

SURGERY REVIEW

This review material is a synthesis of the first few chapters of *Schwartz's Principles of Surgery, 9th edition*, *Absite and Board Review of Schwartz's Principles of Surgery, 9th edition, 2009* *Absite Clinical Review of Surgery and RUSH integrated review of surgery*. Integration with other basic subjects as well as review questions per section are also included to facilitate mastery of the course.

Ready? God bless and enjoy Surgery! ☺

- Dr. Jules Lopez and Dr. Teddy Carpio

P.S.

Ophthalmology, ENT, Orthopedics, and Gynecology topics are not included in this surgery handout.

Any statements, tables, figures marked with a ☺ means that the information highlighted was previously tested in previous board exams. You should master/memorize those. Pay close attention to those in bold, italicized, underlines as these are very important facts to remember for the subject. Master topics written in our quick review, subject cross overs and end of review question boxes because they provide high yield information, not just for surgery but for the rest of the other subjects as well!

General Outline:

- I. Basic Principles in Surgery
 - a. Systemic Response to Injury and Metabolic support
 - b. Fluid and Electrolyte management of the Surgical Patient
 - c. Hemostasis, Surgical bleeding and transfusion
 - d. Surgical Infections and Shock
 - e. Trauma
 - f. Burns
 - g. Wound healing
- II. Organ System Pathologies
 - a. Skin and soft tissues
 - b. Breast
 - c. Head & Neck
 - d. Esophagus
 - e. Stomach
 - f. Small Intestine
 - g. Appendix
 - h. Colon, Rectum & Anus
 - i. Abdominal Wall & Hernia
 - j. Liver, Portal Venous System & Gallbladder

Table 1. Cytokines And Their Responses to Injury ☺

Cytokines and their Responses to Injury	
Tumor Necrosis Factor Alpha (TNF-α)	<ul style="list-style-type: none"> Among earliest responders after injury Induces muscle breakdown and cachexia through increased catabolism
Interleukin 1 (IL-1)	<ul style="list-style-type: none"> Induces fever through prostaglandin activity in anterior hypothalamus Promotes β-endorphin release from pituitary
Interleukin 2 (IL-2)	<ul style="list-style-type: none"> Promotes lymphocyte proliferation, immunoglobulin production, gut barrier integrity Attenuated production after major blood loss leads to immunocompromise
Interleukin 6 (IL-6)	<ul style="list-style-type: none"> Elicited by all immunogenic cells as mediator of acute phase response Prolongs activated neutrophil survival
Interleukin 8 (IL-8)	<ul style="list-style-type: none"> Chemoattractant for neutrophils, basophils, eosinophils, lymphocytes
Interferon (IFN-γ)	<ul style="list-style-type: none"> Activates macrophages via TH1 cells that demonstrate enhanced phagocytosis and microbial killing Found in wounds 5-7 days after injury

2. Heat Shock Proteins

- Group of intracellular proteins that are increasingly expressed during times of stress
- Bind both autologous and foreign proteins and thereby function as intracellular chaperones for ligands such as bacterial DNA and endotoxin
- Protect cells** from the deleterious effects of traumatic stress and, when released by damaged cells, **alert the immune system of the tissue damage**

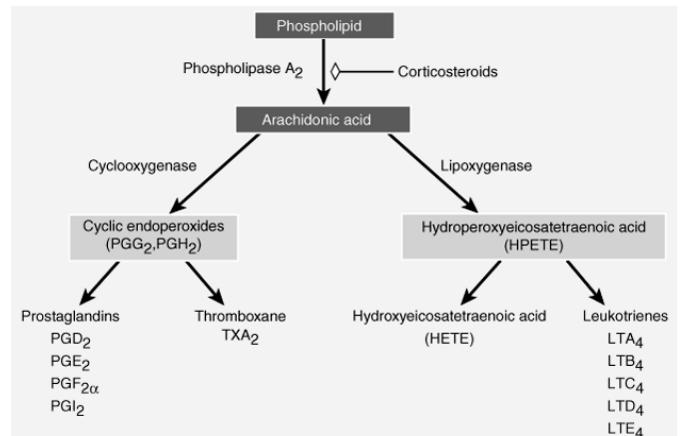
3. Reactive Oxygen Species (ROS)

- Small molecules that are highly reactive due to the presence of unpaired outer orbit electrons
- Cause cellular injury to both host cells and invading pathogens** through the oxidation of unsaturated fatty acids within cell membranes

4. Eicosanoids (Refer to Figure 1 ☺)

- Derived primarily by oxidation of membrane phospholipid, **arachidonic acid**
- Composed of subgroups including **prostaglandins, prostacyclins, hydroxyeicosatetraenoic acid, thromboxanes, and leukotrienes**
- Generate a **proinflammatory response**

Figure 1. Arachidonic acid metabolism ☺. Cyclooxygenase catalyzes the formation of PG and TXA₂ from arachidonic acid. LT = leukotriene; PG = prostaglandin; TXA₂ = thromboxane A₂



A. MEDIATORS OF INFLAMMATION

1. Cytokines (Refer to Table 1 ☺)

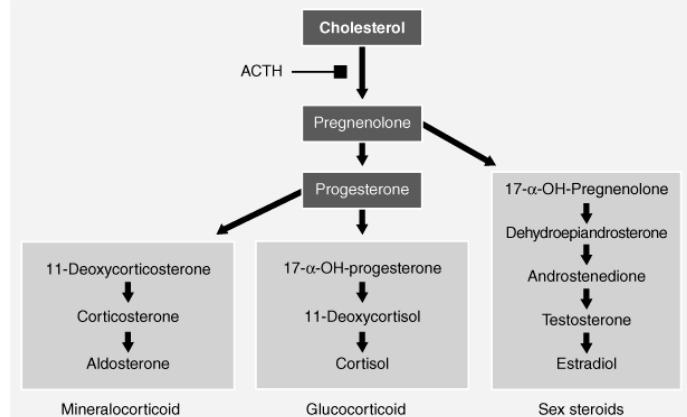
- Protein signaling compounds** that are essential for both innate and adaptive immunity
- Mediate cellular responses, including cell migration and turnover, DNA replication, and immunocyte proliferation

⊗ PHARMACOLOGY

- **Aspirin (Acetylsalicylic acid, ASA)** is one of the **non-steroidal anti-inflammatory drug (NSAID)** prototypes
- **Mechanism of action** ||
 - **Nonselective AND irreversible inhibitor** of the enzyme **cyclooxygenase (COX)**, inhibiting both **cyclooxygenase-1 (COX-1)** and **cyclooxygenase-2 (COX-2)** isoenzymes
 - Anti-inflammatory effect is mediated by COX-2 inhibition via decreasing platelet production of TXA₂, a potent stimulator of platelet aggregation
- **Side effect** || **Gastrointestinal (GI) toxicity** due to inhibition of COX-1 and thereby PG synthesis
- **Notes** || **Uncoupler of oxidative phosphorylation** and is associated with *Reye syndrome* in children
- **Ketorolac and Indomethacin** are both **nonselective BUT reversible** COX inhibitors
- **Celecoxib** is a **selective COX-2 inhibitor** with a reduced risk of GI toxicity

- Wound healing is impaired because it reduces transforming growth factor-beta (TGF-B) and insulin-like growth factor I (IGF-I) in the wound

Figure 2. Steroid synthesis from cholesterol ⊗. ACTH is a principal regulator of steroid synthesis. The end products are mineralocorticoids, glucocorticoids, and sex steroids.



5. Fatty Acid Metabolites

- Omega-3 fatty acids have **anti-inflammatory effects** including **inhibition of TNF release** from hepatic Kupffer cells, leukocyte adhesion and migration

6. Kallikrein-Kinin System

- Group of proteins that contribute to inflammation, BP control, coagulation, and pain responses
- **Kallikrein** levels are increased during gram negative bacteremia, hypotension, hemorrhage, endotoxemia, and tissue injury
- **Kinins** mediate vasodilation, increased capillary permeability, tissue edema, pain pathway activation, inhibition of gluconeogenesis, and increased bronchoconstriction
- Elevated levels of both has been associated with the magnitude of injury and mortality

7. Serotonin

- Released at the site of injury, primarily by platelets
- Stimulates vasoconstriction, bronchoconstriction, and platelet aggregation
- Ex vivo study showed that serotonin receptor blockade is associated with decreased production of TNF and IL-1 in endotoxin-treated monocytes

8. Histamine (H₄)

- Associated with **eosinophil and mast cell chemotaxis**
- Increased release has been documented in hemorrhagic shock, trauma, thermal injury, endotoxemia, and sepsis

B. CNS REGULATION OF INFLAMMATION

- **Vagus nerve** is highly influential in mediating afferent sensory input to the CNS
 - **Parasympathetic nervous system transmits its efferent signals via acetylcholine**
 - Exerts homeostatic influences such as enhancing gut motility, reducing heart rate, and regulating inflammation
 - Allows for a rapid response to inflammatory stimuli and also for the potential regulation of early proinflammatory mediator release, specifically **tumor necrosis factor (TNF)**
 - Inhibit cytokine activity and reduce injury from disease process

C. HORMONAL RESPONSE TO INJURY

1. Cortisol (Refer to Figure 2 ⊗)

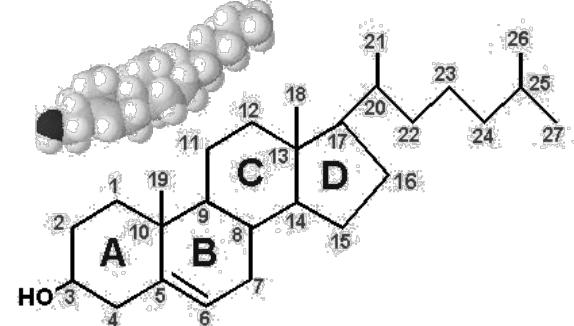
- Glucocorticoid steroid hormone released by the adrenal cortex in response to adrenocorticotrophic hormone (ACTH)
- Release is **increased** during times of stress and may be chronically elevated in certain disease processes (e.g. **burn-injured patients may exhibit elevated levels for 4 weeks**)

- **Cholesterol** is a **steroid alcohol**

- It is a precursor of the following:

1. Cell membranes
2. Vitamin D (*7-dehydrocholesterol*)
3. Bile salts (*cholic* and *chenodeoxycholic acid*)
4. Adrenal hormones (*aldosterone* and *cortisol*)
5. Sex hormones (*testosterone* and *estradiol*)

- It is very **hydrophobic** (which means, it can cross lipid predominant barriers), composed of 4 fused hydrocarbon rings (A-D) and 8-membered branched hydrocarbon chain (20-27) attached to the D-ring
- It has a single hydroxyl group located at carbon 3 of the A-ring to which a fatty acid can be attached to form cholesterol esters



2. Macrophage Migration-Inhibiting Factor

- Neurohormone that is stored and secreted by the anterior pituitary and by intracellular pools within macrophages
- A counter regulatory mediator that potentially **reverses the anti-inflammatory effects of cortisol**

3. Growth Hormones (GH)

- Neurohormone expressed primarily by the pituitary gland that has both metabolic and immunomodulatory effects
- Exerts its downstream effects through direct interaction with GH receptors and secondarily through the enhanced hepatic synthesis of IGF-I
- GH and IGF-I promote **protein synthesis and insulin resistance**, and **enhances mobilization of fat stores**

4. Catecholamines

- Include **epinephrine, norepinephrine, and dopamine**, which have metabolic, immunomodulatory, and vasoactive effects
- After severe injury, plasma catecholamine levels are **increased** threefold to fourfold, with elevations lasting 24 to 48 hours before returning to baseline levels

5. Insulin

- Mediates an overall host **anabolic state**
- **Insulin resistance** and **hyperglycemia** are hallmarks of critical illness due to the catabolic effects of circulating mediators, including *catecholamines*, *cortisol*, *glucagon*, and *GH*
- Hyperglycemia during critical illness has **immunosuppressive effects**, and thus is associated with an **increased risk for infection**
- Insulin therapy (to manage hyperglycemia) decreased mortality and reduced infectious complications in select patient populations

✓ QUICK REVIEW

- Burn patients may exhibit elevated levels of *cortisol* for **4 weeks**
- Plasma catecholamine levels are increased 3-4x lasting for **24 to 48 hours** before returning to baseline

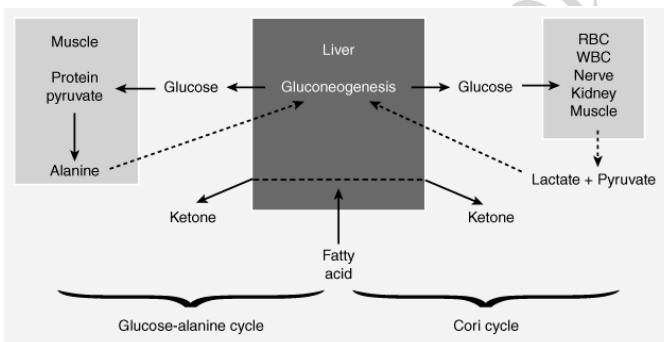
D. SURGICAL METABOLISM

- To maintain basal metabolic needs (i.e. at rest and fasting), a normal healthy adult requires **~22 to 25 kcal/kg/day** from carbohydrate, lipid, and protein sources
- Initial hours after surgical or traumatic injury are metabolically associated with a **reduced total body energy expenditure and urinary nitrogen wasting**

1. Metabolism During Short-term Fasting (<5 days)

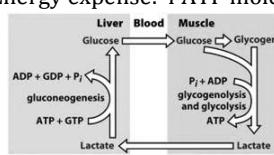
- In the healthy adult, principal sources of fuel are derived from muscle protein and lipids, with **lipids being the most abundant source of energy** (40% or more of caloric expenditure)
- Hepatic glycogen stores are rapidly and preferentially depleted → fall of serum glucose concentration within hours (<16 hours)
- Hepatic gluconeogenesis is then activated using lactate from skeletal muscle as the main precursor (Refer to **Figure 3** ☺)

Figure 3. The recycling of peripheral lactate and pyruvate for hepatic gluconeogenesis is accomplished by the Cori cycle. Alanine within skeletal muscles can also be used as a precursor for hepatic gluconeogenesis ☺.



⊗ BIOCHEMISTRY

- Lactate is generated from the skeletal muscle during anaerobic metabolism
- Muscle **CANNOT** reconvert lactate to glucose
- Lactate MUST first be transported to the liver, where it is converted to glucose via hepatic gluconeogenesis
- Glucose is then brought back to muscles for usage
- This metabolic pathway involving conversion of lactate to glucose; which, in turn, is brought back to the muscle for utilization is the **Cori cycle**
- Energy expense: 4 ATP molecules



- Lactate production is insufficient to maintain systemic glucose needs during short-term fasting; therefore, **significant amounts of protein must be degraded daily** (75 g/d for a 70 kg adult) to provide the amino acid substrate for hepatic gluconeogenesis
- Proteolysis during starvation, which results from decreased *insulin* and increased *cortisol* release, is associated with **elevated urinary nitrogen excretion** from the normal 7-10 g/day up to 30 g or more/day

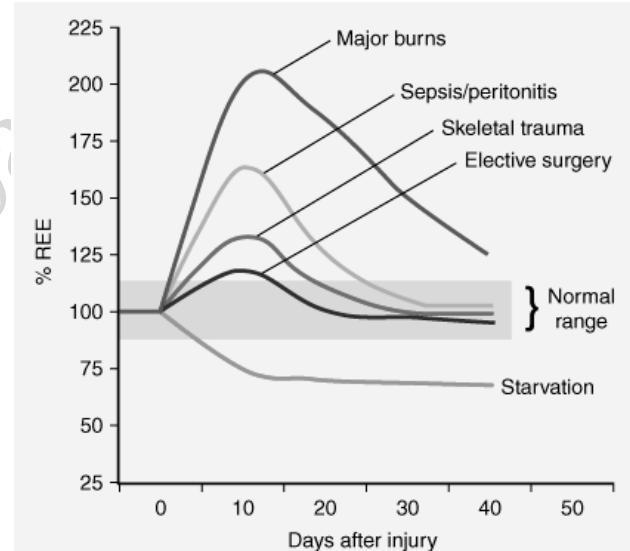
2. Metabolism During Prolonged Fasting

- Systemic proteolysis is **reduced** approximately 20 g/d and urinary nitrogen excretion stabilizes at 2 to 5 g/d due to adaptation by vital organs (e.g. myocardium, brain, renal cortex, and skeletal muscle) to using **ketone bodies** as their principal fuel source
- Ketone bodies become an important fuel source for the brain after 2 days and gradually become the principal fuel source by 24 days

3. Metabolism After Injury

- Injuries or infections induce unique neuroendocrine and immunologic responses that differentiate injury metabolism from that of unstressed fasting
- Magnitude of metabolic expenditure appears to be directly proportional to the severity of insult, with thermal injuries and severe infections having the highest energy demands (Refer to **Figure 4**)

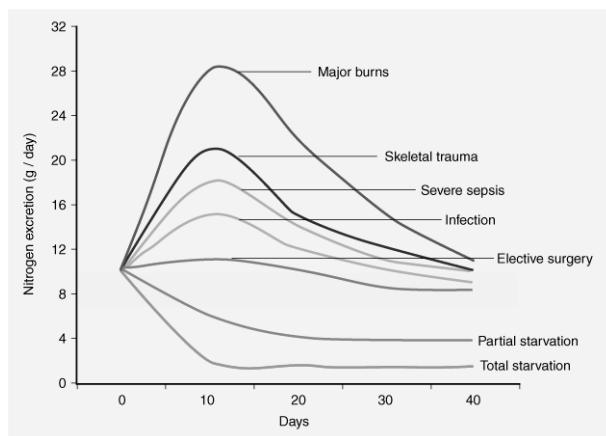
Figure 4. Influence of injury severity on resting metabolism (resting energy expenditure or REE)



- **Lipids** (Triglyceride) become the primary source of energy (50-80%) during **critical illness and stressed states**
 - Minimize protein catabolism in the injured patient
 - Lipolysis occurs mainly in response to catecholamine **stimulus of the hormone-sensitive triglyceride lipase**
- Injury and severe infections induce a state of **peripheral glucose intolerance (insulin resistance)**, despite ample insulin production at levels several-fold above baseline
 - Occur in part due to reduced skeletal muscle *pyruvate dehydrogenase* activity after injury, which diminishes the conversion of *pyruvate* to *acetyl-CoA* and subsequent entry into the TCA cycle
 - Increase in plasma glucose levels is proportional to the severity of injury, and this net hepatic gluconeogenic response is under the influence of *glucagon*
- After injury, the initial systemic proteolysis, mediated primarily by *cortisol*, **increases urinary nitrogen excretion** to levels in excess of 30 g/d, which roughly

corresponds to a loss in lean body mass of 1.5%/d
(Refer to **Figure 5**)

Figure 5. Effect of injury severity on nitrogen wasting



✓ QUICK REVIEW	
• Normal energy requirement: 22 to 25 kcal/kg/day	
• Initial hours after surgical or traumatic injury results to a reduced total body energy expenditure and urinary nitrogen wasting	
• Fat/lipid is the primary source of calories during acute starvation (<5 days fasting) and after acute injury	
• Ketone bodies is the primary fuel source in prolonged starvation	
• Ketone bodies becomes an important fuel source for brain after 2 days and eventually become the principal fuel source by 24 days	

E. NUTRITION IN THE SURGICAL PATIENT

- Goals of nutritional support in the surgical patient are as follows:
 - To meet the energy requirements for metabolic processes, core temperature maintenance, and tissue repair
 - To meet the substrate requirements for protein synthesis
- Energy requirement may be measured by indirect calorimetry and trends in serum markers (e.g. prealbumin level) and estimation from urinary nitrogen excretion, which is proportional to resting energy expenditure
- Basal energy expenditure (BEE)** may also be estimated using Harris-Benedict equations, adjusted for the type of surgical stress (Refer to **Table 2**)
 - BEE (men) = $66.47 + 13.75(\text{weight in kg}) + 5(\text{height in cm}) - 6.76(\text{age in years})$ kcal/d
 - BEE (women) = $655.1 + 9.56(\text{weight in kg}) + 1.85(\text{height in cm}) - 4.68(\text{age in years})$ kcal/d
- The BEE is then multiplied by the type of surgical stress (Refer to **Table 2**) that the patient has to determine the total daily caloric need

Table 2. Caloric Adjustment Above BEE in Hypermetabolic Conditions ☺
Caloric Adjustments Above Basal Energy Expenditures in Hypermetabolic Conditions

Normal or Moderate Malnutrition	25-30 kcal/kg/day
Mild Stress	25-30
Moderate Stress	30
Severe Stress	30-35
Burns	35-40

- Provision of **30 kcal/kg/d** will adequately meet energy requirements in **most postsurgical patients**, with low risk of overfeeding
 - Overfeeding** usually results from overestimation of caloric needs because actual body weight is used to calculate BEE, especially in special patients (e.g. critically ill with significant fluid overload and the obese)
 - Overfeeding may contribute to clinical deterioration via the following: increased O₂

consumption, increased CO₂ production and prolonged need for ventilatory support, suppression of leukocyte function, hyperglycemia, and increased risk of infection

1. **Enteral Nutrition**

- Generally preferred over parenteral nutrition due to:
 - Lower cost
 - Associated risks of the intravenous route
 - Beneficial effects of luminal nutrient contact as it reduces intestinal mucosal atrophy
- Initiation should occur immediately after adequate resuscitation (adequate urine output)
- Presence of bowel sounds and the passage of flatus or stool are NOT absolute prerequisites to start enteral nutrition, EXCEPT in the setting of **gastroparesis**, feedings should be administered distal to the pylorus
- Gastric residuals of 200 ml or more in a 4 to 6 hour period or abdominal distention requires cessation of feeding and adjustment of infusion rate
- The following are options for enteral feeding access (Refer to **Table 3** ☺):

Table 3. Options for Enteral Feeding Access ☺

Options for Enteral Feeding Access	
Nasogastric tube (NGT)	<ul style="list-style-type: none"> Short-term use Aspiration risks Nasopharyngeal trauma Frequent dislodgement
Nasoduodenal / Nasojejunal tube	<ul style="list-style-type: none"> Short-term use Lower aspiration risks in jejunum Placement challenges (radiographic assistance often necessary)
Percutaneous Endoscopic Gastrostomy (PEG)	<ul style="list-style-type: none"> Endoscopy skills required May be used for gastric decompression or bolus feeds Aspiration risks Can last 12-24 months Slightly higher complication rates with placement and site leaks
Surgical Gastrostomy	<ul style="list-style-type: none"> Requires general anesthesia and small laparotomy Procedure may allow placement of extended duodenal/jejunal feeding ports Laparoscopic placement possible
Surgical Jejunostomy	<ul style="list-style-type: none"> Commonly carried out during laparotomy General anesthesia, laparoscopic placement usually requires assistant to thread catheter Laparoscopy offers direct visualization of catheter placement
PEG-jejunal tube	<ul style="list-style-type: none"> Jejunal placement with regular endoscope is operator dependent Jejunal tube often dislodges retrograde Two-stage procedure with PEG placement, followed by fluoroscopic conversion with jejunal feeding tube through PEG

2. **Parenteral Nutrition**

- Continuous infusion of hyperosmolar solution containing carbohydrates, proteins, fat, and other necessary nutrients through an indwelling catheter inserted into the superior vena cava
- Principal indications include malnutrition, sepsis, or surgical or traumatic injury in seriously ill patients for whom use of the gastrointestinal tract for feedings is not possible
- Total (Central) Parenteral Nutrition (TPN)** requires access to a large-diameter vein to deliver the nutritional requirements of the individual
 - Dextrose content of the solution is high (15-25%)
 - All other macronutrients and micronutrients are deliverable by this route
- Peripheral Parenteral Nutrition (PPN)** uses lower osmolarity of the solution to allow its administration via peripheral veins
 - Reduced levels of dextrose (5-10%) and protein (3%)

- Some nutrients cannot be supplemented because they cannot be concentrated into small volumes
- Not appropriate for repleting patients with severe malnutrition
- Used for short periods (<2 weeks); beyond this, TPN should be instituted
- Complications are as follows (Refer to **Table 4** ☺):

Table 4. Complication of Parenteral Nutrition ☺

Complications of Parenteral Nutrition	
Vitamin Deficiencies	<ul style="list-style-type: none"> ● Rare occurrences if IV vitamin preparations are used ● However, Vitamin K is not part of any commercially prepared vitamin solution so it should be supplemented on a weekly basis
Essential Fatty Acid (EFA) Deficiency	<ul style="list-style-type: none"> ● Clinically apparent during prolonged parenteral nutrition with fat-free solutions ● Manifests as dry, scaly dermatitis and loss of hair ● Prevented by periodic infusion of a fat emulsion at a rate equivalent to 10 to 15% of total calories
Trace Mineral Deficiencies	<ul style="list-style-type: none"> ● Essential trace minerals may be required after prolonged TPN ● Zinc deficiency is the most common that manifests as diffuse eczematoid rash at intertriginous areas ● Copper deficiency is associated with Microcytic anemia ● Chromium deficiency is associated with Glucose intolerance
Relative Glucose Intolerance	<ul style="list-style-type: none"> ● May occur after initiation of parenteral nutrition ● Manifests as glycosuria ● If blood glucose levels remain elevated or glycosuria persists, dextrose concentration may be decreased, infusion rate slowed, or regular insulin added to each bottle ● Rise in blood glucose may be temporary, as the normal pancreas increases its output of insulin in response to the continuous carbohydrate infusion
Hypokalemia (and Metabolic Acidosis)	<ul style="list-style-type: none"> ● Due to large glucose infusion, a significant shift of potassium from extracellular to intracellular space may take place ● Manifests as glycosuria, which is treated with potassium, NOT insulin
Intestinal Atrophy	<ul style="list-style-type: none"> ● Lack of intestinal stimulation is associated with intestinal mucosal atrophy, diminished villous height, bacterial overgrowth, reduced lymphoid tissue size, reduced immunoglobulin A production, and impaired gut immunity

REVIEW QUESTIONS

1. Prostacyclin has which of the following effects in systemic inflammation?
- a. Inhibition of platelet aggregation
 - b. Vasoconstriction
 - c. Increased adhesion molecules
 - d. Decreased cardiac output

Answer: A

Prostacyclin is a member of the eicosanoid family and is primarily produced by endothelial cells. It is an effective vasodilator and also **inhibits platelet aggregation**. During systemic inflammation, prostacyclin expression is impaired and thus the endothelium favors a more procoagulant profile.

2. Sepsis increases metabolic needs by approximately what percentage?
- a. 25%
 - b. 50%

- c. 75%
- d. 100%

Answer: B

Sepsis increases metabolic needs to approximately 150-160% of resting energy expenditure, or **50% above normal** (Refer to **Figure 4**). This is mediated in part by sympathetic activation and catecholamine release.

3. Which of the following is the initial enteric formula for the majority of surgical patients?
- a. Low-residue isotonic formula
 - b. Elemental formula
 - c. Calorie dense formula
 - d. High protein formula

Answer: A

Most low-residue isotonic formulas provide a caloric density of 1.0 kcal/ml, and approximately 1500 to 1800 ml are required to meet daily requirements. These provide baseline carbohydrates, protein, electrolytes, water, fat, and fat-soluble vitamins. These solutions usually are considered to be the standard or first-line formulas for stable patients with an intact GI tract.

FLUID AND ELECTROLYTE MANAGEMENT OF THE SURGICAL PATIENT

- A. **Body Fluids and Compartments**
- B. **Body Fluid Changes**
- C. **Fluid Therapy**
- D. **Special Case: Refeeding Syndrome**
- E. **Electrolyte Abnormalities**
- F. **Acid-Base Disorders**

A. BODY FLUIDS AND COMPARTMENTS

- Water constitutes ~**50-60% of total body weight**
- Relationship between total body weight and **total body water (TBW)** is relatively constant for an individual and is primarily a **reflection of body fat**
 - Lean tissues (e.g. muscle and solid organs) have higher water content than fat and bone
 - **TBW of average young adult male and female is 60% and 50%, respectively of total body weight** ☺
- Estimates of %TBW should be adjusted downward ~10-20% for obese individuals and upward by ~10% for malnourished individuals
- Highest percentage of TBW is found in **newborns** (~80%)

✓ QUICK REVIEW

- TBW is ~**50-60%** of total body weight
- TBW (Male): **60%** of total body weight
- TBW (Female): **50%** of total body weight
- Young lean males have a higher proportion of TBW than elderly or obese individuals
- Lower percentage of TBW in females generally correlates with a higher percentage of adipose tissue and lower percentage of muscle mass

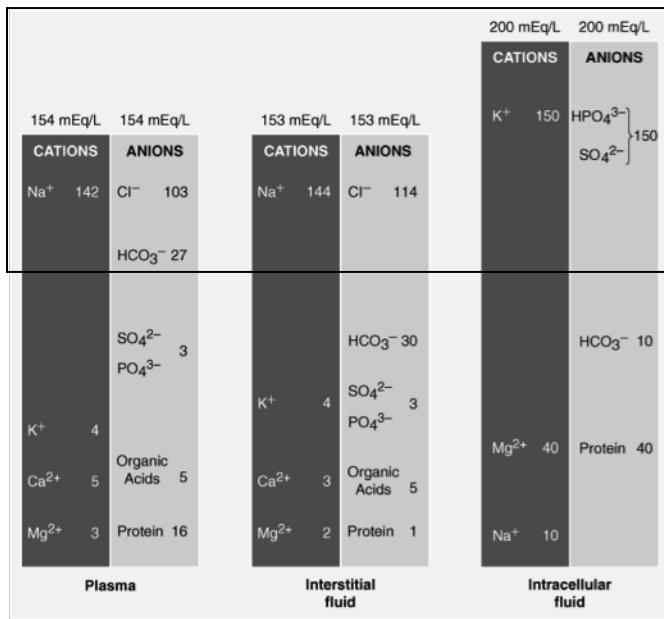
- TBW is divided into 3 functional fluid compartments (Refer to **Table 5** ☺):
- **Plasma** (extracellular)
 - **Interstitial fluid** (extracellular)
 - **Intracellular fluid**

Table 5. Functional Body Fluid Compartments ☺

Total Body Water (TBW)	Extracellular fluid (1/3 of TBW or 20% of total body weight)	PLASMA (1) (5% of total body weight)
		INTERSTITIAL FLUID (2) (15% of total body weight)
		INTRACELLULAR FLUID (3) (2/3 of TBW or 40% of total body weight)

- *Extracellular fluid compartment (ECF) is balanced between **sodium (Na⁺)**, the principal cation, and **chloride (Cl⁻)** and **bicarbonate (HCO₃⁻)**, the principal anions (Refer to Figure 6)*
 - Composition of the *plasma* and *interstitial fluid* differs only slightly in ionic composition
 - Slightly higher protein content (anions) in plasma results in a higher plasma cation composition relative to the interstitial fluid
- *Intracellular fluid compartment (ICF) is comprised of cations, **potassium (K⁺)** and **magnesium (Mg²⁺)**, and the anions, **phosphate (HPO₄²⁻)** and **proteins***
- Concentration gradient between compartments is maintained by *adenosine triphosphate (ATP)* driven *sodium-potassium pumps* located within the cell membranes

Figure 6. Chemical composition of body fluid compartments



- *Water is freely diffusible and distributed evenly throughout all fluid compartments of the body*
- *Sodium is confined to ECF and is associated with water*
 - Sodium-containing fluids are distributed throughout the ECF and add to both *plasma (intravascular)* and *interstitial spaces*
 - Sodium-containing fluids expand the *interstitial space* by ~3x as much as the *plasma*

B. BODY FLUID CHANGES

- A healthy person consumes water an average of **2L/d**, ~75% from oral intake and the rest extracted from solid foods (Refer to Table 6)
- Daily water losses include 800-1200 ml in urine, 250 ml in stool, and 600 ml in insensible losses through both the skin (75%) and lungs (25%)
- Sensible water losses such as sweating or pathologic loss of GI fluids vary widely, but these include loss of electrolytes as well
 - *Sweat* is **hypotonic** and sweating usually results in only a small sodium loss
 - *Pathologic GI losses* are **isotonic to slightly hypotonic** and contribute little to net gain or loss of free water

Table 6. Normal Fluid Balance

	Water Gain	Water Loss
Sensible	Oral fluids 1,500 ml	Urine 800-1200 ml
		Stool 250 ml
Insensible	Solid fluids 500 ml	Sweat 0 ml
	Water of oxidation 250 ml	Skin 450 ml
	Water of solution 0 ml	Lungs 150 ml

1. Extracellular Volume Deficit

- **Most common fluid disorder in surgical patients** ☺
- Can either be *acute* or *chronic* (Refer to Table 7)
 - *Acute volume deficit* is associated with cardiovascular and central nervous system signs
 - *Chronic deficit* displays tissue signs such as decrease in skin turgor and sunken eyes, in addition to acute signs

Table 7. Signs and Symptoms of Volume Disturbances

System	Volume Deficit	Volume Excess
General	Weight loss Decreased skin turgor	Weight gain Peripheral edema
Cardio	Tachycardia Orthostasis / Hypotension Collapsed neck veins	Increased cardiac output Increased central venous pressure Distended neck veins Murmur
Renal	Oliguria Azotemia	--
GI	Ileus	Bowel edema
Pulmo	--	Pulmonary edema

- **Most common cause of volume deficit in surgical patients** is a **loss of GI fluids** from nasogastric suction, vomiting, diarrhea, or enterocutaneous fistula (Refer to Table 8 ☺)
- Third-space or nonfunctional ECF losses that occur with sequestration secondary to soft tissue injuries/infections, burns, and intraabdominal processes such as peritonitis, obstruction, or prolonged surgery can also lead to massive volume deficits

Table 8. Composition of GI Secretions ☺

	Volume (ml/24h)	Na⁺ (mEq/L)	K⁺ (mEq/L)	Cl⁻ (mEq/L)	HCO₃ (mEq/L)
Saliva	1000	10	26	10	30
Stomach	1000-2000	60-90	10	130	0
Duodenum	1500	120-140	5-10	90-120	0
Ileum	3000	140	5	104	30
Colon	750	60	30	40	0
Pancreas	600-800	135-145	5-10	70-90	115
Bile	300-800	135-145	5-10	90-110	30-40

2. Extracellular Volume Excess

- May be iatrogenic or secondary to renal dysfunction, congestive heart failure, or cirrhosis
- Both plasma and interstitial volumes are increased
- Symptoms are primarily pulmonary and cardiovascular (Refer to Table 7)
- In healthy patients, edema and hyperdynamic circulation are common and well tolerated
- However, the elderly and patients with cardiac disease may quickly develop congestive heart failure and pulmonary edema in response to only a moderate volume excess

C. FLUID THERAPY

- Most commonly used solutions are as follows: (Refer to Table 9)

Table 9. Electrolyte Solutions for Parenteral Administration

Solution	Na ⁺	Cl ⁻	K ⁺	Ca ²⁺	Other	mOsm
ECF	142	103	4	27	--	280
Lactated Ringer's (LR)	130	109	4	28	Lactate 28 mEq/l	280
0.9% Sodium chloride (PNSS)	154	154	0	0	--	308
D5 Lactated Ringer's (D5LR)	130	109	4	3	Dextrose 50 g/l Lactate 28 mEq/l	560
D5 Sodium chloride (D5NS)	154	154	0	0	Dextrose 50 g/l	588
D5 0.45% Sodium chloride	77	77	0	0	Dextrose 50 g/l	434
D5 0.25% Sodium chloride	34	34	0	0	Dextrose 50 g/l	357

- Type of fluid administered depends on the patient's volume status and the type of concentration or composition abnormality present (Refer to **Table 10**)

Table 10. Fluid Therapy

Solution	Description
Lactated Ringer's (PLR)	<ul style="list-style-type: none"> Considered isotonic BUT it is slightly hypotonic due to lactate Useful in replacing GI losses and correcting extracellular volume deficits
0.9% Sodium chloride (PNSS)	<ul style="list-style-type: none"> Considered isotonic BUT it is mildly hypertonic Also useful in replacing GI losses and correcting extracellular volume deficits, especially those associated with hyponatremia, hypochloremia, and metabolic alkalosis
D5 0.45% Sodium chloride	<ul style="list-style-type: none"> Useful for replacement of ongoing GI losses as well as for maintenance fluid therapy in the postoperative period Provides sufficient free water for insensible losses and enough sodium to aid the kidneys in adjustment of serum sodium levels
D5 3.5-5% Sodium chloride	<ul style="list-style-type: none"> Hypertonic saline solution Used for correction of severe sodium deficits
D5 7% Sodium chloride	<ul style="list-style-type: none"> Hypertonic saline solution Used as a treatment modality in patients with closed head injuries Shown to increase cerebral perfusion and decrease intracranial pressure, thus decreasing brain edema However, there also have been concerns of increased bleeding, because hypertonic saline is an arteriolar vasodilator

1. Preoperative Fluid Therapy

- Preoperative evaluation of a patient's volume status and pre-existing electrolyte abnormalities is an important part of overall preoperative care
- Administration of **maintenance fluids** is required in an otherwise healthy individual on NPO before surgery
- The following is the formula used for calculating maintenance fluids in the absence of pre-existing abnormalities (Refer to **Table 11**):

Table 11. Maintenance Fluid Computation

First 0-10 kg	Give 100 ml/kg/dor 4 ml/kg/hr
Next 10-20 kg	Give additional 50 ml/kg/dor 2 ml/kg/hr
Weight >20 kg	Give additional 20 ml/kg/dor 1 ml/kg/hr

- However, may surgical patients have volume and/or electrolyte abnormalities associated with their surgical disease
 - Acute volume deficits should be corrected as much as possible
 - Once a volume deficit is diagnosed, prompt fluid replacement should be instituted, usually with an isotonic crystalloid

- Patients whose volume deficit is not corrected after initial volume challenge and those with impaired renal function and the elderly should be considered for more intensive monitoring of central venous pressure or cardiac output in an ICU setting
- If symptomatic electrolyte abnormalities accompany volume deficit, the abnormality should be corrected to the point that the acute symptom is relieved before surgical intervention.

✓ QUICK REVIEW

- Extracellular volume deficit** is the most common fluid disorder in surgical patients
- Most common cause of volume deficit in surgical patients is a **loss of GI fluids**
- Both **PLR and PNS** are considered isotonic and are useful in replacing GI losses and correcting extracellular volume deficits
- Hypertonic saline solution** is used as a treatment modality in patients with closed head injuries

2. Intraoperative Fluid Therapy

- With the induction of anesthesia, compensatory mechanisms are lost, and hypotension will develop if volume deficits are not appropriately managed
- To avoid hemodynamic instability intraoperatively, the following should be ensured:
 - Known fluid losses corrected preoperatively**
 - Adequate maintenance fluid therapy provided**
 - Ongoing losses replaced intraoperatively**
- Among the ongoing losses during surgery include distributional shifts via **third space or nonfunctional ECF losses** seen in the following:
 - Major open abdominal surgeries in the form of bowel wall edema, peritoneal fluid, and the wound edema during surgery
 - Large soft tissue wounds, complex fractures with associated soft tissue injury, and burns
- Replacement of ECF losses during surgery often requires 500 to 1000 ml/hr of a balanced salt solution to support homeostasis
- Addition of albumin or other colloid-containing solutions to intraoperative fluid therapy is NOT necessary

3. Postoperative Fluid Therapy

- Should be based on the patient's current estimated volume status and projected ongoing fluid losses
- Any deficits from either preoperative or intraoperative losses should be corrected and ongoing requirements should be included along with maintenance fluids
- In the initial postoperative period, an **isotonic solution** should be administered
 - Adequacy of resuscitation should be based on vital signs and urine output
 - All measured losses, including losses through vomiting, NGT, drains, and urine output as well as insensible losses should be replaced
- After the initial 24 to 48 hours, fluids can be changed to **5% dextrose to 0.45% saline** in patients unable to tolerate enteral nutrition
- If normal renal function and adequate urine output are present, potassium may be added to the IV fluids

D. SPECIAL CASE: REFEEDING SYNDROME ☺

- Refeeding syndrome** potentially lethal condition that can occur with **rapid and excessive feeding of patients with severe underlying malnutrition** due to starvation, alcoholism, delayed nutritional support, anorexia nervosa, or massive weight loss in obese patients

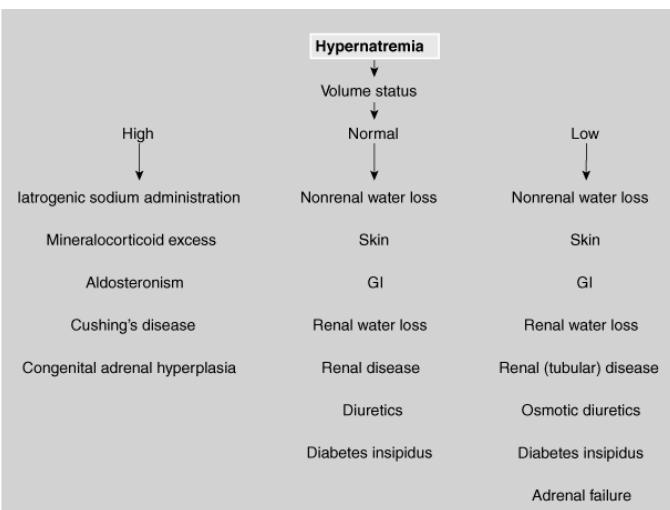
- Shift in metabolism from fat to carbohydrate substrate stimulates insulin release, which results in the cellular uptake of electrolytes, particularly **phosphate**, magnesium, potassium, and calcium
- Severe hyperglycemia may result from blunted basal insulin secretion
- To prevent its development, the following measures should be done:
 - Underlying electrolyte and volume deficits should be corrected
 - Thiamine** should be administered before the initiation of feeding
 - Caloric repletion should be instituted slowly, at 20 kcal/kg per day, and should gradually increase over the first week

E. ELECTROLYTE ABNORMALITIES

1. Hypernatremia

- Results from either a loss of free water or a gain of sodium in excess of water
- Associated with either an increased, normal, or decreased extracellular volume (Refer to **Figure 7**)
- Symptoms are rare until **serum sodium concentration exceeds 160 mEq/l**
- Clinical manifestations** || Mostly central nervous system in nature (*restlessness, irritability, seizures, coma*) due to **hyperosmolarity**
- May lead to subarachnoid hemorrhage and death

Figure 7. Etiology of Hypernatremia

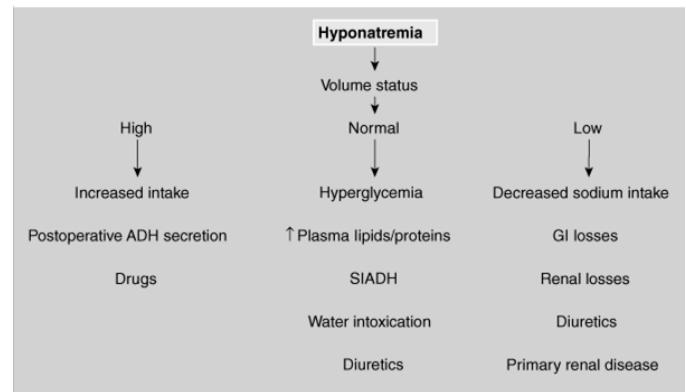


- Treatment** || **Management of water deficit**
- In hypovolemic patients, volume should be restored with normal saline before concentration abnormality is addressed
- Once adequate volume is achieved, water deficit is replaced using a hypotonic fluid
- Rate of fluid administration should be titrated to achieve a **decrease in serum sodium concentration of no more than 1 mEq/l/h**
- Overly rapid correction can lead to **cerebral edema** and **herniation**

2. Hyponatremia

- Occurs when there is an excess of extracellular water relative to sodium
- Extracellular volume can be high, normal, or low (Refer to **Figure 8**)
- In most cases, sodium concentration is decreased as a consequence of either sodium depletion or dilution
- Symptomatic hyponatremia does not occur until **serum sodium level is 20 mEq/l**
- Clinical manifestations** || Primarily central nervous system in origin (*headache, confusion, seizures, coma*) associated increases in intracranial pressure

Figure 8. Etiology of Hyponatremia



- Treatment** || **Water restriction** and, if severe, the **administration of sodium**
- If symptomatic, 3% normal saline should be used to increase the sodium by **no more than 1 mEq/l/h** until the serum sodium reaches 130 mEq/l or symptoms are improved
- If asymptomatic, correction should increase the sodium level by **no more than 0.5 mEq/l/hr** to a maximum increase of 12 mEq/l/d

⊗INTERNAL MEDICINE

- Central Pontine Myelinosis** is a **consequence of rapid correction of hyponatremia**
- Characterized with seizures, weakness, paresis, akinetic movements, and unresponsiveness
- May result in permanent brain damage and death
- MRI may assist in the diagnosis

3. Hyperkalemia

- Serum K⁺ concentration **above the normal range of 3.5-5 mEq/l**
- Caused by excessive K⁺ intake, increased release of K⁺ from cells, or impaired K⁺ excretion by the kidneys (Refer to **Table 12**)
- Clinical manifestations** || Mostly GI (*nausea/vomiting, diarrhea*), neuromuscular (*weakness, paralysis*), and cardiovascular (*arrhythmia, arrest*)
- ECG changes** || **High peaked T waves** (early), widened QRS complex, flattened P wave, prolonged PR interval (first-degree block), sine wave formation and ventricular fibrillation
- Treatment** || Reducing total body K⁺, shifting K⁺ from extracellular to intracellular space, and protecting cells from the effects of increased K⁺
- Exogenous sources of potassium should be removed, including K⁺ supplementation in IV fluids
- K⁺ can be removed from the body using a cation-exchange resin such as **Kayexalate** that binds K⁺ in exchange for Na⁺
- Immediate measures also should include attempts to shift K⁺ intracellularly with **glucose, insulin and bicarbonate infusion** and **nebulized salbutamol** (10-20 mg)
- When ECG changes are present, **calcium chloride or calcium gluconate** (5-10 ml of 10% solution) should be administered immediately
- All measures are temporary, lasting from 1 to 4 hours
- Dialysis** should be considered in severe hyperkalemia when conservative measures fail

4. Hypokalemia

- More common than hyperkalemia in the surgical patient
- Caused by inadequate K⁺ intake, excessive renal K⁺ excretion, K⁺ loss in pathologic GI secretions, or intracellular shifts from metabolic alkalosis or insulin therapy (Refer to **Table 12**)
- Clinical manifestations** || Primarily related to failure of normal contractility of GI smooth muscle (*ileus*,

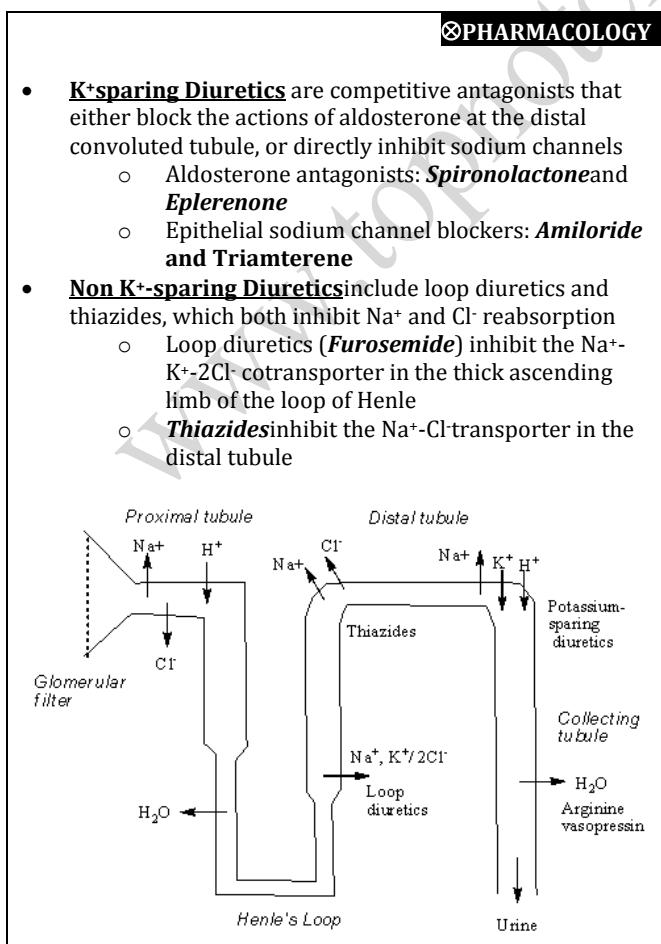
constipation), skeletal muscle (*decreased reflexes, weakness, paralysis*), and cardiac muscle (*arrest*)

- **ECG changes** || U waves, **T-wave flattening**, ST-segment changes, and arrhythmias (with digitalis therapy)

Table 12. Etiology of Potassium Abnormalities

Etiology of Potassium Abnormalities	
Hyperkalemia	Increased Intake <ul style="list-style-type: none"> • Potassium supplementation • Blood transfusions • Endogenous load/destruction: hemodialysis, rhabdomyolysis, crush injury, GI hemorrhage
	Increased Release <ul style="list-style-type: none"> • Acidosis • Rapid rise of extracellular osmolality (hyperglycemia or mannitol)
	Impaired Excretion <ul style="list-style-type: none"> • Potassium-sparing diuretics • Renal insufficiency/failure
Hypokalemia	Inadequate Intake <ul style="list-style-type: none"> • Dietary, potassium-free IV fluids • Potassium-deficient TPN
	Excessive Potassium Excretion <ul style="list-style-type: none"> • Hyperaldosteronism • Medications (Non-K⁺ sparing diuretics)
	GI losses <ul style="list-style-type: none"> • Direct loss of potassium from GI fluid (diarrhea) • Renal loss of potassium

- **Treatment** || **Potassium repletion**, the rate is determined by the symptoms
- Mild, asymptomatic hypokalemia: oral repletion is adequate (KCl 40 mEq per enteral access x 1 dose)
- Asymptomatic hypokalemia, not tolerating enteral nutrition: KCl 20 mEq IV q2h x 2 doses
- If IV repletion is required, usually **no more than 10 mEq/h** is advisable in an unmonitored setting
- K⁺ supplementation can be increased to 40 mEq/h when accompanied by continuous ECG monitoring, and even more in the case of imminent cardiac arrest from a malignant arrhythmia associated hypokalemia
- Caution should be done when oliguria or impaired renal function is coexistent



✓ QUICK REVIEW
• Normal Na ⁺ : 135-145 mEq/l
• Symptomatic hyponatremia are rare until serum sodium exceeds 160 mEq/l
• Symptomatic hyponatremia does not occur until serum sodium level is 20 mEq/l
• Normal K ⁺ : 3.5-5 mEq/l
• Peaked T waves are the first ECG change seen in most patients with hyperkalemia
• T-wave flattening is seen in hypokalemia
• Hypokalemia causes decreased deep tendon reflexes while hypomagnesemia and hypocalcemia causes increased deep tendon reflexes

5. Hypercalcemia

- Serum calcium level **above the normal range of 8.5-10.5 mEq/l** or an increase in ionized calcium **above 4.2-4.8 mg/dl**
- Caused by *primary hyperparathyroidism* in the outpatient setting and *malignancy* in hospitalized patients
- **Clinical manifestations** || Neurologic impairment, musculoskeletal weakness and pain, renal dysfunction, and GI symptoms (Refer to **Table 13**)
- **ECG changes** || Shortened QT interval, prolonged PR and QRS intervals, increased QRS voltage, T-wave flattening and widening, and atrioventricular block
- Treatment is required when hypercalcemia is symptomatic, which usually occurs when the **serum level exceeds 12 mEq/l**
- **Critical level for serum calcium is 15 mEq/l** when symptoms noted earlier may rapidly progress to death
- **Treatment** || Aimed at repleting the associated volume deficit and then inducing a brisk diuresis with normal saline

6. Hypocalcemia

- Serum calcium level **below 8.5 mEq/l** or a decrease in the ionized calcium level **below 4.2 mg/dl**
- Causes include *pancreatitis*, malignancies associated with increased osteoclastic activity (*breast and prostate cancer*), massive soft tissue infections such as *necrotizing fasciitis*, *renal failure*, *pancreatic* and *small bowel fistulas*, *hypoparathyroidism*, *toxic shock syndrome*, and *tumor lysis syndrome*
- Transient hypocalcemia also occurs after removal of a parathyroid adenoma due to atrophy of the remaining gland and avid bone remineralization
- Neuromuscular and cardiac symptoms do not occur until the **ionized fraction falls below 2.5 mg/dl**
- **Clinical manifestations** || Neuromuscular symptoms with decreased cardiac contractility (Refer to **Table 13**)
- **ECG changes** || Prolonged QT interval, T-wave inversion, heart block and ventricular fibrillation

⊗MICROBIOLOGY
• Toxic Shock Syndrome is due to the <i>Staphylococcus aureus</i> toxin, Toxic shock syndrome toxin (TSST-1)
• Clinical manifestations Fever, hypotension, sloughing of the filiform papillae (strawberry tongue), desquamating rash , and multi-organ involvement
• Usually no site of pyogenic inflammation → blood CS negative
• Common in tampon-using menstruating women or in patients with nasal packing for epistaxis
• Treatment Remove the offending agent and to start antibiotics (Clindamycin and Vancomycin)

PATHOLOGY

- Tumor Lysis Syndrome** consists of multiple electrolyte abnormalities that may be seen after initiation of cancer treatment
- Chemotherapy causes release of break-down products of dying cancer cells
- Among the electrolyte abnormalities include **hyperkalemia, hyperphosphatemia, hyperuricemia, and hypocalcemia**
- Clinical consequences are **acute uric acid nephropathy** and **acute renal failure**

- Treatment** || Calcium supplementation and correction of other metabolic derangements
- Asymptomatic hypocalcemia can be treated with **oral or IV calcium**
- Acute symptomatic hypocalcemia should be treated with **IV 10% calcium gluconate** to achieve a serum concentration of 7-9 mg/dl
- Associated deficits in magnesium, potassium, and pH must also be corrected
- Hypocalcemia will be refractory to treatment if coexisting hypomagnesemia is not corrected first**

7. Hypermagnesemia

- Rare but can be seen with *severe renal insufficiency* and *parallel changes in potassium excretion*
 - Magnesium-containing antacids and laxatives can produce toxic levels in patients with renal insufficiency/failure
 - Excess intake in conjunction with TPN, or rarely massive trauma, thermal injury, and severe acidosis, may be associated with symptomatic hypermagnesemia
- Clinical manifestations** || Mainly GI with neuromuscular dysfunction and impaired cardiac conduction (Refer to **Table 13**)
- ECG changes** || (similar to hyperkalemia) Increased PR interval, widened QRS complex, elevated T waves
- Treatment** || Eliminate exogenous sources of magnesium, correct concurrent volume deficits and correct acidosis if present
- To manage acute symptoms, **calcium chloride**(5-10ml) should be administered to immediately antagonize the cardiovascular effects
- If persistently elevated or with symptoms, **dialysis** may be necessary

