosis
- Persistent monocytosis

35 Small Bowel

ANATOMY AND PHYSIOLOGY

- Small intestine – nutrient and water absorption
- Large intestine – water absorption
- Duodenum
  - Bulb (1st portion) – 90% of ulcers here
  - Descending (2nd) – contains ampulla of Vater (duct of Wirsung) and duct of Santorini
  - Transverse (3rd)
  - Ascending (4th)
  - Descending and transverse portions are retroperitoneal
  - 3rd and 4th portions – transition point at the acute angle between the aorta (posterior) and SMA (anterior)
  - Vascular supply is superior (off gastroduodenal artery) and inferior (off SMA) pancreaticoduodenal arteries
    - Both have anterior and posterior branches
    - Many communications between these arteries



Arterial supply to the duodenum.

- Jejunum
  - 100 cm long; long vasa recta, circular muscle folds
  - Is the maximum site of all absorption except for B_{12} (terminal ileum), bile acids (ileum – non-conjugated; terminal ileum – conjugated), iron (duodenum), and folate (terminal ileum)
  - 95% of NaCl absorbed and 90% of water absorbed in jejunum
  - Vascular supply – SMA
- Ileum – 150 cm long; short vasa recta, flat
  - Vascular supply – SMA

- Intestinal brush border – maltase, sucrase, limit dextrinase, lactase
- Normal sizes – small bowel/transverse colon/cecum → 3/6/9 cm
- SMA eventually branches into the ileocolic artery
- Cell types
  - Absorptive cells
  - Goblet cells (mucin secretion)
  - Paneth cells (secretory granules, enzymes)
  - Enterochromaffin cells (APUD, 5-hydroxytryptamine release, carcinoid precursor)
  - Brunner's glands (alkaline solution)
  - Peyer's patches (lymphoid tissue); increased in the ileum
  - M cells – antigen-presenting cells in intestinal wall
- IgA – released into gut; also in mother's milk
- Fe – small bowel has both heme and Fe transporters
- Migrating motor complex (gut motility)
  - Phase I – rest
  - Phase II – acceleration and gallbladder contraction
  - Phase III – peristalsis
  - Phase IV – deceleration
  - Motilin is most important hormone in migrating motor complex (acts on phase III peristalsis)
- Bile salts (acids)
  - 95% of bile salts are reabsorbed
    - 50% passive absorption (non-conjugated bile salts) – 45% ileum, 5% colon
    - 50% active resorption (conjugated bile salts) in terminal ileum (Na/K ATPase); conjugated bile salts are absorbed only in the terminal ileum
  - Gallstones form after terminal ileum resection from malabsorption of bile salts (get cholesterol stones)

SHORT-GUT SYNDROME

- Diagnosis is made on symptoms, not length of bowel
- Symptoms: steatorrhea, weight loss, nutritional deficiency
- Lose fat, B_{12}, electrolytes, water
- Sudan red stain – checks for fecal fat
- Schilling test – checks for B_{12} absorption (radiolabeled B_{12} in urine)
- Probably need at least 75 cm to survive off TPN; 50 cm with competent ileocecal valve
- Tx: restrict fat, PPI to reduce acid, Lomotil (diphenoxylate and atropine)

CAUSES OF STEATORRHEA

- Gastric hypersecretion of acid → ↓ pH → ↑ intestinal motility; interferes with fat absorption
- Interruption of bile salt resorption (eg terminal ileum resection) interferes with micelle formation and fat absorption
- Decreased pancreatic enzymes (eg chronic pancreatitis)
- Steatorrhea causes malnutrition with weight loss as well as deficiency in fat-soluble vitamins (A, D, E, K) and essential fatty acids

NONHEALING FISTULA

- "FRIENDSS" – mnemonic for nonhealing fistula causes: foreign body, radiation, inflammatory bowel disease, epithelialization, neoplasm, distal obstruction, sepsis/infection, steroids
- High-output fistulas are more likely with proximal bowel (duodenum or proximal jejunum) and are less likely to close with conservative management
- Colonic fistulas are more likely to close than those in small bowel
- Patients with persistent fever or sepsis – need to check for abscess (fistulogram, abdominal CT, upper GI with small bowel follow-through)
- Can cause fluid/electrolyte loss, nutritional depletion, and skin erosion of abdominal wall
- Most fistulas are iatrogenic and treated conservatively 1st → NPO, TPN, skin protection (stoma appliance), octreotide
- Majority close spontaneously without surgery
- Surgical options: resect bowel segment containing fistula and perform primary anastomosis

BOWEL OBSTRUCTION

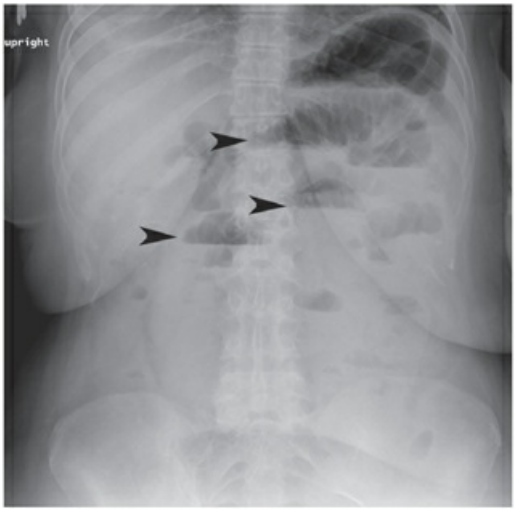
- Without previous surgery (most common)
  - Small bowel – hernia
  - Large bowel – cancer
- With previous surgery (most common)
  - Small bowel – adhesions
  - Large bowel – cancer

Symptoms and Signs of Bowel Obstruction

Symptom or Sign	Proximal Small Bowel (Open Loop)	Distal Small Bowel (Open Loop)	Small Bowel (Closed Loop)	Colon and Rectum
Pain	Intermittent, intense, colicky; often relieved by vomiting	Intermittent to constant	Progressive, intermittent constant; rapidly worsens	Continuous
Vomiting	Large volumes; bilious and frequent	Low volume and frequency; progressively feculent with time	May be prominent (reflex)	Intermittent, not prominent; feculent when present
Tenderness	Epigastric or periumbilical; quite mild unless strangulation is present	Diffuse and progressive	Diffuse, progressive	Diffuse
Distention	Absent	Moderate to marked	Often absent	Marked
Obstipation	May not be present	Present	May not be present	Present

Adapted from Schuffler MD, Sinanan MN. Intestinal obstruction and pseudo-obstruction. In: Sleisenger MH, Fordtran JS, eds. *Gastrointestinal Disease*. 5th ed. Philadelphia, PA: WB Saunders; 1993:898.

- Symptoms: nausea and vomiting, crampy abdominal pain, failure to pass gas or stool
- Abdominal x-ray: air–fluid level, distended loops of small bowel, distal decompression



Plain upright abdominal film of a patient with small intestinal obstruction. Note the air–fluid levels in the stomach and multiple dilated loops of small intestine (*black arrows*) and absence of air in the colon or rectum.

- 3rd spacing of fluid into bowel lumen occurs – need aggressive fluid resuscitation
- Air with bowel obstruction – from swallowed nitrogen
- Tx: bowel rest, NG tube, IV fluids → cures 80% of partial SBO, 40% of complete SBO
- Surgical indications: progressing pain, peritoneal signs, fever, increasing WBCs (all signs of strangulation or perforation), or failure to resolve
- Obstruction from hernias should all be operated on to eliminate the hernia (either emergently if incarcerated or electively if reducible)

GALLSTONE ILEUS

- Small bowel obstruction from gallstone usually in the terminal ileum
- Classically see air in the biliary tree in a patient with small bowel obstruction
- Caused by a fistula between the gallbladder and second portion of duodenum
- Tx: remove stone from terminal ileum
  - Can leave gallbladder and fistula if patient too sick
  - If not too sick, perform cholecystectomy and close duodenum

MECKEL'S DIVERTICULUM

- 2 ft from ileocecal valve; 2% of population; usually presents in 1st 2 years of life with bleeding; is a true diverticulum
- Caused by failure of closure of the omphalomesenteric duct
- Accounts for 50% of all painless lower GI bleeds in children < 2 years
- Pancreas tissue – most common tissue found in Meckel's (can cause diverticulitis)
- Gastric mucosa – most likely to be symptomatic (bleeding most common)
- Obstruction – most common presentation in adults
- Incidental → usually not removed unless gastric mucosa suspected (diverticulum feels thick) or has a very narrow neck
- Dx: can get a Meckel's scan (^{99}Tc) if having trouble localizing (mucosa lights up)
- Tx: diverticulectomy for uncomplicated diverticulitis or bleeding
  - Need segmental resection for complicated diverticulitis (eg perforation), neck > ⅓ the

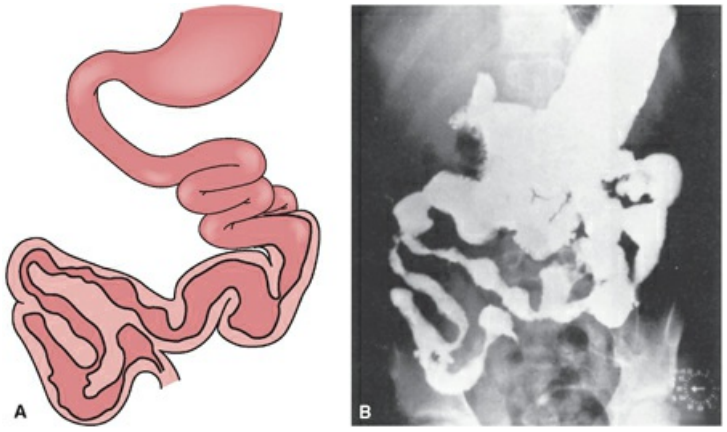
diameter of the normal bowel lumen, or if diverticulitis involves the base

DUODENAL DIVERTICULA

- Need to rule out gallbladder-duodenal fistula
- Observe unless perforated, bleeding, causing obstruction, or highly symptomatic
- Frequency of diverticula: duodenal > jejunal > ileal
- Tx: segmental resection if significantly symptomatic and outside the 2nd portion of the duodenum
  - If juxta-ampullary usually can't get resection and need choledochojejunostomy for biliary or ERCP with stent for pancreatitis symptoms (*avoid* Whipple here)

CROHN'S DISEASE

- Inflammatory bowel disease causing intermittent abdominal pain, diarrhea, and weight loss; can also cause bowel obstructions and fistulas
- 15–35 years old at 1st presentation; ↑ in Ashkenazi Jews
- Extraintestinal manifestations – arthritis, arthralgias, pyoderma gangrenosum, ocular diseases, growth failure, megaloblastic anemia from folate and vitamin B_{12} malabsorption
- Can occur anywhere from mouth to anus; usually spares rectum
- Terminal ileum – most commonly involved bowel segment
- Anal/perianal disease – 1st presentation in 5% (MC: large skin tags – *do not resect*)
- Most common sites for initial presentation
  - Terminal ileum and cecum – 40%
  - Colon only – 35%
  - Small bowel only – 20%
  - Perianal – 5%
- Dx: colonoscopy with biopsies and enteroclysis can help make the diagnosis



Typical radiographic appearance of extensive jejunoileal Crohn's disease.

- Pathology – transmural involvement, segmental disease (skip lesions), cobblestoning, narrow deep ulcers, creeping fat
- Medical Tx: sulfasalazine and loperamide for maintenance; steroids for acute flares
  - Remicade (infliximab; TNF-α inhibitor) – for fistulas or steroid-resistant disease
  - Flagyl – good for fistulas and perianal disease
  - Add Cipro and Flagyl for acute flares if worried about infection or toxic megacolon/colitis

- No agents affect the natural course of disease
- TPN – may induce remission and fistula closure with small bowel Crohn's disease

- 90% eventually need an operation
- Complications related to Crohn's – unlike ulcerative colitis, surgery is not curative
  - Obstruction – often partial and can be initially treated conservatively
  - Abscess – usually treated with percutaneous drainage
  - Toxic megacolon/colitis – unusual but can occur; surgery if refractory
  - Hemorrhage – unusual in Crohn's but can occur
  - Blind loop obstruction – need resection
  - Fissures – *no lateral internal sphincteroplasty in patients with Crohn's disease*
  - Enterocutaneous fistula – can usually be treated conservatively
  - Perineal fistula – rule out abscess; use draining setons; let heal on its own
  - Anorectovaginal fistulas – may need rectal advancement flap; possible colostomy
  - Do not need clear margins; just get 2 cm away from gross disease with surgery
- Patients with diffuse severe disease of colon – proctocolectomy and ileostomy the procedures of choice *(no pouches or ilio-anal anastomosis with Crohn's)*
- Incidental finding of inflammatory bowel disease in patient with presumed appendicitis who has normal appendix – Tx: remove appendix if cecum not involved (avoids future confounding diagnosis)
- Stricturoplasty (longitudinal incision through stricture, close transversely)
  - Consider if patient has multiple bowel strictures to save small bowel length
  - Probably not good for patient's 1st operation as it leaves disease behind
  - 10% leakage/abscess/fistula rate with stricturoplasty (all of which can usually be treated conservatively)
- 50% recurrence rate requiring surgery for Crohn's disease after resection
- Crohn's pancolitis – same colon CA risk as ulcerative colitis
- Complications from removal of terminal ileum
  - ↓ B_{12} uptake can result in megaloblastic anemia
  - ↓ bile salt uptake causes osmotic diarrhea (bile salts) and steatorrhea (fat) in colon
  - ↓ oxalate binding to calcium secondary to ↑ intraluminal fat (fat binds Ca) → oxalate then gets absorbed in colon → released in urine → Ca oxalate kidney stones (hyperoxaluria)
  - Gallstones can form after terminal ileum resection from malabsorption of bile salts

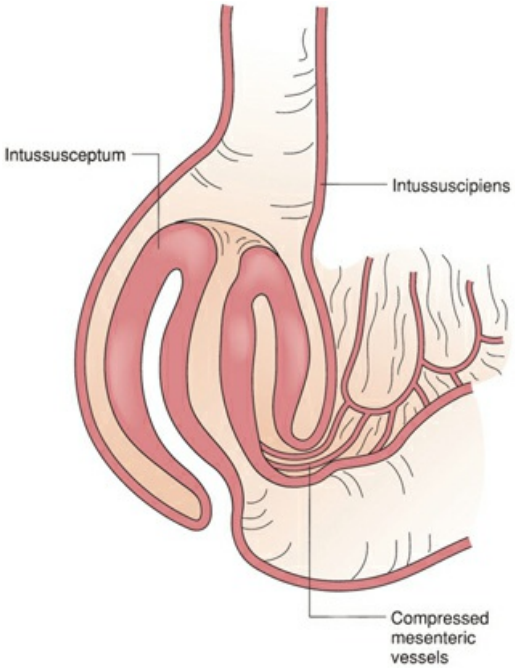
CARCINOID

- Serotonin is produced by Kulchitsky cells (enterochromaffin cell or argentaffin cell)
  - Part of amine precursor uptake decarboxylase system (APUD)
  - 5-HIAA is a breakdown product of serotonin – can measure this in urine
- Carcinoid syndrome – caused by bulky liver metastases
  - Intermittent flushing (kallikrein) and diarrhea (serotonin) – hallmark symptoms
  - Can also get asthma-type symptoms (bradykinin) and right heart valve lesions
  - If patient has carcinoid syndrome with small bowel carcinoid primary, it indicates metastasis to liver (liver usually clears serotonin)
  - If resection of liver metastases is performed, perform cholecystectomy in case of future embolization
  - Octreotide scan – best for *localizing* tumor not seen on CT scan

- Chromogranin A level – highest sensitivity for *detecting* a carcinoid tumor
- Appendix carcinoid – most common site for carcinoid tumor (50% of carcinoids arise here; ileum and rectum next most common)
- Small bowel carcinoid – patients at ↑ risk for multiple primaries and second unrelated malignancies
- Carcinoid Tx:
  - Carcinoid in appendix – < 2 cm → appendectomy; ≥ 2 cm or involving base → right hemicolectomy
  - Chemotherapy – streptozocin and 5FU; usually just for unresectable disease
  - Octreotide – useful for carcinoid syndrome palliation
  - Bronchospasm – Tx: albuterol inhalers
  - Flushing – Tx: **α**-blockers (phenothiazine)
  - False 5-HIAA – fruits

INTUSSUSCEPTION IN ADULTS

- Can occur from small bowel or cecal tumors
- Most common presentation is obstruction
- Worrisome in adults as it often has a malignant lead point (ie cecal CA)
- Tx: resection



Anatomy of intussusception. The intussusceptum is the segment of bowel that invaginates into the intussuscipiens.

BENIGN SMALL BOWEL TUMORS

- Adenomas – most found in duodenum; present with bleeding, obstruction
  - Need resection when identified (often done with endoscope)
- Peutz–Jeghers syndrome (autosomal dominant) – hamartomas throughout GI tract (small and large bowel); mucocutaneous melanotic skin pigmentation; patients have ↑ extraintestinal malignancies (most common – breast CA) and a small risk of GI malignancies; *no*

prophylactic colectomy

MALIGNANT SMALL BOWEL TUMORS (RARE)

- Adenocarcinoma (rare) – most common malignant small bowel tumor
  - High proportion is in the duodenum
  - Symptoms: obstruction, jaundice
  - Can also arise from the ampulla of Vater (Sx's – jaundice, anemia, guaiac positive stools)
  - Tx: resection and adenectomy; Whipple if in 2nd portion of duodenum
- Duodenal CA risk factors: FAP, Gardner's, polyps, adenomas, von Recklinghausen's
- Leiomyosarcoma
  - Usually in jejunum and ileum; most extraluminal
  - Hard to differentiate compared with leiomyoma (> 5 mitoses/50 HPF, atypia, necrosis)
  - Make sure it is not a GIST (check for C-Kit)
  - Tx: resection; no adenectomy required
- Lymphoma
  - Usually in ileum; associated with Wegener's, SLE, AIDS, Crohn's, celiac sprue
  - Usually NHL B cell type
  - Post-transplantation – ↑ risk of bleeding and perforation
  - Dx: abdominal CT, node sampling
  - Tx: wide en bloc resection (include nodes) unless 1st or 2nd portion of the duodenum (chemo-XRT, no Whipple)
  - 40% 5-year survival rate

STOMAS

- Parastomal hernias – highest incidence with colostomies; generally well tolerated and do not need repair unless symptomatic
- *Candida* – most common stomal infection
- Diversion colitis (Hartmann's pouch) – secondary to lack of short-chain fatty acids
  - Tx: short-chain fatty acid enemas
- Ischemia – most common cause of stenosis of stoma
  - Tx: dilation if mild
- Crohn's disease – most common cause of fistula near stoma site
- Abscesses – underneath stoma site, often caused by irrigation device
- Gallstones (loss of bile salts) and uric acid kidney stones (loss of HCO_3^-) – increased in patients with ileostomy

APPENDICITIS

- Appendicitis – 1st: anorexia; 2nd: abdominal pain (periumbilical); 3rd: vomiting
- Pain gradually migrates to the RLQ as peritonitis sets in
- Most commonly occurs in patients 20–35 years
- Patients can have normal WBC count
- CT scan – diameter > 7 mm or wall thickness > 2 mm (looks like a bull's eye), fat stranding, no contrast in appendiceal lumen; try to give rectal contrast
- Midpoint of anti-mesenteric border – area most likely to perforate
- Lymphoid hyperplasia – most common cause in children; can follow a viral illness

- Fecalith – most common cause in adults
- Luminal obstruction is followed by distention of the appendix, venous congestion and thrombosis, ischemia, gangrene necrosis, and finally rupture
- Nonoperative situation – CT scan shows walled-off perforated appendix (usually in elderly)
  - Tx: percutaneous drainage and interval appendectomy at later date as long as symptoms are improving
  - Consider follow-up barium enema or colonoscopy to rule out perforated cecal colon CA
- Children and elderly have higher propensity to rupture secondary to delayed diagnosis
  - Children often have higher fever and more vomiting and diarrhea
  - Elderly – signs and symptoms can be minimal; may need right hemicolectomy if cancer suspected
- Appendicitis is infrequent in infants
- Perforation – patient generally more ill; can have evidence of sepsis
- Appendicitis during pregnancy
  - Most common cause of acute abdominal pain in the 1st trimester
  - More likely to occur in the 2nd trimester but is not the most common cause of abdominal pain
  - More likely to perforate in the 3rd trimester – confused with contractions
  - Need to make the incision where the patient is having pain – the appendix is *displaced superiorly (cephalad)*
  - May have symptoms of RUQ pain in the 3rd trimester
  - 35% fetal mortality with rupture
  - Women with suspected appendicitis need beta-HCG drawn and abdominal ultrasound to rule out OB/GYN causes of abdominal pain

OTHER APPENDIX

- Appendix mucocele – can be benign or malignant mucinous tumor (signet ring cells); needs resection (should open for these so you don't spill tumor contents)
  - Need right hemicolectomy if malignant
  - Can get pseudomyxoma peritonei with rupture (spread of tumor implants throughout the peritoneum)
  - MCC of death – small bowel obstruction from peritoneal tumor spread
- Regional ileitis – can mimic appendicitis; 10% go on to Crohn's disease
- Gastroenteritis – nausea, vomiting, diarrhea
- Presumed appendicitis but find ruptured ovarian cyst, thrombosed ovarian vein, or regional enteritis not involving cecum → still perform appendectomy (prevents future confounding diagnosis)

ILEUS

- Causes include surgery (most common), electrolyte abnormalities (↓ K), peritonitis, ischemia, trauma, drugs
- Ileus – dilatation is uniform throughout the stomach, small bowel, colon, and rectum *without* decompression; no passage of gas; absent bowel sounds
- Obstruction – there is bowel decompression distal to the obstruction

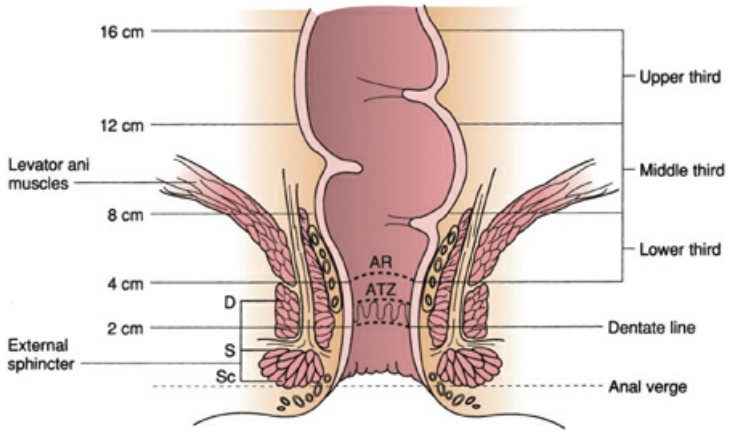
TYPHOID ENTERITIS (SALMONELLA)

- Children; get RLQ pain, diarrhea, fever, headaches, maculopapular rash, leukopenia; rare bleeding/perforation
- Large mesenteric lymph nodes
- Tx: Bactrim

36 Colorectal

ANATOMY AND PHYSIOLOGY

- Colon secretes K and reabsorbs Na and water (mostly in right colon and cecum)
- 4 layers – mucosa (columnar epithelium) → submucosa → muscularis propria → serosa
  - Muscularis mucosa – small interwoven inner muscle layer just below mucosa but above basement membrane
  - Muscularis propria – circular layer of muscle
- Ascending, descending, and sigmoid colon are all retroperitoneal
  - Peritoneum covers anterior upper and middle ⅓ of the rectum
- Plicae semilunares – transverse bands that form haustra
- Taenia coli – 3 bands that run longitudinally along colon. At rectosigmoid junction, the taeniae become broad and completely encircle the bowel.

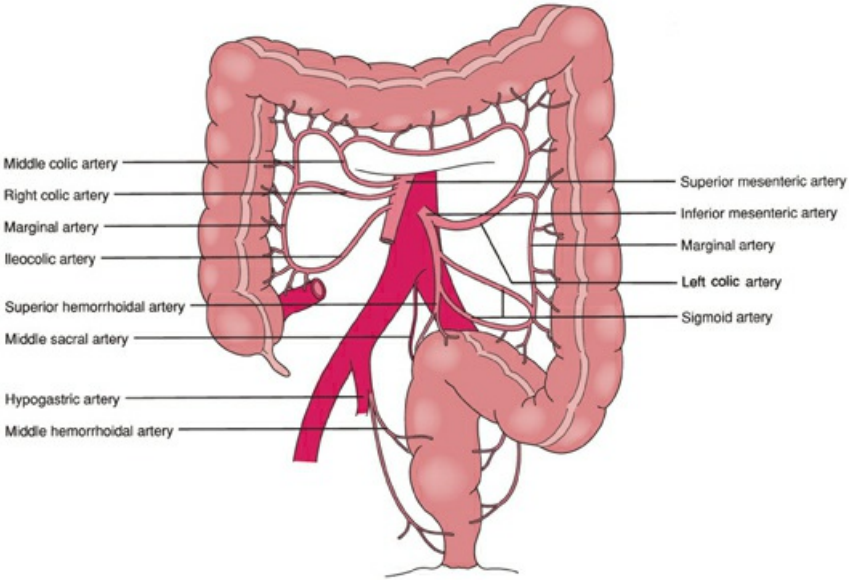


Anorectal anatomy with important landmarks. Approximate measurements are relative to the anal verge. D, deep; S, superficial; Sc, subcutaneous; AR, anorectal ring; ATZ, anal transition zone.

