UTMB ABSITE REVIEW MANUAL

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Barrett’s Esophagus
Peter Chang, DMD, MD

Barrett’s Esophagus
-premalignant condition in which abnormal columnar epithelium replaces the stratified squamous epithelium that normally lines the distal esophagus
-most severe histologic consequence of chronic gastroesophageal reflux
-predisposes to the development of adenocarcinoma of the esophagus

Epidemiology- usually discovered during endoscopy
-mean age of diagnosis is 55 years; 3M>F
-can affect children, but rarely before age 5 (and thus supports an acquired condition vs. a congenital one)
-10-15% Barrett’s are found during endoscopy for symptoms of GERD
-uncommon in African Americans and Asians
-prevalence in Hispanics is similar to Caucasians
-prevalence in the general population is variable
-risk factors: male, white, smoker

Clinical Features- columnar metaplasia in Barrett’s esophagus causes no symptoms
-most patients are seen initially for symptoms of GERD (heartburn, regurgitation, dysphagia)
-GERD associated with Barrett’s esophagus is frequently complicated by esophageal ulceration/perforation, stricture, shortening and hemorrhage
-histologically, 3 different types of columnar epithelia in Barrett’s:
  -specialized intestinal metaplasia (villiform surface and intestinal-type crypts lined by mucous-secreting columnar cells and goblet cells
  -gastric fundic-type epithelium
  -junctional-type epithelium
-specialized intestinal metaplasia is the most common, and likely associated with dysplasia and carcinoma

Diagnosis- sensitivity of endoscopy in detecting Barrett’s is related to the length of involved mucosa (long segment Barrett’s)
-overall reliability of endoscopy for detection of Barrett’s is ~ 80%
-controversy regarding diagnostic criteria for Barrett’s (no reproducible anatomic landmarks that clearly delimit the esophagus-GEJ or squamocolumnar junction)
-3 terms describing the specialized intestinal metaplasia in the esophagus:
  -long segment Barrett’s (range 2-5 cm, but 3 cm is the accepted cutoff)
  -short segment Barrett’s (less than 3 cm), more prevalent
  -junctional intestinal metaplasia (squamocolumnar junction=GEJ)
-long segment has a higher risk of dysplasia and adenocarcinoma

Treatment- endoscopic surveillance is the current recommendation
-reflux control with antireflux procedure to prevent mucosal damage prn
-if confirmed high grade dysplasia or cancer, esophagectomy is recommended
-other procedures with less success: laser ablation, photodynamic therapy, mucosectomy, argon plasma coagulation
Complications of Nissen Fundoplication
Sharla K. Stovall, MD

I. Nissen
360° wrap (left crus approach) used when medical management for GERD fails, severe esophageal injury (ulcer, stricture, or Barrett’s)
- Procedure of choice for patients with normal esophageal motility
- Advantage of direct and early view of short gastrics, spleen

II. Operative
- Position: low lithotomy
- Surgery: Dissect out left crus and greater curvature. Take down short gastrics to mobilize fundus. Mobilize left crus and right crus. Open lesser omentum. Preserve anterior and posterior vagi (both contained by wrap). Reapproximate crura posteriorly. Heavy permanent sutures allow passage of 52F bougie. Wrap created length of 2.5-3cm and anchor to esophagus and bilateral crus at hiatus. Anchor anteriorly and posteriorly.

III. Complications
- 3 – 10% of patients
  A. Operative
- Pneumothorax – most common: 5 – 8%. Violation of pleural space by CO2. No need to evacuate gas. Lung will usually expand without incident. Supplemental O2, repeat CXR 2h after operation.
- Gastric/Esophageal Injuries – less common: <1%. Result of overaggressive tissue manipulation or passage of bougie. May be repaired with suture or automatic stapler if identified at time of surgery. If injury not seen at operation, patient will likely need second operation to repair viscus unless the leak is small and contained.
- Liver/Spleen – reported rarely. Careful retraction of left lobe of liver will prevent significant laceration and subcapsular hematomas. Splenic injury usually results from dissection of fundus and greater curvature.
  B. Post-operative
- Bloating – complaint of bloating in 30% of patients, <4% after 2 months. Difficulty belching secondary to wrap. Vagal trauma may lead to delayed gastric emptying. Patients have tendency to swallow saliva (unconscious effort to relieve symptoms of reflux) and with this a significant amount of air.
- Dysphagia – 20% of patients. Due to dissection of hiatus or suture placement and handling of esophagus will cause some edema. dysphagia is usually short-lived. If the wrap is too tight, unlikely to resolve without dilation.
Motility Disorders of the Esophagus and Treatment
Juan C. Escalon, MD

Definition – Motor disorders of the esophagus are functional disorders that interfere with the normal act of swallowing or produce dysphagia without any associated intraluminal organic obstruction or extrinsic compression.

I. Upper Esophageal Sphincter Dysfunction – oropharyngeal dysphagia and cricopharyngeal dysfunction with symptoms of difficulty in swallowing liquid or solid food from the oropharynx into the upper esophagus.

A. Causes
1. Central and peripheral nervous system abnormalities
2. Metabolic and inflammatory myopathy
3. Gastroesophageal reflux disease
4. Complications of neck and thoracic surgery
5. Anatomic causes
   a. Carcinoma
   b. Caustic stricture
   c. Cervical vertebral bone spurs
   d. Thyromegaly
   e. Trauma
6. Globus hystericus – purely psychological cause of complaints, diagnosis of exclusion

B. Clinical presentation
1. Dysphagia localized between the thyroid cartilage and the suprasternal notch characterized as a lump in the throat or as occasional pain radiating to the jaw and ears.
2. Excessive saliva expectoration in patients unable to swallow
3. Hoarseness
4. Weight loss secondary to impaired caloric intake
5. 30-90% of patients have symptoms of GERD

C. Diagnosis
1. Barium esophagram - may demonstrate hypertonicity of the UES, a posterior cricopharyngeal bar, or a Zenkers diverticulum. Also can rule out a hiatal hernia or distal tumor.
2. Esophagoscopy – Look for neoplasm or reflux esophagitis
3. Esophageal manometry - test for abnormal UES

D. Treatment – Individualized depending on the cause.
1. Cervical Esophagomyotomy for dysphagia without reflux, successful in relieving cervical dysphagia from cricopharyngeal motor dysfunction in 65-85% of patients who undergo procedure.
2. Antireflux medications if evidence of GERD
3. Intermittent bougie dilation to 54-56 French for temporary relief in patients with polymyositis, Parkinson’s disease, or CVA.

II. Disorders of the Esophageal Body – a continuum with hypomotility at one extreme and hypermotility at the other.

A. Achalasia – means “failure or lack of relaxation”, usually a disease of middle age, incidence is same for male vs. female 6/100,000 per year. A primary disorder of the LES causing increased resistance and increased frequency of simultaneous contractions with poor amplitude resulting in near complete absence of peristalsis. The parasym pathetic ganglion cells of myenteric plexus are reduced in number. Risk of carcinoma is 1-10% after having disease for 15-25 years. Lesions develop in the middle 3rd of the esophagus.

1. Clinical presentation
   b. In early stages a sticking sensation at the level of the xiphoid after ingestion of liquids, especially cold liquids, and later after ingestion of solids.
   c. Patients eat slowly and use large volumes of water to help wash food into the stomach.
   d. In later stages, regurgitation of foul-smelling intraesophageal contents leads to aspiration that may cause pneumonia, lung abscess, bronchiectasis, hemoptysis, or bronchospasm.

2. Diagnosis
   a. Radiographic findings
      i. Bird’s beak and dilated esophagus on barium swallow (Fig 37-15, Townsend) along with tortuosity and sigmoid shape in later stages.
      ii. Double mediastinal stripe throughout the length of the chest and a retrocardiac air-fluid level
   b. Manometric and EGD findings
      i. Aperistalsis in esophageal body, partial or absent LES relaxation with swallowing, LES pressure normal to >45 mm Hg, and intraesophageal basal pressure higher than intragastric.
      ii. Residual food seen in esophagus, “popping” through LES with scope, and esophagitis.

3. Treatment - purely palliative directed toward relieving the obstruction caused by non relaxing LES
   a. Early stages – sublingual nitroglycerin before or during meals, long-acting nitrates, and calcium channel blockers may improve swallowing.
b. Temporary relief - passage of mercury weighted bougie dilators 48-54 French will relieve dysphagia up to a few weeks.
c. Balloon dilation - successful in 60% of patients, risk of perforation.
d. Intraspincteric botulinum toxin - efficacy has yet to be established.
e. Surgical therapy - many approaches to myotomy along with fundoplication, currently best results with a laparoscopic Heller myotomy and partial fundoplication. In end stage achalasia, an esophagectomy

B. **Diffuse Esophageal Spasm** – five times more rare than achalasia. A disorder of the esophageal body of unclear etiology resulting in repetitive, simultaneous, high-amplitude esophageal contractions.

1. Clinical presentation – typically in anxious patients and commonly with a history of irritable bowel syndrome, pylorospasm, spastic colon, or other functional GI complaints.
   a. Subternal chest pain that mimics angina pectoris
   b. No association with exercise
   c. Occasional dysphagia
   d. Symptoms often greatest during periods of emotional stress.
   e. Ingestion of cold liquids or foods aggravates DES.
   f. Gallstones, PUD, and pancreatitis can all trigger DES.

2. Diagnosis
   a. Barium swallow
      i. Curling or a corkscrew esophagus caused by segmental contractions.
      ii. Esophageal pulsion diverticulum.
   b. Manometry (Fig 37-17, Townsend)
      i. Simultaneous (non-peristaltic) contractions, repetitive (>3 wks) and increased duration (>6 sec).
      ii. Spontaneous contractions with intermittent normal peristalsis.
      iii. Contractions possibly of increased amplitude.

3. Treatment
   a. Antispasmodics and calcium channel blockers are occasionally helpful.
   b. Nitrates are sometimes helpful, variable response.
   c. Esophageal dilation with bougies 50-60 French may relieve dysphagia and chest pain.
   d. Esophagomyotomy is reserved for patients with incapacitating chest pain since success rates are 50-60%.

C. **Nutcracker Esophagus** – hypermotility disorder characterized by extremely high-amplitude (225-430 mm Hg) progressive peristaltic contractions, often of prolonged duration. Symptoms and treatment is similar to DES.

D. **Hypertensive Lower Esophageal Sphincter** – has high LES pressures (>45 mm Hg) but with normal relaxation and normal esophageal peristalsis. Symptoms and treatment is similar to DES.

III. **Nonspecific Esophageal Motility Disorders** – Manifested by no or decreased amplitude peristalsis with normal LES pressure and normal LES relaxation. Abnormal peristalsis presents with abnormal waveforms, isolated simultaneous contractions, and/or isolated spontaneous contractions.

A. Causes – dermatomyositis, polymyositis, lupus, and scleroderma
B. Symptoms – dysphagia, regurgitation, esophagitis, and GERD
C. Treatment – symptomatic, scleroderma patients have good results with Collis gastroplasty-fundoplication, and esophagectomy for severe cases.
Esophageal Leiomyoma
Angela K. Champion, MD

**Definition**
Most common benign tumor of the esophagus consisting of interlacing bundles of smooth muscle cells
Slow growing
Malignant degeneration rare

**Frequency**
60% of all benign tumors of the esophagus
Benign tumors make up less than 1% of all esophageal neoplasms
Usually adults, often multiple, 80% occur in middle/lower esophagus

**Clinical Features**
Usually asymptomatic, unless large (>5cm)
Often found incidentally at autopsy
Tumors >5cm may cause dysphagia or retrosternal pressure/pain

**Diagnosis**
Esophageal symptoms or mass on CXR prompt barium swallow or endoscopy
Distinct barium swallow appearance- well localized mass with smooth margins, not circumferential (see figure 37-26 Townsend Textbook of Surgery)
Endoscopy shows intact mucosa with lumen narrowing from extrinsic mass
AVOID endoscopic biopsy-may complicate subsequent surgical resection
Esophageal ultrasound confirms diagnosis

**Treatment**
Surgical excision for symptoms or >5cm
Asymptomatic or small tumors may be followed
Anatomy of the Stomach
Juan C. Escalon, MD

I. General
A. Derived from the embryonic foregut
B. Functions
   1. Serves as a reservoir for large quantities of ingested food
   2. Mixes food with gastric secretions to form chyme
   3. Controls food emptying in the duodenum at a rate suitable for proper digestion and absorption

II. Anatomic Regions (Fig 43-1, Townsend)
A. Cardia - small, ill-defined area immediately adjacent to the gastroesophageal junction, located slightly left of midline and is the most fixed portion of the stomach.
B. Fundus – projects upward above the junction of the cardia and gastroesophagus, it is the most superior portion of the stomach and is in contact with the left hemidiaphragm.
C. Body – largest portion the stomach, located immediately below and continuous with the fundus
D. Incisura angularis – located approximately two thirds of the distance from the lesser curvature, marks the border of the gastric body and the antrum. This margin is not distinct externally but can be defined arbitrarily by a line from the incisura angularis on the lesser curvature to a point one fourth of the distance from the pylorus to the esophagogastric junction along the greater curvature.
E. Antrum – most distal portion the stomach, lies between the body and the pylorus.

III. Stomach Wall
A. Forms thick longitudinal folds (rugae) that flatten with distention and consists of four layers.
   1. **Mucosa** - lines the stomach lumen, has a soft velvety appearance and pink color. Most secretory elements are located in the mucosa. The muscularis mucosa is a thin sheet of smooth muscle cells with an inner circular and outer longitudinal layer that forms the boundary between the mucosa and submucosa.
   2. **Submucosa** – is composed of areolar connective tissue, blood and lymphatic vessels. It extends into the rugae, which are made up of both mucosa and submucosa.
   3. **Muscularis propria** – a combination of three muscle layers
      a. **Inner oblique fibers** – are the most internal, found mainly at the cardiac end of the stomach, spread over the anterior and posterior surface.
      b. **Middle circular fibers** – encircle the entire body of the stomach and thicken distally to become the pyloric sphincter.
      c. **Outer longitudinal fibers** – concentrated along the lesser and greater curvature of the stomach
   4. **Serosa** – the outermost layer, is a continuation of the visceral peritoneum and contains some of the larger blood vessels and lymphatics.

IV. Vascular Supply (Fig 43-2, Townsend)
A. **Arteries** - The stomach is supplied blood by a rich network of arteries that give rise to a large number of extramural and intramural collateral vessels. Gastric tissue viability therefore can be preserved by ligation all except one of the primary gastric arteries. This also means that hemorrhage is difficult to control by external ligation of the gastric arteries.
   1. **Left gastric** - branch of the celiac trunk, runs along the superior aspect of the lesser curvature and anastomosis with the right gastric artery.
   2. **Right gastric** – branch of the hepatic or gastroduodenal artery, runs along the inferior aspect of the lesser curvature and anastomosis with the left gastric artery.
   3. **Left gastroepiploic** – branch of the splenic artery, runs along the superior aspect of the greater curvature and anastomosis with the right gastroepiploic artery.
4. **Right gastroepiploic** – branch of the gastroduodenal artery, runs along the inferior aspect of the greater curvature and anastomosis with the left gastroepiploic artery.

5. **Short gastric** – branch of the splenic artery, supplies the gastric fundus and the left most upper aspect of the greater curvature.

### B. Veins
The venous supply of the stomach follows the arterial supply. The veins empty into the portal vein, one of its branches, the splenic vein, or the superior mesenteric veins.

1. **Left gastric vein** (coronary vein) anastomosis with esophageal tributaries and is the basis for varix formation in portal hypertension.

### C. Lymphatics
The lymphatic drainage parallels the venous system.

1. **Lesser curvature** – drains into the gastric nodes, and then to celiac nodes.
2. **Greater curvature** – drains into the gastroepiploic, splenic, pancreatic, omental nodes and then to the celiac nodes.

### V. Innervation

#### A. Parasympathetic (Fig 43-3, Townsend)

1. **Left vagus nerve** – usually closely adhered to the anterior surface of the esophagus, it becomes the anterior vagal trunk of the stomach. It also branches to supply liver and biliary tree.
2. **Right vagus nerve** – often separated from the esophagus, found midway between the esophagus and aorta, it becomes the posterior vagal trunk of the stomach. It branches to the celiac plexus that supplies the small and large intestine up to the splenic flexure.

#### B. Sympathetic
Derived from the 6th to 8th thoracic spinal nerves that synapse within the celiac ganglia and whose postganglionic fibers pass through the celiac plexus and follow the vasculature to the stomach.

### VI. Microanatomy

#### A. The gastric mucosa is composed primarily of a single layer of columnar epithelial cells that is invaginated by gastric pits, which contain specialized cells.

#### B. Cell types

1. **Surface mucosal cells** – found throughout the stomach, secrete mucus and granules by apical expulsion, and are responsible for luminal cytoprotection from acid, pepsin, ingested substances, and pathogens. Renew themselves every 72 hours.
2. **Parietal cells** – found mainly in the fundus and body of the stomach and are responsible for hydrogen ions secretion to concentrations of 150-160 mEq/L.
3. **Mucous neck cells** – closely associated to parietal cells, they synthesize an acidic and sulfated mucus in comparison to the neutral mucus made by surface mucosal cells. Neck cells also function as stem cell precursors for surface mucosal, parietal, chief, and endocrine cells.
4. **Chief cells** – involved in the synthesis and secretion of pepsinogen I and II.
5. **G cells** – found mainly in the antrum and duodenum, responsible for secreting gastrin and thereby regulating gastric acid secretions.
Surgical treatment of peptic ulcer disease
Eric C. Feliberti, MD

I. Indications for surgery
   • Hemorrhage, perforation, obstruction, refractory to medical management

II. Operations
   A. Truncal vagotomy and drainage procedure
      Vagotomy abolishes cholinergic stimulation of the acid-producing fundus. This decreases basal acid output by 80% initially; maximal acid output is decreased by 50% at 1 year.
      Cholinergic denervation of fundus causes loss of receptive relaxation, which regulates gastric emptying of liquids. Vagotomy thus increases the rate of liquid emptying.
      Cholinergic denervation of the pylorus causes loss of pyloric coordination, which regulates emptying of solids to a size less than 1mm. Truncal vagotomy thus increases rate of solid emptying.
      Truncal vagotomy must be accompanied by pyloric drainage procedure, typically a pyloroplasty.
      1. Pyloroplasties
         a. Heineke-Mickulicz pyloroplasty
            Longitudinal incision across pylorus from 2cm proximal to 2cm distal. Incision then closed transversely.
         b. Finney pyloroplasty
            U-shaped incision from dependent antrum across pylorus to duodenum. Then side-to-side anastomosis.
         c. Jaboulay pyloroplasty
            Similar to Finney, but incision spares pylorus, closed as side-to-side anastomosis. Useful when pylorus is scarred.
      2. Outcomes
         Ulcer recurrence 10%; operative mortality 0.5%.
      3. Complications
         a. Diarrhea
            Thought secondary to cholinergic denervation of pylorus and small bowel. Incidence is 20% initially after truncal vagotomy; only 2% have persistent diarrhea.
         b. Dumping
            Incidence 10% initially; 1% chronically.

   B. Truncal vagotomy and antrectomy
   Antrectomy removes gastric production of gastrin, thereby abolishing another stimulant of gastric acid secretion in addition to vagotomy.
   Decreases basal acid output by 85% initially; maximal acid output decreased by 85% at 1 yr.
Reconstruction with Billroth I (gastroduodenostomy) or Billroth II (gastrojejunostomy).

1. Outcomes
   Ulcer recurrence rate 1-2% (*lowest*); operative mortality 1% (*highest*).
   Liquid emptying increased; solid emptying decreased.

2. Complications
   b. Late dumping – Similar symptoms occurring 1-3 hours after meals. Due to hypoglycemia. Transient. Treat with small meals, avoid sugars.
   c. Alkaline reflux gastritis – Nausea, abdominal pain, bilious emesis, bile stained mucosa with gastritis on EGD. May play a role in development of gastric cancer 20-30yrs after operation. Treatment is operative – Roux-en-Y gastrojejunostomy.

C. Highly selective vagotomy (aka parietal cell vagotomy)
   Vagotomy only of fundus, preserving celiac and hepatic branches as well as the nerve of Latarjet to pylorus. Does not require drainage procedure.
   Basal acid output decreased by 80% initially; maximal acid output decreased by 50% at 1 yr.

1. Outcomes
   Ulcer recurrence rate 10% (*highest*); operative mortality <0.5%.
   Liquid emptying increased; solid emptying unchanged.

2. Complications - *lowest incidence*
   a. Dumping - <5%
   b. Diarrhea - <5%.
**Helicobacter pylori**

**Angela K. Champion, MD**

**Definition**
Slow growing, highly mobile gram negative spiral bacteria
Lives on surface of gastric mucosa within the mucus layer
Produces high amounts of urease

**Frequency**
Usually acquired in childhood by age 10 in developing countries
In developed countries, age related increase in prevalence
Major risk factor is low socioeconomic status as child

**Clinical Correlation**
Firmly established cause of gastritis
Close association of H. pylori gastritis and gastric ulcer development
Cure of H. pylori infection greatly reduces ulcer recurrence (~90% cure rate)
Yearly incidence of ulcer development in patients infected with H. pylori is about 1%
Six fold increased risk of gastric cancer in populations with H. pylori infection

**Diagnosis**
Mucosal biopsy and histologic examination of gastric mucosa is gold standard
Serologic testing for antibodies good screening test
Urea breath test good for evaluating success of treatment

**Pathophysiology**
Infection causes significant inflammatory and immune responses, which results in further mucosal injury and ulceration
Associated with a decrease resistance of the mucus layer to acid permeation increasing the risk of ulceration

**Complications**
Bleeding/Hemorrhage-ulcer extends into major vessel (~15-20% of patients develop gross bleeding at some point)
Perforation-ulcer penetrates full thickness; often results in peritonitis (~5-10% of patients)
Gastric Outlet Obstruction-usually as a result of chronic disease when edema or scarring occludes the lumen (<5% of patients)

**Treatment**
Medical treatment-triple therapy (e.g. bismuth, flagyl & tetracycline) or PPI with 2 Antibiotics (e.g. omeprazole with clarithromycin, amoxicillin or flagyl)
Surgical-secondary to complications or intractable ulcer disease
Gastric Emptying Post Vagotomy
Kenneth J. Woodside, MD

Anatomy & Normal Gastric Motility
Traditional divisions: cardia, fundus, corpus, antrum

The stomach also can be modeled as two different regions:
   - Orad, or proximal third of the stomach
     Three distinct muscle layers: outer longitudinal, middle circular, inner oblique
     Electrically stable
     Contractions are tonic and prolonged, without peristalsis, lasting several minutes
     Receptive relaxation of the orad region to an ingested meal is mediated by the vagus nerve
     After ingestion, proximal contractility increases and cause compressive movement of the meal towards the antrum.
     The proximal segment determines the rate of liquid emptying of the stomach via the gastroduodenal pressure gradient resulting from proximal contractions.

   - Caudad, or distal two thirds.
     Inner oblique muscle layer not distinct
     Spontaneous repeated electrical discharges
     Pacesetter potentials (3/minute) originate along the greater curvature, and travel faster along the greater curvature to reach the pylorus at the same time
     Food is propelled towards the pylorus, with closure of the pylorus 2-3 seconds prior to arrival of the contraction. This closure allows a small bolus of liquid and small food particles (<1 mm) to pass and pushes the majority of the contents backwards toward the proximal antrum in a churning action that mixes enzymes, acid, and food.
     The distal segment determines solid emptying via peristalsis and churning activity

Types of Vagotomies
General Comments
   - Decreased cholinergic stimulation of acid secreting parietal cells
   - Diminishes parietal cell responsiveness to gastrin and histamine
   - 80% reduction in acid secretion immediately post-operatively, increasing slightly with time

Truncal Vagotomy (& pyloroplasty)
   - Both vagal nerve trunks are dived at the diaphragmatic hiatus
   - Loss of innervation of antrum and pylorus with greater difficulty to empty solids unless accompanied by a drainage procedure
   - When performed with a pyloroplasty, there are increased solid & liquid emptying rates
   - Hypergastrinemia
   - Decreased pancreatic exocrine secretion (bicarbonate and enzymes) & biliary secretion, and increased gallbladder distention with loss of the hepatic & celiac branches

Vagotomy & Antrectomy
   - Billroth I-gastroduodenostomy
   - Billroth II-gastrojejunostomy & afferent limb
   - Decreased gastrin levels
Proximal Gastric Vagotomy (Highly Selective Vagotomy, Parietal Cell Vagotomy)
Best for duodenal ulcers, but not effective with prepyloric ulcers
Only the nerve fibers to the fundus are divided (acid secretion region), with fibers to the antrum and pylorus left intact as well as hepatic and celiac branches
From 5 cm above the LES to 5 cm before the pylorus along the lesser curvature
Loss of receptive relation, with increased gastric pressure (and gastroduodenal pressure gradient) and resulting accelerated liquid emptying
Retained "churning," with resulting normal emptying of solids

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<th>TV+A</th>
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<tr>
<td>Diarrhea</td>
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Complications of Vagotomy

Early Dumping Syndrome "Early Vasomotor Dumping"
Occurs 1-30 minutes after ingestion of the meal
Associated with release of serotonin, kinins, VIP, and other GI hormones
Sx include nausea, epigastric discomfort, borborygmi (intestinal rumblings), palpitations, diaphoresis, dizziness, or even syncope. Sx worsen with sugar.
Most pt's have resolution with time or with minor dietary changes. A small percentage (1-10%) require low carbohydrate diets or octreotide (50-100 mcg 15-30 m before meal).
Severe cases require conversion of B-I or B-II to Roux-en-Y gastrojejunostomy

Late Dumping Syndrome "Hypoglycemic Dumping"
1-3 hours after the meal
Rapid emptying of carbohydrates into the intestine cause a rapid rise in serum glucose
Hyperosmolar istestinal contents cause release of enteroglucagon, sensitizing pancreatic beta cells for the release of excess insulin. Sx often improve with sugar.
Most cases resolve or are controlled with dietary manipulation.

Postvagotomy Diarrhea
Most common with complete vagotomy with drainage procedure
Loss of control of gastric emptying
Incapacitating in 1-2 % of pts.
Tx with dietary alteration, frequent smaller feedings, increased fiber, or pharmacological therapy with opiates, antidiarrheal medications, or octreotide
Antiperistaltic reversed segment operations (usually jejunal) may work in severe cases

References
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Cameron JL, Current Surgical Therapy, 6/e.
Netter FH, Atlas of Human Anatomy, 1/e.
PRIMARY GASTRIC LYMPHOMA
Buckminster J. Farrow, MD

6% of all gastric malignant tumors
Most common site of GI lymphoma (>50% of all GI lymphomas)
Most gastric lymphoma is secondary to systemic malignant lymphoma, not primary
disease; systemic disease is treated with chemotherapy, treatment of primary
gastric lymphoma is much more controversial (see below)
Low grade MALT-associated lymphoma may be treated by H. pylori eradication alone

Epidemiology
Men 2:1 women, most >50 y.o.
Increased risk with immunosuppression for renal transplant, SLE, or rheumatoid arthritis
H. pylori (present in 64-100% of primary gastric lymphomas)

Pathology
98% are B-cell lymphomas (non-Hodgkin’s)
Lymphoid cells leave other GI tissue, reside in submucosa of stomach
Believed to be due to chronic gastritis and/or H.pylori infection
Most are large at time of diagnosis (>10cm in 50% of pt.)
25% are multifocal within stomach, 30-50% are ulcerated
Spread is through sub-mucosa, then to adjacent organs & lymph nodes like
adenocarcinoma--not to bone marrow & peripheral nodes like systemic
lymphoma

Symptoms/Diagnosis
Asymptomatic until late stage, median 10 months of symptoms until diagnosis
Abdominal pain (80%), nausea/vomiting, early satiety, weight loss
<20% have evident GI bleed, but 50% have occult blood loss
Diagnosis usually via EGD- appear as superficial ulcers, biopsies must be
depth/multiple for accurate diagnosis (disease is submucosal); also EUS to stage
CT chest/abdomen/pelvis, bone marrow aspirate to evaluate for systemic lymphoma

Staging- TNM or Ann Arbor classification (below)
IE confined to GI tract
IIE GI tract/regional lymph nodes
IIIE Distant lymph nodes
IVE spread to other abdominal organs or beyond abdomen (bone marrow)

Treatment
Primarily surgical- subtotal if distal tumor or total gastrectomy with Roux-en-Y
Cure is only 60% for lesions which invade into muscularis or serosa
Use adjuvant therapy for extension into duodenum or esophagus/ residual disease
IE- chemotherapy IIE- chemotherapy and XRT (improves 5 yr survival)
Overall 5 yr survival 34-50% (80-100% for IE, 40% for IIE)
Chemotherapy (CHOP) + XRT may be sufficient treatment, trials underway
**VITAMIN B12 ABSORPTION**

I. B12 derived from cobalamin

II. B12 ingested with dietary protein, released from protein in acidic stomach by pepsin

III. Two B12-binding proteins secreted in stomach
   1. **R Binder** - also secreted in saliva and bile
      a. more efficient than IF at binding B12
   2. **Intrinsic factor** - made in parietal cells
      b. All stimulants and inhibitors of acid secretion in stomach have same effect on intrinsic factor

IV. Most B12 initially binds to R binder

V. In upper small intestine, all B12 complexes are separated by trypsin

VI. The freed B12 then binds to intrinsic factor (protects from proteolytic digestion)

VII. Specific receptors in terminal ileum take up cobalamin-intrinsic factor complex by active transport

VIII. Small amount of B12 taken up by passive absorption

IX. B12 then transported via portal system to liver by transport protein - transcobalamin II

X. IF secretion normally far exceeds that necessary for B12 absorption

XI. Secretory inhibitors (omeprazole, H2-receptor antagonists) ↓ IF secretion, but usually not enough to cause B12 deficiency

XII. Total gastrectomy requires B12 supplementation - 1000 mcg SC/IM qmonth

**Previous treatment for pernicious anemia was eating raw liver (later found that raw liver has large quantity of B12)**

**BILIARY SECRETION**

I. Liver secretes 600-1200 ml/day bile into duodenum
   1. secreted at canalicular membrane of hepatocytes (80%) and ductules (20%) by an active process

II. Bile contains: bile salts, bile pigments (bilirubin), cholesterol, phospholipids, proteins
   1. **Bile salts** - bile acids conjugated with either taurine or glycine (renders more neutral - rapid diffusion into enterocytes)
      a) bile salts secreted by carrier at canalicular membrane (bile acid-sodium symport uses Na-K ATPase)
   2. Biliary secretion is also route for elimination of bilirubin and cholesterol from body

III. **CCK** (stimulated by FA and amino acids in intestinal lumen) stimulates GB contraction, bile secreted into duodenum
   1. gallbladder bile up to 50x more concentrated than liver bile (water uptake via Na/K ATPase)

IV. Acidic chyme causes small intestine to release secretin → bile duct cells release HCO3 (bile neutralizes acid in duodenum)

V. Components of Bile
   1. electrolytes similar to blood plasma (HCO3 higher → alkaline)
   2. **primary bile acids** - cholic acid, chenodeoxycholic acid (synthesized by hepatocytes)
   3. **secondary bile acids** - deoxycholic acid/lithocholic acid (bacteria in GI tract change primary BA’s via dehydroxylation)
      a) secondary bile acids more hydrophobic - promote biliary stasis/gallstone formation
   4. phospholipids - mainly LECITHIN (phosphatidylcholine)
   5. **cholesterol**

VI. Major determinant of bile salt synth/secretion is bile salt concentration in portal blood (negative feedback)
   1. gastrin - stimulates bile secretion (increased acid→increased secretin, and directly stimulates liver)
   2. **estrogens** - inhibit bile secretion
   3. motilin - stimulates GB contraction, may ↑ bile secretion
   4. vagal stimulation - causes contraction GB (vagotomy causes decreased bile secretion)

**ENTEROHEPATIC CIRCULATION**

I. Total bile acid pool 2-5 grams
   1. Cycles approximately 6 times/day (3-5 in light eater, up to 14-16 in heavy eater)

II. Absorption of Fat
   1. Fat emulsified in the stomach
   2. Triglycerides partially hydrolyzed by pancreatic lipase → splits off the 2 exposed fatty acids → leaves central FA attached to glycerol
   3. Monoglyceride and FA’s poorly water soluble → combine with bile salts
   4. Mixed micelle then passes through unstirred water layer
   5. After disaggregation of micelle, bile salts remain within the lumen of the intestine → form other micelles

III. Bile salts in intestinal lumen absorbed 3 ways:
   1. passive diffusion throughout entire small intestine (small amount only)
   2. Most important - bile salts absorbed in terminal ileum via active carrier mediated pathway
      - extremely efficient, only 5% of bile salts escape this pathway
      3. bacteria in terminal ileum and colon deconjugate bile salts to form bile acids → absorbed passively
   4. 200-500mg bile acids lost in feces every day (replenished by synthesis from cholesterol)
   5. absorbed bile salts transported in portal blood bound to albumin or HDL
   6. uptake of bile salts by hepatocytes extremely efficient - 80% in one pass
   7. bile acids again coupled to glycine or taurine and resecreted by hepatocytes
Digestion and Absorption
Dirk C. Johnson, MD

Digestion - the process of actively converting food into chemical substances that can be absorbed and assimilated.

I. Carbohydrates-(Dietary intake 350-450g Sucrose(30%), lactose(10%), and starch(60%))

A. Digestion
   1. Sucrose and lactose processed at the brush border
   2. Starch (amylose:amylopectin, 1:4) requires digestion prior to absorption
      a) Digested by salivary and pancreatic amylase
         Amylase → (α-amalyse) → maltose + malotriose
         Amylopectin → (α-amalyse) → α-limit Dextrins
      b) Proximal lumenal digestion with completion by jejunum
      c) Final digestion occurs at brush border → glucose, galactose, fructose

B. Absorption
   1. Fructose-facilitated diffusion
   2. Glucose and galactose
      a) Absorbed by carrier-mediated active transport
      b) Dependant on sodium pump of basolateral membrane

II. Protein

A. Digestion - 80-90% completed in jejunum
   1. Stomach - Acid denatures proteins
   2. Small bowel - pancreatic enzymatic digestion
      a) Enterokinase secreted by intestinal mucosa converts
         Trypsinogen → trypsin
      b) Trypsin activates the other pancreatic protease precursors
      c) Pancreatic proteases (trypsin, chymotrypsin, elastase, carboxypeptidases)
         (1) Endopeptidases- cleave bonds on the interior of the polypeptide (PP)
         (2) Exopeptidase - serially cleave peptides from the ends of PPs
      d) Cytosolic peptidases complete digestion after transport before delivery

B. Absorption
   1. Carrier mediated active transport of single amino acids and short PP chains
      (2-3AA)

III. Fat - Dietary intake 60-100g largely triglycerides (TG)

A. Digestion - small intestine
   1. Fat is emulsified in the stomach
   2. TG → (Pancreatic lipase) → 2 Fatty Acids + glycerol (2-Monoglyceride)
   3. Fatty Acids and glycerol combine with bile salts → micelles
   4. Mixed micelles may contain lecithin, cholesterol, vitamin ADEK, and/or phospholipids → Enhanced ability to dissolve fat

B. Absorption
   1. Passive transport of micelles with bile salts remaining in intestinal lumen
   2. TG reformatted intracellularly by endoplasmic reticulum enzymes
   3. TGs, cholesterol, phospholipids, and apoproteins combine to form chylomicrons.
   4. Chylomicrons travel through lacteals to lymphatics to enter the venous circulation
IV. **Water, Electrolytes, and Vitamins**

A. **Water**
   1. (8-10L qd) enters SB
   2. absorbed by simple diffusion
   3. osmotic gradient created by active transport of other molecules

B. **Electrolytes & Vitamins**
   1. Sodium and Chloride
      a) active transport with organic molecules
      b) cotransport as NaCl
   2. Bicarbonate Na-H⁺ exchange
   3. Calcium active transport facilitated by acidification, PTH and Vitamin D
   4. Potassium- passive diffusion
   5. Iron active transport dependant on erythropoiesis and total body iron stores
   6. Vitamins
      a) **Fat Soluble (ADEK) carried in mixed micelles**
      b) **Water soluble**
         (1) active transport (Vitamin C, riboflavin, B₁₂, and thiamine)
         (2) simple diffusion (Biotin, nicotinic acid, folic acid, riboflavin, thiamine, C, B₆, some B₁₂)
- The principal role of the small bowel is to digest and absorb nutrients, water, and electrolytes.
- This process is made possible by the contributions of exocrine secretions from the liver and pancreas, bile from the gallbladder and brush border enzymes.
- The final products of digestion of carbohydrates: glucose and galactose are absorbed by a carrier-mediated active transport, and fructose is absorbed through facilitated diffusion. This process occurs mostly in the jejunum.
- Protein digestion yields amino acids (AA) and short peptides (SPs) (dipeptides and tripeptides). AAs are absorbed by a carrier-mediated active transport. SPs are brought into the cell by a peptide-transport mechanism that is active in nature. 80-90% of digestion and absorption of proteins are completed in the jejunum.
- The end product of fat (triglycerides) digestion: fatty acids and 2-monoglyceride aggregate with the help of bile salts to form micelles. Micelles are absorbed via a passive process and disintegrates once inside the cell to form chylomicrons that eventually enter the lymphatics and portal vein.
- Median chain triglycerides (< C10) are absorbed without forming micelles and move directly through the cell, and finally entering the portal vein.
- Unconjugated bile acids are absorbed in the jejunum, but conjugated bile acids with micelles are absorbed in the distal ileum as part of the enterohepatic circulation (EHC).
- The EHC recirculates total bile salts (approximately 5 g) 6 X/day and only loses an average of about 500 mg in stool/day.
- The small bowel absorbs approximately 95% of the 10 L of H2O that is delivered to it daily by simple diffusion.
- Na+ and Cl- are absorbed by active transport by coupling to organic solutes and by co-transport on carriers of neutral sodium chloride.
- HCO3- is absorbed by Na+-H+ exchange (one-to-one).
- Ca2+ is absorbed in the duodenum/jejunum by an active transport mechanism (facilitated by an acid environment and enhanced by Vit. D and PTH).
- K+ is absorbed by passive diffusion.
- Fe2+ is absorbed by an active process in the duodenum as a heme and non-heme component.
- Fat soluble vitamins (A, D, E, K) are incorporated into micelles and absorbed.
- Vit.C is absorbed by an active process via Na+ -coupling as well as a specific carrier system.
- Vit B6, thiamine, and riboflavin are absorbed by simple diffusion in the proximal small bowel.
- Vit B12/Intrinsic Factor is absorbed in the terminal ileum by active transport, and a small amount by passive transport.
- Because the small bowel plays such an instrumental role in digestion and absorption of nutrients and electrolytes, complications are bound to arise whenever there is a resection.
- Most likely etiology of ileal resection includes but not limited to: trauma to small bowel, Crohn's disease, tumors, and intestinal bypass for obesity.
- Reduced absorption of bile acids occurs, rendering bile more lithogenic and a predisposition to cholelithiasis and gallstone pancreatitis.
- Megaloblastic anemia ensues due to the decrease absorption of Vit. B12.
- Reduction in the absorption of the fat-soluble vitamins, which can lead to coagulopathies with decreased vitamin K
- Nephrolithiasis can ensue due to an increase amount of unchelated calcium and oxalate delivery to the large bowel, that eventually is absorbed and can precipitate in the renal tubules.
I. Small Intestine Anatomy
   - Mucosal layer- divided into the Muscularis Mucosa, Lamina Propria, and the epithelial layer
   - Epithelial layer- continuous sheet of cells covering villi, lining crypts
     - Crypt function- cell renewal, water/ion secretion
     - Villi function - digestion, absorption
   - Combination of folds, villi, microvilli increase surface area 1000-fold

II. Ileal Functions: Digestion of fats, absorption of bile salts, Vit B12
   - Digestion of fats: nearly all occurs in small intestine
     A. Emulsification-breaking up fat globules into water soluble particles
     B. Pancreatic Lipase breaks down TG’s into Free F.A.’s + 2 monoglycerides
     C. Micelle Formation-sterol nucleus with water soluble groups projecting out. Micelles are absorbed into the brushborder
     D. Intracellular Processing- reform TG’s, form chylomicrons\(\rightarrow\) lacteals\(\rightarrow\)venous system

III. Enterohepatic Circulation
   - Conjugated bile acids are absorbed by the ileum\(\rightarrow\)lacteal\(\rightarrow\)portal system
   - Once in the portal system, the liver resecretes as bile
   - Bile salt pool is 2-3 grams and recirculates about 6 times every 24 hours

IV. Vitamin B12
   - Absorption: occurs in ileum
     A. Released from food by pepsin in the stomach
     B. Forms complex with R proteins secreted in the stomach
     C. Intrinsic factor is secreted by Parietal Cells
     D. Proteins degraded in duodenum, B12 complexes with intrinsic factor
     E. Intrinsic factor-B12 complex binds ileal receptor and are absorbed
   - Fat Soluble Vitamins- (A,D,E,and K) depend on solubilization with bile salts and micelles for intestinal absorption.