8. Hypomagnesemia

- Magnesium depletion is a common problem in hospitalized patients, particularly in the critically ill
- Result from alterations of intake, renal excretion and pathologic losses
 - Poor intake may occur in cases of *starvation, alcoholism, prolonged IV fluid therapy, and TPN with inadequate supplementation of Magnesium*
 - Losses are seen in cases of *increased renal excretion from alcohol abuse, diuretic use, administration of amphotericin B, and primary aldosteronism, as well as GI losses from diarrhea, malabsorption, and acute pancreatitis*
- Clinical manifestations** || Neuromuscular and central nervous system hyperactivity, similar to those of calcium deficiency
- ECG changes** || Prolonged QT and PR intervals, ST-segment depression, flattening or inversion of P waves, *torsades de pointes*, and arrhythmias
- Can produce hypocalcemia and lead to persistent hypokalemia** ☺

Table 13. Clinical Manifestations of Abnormalities in Ca^{2+} and Mg^{2+}

Increased Serum Levels		
System	Calcium	Magnesium
<i>Gastrointestinal</i>	Anorexia Nausea/vomiting	Nausea/vomiting

	Abdominal pain	
<i>Neuromuscular</i>	Weakness Bone pain Confusion Coma	Weakness Lethargy Decreased reflexes
<i>Cardiovascular</i>	Hypertension Arrhythmia Worsening of digitalis toxicity	Hypotension Arrest
<i>Renal</i>	Polyuria	-
Decreased Serum Levels		
System	Calcium	Magnesium
<i>Neuromuscular</i>	Hyperactive reflexes Paresthesias Muscle cramps Carpopedal spasm Seizures Tetany Trousseau's sign ¹ Chvostek's sign ²	Hyperactive reflexes Muscle tremors Tetany Positive Chvostek's and Trousseau's signs Delirium and seizures (severe)
<i>Cardiovascular</i>	Heart failure	Arrhythmia

¹Spasm resulting from pressure applied to the nerves and vessels of the upper extremity with a blood pressure cuff

²Spasm resulting from tapping over the facial nerve

- Treatment** || Magnesium supplementation
- Correction of magnesium depletion can be oral if asymptomatic and mild or IV if symptomatic and severe
- For those with severe deficits (<1 mEq/L) or those who are symptomatic, **1 to 2 g of magnesium sulfate** may be administered IV over 15 minutes or 2 minutes if under ECG monitoring to correct *torsades*
- To counteract the adverse side effects of a rapidly rising magnesium level and correct hypocalcemia (frequently associated with hypomagnesemia), simultaneous administration of **calcium gluconate** is done

QUICK REVIEW

- Normal Ca^{2+} : **8.5-10.5 mEq/l**
- Normal ionized Ca^{2+} : **4.2-4.8 mg/dl**
- Treatment is required when **hypercalcemia** is symptomatic, when the **serum level exceeds 12 mEq/l**
- Symptomatic **hypocalcemia** do not occur until the **ionized fraction falls below 2.5 mg/dl**
- Hypocalcemia** will be refractory to treatment if coexisting **hypomagnesemia** is not corrected first

F. ACID-BASE DISORDERS

1. Metabolic Acidosis

- Results from an *increased intake of acids, an increased generation of acids, or an increased loss of bicarbonate*
- Body compensates by *producing buffers* (extracellular bicarbonate and intracellular buffers from bone and muscle), *increasing ventilation* (Kussmaul's respirations), *increasing renal reabsorption* and *generation of bicarbonate*, and *increasing renal secretion of hydrogen*
- Evaluation of a patient with metabolic acidosis includes determination of the **anion gap (AG)**, an index of unmeasured anions
 - $\text{AG} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$
 - Normal: <12 mmol/l
- Etiology of metabolic acidosis is listed in **Table 14** ☺

Table 14. Etiology of Metabolic Acidosis ☺

High Anion Gap Metabolic Acidosis (HAGMA)	
Exogenous acid ingestion <ul style="list-style-type: none"> Ethylene glycol Salicylate Methanol 	Mnemonic: "MUDPILES" <ul style="list-style-type: none"> Methanol Uremia (Renal failure) Diabetic ketoacidosis Propylene glycol Paraldehyde Infection, Iron, Isoniazid Lactic acidosis Ethylene glycol Salicylates
Endogenous acid production <ul style="list-style-type: none"> Ketoacidosis Lactic acidosis Renal insufficiency 	

Normal Anion Gap Metabolic Acidosis (NAGMA)	
Acid administration (HCl)	
Loss of bicarbonate	Mnemonic: "HARD UP" <ul style="list-style-type: none"> • Hyperalimentation • Acetazolamide (Carbonic anhydrase inhibitor) • Renal tubular acidosis • Diarrhea • Ureteroenteric fistula • Pancreaticoduodenal fistula
GI losses (diarrhea, fistulas)	
Ureterosigmoidoscopy	
Renal tubular acidosis	
Carbonic anhydrase inhibitor	

- **Lactic acidosis** is a common cause of severe metabolic acidosis in surgical patients
- In circulatory shock, *lactate* is produced in the presence of hypoxia from inadequate tissue perfusion
- **Treatment || Restore perfusion with volume resuscitation** rather than to attempt to correct with exogenous bicarbonate
- With adequate perfusion, lactate is rapidly metabolized by the liver and the pH level returns to normal
- Administration of **bicarbonate** for the treatment of metabolic acidosis is controversial
 - Overzealous administration of bicarbonate can lead to **metabolic alkalosis** and can be associated with **arrhythmias**
 - An additional disadvantage is that sodium bicarbonate actually can exacerbate intracellular acidosis

2. Metabolic Alkalosis

- Results from the *loss of fixed acids* organ of **bicarbonate** (Refer to **Table 15**)
- Majority of patients will have **hypokalemia**, because extracellular potassium ions exchange with intracellular hydrogen ions and allow the hydrogen ions to buffer excess HCO_3^-
- **Treatment || Includes replacement of the volume deficit** with isotonic saline and then potassium replacement once adequate urine output is achieved

Table 15. Etiology of Metabolic Alkalosis

Increased bicarbonate generation	
Chloride losing (urinary chloride > 20 mEq/l)	<ul style="list-style-type: none"> • Mineralocorticoid excess • Profound potassium depletion
Chloride sparing (urinary chloride < 20 mEq/l)	<ul style="list-style-type: none"> • Loss from gastric secretions (emesis or nasogastric suction) • Diuretics
Excess administration of alkali	
<ul style="list-style-type: none"> • Acetate in parenteral nutrition • Citrate in blood transfusions • Antacids • Bicarbonate • Milk-alkali syndrome 	
Impaired bicarbonate excretion	
Decreased glomerular filtration	
Increased bicarbonate reabsorption (hypercarbia or potassium depletion)	

3. Respiratory Acidosis

- Associated with *retention of CO_2* secondary to **decreased alveolar ventilation**
- Principal causes are listed in **Table 16**
- Because compensation is primarily a *renal mechanism*, it is a delayed response
- In the chronic form, partial pressure of arterial CO_2 remains elevated and the bicarbonate concentration rises slowly as renal compensation occurs
- **Treatment || Directed at the underlying cause**
- Measures to ensure adequate ventilation through bilevel positive airway pressure or endotracheal intubation are also initiated

Table 16. Etiology of Respiratory Acidosis

Etiology of Respiratory Acidosis	
Narcotics	
Central nervous system injury	
Pulmonary (secretions, atelectasis, mucus plug, pneumonia, pleural effusion)	
Pain from abdominal or thoracic injuries or incisions	
Limited diaphragmatic excursion from intra-abdominal pathology (abdominal distension, abdominal compartment syndrome, ascites)	

4. Respiratory Alkalosis

- In the surgical patient, most cases are acute and secondary to **alveolar hyperventilation**
- Causes include pain, anxiety, neurologic disorders (*central nervous system injury* and *assisted ventilation*), drugs (*salicylates*), fever, gram-negative bacteremia, thyrotoxicosis, and hypoxemia
- Acute hypocapnia can cause an uptake of potassium and phosphate into cells and increased binding of calcium to albumin, leading to **symptomatic hypokalemia**, **hypophosphatemia**, and **hypocalcemia** with subsequent arrhythmias, paresthesias, muscle cramps, and seizures
- **Treatment ||** Directed at the underlying cause
- Direct treatment of the hyperventilation using controlled ventilation may also be required

✓ QUICK REVIEW

- Evaluation of a patient with **metabolic acidosis** includes determination of the **anion gap (AG)** to differentiate HAGMA from NAGMA (TIP: Memorize the mnemonics!)
- Normal AG is **<12 mmol/l**
- Treatment of **metabolic acidosis** is to **restore perfusion with volume resuscitation** rather than exogenous bicarbonate
- **Metabolic alkalosis** is associated with **hypokalemia**

REVIEW QUESTIONS

1. A patient develops a high output fistula following abdominal surgery. The fluid is sent for evaluation with the following results: Na^+ 135, K^+ 5, Cl^- 70. Which of the following is the most likely source of the fistula?
 - a. Stomach
 - b. Small bowel
 - c. Pancreas
 - d. Biliary tract
- Answer: C
The composition of **pancreatic secretions** is marked by **high level of bicarbonate** (Refer to **Table 8**), compared to other GI secretions. In this example, the patient has a total of 140 mEq of cation ($\text{Na}^+ + \text{K}^+$) and only 70 mEq of anion (Cl^-). The remaining 70 mEq (to balance the 140 mEq of cation) must be bicarbonate.
2. A postoperative patient with a potassium of 2.9 is given 1 mEq/kg replacement with KCl (potassium chloride). Repeat tests after the replacement show the serum K to be 3.0. The most likely diagnosis is:
 - a. Hypomagnesemia
 - b. Hypocalcemia
 - c. Metabolic acidosis
 - d. Metabolic alkalosis

Answer: A

In cases in which potassium deficiency is due to magnesium depletion, **potassium repletion is difficult unless hypomagnesemia is first corrected**. *Alkalosis* will change serum potassium (a decrease in 0.3 mEq/l for every 0.1 increase in pH above normal). This is not enough to explain the lack of response to repletion in the patient. *Metabolic acidosis* would not decrease potassium. Calcium does not play a role in potassium metabolism.

3. Which of the following is a cause of acute hypophosphatemia?
- Chronic ingestion of magnesium containing laxatives
 - Insulin coma
 - Refeeding syndrome
 - Rhabdomyolysis

Answer: C

Acute hypophosphatemia is usually caused by an intracellular shift of phosphate in association with respiratory alkalosis, insulin therapy, **refeeding syndrome**, and hungry bone syndrome. Clinical manifestations include cardiac dysfunction or muscle weakness but are usually absent until levels fall significantly. Refer to page 8 for a discussion on **refeeding syndrome**.

Magnesium containing laxatives can cause **hypermagnesemia** in patients with renal failure but does not affect phosphorous. Patients with insulin coma (hypoglycemia) are not at risk for hypophosphatemia. Rhabdomyolysis is associated with **hyperkalemia** and **hyperphosphatemia**

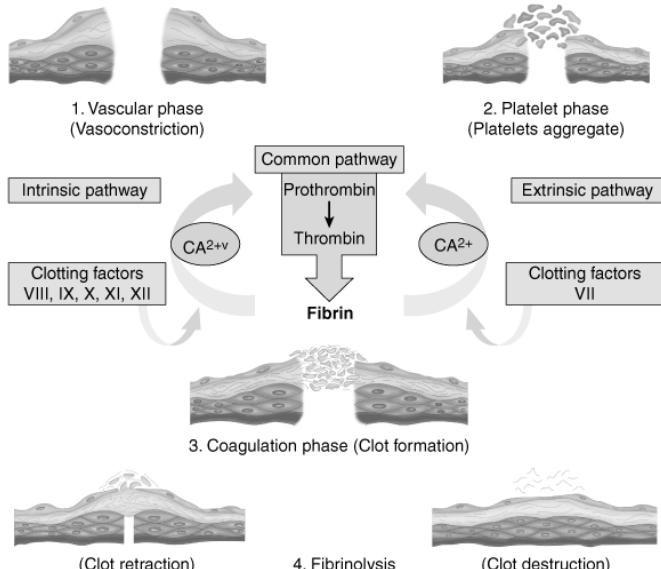
HEMOSTASIS, SURGICAL BLEEDING, AND TRANSFUSION

- Hemostasis
- Evaluation of Hemostatic Risk
- Surgical Bleeding
- Special Cases
- Transfusion

A. HEMOSTASIS

- Function is **to limit blood loss from an injured vessel**
- Four major physiologic events participate in the hemostatic process (Refer to Figure 9):
 - Vascular constriction
 - Platelet plug formation
 - Fibrin formation
 - Fibrinolysis

Figure 9. Biology of Hemostasis



1. Vascular Constriction

- Initial response to vessel injury
- Dependent on local contraction of smooth muscle
 - Thromboxane A₂** (TXA₂) is a potent constrictor of smooth muscle, is produced locally at the site of injury
 - Endothelin** is also a potent vasoconstrictor, is synthesized by injured endothelium and serotonin
 - Bradykinin** and **fibrinopeptides** are capable of contracting vascular smooth muscle.

- Extent of vasoconstriction varies with the degree of vessel injury (more pronounced in vessels with medial smooth muscles)

2. Platelet Plug Formation

- Platelets do not normally adhere to each other or to the vessel wall but during vascular disruption, they form a **hemostatic plug** that aids in cessation of bleeding
- Injury to the intimal layer in the vascular wall exposes **von Willebrand's factor (vWF)**, a subendothelial protein, where platelets adhere via **glycoprotein I/IX/V**
- After adhesion, platelets initiate a *release reaction* that recruits other platelets to seal the disrupted vessel
- The aforementioned process, mediated by **adenosine diphosphate (ADP) and serotonin**, is *reversible* and is known as **primary hemostasis**
- In the second wave of platelet aggregation, another *release reaction* occurs that results in compaction of the platelets via **glycoprotein IIb/IIIa** into a plug
- With **fibrinogen** as a cofactor, this process, mediated by **ADP, Ca²⁺, serotonin, TXA₂**, is *irreversible*

3. Fibrin Formation / Coagulation

- As a consequence of the release reaction, alterations occur in the phospholipids of the platelet membrane that initiates **coagulation**
- Coagulation cascade typically has been depicted as two intersecting pathways
 - Intrinsic pathway** begins with **factor XII** and through a series of enzymatic reactions, which is intrinsic to the circulating plasma and **no surface is required to initiate the process**
 - Extrinsic pathway** requires **exposure of tissue factor on the surface of the injured vessel wall** to initiate the arm of the cascade beginning with **factor VII**
 - The two arms of the coagulation cascade merge to a common pathway at **factor X**, and activation of factors II (prothrombin) and I (fibrinogen) proceeds in sequence
- Secondary hemostasis** or **fibrin clot formation** occurs after conversion of **fibrinogen to fibrin**

4. Fibrinolysis

- During the wound-healing process, the fibrin clot undergoes **fibrinolysis**, which permits restoration of blood flow
- This is initiated at the same time as the clotting mechanism under the influence of circulating kinases, tissue activators, and **kallikrein**, which are present in the vascular endothelium
- Plasmin** degrades the fibrin mesh at various places, which leads to the production of circulating fragments that are cleared by proteases or by the kidney and liver

B. EVALUATION OF HEMOSTATIC RISK

1. Preoperative Evaluation of Hemostasis

- Most important component of the bleeding risk assessment is a *directed bleeding history*
- When history is unreliable or incomplete or when abnormal bleeding is suggested, a *formal evaluation of hemostasis* should be performed before surgery
 - Hemoglobin levels below 7 or 8 g/dl appear to be associated with significantly more perioperative complications
 - Determination of the need for preoperative transfusion must consider factors other than the absolute hemoglobin level, including the presence of cardiopulmonary disease, type of surgery, and likelihood of surgical blood loss
- Laboratory tests of hemostatic parameters in patients with low risk of bleeding are NOT required

2. Evaluation of Intraoperative or Postoperative Bleeding

- Excessive bleeding during or after a surgical procedure may be the result of *ineffective hemostasis*, *blood transfusion*, *undetected hemostatic defect*, *disseminated*

intravascular coagulation (DIC) or consumptive coagulopathy, and/or fibrinolysis

C. SURGICAL BLEEDING

1. Systemic Bleeding Disorders

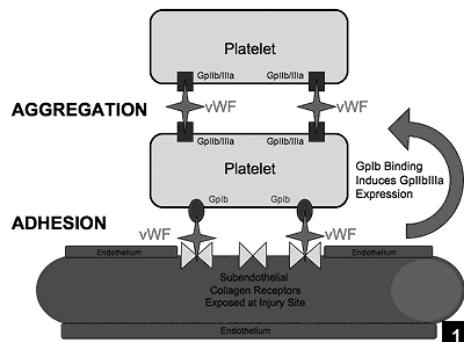
- **Thrombocytopenia**, secondary to any platelet pathology, is the **most common abnormality of hemostasis** that results in bleeding in surgical patients
- Systemic causes of surgical bleeding can either be inherited or acquired (Refer to **Table 17**)
- Inherited platelet functional defects include *abnormalities of platelet surface proteins, abnormalities of platelet granules, and enzyme defects*
- Acquired abnormalities of platelets may be *quantitative* or *qualitative*, although some patients have both types
 - Quantitative defects may be a result of *failure of production* due to bone marrow disorders, *shortened survival*, or *sequestration*
 - Qualitative defects include *massive transfusion* and *drugs that interfere with platelet function*

Table 17. Etiology of Surgical Bleeding

Congenital Factor Deficiencies	
Coagulation Factor Deficiencies	
von Willibrand's Disease	
Platelet Functional Defects	
Acquired Hemostatic Defects	
Platelet Abnormalities: Quantitative	
Failure of Production	Leukemia
	Myeloproliferative disorders
	Vitamin B12 or Folate deficiency
	Chemotherapy or radiation therapy
	Acute alcohol intoxication
	Viral infections
Decreased Survival	Immune-mediated disorders (Idiopathic thrombocytopenia, Heparin-induced thrombocytopenia, Autoimmune disorders or B-cell malignancies, Secondary thrombocytopenia)
	Disseminated intravascular coagulation
	Disorders related to platelet thrombi (Thrombocytopenic purpura, Hemolytic uremic syndrome)
Sequestration	Portal hypertension
	Sarcoid
	Lymphoma
	Gaucher's disease
Platelet Abnormalities: Qualitative	
Massive transfusion	
Therapeutic administration of platelet inhibitors	
Disease states	Myeloproliferative disorders
	Monoclonal gammopathies
	Liver disease

✓PATHOLOGY

- **Bernard-Soulier Syndrome** is caused by a **defect in the glycoprotein Ib/IX/V receptor for vWF**, leading to **defective platelet adhesion**
 - **Decreased** platelet count
 - **Treatment** || Platelet transfusion
- **Glanzmann Thrombasthenia** is caused by a **defect in the platelet glycoprotein IIb/IIIa complex**, leading to **defective platelet aggregation**
 - **Normal** platelet count
 - **Treatment** || Platelet transfusion



- **Treatment** || Depends on the extent and cause of platelet reduction
 - Platelets are given preoperatively to rapidly increase the count in surgical patients
 - A count of >50,000/L generally requires no specific therapy
 - **One unit of platelet concentrate is expected to increase the circulating platelet count by ~10,000/L** in the average 70-kg person
 - In patients whose thrombocytopenia is refractory to standard platelet transfusion, the use of **human leukocyte antigen (HLA) compatible platelets** has proved effective

2. Local Hemostasis

- Significant surgical bleeding usually is caused by **ineffective local hemostasis**
- Goal is to prevent further blood loss from a disrupted vessel that has been incised or transected
- Hemostasis may be accomplished by interrupting the flow of blood to the involved area or by direct closure of the blood vessel wall defect
 - **Mechanical procedure:** When pressure is applied (whether through *direct digital pressure, hemostatic clamp, or tourniquet*) to an artery proximal to an area of bleeding, profuse bleeding may be reduced so that more definitive action is permitted
 - **Thermal agents:** Heat (via *cautery or harmonic scalpel*) achieves hemostasis by denaturation of protein that results in coagulation of large areas of tissue
 - **Topical hemostatic agents:** Include physical or mechanical, caustic, biologic, and physiologic agents that works either by inducing protein coagulation and precipitation or activating biologic responses to bleeding

D. SPECIAL CASES

1. Disseminated Intravascular Coagulation (DIC)

- An acquired syndrome characterized by **intravascular activation of coagulation**
- Can originate from and cause damage to the **microvasculature**, which if sufficiently severe, can produce organ dysfunction
- Excessive thrombin generation leads to microthrombus formation, followed by **consumption and depletion of coagulation factors and platelets**, which leads to the classic picture of diffuse bleeding
- Causes include the following:
 - Central nervous system injuries with embolization of brain matter
 - Fractures with embolization of bone marrow
 - Malignancy
 - Organ injury (severe pancreatitis, liver failure)
 - Certain vascular abnormalities (aneurysms)
 - Others: snakebites, illicit drugs, transfusion reactions, transplant rejection, and sepsis
- Diagnosis is made on the basis of an inciting cause with associated **thrombocytopenia, prolonged PT, low fibrinogen level, and elevated levels of fibrin markers** (fibrin degradation products, D-dimer, soluble fibrin monomers)
- **Treatment** || Relieving the patient's causative primary medical or surgical problem and maintaining adequate perfusion
- If there is active bleeding, hemostatic factors should be replaced using **fresh frozen plasma (FFP)**, which generally is sufficient to correct the **hypofibrinogenemia**

2. Anticoagulation and Bleeding

- Spontaneous bleeding can be a complication of anticoagulant therapy with either *heparin, warfarin, or low molecular weight heparin*
 - Risk of spontaneous bleeding with **heparin** is relatively high but reduced with continuous infusion technique

- Therapeutic anticoagulation is more reliably achieved with **low molecular weight heparin** because laboratory testing is not routinely done, which makes them attractive options for outpatient anticoagulation
- **Warfarin** is used for long-term outpatient anticoagulation in various clinical conditions including *deep vein thrombosis, valvular heart disease (with or without prosthetic valves), atrial fibrillation, and recurrent myocardial infarction*

- **Clopidogrel** inhibit platelet function through selective irreversible inhibition of ADP-induced platelet aggregation

- General recommendation is that a period of **~7 days** is required from the time the drug is stopped until an elective procedure can be performed
- Timing of urgent and emergent surgeries is unclear
- Preoperative platelet transfusions may be beneficial

3. Coagulopathy of Liver Disease

- Liver plays a key role in hemostasis because it synthesizes many coagulation factors
- Most common coagulation abnormalities associated with liver dysfunction are **thrombocytopenia and impaired humoral coagulation function** manifested as **prolonged PT and increase in the International Normalized Ratio (INR)**
- Thrombocytopenia is related to *hypersplenism, reduced production of thrombopoietin, and immune-mediated destruction of platelets*
- Before any therapy for thrombocytopenia is initiated, the actual need for correction should be strongly considered
- **Treatment** || **Platelet transfusions**; however, the effect typically lasts only several hours
- Potential alternative strategy is **administration of interleukin-11**, a cytokine that stimulates proliferation of hematopoietic stem cells and megakaryocyte progenitors
- Less well accepted option is **splenectomy or splenic embolization** to reduce *hypersplenism* but reduced splenic blood flow can reduce portal vein flow with subsequent development of portal vein thrombosis.

4. Coagulopathy of Trauma

- Recognized causes of traumatic coagulopathy include *acidosis, hypothermia, and dilution of coagulation factors*
- Significant proportion of trauma patients arrive at the ER coagulopathic, and this early coagulopathy is associated with increased mortality
- **Shock** has been postulated to induce coagulopathy through systemic activation of anticoagulant and fibrinolytic pathways
- Hypoperfusion causes activation of *thrombomodulin* (on the surface of endothelial cells), which complexes with *circulating thrombin* thereby **inducing not only an anticoagulant state but also enhancing fibrinolysis**

5. Massive Transfusion

- Well-known cause of thrombocytopenia due to *hypothermia, dilutional coagulopathy, platelet dysfunction, fibrinolysis, or hypofibrinogenemia*
- Impaired ADP-stimulated aggregation occurs with **massive transfusion (>10 units of packed RBC)** leading to surgical bleeding

D. TRANSFUSION

- General indications for transfusion is listed in **Table 19**

Table 18. Reversal of anticoagulation for patients undergoing surgery

Reversal of Heparin Therapy	
Not indicated when aPTT is <1.3 times the control value	
Emergency surgery	Discontinue drug and use of protamine sulfate for more rapid reversal of anticoagulation
Reversal of Warfarin Therapy	
Not indicated when the INR is <1.5	
Elective surgery	Discontinue drug several days before the operation with monitoring of prothrombin concentration (>50% is safe)
	Parenteral administration of vitamin K is indicated in patients with <i>biliary obstruction or malabsorption who may be vitamin K deficient</i>
	Low molecular weight heparin should be administered while the INR is decreasing in <i>patients with high risk of thrombosis</i>
Emergency surgery	Rapid reversal of anticoagulation can be accomplished with FFP

- Other drugs that interfere with platelet function are *aspirin, clopidogrel, dipyridamole, and glycoprotein IIb/IIIa inhibitors*
 - **Aspirin** inhibit platelet function through irreversible acetylation of platelet prostaglandin synthase

Table 19. Indications for Replacement of Blood and its Elements

General Indications for Transfusion	
Improvement in Oxygen Carrying Capacity	<ul style="list-style-type: none"> • Oxygen-carrying capacity is primarily a function of RBC • Therefore, transfusion of RBC should augment oxygen-carrying capacity
Treatment of Anemia	<ul style="list-style-type: none"> • Critically ill patients frequently receive transfusions at a hemoglobin level approaching 9 g/dL
Volume Replacement	<ul style="list-style-type: none"> • Most common indication for blood transfusion in surgical patients is the replenishment of the blood volume • Measurements of hemoglobin levels or hematocrit are frequently used to assess blood loss → misleading in acute loss, because levels can be normal in spite of severely contracted blood volume • Estimated total blood volume is 7-8% of TBW • Blood loss of up to 20% of total blood volume: Replaced with crystalloid solution

- Blood loss >20% of total blood volume: **Addition of packed RBC**, and in the case of massive transfusion, the **addition of FFP**

✓ QUICK REVIEW

- **Thrombocytopenia** is the most common abnormality of hemostasis
- Significant surgical bleeding usually is caused by **ineffective local hemostasis**
- Most important management of DIC is **treatment of the underlying cause**
- **Bleeding into the abdominal cavity** is the most common complication of **warfarin** therapy
- **Intramural bowel hematoma** is the most common cause of abdominal pain in patients receiving anticoagulation therapy
- A period of **~7 days** is required from the time **aspirin and/or clopidogrel** is stopped until an elective procedure can be performed
- Most common coagulation abnormalities associated with liver dysfunction are **thrombocytopenia and impaired humoral coagulation function**
- Most common indication for blood transfusion in surgical patients is **volume replacement**

- Complications of transfusion is primarily related to **blood-induced proinflammatory responses**
- Complications (discussed below) occur in approximately 10% of all transfusions, but <0.5% are serious

1. Febrile Non-hemolytic Reactions

- Defined as an **increase in temperature [>1°C (1.8°F)]** associated with a transfusion
- Approximately 1% of all transfusions
- **Preformed cytokines in donated blood and recipient antibodies reacting with donated antibodies** are postulated causes
- Can be reduced by the use of leukocyte-reduced blood products with
- Pretreatment with **paracetamol** reduces the severity of the reaction
- Rare but potentially lethal febrile reaction is secondary to **bacterial contamination of infused blood**
 - **Gram-negative organisms**, especially *Yersinia enterocolitica* and *Pseudomonas* species are the **most common cause**
 - Most cases are associated with the **administration of platelets**
 - Pathogenesis is related to lability of factor V, which appears necessary for this interaction
 - Results in sepsis and death in 25% of patients
 - **Clinical manifestations** ||fever and chills, tachycardia, and hypotension, GI symptoms (abdominal cramps, vomiting, and diarrhea), and hemorrhagic manifestations such as hemoglobinemia, hemoglobinuria, and DIC
 - If suspected, transfusion should be discontinued and the blood cultured
 - **Treatment** ||Administration of oxygen, adrenergic blocking agents, and antibiotics

2. Allergic Reaction

- Occurs in ~1% of all transfusions
- Reactions usually are mild
- **Clinical manifestations** ||rash, urticaria, and fever within 60 to 90 minutes of the start of the transfusion
- In rare instances, anaphylactic shock develops
- Caused by transfusion of antibodies from hypersensitive donors or the transfusion of antigens to which the recipient is hypersensitive
- Can occur after the administration of **any blood product**

- **Treatment** ||Administration of antihistamines or in more serious cases, use of epinephrine or steroids may be indicated

3. Respiratory Complications

- **Circulatory overload** can occur with rapid infusion of blood, plasma expanders, and crystalloids, particularly in older patients with underlying heart disease
- **Clinical manifestations** ||dyspnea, rales, and cough
- **Treatment** ||Initiate diuresis, slow the rate of blood administration, and minimize delivery of fluids while blood products are being transfused
- Another significant respiratory complication is **Transfusion-related Acute Lung Injury (TRALI)**
 - Defined as noncardiogenic pulmonary edema related to transfusion
 - Can occur with the administration of **any plasma-containing blood product**
 - **Clinical manifestations** ||similar to those of circulatory overload and often accompanied by fever, rigors, and bilateral pulmonary infiltrates on chest radiograph
 - Most commonly occurs within 1 to 2 hours after the onset of transfusion, but virtually **always before 6 hours**
 - Etiology is not well established, but TRALI is thought to be **related to anti-HLA or anti-human neutrophil antigen antibodies** in transfused blood that primes neutrophils in the pulmonary circulation.
 - **Treatment** || Discontinuation of any transfusion, notification of the transfusion service, and provision of pulmonary support (from supplemental oxygen to mechanical ventilation)

4. Hemolytic Reactions

- Can be classified as either **acute or delayed** (Refer to **Table 20**)

Table 20. Classification of Hemolytic Reactions

Classification of Hemolytic Reactions	
Acute Hemolytic Reaction	<ul style="list-style-type: none"> • Occur with the administration of ABO-incompatible blood • Fatal in up to 6% of cases • Contributing factors include technical or clerical errors in the laboratory and administration of wrong blood type • Characterized by intravascular hemolysis and consequent hemoglobinemia and hemoglobinuria • Clinical manifestations pain at the site of transfusion, facial flushing, and back and chest pain, associated with fever, respiratory distress, hypotension, and tachycardia • In anesthetized patients, diffuse bleeding and hypotension are the hallmarks • Positive Coombs' test is diagnostic • Treatment stop transfusion, get a sample of the recipient's blood and send along with the suspect unit to the blood bank for comparison with the pretransfusion samples • Urine output should be monitored and adequate hydration maintained to prevent precipitation of hemoglobin within the tubules
Delayed Hemolytic Reaction	<ul style="list-style-type: none"> • Reactions occur 2 to 10 days after transfusion • Occur when an individual has a low antibody titer at the time of transfusion • Characterized by extravascular hemolysis, mild anemia, indirect hyperbilirubinemia, decreased haptoglobin levels, low-grade hemoglobinemia and hemoglobinuria • Clinical manifestations fever and jaundice • Coombs' test usually yields a positive result • Treatment Do not usually require specific intervention

5. Transmission of Disease

- Among the diseases that have been transmitted by transfusion are **malaria, Chagas' disease, brucellosis**, and, very rarely, **syphilis**

- Transmission of *hepatitis C virus* and *HIV-1* has been dramatically minimized by the introduction of better antibody and nucleic acid screening for these pathogens
- Hepatitis B virus* transmission may still occur in about 1 in 100,000 transfusions in nonimmune recipients

QUICK REVIEW

- Gram-negative organisms** are the most common cause of **bacterial contamination of infused blood**, especially with platelet administration
- Transfusion-related Acute Lung Injury (TRALI)** most commonly occurs within 1 to 2 hours after the onset of transfusion, but virtually **always before 6 hours**
- Acute hemolytic reaction** is characterized by **intravascular hemolysis** while **delayed reaction** is characterized by **extravascular hemolysis**

REVIEW QUESTIONS

- What percentage of platelets can be sequestered in the spleen?
 - 15%
 - 30%
 - 45%
 - 60%

Answer: **B**

Platelets are anucleate fragments of megakaryocytes. The normal circulating number of platelets ranges between 150,000 and 400,000/L. **Up to 30% of circulating platelets may be sequestered in the spleen.** If not consumed in a clotting reaction, platelets are normally removed by the spleen and have an average life span of 7 to 10 days.

- A patient on chronic warfarin therapy presents with acute appendicitis. INR is 1.4. Which of the following is the most appropriate management?
 - Proceed immediately with surgery without stopping the warfarin
 - Stop the warfarin, give FFP, and proceed with surgery
 - Stop the warfarin and proceed with surgery in 8-12 hours
 - Stop the warfarin and proceed with surgery in 24-36 hours

Answer: **A**

When the INR <1.5 in a patient taking warfarin, reversal of anticoagulation therapy may not be necessary. (Refer to **Table 18**). However, meticulous surgical technique is mandatory, and the patient must be observed closely throughout the postoperative period.

- What percent of the population is Rh negative?
 - 5%
 - 15%
 - 25%
 - 35%

Answer: **B**

Rh negative recipients should receive transfusion only of Rh negative blood. However, this group represents only **15% of the population**. Therefore, the administration of Rh positive blood is acceptable if Rh negative blood is not available. However, Rh positive blood should not be transfused to Rh negative females who are of childbearing age.

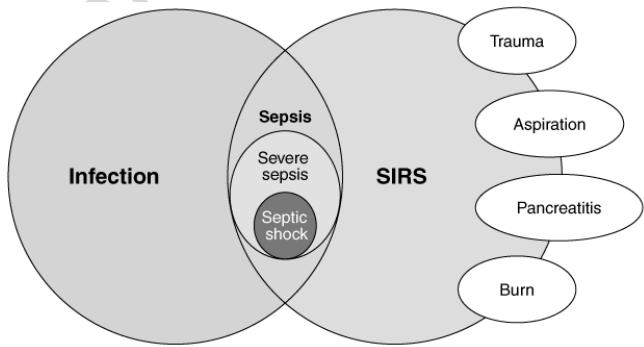
SURGICAL INFECTIONS AND SHOCK

- Definitions**
- Surgical Wounds Classification**
- Prevention and Treatment of Surgical Infections**
- Infections of Significance in Surgical Patients**
- Shock**

A. DEFINITIONS

- Infection** (Refer to **Figure 10**)
 - Identifiable source of microbial insult
- Systemic Inflammatory Response Syndrome (SIRS)**
 - Two or more of the following criteria met:
 - Temperature $\geq 38^{\circ}\text{C}$ or $\leq 36^{\circ}\text{C}$
 - Heart rate ≥ 90 beats per minute
 - Respiratory rate ≥ 20 breaths per minute or $\text{PaCO}_2 \leq 32$ mmHg or mechanical ventilation
 - White blood cell count $\geq 12,000/\mu\text{L}$ or $\leq 4,000/\mu\text{L}$ or $\geq 10\%$ band forms
- Sepsis**
 - SIRS + Identifiable source of infection
- Severe Sepsis**
 - Sepsis + Organ dysfunction
- Septic Shock**
 - Sepsis + Cardiovascular collapse (needs vasopressors)

Figure 10. Relationship between infection and SIRS. Sepsis is the presence both of infection and SIRS, shown here as the intersection of these two areas. Other conditions may cause SIRS as well (trauma, aspiration, etc.). Severe sepsis (and septic shock) are both subsets of sepsis.



B. SURGICAL WOUNDS CLASSIFICATION ☺

*Based on the magnitude of bacterial load at the time of surgery

**IR = Infection rate

- Clean (Class I)**
 - Include those in which **no infection is present**
 - Only skin microflora potentially contaminate the wound
 - No hollow viscus (that contains microbes) is entered
 - Class ID wounds** are similar except that a **prosthetic device (e.g. mesh or valve) is inserted**
 - Example: *Hernia repair, Breast biopsy*(IR: 1-5.4%)
- Clean/Contaminated (Class II)**
 - Include those in which a **hollow viscus** such as respiratory, GI, or GU tracts with inherent bacterial flora **is opened under controlled circumstances without significant spillage of contents**
 - Example: *Cholecystectomy, Elective GI surgery (not colon)* (IR: 2.1-9.5%), *Colorectal surgery*(IR: 9.4-25%)
- Contaminated (Class III)**
 - Include **open accidental wounds encountered early after injury**, those with **extensive introduction of bacteria into a normally sterile area of the body** due to major breaks in sterile technique (e.g. open cardiac massage), **gross spillage of viscous contents** such as from the intestine, or incision through inflamed albeit nonpurulent tissue
 - Example: *Penetrating abdominal trauma, large tissue injury, enterotomy* (IR: 3.4-13.2%)

4. Dirty (Class IV)

- Include **traumatic wounds in which a significant delay in treatment has occurred** and in which necrotic tissue is present, those **created in the presence of overt infection** as evidenced by the presence of purulent material, and those **created to access a perforated viscus** accompanied by a high degree of contamination
- Example: *Perforated diverticulitis, necrotizing soft tissue infections* (IR: 3.1-12.8%)

C. PREVENTION AND TREATMENT OF SURGICAL INFECTIONS

- Resident microflora of the skin and other barrier surfaces represent a potential source of microbes that can invade the body during trauma, thermal injury, or elective or emergent surgical intervention
- Maneuvers to diminish the presence of exogenous (surgeon and operating room environment) and endogenous (patient) microbes consist of the use of *mechanical, chemical, and antimicrobial modalities*, or a *combination of these methods*
- These modalities are NOT capable of sterilizing the hands of the surgeon or the skin or epithelial surfaces of the patient BUT the **inoculum can be reduced considerably**
- Thus, **entry through the skin, into the soft tissue, and into a body cavity or hollow viscus invariably is STILL associated with the introduction of some degree of microbial contamination**
- Therefore, antimicrobial agents should be given in patients who *undergo procedures that may be associated with the ingress of significant numbers of microbes* (e.g., colonic resection) or *in whom the consequences of any type of infection due to said process would be dire* (e.g., prosthetic vascular graft infection)

1. Appropriate Use of Antimicrobial Agents

- Prophylaxis** is the administration of an antimicrobial agent(s) **before and during the operative procedure** to reduce the number of microbes that enter the tissue or body cavity
 - Only a **single dose** of antibiotic is required, and only for certain types of surgical procedures (Refer to **Table 21**)
 - Patients who undergo complex, prolonged procedures in which the *duration of the operation exceeds the serum drug half-life* should **receive an additional dose(s)**
 - Administration of postoperative doses DOES NOT provide additional benefit**, and should be discouraged, as it is costly and is associated with increased rates of microbial drug resistance

Table 21. Prophylactic therapy

Site	Antibiotic	Alternative
Cardiovascular	Cefazolin or Cefuroxime	Vancomycin
Gastroduodenal	Cefazolin, Cefotetan Cefoxitin Ampicillin-sulbactam	Fluoroquinolone
Biliary tract with active infection (cholecystitis)	Ampicillin-sulbactam Ticarcillin-clavulanate Piperacillin-tazobactam	Fluoroquinolone + Clindamycin or Metronidazole
Colorectal, Obstructed small bowel	Cefazolin+Metronidazole Ertapenem Ticarcillin-clavulanate Piperacillin-tazobactam	Gentamicin or Fluoroquinolone plus Clindamycin or Metronidazole
Head and neck	Cefazolin	Aminoglycoside + Clindamycin
Neurosurgery	Cefazolin	Vancomycin
Orthopedics	Cefazolin Ceftriaxone	Vancomycin
Breast, Hernia	Cefazolin	Vancomycin

- Empiric therapy** comprises the use of an antimicrobial agent(s) **when the risk of a surgical infection is high** based on the underlying disease process (e.g. *ruptured appendicitis*), or **when significant contamination during surgery has occurred** (e.g. *inadequate bowel*

preparation or considerable spillage of colon contents)

- Prophylaxis merges into empiric therapy in situations in which the risk of infection increases markedly because of intraoperative findings
- Limited to a **short course of drug** (3-5 days), and should be curtailed based on microbiologic data (i.e. culture and sensitivity pattern) coupled with improvements in the clinical course of the patient
- Manner in which therapy is used differs depending on whether the infection is **monomicrobial** or **polymicrobial**

Table 22. General principles in empiric therapy

Empiric Therapy	
Monomicrobial	<ul style="list-style-type: none"> Frequently are <u>nosocomial infections</u> occurring in postoperative patients, such as <u>UTIs, pneumonia, or bacteremia</u> Therapy should be initiated in patients with evidence of <u>SIRS</u>, coupled with evidence of local infection (e.g., an infiltrate on chest X-ray plus a positive Gram's stain in BAL sample) Within 24 to 72 hours, culture and sensitivity reports will allow directed antibiotic regimen Empiric regimen for common infections are as follows: <ul style="list-style-type: none"> <u>UTI:</u> 3-5 days <u>Pneumonia:</u> 7-10 days <u>Bacteremia:</u> 7-14 days <u>Osteomyelitis, endocarditis, or prosthetic infections:</u> 6-12 weeks
Polymicrobial	<ul style="list-style-type: none"> Primary therapeutic modality is <u>source control</u> (discussed below) but antimicrobial agents play an important role as well <u>Culture results are of lesser importance</u> in managing these infections, as it has been demonstrated that only a limited group of microbes predominate in the established infection, selected from a large number present at the time of initial contamination As such, <u>antibiotic regimen should NOT be modified solely on the basis of culture information</u>

2. Source Control

- Primary precept of surgical infectious disease therapy consists of *drainage of all purulent material, debridement of all infected, devitalized tissue, and debris, and/or removal of foreign bodies at the site of infection, plus remediation of the underlying cause of infection*
 - Discrete, walled-off purulent fluid collection (abscess) requires drainage via percutaneous drain insertion or an incision and drainage
 - Ongoing source of contamination (e.g. bowel perforation) or presence of an aggressive, rapidly-spreading infection (e.g. necrotizing soft tissue infection) requires aggressive operative intervention, both to remove contaminated material and infected tissue (e.g. radical debridement or amputation) and to remove the initial cause of infection (e.g. bowel resection)

D. INFECTIONS OF SIGNIFICANCE IN SURGICAL PATIENTS

1. Surgical Site Infection (SSI)

- Infections of the tissues, organs, or spaces** exposed by surgeons during surgery
- Development of SSI is related to three factors (Refer to **Table 23**):
 - Patient factors**
 - Local factors**
 - Microbial factors**
- Treatment** || Prophylactic antibiotics reduce the incidence of SSI during certain types of procedures
 - Single dose of an antimicrobial agent** should be administered immediately before commencing surgery for **class I, II, III, and IV** types of wounds

- Surgical management of the wound is also a critical determinant of the propensity to develop an SSI
 - Class I and II wounds** may be closed primarily
 - Class III and IV wounds** are allowed to heal by secondary intention where superficial aspects of these wounds should be packed open only

Table 23. Risk factors for development of surgical site infections

Patient Factors	
Older age	
Immunosuppression	
Obesity	
Diabetes Mellitus	
Chronic inflammatory process	
Malnutrition	
Peripheral vascular disease	
Anemia	
Radiation	
Chronic skin disease	
Carrier state (e.g. chronic staphylococcus carriage)	
Recent operation	
Local Factors	
Poor skin penetration	
Contamination of instruments	
Inadequate antibiotic prophylaxis	
Prolonged procedure	
Local tissue necrosis	
Hypoxia, hypothermia	
Microbial Factors	
Prolonged hospitalization (leading to nosocomial organisms)	
Toxin secretion	
Resistance to clearance (e.g. capsule formation)	

- Surgical site infections** are classified into **incisional** and **organ/space infections**
- Incisional infections** are further subclassified into **superficial** (limited to **skin and subcutaneous tissue**) and **deep incisional categories**
 - Treatment** || Effective therapy for **incisional SSIs** consists of **incision and drainage without the addition of antibiotics**
 - Antibiotic therapy is reserved for patients in whom evidence of significant **cellulitis** is present, or who manifest concurrent SIRS
 - Open wound often is allowed to heal by secondary intention, with dressings being changed twice a day
 - Use of topical antibiotics and antiseptics to further wound healing remains unproven
 - Vacuum-assisted closure is increasingly used in management of problem wounds and can be applied to complex wounds in difficult locations
- Treatment of **organ/space infections** is discussed in Intra-Abdominal Infections section

2. Intra-Abdominal Infections/Peritonitis

- Microbial contamination of the **peritoneal cavity**
- Classified according to etiology (Refer to **Table 24**)

Table 24. Intra-abdominal infections

Intra-abdominal Infections	
Primary Microbial Peritonitis	<ul style="list-style-type: none"> Occurs when microbes invade the normally sterile peritoneal cavity via hematogenous dissemination from a distant source of infection or direct inoculation More common among patients with ascites, and in those individuals who are undergoing peritoneal dialysis Often monomicrobial and rarely require surgical intervention Diagnosis is established based on physical examination that reveals diffuse tenderness and guarding without localized findings, absence of pneumoperitoneum, presence of >100 WBCs/ml, and microbes with a single morphology on Gram's stain on fluid obtained via paracentesis Treatment Antibiotic therapy for 14 to 21 days and removal of indwelling devices (e.g., peritoneal dialysis catheter or peritoneovenous shunt)

Secondary Microbial Peritonitis	<ul style="list-style-type: none"> Occurs due to contamination of the peritoneal cavity due to perforation or severe inflammation and infection of an intra-abdominal organ Examples: <i>Appendicitis, perforation of any portion of the GI tract, or diverticulitis</i> Treatment Effective therapy requires source control to resect or repair the diseased organ, debridement of necrotic, infected tissue and debris, and administration of antimicrobial agents directed against aerobes and anaerobe
Tertiary (persistent) Peritonitis or Postoperative Peritonitis	<ul style="list-style-type: none"> Develops by leakage from a GI anastomosis or intra-abdominal abscess in patients in whom standard therapy fails Common in immunosuppressed patients Microbes such as <i>E. faecalis</i> and <i>faecium</i>, <i>S. epidermidis</i>, <i>C. albicans</i>, and <i>P. aeruginosa</i> can be identified Abscess is diagnosed via abdominal CT Treatment CT-guided percutaneous drainage for <i>intra-abdominal abscess</i> Surgical intervention is reserved for <i>patients with multiple abscesses, those with abscesses in proximity to vital structures such that percutaneous drainage would be hazardous, and those in whom an ongoing source of contamination (e.g., enteric leak) is identified</i> Necessity of antimicrobial agent therapy and precise guidelines that dictate duration of catheter drainage have NOT been established Short course (3 to 7 days) of antibiotics that covers for aerobic and anaerobic bacteria can be given Unfortunately, even with effective antimicrobial agent therapy, this disease process is associated with mortality rates of more than 50% Drainage catheter is left in situ until the abscess cavity collapses, its output is less than 10-20 ml/d with no evidence of an ongoing source of contamination and the patient's clinical condition has improved

3. Postoperative Nosocomial Infections

- Include **SSIs, UTIs, pneumonia, and bacteremia**
- Most infections are related to prolonged use of indwelling tubes and catheters for the purpose of urinary drainage, ventilation, and venous and arterial access, respectively (Refer to **Table 25**).

Table 25. Postoperative nosocomial infections

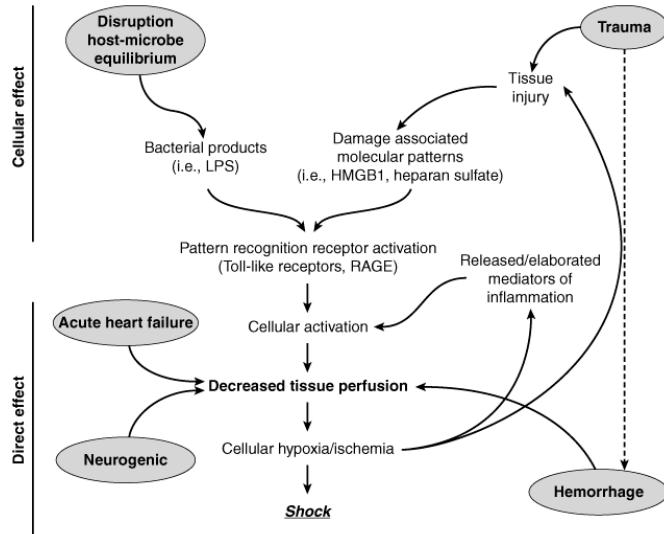
Postoperative nosocomial infections	
Postoperative Urinary Tract Infection (UTI)	<ul style="list-style-type: none"> Should be considered based on urinalysis with WBCs or bacteria, a positive test for leukocyte esterase, or a combination of these elements Diagnosis is established after more than 10⁴ CFU/ml of microbes are identified by culture techniques in symptomatic patients, or more than 10⁵ CFU/ml in asymptomatic individuals Treatment Single antibiotic therapy for 3 to 5 days Indwelling urinary catheters should be removed as quickly as possible, typically within 1 to 2 days, as long as the patients are mobile
Pneumonia	<ul style="list-style-type: none"> Associated with prolonged mechanical ventilation and is frequently due to pathogens common in the nosocomial environment Diagnosis should be made using the presence of a purulent sputum, elevated leukocyte count, fever, and new chest x-ray abnormality Presence of two of the clinical findings, plus chest x-ray findings, significantly increases the likelihood of ventilator-associated pneumonia Treatment Antibiotic therapy for 7 to 10 days Surgical patients should be weaned from mechanical ventilation as soon as feasible, based on oxygenation and inspiratory effort

E. SHOCK

- Failure to meet the metabolic needs of the cell and the consequences that ensue**

- Consists of inadequate tissue perfusion marked by decreased delivery of required metabolic substrates and inadequate removal of cellular waste products (Refer to **Figure 11**)
- Initial cellular injury that occurs is *reversible*; however, injury will become *irreversible* if tissue perfusion is prolonged or severe enough such that, at the cellular level, compensation is no longer possible

Figure 11. Pathways leading to decreased tissue perfusion and shock



- Clinical manifestations of several physiologic responses are most often what lead practitioners to the diagnosis of shock as well as guide the management of patients
- Shock is classified into six types (Refer to **Table 26**)

Table 26. Types of Shock

Postoperative nosocomial infections	
Hypovolemic	<ul style="list-style-type: none"> • Most common type • Results from loss of circulating blood volume due to loss of whole blood (hemorrhagic shock), plasma, interstitial fluid (bowel obstruction) • Clinical and physiologic response is classified according to the magnitude of volume loss (Refer to Table 27) • Treatment Instituted with diagnostic evaluation to identify a bleeding source • Appropriate priorities are secure the airway, control source of blood loss, and IV volume resuscitation • Patients who fail to respond to initial resuscitative efforts should be assumed to have ongoing active hemorrhage and require prompt operative intervention
Vasogenic (Septic)	<ul style="list-style-type: none"> • Results from decreased resistance within capacitance vessels • Evaluation begins with an assessment of the adequacy of airway and ventilation • Treatment Fluid resuscitation and restoration of circulatory volume • Empiric antibiotics must be chosen carefully (gram-negative rods, gram-positive cocci, and anaerobes) • However, IV antibiotics without source control will be insufficient to adequately treat patients with infected fluid collections, infected foreign bodies, and devitalized tissue • Vasopressors may be necessary as well
Neurogenic	<ul style="list-style-type: none"> • Form of vasogenic shock in which spinal cord injury or spinal anesthesia causes vasodilation due to acute loss of sympathetic vascular tone • Treatment After airway is secured and ventilation is adequate, fluid resuscitation and restoration of intravascular volume often will improve perfusion • Administration of vasoconstrictors will improve peripheral vascular tone, decrease vascular capacitance, and increase venous return

Cardiogenic	<ul style="list-style-type: none"> • If the patient's blood pressure has not responded, dopamine may be used • Results from failure of the heart as a pump, as in arrhythmias or acute myocardial infarction (most common) • Hemodynamic criteria include sustained hypotension (i.e. SBP <90 mmHg for at least 30 minutes), reduced cardiac index (<2.2 L/min/m²), and elevated pulmonary artery wedge pressure (>15 mmHg) • Treatment Ensure adequate airway is present and ventilation is sufficient • Treatment of cardiac dysfunction includes maintenance of adequate oxygenation to ensure adequate myocardial O₂ delivery and judicious fluid administration to avoid fluid overload and development of cardiogenic pulmonary edema • Significant dysrhythmias and heart block must be treated with antiarrhythmic drugs, pacing, or cardioversion
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Obstructive	<ul style="list-style-type: none"> • Form of cardiogenic shock that results from mechanical impediment to circulation leading to depressed cardiac output rather than primary cardiac failure • Causes include cardiac tamponade, pulmonary embolism, tension pneumothorax, IVC obstruction (DVT, gravid uterus), increased intrathoracic pressure (neoplasm) • Treatment Dependent on the etiology of the obstructive shock
Traumatic	<ul style="list-style-type: none"> • Soft tissue and bony injury lead to the activation of inflammatory cells and the release of circulating factors that modulate the immune response • These effects of tissue injury are combined with the effects of hemorrhage, creating a more complex and amplified deviation from homeostasis. • Treatment Correction of the individual elements to diminish the cascade of proinflammatory activation, and includes prompt control of hemorrhage, adequate volume resuscitation to correct O₂ debt, debridement of nonviable tissue, stabilization of bony injuries, and appropriate treatment of soft tissue injuries

Table 27. Signs and symptoms of advancing stages of hypovolemic shock ☺

	Class I	Class II	Class III	Class IV
Blood loss (ml)	Up to 750	750-1,500	1,500-2,000	>2,000
Blood loss (%blood volume)	Up to 15%	15-30%	30-40%	>40%
Pulse rate	<100	>100	>120	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate	14-20	20-30	30-40	>35
Urine output (ml/h)	>30	20-30	5-15	Negligible
CNS/mental status	Slightly anxious	Mildly anxious	Anxious and confused	Confused and lethargic

- Ultimate goal in the treatment of shock is restoration of adequate organ perfusion and tissue oxygenation
- Endpoints in resuscitation can be divided into **systemic or global parameters, tissue-specific parameters, and cellular parameters** (Refer to **Table 28**)
- Global endpoints include vital signs, cardiac output, pulmonary artery wedge pressure, O₂ delivery and consumption, lactate, and base deficit

Table 28. Endpoints in resuscitation

Systemic/Global
Lactate
Base deficit
Cardiac output
Oxygen delivery and consumption
Tissue Specific
Gastric tonometry
Tissue pH, Oxygen, Carbon dioxide levels
Near infrared spectroscopy
Cellular
Membrane potential
Adenosine triphosphate

preventing the typical reflex tachycardia that occurs with hypovolemia.

The classic description of **neurogenic shock** consist of **decreased blood pressure associated with bradycardia** (absence of reflex tachycardia due to disrupted sympathetic discharge), warm extremities (loss of peripheral vasoconstriction), motor and sensory deficits indicative of a spinal cord injury, and radiographic evidence of a vertebral column fracture.