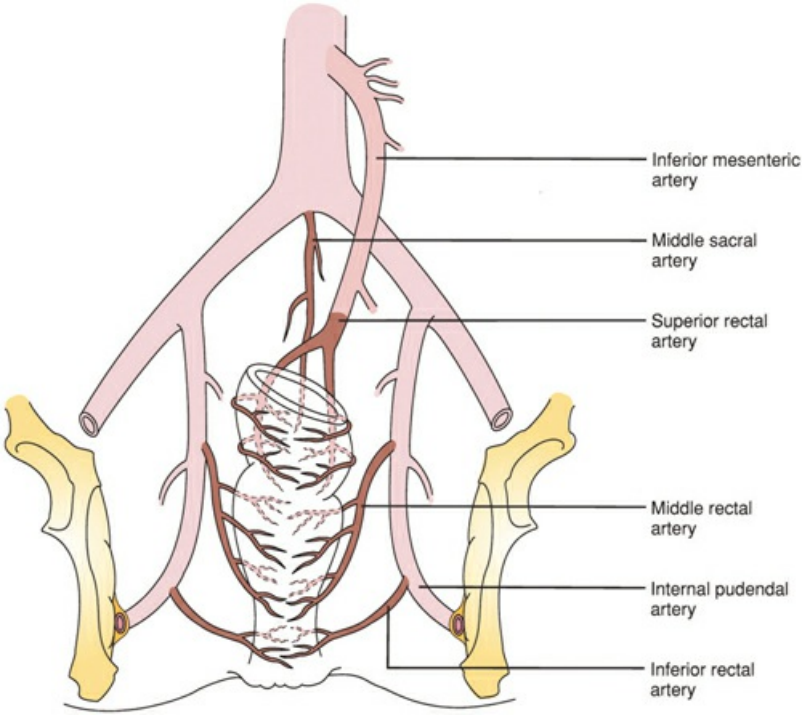
- Vascular supply
  - Ascending and ⅔ of transverse colon supplied by SMA (ileocolic, right and middle colic arteries)
  - ⅓ transverse, descending colon, sigmoid colon, and upper portion of the rectum supplied by IMA (left colic, sigmoid branches, superior rectal artery)
  - Marginal artery – runs along colon margin, connecting SMA to IMA (provides collateral flow)
  - Arc of Riolan – short direct connection between SMA and IMA
  - 80% of blood flow goes to mucosa and submucosa
- Venous drainage follows arterial except IMV, which goes to the splenic vein
  - Splenic vein joins the SMV to form the portal vein behind the pancreas
- Superior rectal artery – branch of IMA
- Middle rectal artery – branch of internal iliac (the lateral stalks during low anterior resection

[LAR] or abdominoperineal resection [APR] contain the middle rectal arteries)

- Inferior rectal artery – branch of internal pudendal (which is a branch of internal iliac)
- Superior and middle rectal veins drain into the IMV and eventually the portal vein
- Inferior rectal veins drain into the internal iliac veins and eventually the caval system



Arterial blood supply of the colon. The superior mesenteric artery (SMA) and inferior mesenteric artery (IMA) are the major blood supplies to the colon.



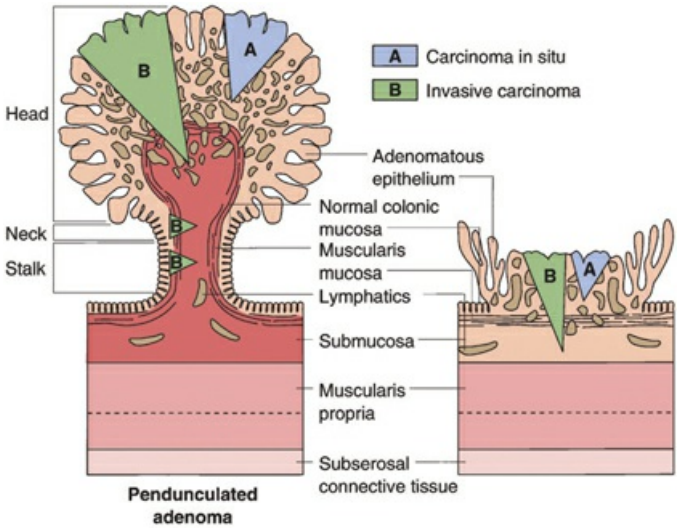
Arterial supply of the rectum and anal canal.

- Superior and middle rectum – drain to IMA nodal lymphatics
- Lower rectum – drains primarily to IMA nodes, also to internal iliac nodes
- Bowel wall contains mucosal and submucosal lymphatics

- Watershed areas
  - Splenic flexure (Griffith's point) – SMA and IMA junction
  - Rectum (Sudak's point) – superior rectal and middle rectal junction
  - Hypotension or low-flow states causes ischemia in these areas
  - Colon more sensitive to ischemia than small bowel secondary to ↓ collaterals
- External sphincter (puborectalis muscle) – under CNS (voluntary) control
  - Inferior rectal branch of internal pudendal nerve
  - Is the continuation of the levator ani muscle (striated muscle)
- Internal sphincter – involuntary control
  - Pelvic splanchnic nerves
  - Is the continuation of the muscularis propria (smooth muscle)
  - Is normally contracted
- Meissner's plexus – inner nerve plexus
- Auerbach's plexus – outer nerve plexus
- Pelvic splanchnic nerves – parasympathetic
- From anal verge – anal canal 0–5 cm, rectum 5–15 cm, rectosigmoid junction 15–18 cm
- Levator ani – marks the transition between anal canal and rectum
- Crypts of Lieberkühn – mucin-secreting goblet cells
- Colonic inertia – slow transit time; patients may need subtotal colectomy
- Short-chain fatty acids – main nutrient of colonocytes
- Stump pouchitis (diversion or disuse proctitis) – Tx: short-chain fatty acid enema
- Infectious pouchitis – Tx: metronidazole (Flagyl)
- Denonvilliers fascia (anterior) – rectovesicular and rectoprostatic fascia in men; rectovaginal fascia in women
- Waldeyer's fascia (posterior) – rectosacral fascia

POLYPS

- Hyperplastic polyps – most common polyp; no cancer risk
- Tubular adenoma – most common (75%) intestinal neoplastic polyp
  - These are generally pedunculated
- Villous adenoma – most likely to produce symptoms
  - These are generally sessile and larger than tubular adenomas
  - 50% of villous adenomas have cancer
- > 2 cm, sessile, or villous lesions have ↑ cancer risk
- Polyps have left-side predominance
- Most pedunculated polyps can be removed endoscopically

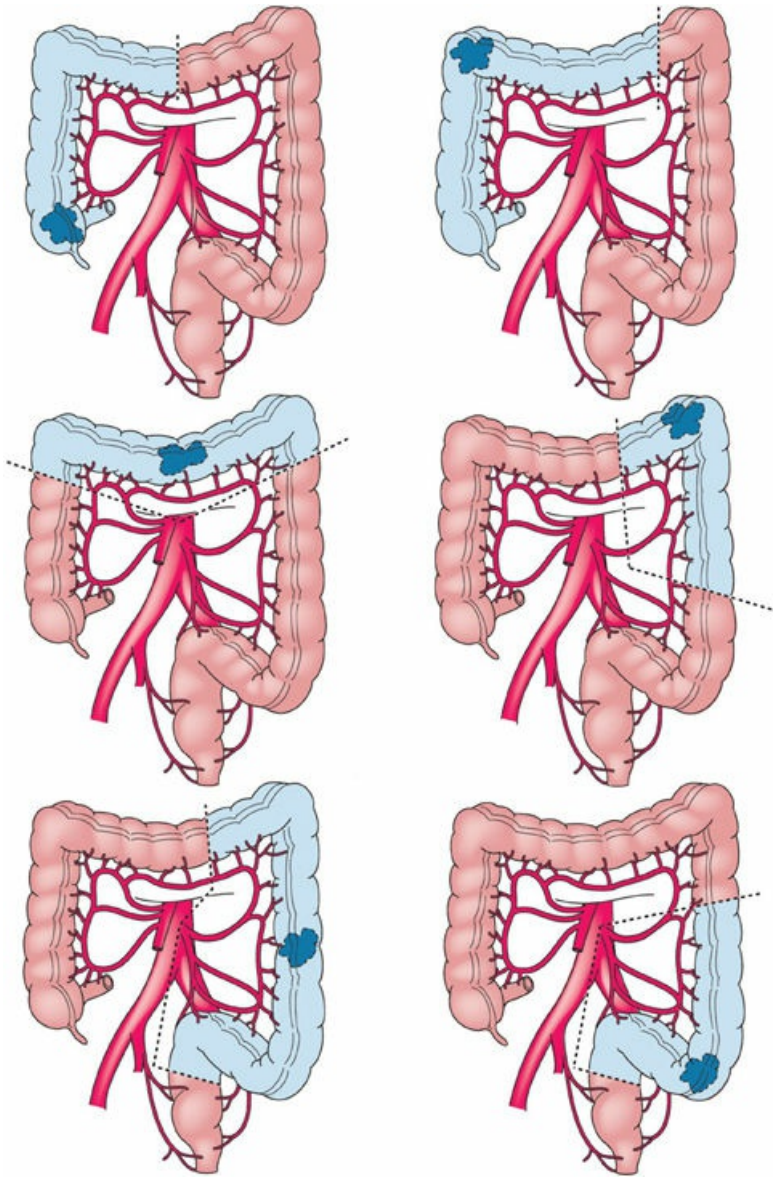


Diagrammatic representation of cancer-containing polyps. Pedunculated adenoma is described on the left and a sessile adenoma on the right. In carcinoma in situ, malignant cells are confined to the mucosa. These lesions are adequately treated by endoscopic polypectomy. Polypectomy is adequate treatment for invasive carcinoma only if the margin is sufficient (2 mm), the carcinoma is not poorly differentiated, and no evidence of venous or lymphatic invasion is found.

- If not able to get all of the polyp (which usually occurs with sessile polyps) → need segmental resection
- High-grade dysplasia – basement membrane is intact (carcinoma in situ)
- Intramucosal cancer – into muscularis mucosa (carcinoma in situ → still has not gone through basement membrane)
- Invasive cancer – into submucosa (T1)
- Screening – at 50 for normal risk, at 40 (or 10 years before youngest case) for intermediate risk (eg family history of colon CA)
- Screening options – 1) colonoscopy every 10 years; *or* 2) high-sensitivity fecal occult blood testing every 3 years and flexible sigmoidoscopy every 5 years; *or* 3) high-sensitivity fecal occult blood testing annually
  - Double contrast barium enema or CT colonography every 5 years may be alternatives to above
  - False-positive guaiac – beef, vitamin C, iron, cimetidine
  - No colonoscopy with recent MI, splenomegaly, pregnancy (if fluoroscopy planned)
- Polypectomy shows T1 lesion – polypectomy is adequate if margins are clear (2 mm), is well differentiated, and has no vascular/lymphatic invasion; otherwise, need formal colon resection
- Extensive low rectal villous adenomas with atypia – Tx: transanal excision (can try mucosectomy) as much of the polyp as possible
  - No APR unless cancer is present
- Pathology shows T1 lesion after transanal excision of villous rectal polyp → transanal excision is adequate if margins are clear (2 mm), it is well differentiated, and it has no vascular/lymphatic invasion
- Pathology shows T2 lesion after transanal excision of villous rectal polyp → patient needs APR or LAR

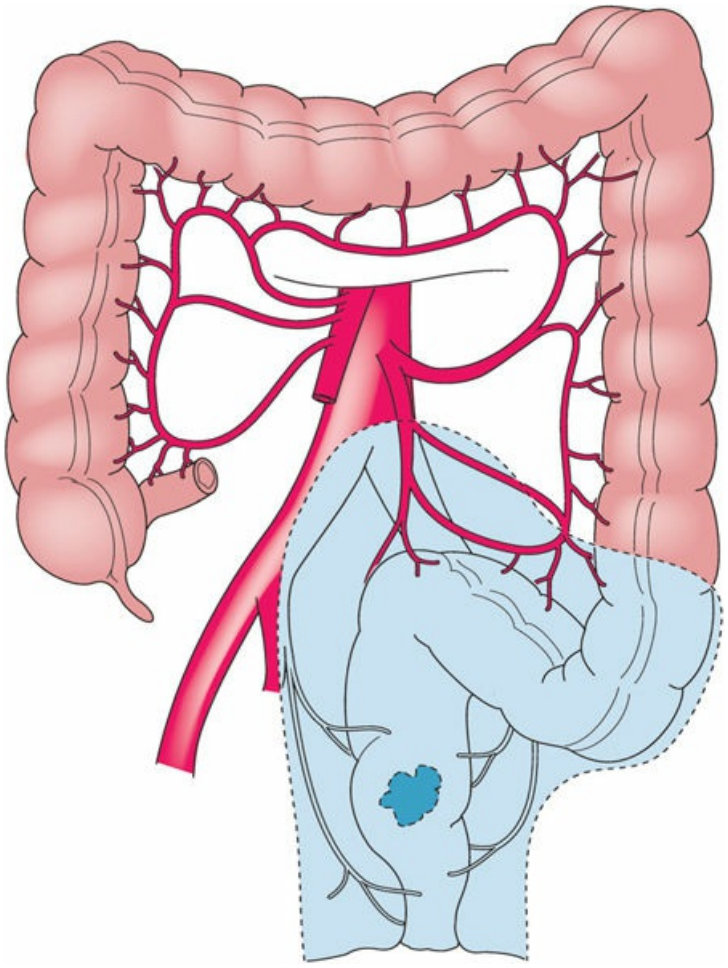
COLORECTAL CANCER

- 2nd leading cause of CA death
- Symptoms: anemia, constipation (narrow caliber stools), and lower GI bleeding
- Red meat and fat → O_2 radicals are thought to have a role
- Colon CA has had an association with *Clostridium septicum* infection
- Colon CA – main gene mutations are APC, DCC, p53, and k-ras
- Sigmoid colon – most common site of primary
- Disease spread
  - Spreads to nodes first
  - Nodal status – most important prognostic factor
  - Liver – #1 site of metastases; lung – #2 site of metastases
    - Portal vein → liver metastases; iliac vein → lung metastases
    - Liver metastases – if resectable and leaves adequate liver function, patients have 35% 5-year survival (5-YS) rate
    - Lung metastases – 25% 5-YS rate in selected patients after resection
    - Isolated liver or lung metastases should be resected
  - 5% get drop metastases to ovaries
  - Rectal CA – can metastasize to spine directly via Batson's plexus (venous)
  - Colon CA typically does not go to bone
  - Colorectal CA growing into adjacent organs can be resected en bloc with a portion of the adjacent organ (ie partial bladder resection)
- Lymphocytic penetration – patients have an improved prognosis
- Mucoepidermoid – worst prognosis
- Transrectal ultrasound (TRUS) – good at assessing depth of invasion (sphincter involvement), recurrence, and presence of enlarged nodes; best test for T and N status
- Need total colonoscopy to rule out synchronous lesions in patients with colorectal CA
- Goals of resection
  - En bloc resection, adequate margins, mesocolon, and regional adenectomy
  - Take Waldeyer's and Denonvillier's fascia for rectal tumors
  - Most right-sided colon CAs can be treated with primary anastomosis without ostomy
  - Rectal pain with rectal CA – patient needs APR
  - Generally need 2-cm margins



Segmental resections for cancers of the colon and upper third of the rectum. Note the blood supply taken with each form of resection.

- Intraoperative ultrasound (U/S) – best method of picking up intrahepatic metastases
  - Conventional U/S resolution: 10 mm
  - Abdominal CT: 5–10 mm
  - Abdominal MRI: 5–10 mm (better resolution than CT)
  - Intraoperative U/S: 3–5 mm
- Abdominoperineal resection (APR)
  - Permanent colostomy; anal canal is excised along with the rectum
  - Can have impotence and bladder dysfunction (injured pudendal nerves)
  - Indicated for malignant lesions only (not benign tumors) that are not amenable to LAR
  - Need at least a 2-cm margin (2 cm from levator ani muscles) for LAR, otherwise will need APR
  - Risk of local recurrence higher with rectal CA than with colon CA in general



Extent of surgery in abdominoperineal resection.

- Preoperative chemo-XRT – produces complete response in some patients with rectal CA; preserves sphincter function in some

TNM Staging System for Colorectal Cancer

- T1: into submucosa. T2: into muscularis propria. T3: into subserosa or through muscularis propria if no serosa is present. T4: through serosa into free peritoneal cavity or into adjacent organs/structures if no serosa is present
- N0: nodes negative. N1: 1–3 nodes positive, N2: ≥ 4 nodes positive, N3: central nodes positive
- M1: distant metastases

Stage	TNM Status
0	Tis, N0, M0
I	T1–2, N0, M0
IIA	T3, N0, M0
IIB	T4, N0, M0
IIIA	T1–2, N1, M0
IIIB	T3–4, N1, M0
IIIC	Any T, N2, M0
IV	Any T, Any N, M1

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- Low rectal T1 (limited to submucosa) – can be excised transanally if < 4 cm, has negative margins (need 2 mm), is well differentiated, and there is no neurologic or vascular invasion; otherwise, patient needs APR or LAR
- Low rectal T2 or higher – Tx: APR or LAR
- Chemotherapy
  - Stage III and IV colon CA (nodes positive or distant metastases) → postop chemo, no XRT
  - Stage II and III rectal CA → pre-op chemo-XRT (neoadjuvant)
  - Stage IV rectal CA → chemo and XRT ± surgery (possibly just colostomy, may want to avoid APR in patients with metastatic disease)
  - Chemo – *5FU*, *leucovorin*, and *oxaliplatin (FOLFOX)*
- XRT
  - ↓ local recurrence and ↑ survival when combined with chemotherapy
  - XRT damage – rectum most common site of injury → vasculitis, thrombosis, ulcers, strictures, bleeding
  - Pre-op chemo-XRT may help shrink rectal tumors, allowing down-staging of the tumor and possibly allowing LAR versus APR
- 20% have a recurrence (usually occurs within 1 year)
  - 5% get another primary – *main reason for surveillance colonoscopy after 1 year*
- Follow-up colonoscopy at 1 year – mainly to check for new primary colon CA (metachronous)

FAMILIAL ADENOMATOUS POLYPOSIS (FAP)

- Autosomal dominant; all have cancer by age 40
- APC gene – chromosome 5
- 20% of FAP syndromes are spontaneous
- Polyps not present at birth; are present in puberty
- Get 1,000s of polyps (carpet the colon)
- Do not need colonoscopy for surveillance in patients with suspected FAP → just need flexible sigmoidoscopy to check for polyps
- All need total colectomy prophylactically at age 20
- Also get duodenal polyps → need to check duodenum with endoscopy every 1–2 years
- Surgery – proctocolectomy, rectal mucosectomy, and ileoanal pouch (J-pouch)
  - Need lifetime surveillance of residual rectal mucosa
  - Total proctocolectomy with end ileostomy is also an option
  - Following colectomy, most common cause of death in FAP patients is periampullary tumors of duodenum
- Gardner's syndrome – patients get colon CA (associated with APC gene) and intra-abdominal desmoid tumors/osteomas
- Turcot's syndrome – patients get colon CA (associated with APC gene) and brain tumors

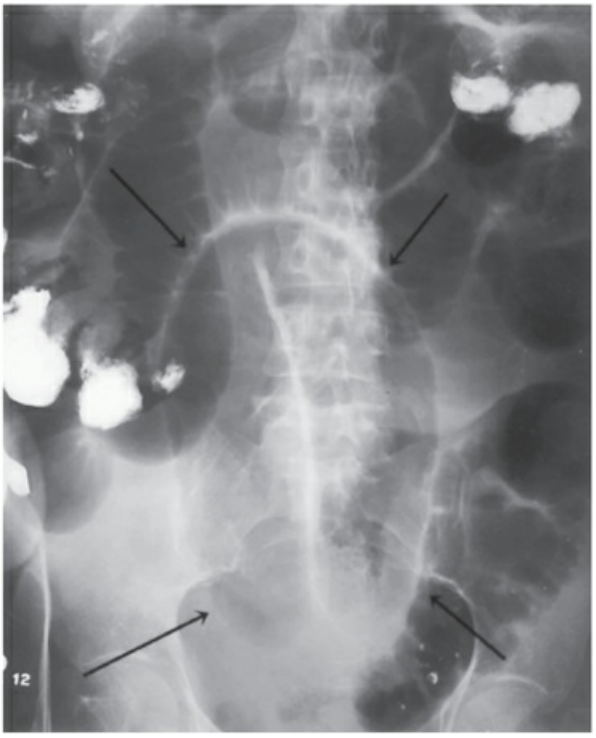
LYNCH SYNDROMES (HEREDITARY NONPOLYPOSIS COLON

CANCER)

- 5% of population, autosomal dominant
- Associated with DNA mismatch repair gene
- Predilection for right-sided and multiple cancers
- Lynch I – just colon CA risk
- Lynch II – patients *also* have ↑ risk of ovarian, endometrial, bladder, and stomach cancer
- Amsterdam criteria for Lynch syndrome – "3, 2, 1" → at least 3 first-degree relatives, over 2 generations, 1 with cancer before age 50
- Need surveillance colonoscopy starting at age 25 or 10 years before primary relative got cancer (also need surveillance program for the other CA types in the family)
- 50% get metachronous lesions within 10 years; often have multiple primaries
- Need total proctocolectomy with first cancer operation

SIGMOID VOLVULUS

- More common with high-fiber diets (Iran, Iraq) and in elderly
- Risk factors – debilitated, psychiatric patients, neurologic dysfunction, laxative abuse
- Symptoms: pain, distention, and obstipation
- Causes closed-loop obstruction – sigmoid colon twists on itself
- Abdominal x-ray – bent inner tube sign and colon distension; Gastrografin enema may show bird's beak sign (tapered colon)
- Do not attempt decompression with gangrenous bowel or peritoneal signs → go to OR for sigmoidectomy
- Tx: decompress with colonoscopy (80% reduce, 50% will recur), give bowel prep (consider rectal tube), and perform sigmoid colectomy during same admission



Plain supine abdominal film of a patient with sigmoid volvulus. The centrally located sigmoid loop is outlined by trapped air. The proximal small intestine is dilated as well, suggesting that the

volvulus has been present for sufficient time to cause accumulation of air and fluid proximally. (Courtesy of John Braver, M.D., Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.)

CECAL VOLVULUS

- Less common than sigmoid volvulus; occurs in 20s–30s
- Can appear as an SBO, with dilated cecum in the RLQ
- Can try to decompress with colonoscopy but unlikely to succeed (only 20%)
- Tx: OR → right hemicolectomy probably best treatment; can try cecopexy if colon is viable and patient is frail

ULCERATIVE COLITIS

- Symptoms: bloody diarrhea, abdominal pain, fever, and weight loss
- Involves the mucosa and submucosa
- Strictures and fistulae unusual with ulcerative colitis
- Spares anus – unlike Crohn's disease
  - Usually starts distally in rectum and is contiguous (no skip areas like Crohn's)
  - Bleeding is universal and has mucosal friability with pseudopolyps and collar button ulcers
  - Always need to rule out infectious etiology
  - Backwash ileitis can occur with proximal disease

Clinicopathologic Features of Ulcerative Colitis versus Crohn Disease

Manifestation	Ulcerative Colitis	Crohn Disease
Transmural inflammation	Seldom	Common
Granulomas	Seldom	>50%
Fissuring	Rare	Common
Fibrosis	Rare	Common
Submucosal inflammation	Rare	Common
Crypt abscesses	Common	Uncommon
Small-bowel involvement	Rare (backwash ileitis)	Common
Anatomic location	Continuous	Skip
Rectal involvement	Common	May be spared
Bleeding	Common	Absent
Fistulas	Rare	Common
Perianal disease	Rare	Common
Ulcers	Rare	Common
Surrounding mucosa	Pseudopolyps	Relatively normal
Cobblestoning of mucosa	None	Long-standing disease
Mucosal friability	Common	Uncommon
Vascular pattern	Absent	Normal
Fat wrapping	Rare	Common

- Barium enema – with chronic disease see loss of haustra, narrow caliber, short colon, and loss of redundancy
- Medical Tx: sulfasalazine (or 5-ASA) and loperamide for maintenance therapy
  - Steroids for acute flares
  - 5-ASA and sulfasalazine can maintain remission in ulcerative colitis
  - Consider cyclosporine or infliximab for steroid-resistant disease

- Add Cipro and Flagyl for acute flares if worried about infection or toxic megacolon/colitis
- Toxic colitis and toxic megacolon
  - Toxic colitis: > 6 bloody stools/d, fever, ↑ HR, drop in Hgb, leukocytosis
  - Toxic megacolon: above plus distension, abdominal pain and tenderness
  - Initial Tx: NG tube, fluids, steroids, bowel rest, and antibiotics (ciprofloxacin and Flagyl) will treat 50% adequately; other 50% require surgery
  - Follow clinical response and abdominal radiographs
  - *Avoid* barium enemas, narcotics, anti-diarrheal agents, and anti-cholinergics

Indications for Surgery with Toxic Colitis and Toxic Megacolon

Absolute	Relative
Pneumoperitoneum	Inability to promptly control sepsis
Diffuse peritonitis	Increasing megacolon
Localized peritonitis with increasing abdominal pain and/or colonic distension >10 cm	Failure to improve within 24–48 h
Uncontrolled sepsis	Increasing toxicity or other signs of clinical deterioration
Major hemorrhage	Continued transfusion requirements

Modified from Rothenberger DA, Bullard KM. Surgery for toxic megacolon. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.