V. Ileal Resection
   - Massive ileal resection occurs as a result of:
     A. Extensive ischemic injury to the gut (e.g., midgut volvulus)
     B. Blunt penetrating trauma to the gut and/or mesentery
     C. Crohn’s disease, requiring resection due to stricture
     E. NEC in neonates

VI. Complication of Ileal Resection:
   - Diarrhea/Steatorrhea-excessive bile salts enter colon\(\rightarrow\)chemical enteritis, and decrease in salt pool \(\rightarrow\) increased CCK \(\rightarrow\)increased colonic motility
   - Malabsorption of vitamins/fat \(\rightarrow\) eg, B12 deficiency
   - Nonintestinal Symptoms: renal calculi, gallstones

VII. Treatment:
    PREVENTION, replace fluid/electrolytes, codeine, lomotil, replace B12
Peyer Patches/Immune Cells of the Gut
Chris T. Stephens, MD

- Small intestine serves as major immunologic barrier to consumed pathogens and therefore, possesses an abundance of lymphoid cells (B and T Lymphocytes) and myeloid cells (macrophages, neutrophils, eosinophils, mast cells) that act to process antigens – gut has evolved into a highly organized and efficient system for antigen processing, humoral immunity, and cellular immunity

- Gut barrier includes epithelial cells, glycocalyx, mucin, intestinal motility, gastric acid, and proteolytic enzymes

- Gut-associated lymphoid tissue (GALT) produces 80% of total immunoglobulins and localized in three areas – Peyer patches, lamina propria lymphoid cells, and intraepithelial lymphocytes

**Peyer Patches** – unencapsulated lymphoid nodules that constitute an afferent limb of the gut-associated lymphoid tissue that recognizes antigens through the specialized sampling mechanism of the microfold (M) cells contained within the follicle-associated epithelium

Antigens that gain access to Peyer patches activate and prime B and T cells within that site – activated lymphocytes from intestinal lymphoid follicles then leave the GI tract and migrate into afferent lymphatics (that drain into mesenteric lymph nodes) and into the lamina propria – B lymphocytes: located in lymphoid follicles and become surface IgA-bearing lymphoblasts when activated by antigens

**Lamina Propria** – connective tissue contains B lymphocytes and plasma cells, T lymphocytes, macrophages, dendritic cells (antigen presenting cells), eosinophils, and mast cells – 60% lymphoid cells are T cells – differentiate into several types of T-effector cells: Cytotoxic T cells directly damage target cells; T helper cells help mediate induction of other T cells or B cells to produce antibodies – 40% lamina propria lymphoid cells are B cells (primarily derived from precursors in Peyer patches) that are focused on IgA synthesis with some IgG, IgM, and IgE synthesis

**Intraepithelial Lymphocytes** – located in the space between the epithelial cells that line the mucosal surface and near the basement membrane – most cells are T cells that acquire cytolytic functions that may contribute to both pathogen and epithelial cell death (good for immunosurveillance)

- IgA is predominant immunoglobulin produced in the intestine – produced by plasma cells within lamina propria and secreted in the intestine where it binds antigen at mucosal surfaces – IgA antibody then traverses the epithelial cell to the lumen via protein carrier (secretory component) – secretory IgA inhibits adherence of bacteria to epithelial cells and prevents their colonization and multiplication – additionally, IgA neutralizes bacterial toxins and viral activity as well as blocks absorption of antigens from the gut
I. General information
   a. Carcinoid tumors of small bowel arise from enterochromaffin cells (Kulchitsky cells) in the crypts of Lieberkuhn. These are pluripotent cells with the potential to secrete several endocrine and vasoactive substances—most commonly serotonin.
   b. Common locations include lungs, bronchi and GI tract.
      i. Appendix most common- 45%.
      ii. Ileum- 28%.
      iii. Rectum- 16%
   c. Clinical manifestations
      i. Nonspecific abdominal pain.
      ii. Small bowel obstruction: may be due to intussusception, mesenteric lymph node involvement, or desmoplastic reaction causing kinking.
      iii. Diarrhea, weight loss.
      iv. Carcinoid syndrome.
   d. Pathology
      i. Slow growing.
      ii. Small, firm submucosal nodules.
      iii. Intense desmoplastic reaction occurs after the tumor invades through the serosa producing mesenteric fibrosis presumably due to the humoral factors elaborated by the tumor.

II. Malignant potential
   a. Related to location, size, depth of invasion and growth pattern.
   b. Location:
      i. Appendiceal- 3% metastasize.
      ii. Ileal- 35% metastasize.
   c. Size:
      i. <1 cm- 2% metastasize.
      ii. 1-2 cm- 50% metastasize.
      iii. >2 cm- 80-90% metastasize.
   d. Multicentricity occurs is 20-30% of patients.
   e. Synchronous tumors occur in 10-20% frequently in the large bowel.
   f. Can be associated with MEN I in 10% of cases.

III. Diagnosis
   a. Rarely diagnosed preoperatively.
   b. Barium radiographs of the small bowel may show filling defects as a result of kinking and fibrosis.
   c. CT scan are helpful in detecting lymph node and hepatic metastasis, as well as the extent of bowel wall and mesenteric involvement.
d. A nuclear medicine study with $^{111}$In-octreotide, a radioactively labeled marker that localizes the presence of somatostatin receptors aids in detecting primary as well as metastatic tumors.

e. Elevated urinary levels of 5-HIAA. 5-HIAA is the metabolite of serotonin and increased levels usually indicate hepatic metastasis and a heavy tumor burden.

IV. Treatment
a. Surgical treatment
   i. For tumors <1 cm- perform segmental intestinal resection.
   ii. For tumors >1 cm, multiple tumors or regional lymph node involvement- wide excision of bowel and mesentery
   iii. When extensive mesenteric or hepatic metastases are present aggressive attempts of resection can be beneficial for survival but also provides symptomatic relief.
   iv. Terminal ileal lesions should be treated with right hemicolecotomy.
   v. Duodenal tumors may require a pancreaticoduodenectomy.
   vi. Anesthesia can provoke a carcinoid crisis in which the patient develops hypotension, bronchospasm, flushing, and tachycardia. Treat this with IV octreotide.

b. Medical therapy
   i. Octreotide relieves symptoms of carcinoid syndrome. It may have a potential role in tumor inhibition.
   ii. Interferon-alpha has shown some symptomatic relief.
   iii. Cytotoxic chemotherapy has had limited success.

V. Prognosis 5-year survival
a. Local disease with resection- 100%.
b. Regional disease- 65%.
c. Distant metastasis- 25-35%.

VI. Carcinoid syndrome
a. Present in less than 10% of patients with carcinoid tumors.
b. The majority of patients who exhibit carcinoid syndrome have massive hepatic replacement by metastatic tumor, with resulting loss of hepatic filtration and metabolism.
c. Symptoms
   i. Cutaneous flushing- 90%.
   ii. Diarrhea- 76%. This is typically episodic, secretory in nature.
   iii. Hepatomegaly- 71%.
   iv. Right sided heart valvular disease- 41-70%. This is a late finding. The three most common lesions are pulmonary stenosis, tricuspid insufficiency and tricuspid stenosis.
   v. Asthma- 25%.
Peutz-Jeghers Syndrome
Peter Chang, DMD, MD

General
-a rare autosomal dominant disorder with multiple hamartomatous polyps in the GI tract associated with mucocutaneous pigmentation
-high degree of penetrance for both polyposis and skin pigmentation; M=F

Genetics:
-mapped to chromosomal 19p13.3
-mutations in a gene encoding a serine threonine kinase (role unknown)
-first cancer syndrome due to inactivating mutations in a protein kinase

Clinical manifestations: 2 types: pigmented lesions and multiple GI polyps
-pigmented spots -also known as melanin spots (present in 95% of pts)
-caused by laden macrophages in the dermis
-typically flat, blue-gray to brown spots 1-5 mm
-looks like freckles, but onset and location are different
-occur most commonly on the lips and perioral region (94%)
-hands (74%), buccal mucosa (66%), feet (62%)
-also occurs on the nose, perianal area, genitals rarely in the gut
-usually occur in first 1-2 years of life
-increases in size and number over ensuing years
-fade after puberty with the exception of those on the buccal mucosa
-GI polyps -hamartomatous polyps present in most pts
-proliferation of smooth muscle extending into lamina propria in an arborization-like fashion; overlying epithelium is normal
-no major distinguishing features may be sessile, pedunculated, and lobulated
-small intestines (64%), colon (64%), stomach (49%), rectum (32%)
-number of polyps range from 1-20 per segment of bowel; can be solitary
-size of polyps range from 0.1 to >5 cm in diameter
-begin to grow in the first decade of life
-symptomatic between age 10-30
-obstruction caused by intussusception or occlusion by polyp (43%)
-abdominal pain caused by infarction (23%)
-acute or chronic rectal bleeding caused by ulceration (14%)
-extrusion of the polyp through the rectum (7%)

Risk of malignancy: increased risk of both GI and non-GI malignancies
-risk of dying of cancer approaches 48% by age 57
-13 % of pts develop GI cancers (not due to increased k-ras oncogene)
-small intestine (48%), stomach (24%), colon (24%), pancreas (5%)
-others include cancers of the biliary tree, gallbladder, and esophagus
-non-GI cancers: females-cervical, uterine, ovarian, breast
-males- sertoli cell testicular tumors

Management:
-predictive genetic testing
-screening for cancers in at risk organs (GI, gonads, breast)
-surveillance for polyps and their prophylactic excision
-endoscopic and laparoscopic approach to treat small bowel intussusception
PATHOPHYSIOLOGY
Obstruction of the appendix followed by infection. Somatic pain occurs when the inflamed serosa comes in contact with the parietal peritoneum leading to right lower quadrant pain. Venous and arterial thromboses leads to gangrene. Gangrene permits bacteria to escape and results in perforation.

CLASSIC HISTORY
Usually begins with epigastric abdominal pain that migrates to the umbilicus, and localizes to the right lower quadrant. Anorexia, nausea, and vomiting follow in that order.

CLINICAL PRESENTATION
Abdominal pain and anorexia are the most common findings. Leukocytosis is usually present. The duration of symptoms (over 48 hrs) is an important factor in those patients that perforate.

RADIOGRAPHIC EVALUATION
CT
The diagnosis of appendicitis can be established (especially in adults) if the appendix is enlarged (>6 cm in diameter), its wall is thickened and enhances with IV contrast, or an appendicolith is visualized. Other inflammatory changes that can be identified include fat stranding, abscess formation, extraluminal gas, or adjacent bowel wall thickening.

US
Suitable in children with low abdominal wall fat content. There is a long learning curve. In children, the criteria for the diagnosis of acute appendicitis includes finding a fluid filled appendix, that is distended, non-compressible, and tender. The diameter of the appendix is usually > 6mm, and on cross section a “bull’s eye” concentric ring configuration may be seen. The surrounding mesentery is echogenic and edematous.
Appendicitis: Antibiotic Therapy and Wound Closure
David W. Hart, MD

Common Pathogens
• Gram Negative Rods: *E.coli, Pseudomonas*
• Gram Positive Cocci: *Enterococcus and Streptococcus*
• Anaerobes: *Bacteriodes*

• Goal of antibiotic therapy is to reduce the incidence of wound and deep peritoneal infections and to protect against the consequences of bacteremia--NOT to treat appendicitis
• Most effective when initiated just before surgery, so as to obtain good tissue levels as the incision is being made

Non-Perforated Appendicitis
• <24 hours coverage with single agent (No controversy)
  – Cefotetan, Cefoxitin, Unasyn
Gangrenous and Locally Perforated Appendicitis
• 5 days with single agent (Length controversial)
  – Cefotetan, Cefoxitin, Unasyn
Grossly Perforated Appendicitis
• 7-10 days with triple antibiotic therapy or extended-spectrum synthetic penicillins and an aminoglycoside (Length controversial)
  – With clinical improvement, can simplify to monotherapy
    • Resolution of fever, resolution of leukocytosis, return of GI function

Duration of Antibiotic Therapy and Infectious Complications
• Several studies have demonstrated equivalent efficacy of antibiotic therapy administered for a set number of days (usually 5-10) with antibiotic therapy administered until fever and leukocytosis resolved and normal GI function returned

Non-operative Management of Appendiceal Abscess or Phlegmon
• 10-14 days with broad spectrum agents

Utility of Operative Cultures
• The case for: identify pathogens
• The case against:
  – Colonic flora can be predicted
  – Cultures are not completely accurate
  – Antibiotic regimens are seldom changed
– Morbidity rate is identical whether or not cultures are taken
– Cultures will be taken when clinically significant complications are identified

Wound Closure

• Wound infection rates:
  – Primary closure 6-18%
  – Delayed primary closure 7-15%
  – Secondary closure 10-18%

• Cost-utility analysis
  – RLQ incision is low-risk incision and the primary sequela of infected appendectomy incision is wound care
APPENDICITS IN PREGNANCY
Buckminister J. Farrow, MD

Epidemiology
Appendicitis and cholecystitis are the most common extrauterine causes of abdominal pain in the pregnant patient
Appendicitis is the most common extrauterine cause of laparotomy in pregnant women

Incidence 1:1500 pregnant women
1st trimester – 30%  2nd trimester – 45%  3rd trimester – 25%

Diagnosis
Physical exam is the most important diagnostic modality and RLQ pain is the most common presenting sign
Fever, WBC count, anorexia, nausea/vomiting are largely unreliable

Anatomical changes associated with pregnancy
After 5th month of gestation, tip of the appendix may be elevated and rotated laterally, as the gravid uterus displaces the appendix upward & outward
Presentation may be of flank or RUQ pain instead of RLQ pain esp. in the 3rd trimester
Increased separation between visceral and parietal peritoneum may lead to decreased perception of somatic pain and localization until late in the disease process

Helical CT may be a useful diagnostic tool in pregnant patients – as accurate as in non-pregnant patients (study of 7 pts. In 2nd/3rd trimester, 5 were spared appendectomy)
With the use of select limited helical scanning, radiation exposure is approximately 300 mrad (about one third of the average abdominal-pelvic CT). This is also well below the accepted safe level of fetal exposure (5 rad).

Incidence of perforation at initial presentation 4 -19% in nonpregnant patients 50% in pregnant women

Complications
More common in later trimesters
Preterm labor- much more common with perforated appendicitis
Negative laparotomy results in minimal fetal loss
Delay in diagnosis and perforation may result in high incidence of fetal mortality and maternal morbidity

Incision is standard McBurney’s despite changes in position
Laparoscopy should be considered, especially in early trimesters

“It is the peritonitis, and not the appendectomy, that poses the risk to mother and fetus alike…”

Maingot’s Abdominal Operations
Tumors of the appendix
Eric C. Feliberti, MD

I. Carcinoid tumor
   A. Most common tumor of the appendix; most common site of carcinoid tumors.
   B. Can present as appendicitis or found incidentally.
   C. Firm, yellow-tan mass composed of neuroendocrine cells that can produce multiple peptides (serotonin, bradykinin, substance P).
   D. Most are found at tip, followed by body and then base of appendix.
   E. Rarely metastasizes; thus do not see carcinoid syndrome.
   F. Malignant potential is related to size – tumors less than 2cm rarely metastasize.
   G. Treatment: Less than 2cm, not at base, no serosal invasion – simple appendectomy
      Greater than 2cm, at base, serosal invasion – right hemicolectomy
   H. 5 yr survival is 55%

II. Adenocarcinoma
   A. Arise from adenomas
   B. Commonly presents as appendicitis
   C. Spreads to regional lymph nodes; occasionally to ovary
   D. Tumor invasion most determining factor of survival
   E. Treatment is right hemicolectomy; simple appendectomy may be done for mucosal invasion only.
   F. Duke’s staging and 5 yr survival: A – 100%; B – 67%; C – 50%; D – 6%.

III. Mucocele
   A. Benign or malignant (cystadenocarcinoma).
   B. Secrete mucin causing enlargement of appendix.
   C. Cystadenocarcinomas can rupture and cause pseudomyxoma peritonei.
   D. Less virulent than adenocarcinoma.
   E. Treatment is right hemicolecetomy and debulking of all apparent mucinous tissue.
   F. 3 yr survival of pseudomyxoma peritonei depends on residual peritoneal disease – 92% for mild, 20% for gross.
Short Chain Fatty Acids (SFCAs)
Michael K. Obeng, MD

- SCFAs are anions and constitute two thirds of the anionic contents in the colon, a concentration of about 70-130 mmol/L.
- There are three main types: acetate, propionate and butyrate.
- They are produced by fermentation of water-soluble non-starch polysaccharides (fiber) by colonic bacteria.
- They serve four main purposes: (T.E.A.M.)
  (i) Exertion of trophic effects on colonocyte (Trophic effects)
  (ii) Provision of energy (Energy)
  (iii) Generated energy is coupled with sodium absorption (Absorption)
  (iv) Enhances colonic motility (Motility)
- Butyrate selectively activates G-protein, thus acts paradoxically on normal and neoplastic colonocytes.
- It exerts trophic effects on normal colonocytes, and arrests the growth of neoplastic colonocytes.
- It may involve hormonal signaling such as peptide YY and myogenic reflexes.
- It also regulates the expression of molecules involved in adhesion of colonocytes.
- SCFAs play a pivotal role in the ileocolonic brake.
- Butyrate serves as the main source of fuel for colonic epithelial cells.
- Absorption of SCFAs provides about 10% of the daily energy expenditure (an important concept in patients with short bowel syndrome with intact colon)
- The energy provided is the driving force behind sodium and water absorption.
- The lack of butyrate causes diarrhea (such as when colonic bacteria are wiped out by broad spectrum antibiotics)
- Conversely, butyrate can be employed to treat diarrhea by feeding dietary fibers to patients
- Other effects of SCFAs on the colon include
  (i) Blood flow stimulation
  (ii) Homeostasis of bacteria flora by regulating intraluminal pH
  (iii) Renewal of mucosal cell
Inflammatory Bowel Disease
Juan C. Escalon, MD

I.  Etiology
   A. Genetic factors
      1. First degree relatives of affected patients have a 4-20 times higher risk of developing IBD and have an absolute risk of 7% for IBD.
      2. The overall prevalence for developing IBD varies among different populations.
      3. In studies of monozygotic and dizygotic twins, there is evidence of greater concordance among monozygotic twins with 45% having IBD.
      4. The IBD1 gene on chromosome 16 is linked to the development of CD, but not UC. This locus encodes for NOD2 (a.k.a. CARD 15), a cytoplasmic protein that is expressed in macrophages.
      5. Genetic abnormalities of MLH1, a DNA repair gene, and class II MHC genes, especially HLA DR2 are expressed in patients with UC.
   B. Environmental and predisposing factors
      1. Current evidence based on murine studies suggests that the presence of luminal bacteria is a requirement for the development of IBD.
      2. The use of NSAIDS is associated with IBD flare ups and is likely related to compromising the intestinal mucosal barrier.
      3. A decreased ratio of interleukin-1 receptor antagonist (IL-1ra) to IL-1 correlates to the severity of IBD in both UC and CD.
      4. Appendectomy is reported as a protective factor in UC but does not affect CD.
      5. Cigarette smoking is also a protective factor for developing IBD, the mechanism of which remains unclear.
   C. Pathophysiology
      1. Current data suggests the aggregate effect of genetic and environmental factors lead to the sustained activation of the mucosal immune response.
      2. It is unclear whether this immune response is activated by an intrinsic defect (constitutive activation or failure in down regulation of immune response) or continued stimulation from changes in the mucosal barrier.
      3. After stimulation of the immune response by bacteria or other antigens, type 1 helper T cells (Th1) in CD or atypical type 2 helper T cells (aTh2) in UC promote activation of macrophages and produce IL-12, IL-18, and macrophage migration inhibitor factor. The macrophages in turn produce inflammatory cytokines IL-1, IL-6, and TNF, which effect other cells. Endothelial cells then facilitate leukocyte recruitment from capillaries to the mucosa and alter epithelial cells.
      4. The cellular pathway for IBD leads to activation of nuclear factor kappa B (NFkB) from bacterial lipopolysaccharides, IL-1, or TNF. NFkB is then responsible for activation of gene transcription of more cytokines and chemokines, and regulates apoptosis in the cell.
II. Clinical Presentation
   A. History and physical examination
      1. Both CD and UC can present in similar fashion with a history of fever, abdominal pain, weight loss, diarrhea, and rectal bleeding.
      2. Key differences that maybe seen on physical exam differentiating CD from UC are anal fistulas, fissures, and abscesses; enteral fistula formation; oral aphthous lesions; small bowel obstruction.
      3. UC is associated with increased risk of primary sclerosing cholangitis
      4. Both are associated with increased risk of colon cancer and extracolonic manifestations including erythema nodosum, pyoderma gangrenosum, episcleritis, ankylosing spondylitis, and peripheral arthritis.
   B. Laboratory Findings
      1. Perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) are positive in 70% of patients with UC.
      2. Anti- Saccharomyces cerevisiae antibodies (ASCA) are positive in >50% of patients with CD.
      3. Iron and Vitamin B12 deficiency may be seen in CD secondary to poor ileal absorption.
      4. Severe anemia maybe seen in UC associated with bleeding.
   C. Radiographic Findings
      1. In CD fistulas, strictures, deep ulcers, and segmental lesions can be seen on contrast enhanced radiographs.
      2. In UC loss of haustration, fine or superficial continuous ulcers, and narrowing of the sigmoid and rectum can be seen on contrast enhanced radiographs.
   D. Endoscopic and pathologic findings
      1. Ulcerative Colitis
         a. Exclusively limited to the colon and appears as a continuous segment of congested, ulcerated, and hemorrhagic mucosa. Pseudopolyps are also commonly seen in the mucosa. The disease is usually distributed from distal to proximally and can involve the entire colon. In rare instances, the right colon can be involved without involvement more distally, and CD must be ruled out. Also may have inflamed and dilated terminal ileum “back-wash ileitis.”
         b. Microscopic appearance of UC shows irregular and branching glands with a central crypt abscesses and increased chronic inflammatory cells in the lamina propria.
      2. Crohn’s Disease
         a. Can occur throughout the GI tract and is characterized by “skip lesions” associated with aphthous and linear ulcers, cobblestone appearance and stricturing.
         b. Microscopic appearance of CD is difficult to differentiate from UC, but granulomas are highly suggestive for CD.

Inflammatory Bowel Disease
Indications for Surgical Management
Farin W. Smith, MD

Crohn’s: 78% will require surgery if dz is active for >20y.
Ulcerative Colitis: 50% will require surgery with in 10y.

Indications for surgery:
   Obstruction
   Perforation – free, with fistula, or with abscess
   Hemorrhage
   Urologic complications
   Cancer – known cancer or to prevent progression of dysplasia
   Treatment of peri-anal disease
   Growth retardation in children

For UC add:
   Toxic Megacolon
   Unresponsiveness to maximum medical mgmt.
   Intolerance to side effects of drug therapy
   10y hx of universal involvement

Operative Considerations:

Crohn’s: Operative mgmt only of the diseased segment w/ only a few centimeters of free margin
   Resection of perforated, hemorrhagic, obstructed, or fistulous segment
   Strictureplasty of narrowed segments (Townsend figure 44-24)
   Resection w/ nodes for ca

UC: treat emergent problems as indicated by situation,
   i.e. subtotal colectomy w/ ileostomy and Hartmann pouch for toxic megacolon
   Definitive tx is colectomy w/ mucosal proctectomy & endorectal ileal pouch-anal anastomosis (Townsend figure 46-8 to 46-13)
TREATMENT OF SESSILE COLORECTAL POLYPS

Yvette M. Carter, MD

Polyp-mass→elevation of the mucosa

**Adenomatous Polyps**

Most common (67%)

Prevalence: 15-20% general population; 33% >50yrs

2x increase w/ 1st degree relative with CRC

Histology: tubular (87%)

D<1.5cm

villous (5%)

finger like projections

D>1.5cm

Tubulovillous (8%)

Location: ascending, transverse and sigmoid colon (23-25% each)

Dx: flexible sigmoidoscopy

Colonoscopy

Rx: pedunculated- excised with polypectomy snare

Large/sessile- piecemeal resection (less precise histo assessment)

perforation and bleeding

laparoscopic excision

**polyps with villous characteristics or >3cm—treat like cancer**

require excision of the mesentery, lymph nodes and colon based on the

blood supply to the region of the colon, in which the polyp is located

**Hyperplastic Polyps**

11%

Histology: <3mm (90%)

sessile, flat

funnel-shaped, nonbranching mucosal crypts

**not pre-cancerous**

can have adenomatous changes and coexist with adenomas

Dx: colonoscopy

Rx: excision

**Juvenile Polyps**

Retention polyps

Sx: bleeding, intussusception

<20yrs

histology: pedunculated, 1-3cm=d

mucus-filled cysts lined by columnar cells

**no malignant potential**

**Polyposis Syndromes**

**Familial Adenomatous Polyposis**

APC gene-chromosome 5q

truncated protein

involved in apoptosis and regulation of cell proliferation

mutations: cluster region-amino terminal(73%)

5’ and 3’ extremes-attenuated FAP

few adenomas; later in life

Sx: asymptomatic

diarrhea→CA (6yrs)

rectal bleeding=sx of CA

gastric polyps=fundic gland hyperplasia

duodenal polyps=adenomatous (harbor dysplasia)

CHRPE (70-80% people w/ APC mutation), osteomas, fibromatosis

Px: increased risk of ampullary CA
extrahepatic biliary duct, GB, pancreatic, thyroid, liver CA
Rx: abdominal colectomy with ileorectal anastomosis
Cancer surveillance in remaining rectum
Sulindac reduces polyp formation
total proctocolectomy with permanent ileostomy
total proctocolectomy with ileoanal anastomosis

**Hereditary Nonpolyposis Colorectal Cancer**
6% of CRC; 15.5% of pts with positive family hx
autosomal dominant inheritance
proximal (70% right side)
mucinous adenoCA
Lynch I- CRC
Lynch II- CRC, endometrial, ovarian, ureteral, renal pelvis, stomach,
small bowel, pancreatic CA
Dx: family hx
Management:
   Lynch I-colonoscopy@ 25yrs
      q2yrs until 35yrs, then q1yr
   Lynch II-same as Lynch I + endometrial vacuum curettage@ 25yrs
      +/- pelvic US and CA-125
Colon CA-abdominal colectomy with ileorectal anastomosis
   Post menopausal women-TAH/BSO
Colorectal Cancer
Treatment: Resections & Chemoradiation Therapy
M. Joseph Elieson, MD

Goals of Surgical treatment of Colorectal Cancer:
• Cure patient’s cancer
• Alleviate symptoms / prevent complications (obstruction / bleeding)

Preoperative Colonoscopy or ACBE to evaluate for synchronous lesion
• synchronous benign polyps: 12-62%
• synchronous cancer: 2-8%

Bowel Prep:
• Mechanical – phosphosoda / GoLytely
• Antibiotics – Neomycin / Erythromycin / IV Abx

Colorectal Cancers spread in a stepwise fashion
• Direct extension into adjacent structures
• Lymphatics in the submucosa on to regional nodes
• Vascular invasion to distant sites such as liver and lungs

Resection should include involved segment of colon and its draining lymphatics.
Lymphatics follow major vascular supply; therefore, large segments of colon are resected with the tumor as directed by the segmental blood supply. Involvement of adjacent organs does not preclude resection for cure. En bloc resection with negative margins has nearly a 50% 5 year survival rate

Right Hemicolecotomy
• Treatment for tumors of the cecum and ascending colon
• Ligation of the ileocolic a., right colic a., and right branch of the middle colic a.
• Anastomosis of the ileum to the transverse colon

Extended Right Hemicolecotomy
• Treatment for tumors of the transverse colon
• Ligation of the ileocolic a., right colic a., and middle colic a.
• Anastomosis of the ilium to the descending colon

Left Hemicolecotomy
• Treatment for tumors of the splenic flexure and descending colon
• Ligation of the left colic a.
• Anastomosis of the transverse colon to the sigmoid colon

Sigmoid Colectomy
• Treatment for tumors of the sigmoid colon
• Ligation of the inferior mesenteric a. distal to the takeoff of the left colic a.
• Anastomosis of the descending colon to the rectum

Subtotal Colectomy
• Treatment for synchronous tumors in different areas of the colon, metachronous tumors after previous resection, and proximal perforation due to distally obstructing tumor
• Ligation of the ileocolic a., right colic a., middle colic a., and either the left colic a. or the inferior mesenteric a.
• Anastomosis of the ilium to the sigmoid colon or rectum

Adjuvant Therapy for Colon Cancer
• Adjuvant chemotherapy for colon cancer includes 5-FU with/without other agents such as leucovorin
• Adjuvant therapy is recommended for all node-positive colon cancer patients
• It is less clear whether node negative patients with locally advanced tumors benefit from adjuvant chemotherapy
• Radiation therapy is indicated for control of locally advanced tumors

Rectal Cancer
• Accurate preoperative staging of rectal cancer is 1st step in its management.
• History & Physical Exam including rectal exam
• Colonoscopy or air-contrast barium enema
• EUS or MRI with endoluminal coils to evaluate the depth of invasion and the presence of any nodal involvement

Adjuvant Chemoradiation for Rectal Cancer
• T3N0, TxN1 – Preoperative CTX/XRT
• 6 week course of 5-FU & leucovorin IV (intermittent/continuous pump)
• concomitant 4000~5000 cGy of radiation
• 6 week rest prior to surgical resection
• 6-8 weeks after surgery, 4 additional months of chemotherapy
• T1N0, T2N0 – Controversial – pre-/post-operative radiation

Transanal Excision – full thickness resection with > 1cm margins
• T1N0 rectal ca with proximal edge within 10cm of anal verge, <4cm wide, < 1/3rd of rectal diameter, well or moderately differentiated by biopsy, without evidence of lymphatic or vascular invasion by biopsy
• Local control in patients with extensive metastasis and poor prognosis
• Patients with significant comorbid conditions who are not candidates for abdominal resection

Low Anterior Resection
• Tumors in the proximal 1/3rd of rectum above peritoneal reflection
• colorectal anastomosis
• Minimum 2cm distal margin must be obtained

Restorative Proctocolectomy
• Tumors of the middle or lower 1/3rd of rectum
• Coloanal anastomosis with or without colonic J-pouch reconstruction
• Minimum 2cm distal margin must be obtained
• Total mesorectal excision should be performed
• IMA is frequently ligated to enable full mobilization of the splenic flexure

Abdominal Peritoneal Resection
• Tumors of the lower 1/3rd of rectum involving the anal musculature or the dentate line
• Performed in 2 steps, rectal excision through the abdomen, and excision through the perineum
• Total mesorectal excision should be performed
I. Origin: Fistula in ano arise as a complication of anorectal abscess in approximately 25% of patients. The fistula may present with the initial episode of anorectal abscess or it may present as a draining sinus within 6 months after the inciting event.

II. Parks Classification of Anorectal Fistulas:

1. Intersphincteric: 70% (most common), the fistula track is confined to the intersphincteric plane between the internal and external sphincter into the ischiorectal fascia. Most commonly the track passes directly to the perineal skin.

2. Transsphincteric: 25%, fistula connects the intersphincteric plane with the ischiorectal fossa by perforating the external sphincter.

3. Suprasphincteric: 4%, the fistula track connects the intersphincteric plane with the ischiorectal fossa as in transsphincteric fistulas but the track loops over the external sphincter and perforates the levator ani. Because the track travels over all muscles involved in continence, treatment by division of the external sphincter will result in incontinence.

4. Extrasphincteric: 1%, the fistulous track is completely outside the sphincter apparatus and passes from the rectum to perineal skin.

III. Treatment

1. Examination under anesthesia: digital rectal exam to evaluate for induration, anoscopy to inspect for internal opening and define abnormal anatomy. Use Goodsall’s rule to anticipate the anatomy of simple fistulas.

2. Drainage of primary infection and the primary track.
   A. Primary fistulotomy for simple fistulas that involve small quantities of sphincter muscle. Opening of the fistulous track, curettage and cautery of the track and healing of the wound bed by secondary intention.
   B. Fistulectomy- complete excision of the fistulous track is not indicated
   C. Seton placement should be considered for anterior fistulas in women and if the fistula involves more the one fourth to one half of the bulk of the sphincter muscles. Seton placement allows fibrosis and gradual sphincter transection.
   D. Consider evaluation by a specialist for complex suprasphincteric and extrasphincteric fistulas. They may require complex advancement flaps for coverage of the internal opening.

3. Follow-up wound care to insure proper wound closure, including Sitz baths, wound irrigation and packing of the deep portions of the wound.

4. Failure of resolution of the fistula may be due to remaining infection, excess granulation tissue and Crohn’s disease.
RECTOVAGINAL FISTULAS
Ricki Y. Fram, MD

- A communication between the epithelial lined surface of the rectum and vagina.
- RVFs are always located above the dentate line.
- A fistula between the anal canal distal to the dentate line and the vagina is an anovaginal fistula.

ETIOLOGY (are numerous)
- Obstetric Trauma 50-90%
- Inflammatory Bowel Disease
- Pelvic Irradiation 7-10%
- Surgical Trauma
- Congenital
- Neoplastic and Hematologic
- Infections such as perianal abscesses or Bartholin’s abscess, as well as TB or Lymphogranuloma Venerum
- Foreign bodies such as pessaries or surgical sponges can cause erosion of the anovaginal septum

CLINICAL EVALUATION
Sx are often dependent on size and location. Complaints range from:
- Passage of flatus and stool per vagina.
- Foul-smelling vaginal discharge with recurrent or chronic vaginitis
- Fecal incontinence secondary to associated sphincter injury.
- Diarrhea, bleeding per rectum, mucus discharge, tenesmus, and abdominal pain.
- May be easily seen and felt on bimanual exam. A thorough PE is essential to determining size, location and underlying cause.

CLASSIFICATION is usually according to location, cause and size.
- Simple: low or mid-vaginal septum; <2.5 cm in diameter; due to trauma or infection
- Complex: high vaginal septum; >2.5 cm in diameter; due to inflammatory bowel disease, radiation or neoplasm; multiple failed repairs.
- An RVF is considered low if the rectal opening is at or above the dentate line or it occurs along the lower one-third of the rectum and lower one-half of the vagina.
- An RVF is considered high if it occurs in the middle one-third of the rectum and the posterior vaginal fornix or when the vaginal opening is behind or near the cervix.

RADIATION
- Radiation therapy plays a significant role in the treatment of carcinoma of the prostate, bladder, rectum, uterus and cervix. But most RVF are associated with radiation treatment for endometrial or cervical cancer.
- Radiation-induced rectovaginal fistulas are usually located high in the vagina.
- They differ from other RVFs because they are frequently associated with varying degrees of tissue loss, commonly associated with rectal fissures and webs, they are frequently very large, and usually located in the upper and middle third of the vaginal wall.
- Most postradiation fistulas occur within six months to two years of therapy.
- Radiation causes vascular changes with narrowing of the arterioles by subintimal fibrosis, telangiectasia of capillaries and postcapillary venules, endothelial degeneration and platelet thrombus formation.
After chronic radiation exposure, these changes can result in tissue contraction, stricture formation, decreased regenerative processes and may result in fistula formation.