TRAUMA

- A. General Principle
- B. Primary Survey
- C. Resuscitation
- D. Secondary Survey
- E. Diagnostic Evaluation
- F. Definitive Care

A. GENERAL PRINCIPLE

- **Trauma or injury** is a cellular disruption caused by an exchange with environmental energy that is beyond the body's resilience
- **Most common cause of death** for all individuals between the ages of 1 and 44 years
- Third most common cause of death regardless of age
- Most common cause of years of productive life lost
- Initial management of seriously injured patients according to the Advanced Trauma Life Support (ATLS) consists of the following:
 - Primary survey
 - Concurrent resuscitation
 - Secondary survey
 - Diagnostic evaluation
 - Definitive care

B. PRIMARY SURVEY

- Goal is to identify and treat conditions that constitute an immediate threat to life (Refer to **Table 29**)
- **Assessment of the "ABCDE"** (Airway with cervical spine protection, Breathing, Circulation, Disability, and Exposure)

Table 29. Life-threatening injuries identified during the primary survey

Airway	
Airway obstruction	
Airway injury	
Breathing	
Tension pneumothorax	
Open pneumothorax	
Flail chest with underlying pulmonary contusion	
Circulation	
Hemorrhagic shock	Massive hemothorax or hemoperitoneum
	Mechanically unstable pelvis fracture
	Extremity losses
Cardiogenic shock: Cardiac tamponade	
Neurogenic shock: Cervical spine injury	
Disability	
Intracranial hemorrhage/mass lesion	

1. Airway management with cervical spine protection

- **Ensuring a patent airway is the first priority in the primary survey**
- Efforts to restore cardiovascular integrity will be futile unless the oxygen content of the blood is adequate
- All patients with **blunt trauma** require **cervical spine immobilization** (hard collar or placing sandbags on both sides of the head with the patient's forehead taped across bags to the backboard) until injury is excluded
- Patients who are *conscious*, *do not show tachypnea*, and have a normal *voice* do not require early attention to the airway EXCEPT the following:
 - Patients with penetrating injuries to the neck and an expanding hematoma

REVIEW QUESTIONS

1. Which of the following is the most effective dosing of antibiotics in a patient undergoing elective colon resection?
 - a. A single dose given within 30 min prior to skin incision
 - b. A single dose given at the time of skin incision
 - c. A single preoperative dose + 24 hours of postoperative antibiotics
 - d. A single preoperative dose + 48 hours of postoperative antibiotics

Answer: A

Prophylaxis is the administration of an antimicrobial agent(s) before and during the operative procedure to reduce the number of microbes that enter the tissue or body cavity. Only a **single dose** of antibiotic is required, and only for certain types of surgical procedures. There is no evidence that administration of postoperative doses provides additional benefit.

2. What percentage of the blood volume is normally in the splanchnic circulation?
 - a. 10%
 - b. 20%
 - c. 30%
 - d. 40%

Answer: B

Most alterations in cardiac output in the normal heart are related to changes in preload. Increases in sympathetic tone have a minor effect on skeletal muscle beds but produce a dramatic reduction in splanchnic blood volume, which holds **20% of the blood volume**.

3. Which of the following best describes the hemodynamic response to neurogenic shock?
 - a. Increased cardiac index, unchanged venous capacitance
 - b. Increased cardiac index, decreased venous capacitance
 - c. Variable change in cardiac index (can increase or decrease), increased venous capacitance
 - d. Variable change in cardiac index (can increase or decrease), decreased venous capacitance

Answer: A

Choice B and D are most commonly associated with septic shock. Choice C, on the other hand, is most likely seen in cardiogenic shock.

4. An unconscious patient with a systolic BP of 80 and a HR of 80 most likely has?
 - a. Cardiogenic shock
 - b. Hemorrhagic shock
 - c. Neurogenic shock
 - d. Obstructive shock

Answer: C

Sympathetic input to the heart, which normally increases heart rate and cardiac contractility, and input to the adrenal medulla, which increases catecholamine release, may also be disrupted (with spinal cord injury).

- Evidence of chemical or thermal injury to the mouth, nares, or hypopharynx
- Extensive subcutaneous air in the neck
- Complex maxillofacial trauma
- Airway bleeding
- Elective intubation should be performed on the cases above before evidence of airway compromise
- **Altered mental status is the most common indication for intubation**
- Options for endotracheal intubation include ***nasotracheal, orotracheal, or surgical routes***
 - **Nasotracheal:** Only done in patients, who are breathing spontaneously, requiring emergent airway support in whom chemical paralysis cannot be used
 - **Ootracheal: most common technique** used to establish a definitive airway
 - **Surgical (cricothyroidotomy):** Done in patients in whom attempts at intubation have failed or who are precluded from intubation due to extensive facial injuries
 - **Surgical (emergent tracheostomy):** Indicated in patients with laryngotracheal separation or laryngeal fractures, in whom *cricothyroidotomy* may cause further damage or result in complete loss of airway

2. Breathing and Ventilation

- Once a secure airway is obtained, adequate oxygenation and ventilation must be assured
- All injured patients should receive supplemental oxygen and be monitored by pulse oximetry
- The following conditions constitute an immediate threat to life due to inadequate ventilation (Refer to **Table 30**)

Table 30. Life-threatening injury identified due to inadequate ventilation

Inadequate Ventilation	
Tension Pneumothorax	<ul style="list-style-type: none"> • Diagnosis is implied by respiratory distress and hypotension in combination with any of the following physical signs in patients with chest trauma: <i>tracheal deviation away from the affected side, lack of or decreased breath sounds on the affected side, and subcutaneous emphysema on the affected side</i>(Refer to Figure 10inset) • Treatment Needle thoracostomy decompressionin the 2nd ICS in the MCL may be indicated in the acute setting(Refer to Figure 10) • Closed tube thoracostomy should be performed immediately before a chest radiograph is obtained
Open Pneumothorax (Sucking chest wound)	<ul style="list-style-type: none"> • Occurs with full thickness loss of the chest wall, permitting free communication between the pleural space and the atmosphere • Compromises ventilation due to equilibration of atmospheric and pleural pressures, which prevents lung inflation and alveolar ventilation, and results in hypoxia and hypercarbia • Complete occlusion of the chest wall defect WITHOUT a tube thoracostomy may convert an open pneumothorax to a tension pneumothorax • Treatment Definitive treatment is closure of the chest wall defect and closed tube thoracostomy remote from the wound (Refer to Figure 11)
Flail chest with underlying pulmonary contusion	<ul style="list-style-type: none"> • Occurs when 3 or more contiguous ribs are fractured in at least 2 locations (Refer to Figure 12) • Paradoxical movement of this free floating segment of chest wall may be evident in patients with spontaneous ventilation, due to the negative intrapleural pressure of inspiration • Associated pulmonary contusion is typically the source of postinjury pulmonary dysfunction (Decreased compliance and increased shunt fraction) • Treatment May require presumptive intubation and mechanical ventilation

Figure 12. Tension Pneumothorax (inset) with Needle Thoracostomy

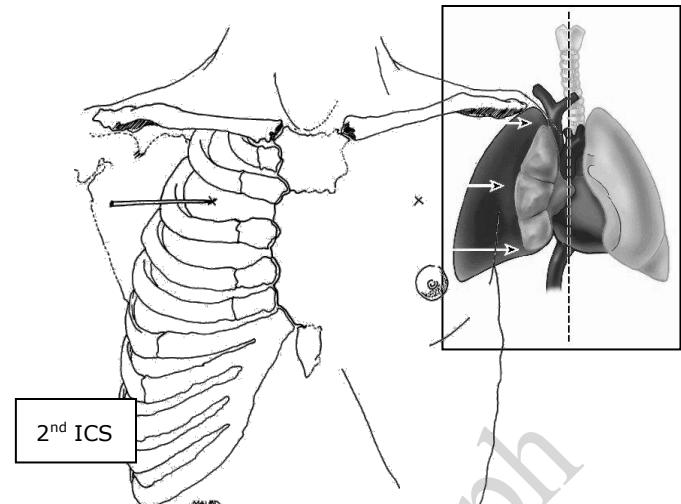


Figure 13. Closed Tube Thoracostomy (CTT).A. Performed in the MCL at the 4th-5th ICS to avoid iatrogenic injury to the liver or spleen. B. Heavy scissors are used to cut through the intercostal muscle into the pleural space done on top of the rib to avoid injury to the intercostal bundle located just beneath the rib. C. Incision is digitally explored to confirm intrathoracic location and identify pleural adhesions. D. A 36F chest tube is directed superiorly and posteriorly with the aid of a large clamp.

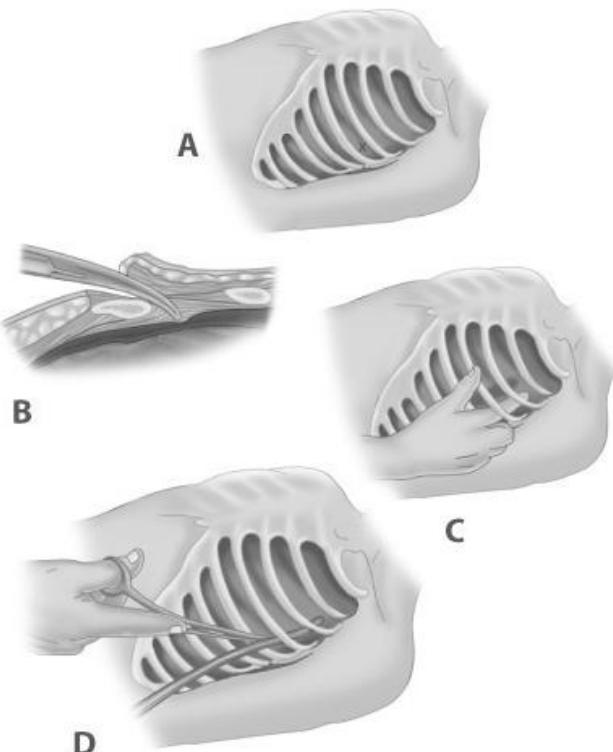
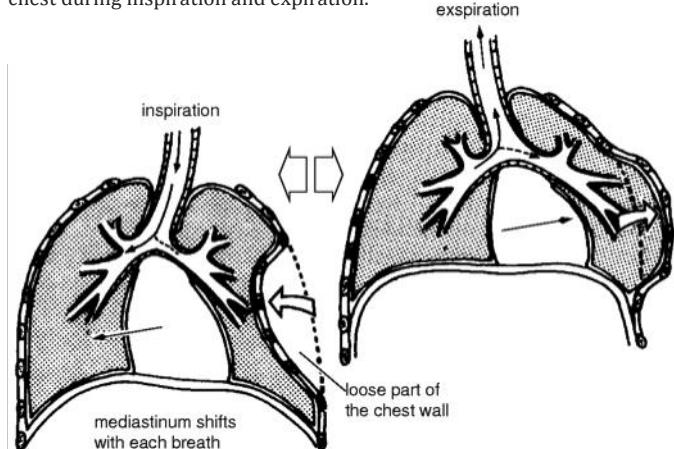


Figure 14. Mechanism of a Flail Chest.Paradoxical movement of the flail chest during inspiration and expiration.



3. Circulation with hemorrhage control

- Initial approximation of the patient's cardiovascular status can be obtained by **palpating peripheral pulses**
 - Carotid pulse: 60 mmHg systolic BP

- Femoral pulse: 70 mmHg
- Radial pulse: 80 mmHg to be palpable
- Any **hypotensive episode (SBP <90 mmHg)** is assumed to be caused by hemorrhage until proven otherwise
- IV access for fluid resuscitation is obtained with 2 peripheral catheters, 16-gauge or larger in adults
- In patients under 6 years old, an intraosseous needle can be placed in the proximal tibia (preferred) or distal femur of an unfractured extremity
- External control of hemorrhage should be achieved promptly while circulating volume is restored
- The following conditions constitute an immediate threat to life due to inadequate circulation (Refer to **Table 31**)

Table 31. Life-threatening injury identified due to inadequate circulation

Inadequate Circulation	
Massive Hemothorax	<ul style="list-style-type: none"> • Defined as >1,500 ml of blood or, in the pediatrics, 1/3 of the patient's blood volume in the pleural space • After a blunt trauma, hemothorax is usually due to multiple rib fractures with severed intercostal arteries, but occasionally bleeding is from lacerated lung parenchyma • After a penetrating trauma, a systemic or pulmonary hilar vessel injury should be presumed • Treatment Operative intervention
Cardiac Tamponade	<ul style="list-style-type: none"> • Occurs most commonly after penetrating thoracic injuries, although occasionally blunt rupture of the heart, particularly the atrial appendage, is seen • ≤100 ml of pericardial blood may cause pericardial tamponade (Refer to Figure 13 right) • Beck's triad (dilated neck veins, muffled heart tones, and a decline in arterial pressure) is NOT often observed Diagnosis is best achieved by ultrasound of the pericardium (Refer to Figure 13 left) • Early in the course of tamponade, blood pressure and cardiac output will transiently improve with fluid administration • Treatment Pericardiocentesis is successful in decompressing tamponade in approximately 80% of cases (Refer to Figure 14) • Removing as little as 15 to 20 ml of blood will often temporarily stabilize the patient's hemodynamic status, prevent subendocardial ischemia, and associated lethal arrhythmias, and allow transport to the OR for sternotomy • Patients with a SBP <70 mmHg warrant emergency department thoracotomy(EDT) with opening of the pericardium to address the injury (Refer to Table 31) • EDT is best accomplished using a left anterolateral thoracotomy, with the incision started to the right of the sternum (Refer to Figure 15)

4. Disability and Exposure

- **Glasgow Coma Scale (GCS) score** should be determined for all injured patients
- **Scores of 13 to 15 indicate mild head injury, 9 to 12 moderate injury, and <9 severe injury**
- Abnormal mental status should prompt an immediate re-evaluation of the ABCs and consideration of central nervous system injury

Figure 15. Cardiac

Tamponade with ultrasound findings (*) on the left.

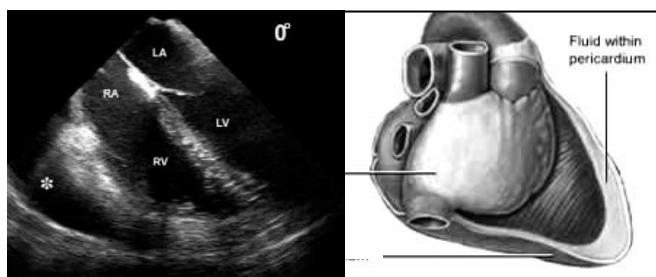


Figure 16. Pericardiocentesis. Access to the pericardium is obtained through a subxiphoid approach, with the needle angled 45 degrees up from the chest wall and toward the left shoulder.

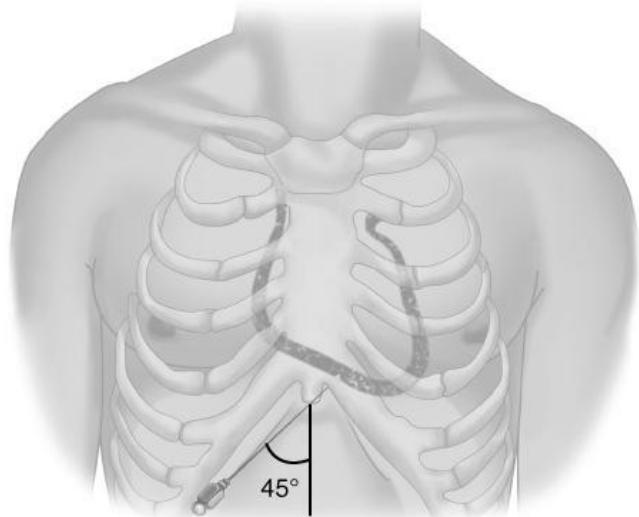
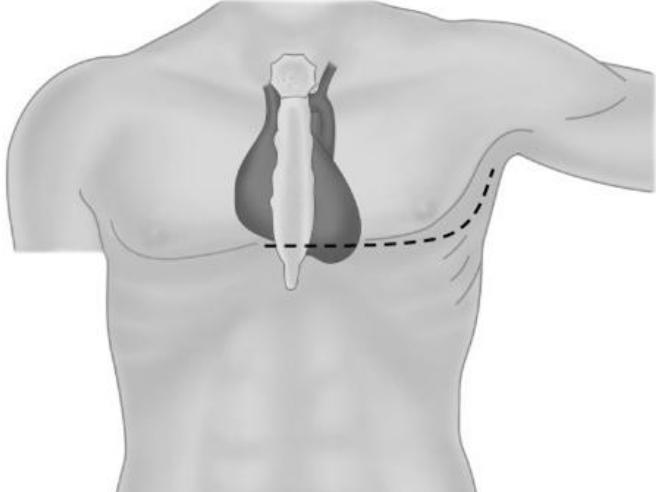


Table 32. Emergency Department Thoracotomy (EDT) Indications and Contraindications. CPR = Cardiopulmonary resuscitation

Indications	
Salvageable postinjury cardiac arrest	Patients sustaining witnessed penetrating trauma with <15 min of prehospital CPR
	Patients sustaining witnessed blunt trauma with <5 min of prehospital CPR
Persistent severe postinjury hypotension (SBP≤60 mmHg)	Cardiac tamponade
	Hemorrhage (intrathoracic, intra-abdominal, extremity, cervical)
	Air embolism
Contraindications	
<i>Penetrating trauma: CPR >15 min and no signs of life (papillary response, respiratory effort, motor activity)</i>	
<i>Blunt trauma: CPR >5 min and no signs of life or asystole</i>	

Figure 17. Emergency department thoracotomy (EDT) is performed through the 5th ICS using the anterolateral approach. Pericardium is opened anterior to the phrenic nerve, and the heart is rotated out for repair



ANATOMY

- **Closed Tube Thoracostomy (CTT)** is done on the superior border of the lower rib on the 4th-5th ICS MCL
 - Directed **superiorly** for air drainage
 - Directed **inferiorly** for fluid drainage
 - Tube passes through the following: Skin → Superficial fascia → Serratus anterior → External intercostals → Internal intercostals → Innermost intercostals → Endothoracic fascia → Parietal pleura

✓ QUICK REVIEW

- **Primary survey** consists of the **assessment of the ABCDE** (Airway with cervical spine protection, Breathing, Circulation, Disability, and Exposure)
- **Ensuring a patent airway** is the first priority in the primary survey
- **Altered mental status** is the most common indication for intubation
- **Massive hemothorax** is defined as **>1,500 ml of blood** or, in the pediatrics, **1/3 of the patient's blood volume in the pleural space**
- **Tension pneumothorax** is the most common cause of cardiogenic shock in trauma patients

C. RESUSCITATION

- Quantity of acute blood loss correlates with physiologic abnormalities (Refer to **Table 26**)
 - **Tachycardia** is often the **earliest sign of ongoing blood loss** but watch out for **relative tachycardia** (HR<90 in patients with a resting pulse rate in the 50s)
 - **Bradycardia**, an ominous sign, occurs with severe blood loss, often **heralding impending cardiovascular collapse**
 - **Hypotension** is NOT a reliable early sign of hypovolemia, because blood volume must decrease by >30% before hypotension occurs
- Goal is to **re-establish tissue perfusion**
 - **Urine output** is a quantitative, reliable indicator of organ perfusion
 - **Adequate urine output is 0.5 ml/kg/hr in an adult, 1 ml/kg/hr in a child, and 2 ml/kg/hr in an infant <1 year of age**
 - Fluid resuscitation begins with a 2L (adult) or 20 ml/kg (child) IV bolus of isotonic crystalloid, typically Ringer's lactate
 - For persistent hypotension, this is repeated once in adult and twice in a child before RBCs are administered
- Based on the initial response to fluid resuscitation, hypovolemic injured patients can be separated into three broad categories: **responders**, **transient responders**, and **nonresponders**
 - **Responders:** Individuals who are stable or have a good response to the initial fluid therapy as evidenced by normalization of vital signs, mental status, and urine output are unlikely to have significant ongoing hemorrhage, and further diagnostic evaluation for occult injuries can proceed in an orderly fashion (Secondary survey)
 - **Transient Responders:** Those who respond initially to volume loading by an increase in blood pressure only to then hemodynamically deteriorate once more
 - **Nonresponders:** These patients have persistent hypotension despite aggressive resuscitation
- Patients with ongoing hemodynamic instability, whether **nonresponders** or **transient responders**, require systematic evaluation and prompt intervention

D. SECONDARY SURVEY

- Once the immediate threats to life have been addressed, a thorough history is obtained and the patient is examined in a systematic fashion
- Patient (or surrogate) should be queried to obtain an **"AMPLE" (Allergies, Medications, Past illnesses or Pregnancy, Last meal, and Events related to the injury)**
- Physical examination should be head to toe with special attention to the patient's back, axilla, and perineum, because injuries here are easily overlooked
- All potentially seriously injured patients should undergo **digital rectal examination** to evaluate for sphincter tone, presence of blood, rectal perforation, or a

high-riding prostate, which is particularly critical in patients with suspected spinal cord injury, pelvic fracture, or transpelvic gunshot wounds

- **Vaginal examination** with a speculum also should be performed in women with **pelvic fractures** to exclude an open fracture

E. DIAGNOSTIC EVALUATION

- Selective radiography and laboratory tests are done early in the evaluation after the **primary survey**
- For patients with **severe blunt trauma**, **lateral cervical spine, chest, and pelvic radiographs** should be obtained, often termed *the big three*
- For patients with **truncal gunshot wounds**, **anteroposterior and lateral radiographs of the chest and abdomen** are warranted
- In **critically injured patients**, blood samples for a routine trauma panel (**type and cross-match, complete blood count, blood chemistries, coagulation studies, lactate level, and arterial blood gas analysis**) should be sent to the laboratory
- For **less severely injured patients** only a **complete blood count and urinalysis** may be required

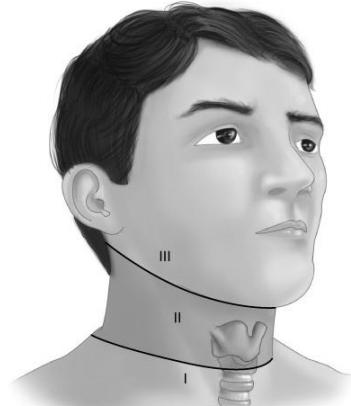
F. DEFINITIVE CARE

- All injured patients undergoing an operation should receive **preoperative antibiotics**
- **Extended postoperative antibiotic therapy** is administered only for *open fractures or significant intra-abdominal contamination*
- **Tetanus prophylaxis** is administered to all patients
- Trauma patients particularly (a) those with *multiple fractures of the pelvis and lower extremities*, (b) those with *coma or spinal cord injury*, and (c) those requiring *ligation of large veins in the abdomen and lower extremities* are at risk for **venous thromboembolism** and its associated complications
 - **Low molecular weight heparin** is initiated as soon as bleeding has been controlled and there is no intracranial pathology
 - In high-risk patients, **removable inferior vena caval filters** should be considered if there are contraindications to administration of low molecular weight heparin
 - **Pulsatile compression stockings** or **sequential compression devices** are used routinely unless there is a fracture
- Another prophylactic measure is **thermal protection** by maintaining a comfortable ambient temperature, covering stabilized patients with warm blankets, and administering warmed IV fluids and blood products.
 - Hemorrhagic shock impairs perfusion and metabolic activity throughout the body, with resultant decrease in heat production and body temperature
 - Hypothermia causes coagulopathy and myocardial irritability
- **PRBC transfusion** should occur once the patient's hemoglobin level is <7 g/dL, in the acute phase of resuscitation the endpoint is 10 g/dL
- **FFP** is transfused to keep the INR <1.5 and PTT <45 sec
- Target of 100,000/L is the target platelet count with massive transfusion

1. Neck

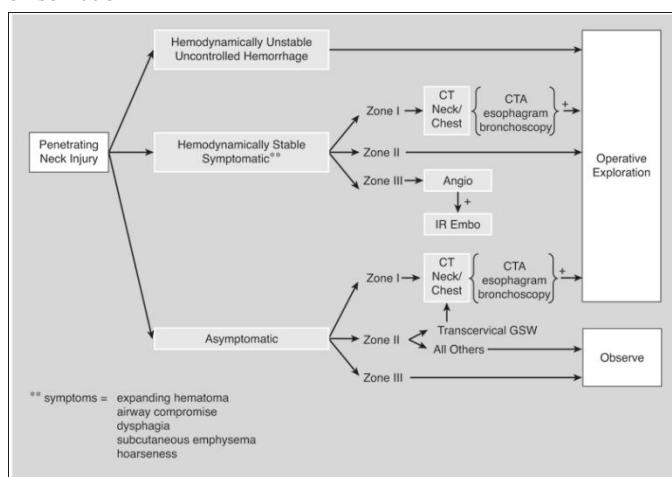
- Divided into three distinct zones that is important in the management of neck injuries (Refer to **Figure 18** ☺)

Figure 18. For the purpose of evaluating *penetrating* injuries, the neck is divided into three zones. **Zone I** is up to the level of the cricoid and is also known as the *thoracic outlet*. **Zone II** is located between the cricoid cartilage and the angle of the mandible. **Zone III** is above the angle of the mandible. ☺



- Imaging options include **CT scan** or **five plain radiograph views of the cervical spine**: lateral view with visualization of C7-T1, anteroposterior view, transoral odontoid views, and bilateral oblique views
- Identification of *penetrating injuries* to the neck with exsanguination, expanding hematomas, and airway obstruction is a priority during the primary survey
- Management algorithm for *penetrating* neck injury patients is based on the presenting symptoms and anatomic location of injury (Refer to **Figure 19**)
- All *blunt* trauma patients should be assumed to have cervical spine injuries until proven otherwise

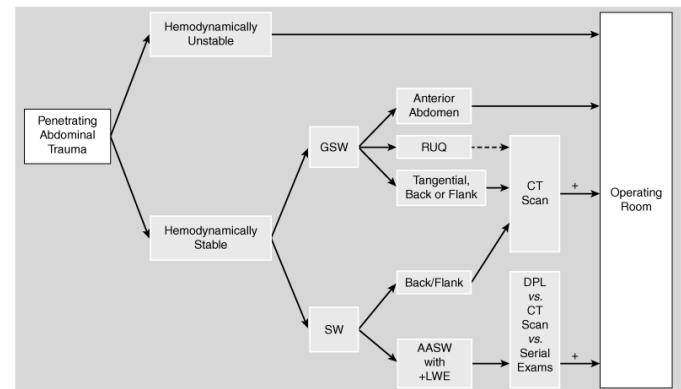
Figure 19. Algorithm for the selective management of *penetrating* neck injuries. CT = computed tomography; CTA = computed tomographic angiography; GSW = gunshot wound; IR Embo = interventional radiology embolization



2. Abdomen

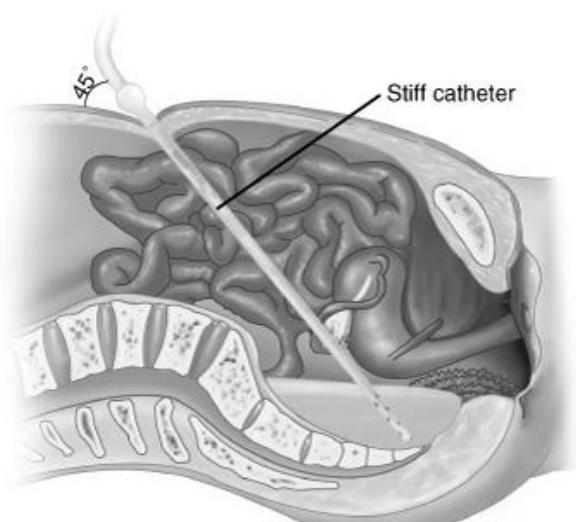
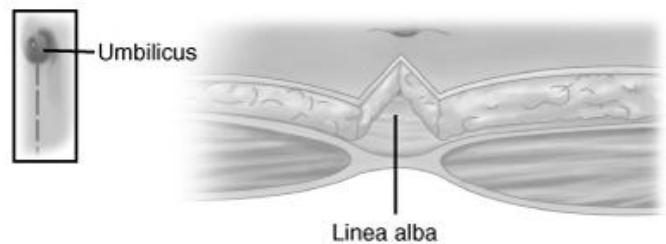
- Diagnostic approach differs for *penetrating* trauma (i.e. gun shot/stab wound) and *blunt* abdominal trauma
- Management algorithm for *penetrating* abdominal injury patients is primarily based on the anatomic location of injury (Refer to **Figure 18**)
- As a rule, minimal evaluation is required before laparotomy for abdominal *gunshot* or *shotgun* wounds because over 90% of patients have significant internal injuries EXCEPT those isolated in the liver by CT scan; in hemodynamically stable patients where nonoperative observation may be considered
- Abdominal *stab* wounds are less likely to injure intra-abdominal organs and thus, diagnostic evaluation can be afforded

Figure 20. Algorithm for the evaluation of *penetrating* abdominal injuries. AASW = anterior abdominal stab wound (from costal margin to inguinal ligament and bilateral MAL); CT = computed tomography; DPL = diagnostic peritoneal lavage; GSW = gunshot wound; LWE = local wound exploration; RUQ = right upper quadrant; SW = stab wound.



- Anterior abdominal stab wounds (AASW) should be explored under local anesthesia in the ED to determine if the fascia has been violated
 - Injuries that do not penetrate the peritoneal cavity do not require further evaluation, and the patient is discharged from the ED
 - Patients with fascial penetration must be further evaluated for intra-abdominal injury, because there is up to a 50% chance of requiring laparotomy
 - Debate remains over whether the optimal diagnostic approach is serial examination, diagnostic peritoneal lavage (Refer to **Figure 20**), or CT scanning
 - Values representing positive findings for diagnostic peritoneal lavage are summarized in **Table 33**

Figure 21. Diagnostic peritoneal lavage (DPL) is performed through an infraumbilical incision unless the patient has a pelvic fracture or is pregnant. Linea alba is sharply incised, and the catheter is directed into the pelvis. Abdominal contents (*diagnostic peritoneal aspiration*) is considered positive if >10 ml of blood is aspirated. If <10 ml is obtained, a liter of NSS is instilled. Effluent is withdrawn via siphoning and sent to the laboratory for analysis.



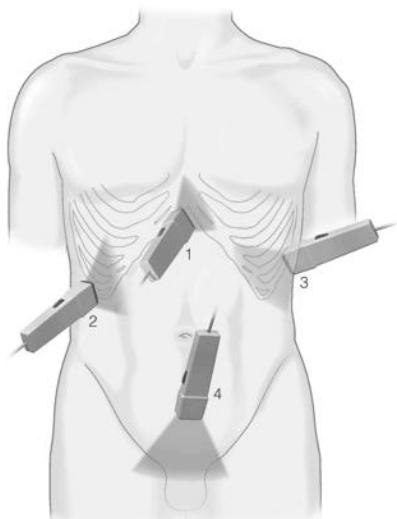
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Table 33. Criteria for positive finding on diagnostic peritoneal lavage. Between 1,000-10,000/ml, do laparoscopy/thoracoscopy ^②

Anterior Abdominal Stab Wound	Thoracoabdominal Stab Wound
Red blood cell (RBC) count	>100,000/ml
White blood cell (WBC) count	>500/ml
Amylase level	>19 IU/l
Alkaline phosphatase level	>2 IU/l
Bilirubin level	>0.01 mg/dl

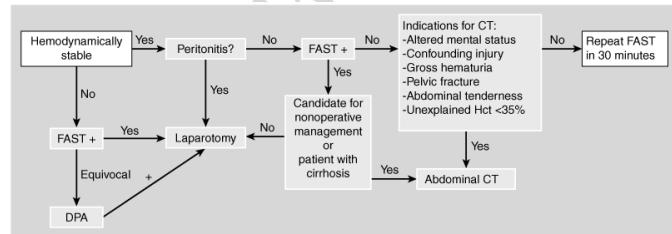
- *Blunt* abdominal trauma initially is evaluated by FAST (Refer to **Figure 22**) exam in major trauma centers
- FAST is not 100% sensitive so diagnostic peritoneal aspiration is still advocated in hemodynamically unstable patients without a defined source of blood loss to rule out abdominal hemorrhage

Figure 22. FAST is used to identify free intraperitoneal fluid in (1) subxiphoid/pericardium, (2) Morison's pouch/hepatorenal recess, (3) left upper quadrant/perisplenic, and (4) pelvis. Although this method is sensitive for detecting intraperitoneal fluid of >250 ml, it does not reliably determine the source of bleeding nor grade solid organ injuries.



- Patients with fluid on FAST examination, considered a "positive FAST," who do not have immediate indications for laparotomy and are hemodynamically stable undergo CT scanning to quantify their injuries
- Management algorithm for *blunt* abdominal injury patients is shown in **Figure 23**

Figure 23. Algorithm for the initial evaluation of a patient with suspected *blunt* abdominal trauma. CT = computed tomography; DPA = diagnostic peritoneal aspiration; FAST = focused abdominal sonography for trauma/focused assessment with sonography for trauma; Hct=hematocrit



✓ QUICK REVIEW

- **Tachycardia** is the earliest sign of ongoing blood loss
- Adequate urine output is **0.5 ml/kg/hr** in an **adult**, **1 ml/kg/hr** in a **child**, and **2 ml/kg/hr** in an **infant <1 year of age**
- **Secondary survey** consists of "**AMPLE**" (**Allergies, Medications, Past illnesses or Pregnancy, Last meal, and Events related to the injury**)

REVIEW QUESTIONS

1. Which of the following trauma patients with airway compromise and failed endotracheal intubation should undergo emergency tracheostomy (rather than a cricothyroidotomy)?
 - a. 84 y/o male with blunt trauma to the neck
 - b. 65 y/o female with a stab wound to the submandibular region
 - c. 16 y/o male with a gun shot wound to the neck
 - d. 6 y/o female with a crush injury to the face

Answer: **D**

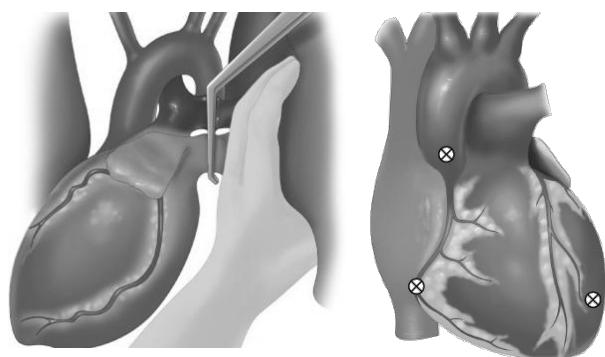
In patients **under the age of 8**, cricothyroidotomy is contraindicated due to the risk of subglottic stenosis, and tracheostomy should be performed.

2. A patient presents with stable vital signs and respiratory distress after a stab wound to the chest. Chest tubes are placed and an air leak is noted. The patient is electively intubated. The patient arrests after positive pressure ventilation is started. What is the most likely diagnosis?
 - a. Unrecognized hemorrhage in the abdomen
 - b. Tension pneumothorax
 - c. Pericardial tamponade
 - d. Air embolism

Answer: **D**

Air emboli can occur after blunt or penetrating trauma, when air from an injured bronchus enters an adjacent injured pulmonary vein and returns air to the left heart. Air accumulation in the left ventricle impedes diastolic filling, and during systole air is pumped into the coronary arteries, disrupting coronary perfusion.

Patient should be placed in Trendelenburg's position to trap the air in the apex of the left ventricle. Emergency thoracotomy is followed by cross clamping (*left picture*) of the pulmonary hilum on the side of the injury to prevent further introduction of air. Air is aspirated from the apex of the left ventricle and the aortic root with an 18-g needle and 50-ml syringe (*right picture*). Vigorous massage is used to force air bubble through the coronary arteries. If unsuccessful, a tuberculin syringe may be used to aspirate air from the right coronary artery. Once circulation is restored, patient should be kept in Trendelenburg's with the pulmonary hilum clamped until pulmonary venous injury is controlled operatively.



3. Which of the following is the expected blood loss in a patient with 6 rib fractures?
 - a. 240 ml
 - b. 480 ml
 - c. 750 ml
 - d. 1500 ml

Answer: **C**

For each rib fracture, there is ~100-200 ml of blood loss; for tibial fractures, 300-500 ml; for femur fractures, 800-1000 ml; and for pelvic fractures, >1000 ml.

Although no single injury may appear to cause a patient's hemodynamic instability, the sum of the injuries may result in life-threatening blood loss

BURNS

- A. Classification of Burns
- B. Burn Depth
- C. Initial Evaluation of Burns
- D. Management of Burns
- E. Inhalational Injury

A. CLASSIFICATION OF BURNS

1. **Thermal**
 - **Flame:** **Most common cause** for hospital admission; highest mortality (due to association with inhalational injury and/or Carbon Monoxide (CO) poisoning)
 - **Contact**
 - **Scald**
2. **Electrical**
 - Potential for **cardiac arrhythmias**; do baseline ECG i
 - **Compartment syndromes** with concurrent **rhabdomyolysis** is more common in high-voltage injuries; check for neurologic or vascular compromise
 - Long-term neurologic and visual symptoms are also common and thus, neurologic and ophthalmologic consultation should be done
3. **Chemical**
 - Less common but usually severe
 - Offending agents can be systematically absorbed; may cause specific metabolic derangements
 - Careful removal of toxic substance from patient and irrigation of the affected area with water (~30 mins) EXCEPT in cases of concrete powder or powdered forms of lye, which should be swept from the patient instead to avoid activation of AlOH with water

B. BURN DEPTH ☺

1. **Superficial (First degree burn)**
 - Painful but DO NOT blister
2. **Partial thickness (Second degree burn)**
 - Extremely painful with weeping and blisters
 - Classified as either **superficial** or **deep** depending on the depth of dermal involvement
 - **Superficial:** Heals with expectant management
 - **Deep:** Requires excision and skin grafting
3. **Full thickness (Third degree burn)**
 - Painless, hard, and non-blanching
4. **Fourth degree burn**
 - Affects underlying soft tissue

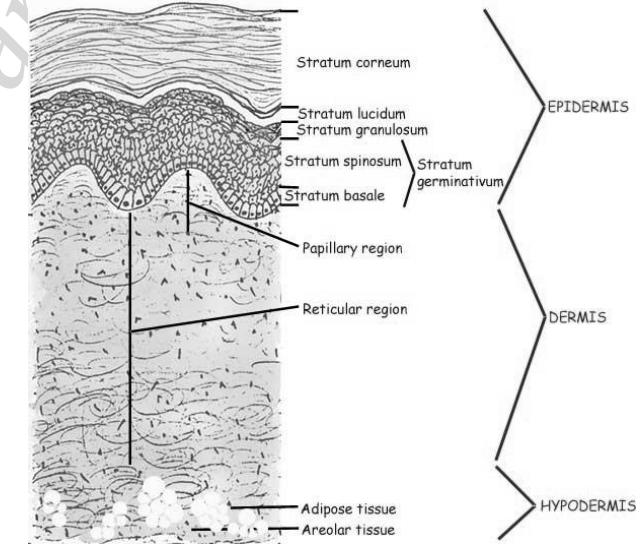
Table 34. Jackson's three zones of tissue injury following burn

Jackson's three zones of tissue injury following burn	
Zone of Coagulation	<ul style="list-style-type: none"> • Most severely burned area (typically the center of the wound) • Affected tissue is coagulated and sometimes necrotic, and will need excision and grafting
Zone of Stasis	<ul style="list-style-type: none"> • Between the first and third zones with local response of vasoconstriction and ischemia • It has marginal perfusion and questionable viability • Resuscitation and wound care may help prevent conversion to a deeper burn • Burn wounds evolve over 48-72 hours after injury
Zone of Hyperemia	<ul style="list-style-type: none"> • Outermost area, usually heals with minimal or no scarring • There is increased blood flow in this area

ANATOMY

LAYERS OF THE SKIN

- **Epidermis** is the **outermost layer** of the integument composed of stratified squamous epithelial layer that is devoid of blood vessels, **consisting of 4-5 layers:**
 - **Stratum Corneum** is a superficial stratum later consisting of flat, anucleated and keratinized cells filled with keratin filaments embedded in a dense matrix of proteins
 - **Stratum Lucidum** is **only found in regions of thick stratum corneum** of palms and soles; not found in thin skin
 - **Stratum Granulosum** is polygonal cells with basophilic keratohyalin granules; **1 layer in thin skin while multiple layers in thin skin**
 - **Stratum Spinosum** is a multilaminar layer of cuboidal-like cells that are bound together by means of numerous desmosomal junctions (tonofibrils) and they produce keratin
 - **Stratum Basale/germinativum** is a **mitotically active**, single layer of columnar or cuboidal cells attached to the dermis via hemidesmosome
 - Mnemonics: "Californians Like Girls in String Bikinis"
- **Dermis** is the connective tissue layer **below the epidermis** and its basement membrane, **consisting of 2 layers:**
 - **Papillary layer** appears **loose** that fills the hollows at the deep surface of the epidermis with frequent capillaries
 - **Reticular layer** appears **denser** and contains fewer cells
- **Hypodermis** is a layer of loose vascular connective tissue infiltrated by adipocytes



C. INITIAL EVALUATION OF BURNS

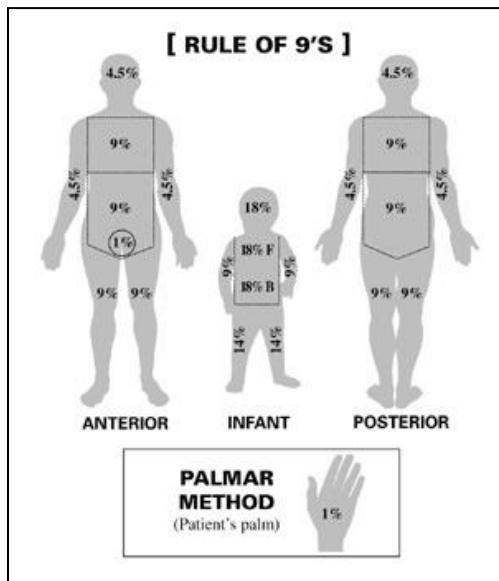
1. **Airway management**
 - With direct thermal injury to the upper airway and/or smoke inhalation (**perioral burns, singed nasal hairs**), **rapid and severe airway edema** is a potentially lethal threat
 - Anticipating the need for intubation and establishing an early airway is critical
 - Signs of impending respiratory compromise: **hoarse voice, wheezing, or stridor**
2. **Evaluation of other injuries**
 - Burn patients should be **first considered traumapatiens** (especially when details of the injury are unclear), as such, a primary survey should be conducted
 - An early and comprehensive secondary survey must also be performed in all burn patients
 - Urgent radiology studies (i.e. CXR) should be performed in the ER, but non urgent skeletal evaluation (i.e.

extremity X-rays) can be done later to avoid hypothermia and delays in burn resuscitation

3. Estimation of burn size

- Most burn resuscitation formulas estimate fluid requirements using the burn size as **% Total Body Surface Area (TBSA)**
- "Rule of nines"** is a crude but quick and effective method of estimating burn size (Refer to **Figure 24** ☺)
- Thorough cleaning of soot and debris is mandatory to avoid confusing areas of soiling with burns
- Superficial (first degree) burns** SHOULD NOT be included when calculating the %TBSA

Figure 24. Rule of nines to estimate burn size ☺



4. Diagnosis of Carbon Monoxide and Cyanide poisoning

- Unexpected neurologic symptoms should raise the level of suspicion for **CO poisoning**
 - Affinity of CO for hemoglobin is 200-250x more than that of O₂, which decreases the levels of normal oxygenated hemoglobin and can quickly lead to anoxia and death
 - Treatment** || Administration of 100% oxygen is the gold standard, and reduces the half-life of CO from 250 mins in room air to 40-60 mins
- Cyanide poisoning** is seen in smoke inhalation injury
 - May have lactic acidosis or ST elevation
 - Cyanide inhibits cytochrome oxidase, which in turn inhibit cellular oxygenation
 - Treatment** || Consists of **sodium thiosulfate, hydroxocobalamin, and 100% oxygen**

D. MANAGEMENT OF BURNS

1. Referral to a burn center (Refer to Table 35)

Table 35. Guidelines for referral to a burn center

Guidelines for referral to a burn center	
1.	Partial thickness burns greater than 10% TBSA
2.	Burns involving the face, hands, feet, genitalia, perineum, or major joints
3.	Third degree burns in any age group
4.	Electric burns (including lightning injury)
5.	Chemical burns
6.	Inhalational injury
7.	Patients with complicated preexisting medical disorders
8.	Patients with burns and concomitant trauma in which the burn is the greatest risk
9.	Burned children in hospitals without qualified personnel for the care of children
10.	Burn injury in patients who will require special social, emotional, or rehabilitative intervention

2. Resuscitation

- Rationale: Burn (and/or inhalational injury) drives inflammatory response that leads to **capillary leak**
- As the plasma leaks into the extravascular space, **crystalloid administration maintains the intravascular volume**

- Therefore, if a patient receives large fluid bolus in a prehospital setting or ER, that fluid has likely leaked into the interstitium and the patient will still require ongoing burn resuscitation
- Several formulas are available to compute for the total fluid requirement but among the most widely used one is the **Parkland formula** (Refer to Table 36 ☺)

Table 36. Parkland formula ☺

Parkland formula	
Total fluid requirement* = 4 mg/kg per %TBSA burn	
$\frac{1}{2}$ volume during first 8 hours	$\frac{1}{2}$ during next 16 hours post-injury

*Use of lactated ringer's solution

- Continuation of fluid volumes should depend on the **time since injury, UO, and MAP**
- As the leak closes, patient will require less volume to maintain the UO and BP
 - Target MAP: **60 mmHg** to ensure optimal end-organ perfusion
 - Target UO: **30 cc/h in adults and 1 to 1.5 cc/kg/hr in pediatric patients**
- Maintenance IV fluid with glucose supplementation** in addition to the calculated resuscitation fluid with LR is given in **children under 20 kg**
 - They do not have sufficient glycogen stores to maintain an adequate glucose level in response to the inflammation.
- Blood transfusions be used only when there is an apparent physiologic need

3. Treatment of burn wound

- Patients with acute burn injuries should NEVER receive prophylactic oral/IV antibiotics
- This intervention has been clearly demonstrated to promote development of fungal infections and resistant organisms
- Silver sulfadiazine:** most widely used
 - Wide range of anti-microbial activity, primarily as topical prophylaxis against burn wound infections rather than treatment of existing infection
 - Not significantly absorbed systemically
 - Side effects** || **Neutropenia** as a result of neutrophil margination due to the inflammatory response to burn injury
 - Destroy skin grafts and is contraindicated on burns in proximity to newly grafted areas
- Others: Mafenide acetate, Silver nitrate, Bacitracin, Neomycin, and Polymyxin B
- Pain management**
 - Important to administer an anxiolytic such as benzodiazepine with the initial narcotics

4. Complications of burn

- Hypothermia** is one of the common pre-hospital complications that contributes to resuscitation failure
 - Patients should be kept wrapped with clean blankets
- Ventilator-associated pneumonia**, like all critically ill patients, is a significant problem in burn patients
 - Simple measures such as elevating the head of the bed and maintaining excellent oral hygiene and pulmonary toilet are recommended to help decrease the risk of postinjury pneumonia

4. Complications of burn (continuation)

- Massive resuscitation of burn patients may lead to an **abdominal compartment syndrome**
 - Characterized by increased airway pressures with hypoventilation, and decreased urine output and hemodynamic compromise
 - Treatment** || **Decompressive laparotomy** is the standard of care for refractory abdominal compartment syndrome but carries an

- o especially lethal prognosis in burn patients
- o Adjunctive measures such as minimizing fluid, performing truncal escharotomies, decreasing tidal volumes, and chemical paralysis should be initiated before resorting to decompressive laparotomy
- Burn patients may be at higher risk for **catheter-related bloodstream infections**
- Full thickness burns with a rigid eschar can form a tourniquet effect as the edema progresses, leading to compromised venous outflow and eventually arterial inflow, leading to **compartment syndrome**
 - o Common in circumferential extremity burns
 - o Warning signs include *paresthesia, pain, decreased capillary refill, and progression to loss of distal pulses*

5. Nutrition of burn patients

- Burn injury causes a **hypermetabolic response** raising baseline metabolic rates by as much as 200%, leading to **catabolism of muscle proteins and decreased lean body mass** that delay functional recovery
- **Early enteral feeding** for patients help prevent loss of lean body mass, slow the hypermetabolic response, and result in a more efficient protein metabolism
- If enteral feeds are started within the first few hours after admission, **gastric ileus** can often be avoided

6. Surgery

- Escharotomies are rarely needed within the first 8 hours following injury and SHOULD NOT be performed unless indicated because of the aesthetic sequelae
- **Burn excision and wound coverage** should ideally start within the first several days, and in larger burns, serial excisions can be performed as the patient's condition allows
- Excision is performed with repeated tangential slices until only non burned tissue remains
- It is appropriate to leave healthy dermis, which will appear white with punctate areas of bleeding

7. Wound coverage/ Grafts

- Split thickness sheet autografts make the most durable wound coverings
- In larger burns, meshing of autografted skin provides a larger area of wound coverage, allowing drainage of blood and serous fluid to prevent accumulation under the skin graft with subsequent graft loss

8. Rehabilitation

- Should be initiated on admission
- Immediate and ongoing physical and occupational therapy is mandatory to prevent loss of physical function

E. INHALATIONAL INJURY

- Commonly seen in tandem with burn injuries
- Drastically increase mortality in burn patients
- Causes injury in 2 ways:
 - o **Direct heat injury to the upper airways**
 - Leads to maximal edema in the first 24 to 48 hours after injury
 - Will require short course of endotracheal intubation for airway protection
 - o **Inhalation of combustion products into the lower airways**
 - Irritants (combustion products) cause direct mucosal injury leading to mucosal sloughing, edema, reactive bronchoconstriction, and eventually obstruction of the lower airways
- Physiologic effects include decrease lung compliance, increase airway resistance work of breathing, increase overall metabolic demands, and an increase in fluid requirements during resuscitation of patients with burn injuries

- **Treatment** ||Supportive care including aggressive pulmonary toilet, routine use of nebulized agents (e.g. Salbutamol) and ventilation for ARDS

REVIEW QUESTIONS

1. Which of the following patients should be immediately referred to a burn center?
 - a. 20 y/o with a 12% partial thickness burn
 - b. 30 y/o with a major liver injury and a 15% partial thickness burn
 - c. 2% TBSA partial thickness burn to the anterior leg, crossing the knee
 - d. 10 y/o with a 7% partial thickness burn

Answer: A

All patients with a partial thickness burn >10% TBSA should be transferred to a burn center. A patient with a burn and other major trauma can be treated in the trauma center first. Burns that involve the entire joint should be transferred to a burn center, but a small burn to the anterior surface of the knee would not necessarily mandate transfer. Children should be transferred if there are no personnel able to care for them, but for a child with a 7% TBSA burn, this would not be mandatory (Refer to **Table 35**)

2. Which of the following is indicated in a 46 y/o patient with a 22% TBSA partial thickness burn?
 - a. Prophylactic 1st generation cephalosporin
 - b. Prophylactic clindamycin
 - c. Tetanus booster
 - d. Tetanus toxoid

Answer: C

Patients with acute burn injuries should never receive prophylactic antibiotics. This intervention promote development of fungal infections and resistant organisms and was abandoned in the mid-1980s. A **tetanus booster** should be administered in the ER.

3. Formic acid burns are associated with?
 - a. Hemoglobinuria
 - b. Rhabdomyolysis
 - c. Hypocalcemia
 - d. Hypokalemia

Answer: A

The offending agents in chemical burns can be systematically absorbed and may causes specific metabolic derangements. **Formic acid** has been known to cause hemolysis and hemoglobinuria.