- Perforation with ulcerative colitis – transverse colon more common
- Perforation with Crohn's – distal ileum most common
- Surgical indications for ulcerative colitis: massive hemorrhage, refractory toxic megacolon, acute fulminant ulcerative colitis (occurs in 15%), obstruction, any dysplasia, cancer, intractability, systemic complications, failure to thrive, and long-standing disease (> 20 years) as prophylaxis against colon CA (some controversy here)
- Emergent/urgent resections – total proctocolectomy and bring up ileostomy
  - Perform definitive hook-up later
- Elective resections
  - Ileoanal anastomosis – rectal mucosectomy, J-pouch, and ileoanal (low rectal) anastomosis; not used with Crohn's disease
    - Can protect bladder and sexual function
    - Need lifetime surveillance of residual rectal area
    - Many ileoanal anastomoses need resection secondary to cancer, dysplastic changes, refractory pouchitis, or pouch failure (incontinence)
    - Need temporary diverting ileostomy (6–8 weeks) while pouch heals
    - Leak (most common major morbidity) – can lead to sepsis (Tx: drainage, antibiotics)
    - Infectious pouchitis – Tx: Flagyl
  - APR with ileostomy – can also be performed
- Cancer risk is 1% per year starting 10 years after initial diagnosis for patients with pancolitis
  - Cancer more evenly distributed throughout colon
  - Need yearly colonoscopy starting 8–10 years after diagnosis
- Extraintestinal manifestations of ulcerative colitis
  - Most common extraintestinal manifestation requiring total colectomy – failure to thrive in children
  - Do not get better with colectomy → primary sclerosing cholangitis, ankylosing

spondylitis
- Get better with colectomy → most ocular problems, arthritis, and anemia
- 50% get better → pyoderma gangrenosum
- HLA B27 – sacroiliitis, ankylosing spondylitis, ulcerative colitis
- Can get thromboembolic disease
- Pyoderma gangrenosum – Tx: steroids

CARCINOID OF THE COLON AND RECTUM

- Represents 15% of all carcinoids; infrequent cause of carcinoid syndrome
- Metastases related to size of tumor
- ⅔ of colon carcinoids have either local or systemic spread
- Low rectal carcinoids
  - < 2 cm → wide local excision with negative margins
  - > 2 cm or invasion of muscularis propria → APR
- Colon or high rectal carcinoids
  - < 1 cm – polypectomy
  - > 1 cm – formal resection

COLONIC OBSTRUCTION

- Colon perforation with obstruction – most likely to occur in cecum
  - Law of LaPlace: tension = pressure × diameter
- Closed-loop obstructions – can be worrisome; can have rapid progression and perforation with minimal distention
  - Competent ileocecal valve can lead to closed-loop obstruction
- Colonic obstruction – #1 cancer; #2 diverticulitis
- Pneumatosis intestinalis – air on the bowel wall, associated with ischemia and dissection of air through areas of bowel wall
- Air in the portal system – usually indicates significant infection or necrosis of the large or small bowel; often an ominous sign

OGILVIE'S SYNDROME

- Pseudoobstruction of colon
- Associated with opiate use; bedridden or older patients; recent surgery, infection, or trauma
- Get a massively dilated colon, which can perforate
- Tx: IVFs; check and replace electrolytes (especially K and Mg); discontinue drugs that slow the gut (eg morphine); NGT; neostigmine
  - If colon > 10 cm (high risk of perforation) → decompression with colonoscopy, rectal tube, and neostigmine; cecostomy if that fails

AMOEBIC COLITIS

- *Entamoeba histolytica*; from contaminated food and water with feces that contain cysts
- Primary infection – occurs in colon; secondary infection – occurs in liver
- Risk factors – travel to Mexico, ETOH; fecal–oral transmission
- Symptoms: similar to ulcerative colitis (dysentery); chronic more common form (3–4 bowel

movements/day, cramping, and fever)
- Dx: endoscopy → ulceration, trophozoites; 90% have anti-amebic antibodies
- Tx: Flagyl, diiodohydroxyquin

ACTINOMYCES

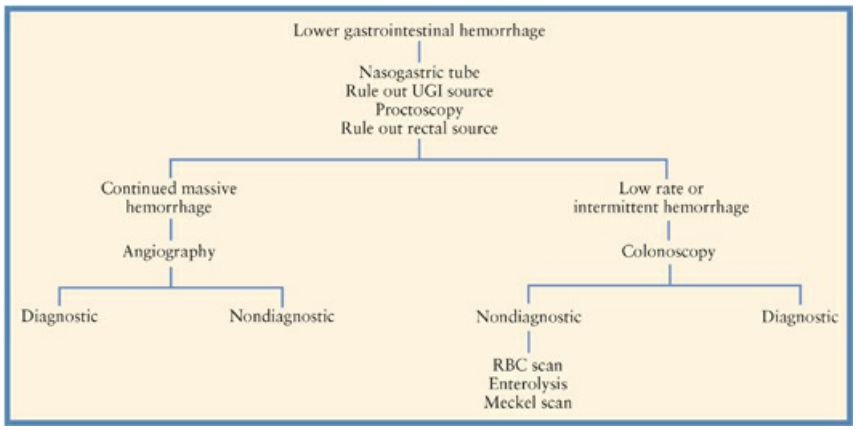
- Can present as a mass, abscess, fistula, or induration; suppurative and granulomatous
- Cecum most common location; can be confused with CA
- Pathology shows yellow-white sulfur granules
- Tx: penicillin or tetracycline, drainage of any abscess

DIVERTICULA

- Herniation of mucosa through the colon wall at sites where arteries enter the muscular wall
- Circular muscle thickens adjacent to diverticulum with luminal narrowing
- Caused by straining (↑ intraluminal pressure)
- Most diverticula occur on left side (80%) in the sigmoid colon (not rectum)
  - Bleeding is more likely with right-sided diverticula (50% of bleeds occur on right)
  - Diverticulitis is more likely to present on the left side
- Present in 35% of the population

LOWER GI BLEEDING

- Stool guaiac can stay positive up to 3 weeks after bleed
- Hematemesis – bleeding anywhere from nose to ligament of Treitz
- Melena – passage of tarry stools; need as little as 50 cc
- Jaundice – from hemoglobin absorption (broken down to bilirubin)
- Azotemia after GI bleed – caused by production of urea from bacterial action on intraluminal blood (↑ BUN; also get elevated total bilirubin)
- Lower GI bleeding can occur from angiodysplasia, diverticulosis, hemorrhoids, polyps, or cancer
- Rule out an upper GI source in patients with melena or red blood per rectum by placing an NG tube
  - If clear fluid is aspirated, need upper endoscopy (pylorus may be closed and duodenum may be the source)
  - If bilious fluid is aspirated, an upper GI source has been ruled out
  - If bloody fluid is aspirated, the diagnosis of upper GI bleeding is made



Diagnostic steps in the evaluation of acute lower gastrointestinal hemorrhage. UGI, upper gastrointestinal; RBC, red blood cell.

- Arteriography – bleeding must be ≥ 0.5 cc/min
- Tagged RBC scan – bleeding must be ≥ 0.1 cc/min
- Video capsule study

DIVERTICULITIS

- Result of mucosal perforations in the diverticulum with adjacent fecal contamination
- Denotes infection and inflammation of the colonic wall as well as surrounding tissue
- LLQ pain, tenderness, fever, ↑ WBCs
- Dx: CT scan is needed only if worried about complications of disease
- Need follow-up colonoscopy after an episode of diverticulitis to rule out colorectal cancer
- Most common complication – abscess formation; can usually percutaneously drain
- Signs of complication – obstruction symptoms, fluctuant mass, peritoneal signs, temperature > 39, WBCs > 20; *all warrant hospital admission*
- Uncomplicated diverticulitis – Tx: levofloxacin and Flagyl; bowel rest for 3–4 days (mild cases – can be treated as an outpatient; moderate to severe cases – NPO and IV fluids)
- Surgery – for significant complications (total obstruction not resolved with medical therapy, perforation, or abscess formation not amenable to percutaneous drainage) or inability to exclude cancer
  - Need to resect all of the sigmoid colon down to the superior rectum (distal margin should be normal rectum)
- Right-sided diverticulitis – 80% discovered at the time of incision for appendectomy
  - Tx: right hemicolectomy
- Colovesicular fistula – fecaluria, pneumaturia
  - MCC – diverticulitis
  - Occurs in men; women are more likely to get colovaginal fistula
  - Cystoscopy is the best diagnostic test
  - Tx: close bladder opening, resect involved segment of colon, and perform reanastomosis, diverting ileostomy; interpose omentum between the bladder and colon

DIVERTICULOSIS BLEEDING

- Most common cause of lower GI bleed
- Usually causes significant bleeding

- 75% stops spontaneously; recurs in 25%
- Caused by disrupted vasa rectum; creates arterial bleeding
- Dx: NG tube to rule out upper GI source
  - Colonoscopy usually as a 1st step → can be therapeutic (hemo-clips best) and can localize bleeding should surgery be required
  - Angio 1st if massive bleed (hypotension, tachycardia) – want to localize area for surgery; may be able to treat at angio with highly selective coil embolization
  - Go to operating room if hypotensive and not responding to resuscitation → colectomy at site of bleeding if identified or total abdominal colectomy if bleeding source has not been localized
  - Tagged RBC scan for intermittent bleeds that are hard to localize (most sensitive test)
- Tx: colonoscopy can ligate bleeder
  - With arteriography, can use vasopressin (to temporize) or highly selective coil embolization; also demonstrates where the bleed is should surgery be required
  - May need segmental colectomy or possible total abdominal colectomy if bleeding is not localized and not controlled
- Patients with recurrent diverticular bleeds should have resection of the area

ANGIODYSPLASIA BLEEDING

- ↑ on right side of colon
- Bleeds are usually less severe than diverticular bleeds but are more likely to recur (80%)
- Causes venous bleeding
- Soft signs of angiodysplasia on angiogram – tufts, slow emptying
- 20% of patients with angiodysplasia have aortic stenosis (usually gets better after valve replacement)

ISCHEMIC COLITIS

- Symptoms: abdominal pain, bright red bleeding
- Generally involves the left colon
- Can be caused by a low-flow state (eg recent MI, CHF), ligation of the IMA at surgery (eg AAA repair), embolus or thrombosis of the IMA, sepsis
- Splenic flexure and upper rectum most vulnerable to low-flow state
- Griffith's point (splenic flexure) – SMA and IMA junction
- Sudeck's point – superior rectal and middle rectal artery junction
- Dx: CT scan or colonoscopy (best test) → cyanotic edematous mucosa covered with exudates
  - Lower ⅔ of the rectum is spared → supplied by the middle and inferior rectal arteries (off internal iliacs)
  - If gangrenous colitis is suspected (peritonitis), no colonoscopy and go to OR → sigmoid resection or left hemicolectomy usual
  - Black bowel on colonoscopy, sepsis, or perforation → go to the OR for resection
- If not going to the OR – Tx: NPO, antibiotics, IVFs

PSEUDOMEMBRANOUS COLITIS (*C. DIFFICILE* COLITIS)

- Symptoms: profuse, watery, green, mucoid diarrhea; pain and cramping; fever
- Can occur up to 3 weeks after antibiotics; increased in postop, elderly, and ICU patients

- Carrier state not eradicated; 15% recurrence
- Key finding – PMN inflammation of mucosa and submucosa
  - Pseudomembranes, plaques, and ringlike lesions
- Most common in the distal colon
- Dx: *C. difficile* toxin (best test)
- Tx: oral – vancomycin or Flagyl; IV – Flagyl
  - Lactobacillus can also help; stop other antibiotics or change them; avoid anti-diarrheals
  - Toxic colitis (or megacolon) can occur requiring emergency colectomy

NEUTROPENIC TYPHLITIS (ENTEROCOLITIS)

- Follows chemotherapy when WBCs are low (nadir)
- Can mimic surgical disease
- Can often see pneumatosis intestinalis (not a surgical indication here)
- Tx: antibiotics; patients will improve when WBCs ↑; surgery *only* for free perforation

OTHER COLON DISEASES

- Other causes of colitis – *Salmonella*, *Shigella*, *Campylobacter*, CMV, *Yersinia* (can mimic appendicitis in children), other viral infections, *Giardia*
- *Yersinia* – can mimic appendicitis; comes from contaminated food (feces/urine)
  - Tx: tetracycline or Bactrim
- Megacolon – propensity for volvulus; enlargement is proximal to non-peristalsing bowel
  - Hirschsprung's disease – rectosigmoid most common. Dx: rectal biopsy
  - *Trypanosoma cruzi* – most common acquired cause, secondary to destruction of nerves

37 Anal and Rectal

INTRODUCTION

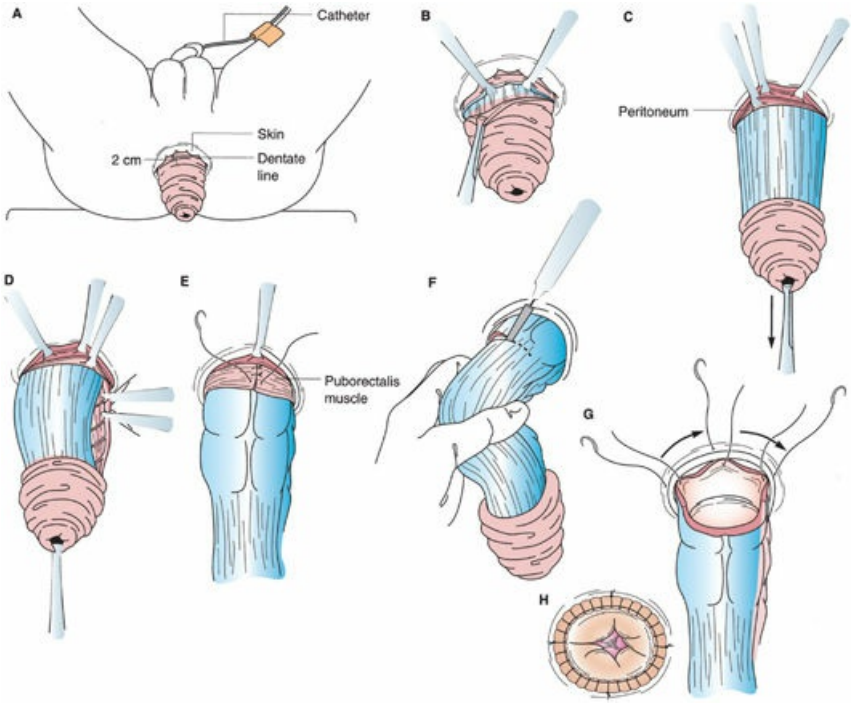
Arterial supply to the anus – inferior rectal artery
Venous drainage – above the dentate is internal hemorrhoid plexus and below the dentate is external hemorrhoid plexus

HEMORRHOIDS

- Caused by straining
- Left lateral, right anterior, and right posterior hemorrhoidal plexuses
- External hemorrhoids cause pain when they thrombose
  - Distal to the dentate line, covered by sensate squamous epithelium; can cause pain, swelling, and itching
- Internal hemorrhoids cause bleeding or prolapse which causes itching
  - Primary – slides below dentate with strain
  - Secondary – prolapse that reduces spontaneously
  - Tertiary – prolapse that has to be manually reduced
  - Quaternary – not able to reduce
- Tx: fiber and stool softeners (prevent straining); sitz baths; drink fluids
- Thrombosed external hemorrhoid → lance open (if > 72 hours) or elliptical excision (if < 72 hours) to relieve pain
- Surgical indications: recurrence, thrombosis multiple times, large external component
- External hemorrhoids can be resected with elliptical excision
- Can band primary and secondary internal hemorrhoids
  - Do not band external hemorrhoids (painful)
- Surgery for tertiary and quaternary internal hemorrhoids – 3 quadrant resection
  - Need to resect down to the internal anal sphincter (do not go through it)
  - Postop – sitz baths, stool softener, high-fiber diet, drink fluids

RECTAL PROLAPSE

- Starts 6–7 cm from anal verge
- Secondary to pudendal neuropathy and laxity of the anal sphincters
- ↑ with female gender, straining, chronic diarrhea, previous pregnancy, and redundant sigmoid colons
- Prolapse involves all layers of the rectum
- Medical Tx: high-fiber diet
- Surgical Tx:
  - Perineal rectosigmoid resection (Altemeier) transanally if patient is older and frail
  - Low anterior resection and pexy of residual colon if good condition patient



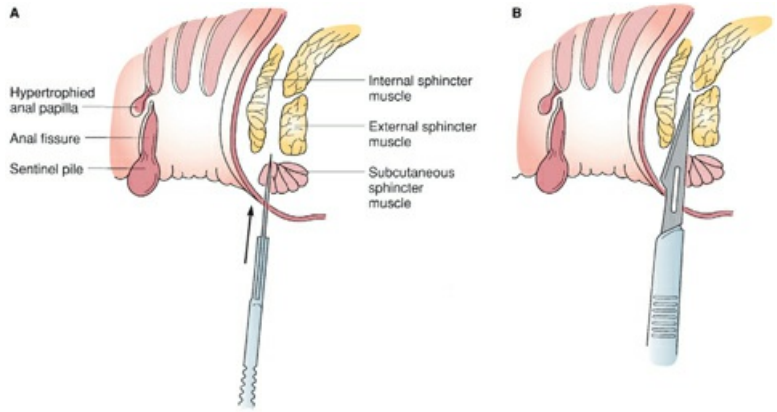
Perineal rectosigmoidectomy. The patient is placed in the lithotomy position with both legs in gynecologic stirrups. *(A and B)* A circular incision is made on the prolapsed rectum 2 cm proximal to the dentate line. *(C)* The peritoneal attachment is dissected from the anterior rectal wall, thus opening into the peritoneal cavity. *(D)* The mesorectum or mesosigmoid is clamped and divided laterally and posteriorly. *(E)* The previously opened peritoneum is sutured to the anterior wall of the rectum or sigmoid colon as high as possible. This is followed by approximation of the puborectalis (optional). *(F)* The anterior wall of the protruding rectum is cut 1 cm distal to the anal verge. *(G)* Stay sutures of 3-0 synthetic absorbable material are placed in four quadrants. *(H)* Anastomosis with running stitches.

CONDYLOMATA ACUMINATA

- Cauliflower mass; papillomavirus (HPV)
- Tx: laser surgery

ANAL FISSURE

- Pain and bleeding after defecation; chronic ones will see a sentinel pile
- Straining bowel movements, constipation
- Caused by a split in the anoderm
- 90% in posterior midline
- First-line medical Tx: sitz baths, bulk, lidocaine jelly, stool softeners, nitroglycerin cream, diltiazem ointment (90% heal with medical Tx)
- Surgical Tx: lateral subcutaneous internal sphincterotomy
- Fecal incontinence is the most serious complication of surgery
- Do not perform surgery if secondary to Crohn's disease or ulcerative colitis
- Lateral or recurrent fissures – worry about inflammatory bowel disease



Lateral internal sphincterotomy (closed technique). *(A)* Triad of fissure, sentinel pile, and hypertrophied anal papilla. With an anal speculum used for exposure of the lateral quadrant, a no. 11 scalpel blade stabs into the subcutaneous tissue from the anal verge to the dentate line, with the knife in the horizontal position. *(B)* The knife is turned 90 degrees, and the internal sphincter muscle is cut while the anal canal is stretched open.

ANORECTAL ABSCESS

- Can cause severe pain; fever
- Perianal, intersphincteric, and ischiorectal abscesses can be drained through the skin (all are below the levator muscles)
  - Intersphincteric and ischiorectal abscesses can form horseshoe abscess
- Supralevator abscesses need to be drained transrectally
- Antibiotics for cellulitis, DM, immunosuppressed, or prosthetic hardware
- Rule out anal cancer

PILONIDAL CYSTS

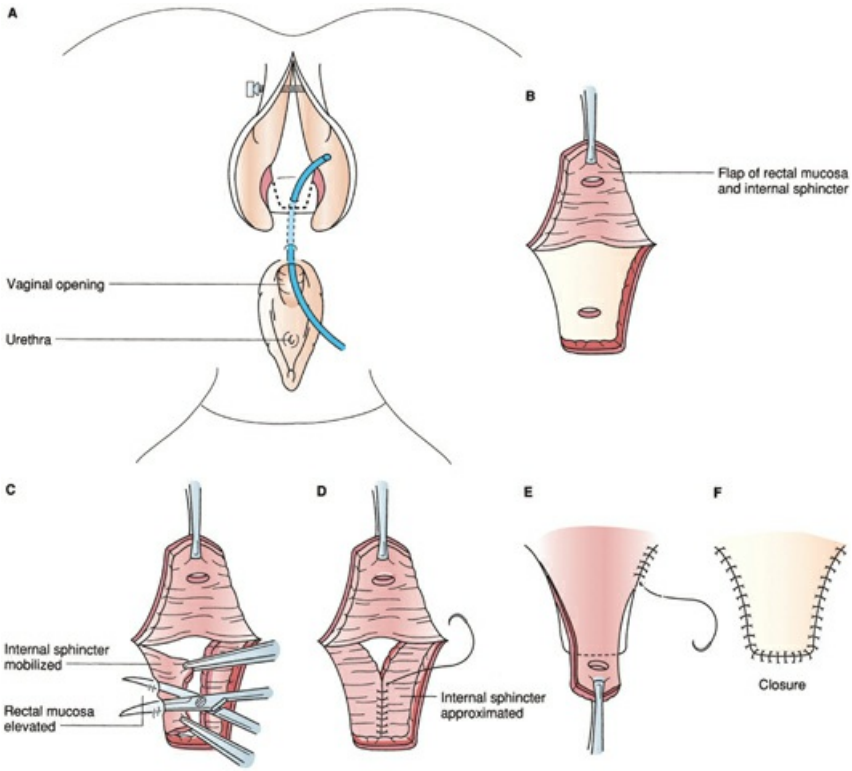
- Sinus or abscess formation over the sacrococcygeal junction; ↑ in men
- Tx: drainage and packing; follow-up surgical resection of cyst

FISTULA-IN-ANO

- Fecal soiling, occasional perianal discomfort
- Do <u>not</u> need to excise the tract
- Often occurs after anorectal abscess formation
- Goodsall's rule
  - Anterior fistulas connect with anus/rectum in a straight line
  - Posterior fistulas go toward a midline internal opening in the anus/rectum
- Tx:
  - Lower ⅓ of the external anal sphincter → draining seton stitch safest but consider fistulotomy (open tract up, curettage out, let it heal by secondary intention)
  - Upper ⅔ of the external anal sphincter → draining seton stitch (use rectal advancement flap if that fails)
  - Most worrisome complication here is risk of incontinence – you want to avoid damage to the external anal sphincter so fistulotomy is not used for fistulas above the lower ⅓ of the external anal sphincter

- Rule out necrotic and draining tumor

RECTOVAGINAL FISTULAS

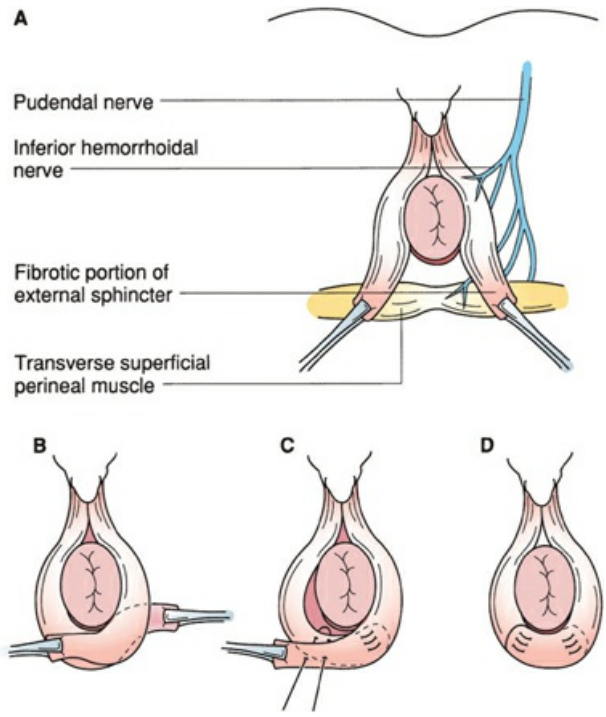


Endorectal advancement of anorectal flap. *(A)* Exposure is gained by an anal speculum, and the fistula is identified. Outline of endorectal flap, extending proximally to 7 cm from the anal verge. *(B)* The full-thickness flap is created to include the internal sphincter muscle. *(C)* Lateral mobilization is made on each side in the submucosal plane. *(D)* Anorectal wall on each side is approximated. *(E and F)* The endorectal flap is pulled down to cover the wound and sutured. The fistula is excised. The aperture in the vagina is not sutured but is left open for drainage.