**SURGICAL OPTIONS**

- Radiation-induced RVFs present unique surgical problems.
- Once a fistula forms it is unlikely to close spontaneously.
- Local repairs of fistulas are generally not feasible because the vascular damage prevents healing of the vaginal or rectal suture line.
- A successful repair must incorporate normal tissue to either replace or cover the fistula.

**Tissue Transposition Procedures**

**Martius Technique**

- The fat pad and bulbocavernosus muscle are mobilized and passed through a subcutaneous tunnel to lie over the rectal closure.
- The vaginal mucosa is closed over the flap.

**Graciloplasty**

- Neighboring muscles such as the sartorius and the gracilis can also be harvested and interposed between the rectum and vagina.
- The vaginal mucosa is closed over the muscle, and if possible, the rectal mucosa is also closed over the graft.

**Abdominal Procedures**

**Onlay Patch Anastomosis**

- The rectosigmoid is divided and an end-sigmoid colostomy is formed.
- The distal rectosigmoid stump is then folded upon itself and the open end anastomosed to the débrided edges of the fistulous opening in the rectum.
- When healing is confirmed radiologically, the end-colostomy is taken down and anastomosed end-to-side to the folded loop of the rectosigmoid.

**Low Anterior Reseption**

- The proximal colon to be used for the low anastomosis should be mobilized from a field outside the area of radiation and must be well vascularized.

**Coloanal Anastomosis**

- The anal sphincter is dilated and a proctoscope is introduced into the anus to the rectosigmoid junction and fixed to the intestinal wall at this level with a heavy silk suture.
- The rectum and lower sigmoid are then everted by downward traction of the obturator.
- The rectal wall is then circumferentially incised 4 cm from the dentate line distal to the RVF.
- The mobile sigmoid is pulled through the everted anorectal stump to cover the site of the RVF with normal colon.
- The sigmoid colon is divided at an appropriate level without tension, and hand-sewn anastomosis of the colon to the rectal stump is performed.

**Colostomy**

- Permanent colostomies are used when diffuse tissue fibrosis makes dissection difficult. Diffuse small vessel endarteritis results in vascular compromise with subsequent tissue loss. There is also often an associated stricture.
Resection of Liver Metastases—Effect on Patient Survival
Chance L. Irwin, MD

I. Indications for Resection
   A. A single, hepatic metastatic lesion can be resected at the time of treatment for the primary lesion
   B. Resection of large symptomatic lesions in the presence of extrahepatic disease
   C. Resection of residual hepatic disease in combination with aggressive chemotherapy
   D. Multiple hepatic lesions (some sources say up to 5) can be resected as long as the 1 cm margin required for cure is attainable

II. Contraindications
   A. Total hepatic involvement
   B. Advanced cirrhosis
   C. Jaundice (except from extrinsic hepatic ductal obstruction)
   D. Vena cava or main portal vein invasion
   E. Extrahepatic tumor involvement (relative contraindication—see above)

III. Effects on Patient Survival
   A. Resection of a solitary metastatic lesion from colorectal carcinoma can have as much as a 60% 5-year survival rate
   B. A review of 345 patients who underwent hepatic resection of colorectal metastases had a cumulative 5-year survival rate of 22%
   C. Those with tumors >5 cm in diameter had a poorer outcome
   D. Survival did not correlate with the time interval between resection of the primary tumor and resection of the metastatic tumor, nor with the extent of liver resection
   E. No difference in survival was found between patients with synchronous and those with metachronous lesions or between patients with solitary lesions and those with multiple lesions in the same lobe
   F. The status of colonic lymph node involvement in the resected primary tumor had no effect on survival

IV. Predictors of Survival
   A. Size of the lesion
   B. Number of metastases
   C. Presence of residual local disease
   D. Several studies suggest females have a better survival than males after hepatic resection for colorectal metastases

V. Prognosis of Untreated Hepatic Metastases for Colorectal Carcinoma
   A. Sixty to 70% will die within 1 year
   B. Close to 100% will die within 3 years

VI. Techniques and Complications
   A. Laparoscopic Evaluation
      1. Only useful to assess the liver surface
      2. Can identify surface lesions as small as 1 mm
      3. >70% of the liver surface can be visualized
      4. 90% of metastases are on the surface
      5. Direct assessment of intraabdominal spread (carcinomatosis)
      6. Laparoscopy and LUS (laparoscopic ultrasound) prevent unnecessary laparotomy in 10% of cases
   B. Intraoperative Ultrasound (IOUS)
      1. May detect 25-35% more lesions than noninvasive imaging techniques such as CT, MRI and transabdominal ultrasound
2. Can detect lesions as small as 5mm wide

C. Hepatic Resection
   1. Technique
      a. Three basic types- major anatomic resection, segmental resection, and nonanatomic resection
      b. Five major resections- right hepatectomy, left hepatectomy, right trisegmentectomy, left trisegmentectomy and left lateral segmentectomy
   2. Perioperative Morbidity and Mortality
      a. Hemorrhage
      b. Hypoglycemia and hyponatremia- usually resolve in 1 week
      c. Alkaline phosphatase and transaminase elevation
      d. Transient hyperbilirubinemia
      e. Overall complication rate exceeds 20% in most series
      f. Pulmonary complications- most common with pleural effusion in 5-10% and pneumonia in 5-22%
      g. Operative mortality rate increases when a major liver resection is performed simultaneously with resection of the primary tumor

D. Ablative Techniques
   1. Cryoablation
   2. Radiofrequency Ablation
   3. Interstitial Laser Hyperthermia
   4. Microwave Coagulation Therapy

E. Benefits of Ablation
   1. Less destruction of normal hepatic parenchyma
   2. Minimization of surgical morbidity and mortality
   3. Less need for blood transfusion
   4. Focal treatment allows potentially curative procedures to be performed in those with multiple tumors or tumors in both lobes of the liver
   5. Patients with inadequate functional reserve (cirrhosis) may receive treatment due to less normal parenchymal loss

F. Why Choose Ablation?
   1. Adequate margins (1cm) or central tumor locations may require major resections for relatively small tumors
   2. Multiple tumors on both sides of the liver may suggest a combination of resection and ablation to decrease blood loss and to preserve adequate liver function
   3. Patients with cardiac or pulmonary disease may benefit from a smaller incision, shorter operative time, and less blood loss

G. Contraindications to Ablation
   1. Tumor >5cm
   2. Tumors close to the largest bile ducts- stricture formation leading to biliary obstruction
   3. Tumors close to major portal or hepatic veins may not be completely killed due to flowing blood in these structures preventing uniform and adequate heating and or cooling

Ref: Sabiston 16th Edition; Current Surgical Therapy 7th Edition
Major Metabolic Functions of the Liver
  Kupffer cell (reticuloendothelial) clearance of antigen
  Glucose & lipid metabolism
  Protein synthesis
  Detoxification & chemical metabolism
  Bile production

Kupffer cells
  Resident macrophages of the liver
  Phagocytosis antigen (portal guardian)
  May be involved in oral (portal) tolerance

Hepatocytes
  Large polyhedral cells (3-4 times the size of an RBC)
  Abundant endoplasmic reticulum, mitochondria, lysosomes, etc
  Abundant lipid and glycogen deposits

Hepatocyte Metabolic Function
  Glycogenesis
    Coverts glucose into storable glycogen
    Stimulated by insulin
    Central metabolite is glucose-6-phosphate
  Glycogenolysis
    Converts glycogen back to glucose for release into the blood
    Stimulated by glucagons
    Central metabolite is glucose-6-phosphate
  Gluconeogenesis
    Converts alanine, lactate, glycerol, or other substrates into glucose
    Stimulated by glucagons
    Enhanced by fasting, anaerobic metabolism, etc

Phosphogluconate Pathway
  Utilized when the liver’s capacity to store glycogen is reached
  Excess glucose is converted to fat

Lipid Metabolism
  Long chain (C-16+) fatty acids are initially part of the chylomicron
  Short and medium chain fatty acids are absorbed directly into the portal circulation
  Free fatty acids are taken up by hepatocytes
  Hepatocytes contain dehydrogenases to make unsaturated fatty acids (e.g. dietary linoleic acid is elongated and dehydrogenated to arachidonic acid)
  Fatty acid CoA esters are synthesized in the cytosol and converted into triglycerides for further metabolism (as acetyl CoA) or storage
  In starvation and other severe states of lipolysis, β-oxidation of the liver may be insufficient, and hepatic storage of triglycerides increases significantly (fatty liver)

Cholesterol Metabolism
  90% of de novo synthesis via hepatocytes
  HMG-CoA reductase, the rate limiting enzyme, is inhibited by dietary intake of cholesterol or by the statins

Other lipids
  Hepatocytes also synthesize lecithins, cephalins, and sphingomyelins
Protein Metabolism
Amino acid deamination results in production of ammonia, which is metabolized by the Krebs-Henseleit cycle in the liver, with a secondary metabolic route in the kidney.

Numerous proteins are produced by hepatocytes:
- Albumin
- Transferrin
- Haptoglobin
- Thyroxine-binding globulin
- Vitamin D binding protein
- Fibrinogen
- Prothrombin
- Factors V, VII, IX, X, XI, XII
- AT-II
- Plasminogen
- Protein C
- Protein S
- C-reactive protein
- Apolipoproteins

Et cetera

Bile Acid Metabolism
Primary bile acids are synthesized by the liver from cholesterol:
- Cholic acid
- Chenodeoxycholic acid

Rate limiting step is cholesterol 7-α-hydroxylase
Regulated by intestinal bile reabsorption

Secondary bile acids form in the intestinal lumen after bacterial metabolism:
- Deoxycholic acid
- Lithocholic acid

Heme Metabolism
75% of bilirubin is from senescent RBCs
Hepatocytes conjugate bilirubin with glucuronide
Bilirubin is reduced by bacteria to urobilinogens
Some urobilinogen is oxidized to urobilin, which gives stool its brown color

Vitamin Metabolism
Involved with the fat-soluble vitamins A, B₁₂, D, & K
- Vitamin A is stored in the liver
- Excess can cause liver injury
- Vitamin D is metabolized to 25-hydroxyvitamin D by hepatocytes
- Vitamin K is required by hepatocytes for production of Factors II, VII, XI, & VI
- Vitamin B₁₂ is stored in the liver

Detoxification
General approach is to convert hydrophobic compounds to hydrophilic conjugates that can be secreted
Phase I reactions—Cytochrome P450 system (oxidation), reduction, and hydrolysis to expose functional groups
Phase II reactions—alter solubility by conjugation

References
- Townsend, 16/e
- Greenfield, 2/e
Benign Liver Tumors
Peter Chang, DMD, MD

Hemangiomas
- Most common benign hepatic tumor
- Liver is the third most common site for hemangiomas besides skin and mucosa
- Women > men in a ratio of 6:1
- Histologically, cavernous types are more common
- Cystically dilated endothelial lined vascular space
- Most are small solitary subcapsular growths
- If >4cm, cause abdominal pain and a palpable mass
- Rarely, spontaneous rupture can cause hemorrhagic shock
- Large congenital hemangiomas may be associated with others on the skin
- May behave as an AVF and produce cardiac hypertrophy and CHF
- Complications include obstructive jaundice, gastric outlet obstruction, consumptive coagulopathy

DX - Biopsy is rarely indicated by FNA
- DX can be made by scintigraphy (technetium labeled RBC), contrast-enhanced CT scans, MRI, or angiography

TX - Excised by lobectomy or enucleation, if symptomatic, otherwise observe
- Radiotherapy or embolization of the hepatic artery for poor surgical candidates

Adenomas
- Occurs almost exclusively in women due to oral contraceptives
- Tumors are soft, yellow-tan, well-circumscribed, measures 2-15 cm
- 2/3 are solitary and the rest are multiple
- 75% in right lobe of liver
- Few are pedunculated
- Rarely become malignant
- Histologically, they consist of an encapsulated homogenous mass of hepatocytes without bile ducts or central veins
- 50% are symptomatic, RUQ pain, palpable mass, spontaneous intra-abdominal hemorrhage
- Acute bleeding episodes may be associated with menstruation

DX - Liver CT and US
- Angiography shows avascular to hypervascular lesions indistinguishable from malignant hepatoma
- FNA is safer than needle core biopsy

TX - Wedge resection or partial hepatectomy for symptomatic bleeding lesions
- Discontinuing oral contraceptives may allow adenomas to regress
- Expectant management for lesions less than 6 cm
- Large adenomas should be removed because they are more likely to bleed or be malignant
- Recurrence is rare
LIVER CYSTS
John J. Bawduniak, MD

a. etiologies
   i. ascending biliary infection
   ii. hematogenous spread via portal system
   iii. generalized septicemia via hepatic artery
   iv. direct extension from intraperitoneal infection
   v. trauma
b. most frequently ascending biliary (calculi or carcinoma)
c. E coli, Klebsiella, streptococcus most common
d. staphylococcus and pseudomonas occasionally
e. mixed bacterial/fungal account for 25%
f. clinical manifestation:
   i. fever most common
   ii. chills, sweating, nausea, vomiting, anorexia
   iii. pain with larger abscess, liver tenderness/enlargement, jaundice sometimes
g. diagnosis
   i. leukocytosis (18-20 is usual)
   ii. positive bld cx in 40%
   iii. CT most accurate (90%), Ultrasound (80%), radionuclide (70%)
h. treatment
   i. antibiotics- IV for 2 weeks, po for 1 month
   ii. drainage- CT/US guided successful 80%
   iii. surgical and percutaneous drainage equivalent success
      1. route of drainage depends on location (thoracic/abdominal)
      2. small group pts with mult foci- resection
i. prognosis
   i. percutaneous/surgical drainage- 7.5-20% mortality
   ii. antibiotics alone- 50% mortality
   iii. mortality greatly increased with multiple abscesses

Amebic abscess (E histolytica)

A. Pathology
   i. Reach liver via portal system from bowel wall ulceration
   ii. Large single abscess with red-brown liquid (“Anchovy Paste”)
   iii. Mostly in right lobe of liver
b. clinical manifestations
   i. fever and liver pain(88%), chills/sweating(75%)
   ii. can be referred to right shoulder
   iii. tender hepatomegaly is almost constant feature
   iv. 30-50% have history of antecedent diarrhea
   v. jaundice is rare
c. Diagnosis
   i. Leukocytosis, LFT’s not helpful
   ii. Amebas found in stool of only 15%
   iii. Indirect hemagglutination positive in almost all cases
   iv. Radiographic findings similar to bacterial abscess
   v. Diagnosis frequently established with aspiration
d. Complications
   i. Most common- secondary infection 22%
   ii. Rupture of abscess
   iii. Pleuropulmonary complications 20%
   iv. Rupture into peritoneal cavity or abdominal viscus (6-9%)
   v. Most serious- extension into pericardial cavity
e. treatment
   i. amebicidal drugs- metronidazole 400 TID x3d
   ii. surgical drainage- not drained until intestinal source controlled
   iii. drug therapy should precede surgery by several days
   iv. indications for aspiration
      1. persistence sx after amebicidals
      2. clinical/radiographic evidence hepatic abscess
      3. absence findings that suggest secondary infection
   v. preferred route 9th or 10th interspace, between ant/post mid ax line
   vi. uncomplicated- mortality<5%, complicated- mortality 43%
Hydatid Cysts

A. echinococcus
   i. intermediate hosts- sheep, pigs, cattle
   ii. most cases US- immigrants from Greece, Italy
   iii. most commonly Echinococcus granulosus
   iv. 70% in liver, 25-30% of these are multiple cysts
   v. right lobe 85%
   vi. fluid under high pressure (300mL), colorless, alkaline

B. complications
   a. intrabiliary rupture (most common) 5-10%
   b. suppuration (2nd most common)- invasion of biliary bacteria, conversion to pyogenic abscess, death of parasite
   c. rupture into peritoneum

C. clinical manifestations
   a. simple/uncomplicated usually asymptomatic
   b. abd pain/tenderness most common, palpable mass (70%)
   c. diffuse hepatic enlargement
   d. “hydatid thrill/feminitus” very rare
   e. secondary infection- tender hepatomegaly, fever, tenderness

D. Diagnosis
   a. Unruptured cyst- round, calcified shadow
   b. Eosinophilia in only 25%
   c. Indirect agglutination positive 85%, Complement fixation test <85%
      a. reaction becomes negative 2-6 months after removal
      b. Casoni skin test positive in 90%, stays positive for years after

E. Treatment
   a. Small calcified cysts/negative serologic tests—no treatment needed
   b. Therapy- removal of cyst contents without gross spillage
   c. Inject hibitane, alcohol, hypertonic saline, then primary closure
   d. Removal of parasite by dissection along plane between germinative layer and adventitia layer
   e. Omentoplasty can manage cavity successful
   f. Resection for multiple or larger cysts.
   g. Marsupialization and partial hepatectomy are alternatives for large or injected cysts
   h. Uncomplicated cases- excellent results with surgery (<5% mortality)
   i. If rupture into peritoneal cavity- laparotomy and thorough cleansing

Nonparasitic Cysts

A. May be single, multiple, diffuse, localized, unilocular, multilocular
B. Include the following lesions:
   1. Blood and degenerative cysts
   2. Dermoid cysts
   3. Lymphatic cysts
   4. Endothelial cysts
   5. Retention cysts
   6. Proliferative cysts (cystadenomas)
C. Autopsy incidence of .15%, CT scans show 1% incidence
D. Polycystic disease
   A. more frequently in women, implicated as rare cause portal HTN, biliary atresia, cholangitis, hemangiomas
   B. 51% associated with polycystic kidneys
   C. Traumatic cysts usually single, filled with bile, no epithelial lining

Cystadenomas

A. grossly smooth, encapsulated, lobular, contain mucoid materialL.
B. Clinical manifestations
   i. Grow slowly, relatively asymptomatic
   ii. Painless RUQ mass
   iii. Sx usually related to compression adjacent structures (early satiety)
   iv. Acute abd pain may accompany complications(torsion, intracystic hemorrhage, intraperitoneal rupture)
   v. LFTs usually wnl, jaundice rare
   vi. CT scan, US, arteriography, scintigraphy may be diagnostic
C. Treatment
   1. Asymptomatic- no treatment
   2. Large, solitary managed electively if uncomplicated- Percutaneous catheter drainage, injection sclerosing agent
   3. Frequent recurrence
   4. Widely unroof cyst (open or lap)
A. Definition
- Any pathophysiologic process that results in interruption or diminution of the normal blood flow out of the liver. However, it commonly implies thrombosis of the hepatic veins and/or the intrahepatic or suprahepatic IVC.

B. Clinical Manifestations
- More common in women, it usually presents in the 3rd to 4th decade of life.
- It may be acute, subacute or chronic.
  1. Acute disease
   - occurs most commonly in women and may be encountered during pregnancy when physiologic changes can unmask an underlying clotting disorder.
   - Patients usually present with severe RUQ pain and hepatomegaly. Ascites is detectable by u/s in more than 90% of patients.
   - Serum aminotransferase levels can range from 100-200 to >600. Alk phos often range from 300-400 and serum bilirubin levels from 3-7.
   - It can present with fulminant hepatic failure.
  2. Subacute disease
   - Having signs and symptoms for less than 6 months without evidence of cirrhosis.
  3. Chronic disease
   - Having signs and symptoms for more than 6 months with evidence of portal hypertension and cirrhosis.
   - For both subacute and chronic, the clinical manifestations and duration of disease prior to presentation depend upon the particular vessels that are occluded, the extent of occlusion and the recruitment of collateral circulation.

C. Major Causes of Budd-Chiari Syndrome
  1. Myeloproliferative Disease, Malignancy (hepatocellular Ca is the most common), Infectious and benign lesions of the liver, OCPs, pregnancy, hypercoagulable states (factor V leiden mutation, prothrombin gene mutation, anti-phospholipid antibody syndrome, anti-thrombin III deficiency, protein C deficiency, protein S deficiency), membranous webs of IVC or hepatic veins, idiopathic.

D. Diagnosis
  1. Doppler Ultrasound
   - most useful non-invasive test
   - non-specific findings include hepatosplenomegaly, ascites, intra–abdominal collateral, caudate lobe hypertrophy (drains separately), atrophy of other hepatic lobes, compression or narrowing of the IVC
   - More specific findings include inability to visualize the junction of hepatic veins with the IVC, thickening, stenosis or dilation of the walls of the hepatic veins, and abnormal flow in the major hepatic veins or IVC.
  2. CT Scan
   - Delayed or absent filling of the three major hepatic veins, rapid clearance of dye from the caudate lobe, narrowing and/or lack of opacification the IVC
  3. Venography
   - The gold standard for diagnosis
   - Performed if non-invasive tests are negative or non-diagnostic but there is a strong clinical suspicion for the disease.

E. Treatment
  1. Medical Therapy
   - includes diuretics and low sodium diet and maximizing nutrition
   - patients may benefit from use of support stocking and large volume paracentesis
   - underlying cause of Budd-Chiari should be investigated and appropriate therapy administered.
   - Thrombolytics, angioplasty and stenting are other options. Most studies have shown these methods to be only beneficial in the short term.
   - TIPS can serve as a temporizing measure in patients with acute fulminant Budd-Chiari syndrome who are in need of transplant.
2. Surgical Treatment
- Most surgical shunts drain the portal or mesenteric system into the IVC or another systemic vein. This allows blood entry into the liver via the hepatic artery to have a low-pressure route by which to drain out of the liver.
- Shunt surgery should be coordinate with the liver transplant team so that shunt placement does not preclude the performance of a later liver transplant.
- Side-to-side portocaval splenorenal and mesocaval shunts are all reasonable if the IVC is patent and without a significant pressure gradient between its infrahepatic and suprahepatic portions.
- Maintenance of shunt patency often requires anticoagulation and doppler u/s to be performed periodically.
- Liver transplant may be the only option for patients with Budd-Chiari syndrome who are not candidates for radiological or surgical decompression.
- Patients who develop Budd-Chiari syndrome as a result of protein S, protein C or anti-thrombin III deficiencies may also be cured of their clotting tendency by liver transplant since the transplanted liver produces normal amount of these enzymes.
HERNIA REPAIR IN A COAGULOPATHIC CIRRHOTIC
Buckminster J. Farrow, MD

Umbilical hernias are present in 17% of all cirrhotics, 7% rupture within 4 yrs with a 11-43% mortality rate, mostly due to infection

Child-Pugh Classification

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>&lt;2</td>
<td>2-3</td>
<td>&gt;3</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt;3.5</td>
<td>2.8-3.5</td>
<td>&lt;2.8</td>
</tr>
<tr>
<td>PT increase in sec</td>
<td>1-3</td>
<td>4-6</td>
<td>&gt;6</td>
</tr>
<tr>
<td>Ascites</td>
<td>none</td>
<td>slight</td>
<td>moderate</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>none</td>
<td>minimal</td>
<td>advanced</td>
</tr>
<tr>
<td>Peri-Operative mortality</td>
<td>10%</td>
<td>30%</td>
<td>80%</td>
</tr>
</tbody>
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Case: 55yo with large abdominal hernia, massive ascites, and PT of 20
Your options are:
1. Fix the hernia right away (please don’t do this, see mortality rate above)
2. Recommend medical management and hope it never ruptures (reasonable)
3. Correct his coagulopathy and improve his ascites, then fix the hernia to prevent spontaneous rupture (probably best and the only choice if the hernia is leaking ascitic fluid). Do a tension free repair! (yes, re-operations are bad)

Management
Control the ascites (cirrhotics have reduced ability to secrete sodium)
Sodium restriction (1g/day) and fluid restriction if Na<130 (1L/day)
Diuresis- spironolactone (inhibits aldosterone) and furosemide (inhibits Na reabsorption in the ascending loop of Henle)
Paracentesis- up to 4-6 L
TIPS- effective to control ascites in 90% of cases
Peritoneovenous shunt- no advantage vs. diuresis+paracentesis many complications including coagulopathy, rapid death
Correct the coagulopathy
Vitamin K up to 5mg IV slowly and/or 10-25mg/day IM or SQ
FFP up to 2U Q2H if needed to normalize PT peri-operatively
Antibiotics if evidence of infection

Surgical repair- mortality is 4X higher in cirrhotic patient for umbilical hernia repair
Make it count, use mesh if you have to, just don’t allow it to recur!!

1Surgery. 122(4):730-5; discussion 735-6, 1997 Oct
also Townsend textbook and Maingot’s Abdominal Operations
SECTION 2

CHAPTER 7

BILIARY
Anatomy of the Extrahepatic Biliary Tree
Robert P. Thomas, MD

I. Extrahepatic biliary tree: (Four features)

- Common hepatic duct (union of R/L hepatic ducts)
- Gallbladder
- Cystic duct
- Common hepatic duct (union of hepatic and cystic duct)

II. Gallbladder

- Average capacity: 30-50 cc
- Four anatomic portions
  - Fundus
  - Body
  - Infundibulum
  - Neck
- Hartman’s pouch (dilation of infundibulum/neck)
- Gallbladder can be entirely within the hepatic parenchyma (intrahepatic gallbladder)
- Inferior surface comes in close contact with colon (fundus) and duodenum (body)

III. Cystic duct

- Length: 2-4 cm
- Usually joins supraduodenal portion of common hepatic duct or may join right hepatic duct or retroduodenal portion of common duct (many variations, must be cautious, See Netter Plate 277)
- Valves of Heister (no valvular function)

IV. Common bile duct

- Length: 8 cm
- Normal diameter: 4-9 mm
- Divided into 1/3’s:
  - Supraduodenal
  - Retroduodenal
  - Intrapancreatic portion
- Anterior to portal vein and to the right of the hepatic artery (upper third), retroduodenal moves lateral to portal vein and anterior to inferior vena cava

V. Hepatocystic Triangle

- Calot triangle: common hepatic duct medially, cystic duct laterally, and cystic artery superiorly
- Hepatocystic triangle: same as Calot, but upper boundary is formed by inferior border of right lobe of liver (aka: hepatobiliary triangle)
- Right replaced hepatic artery (cystic artery arising from SMA) course through medial aspect of triangle, posterior to the cystic duct
GALLSTONE FORMATION
Joseph J. Naoum, MD

Cholesterol solubility depends on the concentration of cholesterol, bile salts, and phospholipids. The formation of micelles (a bile salt-phospholipid-cholesterol complex) and cholesterol-phospholipid vesicles is important to maintain cholesterol in solution. Failure to maintain cholesterol and calcium salts in solution leads to the formation of gallstones. Sludge is a mixture of cholesterol crystals, calcium bilirubinate granules, and a mucin gel matrix. It may serve as a nidus for gallstone formation and growth.

BILE METABOLISM
Hemoglobin is broken down into myoglobin, which is degraded to biliverdin, and then to bilirubin. Over 70% comes as a result of red blood cell breakdown. Less than 30% comes from myoglobin breakdown and liver enzymes.

Direct (conjugated): Bilirubin is conjugated with glucuronide in the liver to form a water soluble complex.

Indirect (unconjugated): Bilirubin forms a complex with albumin that is water insoluble.

ENTEROHEPATIC CIRCULATION
Conjugated bilirubin excreted by the liver drains through the biliary system into the duodenum. Bilirubin is reduced to urobilinogen by small intestinal bacterial flora. Ten to 20% reabsorption occurs in the terminal ileum and is re-excreted by the liver and kidneys.
Biliary Tract Infection----Cholangitis
Katherine M. Trahan, MD

Obstruction of Gallbladder emptying (stone, stricture) + Contamination by Bowel Flora
↓
Pus Under Pressure
↓
Bacterial Spread to Liver (Ascending cholangitis) and to blood stream (bacteremia)

RX: Relieve the Pus…….Antibiotics

I. Most Common Bacteria
   a. Gram Negative-most common
      i. E. Coli
      ii. Klebsiella
   b. Gram Positive-Less frequent
      i. Enterococcus
      ii. Strep Viridans
   c. Anaerobes-found in 10-14% of pts cholecystitis or cholangitis
      i. Bacteroides
      ii. Clostridium
   d. Candida

II. Single vs. Polymicrobial Bacterial Infection
   a. Single most common w/simple choledolithias, acute cholecystitis
   b. Polymicros seen in cholangities (32-37%)
   c. Candida, >2 bacteria associated w/treatment failure

III. Clinical Manifestations:
    Charcots Triad (70%)
    Pain
    Jaundice
    Fever
    Shaking Chill, tachycardia, hypotension

IV. Prophylactic Antibiotics-Recommended for manipulation of biliary tract (ie. Surgery or ERCP)
    Ancef or Unasyn usually sufficient for laproscopic cholecystectomy
    11-30% of people w/gallstone will have bactrobilia

V. Antibiotics for Therapy
   a. Acute cholecystitis/Acute Cholangitis
      i. Unasyn-covers gram neg, positive, some anaerobes and resistance (no pseudomonas coverage), few side effects, cat. B
      ii. 1st or 2nd generation cephalosporin-gram postives, some negative (ecoli and klebsiella), bacteroides for 2nd generation
      iii. aminoglycoside-gram negs, need gram positive and anerobic help (ie. Amp and metronidazole)
      iv. clindamycin-good grm postive, anaerobic, but needs gram neg help
      v. carbapenems-covers pos, negs and anerobes…big gun
      vi. fluoroquinolones + anerobic (Flagyl or clinda)-gram postive, neg, needs anaerobic help
   b. Indwelling Stents/critically ill-often involves pseudomonas
      i. Combo therapy w/ piperacillin + aminoglycoside
Complications of Laproscopic Cholecystectomy

David W. Hart, MD

- Complications of pneumoperitoneum
- Bleeding
- Bowel injury
- Biliary injury
- Leak
- Stricture

Complications of Laparoscopy/Pneumoperitoneum

- Cardiopulmonary alterations
  - ↓ Preload, ↑ Afterload, ↓ CO, ↓ GFR
  - ↓ FRC, Hypercapnea, Acidosis (fetal acidosis)
  - CO₂ embolization
- Elevated ICP
- Needle/Trocar injuries (intestinal, vascular)

Treatment

- Cardiopulmonary embarrassment: Cessation of procedure, release of pneumoperitoneum
- CO₂ embolization: release of pneumoperitoneum, L Lateral Decubitus position
- ICP: no pneumoperitoneum in head injured patients
- Trocar injuries: open technique (?)

Bleeding

- Cystic artery
- Liver bed
- Right hepatic artery

Treatment

- Open procedure with optimal exposure and vision; direct ligation of bleeding vessel

Bowel Injury

- Sharp
- Electrical

Treatment

- Primary closure vs. resection
  - Etiology, extent
  - Time of presentation
  - Location of injury and peritoneal soilage

Biliary Leak

- Cystic stump disruption
- Injury to accessory bile ducts
- Leakage from cystohepatic Ducts of Luschka
- Major CBD disruption/excision

Treatment Strategy

- Establish a controlled fistula
  - Operatively (T-tube, sub-hepatic drain)
  - Percutaneously
  - Endoscopically
- Reduce pressure gradient between biliary system and duodenum
  - Sphincterotomy
  - Transpapillary stent
    - Endoprosthesis
    - Nasobiliary tube
Indications for Surgery
• Complete duct disruption
• Presentation with diffuse bile peritonitis, sepsis, or abscess not amenable to percutaneous drainage
• Failure of percutaneous or endoscopic treatment

Biliary Stricture
• Most present months after biliary injury
  a. Elevated LFT’s
  b. Repeated cholangitis
• Early presentation
  a. Progressive elevation in LFT’s
  b. Increased bile output from drains
  c. Biloma or bile peritonitis

Goals of Management
• Control of sepsis
  a. Antibiotics
  b. Drainage of biliary tree
  c. Drainage of fluid collections
• Define anatomy
• Delay surgical intervention until portal inflammation resolved and patient’s overall condition improved

Immediate Repair of Intraoperative Injury
• Open procedure, cholangiography
• Aberrant ducts <3mm can be ligated
• CHD, CBD injuries of <1cm in length
  a. If opposable without tension, then primary end-to-end anastomosis and placement of T-tube through separate choledochotomy
• Proximal hepatic duct injuries and CHD,CBD injuries >1cm
  a. Roux-en-Y hepaticojejunostomy
• Simple subhepatic drainage (to control biliary fistula) without reconstruction always a good option

Repair of Established Strictures
• Roux-en-Y hepaticojejunostomy
• Bilateral Roux-en-Y hepaticojejunostomy for strictures involving the bifurcation or left or right hepatic ducts
Gallstone Ileus
David B. Loran, MD

I. Demographics
- Usually affects patients >70 years old
- Accounts for <1% of small bowel obstructions
- Occurs in <1% of patients with gallstones
- May account for 25% of SBO in elderly who have not undergone a previous operation and do not have a hernia

II. Symptoms
- Nausea, vomiting
- Abdominal pain – may be episodic as stone temporarily impacts lumen then dislodges
- Obstipation
- Gallbladder related symptoms precede obstruction in 50% of patients

III. Radiology
- Acute Abdominal Series
  - Air-fluid levels and/or small bowel distension
- Pneumobilia
- Misplaced or distant calcified stone

IV. Pathophysiology
- Mechanical obstruction of GI tract
- Stone enters GI tract via biliary-enteric fistula
  - 75% biliary-duodenal fistula
  - other – bilio-gastric, bilio-colonic, choledocho-duodenal
- common sequence:
  - cholecystitis → gangrene → perforation or pressure necrosis from impacted stone → fistula

V. Treatment
- remove the cause of obstruction
- enterotomy and removal of stone
- milk intestine to rule out other stones
Takedown biliary-enteric fistula with cholecystectomy
In septic/unstable patients remove stone then save cholecystectomy for later date
Gall bladder cancer reported at 15% for gallstone ileus patients
CHOLEDCHAL CYSTS
Joseph J. Naoum, MD

DEFINITION
Congenital malformation of the extrahepatic and/or intrahepatic biliary tract.

ETIOLOGY
There is an anomalous pancreaticobiliary junction in over 90% of patients. This anomaly leads to reflux of pancreatic juice into the biliary tree. Other causes include an in-utero accident or an acquired birth defect. Choledochal cysts are most common in women or people of Asian origin.

CLINICAL PRESENTATION
Choledochal cysts occur in 1 in 3000 to 1 in 2 million people. The classic triad of RUQ pain, jaundice, and abdominal mass is present in < 20% of patients. In adults, a palpable mass is uncommon. However, abdominal pain is commonly present in ~80% of patients. A mass can be palpated in 30 to 80% of kids with choledochal cyst, and jaundice is present in approximately 64% of the time. Patients may present with frequent alkaline phosphatase and gamma glutamyl transferase elevation. They may present with a picture of biliary obstruction/ductal dilatation with normal LTF’s (AST and ALT.)

NATURAL HISTORY
They are associated with the development of cholangiocarcinoma and gallbladder cancer in 15% of patients. Having a choledochal cyst carries a twenty-fold increase risk of biliary malignancy. The mechanism for malignancy may be due to the effect of bile stasis, superinfection, or repeated inflammation. Cancers occur at least one decade earlier than commonly found in patients with cholangiocarcinoma.

IMAGING
Ultrasound is quick and easy. Other modalities to establish the diagnosis include CT scan or MRI/MRCP. It is necessary to establish a precise definition of biliary anatomy via PTC, MRCP, or ERCP.

CLASSIFICATION (Todani modification of Alonso-Lej classification) AND TREATMENT
TYPE I: Present 50-60% of the time as a cystic, fusiform saccular extrahepatic biliary dilatation. Treatment consists of cholecystectomy, resection of the extrahepatic biliary tract, and Roux-en-Y hepaticojejunostomy.
TYPE II: present as an extrahepatic biliary diverticulum. It is usually treated by simple cyst excision. The defect in the wall of the CBD must be closed in a transverse fashion to avoid narrowing or stricture.
TYPE III: Present in <10% of cases as a dilatation of the extrahepatic duodenal biliary tree. Treatment consists of lateral duodenostomy in the second portion of the duodenum, followed by identification of bile and pancreatic ducts. The cyst is excised and the CBD and pancreatic duct are re-implanted individually.
TYPE IV: A: Intrahepatic and extrahepatic saccular cystic dilatations (30-40%). B: Multiple extrahepatic cysts (<5%). Extrahepatic biliary resection is recommended.
TYPE V: Caroli’s disease (intrahepatic biliary cysts <10%). If disease is confined to a single lobe, hepatic resection may be indicated. Large cysts confined to one segment can be drained to a Roux-en-Y limb. Liver transplantation may be an alternative.

Internal drainage alone is associated with cholangitis, hepatolithiasis, and the development of cholangiocarcinoma.
SECTION 2

CHAPTER 8

PANCREAS
ANATOMY OF THE PANCREAS
Joseph C. Berardi, MD

Gross Anatomy
- elongated, flattened gland
- 12 to 15 cm long in adults
- head lies within the curvature of the duodenum
- right border is grooved and overlaps the duodenum anteriorly and posteriorly
- neck, body and tail lie obliquely in the posterior abdomen
- tail may extend as far as the hilum of the spleen

Arterial Supply
- supply from the celiac and superior mesenteric arteries
- ant. and post. superior pancreaticoduodenal art./gastroduodenal art./celiac art.
- ant. and post. inferior pancreaticoduodenal art./superior mesenteric art.
- the above vessels lie in groove between head and duodenum and supply both
dorsal pancreatic, pancreatica magna and cauda pancreatic / splenic art.