4. The major improvement in burn survival in the 20th century can be attributed to the introduction of which of the following therapies?
 - a. Antibiotics
 - b. Central venous fluid resuscitation
 - c. Nutritional support
 - d. Early excision of the burn wound

Answer: D

WOUND HEALING

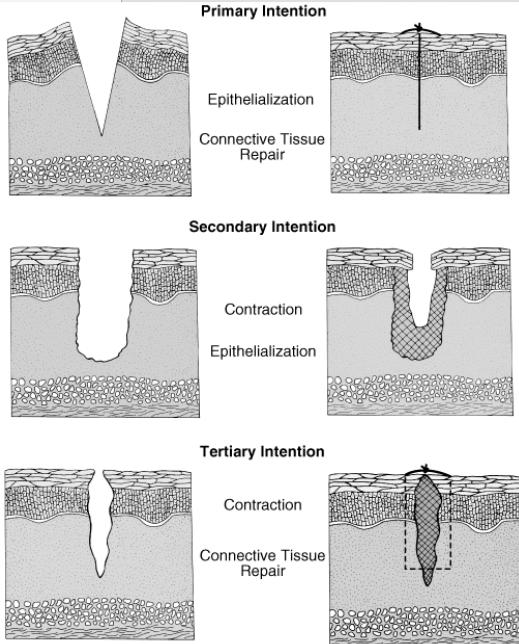
- A. Classification of Wound Healing
- B. Normal Phases of Wound Healing
- C. Classification of Wounds

A. CLASSIFICATION OF WOUND HEALING

- Surgical wounds can heal in several ways (Refer to **Figure 25** ☺)
 - o **Primary intention:** an incised wound that is clean and closed by sutures
 - o **Secondary intention:** Because of bacterial contamination or tissue loss, a wound will be

- left open to heal by granulation tissue formation and contraction
- **Tertiary intention or delayed primary closure:** represents a combination of the first two, consisting of the placement of sutures, allowing the wound to stay open for a few days, and the subsequent closure of the sutures

Figure 25. Different clinical approaches to the closure and healing of acute wounds ☺



B. NORMAL PHASES OF WOUND HEALING ☺

- Normal wound healing follows a predictable pattern that can be divided into three overlapping phases:
 1. *Hemostasis and inflammation*
 2. *Proliferation*
 3. *Maturation and remodeling*

1. Hemostasis and Inflammation

- Hemostasis precedes and initiates inflammation with the ensuing release of chemotactic factors from wound site
- Cellular infiltration after injury follows a characteristic, predetermined sequence
 - **PMNs** are the first infiltrating cells to enter the wound site, peaking at 24 to 48 hours, stimulated by increased vascular permeability, local prostaglandin release, and the presence of chemotactic substances
 - These cells DO NOT play a role in collagen deposition and collagen synthesis

Macrophages (Refer to Figure 26)

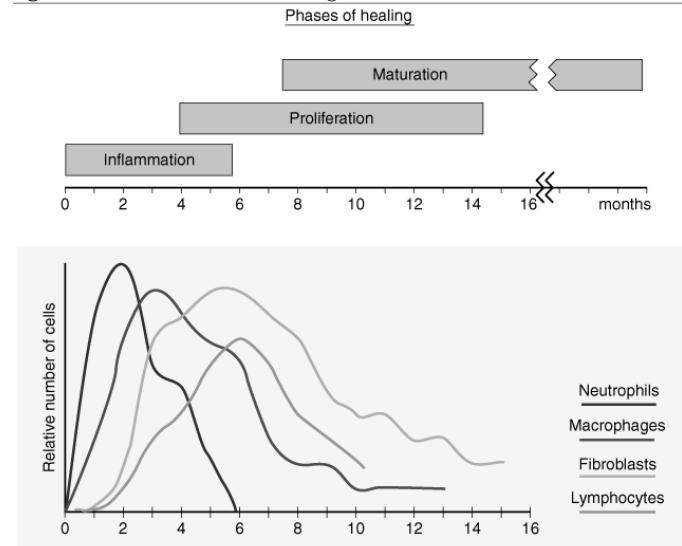
- Recognized to be essential in successful wound healing
- Achieve significant numbers by 48 to 96 hours post injury and remain present until wound healing is complete
- Participate in wound debridement via phagocytosis
- Contribute to microbial stasis via oxygen radical and nitric oxide synthesis
- Activation and recruitment of other cells via mediators as well as directly by cell-cell interaction and intercellular adhesion molecules

T lymphocytes

- Less numerous than macrophages
- Peak at about 1 week post injury and truly bridge the transition from the inflammatory to the proliferative stage of wound healing
- Role is not fully defined
- Theory is that they play an active role in modulation of the wound environment

- Exert a downregulating effect on fibroblast collagen synthesis by cell-associated interferon-gamma, TNF alpha, and IL1

Figure 26. Phases of wound healing



2. Proliferation

- Roughly spans day 4 through 12
- Phase where tissue continuity is re-established
- Fibroblasts and endothelial cells are the last cell populations to infiltrate the healing wound
- Strongest chemotactic factor for fibroblasts is **PDGF**
- Upon entering the wound environment, recruited fibroblasts first need to proliferate, and then become activated, to carry out their primary function of matrix synthesis remodeling
- Fibroblasts from wounds synthesize more collagen, proliferate less, and actively carry out matrix contraction
 - **Type I collagen** is the major component of extracellular matrix in skin
 - **Type III**, which is also normally present in skin, becomes more prominent and important during the repair process
- Endothelial cells also proliferate extensively during this phase of healing, participating in angiogenesis, under the influence of cytokines and growth factors such as TNF-alpha, TGF-beta, and VEGF
- Macrophages represent a major source of VEGF

3. Maturation and Remodeling

- Begins during the fibroplastic phase
- Characterized by a reorganization of previously synthesized collagen
- Collagen is broken down by **matrix metalloproteases**, and the net wound collagen content is the result of a balance between collagenolysis and collagen synthesis
- There is a net shift toward collagen synthesis and eventually the re-establishment of extracellular matrix composed of a relatively acellular collagen-rich scar
- Wound strength and mechanical integrity in the fresh wound are determined by both the quantity and quality of the newly deposited collagen
- The deposition of matrix at the wound site follows a characteristic pattern: fibronectin and **collagen type III** constitute the early matrix scaffolding. Glycosaminoglycans and proteoglycans represent the next significant matrix components, and **collagen type I** is the final matrix
- By several weeks post injury, the amount of collagen in the wound reaches a plateau, but the tensile strength continues to increase for several more months
- Scar remodeling continues for 6 to 12 months post injury, gradually resulting in a mature, avascular, and acellular scar
- Mechanical strength of the scar never achieves that of the uninjured tissue

4. Epithelialization

- While tissue integrity and strength are being re-established, the external barrier must also be restored
- Characterized primarily by **proliferation and migration of epithelial cells adjacent to the wound**
- Process **begin within day 1 of injury** and is seen as thickening of epidermis at the wound edge
- Re-epithelialization is **complete in less than 48 hours** in the case of approximated incised wounds, but may take longer in case of larger wounds, in which there is a significant epidermal/dermal defect
- Mediated by a combination of a loss of contact inhibition, exposure to constituents of the extracellular matrix, particularly fibronectin, and cytokines produced by immune mononuclear cells

5. Wound Contraction

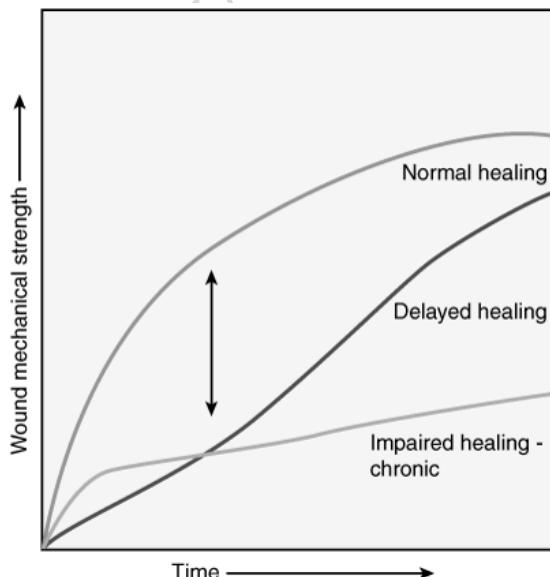
- All wounds undergo some degree of contraction
- **Starts almost immediately after injury** despite the absence of myofibroblasts
- For wounds that do not have surgically approximated edges, the area of the wound will be decreased by this action (healing by secondary intention), the shortening of the scar itself results in contracture
- **Myofibroblast** has been postulated as being the major cell responsible for contraction, and it differs from the normal fibroblast in that it possesses a cytoskeletal structure

C. CLASSIFICATION OF WOUNDS

1. Acute

- Heal in a predictable manner and time frame
- Process occurs with few complications and the end result is a **well-healed wound**
- Normal process of wound healing is characterized by a constant and continual increase that reaches a plateau at some point post injury
- **Wounds with delayed healing** are characterized by decreased wound breaking strength in comparison to wounds that heal at a normal rate, however, they eventually achieve the same integrity and strength as wounds that heal normally
- **Delayed healing** is caused by conditions such as nutritional deficiencies, infections, or severe trauma which reverts to normal with correction of the underlying pathophysiology (Refer to **Figure 27**)
- **Impaired healing** is characterized by a failure to achieve mechanical strength equivalent to normally healed wounds
- Patients with compromised immune system (diabetics, chronic steroid usage, tissues damaged by radiotherapy) are prone to impaired healing (Refer to **Table 37**)

Figure 27. The acquisition of wound mechanical strength over time in normal, delayed, and impaired healing



2. Chronic

- Defined as wounds that have failed to proceed through the orderly process that produces satisfactory anatomic and functional integrity or that have proceeded through the repair process without producing an adequate anatomic and functional result
- Wounds that have NOT healed in **3 months**

Table 37. Factors affecting wound healing

Factors affecting wound healing	
Systemic	
Age	
Nutrition	
Trauma	
Metabolic diseases	
Immunosuppression	
Connective tissue disorders	
Smoking	
Local	
Mechanical injury	
Infection	
Edema	
Ischemic/necrotic tissue	
Topical agents	
Ionizing radiation	
Low oxygen tension	
Foreign bodies	

✓ QUICK REVIEW

- Normal wound healing follows a predictable pattern that can be divided into three overlapping phases: **Hemostasis and inflammation, Proliferation, and Maturation and remodeling**
- **PMNs** are the first infiltrating cells to enter the wound site, peaking at 24 to 48 hours
- **Myofibroblast** has been postulated as being the major cell responsible for contraction

REVIEW QUESTIONS

1. The peak number of fibroblasts in a healing wound occurs?

- 2 days post injury
- 6 days post injury
- 15 days post injury
- 60 days post injury

Answer: **B**

See Figure 26

2. The first cells to migrate into a wound are:

- Macrophages
- T Lymphocytes
- PMNs
- Fibroblasts

Answer: **C**

PMNs are the 1st infiltrating cells to enter the wound site, peaking at 24-48 hours. Increased vascular permeability, local prostaglandin release and the presence of chemotactic substances, such as complement factors, IL-1, TNF-alpha, TGF beta, platelet factor 4, or bacterial products, all stimulate neutrophil migration.

3. The tensile strength of a completely healed wound approaches the strength of uninjured tissue?

- 2 weeks after injury
- 3 months after injury
- 12 months after injury
- NEVER

Answer: **D**

By several weeks postinjury, the amount of collagen in the wound reaches a plateau, but the tensile strength continues to increase for several more months. Fibril formation and fibril cross-linking result in decreased

collagen solubility, increased strength and increased resistance to enzymatic degradation of the collagen matrix. Scar remodeling continues for many months (6-12) post-injury, gradually resulting in a mature, avascular and acellular scar. The mechanical strength of the scar never achieves that of the uninjured tissue.

4. Which layer of the intestine has the greatest tensile strength (ability to hold sutures)?

- a. serosa
- b. muscularis
- c. submucosa
- d. mucosa

Answer: C

The submucosa is the layer that imparts the greatest tensile strength and greatest suture-holding capacity, a characteristic that should be kept in mind during surgical repair of GI tract. Additionally, serosal healing is essential for quickly achieving a watertight seal from the luminal side of the bowel. The importance of the serosa is underscored by the significantly higher rates of anastomotic failure observed clinically in segments of bowel that are extraperitoneal and lack serosa (ex. Esophagus and rectum)

5. A 20 year old male presents to the ER with large contaminated laceration received during a touch football game. It has been irrigated with normal saline and subsequently debrided. Which suture should be used to close the subcutaneous layer?

- a. biologic absorbable monofilament (plain gut)
- b. synthetic absorbable monofilament
- c. absorbable braided
- d. none of the above

Answer: C

In general, the smallest suture required to hold the various layers of the wound in approximation should be selected in order to minimize suture-related inflammation. Nonabsorbable or slowly absorbing monofilament sutures are most suitable for approximating deep fascial layers, particularly in the abdominal wall. Subcutaneous tissues should be closed with braided absorbable sutures, with care to avoid placement of sutures in fat. Although traditional teaching in wound closure emphasized multiple-layer closures, additional layers of suture closure are associated with increased risk of wound infection, especially when placed in fat. Drains may be placed in areas at risk of forming fluid collections.

A. ANATOMY AND PHYSIOLOGY OF THE SKIN

✓ QUICK REVIEW

Layers of the skin - p. 26
Phases of wound healing - p. 29

- **Epidermis**
 - **Keratinocyte transit time** (basal layer to shedding) is approximately **40 to 56 days**.
 - **Melanocytes**
 - Derived from precursor cells of the neural crest/neuroectodermal in origin
 - Produce melanin from **tyrosine and cysteine**
 - **Despite differences in skin tone, the density of melanocytes is constant among individuals. It is the rate of melanin production, transfer to keratinocytes, and melanosome degradation that determine the degree of skin pigmentation**
 - Cutaneous melanocytes play a critical role in neutralizing the sun's harmful rays.
 - **UV-induced damage** affects the function of **tumor suppressor genes**, directly causes cell death, and facilitates neoplastic transformation.

✓ QUICK REVIEW

What factors increase melanin production?

- 1. UV radiation
- 2. Estrogen
- 3. Adrenocorticotropic hormone
- 4. Melanocyte-stimulating hormone

- **Keratinocytes**

- Primarily found in the spindle layer
- Contains intermediate filaments (keratin) → provides flexible **scaffolding** → resist external stress
- Point mutations cause **blistering diseases**, such as **epidermolysis bullosa**, associated with spontaneous release of dermal-epidermal attachments.
- **Langerhans' cells** (not Langhan's cells!) ☺
 - skin's macrophages; from the bone marrow
 - expresses **class II major histocompatibility antigens** → antigen-presenting capabilities.
 - Functions:
 - 1. rejection of foreign bodies
 - 2. immunosurveillance against viral infections
 - 3. immunosurveillance against neoplasms of the skin

- **Dermis**

- **Collagen** (main functional component of the dermis) comprises 70% of its dry weight
- **Skin** is primarily comprised of type I collagen
- **Fetal dermis** is primarily comprised of **type III** collagen (reticulin fibers) → provides tensile strength (property of the skin that resists stretching) to both dermis and epidermis

- **Cutaneous Adnexal Structures**

- 1. **Eccrine glands**: sweat-producing glands located over the entire body but are concentrated on the palms, soles, axillae, and forehead
- 2. **Apocrine glands**: Pheromone producing glands primarily found in the **axillae and anogenital region**. It is these structures that **predispose both regions to suppurative hidradenitis**
- 3. **hair follicles**: contains a reservoir of pluripotential stem cells critical in epidermal reproductivity

ORGAN SYSTEM PATHOLOGIES

SKIN AND SOFT TISSUES

- A. Anatomy and Physiology of the Skin
- B. Injuries to the Skin and subcutaneous
- C. Infections of the skin and the subcutaneous
- D. Inflammatory diseases of the skin and subcutaneous
- E. Benign tumors of the skin and subcutaneous
- F. Malignant tumors of the skin
- G. Syndromic skin malignancies

B. INJURIES TO THE SKIN AND SUBCUTANEOUS

a. Exposure to Caustic substances

Table 38. Difference between acidic and alkali injury ☺

Acidic	Alkali
Coagulative necrosis – can damage nerves, blood vessels and tendons but is less damaging compared to alkali injury	Liquefactive necrosis – causes fat saponification that facilitates tissue penetration and increases tissue damage → producing a longer more sustained injury compared to acidic burns
Tx: copious irrigation with either saline or water for 30 minutes	Tx: continuous irrigation with water for 2 hours or until symptomatic relief is achieved

- **Intravenous fluid (IVF) extravasation:** leakage of injectable fluids into the interstitial space
 - o Is considered a **chemical burn**
 - o Produces chemical toxicity, osmotic toxicity and pressure effects in a closed environment.
 - o Culprits:
 - Cationic substances: K, Ca and bicarbonate
 - Osmotically active agents: TPN, hypertonic dextrose solution
 - Antibiotics
 - Cytotoxic drugs / **chemotherapeutic drugs** – most common cause of extravasation in adults
 - o Most common site of extravasation in adults: **dorsum of the hand**
 - o Most common cause of extravasation in infants causing necrosis: high concentration dextrose, Ca, bicarbonate and TPN

b. Thermal injuries – hypothermic vs hyperthermic injuries

✓ QUICK REVIEW

Jackson's 3 zones of tissue injury for hyperthermic injuries - p. 26

Hypothermic injuries

- o Severe hypothermia primarily exerts its damaging effect by causing direct cellular injury to bv walls and microvascular thrombosis.
- o skin's tensile strength decreases by 20% in a cold environment [12°C, (53.6°F)].
- o **Trench foot:** reactive hyperthermia with blistering as a result of prolonged exposure to ice-cold water after rapidly bringing it back to normal temperature

c. Pressure injury

- **1 hour of 60 mmHg pressure** → can lead to histologically identifiable venous thrombosis, muscle degeneration, and tissue necrosis
- **Pressures:**
 - Normal arteriole: 32 mmHg
 - Normal capillary: 20 mmHg
 - Normal venule: 12 mmHg
 - Sitting: 300 mmHg
 - Sacral pressure at hospital mattress bed: 150 mmHg
- **Muscle tissue is more sensitive to ischemia than skin.** Implication: necrosis usually extends to a deeper area than that apparent on superficial inspection
- **Treatment:** relief of pressure, wound care, systemic enhancement (nutritional optimization) and surgical management (debridement of all necrotic tissue followed by irrigation; if shallow ulcer → close by secondary intention; if deeper ulcer → require surgical debridement and coverage)

d. Radiation exposure

- **Solar or UV radiation:** most common form of radiation exposure
- **Melanin:** most important protective factor from UV related damage
- **UV spectrum:**
 - **UVA (400 to 315 nm):** majority of solar radiation that reaches the Earth
 - **UVB (315 to 290 nm):** less than 5% of all solar UV radiation; responsible for acute sunburn and chronic skin damage leading to malignant degeneration (known risk factor in the development of **melanoma**)
 - **UVC (290 to 200 nm):** absorbed by the ozone layer

C. INFECTIONS OF THE SKIN AND THE SUBCUTANEOUS

a. Cellulitis, Folliculitis, furuncles & carbuncles

Table 39: Comparison of skin infections ☺

Cellulitis	Folliculitis	Furuncles	Carbuncles
<ul style="list-style-type: none"> - Superficial, spreading infection of the skin and subQ - usual cause: Grp. A strep & S. aureus - tx for uncomplicated cellulitis with no morbidities: outpatient oral antibiotics 	<ul style="list-style-type: none"> -infection of the hair follicle -usual cause: Staphylococcus, followed by G(-) organisms -tx: adequate hygiene 	<ul style="list-style-type: none"> -begins as folliculitis but progresses as a fluctuant nodule (boil/furuncle) -tx: warm water hastens liquefaction & spontaneous rupture; incision and drainage if necessary 	<ul style="list-style-type: none"> - deep seated infections that result in multiple draining sinuses -tx: incision and drainage

b. Necrotizing soft tissue infections

- Basis of classification:
 - the tissue plane affected and extent of invasion
 - **necrotizing fascitis:** rapid, extensive infection of the fascia deep to the adipose tissue
 - **necrotizing myositis:** primarily involves the muscles but typically spreads to adjacent soft tissues
 - the anatomic site
 - Most common sites: the external genitalia, perineum, or **abdominal wall (Fournier gangrene)**
 - the causative pathogen
 - **polymicrobial more common than single organism infections**
 - most common causative organisms: group A streptococci, enterococci, coagulase-negative staphylococci, *S. aureus*, *S. epidermidis*, and *Clostridium* species
 - others (Gram negatives): *Escherichia coli*, *Enterobacter*, *Pseudomonas* species, *Proteus* species, *Serratia* species, and *bacteroides*
 - risk factors: diabetes mellitus, malnutrition, obesity, chronic alcoholism, peripheral vascular disease, CLL, steroid use, renal failure, cirrhosis, and autoimmune deficiency syndrome
 - tx: **prompt recognition**, broad-spectrum IV antibiotics, aggressive surgical debridement (should be extensive-including all skin, subcutaneous tissue, and muscle, until there is no further evidence of infected tissue followed by as needed debridement), and **aggressive fluid replacement** (needed to offset acute renal failure from ongoing sepsis)

c. Hidradenitis suppurativa

- is a defect of the terminal follicular epithelium → leading to **apocrine gland blockage** → gives rise to abscess formation in the **axillary, inguinal, and perianal regions**
- Tx: warm compresses, antibiotics, and open drainage if **acute**; wide excision with closure using skin graft or local flap placement if **chronic**

d. Actinomycosis

- is a granulomatous suppurative bacterial disease & deep cutaneous infections that present as nodules and spread to form draining tracts caused by **Actinomyces**

(pathognomonic: (+) sulfur granules within purulent specimen).

- Usual site: face or head (60%)
- Risk factors: tooth extraction, odontogenic infection, or facial trauma.
- Tx: Penicillin and sulfonamides; surgery for deep seated infections.

e. Viral infections - HPV

- Warts are epidermal growths resulting from human papillomavirus (HPV) infection.

Table 40: Comparison of HPV infections

Common wart (verruca vulgaris)	Plantar warts (verruca plantaris)	Flat warts (verruca plana)	Venereal warts (condylomata acuminata)
-fingers and toes -described as rough and bulbous	-soles and palms -resemble a common callus	- the face, legs, and hands - slightly raised and flat.	- the vulva, anus, and scrotum (relatively moist areas) - STD - HPV 6 & 11 buschke Lowenstein tumor: Extensive growths, facilitated by concomitant HIV infection

- histopathology: **hyperkeratosis (hypertrophy of the horny layer), acanthosis (hypertrophy of the spinous layer), and papillomatosis**
- Tx: formalin, podophyllium, and phenol-nitric acid; Curettage with electrodesiccation also can be used for scattered lesions
- **HPV types 5, 8, and 10:** (+) association with squamous cell carcinoma:
 - lesions that grow rapidly, atypically, or ulcerate should be biopsied

D. INFLAMMATORY DISEASES OF THE SKIN AND SUBCUTANEOUS

a. Pyoderma gangrenosum

- Main characteristic: rapidly enlarging, destructive, cutaneous necrotic lesion with undermined border and surrounding erythema
- (+) associated with a systemic disease 50% of the time (inflammatory bowel disease, rheumatoid arthritis, hematologic malignancy, and monoclonal immunoglobulin A gammopathy)
- Tx: Recognition of the underlying disease, systemic steroids or cyclosporine & chemotherapy with aggressive wound care and skin graft coverage

b. SSS vs TEN

Table 41: comparison between SSS & TEN ☺

SSSS	TEN
Difference:	
-caused by an exotoxin (TSS toxin-1) produced during staph infection of the nasopharynx or middle ear → cytokine release throughout the body causing diffuse injury and systemic symptoms	-caused by an immune response to certain drugs (sulfonamides, phenytoin, barbiturates, tetracycline) -more than 30% TBSA involved (if less than 10% TBSA → SJS)
Similarity:	
-histopath: cleavage plane in the granular layer of epidermis	- histopath: structural defect at dermoepidermal jxn; similar to a 2nd degree burn
Similarity:	
- appearance: skin erythema, bullae formation, wide area of tissue loss	- diagnosis: skin biopsy
treatment: fluid and electrolyte replacement, as well as wound care similar to burn therapy	
- appearance: skin erythema, bullae formation, wide area of tissue loss	- diagnosis: skin biopsy
treatment: fluid and electrolyte replacement, as well as wound care similar to burn therapy	

E. BENIGN TUMORS OF THE SKIN AND SUBCUTANEOUS

a. Cutaneous cysts: Epidermal, dermoid or trichilemmal

Table 42: Comparison between epidermal, dermoid & trichilemmal cyst:

Epidermal cyst	Dermoid cyst	Trichilemmal (pilar) cyst
Difference:		
- most common - single, firm nodule -location: anywhere in the body	- congenital lesions that result when epithelium is trapped during fetal midline closure - most common location: eyebrow -histopath: mature epidermis complete with granular layer	-2 nd most common - when ruptured: produce an intense characteristic odor -location: scalp (of females) -histopath: no granular layer
Similarity:		
-contain keratin (not sebum) -appear the same clinically (subcutaneous, thin-walled nodule containing a white, creamy material) -treatment: excision; incision and drainage if infected; make sure to remove the cyst wall to prevent recurrence		

b. Keratosis - seborrheic vs solar

Table 43. Comparison between seborrheic keratosis and actinic keratosis:

Seborrheic (or solar) keratosis	Actinic keratosis
- considered as a premalignant lesion of SCC - appearance: light brown or yellow with a velvety, greasy texture - arise in sun exposed areas (face, forearms, back of hands) - common in old age groups - sudden eruptions are associated with internal malignancies - treatment: topical 5-fluorouracil, surgical excision, electrodesiccation, and dermabrasion	- considered as a premalignant lesion of SCC (although at least 25% spontaneously regress)

- **Nevi - acquired vs congenital:** both are histologically similar.

Acquired melanocytic nevi

- Classification is based on different stages of maturation
 - Junctional: epidermis
 - Compound: extend partially into dermis
 - Dermal: dermis

Congenital nevi

- Rare (less than 1% of neonates)
- Giant congenital lesions (giant hairy nevi): appear in a swim trunk distribution, chest, or back
- may develop into **malignant melanoma** in 1 to 5% of cases
- tx: total excision of nevus

d. Vascular tumors of the skin and subcutaneous

Table 44: Comparison between hemangioma, vascular malformation, port wine stain and glomus tumors.

Hemangioma	Vascular malformation	Capillary malformation (port wine stain)	Glomus tumors
<ul style="list-style-type: none"> most common cutaneous lesion of infancy -benign lesion that present soon after birth (not at birth!) -histopath: mitotically active endothelial cells surrounding several, confluent blood-filled spaces -enlarge at 1st year of life → 90% eventually involute -tx: if it interferes with airway, vision, and feeding or results to systemic problems (thrombocytopenia or high-output cardiac failure) → resection and prednisone/interferon alpha 2 (for rapidly enlarging lesions) 	<ul style="list-style-type: none"> - vascular malformations are a result of structural abnormalities formed during fetal development -histopath: enlarged vascular spaces lined by nonproliferating endothelium. - grow in proportion to the body and never involute 	<ul style="list-style-type: none"> -flat, dull-red lesion often located on the trigeminal (CN V) distribution on the face, trunk, or extremities; associated with sturge-weber syndrome (leptomeningeal angiomas, epilepsy, and glaucoma) 	<ul style="list-style-type: none"> -benign -located at the extremities -arise from dermal neuromyoarterial apparatus (glomus bodies). - usually presents with severe pain, point tenderness and cold sensitivity -tx: tumor excision

e. Soft tissue tumors

Table 45: Comparison of lipoma, dermatofibroma & achrochordon

Lipoma	Dermatofibroma	Achrochordon (skin tags)
<ul style="list-style-type: none"> most common subcutaneous neoplasm - soft and fleshy on palpation --usual location: back -histopath: lobulated tumor composed of normal fat cells -tx: excision 	<ul style="list-style-type: none"> - solitary, soft-tissue nodules measuring 1 to 2 cm -usual location: legs and flanks -histopath: unencapsulated connective tissue whorls containing fibroblasts - do biopsy for atypical presentation -tx: excision 	<ul style="list-style-type: none"> -fleshy, pedunculated masses -usual location: preauricular areas, axillae, trunk, and eyelids -tx: "tying-off" or resection

f. Neural tumors

- Benign**
- Arise from the nerve sheath

Table 46: Comparison of neurofibroma, neurilemoma & granular cell tumor

Neurofibroma	Neurilemoma	Granular cell tumor
<ul style="list-style-type: none"> -sporadic, solitary -can be syndromic (von Recklinghausen's disease): café au lait spots, Lisch nodules, and an autosomal dominant inheritance) - with direct nerve attachment - histopath: proliferation of perineurial and endoneurial fibroblasts with Schwann cells embedded in collagen 	<ul style="list-style-type: none"> - solitary tumors arising from cells of the peripheral nerve sheath 	<ul style="list-style-type: none"> - solitary lesions of the skin or, more commonly, the tongue

F. Malignant tumors of the skin

Basal cell carcinoma ☺

- most common type of skin cancer.**
- Arises from the pluripotential basal epithelial cells of epidermis and NOT DERMIS!
- **Slow growing and metastasis is rare** but are capable of extensive local tissue destruction
- Subtypes:
 - **Nodulocystic/noduloulcerative**
 - 70% of BCC tumors (most frequent form)
 - Waxy and frequently cream colored/translucent; over time, can present as a rolled, pearly borders surrounding a central ulcer (**rodent ulcer**)
 - **Morpheaphorm**
 - flat, plaque-like lesion
 - most aggressive clinically (due to presence of type IV collagenase that facilitates local spread) → early excision
 - **basosquamous type**
 - combination of both BCC + SCC
 - aggressive → treated right away!
- Tx:
 - Less than 2mm nodular lesions: curettage, electrodesiccation, or laser vaporization.
 - If located at cheek, nose, or lip: **Mohs' surgery**
 - Large tumors, those that invade surrounding structures, & aggressive histologic types (morpheiform, infiltrative, and basosquamous): surgical excision with 0.5-cm to 1-cm margins.

Syndromic skin malignancies associated with BCC:

➤ **basal cell nevus (Gorlin's) syndrome:**

- autosomal dominant disorder characterized by the growth of hundreds of BCCs during young adulthood.
- Palmar and plantar pits: common physical finding
- Tx: excision of aggressive and symptomatic lesions

➤ **nevus sebaceus of Jadassohn:**

- lesion containing several cutaneous tissue elements that develops during childhood.

Squamous cell carcinoma ☺

- Arise from **epidermal keratinocytes**
- **Less common than BCC**
- **Highly invasive and tends to metastasize**
- Tend to occur in persons with blond hair, light, thin, dry and irritated skin.
- In situ lesions: **Bowen's disease;** if in the penis → **erythroplasia of Queyrat**
- Risk factors:
 - Skin lesions: **actinic keratosis, atrophic dermatitis**
 - Occupational exposure: **arsenics, nitrates and hydrocarbons**
 - Syndromic malignancies associated with SCC:
 - epidermolysis bullosa
 - lupus erythematosus
 - **Epidermodysplasia verruciformis**
 - rare autosomal recessive disease associated with infection with HPV
 - **Xeroderma pigmentosum**
 - autosomal recessive disease associated with a defect in cellular repair of DNA damage.
 - **tumor thickness correlates well with malignant behavior.**
 - more than 4 mm: Tumor recurrence is more prevalent
 - if 10 mm or more: these lesions usually have associated metastasis

- **Burn scars (Marjolin's ulcer)**, areas of chronic osteomyelitis, and areas of previous injury → tend to metastasize early.
- Tx:
 - Excision with 1 cm margin + histologic confirmation of tumor free borders
 - If located at cheek, nose, or lip: Mohs' surgery
 - **Regional LN excision is indicated for clinically palpable nodes**
 - If SCC arises from chronic wounds, lymphadenectomy before development of palpable nodes (**prophylactic LN dissection is indicated**) because it is more aggressive and lymph node metastases are observed more frequently
- Metastatic disease is a poor prognostic sign (13% survival after 10 years).

✓ MUST KNOW

Keratoacanthoma, which is characterized by rapid growth, rolled edges and a crater filled with keratin, *can be confused with SCC or BCC*. It spontaneously involutes over time.
 Biopsy lesion to rule out carcinoma.

Moh's surgery for BCC and SCC (nice to know!)

- This precise, specialized surgical technique uses minimal tissue resection and immediate microscopic analysis to confirm appropriate resection yet limit removal of valuable anatomy.
- Done for aesthetic purposes
- uses serial excision in small increments coupled with immediate microscopic analysis to ensure tumor removal → all specimen margins are evaluated.
 Recurrence and metastases rates are comparable to those of wide local excision.

Malignant Melanoma ☺

- Arise from **melanocytes**
- **Premalignant lesion: dysplastic nevi** (vs freckles - benign melanocytic neoplasms found on the skin)
- Most common location: skin (>90%); other sites: anus, eyes
- 4%: discovered as metastases without any identifiable primary site.
- Suspicious features: **pigmented lesion with an irregular border, darkening coloration, ulceration, raised surface and recent changes in nevus appearance**
- Risk factors:
 - increased sun exposure of fair skinned people to solar radiation
 - **Familial dysplastic nevus syndrome**
 - autosomal dominant disorder
- Subtypes:

Table 47. comparison of malignant melanoma subtypes:

Superficial spreading	Nodular	Lentigo maligna	Acral lentiginous
- most common type (70% of melanomas)	-15 to 30% of melanomas	-4 to 15% of melanomas	-2 to 8% of melanomas (least common)
- location: anywhere on the skin except the hands and feet	- darker coloration and often raised lack radial growth	- occur on neck, face, and hands of elderly best prognosis	- occurs at palms, soles, and subungual regions Hutchinson's sign: presence of pigmentation in the proximal or lateral nail folds; diagnostic of subungual melanoma dark skinned + acral lentiginous melanoma: increased risk of malignancy
- flat and measure 1 to 2 cm in diameter at diagnosis			
- Before vertical extension, a prolonged radial growth phase is characteristic of these lesions	aggressive but same prognosis with superficial spreading		

- Prognostic indicators:

- Location: lesions of the extremities have a better prognosis than patients with melanomas of the head, neck, or trunk
- (+) ulceration (due to increased angiogenesis): worse prognosis
- Gender: females have higher survival rates than men
- Tumor types:
 - **Best: lentigo maligna**
 - **Worse: acral lentiginous**
- Staging from AJCC: breslow and clark level
- **Breslow thickness:** the vertical thickness of the primary tumor (from the granular layer of the epidermis or base of ulcer to the greatest depth of the tumor); **most important prognostic variable predicting survival in those with cutaneous melanoma;** considered to be more precise in predicting biologic behavior
 - I: 0.75 mm or less
 - II: 0.76 to 1.5 mm
 - III: 1.51 to 4.0 mm
 - IV: 4.0 mm or more
- **Clark level:** anatomic depth of invasion
 - I: superficial to basement membrane (**in situ**)
 - II: papillary dermis
 - III: papillary/reticular dermal junction
 - IV: reticular dermis
 - V: subcutaneous fat
- LN status & Metastasis:
 - Evidence of tumor in regional LNs is a poor prognostic sign (automatic stage III)
 - Identification of distant metastasis is the worst prognostic sign (automatic stage IV)
- Dx: excisional biopsy
- Tx:
 - Melanoma in situ/lentigo maligna melanoma in face: 0.5 cm margins
 - 1mm or less: excision with 1 cm margin
 - 1 to 4 mm: excision with 2 cm margin
 - More than 4 mm or (+) satelliosis: 3-5 cm margin
 - High dose interferon has a role in high risk melanoma
 - LN dissection:
 - **Sentinel LN biopsy:** 1mm or thicker with clinically negative nodes or 0.75 mm thick + clark level IV or ulcerated
 - **Radical regional lymphadenectomy:** clinically (+) nodes with no evidence of distant disease on metastatic work up.

✓ QUICK REVIEW

Remember:

- **Moh's surgery is not appropriate for any type of melanoma**
- **If melanoma is 4mm or greater + clinically negative nodes → perform metastatic work up first**

Merkel cell carcinoma

- Primary Neuroendocrine Carcinoma of the Skin
- associated with a synchronous or metasynchronous SCC 25% of the time.
- Tx: wide local resection with 3-cm margins + Prophylactic regional LN dissection + adjuvant radiation therapy are recommended.
- Prognosis: worse than malignant melanoma

Kaposi's sarcoma

- rubbery bluish nodules that occur primarily on the extremities (also skin and viscera)
- usually multifocal rather than metastatic.
- Histopath: capillaries lined by atypical endothelial cells.
- seen in people of Eastern Europe or sub-Saharan Africa, AIDS or immunosuppression with chemotx
- locally aggressive but undergo periods of remission

Extramammary Paget's disease

- cutaneous lesion that appears as a pruritic red patch that does not resolve
- histologically similar to the mammary type.

REVIEW QUESTIONS

1. Match the item in the left hand column with the appropriate item in the right hand column

a. modulate cold sensation	a. Ruffini's endings
b. modulate sensitivity to warmth	b. Krause' end-bulb
c. modulate sensation of pressure	c. Meissner's corpuscles
d. modulate tactile sensation	d. Pacinian corpuscles
e. modulate thermoregulation	e. autonomic endings

Answer: A-b; B-a; C-d; D-c; E-e

A variety of highly specialized structures are responsible for modulating the skin's various sensory functions. The numbers of these structures vary with the region of the body. **Pacinian corpuscles** are found in the subcutaneous tissue, in the nerves of the palm of the hand and the sole of the foot, and in other areas. Each of these corpuscles is attached to and encloses the termination of a single nerve fiber. They are involved in the sensation of pressure. **Ruffini's endings** are a variety of nerve endings in the subcutaneous tissue of the fingers and modulate sensitivity to warmth. **Krause's end-bulbs** are formed by the expansion of the connective tissue sheath of medullated fibers and are involved in the sensation of cold. **Meissner's corpuscles** occur in the papillae of the corium of the hands, the feet, the skin of the lips and other areas concerned with tactile sensation. **Autonomic fibers** that synapse to sweat glands and receptors in the vasculature govern thermoregulation.

2. Select the treatment options(s) in the 1st set of choices (UPPER CASE) that is/are most appropriate for the melanoma case summaries outlined in the 2nd set of choices (lower case)

A. Level III superficial spreading melanoma (0.4 mm thick with clinically negative regional lymph nodes
B. Level IV nodular melanoma (2mm thick) with satelloysis and clinically negative regional lymph nodes
C. Level IV superficial spreading melanoma (1.5 mm thick) with palpable regional lymph nodes
D. Level IV acral lentiginous melanoma (2 mm thick) with clinically negative regional lymph nodes
E. Level II lentigo maligna melanoma (0.3 mm)
f. Moh's micrographic surgery
g. Wide local excision with 0.5 cm margins
h. Wise local excision with 1.0 cm margins
i. Wide local excision with 2.0 cm margins
j. Wide local excision with 4.0 cm margins
k. Sentinel lymph node biopsy
l. Regional lymph node biopsy
m. Radical regional lymphadenectomy

Answer: A - c; B - e,f; C - d,h; D - d,f; E - b

Virtually all melanomas are best treated by wide excision. The excision margin that minimizes the risk of local recurrence depends on the thickness of the tumor. Melanoma in situ and thin lentigo maligna melanomas of the face are treated adequately by margins of 0.5 cm. For melanomas less than 1.0 mm thick, 1 cm excision margins are appropriate. For intermediate thickness melanoma (1-4 mm), a 2 cm margin is sufficient. Margins of 3-5 cm are generally employed for

melanomas 4 mm in thickness and for those with associated satelloysis. Moh's chemosurgery is not appropriate for the treatment of any melanomas. The indications for elective lymph node dissection remain controversial. Sentinel lymph node biopsy is indicated for patients with melanoma 1 mm or thicker with clinically negative nodes. The indication is extended to patients with 0.75 mm thick melanomas if they are Clark's level IV or ulcerated. Patients with clinically positive lymph nodes with no evidence of distant disease on metastatic workup (CT of chest, abdomen and pelvis; MRI of brain; PET) should undergo radical regional lymphadenectomy. Patients with primary tumors 4 mm or greater with clinically negative nodes should undergo metastatic workup before undergoing sentinel node biopsy and wide local excision.

3. With regards to keloids and hypertrophic scars, which of the following statements is/are true?
 - A. There are no histologic differences between the two
 - B. The differences between hypertrophic scar and keloid are clinical, not pathologic
 - C. Hypertrophic scars outgrow their original borders
 - D. Hypertrophic scars and keloids have been treated successfully with intralesional injection of steroids
 - E. Keloids are seen in dark-skinned individuals, whereas hypertrophic scars are seen in fair-skinned individuals

Answer: A,B,D

Histologically, keloids and hypertrophic scars appear the same. **Hypertrophic scars are thick, red, raised scars that do not outgrow their original borders, whereas keloids do.** Keloids are dense accumulations of fibrous tissue that form at the surface of the skin. The defect appears to result from a failure in collagen breakdown rather than an increase in its production. Keloids and hypertrophic scars have been successfully treated with intralesional steroid injection, radiation, pressure and the use of silicone gel sheets.

BREAST

- A. **Embryology of the breast**
- B. **functional anatomy of the breast**
- C. **Physiology of breast**
- D. **infectious and inflammatory disorders of the breast**
- E. **common benign disorders and diseases of the breast**
- F. **breast cancer**
- G. **special clinical situations**

A. EMBRYOLOGY OF THE BREAST

- 5th or 6th week of fetal development → mammary ridges (thickened ectoderm): precursors of breast
 - Extends from the base of the forelimb (future axilla) to the hind limb (future inguinal region)
- **Witch's milk:** (+) breast secretions in an infant secondary to maternal hormones that crosses the placenta
- **Anomalies in embryology:**
 - **Polymastia:** accessory breast; can be seen in Turner's syndrome (ovarian agenesis and dysgenesis) and Fleischer's syndrome (displacement of the nipples and bilateral renal hypoplasia); can enlarge during pregnancy & lactation
 - **Polythelia:** accessory nipples; maybe associated with CVS and urinary tract anomalies
 - **Amastia:** congenital absence of breast due to arrest in mammary ridge development during the 6th week
 - **Poland's syndrome:** hypoplasia or complete absence of the breast, costal cartilage and rib

- defects, hypoplasia of the subcutaneous tissues of the chest wall, and brachysyndactyly
- **Symmastia:** webbing between the breasts across the midline (no cleavage)
- **Inverted nipple:** occurs in 4% of infants

B. FUNCTIONAL ANATOMY OF THE BREAST

- It extends from the level of the **2nd or 3rd rib to the inframammary fold at the 6th or 7th rib.**
- It extends transversely from **the lateral border of the sternum to the anterior axillary line.**
- The deep or posterior surface of the breast rests on the fascia of the pectoralis major, serratus anterior, external oblique abdominal muscles, & the upper extent of the rectus sheath.
- **retromammary bursa:** located at posterior aspect of the breast between the investing fascia of the breast and the fascia of the pectoralis major muscles.
- The **axillary tail of Spence** extends laterally across the anterior axillary fold.
- **upper outer quadrant:** greatest volume; **most common site of breast cancer** ☺
- Blood supply:

Table 48. Blood supply of the breast

Arterial blood supply	Venous blood supply
- perforating branches of the internal mammary artery	- perforating branches of the internal thoracic vein
- lateral branches of the posterior intercostal arteries	- perforating branches of the posterior intercostal veins
- branches from axillary artery (highest thoracic, lateral thoracic, and pectoral branches of the thoracoacromial artery)	- tributaries of the axillary vein .
	- Batson's vertebral venous plexus ☺: possible route for breast cancer metastases to the vertebrae, skull, pelvic bones, and central nervous system.

- Innervation:

- Sensory innervation to breast & anterolateral chest wall: **Lateral cutaneous branches of the 3rd – 6th intercostal nerves** (slips out in between serratus anterior muscles)
 - **Intercostobrachial nerve:** lateral cutaneous branch of the **second intercostal nerve**; **injury to this nerve results to loss of sensation over the medial aspect of the upper arm.**
- Cutaneous branches from cervical plexus (anterior branches of the **suprascapular nerve**): supply a limited area of skin over the upper portion of the breast.

- Lymphatics:

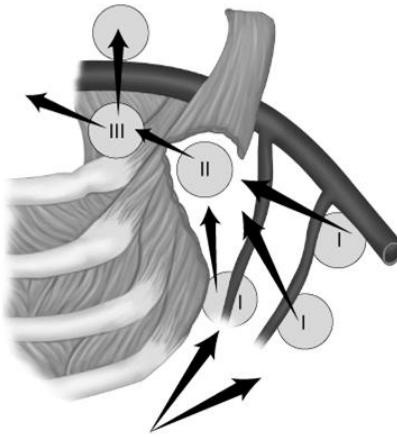
- 6 axillary lymph node groups:

Table 49. Location and drainage pattern of breast ☺

Name	location	drainage
Lateral (axillary vein group) – level I	medial or posterior to the vein	upper extremity; receives 75% drainage of the breast; most common site of axillary LN metastasis
Anterior or pectoral (external mammary group) – level I	lower border of the pectoralis minor muscle contiguous with the lateral thoracic vessels	lateral aspect of the breast
Posterior of subscapular (scapular group) – level I	posterior wall of the axilla at the lateral border of the scapula contiguous with the subscapular vessels	lower posterior neck, the posterior trunk, and the posterior shoulder
Central group – level II	embedded in the fat of the axilla lying immediately posterior to the pectoralis minor muscle	receive lymph drainage both from the axillary vein, external mammary, and scapular groups of lymph nodes, and directly from the breast
Apical (subclavicular group)	posterior and superior to the upper border of	from all of the other groups of axillary lymph nodes

- level III	the pectoralis minor muscle	
<u>Interpectoral group (Rotter's nodes)</u> - level II	interposed between the pectoralis major and pectoralis minor muscles	receive lymph drainage directly from the breast. The lymph fluid that passes through the interpectoral group of lymph nodes passes directly into the central and subclavicular groups.

Figure 28. Axillary lymph node groups ☺



Reference point:
pectoralis minor
(not major!)

Level I: lateral to the pectoralis minor muscle (PM)
Level II: deep to PM

Level III: medial to the PM.

Arrows indicate the direction of lymph flow.

Also seen: axillary vein & its major tributaries, supraclavicular LN

C. PHYSIOLOGY OF BREAST

- Breast development and function

➤ Hormonal stimuli:

- **Estrogen:** ductal development
- **Progesterone:** differentiation of epithelium & lobular development
- **Prolactin:** 1^o hormonal stimulus for lactogenesis in late pregnancy & the postpartum period.

Gynecomastia: enlarged breast in males measuring at least 2 cm in diameter

- Gynecomastia generally does not predispose the male breast to cancer unless syndromic
- Physiologic gynecomastia occurs due to excess in circulating estrogens (in relation to circulating testosterone):
 - neonatal period: action of placental estrogens on neonatal breast tissues
 - adolescence: excess of estradiol relative to testosterone; can be unilateral
 - senescence: circulating testosterone level falls; usually bilateral

D. INFECTIOUS AND INFLAMMATORY DISORDERS OF THE BREAST

a. Breast abscess

- **Staphylococcus aureus** (more localized & deep) and **Streptococcus** (diffuse superficial involvement) species: causative organisms
- SSx: point tenderness, erythema, and hyperthermia.
- Risk factor: lactation (because a lactating breast is an excellent culture medium)
- Tx: preoperative UTZ + incision & drainage (if already with suppuration) + local wound care (warm compresses & IV antibiotics - penicillins or cephalosporins).
 - Remember: Biopsy of the abscess cavity wall is recommended at the time of I&D → rule out breast cancer with necrotic tumor.
- Chronic breast abscesses: consider acid-fast bacilli, anaerobic and aerobic bacteria, and fungi.
- If fungal. Consider blastomycosis or sporotrichosis (rare)

b. Epidemic puerperal mastitis

- MRSA: causative organism
- Transmission via suckling neonate
- Tx: stop breastfeeding, antibiotics & I&D

c. Nonepidemic (sporadic) puerperal mastitis

- involvement of the interlobular CT of the breast
- tx: Emptying of the breast using breast suction pumps + antibiotics

d. Zuska's disease (recurrent periductal mastitis)

- recurrent retroareolar infections and abscesses.
- Risk factor: smoking
- Tx: antibiotics + I&D as necessary.

e. Hidradenitis suppurativa

- can also occur in the nipple-areola complex
- originates within the Montgomery glands or axillary sebaceous glands.
- Risk factor: chronic acne
- may mimic Paget's disease of the nipple or invasive breast cancer.
- Tx: Antibiotic + I&D

f. Mondor's disease

- a benign self limited condition which is a variant of thrombophlebitis that involves the superficial veins of the anterior chest wall and breast.
- Involved veins: lateral thoracic vein, the thoracoepigastric vein, and, less commonly, the superficial epigastric vein.
- SSx: acute pain in the lateral aspect of the breast or the anterior chest wall with palpation of a tender, firm cord along the distribution of the major superficial veins.
- Tx: anti-inflammatory medications + warm compresses along the symptomatic vein + Restriction of motion of the ipsilateral extremity and shoulder + brassiere support of the breast are important (4 to 6 weeks) or excision of vein (if not improving)

E. COMMON BENIGN DISORDERS AND DISEASES OF THE BREAST

a. Fibroadenoma ☺

- seen predominantly in younger women aged 15 to 25 years
- can be self limiting
- if greater than 3cm → consider giant fibroadenoma
- if multiple (more than 5 lesions in 1 breast)
→ considered as abnormal
- tx: cryoablation, surgical removal or observation

b. Cyclical mastalgia and nodularity

- associated with premenstrual enlargement of the breast physiologic.
- If Painful nodularity persists for >1 week of the menstrual cycle → consider a disorder.
- bilateral bloody nipple discharge → can be seen in epithelial hyperplasia of pregnancy

c. Breast cysts ☺

- **occurs when the stroma involutes too quickly**, and alveoli remain → forming microcysts & macrocysts
- characteristics of benign lesions: sharp, smooth margins, a homogenous interior and posterior enhancement (*vs malignancy which will show irregular and jagged margins, heterogeneous interior and posterior shadowing*)
- **management: needle biopsy** (1st line investigation for palpable breast masses)
 - if (+) fluid on aspiration → aspirate to dryness, no need to do cytologic examination
 - If after aspiration, (+) residual mass → do UTZ guided needle biopsy
 - If blood stained fluid → aspirate 2 mL for cytologic examination, utz imaging and biopsy solid areas
- If complex cyst → rule out malignancy.

d. Calcium deposits ☺

- benign
- cause: cellular secretions, debris or by **trauma** and inflammation.
- (+) cancer if <0.5 mm in size, fine, linear calcifications, may branch (**microcalcifications**).

e. Sclerosing adenosis

- Common in childbearing and perimenopausal years
- no malignant potential.
- characterized by distorted breast lobules + multiple microcysts + benign calcifications

f. Radial scars (1 cm or less) or Complex central sclerosis (more than 1 cm)

- characterized by central sclerosis, epithelial proliferation, apocrine metaplasia, and papilloma formation
- can mimic cancer hence an excisional biopsy is done to exclude diagnosis of cancer

g. Ductal hyperplasia

- Severity:
 - Mild: 3-4 cell layers above the basement membrane.
 - Moderate: 5 or more cell layers above the basement membrane.
 - Florid ductal epithelial hyperplasia: occupies at least 70% of a minor duct lumen.
- associated with an increased cancer risk

h. Intraductal papillomas ☺

- Seen in premenopausal women.
- **common symptom: serous or bloody nipple discharge**
- Gross appearance: pinkish tan, friable,
- rarely undergo malignant transformation & no increased risk of breast cancer, unless multiple

i. Atypical proliferative disease

- has some of the features of Ca in situ but lack a major defining feature of Ca in situ or have the features in less than fully developed form
- **Atypical ductal hyperplasia & lobular hyperplasia**
 - Increases risk of breast cancer 4x; if with (+) family hx, 10x

F. BREAST CANCER ☺

risk factors

- **increased exposure to estrogen:** early menarche, nulliparity, late menopause, older age at first live birth (after the age of 30 yo), HRT, obesity, (major source of estrogen in postmenopausal women is the conversion of androstenedione to estrone by adipose tissue)
- **radiation exposure:** patients with multiple fluoroscopies, mantle radiation for treatment of hodgkin's lymphoma
- **increased alcohol intake** (leads to increased estradiol levels)
- **high fat diet** (increased serum estrogen levels)
- **prolonged use of OCPs** (particularly estrogen-plus-progesterone) and HRT
- **(+)** **family history of breast cancer:** the greater the number of relatives affected, the closer the genetic relationship, the younger the age at diagnosis, and the presence of bilateral versus unilateral disease all increased the likelihood of development of breast cancer in an individual.

✓ MUST KNOW

Remember:

Smoking is not considered a risk factor for breast cancer!!!!!! Please don't make the mistake of answering this as part of the risk factors in breast cancer.

- risk management

- **Postmenopausal hormone replacement tx**
 - Widely prescribed because it is effective in controlling symptoms of estrogen deficiency (vasomotor symptoms such as hot flashes, night sweats and their associated sleep

- deprivation, osteoporosis, and cognitive changes)
- Results of Women's health initiative study (2002): **breast Ca risk is increased to 3-4fold after > 4 years of use + no reduction in CAD or CVD**

➤ **screening mammogram**

- routine screening mammography starting 50 years old age reduces mortality from breast cancer by 33%
- baseline mammography at age 35
- **annual mammographic screening beginning at age 40.**
- If (+) family history for breast cancer
 - Baseline mammogram 10 years before the youngest age of diagnosis of breast ca among 1st degree relatives. (this rule is modified if age of diagnosis is less than 35)

➤ **Chemoprevention**

- **Tamoxifen:** selective estrogen receptor modulator
 - recommended only for women who have a Gail relative risk of 1.70 or ↑er.
 - SE: deep vein thrombosis, pulmonary emboli, **endometrial cancer**
 - reduce the incidence of LCIS and ductal carcinoma in situ (DCIS)
- **Raloxifene:** estrogen receptor modulator
 - Equivalent to tamoxifen
 - **associated with a more favorable adverse event profile**
 - **no effect on LCIS or DCIS**

➤ **prophylactic mastectomy**

- greatly reduces risk for breast cancer
- only for high risk populations
- + 3 years → if with 40% risk of having breast Ca
- + 5 years → if with 85% risk of having breast cancer

- **BRCA mutation**

- Constitutes 5-10% of breast cancers
- Autosomal dominant inheritance
- tumor-suppressor genes
- prevalent in Ashkenazi Jews

Table 50. Comparison of BRCA 1 & 2

BRCA 1	BRCA 2
- location: ch arm 17q	-location: ch arm 13q
- predisposing genetic factor: 45% of breast Ca & 85% of ovarian Ca	- lifetime risk for carrier → Ca: 85% for breast ca & 20% for ovarian ca ; if male carrier: 6%
- lifetime risk for carrier → Ca: 90% for breast ca & 40% for ovarian ca	-usually develops invasive ductal carcinomas: well differentiated, hormone receptors (+)
- usually develops invasive ductal carcinomas: poorly differentiated and hormone receptor (-)	-early age of onset, bilateral breast cancer, & other associated ca: ovarian, colon, prostate, pancreatic, gallbladder, bile duct & stomach cancers, melanoma.
- early age of onset, bilateral breast cancer and other associated ca: ovarian, colon and prostate	

- Risk mgt strategies for **BRCA** carriers:
 - Prophylactic mastectomy and reconstruction
 - Prophylactic oophorectomy (because of ↑ risk of ovarian ca) at the completion of childbearing or menopause + HRT
 - Intensive surveillance for breast and ovarian cancer
 - Chemoprevention
- **BRCA** mutation carriers who do not undergo prophylactic mastectomy must do clinical breast examination every 6 months and mammography every 12 months beginning at age 25 years

(because the risk of breast cancer in **BRCA** mutation carriers increases after age 30 years)

- **HER-2 gene**

- Encodes transmembrane tyrosine kinase, a protein with potent growth stimulating activity
- In breast cancer, this gene is amplified (indicating more rapid growth & aggressive behavior)
- Treatment if there is a mutation: **Herceptin**

- **Breast cancer signs and symptoms:**

- **mass (most common)**
 - if size is 1 cm → mass has been present for 5 years
 - breast enlargement or asymmetry
 - nipple changes - retraction, or discharge (due to shortening of Cooper's suspensory ligament)
 - skin dimpling
 - ulceration / erythema of the skin
 - axillary mass or mets
 - firm or hard with continued growth of the metastatic cancer.
 - involved sequentially from the low (level I) to the central (level II) to the apical (level III) lymph node groups.
 - **axillary lymph node status: most important prognostic correlate of disease-free and overall survival**
- **peau d'orange (Localized edema):** blocked drainage of lymph fluid
- musculoskeletal discomfort.
- **Distant metastases:** most common cause of death in breast cancer patients
 - Due to **neovascularization (hematogenous spread)** → cancer cells shed directly to axillary and intercostal veins or vertebral column via **batson's plexus of veins**.
 - Metastatic foci occurs after the 10 ca exceeds **0.5 cm** in diameter
 - Common sites of involvement (in order of frequency): bone, lung, pleura, soft tissues, and liver

✓ **MUST KNOW**

Remember:

- **Breast pain is usually associated with benign disease.**

- **In situ breast cancer**

- **Multicentricity:** occurrence of a second breast cancer outside the breast quadrant of the primary cancer (or at least 4 cm away)
- **Multifocality:** the occurrence of a second cancer within the same breast quadrant as the primary cancer (or within 4 cm of it)
- Difficult to differentiate from atypical hyperplasia or cancers with early invasion
- **Subtypes:**

Table 51. Comparison of LCIS vs DCIS

	LCIS	DCIS
Age	44-47	54-58
Incidence	2-5	5-10
Clinical sx	None	Mass, pain & nipple discharge
Mammographic sx	None / mammographically featureless; may have calcifications in adjacent tissues occasionally	Microcalcifications (usually in areas of necrosis)
Premenopausal	2/3 (more common)	1/3
Incidence of synchronous invasive ca	5%	2-46%
Multicentricity	60-90 %	40-80% (more common if comedo type)
Bilaterality	50-70% (more common)	10-20%

	LCIS	DCIS
Axillary metastasis	1%	1-2%
Subsequent carcinoma		
Laterality	Bilateral	Ipsilateral
Interval to diagnosis	15-20 y	5-10 y
Histo type	Ductal; cytoplasmic mucoid globules are characteristic	ductal
Specifics	Only in ♀ breast; more common in whites; <u>not considered an anatomic precursor of breast ca; only a risk marker (increases risk of breast ca 9x)</u>	Other name: intraductal carcinoma (true anatomic precursor) ; 5% of male cancers

- **Tx:**
 - **LCIS:** observation, **chemoprevention with tamoxifen**, and bilateral total mastectomy or may opt to do close follow up + periodic PE + bilateral mammograms for a more conservative approach
 - **DCIS:**
 - > 4 cm or disease in >1 quadrant: mastectomy
 - Low-grade DCIS of the solid, cribriform, or papillary subtype that is <0.5 cm: lumpectomy (If margins are free of disease)
 - Adjuvant tamoxifen therapy has a role for DCIS pt.