- Simple – low to mid-vagina; MCC – obstetrical trauma
  - Tx: trans-anal rectal mucosa advancement flap
  - Many obstetrical fistulas heal spontaneously
- Complex – high in vagina; MCC – diverticulitis
  - Tx: abdominal or combined abdominal and perineal approach usual; resection and re-anastomosis of rectum, close hole in vagina, interpose omentum, temporary ileostomy

ANAL INCONTINENCE

- Neurogenic (gaping hole) – no good treatment
- Abdominoperineal descent – chronic damage to levator ani muscle and pudendal nerves (obesity, multiparous women) and anus falls below levators; Tx: high-fiber diet, limit to 1 bowel movement a day; hard to treat
- Obstetrical trauma – Tx: anterior anal sphincteroplasty



Overlapping anal sphincteroplasty.

AIDS ANORECTAL PROBLEMS

- Kaposi's sarcoma – see nodule with ulceration; most common cancer in patients with AIDS
- CMV – see shallow ulcers; similar presentation as appendicitis. Tx: ganciclovir
- HSV – #1 rectal ulcer
- B cell lymphoma – can look like abscess or ulcer
- Need biopsies of these ulcers to rule out cancer and figure out above

ANAL CANCER

- Association with HPV, HIV, and XRT
- Anal canal – above dentate line
- Anal margin – below dentate line
- Anal canal lesions *(above dentate line)*
  - Squamous cell CA (eg epidermoid CA, mucoepidermoid CA, cloacogenic CA, basaloid CA)
    - Symptoms: pruritus, bleeding, and palpable mass; may have palpable inguinal nodes
    - Tx: *Nigro protocol (chemo-XRT with 5FU and mitomycin),* not surgery
    - Cures 80%
    - APR for treatment failures or recurrent cancer
  - Adenocarcinoma
    - Tx: APR usual; WLE if < 4 cm, < ½ circumference, limited to submucosa (T1 tumors, 2–3 mm margin needed), well differentiated, and no vascular/lymphatic/nerve invasion
    - Postoperative chemo/XRT same as rectal CA
  - Melanoma
    - 3rd most common site for melanoma (skin and eyes #1 and #2)
    - ⅓ has spread to mesenteric lymph nodes

    - Hematogenous spread to the liver and the lung is early and accounts for most deaths
    - Symptomatic disease is often associated with significant metastatic disease
    - Most common symptom – rectal bleeding
    - Most tumors are lightly pigmented or not pigmented at all
    - Tx: APR usual; margin dictated by depth of lesion standard for melanoma
- Anal margin lesions *(below dentate line)* – have better prognosis than anal canal lesions
  - Squamous cell CA
    - Ulcerating, slow growing; men with better prognosis
    - Metastases – go to inguinal nodes
    - WLE for lesions < 5 cm (need 0.5 cm margin)
    - Chemo-XRT (5-FU and cisplatin) primary Tx for lesions > 5 cm, if involving sphincter or if positive nodes (trying to preserve the sphincter here and avoid APR)
    - Need inguinal node dissection if clinically positive
  - Basal cell CA – central ulcer, raised edges, rare metastases
    - Tx: WLE usually sufficient, only need 3-mm margins; rare need for APR unless sphincter involved

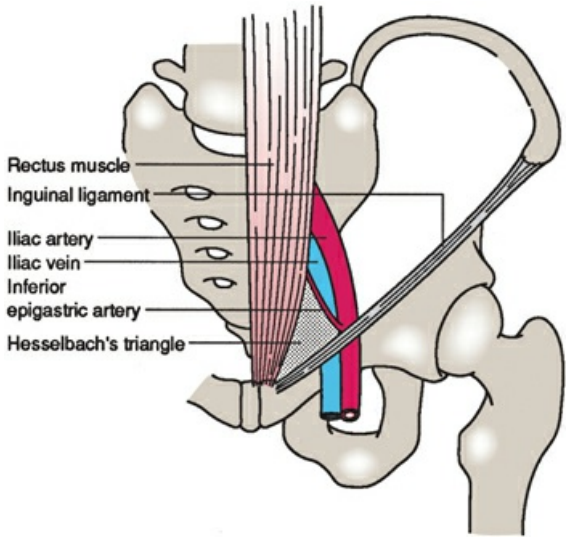
NODAL METASTASES

- Superior and middle rectum – IMA nodes
- Lower rectum – primarily IMA nodes, also to internal iliac nodes
- Anal canal – internal iliac nodes
- Anal margin – inguinal nodes

38 Hernias, Abdomen, and Surgical Technology

INGUINAL HERNIAS

- External abdominal oblique fascia – forms the inguinal ligament (shelving edge and roof) at inferior portion of the inguinal canal
- Internal abdominal oblique – forms cremasteric muscles
- Transversalis muscle – along with the conjoined tendon, forms inguinal canal floor
- Conjoined tendon – composed of the aponeurosis of the internal abdominal oblique and transversalis fascia
- Inguinal ligament (Poupart's ligament) – from external abdominal oblique fascia, runs from anterior superior iliac spine to the pubis; anterior to the femoral vessels
  - Lacunar ligament – where the inguinal ligament splays out to insert in the pubis
- Cooper's ligament – pectineal ligament; posterior to the femoral vessels; lies against bone
- Vas deferens – runs medial to cord structures
- Hesselbach's triangle – rectus muscle, inferior inguinal ligament, and inferior epigastrics
  - Direct hernias are inferior/medial to the epigastric vessels
  - Indirect hernias are superior/lateral to the epigastric vessels



The inguinal (Hesselbach's) triangle.

- Indirect hernias – most common; from persistently patent processus vaginalis
- Direct hernias – lower risk of incarceration; rare in females, higher recurrence than indirect
- Pantaloon hernia – direct and indirect components
- Risk factors for inguinal hernia in adults: age, obesity, heavy lifting, COPD (coughing), chronic constipation, straining (BPH), ascites, pregnancy, peritoneal dialysis
- Incarcerated hernia – can lead to bowel strangulation; should be repaired emergently
- Sliding hernias – retroperitoneal organ makes up part of the hernia sac

    - Females – ovaries or fallopian tubes most common
    - Males – cecum or sigmoid most common
    - Bladder can also be involved
- Females with ovary in canal
    - Ligate the round ligament (found in the inguinal canal in women)
    - Return ovary to peritoneum
    - Perform biopsy if looks abnormal
- Hernias in infants and children
    - Just perform high ligation (nearly always indirect)
    - Open sac prior to ligation
- Lichtenstein repair = mesh; recurrence ↓ with use of mesh (↓ tension)
- Bassini repair – approximation of the conjoined tendon to the free edge of the inguinal ligament (shelving edge, inferior)
- Cooper's ligament repair – approximation of the conjoined tendon to Cooper's ligament (pectineal ligament, inferior)
    - Needs a relaxing incision in the external abdominal oblique fascia
    - Can use this for femoral hernia repair
- Laparoscopic hernia repair – indicated for bilateral or recurrent inguinal hernia
- Urinary retention – most common early complication following hernia repair
- Wound infection – 1%
- Recurrence rate – 2%
- Testicular atrophy – usually secondary to dissection of the distal component of the hernia sac causing vessel disruption
    - Thrombosis of spermatic cord veins
    - Usually occurs with indirect hernias
- Pain after hernia – usually compression of ilioinguinal nerve
    - Tx: local infiltration can be diagnostic and therapeutic (near anterior superior iliac spine)
- Ilioinguinal nerve injury – loss of cremasteric reflex; numbness on ipsilateral penis, scrotum, and thigh
    - Nerve is usually injured at the external ring; nerve runs on top of cord (anterior)
- Genitofemoral nerve injury – usually injured with laparoscopic hernia repair
    - Genital branch – cremaster (motor) and scrotum (sensory)
    - Femoral branch – upper lateral thigh (sensory)
- Cord lipomas – should be removed

FEMORAL HERNIA

- Most common in males, although incidence is increased in females compared to inguinal hernias
- Femoral canal boundaries – Cooper's ligament (pectineal, posterior), inguinal ligament (anterior), femoral vein (lateral), and lacunar ligament (medial)
- Femoral hernia is medial to the femoral vein and lateral to the lymphatics (in empty space)
- High risk of incarceration → may need to divide the inguinal ligament to reduce the bowel
- Hernia passes under the inguinal ligament
- Characteristic bulge on the anterior–medial thigh below the ligament
- Hernia is usually repaired through an inguinal approach with Cooper's ligament repair

OTHER HERNIAS

- Umbilical hernia
  - ↑ incidence in African Americans; often close on their own
  - Delay repair until age 5 years
  - Risk of incarceration in adults, not children
- Spigelian hernia
  - Lateral border of rectus muscle, adjacent to the linea semilunaris
  - Almost always inferior to the semicircularis
  - Occurs between the muscle fibers of the internal abdominal oblique muscle and insertion of the external abdominal oblique aponeurosis into the rectus sheath
- Obturator hernia (anterior pelvis)
  - Can present as tender medial thigh mass or as small bowel obstruction
  - Howship–Romberg sign – inner thigh pain with internal rotation
  - Elderly women, previous pregnancy, bowel gas below superior pubic ramus
  - Tx: operative reduction, may need mesh; check other side for similar defect
- Sciatic hernia (posterior pelvis)
  - Herniation through the greater sciatic foramen; high rate of strangulation
- Incisional hernia – most likely to recur; inadequate closure is the most common cause

RECTUS SHEATH

- Anterior – complete
- Posterior – absent below semicircularis (below umbilicus)
- The posterior aponeurosis of the internal abdominal oblique and transversalis moves anterior below the umbilicus
- Rectus sheath hematomas
  - Most common after trauma; epigastric vessel injury
  - Painful abdominal wall mass
  - Mass more prominent and painful with flexion of the rectus muscle (Fothergill's sign)
  - Tx: nonoperative usual, surgery if expanding

DESMOID TUMORS

- Women, benign but locally invasive; ↑ recurrences
- Gardner's syndrome
- Painless mass
- Tx: wide local excision if possible; if involving significant small bowel mesentery, excision may not be indicated → often not completely resectable
  - Medical Tx: sulindac and tamoxifen

RETROPERITONEAL FIBROSIS

- Can occur with hypersensitivity to methysergide
- IVP most sensitive test (constricted ureters)
- Symptoms usually related to trapped ureters and lymphatic obstruction
- Tx: steroids, nephrostomy if infection is present, and surgery if renal function becomes compromised (free up ureters and wrap in omentum)

MESENTERIC TUMORS

- Of the primary tumors, most are cystic
  - Malignant tumors – closer to the root of the mesentery
  - Benign tumors – more peripheral
- Malignant – liposarcoma (#1), leiomyosarcoma
- Dx: abdominal CT
- Tx: resection

RETROPERITONEAL TUMORS

- 15% in children, others in 5th–6th decade
- Malignant > benign
- Most common malignant retroperitoneal tumor – #1 lymphoma, #2 liposarcoma
- Symptoms: vague abdominal and back pain
- Retroperitoneal sarcomas
  - < 25% resectable; local recurrence in 40%; 10% 5-year survival rate
  - Have pseudocapsule but cannot shell out → would leave residual tumor
  - Metastases go to the lung

OMENTAL TUMORS

- Most common omental solid tumor is metastatic disease
- Omentectomy for metastatic cancer has a role for some cancers (eg ovarian CA)
- Omental cysts are usually asymptomatic, can undergo torsion
- Primary solid omental tumors are rare; ⅓ are malignant
  - No biopsy → can bleed
  - Tx: resection

PERITONEAL MEMBRANE

- Blood is absorbed through fenestrated lymphatic channels in the peritoneum
- Most drugs are not removed with peritoneal dialysis
- NH_3, Ca, Fe, and lead are removed
- Movement of fluid into the peritoneal cavity can occur with hypertonic intra-peritoneal saline load (mechanism of peritoneal dialysis); can cause hypotension

CO_2 PNEUMOPERITONEUM

- Normal is 10–15
- Cardiopulmonary dysfunction can occur with intra-abdominal pressure > 20
- *Increased*: mean arterial pressure, pulmonary artery pressure, HR, systemic vascular resistance, central venous pressure, mean airway pressure, peak inspiratory pressure, and CO_2
- *Decreased*: pH, venous return (IVC compression), cardiac output, renal flow secondary to decreased cardiac output
- Hypovolemia lowers pressure necessary to cause compromise
- PEEP worsens effects of pneumoperitoneum
- CO_2 can cause some ↓ in myocardial contractility

- CO_2 embolus (sudden transient rise in $ETCO_2$, followed by a drop, then hypotension) – Tx: head down, turn patient to the left; can try to aspirate CO_2 through central line; prolonged CPR

SURGICAL TECHNOLOGY

- Harmonic scalpel
  - Cost-effective for medium vessels (short gastrics)
  - Disrupts protein H-bonds, causes coagulation
- Ultrasound
  - B-mode used most commonly (B = brightness; assesses relative density of structures)
  - Shadowing – dark area posterior to object indicates mass
  - Enhancement – brighter area posterior to object indicates fluid-filled cyst
  - Lower frequencies – deep structures
  - Higher frequencies – superficial structures
  - Duplex – adds Doppler; color visual description of blood flow (direction, stenosis, velocity)
- Argon beam – energy transferred across argon gas
  - Depth of necrosis related to power setting (2 mm); causes superficial coagulation
  - Is non-contact – good for hemostasis of the liver and spleen; smokeless
- Laser – return of electrons to ground state releases energy as heat → coagulates and vaporizes
  - Used for condylomata acuminata (wear mask)
- Nd:YAG laser – good for deep tissue penetration; good for bronchial lesions
  - 1–2 mm cuts, 3–10 mm vaporizes, and 1–2 cm coagulates
- Gore-Tex (PTFE) – cannot get fibroblast ingrowth
- Dacron (polypropylene) – allows fibroblast ingrowth
- Incidence of vascular or bowel injury with Veress needle or trocar – 0.1%

39 Urology

ANATOMY AND PHYSIOLOGY

- Gerota's fascia – around kidney
- Anterior to posterior – renal vein, renal artery, and renal pelvis
  - Right renal artery crosses posterior to the IVC
  - Left renal vein is anterior to the aorta
- Ureters cross over iliac vessels
- Left renal vein – can be ligated from IVC secondary to increased collaterals (left adrenal vein, left gonadal vein, and left ascending lumbar vein); right renal vein lacks collaterals
  - Left renal vein usually crosses anterior aorta
- Epididymis – connects to vas deferens
- Seminal vesicles are connected to the vas deferens
- Spermatic cord structures – testicular artery, pampiniform plexus, vas deferens, cremasteric muscle, ilioinguinal nerve, genital branch of the genitofemoral nerve
- Erection – parasympathetic
- Ejaculation – sympathetic
- Hypotension – most common cause of acute renal insufficiency following surgery

KIDNEY STONES

- Symptoms: severe, colicky, flank (back) pain; restlessness; nausea and vomiting
- Urinalysis – blood or stones
- Abdominal CT – can demonstrate stones and associated hydronephrosis
- Calcium oxalate stones – most common (75%); radiopaque; ↑ in patients with terminal ileum resection due to ↑ oxalate absorption in colon
- Struvite stones (magnesium ammonium phosphate; radiopaque) – occur with infections (*Proteus mirabilis*) that are urease producing; cause staghorn calculi (fill renal pelvis)
- Uric acid stones (radiolucent) – ↑ in patients with ileostomies, gout, and myeloproliferative disorders
- Cysteine stones (radiolucent) – associated with congenital disorders in the reabsorption of cysteine (cystinuria); prevention – tiopronin
- Medical Tx: IV fluids, analgesics, watchful waiting
- Surgery indications for kidney stones:
  - Intractable pain or infection
  - Progressive obstruction
  - Progressive renal damage
  - Solitary kidney
  - Stones with low probability of passing
- 90% of kidney stones opaque; > 6 mm not likely to pass
- Tx: ESWL (extra-corporeal shock wave lithotripsy; not used in pregnancy, with bleeding diathesis, or stones that are several centimeters in size); other options – ureteroscopy with

stone extraction or placement of stent past obstruction, percutaneous nephrostomy tube, open nephrolithotomy

TESTICULAR CANCER

- #1 cancer killer in men 25–35
- Symptom: painless hard mass
- Testicular mass – patient needs an orchiectomy through an inguinal incision (not a transscrotal incision → do not want to disrupt lymphatics)
  - The testicle and attached mass constitute the biopsy specimen
- Most testicular masses are malignant
- Ultrasound can help with diagnosis
- Chest and abdominal CT – to check for retroperitoneal and chest metastases
- LDH correlates with tumor bulk
- Check B-HCG and AFP level
- 90% are germ cell – seminoma or nonseminoma
- Undescended testicles (cryptorchidism) – ↑ risk of testicular CA
  - Most likely to get seminoma
- Seminoma
  - #1 testicular tumor
  - 10% of seminomatous tumors have beta-HCG elevation
  - Should not have AFP elevation (if elevated, need to treat like non-seminomatous)
  - Seminoma is extremely sensitive to XRT
  - Tx: all stages get *orchiectomy and retroperitoneal XRT*
    - Chemo reserved for metastatic disease or bulky retroperitoneal disease (cisplatin, bleomycin, VP-16)
    - Surgical resection of residual disease after above
- Nonseminomatous testicular CA
  - Types – embryonal, teratoma, choriocarcinoma, yolk sac
  - Alpha fetoprotein and beta-HCG – 90% have these markers
  - Classically, tumors with ↑ teratoma components are more likely to metastasize to the retroperitoneum
  - Tx: all stages get *orchiectomy and retroperitoneal node dissection*
    - *Stage II or greater – also give chemo (cisplatin, bleomycin, VP-16)*
    - Surgical resection of residual disease after above

PROSTATE CANCER

- Posterior lobe – most common site
- Bone – most common site of metastases
  - Osteoblastic; x-ray demonstrates hyperdense areas
- Many patients become impotent after resection; can get incontinence
- Can also get urethral strictures
- Dx: transrectal Bx, chest/abdomen/pelvic CT, PSA, alkaline phosphatase; possible bone scan
- Intracapsular tumors and no metastases (T1 and T2) → options:
  - XRT *or*
  - Radical prostatectomy + pelvic lymph node dissection (if life span > 10 years) *or*

- Nothing (depending on age and health)
- Extracapsular invasion or metastatic disease
  - Tx: XRT and androgen ablation (leuprolide [GnRH agonist], flutamide [testosterone receptor blocker], or bilateral orchiectomy)
- Stage IA disease found with TURP – Tx: nothing
- With prostatectomy, PSA should go to 0 after 3 weeks → if not, get bone scan to check for metastases
- A normal PSA is < 4 in a patient who has a prostate gland
  - PSA can be ↑ with prostatitis, BPH, and chronic catheterization
- ↑ alkaline phosphatase in a patient with prostate CA → worrisome for metastases or extracapsular disease

RENAL CELL CARCINOMA (RCC, HYPERNEPHROMA)

- #1 primary tumor of kidney (15% calcified)
- Risk factor: smoking
- Flank pain, mass, and hematuria
- Dx: CT scan – ⅓ have metastatic disease at the time of diagnosis → can perform wedge resection of isolated lung or colon metastases
- Lung – most common location for RCC metastases
- Erythrocytosis can occur secondary to ↑ erythropoietin (HTN)
- Tx: radical nephrectomy with regional nodes; XRT, chemotherapy
  - Radical nephrectomy takes kidney, adrenal, fat, Gerota's fascia, and regional nodes
  - Predilection for growth in the IVC; can still resect even if going up IVC → can pull the tumor thrombus out of the IVC
  - Partial nephrectomies should be considered only for patients who would require dialysis after nephrectomy (tumors < 4 cm, creatinine ≥ 2.5)
- Most common tumor in kidney – metastasis from breast CA
- RCC paraneoplastic syndromes – renin, erythropoietin, PTHrp, ACTH, insulin
- Transitional cell CA of renal pelvis – Tx: radical nephroureterectomy
- Oncocytomas – benign
- Angiomyolipomas – hamartomas; can occur with tuberous sclerosis; benign
- Von Hippel–Lindau syndrome – multifocal and recurrent RCC, renal cysts, CNS tumors, and pheochromocytomas

BLADDER CANCER

- Usually transitional cell CA
- Painless hematuria
- Males; prognosis based on stage and grade
- Risk factors: smoking, aniline dyes, and cyclophosphamide
- Dx: cystoscopy
- Tx: intravesical BCG or transurethral resection if muscle is not involved (T1)
  - If muscle wall is invaded (T2 or greater) → cystectomy with ileal conduit, chemotherapy (MVAC: methotrexate, vinblastine, Adriamycin [doxorubicin], and cisplatin), and XRT
  - Metastatic disease – chemotherapy
- Ileal conduit is standard reconstruction option – avoid stasis as this predisposes to infection,

stones (calcium resorption), and ureteral reflux
- Reservoirs or neobladders may also be options
- Squamous cell CA of bladder – schistosomiasis infection

TESTICULAR TORSION

- Peaks in 15-year-olds; sudden onset of severe testicular pain
- Testis is swollen, tender, high riding, and may have a horizontal lie
- Torsion is usually toward the midline
- Tx: emergency detorsion and bilateral orchiopexy
  - If testicle not viable, resection and orchiopexy of contralateral testis

URETERAL TRAUMA

- If going to repair end-to-end →
  - Spatulate ends
  - Use absorbable suture to avoid stone formation
  - Stent the ureter to avoid stenosis
  - Place drains to identify and potentially help treat leaks
- Avoid stripping the soft tissue on the ureter, as it will compromise blood supply

BENIGN PROSTATIC HYPERTROPHY (BPH)

- Arises in transitional zone
- Symptoms: nocturia, frequency, dysuria, weak stream, urinary retention
- Initial therapy
  - Alpha blockers – terazosin, doxazosin (relax smooth muscle)
  - 5-alpha-reductase inhibitors – finasteride (inhibits the conversion of testosterone to dihydrotestosterone → inhibits prostate hypertrophy)
- Surgery (trans-urethral resection of prostate; TURP): for recurrent UTIs, gross hematuria, stones, renal insufficiency, or failure of medical therapy
  - Post-TURP syndrome – hyponatremia secondary to irrigation with water; can precipitate seizures from cerebral edema
  - Tx: careful correction of Na with diuresis
- Most patients with TURP have retrograde ejaculation

NEUROGENIC BLADDER

- Most commonly secondary to spinal compression
- Patient urinates all the time
- Nerve injury above T-12
- Tx: surgery to improve bladder resistance

NEUROGENIC OBSTRUCTIVE UROPATHY

- Incomplete emptying
- Nerve injury below T-12; can occur with APR
- Tx: intermittent catheterization

INCONTINENCE

- Stress incontinence (cough, sneeze)
  - Because of hypermobile urethra or loss of sphincter mechanism; women; multiple pregnancies and vaginal deliveries
  - Tx: Kegel exercises, alpha-adrenergic agents, surgery for urethral suspension or pubovaginal sling
- Overflow incontinence
  - Incomplete emptying of an enlarged bladder
  - Obstruction (BPH) leads to the distention and leakage
  - Tx: tamsulosin (Flomax); TURP