Venous drainage
- all flow into the portal system
- pancreatic veins drain the tail and body and join splenic vein
- pancreaticoduodenal veins drain into either splenic vein or SMV

Lymphatic drainage
- most drain into the pancreaticosplenic nodes
- some drain into preaortic and pancreaticoduodenal nodes

Innervation
- visceral efferent innervation through vagal and splanchnic nerves from hepatic and celiac plexuses
- bodies of sympathetic efferent nerves from thoracic & lumbar paravertebral ganglia
- autonomic efferent and afferent are found near blood vessels of pancreas

Histology
- compound, nodular, similar to salivary gland but less dense
- surrounded by fine connective tissue, though not a well defined capsule
- lobules evident by gross exam, connected by connective tissue septa
- septa contain vessels, nerves, lymphatic, and ducts
- 80% exocrine, 2% endocrine, 18% connective tissue
- islets of Langerhans (endocrine) round clusters of light staining cell throughout pancreas
- acinar cells (exocrine) form lobules, lead into intralobular ducts, which empty into main pancreatic duct

Embryology
- first appears in the fourth week of gestation
-two outpouchings from the endodermal lining of the duodenum (ventral and dorsal pancreas)
dorsal pancreas grow more quickly, elongates into the dorsal mesentery and continues to grow
ventral pancreas remains small and is carried away from the duodenum by the connection to the common bile duct
two portions are brought together by uneven growth to the duodenum and fuse by 7th week
tail, body and part of head formed from dorsal pancreas
remainder of head and uncinate formed by the ventral pancreas
two portions are still distinguishable in adults
ventral duct (formed from common bile duct) fuses with the dorsal duct (formed from the duodenal wall) at the 7th week forming the main pancreatic duct

**Ductal Anatomy**
-proximal end of the dorsal duct becomes accessory duct, patent in 70% of adults
-common outlet of common bile duct and pancreatic duct arises from the common origin
-pancreatic duct (duct of Wirsung) begins in the tail and joins the common bile duct
-the ampulla terminates in the duodenum
-accessory pancreatic duct (duct of Santorini) may terminate in the main pancreatic duct or separately
-5-10% of main ducts terminate in the accessory duct with no connection to common bile duct
Chronic Pancreatitis
Kenneth J. Woodside, MD

Etiology
- Alcohol (85%)
- Idiopathic (10%)
- Other (5%): Hereditary & juvenile chronic pancreatitis, Hypercalcemia, Cystic fibrosis, Hypertriglyceridemia, Drug reaction, Hypercholesterolemia, Trauma, Hyperparathyroidism, Certain scorpion stings (no, they don’t bite), Congenital abnormalities (e.g. pancreas divisum)

Statistics
- Incidence: 4 new cases per 100,000 individuals per year
- 2:1 Male to Female ratio
- Usually in 4th or 5th decade of life

Diagnosis
- Hx & PE:
  - Abdominal pain (LUQ/midepigastriatic radiating to the back, may be episodic or constant)
  - Weight loss & scaphoid appearance
  - Abdominal masses (pseudocyst/inflammatory mass)
  - Sn & Sx of EtOH, biliary obstruction, malabsorption (exocrine insufficiency)
    - Steatorrhea, et cetera
  - Sn & Sx of endocrine deficiency (less common)
    - Diabetes, polyuria, nocturia, et cetera
- Laboratory tests:
  - Amylase & lipase rarely elevated
  - LFT’s may be helpful, especially if the lower biliary tree is obstructed
  - Fecal fat (72 h stool collection—save for the patients you really like)
    - In a diet with 100 g of fat, > 7 g/day in the stool is diagnostic
  - Pancreatic endocrine function tests
    - Fasting & 2 h postprandial glucose tolerance tests abnormal in 90% of chronic pancreatitis patients with calcifications
  - Pancreas stimulation tests (e.g. secretin-CCK test)
  - CA19-9 is elevated in pancreatic cancer (non-specific)
- Radiology:
  - X-rays may show diffuse calcifications of the pancreas (30-50%)
  - Ultrasound is 60% sensitive for ductal or parenchymal disease
  - CT is 75% sensitive for ductal or parenchymal disease
  - ERCP is the gold standard (85-90%) → Chain of lakes
  - MRCP

Complications
- Common bile duct obstruction & strictures
  - Strictures usually are long and smooth (2-4 cm)
  - Present in 3-30%
  - Must differentiate from pancreatic cancer
- Duodenal obstruction → Occurs with acute flare, chronic fibrotic reactions, pseudocysts, and cancers
- Pancreatic fistulata & pseudocysts
- Splenic vein thrombosis
  - Sn/Sx include hematemesis, melena, anemia, abd pain, splenomegalay
  - Tx Splenectomy has 90% ‘cure’ rate
- Pancreatic carcinoma (2-3 fold increase in risk)
- Narcotic dependence
Treatment
Medical
Malabsorption & steatorrhea
  Oral pancreatic enzyme replacement
Diabetes
  Problem is endocrine insufficiency—not insulin resistance—so use insulin
Analgesia
  Often, substance abuse is a baseline problem--good luck
Alcohol avoidance
Octreotide (?)
  H₂ blocker or PPI reduces gastric acid degradation of native or supplemental pancreatic enzymes

Endoscopic
Sphincterotomy
Ductal stenting

Surgical pancreatic drainage
Denervation procedures
  Option for painful chronic pancreatitis
  Can be done surgically or by interventional radiology
Ductal drainage procedures
  Peustow & Gillesby “Side-to-side longitudinal pancreaticojejunostomy”
    60-90% success for relief of pain
    Decompresses the entire pancreatic duct
    Best if pancreatic duct is dilated to > 1 cm & anastomosis > 6 cm
Drainage procedures
  Left sided
    Distal pancreatectomy
      40-80% pancreatectomy with or without splenectomy
      Extends no further than the neck of the pancreas
      Useful in patients with isolated parenchymal disease
    Subtotal distal pancreatectomy (Child’s procedure)
      95% pancreatectomy
      Universal risk of diabetes
      60-80% pain relief
      Almost never used
  Right sided
    Pylorus sparing (modified Whipple procedure-pancreaticoduodenectomy)
      For parenchymal disease of pancreatic head without ductal dilatation
      75-90% of patients have pain relief
      Operative mortality of < 5%
    Frey’s Procedure
      Local pancreatic head resection with longitudinal pancreaticojejunostomy
    Beger’s Procedure
      Duodenum-preserving pancreatic head resection
Total pancreatectomy
  Usually as a completion pancreatectomy in patients with refractory pain
  Reported 60% pain relief
  Extreme morbidity
    Labile insulin sensitivity
    Steatorrhea & weight loss

References
  Cameron, 6/e, & Townsend, 16/e
Splenic Vein Thrombosis
Peter Chang, DMD, MD

Splenic Vein Thrombosis
-isolated thrombosis of the splenic vein is a rare cause of variceal bleeding
-95% likelihood of splenic vein thrombosis if splenomegaly and esophageal and gastric varices are present in a pt with acute or chronic pancreatitis

Pathophysiology
-splenic venous blood is blocked from its normal route:
  -splenic v. provides the main venous outflow of the spleen
  -splenic v. and superior mesenteric v. join to form portal v.
-flows through the short gastric vessels to the gastric fundus
-then into the left gastric vein
-continues toward the liver
-as the blood goes through the stomach, large gastric varices develop and may rupture or bleed
-esophageal varices are rare

Etiology
-common causes are of pancreatic origin
  -acute/chronic pancreatitis (most common) - 50%
  -pancreatic pseudocyst and carcinoma
  -penetrating gastric ulcer
  -endothelial injury, venous stasis, hematologic disorders

Diagnosis
-highly suspicious when bleeding gastric varices develop in a pt with a h/o chronic pancreatitis
-abdominal CT (spiral) - 80-90% sensitive
-duplex US – 100% specific
-selective splenic arteriography- gold standard

Treatment
-depends on the cause of bleeding varices (must r/o other causes of portal HTN) and patency of the splenic vein
-splenectomy is curative, only recommended for symptomatic bleeding varices
-splenectomy should be included when splenic vein thrombosis is found during surgery
Endocrine Tumors of the Pancreas
David W. Hart, MD

Clinically rare
Prevalence 1/100 person years
— Most found incidentally at autopsy and not related to recognizable clinical syndrome
Originate from neural crest cells

Biologic Behavior
Not predictable by routine histologic examination
Multiple immunofluorescence techniques and stains
Malignancy determined by presence of local invasion, distant spread

Insulinoma
Most common pancreatic endocrine tumor
Whipple triad: A) hypoglycemia during fasting,
       B) blood glucose<50,
       C) relief of hypoglycemic symptoms with exogenous glucose
Neuroglycopenic sx: confusion, seizure, obtundation, personality change, coma
Catecholamine surge: trembling, diaphoresis, tachycardia, palpitations

Diagnosis of Insulinoma
Monitored fast
Insulin: Glucose ratio >0.4
Elevated C peptide and proinsulin
Check for antibodies to exogenous insulin; toxicologic screening for sulfonylureas

Localization of Insulinoma
Spiral CT
Endoscopic USG
Provocative angiography
   Intraarterial (SMA, GDA, Spl) Calcium
   Hepatic venous sampling
Operative palpation and intraoperative USG

Natural History of Insulinoma
Evenly distributed in pancreas
90% benign solitary adenomas; 10% malignant (peripancreatic nodes, liver)
-malignant tumors are indolent
<10% associated with MEN-1 (more likely to be multiple and recurrent)

Surgical Treatment of Insulinoma
± intraoperative ultrasound
Small tumors not close to duct: enucleation
Body and tail tumors, large or close to duct: distal pancreatectomy
Head and uncinate tumors, large or deep: pancreaticoduodenectomy
“Blind” Pancreatectomy usually not indicated

Treatment of Malignant Insulinoma
Resection of primary and debulking of mets lessens hypoglycemic symptoms
Dietary and pharmacologic manipulations
-octreotide
Combination chemotherapy
Gastrinoma
1/1000 patients with 1° duodenal PUD
1/50 patients with recurrent ulcer after ulcer surgery
75% sporadic; 25% associated with MEN-1
Frequently extrapancreatic
Frequently malignant (>50%)
Amplification of Her-2/neu protooncogene
Gastrinoma Triangle – Duodenum & head of pancreas

Symptoms of Gastrinoma
Peptic ulcer diathesis--90%
Diarrhea--50%
Diarrhea alone in 10%
Esophagitis, GERD--50%

Diagnosis of Gastrinoma
Fasting serum gastrin > 200pg/ml
>1000pg/ml is diagnostic
Gastric acid analysis:
   Basal acid output > 15 mEq/h (or >5mEq/h after vagotomy)
Proconvective secretin stimulation test
   Increase in peripheral, fasting serum gastrin >200 pg/ml over basal rate after
   2 U/kg secretin bolus

Treatment of Gastrinoma
PPI
Surgery, after localization and staging

Localization and Staging of Gastrinoma
Spiral CT
Somatostatin receptor scintigraphy
   -Indium 111-octreotide tracer (75-80% sensitivity)
EUS
Proconvective angiography
   -Intraarterial (SMA, GDA, Spl) secretin
   -Hepatic venous sampling

Surgical Exploration for Cure
Exploration of entire gastrinoma triangle
   – Intraoperative ultrasound
   – Intraoperative endoscopy with transillumination of duodenal wall
   – Longitudinal duodenotomy
   – Resection of peripancreatic lymph nodes
Small, well encapsulated pancreatic tumors: enucleation
Tumors deep in pancreatic parenchyma: partial pancreatectomy

Treatment of Malignant Gastrinoma
PPI. No indication for debulking
Rarely perform total gastrectomy for non-compliant patients

Outcome of Gastrinoma
Only 35% of patients explored for cure achieve eugastrinemia
   - 60-70% cure rate with “successful” resection
Combination chemotherapy for metastatic gastrinoma assocaited with <50% response rate
Octreotide may relieve sx, but no clear evidence of reduction of tumor volume
VIPoma (Verner-Morrison Syndrome)
- WDHA syndrome; pancreatic cholera syndrome
- Watery diarrhea (5 L/d), weakness, lethargy
- Hypokalemia, achlorhydria, metabolic acidosis
- Elevated fasting VIP level is diagnostic

Localization of VIPoma
- Spiral CT of abdomen (and chest)
- Other studies rarely necessary

Treatment of VIPoma
- Most tumors are in distal pancreas and amenable to distal pancreatectomy
- High prevalence of metastatic disease to lymph nodes and liver--safe, palliative debulking is indicated
- Octreotide for recurrent or unresectable VIPoma

Glucagonoma
- Symptoms: severe dermatitis, mild diabetes, stomatitis, anemia, weight loss
  - Migratory necrolytic erythema
- Elevated fasting serum glucagon is diagnostic
- Spiral CT is usually successful at localizing tumors
  - most are large and solitary
  - located in body and tail of pancreas

Treatment of Glucagonoma
- TPN to treat malnutrition and relieve dermatitis
- Octreotide to decrease glucagon levels and reverse catabolic state
- Distal pancreatectomy with debulking of metastatic lesions if possible

Somatostatinoma
- Very rare
- Steatorrhea, diabetes, hypochlorhydria, cholelithiasis
  - Elevated fasting somatostatin level is diagnostic
- Spiral CT is usually successful at localizing tumors
  - most are large and solitary
  - located in head of pancreas

Treatment of Somatostatinoma
- Treat hyperglycemia and malnutrition
- Usually metastatic at diagnosis
- Resection of primary tumor, debulking of mets, cholecystectomy are indicated

Non-functional Islet Cell Tumors
- 30-50% of neoplasms of endocrine pancreas
- Elevated Pancreatic Polypeptide (PP)
  - Abdominal pain, weight loss, jaundice, pancreatic mass
  - 50-90% malignant, but indolent
  - Whipple for pancreatic head masses, distal pancreatectomy for body/tail masses
SECTION 3

CHAPTER 9

ENDOCRINE
HYPERKALEMIA
John J. Bawduniak, MD

Effects on electrically excitable tissue (cardiac/skeletal muscle)
Depolarization is more likely with hyperkalemia

**CAUSES**
1. **Exogenous**
   - K+ supplements
   - Diet
   - RBC transfusion
   - K+ penicillin G

2. **Endogenous**
   - Fasting
   - Rhabdomyolysis
   - Limb ischemia
   - Rapid tumor lysis

3. **Impaired removal**
   - Renal failure
   - Hypoaldosteronism
   - Drugs
     - Cyclosporine
     - Tacrolimus
     - Trimethoprim

4. **Intracellular to extracellular exchange**
   - Metabolic acidosis
   - Hyperglycemia
   - Drugs
     - B-Blockers
     - A-blockers
     - Digoxin
     - Succinylcholine

**EFFECTS**
- Muscle weakness
- Paralysis
- Sinus bradycardia
- Sinus arrest
- Slow idioventricular rhythms
- Ventricular tachycardia
- Ventricular fibrillation
- Asystole

**EKG CHANGES** (do not necessarily happen in orderly sequence)
- Peaked T-waves
- Lowering of P-wave amplitude
- Prolonged PR interval
- Second degree AV block
- Loss of P-waves altogether
- Bundle branch block
- Widened QRS combine into “sine waves”
  **EKG is insensitive way to detect hyperkalemia (64% with K+>6 had typical changes)**

**TREATMENT** (treat when >5.9, or clinical judgement calls for treatment)
1. STAT repeat K+ level
2. STAT EKG
3. Calcium Gluconate 1amp SIVP
   - a. antagonizes EKG changes, stabilizes membrane
   - b. if Ca chloride given, give 1/3 as much as Ca gluconate
   - c. duration action 30-60 minutes, can be repeated until hyperkalemia resolves
4. Insulin
   - a. 10U with D50 (to prevent hypoglycemia)
   - b. effects within 10-15 minutes
5. B2-agonists
   - a. promote potassium uptake into cells
   - b. given IV or inhalational (albuterol)
   - c. not always uniformly effective, tachycardia/tremors main side effect
6. bicarbonate no longer recommended due to lack of efficacy
7. Exchange resins
   - a. Kayexelate (polystyrene sulfonate)- po/enema, binds K+ for excretion
   - b. Sorbitol/resin associated with 1.8% risk intestinal necrosis
8. Dialysis
Management of Hypercalcemia
Peter Chang, DMD, MD

Therapy for acute severe hypercalcemia

Vigorous IV hydration with NS followed by IV lasix q4-6h
- NS infusion will increase urinary calcium excretion by inhibiting proximal tubular sodium and calcium reabsorption
- adding lasix will further inhibit calcium and sodium transport downstream from the proximal tubule
- complications of IV hydration includes fluid overload, electrolyte abnormalities

Calcitonin: 4 U/kg q12h
- initial dose given IV, subsequent doses may be given SC
- useful in hypercalcemia associated hyperphosphatemia because it also increases urinary phosphate excretion
- only indicated when IV hydration and lasix have failed

Mithramycin: 25 mcg/kg slow IV infusion (over 6 h)
- most potent of all antihypercalcemic agents
- lowers serum Ca within 12-24 h by inhibiting bone resorption
- only for emergency use
- may cause hepatotoxicity, nephrotoxicity, and thrombocytopenia (usually seen with repeated IV doses)

Biphosphonates: pamidronate (60-90 mg IV infusion over 24 h)
- inhibits bone resorption by osteoclasts and is effective in lowering hypercalcemia in pts with malignant disease
- serum Ca will be lowered to normal within 2-5 days in about 75% of pts

Therapy for chronic hypercalcemia

Identify and treat underlying disease (vit. D intoxication, sarcoidosis, etc.)

Discontinue potential hypercalcemic agents (thiazide diuretics)

Parathyroidectomy is the treatment of choice for hypercalcemia caused by a parathyroid adenoma.

Maintain high daily intake of fluids (3-5 L/d) and of sodium chloride (>400 mEq/dy) to increase renal calcium excretion

Medications
- glucocorticoids: hydrocortisone, 3-5 mg/kg/d IV initially, then
prednisone 30 mg PO bid
- calcium lowering action of corticosteroids occurs via decreased intestinal calcium absorption
- very effective in hypercalcemia due to breast CA, myeloma, sarcoidosis, and vit. D intoxication
- limited use in acute hypercalcemia because it takes 48-72 h before calcium declines

- oral phosphates: 1-3 g/d in divided doses (Neutra-Phos 250-500 mg PO q6h)
  - lowers calcium by decreasing GI calcium absorption and bone resorption
  - not useful in acute cases because their effects take 2-3 days
  - contraindicated in renal insufficiency or in medical conditions with elevated phosphate levels

- indomethacin (prostaglandin synthetase inhibitor) 75-150 mg/d
  - useful in prostaglandin-mediated hypercalcemia
CUSHING’S SYNDROME AND DISEASE
Joseph C. Berardi, MD

Adrenal glands
- retroperitoneal and located at the superiomedial aspect of the kidneys
- pyramid shaped, weigh approx. 4 grams
- bright yellow cortex and red-brown medulla

Blood Supply
- superior adrenal artery from inferior phrenic artery
- middle adrenal artery from aorta
- inferior adrenal artery from renal artery
- primary arterial supply for right adrenal gland is the superior and inferior arteries
- primary arterial supply for the left adrenal gland is the middle and inferior arteries
- venous drainage on left is left renal vein, drainage for the right in the inferior vena cava

Adrenal Cortex
- formed from coelomic mesoderm at the 4th to 6th week of gestation
- differentiates into thin outer definitive cortex and thick inner fetal cortex
- aberrant tissue may be found along the urogenital ridge, its course of migration

Fetal Cortex
- produces fetal steroids during gestation
- does not persist long after birth

Definitive Cortex
- zona glomerulosa develops at birth, makes up 15% of cortex, produces mineralcorticoids (aldosterone)
- zona fasciculata develops at birth, makes up 75% of cortex, produces glucocorticoids (cortisol)
- zona reticularis develops during the 1st year of life, makes up the remainder of cortex, produces adrenal androgens (DHEA)

Cushing’s Syndrome vs. Cushing’s Disease
- syndrome = signs and symptoms of hypercortisolism, regardless of the cause
- disease = syndrome caused by pituitary adenoma

Cushing’s Syndrome
- incidence in 1:100,000
- most common cause is exogenous synthetic corticosteroid, see Townsend table 35-5
- endogenous hypercortisolism causes increased adrenal cortisol production (ACTH dependent or independent)

ACTH Dependent
- 80% of the cases
- ACTH secreting tumor, ectopic ACTH secreting tumor (most commonly bronchial carcinoid or small cell lung cancer
- always associated with bilateral adrenal hyperplasia

Signs and Symptoms
- fairly specific to Cushing’s syndrome include: central obesity, plethora, wide purple striae, and inappropriate osteopenia
- please refer to Townsend table 35-6 for more detail

24 Hour Urine Free Cortisol
- most sensitive and specific
- include concurrent creatinine
- distinguishes syndrome vs. hypercortisolism from obesity and affective psychiatric d/o
-no etoh 1-2 months prior to test

**Overnight Low-Dose Dexamethasone-Suppression Test**
-3-5 ug/100ml in normal patient
-<3ug/100ml in Cushing’s syndrome

**Corticotropin-Releasing Hormone/ Dexamethasone-Suppression Test**
-confirmation test
-useful in patients with borderline screening test
-identify suppressible vs. non-suppressible
-15 minute level of 1.4ug/100ml = Cushing’s syndrome

**Plasma Adrenocorticotropic Hormone Level**
-performed once the Cushing’s syndrome is established
-normal level of ACTH 10-100 pg/1ml
-suppression below 5pg/1ml = adrenocortical neoplasm
-levels 15 – 500pg/1ml = pituitary neoplasm and secondary adrenocortical hyperplasia

**High-Dose Dexamethasone-Suppression Test**
-48 hour test
-the differential diagnosis for patients with non-suppressed or elevated ACTH level includes pituitary or ectopic source of ACTH
-8mg overnight test has similar accuracy
-urine cortisol suppressed by 90% in 60-70% of pituitary adenomas
-failure to suppress suggests ectopic source, adrenal neoplasm or primary bilateral nodular hyperplasia

**Corticotropin-Releasing Hormone Test**
-used to distinguish between ACTH dependent and non-dependent
-dependent have more pronounced peak, >30pg/ml
-independent have blunted peak, <10pg/ml
-used to determine ectopic source vs. Cushing’s disease

**Imaging**
- MRI for pituitary mass
- thin cut MRI or CT for adrenal mass
- suspected ectopic source then image chest

**Treatment**
-removal of source
-resection of mass

**Tumors of Adrenal Cortex**
-with endogenous Cushing’s 80-90% have solitary adrenal adenoma
-adrenal adenomas cured by adrenalectomy, size determines procedure
-adrenal adenomas may secrete aldosterone
-all patients need post-surgical glucocorticoid replacement
-adrenalcortical carcinoma is rare (0.2% of all cancers), aggressive and usually in advanced stages at time of discovery
-cure is infrequent
Adrenal Incidentaloma
Carlos Rosales, MD

1. Diagnosis
   - The discovery of adrenal masses raises two important questions:
     1. Is it malignant?
     2. Is it functional?
   - Mayo clinic evaluated 61,054 abdominal CT scans from 1985 to 1990. Adrenal masses were seen in 3.4% of these CT scans. Of these, half were obvious metastatic lesions. 25% were other known lesions. 7.5% were symptomatic tumors and 16.5% were incidental tumors. So, the overall rate of true incidentaloma was approximately 0.4%.

2. Evaluation for Malignancy
   - Primary adrenal carcinomas are quite rare, but other cancers such as lung CA commonly metastasize to the adrenal glands.
     A. Size
        - Risk of cancer is high if the mass is greater than 6 cm.
        - Of 20 adrenal cancers found in the Mayo study, all were between 4 and 6 cm. As a result, the authors recommend removal of masses greater than 4 cm.
        - In the Mayo clinic series, removal of all tumors greater than 4 cm would have meant removal of 8 benign masses for every 1 malignant mass.
        - Further support for this 4 cm cutoff comes from a retrospective multi-center survey of 1,096 cases. Using this cutoff, there was a 93% sensitivity for distinguishing between benign and malignant tumors.
     B. MRI and CT
        - The typical benign adenoma is smooth, round, homogenous and low intensity on unenhanced CT scans. In contrast, carcinomas are usually heterogenous and may have calcifications.
        - Adenomas are isointense with the liver on T2 MRI whereas carcinomas have a hyperintense signal compared with the liver.
     C. FNA
        - Cytology from FNA CANNOT distinguish a benign adrenal mass from the rare adrenal carcinoma. However, it is able to distinguish between an adrenal tumor vs. a metastatic tumor. Therefore, FNA is helpful when there is a suspicion for cancer outside the adrenal gland and a differentiation between metastatic vs. primary tumor needs to be made.
     D. Adrenal Scintigraphy
        - Done with iodinated cholesterol derivative NP-59.
        - Will usually show uptake of the isotope in functioning adrenal cortical tissue
        - In a study of 229 patients with unilateral adrenal masses found on CT, masses that took up NP-59 were almost certainly benign.

3. Evaluation for Hormonal Function
   - Most incidentalomas are non-functional.
   - In the previously mentioned retrospective, multi-center study, 85% were non-functioning. 9.2% secreted cortisol and caused subclinical Cushing’s syndrome. 4.2% were pheochromocytomas and 1.6% were aldosteronomas.
   - The possibility of functioning mass can be suggested by history (palpitations, sweating, headaches), physical exam (features of cushings, hypertension) and routine labs (hypokalemia).
   - See table for clinical and laboratory evaluation of these masses.

4. Treatment
   - Adrenal masses larger than 4 cm in size should be removed if there is no evidence that the mass is metastatic or if the mass is an isolated metastatic lesion and the primary tumor is amicable to resection. In the latter case, it is reasonable to consider removing both lesions.
   - Patients with non-functional tumors less than 4 cm should be followed with repeat CT scan at 3 months and at 1 year. Most tumors will not change in size in which case then the frequency of scans can be decreased to 2 to 3 years.
Current practice is to remove any tumor that enlarges during the follow-up period. However, in one series of 75 patients followed for an average of 4 years in which the cumulative risk of enlargement was 8% at one year and 18% at 5 years, no patient had a carcinoma.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Suggestive clinical features</th>
<th>Lab screening tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pheocromocytoma</td>
<td>paroxysmal hypertension</td>
<td>spot urine metanephrines</td>
</tr>
<tr>
<td></td>
<td>Sweating, headache, palps</td>
<td>normal: &lt;1ug (5.5 umol)/mg Of creatinine</td>
</tr>
<tr>
<td>Cushing’s syndrome</td>
<td>truncal obesity, thin skin, muscle</td>
<td>24h urine cortisol &gt;3X NL or 8AM serum cortisol after 1 mg of dexamethasone at 11pm</td>
</tr>
<tr>
<td></td>
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<td>nl &lt;5 ug/dl (138nmol/L)</td>
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<tr>
<td>Primary aldosteronism</td>
<td>weakness, hypokalemia</td>
<td>serum potassium</td>
</tr>
<tr>
<td></td>
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<td>Serum aldosterone:plasma renin Activity ratio (nl &lt; 30:1)</td>
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<tr>
<td>Adrenocortical CA</td>
<td>virilization or feminization</td>
<td>serum dehydroepiandrosterone</td>
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<td></td>
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<td>Sulfate (nl = 5.44 – 9.2umol/L) Urine 17-ketosteroid excretion</td>
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<td></td>
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<td>Normal:</td>
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<tr>
<td></td>
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<td>Men: 5-15mg (17-52 umol)/24h</td>
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<td>Women: 10-20mg (34-69 umol) /24h</td>
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Adrenal Medulla/Pheochromocytoma
Chris T. Stephens, MD

Adrenal Medulla

Embryology/Anatomy
- Adrenal medulla and sympathetic nervous system develop together – during fifth gestational week, neural crest cells migrate to the para-aortic and paravertebral regions and along adrenal vein toward medial aspect of the developing adrenal fetal cortex
- Most extra-adrenal chromaffin cells regress, while some remain to form the organ of Zuckerkandl, located generally to left of the aortic bifurcation near the origin of inferior mesenteric artery. It can persist anywhere along path of neural crest cell migration.
- Adrenal medulla is smaller than cortex and contributes to 10% of total gland weight – cells are polyhedral, arranged in cords, and contain catecholamines that precipitate chromium salts (derivation of the term *chromaffin cells*) – core vesicles within the medulla store catecholamines – epinephrine and norepinephrine
- Nerve supply to adrenal medulla is via preganglionic sympathetic nerves

Biochemistry/Physiology
- Chromaffin cells store and secrete active amines including dopamine, norepinephrine, and epinephrine
- Synthesis of catecholamines begins with tyrosine and involves 4 enzymes

\[
\text{Tyrosine} \rightarrow \text{Dopa} \rightarrow \text{Dopamine} \rightarrow \text{Norepi} \rightarrow \text{Epi} \\
\uparrow \quad \uparrow \quad \uparrow \quad \uparrow
\text{Tyrosine} \text{Hydroxylase} \text{Aromatic} \text{L-amino acid} \text{Dopamine-\(\beta\)-hydroxylase} \text{Phenylenethanolamine-} \text{N-methyltransferase}
\]

- Phenylethanolamine-N-methyltransferase is exclusively located in medullary chromaffin cells and organ of Zuckerkandl, therefore, epi-secreting tumors arise only in these anatomical regions
- Excitation of chromaffin granules by sympathetic nerves causes release of catecholamines into the circulation which then travel to adrenergic receptors in various organ systems
- Catecholamine clearance (3 mechanisms) – uptake by sympathetic neurons, uptake/degradation by tissues, clearance via kidneys; norepi and epi metabolized by liver/kidney by monoamine oxidase and catechol-O-methyl transferase into following metabolites – *Methoxyhydroxymetanephrine*, *Vanillylmandelic acid (VMA)*, *Normetanephrine*, *Metanephrine*
- These metabolites can be measured in the urine – VMA routinely used as a screen for catecholamines
**Pheochromocytoma**

**Background**

- Catecholamine-secreting adrenal tumors that arise from chromaffin cells of the adrenal medulla (90% of cases) – extra-adrenal pheochromocytomas (also called functional paragangliomas) may occur in sympathetic ganglia in neck, mediastinum, abdomen, pelvis, and organs of Zuckerkandl
- Rare – occur in 2-8 persons per million; however, found with increased frequency in screened hypertensive populations and in people with MEN II, von Recklinghausen’s neurofibromatosis, and von Hippel-Lindau disease
- Rule of 10’s – 10% bilateral, extra-adrenal, familial, malignant, present in children

**Signs and Symptoms**

- Presentation is that of catecholamine excess – hypertension (sustained 50%), (paroxysmal 33%), (absent 20%)
- Also see palpitations, anxiety, headache, flushing
- MI, stroke, dysrhythmias,
- Orthostatic hypotension, depressed GI motility
- VERY UNCOMMON to be asymptomatic

**Diagnosis/non-surgical management**

- Increased urinary excretion of catecholamines and their metabolites is the gold standard for diagnosis (90% sensitive) – urine tested for catecholamines, metanephrine and VMA
- I-MIBG – accumulates in chromaffin tissues more rapidly in pheochromocytomas and is useful to detect small, functional foci of tumor that is extra-adrenal
- Preoperative management focuses on – control of HTN, alpha adrenergic blockade to prevent intraoperative hypertensive crisis (phenoxybenzamine), fluid resuscitation to prevent circulatory collapse post-op, then beta blockade if needed to lower the HR

**Operative Management**

- Open anterior approach used classically and allows for complete abdominal exploration to eval for extra-adrenal tumor, mets, and multifocal lesions
- Today MRI, CT, and nuclear scans allow for a more precise approach via posterior or laparoscopic approach – allows for decreased handling of tumor
- Post op – fluid resuscitation and close hemodynamic monitoring are crucial!
**Multiple Endocrine Neoplasia Syndromes (MEN-1, MEN-2)**

**Classification & Management**

Nicole L. Nemeth, MD

MEN Syndromes are familial, inherited in an autosomal dominant fashion.

**CLASSIFICATION—**

<table>
<thead>
<tr>
<th>MEN</th>
<th>SYNDROME</th>
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| I   | Parathyroid Hyperplasia  
     | Pituitary Tumors  
     | Pancreatic Islet Cell Tumors |
| IIa | Parathyroid Hyperplasia  
     | Pheochromocytoma  
     | Medullary Thyroid Carcinoma |
| IIb | Medullary Thyroid Carcinoma  
     | Pheochromocytoma  
     | Mucosal Neuromas |

**MANAGEMENT—**

A) **Hyperparathyroidism**

- most common manifestation of MEN-I, usually due to parathyroid hyperplasia
- elevated serum calcium levels with intact parathyroid hormone level (↑↑ serum Ca, w/ manifestations such as kidney stones, bone abnormalities, gastrointestinal and musculoskeletal symptoms)
- surgical exploration, resection and reimplantation (non-dominant forearm) of parathyroid tissue for symptomatic pt.’s (those with renal dysfunction, stones, osteopenia, ↑↑ gastrin levels / ZES)

B) **Pancreatic Islet Cell Tumors**

- second most common manifestation of MEN-I (usually occurs with hyperparathyroidism)
- Increased gastrin levels = gastrinoma (Zollinger-Ellison syndrome); increased basal serum gastrin level and exaggerated response of gastrin to secretin
- Insulinomas → fasting hypoglycemia with inappropriate increase in serum insulin and C-peptide levels
- Glucagonomas (rarely) → hyperglycemia, rash, anorexia, diarrhea, glossitis, depression (1/2 of pt.’s may have ↑↑ glucagon levels)
- Increased VIP → Verner-Morrison (watery diarrhea) – pancreatic cholera
- islet cell tumors are malignant 1/3 of the time and frequently metastasize to the liver: hepatic aa. embolization, chemoRx, (5-FU, streptozocin, doxorubicine) to control sx.’s and ↓↓ tumor mass
- resect insulin, glucagon, VIP and GHRH-or CRH-producing tumors
C) Pituitary Adenomas
- occur in >1/2 MEN-I pt.’s
- Prolactinomas most common (serum prolactin levels > 200µg/L, evidence of mass on MRI, bitemporal hemianopsia on PE)
- ↑↑ GH production → acromegaly
- ↑↑ ACTH production → Cushing’s disease
- treat Prolactinomas with bromocriptine
- surgical resection helpful to relieve mass effects
- radiation treatment therapy for large or recurrent tumors

D) Medullary Thyroid Carcinoma
- most common manifestation of MEN-IIA (bilateral neck mass → horaseness, dysphagia), more aggressive in MEN-IIb
- dx. early in family members by yearly serum calcitonin levels (pentagastrin test) or c-ret protooncogene identification in pt.’s with positive family history
- Total thyroidectomy once identified vs. yearly screening until pentagastrin test is abnormal

E) Pheochromocytoma
- sx.’s include nervousness, palpitations, headaches, sweating
- 10% are bilateral
- treatment includes surgical resection of either 1 or both adrenal glands (>50% of pt.’s with unilateral disease will develop pheochromocytoma contralaterally in 10 yrs.)

<table>
<thead>
<tr>
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<th>MEN-I</th>
<th>MEN-IIa</th>
<th>MEN-IIb</th>
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<tbody>
<tr>
<td>Chromosome</td>
<td>11</td>
<td>10</td>
<td>10</td>
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<tr>
<td>Autosomal Dominant</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Medullary Thyroid Cancer</td>
<td>No</td>
<td>Bilateral</td>
<td>Bilateral</td>
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<tr>
<td>MTC Course</td>
<td>None</td>
<td>Indolent</td>
<td>Aggressive</td>
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<tr>
<td>Parathyroid Disease</td>
<td>Hyperplasia (95%)</td>
<td>Hyperplasia (50%)</td>
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<tr>
<td>Pheochromocytoma</td>
<td>No</td>
<td>Bilateral (50%)</td>
<td>Bilateral</td>
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<td>Pancreatic Tumors</td>
<td>Islet Cell</td>
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<td>No</td>
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<td>Phenotype</td>
<td>No</td>
<td>No</td>
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<td>Duodenal Tumors</td>
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<td>Common Presentation</td>
<td>Hyperparathyroid</td>
<td>Hyperthyroid</td>
<td>Hyperthyroid</td>
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<tr>
<td>Other</td>
<td>Pituitary tumors</td>
<td>Multiple mucosal neuromas</td>
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SECTION 3

CHAPTER 10

THYROID & PARATHYROID
Thyroid and Parathyroid Anatomy
David W. Hart, MD

**Thyroid**

1. Originates from alimentary tract as midline diverticulum from floor of pharynx (foramen cecum)
2. Descends caudally into neck from thyroglossal duct (frequently through center of hyoid bone)
3. Ultimobrachial 4th pharyngeal pouches give rise to calcitonin-producing C cells in upper, posterior, middle portions of gland
4. Ectopic thyroid tissue may be found within central portion of neck or anterior mediastinum
   a. LATERAL aberrant thyroid is misnomer for welldifferentiated thyroid carcinoma
5. Invested by pretracheal fascia
   a. Anterior suspensory ligament above isthmus
   b. **Ligament of Berry:** Posteromedial suspensory ligament is condensed and firmly attaches to upper two or three tracheal rings and cricoid cartilage—RLN usually just lateral to ligament, but in 25% nerve is surrounded by ligament before entrance into larynx
6. Arterial supply—2 superior arteries, 2 inferior arteries
   a. Superior thyroid artery from 1st anterior branch of external carotid artery
      i. Close to external branch of superior laryngeal nerve
   b. Inferior thyroid artery from thyrocervical trunk
      i. Principle blood supply of both superior and inferior parathyroid glands
      ii. Enters gland at middle portion
      iii. Intimately involved with RLN
7. Venous drainage—superior, middle, inferior paired veins
8. Lymphatic drainage
   i. Intraglandular—through isthmus to opposite lobe
   ii. Regional nodes: paraglandular, pretracheal superior to isthmus, paratracheal, anterior mediastinal, jugular, retropharyngeal, lateral; RARELY submandibular
9. Relation to nerves
   a. Right RLN—arises from vagus at crossing with subclavian vein; usually ascends 1-2 cm lateral to tracheoesophageal groove
      i. Junction of right RLN with inferior thyroid A—nerve may be anterior, posterior, or interdigitated with arterial branches
      ii. Directly posterior to tubercle of Zuckerkandl
      iii. Traverses ligament of Berry 25% of time
      iv. Non-recurrent 1%
      v. Recurrent AND non-recurrent 0.2%
   b. Left RLN—arises from vagus passing behind aortic arch; typically arises in tracheoesophageal groove
      i. Occassionally, left RLN very medial—on trachea
      ii. Non-recurrent extremely rare (only with situs inversus)
   c. Superior laryngeal nerve—arises from vagus, descends along internal carotid A.
      i. Internal branch is sensory and enters larynx via thyrohyoid membrane
      ii. External branch descends just medial to the superior thyroid artery and enters cricothyroid muscle

**Parathyroid**

1. 2 superior, 2 inferior glands
2. Flat, ovoid, red-brown to yellow
3. Typically weigh 30-50 mg.
4. Superior glands are most often embedded in the fat on the posterior surface of the upper thyroid lobe near site where RLN enters larynx.
5. Inferior glands usually more ventral—close to or within thymus
6. Anatomic variations common, caused by differences in embryogenesis
   a. Superior gland arises from 4th pharyngeal pouch (with lateral thyroid)
   b. Inferior gland arises from 3rd pouch (with thymus)
   c. Migration of inferior gland more variable— anywhere from pharynx to mediastinum, usually adherent to thymus or within thyrothymic ligament
   d. Supranumary glands in 15% patients
7. Vascular supply of superior and inferior glands usually from inferior thyroid artery; usually end-arterial supply
Treatment of Hyperthyroidism
Katherine M. Trahan, MD

Hyperthyroidism is a disease process associated with increased thyroid secretion resulting in a hypermetabolic state. Can be caused by increased secretion w/primary alterations of the gland (Grave’s disease, toxic nodular goiter, toxic thyroid adenoma), central nervous system disorders with increased TSH, exogenous thyroid ingestion, or thyroid malignancy with overproduction. Treatment is aimed at limiting quantity of thyroid hormone release (ie. blocking synthesis) or ablation of tissue (surgery, radioactive iodine, xrt).