✓ MUST KNOW

Remember:

- Mastectomy vs lumpectomy + adjuvant RT: same mortality rate (<2%) but lumpectomy + adjuvant RT has a higher local recurrence rate (up to 9%, compared to 2% for mastectomy)
- Role of RT: markedly **decreases the risk of in-breast recurrence** and significantly reduces the risk that any recurrence will be invasive disease
- High recurrence rate for **DCIS comedo type**

- **Invasive Breast Cancer**

- **Paget's disease of the nipple** (unrelated to Paget's disease of the bone)
 - chronic, erythematous, eczematoid rash or ulcer
 - associated with DCIS & invasive cancer.
 - **Pathognomonic sign: large, pale, vacuolated cells (Paget cells) in the rete pegs of the epithelium.**
 - Rule out superficial spreading melanoma
 - (+) s-100 antigen in immunostaining (vs paget's disease which is (+) in carcinoembryonic antigen immunostaining)
 - Tx: lumpectomy, mastectomy, or MRM (depending on the extent of involvement and the presence of invasive cancer)
- **Invasive ductal carcinoma**
 - Occurs in perimenopausal or postmenopausal ♀ (5th-6th decade)
 - Most common carcinoma presenting as a breast mass
 - poorly defined margin, central stellate configuration with chalky white or yellow streaks extending into surrounding breast tissues
 - macroscopic/microscopic axillary LN metastases in 60% of cases
- **Medullary carcinoma**
 - Associated with *BRCA1* phenotype & DCIS

- Gross appearance: well circumscribed, soft & hemorrhagic (when accompanied with a rapid increase in size)
- PE: bulky and mass is positioned deep within the breast.
- **Can mimic a benign condition on diagnostic imaging (looks like a fibroadenoma on UTZ)**
- Occurs bilaterally in 20% of cases.
- Microscopically: **dense lymphoreticular infiltrate**

➤ **Mucinous (colloid) carcinoma**

- Occurs in the elderly
- Characteristic lesion: extracellular pools of mucin
- Gross appearance: glistening & gelatinous with a firm consistency

➤ **Papillary carcinoma**

- Usually occurs in the 7th decade of life
- More common in nonwhite ♀.
- **defined by papillae with fibrovascular stalks and multilayered epithelium.**

➤ **Tubular carcinoma**

- Usually occurs during perimenopausal or early menopausal periods.
- Microscopically: haphazard array of small, randomly arranged tubular elements is seen.
- Well-differentiated type of infiltrating ductal cancer
- Favorable diagnosis

➤ **Invasive lobular carcinoma**

- **Histopath:** small cells with rounded nuclei, inconspicuous nucleoli, and scant cytoplasm; (+) intracytoplasmic mucin, which may displace the nucleus (**signet-ring cell carcinoma**).
- frequently **multifocal, multicentric, and bilateral**.
- Hard to detect mammographically

- **Diagnosis of breast cancer**

➤ **Mammography:**

- **Views:**
 - Craniocaudal (CC) view: medial aspect of the breast; permits greater breast compression
 - mediolateral oblique (MLO) view: images the greatest volume of breast tissue & upper outer quadrant and the axillary tail of Spence
 - Features suggestive of breast cancer:
 - solid mass +/- stellate features
 - asymmetric thickening of breast tissues
 - clustered microcalcifications
 - presence of fine, stippled calcium in & around a suspicious lesion is suggestive of breast cancer; occurs in 50% of nonpalpable cancers.
 - **Mimickers of breast ca mammographically: radial scars, fibromatosis, granular cell tumor and fat necrosis** (surgical excision is indicated for these lesions, owing to their resemblance to ca)
 - % reduction in mortality for women after screening mammography.
 - Recommendations:
 - normal-risk women at 20 yo → breast examination every 3 years
 - at age 40 yo → annual breast examination / mammography
 - **false (-)/(+) rate: 10%**

➤ **Ductography**

- Indication: is nipple discharge, (particularly when bloody)
- Intraductal papillomas are seen as small filling defects surrounded by contrast media
- Ca: may appear as irregular masses or as multiple intraluminal filling defects

➤ **Ultrasonography**

- Ideal for younger patients (because of tendency to have denser breasts – can affect results if mammography is used)
- Useful for resolving equivocal mammographic findings, defining cystic masses, and demonstrating the echogenic qualities of specific solid abnormalities.
- breast cysts: well circumscribed, with smooth margins and an echo-free center
- features of benign breast masses: smooth contours, round or oval shapes, weak internal echoes, and well-defined margins.
- Features of breast ca: irregular walls but may have smooth margins with acoustic enhancement.
- does not reliably detect lesions that are 1cm.

- **Breast cancer staging**

- Clinically based
- tumor size correlates with the presence of axillary lymph node metastases
- **The single most important predictor of 10- and 20-year survival rates in breast cancer is the number of axillary lymph nodes involved with metastatic disease.**

Table 52. TNM breast cancer staging

T	N	M
T1: <2cm	N1: suspicious mobile axillary nodes	M1: (+) lung, liver or bone involvement
T2: 2-5 cm	N2: matted or fixed axillary nodes	
T3: >5cm	N3: ipsilateral internal mammary nodes	
T4: (+) chest wall & direct skin involvement		

- (+) supraclavicular nodes: stage III disease (not stage IV as formerly classified)

- **Treatment for breast cancer**

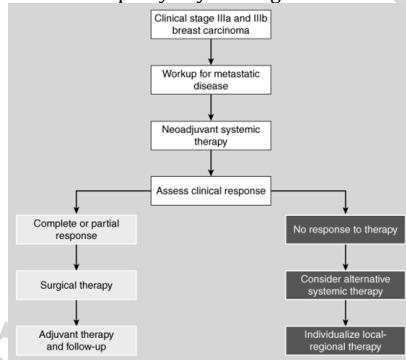
- Treatment is dependent on the stage at diagnosis
- **Early invasive breast cancer (stage I, IIa, IIb)**
 - Lumpectomy +/- RT (breast conservation sx) is an acceptable tx option since survival rates are comparable to total mastectomy.
 - However, recurrence ↑er in the lumpectomy with no RT stage I and II breast cancer.
 - **CI to breast conservation sx:**
 - prior RT to the breast or chest wall
 - involved surgical margins or unknown margin status after re-excision
 - multicentric disease
 - scleroderma or lupus erythematosus.
 - **If clinically negative nodes but with T1-T2 primary ca → perform sentinel LN dissection**
 - **If (+): perform axillary lymph node dissection** should be performed.
 - Adjuvant chemotherapy is indicated for node-positive cancers, >1 cm, and node-negative cancers of >0.5 cm when adverse prognostic features (blood vessel or lymph vessel invasion, high nuclear grade, high histologic grade, HER-2/neu overexpression, and negative hormone receptor status).
 - Tamoxifen therapy: women with hormone receptor (+) cancer that are >1 cm.

- HER-2/neu expression is determined for node (-) breast ca
 - Trastuzumab: medication for HER-2/neu (-)
 - doxorubicin, cyclophosphamide, & paclitaxel: medication for HER-2/neu (+) & node (+) breast cancer.

➤ **Advanced local regional breast cancer (stage IIIa or IIIb)**

- Surgery (MRM) + adjuvant RT + CT (neoadjuvant)
 - Role of CT: maximize distant disease-free survival
 - Role of RT: maximize local-regional disease-free survival.
 - If stage IIIA ca: neoadjuvant (preoperative) CT → reduce the size of the primary ca & permit breast-conserving surgery.

Figure 29. Treatment pathway for stage IIIa & IIIb cancer



➤ **Distant metastases (stage IV)**

- Not anymore curative but may prolong survival

- **Breast cancer prognosis**

➤

- 5 year survival rate
 - Stage I: 94%
 - stage IIA: 85%
 - stage IIB: 70%
 - stage IIIA: 52%
 - stage IIIB: 48%
 - stage IV: 18%

- **surgical techniques in breast cancer tx**

- **sentinel LN dissection:** used to assess the regional LN in women with early breast ca who are clinically node negative by PE & imaging studies
- **breast conservation therapy (BCT)**
 - if stage 0, I & II, BCT is preferable to total mastectomy (with equivalent survival rates)
- **mastectomy and axillary dissection**
 - **simple mastectomy:** removes all breast tissue, the nipple-areola complex, skin & level I LN
 - **Modified radical mastectomy:** removes all breast tissue, the nipple-areola complex, skin, & level I and level II LN.
 - **preserves pectoralis major**, pectoralis minor, level III LN & medial (anterior thoracic) pectoral nerve
 - **complications**
 - **most frequent:** Seromas beneath the skin flaps or in the axilla
 - **injury to the long thoracic nerve (affects serratus anterior) → winging of scapula**
 - **lymphatic fibrosis** → painless, slow progressive swelling of the involved arm
 - **injury to the axillary vein** → sudden painful early postoperative swelling of the involved arm (due to acute thrombosis as the collateral

- channels do not have the chance to develop → acute and painful)
- o **injury to the thoracodorsal vascular pedicle** → ischemic loss of the entire latissimus dorsi flap utilized for reconstruction
- o **injury to the medial pectoral pedicle** → progressive atrophy of the pectoralis muscle
- o **injury to the 2nd intercostals brachiocephalic nerve** → hypesthesia of the upper inner aspect of the ipsilateral arm
- **Halsted radical mastectomy:** removes all breast tissue and skin, the nipple-areola complex, the pectoralis major and pectoralis minor muscles & the level I, II, and III LN.

- Non surgical breast cancer tx

- **RT**
 - **Adjuvant RT after mastectomy → decrease local recurrence rates but will not prolong survival**
 - o Indicated for those with high risk for local recurrence: large tumors, skin involvement, > 4 axillary LN involved
- **Chemotherapy**
 - Adjuvant chemotherapy
 - Indicated if node (-) tumor >1cm that are ER (-)
 - Neoadjuvant chemotherapy
 - Neoadjuvant endocrine therapy
 - Tamoxifen: indicated if node (-) tumor >1cm that are ER (+)
 - Herceptin: (+) her2/neu

- **breast cancer in pregnancy**

- occurs in 1 of every 3000 pregnant ♀
- TX:
 - MRM: 1st & 2nd trimesters of pregnancy
 - lumpectomy with axillary node dissection: 3rd trimester
 - adjuvant RT: after delivery.

- **male breast cancer**

- <1% of all breast cancers occur in men
- preceded by gynecomastia in 20% of men.
- associated with radiation, estrogen tx, testicular feminizing syndromes, and Klinefelter's syndrome (XXY)
- usual types of cancer: DCIS, infiltrating ductal ca
- Overall, men do worse because of the advanced stage of their ca (stage III or IV) at the time of diagnosis and poorer prognosis. But stage for stage, the results of treatment are similar to those in women.

G. special clinical situations

a. nipple discharge

- **suggestive of cancerous lesion:** spontaneous, unilateral, localized to a single duct, present in women 40 years of age, bloody, clear, serous, or associated with a mass.
- **Suggestive of a benign condition:** bilateral, multiductal in origin, occurs in women 39 years of age, or is milky or blue-green.
 - Consider prolactin-secreting pituitary adenomas (↑ serum prolactin levels, Optic nerve compression, visual field loss, & infertility)

b. Cystosarcoma phyllodes tumor

- Resembles a giant fibroadenoma
- Can occur in benign and malignant forms
- gross appearance: classical leaf-like (phyllodes) appearance; greater cellular activity than fibroadenoma
- **metastasis is usually vascular** and no axillary LN involvement is expected.

- tx:
 - if benign → total excision with 2-3 cm margin
 - if malignant → total mastectomy w/o axillary LN dissection; if small → wide excision with 2cm margin is acceptable
 - if large → mastectomy.
 - Follow up is important due to high local recurrence rate

c. Inflammatory breast cancer ☺

- variant of infiltrating ductal ca
- characterized by the skin changes of brawny induration, erythema with a raised edge, and edema or peau d'orange (hence the name inflammatory) + breast mass
- appearance is due to a **dermal lymphatic invasion**

REVIEW QUESTIONS

1. a 58 yo woman presents with chronic, erythematous, oozing, eczematoid rash involving the left nipple and areola. There are no breast masses palpable, and her mammogram is normal. Which of the following recommendations is appropriate?
 - a. Referral to a dermatologist
 - b. Oral vitamin E and topical aloe and lanolin
 - c. Biopsy
 - d. Non allergenic brassiere
 - e. Standard treatment that includes breast conservation

Answer: C

This is a case of **Paget's disease of the breast**. It is a case of primary ductal carcinoma that secondarily invades the epithelium of the nipple and areola. Biopsy of any chronic nipple rash is mandatory and will show the distinctive pagetoid cells. Because of the possible invasion of the tumor on the underlying rich lymphatics of the nipple areolar complex, mastectomy is usually indicated. In selected cases, breast conservation therapies can also be employed.

2. If patient with metastatic breast ca is ER (+), which of the following statements are appropriate?
 - a. Bilateral oophorectomy
 - b. Antiestrogen drugs (tamoxifen)
 - c. Hypophysectomy
 - d. Adrenalectomy
 - e. Aromatase inhibitor

Answer: A,B,E

Patients with high ER & PR levels (based on immunohistochemical stains) have better prognosis compared to those with zero or low levels. The most common hormonal manipulation is estrogen withdrawal, usually with a receptor-blocking agent (**tamoxifen**). However, **bilateral oophorectomy** in premenopausal women is still considered a reasonable option. Surgical **hypophysectomy & adrenalectomy** were at one point considered forms of hormonal manipulation, but are now being replaced by "medical adrenalectomy" in the form of **anastrazole**, which inhibit the production of adrenal steroids and conversion of androgens to estrogens in the adrenal gland and peripherally. The aromatase inhibitors are beneficial only in postmenopausal women.

3. a 39 year old woman presents with an ill-defined 2 cm mass in the outer quadrant of her breast. Mammography shows very dense tissue but no discrete lesion. Ultrasound examination shows a solid lesion. An ultrasound-guided fine needle aspiration (FNA) is performed, and the aspirate is plated, fixed, and sent to the laboratory for cytologic study. A highly cellular

monomorphic pattern is seen, with poorly cohesive intact cells, nuclear "crowding" with a variation in nuclear size, radial dispersion and clumping of the chromatin, and prominent nucleoli. Which of the following management choices is/are appropriate?

- MRM
- Reassuring the patient that the process is benign
- Lumpectomy, sentinel lymph node biopsy and irradiation
- Excision of a fibroadenoma with narrow margins
- Lumpectomy and sentinel lymph node biopsy without irradiation

Answer: A,C

Aspiration biopsy with a 22 gauge needle is an effective and safe way of assessing palpable breast lesions. Performing the aspiration under ultrasound guidance ensures that the lesion has been sampled thoroughly while under direct vision. Although a smaller volume of tissue is obtained than the core needle biopsy, FNA frequently yields results that may be equal to core biopsy if read by an experienced cytopathologist. A **fibroadenoma** would show *broad sheets of cohesive cells with nuclei that are uniform in size and shape. The chromatin pattern would be finely granular and large numbers of bare nuclei would be present. The cytologic findings described in this question is diagnostic of carcinoma.* Appropriate management, therefore, includes either a modified radical mastectomy or lumpectomy, axillary evaluation by either a sentinel lymph node biopsy or an axillary nodal dissection, and whole-breast irradiation.

HEAD and NECK: BENIGN CONDITIONS & TUMORS

- Risk factors for tumors of head and neck
- Anatomy of Oral cavity
- Cancer of the Lip
- Cancer of the Tongue
- Tumors of Alveolus/gingiva
- Anatomy of pharynx
- Tumors of Nasopharynx
- Tumors of Oropharynx
- Tumors of Hypopharynx/cervical esophagus
- Anatomy Larynx
- Benign conditions of the Larynx
- Laryngeal Carcinoma
- Neck and associated conditions
- Salivary gland tumors
- Thyroid and associated conditions

A. RISK FACTORS FOR TUMORS OF HEAD AND NECK

- **tobacco & alcohol: most common preventable risk factors associated with head and neck CA.**
- betel nut chewing
- reverse smoking
- **HPV 16 and 18.**
- UV light exposure (for lip CA)
- Patients with H&N CA are predisposed to the development of a 2nd tumor within the aerodigestive tract.
 - **presentation of a new-onset dysphagia, unexplained weight loss, or chronic cough/hemoptysis must be assessed thoroughly in patients with a history of prior treatment for a head and neck cancer**
 - ex. If (+) primary malignancy of oral cavity oropharynx → secondary malignancy at cervical esophagus; (+) primary malignancy at larynx → secondary malignancy at lungs

- **Synchronous neoplasm:** a 2nd 1^o tumor detected within 6 months of the diagnosis of the initial primary lesion
- **Metachronous tumor:** detection of a 2nd 1^o lesion more than 6 months after the initial.
- Initial evaluation of patients with primary CA of H&N: "panendoscopy."

B. ANATOMY OF ORAL CAVITY

- Borders:
 - Anterior: vermillion border of the lip
 - Superior: hard-palate/soft-palate junction
 - Inferior: circumvallate papillae
 - Lateral: anterior tonsillar pillars
- The oral cavity includes **lips, alveolar ridges, oral tongue, retromolar trigone, floor of mouth, buccal mucosa, and hard palate.**
- Regional metastatic spread of lesions of the oral cavity is to the lymphatics of the **submandibular and the upper jugular region (levels I, II, and III) ⊕**
- **Majority of tumors in the oral cavity are squamous cell carcinoma (>90%)**

C. CANCER OF THE LIP

- most commonly seen old people (50-70 years old) with fair complexion
- Risk factors: prolonged exposure to sunlight, fair complexion, immunosuppression, and tobacco use.
- **Most common location: lower lip (88 to 98%)**, upper lip (2 to 7%) & oral commissure (1%).
- Predominantly **squamous cell CA**
- Basal cell carcinoma presents more frequently on the upper lip than lower.
- Clinical findings:
 - ulcerated lesion on the vermillion or cutaneous surface.
 - **(+) paresthesia in the area of lesion: mental nerve involvement.**
- unfavorable prognosticating factors: perineural invasion, involvement of maxilla/mandible, upper lip or commissure involvement, regional lymphatic metastasis, and age younger than 40 years at onset.
- **primary echelon of nodes at risk is in the submandibular and submental regions**
- Tx:
 - T1 & T2 ($\leq 4\text{cm}$): Surgery = RT
 - T3 & T4: surgical excision with histologic confirmation of tumor-free margins + postop RT
 - Prophylactic supraomohyoid neck dissection should be considered for patients with tumors greater than 4 cm, desmoplastic tumor & (+) perineural invasion
 - **Realignment of the vermillion border during the reconstruction and preservation of the oral commissure** (when possible) are important principles in attempting to attain an acceptable cosmetic result.
- **Prognosis is most favorable for all H&N CA**

D. CANCER OF THE TONGUE

- muscular structure with overlying **nonkeratinizing squamous epithelium.**
- Posterior border: circumvallate papillae
- **Tongue cancer**
 - Same risk factors with other H&N CA
 - Associated with **plummer-vinson syndrome** (cervical dysphagia, IDA, atrophic oral mucosa, brittle spoon finger nails)
 - Clinical findings: ulcerations or as exophytic masses
 - The regional lymphatics of the oral cavity are to the **submandibular space and the upper cervical lymph nodes**
 - Involvement of lingual nerve → ipsilateral paresthesias
 - Involvement of hypoglossal nerve → deviation of tongue on protrusion + fasciculations → atrophy
 - most common location: lateral and ventral surfaces

- if base of the tongue → advanced stage and poorer prognosis
- tx:
 - Surgical treatment of small (T1-T2) primary tumors is wide local excision with either primary closure or healing by secondary intention.
 - If base of tongue → Partial glossectomy with supraomohyoid dissection if N0 or MRND if N(+)

E. TUMORS OF ALVEOLUS/GINGIVAL

- Because of the tight attachment of the alveolar mucosa to the mandibular and maxillary periosteum, treatment of lesions of the alveolar mucosa frequently requires resection of the underlying bone.
- Diagnosis for alveolar or gingival cancer
 - **Panorex:** demonstrate gross cortical invasion
 - **CT:** imaging subtle cortical invasion
 - **MRI:** demonstrates invasion of the medullary cavity
- Tx for alveolar or gingival cancer
 - If minimal bone invasion: mandibular resection
 - If (+) medullary cavity invasion: segmental mandibulectomy

F. ANATOMY OF PHARYNX

- three regions:
 - nasopharynx
 - extends from the posterior nasal septum and choana to the skull base
 - includes fossa of rossenmuller, Eustachian tube orifices (torus tuberosus) and adenoid pad
 - bilateral regional metastatic spread in this area is common
 - Lymphadenopathy of the **posterior triangle (level V)** of the neck should provoke consideration for a nasopharyngeal primary
 - Oropharynx:
 - Includes tonsillar region, base of tongue, soft palate, and posterolateral pharyngeal walls
 - Regional lymphatic drainage for oropharyngeal lesions frequently occurs to the **upper and lower cervical lymphatics (levels II, III, IV)** + Retropharyngeal metastatic spread
 - hypopharynx.
 - extends from the vallecula to the lower border of the cricoid posterior and lateral to the larynx.
 - includes pyriform fossa, the postcricoid space, and posterior pharyngeal wall.
 - Regional lymphatic spread is frequently **bilateral** and to the **mid- and lower cervical lymph nodes (levels III, IV)**

G. TUMORS OF THE NASOPHARYNX

- Tumors arising in the nasopharynx are usually of **squamous cell origin**
- **Most common nasopharyngeal malignancy in the pediatric age group: lymphoma**
- **Risk factors for nasopharyngeal carcinoma: area of habitation & ethnicity (southern China, Africa, Alaska, and in Greenland Eskimos.), EBV infection, & tobacco use.**
- Symptoms:
 - **nasal obstruction, posterior (level V) neck mass, epistaxis, headache, serous otitis media with hearing loss, and otalgia.**
 - Cranial nerve involvement is indicative of skull base extension and advanced disease.
- Lymphatic spread occurs to the **posterior cervical, upper jugular, and retropharyngeal nodes.**
- **Bilateral regional metastatic spread is common.**
- Diagnosis for nasopharyngeal CA:
 - flexible or rigid fiber-optic endoscope
 - CT with contrast: determining bone destruction

- MRI: assess for intracranial and soft-tissue extension.
- Tx: chemoradiation

H. TUMORS OF THE OROPHARYNX

- Direct extension of tumors from the oropharynx into these lateral tissues may involve spread into the parapharyngeal space
- histology of the majority of tumors in this region is **squamous cell carcinoma**
- (+) asymmetrical enlargement of the tonsils and tongue base → think lymphoma
- Clinical findings: ulcerative lesion, exophytic mass, tumor fetor, muffled or "hot potato" voice (large tongue base tumors), Dysphagia, weight loss, Referred otalgia, (tympanic branches of CN IX & CN X), Trismus (involvement of the pterygoid musculature), ipsilateral or bilateral nontender cervical lymphadenopathy
- LN metastasis from oropharyngeal cancer **most commonly occurs in the subdigastric area of level II.** Others - levels III, IV, & V, retropharyngeal & parapharyngeal LN.
 - Bilateral metastases: seen in tumors originating from the tongue base and soft palate; if found in these areas → associated with poor survival
- Tx:
 - Options: surgery, primary radiation alone, surgery with postoperative radiation, & combined chemotherapy with radiation therapy.
 - If tongue base crossing middling: do total glossectomy with possible total laryngectomy
 - Tumors of the oropharynx tend to be **radiosensitive.**

I. TUMORS OF THE HYPOPHARYNX/CERVICAL ESOPHAGUS

- Squamous cancers of the hypopharynx frequently present at an advanced stage, hence are associated with poorer survival rates
- Clinical findings: neck mass, muffled or hoarse voice, referred otalgia, **progressive dysphagia to solids → liquids**, weight loss.
- **Invasion of the larynx by direct extension → vocal cord paralysis (if unilaterally affected) → airway compromise (if bilaterally affected)**
- Diagnosis:
 - flexible fiber-optic laryngoscopy
 - CT and/or MRI imaging: check for regional metastases (paratracheal and upper mediastinal lymph nodes)
- Tx:
 - T1: RT
 - T2 & T3: chemoradiation
 - Larynx-preserving surgical procedures: only if the tumor must not involve the apex of the pyriform sinus, vocal cord mobility must be unimpaired, and the patient must have adequate pulmonary reserve.
 - Bilateral neck dissection is frequently indicated given the elevated risk of nodal metastases found with these lesions

J. ANATOMY OF LARYNX:

- divided into 3 regions:
 - **supraglottis:** epiglottis (lined by stratified, nonkeratinizing squamous epithelium), false vocal cords (lined by pseudostratified, ciliated respiratory epithelium), medial surface of the aryepiglottic folds, and the roof of the laryngeal ventricles
 - has a **rich lymphatic network**, which accounts for the **high rate of bilateral spread of metastatic disease**
 - **glottis:** the true vocal cords, anterior and posterior commissure, and the floor of the laryngeal ventricle.

- **Subglottis:** extends from below the true vocal cords to the cephalic border of the cricoid within the airway
 - pseudostratified, ciliated respiratory epithelium
 - Glottic and subglottic lesions: spread to the cervical chain, paralaryngeal and paratracheal LN

K. BENIGN CONDITIONS OF THE LARYNX

Recurrent respiratory papillomatosis (RRP)

- (+)HPV 6 & 11
- larynx is the most frequently involved site
- presents in early childhood, secondary to viral acquisition during vaginal delivery.
- Sx: hoarseness, airway compromise
- Diagnosis: endoscopy
- Tx: operative microlaryngoscopy with excision or laser ablation
- High tendency to recur

Laryngeal granulomas

- typically occur in the posterior larynx on the arytenoid mucosa
- risk factors: reflux, voice abuse, chronic throat clearing, endotracheal intubation, and vocal fold paralysis
- Sx: pain often with swallowing (less commonly: vocal changes)
- Dx: fiber-optic laryngoscopy, voice analysis, laryngeal electromyography (EMG), and pH probe testing.
- Tx: voice rest, voice retraining therapy, and antireflux therapy.

Reinke's edema

- located at the superficial lamina propria due to injury to the capillaries that exist in this layer, with subsequent extravasation of fluid.
- Sx: rough, low-pitched voice.
- Risk factors: smoking, laryngopharyngeal reflux, hypothyroidism, and vocal hyperfunction.

Vocal cord cyst

- may occur under the laryngeal mucosa (in regions containing mucous-secreting glands)
- Cysts of the vocal cord may be difficult to distinguish from vocal polyps
- Diagnosis: video stroboscopic laryngoscopy
- Tx: Large cysts of the supraglottic larynx are treated by marsupialization with cold steel or a CO₂ laser.

Vocal cord paralysis

- **most commonly is iatrogenic** (s/p thyroid, parathyroid, carotid, or cardiothoracic surgeries)
- can be **secondary to malignant processes** in the lungs, thyroid, esophagus, thoracic cavity, skull base, or neck.
- Sx: presents with hoarseness and "breathy" voice
 - If superior laryngeal nerve is affected → demonstrate aspiration secondary to diminished supraglottic sensation
 - left vocal cord is more commonly involved secondary to its longer course of the recurrent laryngeal nerve (RLN) on that side
 - if anterior surgical approaches to the cervical spine are performed → right RLN is at an increased risk (courses more laterally to the tracheoesophageal complex)

L. LARYNGEAL CARCINOMA

- Suspect if with (+) Hx of smoking & complaint of a change in vocal quality
- are primarily **squamous cell carcinoma**
- Sx:
 - **supraglottic larynx:** chronic sore throat, dysphonia ("hot potato" voice), dysphagia, or a neck mass secondary to regional metastasis,
 - Referred otalgia or odynophagia is encountered with advanced supraglottic cancers.**

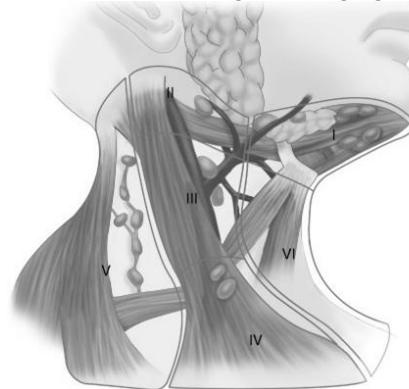
- **Glottic larynx:** hoarseness (early; because only a small degree of change is required to produce hoarseness), Airway obstruction (late), Decreased vocal cord mobility may be caused by direct muscle invasion or involvement of the RLN.
- **Subglottic larynx:** vocal cord paralysis (usually unilateral) and/or airway compromise (are relatively uncommon).
- Lymphatic drainage:
 - **Supraglottic larynx:** subdigastric and superior jugular nodes
 - **glottic and subglottic larynx:** prelaryngeal node (the Delphian node), the paratracheal nodes, and the deep cervical nodes
 - glottic cancers have limited lymphatic access → regional nodal metastases is low
- treatment
 - early stage glottis & supraglottic cancer: RT
 - small glottic cancers: Partial laryngectomy
 - supraglottic cancers w/o arytenoid or vocal cord extension: supraglottic laryngectomy
 - advanced tumors with extension : total laryngectomy + postop RT
 - Subglottic cancers: total laryngectomy.

M. NECK AND ASSOCIATED CONDITIONS ☺

- differential diagnosis of neck masses is dependent on its location and patient's age
 - pediatric age: think congenital or inflammatory conditions
 - adult + risk factors: rule out malignancy
 - in terms of location, think about patterns of drainage

Lymphatic drainage of the neck is divided into 7 levels.

Figure 30. levels of the neck bearing LN bearing regions



1. Level I: submental & submandibular nodes

- **Level Ia:** the submental nodes; medial to the anterior belly of the digastric muscle bilaterally, symphysis of mandible superiorly, and hyoid inferiorly
- **Level Ib:** the submandibular nodes and gland; posterior to the anterior belly of digastric, anterior to the posterior belly of digastric, and inferior to the body of the mandible

2. Level II: upper jugular chain nodes

- **Level IIa:** jugulodigastric nodes; deep to sternocleidomastoid (SCM) muscle, anterior to the posterior border of the muscle, posterior to the posterior aspect of the posterior belly of digastric, superior to the level of the hyoid, inferior to spinal accessory nerve (CN XI)
- **Level IIb:** submuscular recess; superior to spinal accessory nerve to the level of the skull base

3. Level III: middle jugular chain nodes

- inferior to the hyoid, superior to the level of the cricoid, deep to SCM muscle from posterior border of the muscle to the strap muscles medially

4. Level IV: lower jugular chain nodes

- inferior to the level of the cricoid, superior to the clavicle, deep to SCM muscle from posterior border of the muscle to the strap muscles medially

jaime is the best!!

5. Level V: posterior triangle nodes

- **Level Va:** lateral to the posterior aspect of the SCM muscle, inferior and medial to splenius capitis and trapezius, superior to the spinal accessory nerve
- **Level Vb:** lateral to the posterior aspect of SCM muscle, medial to trapezius, inferior to the spinal accessory nerve, superior to the clavicle

6. Level VI: anterior compartment nodes

- inferior to the hyoid, superior to suprasternal notch, medial to the lateral extent of the strap muscles bilaterally

7. Level VII: paratracheal nodes

- inferior to the suprasternal notch in the upper mediastinum

Patterns of spread from primary tumor sites:

- **oral cavity and lip:** levels I, II, and III
 - **Skip metastases may occur with oral tongue cancers** such that involvement of nodes in level III or IV may occur **without involvement of higher echelon nodes (levels I & II).**
- **oropharynx, hypopharynx, and larynx:** levels II, III, and IV.
- **nasopharynx and thyroid:** **level V** nodes in addition to the jugular chain nodes.
- **nasopharynx, soft palate, and lateral and posterior walls of the oropharynx and hypopharynx:** Retropharyngeal lymph nodes
- **hypopharynx, cervical esophagus, and thyroid:** paratracheal nodal compartment + upper mediastinum nodes (level VII).
- **advanced tumors of the glottis with subglottic spread:** Delphian node

Neck dissections:

- **Radical neck dissection (RND or CRILE method):** removes levels I to V of the cervical lymphatics + SCM + internal jugular vein + CN XI
- **Modified radical neck dissection (MRND) or functional neck dissection:** Any modification of the RND that preserves nonlymphatic structures (i.e., CN XI, SCM muscle, or internal jugular vein)
 - **Comparable to RND in controlling regional metastasis** with superior functional results
- **Selective neck dissection (SND):** any modification of the RND that preserves lymphatic compartments normally removed in RND
 - **Also comparable to RND in controlling regional metastasis with superior functional results**
 - Types:

1. supraomohyoid neck dissection

- used with oral cavity malignancies
- removes lymph nodes in levels I to III

2. lateral neck dissection

- used for laryngeal malignancies
- removes lymph nodes in levels II through IV

3. posterolateral neck dissection

- Used for thyroid cancer
- removes lymph nodes in levels II to V
- if clinically N(+) necks: do MRND or RND or SND (only if limited N1 disease)
- if (+) extracapsular spread, perineural invasion, vascular invasion, and the presence of multiple involved lymph nodes are noted → neck dissection of choice + Adjuvant RT +/- chemoRT

Parapharyngeal space masses

- Is a potential space, shaped like an inverted pyramid spanning the skull base to the hyoid.
- Contents of the prestyloid space: parotid, fat, and lymph nodes.

- **Contents of poststyloid compartment:** CNs IX to XII, the carotid space contents, cervical sympathetic chain, fat, and lymph nodes.

- Tumors in this space can **produce displacement of the lateral pharyngeal wall medially into the oropharynx, dysphagia, cranial nerve dysfunction**, Horner's syndrome, or vascular compression.

- Tumors found in the parapharyngeal space:
 - 40 to 50% of the tumors are of **salivary gland origin**
 - usually arising **anterior to the styloid process**

- 20 to 25% of tumors are of **neurogenic origin** such as paragangliomas (glomus vagale, carotid body tumor), schwannomas, and neurofibroma
 - usually arising **posterior to the styloid process**
 - angiography has a role if the tumor in question is located posterior to the styloid process
 - if a paraganglioma is suspected → request for a 24-hour urinary catecholamine
- 15% represent **LN metastases & 1^o lymphoma**

Benign neck masses ☺

Thyroglossal duct cyst

- most commonly encountered congenital cervical anomalies
- represents the **vestigial remainder of the tract of the descending thyroid gland** from the foramen cecum, at the tongue base, into the lower anterior neck during fetal development.
- An embryological anomaly wherein there is **failure of obliteration of the midline pharyngeal diverticulum** during thyroid descent
- present as a **midline or paramedian cystic mass adjacent to the hyoid bone**.
- After an upper respiratory infection, the cyst may enlarge or become infected.
- Tx: removal of the cyst, the tract, and the central portion of the hyoid bone (**Sistrunk procedure**) + portion of the tongue base up to the foramen cecum.
- Check 1st for normal thyroid tissue in the lower neck area & if ensure that patient is euthyroid
- 1% of thyroglossal duct cysts contain **cancer (85% is usually papillary)**

Congenital branchial cleft anomalies:

- remnants are derived from the branchial cleft apparatus that persists after fetal development.
- **1st branchial cleft:** EAC & parotid gland.
- **2nd branchial cleft:** courses between the internal and external carotid arteries and proceeds into the tonsillar fossa
- **3rd branchial cleft:** courses posterior to the common carotid artery, ending in the pyriform sinus region.

Dermoid cysts

- midline masses and represent trapped epithelium originating from the embryonic closure of the midline.

N. SALIVARY GLAND TUMORS

- Majority of neoplasms are benign
- **Most common gland involved: parotid gland** (85% of all salivary gland neoplasms)
- **Most common benign tumor of the salivary gland: pleomorphic adenoma**
- **Most common malignant epithelial neoplasm of salivary gland: mucoepidermoid carcinoma**
- **2nd most common malignant epithelial neoplasm of salivary gland:** Adenoid cystic carcinoma, which has a propensity for neural invasion,
- **Risk of malignancy depending on location: minor salivary gland > submandibular, sublingual > parotid gland**
- Symptoms suggestive of malignancy: pain, paresthesias, facial nerve weakness, skin invasion, fixation to the

- mastoid tip and trismus (invasion of the masseter or pterygoid muscles)
- Tx:
 - If benign neoplasm: do surgical excision
 - If parotid: minimal surgical procedure for neoplasms of the parotid is superficial parotidectomy with preservation of the facial nerve.
 - **Most frequently injured nerve in parotid surgery: greater auricular nerve** (not facial nerve); if transected, will produce numbness of the lower portion of the auricle & periauricular skin
 - **If the auriculotemporal nerve is injured → Frey's syndrome (postoperative gustatory sweating)**
 - If malignant: do en bloc removal of the involved gland with preservation of all nerves unless directly invaded by tumor.
 - if **parotid tumor arising from the lateral lobe**: superficial parotidectomy with ecpreservation of CN VII is indicated.
 - If the tumor extends into the **deep lobe of the parotid**: a total parotidectomy with nerve preservation is performed
 - If **submandibular involvement**: en bloc resection of the gland and submental and submandibular lymph nodes.
 - **Nerves at risk for a submandibular gland removal: lingual and hypoglossal nerve**
 - **Postoperative radiation treatment** plays an important role in the treatment of salivary malignancies. **The presence of extraglandular disease, perineural invasion, direct invasion of regional structures, regional metastasis, and high-grade histology are all indications for radiation treatment**

O. THYROID AND ASSOCIATED CONDITIONS

Important facts about Thyroid anatomy:

- **Weight of a normal thyroid gland: 20 g** ☺
- **pyramidal lobe** is present in about 50% of patients
 - in disorders resulting in thyroid hypertrophy (e.g., Graves' disease, diffuse nodular goiter, or lymphocytic thyroiditis), the pyramidal lobe usually is enlarged and palpable
- enveloped by a **loosely connecting fascia**
- **thyroidea ima artery**: arises directly from the aorta or innominate in 1-4% of individuals
- **ligament of berry**: posteromedial suspensory ligament; has a close relationship with the recurrent laryngeal nerve
- **inferior thyroid artery crosses recurrent laryngeal nerve (RLN)** ☺, necessitating identification of the RLN before ligation
- **RLNs innervate all the intrinsic muscles of the larynx, except the cricothyroid muscles, which are innervated by the external laryngeal nerves** ☺
 - **Injury to one RLN**: paralysis of the ipsilateral vocal cord (lie in the paramedian or the abducted position)
 - **Injury to Bilateral RLN**: airway obstruction, necessitating emergency tracheostomy, or loss of voice.
 - **Most common position of right RLN**: posterior to the inferior thyroid artery
- **Injury to the internal branch of the superior laryngeal nerve** → aspiration.
- **Injury to the external branch of the superior laryngeal nerve** → inability to tense the ipsilateral vocal cord and hence difficulty "hitting high notes"

- **Loop of galen**: where the pharyngeal branches of the recurrent laryngeal nerve communicate with the branches of the superior laryngeal nerve. **Maybe injured when dissecting or ligating the superior thyroid artery**
- Regional lymph nodes include pretracheal, paratracheal, perithyroidal, RLN, superior mediastinal, retropharyngeal, esophageal, and upper, middle, and lower jugular chain nodes.
- **Histology**:
 - the thyroid is divided into lobules that contain 20 to 40 follicles
 - Each follicle is lined by **cuboidal epithelial cells**
 - **C cells or parafollicular cells**: secrete the hormone calcitonin.

Evaluation of patients with thyroid disease:

Tests of thyroid function:

1. **Serum TSH**
 - normal: 0.5 – 5 μ U/mL
 - only test necessary in most patients with thyroid nodules that clinically appear euthyroid
 - serum TSH levels reflect the ability of the anterior pituitary to **detect free T₄ levels**
 - ultrasensitive TSH assay: most sensitive and most specific test for the diagnosis of hyperthyroidism and hypothyroidism
2. **Total T₄**
 - normal: T₄: 55 – 150 nmol/L
 - Total T₄ levels reflect the output from the thyroid gland
 - Not suitable as a general screening test
 - Increased levels seen in hyperthyroid patients, elevated Tg levels secondary to pregnancy, estrogen/progesterone use or congenital diseases
 - Decreased levels seen in hypothyroid patients, decreased Tg levels secondary to anabolic steroid use and protein losing disorders (i.e. nephrotic syndrome)
 - These individuals maybe euthyroid if their free T₄levels are normal
3. **Total T₃**
 - Normal: 1.5 – 3.5 nmol/L
 - Total T₃ levels reflect peripheral thyroid hormone metabolism
 - Not suitable as a general screening test
 - Measurement of total T₃ levels is important for clinically hyperthyroid patients with normal T₄ levels → think T₃ thyrotoxicosis
4. **Free T₄**
 - Normal: 12 – 28 pmol/L
 - Measures the biologically active hormone
 - Not performed as a routine screening test in thyroid disease
 - Its utility is in detecting early hyperthyroidism in which total T₄ levels maybe normal but free T₄ levels are raised
 - Refetoff syndrome: end-organ resistance to T₄ wherein free T₄ are increased and TSH levels are normal
5. **Free T₃**
 - normal: 3 – 9 pmol/L
 - most useful in the diagnosis of early hyperthyroidism in which levels of free T₃ and T₄ rise before total T₃ and T₄
6. **Serum TRH**
 - used for the evaluation of pituitary TASH secretory function
7. **Thyroid antibodies**
 - include anti-Tg, antimicrosomal, or anti-TPO and TSI
 - anti-Tg & anti-TPO antibody levels: elevated if with autoimmune thyroiditis
 - can be elevated in Hashimoto's, Graves', multinodular goiter & thyroid neoplasms

8. Serum Thyroglobulin

- amount is increased in destructive processes of the thyroid gland (thyroiditis) or overactive states (graves' or toxic multinodular goiter)
- **most important use is for the monitoring of differentiated thyroid cancer recurrence, after total thyroidectomy and RAI ablation**
 - elevated anti-Tg antibodies can interfere with the accuracy of Tg levels and should always be measured when interpreting Tg levels.

9. Serum Calcitonin

- normal: 0-4 pg/mL basal
- secreted by C cells
- function: lower serum calcium
- **sensitive marker for medullary thyroid cancer**

Thyroid Imaging:

1. Radionuclide imaging

Types:

1. iodine 123 (¹²³I)

- emits low dose radiation
- t 1/2 : 12 – 14 hours
- **used to image lingual thyroids or goiter**

2. iodine 131 (¹³¹I)

- higher dose radiation exposure because of longer t 1/2
- t 1/2 : 8 to 10 days
- used to screen and treat patients with differentiated thyroid cancers for metastatic disease

**** Cold: trap less radioactivity compared to the surrounding gland, risk of malignancy is higher in cold lesions (20%) compared to hot lesions (<5%)**

**** Hot: trap more radioactivity, therefore, with increased acitivity**

3. technetium Tc 99m pertechnetate (^{99m}Tc)

- this isotope is taken up by the mitochondria
- shorter t 1/2, therefore, less radiation exposure
- **sensitive for nodal metastases**

4. F-fluorodeoxyglucose PET scan

- used to screen for **metastases in patients with thyroid cancer in whom other imaging studies are negative**.
- May show clinically occult lesions

2. Ultrasound

- excellent noninvasive imaging study of thyroid gland
- no radiation exposure
- useful for the **evaluation of thyroid nodules**, distinguishing cystic from solid ones, size, multicentricity and cervical lymphadenopathy

3. CT/MRI

- useful for the **evaluation of extent of large, fixed or substernal goiters and their relationship to the airway and vascular structures**

Developmental abnormalities:

Thyroglossal duct cyst (see Neck)

Lingual thyroid

- **failure of the median thyroid anlage to descend normally**
- may appear as reddish brown mass at the base of the tongue
- **may be the only thyroid tissue present (hence, if surgical tx is warranted, evaluation of normal thyroid tissue in the neck must be carried out 1st)**
- Intervention becomes necessary for obstructive symptoms such as choking, dysphagia, airway obstruction, or hemorrhage or if suspicious for malignancy
- Tx: administration of exogenous **ORAL thyroid hormone** to suppress thyroid-stimulating hormone

(TSH) and **radioactive iodine (RAI) ablation** followed by hormone replacement.

Ectopic thyroid

- Normal thyroid tissue in aberrant locations (esophagus, trachea and anterior mediastinum)

Pyramidal lobe

- The distal end of the atrophied thyroglossal duct that connects to the thyroid, projecting up to the isthmus, lying just to the left or right of the midline.

Benign thyroid disorders

Hyperthyroidism

Grave's disease

- **autoimmune disease with a strong familial predisposition, female preponderance (5:1), and peak incidence between the ages of 40 to 60 years.**
- **Most common cause of hyperthyroidism in North America**
- characterized by **thyrotoxicosis, diffuse goiter, and extrathyroidal conditions** including ophthalmopathy, dermopathy (pretibial myxedema), thyroid acropachy
- hallmark: **thyroid-stimulating antibodies stimulate the thyrocytes to grow and synthesize excess thyroid hormone**
- associated with other autoimmune conditions (ex. type I DM, Addison's disease, pernicious anemia, and myasthenia gravis)
- Macroscopic appearance: **diffusely and smoothly enlarged, increase in vascularity**
- Microscopic appearance: hyperplastic gland, minimal colloid present
- Clinical features:
 - **Hyperthyroid Sx:** heat intolerance, ↑ sweating, ↑ thirst, ↑ weight loss despite adequate caloric intake
 - **adrenergic excess:** palpitations, nervousness, fatigue, emotional lability, hyperkinesis, and tremors
 - **most common GI symptom: diarrhea**
 - can also develop amenorrhea, decreased fertility, and an increased incidence of miscarriages
- PE: facial flushing, warm & moist skin, Tachycardia, atrial fibrillation, fine tremor, muscle wasting, and proximal muscle group weakness with hyperactive tendon reflexes
- 50% of patients → ophthalmopathy
 - lid lag (**von Graefe's sign**)
 - spasm of the upper eyelid
 - revealing the sclera above the corneoscleral limbus (**Dalrymple's sign**)
 - prominent stare
- 1 to 2% of patients → dermopathy (deposition of glycosaminoglycans leading to thickened skin in the pretibial region and dorsum of the foot)

Diagnostic: suppressed TSH with or without an elevated free T₄ or T₃ level.

- If eye signs are present, other tests are generally not needed.
- ¹²³I uptake and scan: elevated uptake, with a diffusely enlarged gland, confirms the diagnosis

Treatment:

➤ Antithyroid drugs:

- **propylthiouracil** (PTU, 100 to 300 mg three times daily) or **methimazole** (10 to 30 mg three times daily, then once daily – because it has a longer half t 1/2)
 - MOA: inhibits the organic binding of iodine and the coupling of iodothyrosines (mediated by TPO).
 - PTU also inhibits the peripheral conversion of T₄ to T₃
 - **Most patients have improved symptoms in 2 weeks and become euthyroid in about 6 weeks.**

- **IMPORTANT SIDE EFFECT OF PTU: AGRANULOCYTOSIS**
- **Propranolol** is the most commonly prescribed medication in doses of about 20 to 40 mg four times daily for control of adrenergic symptoms
- **RAI:** most often used in older patients with small or moderate-sized goiters, those who have relapsed after medical or surgical therapy, and those in whom antithyroid drugs or surgery are contraindicated.
 - Absolute CI: women who are pregnant or breastfeeding
 - Relative contraindications:
 - young patients (i.e., especially children and adolescents)
 - those with thyroid nodules
 - those with ophthalmopathy
- **Surgery:**
 - Patients should be rendered euthyroid before operation
 - **Lugol's iodide solution or saturated potassium iodide** generally is administered beginning 7 to 10 days preoperatively (three drops twice daily) **to reduce vascularity of the gland and decrease the risk of precipitating thyroid storm.**
 - **Indications for Total or near-total thyroidectomy:** Patients with coexistent thyroid cancer, and those who refuse RAI therapy or have severe ophthalmopathy or have life-threatening reactions to antithyroid medications (vasculitis, agranulocytosis, or liver failure)

✓ REMEMBER:

How would you know if there is an undiagnosed hyperthyroid problem intraoperatively?

Increased vascularity → increased bleeding in a sedated patient ☺

Toxic multinodular goiter

- Symptoms and signs of hyperthyroidism are similar to Graves' disease, **but extrathyroidal manifestations are absent**
- Possible presence of cervical compressive symptoms
- Diagnosis:
 - suppressed TSH level and elevated free T₄ or T₃ levels.
 - RAI uptake also is increased, showing multiple nodules with increased uptake
 - Treatment: subtotal thyroidectomy

Toxic adenoma (Plummer's disease)

- Hyperthyroidism from a single hyperfunctioning nodule typically occurs in younger patients
- PE: solitary thyroid nodule without palpable thyroid tissue on the contralateral side
- RAI: "hot" nodule
- rarely malignant.
- Tx: Surgery (lobectomy and isthmusectomy on the affected side) is preferred to treat young patients and those with larger nodules.

Thyroid storm

- hyperthyroidism + fever, central nervous system agitation or depression, cardiovascular dysfunction due to infection, surgery, trauma or **amiodarone** administration.
- Tx: ICU, Beta blockers, Oxygen supplementation, Fever reduction, fluids, hemodynamic support, PTU, Corticosteroids (to prevent adrenal exhaustion and block hepatic thyroid hormone conversion)

Acute (*suppurative*) thyroiditis

- more common in children and often is preceded by an upper respiratory tract infection or otitis media.
- It is characterized by severe neck pain radiating to the jaws or ear, fever, chills, odynophagia, and dysphonia.
- Complications: systemic sepsis, tracheal or esophageal rupture, jugular vein thrombosis, laryngeal chondritis, and perichondritis or sympathetic trunk paralysis
- ***Streptococcus* and anaerobes account for about 70% of cases**
- Diagnosis: leukocytosis on blood tests and FNAB for Gram's stain, culture, and cytology.
- Tx: parenteral antibiotics & drainage of abscesses.

Subacute (*de quervain's*) thyroiditis

- strong association with the HLA-B35 haplotype.
- Self-limiting painful thyroiditis most commonly occurs in 30- to 40-year-old women
- characterized by the sudden or gradual onset of neck pain, which may radiate toward the mandible or ear.
- **History of a preceding upper respiratory tract infection often can be elicited.**
- The gland is enlarged, exquisitely tender, and firm.
- Diagnosis: TSH is decreased, and T_g, T₄, and T₃ levels are elevated (during the early phase)
- tx: symptomatic; NSAIDs are used for pain relief (steroids may be indicated in more severe cases)

Hashimoto's thyroiditis (chronic thyroiditis)

- autoimmune process leads to destruction of thyrocytes by autoantibodies, which lead to complement fixation and killing by natural killer cells
- Antibodies directed against three main antigens—Tg (60%), TPO (95%), the TSH-R (60%), and, less commonly, to the sodium/iodine symporter (25%)
- more common in women (male:female ratio 1:10 to 20) between the ages of 30 and 50 years old.
- **The most common presentation is that of a minimally or moderately enlarged firm granular gland discovered on routine PE or the awareness of a painless anterior neck mass**
- Gross appearance: mildly enlarged, pale, gray-tan cut surface that is granular, nodular, and firm.
- microscopic examination: the gland is diffusely infiltrated by small lymphocytes and plasma cells and occasionally shows well-developed germinal centers, follicles are lined by Hürthle or Askanazy cells
- **Dx: elevated TSH and the presence of thyroid autoantibodies usually confirm the diagnosis.**
- Tx: Thyroid hormone replacement therapy or surgery (if with compressive symptoms)

Reidel's thyroiditis

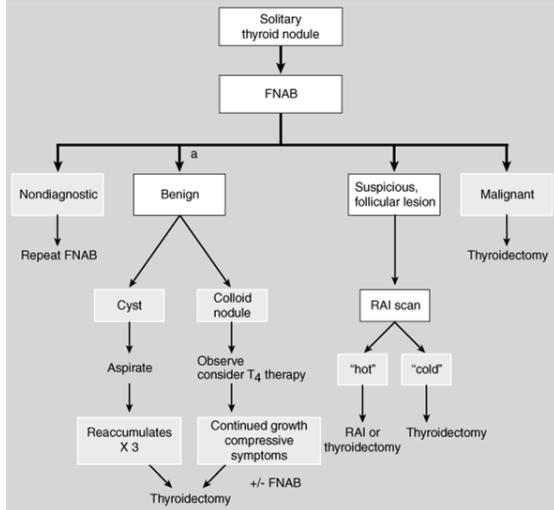
- characterized by the **replacement of all or part of the thyroid parenchyma by fibrous tissue**
- primary autoimmune etiology
- occurs predominantly in women between the ages of 30 to 60 years old.
- presents as a painless, hard anterior neck mass, which progresses over weeks to years to **produce symptoms of compression, including dysphagia, dyspnea, choking, and hoarseness.**
- Can result to hypothyroidism
- Associated with retroperitoneal fibrosis and sclerosing mediastinitis
- **PE: hard, "woody" thyroid gland with fixation to surrounding tissues.**
- Tx: surgery
 - Goal of surgery: to decompress the trachea by wedge excision of the thyroid isthmus and to make a tissue diagnosis

Solitary thyroid nodule

- History: time of onset (usually slow and indolent), change in size, and associated symptoms such as pain, dysphagia, dyspnea, choking, hoarseness (secondary to malignant involvement of the RLNs)
- **Risk factors for malignancy:**
 1. exposure to ionizing radiation

- 2. (+) FH of thyroid and other malignancies associated with thyroid cancer
- 3. Men > women
- 4. Children > adults
- PE: nodules that are hard, gritty, or fixed to surrounding structures (if malignant)
- Diagnosis:

Figure 31. Management of a solitary thyroid nodule ☺



➤ **FNAB: single most important test in the evaluation of thyroid masses: 1st diagnostic test ordered in a patient with a solitary thyroid nodule**

- Results: benign – cysts & colloid nodules (65%), suspicious – follicular or hurthle cell neoplasms (20%), malignant (5%), and nondiagnostic (10%)
- false-positive results is about 1%
- false-negative results occur in approximately 3%
- a negative FNAB does not rule out CA
 - if suspicious result, the diagnosis of malignancy relies on demonstrating capsular or vascular invasion, features that cannot be determined via FNAB.

- **RAI scan:**
- Single, cold, solid nodule → malignant
 - Multiply, Hot, cystic → benign
- **Labs:**
- **TSH:** expect euthyroid
 - **Tg levels:** useful for patients who have undergone total thyroidectomy for thyroid cancer & for serial evaluation of patients undergoing nonoperative management of thyroid nodules.
 - **Serum calcitonin:** obtained in patients with MTC or a family history of MTC or MEN2
 - **RET oncogene mutations:** All patients with MTC should be tested for *RET* oncogene mutations and have a 24-hour urine collection with measurement of levels of vanillylmandelic acid (VMA), metanephrine, and catecholamine to rule out a coexisting **pheochromocytoma**.
- Ultrasound: helpful for detecting nonpalpable thyroid nodules, differentiating solid from cystic nodules, and identifying adjacent lymphadenopathy

- Tx:
- Malignant tumors are treated by thyroidectomy
 - Simple thyroid cysts resolve with aspiration; if persists after 3 attempts at aspiration → unilateral thyroid lobectomy is recommended.
 - Lobectomy is recommended for cysts >4 cm in diameter or complex cysts with solid and cystic components
 - Colloid nodule → observe with serial ultrasound and Tg measurements.