OTHER UROLOGIC DISEASES

- Ureteropelvic obstruction – Tx: pyeloplasty
- Vesicoureteral reflux – prophylactic antibiotics and see if the child outgrows it; failure to suppress infections or complicated disease requires surgery
  - Dx: voiding cystourethrogram
  - Surgical Tx: reimplantation of ureter with long bladder portion
- Ureteral duplication – most common urinary tract abnormality; Tx: reimplantation if obstruction occurs
- Ectopic ureter – often seen with ureteral duplication; can connect to urethra (usually asymptomatic unless obstruction occurs; usually no Tx necessary) or vagina (need to re-implant in the bladder)
- Ureterocele – Tx: resect and reimplant if symptomatic
- Posterior urethral valves – most common reason for newborn boy not to urinate
  - Place urinary catheter to temporize (valves will not block catheter)
  - Dx: voiding cystourethrogram
  - Tx: resection of valves
- Hypospadias – ventral urethral opening; Tx: repair at 6 months with penile skin (use foreskin; *no circumcision in these patients*)
- Epispadias – dorsal urethral opening; Tx: surgery
- Horseshoe kidney – usually joined at lower poles
  - Complications: UTI, urolithiasis, and hydronephrosis
  - Tx: may need pyeloplasty
- Polycystic kidney disease – resection only if symptomatic
- Failure of closure of urachus – connection between umbilicus and bladder; occurs in patients with bladder outlet obstructive disease (wet umbilicus)
  - Tx: resection of sinus/cyst and closure of the bladder; relieve bladder outlet obstruction
- Epididymitis – sterile epididymitis can occur from ↑ abdominal straining
- Infectious acute epididymitis – sexually active; severe testicular pain of sudden onset; fever and pyuria; swollen and tender testis; cord is tender as well; get U/S to rule out testicular torsion; Tx: antibiotics
- Acute bacterial prostatitis – older men with fever, chills, dysuria, frequency, diffuse back pain, and tender prostate; Tx: antibiotics (avoid prostate compression, which could lead to sepsis)
- Varicocele – worrisome for renal cell CA (left gonadal vein inserts into left renal vein;

obstruction by renal tumor causes varicocele); could also be caused by another retroperitoneal malignancy

- Spermatocele – fluid-filled cystic structure separate from and superior to the testis along the epididymis; Tx: surgical removal if symptomatic
- Hydrocele in adult – if acute, suspect tumor elsewhere (pelvic, abdominal); translucent
- Pneumaturia – most common cause is diverticulitis and subsequent formation of colovesical fistula; Dx – cystoscopy
- WBC casts – pyelonephritis, glomerulonephritis
- RBC casts – glomerulonephritis
- Pyelonephritis – fever, chills, flank pain, nausea, vomiting
  - Dx: CT or U/S to rule out obstruction
  - Tx: antibiotics and relief of any obstruction (eg ureteral stone) with stent, stone removal, or percutaneous nephrostomy tube
- Interstitial nephritis – fever, rash, arthralgias, eosinophils
- Vasectomy – 50% pregnancy rate after repair of vasectomy
- Priapism (erection lasting more than 4 hours) – Tx: aspiration of the corpus cavernosum with dilute epinephrine or phenylephrine
  - May need to create a communication through the glans with scalpel
  - Risk factors: sickle-cell anemia, hypercoagulable states, trauma, intracorporeal injections for impotence
- SCC of penis – penectomy with 2-cm margin
- Indigo carmine or methylene blue (intravenous) – used to check for urine leak
- Phimosis found at time of laparotomy – Tx: dorsal slit
- Erythropoietin – ↓ production in patients with renal failure

40 Gynecology

LIGAMENTS

- Round ligament – allows anteversion of the uterus
- Broad ligament – contains uterine vessels
- Infundibular ligament – contains ovarian artery, nerve, and vein
- Cardinal ligament – holds cervix and vagina

ULTRASOUND

- Very good at diagnosing disorders of the female genital tract

PREGNANCY

- Can see most pregnancies on ultrasound at 6 weeks
- Gestational sac is seen with beta-HCG of 1,500
- Fetal pole usually is seen with beta-HCG of 6,000

ABORTIONS

- Missed – 1st-trimester bleeding, closed os, positive sac on ultrasound, and no heartbeat
- Threatened – 1st-trimester bleeding, positive heartbeat
- Incomplete – tissue protrudes through os
- Ectopic pregnancy (life threatening) – acute abdominal pain; positive beta-HCG, negative ultrasound for sac; can also have missed period, vaginal bleeding, hypotension
  - Risk factors for ectopic pregnancy: previous tubal manipulation, PID, previous ectopic pregnancy
  - MC site – ampullary portion of the fallopian tubes
  - Significant shock and hemorrhage can occur from an ectopic pregnancy
  - Stable – methotrexate or salpingotomy
  - Unstable – salpingectomy

ENDOMETRIOSIS

- Symptoms: dysmenorrhea, infertility, dyspareunia
- Can involve the rectum and cause bleeding during menses → endoscopy shows blue mass
- Ovaries – most common site
- Tx: OCPs

PELVIC INFLAMMATORY DISEASE

- Has ↑ risk of infertility and ectopic pregnancy
- Symptoms: pain, nausea, vomiting, fever, vaginal discharge
  - Most commonly occurs in the first ½ of the menstrual cycle
- Risk factors: multiple sexual partners

- Dx: cervical motion tenderness, cervical cultures, positive Gram stain
- Tx: ceftriaxone, doxycycline
- Complications: persistent pain, infertility, ectopic pregnancy
- HSV – vesicles; HPV – condylomata
- Syphilis – positive dark-field microscopy, chancre
- Gonococcus – diplococci

MITTELSCHMERZ

- Rupture of graafian follicle
- Causes pain that can be confused with appendicitis
- Occurs 14 days after the 1st day of menses

VAGINAL CANCER

- #1 primary – squamous cell CA
- DES (diethylstilbestrol) – can cause clear cell CA of vagina
- Botryoides – rhabdosarcoma that occurs in young girls
- XRT – used for most cancers of vagina

VULVAR CANCER

- Elderly, nulliparous, obese; usually unilateral
- Majority squamous cell CA
- Tx: < 2 cm (stage I) – WLE and ipsilateral inguinal node dissection (2-cm margins)
  - > 2 cm (stage II or greater) – radical vulvectomy (bilateral labia) with bilateral inguinal dissection, postop XRT if close margins (< 1 cm)
  - Paget's VIN III or higher – premalignant
  - VIN – vulvar intra-epithelial neoplasia

OVARIAN CANCER

- Leading cause of gynecologic death
- Abdominal or pelvic pain; change in stool or urinary habits; vaginal bleeding
- ↓ risk – OCPs, bilateral tubal ligation
- ↑ risk – nulliparity, late menopause, early menarche
- Types – teratoma, granulosa-theca (estrogen secreting, precocious puberty); Sertoli–Leydig (androgens, masculinization); struma ovarii (thyroid tissues); choriocarcinoma (beta-HCG); mucinous; serous; and papillary
- Clear cell type – worst prognosis

Staging of Ovarian Cancer

Stage	Location
I	One or both ovaries only
II	Limited to pelvis
III	Spread throughout abdomen
IV	Distant metastases

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Springer Science and Business Media LLC, www.springer.com.

- Bilateral ovary involvement still stage I
- MC initial site of regional spread – other ovary
- Debulking tumor – can be effective; including omentectomy (helps intraperitoneal chemo and XRT)
- Tx: total abdominal hysterectomy and bilateral oophorectomy for all stages; *plus*:
  - Pelvic and para-aortic LN dissection
  - Omentectomy
  - 4 quadrant washes
  - Chemotherapy: cisplatin and paclitaxel (Taxol)
- Krukenberg tumor – stomach CA that has metastasized to ovary
  - Pathology classically shows signet ring cells
- Meige's syndrome – pelvic ovarian fibroma that causes ascites and hydrothorax
  - Excision of tumor cures syndrome

ENDOMETRIAL CANCER

- Most common malignant tumor in female genital tract
- Risk factors – nulliparity, late 1st pregnancy, obesity, tamoxifen, unopposed estrogen
- Vaginal bleeding in postmenopausal patient is endometrial CA until proved otherwise
- Uterine polyps have very low chance of malignancy (0.1%)
- Clear cell subtype – worst prognosis
- Abdominal approach with surgery (not trans-vaginal)

Staging and Treatment

Stage	Location	Treatment
I	Endometrium	Total abdominal hysterectomy and BSO or XRT
II	Cervix	Total abdominal hysterectomy and BSO or XRT
III	Vagina, peritoneum, and ovary	Total abdominal hysterectomy and BSO and XRT
IV	Bladder and rectum	Total abdominal hysterectomy and BSO and XRT

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CERVICAL CANCER

- Goes to obturator nodes 1st
- Associated with HPV 16 and 18
- Squamous cell CA – most common

Staging of Cervical Cancer

Stage	Location
I	Cervix
II	Upper ⅔ of vagina
III	Pelvis, side wall, and lower ⅓ of vagina; hydronephrosis
IV	Bladder and rectum

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- Tx: microscopic disease without basement membrane invasion → cone biopsy (conization sufficient to remove disease; inner lining of the cervix is removed)
- Stages I and IIa – total abdominal hysterectomy (TAH)
- Stages IIb to IV – chemo-XRT (cisplatin and paclitaxel [Taxol])

OVARIAN CYSTS

- Postmenopausal patient
  - If septated, has ↑ vascular flow on Doppler, has solid components, or has papillary projections → oophorectomy with intraoperative frozen sections; TAH if ovarian CA
  - If none of the above are present, follow with ultrasound for 1 year → if persists or gets larger → oophorectomy with intraoperative frozen sections; TAH if ovarian CA
- Premenopausal patient
  - If septated, has ↑ vascular flow on Doppler, has solid components, or has papillary projections → oophorectomy with intraoperative frozen sections usual
    - Algorithm becomes very complicated after this, weighing how aggressive the cancer is (based on histology and stage at the time of operation) compared with whether the patient desires future pregnancy
  - If none of the above are present → can follow with ultrasound; surgery if suspicious findings appear

ABNORMAL UTERINE BLEEDING

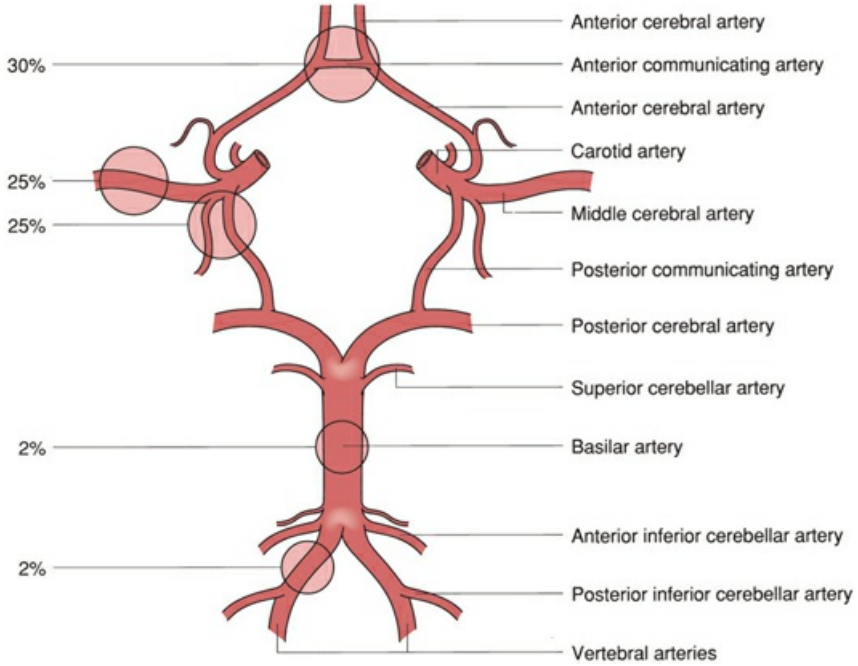
- < 40 years old – if anovulation. Tx: clomiphene citrate
  - If leiomyomas → Tx: GnRH agonists (leuprolide)
- > 40 years old – cancer or menopause → need biopsy

OTHER GYNECOLOGIC CONSIDERATIONS

- Contraindications to estrogen therapy – endometrial CA, thromboembolic disease, undiagnosed vaginal bleeding, breast CA
- Uterine endometrial polyp – can present as progressively heavier menses
- Uterine fibroids (leiomyomas) – under hormonal influence; recurrent abortions, infertility, bleeding
- Most common vaginal tumor – invasion from surrounding or distant structure
- Hydatidiform mole – malignancy risk with partial mole; complete mole is of paternal origin; Tx: chemo (methotrexate)
- Toxic shock syndrome – fever, erythema, diffuse desquamation, nausea, vomiting; associated with highly absorbent tampons
- Ovarian torsion – Tx: remove torsion and check for viability
- Adnexal torsion with vascular necrosis – Tx: adnexectomy
- Ruptured tuboovarian abscess – Tx: percutaneous drainage and antibiotics
- Ovarian vein thrombosis – Dx: CT scan; Tx: heparin
- Postpartum pelvic thrombophlebitis – can lead to ovarian vein, IVC, and hepatic vein thrombosis; get liver failure with ascites after pregnancy; Tx: heparin and antibiotics

41 Neurosurgery

INTRODUCTION



Locations of aneurysms of the circle of Willis and their relative occurrence.

CIRCLE OF WILLIS

- Vertebral arteries – come together to form a single basilar artery, which branches into 2 posterior cerebral arteries
- Posterior communicating arteries – connect middle cerebral arteries to posterior cerebral arteries
- Anterior cerebral arteries – branches off middle cerebral arteries and are connected to each other through the 1 anterior communicating artery

NERVE INJURY

- Neurapraxia – no axonal injury (temporary loss of function, foot falls asleep)
- Axonotmesis – disruption of axon with preservation of axon sheath, will improve
- Neurotmesis – disruption of axon and myelin sheath (whole nerve is disrupted), may need surgery for recovery
- Regeneration of nerves occurs at a rate of 1 mm/day
- Nodes of Ranvier – bare sections; allow salutatory conduction

ANTIDIURETIC HORMONE (ADH)

- Release controlled by supraoptic nucleus of hypothalamus, which descends into the

posterior pituitary gland

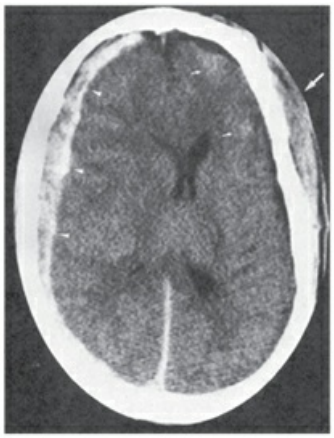
- Released in response to high plasma osmolarity; ADH increases water absorption in collecting ducts

STROKE

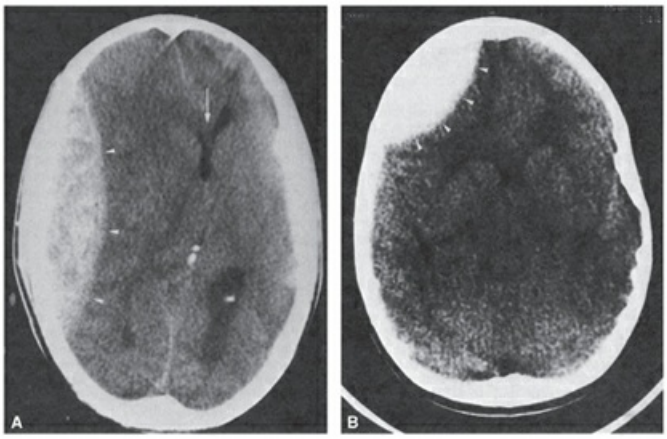
- CT scan to rule out hemorrhage (can't use tPA)
- Tx: tPA if within 3 hours of symptoms; endovascular stent retriever can be used for large emboli or failure of tPA if within 6 hours of stroke

HEMORRHAGE

- Arteriovenous malformations – 50% present with hemorrhage; are congenital
  - Usually in patients < 30; sudden headache and loss of consciousness
  - Tx: resection if symptomatic
  - Can coil embolize these prior to resection
- Cerebral aneurysms – usually occur in patients > 40; most are congenital
  - Can present with bleeding, mass effect, seizures, or infarcts
  - Occur at branch points in artery, most off middle cerebral artery
  - Tx: often place coils before clipping and resecting aneurysm
- Subdural hematoma – caused by torn bridging veins
  - Has crescent shape on head CT and conforms to brain
  - Higher mortality than epidural hematoma
  - Tx: operate for significant neurologic degeneration or mass effect (shift > 1 cm)



Acute subdural hematoma imaged by noncontrast computed tomography.



Two examples of acute epidural hematoma imaged by noncontrast computed tomography.

- Epidural hematoma – caused by injury to middle meningeal artery
  - Has lens shape on head CT and pushes brain away
  - Patients classically lose consciousness, have a lucid interval, and then lose consciousness again
  - Tx: operate for significant neurologic degeneration or mass effect (shift > 0.5 cm)
- Subarachnoid hemorrhage (nontraumatic)
  - Caused by cerebral aneurysms (50% middle cerebral artery) and AVMs
  - Symptoms: stiff neck (nuchal rigidity), severe headache, photophobia, neurologic defects
  - Tx: goal is to isolate the aneurysm from systemic circulation (clipping vascular supply), maximize cerebral perfusion to overcome vasospasm, and prevent rebleeding; use hypervolemia and calcium channel blockers to overcome vasospasm
  - Go to OR only if neurologically intact
  - Can get subarachnoid hemorrhages with trauma as well
- Intracerebral hematomas – temporal lobe most often affected
  - Those that are large and cause focal deficits should be drained
- Symptoms of ↑ ICP – stupor, headache, nausea and vomiting, stiff neck
- Signs of ↑ ICP – hypertension, HR lability, slow respirations
  - Intermittent bradycardia is a sign of severely elevated ICP and impending herniation
  - Cushing's triad – hypertension, bradycardia, slow respiratory rate

SPINAL CORD INJURY

- Cord injury with deficit → give high-dose steroids (↓ swelling)
- Most sensitive test for spinal cord injury – MRI
- Spinal shock – hypotension, normal or slow heart rate, and warm extremities (vasodilated)
  - Occurs with spinal cord injuries above T6 (loss of sympathetic tone)
  - Tx: fluids initially, may need phenylephrine drip (alpha agonist)
- Complete cord transection – bilateral areflexia, flaccidity, anesthesia, and paralysis below the level of the lesion
- Anterior spinal artery syndrome (anterior spinal cord syndrome) – occurs from compromise of the anterior spinal artery
  - Causes – aortic dissection, aneurysm, or atherosclerosis; ruptured disc; vertebral body burst fracture
  - Bilateral loss of motor, pain, and temperature sensation below the level of lesion

- Preservation of position–vibratory sensation and light touch
- About 10% recover to ambulation

- Hemisection (Brown-Sequard syndrome) – incomplete cord transection (hemisection); most commonly due to penetrating injury
  - Loss of ipsilateral motor and contralateral pain/temperature below level of lesion
  - About 90% recover to ambulation
- Central cord syndrome – most commonly occurs with hyperextension of the cervical spine (eg rear-end collision; often in elderly patients with preexisting cervical spondylosis)
  - Most common cervical spinal cord injury
  - Bilateral loss motor, pain, and temperature sensation in upper extremities; lower extremities spared
- Cauda equina syndrome – pain and weakness in lower extremities due to compression of lumbar nerve roots
- Spinothalamic tract (dorsal) – carries pain and temperature sensory neurons
- Corticospinal tract (ventral) – carries motor neurons
- Rubrospinal tract (ventral) – carries motor neurons
- Dorsal nerve roots – are generally afferent; carry sensory fibers
- Ventral nerve roots – are generally efferent; carry motor neuron fibers

BRAIN TUMORS

- Most are metastatic from other primary sites (eg breast, lung)
- Symptoms: headache, seizures, blurred vision, progressive neurologic deficit, and persistent vomiting
- High-dose steroids can help reduce intracranial pressure
- Cushing reflex – HTN and bradycardia from increased intra-cranial pressure
- Adults – ⅔ supratentorial
- Children – ⅔ infratentorial (cerebellum; Sx's: ataxia, stumbling)
- Gliomas – most common primary brain tumor in adults and overall
  - Glioma multiforme – most common subtype, uniformly fatal
- Meningioma – benign; Tx: resection
- Lung – #1 metastasis to brain
- Most common brain tumor in children – medulloblastoma
- Most common metastatic brain tumor in children – neuroblastoma
- Acoustic neuroma – arises from the 8th cranial nerve at cerebellopontine angle
  - Symptoms – hearing loss, unsteadiness, vertigo, nausea, and vomiting
  - Tx: surgery usual

SPINE TUMORS

- Overall, most are benign; #1 tumor overall neurofibroma
- Intradural tumors are more likely benign, and extradural tumors are more likely malignant
- Paraganglionoma – check for metanephrines in urine

PEDIATRIC NEUROSURGERY

- Intraventricular hemorrhage (subependymal hemorrhage)
  - Seen in premature infants secondary to rupture of the fragile vessels in germinal matrix

- Risk factors: ECMO, cyanotic congenital heart disease
- Symptoms: bulging fontanelle, neurologic deficits, ↓ BP, and ↓ Hct
- Tx: ventricular catheter for drainage and prevention of hydrocephalus

- Myelomeningocele
  - Neural cord defect – herniation of spinal cord and nerve roots through defect in vertebra
  - Most commonly occurs in the lumbar region

MISCELLANEOUS

- Wernicke's area – speech comprehension, temporal lobe
- Broca's area – speech motor, posterior part of anterior lobe
- Pituitary adenoma, undergoing XRT, patient now in shock
  - Dx: pituitary apoplexy
  - Tx: steroids
- Cervical nerves roots 3–5 innervate diaphragm (phrenic nerve)
- Microglial cells – act as brain macrophages

Cranial Nerves

Nerve	Name	Function	Muscle
I	Olfactory	Smell	
II	Optic	Sight	
III	Oculomotor		Motor to eye
IV	Trochlear		Superior oblique (eye)
V	Trigeminal: ophthalmic, maxillary, and mandibular branches	Sensory to face	Muscles of mastication
VI	Abducens		Lateral rectus (eye)
VII	Facial	Taste to anterior ⅔ of tongue	Motor to face
VIII	Vestibulocochlear	Hearing	
IX	Glossopharyngeal	Taste to posterior ⅓ of tongue	Swallowing muscles
X	Vagus	Many functions	
XI	Accessory		Trapezius Sternocleidomastoid
XII	Hypoglossal		Tongue

- Brain abscess – usually from adjacent otitis media or mastoiditis; fever; elevated ICP symptoms
  - Tx: need drainage if > 2.5 cm, otherwise just antibiotics
- Reflex sympathetic dystrophy (causalgia)
  - Develops several months after initial injury
  - Constant burning pain; aggravated by stimulation of area; area may be cold, cyanotic, and moist
  - Tx: sympathectomy

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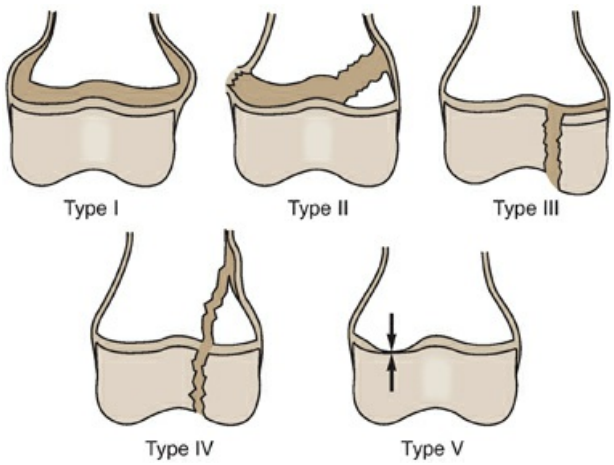
BACKGROUND

- Osteoblasts – synthesize nonmineralized bone cortex
- Osteoclasts – reabsorb bone
  - Stages of bone healing – 1) inflammation, 2) soft callus formation, 3) mineralization of the callus, 4) remodeling of the callus
- Cartilage receives nutrients from synovial fluid (osmotic)
- Salter-Harris fractures III, IV, and V – cross the epiphyseal plate and can affect the growth plate of the bone (growth plate is in 2 pieces); need open reduction and internal fixation (ORIF)
- Salter-Harris fractures I and II – closed reduction
- Greenstick fracture – buckling of the cortex



Salter-Harris classification of epiphyseal injuries. Type I injury is an epiphysiolysis of the involved growth plate without associated fracture. Type II has an additional metaphyseal fracture fragment; type I and II injuries have a good prognosis and are usually treated with closed reduction and casting. Type III injury results in a fracture through the growth plate and epiphysis. Type IV fracture crosses the epiphysis, growth plate (physis), and metaphysis. Type III and IV injuries require careful open reduction and internal fixation if displaced. Type V injury involves a crush of the growth plate without a fracture and is usually detected late by asymmetric or premature closure of the growth plate.