I. Drugs: often 1st choice in treatment especially in children or adolescence.

A. Prophylthiouracil (PTU)/methimazole (Tapazole)-thioamide class
   a. Mechanism: inhibits organification and oxidation of inorganic iodine. Also inhibits linking of iodothyronine molecules to MIT and DIT.
   b. Benefits: PTU-rapid control of hyperthyroid; does not cross placenta
                  Methimazole-single daily dose
   c. Risks: agranulocytosis in <1%
                  Rash, neuritis, liver dysfunction, fever
   d. Dosage: PTU-100-150 mg q6-8hr for 12-24 months
                  *may benefit from addition of adrenergic antagonist

B. Iodine-best used for impending/actual thyrotoxic crisis or severe cardiac disease
   a. Mechanism: large dose can inhibit thyroid hormone release by altering binding process
   b. Benefits: Very rapid action
      Rx for hyperactivity preop/prevention of thyrotoxicosis after I131
   c. Risks: transient effect/allergy
                  PTU/Methimazole should be given 1st-iodine may prolong latency response to antithyroid drug

C. Steroids
      Inhibit peripheral conversion of T4-T3
   b. Benefits: rapidly lowers T3 levels
                  Lowers TSH-good for severe, resistant hyperthyroidism
   c. Risks:cushingoid features, osteoporosis, poor wound healing
   d. Dosage: Dexamethasone 2 mg q6h
                  Sodium iodate 1 gm qd with antithyroid drug

D. Beta Blockers-good for thyrotoxicosis (increased sensitivity to catecholamines)
   a. Mechanism: adrenergic antagonist that blocks peripheral effects of catecolamines
   b. Benefits: reduces heart rate, tremor, anxiety
   c. Risks: bradycardia, hypermetabolic state remains.

II. Methods of Ablation

A. Radionuclide Therapy-most common therapy for Grave’s disease in US. Most commonly used radionuclide is I-131.
   Pretreatment to achieve euthyroid state 3-4 weeks prior to treatment is indicated and then drugs should be stopped to allow proper uptake of nuclide. Best used for patients with small to moderate enlargement of gland w/poor medical results. Also indicated for those unable to undergo surgery.
   a. Mechanism: Cell death & apoptosis
   b. Benefits: Cure rate of 90%
                  Avoids risk of surgery
   c. Risks: 10-15% incidence of hypothyroidism within 12 months and w/ increased risk of 3% per year (40-70% of pt hypothyroid after 10 years)
                  Exacerbation of cardiac arrhythmias, fetal damage, worsening ophthalmic problems
                  Need close followup of TSH and Thyroid level
                  Contraindicated in children, pregnancy
                  Radiation thyroiditis-usually 7-10 days after rx in elderly w/other disease
   d. Dosage: precalculated per patient but usually 8-12 mCi

B. Thyroid Resection-indications include obvious medical failure, younger patients, pregnancy, associated suspicious mass, cosmetic defects, tracheal compression. Attempts should be made to render pt euthyroid before surgery and beta blocked. Lugol’s solution (5 drops) for 7 days preop may decrease vascularity of thyroid tissue.
   a. Methods: Complete ablation requires total thyroidectomy
   b. Benefits: rapid, without side effects of medication
                  lowest rate of relapse
   c. Risks: hypoparathyroidism, hemorrhage, hypothyroidism, infection
                  recurrent laryngeal nerve damage
                  recurrence if tissue left
                  thyroid storm-severe tachycardia, fever, confusion, vomiting 2nd to adrenergic overstimulation after thyroid resection in untreated patients (best to prevent with preop)
                  RX: rapid fluid replacement, antithyroid drugs, beta blockers before alpha blockers,
                  iodine, steroids..HD to remove T4 and T3
Work-up of a Thyroid Nodule
David B. Loran, MD

Differential diagnosis:
- Benign – colloid nodule, benign cyst, adenoma, goiter
- Malignant – carcinoma, lymphoma, squamous cell, metastatic disease

Important history & physical exam questions:
- Is the nodule firm? rapidly growing? unilateral? tender? multinodular?
- Is the pt male? greater than 50? had radiation exposure? lost weight? complained of hoarseness?
- Is there a family history of polyposis? thyroid cancer?
- Are there signs of hyper-/hypo-thyroidism? cervical adenopathy?

Laboratory work-up:
- for screening, only a thyroid panel is needed… TSH, T3/T4, calcitonin (if medullary ca suspected)

Radiological work-up:
- Ultrasound – can help determine whether a mass is solid/cystic, multifocal
  o Can also help with accurate measurements when following a nodule
  o 25% of well-differentiated cancers have cystic component
- Nuclear medicine scans – not necessary to determine cancer
  o 16% cold and 4% hot nodules turn out to be cancer
  o can be used to determine if solitary nodule is functional in setting of hyperthyroid patient

Fine-needle aspiration:
- 86 – 90% sensitive
- 91 – 93% specific for diagnosing thyroid cancer, esp papillary
- “follicular cells” by FNA – 6 – 20% incidence of cancer
- “colloid” by FNA – this is a benign dx but 1-6% false negative rate
- “indeterminent” by FNA – repeat id suspicion is high vs. close f/u
- “suspicious” by FNA – up to 50% can have cancers, usually require lobectomy or repeat FNA

Summary:
- once a thyroid nodule is found……FNA
Complications of Thyroidectomy
Juan C. Escalon, MD

Complications of a thyroidectomy are best understood in terms of the operative procedure.

I. Definitions
   A. Total Thyroidectomy – division of all thyroid tissue between the entrance of the recurrent laryngeal nerves bilaterally by the ligament of Berry, resulting in complete removal of all visible thyroid tissue bilaterally.
   B. Near-Total Thyroidectomy – complete dissection on one side while leaving a remnant of thyroid tissue laterally on the contralateral side.
   C. Subtotal Thyroidectomy – leaves a rim of thyroid tissue bilaterally to ensure parathyroid viability and avoiding the recurrent laryngeal nerves.

II. Operative procedure
   A. Transverse incision along normal skin lines and development of subplatysmal flaps superior and inferior. Midline dissection through a bloodless plane of the sternohyoid/ sternothyroid muscles and ligation of any jugular vein branches running along the midline. Also identification of the middle thyroid vein and ligation. (Townsend, Fig 32-17)
   B. Placement of Babcock clamp for downward traction to expose the superior pole. Identification of the superior artery, vein, and superficial laryngeal nerve. The artery and veins branches should be ligated as close to the gland as possible in order to reduce the risk of superficial laryngeal nerve injury. The superficial laryngeal nerve controls tension of the vocal cords and usually is separate (75-80%) from the superior vessels, running on the cricothyroid muscle. (Fig 32-19)
   C. The thyroid in retracted anterior and medially. The inferior thyroid artery, vein, parathyroids, and recurrent laryngeal nerve are identified. (Fig 32-20)
   D. The recurrent laryngeal nerve is at risk for injury during ligation of the inferior thyroid artery and division of the ligament of Berry. Only after the nerve is directly visualized and its cephalad course into the trachea is identified should ligation of the inferior vessels and division of the ligament of Berry be done. (Fig 32-21, 32-26)
   E. If nerve is injured during procedure, attempts should be made to perform a microvascular repair using 8-0 or 9-0 monofilament suture.
   F. The parathyroid glands should also be isolated at this time and mobilized with their vascular supply to preserve their function. Risk for hypocalcemia if not done.
   G. For lobectomy, the dissection may be extended past the isthmus by cauterizing the loose connective tissue separating the lobe and isthmus from the trachea. (Fig 32-22)
   H. Clamps are then place along the line of resection and the tissue suture-ligated after being resected. (Fig 32-25)
I. For subtotal thyroidectomy the inferior vessels, parathyroids, and recurrent laryngeal nerve are identified and transection of the thyroid is done to preserve these structures. (Fig 32-23)

III. Hypocalcemia
A. Reported incidence of permanent hypocalcemia in children with thyroid cancer by Newman et al
   1. after lobectomy 4%
   2. after total thyroidectomy 17%

B. Reported incidence of temporary hypocalcemia in series stated above
   1. after total thyroidectomy 46%
PAPILLARY THYROID CARCINOMA (PTC)
Joseph J. Naoum, MD

PTC is the most common thyroid neoplasm comprising 70-80% of cases. Good prognosis is associated with women younger than 40 years of age. External beam radiation and nuclear fallout contamination have been associated with an increased incidence of PTC.

Pathologic Classification
Histologic evaluation shows intranuclear inclusion bodies and cellular “grooving”. Calcified clumps of cells called psammoma bodies are diagnostic of PTC. The neoplasm may form well-differentiated follicles with only minimal papillary architecture which is classified as the follicular variant of papillary carcinoma. Insular, columnar, and tall cell carcinomas are aggressive, tend to occur in older patients, and represent less than 1% of PTC.

Clinical Presentation
Diagnosis of a palpable thyroid mass may be initiated by ultrasound followed by FNA of a solid lesion. Multicentricity can be expected in 70% of patients. Younger patients have been shown to have a higher rate of lymph node metastasis. 95% ten-year survival has been reported. Age at diagnosis (<40), size less than 4 cm without extension through the capsule, and absence of distant metastasis are important prognostic factors for long term survival.

Treatment
Less than 1 cm lesions are treated with lobectomy and isthmectomy. Treatment for 1-2 cm lesions is controversial but may involve total thyroidectomy vs lobectomy with isthmectomy. Greater than 2 cm lesions are treated with total or near total thyroidectomy. Palpable adenopathy requires a modified radical neck dissection and total thyroidectomy. Recurrence in local or regional lymph nodes should be treated with completion thyroidectomy plus regional lymph node dissection. Radioiodine therapy should be used as adjunctive therapy. In patients with total thyroidectomy, postoperative thyroglobulin levels may be followed to monitor recurrence.
I. Embryology of parathyroid glands
   A. Superior parathyroids arise from the 4th pharyngeal pouch.
   B. Inferior parathyroids arise from the 3rd pharyngeal pouch.
   C. Inferior glands migrate caudad and are more variable in location.

II. Primary Hyperparathyroidism
   A. Etiology is unclear.
   B. Increased production of PTH due to disrupted feedback loop of calcium on the production of PTH.
   C. 85% of cases are caused by single gland adenoma.
   D. Multi-gland enlargement can occur sporadically, but is also seen with MEN I and IIA.
   E. Presentation is usually asymptomatic hypercalcemia detected by routine laboratory studies.
   F. Chronic symptoms are due to secondary changes in the genitourinary system and skeleton.
      i. Weakness, myalgia, arthralgia, nephrolitiasis, constipation.
      ii. Renal complications
         1. frequency, nocturia, and polydipsia.
         2. nephrolithiasis- 25-30% of cases.
         3. nephrocalcinosis- calcification within the kidney parenchyma, 5-10% of cases.
         4. hypertension.
      iii. Skeleton
         1. Osteitis fibrosa cystica- diffuse demineralization of bone.
         2. Subperiosteal resorption is pathognomonic.
         3. Radial aspect of middle phalanx of 2nd or 3rd fingers is most commonly involved; skull is second.
         4. Osteoclastomas (brown tumors) present in advanced disease.
         5. Chondrocalcinosis and pseudogout in 3-7%.
      iv. Gastrointestinal
         1. Increased incidence of peptic ulcer disease- increased Ca causes increased gastric acid secretion.
         2. Pancreatitis.
         3. Cholelithiasis.
   G. Laboratory data
      i. Increased serum Ca.
      ii. Simultaneous increased serum PTH.
      iii. Increased urinary Ca.
      iv. Hyperchloremic metabolic acidosis.
III. Secondary hyperparathyroidism
   A. Occurs as the result of metabolic alterations of chronic renal failure.
   B. Increased phosphorus and decreased production of 1,25-D3 by the kidney causes hypocalcemia.
   C. The resulting hypocalcemia causes elevated PTH levels.
   D. Tertiary hyperparathyroidism results from chronically stimulated parathyroid glands in renal failure and the patient develops autonomous function of the parathyroids after renal transplantation.

IV. Indications for operation in primary hyperparathyroidism
   A. On initial evaluation
      i. Markedly elevated serum calcium
      ii. History of an episode of life-threatening hypercalcemia.
      iii. Reduced creatinine clearance.
      v. Decreased bone mass evidenced by direct measurement.
   B. During monitoring of asymptomatic patient one of these develops
      i. Skeletal, renal, or GI symptoms as above.
      ii. Sustained serum Ca >1-1.6 mg/100ml above normal.
      iii. Decreased creatinine clearance by >30%.
      iv. Nephrolithiasis or worsening calciuria.
      v. Decrease in bone mass.
      vi. Neuromuscular or psychologic symptoms.
      vii. Patient desires surgical therapy.

V. Indications for operation in secondary hyperparathyroidism
   A. Persistent and symptomatic hypercalcemia in prospective renal transplant patients.
   B. Bone pain or pathologic fractures.
   C. Ectopic calcification.
   D. Intractable itching.

VI. Treatment
   A. Surgical removal is only treatment and is highly successful.
   B. Localization techniques- should always be done when treating recurrent or persistent disease.
      i. Standard exploration- bilateral cervical exploration.
      ii. Sestamibi scan for pre-op localization.
      iii. Intra-op PTH measurement.
      iv. Videoscopic neck exploration and parathyroidectomy.
   C. Single gland enlargement is treated by removal of only the enlarged gland.
   D. If 2 or 3 glands are enlarged resect them and leave the normal appearing glands.
   E. Generalized hyperplasia is treated with radical subtotal (3.5 gland) parathyroidectomy or total parathyroidectomy with heterotopic autotransplantation.
SECTION 3

CHAPTER 11

HEAD & NECK
Work-up for enlarged neck node
Tammy Lee, MD

Frequency of Disease
• Pediatric and Young Adults: Inflammatory > congenital > neoplastic
• Older Adults: Neoplasia > inflammatory > congenital

LOCATION
• Congenital, developmental, and traumatic masses are quite consistent in their locations.
• In neoplastic masses, their locations are both diagnostically and prognostically significant

Diagnostic Steps
• Most important diagnostic tool: History and Physical Exam
  1) Thorough review of the developmental time course of the mass
  2) Associated symptoms
  3) Personal habits (smoking, drinking)
  4) Prior trauma, irradiation, or surgery
• Complete exam of Head and Neck
  1) View all mucosal surfaces of the various oral and pharyngeal regions by direct examination or by indirect mirror or fiberoptic visualization
  2) Touch all oral and pharyngeal regions as well as the neck structures and masses in question
  3) Listen for bruits

Clinical Antibiotic Trial
• When inflammatory adenopathy is suspected and the examination is otherwise negative
• A clinical test in the form of a trial of antibiotics and observation not to exceed 2 weeks
• If the mass persists or increases in size, additional investigation is necessary

Diagnostic Steps
• Prime diagnostic tool: Fine-Needle Aspiration - Single most helpful test
• Computed tomography (CT)
• Ultrasonography - solid vs cystic masses
• X-rays – Rarely helpful
  • MRI provides much of the same information as CT- both delineate cysts from solid tumors, establishes location within a nodal group or gland, and with infusion delineates vascularity
  • Currently, MRI is better for upper neck and skull base masses while CT is better for lower midneck masses b/c of motion artifact caused by breathing, swallowing, and vascular pulsations.

Limitations of FNA
• In a chronic user of tobacco, alcohol, or both with no obvious primary head and neck mucosal tumor, results of the FNA may be equivocal or negative
• In this situation, the patient requires endoscopy and possible subsequent open biopsy because of the high index of suspicion.
• Neck mass positive for cancer on FNA but primary source unknown, then examine aerodigestive tract panendoscopically, paying special attention to area drained by lymphatics leading to the mass.
• Biopsies should be performed on any obvious lesions
• If no lesion seen or palpated on endoscopy, perform guided biopsies in the most logical areas of primary tumor origin.
• If none of the previous measures of office examination, fine-needle aspiration, endoscopy, or guided biopsy delineates the origin of the neck mass, open excisional biopsy is the next step
• Open biopsy for diagnosis is needed in fewer than 5% of cancer patients whose problem starts out as a neck mass.
Otalgia
Peter Chang, DMD, MD

Ear Pain- Otalgia
-a symptom that does not always signify primary ear disease
-may represent referred pain from a regional or distant abnormality
-50% of adults and 80% of children c/o ear pain suffer from local disease
-may be referred from head and neck cancers, especially in males if alcohol and tobacco are risk factors

Work-Up
Detailed H & P
-history should include characteristics of the pain, associated medical conditions such as hoarseness, hearing loss, TMJ pain, dental disease, weight loss, GI disease.
-physical exam should include careful evaluation of the oral cavity, oropharynx, nasopharynx, larynx, or any specific area in the head and neck, or thorax for lesions or masses
-studies may include laryngoscopy, endoscopy, otoscopy, CT/MRI, plain films

Differential Diagnosis:
Local Causes of Otalgia
Auricle
- Trauma- sunburn, lacerations, subperichondrial hematoma
- Perichondritis/Abscess of the auricle - infection or inflammation
- Radiation-induced chondritis
- Malignant or benign growth- skin cancers
External Auditory Canal
- Otitis externa- Pseudomonas aeruginosa
- Foreign body
- Impacted cerumen
- Herpes zoster oticus (Ramsay Hunt Syndrome)
- Trauma- cotton-tipped applicators
- Malignant or benign growth
Tympanic Membrane or Middle Ear
- Acute otitis media
- Acute mastoiditis
- Acute eustachian tube obstruction
- Trauma- barotrauma from diving or flying
- Malignant or benign growth

Regional Causes of Otalgia
- Dental Neuralgias- bad teeth, impacted molars, malocclusion
- Bruxism
- Temporomandibular joint disease
- Myofacial pain dysfunction syndrome
Malignant or benign growths of the maxilla or mandible

Distant Causes of Otalgia
Nasal Cavity and Nasopharynx
- sinusitis
- malignant or benign growth
Oral cavity and Pharyngeal lesions
- Acute glossitis or stomatitis
- pharyngitis, tonsillitis
- peritonsillar abscess
- ulceration
- post adenoidectomy or tonsillectomy
- malignant or benign growth (floor of mouth, base of tongue)
Larynx
- ulceration
- perichondritis and chondritis
- arthritis of cricoarytenoid joint
- malignant or benign growth
Esophagus
- foreign body
- hiatal hernia
- GERD
- malignant or benign growth
Lung and Bronchus
- inflammation or infection
- malignant or benign growth
Cardiovascular System
- angina pectoris
- thoracic or innominate artery aneurysm
Cervical Spine
- osteoarthritis
- whiplash injury
- subluxation of the atlantoaxial joint
- malignant or benign growth
Idiopathic- ticlike pain confined to the ear
I. Clinical Presentation
   a. Account for < 4% of head and neck tumors
   b. 20% of parotid tumors = malignant (1-2/100,000)
   c. Risk factors - radiation, unknown
   d. Any age/no gender

II. Patient Evaluation
   a. Presentation
      i. Usually asymptomatic lump present for years - painless near ear
   b. Studies
      i. FNA (esp. if large or close to facial nerve)
      ii. CT/MRI - only nec. for malignant tumors

III. Classification and Stage - very difficult (>20 types of tumors)
   a. Benign (most to least common) (65-70%) - usually in tail of gland, 15% recurrence at 20 years (recurrence highest w/enucleation, lower w/superficial parotidectomy and or radiation)
      i. Pleomorphic adenoma (90% superficial to facial nerve) - most common
      ii. Warthin’s tumor - male, assoc. w/tobacco, 10% bilateral
      iii. Benign cyst
      iv. Lymphoepithelial lesion
      v. Oncocytoma
      vi. Monomorphic adenoma - painless superficial mass
   b. Malignant 30% - stage is more important than histologic subtype, occur in 5-6th decade of life, pain or involvement of facial nerve = more advanced.
      High grade recurrence rate 50-60% w/surgery alone
      i. Mucoepidermoid carcinoma - most common
      ii. Adenoid cystic carcinoma - can travel along nerves
      iii. Adenocarcinoma
      iv. Malignant mixed tumor
      v. Acinic Cell carcinoma
      vi. Epidermoid carcinoma
      vii. Anaplastic and others
   c. Stage
      i. Low - tumors up to 6 cm w/ no extension to adjacent structure or 4 cm or less w/ extension
      ii. High - 4-6 cm w/ extension, > 6 cm, any size w/nodal mets

IV. Treatment
   a. Surgical Resection - resect facial nerve if involved. Benign usually can be enucleated or undergo superficial parotidectomy. Malignant tumor especially from deep lobe require total parotidectomy
   b. Adjuvant Therapy - Radiation for high grade neoplasms or low grade recurrent neoplasm or positive margins. Radiation is treatment of choice for inoperable lesions. Chemotherapy generally by clinical trial only.

V. Complications
   a. Frey Syndrome - gustatory sweating secondary to parasympathetic damage to auriculotemporal nerve
   b. Recurrence
   c. Salivary Fistula
SECTION 3

CHAPTER 12

GENITOURINARY, UROLOGY, & GYNECOLOGY
VARICOCELE
John J. Bawduniak, MD

I. Anatomy
A. Normal venous anatomy
   1. Pampiniform plexus encircles the arteries and drains testis
   2. plexus is countercurrent heat exchanger- cool blood into the scrotum
   3. Varicosities impede this countercurrent exchange

II. Varicocele
A. Abnormal dilated veins of spermatic cord (peritesticular pampiniform plexus)
   1. Obstruction to blood return from testis or abnormal valves
   2. Incompetence of valve between internal spermatic vein and renal vein
C. Incidence- 10-15% general population, 20-40% infertile men
D. 90% idiopathic varicoceles arise on the left
   1. R spermatic vein/IVC forms acute angle- acts as valve
   2. L spermatic vein/renal vein- more obtuse angle, more retrograde pressure
   3. Left renal vein may also be compressed between SMA and aorta
E. Varicoceles that are: bilateral, unilateral right, sudden onset, does not reduce in size in supine position…. should prompt search for cause
   1. IVC occlusion, tumor, thrombosis, situs inversus
F. Varicoceles associated with smaller ipsilateral testis (atrophy)
H. Most common treatable cause of male infertility (1/3 infertile men)
   1. Most men with varicoceles are fertile
   2. Mechanism of infertility unknown (90% have decreased sperm motility)
      a. Increased temperature
      b. Reflux renal/adrenal metabolites from renal vein
      c. Decreased blood flow/Hypoxia

III. Differential Diagnosis
Tumor Spermatocele
Epididymitis/epididymo-orchitis, acute and Varicocele
   chronic Cord lipoma
   Communicating Dermatologic lesions
   Hydrocele Inflammatory vasculitis (Honoch-Schonlein purpura)
   Communicating Hydrocele of the cord Scrotal wall swelling
   Torsion Urinary extravasation
   Testis Trauma/insect bite
   Appendix testis Edema from cardiac, hepatic, or renal failure
   Spermatic cord Fungal infection
Inguinal hernia

Diagnosis
A. Physical exam- presents as painless, compressible mass above, sometimes surrounding, testis
   a. classically “bag of worms” that decompresses in supine position
   b. valsalva/upright position increases varicocele in size
   C. transfusion- solid(tumor) vs cystic(hydrocele, spermatocele)
B. Diagnosis made when 2-3 veins of >3mm size, enlarge on standing, reflux supine
C. Graded:
   III- large, visible through scrotal skin
   II- moderate sized, easily palpable without valsalva
   I- small, palpable only with valsalva
D. Rarely present with pain (inguinal/scrotal ache relieved by supine position)
E. Semen analysis- usually nonspecific, decreased sperm density with medium/large varicoceles
F. Transscrotal ultrasound with doppler
**Treatment**

A. Surgical repair- Ligation/occlusion dilated testicular veins, preservation artery/lymphatics
   1. Ipsilateral testis volume loss >2ml reasonable indication for adolescent varicocele ablation
   2. Different surgical approaches
      a. Retroperitoneal approach
      b. Inguinal approach- ligate cord veins, except those associated with vas
      c. Subinguinal approach- incision below inguinal ring at level of pub tub
      d. Microsurgical- allows visualization lymphatics/artery, less damage
      e. Laparoscopic
   6. Improvement in seminal parameters in 70%
   7. Complications-
      a. Hydrocele- most common (3-33%)
         1) Due to lymphatic obstruction
         2) 50% warrant later surgical correction
         3) risk eliminated/decreased with coil embolization/microsurgical
      b. Testicular artery injury
         1) 14% testicular atrophy with intentional ligation (infarction)
         2) risk eliminated by coil embolization, decreased with microsurg
      c. Recurrence (.6-45%)
         1) Periarterial/parallel inguinal/midretroperitoneal collaterals
         2) Nonmagnified operations have higher incidence
            a. Microsurgical- 1-2% incidence
            b. Nonmicrosurgical- 9-16% incidence

B. Percutaneous transcatheter placement of coils in spermatic vein (via left renal vein)
   2. 4-11% recurrence
   3. successful in 75-90% attempts (many will still require surgery)
   4. takes 1-3 hours (surgery 25-45min)
   5. rare- coil migrates to renal vein-lose kidney or pulm embolism, fem vein perf
Testicular Emergencies
John W. Antonetti, MD

Male patient presents with acute onset of swollen tender scrotum.

Differential Diagnosis: Incarcerated hernia, tense hydrocele, acute epidymo-orchitis, testicular torsion, or torsion of testicular appendage.

1. Testicular Torsion: Twisting of the testicular pedicle results in acute ischemia to the testis with permanent damage as soon as four hours after onset of symptoms

   Extravaginal- Type seen in neonates, the entire testis and tunica vaginalis twist along the axis of the spermatic cord.

   Intravaginal- Seen most often in teenage years, high placement of tunica vaginalis allows for rotation within the scrotum.

Diagnosis:
   Physical Exam- The testicle in patients with torsion may present with elevated testicle on the affected side and anterior placed epididymis.
   Studies- Doppler duplex sonography, Tc pertechnium.

Treatment of Testicular torsion
   Possible manual detorsion under local anesthesia.
   Orchidopexy- Bilateral because “Bell Clapper” deformity is usually bilateral and if both testicles are not fixed, there is a high incidence of recurrence on the contralateral side.

2. Acute Epididymo-orchitis: Age groups run from sexually active teenager to the elderly. Onset of pain is not as acute. Scrotal lifting reduces pain in testicles. Likely urinary or prostatic infection.

3. Torsion of testicular appendage (appendix testis): Results from torsion of the vestigial appendage resulting in acute pain often with dark blue spot identified on physical exam representing the underlying ischemic testicular appendage.
A. Ectopic Pregnancy
   1. Define as an ovum that implants and develops outside the uterine cavity
      - 95% are tubal and most of those are in the ampulla
      - 6 to 8 weeks is the most common time for rupture
      - Incidence about 3 per 100 pregnancies
      - Hx of PID or infertility
   2. Symptoms
      - Light vaginal bleeding 2 to 4 weeks after missed period
      - Sharp episodic abdominal pain eventually sudden severe pain when tube
        ruptures
   3. Physical Exam
      - Unilateral tender mass on palpation
      - Cyanosis and softening of the cervix
      - Possible signs of peritoneal irritation (not very reliable)
      - Febrile and leukocytosis if ruptured
   4. Lab Values
      - Progressive anemia
      - If beta-HCG >1600 Transvaginal U/S should show intrauterine pregnancy
      - If no intrauterine pregnancy visualized repeat BHCG in 48 hrs which
        should double in a normal pregnancy
      - May attempt to locate pregnancy by U/S and diagnostic laparoscopy if
        necessary
   5. Treatment
      - Medical treatment most of the time now if unruptured (methotrexate)
      - Linear salpingostomy vs segmental salpingectomy with possible re-
        anastomosis vs total salpingectomy depending on situation
      - Linear salpingostomy associated with highest rate of recurrent ectopics in
        future
      - Must follow BHCG to zero post op to confirm complete removal

B. Tuboovarian Abscess
   1. Diagnosis
      - Should be considered in any pt with PID
      - Over 90% present with abdominal or pelvic pain
      - Fever and leukocytosis in 60-80% of patients
      - Most are appreciated on pelvic exam (90% in one study)
      - U/S, Pelvic CT, Laproscopy may all be used to help with diagnosis
      - U/S is the test of choice for diagnosis
   2. Treatment
      - If pt stable treatment with one of the following (amp+gent+Flagyl;
        ofloxacin + Flagyl; ortimentin or Zosyn)
- Surgical therapy indicated for unstable pts or failed medical therapy after 4 days
- Depending on involvement of TOA determines surgery (TAH, BSO, drainage)

C. Ovarian Torsion

1. Diagnosis
   - Hx of recurrent pain since torsion may spontaneously resolve
   - More common on the right side and usually due to ovarian mass
   - Pt c/o sharp pain N/V, difficult to separate from TOA

2. Physical Exam and Studies
   - LQ Abdominal pain, usually no peritoneal signs
   - Tender adnexa on pelvic exam
   - Check BHCG to r/o ectopic pregnancy
   - U/S can be used of diagnostic laparoscopy

3. Treatment
   - If ovary infarcted: salpingo-oophorectomy
   - If ovary viable: untwist and secure the ovary
Ovarian carcinoma primarily affects peri- and post-menopausal women (mean age = 51). 1 / 70 women affected and risk increases significantly after age 70. Ovarian CA accounts for > 50% of all gynecologic cancer-related deaths, making it the most deadly of the gynecologic malignancies.

RISKS

- Higher incidence in industrialized countries (↑↑ dietary fat intake)
- Nulliparity
- Infertility
- Late child-bearing
- Delayed menopause
- Personal or family h/o endometrial, breast, or colon CA
- *BRCA1 or BRCA2* mutation

Note: The use of oral contraceptives greatly reduces the risk of ovarian cancer.

HISTOPATHOLOGY

Distinct histologic subtypes include epithelial, sex-cord stromal, germ cell, and metastatic lesions. Serous cystadenocarcinoma is the most common among the malignant ovarian carcinomas. Lesions that are bilateral, hard, and fixed upon examination (including evidence of ascites, capsule rupture, peritoneal implantation, and/or hemorrhagic or necrotic) are most likely to represent malignancy.

Pseudomyxoma peritonei and Krukenberg tumors are examples of metastatic ovarian cancers. Most common sites of metastatic primaries are: Colon (52%)
  - Breast (17%)
  - Stomach (10%)
  - Pancreas (10%)

DIAGNOSIS

Diagnosis is usually made when disease is already in advanced stage. Only ~30% of cases are confined only to the ovaries at the time of initial diagnosis.

- History and Physical Exam
- Transvaginal Ultrasound (with or without Color Doppler imaging)
- Tumor Markers (CA-125, CA 19-9, AFP, LDH, HCG, CEA)

STAGING, SPREAD & METASTASIS

Ovarian CA spreads via local intraperitoneal extension, hematogenous and lymphatic dissemination, as well as transdiaphragmatic passage.

*Stage I* – confined to one or both ovaries.
*Stage II* – involves one or both ovaries and extends into local pelvic structures.
*Stage III* – involves one or both ovaries with intraperitoneal / abdominal metastases.
*Stage IV* – involves one or both ovaries with distant metastases.

(ref. Townsend, p. 1641 – 1642)
TREATMENT

- Staging laparotomy + surgical debulking (includes TAH w/ BSO, omentectomy, lymph node sampling, peritoneal biopsies, peritoneal washings, and complete peritoneal inspection).

- Chemotherapy indicated for stages I, II, III, and IV with post-chemotherapy “Second Look” surgery for further debulking.

- “Second Look” debulking may be beneficial as both a treatment modality and prognostic indicator.

- Follow-up Ovarian CA patient with a thorough history and physical exam, rectovaginal pelvic exam, and CA-125 level every 3 to 4 months for 2 years post-treatment, then less frequently thereafter.
Transitional Cell Carcinoma of Bladder
Tammy Lee, MD

Intro
- 5th most common CA in US
- 3:1 male:female ratio
- Median age at diagnosis: 65yo
- Frequent recurrences

Epidemiology
- 4x more prevalent in smokers
- 9x more prevalent with chronic cyclophosphamide txt (believed to be secondary to urinary metabolite acrolin)
- Schistosoma haematobium (30% of time cause transitional CA not squamous)
- Other agents: aniline dyes, external beam radiation, meds such as phenacetin and chlornaphazin

Pathology
- 90% of bladder CA is transitional cell (70% papillary, 20% mixed, 10% sessile)
- 75% present as superficial lesions, 20% muscle invasion, 5 % mets
- STRONG correlation exists between tumor stage and grade.
- CIS is poorly differentiated high grade tumor confined to urothelium

CIS
- may be found as a solitary or multifocal process
- found in association with invasive CA 25% of cases
- POOR PROGNOSIS

Clinical Presentation
- Gross painless hematuria is common presenting sign
- 20% of cases may present with only microscopic hematuria
- Irritative voiding symptoms (frequency, urgency) may suggest malignancy, particularly CIS

Clinical Diagnosis
- eval of upper tracts (IVP or CT), cystoscopy, and urine cytology
- Confirmation of diagnosis with transurethral biopsy or resection

Management
- depends on tumor stage- has tumor invaded muscle layer
- most superficial bladder CA can be treated only with transurethral resection
- CIS, high grade superficial tumors, involvement of lamina propria (T1), and rapidly recurrent tumors need intravesical chemotherapy (thiotepa, doxorubicin, mitomycin C, interferon) or intravesical bacillus Calmette-Guetin (BCG) txt

Bladder Surveillance
- MANDATORY – 50% recurrence rate at 5 years
- Protocol – Cystoscopy and Urinary cytology studies (1st yr q3 months, 2nd yr q4 mo, 3rd yr semiannual, annually thereafter)
- Periodic eval of upper tracts to r/o upper tract occurrence – 3-5% of cases, BUT in pts with high-grade lesions or CIS can be as high as 20% with long term f/u
Radical Cystectomy
- Removal of bladder and pelvic lymph nodes (men- also prostate, seminal vesicle, perivesical fat, proximal urethra—women- also uterus, anterior vaginal wall, urethra, surrounding fascia, fallopian tubes, ovaries)
- 5 year survival rate - T2a (inner ½ muscle) 85%, T2b (outer ½ muscle) 60%, T3a (micro perivesical) 60%, T3b (macro perivesical) 40%, Node + dz <3%

Urinary Diversion
- Ileal or colon conduit which requires collection appliance
- Continent cutaneous diversion  (1) Indiana pouch – using Rt colon with a tapered and catheterizable efferent limb of ileum  (2) Koch pouch - creation of a nipple valve
- Orthotopic Neobladder – creation of reservoir using detubularized ileum or colon with direct anastomosis to the urethra

Metastatic Dz
- MVAC is standard txt but with significant toxicities (neutropenia/fever, mucositis, decreased renal and auditory function, peripheral neuropathy)
- Recent 2-3 drug combos with cisplatin, paclitaxel, and gemcitabine show similar response and survival rates to MVAC with fewer side effects.
- 10 – 15 % 5 year survival

Adjuvant chemotherapy
- for pts T3b, T4, N1, N2 dz
- MVAC is standard (methotrexate, vinblastine, adriamycin, cisplatin)
- Durable complete response rate < 15%
- Other chemo agents being explored (gemcitabine, paclitaxel, ifosfamide)
SECTION 4

CHAPTER 13

BREAST
Benign Breast Lesions
Kenneth J. Woodside, MD

Gynecomastia

Pubertal Hypertrophy
13 – 17 year old boys
Frequently bilateral
Usually ‘unnoticed’ (according to textbooks, not junior high boys)
Regresses with adulthood
Tx is reassurance

Senescent Hypertrophy
Often unilateral, sometimes tender
PE is smooth, firm, and symmetric underneath areola—no dominant mass
May be exacerbated by digoxin, thiazides, estrogens, phenothiazines, theophylline
Associated with cirrhosis, renal failure, and malnutrition
May require MMG and/or biopsy, if suspicious
Usually left untreated

Galactocele
Milk filled cyst
PE is round, well circumscribed, easily mobile, usually centrally located under the nipple
Usually occurs after cessation of lactation or decreased frequency of feedings
Tx by needle aspiration, although excision can be performed if difficult cysts
Aspiration yields a thick creamy material that is usually sterile

Breast Cysts
Fluid-filled epithelium-lined cavity, usually (but not always) unilocular
Palpable cyst in 1/14 women
50% multiple or recurrent

Pathogenesis
Destruction and dilatation of lobules and terminal ductules
Stricture and fibrosis near terminal branching of small ductules
Continued secretion by distal lobule results in expansion of a cavity

Macrocyts versus microscopic disease
Microscopic cyst disease is frequently bilateral and is not associated with increased cancer risk
Macrocyts can be unilateral, and may or may not be associated with a 2-4 fold increase in risk

Ovarian cycle effects
Often new cysts are first seen after 35 (rarely before 25)
Incidence increases sharply until menopause, then drops off
If found in postmenopausal women, they are often associated with HRT
Tx by aspiration. Excision is indicated in recurrence to r/o intracystic tumor

Fibroadenoma (Adenofibroma)
Stromal and epithelial elements
Most common tumor in women < 30 y/o
PE demonstrates a palpable mass that may be lobulated, but is easily mobile
Well encapsulated, with a variable proportion of epithelial and stromal proliferation
No specifically attributed increased cancer risk
Risk of carcinoma about the same as patients who underwent needle biopsy (2 fold)
Intraadenoma carcinomas are possible (same risk as other breast tissue)
Tx typically follow clinically (needle biopsy).
Elective excision if patient wants it removed or if the lesion is larger or growing (>2 cm ?)