Thyroid cancer

Papillary CA

- **80% of all thyroid malignancies in iodine-sufficient areas**
- **predominant thyroid cancer in children and individuals exposed to external radiation.**
- occurs more often in women, 2:1
- symptoms of locally advanced disease: Dysphagia, dyspnea, and dysphonia
- Diagnosis:
 - FNAB of the thyroid mass or lymph node.
 - Complete neck UTZ: to evaluate the contralateral lobe and for LN metastases in the central and lateral neck compartments.
- **The most common sites are lungs, followed by bone, liver, and brain.**
- **Spread via lymphatic route**
- Gross appearance: hard and whitish and remain flat on sectioning with a blade, macroscopic calcification, necrosis, or cystic change may be apparent.
- Microscopically:
 - papillary projections - a mixed pattern of papillary and follicular structures
 - pure follicular pattern (follicular variant).
 - **Cells are cuboidal with pale, abundant cytoplasm, large nuclei that may demonstrate "grooving," and intranuclear cytoplasmic inclusions (Orphan Annie nuclei)☺**
 - **Psammoma bodies☺:** microscopic, calcified deposits representing clumps of sloughed cells, also may be present
 - Multifocality: associated with an increased risk of cervical nodal metastases
 - Other variants: tall cell, insular, columnar, diffuse sclerosing, clear cell, trabecular, and poorly differentiated types.
 - are generally associated with a worse prognosis.

- Tx:

- If less than 1.5 cm: lobectomy + isthmusectomy
- If multicentric: near total or total thyroidectomy
- (+) cervical node mets: MDRD
 - **patients with papillary thyroid CA have an excellent prognosis with a >95% 10-year survival rate.**
 - **Age is the most important prognostic factor in determining long term survival**

Follicular CA

- account for 10% of thyroid cancers
- occur more commonly in iodine-deficient areas.
- Women have a higher incidence of follicular cancer, with a female-to-male ratio of 3:1
- usually present as solitary thyroid nodules, occasionally with a history of rapid size increase, and long-standing goiter.
- In <1% of cases, follicular cancers may be hyperfunctioning, leading patients to present with signs and symptoms of thyrotoxicosis.
- **Spread via hematogenous route, hence their spread is more distant, than regional**
- **Most common site of distant metastasis: lung & bone**
- Diagnosis:
 - FNAB shows follicular type → must do lobectomy to demonstrate capsular or vascular invasion (criteria for malignancy)
- Microscopically: follicles are present, but the lumen may be devoid of colloid.
- Tx:
 - If follicular lesion → thyroid lobectomy + isthmusectomy because at least 80% of these patients will have benign adenomas.
 - older patients with follicular lesions >4 cm: total thyroidectomy
 - if (+) thyroid CA: do Total thyroidectomy
 - (+) cervical node mets: MDRD

- mortality from follicular thyroid cancer is approximately 15% at 10 years and 30% at 20 years.
- Poor long-term prognosis: age over 50 years old at presentation, tumor size >4 cm, higher tumor grade, marked vascular invasion, extrathyroidal invasion, and distant metastases at the time of diagnosis.

Hurtle cell CA

- account for approximately 3% of all thyroid malignancies
- **considered to be a subtype of follicular thyroid cancer.**
- Cannot be diagnosed by FNAB.
- Microscopically: hurthle cells (**variable enlargement, hyperchromatic nuclei and granular cytoplasm**)
- Difference from follicular CA:
 - multifocal
 - bilateral (about 30%)
 - usually do not take up RAI (about 5%)
 - more likely to metastasize to local nodes (25%)
 - associated with a higher mortality rate (about 20% at 10 years)
 - higher recurrence rate
- Same management with follicular neoplasms
- If (+) for hurthle malignancy: perform total thyroidectomy + routine central neck (level 6) node removal or MDRD when lateral neck nodes are palpable.

Medullary thyroid CA (MTC)

- accounts for about 5% of thyroid malignancies
- arises from the **parafollicular or C cells** of the thyroid usually located **superolaterally** in the thyroid lobes (usual site of MTC)
- female-to-male ratio is 1.5:1
- Most patients present between 50 and 60 years old
- Most MTCs occur sporadically.
 - Occur singly
 - unilateral (80%)
 - no familial predisposition
- approximately 25% occur within the spectrum familial MTC - **MEN2A** (pheochromocytoma + parathyroid hyperplasia), and **MEN2B** (pheochromocytoma + neuromas)
 - due to germline mutations in the **RET proto-oncogene**
 - encodes for tyrosine-kinase receptor in the cell membrane
 - RET protein is expressed in tissues derived from embryonic nervous and excretory systems
 - present at a younger age
 - multicentric
 - **(+)** **C cell hyperplasia: premalignant lesion**
- clinical features:
 - present with a neck mass that may be associated with palpable cervical lymphadenopathy (15 to 20%).
 - Pain or aching is common
 - dysphagia, dyspnea, or dysphonia – already invasive
 - diarrhea – indicates metastatic disease (due to increased intestinal motility and impaired intestinal water and electrolyte flux)
 - 2 to 4% of patients develop Cushing's syndrome as a result of ectopic production of adrenocorticotrophic hormone (ACTH)
- tumor markers: **calcitonin (diagnostic, most sensitive tumor marker)**, CEA (better predictor of prognosis), calcitonin gene-related peptide, histaminades, prostaglandins E₂ and F₂ & serotonin.
- Microscopically:
 - Heterogenous
 - Cells are polygonal or spindle shaped
 - infiltrating neoplastic cells separated by collagen and amyloid
 - **presence of amyloid is a diagnostic finding**
- Diagnosis:

- history, physical examination, raised serum calcitonin, or CEA levels, and FNAB cytology of the thyroid mass
- **all new patients with MTC should be screened for RET point mutations, pheochromocytoma, and HPT.** If (+) carrier, perform total thyroidectomy

- Tx:

- Total thyroidectomy + bilateral central node dissection (level 6) because of high incidence of multicentricity
- If (+) pheochromocytoma → manage this 1st
- If with palpable cervical nodes or involved central neck nodes: ipsilateral or bilateral MDRD
- If tumors >1 cm, ipsilateral prophylactic modified radical neck dissection is recommended because >60% of these patients have nodal metastases. → if ipsilateral nodes are positive → do contralateral node dissection
- Postoperative Follow-Up: annual measurements of calcitonin and CEA levels
- Prognosis:
 - 10-year survival rate is approximately 80% but decreases to 45% in patients with lymph node involvement.
 - best in patients with non-MEN familial MTC, followed by those with MEN2A
 - **Prognosis is the worst (survival 35% at 10 years) in patients with MEN2B.**

Anaplastic CA

- approximately 1% of all thyroid malignancies
- **the most aggressive of thyroid malignancies**
- Women are more commonly affected
- present in the 7th & 8th decade of life
- Clinical features:
 - Presents as a **long-standing neck mass, which rapidly enlarges and may be painful.** Associated symptoms such as dysphonia, dysphagia, and dyspnea are common.
 - Lymph nodes usually are palpable at presentation.
- Gross appearance: firm and whitish in appearance.
- **Microscopically: characteristic giant and multinucleated cells.** with marked heterogeneity are seen (spindle shaped, polygonal, or large, multinucleated cells)
- Tx: if resectable mass → surgery will only give small improvement in survival
- Prognosis: 6 months

Thyroid Lymphoma

- <1% of thyroid malignancies
- Most common: non-Hodgkin's B-cell type.
- develop in patients with chronic lymphocytic thyroiditis.
- present with a rapidly enlarging neck mass that is often painless.
- may present with acute respiratory distress.
- Tx:
 - **CT(CHOP—cyclophosphamide, doxorubicin, vincristine, and prednisone) + RT**
 - Thyroidectomy and nodal resection: for alleviation of airway obstructive symptoms who do not respond quickly to the above regimens or who have completed the regimen before diagnosis.
- The overall 5-year survival rate is about 50%; patients with extrathyroidal disease have markedly lower survival rates.

Thyroid surgeries:

Total thyroidectomy: dissection and removal of all visible thyroid tissue bilaterally, which usually reveals the entrance of the recurrent laryngeal nerve as they enter the ligament of berry

Near total thyroidectomy: complete hemithyroidectomy and isthmusectomy; most of the contralateral side is removed but a remnant is left to prevent damage to parathyroid glands

Subtotal thyroidectomy: removes all visible thyroid tissue except for a rim of thyroid tissue bilaterally to ensure parathyroid viability and avoids damage to the recurrent laryngeal nerve

REVIEW QUESTIONS

1. Regarding salivary gland tumors, which one of the following statements is true?
 - a. The majority of malignant salivary gland tumors arise in the parotid gland
 - b. Most parotid neoplasms are malignant
 - c. Fine needle aspiration biopsy is recommended for all suspected salivary gland malignancies
 - d. Minor salivary gland tumors occur most commonly in the floor of the mouth

Answer: A

The likelihood of a given tumor's being malignant is lowest in the parotid gland (approximately 20%), followed by the submandibular salivary gland (approximately 50%) and sublingual glands (nearly 100%). However, because more than 75% of all salivary gland tumors occur in the parotid gland, the parotid gland accounts for the majority of the malignant salivary gland tumors. The diagnostic evaluation of a salivary gland mass depends on the location and clinical scenario. FNAB is not indicated for all parotid tumors, since a tissue diagnosis does not change the treatment plan for a patient with a small, mobile mass clearly within the gland. When the location is uncertain, the history suggests the possibility of metastatic disease, or the tumor size or location indicates a difficult facial nerve dissection, FNAB may be helpful. Biopsy, usually a punch or excisional biopsy, should be performed for suspected minor salivary gland tumors, the most common site of which is the palate, usually at the junction of the hard and soft palate. Like FNAB, imaging studies (CT or MRI) should be used when they are likely to augment the clinical assessment of staging and affect treatment planning.

2. A 40 year-old woman comes to the clinician's office with a thyroid mass, which is confirmed on FNA and UTZ to be unilateral, 3.2 cm follicular neoplasm. She has been completely asymptomatic. What will the next intervention be?
 - a. Total thyroidectomy
 - b. Hemithyroidectomy or isthmusectomy
 - c. Excisional biopsy
 - d. Core-needle biopsy
 - e. Thyroid suppression via T₃ or T₄ analogues

Answer: A, B

The presence of a follicular neoplasm as confirmed by FNA mandates further evaluation, since FNA does not provide enough information about tissue architecture to differentiate between a benign follicular adenoma and a follicular carcinoma. Vascular or capsular invasion confirms the presence of carcinoma. The management of small, unilateral follicular lesions is controversial (total versus hemithyroidectomy with frozen section). However, lesions larger than 4 cm should be treated with total thyroidectomy, since multicentricity becomes more common as tumor size increases. Total thyroidectomy also facilitates the effectiveness of postoperative radioactive iodine, since no residual thyroid tissue remains to serve as a sink for the radioisotope.

3. During a total thyroidectomy for papillary cancer, the clinician observes an intact recurrent laryngeal nerve on the right side and a completely transected nerve on the left, with both ends in view. What

should management of this patient at this point entail?

- a. Complete the operation and evaluate the vocal cords postoperatively via flexible bronchoscopy
- b. Perform intraoperative flexible bronchoscopy to evaluate vocal cords
- c. Repair the nerve using 8.0 monofilament sutures
- d. None of the above

Answer: D

If the recurrent laryngeal nerve is injured or transected during an otherwise uncomplicated operation, it should be repaired using loupes or an operating microscope to visualize the field, and 8.0 or 9.0 monofilament sutures to anastomose the cut ends of the nerves. There is no role for flexible bronchoscopy either intraoperatively or postoperatively unless there is uncertainty about the injury or the function of the contralateral nerve.

ESOPHAGUS

- A. Diagnostic tests for esophageal function
- B. GERD
- C. Diaphragmatic hernia
- D. Schatzki's ring
- E. Scleroderma of esophagus
- F. Zenker's diverticulum
- G. Achalasia
- H. Diffuse and segmental esophageal spasm
- I. Nutcracker esophagus
- J. Hypertensive LES
- K. Esophageal diverticulum
- L. Esophageal perforation
- M. Mallory weiss syndrome
- N. Caustic injury
- O. Esophageal carcinoma

A. DIAGNOSTIC TESTS FOR ESOPHAGEAL FUNCTION

Tests to detect structural abnormalities

1. Barium swallow

- 1st diagnostic test in patients with suspected esophageal disease (with full assessment of stomach and duodenum)
- can reveal anatomic problems
- if patient complains of dysphagia and no obstructing lesion seen in barium swallow → use a barium-impregnated marshmallow, barium-soaked bread or barium hamburger
- will bring out the functional disturbance in the esophageal transport that can be missed when liquid barium is used.

2. Endoscopic evaluation

- endoscopy is indicated in patients complaining of dysphagia even with a normal radiographic study

Tests to detect functional abnormalities

1. manometry

- indicated when a motor abnormality of the esophagus is considered on the basis of complaints (dysphagia, odynophagia, or noncardiac chest pain) and barium swallow and endoscopy does not show a structural abnormality
- essential tool in preoperative evaluation of patients before antireflux surgery

Tests to detect increased exposure to gastric juice

1. 24 hour ambulatory pH monitoring

- most direct method of measuring increased esophageal exposure to gastric juice (not reflux)

- sensitivity and specificity of 96%
 - **gold standard for the diagnosis of GERD**
- 2. radiographic exposure of gastroesophageal reflux**
- radiographic demonstration of spontaneous regurgitation of barium into the esophagus in the upright position is a reliable indicator that reflux is present
 - note: failure to see this does not indicate absence of disease
- B. GERD**
- Clinical features:
 1. **Heartburn:** substernal burning-type discomfort, beginning in the epigastrium and radiating upward.
 -It is often aggravated by meals, spicy or fatty foods, chocolate, alcohol, and coffee
 -worse in the supine position
 2. **Regurgitation:** effortless return of acid or bitter gastric contents into the chest, pharynx, or mouth; highly suggestive of foregut pathology
 -severe at night when supine or when bending over
 -secondary to either an incompetent GEJ
 -explains the associated pulmonary symptoms, including cough, hoarseness, asthma, and recurrent pneumonia.
 2. **Dysphagia:** most specific symptom of foregut disease; sensation of difficulty in the passage of food from the mouth to the stomach
 3. **Chest pain**
 - primary cause of GERD: **permanent attenuation of the collar sling musculature, with a resultant opening of the gastric cardia and loss of the high-pressure zone as measured with esophageal manometry**
 - characteristics of a defective sphincter
 - 1. LES with a mean resting pressure of less than 6 mmHg
 - 2. overall sphincter length of <2 cm
 - 3. **intra-abdominal sphincter length of <1 cm (most important consideration affecting the competence of the GE jxn)**
 - diagnosis:
 - **24 hour pH monitoring (gold standard): most sensitive for the detection of reflux**
 - Endoscopic examination: assessing anatomic damage produced by reflux (esophagitis, ulceration and strictures) & for ruling out CA
 - **Grading of esophagitis**
 - Grade I: small circular nonconfluent erosions
 - Grade II: presence of linear erosions lined with granulation tissue that bleeds easily when touched
 - Grade III: linear erosions coalesce into a circumferential loss of the epithelium; cobblestone mucosa
 - Grade IV: (+) stricture
- **absence of esophagitis above a stricture suggest chemical induced injury or neoplasm as a cause.
- i.
- Manometric studies: rule out motility DO
- Complications:
1. **Metaplastic (Barrett's Esophagus)**
 - condition whereby the tubular esophagus is lined with columnar epithelium rather than squamous epithelium
 - occurs in 10 to 15% of patients with GERD
 - end stage of natural Hx of GERD
 - **hallmark: presence of intestinal goblet cells in esophageal epithelium (intestinal metaplasia)**
 - endoscopically: difficulty visualizing the squamocolumnar junction at its normal location & appearance of redder mucosa than normally seen in lower esophagus
 - earliest sign for malignant degeneration: severe dysplasia or intramucosal adenocarcinoma
- antireflux surgery is an excellent means of long-term control for most patients
 - one third of all patients with BE present with malignancy
 - should undergo surveillance with biopsy every 2 years
 - if (+) low grade dysplasia, increase frequency to 6 months
- 2. Esophageal Adenocarcinoma**
- Most important etiologic factor in its development is barrett's esophagus
- 3. Respiratory symptoms**
- LERD
 - Adult-onset asthma
 - Idiopathic pulmonary fibrosis
- Treatment:
- Medical:
 - Uncomplicated GERD: 12 weeks of empiric treatment of antacid
 - Persistent sx: PPIs or H2 antagonists
 - **A structurally defective LES is the most important factor predicting failure of medical therapy**
 - They don't respond to medical therapy well; candidates for anti-reflux surgery
 - Lifestyle changes: elevate the head of the bed during sleep; avoid tight-fitting clothing; eat small, frequent meals; avoid eating the nighttime meal immediately prior to bedtime; and avoid alcohol, coffee, chocolate, and peppermint (which are known to reduce resting LES pressure)
 - Surgical
 - **Nissen fundiplication:** a abdominal or thoracic approach using a 360 degree circumferential wrap of the gastric fundus
 - **Belsey operation:** difficult to learn, performed through the chest, involves placement of 2 layers of placating structures between the gastric fundus and lower esophagus with subsequent creation of 280 degree anterior gastric wrap and posterior approximation of the crura
 - **Hill operation:** approach is through the abdomen, posterior approximation of the crura followed by anchoring of the posterior and anterior aspects of the GEJ to the median arcuate ligament adjacent to the aorta, creating a 180 degree gastric wrap
 - **Collis gastroplasty:** esophageal lengthening procedure
 - **Angelchik prosthesis:** horseshoe shape silastic device placed around the distal esophagus, keeping this segment in the abdomen

✓ MUST KNOW

Principles of surgical therapy in reflux disease ☺

1. the operation should restore the pressure of the distal esophageal sphincter to a level twice the resting gastric pressure
2. the operation should place an adequate length of the distal esophageal sphincter in the positive-pressure environment of the abdomen by a method that ensures its response to changes in intra-abdominal pressure
3. the operation should allow the reconstructed cardia to relax on deglutition
4. the fundoplication should not increase the resistance of the relaxed sphincter to a level that exceeds the peristaltic power of the body of the esophagus
5. the operation should ensure that the fundoplication can be placed in the abdomen without undue tension, and maintained there by approximating the crura of the diaphragm above the repair

C. DIAPHRAGMATIC HERNIA

- Types:

1. **type I (sliding hernia)**

- upward dislocation of the cardia in the posterior mediastinum
 - **the phrenoesophageal ligament is stretched but intact**
 - most common
 - can evolve into a type III hernia
- 2. type II (rolling or paraesophageal or giant hiatal hernia)**
- upward dislocation of the gastric fundus alongside a normally positioned cardia
 - **defect in the phrenoesophageal membrane**
 - rare
 - more likely to occur in women (4:1)
- 3. type III (the combined sliding-rolling or mixed hernia)**
- upward dislocation of both the cardia and the gastric fundus; therefore
 - **the esophagogastric junction is in the mediastinum**
- 4. type IV: colon, herniates as well (in some classifications)**
- 5. intrathoracic abdomen**
- the end stage of type I and type II hernias occurs when the whole stomach migrates up into the chest by rotating 180° around its longitudinal axis, with the cardia and pylorus as fixed points
- **most common complications:**
- > occult GI bleeding from gastritis
 - > ulceration in the herniated portion of the stomach
 - > **gastric volvulus (surgical emergency): or Borchardt's triad** of pain, nausea with inability to vomit and inability to pass NGT
- **Diagnosis:**
- > **Barium esophagogram:** for diagnosis of paraesophageal hiatal hernia
 - > Fiber-optic esophagoscopy
 - Detection of pouch lined with gastric rugal folds lying 2 cm or more above the margins of the diaphragmatic crura (identified by having the patient sniff)
- Treatment: surgical
- > Important principles
 - Reduce the hernia contents
 - After reduction, excise the sac
 - The use of mesh can reduce recurrence rates of hernia is > than 8 cm
- D. SCHATZKI'S RING**
- thin submucosal circumferential ring in the lower esophagus at the squamocolumnar junction, often associated with a hiatal hernia.
 - probably an **acquired lesion** that can lead to stenosis from chemical-induced injury by pill lodgment in the distal esophagus, or from reflux-induced injury to the lower esophageal mucosa
 - **Symptoms:** brief episodes of dysphagia during hurried ingestion of solid foods.
 - **Treatment options:** dilation alone, dilation with antireflux measures, antireflux procedure alone, incision, and excision of the ring
- E. SCLERODERMA OF ESOPHAGUS**
- Scleroderma is a systemic disease accompanied by **esophageal abnormalities in approximately 80% of patients.**
 - onset of the disease is usually in the **third or fourth decade of life, occurring twice as frequently in women as in men.**
 - **Small vessel inflammation appears to be an initiating event, with subsequent perivascular deposition of normal collagen, which may lead to vascular compromise.**
 - Muscle ischemia due to perivascular compression has been suggested as a possible mechanism for the motility abnormality in scleroderma.
 - predominant feature at GI tract: smooth muscle atrophy.
 - Diagnosis:
- > **Manometrically:** observation of normal peristalsis in the proximal striated esophagus, with absent peristalsis in the distal smooth muscle portion
- > **Barium swallow:** dilated, barium-filled esophagus, stomach, and duodenum, or a hiatal hernia with distal esophageal stricture and proximal dilatation
- F. ZENKER'S DIVERTICULUM**
- most common esophageal diverticulum
 - classified as **false diverticulum**
 - clinical features: **dysphagia associated with the spontaneous regurgitation of undigested food, halitosis**, weight loss, chronic aspiration and repetitive respiratory infection
 - due to weakness of the cricopharyngeal muscle → weakness at the Killian's area
 - Diagnosis: Barium swallow (to exclude neoplasia or ulceration)
 - Treatment:
 - > Pharyngomyotomy: 2 cm or less
 - > Diverticulectomy/diverticuopexy: >2cm
- G. ACHALASIA**
- Characterized by complete absence of peristalsis in the esophageal body and failure of LES relaxation
 - **Classic triad of symptoms: dysphagia, regurgitation and weight loss;** also associated with nocturnal asthma and foul smelling esophageal contents
 - pathogenesis of achalasia is presumed to be a neurogenic degeneration, which is either idiopathic or due to infection.
 - Can be caused by T. cruzi which demonstrates destruction of smooth muscle myenteric auerbach's plexus
 - Diagnosis:
 - > Barium Esophagogram: dilated esophagus with a tapering or other wise known as "**bird's beak**"
 - > Manometric studies: failure of the LES to relax, progressive peristalsis in proximal esophagus (if late disease)
 - > Has a 10% chance of developing carcinoma due to prolonged mucosal irritation
 - Tx:
 - > **heller's myotomy** (surgical myotomy of the LES)
 - > goal of surgery: relieve functional obstruction at the LES
- H. DIFFUSE AND SEGMENTAL ESOPHAGEAL SPASM**
- characterized by **substernal chest pain and/or dysphagia.**
 - The LES in patients with DES usually shows a normal resting pressure and relaxation on swallowing
 - Diagnosis:
 - > **Manometric studies:** frequent occurrence of simultaneous waveforms and multipeaked esophageal contractions, which may be of abnormally high amplitude or long duration.
 - > Esophagogram: **corkscrew esophagus or pseudodiverticulosis**
- I. NUTCRACKER ESOPHAGUS**
- Other name: supersqueezes esophagus
 - **most common of the primary esophageal motility disorders**
 - characterized by peristaltic esophageal contractions with peak amplitudes greater than two SDs above the normal values (up to 400 mmHg)
 - Treatment in these patients should be aimed at the treatment of GERD
- J. HYPERTENSIVE LES**
- This disorder is characterized by an elevated basal pressure of the LES with normal relaxation and normal propulsion in the esophageal body.
 - Treatment: Myotomy of the LES may be indicated in patients not responding to medical therapy or dilation.
- K. ESOPHAGEAL DIVERTICULUM**

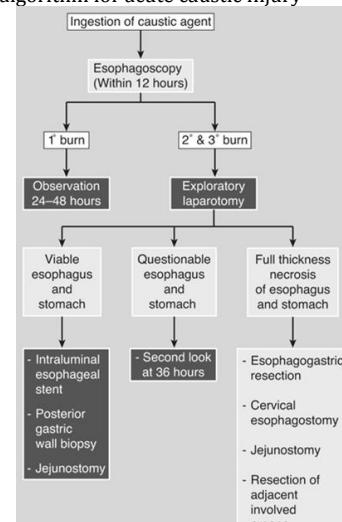
- Classification:
 - Location: proximal, mid, distal
 - Pathology
 - Pulsion: motor DO
 - Traction: inflammatory DO
 - **Epiphrenic diverticula:**
 - terminal 3rd of the thoracic esophagus & are usually found adjacent to the diaphragm
 - associated with distal esophageal muscular hypertrophy, esophageal motility abnormalities, and increased luminal pressure
 - considered as "pulsion" diverticula
 - classified as false diverticulum (pouch of mucosa that is protruding in the wall of the esophagus)
 - **Midesophageal or traction diverticula**
 - Classified as true diverticulum (composed of all layers of the esophageal wall)
 - noted in patients who had mediastinal LN involvement with tuberculosis, mediastinal lymphadenopathy, such as pulmonary fungal infections (e.g., aspergillosis), lymphoma, or sarcoid
- L. ESOPHAGEAL PERFORATION**
- true emergency.
 - **It most commonly occurs following diagnostic or therapeutic procedures (endoscopy).**
 - **Boerhaave's syndrome:** spontaneous perforation, Clinical features: chest pain (very striking and consistent symptom), fever, tachycardia, subcutaneous emphysema, dysphagia, dysnea
 - Diagnosis:
 - **contrast esophagogram with water soluble (like gastrografin) medium: (+) extravasation (diagnostic)**
 - chest xray: air or effusion in pleural space, mediastinal or cervical emphysema
 - treatment:
 - the incidence of mortality is related to the time interval between perforation and treatment; **hence the key to optimum management is early diagnosis.**
 - The most favorable outcome is obtained following **primary closure of the perforation within 24 hours, resulting in 80 to 90% survival.**
 - The most common location for the injury is the left lateral wall of the esophagus, just above the GEJ
 - non-operative management
 - usually follows an injury occurring during dilation of esophageal strictures or pneumatic dilations of achalasia
 - indications
 1. barium swallow must show the perforation to be contained within the mediastinum and drain well back into the esophagus
 2. mild symptoms
 3. minimal evidence of clinical sepsis
 - approach:
 - hyperalimentation
 - antibiotics
 - cimetidine: to decreased acid secretion, diminish pepsin activity

M. MALLORY WEISS SYNDROME

- Longitudinal tear in the mucosa of the GE junction
- Characterized by **acute upper GI bleeding** caused by **forceful vomiting and/or retching**
- Commonly seen in **alcoholics**
- arterial → massive
- mechanism: an acute increase in intra-abdominal pressure against a closed glottis in a patient with a hiatal hernia.
- Diagnosis:
 - requires a high index of suspicion (**the pattern of sudden upper GI bleeding following prolonged vomiting or retching is indicative**).

- Upper endoscopy: longitudinal fissures in the mucosa of the herniated stomach as the source of bleeding.
 - Treatment:
 - **bleeding will stop 90% of the time spontaneously with nonoperative management.**
 - Decompression
 - antiemetics
- N. CAUSTIC INJURY**
- Alkalies vs acids
 - **Alkalies dissolve tissue, and therefore penetrate more deeply (more serious)**
 - **acids cause a coagulative necrosis that limits their penetration**
 - The strength of esophageal contractions varies according to the level of the esophagus
 - weakest at the striated muscle-smooth muscle interface
 - slower clearance → allowing caustic substances to remain in contact with the mucosa longer → explains why the esophagus is preferentially and more severely affected at this level than in the lower portions.
 - **Phases of injury:**
 - acute necrotic phase:
 - lasting 1 to 4 days after injury
 - coagulation of intracellular proteins results in cell necrosis
 - living tissue surrounding the area of necrosis develops an intense inflammatory reaction.
 - ulceration and granulation phase:
 - 3 to 5 days after injury
 - Considered a quiescent period because symptoms seem to disappear
 - the superficial necrotic tissue sloughs, leaving an ulcerated, acutely inflamed base, and granulation tissue fills the defect left by the sloughed mucosa.
 - This phase lasts 10 to 12 days
 - **period that the esophagus is the weakest**
 - cicatrization and scarring
 - begins third week following injury.
 - previously formed connective tissue begins to contract, resulting in narrowing of the esophagus
 - **characterized by dysphagia**
 - It is during this period that efforts must be made to reduce stricture formation.
 - Clinical features: pain in the mouth and substernal region, hypersalivation, pain on swallowing, and dysphagia, **fever (strongly correlated with the presence of an esophageal lesion)**
 - Diagnosis: **early esophagoscopy** is advocated to establish the presence of an esophageal injury
 - To lessen the chance of perforation, the scope should not be introduced beyond the proximal esophageal lesion.
 - Treatment:

Figure 32. algorithm for acute caustic injury



O. ESOPHAGEAL CARCINOMA

- **Squamous carcinoma accounts for the majority of esophageal carcinomas worldwide.**
- Risk factors:
 - nitroso compounds in pickled vegetables and smoked meats
 - zinc & molybdenum deficiency
 - smoking (more squamous CA)
 - alcohol consumption (more squamous CA)
 - achalasia
 - lye strictures
 - tylosis (an autosomal dominant disorder characterized by hyperkeratosis of the palms and soles)
 - human papillomavirus.
 - Barrett's esophagus (more adenocarcinoma)
- **Most common presenting symptom: dysphagia** (already a late symptom)
- Diagnosis:
 - barium esophagogram → (if with lesion) → upper endoscopy
 - CT scan of chest and abdomen: delineate the tumor and detect distant pulmonary or hepatic metastasis
- Characteristics based on tumor location and treatment:
 - Cervical esophagus (proximal 1/3)
 - Almost always squamous carcinoma
 - Frequently unresectable because of early invasion of larynx, great vessels or trachea
 - Tx: stereotactic radiation with concomitant chemotherapy
 - thoracic esophagus (middle 1/3)
 - almost always squamous carcinoma with LN metastasis
 - tx: video assisted thoracic surgery (VATS) ± thoracotomy
 - distal 1/3 or near/at cardia
 - almost always adenocarcinoma
 - tx: curative resection requires cervical division of esophagus + >50% proximal gastrectomy
- Staging:
 - Stage 0: in situ, high-grade dysplasia, no LN mets
 - Stage I: invaded lamina propria
 - Stage IIA: invaded esophageal wall but not surrounding structures
 - Stage IIB: LN (+); primary tumor has only invaded submucosa or muscularis propria
 - Stage III: invaded the adventitia and surrounding structures (pericardium, pleura and aorta)
 - Stage IV: (+) metastasis
- Clinical factors that indicate advanced stage (and therefore exclude surgery for curative intent):
 - Horner's syndrome
 - Persistent spinal pain
 - Paralysis of diaphragm
 - Fistula formation
 - Malignant pleural effusion
- Treatment:
 - Surgery:
 - **Ivor lewis procedure:**
 - primarily for middle esophageal lesion; all LNs are removed en bloc with the lesser curvature of the stomach
 - most radical → highest number of complication rate
 - **Left thoracoabdominal approach**
 - excellent exposure of distal esophagus
 - **Transhiatal blunt resection:** resection of the thoracic esophagus from abdomen with subsequent pull-up of stomach and esophagogastric anastomosis in the neck
 - **Goes against the principle of en-bloc resection of cancer surgery**
 - **Minimized morbidity and mortality compared to the other procedures**

REVIEW QUESTIONS

1. a 4 year old child is brought to the ER 15 minutes after accidentally ingesting a drain cleaner. The child exhibits a hoarse voice and is stridorous. Which of the following apply?

- Laryngeal ulceration
- Instillation of vinegar into the stomach
- Immediate fiberoptic endoscopy
- tracheostomy

Answer: A & D

This is a case of caustic ingestion. Since the child already exhibits laryngeal and epiglottic edema, preservation of the airway must be the priority. Therefore, endoscopy is deferred.

2. A 50 year old healthy man is brought to the ER with retching followed by hematemesis.

- Treatment is by balloon tamponade
- Bleeding often stops spontaneously
- It is not caused by forceful vomiting
- There is air in the mediastinum
- Diagnosis is not made by endoscopic examination

Answer: B

This is a case of **Mallory-weiss tear**. The mechanism is similar to boerhave syndrome (postemetic esophageal rupture) in which there is associated perforation and vomiting against a closed cardia. It is diagnosed by endoscopic examination, and the bleeding usually stops spontaneously. Because the bleeding is arterial, a pressure tamponade (i.e. Sengstaken-blakemore tube) does not help and may lead to esophageal disruption. If bleeding does not stop, gastroscopy and oversewing of the bleeding point is the proper therapy, although nonsurgical alternatives, such as endoscopic injection of epinephrine and cautery have been attempted.

3. After diagnostic esophagoscopy, a patient complains of odynophagia and chest pain, but results of water-soluble contrast swallow are negative. Which of the following apply?

- Discharge the patient if ECG is normal.
- Use of barium in the chest is devastating
- Esophageal manometry should be performed immediately
- Repeat swallow with barium

Answer: D

Chest pain, fever, tachycardia, subcutaneous emphysema, dysphagia and dyspnea are typical of **esophageal perforation**. Perforation may result from iatrogenic operations, external trauma, primary esophageal disease or postemetic ("spontaneous") esophageal hypertension. The incidence of mortality from esophageal perforation is clearly related to the time interval between perforation and definitive treatment. Whenever perforation is suspected, a contrast study should be performed with water-soluble contrast material. However, if this study does not demonstrate the perforation, it should be repeated with barium. Although barium is contraindicated in the presence of colonic injuries because of the harmful effects of feces and barium, it does not cause a problem in the chest. Barium is more accurate than water in detecting esophageal leakage. Contrast studies are important not just for verifying esophageal rupture but also for documenting the level of injury, which has important implications for treatment.



STOMACH

- A. Anatomy
- B. Diagnostic tests for stomach
- C. Peptic ulcer disease
- D. Zollinger-Ellison syndrome
- E. Gastritis
- F. Stress ulcer
- G. Malignant neoplasms of the stomach
- H. Benign gastric neoplasms: polyps
- I. Gastric volvulus
- J. Postgastrectomy problems

A. ANATOMY

- Stomach is composed of 3 smooth muscle layers:
 - 1. **Outer longitudinal layer** – greater and lesser curvatures of the stomach
 - 2. **Middle circular** – pylorus
 - 3. **Inner oblique**
- Majority of parietal cells are in the **Body of the stomach**
- Largest artery to the stomach is the **left gastric artery** (from the celiac trunk)
- Gastric contraction is via the **vagus nerve** (primarily due to parasympathetic fibers) ☺
 - 1. The vagus nerves forms **LARP (left:anterior & right:posterior)** at the esophageal hiatus as it descends from the mediastinum
 - 2. **Anterior** branch of vagus: **nerves of Larterjet**
 - they send segmental branches to the **body of the stomach** before they terminate near the **angularis incisura** as the "crow's foot"
 - 3. **Posterior** branch: **Criminal nerve of Grassi (posterior fundus)**
 - easily missed during **truncal or highly selective vagotomy (HSV)**.
- **Gastric relaxation** is due to CCK, distention of duodenum and **presence of glucose in the duodenum**

✓ MUST KNOW

Atonic gastritis and abnormal distention and failure to empty of the stomach can occur in the postoperative patient due to electrolyte disturbances, hyperglycemia and uremia.

Gastric ulcers located in the PYLORUS are associated with increased gastric production (see below – Type II & III ulcers)

B. DIAGNOSTIC TEST FOR STOMACH

1. EGD

- patients with one or more of the alarm symptoms must undergo immediate upper endoscopy

Table 53. Alarm symptoms

Alarm symptoms that indicate the need for upper endoscopy	
Weight loss	
Recurrent vomiting	
Dysphagia	
Bleeding	
Anemia	

- requires an 8 hour fasting
- more sensitive than double contrast upper GI series
- **most serious complication: esophageal perforation**

2. Radiologic tests

Plain abdominal xray

- helpful in the diagnosis of gastric perforation (pneumoperitoneum) or delayed gastric emptying (large air-fluid level)

Double contrast upper GI series

- better than EGD in detecting the ff: diverticula, fistula, tortuosity or stricture location, and size of hiatal hernia
- **CT and MRI**
- is part of routine staging work-up for most patients with a malignant gastric tumor
- **Gastric secretory analysis**
- maybe useful in the evaluation of patients with hypergastrinemia, including Zollinger-Ellison syndrome, patients with refractory ulcer or GERD or recurrent ulcer after operation

5. Tests for Helicobacter pylori

Serologic test for H. pylori

- a positive test is a presumptive evidence of active infection if the patient has never been treated for H. pylori infection

Histologic examination of antral mucosal biopsy (with special stains)

- gold standard for *H. pylori*

Urease breath test

- standard test for to confirm eradication of *H. pylori* post-treatment
- basis: the patient ingests urea labeled with nonradioactive ¹³C → labeled urea is acted upon by the urease present in *H. pylori* → converts urea into ammonia and carbon dioxide → radiolabeled carbon dioxide is excreted from lungs and is detected in expired air.

✓ MUST KNOW

H. pylori has the enzyme **urease**, which converts urea into **ammonia and bicarbonate**, thus creating an environment around the bacteria that buffers the acid secreted by the stomach.

***H. pylori* fecal antigen test**

- sensitive and specific for active *H. pylori* infection
- can also be used to confirm cure

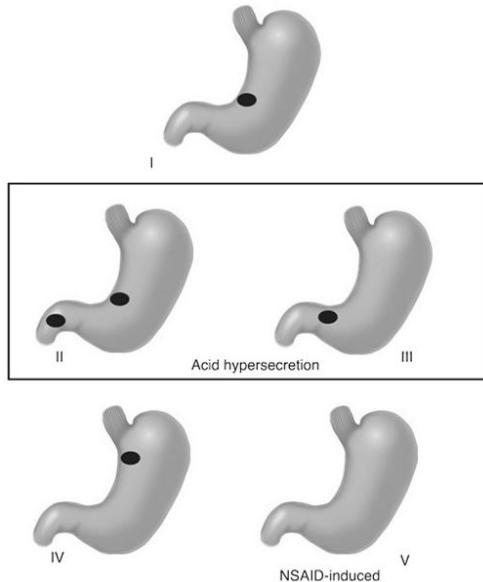
C. PEPTIC ULCER DISEASE

- focal defects in the gastric or duodenal mucosa that extend into the submucosa or deeper
- caused by an imbalance between mucosal defenses and acid/peptic injury.

Etiology

- ***H. Pylori***: associated with both gastric and duodenal ulcer but is a **higher predictor of duodenal ulcer formation**
- **NSAID** – patients taking NSAID and/or aspirin need acid suppressing medication if any of the ff are present: age over 60 yo, hx of PUD, concomitant steroid/anticogulant/high dose NSAIDs intake
- **Smoking** – largest positive predictor of risk (also with alcoholic drinking)
- **Stress** – both physiologic and psychologic stress
- **Others**
 - More common in **Type A personality**
 - Sex: duodenal ulcer is twice more common in males; same incidence between sexes for gastric ulcer
 - Blood type:
 - **Type O**: duodenal ulcer
 - **Type A**: gastric ulcer
- **Types of ulcer based on location and pathophysiology**
- **Duodenal ulcers patients** have ↑ daytime and nocturnal acid secretion, ↑ BAO and MAO, ↑ gastric emptying compared to gastric ulcer patients
- **Gastric ulcers patients** have variable patterns of secretion

Figure 33. Modified Johnson classification of gastric ulcer



Type I: located near the angularis incisura on the lesser curvature; usually have normal or decreased acid secretion; **most common**

Type II: same with type I but with an associated active or quiescent duodenal ulcer; associated with normal or increased gastric acid secretion

Type III: prepyloric ulcer disease; associated with normal or increased gastric acid secretion

Type IV: occur near the GE junction, and acid secretion is normal or below normal

Type V: NSAID induced, can occur anywhere in the stomach

✓ MUST KNOW

Curling ulcers: peptic ulcers formed after **severe burn injury**

Cushing's ulcers: peptic ulcers formed after **severe brain damage**

- Pathophysiology, Clinical manifestations, diagnosis and treatment

Table 54: Comparison between gastric vs duodenal ulcer

	Gastric ulcer	Duodenal ulcer
Pathophysiology	H.pylori, overuse of NSAIDS & steroids	↑ acid production & H.pylori
Clinical manifestation	Sharp burning pain in epigastrium shortly after eating; nausea, vomiting and anorexia	Severe epigastric pain 2-3 hours after eating; epigastric pain can also awaken them from sleep
Diagnosis	Endoscopy and biopsy (must for all gastric ulcers to rule out cancer; test for H.pylori)	Endoscopy, history, PE, test for H pylori
Best test to confirm eradication of H. pylori: negative urea breath test		
treatment	Triple therapy; PPI, antacids and H2 blockers	Triple therapy; stop smoking, alcohol consumption

- More than 90% of patients with PUD complain of **abdominal pain** (non-radiating, burning in quality & epigastric in location)
- **Indication for endoscopy in PUD:**
 - Any symptomatic patient 45 yo and up
 - Any symptomatic patient regardless of age with **alarm symptoms (see table 54) ☺**
- Medical treatment for PUD: **PPIs** are the mainstay of therapy for PUD.

table 50. treatment regimens for H. pylori

PPI + clarithromycin 500 mg BID + amoxicillin 1000 mg BID	10-14 d
PPI + clarithromycin 500 mg BID + metronidazole 500 mg BID	10-14 d
PPI ++ amoxicillin 1000 mg BID, then	5 d
PPI + clarithromycin 500 mg BID + tinidazole mg BID	

Salvage regimens for patients who fail one of the above initial regimens

Bismuth subsalicylate 525 mg qid + metronidazole 250 mg qid + tetracycline 500 mg qid + PPI	10-14 d
PPI + amoxicillin 1000 mg bid + levofloxacin 500 mg daily	10 d

- Indications for surgical treatment for PUD
 - bleeding
 - perforation
 - obstruction
 - intractability or nonhealing ulcers (with discretion)
- For nonhealing PUD
 - Rare indication for surgery
 - Consider possible differentials for nonhealing PUD first
 - Surgical treatment is considered in patients with nonhealing or intractable PUD who have multiple recurrences, large ulcers (>2 cm), complications (obstruction, perforation, or hemorrhage), or suspected malignancy
- Complications of PUD:

Table 55: Comparison of complications of PUD ☺

Bleeding PUD	Perforation	Gastric outlet Obstruction
<ul style="list-style-type: none"> -most common cause of ulcer related death -most common cause of UGIB in admitted patients -presents with melena, hematemesis, shock -abdominal pain is uncommon -tx: acid suppression and NPO, transfusion and endoscopic tx (electrocautery + epi) for high risk group 	<ul style="list-style-type: none"> -2nd most common complication of PUD -classic symptom: patient can remember the exact time of onset of abdominal pain -presents acute abdomen with peritoneal signs (+) pneumoperitoneum on upright chest xray (80% of patients) -Tx: analgesia, antibiotics, isotonic fluid resuscitation, immediate OR 	<ul style="list-style-type: none"> -rare (5% of all PUD complications) -usually due to duodenal or prepyloric disease -presents with bilious vomiting, profound hypochloremic, metabolic alkalosis -tx: nasogastric suction, IV hydration and electrolyte repletion, and antisecretory medication, OR -rule out pancreatic, gastric & duodenal CA as a cause of obstruction

✓ MUST KNOW

High risk lesions for massive bleeding (based on location):

- posterior duodenal ulcer** with erosion of **gastroduodenal artery**
- lesser curvature gastric ulcer** with erosion of **left gastric artery or branch**

- Surgical options for PUD

1. **HSV or parietal cell vagotomy or proximal gastric vagotomy**
 - safe (mortality risk <0.5%) with minimal side effects
 - done by severing the vagal nerve supply to the proximal 2/3 of the stomach (where essentially all parietal cells are located) & preserves the vagal innervation to the antrum and pylorus and remaining abdominal viscera.
2. **Taylor procedure**
 - posterior truncal vagotomy and anterior seromyotomy
 - attractive to HSV with similar results
3. **Vagotomy + drainage (V+D) procedures**
 - Truncal vagotomy denerves the antral mechanism, therefore, some sort of procedure is needed to bypass or ablate the pylorus
 - Types:
 - Truncal vagotomy and pyroplasty
 - Pyroplasty – useful in patients who require pyloromyotomy to deal with the ulcer complication (i.e. posterior bleeding duodenal ulcer), limited focal scarring in the pyloric region
 - Truncal vagotomy and gastrojejunostomy
 -
 - disadvantage: 10% of significant dumping / diarrhea

4. Vagotomy and distal gastrectomy

D. ZOLLINGER-ELLISON SYNDROME

- uncontrolled secretion of abnormal amounts of gastrin by a duodenal or pancreatic neuroendocrine tumor (i.e., gastrinoma) **leading to excessive production of HCl by the parietal cells, further exacerbating PUD.**
- The inherited or familial form of gastrinoma is associated with **multiple endocrine neoplasia type 1** or **MEN1** (parathyroid, pituitary, and pancreatic or duodenal tumors)

⊗ PHYSIOLOGY

Gastrin

- produced by **antral G cells**
- major hormonal stimulant of acid secretion during the gastric phase.
- The biologically active pentapeptide sequence at the C-terminal end of gastrin is **identical to that of CCK**
- **Luminal peptides and amino acids** are the most potent stimulants of gastrin release
- **luminal acid** is the most potent inhibitor of gastrin secretion.
- principal mediator of gastrin-stimulated acid production is **histamine from mucosal ECL cells**

- **Gastrinoma triangle (or Pasaro's triangle)** ☺: where 90% of ZES tumors are found
 - boundaries: jxn of cystic & CBD, confluence of 2nd & 3rd segments of the duodenum and jxn of body and neck of pancreas
- most common symptoms of ZES are epigastric pain, GERD & diarrhea. Can also be associated with steatorrhea and other symptoms of malabsorption.
- Diagnosis:
 - Fasting gastrin of 1mg/L, BAO >15 mEq/h or >5 mEq/h (if with previous procedure for peptic ulcer) are suggestive of ZES
 - **Confirmatory test: secretin stimulation test**
 - (+) secretin stimulation test: paradoxical rise in gastrin levels (200 pg/mL or greater) upon administration of IV bolus of secretin (*an inhibitor of gastrin*)
 - **Should also check for serum calcium and PTH levels to rule out MEN1.**
 - **Preoperative imaging of choice for gastrinoma: somatostatin receptor scintigraphy (octreotide scan)**
 - Basis: Gastrinoma cells contain type 2 somatostatin receptors that bind the indium-labeled somatostatin analogue (octreotide) with high affinity, making imaging with a gamma camera possible

⊗ PHYSIOLOGY

Somatostatin

- produced by **D cells** located throughout the gastric mucosa.
- major stimulus for somatostatin release is **antral acidification**
- **acetylcholine inhibits its release**
- Somatostatin effects: **inhibits acid secretion from parietal cells, inhibits gastrin release from G cells & decreases histamine release from ECL cells.**
- **Octreotide** is a somatostatin analogue

Treatment:

- Surgical resection of gastrinoma
 - If (+) MEN1, perform parathyroidectomy 1st before resection of gastrinoma
- PPI for symptomatic relief

E. GASTRITIS

- Definition: Mucosal inflammation
- **Most common cause: H. pylori**

- Other causes: alcohol, NSAIDs, Crohn's disease, tuberculosis, and bile reflux

- Pathophysiology:

- infectious and inflammatory causes: result in immune cell infiltration and cytokine production which damage mucosal cells.
- chemical agents (alcohol, aspirin, and bile): disrupt the mucosal barrier, allowing mucosal damage by back diffusion of luminal hydrogen ions.

F. STRESS ULCER

- Pathophysiology: due to inadequate gastric mucosal blood flow during periods of intense physiologic stress.

- Adequate mucosal blood flow is important to maintain the mucosal barrier, and to buffer any back-diffused hydrogen ions. When blood flow is inadequate, these processes fail and mucosal breakdown occurs

G. MALIGNANT NEOPLASMS OF THE STOMACH

- The three most common primary malignant gastric neoplasms are **adenocarcinoma (95%), lymphoma (4%), and malignant GIST (1%)**

GASTRIC ADENOCARCINOMA

- Epidemiology & etiology

- Gastric adenoCA is a disease of the elderly
- Risk factors:
 - Black race: twice more common in blacks compared to whites
 - Pernicious anemia
 - Blood group A
 - FH of gastric CA
 - Diet: starchy diet high in pickled, salted, or smoked food, nitrates increases risk
 - H. pylori
 - Smoking
 - EBV infections
 - **Remember: Alcohol has no role in gastric CA**
- protective factors: aspirin (*Yes! Schwartz says so. You don't believe me? Check p. 927, 9th edition*), vitamin C and diet high in fruits and vegetables
- premalignant conditions:
 - polyps
 - **hyperplastic and adenomas** are the types associated with carcinoma
 - inflammatory, hamartomatous and heterotrophic polyps are considered benign lesions
 - **atrophic gastritis**: most common precancerous lesion / precursor of gastric cancer
 - intestinal metaplasia: can be caused by H. pylori

- Pathology

- **Gastric Dysplasia**: universal precursor to gastric adenocarcinoma
- **Early gastric cancer**: adenocarcinoma limited to the mucosa and submucosa of the stomach, regardless of lymph node status.
- **4 forms of gastric cancer (Gross morphology):**
 1. **Polypoid**: bulk of tumor is intraluminal, not ulcerated
 2. **Fungating**: bulk of tumor is intraluminal, ulcerated
 3. **Ulcerative**: bulk of tumor is within the stomach wall
 4. **Scirrhous (linitis plastica)**: bulk of tumor is within the stomach wall; infiltrate the entire thickness of stomach and cover a large surface area, poor prognosis
- Location of primary tumor: 40% distal stomach, 30% middle stomach and 30% proximal stomach
- **Most important prognosticating factors: lymph node involvement and depth of tumor invasion**

- Clinical manifestations:

- Most patients diagnosed with gastric CA have **advanced stage III or IV disease**
- S/Sx:

- weight loss and decreased food intake due to anorexia and early satiety (most common)
- Abdominal pain (usually not severe and often ignored)
 - nausea, vomiting, & bloating.
 - Acute GI bleeding (unusual)
 - chronic occult blood loss (iron deficiency anemia and heme+ stool)
 - Dysphagia: if the tumor involves the cardia of the stomach.
 - Paraneoplastic syndromes - Trousseau's syndrome (thrombophlebitis), acanthosis nigricans (hyperpigmentation of the axilla and groin), or peripheral neuropathy can be present.
- Physical examination:
 - Enlarged Cervical, supraclavicular (on the left referred to as Virchow's node), and axillary lymph nodes
 - **Sister Joseph's nodule:** palpable umbilical nodule; **pathognomonic for advanced disease**
 - **Blumer nodes:** palpable nodularity in the pouch of douglas; evidence of **drop metastasis**
- Diagnosis
 - Do endoscopy and biopsy
 - Pre-operative staging: abdominal/pelvic CT scanning with IV and oral contrast
- Treatment
 - Surgery is the only curative treatment for gastric cancer (radical subtotal gastrectomy)
 - Goal in resecting gastric adenocarcinoma: **grossly negative margin of at least 5 cm to achieve R0 resection**

GASTRIC LYMPHOMA

- stomach is the most common site of primary GI lymphoma
- over 95% are non-Hodgkin's type.
- Most are B-cell type, thought to arise in MALT
- MALT lymphomas is a form of NHL arising from the B cells in the marginal zone of MALT
- Is associated with chronic inflammation due to H. pylori
- Diligent search for extragastic disease should be done before giving a diagnosis of primary gastric lymphoma
- Treatment: chemotx is equivalent to surgery

GASTROINTESTINAL STROMAL TUMOR (GIST)

- Are submucosal solitary slow growing tumors arising from **interstitial cells of Cajal (ICC)**
- **2/3 of all GISTS occur in the stomach, occurring commonly in the body**
- defining feature of GISTS is their gain of function mutation of protooncogene KIT, a receptor tyrosine kinase (majority of GISTS have activated mutation in the c-kit protooncogene, which causes KIT to be constitutively activated, presumably leading to persistence of cellular growth or survival signals)
- **Epithelial cell stromal GIST:** most common cell type arising in the stomach; **cellular spindle type** is the next most common; **glomus tumor type** is seen only in the stomach.
- Markers: (+) c-KIT, a protooncogene; a characteristic shared with ICC
- Diagnosis: endoscopy and biopsy,
- Mode of metastasis: **hematogenous route**; most common sites: liver and lung
- Treatment:
 - **Wedge resection with clear margins** is adequate surgical treatment
 - **Imatinib (Gleevec):** a chemotherapeutic agent that **blocks the activity of the tyrosine kinase product of c-kit**, is reserved for metastatic or unresectable GIST. benign gastric neoplasms

- H. **BENIGN GASTRIC NEOPLASMS: POLYP** (see also premalignant conditions of gastric adenoCA)
 - **most common benign tumor of the stomach**
 - 5 types:
 1. **Adenomatous:** (+) malignant potential; 10-15% of all gastric polyps
 2. **hyperplastic** (regenerative): **most common gastric polyp (75% of all gastric polyps)**; occurs in the setting of gastritis and has a low malignant potential
 3. hamartomatous: benign
 4. inflammatory: benign
 5. heterotopic (e.g. ectopic pancreas): benign
*****Polyps that are symptomatic, >2 cm, large hyperplastic or adenomatous should be removed, usually by endoscopic snare polypectomy.**

I. GASTRIC VOLVULUS

- is a twist of the stomach that usually occurs in association with a large hiatal hernia or unusually mobile stomach without hiatal hernia.
- Gastric volvulus is a chronic condition that can be surprisingly asymptomatic.
- Clinical manifestations: abdominal pain and pressure related to the intermittently distending and poorly emptying twisted stomach, dyspnea (due to pressure on the lung), palpitations (due to pressure on the pericardium) and dysphagia (pressure on the esophagus)
- Management:
 - Vomiting and passage of a NGT may relieve symptoms
 - **Gastric infarction is a surgical emergency**

J. POSTGASTRECTOMY PROBLEMS

DUMPING SYNDROME

- occurs after bariatric surgery and PUD repair (after pyloroplasty, pyloromyotomy or distal gastrectomy)
- mechanism: there is accumulation of digested food in the small intestine (or abrupt delivery of hyperosmolar load into the small bowel) leading to circumferential expansion, additional accumulation of fluids emptying from stomach to duodenum and sudden expulsion of food to GIT → possibly due to ablation of the pylorus or decreased gastric compliance with accelerated emptying of liquids (after highly selective vagotomy)
- clinical manifestation: tachycardia, crampy abdominal pain and diarrhea, dizziness, lightheadedness, diaphoresis, nausea and vomiting after ingestion of a fatty or carbohydrate laden meal
 - due to sudden shift in electrolytes and fluids combined with increased blood flow to small intestine
- treatment:
 - decreasing fluid and food intake to small frequent portions
 - avoid fatty and simple sugars

AFFERENT LIMB OBSTRUCTION (BLIND LOOP SYNDROME)

- occurs usually after a **Billroth II procedure** (distal gastric resection followed by gastrojejunral anastomosis)
- location of obstruction: at the limb associated with the gastric remnant going to the duodenum
- clinical manifestations: severe epigastric pain following eating, bilious emesis without food
- treatment: convert Billroth II to roux en-Y gastric bypass (possible problem: can delay gastric emptying)

GASTRIC OUTLET OBSTRUCTION (see complications of PUD as well)

- presents with **hypochloremic, hypokalemic metabolic alkalosis** ☺ → dehydration
- as a compensatory response due to worsening dehydration, Na conservation occurs in the kidney,

leading to renal tubular acidosis with subsequent aciduria

REVIEW QUESTIONS

1. A patient with a vagotomy and pyloroplasty returns with a recurrent ulcer. The best method for determining if there was an inadequate vagotomy performed is
 - a. Direct vagal stimulation
 - b. Stimulated gastric analysis
 - c. Stimulated PPI (pancreatic polypeptide) levels
 - d. None of the above – there is no good test to determine inadequate vagotomy

Answer: C

Historically, gastric analysis was performed most commonly to test for the adequacy of vagotomy in postoperative patients with recurrent or persistent ulcer. Now this can be done by assessing peripheral pancreatic polypeptide levels in response to sham feeding. A 50% increase in pancreatic polypeptide within 30 minutes of sham feeding suggests vagal integrity.