- Fractures associated with avascular necrosis (AVN) – scaphoid, femoral neck, talus, hip dislocation
- Fractures associated with nonunion – clavicle, 5th metatarsal fracture (Jones' fracture)
- Fractures associated with compartment syndrome – supracondylar humerus, tibia, calcaneus
- Biggest risk factor for nonunion – smoking

LOWER EXTREMITY NERVES

- Obturator nerve – hip adduction
- Superior gluteal nerve – hip abduction
- Inferior gluteal nerve – hip extension
- Femoral nerve – knee extension

LUMBAR DISC HERNIATION

- Presents with back pain, sciatica
- Herniated nucleus pulposus
- Nerve root compression affects 1 nerve root below disc:
  - L3 nerve compression (L2–3 disc) – weak hip flexion
  - L4 nerve compression (most common; L3–4 disc) – weak knee extension (quadriceps), weak patellar reflex
  - L5 nerve compression (L4–5 disc) – weak dorsiflexion (foot drop)
    - ↓ sensation in big toe web space
  - S1 nerve compression (L5–S1 disc) – weak plantar flexion, weak Achilles reflex
    - ↓ sensation in lateral foot
- Dx: patients with neurologic findings need MRI
- Tx: NSAIDs, heat, and rest for majority; surgery for substantial/progressive neurologic deficit, refractory cases, severe sciatica, or disc fragments that have herniated into the cord (laminectomy)
- Cauda equina syndrome – distended bladder, flaccid rectal sphincter, perineal saddle anesthesia; Tx: emergency decompression

TERMINAL BRANCHES OF BRACHIAL PLEXUS

- Ulnar nerve
  - Motor – intrinsic musculature of hand (palmar interossei, palmaris brevis, adductor pollicis, and hypothenar eminence); finger abduction (spread fingers); wrist flexion
  - Sensory – all of 5th and ½ 4th fingers, back of hand
  - Injury results in claw hand
- Median nerve
  - Motor – thumb apposition (anterior interosseous muscle, OK sign); finger flexors
  - Sensory – most of palm and 1st 3 and ½ 4th fingers on palmar side
  - Nerve is involved in carpal tunnel syndrome
- Radial nerve
  - Motor – wrist extension, finger extension, thumb extension, and triceps; no hand muscles
  - Sensory – 1st 3 and ½ 4th fingers on dorsal side
- Axillary nerve – motor to deltoid (abduction)
- Musculocutaneous nerve – motor to biceps, brachialis, and coracobrachialis
- Radial nerve roots – on the superior portion of the brachial plexus
- Ulnar nerve roots – on the inferior portion of the brachial plexus

UPPER EXTREMITY

- Clavicle fracture – usually just treated with sling (risk of vascular impingement)
- Shoulder dislocation
  - Anterior (90%) risk of axillary nerve injury. Tx: closed reduction

- Posterior (seizures, electrocution) risk of axillary artery injury. Tx: closed reduction
- Acromioclavicular separation – Tx: sling (risk of brachial plexus and subclavian vessel injury)
- Scapula fracture – sling unless glenoid fossa involved, then need internal fixation
- Midshaft humeral fracture – Tx: sling for almost all
- Supracondylar humeral fracture – adults → ORIF
  - Children: nondisplaced → closed reduction; displaced → ORIF
- Monteggia fracture – fall on outstretched hand; proximal ulnar fracture and radial head dislocation
  - Tx: ORIF
- Colles fracture – fall on outstretched hand, distal radius. Tx: closed reduction
- Nursemaid's elbow – subluxation of the radius at the elbow caused by pulling on an extended, pronated arm. Tx: closed reduction
- Combined radial and ulnar fracture
  - Adults – ORIF
  - Children – closed reduction
- Scaphoid fracture – snuffbox tenderness; can have negative x-ray
  - MC carpal bone fracture
  - Tx: all patients require cast to elbow, may need ORIF if displaced and angulated
  - High risk of avascular necrosis and non-union
- Metacarpal fracture – typically 4th or 5th (when closed fist hits solid surface)
  - Tx: closed reduction with ulnar gutter splint; Kirschner wires if severely displaced
- Volkmann's contracture: supracondylar humerus fracture → occluded anterior interosseous artery → closed reduction of humerus → artery opens up → reperfusion injury, edema, and forearm compartment syndrome (flexor compartment most affected)
  - Symptoms: forearm pain with passive extension; weakness, tense forearm, hypesthesia
  - Median nerve most affected by swelling
  - Tx: forearm fasciotomies
- Forearm fasciotomies – need to open volar and dorsal compartments
- Dupuytren's contracture – associated with diabetes, ETOH, Norwegian descent
  - Progressive proliferation of the palmar fascia of hand results in contractures that usually affect the 4th and 5th digits (cannot extend fingers)
  - Tx: NSAIDs, steroid injections; excision of involved fascia for significant contraction
- Carpal tunnel syndrome – median nerve compression by transverse carpal ligament
  - Tx: splint, NSAIDs, and steroid injections; transverse carpal ligament release if that fails
- Trigger finger – tenosynovitis of the flexor tendon that catches at the MCP joint when trying to extend finger
  - Tx: splint, tendon sheath steroid injections (not the tendon itself); if that fails, can release the pulley system at the MCP joint
- Suppurative tenosynovitis
  - Infection that spreads along flexor tendon sheaths of digits (can destroy sheath)
  - 4 classic signs: tendon sheath tenderness, pain with passive motion, swelling along sheath, and semi-flexed posture of the involved digit
  - Tx: *midaxial longitudinal incision and drainage*
- Rotator cuff tears – supraspinatus, infraspinatus, teres minor, and subscapularis
  - Acutely → sling and conservative treatment
  - Surgical repair if the patient needs to retain a high level of activity or if ADL affected

- Paronychia – infection under nail bed; painful. Tx: antibiotics; remove nail if purulent
- Felon – fingertip (pad) abscess
  - Tx: incision over the tip of the finger and along the medial and lateral aspects to prevent necrosis of tip of finger

LOWER EXTREMITY

- Isolated anterior ring with minimal ischial displacement – Tx: weight-bearing as tolerated
- Hip dislocation
  - Posterior (90%) – patients have internal rotation and adduction of leg; risk of sciatic nerve injury. Tx: closed reduction
  - Anterior (10%) – patients have external rotation and abduction of leg; risk of injury to femoral artery. Tx: closed reduction
  - Reduce within 24 hours to prevent avascular necrosis
- Hip fracture
  - Femoral shaft – ORIF with intramedullary rod
  - Intertrochanteric – ORIF
  - Femoral neck – ORIF; risk of avascular necrosis if open reduction delayed
- Lateral knee trauma – can result in injury to anterior cruciate ligament, posterior cruciate ligament, and medial meniscus
- Anterior cruciate ligament injury – positive anterior drawer test
  - Present with knee effusion and pain with pivoting action; MRI confirms diagnosis
  - Tx: surgery with knee instability (reconstruction with patellar tendon or hamstring tendon); otherwise physical therapy with leg-strengthening exercise
- Posterior cruciate ligament injury – positive posterior drawer test
  - Much less common than ACL injury; present with knee pain and joint effusion
  - Tx: conservative therapy initially; surgery for failure of medical management
- Collateral ligaments
  - Medial collateral ligament injury – lateral blow to knee
  - Lateral collateral ligament injury – medial blow to knee
  - Tx: small tear – brace; large tear – surgery
  - These injuries are associated with injuries to the corresponding meniscus
- Meniscus tears – joint line tenderness; can treat with arthroscopic repair or debridement
- Tibial stress fracture – young men in forced marches; point tibial tenderness; x-rays initially normal; Tx – cast and repeat x-ray in 2 weeks
- Posterior knee dislocation – all patients need angiogram to rule out popliteal artery injury
- Patellar fracture – long leg cast unless comminuted, then need internal fixation
- Tibial plateau fracture and tibia–fibula fracture – ORIF fixation unless open, then need external fixator until tissue heals
- Plantaris muscle rupture – pain and mass below popliteal fossa (contracted plantaris) and ankle ecchymosis; Tx: conservative
- Achilles tendon rupture – have limited plantar flexion; Tx: open repair for younger patients; casting in older patients
- Ankle fracture – most treated with cast and immobilization; bimalleolar or trimalleolar fractures need ORIF
- Metatarsal fracture – cast immobilization or brace for 6 weeks
- Calcaneus fracture – cast and immobilization if nondisplaced; ORIF for any displacement

- Talus fracture – closed reduction for most; ORIF for severe displacement
- Plantar fasciitis – older, over-weight patients; pain in heel when it strikes ground; Tx: NSAIDs, steroid injections; if conservative measures fail, surgery requires detaching fascia from heel
- Morton neuroma – usually between 3rd and 4th toes; very tender; from pointed shoes; Tx: NSAIDs, can be resected if conservative measures fail
- Nerve most commonly injured with lower extremity fasciotomy – superficial peroneal nerve (foot eversion)
- Footdrop after lithotomy position or after crossing legs for long periods or fibula head fracture – common peroneal nerve (foot-drop)

LEG COMPARTMENTS

- Anterior – anterior tibial artery, deep peroneal nerve
  - Muscles – anterior tibialis, extensor hallucis longus, extensor digitorum longus, and communis
- Lateral – superficial peroneal nerve
  - Muscles – peroneal muscles
- Deep posterior – posterior tibial artery, peroneal artery, and tibial nerve
  - Muscles – flexor hallucis longus, flexor digitorum longus, and posterior tibialis
- Superficial posterior – sural nerve
  - Muscles – gastrocnemius, soleus, and plantaris

COMPARTMENT SYNDROME

- Most common in the anterior compartment of leg (get footdrop) after vascular compromise, restoration of blood flow, and subsequent reperfusion injury (PMNs) with swelling of the compartment
- Can also occur from crush injuries
- Symptoms: swollen and tight extremity: pain with passive motion → paresthesia → anesthesia → paralysis → poikilothermia → pulselessness (late finding)
- Distal pulses can be present with compartment syndrome → last thing to go
- Pressure > 20–30 mm Hg abnormal
- Pain under a cast – remove cast and examine limb
- Dx: based on clinical suspicion
- Tx: fasciotomy

PEDIATRIC ORTHOPEDICS

- Hip problems in children can present with knee pain (compensation)
- Remodeling and straightening of bone fractures in children occurs even with significant angulation deformities
- Children heal faster than adults
- Children do have problems with supracondylar fractures and fractures affecting the growth plate
- Idiopathic adolescent scoliosis – prepubertal females, right thoracic curve most common, usually asymptomatic
  - Curves 20–45 degrees need bracing to slow progression, which can occur with growth

spurt
    - Curves > 45 degrees or those likely to progress → spinal fusion
- Acute hematogenous osteomyelitis – can occur in metaphysis of long bones in children; most commonly staph
    - Symptoms: febrile illness, pain, decreased use of extremity
    - Dx: MRI
    - Tx: antibiotics
- Septic hip
    - Toddlers with a febrile illness; refuse to move hip; have elevated ESR
    - Dx: hip aspiration (shows pus)
    - Tx: open drainage
- Legg–Calvé–Perthes disease – AVN of the femoral head; children around age 6
    - Can result from a hypercoagulable state; bilateral in 10%
    - Symptoms: painful gait limp; decreased hip motion
    - X-ray: flattening of the femoral head
    - Tx: maintain range of motion with limited exercise; femoral head will remodel without sequelae
    - Surgery if femoral head is not covered by the acetabulum (casting, crutches)
- Slipped capital femoral epiphysis
    - Males aged 10–13; ↑ risk of AVN of the femoral head; painful gait; hip motion limited
    - X-ray: widening and irregularity of the epiphyseal plate
    - Orthopedic emergency
    - Tx: surgical pinning of the femoral head
- Developmental hip dysplasia (congenital dislocation of the hip)
    - More common in females; generally diagnosed right after birth
    - Hip can be easily dislocated posteriorly; uneven gluteal folds
    - Dx: sonogram (not XR's as hip is not calcified in newborns)
    - Tx: Pavlik harness for 6 months, which keeps the legs abducted and the femoral head reduced in the acetabulum
- Osgood–Schlatter disease – tibial tubercle apophysitis (osteochondrosis); caused by traction injury from the quadriceps in adolescents aged 13–15; have pain over tibial tubercle (there is no knee swelling)
    - X-ray: irregular shape or fragmenting of the tibial tubercle
    - Tx: mild symptoms → activity limitation; severe symptoms → cast 6 weeks followed by activity limitation
- Genu varum (bow legs) – normal up to age 3
    - If it persists, likely is Blount disease (medial tibial growth plate abnormality) for which surgery can be done
- Genu valgus (knock knee) – normal between ages 4 and 8
- Talipes equinovarus (clubfoot)
    - Seen at birth
    - Tx: serial casting starts in neonatal period

BONE TUMORS

- Most common is metastatic disease (#1 breast [lytic lesions], #2 prostate [blastic lesions])
    - Can have localized pain; pathologic fracture may be the initial symptom

- Tx: internal fixation with impending fracture (> 50% cortical involvement); followed by XRT
- Bone pain + lesion → very likely malignant
- Primary bone tumors usually present with persistent, low grade pain for several months
- Multiple myeloma – most common primary malignant tumor of bone
  - Usually in elderly men; fatigue, anemia, and localized bone pain
  - X-ray – multiple lytic lesions
  - Urine – Bence Jones protein
  - Blood – abnormal immunoglobulins
  - Tx: chemotherapy for systemic disease; internal fixation for impending fractures
- Pathologic fractures – treat with internal fixation
  - XRT can be used for pain relief in patients with painful bony metastases
- Osteogenic sarcoma – most common primary bone sarcoma, usually around the knee
  - Patients aged 10–25
  - X-ray: Codman's triangle → periosteal reaction (sunburst pattern)
  - Tx: limb-sparing resection if possible; XRT and doxorubicin-based chemotherapy can be used preoperatively to increase chance of limb-sparing resection
- Ewing's sarcoma – 2nd most common primary bone sarcoma
  - Patients aged 5–15; grows in diaphysis of long bones
  - X-ray – onion skinning pattern
- Benign bone tumors treated with curettage ± bone graft – osteochondroma (MC benign bone tumor; resection only if cosmetic defect or causing symptoms), osteoid osteoma, endochondroma (may be able to observe), chondroblastoma, nonossifying fibroma (may be observed), and fibrodysplasia
- Giant cell tumor of bone – total resection ± XRT (benign but 30% risk of recurrence; also has malignant degeneration risk)

OTHER ORTHOPEDIC CONDITIONS

- Spondylolisthesis – formed by subluxation or slip of one vertebral body over another
  - Most commonly occurs in lumbar region
  - Most common cause of lumbar pain in adolescents (gymnasts)
  - Tx: depends on degree of subluxation and symptoms – ranges from conservative treatment to surgical fusion
- Cervical stenosis – surgical decompression if significant myelopathy present
- Lumbar stenosis – surgical decompression for cases refractory to medical treatment
- Torus fracture – buckling of the metaphyseal cortex seen in children (ie distal radius)
- Open fractures – need incision and drainage, antibiotics, fracture stabilization, and soft tissue coverage

43 Pediatric Surgery

INTRODUCTION

- Foregut – lungs, esophagus, stomach, pancreas, liver, gallbladder, bile duct, and duodenum proximal to ampulla
- Midgut – duodenum distal to ampulla, small bowel, and large bowel to distal ⅓ of transverse colon
- Hindgut – distal ⅓ of transverse colon to anal canal
- Midgut rotates 270 degrees counterclockwise normally
- Low birth weight < 2,500 g; premature < 37 weeks
- Immunity at birth – IgA from mother's milk; IgG crosses the placenta
- #1 cause of childhood death – trauma
  - Trauma bolus – 20 cc/kg × 2, then give blood 10 cc/kg
  - Tachycardia – best indicator of shock (neonate > 150; < 1 year > 120; rest > 100)
  - Want urine output > 2–4 cc/kg/hr
  - Children (< 6 months) only have 25% the GFR capacity of adults – poor concentrating ability
- ↑ alkaline phosphatase in children compared with adults → bone growth
- Umbilical vessels – 2 arteries and 1 vein
- Unilateral earache, rhinorrhea, or wheezing in a toddler – may be foreign body (Dx/Tx: appropriate endoscopy and removal)

MAINTENANCE INTRAVENOUS FLUIDS

- 4 cc/kg/hr for 1st 10 kg
- 2 cc/kg/hr for 2nd 10 kg
- 1 cc/kg/hr for everything after that

CONGENITAL CYSTIC DISEASE OF THE LUNG

- Pulmonary sequestration
  - Lung tissue has anomalous systemic arterial supply (thoracic aorta [MC] or abdominal aorta through inferior pulmonary ligament)
  - Have either systemic venous or pulmonary vein drainage
  - Extra-lobar – more likely to have systemic venous drainage (azygous system)
  - Intra-lobar – more likely to have pulmonary vein drainage
  - Do not communicate with tracheobronchial tree
  - Most commonly presents with infection; can also have respiratory compromise or an abnormal CXR
  - Tx: ligate arterial supply first (risk of severe hemorrhage), then lobectomy
- Congenital lobar overinflation (emphysema)
  - Cartilage fails to develop in bronchus, leading to air trapping with expiration
  - Vascular supply and other lobes are normal (except compressed by hyperinflated lobe)

- Can develop hemodynamic instability (same mechanism as tension PTX) or respiratory compromise
- LUL most commonly affected
- Tx: lobectomy

- Congenital cystic adenoid malformation (CCAM)
  - Communicates with airway
  - Alveolar structure is poorly developed, although lung tissue is present
  - Symptoms: respiratory compromise or recurrent infection
  - Tx: lobectomy
- Bronchiogenic cyst
  - Most common cysts of the mediastinum; usually posterior to the carina
  - Are extra-pulmonary cysts formed from bronchial tissue and cartilage wall
  - Usually present with a mediastinal mass filled with milky liquid
  - Can compress adjacent structures or become infected; have malignant potential
  - Occasionally are intra-pulmonary
  - Tx: resect cyst

MEDIASTINAL MASSES IN CHILDREN

- Neurogenic tumors (neurofibroma, neuroganglioma, neuroblastoma) – most common mediastinal tumor in children; usually located posteriorly
- Respiratory symptoms, dysphagia – common to all mediastinal masses regardless of location
- Anterior – T cell lymphoma, teratoma (and other germ cell tumors; most common type of anterior mediastinal mass in children), thyroid CA
- Middle – T cell lymphoma, teratoma, cyst (cardiogenic or bronchiogenic)
- Posterior – T cell lymphoma, neuroblastoma, neurogenic tumor
- *Thymoma is rare in children*

CHOLEDOCHAL CYST

- Need to resect – risk of cholangiocarcinoma, pancreatitis, cholangitis, and obstructive jaundice; caused by reflux of pancreatic enzymes into the biliary system in utero

Choledochal Cysts

Type	%	Description	Treatment
I	85%	Fusiform dilation of entire common bile duct, mildly dilated common hepatic duct, normal intrahepatic ducts	Resection, hepaticojejunostomy
II	3%	A true diverticulum that hangs off the common bile duct	Resection off common bile duct; may be able to preserve common bile duct and avoid hepaticojejunostomy
III	1%	Dilation of distal intramural common bile duct; involves sphincter of Oddi	Resection or marsupialization
IV	10%	Multiple cysts, both intrahepatic and extrahepatic	Resection; may need liver lobectomy; possible TXP
V	1%	Caroli's disease: intrahepatic cysts; get hepatic fibrosis; may be associated with congenital hepatic fibrosis and medullary sponge kidney	Resection; may need lobectomy; possible liver TXP

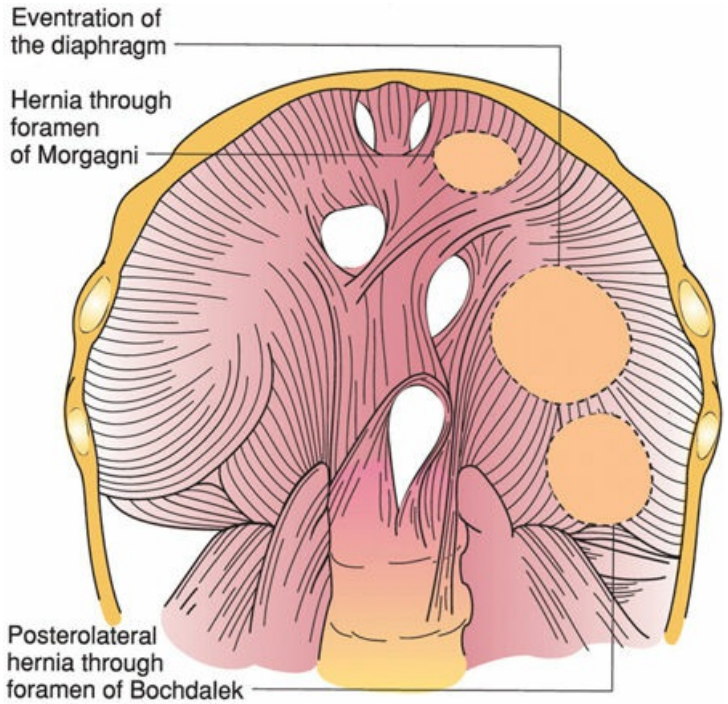
LYMPHADENOPATHY

- Usually acute suppurative adenitis associated with URI or pharyngitis

- If fluctuant → FNA, culture and sensitivity, and antibiotics; may need incision and drainage if it fails to resolve
  - Chronic causes – cat scratch fever, atypical mycoplasma
- Asymptomatic – antibiotics for 10 days → excisional biopsy if no improvement
  - This is lymphoma until proved otherwise
- Cystic hygroma (lymphangioma) – usually found in lateral cervical regions in neck; gets infected; is usually lateral to the sternocleidomastoid (SCM) muscle
  - Tx: resection

DIAPHRAGMATIC HERNIAS AND CHEST WALL

- Overall survival 50%
- Increased on left side (80%); can have severe pulmonary HTN
- 80% have associated anomalies (cardiac and neural tube defects mostly; malrotation)
- Diagnosis can be made with prenatal ultrasound
- Symptoms: respiratory distress
- CXR – bowel in chest
- Both lungs are dysfunctional (hernia side is hypoplastic; contralateral side has pulmonary HTN)
- Tx: high-frequency ventilation; inhaled nitric oxide; may need ECMO
  - Stabilize these patients before operating on them
  - Need to reduce bowel and repair defect ± mesh (abdominal approach)
  - Look for visceral anomalies (run the bowel)
- Bochdalek's hernia – most common, located posteriorly
- Morgagni's hernia – rare, located anteriorly



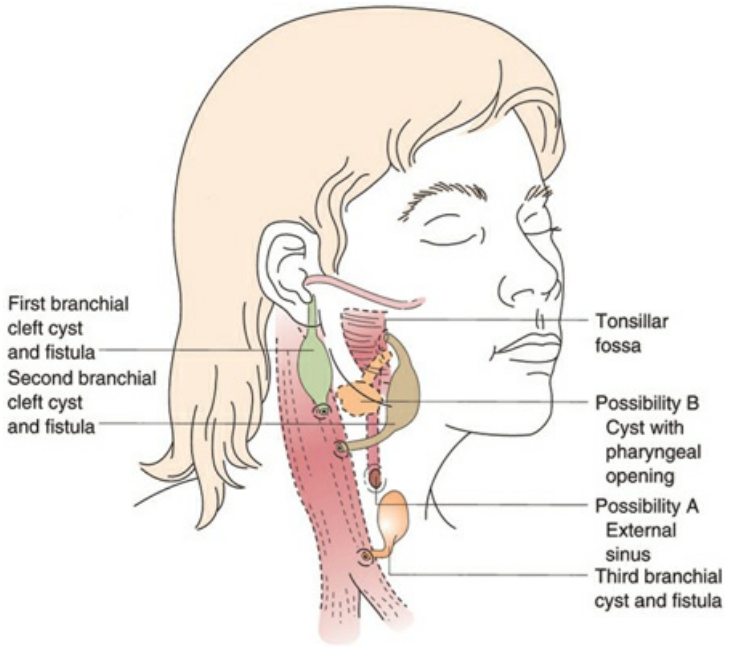
Anatomy of the diaphragm showing the location of congenital diaphragmatic defects.

- Pectus excavatum (sinks in) – sternal osteotomy, need strut; performed if causing respiratory symptoms or emotional stress

- Pectus carinatum (pigeon chest) – strut not necessary; repair for emotional stress

BRANCHIAL CLEFT CYST

- Leads to cysts, sinuses, and fistulas
- 1st branchial cleft cyst – angle of mandible; may connect with external auditory canal
  - Often associated with facial nerve
- 2nd branchial cleft cyst (most common) – on anterior border of mid-SCM muscle
  - Goes through carotid bifurcation into tonsillar pillar
- 3rd branchial cleft cyst – lower neck, medial to or through the lower SCM, to the piriform sinus
- Tx for all branchial cysts: resection



Types of first, second, and third branchial cleft remnants. Sinuses and fistulas are seen most often in infants and young children, whereas cysts usually appear at a later age.