Giant fibroadenoma and Juvenile fibroadenoma
Typically greater than 5 cm--may be rapidly growing
Surgical removal is curative
Hamartoma
Benign discrete nodule
Closely packed lobules and prominent ecstatic extralobular ducts
PE and MMG is the same as a fibroadenoma
Excision is curative

<table>
<thead>
<tr>
<th>Risk Increased</th>
<th>Condition</th>
</tr>
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<tbody>
<tr>
<td>No increased risk</td>
<td>Adenosis, Cysts, Duct Ectasia, Fibroadenoma, Fibrosis, Apocrine Metaplasia</td>
</tr>
<tr>
<td>1.5 to 2 fold increase</td>
<td>Moderate Hyperplasia, Florid Hyperplasia, Papilloma with Fibrovascular Core</td>
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<tr>
<td>4 to 5 fold increase</td>
<td>Atypical Ductal Hyperplasia, Atypical Lobular Hyperplasia</td>
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Breast Abscesses
Often in subareolar breast tissue
Frequently recurrent
Subareolar duct ectasia and duct obstruction can lead to fluid collection
Subsequent bacterial seeding can lead to abscess formation
While mastitis is treated by Abx, abscesses require I&D
Chronic inflammation can lead to a mammary fistula, which is tx by excision of epithelialized tract

Papilloma
Epithelium lined polyps of the breast duct
Usually subareolar when solitary. Multiple intraductal papillomas are more likely peripheral
May arise within a cystic duct
Usually < 1 cm, but can be much larger
PE may demonstrate bloody nipple discharge or mass
Tx is excision through a circumareolar incision

Papillomatosis
Epithelial hyperplasia associated with fibrocystic changes
Not true papillomas—no stalk of fibrovascular tissue
Benign, with increased cancer risk only associated with atypical epithelial proliferation

Sclerosing Adenosis
Increased small terminal ductules or acini associated with proliferation of stromal tissue
May be calcified and confused with carcinoma
No increased malignant potential

Radial Scar
Complex sclerosing lesions
Also can be confused with carcinoma
May contain microcysts, epithelial hyperplasia, adenosis, and central sclerosis
Associated with a 2 fold increase of cancer risk
Biopsy is always recommended

Fat Necrosis
May produce a mass on PE or density on MMG
Often results from trauma
Composed of lipid laden macrophages, scar tissue, and chronic inflammatory cells
No malignant potential

References
Townsend CM, et al. Textbook of Surgery, 16/e
Cameron JL. Current Surgical Therapy, 6/e
## Risk Factors for Breast Cancer

Angela K. Champion, MD

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
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<tbody>
<tr>
<td>Gender</td>
<td>Early Menarche</td>
</tr>
<tr>
<td>Age</td>
<td>Late Menopause</td>
</tr>
<tr>
<td>Personal history of breast cancer</td>
<td>Obesity</td>
</tr>
<tr>
<td>Family history of breast cancer</td>
<td>Low dose Radiation</td>
</tr>
<tr>
<td>Benign Proliferative changes with atypia</td>
<td></td>
</tr>
<tr>
<td>Noninvasive cancer</td>
<td></td>
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### Age and Gender
- Females > Males
- Incidence in males <1% of incidence in females
- Incidence of breast cancer increases with age
- Patients younger than 30 years of age constitute <2% of cases

### Personal History
- Previous history of breast cancer increases risk of 2\textsuperscript{nd} primary in other breast
- Risk based on age at diagnosis of first primary
- Patients <45yrs at initial diagnosis increases risk by 5-6X
- Older patients risk decreases to twofold

### Family History
- History of first degree relative (mother, daughter, sister) increases risk 2-3X
- Risk even higher if relative had premenopausal or bilateral disease
- Risk approaches 50% with multiple affected members
- Risk decreases significantly for distant relatives (cousins, aunts, grandmothers)

### Benign Proliferative Changes with Atypia
- Fibrocystic disease with biopsy showing cellular atypia
- Increases risk 4-5X
- Risk increases with additional factors (family history) to >9X

### Noninvasive Cancer
- History of DCIS or LCIS predispose to subsequent cancer
- Most often seen in contra-lateral breast
- Risk increases with age and time
- Requires lifelong close observation

### Minor Factors
- BCDDP study examined many variables to determine factors for increase risk
- Early menarche, late menopause, age at first birth, # of breast biopsies, # of first degree relatives with breast cancer all showed an increase risk
- Rejected previous ideas regarding smoking, alcohol, OCP and HRT
Tamoxifen & Herceptin in Breast Cancer
Angela K. Champion, MD

**Tamoxifen**
- Estrogen agonist-antagonist
- Acts as competitive antagonist of estrogen activity in breast
- Acts as agonist in other tissue (uterus)
- Hormonal treatment of choice for estrogen receptor positive breast cancer in pre and postmenopausal women

**Mechanism**
- Competes with estrogen at binding sites in breast
- Decreases the induction of numerous gene products

**Indications**
- Tamoxifen indicated for estrogen ± progesterone receptor positive breast cancers
- >10% tumor cells stain +, response to hormone therapy likely
- The presence of both receptors shows an 80% chance of favorable response
- Tamoxifen shown to increase disease free interval and overall survival rates
- Early Breast Cancer Trials show reduction in second breast cancer by 47%
- NSABP trial found a 49% reduction in invasive breast cancer
- Effective results may take up to 5 years

**Contraindications**
- Known uterine cancer, hypersensitivity, history of DVT or PE

**Side Effects**
- Risk of uterine cancer increased by 2.5X, outweighed by benefits
- Estrogen-like effects on cardiac and skeletal muscle
- Decreases postmenopausal bone loss

**Herceptin**
- Recombinant DNA derived monoclonal antibody
- Selectively binds to human epidermal growth factor receptor 2 protein (HER-2)

**HER-2**
- Proto-oncogene which encodes a transmembrane receptor protein
- HER-2 overexpression seen in 25-30% of primary breast cancers
- Herceptin inhibits proliferation of human tumor cells which express HER2

**Indications**
- Approved for use in metastatic breast cancers
- Shown when added to chemotherapy tripled time to progression and improved survival by 4-6 months
- Risk of cardiomyopathy-evaluate LV function prior to use
Treatment of DCIS
Angela K. Champion, MD

**Definition:**
- Proliferating malignant epithelium of breast ducts without detectable invasion through the basement membrane
- Tumor cells fill and expand ducts
- Undergo necrosis, filling ducts with necrotic debris, which may calcify

**Presentation**
- Screening mammography
  - Seen as clusters of dystrophic calcifications
  - Represent 30-40% of newly diagnosed cancers
- Palpable mass if multiple ducts involved or bloody nipple discharge

**Treatment**
- Total Mastectomy
- Wide Local Excision ± radiation
- Tamoxifen

**Mastectomy**
- Total mastectomy typically without axillary node dissection
- Attractive option for extensive, multicentric disease
- Procedure of choice for tumors not amenable to complete resection
- Less than 2% recurrence rate at 10 years

**Excision with Radiation**
- Patients who desire breast conservation
- Local recurrence after DCIS excision is reduced by 50% with use of radiation
- Recurrence rate slightly higher than mastectomy, about 12%
- No change in mortality compared to mastectomy

**Excision without Radiation**
- Patients desire breast conservation, do not want radiation
- Attractive option for small tumors, <1cm
- Recurrence rate estimated 27% compared to mastectomy
- No change in mortality compared to other treatments

**Tamoxifen**
- NSABP trial showed adding tamoxifen to treatment of DCIS decreases recurrence rate of breast cancer
- Recurrence rate of invasive cancer in same breast decreased by 30%
- Recurrence of DCIS in opposite breast decreased by 52%
- Treatment based on oral tamoxifen for 5 years
- Short follow-up and liberal inclusion criteria
Management of Lobular Carcinoma in situ and BRCA
Juan C. Escalon, MD

I. Lobular Carcinoma in situ (LCIS)
   A. First described by Foote and Stewart in 1941. Later called lobular neoplasia by Haagensen 1978 in order to include atypical lobular hyperplasia (ALH).
      1. LCIS is histologically composed of monomorphic small round cells with a thin rim of clear cytoplasm and a high nuclear-to-cytoplasmic ration. More than half the acini within the lobular unit must be distended and there must not be any central lumina.
      2. ALH has similar cellular characteristics as LCIS except that cells only partially occlude the lumen and lobules are only slightly distended. Central lumina may be present and less than half the lobule is affected by proliferation.
      3. It is now believed that LCIS and ALH are not biologically distinct lesions and have the same risk for development of invasive carcinoma.
   B. LCIS and ALH are found incidentally
      1. Never forms a palpable mass by itself and therefore not found on physical examination.
      2. There are no mammographic findings present, it does not form a density and rarely calcifies.
      3. It is recognized incidentally after biopsy for another abnormality producing clinical or mammographic findings.
      4. Reported to be found in 0.5 – 8% of benign breast biopsies.
   C. LCIS/ALH occurs in premenopausal women
      1. Average age at diagnosis is 44-49 years old; this is 10-15 years earlier than invasive breast cancer.
      2. Not present in men since lobular breast elements are not usually present.
      3. Studies show that 40% of women with LCIS had carcinoma in situ lesions on follow up and of those 50% were in the contralateral breast.
      4. Invasive carcinoma will develop in 30% of women with LCIS/ALH, relative risk increase of 8-10.
   D. Management for LCIS/ALH
      1. Surveillance is the most commonly recommended management option.
         a. Strang-Cornell Breast Center: every 3-4 month physician exam, annual mammography, genetic counseling, and nutritional advice.
         b. Blind contralateral breast biopsy is not recommended.
      2. Chemoprevention with tamoxifen has proven a 49-50% decreased risk for developing invasive carcinoma as shown in the National Surgical Adjuvant Breast and Bowel Project (NSABP P-1) for patients with LCIS when taken for five years.
      3. Bilateral prophylactic mastectomy (BPM) is reserved for patient with extreme anxiety regarding condition and those who elect surgical intervention instead of close follow up.

II. BRCA genes are tumor suppressor genes identified with increased risk for breast and ovarian cancers in patients with mutations.
   A. They are responsible for 5-10% of all breast cancers. The lifetime risk of developing breast cancer for BRCA1/2 carriers is 40-85%.
   B. The risk of breast cancer increases in BRCA1/2 carriers with childbearing and subsequent pregnancies.
   C. BRCA1 is located on chromosome 17q21 and is associated with a lifetime risk for developing ovarian cancer of 16-40%.
      1. The age of onset is 48-54 years old, which is 8-14 years younger then average (62 years old).
D. BRCA2 is found on chromosome 13q12-q13 and is associated with a lifetime risk for
developing ovarian cancer of 10-20%.
   1. The age of onset is similar to average age of onset in non-BRCA associated ovarian
cancer.
   2. BRCA2 was linked to LCIS in one study, yet overall data is inconclusive.
   3. Men having BRCA2 mutations have an estimated 6% lifetime risk for developing breast
cancer.

E. Management of BRCA
   1. Surveillance recommendations by the Cancer Genetics Studies Consortium
      a. Monthly self exam starting at 18-21 years old
      b. Clinical breast exam every 6-12 months starting at 25-35 years old
      c. Annual mammography starting at 25-35 years old
      d. Annual transvaginal ultrasound
      e. Annual measurement of CA-125
   2. Chemoprevention with tamoxifen showed a 50% reduction in cancer incidence as seen in
      the NSABP P-1 trial.
      a. Increased risk of endometrial cancer with tamoxifen lead to the NSABP P-2 trial in
         which raloxifene, a selective estrogen receptor modulator is being evaluated, with
         favorable results thus far.
   3. Bilateral prophylactic mastectomy (BPM) has shown a 90-94% risk reduction for breast
      cancer and an 81-94% reduction in the death from breast cancer.
      a. Minimal survival gains were seen for women having BPM after age 60.
   4. Oophorectomy in premenopausal women has shown a 50% risk reduction in BRCA1
      carriers and is considered as an alternative to BPM in these patients.
Phyllodes Tumor
John W. Antonetti, MD

“Cystosarcoma”

Originally named cystosarcoma phyllodes, the phyllodes tumor presents a challenge when evaluating the majority of benign tumors from the few that have malignant potential. The name cystosarcoma describes the histologic morphology of the tumor. “Cyst” describes the cystic components due to infarction and necrosis and “sarcoma” describes the connective tissue origin of the tumor. Phyllodes, derived from the Greek word for leaf describes the appearance of the breast with underlying bulky tumor.

Similar in appearance to the fibroadenoma, the phyllodes tumor has a sharply defined border that leads to compression of surrounding tissue. In contrast to the fibroadenoma, the phyllodes tumor presents later in life with the majority of tumors diagnosed in the sixth decade.

Diagnosis: Biopsy or excision. The phyllodes tumor is distinguished from the fibroadenoma by its increased cellularity, mitotic rate, nuclear pleomorphism, stromal overgrowth, and infiltrative borders.

Treatment: Smaller tumors require at least a one-centimeter margin with the average tumor measuring 4-5 centimeters. Larger tumors require mastectomy. Nodal resection may or may not be performed due to rare nodal metastasis of phyllodes that have preponderance for the lungs.

Prognosis: Half of all resected phyllodes tumors may recur locally. When local recurrence occurs total mastectomy is recommended with lymph node resection of questionable value. With less than one percent metastatic rate, the phyllodes tumor rarely undergoes metastasis.

Phyllodes sarcoma—malignant, low occurrence.
SECTION 4

CHAPTER 14

ONCOLOGY
OVERVIEW
- Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma are among the most common cancers in the world
- If a person develops one the above cancers there is 35% risk at 3 years and 50% risk at 5 years of developing another skin cancer
- Destructive, but low mortality
- Mortality associated with refusal of treatment
- Invasive and rarely metastasize (10 month survival)
- Metastasis associated with neglect or multiple incomplete excisions
- No precursor lesions
- Most common malignancy in humans
- Lifetime risk 28% to 33%

RISK FACTORS
- White, elderly, fair skinned Caucasians
- Ultraviolet radiation is greatest risk factor with 20 to 50 year latency
- Immunocompromised
- Genetic disorders i.e. xeroderma pigmentosum
- Arsenic exposure causes multiple lesions other than head and neck

PRESENTATION
- Most common on head and neck
- Non-healing, ulcerated, bleeding tendency, scaling
- Crusted, eroded, rolled edges or raised borders
- May enlarge over months to years
- Telangiectasia

TYPES AND APPEARANCE
- Nodular
  - pearly, waxy papules or nodules
  - most common
- Cystic
  - filled with fluid
  - translucent blue/gray
  - mistaken for benign hidrocystoma
- Pigmented
  - brown or black
-dark skinned individual
-may mimic mole or melanoma
-Superficial
- pink to reddish brown scaly plaques
- mistaken for eczema or psoriasis
- more common on the trunk
- associated with arsenic exposure

-Aggressive
- flat, pale, smooth surfaced lesion
- poorly defined borders
- deep extension difficult to clinically assess (subclinical extension)
- associated with morpheaform, infiltrative and micronodular subtypes, which may extend through tissue with distortion of normal tissue

PHYSIOLOGY AND GENETICS
- Arise from basal keratinocytes of the epidermis and other adnexal structures i.e. hair follicles
- PATCHED gene mutated in 90% of BCC
- p53 gene mutated in 50% of BCC

TREATMENT
- Excision with 4mm margins and send to pathology
- Excise with 7mm margins for aggressive type
- Ninety percent cure rate with the above method
- Moh’s micrographic excision recommended in areas which have been previously treated or areas such as noses, ears
Melanoma
Chris T. Stephens, MD

**Epidemiology**
- eighth most common cancer in the U.S. – approx. 40,000 new diagnoses per year (4-5% of total skin malignancies)
- increasing risk of whites developing disease (1:75 risk); risk ratio white:black 20:1
- highest risk: pale skin, freckles, blonde/red hair, light-colored eyes
- men- lesions more common on trunk, head/neck; women- lower extremities
- environmental factors- sun exposure only avoidable risk factor; UVA/UVB radiation known to be carcinogenic in experimental models
- severe sunburns in childhood increase risk for melanoma in adult life

**Precursor Lesions**
- all lesions should be excised
- dysplastic nevus: large nevus with indistinct border and color variation – may be mistaken for melanoma	dysplastic nevus syndrome- multiple pigmented lesions on upper back, chest, and arms; increased risk of melanoma development
- spitz nevus- most common in children/young adults – also mistaken for melanoma – well circumscribed and raised
- giant congenital nevus- (1:20,000 newborns) risk of melanoma is 5-8% - risk occurs in early childhood; early excision recommended

**Pathology**
- abnormal proliferation of atypical melanocytes near dermal-epidermal junction
- growth phases – radial growth phase: tumor cells proliferate and expand radially
  - vertical growth phase: tumor cells invade more deeply into dermis and can result in a palpable nodule
- major histopathological types:
  o superficial spreading melanoma (most common – 70% of all melanomas): found on both sun-exposed and non-sun-exposed areas – lesions progress from radial growth to vertical growth and prognosis worsens
  o lentigo maligna melanoma: presents as a thin melanoma – better prognosis than other types – typically arises on sun-exposed areas in older people (50-80 y/o)
  o acral-lentiginous melanoma: common on palms, soles, subungual – most common type in mucosal lesions – more common in blacks- commonly misdiagnosed and therefore worse prognosis with delay in Tx
  o nodular melanoma: vertical growth phase only – demonstrates upwards growth resulting in nodule – rapid dermal invasion and poor prognosis characteristic

**Clinical Features**
- cutaneous melanoma: pigmented skin lesion accounts for 90-95% of melanomas (may arise from pre-existing lesion or de novo)
- 5 most common features of melanoma (ABCDE’s): Asymmetry, Border irregularity, Color variation, Diameter >6mm, Elevation
- beware of any recent changes in lesion characteristic – increases suspicion of malignant transformation
- characteristics of these lesions can include bleeding, itching, ulceration, different shades of pigmentation, no pigmentation (amelanotic melanoma)
Clinical Management
- biopsy any suspicious lesion! Always perform full thickness biopsy for staging
- complete excision with narrow margin (1mm) of normal skin is best
- features of primary lesion: depth of invasion- Clark’s level: depth characterized anatomically; Breslow’s thickness: depth measured in mm
- ulceration more common in thicker lesions and associated with worse prognosis

Staging (New 2002 Melanoma Staging System – AJCC)
- TNM staging: T – primary tumor; N – nodal mets; M – distant mets
- T0: no evidence of primary tumor; T1: 1.0mm or less in thickness; T2: 1.01 to 2.0mm; T3: 2.01 to 4.0mm; T4: >4.0mm
- N0: no regional mets detected; N1: one node; N2: two-three nodes; N3: four or more nodes detected
- M0: No detected distant mets; M1a: mets to skin, subcutaneous, or distant lymph nodes; M1b: mets to lung; M1c: mets to all other visceral sites

Treatment
- surgical management includes wide local excision
- lesions thicker than 1.5mm = higher incidence of nodal mets (nodes are first site of mets in >60% cases)
- elective node dissection thought to improve outcome
- sentinel lymph node biopsy – involves lymphatic mapping with radioactive tracers – sentinel nodes resected with benefit of minimizing morbidity – standard of care for primary cutaneous melanoma – believed to reflect status of entire nodal basin in 98-99% of cases
- local/regional recurrence managed with complete excision when possible
- adjuvant radiation therapy may improve outcome in people with multiple nodes involved or extranodal extension of mets
- distant mets Tx with resection and/or systemic therapy based on individual cases (most common visceral mets include lung and liver but can occur anywhere)

Systemic Therapy:
- cytotoxic chemotherapy - dacarbazine (20-40% response rate)
- immunotherapy includes vaccines and cytokines (IL-2)
- adjuvant therapy for resected disease – INF-α used for high risk melanoma (limited due to toxicity)

IL-2: Cytokine produced by human T-helper lymphocytes that induce the expansion of lymphocytes following activation by a specific antigen – these activated lymphocytes have anti-tumor activity

Vaccines – based either on cancer cells or on the genetic identification of cancer antigens – vaccines based on T-cell recognition of tumor antigens
- Vaccines based on cancer cells derived from whole cancer cells, gene-modified cancer cells, cancer cell extracts (lysates, membranes, heat shock proteins), and cancer cells fused to APC’s
- Vaccines based on genetic identification of cancer antigens – use purified cancer antigens, synthetic peptides (naked DNA), recombinant viruses, and recombinant bacteria
Proto-oncogenes
Carlos A. Murillo, MD

Colorectal cancer
- Associated with an overexpression of proto-oncogenes or risk-modifier genes,
- Underexpression of mismatch repair genes or tumor suppressor genes

Proto-oncogenes
- K-ras – most commonly mutated oncogene in sporadic colonic neoplasia
  - Codes for a small guanosine triphosphate-binding protein (G protein) that normally functions as a switch in the transduction of signals from the cell surface to intracellular targets
  - Mutations cause an abnormal G protein that can not be inactivated
  - Found in 40-50% of all sporadic colorectal adenomas and carcinomas
  - Found in adjacent tissue to CRC’s – dysplastic precursor
- Src – first tyrosine kinase protein identified
  - Involved in signal transduction
- c-myc – stimulated by B-catenin
  - Produces a protein c-Myc which is a powerful stimulator of cell growth and proliferation
  - Normally not mutated, but overexpressed
    - in Burkitt’s lymphomas, c-myc gene is translocated downstream of control sequences that normally drive expression of antibodies in B-cells, leading to overexpression

Tumor suppressor
- Rb – retinoblastoma genes
  - Codes for a protein involved in cell-cycle regulation
  - Two hit hypotheses – mutations and translocations
  - Found in retinoblastomas, lung, breast, and bladder
- APC (adenomatous polyposis coli) – located on the long arm of chromosome 5
  - Inherited mutation leads to familial polyposis coli and Gardner’s syndrome
  - Located on the 5q21 chromosomal region
  - Functions in cell-cell interaction (binds to B-catenin) and the regulation of the cell cycle
  - Most common mutation is the loss of the second allele leading to “Loss of Heterozygosity” within the cell(s)
    - seen in 50-85% of sporadic CRC and adenomas
    - also seen in 33-50% of all UC-related dysplasias and carcinomas
- DCC (deleted in colon cancer) – located on the long arm of chromosome 18 (18q)
  - Protein sequence is homologous to adhesion molecules
  - Believed to function in cell-cell adhesion and attachment
  - LOH for DCC locus is seen in 70% of all sporadic carcinomas
- p53 – mutations occur in 50% of all human cancers
  - Located in the short arm of chromosome 17 (17p)
- Codes for a nuclear phosphoprotein that functions as a transcription factor
- Expression increases in response to DNA damage
- Regulates the transcription of genes that lead to apoptosis
- Mutation found in 80-90% of sporadic CRC, 45-100% of UC-related cancers

MCC (mutated in colon cancer)
- Located on chromosome 5q21
- Mutations are associated with cell cycle progression
- Overexpression leads to cell cycle arrest

DPC4 – located in chromosome 18q
- Codes for Smad protein
- Seen homozygously deleted in 30% of pancreatic cancers
- Inactivated in 55% of infiltrating pancreatic cancers
- Leads to transcription of specific genes

BRCA1,2 – located on chromosome 17q21, 18q
- Negative regulation of cell proliferation

Mismatch repair gene (DNA repair genes)
- Germ line mutations seen in HMPCC
- Leads to defective DNA mismatch repair leading to microsatellite Instability (MIS)
  - Caused by the failure of correct replication of nucleotide repeat sequences
  - Results in expansion or contraction of the size of the repeated sequences, disrupting genes that may have these sequences
    - transforming growth factor beta
    - bax gene
- Flavors: hMSH2 (chromosome 2p), hMSH1 (chromosome 3), MLH1, PMS1, PMS2, GTBP

Risk modifier genes
- Phospholipase A2
- COX2 (cyclooxygenase 2)
  - Overexpression has been linked to resistance to apoptotic signals, and
  - COX2-specific NSAIDs have been shown to increase apoptosis
- CD44v – involved in cell-cell adhesion activities
  - Associated with advanced disease and metastasis, i.e. multiple myeloma,
  - Unclear mechanism of action
Tumor Markers
Carlos A. Murillo, MD

Tumor markers
1. Molecules that are associated with cancer
2. Can be any kind of molecule: protein, DNA, RNA, ganglioside, immunoglobulin, glycoprotein
3. Few are shared by many cancers
4. Classified into two classes: tumor-specific markers (markers produced only by tumors) and tumor-associated markers (produced by tumor cells and normal cells)
5. Number of tumor markers has increased with advanced in molecular biology
6. Arise from genetic changes associated with the initiation and development of tumors
   a. Viral genes and Chromosomal Translocations
      i. May see viral gene products in viral induced tumors
         1. EBV (Burkitt’s lymphoma), HPV (cervical cancer), HBV (hepatocellular carcinoma), HTLV-1 (T-cell leukemia)
      ii. Hybrid proteins
         1. Produced from chromosomal translocations; breakpoints in gene sequence
         2. Examples:
            a. Philadelphia chromosome (90% of CML)
            b. Short chromosome 22 from 9-22 translocation
            c. Epidermal growth factor receptor (40% of glioblastomas)
      iii. Fusion protein from internal deletion in sequence
         1. producing a more stable protein than wild-type EGF-R
   b. Genetic changes
      i. Alter transcription levels of genes leading to gene silencing or overexpression
         i.e. mutated p53, ras
      ii. May alter intro-exon splicing sites producing aberrant mRNA and altered proteins
         i.e. gp100 tumor antigen-encoding gene in malignant melanoma
         TRP-1/gp75 (a tyrosinase-related protein) in melanoma

Tumor-specific Markers
1. Produced my a variety of causes
2. Carcinogen-induced protein alterations
3. Germ-line mutations: BRCA1, BRCA2, APC, ret genes
   a. Include mutations in tumor suppressor genes and oncogenes:
      i.e. BRCA-1, BRCA-2, APC, p53, nm23 and ret, β-catenin, ras, bcl)
4. Fusion proteins from internal deletions, altered reading frames, translocations
   i.e. EGF-R
   i. Viral-encoded genes
      i.e. EBV (EBV nuclear protein in 80% of BL), HPV (E6, E& in associated cancers), HBV, HTLV-1
Tumor-associated Markers

1. Three large categories: differentiation, oncofetal, clonal
   a. Differentiation (largest group)
      i. Lineage specific – can trace origin of tumor cells
   b. Oncofetal
      i. Proteins that are expressed primarily in the embryonic or fetal stage development but not, or in low levels, in adult stages
   c. Clonal
      i. Proteins produced at low frequencies in normal cells

2. Some cancers may secrete parts of a molecule
   a. Prostate-specific antigen (PSA) or prostate serum acid phosphatase (PSAP) in prostate cancer; CA125 in ovarian; MUC-1 in breast cancer
   CEA in pancreatic, breast, and colon cancer

3. Some cancers may also secrete whole proteins, i.e. hormones
   a. Chorionic gonadotropin hormone in trophoblastic and testicular cancers
   Calcitonin in medullary thyroid cancers
BRCA and Breast Cancer
Eric C. Feliberti, MD

I. Molecular biology
- BRCA-1 found on chromosome 17; BRCA-2 found on chromosome 13.
- Both are tumor suppressor genes.
- Genes have high densities of repetitive elements, making them unstable.
- Proteins of BRCA-1 and -2 are involved in double strand DNA repair.
- Cells lacking BRCA-1 or -2 accumulate chromosomal abnormalities, chromosomal breaks and aneuploidy.

II. Epidemiology
- 50-70% of sporadic breast cancers and ovarian cancers have loss of BRCA-1, and 30-50% have loss of BRCA-2.
- 5%-10% of breast cancers are familial.
- 90% of familial breast cancers have loss of BRCA-1 or –2.
- Risk factors for familial breast cancer include personal history of breast or ovarian cancer, family history of breast or ovarian cancer, young age at time of diagnosis.

III. Breast-ovarian syndrome
- Associated with loss of BRCA-1 gene.
- Patients have 50% risk of breast cancer and 16% risk of ovarian cancer.
- Loss of BRCA-2 has a high incidence of breast cancer, but only limited risk of ovarian cancer.

IV. Treatment
- Prophylactic mastectomy is only current modality to reduce breast cancer risk – reduced by 90%; 5-7 year gain in life expectancy.
- Tamoxifen as chemoprevention currently in trials.
- Oral contraception and prophylactic and prophylactic oophorectomy are options for prevention of ovarian cancer.
RET proto-oncogene in thyroid cancer
Brittany B. DeBerry, MD

I. General information
   a. Proto-oncogene - a gene that can give rise to an oncogene after genetic alteration or through modification of the genetic proteins, which are expressed.
   b. RET proto-oncogene - encodes a tyrosine kinase receptor on the cell membrane. Cells of neural crest origin have increased expression of this oncogene. It has been found in neuroblastoma, pheochromocytoma and medullary thyroid cancer tissue.
   c. RET proto-oncogene has been localized to chromosome 10q.
   d. The function of the RET gene was determined in mice having null-mutation in the gene to be kidney development and enteric neurogenesis.

II. Involvement in papillary thyroid cancer
   a. PTC represents about 80% of all thyroid cancers.
   b. Ionizing radiation can induce RET/PTC rearrangements. RET/PTC rearrangements are highly prevalent in papillary carcinoma found in patients after the Chernobyl nuclear accident.
   c. External radiation is also associated with PTC however a longer interval to diagnosis is present when comparing external radiation which usually develops 10-20 years post-radiation to post-Chernobyl PTC which typically presents much earlier.
   d. RET/PTC may have implications is prognosis with some studies showing a greater incidence of metastasis when the mutation is present.

III. Involvement in MEN
   a. RET oncogene mutations have been associated with MEN 2 and FMTC.
   b. In one report 95% of 79 families with MEN 2B 98% of 203 families with MEN 2A and 88% of 34 families with FMTC were found to have mutations in the RET gene.
   c. Screening for RET mutations allows the detection of gene carriers when they are clinically unaffected or at a very early stage of disease.
   d. Once a carrier is identified the patient must undergo a clinical and biochemical examination
      i. Neck palpation and ultrasound.
      ii. Measurement of basal and penagastin-stimulated serum calcitonin.
      iii. Measurement of serum calcium and parathyroid hormone.
      iv. Measurement of serum or urinary catecholamines.
   e. Treatment
      i. When clinical or biochemical evidence of disease is found surgery is the treatment of choice.
      ii. This is the same as any patient with MTC- total thyroidectomy and lymph node dissection.
      iii. Prophylactic thyroidectomy can be performed when no evidence of disease is found. Discuss with the patient the risks of morbidity of the operation.
I. Sporadic desmoid tumors
   a. 2-5/1,000,000 occurrence per year
   b. Usually located on the anterior abdominal wall, some involve the shoulder girdle.
   c. Arise from the musculoaponeurosis of the rectus abdominus muscle and its sheath; can arise in surgical scars or other areas of trauma
   d. More frequent in females, especially after pregnancy. A hormonal component to development is suggested because of this phenomenon and because desmoids have been seen to regress at menopause.
   e. Lack the capacity to metastasize but can be locally aggressive
   f. Local recurrence rate after surgery can be as high as 25-50%

II. Desmoids in association with FAP
   a. FAP is an autosomal dominant condition resulting from homozygous inactivation of APC gene.
   b. Historically called Gardner’s syndrome
   c. 10% of FAP patients have clinically significant desmoids
   d. 70% are intra-abdominal, largely involving the small bowel mesentery; 15% are in the abdominal wall and 15% are extra-abdominal
   e. Can be associated with significant complications such as SBO, ureteric obstruction, bowel perforation, hemorrhage, and DVT
   f. Prognostic indicators:
      i. Size >10cm
      ii. Multiple lesions
      iii. Bilateral hydronephrosis
      iv. Extensive small bowel involvement
   g. Operative management is patients of FAP associated DTs have an exceptionally high recurrence rate and some authors suggest operative management only if symptoms such as bowel or urinary obstruction, fistulas or abscess formation.

III. Presentation and diagnosis
   a. Most commonly present as a slowly enlarging mass.
   b. Symptoms depend on location.
   c. Diagnosis is based on clinical suspicion. History of FAP, trauma or pregnancy is common.
   d. Radiographic studies including CT and MRI can help define anatomy prior to operation especially in intra-abdominal tumors.
e. FNA usually is not helpful in diagnosis because of the lack of cellularity present in these tumors. Incisional biopsy is usually necessary to establish a definitive diagnosis.

IV. Treatment
  a. Medical management
     i. Radiation therapy- used when a patient’s overall medical condition will not permit operation or with recurrent tumors. Controversial results in the literature. Complications include soft tissue fibrosis, skin necrosis, bowel obstruction and fistula formation.
     ii. Chemotherapeutic agents- not used frequently due to side effects, and lack of clearly documented results. Cytotoxic drugs can be used when unresectable tumors are present, or the tumor is rapidly growing.
     iii. cAMP modulators (theophylline, testolactone)- mechanism of action is largely unknown, possibly blocks the conversion of testosterone and androstenedione to estrogen. Few studies have been done.
     iv. NSAIDS- Indomethacin and Sulindac. Possible mechanisms of action include blocking the induction of ornithine decarboxylase thereby decreasing cellular proliferation or via prostaglandin suppression they may improve immune surveillance. Again few studies with variable results.
     v. Anti-hormonal therapy- thought to be beneficial due to association with estrogen.

b. Operative management
   i. Wide local excision- frequent local recurrence highly dependent on tumor location.
      1. Overall recurrence rate 40%
      2. Abdominal wall tumors 24%
      3. Mesenteric tumors 77%
   ii. Margin of resection- no conclusive evidence that there is any difference when positive vs negative margins are present.
   iii. Recurrent disease
      1. Symptomatic- re-operation.
   iv. New protocols- neoadjuvant chemotherapy and radiation followed by surgical resection provided an 85% local control rate
Sarcoma of the Extremity
John W. Antonetti, MD

About 8000 total cases of sarcoma are diagnosed in the US each year. Although rare, these tumors have a high rate of metastasis and local recurrence.

**Soft Tissue Sarcomas of the Extremity:** With high local recurrence rate, sarcomas of the extremity have a propensity to spread to the lungs when metastasis occurs.

1. Malignant Fibrous Histiocytoma
2. Liposarcoma

Diagnosis: Although presenting as a painless mass most often, pain is noted in 33% of patients. Soft tissue sarcomas of the extremity may present as muscle strains or hematomas leading to a delay in diagnosis. For masses larger than 5cm or persisting longer than a month, incisional biopsy is preferred with subsequent en bloc resection of scar when definitive surgery is to take place.

**Evaluation and Staging:**

Low grade lesion- Mandates chest x-ray to evaluate for metastasis
High grade lesion- Chest CT Scan

Staging: Determined by histological grade, size, nodal involvement, and presence of distant metastasis.

Stage I and II: Low grade tumor
Stage III and IV: High-grade tumor

**Treatment and Management**

Surgical Treatment: Preoperative MRI of involved extremity. Should achieve total resection of tumor with optimized conservation of function. Preferred margins are at 2-3cm. Pulmonary resection is advised when possible.

Adjuvant Radiation: Improve local control of large (>5cm) high or low-grade lesions. Increases likelihood of limb-sparing resection.

Adjuvant Chemotherapy: Not proven to be efficacious. Investigational trial is used for some high-grade lesions.

**Inadequate resection:**
- Tumor alone: 90% recurrence, due to “pseudocapsule” outer sheath of viable tumor cells left behind after simple excision.
- Extensive resection: 40% recurrence
- Radical muscle group resection: 10-25% recurrence
**Prognostic Factors**

Local recurrence- (presenting as nodularity along the scar) age greater than 50, positive margins, subtypes fibrosarcoma and malignant peripheral nerve tumor.

Distant recurrence- large tumor size, deep location, high histological grade, recurrent disease.

*Long term follow up is important beyond five years to evaluate for recurrence.*

**Osteosarcoma**

Age of presentation: Bimodal, 10-20 years with second peak around age 60

Gender distribution: Affects men more than women

Location: 66% of lesions occur in the distal femur and proximal tibia, other common site includes the proximal humerus

Radiographic findings: Poorly defined borders with tumor eroding through cortex, will find bone formation within the tumor

Treatment: Resection plus chemotherapy

Five-year survival rate: 15%

Metastasis: Lungs

**Ewing’s Sarcoma:**

Presents as pain, swelling of the involved bone. Rapid growth of tumor, with occasion pathologic fracture being the presenting feature.