2. Which of the following procedures for PUD has the highest incidence of postoperative diarrhea?
 - a. Graham patch
 - b. Parietal cell vagotomy
 - c. Truncal vagotomy and pyloroplasty
 - d. Distal gastrectomy without vagotomy

Answer: C

	Parietal Cell vagotomy	Truncal vagotomy & pyloroplasty	Truncal vagotomy & Antrectomy
Operative mortality rate (%)	0	<1	1
Ulcer recurrence (%)	5-15	5-15	<2
Dumping(%)			
Mild	<5	10	10-15
Severe	0	1	1-2
Diarrhea			
Mild	<5	25	20
Severe	0	2	1-2

- Layers of the small intestine (from innermost to outermost layers): mucosa, submucosa, muscularis propria and serosa
 - Contraction of the inner circular layer causes results in luminal narrowing
 - Contraction of the outer longitudinal layer results in bowel shortening
 - Contraction of the muscularis mucosa contribute to mucosal or villus motility (but not peristalsis)
- Mucosal folds: **plicae circulares / valvulae conniventes**
- **Peyer's patches:** most commonly located in the ileum which are aggregates of lymphoid follicles and is a local source of IgA
- **Difference between jejunum and ileum: jejunum has larger circumference, thicker wall, less fatty mesentery, and longer vasa recta**
- **Calcium** is primarily absorbed in the **duodenum** through both transcellular transport and paracellular diffusion.

⊗ PHYSIOLOGY

Representative Regulatory Peptides produced in the small Intestine:

Hormone	Source	Actions
Somatostatin	D Cell	Inhibits GI secretion, motility & splanchnic perfusion
Secretin (1 st hormone discovered in the human body)	S cell	Stimulates exocrine pancreatic secretion; stimulates intestinal secretion
Cholecystokinin	I cell	Stimulates exocrine pancreatic secretion; Stimulates GB emptying; Inhibits sphincter of Oddi contraction
Motilin	M cell	Stimulates intestinal motility
Glucagon-like peptide 2	L cell	Stimulates intestinal proliferation
Peptide YY	L cell	Inhibits intestinal motility & secretion

B. SMALL BOWEL OBSTRUCTION

- Epidemiology:
 - **most frequently encountered surgical disorder of the small intestine.**
 - Lesions can be described as:
 - Intraluminal: foreign bodies, gallstones, meconium
 - Intramural: tumors, Crohn's disease associated inflammatory strictures
 - Extrinsic: adhesions, hernias, carcinomatosis
- Etiology:
 - **Intra-abdominal adhesions related to prior abdominal surgery: most common cause (75% of cases)**
 - Hernias
 - **Malignancy:** due to extrinsic compression or invasion by advanced malignancies arising in organs other than the small bowel
 - Crohn's disease.
 - Congenital abnormalities (i.e. midgut volvulus and intestinal malrotation) diagnosed at adulthood.
 - **superior mesenteric artery syndrome:** rare; compression of the 3rd portion of the duodenum by the superior mesenteric artery as it crosses over this portion of the duodenum; seen in young asthenic individuals who have chronic symptoms suggestive of proximal small bowel obstruction.

- Pathophysiology

- Gas (usually from swallowed air) and fluid (from swallowed liquids and GI secretions) accumulate within the intestinal lumen proximal to the site of obstruction → intestinal activity ↑ to overcome the

SMALL INTESTINE

- A. Gross Anatomy and Histology
- B. Small bowel obstruction
- C. Ileus & other disorders of intestinal motility
- D. Crohn's disease
- E. Intestinal fistulas
- F. Small bowel neoplasms
- G. Radiation enteritis
- H. Meckel's diverticulum
- I. Acquired diverticulum
- J. Mesenteric Ischemia
- K. Obscure GI bleeding
- L. Intussusception
- M. Short bowel syndrome

A. GROSS ANATOMY AND HISTOLOGY

- **raison d'être of the GI tract** because it is the principle site of nutrient digestion and absorption.

- obstruction (seen as colicky pain and diarrhea) → bowel distention → ↑ intraluminal and intramural pressures rise → intestinal motility is eventually reduced with fewer contractions → If intramural pressure becomes high enough → impaired intestinal microvascular perfusion → intestinal ischemia → necrosis (**strangulated bowel obstruction**)
- With obstruction, the luminal flora of the small bowel (which is usually sterile) changes → Translocation of these bacteria to regional lymph nodes

Partial SBO: only a portion of the intestinal lumen is occluded, allowing passage of some gas and fluid.

Complete SBO: complete occlusion

Closed loop obstruction: dangerous form of SBO, in which a segment of intestine is obstructed both proximally and distally (e.g., with volvulus). *In such cases, the accumulating gas and fluid cannot escape either proximally or distally from the obstructed segment, leading to a rapid rise in luminal pressure, and a rapid progression to strangulation.*

- Clinical presentation

- **Symptoms:** colicky abdominal pain, nausea, vomiting (a more prominent symptom with proximal obstructions than distal; vomitus is usually feculent), and obstipation, continued passage of flatus and/or stool beyond 6 to 12 hours after onset of symptoms (more for partial SBO than complete SBO)
- **Signs:** abdominal distension (pronounced if the site of obstruction is distal ileum & absent if the site of obstruction is in the proximal small intestine), initially hyperactive bowel sounds (maybe minimal towards the late stages of bowel obstruction)
- **Lab findings:** hemoconcentration and electrolyte abnormalities (reflect intravascular volume depletion) & Mild leukocytosis
- **Features of strangulated SBO:** abdominal pain often disproportionate to the degree of abdominal findings (suggestive of intestinal ischemia), tachycardia, localized abdominal tenderness, fever, marked leukocytosis, & acidosis.

- Diagnosis

- **Confirmatory test: abdominal series** (radiograph of the abdomen with the patient in a supine position, upright position & radiograph of the chest with the patient in an upright position)
 - **Sensitivity of abdominal radiographs for detecting SBO is 70-80%**
 - **Triad of dilated small bowel loops (>3 cm in diameter), air-fluid levels seen on upright films, and a paucity of air in the colon is MOST SPECIFIC**
- CT scan
 - 80 to 90% sensitive
 - 70 to 90% specific
 - **Appearance of closed-loop obstruction in CT:** presence of U-shaped or C-shaped dilated bowel loop associated with a radial distribution of mesenteric vessels converging toward a torsion point.
 - **Appearance of strangulation in CT:** thickening of the bowel wall, pneumatisis intestinalis (air in bowel wall), portal venous gas, mesenteric haziness and poor uptake of IV contrast into the wall of the affected bowel.

- Treatment

- Fluid resuscitation: isotonic replacement
- Broad spectrum antibiotics
- NGT placement for decompression
- If complete SBO, perform surgery

- If partial SBO, may be approached conservatively given that there is no fever, tachycardia, tenderness, or an increase in white cell count (indicates perforation)
- **most patients with partial small obstruction whose symptoms do not improve within 48 hours after initiation of nonoperative therapy should undergo surgery.**
- Obstruction presenting in **the early postoperative period** (particularly those undergoing pelvic surgery, especially colorectal procedures) pose the **greatest risk for developing early postoperative small bowel obstruction.**
 - obstruction should be considered if **Sx of intestinal obstruction occur after the initial return of bowel function or if bowel function fails to return within the expected 3 to 5 days after abdominal surgery.**
- Regardless of etiology, the affected intestine should be examined, and nonviable bowel resected.
 - **Criteria for viability: normal color (pinkish), (+)peristalsis, and marginal arterial pulsations.**

Ogilvie syndrome

- Distention of the abdomen leading to obstruction
- Tends to occur following non-abdominal procedures (i.e. cardiac surgery)
- Due to a neurologic dysfunction, electrolyte abnormality and age
- Treatment: NGT, **IV neostigmine**, IV atropine (to counter bradycardia as SE of neostigmine), exploratory laparotomy during worst case scenario)

C. ILEUS & OTHER DISORDERS OF INTESTINAL MOTILITY

- Ileus is a **temporary** motility disorder
- **Postoperative ileus: most frequently implicated cause of delayed discharge following abdominal operations**
- **Pathophysiology:**
 - Common etiologies: abdominal operations, infection and inflammation, electrolyte abnormalities (↓K, ↓&↑Mg, ↓Na) & drugs (anticholinergics, opiates, phenothiazine, CCB, Tricyclic antidepressants)
 - Proposed mechanisms: surgical stress-induced sympathetic reflexes, inflammatory response mediator release, and anesthetic/analgesic effects
 - **Normal temporal pattern of return of GI motility** ☺: **small intestinal motility (1st 24 hours), gastric motility (48 hours) and colonic motility (3 to 5 days)**
- Clinical presentation (usually resembles SBO): Inability to tolerate liquids and solids by mouth, nausea, and lack of flatus or bowel movements, vomiting, abdominal distention & diminished or absent bowel sounds
- **diagnosis:** If **ileus persists beyond 3 to 5 days postoperatively** ☺ or occurs in the absence of abdominal surgery, further investigation is warranted to rule out possibility of mechanical obstruction

⊗ CLINICAL PEARLS

Measures to REDUCE postoperative ileus:

Intraoperative measures:

- minimize handling of bowel
- laparoscopic approach, if possible
- avoid excessive intraoperative fluid administration

Postoperative measures

- early enteral feeding
- epidural anesthesia, if indicated
- avoid excessive IV fluid administration
- correct electrolyte abnormalities
- consider m-opioid antagonists (

***Remember, though often recommended, the **use of early ambulation and routine NG intubation** has **NOT** been demonstrated to be associated with earlier resolution of postoperative ileus.

D. INFLAMMATORY BOWEL SYNDROME: CROHN'S DISEASE VS ULCERATIVE COLITIS ☺

table 56. Inflammatory bowel syndrome

	Crohn's disease	Ulcerative colitis
description	chronic, idiopathic transmural inflammatory disease with a propensity to affect the distal ileum	Chronic inflammatory disease affecting only the colonic mucosa and submucosa
Etiology & epidemiology	-more common in Ashkenazi jews & caucasians, females, has a bimodal age distribution (3 rd & 6 th decade), (+) strong pattern of family inheritance, smokers & higher Socio-eco status	Higher chance of leading to colorectal cancer
Pathology	<p>Focal transmural inflammation, aphthous ulcers (earliest lesion of Crohn's), non caseating granulomas, cobblestoning, **fat wrapping (encroachment of mesenteric fat onto the serosal surface of the bowel): <i>pathognomonic of crohn's</i></p> <p>spares rectum, can occur anywhere in the GI tract, skip lesions, targets terminal ileum</p> <p>fistula,</p>	<p>Inflammation is limited to mucosa and submucosa only; lead pipe colon (lacks haustral markings); no granulomas</p> <p>Primarily affects the colon & rectum and is continuous; can also manifest with backwash ileitis</p>
S/Sx	<p>Inisiduous onset with waxing and waning course of abdominal pain (usually RLQ), nonbloody diarrhea & weight loss;</p> <p>(+) extraintestinal manifestation: arthritis, uveitis, iritis, erythema nodosum, pyoderma gangrenosum, primary sclerosing cholangitis, nephrolithiasis</p>	<p>bloody diarrhea and crampy abdominal pain. Proctitis may produce tenesmus; can proceed to fulminant colitis and toxic megacolon</p>
Diagnosis	Endoscopy (skip lesions, cobblestoning, abscess formation and fistulas); histology demonstrate granulomas; (+) (pANCA) and anti-Saccharomyces cerevisiae antibody (ASCA)	Endoscopy & proctoscopy (earliest manifestation is mucosal edema; mucosal friability; ulceration; (+) Pus and mucus)
Treatment	Sulfasalazine + steroids; surgery if unresponsive to aggressive medical Tx	Similar to Crohn's; colectomy after 15 years of symptoms

E. INTESTINAL FISTULAS

- abnormal communication between two epithelialized surfaces
- can be internal (within GI tract or adjacent organs) or external (with communication to external environment)
- Kinds:
 - **low output fistulas** - drain less than 200 mL of fluid/day
 - **high output fistulas** - drain more than 500 mL of fluid/day
- **80% of enterocutaneous fistulas are due to iatrogenic complications**
- Clinical presentation

- usually become clinically evident between the 5th & 10th postop
- initial signs: Fever, leukocytosis, prolonged ileus, abdominal tenderness, and wound infection
- (+) drainage of enteric material through the abdominal wound or through existing drains: associated with intra-abdominal abscesses.

Diagnosis

- CT scan: most useful initial test
- small bowel series or enteroclysis examination: can be obtained to demonstrate the fistula's site of origin in the bowel.
- Fistulogram: greater sensitivity in localizing the fistula origin.

Treatment

- Should follow orderly steps (*done to maximize spontaneous closure*)
 - Stabilization: fluid & electrolyte resuscitation, TPN, antibiotics,
 - Investigation: see diagnosis
 - Decision to do perform surgery or do conservative treatment
 - Surgeons usually do **2 to 3 months of conservative therapy before considering surgical intervention**.
 - This approach is based on evidence that **90% of fistulas that are going to close, close within a 5-week interval**
- Definitive management: surgery (if failure of spontaneous closure during time period or with complications and risk factors)
- rehabilitation

✓ MUST KNOW

Remember **FRIEND** (factors that inhibit spontaneous closure of fistulas):
Foreign body within the fistula tract
Radiation enteritis
Infection/Inflammation at the fistula origin **Epithelialization** of the fistula tract
Neoplasm at the fistula origin
Distal obstruction of the intestine

F. SMALL BOWEL NEOPLASMS

- **Adenomas** are the most common benign neoplasm of the small intestine
- Most common location for primary adenocarcinoma and adenomas of the small bowel is **DUODENUM (EXCEPT** in patient's with Crohn's disease, which is found mostly in the ileum)
- **Primary small bowel cancers are rare:** 1.1 to 2.4% of all GI malignancies
 - Adenocarcinomas: 35 - 50%
 - Carcinoid tumors: 20 to 40%
 - Lymphomas: 10 to 15 %
 - GISTs: most common location is **STOMACH (60-70%)**, 2nd most common location is small intestine (25-35%)

Pathophysiology:

- proposed explanations for the low frequency of small intestinal neoplasms
- dilution of environmental carcinogens in the liquid chyme present in the SI lumen
 - rapid transit of chime (limiting the contact time between carcinogens and the intestinal mucosa)
 - relatively low concentration of bacteria in small intestinal chyme (therefore, low concentration of carcinogenic products of bacterial metabolism)
 - mucosal protection by secretory IgA and hydrolases such as benzpyrene hydroxylase → render carcinogens less active
 - efficient epithelial cellular apoptotic mechanisms that serve to eliminate clones harboring genetic mutations.

- **Clinical presentation**
 - **Partial SBO** is the most common mode of presentation
 - Only becomes symptomatic when it becomes large
- **Diagnosis:** Because of the absent or nonspecific symptoms associated with most small intestinal neoplasms, *these lesions rarely are diagnosed preoperatively*
- **Treatment:** surgical resection

G. RADIATION ENTERITIS

- An undesired side effect of radiation therapy is radiation-induced injury to the small intestine
- **The SI is susceptible to radiation-induced injury because it has a high rate of rapidly proliferating cells compared to the other portions of the GI tract**
- **Pathophysiology**
 - principal mechanism of radiation-induced cell death is believed to be apoptosis resulting from free-radical-induced breaks in double-stranded DNA
 - The intensity of injury is related to the dose of radiation administered
- **Pathology**
 - **acute injury:** villus blunting, dense infiltrate of leukocytes and plasma cells within the crypts, mucosal sloughing, ulceration, and hemorrhage
 - **chronic injury:** progressive occlusive vasculitis that leads to chronic ischemia and fibrosis that affects all layers of the intestinal wall, rather than the mucosa alone → leading to strictures, abscesses, and fistulas
- **Clinical presentation**
 - Acute: nausea, vomiting, diarrhea, and crampy abdominal pain.
 - Chronic: becomes evident within 2 years of radiation administration, most commonly presents with **partial small bowel obstruction** with nausea, vomiting, intermittent abdominal distention, crampy abdominal pain, and weight loss. The **terminal ileum** is the most frequently affected segment
- **Diagnosis**
 - Enteroclysis: most accurate imaging test for diagnosing chronic radiation enteritis,
 - CT scan findings are neither very sensitive nor specific for chronic radiation enteritis; should be obtained to rule out the presence of recurrent cancer (because of overlap in clinical manifestations)
- **Treatment: supportive therapy**

H. MECKEL'S DIVERTICULUM ☺

- **most prevalent congenital anomaly of the GI tract**
- considered a **true diverticula**
- location is usually found in the **ileum within 100 cm of the ileocecal valve**
- 60% of Meckel's diverticula contain **heterotopic mucosa** (**most common: gastric mucosa** – 60%; others: Pancreatic acini, Brunner's glands, pancreatic islets, colonic mucosa, endometriosis, and hepatobiliary tissues).

✓ MUST KNOW

rule of TWOs of Meckel's diverticulum:

2% prevalence
 2:1 female predominance
 location 2 ft proximal to the ileocecal valve in adults
 one half of those who are symptomatic are under 2 years of age

- **Pathophysiology**
 - **Failure of the the omphalomesenteric (vitelline) duct to undergo obliteration** during the **8th week of gestation**

- **Littre's hernia:** Meckel's diverticula found in an **inguinal or femoral hernia** sacs; when incarcerated, can cause intestinal obstruction
- **Clinical presentation**
 - most common presentations associated with symptomatic Meckel's diverticula: **bleeding (most common in pediatric age), intestinal obstruction (most common in adults), and diverticulitis**
- **Diagnosis**
 - Usually *discovered incidentally* on radiographic imaging, during endoscopy, or at the time of surgery.
 - **CT scan:** low sensitivity and specificity
 - **Enteroclysis:** has 75% accuracy but not applicable during acute presentations
 - **Radionuclide scans** (^{99m}Tc-pertechnetate): positive only when the diverticulum contains associated ectopic gastric mucosa that is capable of uptake of the tracer
- **Treatment: surgical**
 - diverticulectomy
 - If the indication for diverticulectomy is bleeding, segmental resection of ileum that includes both the diverticulum and the adjacent ileal peptic ulcer should be performed.
 - Segmental ileal resection may also be necessary if the diverticulum contains a tumor or if the base of the diverticulum is inflamed or perforated.
 - The management of incidentally found (asymptomatic) Meckel's diverticula is controversial.

I. ACQUIRED DIVERTICULUM

- Considered as **false diverticula** (because their walls consist of mucosa and submucosa but lack a complete muscularis)
- more common in the duodenum, near the ampulla (*periampullary, juxtapapillary, or peri-Vaterian diverticula*)
- Diverticula in the jejunum tend to be large and accompanied by multiple other diverticula, whereas those in the ileum tend to be small and solitary.
- **Pathophysiology**
 - Due to acquired abnormalities of intestinal smooth muscle or dysregulated motility → leading to herniation of mucosa and submucosa through weakened areas of muscularis.
- **Clinical presentation**
 - Acquired diverticula are asymptomatic unless associated complications arise
 - Complications (6 to 10% of patients): intestinal obstruction, diverticulitis, hemorrhage, perforation, and malabsorption.
- **Diagnosis**
 - Most acquired diverticula are discovered incidentally on radiographic imaging, during endoscopy, or at the time of surgery.
 - **Enteroclysis** is the most sensitive test for detecting jejunoileal diverticula
- **Treatment**
 - If **asymptomatic, observe**
 - If (+)complications, such as bleeding and diverticulitis: segmental intestinal resection for diverticula located in the jejunum or ileum.

J. MESENTERIC ISCHEMIA

Table 57: comparison of acute vs chronic mesenteric ischemia

Acute mesenteric ischemia	Chronic mesenteric ischemia
Causes:	
- arterial embolus: most common cause; most common source: heart; most common location: SMA	- results from atherosclerotic lesions in the main splanchnic arteries (celiac, superior mesenteric, and inferior mesenteric arteries
- arterial thrombosis: occur in proximal mesenteric arteries	-rarely leads to infarction
- vasospasm (nonocclusive mesenteric ischemia): diagnosed in critically ill	- Postprandial abdominal pain is the most prevalent symptom , producing a

Acute mesenteric ischemia	Chronic mesenteric ischemia
<p>patients receiving vasopressor agents.</p> <p>-venous thrombosis: involves the superior mesenteric vein in 95% of cases; associated with heritable or acquired coagulation DO</p> <p>Golden period: 3 hours – intestinal sloughing; 6 hours: full thickness intestinal infarction</p> <p>Hallmark of acute mesenteric ischemia: Severe abdominal pain, out of proportion to the degree of tenderness on examination</p>	<p>characteristic aversion to food ("food-fear") and weight loss (can be mistaken as a symptom of malignancy)</p>

K. INTUSSUSCEPTION ☺

- refers to a condition where one segment of the intestine becomes drawn in to the lumen of the proximal segment of the bowel
- usually is seen in the pediatric population
- Adult intussusceptions are rare; usually with distinct pathologic lead point (which can be malignant)
- commonly present with a history of intermittent abdominal pain and signs and symptoms of bowel obstruction
- **CT scan: diagnostic of choice**
 - **Finding: "target sign"**
- Treatment: surgical resection of the involved segment and the lead point, which needs to undergo pathologic evaluation to rule out an underlying malignancy.

L. SHORT BOWEL SYNDROME

- presence of less than 200 cm of residual small bowel in adult patients
- usually acquired (s/p intestinal resection)
- can result to malabsorptive symptoms: diarrhea, dehydration, and malnutrition,
- most common etiologies:
 - adults: acute mesenteric ischemia, malignancy, and Crohn's disease
 - pediatrics: intestinal atresias, volvulus, and necrotizing enterocolitis
- Pathophysiology
 - Normal: Resection of less than 50% of the small intestine is generally well tolerated.
 - Symptomatic when greater than 50 to 80% of the small intestine has been resected.
 - Malabsorption in patients who have undergone massive small bowel resection is exacerbated by a characteristic **hypergastrinemia-associated gastric acid hypersecretion** that persists for 1 to 2 years postoperatively
- Treatment:
 - TPN & enteral nutrition
 - Pharmacotherapy

REVIEW QUESTIONS

1. Vitamin B12 deficiency can occur after
 - a. Gastrectomy
 - b. Gastric bypass
 - c. Ileal resection
 - d. ALL OF THE ABOVE

Answer: D

Vitamin B12 (cobalamin) malabsorption can result from a variety of surgical manipulations. The vitamin is initially bound by saliva-derived R protein. In the duodenum, R protein is hydrolyzed by pancreatic enzymes, allowing free cobalamin to bind to gastric parietal cell-derived intrinsic factor. The cobalamin-intrinsic factor complex is able to escape hydrolysis by pancreatic enzymes, allowing it to reach the terminal ileum, which expresses specific receptors for intrinsic factor. Subsequent

events in cobalamin absorption are poorly characterized, but the intact complex probably enters enterocytes through translocation. Because each of these steps is necessary for cobalamin assimilation, gastric resection, gastric bypass and ileal resection can each result in Vitamin B 12 insufficiency.

2. Which of the following is the LAST to recover from postoperative ileus?
 - a. Stomach
 - b. Small Bowel
 - c. Colon
 - d. NONE of the above – recovery is simultaneous

Answer: C

The return of normal motility generally follows a characteristic temporal sequence, with small intestinal motility returning to normal within the 1st 24 hours after laparotomy and gastric and colonic motility returning to normal by 48 hours and 3 to 5 days, respectively. Because small bowel motility is returned before colonic and gastric motility, listening for bowel sounds is not a reliable indicator that ileus has fully resolved. Functional evidence of coordinated GI motility in the form of passing flatus or bowel movement is a more useful indicator.

APPENDIX

- A. Anatomy
- B. Acute appendicitis
- C. Appendiceal tumors - Carcinoid

A. ANATOMY

- Function: immunologic organ; a GALT tissue that secretes immunoglobulins
- The **base of the appendix** can always be found at the **confluence of the taenia**
- Tip of the appendix varies: retrocecal (most common), pelvic, subcecal, preileal, or right pericolic position
 - ***The location of the tip of the appendix determine the location of physical findings produced by irritation of parietal peritoneum
- the luminal capacity if the normal appendix is 0.1 cc. secretion of as little as 0.5 cc of fluid distal to the obstruction raises intraluminal pressure to 60 cm H₂O.

B. ACUTE APPENDICITIS

- **Etiology**
 - **Fecalith:** most common cause of appendiceal obstruction; usually in adults
 - **Lymphoid hyperplasia:** most common cause of appendiceal obstruction in patients of pediatric age
- **Pathogenesis:** Luminal obstruction → bacterial overgrowth, active mucosal secretion & increased luminal pressure
- **Natural history:** rarely resolves; ultimately lead to gangrene and perforation
- **Clinical presentation**
 - Hallmark of appendicitis: *poorly localized pain* (due to distension stimulates visceral afferent pain fibers) *that is referred to the perumbilical region (via autonomic innervations) → Right lower quadrant pain and tenderness (via somatic innervations due to involvement of the parietal peritoneum)*
 - Vomiting usually follows abdominal pain
 - Anorexia is a constant symptom; if not present, question diagnosis; usually precedes abdominal pain
 - Variations in the anatomic location of the appendiceal tip account for the different manifestation of the abdominal pain

- Retrocecal: flank or back pain
- Pelvis: findings maybe absent; painful DRE exam
- PE maneuvers:
 - **Dumphy's sign:** increased pain during coughing or jumping
 - **Rovsing's sign:** pain in the RLQ when pressure is applied on the LLQ; this suggests peritoneal irritation
 - **Psoas sign:** pain on extension of the right thigh with the patient lying on the left side; this is due to the pain elicited by the stretched psoas muscle irritating the inflamed appendix
 - **Obturator's sign:** pain with passive rotation of the flexed right hip; suggests that the inflamed tip lies in the appendix
- **Diagnosis:** usually based on history and physical examination even in the absence of laboratories and imaging
 - **Laboratory findings**
 1. Moderate leukocytosis with polymorphonuclear predominance (if above 18,000 – suspect abscess or perforation)
 2. Can also have normal WBC count (1/3 of patients)
 3. Minimal albuminuria, (+) WBC and RBC in urine if appendix is retrocecal
 4. Anemia in elderly should raise suspicion of carcinoma of the cecum
 - **Imaging**
 1. **Plain abdominal films:** fecalith, localized ileus on the RLQ & loss of peritoneal fat strip
 2. **UTZ:** tubular, immobile and noncompressible appendix, wall thickness of >2mm and outer diameter of at least 6 mm are indicative of appendicitis
 3. **CT scan:** thickened by more than 5-7mm&fluid filled, periappendiceal inflammation along with fat stranding, fluid collections & phlegmons
- **Differential diagnosis**
 - **Acute mesenteric adenitis:** associated with URTI and presents with a more diffused abdominal pain also with generalized lymphadenopathy with lymphocytosis
 - **Acute gastroenteritis:** crampy abdominal pain with watery stools, nausea and vomiting
 - **Diverticulitis:** of cecum or perforated carcinoma of cecum is difficult to distinguish clinically from appendicitis; diagnosis is usually done intraoperatively
 - **Epiploic appendagitis:** infarction of the appendage due to torsion; pain shift is unusual and patient is usually not ill
 - **Gynecologic conditions:** ruptured ectopic pregnancy, PID, ruptured graafian follicle, twisted ovarian cyst
 - **Intussusception:** patient's age, type of pain, palpable mass in the lower quadrant and passage of currant jelly stool may help with diagnosis; barium enema offers both diagnostic and therapeutic option for intussusception.
- **Special conditions:**
 - AP IN THE YOUNG**
 - Diagnostic accuracy in these age group is lower compared to adults due to imprecise history and nonspecific abdominal complaints
 - Hx: vomiting, fever and diarrhea are common complaints
 - PE: abdominal distention, maximal tenderness in the right lower quadrant, the inability to walk or walking with a limp, and pain with percussion, coughing, and hopping
 - Gangrene and rupture are more common in these age group because of delays in diagnosis

AP IN THE ELDERLY

- Usually with atypical presentation: fever, leukocytosis and RLQ pain maybe minimal or absent
- Have 60-90% rupture rate
- The atrophic omentum is less capable of walling off a perforated appendix → diffuse peritonitis or distant intra-abdominal abscess are expected
- If patient is older than 60yo, always rule out cancer because the definitive treatment for that is right hemicolectomy (if affecting the cecum)

AP IN PREGNANCY

- **Most common surgical emergency in pregnancy**
- In pregnancy, the gravid uterus pushes the appendix superiorly and the tip medially
- Most consistent sign of AP in pregnant women: pain in the right side of the abdomen
- Common occurrence of abdominal pain, nausea and leukocytosis in the normal course of pregnancy makes diagnosis difficult
- Most cases occur during 2nd trimester
- Fetal mortality is 2-8.5%; increases to 35% with rupture

AP IN HIV OR AIDS PATIENTS

- Similar presentation to non-infected patients
- Risk of appendiceal rupture is higher for these patients
- DDx: CMV enteritis, typhilitis, fungal, protozoal and mycobacterial infections

Treatment: appendectomy

C. APPENDICEAL TUMORS - CARCINOID

- most common location is appendix (50%), ileum (25%) then rectum (20%)
- ileal carcinoid has the highest potential for metastasis (around 35%) vs appendiceal carcinoid which has lowest potential for metastasis (3%)
- Gross appearance: small, firm, circumscribed, yellowish tumor
- **Treatment:**
 - <2cm at distal appendix: appendectomy
 - >2cm or at base: right hemicolectomy

REVIEW QUESTIONS

1. A patient suspected of having appendicitis underwent exploration, Crohn's disease was found. Which of the following are true?
 - a. The normal appendix should always be removed
 - b. All grossly involved bowel, including the appendix, should be resected.
 - c. An inflamed appendix, cecum and terminal ileum, should be resected
 - d. Perforated bowel and advanced Crohn's disease with obstruction should be resected.

Answer: D

If a normal appendix is found at the time of laparotomy, other causes should be sought. If Crohn's disease is encountered and the cecum and base of the appendix are normal, an appendectomy should be performed. If the base is involved with Crohn's disease and the appendix is normal, appendectomy should not be performed. If the finding of Crohn's disease is uncomplicated by perforation or obstruction, ileal resection is not indicated. However, in the case of perforation or Crohn's disease with obstruction, the involved bowel should be resected.

COLON, RECTUM, ANUS

- A. Embryology
- B. Diagnostic evaluation of Colon, Rectum and Anus
- C. Evaluation of Common symptoms
- D. Diverticular disease
- E. Colorectal adenocarcinoma
- F. Colorectal carcinoid tumors
- G. Anal intraepithelial neoplasia (Bowen's disease)
- H. Volvulus
- I. Colonic pseudoobstruction (Ogilvie's syndrome)
- J. Hemorrhoids
- K. Anal fissure
- L. Anorectal abscess
- M. Fistula in ano

A. EMBRYOLOGY

- Embryonic GI tract begins developing during **4th week of gestation**

Table 57. Embryology of GI tract

FOREGUT	MIDGUT	HINDGUT
Esophagus, stomach, pancreas, liver, duodenum	small intestine, ascending colon, and proximal transverse colon	distal transverse colon, descending colon, rectum, and proximal anus
Celiac artery	SMA	IMA

***distal anus is derived from the ectoderm; BS: internal pudendal artery

- The colon has 5 distinct layers: mucosa, submucosa, inner circular muscle, outer longitudinal muscle, and serosa

✓ MUST KNOW

Most common bacterium within the colon is **B. fragilis** followed by **E. coli** and **Enterococcus sp.**

B. DIAGNOSTIC EVALUATION OF COLON, RECTUM AND ANUS

ENDOSCOPY:

1. Anoscopy

- useful instrument for the examination of the anal canal
- not attempted without anesthesia if patient complains of severe perianal pain and does not tolerate digital rectal examination

2. Proctoscopy

- useful for the examination of the rectum and distal sigmoid colon
- can be both therapeutic and diagnostic
- length: 25 cm
- 15-19 mm diameter proctoscope is useful for diagnostic examination
- useful for polypectomy, electrocoagulation, detorsion of sigmoid volvulus

3. Flexible sigmoidoscopy and colonoscopy

- provides excellent visualization of colon and rectum
- can be both diagnostic and therapeutic
- length:
 - 60 cm: sigmoidoscope
 - 100-160 cm: colonoscope
- full length insertion:
 - may allow visualization as far as splenic flexure: sigmoidoscope
 - may allow visualization as far as terminal ileum: colonoscope

IMAGING:

1. Plain x-ray and contrast studies

- **plain x-rays of abdomen** (upright, supine and diaphragmatic views) are useful for detecting free intra-

abdominal air, bowel gas patterns suggestive of small or large bowel obstruction and volvulus

- **contrast studies** are useful for evaluating obstructive symptoms, delineating fistulous tracts and diagnosing small perforations or anastomotic leaks.
- **Gastrografin** (water soluble contrast agent) is recommended if perforation or leak is suspected
- **Double contrast barium enema** is 70-90% sensitive for the detection of mass lesions **greater than 1 cm in diameter**
 - If a small, non obstructing lesion is considered, **colonoscopy** is the preferred imaging modality of choice

2. CT

- the utility of CT is in the **detection of extraluminal disease**, such as intra-abdominal abscesses and pericolic inflammation and in **staging colorectal carcinoma** (because of its sensitivity in detecting hepatic metastasis)
 - **REMEMBER: a standard CT scan is INSENSITIVE for detection of intraluminal lesions**
- **If considering a perforation / anastomotic leak:** check for extravasation of oral or rectal contrast
- **Bowel wall thickening / mesenteric stranding** suggests inflammatory bowel disease, enteritis/colitis or ischemia

3. MRI

- the main use of MRI in colorectal DO is in the evaluation of **pelvic lesions**
- more sensitive than CT for detecting **bony involvement or pelvic sidewall extension of rectal tumors**.
- Can be useful in the detection and delineation of **complex fistulas in ano**.

4. Positron Emission Tomography

- useful for imaging tissues with high levels of anaerobic glycolysis, such as **malignant tumors**
- **F-fluorodeoxyglucose** is injected as a tracer → its metabolism results in positron emission
- Used as an adjunct to CT in staging colorectal cancer

5. Angiography

- used for the detection of bleeding within the colon or small bowel
- to visualize hemorrhage angiographically, bleeding must be relatively brisk (0.5 to 1 cc per minute)
- if extravasation of contrast is identified, infusion with vasopressin or angiographic embolization can be therapeutic.

6. Endorectal and Endoanal UTZ

- is used primarily to evaluate the depth of invasion of **neoplastic lesions in the rectum** and detecting sphincter defects & outlining complex anal fistulas
- normal rectal wall can be seen as a 5 layer structure
- UTZ can reliably differentiate benign polyps from invasive tumors based upon the **integrity of the submucosal layer**.
- Accuracy in detecting depth of mural invasion is 81-94%

PHYSIOLOGIC AND PELVIC FLOOR INVESTIGATIONS:

useful in the evaluation of patients with incontinence, constipation, rectal prolapse, obstructed defecation and other pelvic floor disorders

1. Manometry

- procedure: pressure-sensitive catheter is placed in the lower rectum → catheter is withdrawn through the anal canal and pressures recorded
- values:
 - **resting pressure** (normal: 40-80 mmHg): reflects the function of the internal anal sphincter
 - **Squeeze pressure** (normal: 40-80 mmHg above resting pressure): maximum voluntary contraction pressure minus resting pressure, reflects the function of the external anal sphincter

- **High pressure zone** (normal: 2-4 cm): estimates the length of the anal canal
- **Absence of rectoanal inhibitory reflex is characteristic of Hirschsprung's disease**

- 2. Neurophysiology**
- Neurophysiologic testing assesses function of the pudendal nerve and recruitment of puborectalis muscle fibers

LABORATORY STUDIES:

- 1. Fecal Occult Blood testing (FOBT)**
- is a screening test for colonic neoplasms in asymptomatic, average-risk individuals
- occult bleeding from any GI source will produce a positive result (since it is a non specific test for peroxidase contained in hemoglobin)
- any positive FOBT mandates further investigation, usually by colonoscopy

- 2. Stool studies**
- helpful in the evaluation of etiology of diarrhea
- wet mount examination: (+) fecal leukocytes indicate colonic inflammation or presence of invasive organisms (such as E. coli or Shigella)
- Sudan red stain to stool sample: to evaluate steatorrhea

- 3. CEA: tumor marker**
- elevated in 60-90% of patients with colorectal cancer; however, not an effective screening agent for colorectal CA
- serial monitoring used after curative-intent surgery is done

- C. EVALUATION OF COMMON SYMPTOMS**
- 1. Pain**
- abdominal pain related to colon and rectum can result from obstruction (inflammatory or neoplastic), inflammation, perforation or ischemia
- pelvic pain can originate from distal colon and rectum or adjacent urogenital structures
 - tenesmus: due to proctitis or from rectal or rectorectal mass
 - cyclical pain + menses + rectal bleeding: endometriosis
- anorectal pain is most often secondary to anal fissure, perirectal abscess and/or fistula, or a thrombosed hemorrhoids

- 2. Lower GI bleeding**
- first goal in managing a patient with GI hemorrhage: **ADEQUATE RESUSCITATION**
- **insert NGT** (1st test that should be performed) since the most common cause of bleeding can either be esophageal, gastric or duodenal
 - if (+) return of bile → suggests that bleeding is distal to the ligament of Treitz
 - if bloody/non-bile secretions → suggests an upper intestinal source; do EGD right away
- technetium-99-tagged RBC scan: highly sensitive (as little as 0.1 cc/hour of bleeding can be detected); however location is imprecise → perform angiography to localize bleeding
- if sharp, knife-like pain + bright red rectal bleeding with bowel movements → anal fissure
- if painless, bright red rectal bleeding secondary to bowel movements → internal hemorrhoids

- 3. Constipation and obstructed defecation**
- A very common problem
- rule out an underlying metabolic, pharmacologic, endocrine, psychological and neurologic causes first before work up
- a stricture or mass lesion should be excluded by colonoscopy or barium enema
- once other causes have been ruled out, perform transit studies
- Medical management is the mainstay of treatment for constipation (High fiber, increase fluids & laxatives)

4. Diarrhea and irritable bowel syndrome

- Acute bloody diarrhea and pain can be due to infection or inflammation
- chronic diarrhea has a more difficult diagnostic dilemma since causes are myriad (ulcerative colitis, crohn's colitis, malabsorption, short-gut syndrome, carcinoid, islet cell tumors, etc)

5. Incontinence

- ranges in severity from occasional leakage of gas and liquid stool to daily loss of solid stool
- can be neurogenic or anatomic
 - Neurogenic: diseases of CNS, spinal cord, pudendal nerve injury
 - Anatomic: congenital abnormalities, procidentia, overflow incontinence secondary to impaction, neoplasm or trauma
- Most common traumatic cause of incontinence is injury to the anal sphincter during vaginal delivery

D. DIVERTICULAR DISEASE

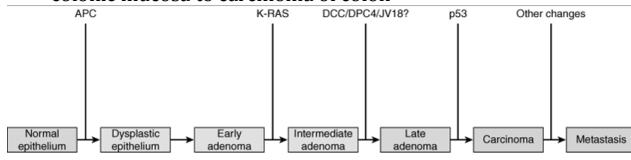
- **Diverticulosis:** presence of diverticula without inflammation.
 - Common in patients with low fiber diet
 - Majority tend to occur after the age of 85
 - **Sigmoid colon: most common site of diverticulosis**
 - Common symptom: massive LGIB
- **Diverticulitis:** inflammation and infection associated with diverticula.
 - **5% of complicated diverticulitis develop a fistula to an adjacent organ.** Most common of which is a **colovesical fistula**.
 - More common is false diverticula type
 - Only mucosa and muscularis mucosa have herniated (also called pulsion diverticula) through the colonic wall, in between taenia coli (area of weakness)
 - True diverticula, comprises all layers of the bowel, is congenital and rare
 - Clinical manifestations of diverticulitis:
 - Uncomplicated diverticulitis: left-sided abdominal pain, with or without fever, mass and leukocytosis
 - complicated diverticulitis: abscess, obstruction, diffuse peritonitis (free perforation), or fistulas (most common is colovesical fistula)
- **Hinchey staging for complicated diverticulitis**
 - Stage I:** colonic inflammation with an associated pericolic abscess
 - Stage II:** colonic inflammation with a retroperitoneal or pelvic abscess
 - Stage III:** purulent peritonitis
 - Stage IV:** fecal peritonitis.
- Diagnosis: **CT scan**
 - Appears as **pericolic soft tissue stranding, colonic wall thickening, and/or phlegmon**
- Treatment:
 - Uncomplicated diverticulitis: outpatient therapy with broad-spectrum oral antibiotics for 7-10 days & low-residue diet; failure to improve within 48-72 hours indicates abscess formation
 - If 2nd episode of uncomplicated diverticulitis or 1st episode of complicated diverticulitis: elective sigmoid colectomy is recommended
 - Small abscesses (<2 cm diameter) may be treated with parenteral antibiotics.
 - Larger abscesses are best treated with CT-guided percutaneous drainage

E. COLORECTAL ADENOCARCINOMA

- Most common malignancy of the GIT
- Risk factors:
 1. Aging: dominant risk factor for colorectal cancer; incidence increases after 50 yo
 2. Known FH of cancer: accounts for 20% of cases
 3. Diet: high in animal fat and low in fiber
 4. Inflammatory bowel syndrome
 5. Cigarette smoking

- Pathogenesis: genetic defects

Figure 34. Schematic diagram showing progression from normal colonic mucosa to carcinoma of colon



APC

- Tumor suppressor gene located at chromosome 5
- Function: the protein product of APC is for maintaining cellular adhesions and suppressing neoplastic growth
- **APC inactivation** leads to sporadic colorectal cancer
- Mutated in individuals with familial adenomatous polyposis (FAP)

K-RAS

- Proto-oncogene located in chromosome 12
- Function: encodes for plasma membrane based protein involved in transduction of growth and differential signals
- Mutation leads to uncontrolled cell division
- **K-RAS activation** leads to colorectal cancer
-

DCC

- Tumor suppressor gene located at chromosome 18
- Function: encodes for a protein responsible for cell to cell contact
- Loss of DCC gene (or inactivation) tends to present in more advanced carcinomas
- Present in 70% of colorectal carcinomas

P53

- Tumor suppressor gene located at chromosome 17
- **Mutations of this gene are the most common genetic abnormality found in human cancer genes**
- Function: crucial for initiating apoptosis in cells with irreparable genetic damage.
- Mutations in p53 are present in 75% of colorectal cancers
- **p53 inactivation** leads to colorectal cancer

Polyps:

- Non-neoplastic polyps (no malignant potential)
 - **Hyperplastic polyp: most common type of all polyps;** usually small, multiple and sessile; occur frequently in the rectosigmoid region
 - **Pseudopolyps (or inflammatory polyps):** occur most commonly in the context of inflammatory bowel disease, amebic colitis, ischemic colitis, and schistosomal colitis; not premalignant, but they cannot be distinguished from adenomatous polyps based upon gross appearance & therefore should be removed.
- **Hamartomas:** similar appearance to adenomatous polyps but is not considered to be premalignant
 - **Familial juvenile polyposis:** autosomal dominant DO in which patients develop hundreds of polyps in the colon and rectum; degenerate into adenomas → carcinoma
 - **Peutz-Jeghers syndrome:** characterized by polyposis of the small intestine and, to a lesser extent, of the colon and rectum. ; Characteristic melanin spots are noted on the buccal mucosa and lips of these patients.
 - **Cronkite-Canada syndrome:** GI polyposis + alopecia + cutaneous pigmentation + atrophy of the fingernails and toenails; SSx: Diarrhea, vomiting, malabsorption, and protein-losing enteropathy

- **Cowden syndrome:** autosomal dominant disorder with hamartomas of all three embryonal cell layers; Facial trichilemmomas, breast cancer, thyroid disease, and GI polyps are typical of the syndrome.

➤ Neoplastic polyps

- **Tubular adenomas: most common type of neoplastic polyps;** asymptomatic, pedunculated, less than 1 cm in size and occur commonly in the rectosigmoid region
<1cm: rare chance for malignancy
1-2cm: 10% chance for malignancy
>2 cm: 30% chance for malignancy
- **Tubulovillous adenoma:** mixed; 22% chance for malignancy
- **Villous adenoma:** sessile, larger and symptomatic, can cause malignancy by 40-50%; **highest risk of cancer**
- **Sessile adenomas are more likely to harbor malignancy compared to pedunculated ones**

Inherited colorectal carcinoma

➤ **Familial adenomatosis polyposis**

- rare autosomal dominant condition accounts for only about 1% of all colorectal adenocarcinomas.
- Due to mutation in the APC gene, located on chromosome 5q
- Clinically, patients develop hundreds to thousands of adenomatous polyps shortly after puberty.
- The lifetime risk of colorectal cancer in FAP patients approaches 100% by age 50 years.
- Flexible sigmoidoscopy of first-degree relatives of FAP patients beginning at age 10 to 15 years
- FAP may be associated with extraintestinal manifestations such as congenital hypertrophy of the retinal pigmented epithelium, desmoid tumors, epidermoid cysts, mandibular osteomas (Gardner's syndrome), and central nervous system tumors (Turcot's syndrome).

➤ **HNPCC or Lynch syndrome**

- Rare autosomal dominant disorder arising from errors in mismatch repair
- is characterized by the development of colorectal carcinoma at an early age (average age: 40 to 45 years).
- The risk of synchronous or metachronous colorectal carcinoma is 40%.
- HNPCC also may be associated with extracolonic malignancies, including endometrial (most common), ovarian, pancreas, stomach, small bowel, biliary, and urinary tract carcinomas.
- Diagnosis: *Amsterdam criteria* for clinical diagnosis of HNPCC are three affected relatives with histologically verified adenocarcinoma of the large bowel (one must be a 1st degree relative of one of the others) in 2 successive generations of a family with 1 patient diagnosed before age 50 years.
- Screening colonoscopy is recommended annually for at-risk patients beginning at either age 20 to 25 years or 10 years younger than the youngest age at diagnosis in the family, whichever comes first.

➤ **Familial colorectal cancer**

- Nonsyndromic familial colorectal cancer accounts for 10 to 15% of patients with colorectal cancer
- Screening colonoscopy is recommended every 5 years beginning at age 40 years or beginning 10 years before the age of the earliest diagnosed patient in the pedigree.

- Routes of spread & natural history:

- **Regional lymph node involvement** is the most common form of spread of colorectal carcinoma and usually precedes distant metastasis
- **T stage (depth of invasion)** is the single most significant predictor of lymph node spread
- The number of lymph nodes with metastases correlates with the presence of distant disease and inversely with survival: 4 or more involved lymph nodes predict a poor prognosis
- **most common site of distant metastasis from colorectal cancer is the liver** (via **hematogenous spread** to the portal venous system)

- Screening:
 - annual DRE at age 40
 - FOB at age 50
 - Flexible sigmoidoscopy every 5 years at age 50
 - Colonoscopy if with risk factors
- Clinical presentation: **change in bowel habits, rectal bleeding, melena, unexplained anemia, or weight loss**
- Staging and treatment

Table 58. Duke staging of colorectal cancer & treatment

Stage	description	5 year survival	Treatment
Stage A	Cancer limited to mucosa & submucosa	90%	Wide resection of colon with sampling of LN (to rule out T1 disease stage); stage B can also employ RT+CT
Stage B	Cancer invades the muscularis propria	70%	
Stage C	Invasion of local LN	30%	Surgery + chemox (5-fluorouracil + leucovorin) + RT
Stage D	Distant metastasis	Limited survival	palliative

- **LAR:** for tumors located 5-10 cm from anal verge
- **APR:** tumors less than 5 cm from anal verge and if recurrent cancer at LAR site

F. COLORECTAL CARCINOID TUMORS

- Result of a neuroendocrine tumor that secretes neurotransmitters (serotonin, ACTH, histamine, dopamine, tryptophan, substance P, bradykinin)
- occur most commonly in the GI tract
- most common location is appendix (50%), ileum (25%) then rectum (20%)
- ileal carcinoid has the highest potential for metastasis
- appendiceal has lowest potential for metastasis
- Carcinoid tumors in the proximal colon are less common and are more likely to be malignant.
- Can be part of MEN type I
- risk of malignancy increases with size (more than 60% of tumors greater than 2 cm in diameter are associated with distant metastases)
- clinical manifestation:
 - triad of flushing (due to excess bradykinin), diarrhea (due to excess serotonin) & valvular heart disease (primarily affects the mitral valve from excess serotonin)
 - others: hypotension, tachycardia, alcohol intolerance
- diagnosis:
 - 24 hour 5-HIAA collection (5-HIAA is a metabolite of serotonin)
- treatment:
 - Small carcinoids can be locally resected, either transanally or using transanal endoscopic microsurgery.
 - Larger tumors or tumors with obvious invasion into the muscularis require more radical resection
 - Medical: somatostatin analogues (octreotide)
 - RT

G. ANAL INTRAEPITHELIAL NEOPLASIA (BOWEN'S DISEASE)

- **refers to squamous cell carcinoma in situ of the anus.**
- precursor to an invasive squamous cell carcinoma (epidermoid carcinoma)
- may appear as a plaque-like lesion, or may **only be apparent with high-resolution anoscopy and application of acetic acid or Lugol's iodine solution.**
- associated with HPV infection types 16 and 18.
- Incidence has increased dramatically **among HIV-positive, homosexual men.**
- Treatment:
 - **Ablation**
 - Topical immunomodulators such as imiquimod, Topical 5-FU

H. VOLVULUS

- occurs when an air-filled segment of the colon twists about its mesentery
- clinical manifestations: similar to SBO; abdominal distention, nausea, and vomiting; can rapidly progress to generalized abdominal pain and tenderness; **Fever and leukocytosis are heralds of gangrene and/or perforation**

Table 59. Comparison of sigmoid vs cecal volvulus

Sigmoid volvulus	Cecal volvulus
-90% of cases	<20% of cases
-plain abdominal xray: bent inner tube or coffee bean appearance with the convexity of the loop lying in the RUQ (opposite site of obstruction) -gastrografin enema: bird's beak (pathognomonic)	-plain abdominal xray: kidney-shaped air-filled structure in the LUQ
Initial management: fluid resuscitation followed by endoscopic detorsion (rigid proctoscope); if suspecting gangrene or perforation, perform immediate surgical exploration	-surgical exploration once diagnosis is made; no room for endoscopic detorsion

✓ MUST KNOW

Bird's beak is also seen in barium esophagogram of achalasia!

I. COLONIC PSEUDOObSTRUCTION (OGILVIE'S SYNDROME)

- Distention of the abdomen leading to colonic obstruction (even if there is no obvious signs of obstruction)
- most commonly occurs in hospitalized patients and is associated with the use of narcotics, bedrest, and comorbid disease.
- Due to a neurologic dysfunction, electrolyte abnormality and age
- Treatment: NGT, **IV neostigmine**, IV atropine (to counter bradycardia as SE of neostigmine), exploratory laparotomy during worst case scenario)

J. HEMORRHOIDS

- are cushions of submucosal tissue containing venules, arterioles, and smooth-muscle fibers that are located in the anal canal
- Excessive straining, increased abdominal pressure, and hard stools lead to further prolapse of hemorrhoids
- Difference between internal and external hemorrhoids:

Table 60: comparison of internal and external hemorrhoids

Internal hemorrhoids	External hemorrhoids
- Exaggerated submucosal vascular cushions normally <u>located above dentate line</u> ; <u>covered by insensate transitional mucosa of the anal canal and not by anoderm</u> ; only become painful when already thrombosed / necrosis	- are dilated veins of the inferior hemorrhoidal plexus <u>located below the dentate line and covered by anoderm</u> ; can cause significant pain
- prolapsing hemorrhoids: are internal hemorrhoids beyond the dentate line	

- **Types of internal hemorrhoids:** graded according to extent of prolapsed ☺
 - 1st degree:** bulge into the anal canal and may prolapse beyond the dentate line on straining
 - 2nd degree:** prolapse through the anus but reduce spontaneously
 - 3rd degree:** prolapse through the anal canal and require manual reduction
 - 4th degree:** prolapse but cannot be reduced and are at risk for strangulation
- **Combined internal and external hemorrhoids:** straddle the dentate line; mixed characteristics
- **Post partum hemorrhoids:** result from straining during labor, which results in edema, thrombosis, and/or strangulation.
- Treatment:
 - Dietary fiber, stool softeners, ↑OFL, avoid straining: for 1st & 2nd degree hemorrhoids
 - Rubber band ligation: for persistent 1st & 2nd degree hemorrhoids & selected 3rd degree hemorrhoids
 - If thrombosed hemorrhoids, perform excision
 - **Most common complication of hemorrhoidectomy:** urinary retention

K. ANAL FISSURE

- is a tear in the anoderm distal to the dentate line
- **90% of fissures are located at the posterior midline**, an area where the anoderm is least supported by the sphincter
- **Fissures located laterally should arouse suspicion of Crohn's, UC, syphilis, TB,leukemia**
- **Clinical manifestation:** tearing pain with defecation and hematochezia; often too tender to tolerate DRE
- Treatment
 - Initially, can be **managed conservatively with lubricants, warm sitz bath and bulk laxatives (treatment of choice)**
 - Surgery: lateral subQ partial internal sphincterectomy
 - **Posterior fissurectomy & sphincterectomy can lead to keyhole defect & constant soiling**

L. ANORECTAL ABSCESS ☺

- **Perianal abscess:** most common manifestation and appears as a painful swelling at the anal verge
- **Ischiorectal abscess:** happens when there is Spread through the external sphincter below the level of the puborectalis; may become extremely large and may not be visible externally; DRE will reveal a painful swelling laterally in the ischiorectal fossa
- **Intersphincteric abscess:** occur in the intersphincteric space and are notoriously difficult to diagnose; causes deep pain in the rectum without external manifestation
- **Pelvic and superior levator abscess:** rare; may result from extension of an intersphincteric or ischiorectal abscess upward, or extension of an intraperitoneal abscess downward
- **Horseshoe abscess:** bilateral ischiorectal, supralevator or perianal abscesses that communicate; begins as a posterior midline infection
- Treatment: drainage with local anesthesia

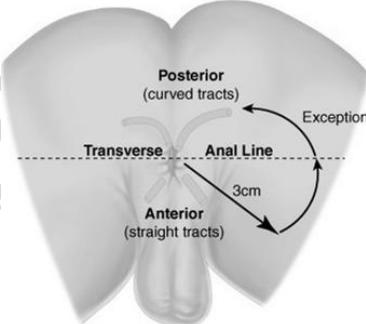
- Signs of (+) fistula: nonhealing of an abscess wounds or recurrence of an abscess at the same location

M. FISTULA IN ANO

- **Classification** (based on relationship to the anal sphincter complex)
 1. **Intersphincteric (most common)** ☺: tracks through the distal internal sphincter and intersphincteric space to an external opening near the anal verge
 2. **Transsphincteric:** often results from an ischiorectal abscess and extends through both the internal and external sphincters
 3. **Suprasphincteric:** originates in the intersphincteric plane and tracks up and around the entire external sphincter
 4. **Extrasphincteric:** originates in the rectal wall and tracks around both sphincters to exit laterally, usually in the ischiorectal fossa
- **Goodsall's rule** ☺: states that, if the external opening is anterior to the imaginary line drawn between the ischial tuberosities, the fistula runs directly into the anal canal. If the external opening is posterior, the tract curves to the posterior midline.