CYSTIC HYGROMA

- Mass-like lesion usually found in the base of the lateral neck (posterior neck triangle)
- Is a macrocytic lymphatic malformation; can get infected, form sinuses
- Dx: CT scan (want to assess depth; can involve mediastinum)
- Tx: resection

THYROGLOSSAL DUCT CYST

- From the descent of the thyroid gland from the foramen cecum
- May be only thyroid tissue patient has
- Presents as a midline cervical mass
- Goes through the hyoid bone
- Tx: excision of cyst, tract, and hyoid bone (at least the central portion)

HEMANGIOMA

- Appears at birth or shortly after
- Rapid growth during first 6–12 months of life, then begins to involute
- Tx: observation – most resolve by age 7–8
- If lesion has uncontrollable growth, impairs function (eyelid or ear canal), or is persistent after age 8 → can treat with oral steroids → laser or resection if steroids are not successful

NEUROBLASTOMA

- #1 solid abdominal malignancy in children
- Usually presents as asymptomatic mass
- Can have secretory diarrhea, raccoon eyes (orbital metastases), HTN, and opsomyoclonus syndrome (unsteady gait)
- Most often on adrenals; can occur anywhere along the sympathetic chain
- Most common in 1st 2 years of life
  - Children < 1 year have best prognosis (the younger the patient, the better the cure rate)
- Most have ↑ catecholamines, VMA, HVA, and metanephrines (HTN)
- Derived from neural crest cells
- Encases vasculature rather than invades
- Rare metastases – go to lung and bone
- Abdominal x-ray: may show stippled calcifications in the tumor
- NSE, LDH, HVA, diploid tumors, and N-myc amplification (> 3 copies) – have *worse* prognosis
- NSE is ↑ in all patients with metastases
- Tx: resection (adrenal gland and kidney taken; 40% cured)
- Initially unresectable tumors may be resectable after doxorubicin-based chemo
- One of the few tumors that can involute spontaneously and turn into a benign neuroma

Staging of Neuroblastoma

Stage	Description
I	Localized, complete excision
II	Incomplete excision but does not cross midline
III	Crosses midline ± regional nodes
IV	Distant metastases (nodes or solid organ)
IV-S	Localized tumor with distant metastases

This table as well as subsequent staging tables used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springer.com.

WILMS TUMOR (NEPHROBLASTOMA)

- Usually presents as asymptomatic mass; can have hematuria or HTN; 10% bilateral
- Mean age at diagnosis – 3 years
- Prognosis based on tumor grade (anaplastic and sarcomatous variations have worse prognosis)
- Frequent metastases to bone and lung
- Pulmonary metastases – whole lung XRT
- Abdominal CT – replacement of renal parenchyma and not displacement (differentiates it from neuroblastoma)
- Tx: nephrectomy (90% cured)

- If venous extension occurs in the renal vein, the tumor can be extracted from the vein
- Need to examine the contralateral kidney and look for peritoneal implants
- Avoid rupture of tumor with resection, which will ↑ stage
- Actinomycin and vincristine based chemo in all unless Stage I and < 500 g tumor
- Need nephron-sparing surgery for stage V disease

Staging of Wilms Tumor	
Stage	Description
I	Limited to kidney, completely excised
II	Beyond kidney but completely excised
III	Residual nonhematogenous tumor
IV	Hematogenous metastases
V	Bilateral renal involvement

HEPATOBLASTOMA

- Most common malignant liver tumor in children; ↑ AFP in 90%
- Fractures, precocious puberty (from beta-HCG release)
- Better prognosis than hepatocellular CA
- Can be pedunculated; vascular invasion common
- Tx: resection optimal; otherwise doxorubicin-based chemotherapy → may downstage tumors and make them resectable
- Survival is primarily related to resectability
- Fetal histology has best prognosis

MOST COMMONS

#1 children's malignancy overall – leukemia (ALL)
#1 solid tumor class – CNS tumors
#1 general surgery tumor – neuroblastoma
  #1 in child < 2 years → neuroblastoma
  #1 in child > 2 years → Wilms tumor
#1 cause of duodenal obstruction in newborns (< 1 week) – duodenal atresia
#1 cause of duodenal obstruction after newborn period (> 1 week) and overall – malrotation
#1 cause of colon obstruction – Hirschsprung's disease
#1 liver tumor in children – hepatoblastoma; ⅔ of liver tumors in children are malignant
#1 lung tumor in children – carcinoid
Painful lower GI bleeding – #1 benign anorectal lesions (fissures, etc.)
Painless lower GI bleeding – #1 Meckel's diverticulum
Upper GI bleeding – 0–1 year → gastritis, esophagitis
  1 year to adult → esophageal varices, esophagitis

MECKEL'S DIVERTICULUM

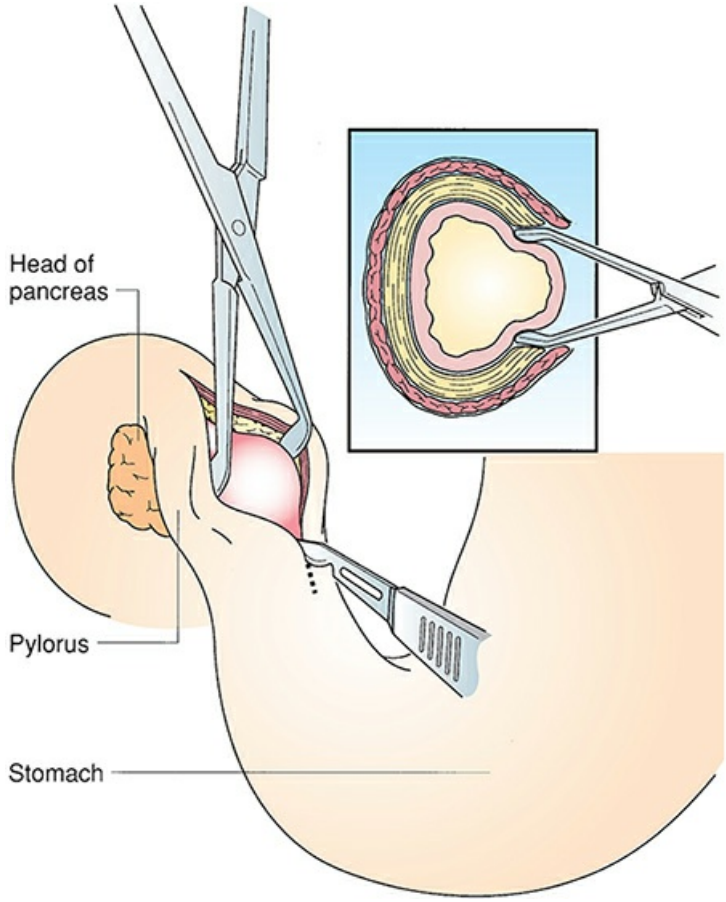
- Found on antimesenteric border of small bowel
- Embryology – persistent vitelline duct
- Rule of 2s – 2 feet from ileocecal valve, 2% population, 2% symptomatic, 2 tissue types (pancreatic – most common; gastric – most likely to be symptomatic), and 2 presentations

(diverticulitis and bleeding)

- #1 cause of painless lower GI bleeding in children
- Can get Meckel's scan (pertechnetate) if suspicious of Meckel's diverticulum and having trouble locating
- Tx: resection with symptoms, suspicion of gastric mucosa, narrow neck, or complication (eg perforation)
  - Diverticulitis involving the base or if the base is > ⅓ the size of the bowel, need to perform segmental resection

PYLORIC STENOSIS

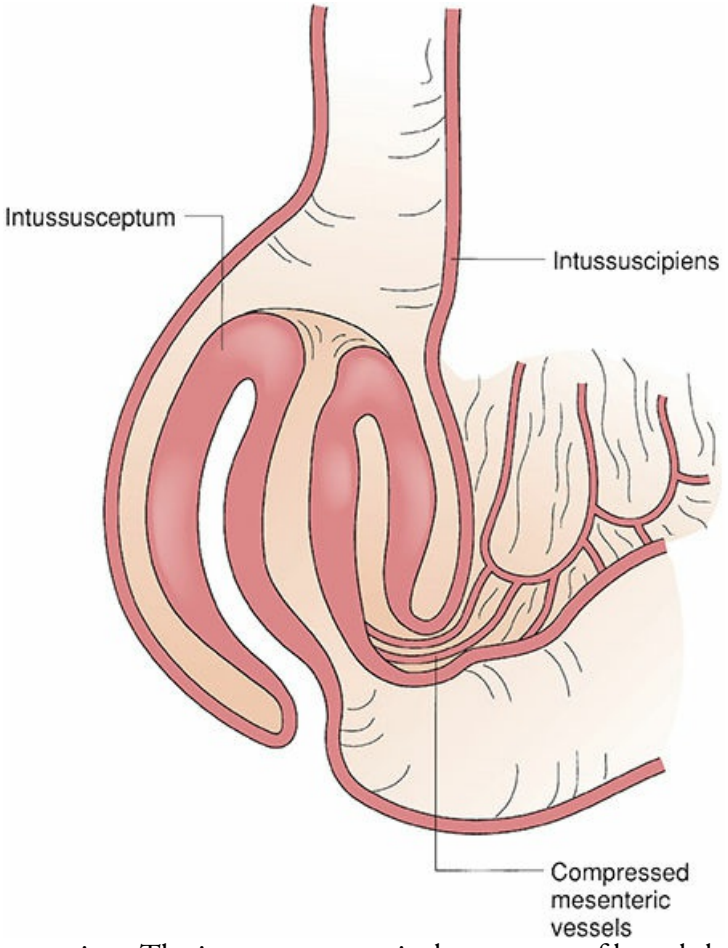
- 3–12 weeks, firstborn males
- Sx's – projectile vomiting (nonbilious) and dehydration
- Can feel olive mass in stomach
- Get hypochloremic, hypokalemic metabolic alkalosis
- Ultrasound – pylorus ≥ 4-mm thick, ≥ 14-mm long
- For severe dehydration, resuscitate with normal saline boluses until making urine, then switch to D5 normal saline with 10 mEq K maintenance
  - *Avoid fluid resuscitation with K-containing fluids in children with severe dehydration as hyperkalemia can quickly develop*
  - *Avoid non–salt-containing solutions in infants as hyponatremia can quickly develop*
  - *Infants should always have a maintenance fluid with glucose because of their limited reserves for gluconeogenesis and vulnerability for hypoglycemia*
- Tx: pyloromyotomy (RUQ incision; proximal extent should be the circular muscles of stomach)



Ramstedt pyloromyotomy for infantile hypertrophic pyloric stenosis. The cross-sectional view shows herniation of the submucosa into the myotomy site, indicative of an adequate myotomy

INTUSSUSCEPTION

- Usually 3 months to 3 years
- Currant jelly stools (from vascular congestion, not an indication for resection), sausage mass, abdominal distention, RUQ pain, and vomiting
- Invagination of one loop of intestine into another (MC – ileum into right colon)
- Lead points in children – enlarged Peyer's patches (#1), lymphoma, and Meckel's diverticulum
- 15% recurrence after reduction
- Tx: reduce with air-contrast enema → 80% successful; no surgery required if reduced
  - Max pressure with air-contrast enema – 120 mm Hg
  - Max column height with barium enema – 1 meter (3 feet)
  - High perforation risk beyond these values → need to proceed to OR if you have reached these values after 1 hour
  - Need to go to OR with peritonitis or free air, or if unable to reduce
    - When reducing in OR, do not place traction on proximal limb of bowel; need to apply pressure to the distal limb
    - Usually do not require resection unless associated with lead point (Meckel's, etc.)
- Adults presenting with intussusception – patient most likely has malignant lead point (ie colon CA in cecum) → OR for resection



Anatomy of intussusception. The intussusceptum is the segment of bowel that invaginates into the intussuscipiens.

INTESTINAL ATRESIAS

- Develop as a result of intrauterine vascular accidents
- Symptoms: bilious emesis, distention; most do not pass meconium
- More common in jejunum; can be multiple
- Get rectal biopsy to R/O Hirschsprung's before surgery
- Tx: resection

DUODENAL ATRESIA

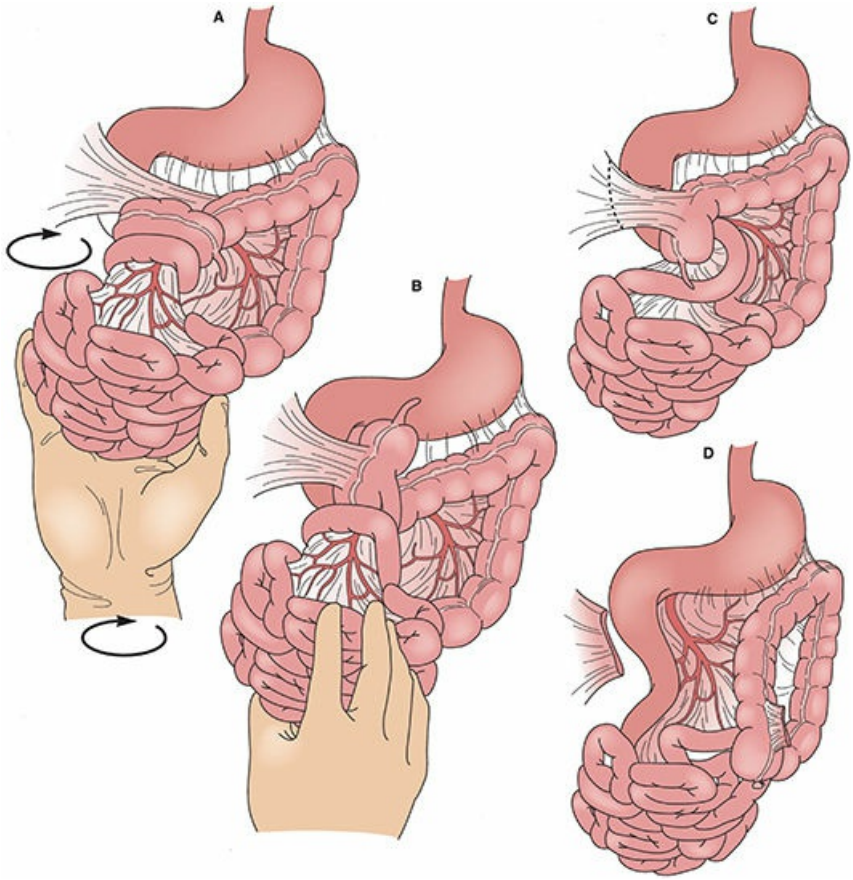
- #1 cause of duodenal obstruction in newborns (< 1 week)
- Usually distal to ampulla of Vater; causes bilious vomiting and feeding intolerance immediately after birth
- Associated with polyhydramnios in mother
- Associated with cardiac, renal, and other GI anomalies
- 20% of these patients have Down's syndrome (check chromosomal studies)
- Abdominal x-ray – shows double-bubble sign
- Tx: resuscitation; duodenoduodenostomy or duodenojejunostomy

TRACHEOESOPHAGEAL FISTULAS (TEF)

- Type C – most common type (85%)
  - Proximal esophageal atresia (blind pouch) and distal TE fistula
  - Symptoms: newborn spits up feeds, has excessive drooling, and respiratory symptoms with feeding; cannot place NG tube in stomach
  - Abdominal x-ray – distended, gas-filled stomach
- Type A – second most common type (5%)
  - Esophageal atresia and no fistula
  - Symptoms: similar to type C
  - Abdominal x-ray – patients have gasless abdomen
- VACTERL syndrome – vertebral, anorectal (imperforate anus), cardiac, TE fistula, radius/renal, and limb anomalies
- Before surgery, look at anus for imperforation, x-ray for vertebral anomalies, echocardiogram for congenital heart problems, and renal U/S
- Tx: right extrapleural thoracotomy for most; perform primary repair; and place G-tube
  - Azygous vein often needs to be divided
- Infants that are premature, < 2,500 g, or sick → Replogle tube, treat respiratory symptoms; place gastrostomy-tube (for type C; drains stomach and prevents reflux into the lungs); delay repair
- Complications of repair – GERD, leak, stricture, and fistula
- Survival related to birth weight and associated anomalies

MALROTATION

- Sudden onset of bilious vomiting (Ladd's bands cause duodenal obstruction, coming out from the right retroperitoneum)
- Volvulus associated with compromise of the SMA, leading to infarction of the intestine
- Failure of normal counterclockwise rotation (270 degrees)
- 75% in the 1st month; 90% present by 1 year of age
- *Any child with bilious vomiting needs an emergent UGI to rule out malrotation*
- Dx: UGI – duodenum does not cross midline; duodenal-jejunal junction displaced to the right
- Tx: resect Ladd's bands, counterclockwise rotation (may require multiple turns), place cecum in LLQ (cecopexy), place duodenum in RUQ, and appendectomy



Correction of malrotation. *(A and B)* Detorsion of midgut. *(C and D)* Division of peritoneal attachments (Ladd's bands) of cecum to abdominal cavity.

MECONIUM ILEUS

- Causes distal ileal obstruction, abdominal distention, bilious vomiting, and distended loops of bowel
- Need sweat chloride test or PCR for Cl channel defect
- Occurs in 10% of children with cystic fibrosis
- Abdominal x-ray: dilated loops of small bowel without air-fluid levels (because the meconium is too thick to separate from the bowel wall); can have ground glass or soapsuds appearance
- Can cause perforation, leading to meconium pseudocyst or free perforation → requires laparotomy
- Tx: Gastrografin enema (effective in 80%); can also make the diagnosis and potentially treat the patient
- Can also use *N*-acetylcysteine enema
  - If surgery required, manual decompression and create a vent for *N*-acetylcysteine antegrade enemas

NECROTIZING ENTEROCOLITIS (NEC)

- Classically presents with bloody stools after 1st feeding in premature neonate
- Risk factors: prematurity, hypoxia, sepsis
- Symptoms: lethargy, respiratory decompensation, abdominal distention, vomiting, blood per rectum, thrombocytopenia (sign of sepsis in infants)

- Abdominal x-ray: may show pneumatosis intestinalis, free air, or portal vein air
- Need serial lateral decubitus films to look for perforation
- Initial Tx: resuscitation, NPO, antibiotics, TPN, and orogastric tube
- Indications for operation: free air, peritonitis, clinical deterioration, abdominal wall erythema → resect dead bowel and bring up ostomies
- Need barium contrast enema before taking down ostomies to rule out distal obstruction from stenosis
- Mortality 10%

CONGENITAL VASCULAR MALFORMATION

- Surgery for hemorrhage, ischemia, CHF, nonbleeding ulcers, functional impairment, or limb-length discrepancy
- Tx: embolization (may be sufficient on its own) and/or resection

IMPERFORATE ANUS

- More common in males
- Check for associated renal, cardiac, and vertebral (VACTERL) anomalies
- High (above levators) – meconium in urine or vagina (fistula to bladder/vagina/prostatic urethra)
  - Tx: colostomy, later anal reconstruction with posterior sagittal anoplasty
- Low (below levators) – fistula carries meconium to perineal skin; perform posterior sagittal anoplasty (pull anus down into sphincter mechanism); no colostomy needed
- Need postop anal dilatation to avoid stricture; these patients are prone to constipation

GASTROSCHISIS

- Abdominal wall defect
- Intrauterine rupture of umbilical vein; does <u>not</u> have a peritoneal sac
- ↓ congenital anomalies (only 10%) except intestinal atresia (MC associated GI finding)
- To the right of midline, no peritoneal sac, stiff bowel from exposure to amniotic fluid
- Tx: initially place saline-soaked gauzes and resuscitate the patient; can lose a lot of fluid from the exposed bowel; TPN, NPO
  - Repair when patient is stable
  - At operation, try to place bowel back in abdomen, may need silastic mesh silo (abdominal contents are gently squeezed back into the abdomen over a week or so)
  - Primary closure at a later date if silo used

OMPHALOCELE

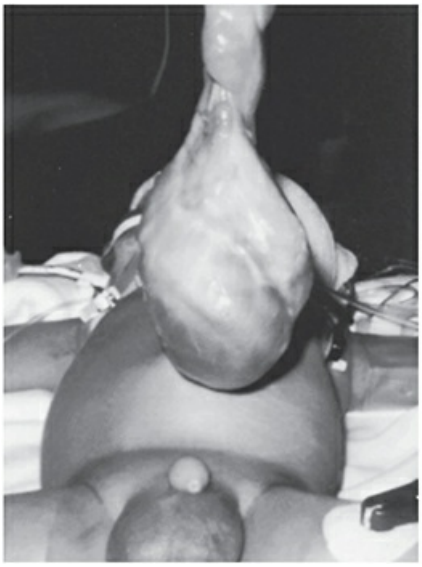
- Failure of embryonal development; <u>has peritoneal sac</u> with cord attached
- ↑ congenital anomalies (50%); midline defect
- Sac can contain intra-abdominal structures other than bowel (liver, spleen, etc.)
- Associated with Down's syndrome
- MC associated GI finding – malrotation
- Cantrell pentalogy
  - Cardiac defects

- Pericardium defects (usually at diaphragmatic pericardium)
- Sternal cleft or absence of lower sternum
- Diaphragmatic septum transversum absence
- Omphalocele

- Tx: initially place saline-soaked gauzes and resuscitate the patient; can lose a lot of fluid from the exposed bowel; TPN, NPO
  - Repair when patient is stable
  - At operation, try to place bowel back in abdomen; may need silastic mesh silo
  - Primary closure at a later date if mesh used
- Worse overall prognosis compared with gastroschisis secondary to congenital anomalies
- Malrotation can occur with both gastroschisis and omphalocele

EXSTROPHY OF URINARY BLADDER

- Abdominal wall defect over the pubis (which is not fused)
- Bladder mucosa comes through defect
- Tx: surgery to close defect and repair bladder



Omphalocele. The herniated intestines and liver are visible inside the sac. The umbilical cord attaches to the sac.

Silastic chimney or silo for temporary coverage of giant omphalocele.

HIRSCHSPRUNG'S DISEASE

- #1 cause of colonic obstruction in infants; more common in males
- Most common sign → infants fail to pass meconium in 1st 24 hours
  - Can also present in older age groups as chronic constipation (age 2–3)
- Abdominal distention; occasionally get colitis
- Can get explosive release of watery stool with anorectal exam
- Rectal biopsy diagnostic (full thickness; absence of ganglion cells in myenteric plexus)
- AXR – dilated proximal colon
- Is due to failure of the neural crest cells (ganglion cells) to progress in caudad direction
- Need to resect rectum and colon until proximal to where ganglion cells appear
- Tx: may need to bring up a colostomy initially, eventually connect the colon to the anus (Soave or Duhamel procedure)
- Hirschsprung's colitis – may be rapidly progressive; manifested by abdominal distention and foul-smelling diarrhea
  - Lethargy and signs of sepsis may be present
  - Tx: rectal irrigation to try and empty colon; may need emergency colectomy

UMBILICAL HERNIA

- Failure of closure of linea alba; most close by age 3, rare incarceration
- Increased in African Americans and premature infants
- Tx: surgery if not closed by age 5, incarceration, or if patient has a VP shunt

INGUINAL HERNIA

- Due to persistent processus vaginalis; 3% of infants, M > F
- Right in 60%, left in 30%, bilateral in 10%
- Extension of the hernia sac into the internal ring differentiates hernia from hydrocele
- Tx: emergent operation if not able to reduce; otherwise, elective repair with high ligation of the hernia sac
- Consider exploring the contralateral side if left sided, female, or child < 1 year

- Need operation within 24 hours after reduction

HYDROCELE

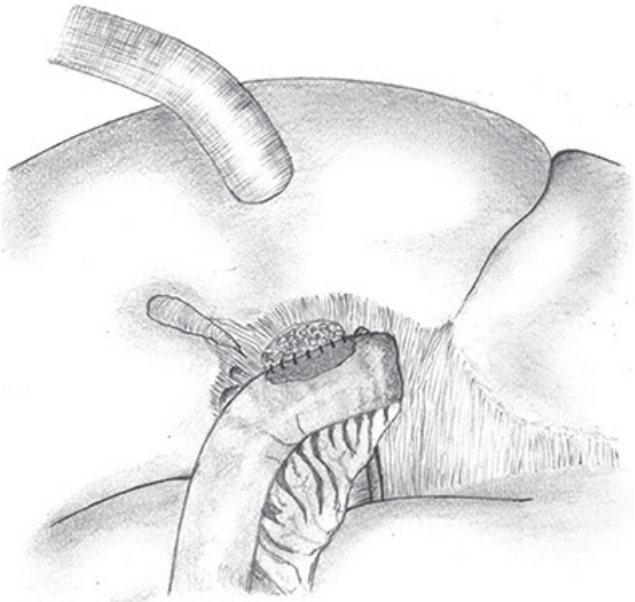
- Most disappear by 1 year; noncommunicating will resolve; should transilluminate
- Tx: surgery at 1 year if not resolved or if thought to be communicating (waxing and waning size); resect hydrocele and ligate processus vaginalis

CYSTIC DUPLICATION

- Most common in ileum; often on mesenteric border
- Tx: resect cyst

BILIARY ATRESIA

- Most common cause of neonatal jaundice requiring surgery
- Most common indication for liver TXP in children
- Progressive jaundice persisting > 2 weeks after birth suggests atresia
- Can involve either the extrahepatic or intrahepatic biliary tree or both



Anastomosis of Roux-en-Y hepatoportoenterostomy to liver. (From Qureshi FG, Ergun O, Ford HR. Biliary atresia. In: Fischer JE, Bland KI, et al, eds. *Mastery of Surgery*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007, with permission.)