Location: Distal femur, proximal tibia

Age: Less than 20 years

Radiographic findings: Lytic lesion with periosteal reaction “onion skinning” calcified layering. Can spread up and down the marrow, giving the bone a moth eaten appearance.
SECTION 5

CHAPTER 15

THORACIC
Aspiration Pneumonitis & Pneumonia  
Kenneth J. Woodside, MD

Aspiration Pneumonitis  
Results from aspiration of infectious or caustic material (e.g. gastric acid)  
Contributing factors include the aspirate pH (< 2.5 induces a severe pneumonitis), food particles, volume, and distribution  
Clinical manifestations include apnea, hypotension, dyspnea, cough, frothy sputum, respiratory failure, tachypnea, cyanosis, rhonchi, etc  
Laboratory examination is variable, with a moderate leukocytosis and left shift most common. Hypoxemia may be evident.  
Chest x-ray findings are extremely variable, and do not correlate with clinical outcome. RLL most common.  
Food particles or gastric contents are diagnostic if found on bronchoscopy.  
Treatment Approach  
ABC’s  
Supplemental oxygen  
Bronchoscopy  
Prevent future episodes (NG suction, PPI’s)

Aspiration Pneumonia  
Results from the bacterial content of the aspirate  
Usually anaerobes, but may contain mixed flora  
Sn/Sx include fever, productive cough, tachypnea, cyanosis, rhonchi, etc  
Can progress to lung abscess (look for fluid filled cavity on chest x-ray) or empyema  
Treatment includes early bronchoscopy with aspiration and cultures, respiratory support, and antibiotics.
**PNEUMOTHORACES**

JOSEPH C. BERARDI, MD

**Definition and characteristics**
- accumulation of air in the pleural space.
- may be spontaneous or secondary to disease, trauma, therapeutics or surgical procedures.
- positive pressure develops causing compression of the lung leading to respiratory compromise and hemodynamic collapse

**Primary Spontaneous Pneumothorax**
- occurs in males > females
- occurs between the second and third decade
- those with tall and thin build
- smokers at greater risk (22x in male, 9x in female)
- peak in fall and winter
- unilateral, occurs at rest, acute onset
- ruptures bleb at apex, visceral tear
- risk of recurrence increases with each subsequent episode
- dyspnea, pleuritic chest pain, hyperresonance, decrease to absent breath sounds, tachycardia,
- symptoms may abate

**Secondary Spontaneous Pneumothorax**
- occurs with many diseases, COPD being the most common
- incidence is similar to primary spontaneous pneumothorax, but occurs later in life (60s), likely secondary to increase in pulmonary disease
- results from hyperexpansion of distal airspaces or pleural tear
- dyspnea is more severe, symptoms and pleuritic pain is less when compare to primary pneumothorax, symptoms may not abate

**Iatrogenic Pneumothorax**
- represents the majority of pneumothoraces in hospitals
- leading cause is transthoracic needle aspiration biopsy
- other causes include nasal feeding tubes, thoracentesis, mechanical ventilation, central lines
- may be asymptomatic or develop slowly
- typically discovered secondary to f/u chest x-ray

**Traumatic Pneumothorax**
- visceral pleura tear from penetrating injury or blunt injury with rib fractures

**Tension Pneumothorax**
- occurs when intrapleural pressure exceeds atmospheric pressure
- unidirectional airflow from injured lung or chest wall
- ipsilateral lung collapse
- acute tachypnea, tachycardia, cyanosis, hypotension,
- these are in addition to typical findings of spontaneous pneumothorax
- very common with traumatic pneumothorax
- difficult to detect with underlying lung disease

**Radiographic findings**
- separation of the visceral pleura from chest wall
- end expiratory study may help detect small pneumothorax or lateral decubitus with affected side superior
- should be evaluated by percent lung volume lost
- if equal linear separation a 1cm or less, separation equates to approx 15% volume loss, whereas as 2.0 to 2.5cm separation equates to approx 30% volume loss.
- secondary pneumothorax may be more difficult to evaluate secondary to lung parenchymal disease
-tension pneumothorax may present as hyperexpansion of hemithorax, depression of ipsilateral hemidiaphragm, mediastinal shift as well as tracheal shift
-may occur without these findings i.e. mechanically ventilated patients with underlying lung disease
-associated pneumomediastinum may be present

Management
-goal is to remove air from pleural space, to expand the lung and decrease likelihood of recurrence
-1% resolution per day
-observation may be treatment option in primary and secondary pneumothorax if <15%, pt vitals sign are stable, patient is asymptomatic, chest x-ray shows no other abnormalities, follow up chest x-ray show no progression
-observation less successful in those with secondary pneumothorax
-supplemental oxygen increases rate of absorption 4 fold by washing out nitrogen from bloodstream and increasing the gradient across pleura
-catheter aspiration is a means of treatment for primary spontaneous pneumothorax
-tube thoracostomy (8-16 fr) for those with secondary pneumothorax >15%, primary pneumothorax who failed catheter tx or are symptomatic, traumatic pneumothorax (24-40 fr)
-chemical pleurodesis appropriate tx for recurrent pneumothorax, primary or secondary pneumothorax
-thoracotomy indicated for persistent air leak >7 days, failed pleurodesis, inability to expand lung with tube thoracostomy.
Treatment of Large Air Leak After Trauma
Sharla K. Stovall, MD

I. Pneumothorax
- Occurs in 40-50% of patients with chest trauma
- May be a result of blunt trauma, unrestrained head-on MVA, or penetrating wound into the pleural space
- Asymptomatic chest stab wounds may develop a delayed pneumothorax, check CXR in 6h
- Management is usually accomplished with chest tube insertion with resolution in 5-7 days

II. Persistent Air Leak
- Occurs in 4-23% of injured patients
- May be the result of a mechanical air leak, bronchopleural fistula, parenchymal lung leak, bronchial injury, or esophageal perforation
- May lead to a tension pneumothorax or the formation of intrapulmonary cysts

III. Clinical Findings
- Pneumomediastinum
- Substernal chest pain that may radiate to back
- Subcutaneous emphysema: crepitus over suprasternal notch, chest wall, and neck
- Respiratory distress
- Hemoptyysis
- If large air leak continues greater than 72h despite chest tube or is associated with the inability to re-expand the lung, inability to adequately oxygenate, or the presence of significant hemoptyysis, then surgical intervention is indicated

IV. Management
- Bronchoscopy- assess for bronchial injury or blood in airway. If no injury to airway, then patient can be intubated
- Esophagoscopy or water-soluble contrast esophagram to identify esophageal lesions
- Video-assisted thoracic surgery (VATS) to guide therapy; has been shown to decrease number of days of chest tube
- Thoracotomy – to seal large parenchymal leaks (via stapling or resection), treat bronchial injury, and re-establish normal ventilation. Approach is from posterior lateral chest wall.
FAT EMBOLI SYNDROME
Yvette M. Carter, MD

After bony trauma; prosthetic joint replacement; closed chest cardiac massage
Liver trauma, extra-corporeal oxygenation; liposuction, bone marrow transplant,
acute hemorrhagic pancreatitis
Sx: acute respiratory failure (resp insufficiency by 48-72h post injury)
Decreased PaO2 (not reversed by supplemental O2)
Altered mental status (precede lung symptoms by 6-12hr)
Petechiae-head, torso, sclera, neck, skin folds, oral mucosa
Disappears after 12-24hr
Diff dx: fat globules in peripheral circulation and lung parenchyma
After long bone fx or multiple trauma
Incidence: 0.5-2% isolated long bone fx
5-10% multiple long bone or concomitant pelvic fx
Dx: Physical exam
CXR: bilateral aleolar infiltrates
Labs: decreased HCt, platelets, Ca²⁺, albumin
increased lipase
Pathology: release of marrow substances and fat from
damaged marrow→intravascular→pulmonary-capillary bed
Histology: petechial hemorrhages of cortical white matter, brainstem and spinal cord
Rx: early surgical immobilization and fixation of fractures
Fluid resuscitation
Transfusion
Ventilatory support
TPN for nutrition
Solitary Lung Nodule
Farin W. Smith, MD

Basics
- **Definition** - single lesion, less than 3 cm of size, surrounded at least 2/3 by parenchyma and not touching hilum or mediastinum, and w/o atelectasis or pleural effusion
- 33% are malignant (if greater than 50 years old, 50% are malignant)
- Pt’s present w/ a wide range of symptoms from asymptomatic to cough, dyspnea, hemoptysis, chest pain, recurrent pneumonia, hoarsness, fever, weight loss, bone pain, weakness, HA, confusion, atxia……
- Differential diagnosis – Foreign bodies, pneumonia, TB, systemic mycoses, autoimmune disease, metastatic disease

Work-up
- **H&P, CXR, CT chest through adrenals**
- **Tissue diagnosis** – procedures should be used w/ the least invasiveness and highest diagnostic yield based on location of lesion
  1. Central 1/3 – use bronchoscopy w/ FNA
  2. Periferal 2/3 –
     - >1.5 cm Fluoroscopic FNA
     - <1.5cm CT FNA
  3. Abuts pleura – U/S FNA
  4. If above are negative after 2 attempts
     - 2-3 cm form pleura – VATS
     - Deeper – muscle sparing thoracotomy and wedge bx
- **Nodal Evaluation** – procedures should be used w/ least morbidity and mortality based on location
  1. Anterior mediastinum – CT FNA
  2. Middle mediastinum – CT FNA
  3. Sub-carinal - EUS FNA
  4. Posterior mediastinum – EUS FNA
  5. AP Window – EUS or CT FNA depending on size

Treatment
- **Stage I** – resection
- **Stage II** – resection w/ lymph node mapping
- Exceptions to resection
  1. Mass unchanged for greater than 2 years on serial CXR
  2. Benign patterns of calcification (i.e. hamartoma)
  3. Obvious inflammatory/infectious process (i.e. TB)
  4. High operative risk
  5. Small cell carcinoma is suspected
- For noncancerous diagnosis, lobectomy is recommended
SECTION 5

CHAPTER 16

CARDIAC
Pericardial Tamponade: Diagnosis and Treatment
Michael K. Obeng, MD

Pericardial tamponade is an increase in intra-pericardial pressure secondary to accumulation of fluid or blood in the pericardial sac.

Common causes include: Trauma, cardiac surgery, neoplastic dz, uremia, and idiopathic pericarditis.

The pathophysiology encompasses:
• Filling of the pericardial sac
• Elevation of the intrapericardial pressure
• Decline in the transmural filling pressures
• Decrease cardiac output (CO) \( CO = SV \times HR \)
• Reduction in the stroke volume (SV)
• Compensatory increase in adrenergic tone
• Heart rate (HR) increases
• Compensatory mechanism is only temporary
• Drop in systemic arterial pressures
• Decrease coronary perfusion circulation
• Impaired perfusion of vital organs

The diagnosis is mainly based on clinical findings, signs and symptoms include:
• Classic signs and symptoms (Beck’s triad, only present in 1/3 of cases)
  – Hypotension
  – Elevated venous pressure (distended neck veins)
  – Decreased heart sounds (muffled heart sounds)
• Other signs and symptoms include
  – Tachycardia
  – Tachypnea
  – Pale, cool, clammy skin
  – Oliguria
  – Pulsus paradoxus (pathognomonic)
  – Kussmaul’s sign
  – Electrical alternans on EKG
(abscence of distended neck veins does not rule out a dx of pericardial tamponade)

Diagnostic modalities include:
• Pericardiocentesis- diagnostic and therapeutic, 15% false negative results.
• Chest X-rays- unreliable, cardiomegaly and mediastinal widening, requires about 250cc of blood/fluid to see changes on cardiac silhouette.
• Electrocardiogram- unreliable, electrical alternans, non-specific reduction in QRS and flattening T-waves
• Echocardiogram- most reliable, can detect as little as 20 cc of fluid

Treatment includes:
1. Standard initial resuscitative measures (ABC’s, fluid replacement)
2. Pericardiocentesis- only in stable patients, may be temporary.
3. Pericardial window- in the OR
4. Thoracotomy- left thoracotomy preferred over median sternotomy.
Valvular Heart Disease
Dirk C. Johnson, MD

Diagnosis: cardiac catheterization and echocardiograms are the diagnostic tools for all heart valve disease.

- **Aortic valve**
  - **Aortic Stenosis**
    - Left ventricle (LV) outflow obstruction at subvalvular, valvular, or supravalvular levels
  - **Pathology**
    - usually the result of degeneration/calcification of normal or bicuspid valve
    - can develop as sequelae of rheumatic fever
  - **Poor prognostic factors**- angina< syncope< congestive heart failure
  - **Signs/symptoms**
    - Systolic murmur
    - Pulsus parvus et tardes
    - Valve area <1-0.7 cm² are usually symptomatic
  - **Treatment** (when symptoms and/or valve area < 0.7cm² or gradient > 50mm Hg)
    - Aortic valve replacement (AVR)
    - balloon dilation in poor candidates

- **Aortic Insufficiency**
  - **Etiology**
    - Rheumatic heart disease (RHD) 50% of cases
    - Myxomatous degeneration, endocarditis, ascending aortic dissection, Marfan’s Syndrome, Syphilis, ankylosing spondylitis, hypertension
  - **Signs/symptoms**
    - Diastolic Murmur
    - Exercise intolerance, atypical chest pain, DOE, palpitations
  - **Treatment**
    - Medical Afterload reduction, diuretics,
    - Surgical-AVR when medical treatment fails or when LV enlargement (concomitant CABG PRN)

- **Mitral Valve**
  - **Mitral Stenosis**
    - **Etiology**
      - usually RHD although history is often hard to verify
      - Other causes: collagen vascular disease, amyloidosis, and congenital stenosis
    - **Signs/symptoms**
      - Diastolic murmur with opening snap, loud S1,
      - DOE, orthopnea, hemoptysis, and peripheral emboli
    - **Symptoms develop when valve area is <0.5-0.8 cm²**
  - **Treatment**
    - Mitral valve replacement or repair (MVR)
    - 5-year survival without surgery 50-60%

- **Mitral Regurgitation**
  - Acute or chronic abnormality
  - **Etiology**
    - Dysfunction of the chordae tendineae, papillary muscles, anomaly of the annulus, or with endocarditis
    - Can occur following an acute MI
  - **Signs/symptoms**
    - Apical murmur
    - DOE, fatigue, palpitations
  - **Treatment** (when patient can tolerate it for moderate to severe disease) MVR

- **Tricuspid Valve insufficiency**
  - **Etiology**
    - usually functional dilation of annulus secondary to pulmonary hypertension
    - RHD, bacterial endocarditis, carcinoid tumors, blunt trauma

- **Pulmonary Valve**
  - Rarely significant clinically
VENTRICULAR SEPTAL DEFECT
Interventricular septum infarction → rupture
Location: 75% anterior/apical
LAD occlusion
25% posterior
assoc. with inferior MI
±mitral valve incompetence (papillary muscles)
RCA or circumflex artery
Cause: lack of collateral circulation
Timing: 2 weeks post-MI
Symptoms: pansystolic murmur
Worsening CHF
Dx: color-flow Doppler-site of VSD, size of L → R shunt
Swan-Ganz catheter-monitor pulmonary artery pressures
Cardiac catheterization-quantitate L → R shunt
Measure PA pressures and resistances
Px: 75% survive first 24h
50% alive at 1 week
Rx: emergency CAG + VSD closure on bypass
Left ventriculotomy and double-patch with Dacron
In hospital mortality after repair 20-30%

MITRAL VALVE REGURGITATION
Incidence: 40% detectable by echo
3.5% moderate or severe MR with CHF
**often mild MR and resolves prior to discharge
Cause: epicardial arteries obstruct → decreased supply to penetrating vessels to
Papillary muscles
Location: posterior = 3-6X anterior muscle
Types: Acute severe MR
0.4-0.9%
rupture of papillary muscle trunk
pulmonary edema, CHF
**surgical emergency
rupture of papillary muscle tip
s/sx: chest pain, dyspnea, pulmonary edema, hypotension,
holosystolic murmur → L axilla
right heart cath: elevate PA pressures, prominent V waves
decreased SvO2, decreased CO
Px: severe CHF, # of comorbidities, reduced EF, # diseased
coronary arteries
In hospital mortality 10-20%
Rx: IABP (for afterload reduction), prosthetic valve
Chronic MR
S/sx: pulmonary edema and SOB episodes
+ angina
Rx: elective MV repair
Elective MV replacement + CABG (5-7% mortality)
CABG
LEFT VENTRICULAR ANEURYSM
Large area of LV dyskinesia
Incidence: 7.6%
Timing: after transmural infarct
Cause: acute LAD or dominant RCA occlusion
   Anterior infarct (88%)
   Inferior infarct (12%)
Systolic bulging and thinning of the infarct after loss of systolic contraction in the infarct region, with preserved surrounding region
Rx: resection
Px: in hospital mortality-9%
   10y survival-57%

CARDIOGENIC SHOCK
85-90% mortality without Rx
>40% functioning LV mass lost
incidence: 7.5% of acute MI patients
s/sx: SBP<80mmHg with adequate filling pressures
   peripheral vasoconstriction
   cerebral vascular hypoperfusion
   decreased UOP, CI (<1.8L/min/m²)
Px: in-hospital mortality-80%
Rx: beta blockers, digoxin, PTCA
   CABG
A. **General**
1. Congenital heart disease accounts for 0.8-1.0% of all live births
2. Majority of lesions divided into cyanotic vs noncyanotic heart defects

B. **Noncyanotic**-left to right shunt, increased pulmonary blood flow → pulmonary congestion/CHF
1. **PDA**: 1/2000 births
   - Ductus arteriosus diverts blood away from the pulmonary system to the aorta: Failure to close within 3 months considered pathologic
   - "machinery" murmur in neonates or pulmonary congestion, FTT or ventilatory difficulties
   - in premature infants- surgery after 3 failed indomethacin treatment
   - in full term infants- surgical PDA closure within 6 months; open approach via left posterolateral thoracotomy vs. transcatheter devices

2. **Atrial Septal Defects**: most common cardiac anomaly
   - Defects caused by failure of septum primum to develop or regression of interatrial folds at superior/inferior vena cava. PFO allows the circulation to function
   - Diagnosis in the young by murmur on PE; in older patients with sx of CHF, exercise intolerance, and arrhythmias
   - Closure indicated in all with sx disease or children with significant ASD
   - Open surgery vs percutaneous transcatheter device

3. **Atrioventricular (AV) Canal Defects**
   - Fibrous center of the heart is deficient and the conduction system is in abnormal position
   - Three components criteria complete: (1) AV septal defect (2) interventricular septum (3) abnormal AV valve
   - Partial defects-surgery at preschool age
   - Complete defects- ideal age for repair related to risk for developing pulmonary vascular disease

4. **Ventricular Septal Defects**
   - 1-2/1000 live births
   - Failure of ventricular septum to completely close
   - Clinical presentation depends on size of shunt and PVR
   - 80% close spontaneously by 1 month of age
   - Prosthetic patch closure

C. **Cyanotic**- right to left shunt, resulting in decreased pulmonary flow → cyanosis

1. **Tetralogy of Fallot**
   - Defect resulting from anterior malalignment of infundibular septum giving rise to four components: VSD, overriding aorta, right ventricular obstruction, RVH
   - Can present with sudden death due to arrhythmias, syncope, CHF
   - Hypoxic spells, cyanosis, clubbing, SEM and CXR with boot shaped heart
   - Conservative-knee to chest, oxygen, sedation, and volume expansion
   - Palliative repair for those not able to tolerate complete repair: systemic-pulmonary artery shunt (Blalock-Taussig)
   - Complete: repair of VSD, relief of RVOTO with muscle resection

2. **Truncus Arteriosus**
   - Single arterial trunk arises both ventricles from which the coronary and pulmonary arteries originate; associated with VSD
   - Complete repair recommended in neonatal period for severe CHF
   - Mortality depends on the associated conditions
3. Total Anomalous Pulmonary Venous Return (TAPVR)
- Partial or complete
- Most common anomalies are:
  - right upper pulmonary veins draining to the superior vena cava
  - drainage of the right-sided pulmonary veins to the inferior vena cava
  - isolated left upper pulmonary veins draining to left innominate vein via a vertical vein
- Diagnosis depends on the magnitude of the associated shunt, degree of systemic desaturation, and the presence or absence of pulmonary venous obstruction
- Treatment: redirecting of the pulmonary venous return with closure of the ASD or reconnecting the pulmonary veins to the left atrium and division of the systemic venous connection
- Surgery is low risk

4. Tricuspid Atresia
- Rare, 0.3 to 3.7% of congenital heart patients
- Absence of communication between the RA and the RV
- Associated with ASD, enlargement of the MV and LV, and varying degree of RV hypoplasia
- Treatment: patients with inadequate pulmonary blood flow will require shunting with unobstructed pulmonary system, a pulmonary artery band is applied early in life
- Most neonates undergo early balloon atrial septostomy prior to other treatments to restore pulmonary blood flow

5. Transposition of the Great Vessels
- 5-8% of all congenital cardiac malformations
- Defined as an aorta arising from an anatomic right ventricle and the pulmonary artery arising from an anatomic left ventricle
- Associated with VSD, coarctation, and left ventricular outflow obstruction
- Simple defect: interventricular septum is intact or almost intact, cyanosis profound after birth with closure of PDA, survival depends on size of ASD
- Complex defect: VSD(s) allow mixing at an additional level with a tendency to higher systemic saturations and CHF
- Treatment: left ventricle must be able to support the increased systemic workload
  surgery should be undertaken prior to 3 months
- "Gold Standard" is the arterial switch operation: great vessels are transected and the orifices and the course of the coronary arteries are inspected and reimplanted into the aorta; continuity between the aorta and the LV and the pulmonary artery and the RV is reestablished
Cardiopulmonary Bypass and Blood Flow
David B. Loran, MD

I. Simple Circuit
   a. Venous catheter $\rightarrow$ blood reservoir $\rightarrow$ pump $\rightarrow$ oxygenator $\rightarrow$ heat exchanger $\rightarrow$ filter $\rightarrow$ arterial catheter
   b. Normally blood flow (BF) is pulsatile, but in cardiopulmonary bypass (CPB) it is non-pulsatile

Consequences on Organ Systems
   - Brain
     a. No change in total BF or distribution of flow in brain
     b. Oxygenation of tissue is not changed
     c. Mean pressure should be kept $>$50mmHg
     d. Slight increase in cerebral edema due to effects of hemodilution and reduced colloid osmotic pressure
   - Lungs
     a. Not perfused directly on CPB, lungs are excluded from the circuit
     b. Following CPB there is a slight increase in airway and pulmonary vascular resistance, decrease in lung compliance
     c. Easily tolerated by most patients
   - Kidneys
     a. CPB does not change total renal BF but does change the distribution of flow by decreasing cortex perfusion
        - Causes decreased sodium, creatinine, and free water clearance
     b. Hypothermia reduces renal BF and increases renal vascular resistance
     c. Trauma to RBC’s releases vasoactive substances and free hemoglobin which reduces renal BF
     d. Microemboli debris affect cortex to further alter distribution of flow
     e. GFR and urine output fall during CPB
   - Heart
     a. Gets perfused during CPB via coronary arteries
     b. Total BF and distribution of flow are not altered
     c. Myocardial and subendocardial perfusion is not affected
   - Gut Perfusion
     a. Overall BF is increased with CPB
     b. Complications of intestinal ischemia and pancreatitis are thought to be due to microemboli
SECTION 5

CHAPTER 17

VASCULAR
Heparin
Juan C. Escalon, MD

I. Mechanism of Action
A. Heparin binds to anti-thrombin III (ATIII) in a 1:1 ratio. This complex then binds to thrombin and other serine proteases.
B. The heparin-ATIII complex inhibits IIa, IXa, Xa, XIa, and XIIa.
C. A dose of heparin is cleared from the bloodstream in 6 hrs.
D. Heparin affects both PT and PTT, but is most sensitive for PTT.
E. Heparin is a strongly negatively charged molecule.

II. Low Molecular Weight Heparin
A. LMWH binds to ATIII and Xa.
B. Interacts with Xa to inhibit coagulation.
C. Has longer half-life than heparin
D. Approved for DVT prophylaxis, treatment of acute DVT, pulmonary embolism, prevent complications of unstable angina and Non-Q wave MI’s.

III. Side Effects
A. Osteoporosis
B. Skin reactions
C. Alopecia
D. Hyperkalemia
E. Priapism
F. Heparin induced thrombocytopenia

IV. Heparin Induced Thrombocytopenia
A. Forms:
   1. Type I
      a. decrease in platelet count that has no clinical significance
      b. becomes apparent 2-3 days after initiation of heparin therapy
      c. resolves with d/c of heparin; no long-term sequela
      d. not associated with specific antibody
   2. Type II
      a. can have serious clinical significance
      b. becomes apparent 4-5 days after heparin therapy initiated
      c. most are asymptomatic but platelet count can fall <100,000
      d. linked to serious thrombotic complications
      e. Resolves in 5-15 days if heparin stopped
B. Incidence
   1. occurs in 1-3% of patients getting heparin
   2. incidence is lower when using LMWH
   3. not related to route of administration (SC vs. IV)
   4. associated more often with bovine derived heparin
C. Pathophysiology: caused by IgG Ab that activates platelets through Fc receptors
   1. the Ab initiates a cascade of platelet activation and aggregation in the presence of heparin
   2. the Ab does not initiate the full clotting cascade
   3. Platelet Factor -4 is a surface adhesion protein on platelets
   4. the Ab + Heparin increases the PF4 production and platelet adhesion
   5. this dynamic process forms a platelet meshwork leading to clot formation
D. Histology:
   1. “onion skin” appearance microscopically
   2. decreased fibrin content because it does not initiate the clotting cascade
   3. increased IgG
E. Diagnosis:
1. Clinically: highly suspicious if platelets fall after heparin
2. Testing:
   a. check for heparin induced antibodies
   b. platelet aggregation test
   c. (14)C-serotonin release assay
   d. ELISA to identify the anti-heparin/platelet factor 4 complex (most sensitive)

F. Treatment
1. STOP HEPARIN IMMEDIATELY
2. Argatroban - synthetic anti-thrombin, short half life, no cross reactivity for HIT antibodies, potent AT activity, metabolized in liver
3. Danaparoid - anticoagulant with rapid anti-Xa effects and long half-life, approximately 25 hours, cross-reacts with HIT antibodies in vitro
4. Lepirudin - potent thrombin inhibitor, no cross reactivity with HIT antibodies, followed with PT/INR, metabolized by the kidney
5. ASA - only a modest inhibitory effect in platelet activation

V. Protamine Sulfate
   A. Protamine is a strongly positively charged molecule.
   B. Neutralizes the effects of heparin by binding the heparin molecule.
   C. Dose is 1mg of protamine sulfate for each 100u of heparin.
Carotid Disease
Robert P. Thomas, MD

Background
- 500,000 new strokes/year in USA
- 30% (or more) due to carotid disease
- Annual stroke rate for symptomatic patients: 2-5%
- Progressive occlusion is unpredictable

Symptomatic Carotid disease
- TIA or Stroke: focal neurologic deficit (not vertigo or dizziness)

North American Symptomatic Carotid Endarterectomy Trial [NASCET]
- Patients selected had suffered TIA or stroke
- Three categories if internal carotid (ICA) stenosis
  - 0-29%
  - 30-69%
  - 70-99%
- Endpoint was stroke (ipsilateral)
- Data
  - >=70% stenosis: Medical therapy (ASA plus HTN, DM, smoking control) = 26% rec. stroke
    Medical therapy + CEA = 9% rec. stroke * CEA prevents stroke in severe stenosis
  - 50-69% stenosis: Medical therapy = 23% rec. stroke
    Medical therapy + CEA = 16% * CEA prevents stroke, but benefit is less
  - Less than 50%: CEA no benefit

Symptomatic Carotid disease
- Greater than 60% stenosis, no symptoms

Asymptomatic Carotid Atherosclerosis Study [ACAS]
(JAMA 1995; 273: 1421-8)
- 1662 patients: 60-99% stenosis, 40-79 y.o.
- Endpoints: Stroke and operative death
- Greater than 60% stenosis: Medical therapy = 11% stroke rate VS. Medical + CEA = 5.1% * CEA prevents stroke in severe stenosis/asymptomatic patients

Summary
- CEA recommended for asymptomatic and symptomatic patients with 70% ICA stenosis
- CEA is beneficial in symptomatic 50-69% stenosis, and asymptomatic patients if stroke rate from operative can be kept low (1-2%)
Suggested Management of Symptomatic Carotid Disease

Stroke, TIA or Amaurosis
\[ \downarrow \text{CT or MRI Brain} \]
Cardiac Evaluation
ECG & ECHO
Cardio-Emolic Etiology
\[ \rightarrow \text{Carotid Duplex*} \]
\[ \rightarrow \text{Ulcerated Plaque} \]
\[ \downarrow \text{or} \]
\[ \rightarrow \text{Platelet Inhibition} \]
\[ \rightarrow \text{Anticoagulate (+ Platelet Inhibition)} \]

\[ \text{< 50%} \]
\[ \rightarrow \text{Platelet Inhibition} \]
\[ \rightarrow \text{Risk Factors Modification} \]
\[ \rightarrow \text{Platelet Inhibition} \]

\[ \text{> 50 - 99%} \]
\[ \rightarrow \text{Occlusion} \]

\[ \rightarrow \text{Angio vs. MRA} \]

\[ \rightarrow \text{CEA + Platelet Inhibition} \]

\[ \rightarrow \text{Good Quality Duplex} \]
\[ \rightarrow \text{No**} \]
\[ \rightarrow \text{YES} \]

* Treatment on basis of duplex alone assumes a good quality examination with conclusive findings. Others should have angio or MRA.

** Angiogram or MRA confirmation of occlusion should receive platelet inhibition.

Suggested Management of Asymptomatic Carotid Disease

Positive Risk Factors
Bruit
\[ \rightarrow \text{Carotid Duplex} \]
Good Quality Duplex with Conclusive Findings*
\[ \rightarrow \text{Yes} \]
\[ \rightarrow \text{< 50% Stenosis} \]
\[ \rightarrow \text{50-69% Stenosis} \]
\[ \rightarrow \text{70-99% Stenosis} \]
\[ \rightarrow \text{Occlusion} \]
Risk Factor Modification
Platelet Inhibition

\[ \rightarrow \text{Repeat Duplex 1-2 years} \]
\[ \rightarrow \text{Repeat Duplex 6-12 months} \]
Endarterectomy

* Confirmatory MRA or arteriogram required in patients with an inconclusive duplex.
Abdominal Artery Aneurysms
Chance L. Irwin, MD

I. Definition
A. An arterial aneurysm is defined as a permanent, localized enlargement of an artery to more than 1.5 times its expected diameter.

II. Pathogenesis
A. Genetic (not the sole cause)
   1. Familial clustering - 10-20% of first degree relatives
   2. Marfan’s - defect in fibrillin
   3. Ehlers-Danlos type 4 - procollagen type III
   4. Decreased type III collagen in the aortic media of familial aneurysms
   5. Polymorphisms on the gene for pro-alpha 1 (III) chain of type III collagen
   6. Haptoglobin alpha allele
   7. Abnormalities on the long arm of chromosome 16

B. Proteolytic
   1. Primary determinants of aortic structural integrity and stability are musculoelastic fascicles in the media and the collagen scaffold structure of the adventitia (degradation of the above results in aneurysmal dilatation)
   2. Marked decrease in the quality of elastin in the aneurysm wall while the quality of collagen remains the same
   3. Increased and altered metalloproteinases, with decreased TIMP activity, resulting in vascular remodeling with decreased elastic potential.

C. Atherosclerosis
   1. Most common etiology
   2. Occurs in the elderly, mostly males, and smokers
   3. Focal intimal thickening encroaching on the lumen and consequent compensatory arterial dilation
   4. Remodeling occurs by thinning of the media underneath the plaque and loss of normal arterial architecture

III. Epidemiology
A. Distribution
   1. Most commonly in the infrarenal aorta with sparing of the segment just below the renal arteries (juxtarenal aneurysms)
   2. Suprarenal
   3. Thoracoabdominal (2%)- involving the abdominal aorta, celiac, superior mesenteric, and renal arteries
   4. Iliac arteries are involved in 40% of patients with abdominal aortic aneurysms (AAA)- 90% common iliac and 10% hypogastric artery involvement
   5. External iliacs are almost never involved

B. Prevalence of AAA
   1. 1.8-6.6% at autopsy
   2. Large autopsy study- prevalence was 4.3% in men, increasing rapidly after the age of 55 and peaking at 80; prevalence in women was 2.1%, increasing after 70 and continuing past 90 y/o
   3. Up to 40% of those with infrarenal AAA have an aneurysm elsewhere in the aorta
   4. Incidence of newly diagnosed aortic aneurysms is 21 in 100,000 patient years
   5. Average age is 75 y/o
   6. Male-to-female ratio of 8:1
   7. White males have higher prevalence than black males or females
   8. Smoking is the most important risk factor and is associated with 78% of aneurysms discovered on screening
   9. 10-20% and 11.6 fold increase in the relative risk in first degree relatives of patients with AAA- familial aneurysms affect patients at a much younger age and more women affected
   10. Rupture is cause of death in 1.2% of males and 0.6% of females in the US
   11. Rupture is the 13th most common cause of death in the US- 15,000 annually

IV. Natural History
A. Enlarge and rupture
B. Only 50% arrive alive after rupture, of those, 24% or more die before surgery and 42% die after operation- overall mortality rate of 78-94%
C. Most important factor- cross-sectional aneurysm diameter
D. Risk of rupture
   1. 1-3% per year for 4-5cm
   2. 6-11% per year for 5-7cm
   3. 20% per year for >7cm
   4. <4cm very low risk
   5. Hypertension, COPD and female gender have increased risk
E. Enlarge at an average rate of 0.4cm per year (variable)
V. Clinical Presentation
   A. Most asymptomatic before rupture
   B. Most discovered on routine PE with palpation of a pulsatile abdominal mass or imaging of an unrelated problem
   C. 80% identified incidentally by abdominal US, CT, MRI, or plain film
   D. Can be associated with vague abdominal and back discomfort
   E. Spinal erosion can cause back pain
   F. Large aneurysms can cause early satiety and occasional vomiting
   G. Actively expanding aneurysms produce severe, deep back pain or abdominal pain radiating to the back
   H. <5% have evidence of embolization, usually small, to distal arteries of LE
   I. As many as 12% present for the first time with acute rupture
   J. 5% present with nonspecific, idiopathic retroperitoneal inflammation and fibrosis

VI. Diagnosis
   A. Physical exam is useful
   B. Occasionally found on plain abdominal or a lumbar spine radiograph by characteristic "eggshell" pattern of calcification- not reliable for diagnosis or exclusion
   C. Abdominal US- most widely used noninvasive test for diagnosis
   D. CT Scan- most precise, clearly demonstrates the size and extent and relation to renal and iliac vessels
   E. MRI- rival CT quality, can use MR angiography, useful for planning and follow-up of endovascular repair
   F. Arteriography- reliable for lumen diameter and branch vessel disease, size assessment is unreliable

VII. Preoperative Evaluation
   A. Cardiac Evaluation- most important
      1. Uncorrected CAD raises risk of death from <3% to 5-10%, risk of fatal MI to 4.7% and risk of nonfatal MI to 16%
      2. No CAD- perioperative mortality rate is 1.1%
      3. After coronary revascularization the mortality rate is 0.4%
      4. History, PE, and EKG do not identify all at risk so noninvasive tests are used such as dipyridamole thallium cardiac scintillation scan and dobutamine stress echo
      5. Significant CAD- cardiac catheterization or CABG
      6. COPD and impaired renal function are other important risk factors

VIII. Selection of Patients for Open Surgical Repair
   A. Most with aneurysms >5cm and have life expectancy of >2years and are good surgical candidates
   B. If >6-7cm, higher surgical risk patients can be considered
   C. Between 4-5cm considered if evidence of >0.5cm aneurysmal enlargement over a 6 month period
   D. Evidence of rapid expansion, tenderness over the aneurysm, and back or abdominal pain need urgent repair

IX. Open Technique
   A. Transperitoneal or retroperitoneal approach under GETA

X. Endovascular Aortic Aneurysm Repair
   A. Prosthetic graft is introduced through the femoral arteries and fixed in place with self-expanding or balloon stents
   B. Candidates- proximal infrarenal neck at least 1-2cm in length and non-tortuous common iliac arteries
   C. No long-term follow-up data

XI. Results and Complications
   A. Preoperative evaluation has decreased mortality rates for both open (0-5%) and endovascular repair (1-3%)
   B. Overall mortality rate for elective repair is 10-30%
   C. Complications
      1. Most common is myocardial ischemia in 3-16% usually within 2 days of surgery
      2. Myocardial infarction is the most common cause of post-operative death
      3. Second most common is mild renal failure in 6% of elective repairs due to renal hypoperfusion, contrast nephropathy, and atheroembolism
      4. Post-operative pneumonia in 5%
      5. Post-operative bleeding occasionally from anastomotic suture line, venous injuries, and coagulopathy from intraoperative hypothermia or excessive blood loss
      6. Lower limb ischemia- emboli or graft thrombosis
      7. Post-operative paralytic ileus for 3-4 days
      8. Colon ischemia after 1% of repairs
      9. Paraplegia in 0.2%
      10. Sexual dysfunction- impotence or retrograde ejaculation
      11. Late complications are rare- pseudoaneurysm and graft rejection
   D. Five year survival rate is 67% with a range of 49-84%
   E. Mean duration of survival is 7.4 years
   F. Endovascular complications
      1. Endoleak-9-44%
      2. Graft migration
      3. Stent graft occlusion
Splenic Artery Aneurysms
- Comprise 60% of all reported visceral artery aneurysms
- Male:Female Ratio 1:4
- Etiology: medial fibrodysplasia, multiple pregnancies, portal hypertension with splenomegaly, chronic pancreatitis and penetrating trauma
- Most are saccular and occur at vessel branchings.
- Diagnosis: abdominal radiographs show vascular calcifications with a “signet ring” appearance, US, CT and MRI.
- Symptoms: Often asymptomatic, but can have LUQ or epigastric pain; a minority of patients may have vague abdominal discomfort; RUQ pain may indicate hemorrhage.
- Rupture occurs in 2% of cases with 25% of ruptures occurring in mortality.
- Treatment: splenectomy was the most common treatment in the past, now ligature obliteration or excision is preferred.