*****EXCEPTION:** if an anterior external opening is greater than 3 cm from the anal margin, these fistulas usually track to the posterior midline!!!

Figure 35. Goodsall's rule



- **Treatment:** fistulotomy with adequate drainage or seton placement

REVIEW QUESTIONS

1. Which of the following is important in maintaining the integrity of the colonic mucosa?
 - a. short-chain fatty acids
 - b. alanine
 - c. medium-chain fatty acids
 - d. glutamine

Answer: A

Short chain fatty acids are produced by bacterial fermentation of dietary carbohydrates. Short chain fatty acids are an important source of energy for the colonic mucosa, and metabolism by colonocytes provides energy for processes such as active transport of sodium. Lack of a dietary source for production of short chain fatty acids, or diversion of the fecal stream by an ileostomy or colostomy, may result in mucosal atrophy and diversion colitis.

2. Match the organs in the left hand column with the location of their referred pain in the right hand column. (items in the right may be used more than once)

- | | |
|----------------|-----------------|
| A. Gallbladder | a. epigastrium |
| B. Jejunum | b. perumbilical |
| C. Rectum | c. hypogastrium |
| D. Pancreas | d. shoulder |
| E. Appendix | |

Answer: A - a,d; B - b; C - c; D - a; E - b

The visceral peritoneum is innervated by C fibers coursing with the autonomic ganglia. C fibers are unmyelinated, slow-conducting (0.5-5.0 m/s), polymodal nociceptors that travel bilaterally with the sympathetic and parasympathetic fibers. Visceral pain is a response to injury of the visceral peritoneum.

Distension, stretch, traction, compression, torsion, ischemia and inflammation trigger visceral pain fibers. Abdominal organs are insensate to heat, cutting and electrical stimulation.

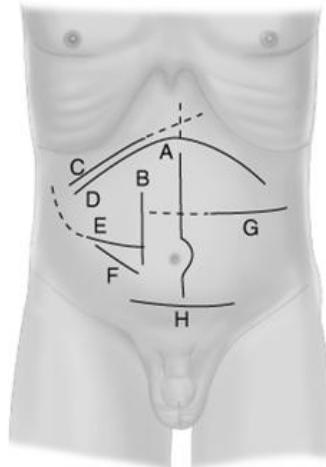
Visceral pain is typically vague and crampy and is perceived in the region of origin of the embryologically derived autonomic ganglia. **Foregut organs** (proximal to the ligament of treitz) refer pain to the celiac chain, and the pain is felt in the epigastrium. The **organs of the midgut** (small intestine, ascending colon) refer pain to the superior mesenteric chain (periumbilical chain) and those of the **hindgut** (transverse and descending colon, sigmoid colon and rectum) to the inferior mesenteric ganglia and hypogastrium.

ABDOMINAL WALL & HERNIAS

- A. Abdominal Incisions
- B. Rectus abdominis diastasis
- C. Rectus sheath hematoma
- D. Abdominal wall hernias
- E. Incisional hernias
- F. Retroperitoneal fibrosis
- G. Inguinal hernias
- H. Femoral hernia

A. ABDOMINAL INCISIONS

Figure 36. Abdominal incisions



A.Midline incision	-are used because of the flexibility offered by this approach in establishing adequate exposure. -the incision in the fused midline aponeurotic tissue (linea alba) is simple and requires no division of skeletal muscle.
B.paramedian incision	-made longitudinally 3 cm off the midline, through the rectus abdominis sheath structures, and have largely been abandoned in favor of midline or nonlongitudinal access methods
C.right subcostal incision D.bilateral subcostal	-Subcostal incisions on the right (Kocher incision for cholecystectomy) or left (for splenectomy) are archetypal muscle-dividing incisions that generally result in the transaction of some or all of the rectus abdominis muscle fibers and investing aponeuroses. -These incisions generally are closed in two layers (anterior aponeurotic sheath of the rectus muscle medially, transitioning to external oblique muscle and aponeurosis more laterally & posterior, deeper layer consists of internal oblique and transverses abdominis muscle)

E.Rocky davis incision	Right lower quadrant incision or muscle splitting incision for appendectomy
F.McBurney incision	it begins 2 to 5 centimeters above the anterior superior iliac spine and continues to a point one-third of the way to the umbilicus (McBurney's point). Thus, the incision is parallel to the external oblique muscle
G.Transverse incision	Similar to kocher incision (subcostal incision). Preferred for newborns and infants because more abdominal exposure is gained per length of the incision compared to vertical exposure
H.Pfannenstiel incision	Pfannenstiel incision, used commonly for pelvic procedures, is distinguished by transverse skin and anterior rectus sheath incisions, followed by rectus muscle retraction and longitudinal incision of the peritoneum.

B. RECTUS ABDOMINIS DIASTASIS

- Other name: diastasis recti
- is a clinically evident separation of the rectus abdominis muscle pillars resulting to a **characteristic bulging of the abdominal wall in the epigastrium** (sometimes mistaken for a ventral hernia)
- may be congenital
- can be associated with advancing age, in obesity, or after pregnancy
- In the postpartum setting, rectus diastasis tends to occur in women who are of advanced maternal age, who have a multiple or twin pregnancy, or who deliver a high-birth-weight infant.
- Diagnosis:
 - CT scan: can differentiate rectus diastasis from a true ventral hernia
- Treatment: surgery

C. RECTUS SHEATH HEMATOMA

- As a result of hemorrhage from any of the network of collateralizing vessels (superior and inferior epigastric arteries or veins) within the rectus sheath and muscles
- History: trauma, sudden contraction of the rectus muscles with coughing, sneezing, or any vigorous physical activity.
- Clinical manifestations: sudden onset of unilateral abdominal pain that increases with contraction of the rectus muscles; palpable tender mass
- **(+)Fothergill's sign: palpable abdominal mass that remains unchanged with contraction of the rectus muscles**
- Diagnosis:
 - Abdominal UTZ may show a solid or cystic mass within the abdominal wall
 - CT scan: most definitive study to establish the correct diagnosis and to exclude other disorders
- Treatment: nonoperative; surgery is indicated in instances of expensing hematoma and hemodynamic instability

D. ABDOMINAL WALL HERNIAS

- This is due to defects in the parietal abdominal wall fascia and muscle through which intra-abdominal or preperitoneal contents can protrude
- **ACQUIRED HERNIAS**
 - may develop through slow architectural deterioration of the muscular aponeuroses or they may develop from failed healing of an anterior abdominal wall incision (**incisional hernia**).
 - most common finding is a mass or bulge on the anterior abdominal wall, which may increase in size with a Valsalva maneuver
 - PE reveals a bulge on the anterior abdominal wall that may reduce spontaneously, with recumbency, or with manual pressure
 - Treatment: if incarcerated (cannot be reduced) or strangulated (BS is compromised) → do surgical correction
- **PRIMARY VENTRAL HERNIAS**
 - Non incisional or true ventral hernias
 - Examples:

Epigastric hernias: congenital due to defective midline fusion of lateral abdominal wall; occurs in multiples and are small; located in the midline between the xiphoid process and the umbilicus; found to contain omentum or a portion of the falciform ligament.

Umbilical hernias: due to a patent umbilical ring; more common in premature infants; spontaneous closure can occur at age of 5, no closure by that time, do elective surgical repair

Spigelian hernias: occur anywhere along the length of the Spigelian line or zone—an aponeurotic band of variable width at the lateral border of the rectus abdominis.

E. RETROPERITONEAL FIBROSIS

- class of disorders characterized by hyperproliferation of fibrous tissue in the retroperitoneum
- if primary, it is known as **Ormond disease**
- may be secondary to inflammatory process, malignancy, or **medication (methysergide, ergotamine, hydralazine, methyldopa and B blockers)**
- Men are twice as likely to be affected as women
- primarily affects individuals in the 4th-6th decades of life.
- Clinical manifestations:
 - > Sx: insidious onset of dull, poorly localized abdominal pain, unilateral leg swelling, intermittent claudication, oliguria, hematuria, & dysuria.
 - > PE: hypertension, the palpation of an abdominal or flank mass, lower extremity edema (unilateral or bilateral), or diminished lower extremity pulses (unilateral or bilateral).
- Diagnosis:
 - > ↑ESR, BUN & creatinine
 - > **Most definitive noninvasive diagnostic test: intravenous pyelography**
- Treatment: corticosteroids with or without surgery (only indicated when renal function is compromised)

F. INGUINAL HERNIAS

Table 61. comparison of Inguinal hernias

	Indirect inguinal hernia	Direct inguinal hernia
etiology	- usually congenital; due to patent processus vaginalis	-Usually acquired; weakness in the abdominal wall musculature
Risk factors:	Strenuous physical activity, obesity, ehler's danlos, smoking	
anatomy	protrude lateral to the inferior epigastric vessels, through the deep inguinal ring	protrusions medial to the inferior epigastric vessels, in Hesselbach's triangle
PE: inguinal occlusion test	cough impulse is controlled; felt on the dorsum of fingertip	Cough impulse is manifest; felt on the fingertip

- Clinical manifestations: groin pain
- Diagnosis: usually employed for ambiguous diagnosis (i.e. obese patients)
- **Treatment: definitive treatment is surgical repair**

Bassini repair: anterior approach, nonprosthetic, hernia reduced and the defect oversewn, & reconstruction the site of weakness; disadvantage: (+) tension on the reconstructed tissue

Shouldice repair: anterior approach, nonprosthetic, multilayer (4-layer suture repair) reconstruction distributes the tension, effectively resulting in a tension-free repair; lowest recurrence rate

Pott's repair: high ligation of the sac only, with no repair of the inguinal canal; used for indirect hernias only

McVay repair: anterior approach, nonprosthetic; the conjoined tendon is sutured to the cooper's ligament laterally; can be used for indirect, direct & **femoral hernias**

*****problem with anterior non prosthetic approaches: high recurrence rates**

Lichtenstein tension free repair: addition of a mesh prosthesis effected a reconstruction of the posterior inguinal canal, without placing tension on the floor itself

Read-rives repair: anterior preperitoneal approach

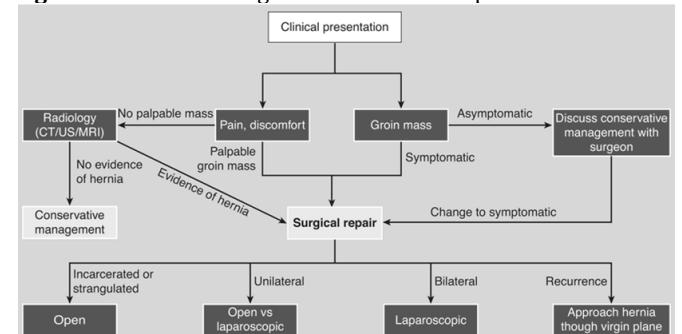
Rives, stoppa, wanz repair: giant prosthetic reinforcement of the visceral sac; preperitoneal approach

Kugel repair: maximize on the preperitoneal approach while minimizing on the length of the skin and fascia incision

Laparoscopic repair: uses preperitoneal approach with small incisions; can asses and repair unilateral or bilateral inguinal hernias

Emergency inguinal hernia repair: reserved for strangulated, incarcerated and sliding hernias

Figure 37: treatment algorithm for hernia repair



✓ MUST KNOW

Hesselbach's triangle:

Inferior: inguinal ligament

Medial: rectus abdominis

Superolateral border: inferior epigastric vessels

✓ MUST KNOW

Femoral hernias are more prevalent in females compared to males but the most common type of groin hernia in females is still indirect inguinal hernia.

REVIEW QUESTIONS

1. Which of the following is the most important initial therapy for a patient with portal hypertension, ascites, and a tense umbilical hernia?
 - a. Primary repair with concurrent placement of a peritoneal venous shunt
 - b. Emergency primary repair to avoid hernia rupture
 - c. Medical therapy to control ascites
 - d. Transjugular intrahepatic portacaval shunt followed by umbilical hernia repair

Answer: C

Treatment and control of the ascites with diuretic, dietary management and paracentesis is the most appropriate initial therapy. Patients with refractory ascites may be candidates for transjugular intrahepatic portacaval shunting or eventual liver transplantation. Umbilical hernia repair should be deferred until after the ascites is controlled.

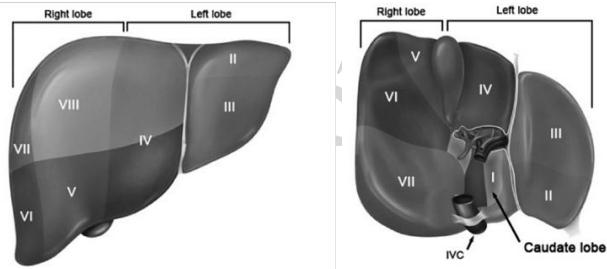
2. In the setting of an equivocal examination, which of the following has the greatest sensitivity in diagnosing an inguinal hernia?
 - a. Repeat examination by a second surgeon
 - b. Ultrasound
 - c. CT scan
 - d. MRI

Answer: D

Although Ct scan is useful in ambiguous clinical presentations, little data exist to support its routine use in diagnosis. The use of MRI in assessing groin hernias was examined in a group of 41 patients scheduled to undergo laparoscopic inguinal hernia repair. Preoperatively, all patients underwent US and MRI. Laparoscopic confirmation of the presence of inguinal hernia was deemed as gold standard. Physical examination was found to be the least sensitive. False positives were low on physical examination and MRI (one finding), but higher with US (four findings). With further refinement of technology, radiologic techniques will continue to improve sensitivity and specificity rates of diagnosis, thereby serving a supplementary role in cases of uncertain diagnosis.

- **Pringle maneuver:** used to clamp this ligament in the event of injury to the right hepatic artery during cholecystectomy
- Relationship: CBD is located at the right of the hepatic artery and anterior to the portal vein
- From the right and deep to the porta hepatis is the **foramen of Winslow (or epiploic foramen)**
- Segmental anatomy
- **Cantlie's line:** plane from the gallbladder fossa to the IVC that **separates the liver's right and left lobes grossly**.
- **Falciform ligament:** separates the left lateral and left medial segments along the umbilical fissure and anchors the liver to the anterior abdominal wall; does not separate the liver to right and left lobes
- **Couinaud's segments:** divides liver into 8 segments, in clockwise direction with caudate lobe as segment 1

Figure 38. Segmental anatomy of liver



Notes to figure

Segments	part	Corresponding side	Venous drainage
Segment I	Caudate lobe		IVC
Segment II	Left lateral superior segment	Left lobe	Left hepatic vein
Segment III	Left lateral inferior segment	Left lobe	Left hepatic vein
Segment IV	Left medial segment (quadrate lobe - outdated)	Left lobe	Middle hepatic vein
Segment V	Right anterior inferior segment	Right lobe	Right & middle hepatic vein
Segment VI	Right posterior inferior segment	Right lobe	Right hepatic vein
Segment VII	Right posterior superior segment	Right lobe	Right hepatic vein
Segment VIII	Right anterior superior segment	Right lobe	Right & middle hepatic vein

- The hepatic veins divides the liver into 4 sectors
- The liver has **dual blood supply:**
 - **hepatic artery:** 25%
 - branch of celiac artery
 - most common variation: right hepatic artery from SMA
 - **portal vein:** 75% (majority)
 - confluence of splenic vein and SMV
- normal pressure: 3-5 mmHg
- communication of portal vein and systemic circulation (important for location of varices & bleeding in portal hypertension): **gastroesophageal junction, anal canal, falciform ligament, splenic venous bed and left renal vein, and retroperitoneum**
- Biliary tree
 - Hepatic ducts follow arterial branching of the liver
 - Left hepatic duct has a longer extrahepatic course

B. LIVER FUNCTION TESTS ☺

- Term used to frequently measure the levels of group of serum markers for evaluation of liver dysfunction.
- A misnomer because the panel measures cell damage, and not liver function

Table 62. Different components of liver function tests

Serum albumin, prothrombin time & clotting factors (except factor VIII)	<ul style="list-style-type: none"> - Measures liver's synthetic function - prothrombin time and INR: best test among the 3 to measure the liver's synthetic function - PT is prolonged with conditions such as vitamin K deficiency or warfarin therapy (because vitamin K is involved in the Y-carboxylation of factors used to measure prothrombin time) ***factor VIII: not synthesized exclusively in the liver; has the shortest half-life; useful for determining liver failure
AST (formerly GGT)	- Indicators of integrity of hepatocellular

LIVER, PORTAL VENOUS SYSTEM & GALLBLADDER

- A. Anatomy
- B. Liver function tests
- C. Radiographic evaluation
- D. Liver cirrhosis
- E. Portal Hypertension
- F. Budd-Chiari syndrome
- G. Infections of the liver
- H. Benign neoplasms of the liver
- I. Malignant tumors
- J. Gallstone disease
- K. Acute cholecystitis
- L. Choledocholithiasis
- M. Cholangitis
- N. Biliary pancreatitis
- O. Acalculous cholecystitis
- P. Biliary or choledochal cysts
- Q. Sclerosing cholangitis

A. ANATOMY

Liver

- Largest organ, weighing approximately 1500 g
- **Hepatoduodenal ligament** ☺ contains the porta hepatis (portal vein, hepatic artery and common bile duct)

SGOT) & ALT (formerly SGPT)	membranes; increased levels reflect hepatocellular injury with leakage -AST: can also be found in liver, cardiac muscle, skeletal muscle, kidney, brain, pancreas, lungs, and red blood cells and thus is less specific -ALT: more specific for liver disease -AST:ALT ratio of >2:1 → alcoholic liver disease moderate increases: viral hepatitis -in the thousands → ischemia, toxin ingestion (acetaminophen), fulminant hepatitis
Indirect (unconjugated) bilirubin	-elevations point to intrahepatic cholestasis, hemolytic disorders (hemolytic anemia, resorption of hematomas), bilirubin defects in hepatic uptake or conjugation (acquired or inherited)
Direct (conjugated) bilirubin	-elevations point to extrahepatic or obstructive cholestasis, inherited or acquired disorders of intrahepatic excretion or extrahepatic obstruction
Alkaline phosphatase	-found in liver and bones; -indicative of biliary obstruction - since half life of AP is 7 days, it may take several days for the levels to normalize even after resolution of biliary obstruction
GGTP	-early marker and sensitive test for hepatobiliary disease -nonspecific; can also be elevated in overdose of certain medications, alcohol abuse, pancreatic disease, myocardial infarction, renal failure, & obstructive pulmonary disease - interpret GGTP elevations with other enzyme abnormalities

BIOCHEMISTRY

AST (aspartate transaminase): an enzyme in gluconeogenesis that transfers amino groups from **aspartic acid** to **ketoglutaric acid** to produce **oxaloacetate**.

ALT (alanine transaminase): an enzyme in gluconeogenesis that transfers amino groups from **alanine** to **ketoglutaric acid** to produce **pyruvic acid**

C. RADIOGRAPHIC EVALUATION

ULTRASOUND

Liver

- Useful initial test imaging test of the liver because it is inexpensive, involves no radiation exposure, and is well tolerated by patients
- It is excellent for diagnosing biliary pathology and liver lesions.
- Limitations:
 - Incomplete imaging: dome or beneath the ribs on the surface, lesion boundaries are not as visualized
 - Obesity
 - Overlying gas bowels
- If a mass is detected, further evaluation by CT or MRI is required since UTZ has lower sensitivity and specificity
- **Intraoperative ultrasound:**
 - Gold standard for diagnosing liver lesions
 - Useful for tumor staging, visualization of intrahepatic vascular structures, guidance of resection plane by assessment of relationship of mass to vessels, for biopsy of tumors and tumor ablation

Gallbladder

- UTZ is the **initial investigation used for any patient suspected of disease in the biliary tree**.
- UTZ will show gallbladder stones with sensitivity and specificity of >90%
 - Appearance of GB Stones: (+) acoustic shadow, move with changes in position (vs polyps: may also have a shadow but does not move with changes in position)
 - If a stone obstructs the neck of the GB: large GB but thin walled

- if **acute cholecystitis**: (+) edema within the wall of the GB or between the GB and liver in association with localized tenderness
- if **chronic cholecystitis**: contracted thick-walled GB
- **Extrahepatic ducts** are well visualized using UTZ (except for retroduodenal portion)
- Dilatation of the ducts + stones in the GB + jaundiced patient → think extrahepatic obstruction
 - **Periampullary tumors** can be difficult to diagnose on UTZ
 - UTZ is useful for evaluating tumor invasion and flow in the portal vein – an important guideline in the resectability of periampullary and pancreatic head tumors

ORAL CHOLECYSTOGRAPHY

- Considered as a diagnostic procedure of choice for gallstones but it largely replaced now by UTZ.
- Mechanism: oral administration of radiopaque compound that is absorbed and excreted by the liver, passed into the GB → stones are noted on a film as a filling defect in a visualized, opacified GB

BILIARY RADIONUCLIDE SCANNING (HIDA SCAN)

- Provides a noninvasive evaluation of the liver, GB, bile ducts and duodenum with both anatomic and functional information
- Mechanism: **Technetium-labeled derivatives of dimethyl iminodiacetic acid (HIDA)** are injected IV → cleared by Kupffer cells in the liver → excreted in the bile
 - 10 minutes: time it takes for the liver to detect it
 - 60 minutes: time it takes for the GB, bile ducts and duodenum to detect it
- **the primary use of biliary scintigraphy is the diagnosis of acute cholecystitis**
 - appearance: nonvisualized GB, with prompt filling of the common bil duct and duodenum, biliary obstruction
 - sensitivity & specificity: 95%
 - can also detect obstruction of the ampulla
 - appearance: filling of the GB and CBD with delayed and absent filling of the duodenum
 - can also be used for detection of biliary leaks as a complication of GB surgery

COMPUTED TOMOGRAPHY

Liver

- **Contrast medium** is routinely used for liver evaluation because of the **similar densities of most pathologic liver masses and normal hepatic parenchyma**.
 - Uses **dual or triple phase bolus of IV contrast**
 - Exploits the dual blood supply of the liver: **most liver tumors receive their blood supply from the hepatic artery and normal hepatic parenchyma from portal vein**
 - 2 phases:
 1. **Arterial dominant phase** (20 to 30 seconds after beginning of contrast injection) – the phase where hepatic tumors and other hypervascular lesions are well delineated.
 2. **Venous or portal dominant phase** (60 to 70 seconds after contrast injection) – the phase where there is optimal enhancement of normal liver parenchyma and hypovascular lesions (will appear attenuated in contrast with brighter normal liver parenchyma)

gallbladder

- It is the **test of choice** in evaluating patients with **suspected malignancy of the GB, extrahepatic biliary system or nearby organs, in particular, the head of pancreas**

- Abdominal CT scan is inferior to UTZ in diagnosing gallstones

PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY

- Useful in patients with **bile duct strictures and tumors**, as it defines the anatomy of the biliary tree proximal to the affected segment
- Mechanism: intrahepatic ducts are accessed percutaneously with a small needle under fluoroscopic guidance → catheter is placed → cholangiogram performed → **can do therapeutic interventions as well** (biliary drain insertion, stent placement)
- Very little role in management of uncomplicated gallstone disease

MAGNETIC RESONANCE IMAGING

Liver

- Also uses contrast agent, just like in CT scan, to differentiate normal and pathologic lesion in the liver
- Types:
 - Gadopentate dimeglumine – behaves in a manner similar to iodine in CT
 - Feruxomide – excretion of kupffer cells
 - Iminoacetic acid-derivative radionuclide – secretion in bile by hepatocytes

Gallbladder

- **MRI with MRCP (magnetic resonance cholangiopancreatography) →** offers a single noninvasive test for the diagnosis of biliary tract and pancreatic disease

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

- It is the **diagnostic and therapeutic procedure of choice** for stones in the CBD associated with **obstructive jaundice, cholangitis and gallstone pancreatitis**
- Provides direct visualization of the biliary and pancreatic ducts, particularly the ampullary region and distal common bile duct
- Therapeutic interventions include sphincterotomy, stone extraction if indicated

POSITRON EMISSION TOMOGRAPHY

liver

- PET offers functional imaging of tissues with high metabolic activity, including most types of metastatic tumors
- With high value for colorectal cancer with liver metastases
 - 20% of patients with colorectal cancer present initially with liver metastasis
 - presence of extrahepatic disease is a poor prognosticator and precludes surgical intervention
 - valuable tool for the diagnostic work up of patient with potentially resectable hepatic disease
 - must be combined with CT to improve diagnostic accuracy

D. LIVER CIRRHOSIS

- final sequela of chronic hepatic insult, is characterized by the **presence of fibrous septa (due to accumulation to ECM matrix or scar tissue)** throughout the liver subdividing the parenchyma into hepatocellular nodules
- 2 consequences: hepatocellular failure and portal hypertension
- **Classification**
 - **Micronodular cirrhosis:** characterized by thick regular septa, small uniform regenerative nodules, and involvement of virtually every hepatic lobule

- **Macronodular cirrhosis:** frequently has septa and regenerative nodules (irregularly sized hepatocytes with large nuclei and cell plates of varying thickness)
- **Mixed cirrhosis:** present when regeneration is occurring in a micronodular liver and over time converts to a macronodular pattern
- **Etiology:** viral, autoimmune, drug-induced, cholestatic, and metabolic diseases
- **Clinical manifestation**
 - Fat stores and muscle mass are reduced
 - resting energy expenditure is increased
 - (+) Muscle cramps: respond to administration of quinine sulfate and human albumin
 - increased CO & HR
 - Prone to infections → due to impaired phagocytic activity of the RES

Diagnosis

- mild normocytic normochromic anemia.
- Decreased WBC & PC
- bone marrow: macronormoblastic
- prothrombin time is prolonged & does not respond to vitamin K tx
- serum albumin level is decreased
- serum levels of bilirubin, transaminases, and alkaline phosphatase are all elevated

- **CHILD-TURCOTTE-PUGH SCORE:** evaluate the risk of portacaval shunt procedures secondary to portal hypertension and also **useful in predicting surgical risks of other intra-abdominal operations performed on cirrhotic patients**

Table 63. Child-Turcotte-Pugh Score

variable	1 point	2 points	3 points
Bilirubin	< 2 mg/dL	2-3 mg/dL	>3 mg/dL
Albumin	>3.5 g/dL	2.8-3.5 g/dL	<2.8 g/dL
INR	<1.7	1.7-2.2	>2.2
Encephalopathy	none	controlled	uncontrolled
Ascites	none	controlled	uncontrolled
Child-Turcotte-Pugh Class & overall surgical mortality rates			
Class A = 5-6 points → 10%			
Class B= 7-9 points → 30%			
Class C= 10-15 points → 75-80%			

E. PORTAL HYPERTENSION

- definition: direct portal venous pressure that is >5 mmHg greater than the IVC pressure, a splenic pressure of >15 mmHg, or a portal venous pressure measured at surgery of >20 mmHg
- normal portal venous pressure: 5 to 10 mmHg
 - at this pressure, very little blood is shunted from the portal venous system into the systemic circulation
 - as portal venous pressure increases, the communication with the systemic circulation dilate → Large amount of blood is shunted around the liver and into the systemic circulation → complications
 - A portal pressure of >12 mmHg is necessary for varices to form and subsequently bleed
- **Etiology: most common cause is **cirrhosis (intrahepatic)****
- **Clinical manifestation**
 - **Most significant clinical finding: gastroesophageal varices**
 - Major BS of GE varices: anterior branch of the left gastric or coronary vein
 - May present with splenomegaly, hemorrhoids, ascites, caput medusa & **upper GI bleeding due to variceal bleeding (leading cause of morbidity and mortality)**
- **Diagnosis:** most accurate method of determining portal hypertension is **hepatic venography**
- **Management**
 - Prevention of variceal bleeding: improve liver function (avoid alcohol), avoid aspirin & NSAID, beta blockers

- Management of acute variceal bleeding
 - Specifics:
 - **ICU admission:** must!
 - **Blood resuscitation:** goal is Hgb of 8g/dL and above
 - **FFP and platelets** for patients with severe coagulopathy
 - Short term prophylactic antibiotics: **ceftriaxone 1g/day** (proven to decrease the rate of bacterial infections and increase survival)
 - **Vassopressin** at 0.2 to 0.8 units/min IV for vasoconstriction (most potent)
 - **Octreotide/somatostatin** for splanchnic vasoconstriction
 - Endoscopic variceal ligation (EVL)
 - Balloon tamponade using sengstaken-blakemore tube
 - **Shunt therapy (surgical shunts or TIPS)**
 - Even with aggressive pharmacologic and endoscopic therapy, **10-20% of patients with variceal bleeding will continue to rebleed**
 - **Shunt therapy (surgical shunt or TIPS)**, on the other hand, has been shown to **control refractory variceal bleeding in >90% of treated individuals**
 - **Surgical shunt:** CTP class A
 - **TIPS:** CTP class B & C
 - Balloon tamponade using sengstaken-blakemore tube can **control refractory bleeding in >80% of patients**
 - Complication: aspiration, esophageal perforation

Table.64 Comparison of Surgical shunts vs TIPS

Surgical shunts (can be selective or non selective shunts)	TIPS (Transjugular Intrahepatic Portosystemic Shunt)
-aim: reduce portal venous pressure, maintain total hepatic and portal blood flow and avoid a high incidence of complicating hepatic encephalopathy	-considered as a nonselective shunt -involves implantation of a metallic stent between an intrahepatic branch of the portal vein and a hepatic vein radical TIPS can control variceal bleeding in >90% of cases refractory to medical treatment -disadvantages: bleeding either intra-abdominally or via the biliary tree, infections, renal failure, decreased hepatic function, and ter hepatic encephalopathy (because it is a non selective shunt)
- non-selective shunt (ex. portacaval shunt or eck fistula: joins the portal vein to the IVC in an end-to-side fashion & disrupts portal vein flow to the liver, or joins it in a side-to-side fashion and maintains partial portal venous flow to the liver; non selective; rarely performed now because it has a higher incidence of hepatic encephalopathy and decreased liver function resulting from the reduction of portal perfusion; controls bleeding effectively)	
- selective shunt (ex. Warren shunt – distal splenorenal & left gastric caval shunt) have ↓er incidence of hepatic encephalopathy	

F. BUDD-CHIARI SYNDROME

- uncommon congestive hepatopathy characterized by the obstruction of hepatic venous outflow due to endoluminal venous thrombosis (primary) or compressive lesion external to the veins (secondary)
- risk factors: coagulopathies, thrombotic disease
- most patients are women
- mean age of diagnosis: 30 yo
- clinical manifestations: abdominal pain (RUQ), ascites, and hepatomegaly or long standing portal hypertension
- diagnosis
- abdominal UTZ: initial investigation of choice
 - check for absence of hepatic vein flow, spider web hepatic veins & collateral circulation

- **definitive imaging: hepatic venography**
- **initial treatment: anticoagulation**

G. INFECTIONS OF THE LIVER

PYOGENIC LIVER ABSCESS

- **most common liver abscesses seen in the United States.**
- Risk factors: IV drug abuse, teeth cleaning, diverticulitis, Crohn's disease, subacute bacterial endocarditis, (+) infected indwelling catheters & immunocompromised states
- may be single or multiple
- more frequently found in the **right lobe of the liver**
- causative organisms:
 - **monomicrobial: 40%; polymicrobial: 40%; culture negative: 20%**
 - **most common: gram-negative organisms** (*Escherichia coli* - 2/3; *Streptococcus faecalis*, *Klebsiella*, and *Proteus vulgaris* are also common)
 - Anaerobic organisms (ex. *Bacteroides fragilis*) are also seen frequently
 - If (+) endocarditis / indwelling catheter: think *Staphylococcus* and *Streptococcus*
- Clinical manifestations: RUQ pain, fever & jaundice (1/3 of patients)
- Diagnosis:
 - **Leucocytosis, ↑ESR & AP** (most common laboratory findings)
 - Blood cultures reveal the causative organism in approximately 50% of cases.
 - **Liver UTZ: round or oval hypoechoic lesions with well-defined borders and a variable number of internal echoes.**
 - **CT scan: highly sensitive in the localization; appear as hypodense mass with air-fluid levels (indicating a gas-producing organisms) & peripheral enhancement**
- Treatment: cornerstones of treatment include correction of the underlying cause, percutaneous needle aspiration, and IV antibiotic therapy
 - **Initial antibiotic therapy needs to cover gram-negative as well as anaerobic organisms; must be continued for at least 8 weeks.**
 - If aspiration and IV antibiotics fail, undergo surgical therapy (either laparoscopic or open drainage)
 - Anatomic surgical resection is reserved for patients with recalcitrant abscesses.
 - **Always rule out necrotic hepatic malignancy**

AMEBIC ABSCESS

- **most common type of liver abscesses worldwide.**
- Causative agent: *Entamoeba histolytica*
- can be single or multiple
- most commonly located in the **superior-anterior aspect of the right lobe** of the liver near the diaphragm
- Gross: **necrotic central portion that contains a thick, reddish brown, pus-like material (anchovy paste or chocolate sauce)**
- Clinical manifestation: RUQ pain + fever + hepatomegaly + travel to an endemic area
- Diagnosis:
 - most common biochemical abnormality: **↑ AP level.**
 - (+) Leukocytosis
 - Transaminase levels and jaundice are unusual.
 - (+) fluorescent antibody test for *E. histolytica*
 - Ultrasound and CT scanning: very sensitive but nonspecific for the detection of amebic abscesses
 - Appears to be as a well-defined low-density round lesions that have enhancement of the wall, ragged in appearance with a peripheral zone of edema; has a central cavity with septations & fluid levels
- **Treatment**
 - **Metronidazole 750 mg tid for 7 to 10 days is the treatment of choice and is successful in 95% of cases.**

- Defervescence usually occurs in **3 to 5 days**.
- Time of resolution of abscess: **30 to 300 days** from presentation
- Aspiration of the abscess is rarely needed and should be reserved for patients with large abscesses, abscesses that do not respond to medical therapy, abscesses that appear to be superinfected, and abscesses of the left lobe of the liver that may rupture into the pericardium

HYDATID DISEASE

- due to the larval or cyst stage of infection by the tapeworm ***Echinococcus granulosus*** (causative agents)
 - intermediate hosts: Humans, sheep, and cattle
 - definitive host: dogs
- commonly involve **the right lobe of the liver**, usually the **anterior-inferior or posterior-inferior segments**
- clinical manifestations: dull RUQ or abdominal distention; can be clinically silent; if ruptured, may lead to **an allergic or anaphylactic reaction**.
- Diagnosis:
 - (+)ELISA for echinococcal antigens; maybe (-) if cyst has not leaked or does not contain scolices, or if the parasite is no longer viable
 - Eosinophilia of >7% is found in approximately 30% of infected patients.
 - UTZ & CT scan of the abdomen: sensitive for detecting hydatid cysts.
 - hydatid cysts: appear as **well-defined hypodense lesions with a distinct wall; (+) Ring-like calcifications of the pericyst** (present in 20 to 30% of cases); healing occurs → the entire cyst calcifies densely, and a lesion with this appearance is usually dead or inactive. Daughter cysts: occur in a peripheral location & are slightly hypodense compared with the mother cyst.
- Treatment:
 - Unless the cysts are small or the patient is not a suitable candidate for surgery, treatment of hydatid disease is **surgically based** (laparoscopic or open complete cyst removal + instillation of scolicidal agent)
 - **caution must be exercised to avoid rupture of the cyst** with release of protoscolices into the peritoneal cavity.
 - **Peritoneal contamination can result in an acute anaphylactic reaction or peritoneal implantation of scolices with daughter cyst formation and inevitable recurrence**
 - Medical treatment of choice: **albendazole** - initial treatment for small, asymptomatic cysts.

H. BENIGN NEOPLASMS OF THE LIVER

HEPATIC CYST

- **most common benign lesion found in the liver is the congenital or simple cyst**
- female:male ratio is approximately 4:1
- Clinical manifestation: asymptomatic if small; Large simple cysts may cause abdominal pain, epigastric fullness, and early satiety. Occasionally the affected patient presents with an abdominal mass.
- Diagnosis: appear as **thin-walled, homogeneous, fluid-filled structures with few to no septations**.
- Treatment:
 - **Observation if asymptomatic**
 - If symptomatic, perform UTZ- or CT-guided percutaneous cyst aspiration followed by sclerotherapy
 - excised cyst wall is sent for pathologic analysis to rule out carcinoma, and the remaining cyst wall must be carefully inspected for evidence of neoplastic change.

HEMANGIOMA

- consist of large endothelial-lined vascular spaces and represent congenital vascular lesions that contain

fibrous tissue and small blood vessels which eventually grow

- **most common solid benign masses that occur in the liver**
- more common in women
- clinical manifestation:
 - **most common symptom is abdominal pain**
 - can be asymptomatic as well
- **diagnosis:**
 - biphasic contrast CT scan: asymmetrical nodular **peripheral enhancement** that is isodense with large vessels and exhibit progressive centripetal enhancement fill-in over time
 - MRI: hypointense on T1-weighted images and hyperintense on T2-weighted images
 - Caution should be exercised in ordering a liver biopsy if the suspected diagnosis is hemangioma because of the risk of bleeding from the biopsy site
- **treatment: Surgical resection (enucleation or formal hepatic resection) only if symptomatic; observation if asymptomatic**

HEPATIC ADENOMA

- benign solid neoplasms of the liver
- most commonly seen in young women (aged 20-40)
- typically solitary
- risk factors: **Prior or current use of estrogens (oral contraceptives)**
- Gross appearance: soft and encapsulated and are tan to light brown.
- Histology: **does not contain Kupffer cells**
- **(+) risk of malignant transformation to a well-differentiated HCC**
- **Clinical manifestation:**
 - **carry a significant risk of spontaneous rupture with intraperitoneal bleeding.**
 - The clinical presentation may be abdominal pain
- Diagnosis:
 - CT scan: with sharply defined borders; can be confused with metastatic tumors
 - venous phase contrast: hypodense or isodense (in comparison with background liver)
 - arterial phase contrast: subtle hypervascular enhancement
 - MRI: hyperintense on T1-weighted images and enhance early after gadolinium injection.
 - nuclear imaging: "cold"; **no uptake of radioisotope**
- Treatment: surgical resection

FOCAL NODULAR HYPERPLASIA

- A benign, solid neoplasm of the liver
- more common in women of childbearing age
- FNH lesions **usually do not rupture spontaneously and have no significant risk of malignant transformation**.
- diagnosis:
 - biphasic CT scan: **well circumscribed with a typical central scar**
 - Arterial phase contrast: intense homogeneous enhancement
 - Venous phase contrast: isodense or invisible
 - MRI scans: hypointense on T1-weighted images & isointense to hyperintense on T2-weighted images
 - After gadolinium administration, lesions are hyperintense but become isointense on delayed images.
 - nuclear imaging: **(+) uptake by Kupffer cells**.
- Treatment: surgical resection only if symptomatic

BILE DUCT HAMARTOMA

- small liver lesions (2 - 4 mm)
- usually visualized on the surface of the liver at laparotomy.
- Gross appearance: firm, smooth, and whitish yellow in appearance.

- can be difficult to differentiate from small metastatic lesions
- excisional biopsy often is required to establish the diagnosis

I. MALIGNANT TUMORS

HEPATOCELLULAR CARCINOMA (HCC)

- 5th most common malignancy worldwide
- Risk factors: viral hepatitis (B or C), alcoholic cirrhosis, hemochromatosis, and nonalcoholic steatohepatitis
- HCCs are typically **hypervascular** with blood supplied predominantly from the hepatic artery
- Most common site of metastasis is **Lungs**
- Clinical manifestations: jaundice, pruritus, hepatosplenomegaly, bleeding diathesis, cachexia, encephalopathy, asterixis, ascites and varices
- Diagnosis:
 - CT scan: appears hypervascular during the arterial phase of CT studies & relatively hypodense during the delayed phases due to early washout of the contrast medium by the arterial blood.
 - MRI: HCC is variable on T1-weighted images and usually hyperintense on T2-weighted images; HCC enhances in the arterial phase after gadolinium injection because of its hypervascularity and becomes hypointense in the delayed phases due to contrast washout
 - (+) **thrombus in portal vein** is highly suggestive of HCC
 - ↑AST,ALT,AFP
- treatment options for liver cancer
 - **hepatic resection:** reserved for patients without cirrhosis & Child's class A cirrhosis with preserved liver function and no portal hypertension
 - liver transplantation: if with poor liver function and the HCC meets the Milan criteria (one nodule <5 cm, or two or three nodules all <3 cm, no gross vascular invasion or extrahepatic spread)
 - **Chemoembolization** can also be of benefit
 - 5 year survival after complete resection: 30%

CHOLANGIOPANCREATIC CANCER

- 2nd most common primary malignancy within the liver
- It is the adenocarcinoma of the bile ducts that forms in the biliary epithelial cells
- Most commonly occurs at the bifurcation of the common hepatic duct
- Subclassification:
 - peripheral (intrahepatic) bile duct cancer
 - tumor mass is within the lobe or peripheral of the liver
 - less common than extrahepatic bile duct Cancer
 - central (extrahepatic) bile duct cancer
 - if it is proximally located, referred to as a **hilar cholangiocarcinoma (Klatskin's tumor)**.
 - presents with **obstructive and painless jaundice** rather than an actual liver mass
- treatment:
 - surgical resection is the treatment of choice
 - **hilar cholangiocarcinoma + primary sclerosing cholangitis:** surgical resection has no role & transplantation provided dismal results
 - **neoadjuvant chemoradiation has a role**

GALLBLADDER CANCER

- rare aggressive tumor with a very poor prognosis.
- Chololithiasis is the most important risk factor for gallbladder carcinoma
- 80-90% of gallbladder tumors are adenocarcinomas
- signs and symptoms of GB carcinoma are indistinguishable from cholecystitis and cholelithiasis
- sensitivity of UTZ in detecting GB carcinoma ranges from 70-100%.

- Treatment: surgery is the only curative option for gallbladder cancer
 - reoperation for an incidental finding of gallbladder cancer after cholecystectomy (central liver resection, hilar lymphadenectomy, and evaluation of cystic duct stump)
 - reoperation should be considered for all patients who have T2 or T3 tumors or for whom the accuracy of staging is in question
 - radical resection in patients with advanced disease
 - usually with dismal results if already with (+) hilar LN

METASTATIC COLORECTAL CANCER

- Over 50% of patients diagnosed with colorectal cancer will develop hepatic metastases during their lifetime.
- Resection is the preferred treatment for liver metastases from colorectal CA, provided that patient has adequate liver reserve, no extrahepatic metastases, total hepatic involvement and advanced cirrhosis, vena cava or portal vein invasion
- volume of future liver remnant and the health of the background liver, and not actual tumor number, as the primary determinants in selection for an operative approach.

J. GALLSTONE DISEASE

Prevalence and incidence

- most common problems affecting the digestive tract
- Women are 3x more likely to develop gallstones than men
- **risk factors:** Obesity, pregnancy, dietary factors, Crohn's disease, terminal ileal resection, gastric surgery, hereditary spherocytosis, sickle cell disease, and thalassemia
- **Natural history**
 - Most patients will remain asymptomatic
 - **prophylactic cholecystectomy in asymptomatic persons with gallstones is rarely indicated**
 - cholecystectomy is advisable for the ff asymptomatic patients:

1. **elderly patients with diabetes**
2. individuals isolated from medical care for extended periods of time
3. in populations with increased risk of gallbladder cancer (**porcelain gallbladder - premalignant lesion**)
4. **symptomatic Cholesterolosis:** accumulation of cholesterol in macrophages in the gallbladder mucosa, either locally or as polyps; produces the classic macroscopic appearance of a "**strawberry gallbladder**."
5. **symptomatic Adenomyomatosis or cholecystitis glandularis proliferans:** characterized on microscopy by hypertrophic smooth muscle bundles and by the ingrowths of mucosal glands into the muscle layer (epithelial sinus formation)
6. **symptomatic granulomatous polyps**

Gallstone formation

- **Cholesterol stones (80% of gallstones)**
 - multiple, variable size, may be hard and faceted or irregular, mulberry-shaped, and soft; colors range from whitish yellow and green to black
 - Most cholesterol stones are radiolucent
 - formation is due to supersaturation of bile with cholesterol
- **Pigment stones (15-20% of gallstones)**
 - dark because of the presence of calcium bilirubinate
 - **Black pigment stones:** small, brittle, black, and sometimes speculated; In Asian countries such as Japan, black stones account for a much higher percentage of gallstones than in the Western hemisphere; typically occur in **patients with cirrhosis and hemolysis**

- **Brown pigment stones:** <1 cm in diameter, brownish-yellow, soft, and often mushy; they are formed usually due to secondary to bacterial infection (ex. E. coli) caused by bile stasis; associated with stasis secondary to parasite infection
 - Clinical presentation
 - Abdominal pain: epigastrium or RUQ, constant, increasing in severity, episodic, usually after a fatty meal, nausea, vomiting
 - **Hydrops of gallbladder:** manifests as a palpable nontender gallbladder
 - Usually due to impacted stone without cholecystitis (pathophysio: bile gets absorbed, but the gallbladder epithelium continues to secrete mucus, and the gallbladder becomes distended with mucinous material)
 - Is usually an indication for cholecystectomy
 - Diagnosis
 - **Abdominal UTZ:** standard diagnostic test for gallstones
 - Presence of hyperechoic intraluminal focus
 - Shadowing posterior to the focus
 - Movement of the focus with positional changes of the patient
 - Management: Patients with symptomatic gallstones should be advised to have elective laparoscopic cholecystectomy
- K. ACUTE CHOLECYSTITIS**
- **Pathogenesis:**
 - Acute cholecystitis is secondary to gallstones in 90 to 95% of cases
 - In <1% of acute cholecystitis, the cause is a tumor obstructing the cystic duct (leads to gallbladder distention, inflammation, and edema of the gallbladder wall)
 - Gross appearance: gallbladder wall is grossly thickened & reddish with subserosal hemorrhages; (+) pericholecystic fluid often; mucosal hyperemia & patchy necrosis
 - When the gallbladder remains obstructed and secondary bacterial infection supervenes → an acute gangrenous cholecystitis develops → abscess or empyema forms within the gallbladder; can also lead to perforation of ischemic areas
 - **emphysematous gallbladder :** (+) gas may be seen in the gallbladder lumen and in the wall of the gallbladder on abdominal radiographs and CT scans due to gas-forming organisms as part of the secondary bacterial infection
 - **clinical manifestations:**
 - unremitting epigastric or RUQ pain, may persist for several days, may radiate to the right upper part of the back or the interscapular area; febrile, anorexia, nausea, and vomiting, reluctant to move, (+) focal tenderness and guarding on the RUQ, (+) Murphy's sign (an inspiratory arrest with deep palpation in the right subcostal area) is characteristic
 - **Mirizzi's syndrome:** Severe jaundice due to common bile duct stones or obstruction of the bile ducts by severe pericholecystic inflammation secondary to impaction of a stone in the infundibulum of the gallbladder that mechanically obstructs the bile duct
 - in elderly patients and in those with diabetes mellitus, acute cholecystitis may have a subtle presentation resulting in a delay in diagnosis.
 - **Laboratory diagnosis:**
 - A mild to moderate leukocytosis (12,000 to 15,000 cells/mm³)
 - if high WBC (above 20,000): suggests a complicated form of cholecystitis such as gangrenous cholecystitis, perforation, or associated cholangitis.
 - mild elevation of serum bilirubin, <4 mg/mL
- mild elevation of alkaline phosphatase, transaminases, and amylase.
 - **diagnosis:**
 - **UTZ: most useful radiologic test for diagnosing acute cholecystitis**
 - Is 95% sensitive and specific
 - Appears as thickening of the gallbladder wall and (+) pericholecystic fluid
 - (+) sonographic murphy's sign
 - **Biliary radionuclide scanning (HIDA scan): most accurate in the diagnosis of acute cholecystitis**
 - **Treatment**
 - IV fluids
 - Antibiotics: should cover Gram (-) aerobes + anaerobes - 3rd generation cephalosporin or 2nd generation cephalosporin + metronidazole
 - Analgesia
 - Cholecystectomy: definitive treatment
 - Laparoscopic cholecystectomy: procedure of choice
- L. CHOLEDOCHOLITHIASIS**
- Common bile duct stones
 - Common over the age of 60
 - clinical manifestations: may be silent or incidental; if symptomatic, may cause pain, nausea and vomiting with mild epigastric or RUQ tenderness + mild icterus
 - **diagnosis:**
 - ↑ of serum bilirubin, alkaline phosphatase, and transaminases
 - UTZ: dilated common bile duct (>8 mm in diameter)
 - Endoscopic cholangiography: gold standard for diagnosing CBD stones; can be therapeutic as well
 - IOC can be done to evaluate CBD stones
 - **Treatment:** sphincterotomy and ductal clearance of the stones is appropriate, followed by a laparoscopic cholecystectomy
- M. CHOLANGITIS**
- Complication of choledochal stones
 - Gallstones are the most common cause of obstruction in cholangitis
 - Normal: bile is sterile
 - Causative organisms: *E. coli*, *Klebsiella pneumoniae*, *Streptococcus faecalis*, Enterobacter, and *Bacteroides fragilis*
 - **Clinical manifestations :**
 - most common presentation is **fever, epigastric or right upper quadrant pain, and jaundice (Charcot's triad)**
 - charcot's triad + **septic shock + mental status changes** → reynaud's pentad
 - **diagnosis:**
 - Leukocytosis, hyperbilirubinemia, and elevation of alkaline phosphatase and transaminases are seen
 - UTZ: (+) gallbladder stones, dilated ducts
 - **ERC: Definitive diagnosis**
 - **Treatment**
 - **IV antibiotics: initial management; cover for gram (-)**
 - **Fluid resuscitation: initial management**
 - Emergency biliary decompression: if failed to improve with IV antibiotics and resuscitation measures
- N. BILIARY PANCREATITIS**
- Obstruction of the pancreatic duct by an impacted stone or temporary obstruction by a stone passing through the ampulla leads to this condition
 - Diagnosis: UTZ of biliary tree
 - Treatment: ERC with sphincterotomy and stone extraction + cholecystectomy (upon resolution of pancreatitis during same admission)
- O. ACALCULOUS CHOLECYSTITIS**
- develops in critically ill patients in ICU (patients on parenteral nutrition with extensive burns, sepsis, major

operations, multiple trauma, or prolonged illness with multiple organ system failure)

- histopathology: reveals edema of the serosa and muscular layers, with patchy thrombosis of arterioles and venules
- clinical manifestations:
 - alert patient: right upper quadrant pain and tenderness, fever, and leukocytosis
 - sedated or unconscious patient: fever and elevated WBC count, as well as elevation of alkaline phosphatase and bilirubin
- diagnosis:
 - UTZ: diagnostic test of choice; appears as distended gallbladder with thickened wall, biliary sludge, pericholecystic fluid, and (+) abscess formation
- Treatment of choice: Percutaneous ultrasound- or CT-guided cholecystostomy

P. BILIARY or CHOLEDOCHAL CYSTS

- congenital cystic dilatations of the extrahepatic and/or intrahepatic biliary tree
- rare
- more common in women
- more frequently diagnosed during childhood
- types:
 - type I: cystic dilatation of the extrahepatic bile duct; most common type**
 - type II:** diverticulum of the CBD
 - type III:** a "choledochocele" extending from the distal duct into the duodenum
 - type IV:** combined intrahepatic and extrahepatic cysts
 - type V:** cystic disease confined to intrahepatic ducts
- clinical manifestations: jaundice or cholangitis (for adults); less than ½ of patients present with the classic clinical triad of abdominal pain, jaundice, and a mass
- diagnosis: Ultrasonography or CT scanning will confirm the diagnosis, but endoscopic, transhepatic, or MRC is required to assess the biliary anatomy and to plan the appropriate surgical treatment
- treatment: complete cyst excision with roux-en-Y hepaticojjunostomy

Q. SCLEROSING CHOLANGITIS

- is a progressive disease that eventually results in secondary biliary cirrhosis characterized by inflammatory strictures involving the intrahepatic and extrahepatic biliary tree
- associated with ulcerative colitis, Riedel's thyroiditis and retroperitoneal fibrosis
- increased risk for developing cholangiocarcinoma.
- mean age of presentation is 30 to 45 years
- men are affected twice as commonly as women
- clinical manifestations: jaundice, fatigue, weight loss, pruritus, and abdominal pain; usually with cyclic remissions and exacerbations
- diagnosis:
 - elevated ALP & bilirubin
 - ERCP: confirmatory test
 - **multiple dilatations and strictures (beading) of both the intra- and extrahepatic biliary tree**

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REVIEW QUESTIONS

1. A patient presents with biliary colic. On ultrasound there are multiple small gallstones in the gallbladder and the common bile duct measures 9mm in diameter. No stone is visualized in the common bile duct. Which of the following is the most reasonable next step?
 - a. Repeat UTZ in 24-48 hours
 - b. MRCP with contrast
 - c. Percutaneous cholangiography
 - d. Laparoscopic cholecystectomy and intraoperative cholangiography

Answer: **D**

For patients with symptomatic gallstones and suspected CBD stones, either preoperative endoscopic cholangiography or an intraoperative cholangiogram will document the bile duct stones. If an endoscopic cholangiogram reveals stones, sphincterotomy and ductal clearance of the stones is appropriate, followed by a laparoscopic cholecystectomy. An intraoperative cholangiogram at the time of cholecystectomy will also document the presence or absence of bile duct stones. Laparoscopic common bile duct exploration via the cystic duct or with formal choledochotomy allows the stones to be retrieved in the same setting. If the expertise and/or the instrumentation for laparoscopic common bile duct exploration are not available, a drain should be left adjacent to the cystic duct and the patient scheduled for endoscopic sphincterotomy the following day. An open common bile duct exploration is an option of the endoscopic method has already been tried or is, for some reason, not feasible.

2. Which hepatic cells provides the primary defense against lipopolysaccharide (LPS)?
 - a. Hepatocytes
 - b. Kuppfer cells
 - c. Bile duct epithelial cells
 - d. Intrahepatic endothelial cells

Answer: **B**

The complications of Gram negative sepsis is initiated by the endotoxin LPS. The liver is the main organ in the clearance of LPS in the bloodstream and plays a critical role in the identification and processing of LPS. Kuppfer cells are the resident macrophages in the liver and have been shown to participate in LPS clearance.