- Dx: liver biopsy → periportal fibrosis, bile plugging, eventual cirrhosis
  - Ultrasound and HIDA can reveal atretic biliary tree
- Get continued cirrhosis and eventual hepatic failure
- Try Kasai procedure (hepaticoportojejunostomy) – ⅓ get better, ⅓ go on to liver transplant, and ⅓ die
  - Involves resecting the atretic extrahepatic bile duct segment
  - Choleretic agents (eg phenobarbital) and steroids are used to try and increase bile flow
- Need to perform Kasai procedure before age 3 months, to avoid irreversible liver damage

TERATOMA

- ↑ AFP and beta-HCG (elevated markers suggest transformation to malignancy)
- Neonates – sacrococcygeal; adolescents – germ cell
- Tx: excision
- Sacrococcygeal teratomas
  - 90% benign at birth (almost all have exophytic component)
  - Great potential for malignancy
  - AFP – good marker
  - 2-month mark is a huge transition – < 2 months → usually benign; > 2 months → usually malignant
  - Tx: coccygectomy and long-term follow-up

UNDESCENDED TESTICLES

- Wait 6 months to treat
- Higher risk of testicular CA in these children
- Cancer risk stays the same even if testicles brought into scrotum
- Get seminoma
- If undescended bilaterally, get chromosomal studies
- If you cannot feel the testes in the inguinal canal, you need to get an MRI to confirm their presence
- If the testicle can be brought into the scrotum, surgery generally not required (is due to overactive cremasteric muscle; 95% will outgrow this and the testicle will remain in the scrotum)
- Tx: orchiopexy through inguinal incision; if not able to get testicles down → close and wait 6 months and try again; if will not come down, perform division of spermatic vessels (vas deferens blood supply will collateralize to the testicles)

TRACHEOMALACIA

- Elliptical, fragmented tracheal rings instead of C-shaped; collapse with inspiration
- Inspiratory wheezing, usually get better after 1–2 years
- Risk factor – TE fistula
- Surgical indications – dying spell (MC), failure to wean from ventilator, recurrent infections
- Surgery – aortopexy (aorta sutured to the back of the sternum, opens up trachea)

LARYNGOMALACIA

- Most common cause of airway obstruction in infants
- Symptoms: intermittent respiratory distress and stridor exacerbation in the supine position
- Caused by immature epiglottis cartilage with intermittent collapse of the airway
- Most children outgrow this by 12 months
- Surgical tracheostomy reserved for a very small number of patients

CHOANAL ATRESIA

- Obstruction of choanal opening (nasal passage) by either bone or mucous membrane, usually unilateral

- Symptoms: intermittent respiratory distress, poor suckling
- Tx: surgical correction

LARYNGEAL PAPILLOMATOSIS

- Most common tumor of the pediatric larynx
- Frequently involutes after puberty
- Can treat with endoscopic removal or laser but frequently comes back
- Thought to be caused from HPV in the mother during passage through the birth canal

CEREBRAL PALSY

- Many develop GERD

Neonatal Intestinal Obstruction

Diagnosis	History	Physical Examination	Diagnostic Studies
Intestinal atresia or stenosis	Bilious emesis	Abdominal distention	Plain abdominal film
Duodenal atresia or stenosis	Failure to pass meconium	Acholic meconium	Contrast enema
		Gastric distention	Plain abdominal film
	Bilious emesis	Trisomy 21	Upper GI contrast study
Imperforate anus	Failure to pass meconium	Absent anus or visible fistula	Plain chest, abdominal film
	Bilious emesis (late)	Abdominal distention	Ultrasound kidneys, sacrum, rectum
		VACTERL association	Echocardiogram
Necrotizing enterocolitis	High-risk, premature infant	Abdominal distention	Plain abdominal film
	Bilious emesis	Hematochezia, guaiac-positive stool	
Meconium ileus	Cystic fibrosis (10%)	Acholic meconium	Plain abdominal film
	Bilious emesis	Abdominal distention	Contrast enema
Malrotation	Bilious emesis	No abdominal distention	Plain abdominal film
	Term, healthy infant		Upper GI contrast study
Hirschsprung's disease	Delayed passage of meconium	Abdominal distention	Plain abdominal film
	Bilious emesis	Trisomy 21	Contrast enema

GI, gastrointestinal; VACTERL, vertebral, anal, cardiac, tracheal, esophageal, renal, and limb anomalies.

44 Statistics and Patient Safety

INTRODUCTION

- Type I error – rejects null hypothesis incorrectly → falsely assumed there was a difference when no difference exists
- Type II error – accepts null hypothesis incorrectly because of small sample size → the treatments are interpreted as equal when there is actually a difference
- Null hypothesis – hypothesis that no difference exists between groups
- $p < 0.05$ rejects the null hypothesis
  - $p < 0.05$ = > 95% likelihood that the difference between the populations is true
  - < 5% likelihood that the difference is not true and occurred by chance alone
- Variance – spread of data around a mean
- Parameter – population
- Numeric terms – example: 2, 7, 7, 8, 9, 11, 15
  - Mode – most frequently occurring value = 7
  - Mean – average = 9
  - Median – middle value of a set of data (50th percentile) = 8 (used if you have a lot of outliers)

TRIALS AND STUDIES

- Randomized controlled trial – prospective study with random assignment to treatment and nontreatment groups
  - Avoids treatment biases
- Double-blind controlled trial – prospective study in which patient and doctor are blind to the treatment
  - Avoids observational biases
- Cohort study – prospective study → compares disease rate between exposed and unexposed groups (nonrandom assignment)
- Case-control study – retrospective study in which those who have the disease are compared with a similar population who do not have the disease; the frequency of the suspected risk factor is then compared between the 2 groups (has selection bias)
- Meta-analysis – combining data from different studies

QUANTITATIVE VARIABLES

- Student's t test – 2 independent groups and variable is quantitative → compares means (mean weight between 2 groups)
- Paired t tests – variable is quantitative; before and after studies (eg weight before and after, drug versus placebo)
- ANOVA – compares quantitative variables (means) for more than 2 groups

QUALITATIVE VARIABLES

- Nonparametric statistics – compare categorical (qualitative) variables (race, sex, medical problems and diseases, medications)
- Chi-squared test – compares 2 groups with categorical (qualitative) variables (number of obese patients with and without diabetes versus number of nonobese patients with and without diabetes)
- Kaplan-Meyer – small groups → estimates survival
- Relative risk = incidence in exposed/incidence in unexposed
- Power of test = probability of making the correct conclusion = 1 – probability of type II error
  - Likelihood that the conclusion of the test is true
  - Larger sample size increases power of a test
- Prevalence – number of people with disease in a population (eg number of patients in United States with colon CA)
  - Long-standing disease increases prevalence
- Incidence – number of new cases diagnosed over a certain time frame in a population (eg number of patients in United States newly diagnosed with colon CA in 2003)
- Sensitivity – ability to detect disease = true-positives/(true-positives + false-negatives)
  - Indicates the number of people who have the disease who test positive
  - With high sensitivity, a negative test result means patient is very unlikely to have disease

	Positive Test	Negative Test
Have disease	True-positive (TP)	False-negative (FN)
No disease	False-positive (FP)	True-negative (TN)

- Specificity – ability to state no disease is present = true-negatives/(true-negatives + false-positives)
  - Indicates the number of people who do not have the disease who test negative
  - With high specificity, a positive test result means patient is very likely to have disease
- Positive predictive value = true-positives/(true-positives + false-positives)
  - Likelihood that with a positive result, the patient actually has the disease
- Negative predictive value = true-negatives/(true-negatives + false-negatives)
  - Likelihood that with a negative result, the patient does not have the disease
- Accuracy = true-positives + true-negatives/true-positives + true-negatives + false-positives + false-negatives
- Predictive value – depends on disease prevalence
- Sensitivity and specificity – are independent of prevalence

PATIENT SAFETY

- National Surgical Quality Improvement Program (NSQIP) – seeks to collect outcome data to measure and improve surgical quality in the United States. Outcomes are reported as observed vs. expected ratios.
- JCAHO prevention of wrong site/procedure/patient protocol:
  - Pre-op verification of patient and procedure
  - Operative site and side (marking if left or right or multiple levels; must be visible after the patient is prepped)
  - Time out before incision made (verifying patient, procedure, position site + side, and availability of implants or special requirements)

- Promoting culture of safety
  - Confidential system of reporting errors
  - Emphasis on learning over accountability
  - Flexibility in adapting to new situations or problems
- RFs for retained object after surgery (MC sponge) – emergency procedure, unplanned change in procedure, obesity, towel used for closure
- Sentinel Event (JCAHO) – unexpected occurrence involving death or serious injury, or the risk thereof; hospital undergoes root cause analysis to prevent and minimize future occurrences (eg wrong site surgery)
- GAP protection technique – gaps in care (eg change in caregiver, divisions of labor, shift changes, transfers) can lead to loss of information and error; prevention – structured handoffs and checklists (face to face if possible); standardizing orders; reading back orders if verbal

APPENDIX Common Abbreviations and Eponyms

↑	increased *or* high
↓	decreased *or* low
2,3-DPG	2,3-diphosphoglycerate
5FU	5-fluorouracil
AAA	abdominal aortic aneurysm
Ab	antibody
Abd	abdominal
ABI	ankle brachial index
abx	antibiotic
AC	doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan)
ACE	angiotensin-converting enzyme
Ach	acetylcholine
ACT	activated clotting time
ACTH	adrenocorticotropic hormone
AD	autosomal dominant
ADH	antidiuretic hormone
ADL	activities of daily living
AFP	alpha-fetoprotein
Ag	antigen
AIDS	acquired immunodeficiency syndrome
AKA	above-knee amputation
ALL	acute lymphoblastic leukemia
ALND	axillary lymph node dissection
ALT	alanine aminotransferase
angio	angiography
ANOVA	analysis of variance
AP	aortopulmonary
APACHE	acute physiology and chronic health evaluation
APC	antigen-presenting cells
APR	abdominoperineal resection
APUD	amine precursor uptake and decarboxylation
ARDS	acute respiratory distress syndrome
ARF	acute renal failure
ASA	acetylsalicylic acid
ASD	atrial septal defect
AST	aspartate aminotransferase
ATGAM	antithymocyte gamma globulin
AT-III	antithrombin III
ATN	acute tubular necrosis
ATP	adenosine triphosphate
ATPase	adenosine triphosphatase
A-V	arteriovenous
AV	atrioventricular
AVM	arteriovenous malformation
AVN	avascular necrosis
AXR	abdominal radiograph
BCG	bacille Calmette-Guérin

BCT	breast-conserving therapy
BKA	below-knee amputation
BM	bowel movement
BPH	benign prostatic hypertrophy
BSA	body surface area
BT shunt	Blalock-Taussig shunt
BUN	blood urea nitrogen
Bx	biopsy
Ca	calcium
CA	cancer, carcinoma
CABG	coronary artery bypass graft
cAMP	cyclic adenosine monophosphate
CaO_2	arterial oxygen content
CBD	common bile duct
CCAM	congenital cystic adenoid malformation
CCK	cholecystokinin
cCMP	3,5-cyclic monophosphate (cytidine)
CD	cluster of differentiation (eg CD4, CD8)
CEA	carcinoembryonic antigen
CEA	carotid endarterectomy
cGMP	cyclic guanosine-3, 5-monophosphate
chemo	chemotherapy
CHF	chronic heart failure
CI	cardiac index
CLL	chronic lymphocytic leukemia
CMF	cyclophosphamide (Cytoxan), methotrexate, and 5-fluorouracil
CML	chronic myelogenous leukemia
CMV	cytomegalovirus
CN	cranial nerve
CNS	central nervous system
CO	cardiac output
COPD	chronic obstructive pulmonary disease
COX	cyclooxygenase
CPAP	continuous positive airway pressure
CPP	cerebral perfusion pressure
CPR	cardiopulmonary resuscitation
Cr	creatinine
CRH	corticotropin-releasing hormone
CSA	cyclosporin
CSF	cerebrospinal fluid
CT	computed tomography
CVA	cerebrovascular accident (stroke)
CVHD	continuous venovenous hemodialysis
CvO_2	venous oxygen content
CVP	central venous pressure
Cx	complication
CXR	chest radiograph
D/C	discontinue
DAG	diacylglycerol
DBP	diastolic blood pressure
DCIS	ductal carcinoma in situ
DDAVP	desmopressin acetate, 1-deamino-8-d-arginine-vasopressin
DES	diethylstilbestrol
DIC	disseminated intravascular coagulation
DIT	diiodotyrosine

DKA	diabetic ketoacidosis
DLCO	diffusing capacity of the lung for carbon monoxide
DM	diabetes mellitus
DPL	diagnostic peritoneal lavage
DVT	deep venous thrombosis
Dx	diagnosis
DZ	disease
EBV	Epstein-Barr virus
ECA	external carotid artery
ECHO	echocardiogram
ECMO	extracorporeal membrane oxygenation
EDRF	endothelium-derived relaxing factor
EDV	end-diastolic volume
EEG	electroencephalogram
EF	ejection fraction
EGD	esophagogastroduodenoscopy
EGF	epidermal growth factor
EKG	electrocardiogram
ELAM	endothelial leukocyte adhesion molecule
EPI	epinephrine
ER	emergency room *or* endoplasmic reticulum
ERCP	endoscopic retrograde cholangiopancreatography
ERV	expiratory reserve volume
ESR	erythrocyte sedimentation rate
ESWL	extracorporeal shock wave lithotripsy
ET	endotracheal
$ETCO_2$	end-tidal CO_2
ETOH	ethanol, alcohol
EVAR	endovascular aortic repair
F/U	follow-up
FAP	familial adenomatous polyposis
FAST	focused abdominal sonography for trauma
Fc	antibody fragment, crystallizable
FEV_1	forced expiratory volume in 1 second
FFP	fresh frozen plasma
FGF	fibroblastic growth factor
FIO_2	fraction of inspired oxygen
FMD	fibromuscular dysplasia
FNA	fine needle aspiration
FRC	functional residual capacity
FSH	follicle-stimulating hormone
FTSG	full-thickness skin graft
FTT	failure to thrive
Fx	fracture
G6PD	glucose-6-phosphate dehydrogenase
GABA	gamma-aminobutyric acid
GCS	Glasgow Coma Scale
GCSF	granulocyte colony–stimulating factor
GDA	gastroduodenal artery
GERD	gastroesophageal reflux disease
GFR	glomerular filtration rate
GH	growth hormone
GHRH	growth hormone–releasing hormone
GI	gastrointestinal
GIP	gastric inhibitory peptide

GIST	gastrointestinal stromal tumor
GNR	gram-negative rod
GnRH	gonadotropin-releasing hormone
GPC	gram-positive cocci
GPR	gram-positive rod
GRP	gastrin-releasing peptide
GSH	glutathione
GU	genitourinary
H and P	history and physical
HA	headache
HBIG	hepatitis B immunoglobulin
HBV	hepatitis B virus
HCG	human chorionic gonadotropin
HCl	hydrochloric acid; hydrochloride
Hct	hematocrit
HCV	hepatitis C virus
HETE	hydroxyeicosatetraenoic acid
Hgb	hemoglobin
HGD	high grade dysplasia
HIDA	hepatic iminodiacetic acid
HIT	heparin-induced thrombocytopenia
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HMG CoA	_-hydroxy-_-methylglutaryl-CoA
HMW	high molecular weight
HPETE	hydroperoxyeicosatetraenoic acid
HPF	high-power field
HPV	human papillomavirus
HR	heart rate
HSV	herpes simplex virus
HTLV-1	human T-cell leukemia virus 1
HTN	hypertension
HUS	hemolytic uremic syndrome
HVA	homovanillic acid
IABP	intra-aortic balloon pump
IBW	ideal body weight
ICA	internal carotid artery
ICAM	intracellular adhesion molecule
ICP	intracranial pressure
ICU	intensive care unit
Ig	immunoglobulin
IJ	internal jugular
IL	interleukin
IMA	inferior mesenteric artery *or* internal mammary artery
IMF	intramaxillary fixation
IMV	inferior mesenteric vein
INF	interferon
INH	isoniazid
INR	international normalized ratio
IP_3	inositol 1,4,5-triphosphate
ITP	idiopathic thrombocytopenic purpura
IV	intravenous
IVC	inferior vena cava
IVF	intravenous fluid
IVP	intravenous pyelogram

L	liter
LA	left atrium
LAD	left anterior descending (coronary artery)
LAK	lymphokine-activated killer
LAR	low anterior resection
LATS	long-acting thyroid stimulator
LCIS	lobular carcinoma in situ
LD_{50}	dose that will kill 50% of test subjects
LDH	lactate dehydrogenase
LES	lower esophageal sphincter
LFT	liver function test
LH	luteotropic hormone
LHRH	luteinizing hormone–releasing hormone
LLQ	left lower quadrant
LR	lactated Ringer's
LS ratio	lecithin:sphingomyelin ratio
LTA_4	leukotriene A_4
LTB_4	leukotriene B_4
LTC_4	leukotriene C_4
LTD_4	leukotriene D_4
LTE_4	leukotriene E_4
LV	left ventricle *or* left ventricular
LVEDV	left ventricular end-diastolic volume
LVEF	left ventricular ejection fraction
LVESV	left ventricular end-systolic volume
LVOT	left ventricular outflow tract
MAC	minimum alveolar concentration
MALT	mucosa-associated lymphoid tissue
MAO	monoamine oxidase
MAOI	monoamine oxidase inhibitor
MAP	mean arterial pressure
MEN	multiple endocrine neoplasia
MHC	major histocompatibility complex
MI	myocardial infarction
MIBG	radioactive iodine meta-idobenzoguanidine
MIT	monoiodotyrosine
MRA	magnetic resonance angiogram
MRI	magnetic resonance imaging
MRCP	magnetic resonance cholangiopancreatography
MRM	modified radical mastectomy
MRND	modified radical neck dissection
MRSA	methicillin-resistant *S. aureus*
MS	mental status
MSH	melanocyte-stimulating hormone
MSOF	multisystem organ failure
MTP	metatarsophalangeal
MTX	methotrexate
N/V	nausea and vomiting
NADH	nicotinamide adenine dinucleotide
NADPH	nicotinamide adenine dinucleotide phosphate
NAPA	*N*-acetylprocainamide
NE	norepinephrine
NEC	necrotizing enterocolitis
NGT	nasogastric tube

NHL	non-Hodgkin's lymphoma
NIF	negative inspiratory force
NO	nitric oxide
NOMI	nonocclussive mesenteric ischemia
NPO	nil per os (nothing by mouth)
NS	normal saline (solution)
NSAID	nonsteroidal anti-inflammatory drug
NSE	neuron-specific enolase
NTG	nitroglycerine
OCP	oral contraceptive pills
OKT3	murine monoclonal anti-CD3 antibody therapy
Op-DDD	2,4-dichlorodiphenyl-dichloroethane (mitotane)
OR	operating room
ORIF	open reduction and internal fixation
PA	pulmonary artery
PABA	*p*-aminobenzoic acid
PADP	pulmonary artery diastolic pressure
PAF	platelet-activating factor
PAS	periodic acid–Schiff stain
PCN	penicillin
PCR	polymerase chain
PDA	patent ductus arteriosus
PDGF	platelet-derived growth factor
PE	pulmonary embolism
PECAM	platelet/endothelial cell adhesion molecule
PEEP	positive end-expiratory pressure
PEG	percutaneous endoscopic gastrostomy
PGD_2	prostaglandin D_2
PGE_1	prostaglandin E_1
PGE_2	prostaglandin E_2
PGF_2	prostaglandin F_2
PGG_2	prostaglandin G_2
PGH_2	prostaglandin H_2
PGI_2	prostaglandin I_2 (prostacyclin)
PIP_3	phosphatidylinositol 4,5-bisphosphonate
PMHx	past medical history
PMN	polymorphonuclear leukocytes
PNA	pneumonia
PNMT	phenylethanolamine-*N*-methyl-transferase
POD	postoperative day
PPI	proton pump inhibitor
PPN	peripheral line parenteral nutrition
pRBC	packed red blood cells
PSA	prostate-specific antigen
PSSS	postsplenectomy sepsis syndrome
PT	prothrombin time
PTA	percutaneous transluminal angioplasty
PTC	percutaneous transhepatic cholangiography
PTCA	percutaneous transluminal coronary angioplasty
PTFE	polytetrafluoroethylene
PTH	parathyroid hormone
PTHrP	parathyroid hormone–related peptide
PTLD	posttransplant lymphoproliferative disease
PTT	partial thromboplastin time

PTU	propylthiouracil
PTX	pneumothorax
PUD	peptic ulcer disease
PVC	premature ventricular contraction
PVR	pulmonary vascular resistance
Qp/Qs	pulmonary-to-systemic flow ratio
R/O	rule out
RA	right atrium
RBC	red blood cell
RLL	right lower lobe
RLN	recurrent laryngeal nerve
RND	radical neck dissection
ROM	range of motion
RPR	rapid plasma reagin
RQ	respiratory quotient
RR	respiratory rate
RUG	retrograde urethrogram
RUL	right upper lobe
RUQ	right upper quadrant
RV	residual volume *or* right ventricle
S/E	side effect
S–B	Sengstaken–Blakemore (tube)
SBFT	small bowel follow-through
SBO	small bowel obstruction
SBP	spontaneous bacterial peritonitis
SBP	systolic blood pressure
SCC	squamous cell carcinoma
SCD	sequential compression device
SCM	sternocleidomastoid
SCV	subclavian
SFA	superficial femoral artery
SIADH	syndrome of inappropriate antidiuretic hormone
SIRS	systemic inflammatory response syndrome
SLE	systemic lupus erythematosus
SLNBx	sentinel lymph node biopsy
SMA	superior mesenteric artery
SMV	superior mesenteric vein
SOB	shortness of breath
STEMI	ST segment elevation myocardial infarction
STSG	split-thickness skin graft
SVC	superior vena cava
SvO_2	mixed venous oxygen saturation
SVR	systemic vascular resistance
SVRI	systemic vascular resistance index
SVT	supraventricular tachycardia
Sx	symptom
T bili	total bilirubin
TAG	triacylglyceride
TAH	total abdominal hysterectomy
TB	tuberculosis
TBG	thyroid-binding globulin
TCOM	transcutaneous oxygen measurement
TCR	T-cell receptor
TE	tracheoesophageal
TEN	toxic epidermal necrolysis

TFT	thyroid function test
TGF-β	transforming growth factor-beta
TIA	transient ischemic attack
TIPS	transjugular intrahepatic portosystemic shunt
TLC	total lung capacity
TLSO	thoracolumbosacral orthosis
TMJ	temporomandibular joint
TNF	tumor necrosis factor
TOS	thoracic outlet syndrome
tPA	tissue plasminogen activator
TPN	total parenteral nutrition
TRALI	transfusion-related acute lung injury
TRAM	transverse rectus abdominis myocutaneous
TRH	thyrotropin-releasing hormone
TRUS	transrectal ultrasound
TSH	thyroid-stimulating hormone
TSI	thyroid-stimulating immunoglobulin
TTP	thrombotic thrombocytopenic purpura
TURP	transurethral resection of the prostate; transurethral prostatectomy
TV	tidal volume
Tx	treatment
TXA_2	thromboxane A_2
TXP	transplant
U/S	ultrasound
UC	ulcerative colitis
UDCA	ursodeoxycholic acid
UES	upper esophageal sphincter
UGI	upper gastrointestinal
URI	upper respiratory tract infection
UTI	urinary tract infection
UV	ultraviolet
V/Q	ventilation/perfusion
VC	vital capacity
VCAM	vascular cell adhesion molecule
V-fib	ventricular fibrillation
VIP	vasoactive intestinal peptide
VIPoma	vasoactive intestinal peptide–producing tumor
VLDL	very-low-density lipids
VMA	vanillylmandelic acid
VO_2	oxygen consumption
VP-16	etoposide
VRE	vancomycin-resistant *Enterococcus*
VSD	ventricular septal defect
V-tach	ventricular tachycardia
vWD	von Willebrand's disease
vWF	von Willebrand factor
W/U	workup
WBC	white blood cell
WDHA	watery diarrhea, hypokalemia, achlorhydria
wedge	pulmonary artery wedge pressure
WLE	wide local excision
XRT	radiation therapy
Z–E/ZES	Zollinger–Ellison syndrome

INDEX

Note: Page numbers in *italics* denote figures; those followed by t denote tables.