Hepatic Artery Aneurysms
- Comprise 20% of all visceral artery aneurysms
- Male:Female Ratio 2:1
- Etiology: Arteriosclerosis, medial degeneration, trauma and infection
- Usually solitary, being extrahepatic in 80% and intrahepatic in 20%
- Fusiform when less than 2cm in diameter and saccular when larger
- Diagnosis: Usually found as incidental findings on CT scan and US
- Symptoms: usually asymptomatic, but can have RUQ or epigastric pain, severe abdominal discomfort, obstructive jaundice
- Incidence of rupture around 20% with 35% of ruptures leading to mortality
- Treatment: aneurysmectomy with or without arterial reconstruction, hepatic resection, transcatheter aneurysm obliteration.

Others in general
- Majority affect patients older than 50 years of age
- Each comprise <5% of all visceral artery aneurysms.
- Etiology: infection related to bacterial endocarditis, medial degeneration, periarterial inflammation and trauma.
- Diagnosis: Arteriography, sometimes US or CT, usually found incidentally
- Symptoms: Usually asymptomatic or with vague abdominal discomfort.
- Treatment: aneurysmectomy with reconstruction; ligation if collateral circulation is adequate.

Specifically:

Gastric and Gastroepiploic Artery Aneurysms
- Symptoms: Usually present as emergencies without preceding symptoms.
- Rupture occurs in 90% of cases and leads to mortality in 70%.

Pancreaticoduodenal, Pancreatic and Gastroduodenal Artery Aneurysms
- Etiology: Pancreatitis-related vascular necrosis or vessel erosion by an adjacent pseudocyst; medial degeneration, traumatic lesions.
- Rupture occurs in 50% of cases; overall mortality in rupture is 25%.

Superior Mesenteric Artery Aneurysms
Celiac Artery Aneurysms
Jejunal, Ileal and Colic Artery Aneurysms
Peripheral Vascular Aneurysms
Carlos A. Murillo, MD

1) Lower Extremity
   a. Two Types: popliteal and femoral
      i. Popliteal aneurysms
         1. Account for 70% of all peripheral aneurysms
      ii. Femoral aneurysms
         1. Account for 20% of all peripheral aneurysms not involving the aortoiliac arteries
   b. Etiology:
      i. Unknown etiology
         1. Repeated knee flexion; turbulence beyond a relative stenosis at the tendinous hiatus of the adductor magnus?
      ii. Degenerative type of aneurysms
      iii. Demographics
         Males 20-30:1 females
         Mean age of presentation 65
         >50% are bilateral
      iv. 75% of femoral and 33% of popliteal are associated with an aortic aneurysm
   c. Symptoms
      i. Mostly asymptomatic
      ii. Most important manifestation is distal embolization
         {25% of popliteal, 10% of femoral}
      iii. Most common symptom is ischemia
         1. Limb-threatening in 44% of cases
      iv. Thrombosis common in 40% of popliteal and 1-16% of femoral cases
      v. Nerve compression and compression of adjacent veins with resulting edema and/or venous thrombosis
   d. Diagnosis:
      i. Physical examination:
         1. Femoral aneurysms are easier to palpate in most cases
         2. Popliteal are much harder to appreciate due to the relative deep location of the lesion, unless abnormally pronounced; easily mistaken for Baker cysts or tumors.
      ii. Duplex ultrasonography examination is the best initial study
      iii. Arteriography is important to show the extent of the aneurysm, the patency and quality of runoff vessel and detect distal embolic disease; Search for other associated aneurysms
   e. Treatment:
      i. Indications: acute ischemia from acute occlusion, distal emboli and transverse diameter (2.5 cm in popliteal and 2 cm in common femoral aneurysms)
      ii. Exclusion of the aneurysm and restoration of distal blood flow
      iii. Femoral aneurysms are often replaced with prosthetic graft
      iv. Popliteal aneurysms are replaced with autogenous material (greater saphenous vein)
      v. Resection of the aneurysm in unnecessary
      vi. Thromboembolectomy or thrombolysis is performed when the aneurysm is thrombosed or there is evidence is distal emboli
      vii. Endovascular treatment is being evaluated
   f. Complications:
      i. Rupture occurs 1-14% in femoral, <5% in popliteal aneurysms
      ii. Death is rare
iii. Asymptomatic patients: limb-salvage rate is 90-98%
iv. Symptomatic patients: graft patency is 59-85%; limb-salvage rate is 70-80%.
v. Approximately 25% of patients with distal thromboembolism from femoral popliteal aneurysms lead to amputation due to progressive chronic occlusion of the runoff vessels before thrombosis

2) Upper Extremity Aneurysms
   a. Rare compared to other peripheral aneurysms
   b. Most common: Subclavian artery aneurysms
      i. Caused by atherosclerosis (proximal), compression of the thoracic outlet (distal), and trauma
      ii. 50% are associated with aortoiliac and other peripheral aneurysms
      iii. Symptoms: nerve compression (pain, impaired motor or sensory function, hoarseness, resp. insufficiency – recurrent laryngeal, brachial plexus nerves or tracheal compression), TIA, strokes from thromboembolism.
   iv. Diagnosis: duplex ultrasonography or CT; arteriography to show extent of aneurysm, thromboembolic disease, and relation to vertebral artery and carotid artery (right side)
   v. Treatment:
      1. Aneurysm resection and arterial interposition graft.
      Right proximal: media sternotomy with incision into the supraclavicular fossa
      Left proximal: left anterior thoracotomy
      Mid and distal: Supra- and infraclavicular incision, possible resection of the mid-clavicle
      2. Balloon thromboembolectomy if recent embolic events occurred
      3. Reimplantation of the vertebral artery as necessary.
   c. Axillary
      i. Aneurysm and pseudoaneurysms are associated with trauma (blunt or penetrating), or congenital (rare)
      ii. Sx: related to nerve compression and ischemia from thrombosis/thromboembolism
      iii. Treatment: resection of the aneurysmal artery and primary repair, and possible repair with a short interposition vein graft
   d. Ulnar artery
      i. Associated with repeated trauma to the dominant hand, i.e. “hypothenar hammer syndrome”
      ii. Complications: distal thromboembolism, rest pain, numbness, cyanosis, and gangrene of the hand and digits (3rd and 4th), and ulnar nerve compression
      iii. Treatment: resection of the aneurysm and microvascular reconstruction with a vein interposition graft
Angioplasty
Eric C. Feliberti, MD

I. Definition
- Endovascular balloon used to fracture atherosclerotic media, stretching the muscle fibers and irreversibly stretching the adventitia.
- Ideal for *focal stenosis in large arteries* – not used for occlusion or small arteries.

II. Technical
- Balloon length must be longer than lesion so there is contact with normal vessel proximally and distally. This limits fissuring.
- Balloon is inflated to 4-12atm.
- Heparin is given just prior to angioplasty.
- Considered successful if residual stenosis < 30%.

III. Site specific angioplasty
   A. Common iliac artery
      - Ideal since it is a large artery, stenosis tend to be focal, and there is high flow.
      - Can also be used to increase inflow in infrainguinal disease.
      - 2yr patency – 81%; 5yr patency – 72%.
   B. Renal artery
      - Fibromuscular dysplasia amenable to angioplasty – 33% cure rate from hypertension; 50% alleviation of hypertension.
      - Not used for ostial lesions or atherosclerotic plaques.
   C. Other sites
      - Aorta – Uncommon to have focal lesions.
      - Femoral/popliteal – lesions tend to be >5cm, eccentric and diffuse, all limiting angioplasty.
      - Carotid – ongoing trials with stents.

IV. Complications
- Puncture site infections, acute occlusion, dissection - >5%.
- Pseudoaneurysm at puncture site, distal embolization – 1-5%.
- AV fistula at puncture site - <1%.
SECTION 5

CHAPTER 18

EXTREMITIES
Neurovascular Supply to the Leg and Foot
Sharla K. Stovall, MD

Nerve Supply
- Sciatic Nerve- arises from sacral plexus, divides into:
  - Common Peroneal-descends through popliteal fossa to divide into
    o Superficial-innervates lateral compartment
    o Deep- anterior muscles of the leg, first two digits of the foot
  - Tibial-descends through popliteal fossa, gives off 3 articular branches to knee and 3 branches to posterior muscles. Divides into
    o Medial sural cutaneous and medial calcaneal- supplies heel and sole
    o Terminates beneath flexor retinaculum and divides into medial and lateral plantar nerves to supply foot and toes

Lesions of Peripheral Nerves
- Common Peroneal- foot drop, loss of sensation on dorsum of foot, lateral leg
- Tibial- Loss of plantar flexion, impaired inversion, shuffling gait
- Deep Peroneal- foot drop, high stepping gait
- Superficial- loss of eversion

Arterial Supply
- Popliteal Artery- continuation of femoral artery at the adductor hiatus; descends through fossa and divides into:
  o Posterior Tibial- arise between tibia and fibula
    - Peroneal artery-supply lateral muscles in posterior compartment, ends in branches to ankle/heel
    - Medial Plantar-supplies big toe and 3 digits
    - Lateral Plantar- forms the plantar arch and gives rise to 4 plantar metatarsal arteries
  o Anterior Tibial-enter anterior compartment through the IOM, gives rise to recurrent branch to knee, anterior medial and lateral malleolar arteries at the ankle, continues onto dorsum of foot as dorsalis pedis
  o Dorsalis Pedis- terminates as deep plantar artery, joins lateral plantar to complete the plantar arch

Acute Compartment Syndrome
- Early recognition and treatment is critical to avoid amputation, limb dysfunction, and death
- Causes are numerous-open and closed fractures, arterial injury, GSW’s, burns, snake bites, compression

Pathogenesis
- Develops secondary to increased pressure in an enclosed space
- Most common cause in orthopedic patients is muscle edema from direct trauma or reperfusion after vascular injury
- Edema \( \rightarrow \) increased compartment pressure \( \rightarrow \) muscle ischemia

Diagnosis
- High degree of clinical suspicion based on mechanism
- Most sensitive clinical finding is exquisite pain with passive stretching of muscle group
Any evidence of increased tension or fullness should raise suspicion

Pitfalls
- Over time, pain will diminish with further ischemia
- In intoxicated, uncooperative, or the neurologically impaired, diagnosis may depend on compartment pressures

Tissue Pressure Measurements
- Most common method uses Stryker Stic device; obtain measurements by inserting needle into each compartment (highest pressure at level of fx or within 5 cm)
- Much controversy regarding level of pressure that requires surgical intervention (20mmHg – Diastolic, 30, 45)

Ischemia
- Peripheral nerves/muscles can survive 4 hours under ischemic conditions without irreversible damage
- 6 hours results invariable return to function in both muscle and nerve tissue

Surgical Treatment
- 2 incision approach: anterolateral incision over anterior and lateral compartments and a medial incision just posterior to medial aspect of the tibia
- Make small transverse incisions in the fascia to protect peroneal and saphenous vein and nerve respectively
INFECTIONS OF THE HAND AND TREATMENT
Michael K. Obeng, M.D.

Infections of the hand can be grouped into 6 different kinds:

1. Paronychia
2. Felon
3. Suppurative tenosynovitis
4. Deep Space infections
5. Herpes infections
6. Human bites

Paronychia results usually from a traumatic injury to the nail fold
- Presents with erythema.
- Staphylococcus aureus is the most common causative organism.
- Early infections can be treated with antibiotics and hygiene.
- Incision and drainage, if fluctuant, followed by antibiotics.
- Sometimes nail bed removal for total cure.

Felon is an abscess in the fingertip pulp as a result of penetrating injury.
- Staph among the most common organism.
- Very painful.
- Incision and drainage through a dorsal longitudinal skin incision on the side of the fingertip.
- Antibiotics to cover gram positives, esp. staph.
- Untreated infections can result in septic tenosynovitis, osteomyelitis of the phalanges and skin necrosis.

Suppurative tenosynovitis is an infection of the flexor tendon sheath mostly as a result of penetrating trauma.
- Most common organism is staph. Aureus
- Four cardinal signs may be present (Kanavel’s)
  - Fusiform swelling
  - Digit held in flexed position
  - Tendon sheath tender on palpitation
  - Pain with passive extension of the digit
- Elevation, worn soaks and IV abx
- Incision and drainage if no improvement seen with conservative management after 6 hours.
- A small drain can be placed in the tendon sheath for 36-48 hrs with continuous saline infusion until improvement in chemical signs and symptoms.
- Untreated cases can lead to tendon sheath necrosis, necrosis of the pulley system, and osteomyelitis and abscesses.
Herpes infection; (Whitlow) of a digit is caused by HSV
- Often seen in health care workers.
- Infections are often from orotracheal secretions
- Incubation period is between 2-14 days
- Signs include fluid-filled vesicles on the fingertip
- Diagnosis made from KOH prep or Tzanck smear.
- Viral culture, immunofluorescence and anti herpes antibodies can be helpful.
- Self-limiting, no incision and drainage needed.
- Incision and drainage can lead to systemic involvement and possibly viral encephalitis

Fungal hand infections often mimic the other type of infection.
- Often fails antibiotic therapy
- Antifungal mainstay of treatment.

Human bites are conglomerate of mouth flora
- Common organisms include staph-aureus, strep, bacteroides spp, and eikenella spp.
- Often occurs when someone with a clenched fist hits someone in the mouth.
- Incision and drainage with jet lavage is mandatory.
- No primary closure, wound should be allowed to heal by secondary intention.
- Antibiotic coverage should include PCN or cephalosporin after incision and drainage.

Don’t forget to elevate affected hand at all times.
Fractures of Humerus and Scaphoid
Dirk C. Johnson, MD

Fracture- a linear deformation or discontinuity of bone produced by forces that exceed the ultimate strength of the material

Fracture descriptions:
- Location: Intraarticular, epiphyseal, metaphyseal, diaphyseal
- Plane: Transverse, oblique, spiral
- Fragments: number and type
- Open or closed
- Displacement: based on direction of displacement of distal fragment
- Angulation: based on long access of fracture proximally to distal

Diagnosis
- Pain, swelling, deformity, ecchymosis, instability, crepitus
- Radiographic confirmation with films at perpendicular angles

Evaluation
- Neurologic: strength, sensation,
- Vascular: color, pulses, capillary refill
- Joint stability

Open Fractures
- Orthopedic emergency
- Risk of deep tissue infections, osteomyelitis,

Classification of Open fractures
I. Puncture wound <1cm
II. > 1cm with moderate tissue damage
III. Severe tissue damage or loss

Management of open fractures
- Cover wound and splint
- Broad-spectrum antibiotics
- Operative washout and debridement
- Reduce fracture and loosely reapproximate soft tissue
- Fracture stabilization
- Tissue coverage for defects

Compartment syndrome
- Pain, Pallor, Pulselessness, and Paresthesias
- Compartment pressures
- Treatment Fasciotomies

Humeral fractures
- Surgical Neck Proximal Metaphysis (adults)
- Anatomic Neck Epiphyseal Metaphyseal Junction
- Classification (Neer) based on number of displaced fragments
- Risk of Avascular Necrosis (AVN) if multiple proximal fragments
- Rehab is dependant on early rehabilitation to avoid stiffness (Codman) exercises

Supracondylar fractures
- Most common in children
- Volkmann’s contracture
Compartment syndrome
Brachial artery injuries
Median/Radial nerve injuries

Treatment
- Splint with elbow at 90 degrees
- ORIF
- Percutaneous pinning

Lateral epicondyle
Fracture is intraarticular and crosses the growth plate
Classification
I. Nondisplaced
II. Minimally displaced <2cm
III. Displaced and rotated
Treatment-ORIF

Medial epicondyle
ORIF if intraarticular

Colles Fracture
Fall on outstretched hand
Distal radius fracture with comminution, dorsal angulation

Smith’s fracture (reverse Collies)

Treat both with closed reduction and casting

Scaphoid fractures
Associated with wrist fractures
Most common carpal fracture
Pain at anatomic snuffbox
Radiographic studies-AP, lateral, 17-degree oblique (navicular view)
Can be missed on plain films→ CT scan if high clinical suspicion
Treat with long arm spica cast
Empiric treatment
High risk for acute vascular necrosis (blood supply enters from distal segment)


EXTREMITY VASCULAR INJURIES
Yvette M. Carter, MD

EPIDEMIOLOGY
Penetrating- GSW
Iatrogenic- endovascular therapy (1/3)

PATHOPHYSIOLOGY
Hemorrhage
Inadequate distal perfusion
Hypovolemic shock
Local
Thrombosis → acute arterial occlusion → distal ischemia
Tissue loss proportional to collateral blood flow
Tissue sensitivity to ischemia
Delay in flow restoration
Peripheral nerves and muscles
Tolerate 4 hours of ischemia without permanent injury
Ischemia/reperfusion injury
Ischemia → anoxic cell death
Xanthine dehydrogenase → xanthine oxidase → + hypoxanthine
↓ O2
↓ perfusion
xanthine + O2
→ lipid peroxidation → microvascular endothelial injury → P_interstitial → ↓ flow
→ → → "no flow" phenomenon + muscle necrosis
hypokalemia, myoglobinemia, metabolic acidosis, renal failure

TYPES OF INJURY
Incomplete laceration-no retraction, vasoconstriction or thrombosis → ↑ hemorrhage
Complete laceration
Complications-Acute: intimal flap occlusion
Arterial contusion with thrombosis
Arteriovenous fistula
Chronic: pseudoaneurysm
Thrombosis
Distal emboli
Blunt Trauma: deceleration injuries
Complete/partial vessel wall disruption
Elastic adventitia + muscular layers intact; intima fractures
Blood dissects under intima → thrombosis
High velocity wounds
“shock wave” vessel injuries
Shock wave displaces tissue 90° away from bullet path → intimal tears with local
dissection, thrombosis, embolization

DIAGNOSIS
H&P
Sx: pain, pallor, ↓ pulse, paresthesia, ↓ perfusion (complete occlusion)
Segmental artery pressures
ABI = 1.1 (normal)
<0.9 or 20mmHg difference between extremities
affected by hypovolemia
Duplex Scanning
Arteriography
Indications: moderate hemorrhage
Injury near major arteries
Diminished pulses
Peripheral nerve injury
Biplanar views >15cm above and below injury site
Early and late views:  
- r/o venous filling from AV fistula
- r/o late filling of pseudoaneurysm

**TREATMENT**

**NON-OPERATIVE**

Endovascular therapy
- Stents and grafts (experimental for non iatrogenic injuries)
- Embolization for branch vessel hemorrhage
  - Coils + thrombotic protein foam
- Biologic glues
- Balloon catheter occlusion

US guided therapy
- Iatrogenic femoral artery pseudoaneurysms
  - > 3 cm
- 0.5-1 ml (1000U/mL) thrombin

**OPERATIVE**

Avoid blind clamp placement
- IV abx
- Systemic heparin (isolated extremity injuries)
- Tetanus

**#1 repair vascular injury**

**#2 stabilize skeletal injury**

1. proximal and distal control thru uninjured area
2. thrombectomy of proximal and distal artery
3. heparinized saline proximal and distal
4. end-to-end anastomosis (< 2 cm between segments)
5. interposition graft #1 reversed SVG; #2 PTFE
6. venous ligation if hemodynamically unstable
7. intraluminal shunts
6. decrease limb ischemia time
   - place interposition graft over shunt
9. LMW dextran to prevent early thrombosis
    - improves microvascular circulation
    - dextran 40 @ 40-50 cc/hr x 24 h

**COMPLICATIONS**

Compartment Syndrome

**Calf >> thigh and forearm**
- Pain on passive stretch
- Fasciotomy 6h b/t injury and reperfusion
  - Associated crush injury
  - Pre-op calf swelling
  - Artery and vein injury
  - Extensive venous ligation
  - Increased compartment pressures

Early: thrombosis (significant post-op swelling)
- Rx: heparin + coumadin
- infection disrupt suture line + hemorrhage
- Rx: ligation + extra-anatomic bypass

Late: stenosis or occlusion of arterial repair
- Aneurysmal changes to vein graft
- Venous thrombosis/ligation  post-thrombotic syndrome

**Brachial a. proximal to profunda brachii**
- Posterior knee dislocation

**Ulnar a. + radial a.-repair**
- Femoral a.-direct repair
- Popliteal a.- interposition graft
- isolated tibial a.-no repair required
Compartment syndrome
Eric C. Feliberti, MD

I. Definition
Elevation of interstitial pressure in a closed osseofascial compartment resulting in microvascular compromise.

II. Physiology
A. Any insult that causes a decrease in compartment size or an increase in compartment pressure can initiate compartment syndrome. Increase in interstitial pressure overcomes intravascular pressure of venules and capillaries, arresting blood flow. The tissue ischemia causes edema, increasing the compartment pressure further.
B. Critical warm ischemia time is 6 hours – irreversible nerve and muscle injury.

III. Etiology
A. General
Crush injuries, fractures, prolonged compression, bleeding, burns, excessive exercise.
B. Specific
1. Hand, thigh – crush injuries
2. Forearm – supracondylar humeral fracture (Volkmann’s contracture).
3. Leg – Tibial shaft and plateau fractures
4. Foot – calcaneal fractures

IV. Symptoms/signs
Pain out of proportion to injury – most sensitive sign
Pain with passive stretching of compartment
Paresthesia – may be an unreliable or late sign, since nerve conduction continues 1 hour after ischemia.

V. Diagnosis
A. Clinical diagnosis based on etiology and symptoms
B. Compartment pressure
   1. Compartment pressure of 30-45mmHg and symptoms
   2. Difference less than 30mmHg between diastolic and compartment pressure.

VI. Compartments
A. Thigh – anterior, posterior, obturator (medial)
B. Leg – anterior, lateral, superficial posterior, deep posterior
C. Forearm – superficial volar, deep volar, dorsal (mobile wad of Henry)

VII. Treatment
A. Fasciotomy – incise fascia of all compartments
B. Escharotomy – only indicated for burns; incise to subcutaneous fat.
VIII. Procedure

A. Thigh fasciotomy
Make an incision from the intertrochanteric line to the lateral epicondyle and incise the iliotibial band. The vastus lateralis is reflected off the lateral intermuscular septum. A 1.5-cm incision is made in the lateral intermuscular septum and, using Metzenbaum scissors, it is extended proximally and distally the length of the incision, releasing the anterior and posterior compartments. A separate medial incision is made over the adductor compartment.

B. Fasciotomy of the leg
Make an incision halfway between the fibular shaft and the crest of the tibia medially and a transverse incision is made to expose the lateral intermuscular septum and identify the superficial peroneal nerve just posterior to the septum. The anterior and posterior compartments are incised proximally and distally. A second longitudinal incision 2 cm posterior to the posterior margin of the tibia is made and the saphenous vein and nerve anteriorly are retracted. The septum between the deep and superficial posterior compartments is incised and fasciotomies are performed.

C. Fasciotomy of the forearm
Make a curvilinear incision on volar aspect (to avoid contracture) and carry the incision distally into the palm to allow for a carpal tunnel release. Release the superficial volar compartment throughout its length. Identify the flexor carpi ulnaris and retract it with its underlying ulnar neurovascular bundle medially. Retract the flexor digitorum superficialis and median nerve laterally to expose the flexor digitorum profundus in its deep compartment and incise it longitudinally. For the dorsal compartment, an incision is made distal to the lateral epicondyle extending distally. The fascia overlying the mobile wad of Henry and the extensor retinaculum is incised.

D. Fasciotomy of the hand
Make two dorsal parallel incisions overlying the second and fourth metacarpals and incise the fascia. If the thenar and hypothenar muscles are involved, additional palmar radial and palmar ulnar incisions are made to allow for their separate decompression. Digital fasciotomies are made through midlateral incisions along the radial border of the ring and small fingers and the ulnar border of the index and long fingers.
Nerve Supply to Arm and Hand
Farin W. Smith, MD

Hand innervation:
- Radial nerve – motor innervation to extrinsic extensors of the hand, wrist extensors, and supinator
  - Superficial branch of radial nerve provides sensation to the dorsum of the thumb, the proximal radial three digits, and the accompanying dorsum of the hand
- Median nerve – the flexor digitorum superficialis (FDS), the two radial flexor digitorum profundus (FDP), the flexor pollicis longus, the radial lumbricals (first two), and the thenar musculature
  - Median nerve sensory – radial palm, the palmar skin of the radial 3rd digits, and the dorsal skin of the distal (radial) 3rd digits
- Ulnar nerve – motor innervation to flexor carpi ulnaris, the two ulnar FDP and lumbricals, the hypothenar muscles, the interossei, the adductor pollicis, and the deep portion of the flexor pollicis brevis
  - Sensation: ulnar hand and the ulnar 1st digit, both dorsal and ulnar sides

Nerve injuries
- Three types:
  - Neurapraxia – interruption of nerve conduction but anatomic preservation (recovery in 60 days)
  - Axonotmesis – wallerian degeneration, reinnervation occurs when tubular structure is intact
  - Neurotmesis – anatomic disruption of nerve (needs surgical repair); regeneration rate of approx. 1 mm per day, age is strong prognostic factor

Nerve compression syndromes
- Median nerve compressions:
  - Carpal tunnel syndrome – pain and numbness at night, pain prox. to elbow suggests involvement of shoulder or cervical spine; synovitis most common cause: positive Tinel’s sign; initial management is conservative, if symptoms persist, or there is thenal weakness, surgical release
  - Pronator syndrome – similar to carpal tunnel, but no nocturnal symptoms; pronator teres, lacertus fibrosus, FDS fascial arch, and the ligament of Struthers cause compression, surgical release of pronator teres muscle and FDS fascial arch at the elbow
- Ulnar nerve compressions:
  - Cubial tunnel syndrome – aching pain and numbness and paresthesias in the ring and small fingers, positive Tinel’s sign at elbow, weak grip and key pinch; symptoms reproducible when elbow is flexed; initial management is splinting in neutral position, then surgical release
  - Guyon’s canal – hook of the hammate, pisiform, pisohamate ligament, and palmar capsular ligament; treatment consists of exploration of canal for space occupying lesion
- Radial nerve compression:
  - Upper arm compression by triceps, or, more commonly, in the forearm at the supinator muscle
- Thoracic outlet syndrome:
  - Outlet is bounded by first rib inferiorly, the scalenus anterior anteriorly, the scalenus muscle posteriorly, and the clavicle; women 18-25 years of age; usually compression of lower plexus (ulnar nerve distribution); upper compression – lateral arm and face jaw, or ear paresthesias; Roos test (arm overhead), Adson test (head turned to examining side, palpate radial nerve and breathe); passively flexing the neck away from the affected side usually reproduces symptoms; x-rays a must; electrophysiological studies frequently normal; treatment is conservative initially, then includes cervical rib resection, first rib resection, and scalenectomies
SECTION 6

CHAPTER 19

TRAUMA
Hemorrhagic Shock and Physiologic Responses
Chris T. Stephens, MD

Introduction: Hemorrhage is defined as an acute loss of circulating blood volume – most common cause of shock in the trauma patient. The response to blood loss is complex and involves the shift of fluid from the interstitium into the vascular space, as well as other fluid shifts. Classes of hemorrhage are based on the percentage of acute blood volume loss – this classification is useful in demonstrating the early signs and pathophysiology of the shock state. Hemorrhage results in a complex cascade of physiologic responses – increased circulating levels of norepinephrine are the first response in mild hemorrhage resulting in tachycardia to compensate for decreased stroke volume/cardiac output, diminished preload, decreased right and left ventricular end diastolic volumes, followed by release of epinephrine and activation of the renin-angiotensin system with greater volume deficits to allow for increased systemic vascular resistance and sodium/free water conservation – as a consequence of vasopressor release, blood flow to skin/skeletal muscle decreases as SVR increases – perfusion to heart, lungs, and brain is preserved, while visceral perfusion reduced.

Class I Hemorrhage – Blood volume loss of up to 15%
- clinical symptoms minimal
- minimal tachycardia may be appreciated to maintain CO
- arterial vasoconstriction
- no measurable change in blood pressure, pulse pressure, or respiratory rate
- generally does not require volume replacement
- transcapillary refill and other compensatory mechanisms restore blood volume in 24 hrs
- if patient is symptomatic – replacement of primary fluid losses corrects circulatory state

Class II Hemorrhage – 15% to 30% blood volume loss
- 70 kg male – volume loss is 750-1500 ml of blood
- tachycardia (HR>100), tachypnea, decreased pulse pressure (secondary to rise in diastolic component of BP due to increased release in circulating catecholamines – inotropes produce increase in peripheral vascular tone and resistance
- systolic blood pressure changes minimally in early shock – eval pulse pressure instead!!
- subtle CNS disturbances may be seen – anxiety, fright, or hostility
- urine output mildly affected – usually 20-30 cc/hr in adults
- require crystalloid replacement and may eventually require blood transfusions

Class III Hemorrhage – 30% to 40% blood volume loss
- approximately 2000 ml blood volume loss in adults – can be devastating
- patients present with classic signs of inadequate perfusion – marked tachycardia, tachypnea, fall in systolic blood pressure (in uncomplicated cases, this is the least amount of blood loss that consistently lowers SBP)
- CNS changes include altered mental status (confusion, combativeness)
- almost always require blood transfusion in addition to crystalloid replacement
- decision to transfuse based on patient’s response to crystalloid resuscitation

Class IV Hemorrhage - >40% blood volume loss
- this degree of hemorrhage is immediately life threatening
- physiologic responses demonstrate marked tachycardia (possibly bradycardia if profound irreversible shock and death is imminent), a significant decrease in systolic blood pressure, very narrow pulse pressure (diastolic pressure may be unobtainable), urine output negligible, marked altered mental status, pale, cool, diaphoretic skin signs
- loss of >50% blood volume results in rapid loss of consciousness, pulse, and blood pressure
## HEMORRHAGIC SHOCK CLASSES
### And Physiologic Responses

<table>
<thead>
<tr>
<th></th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood Loss (mL)</strong></td>
<td>Up to 750</td>
<td>750-1500</td>
<td>1500-2000</td>
<td>&gt;2000</td>
</tr>
<tr>
<td><strong>Blood Loss</strong> (% Blood Volume)</td>
<td>Up to 15%</td>
<td>15-30%</td>
<td>30-40%</td>
<td>&gt;40%</td>
</tr>
<tr>
<td><strong>Pulse Rate</strong></td>
<td>&lt;100</td>
<td>&gt;100</td>
<td>&gt;120</td>
<td>&gt;140</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Pulse Pressure</strong></td>
<td>Normal/ Increased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
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<tr>
<td><strong>Respiratory Rate</strong></td>
<td>14-20</td>
<td>20-30</td>
<td>30-40</td>
<td>&gt;35</td>
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<tr>
<td><strong>Urine Output</strong></td>
<td>&gt;30</td>
<td>20-30</td>
<td>5-15</td>
<td>Negligible</td>
</tr>
<tr>
<td><strong>CNS/Mental Status</strong></td>
<td>Slightly anxious</td>
<td>Mildly anxious</td>
<td>Anxious, confused</td>
<td>Confused, lethargic</td>
</tr>
<tr>
<td><strong>Fluid Replacement</strong></td>
<td>Crystalloid</td>
<td>Crystalloid</td>
<td>Crystalloid and blood</td>
<td>Crystalloid and blood</td>
</tr>
</tbody>
</table>
Epidural/Subdural Hematomas
Carlos Rosales, MD

Epidural Hematoma

Epidural hematomas are located within the skull but outside the dura. A brief loss of consciousness is followed by a several hour lucid interval, followed by a rapid decline in consciousness, ipsilateral pupillary dilation, contralateral hemiparesis and cushing’s triad (hypertension, bradycardia, respiratory irregularity) due to mid-brain compression from temporal lobe herniation. The lucid interval phenomenon is seen in less than 25% of epidural hematomas. 10 to 20% of epidural hematomas are associated with “Kernohan’s phenomenon”: contralateral cerebral peduncle compression against the tentorial notch, resulting in contralateral dilated pupil and ipsilateral hemiparesis. They are usually arterial in origin and the most common cause is tearing of the middle meningeal secondary to trauma. The hematoma can also be the result of dural sinus bleeds in up to 15% of cases. On CT scan, these hematomas typically have a biconcave or lenticular shape and are hyperdense. They can be located anywhere but are most commonly located in the temporal parietal region of the skull. Treatment consists of immediate craniotomy to control the bleeding and evacuation of the hematoma. Early treatment usually results in a good prognosis. Outcome is directly related to the neurological exam of the patient prior to surgery.

Subdural Hematomas

A subdural hematoma is a collection of blood below the dura and above the subarachnoid membrane. Bleeding is usually the result of tearing of small bridging veins that traverse the brain to the dural sinuses. Trauma as insignificant as falling from a standing position in the elderly can lead to this. A hyperdense, crescent-shaped fluid collection displacing the brain on CT scan is a classical appearance. Simple subdural hematomas are not associated with brain injury and have a mortality rate of 20%. Complex subdural hematomas are often associated with frontal temporal contracoup parenchymal lesions and have a mortality rate of 50-90%. Immediate surgical evacuation of the hematoma by burr holes is the treatment for an acute subdural hematoma.
Aortic Transection
Tammy Lee, MD

Definition
• Aortic transection is a cross-sectional cut through the aorta; also described as a traumatic aneurysm, traumatic dissection, or thoracic aortic rupture.

Presentation
• Diagnosis requires a high index of suspicion. Symptoms are nonspecific and often referable to other injuries. Symptoms include dyspnea and chest or back pain.
• Less than one third of patients have unequal upper extremity blood pressures with decreased femoral pulses and reduced lower extremity blood pressures—the so-called "pseudocoarctation syndrome."
• 10% to 20% have a precordial systolic or interscapular murmur.
• 2% to 5% present with paraplegia caused by direct cord trauma or spinal cord ischemia secondary to the aortic disruption.

Diagnosis
• Chest radiography is the most helpful initial test: Fractures of the sternum, scapula, multiple ribs, or clavicle; Lateral chest radiography findings of anterior trachea displacement or opacified aortic pulmonary window; Obliteration of the aortic nob; Widening of the mediastinum; Displacement of the left mainstem bronchus; Widened paraspinal interspace; Apical pleural hematoma; Massive left hemothorax
• Angiography remains the "gold standard"; it has nearly 100% sensitivity and specificity, and it provides a "road map" of the aorta and the extent of injury.
• Chest spiral CT is improving for excluding aortic disruption in patients with a low index of suspicion for an aortic tear.
• MR imaging has proved to be an excellent modality to visualize the thoracic aorta, particularly for aneurysms and dissections.
• Transesophageal echocardiography has emerged as an excellent tool for examining both the heart and the aorta; Two problems impede its widespread acceptance: (1) the inability to adequately visualize the aortic arch and its main branches and (2) too few operators available with expertise with traumatic aortic injuries.

Treatment
• Definitive treatment is surgical repair.
• Most descending aortic injuries are repaired through a left thoracotomy; Sternotomy is used for ascending aorta, aortic arch, and some descending aortic injuries.
• A primary reanastomosis is attempted or prosthetic graft material is used. Ischemia of the spinal cord or abdominal organs is a risk during repair. Perfusion of the spinal cord can be compromised by damage to the blood supply at the time
of injury or during surgical exposure, as well as during aortic clamping and artery cannulation.
Spleen trauma
Dirk C. Johnson, MD

- The spleen is the most frequently injured abdominal organ in blunt trauma
- Non-operative management is gaining popularity as a treatment alternative in the hemodynamically stable patient
- Suspect spleen injury after trauma to left chest, flank or abdomen
- CT scan with IV contrast to confirm diagnosis

Non-operative Management
- preferred in pediatric population when possible
- Serial hematocrits
- Serial abdominal exams
- Bed rest
- Ambulate after 72 hours
- Repeat CT if condition deteriorates
- Do not need to repeat CT for stable patient at discharge or follow up
- Avoid intense physical activity and contact sports for 3 months
- 90% success: safe and effective

Indication for splenectomy
- Transfusion requirement greater than half of patients blood volume
- Hemodynamic instability
- Accumulation of blood in the pelvis (grade III+)
- Coagulopathy

Post Splenectomy
- Overwhelming postsplenectomy infection
  - Rapid onset
  - Last 12-18 hours
  - Common organisms Pnuemococcus, E.Coli, H. Flu, Meningococcus, staph, and strep
- Impaired phagocytosis of particles in blood
- Capsulated bacterial infections increased because of impaired immune response (opsonization) to these organisms
- Prepubertal children sepsis rate 0.5% with 50% mortality
- All splenectomies should receive pneumococcal, H. Flu, and meningococcal vaccines 1-2 weeks postoperatively
- Prophylactic antibiotics are controversial

Splenic Salvage
- 40-60% success rate
- capsular tears, hilar disruptions,
- several techniques (argon beam, horizontal mattress sutures, dacron mesh, fibrin glue)
Injuries of the Duodenum and Pancreas

M. Joseph Elieson, MD

The retroperitoneal location of pancreas & duodenum contribute to unique presentations of traumatic injuries involving these organs; significant bleeding is rare in blunt trauma, identification of physical findings are usually delayed, DPL is frequently negative (50%), CT scan often shows nonspecific findings. Most patients who die of pancreatic or duodenal injury, due so within the first 48 hours. This is most often a result of associated injuries. Isolated duodenal or pancreatic injuries are uncommon. Overall, 90% of patients will have at least one associated injury (3.5 to 4.1 additional injuries per patient). Associated injuries are usually those of neighboring vascular, solid and soft organs.

I. Duodenal Injuries

A. Diagnosis: Similar to pancreatic injuries, early clinical signs of duodenal injuries are frequently nonspecific and injuries are often determined intraoperatively. Findings on plain abdominal film are usually subtle, but may show retroperitoneal air in the epigastric area or along the lateral border of the right psoas, mild scoliosis, or obliteration of the right psoas. Injury is usually confirmed by double contrast CT scan of the retroperitoneum or by UGI with gastrografin followed by barium when negative. These studies are diagnostic when they show extravasation of contrast or paraduodenal air.

B. Treatment: A thorough exploration of duodenum requires Kocher maneuver, mobilization of duodenum to ligament of Treitz, inspection of posterior duodenum and evaluation of pancreas for potential associated injuries. The first priority is control of associated hemorrhage. Limiting bacterial contamination to prevent late infections as a second priority with an ultimate goal of reestablishing duodenal continuity without leakage.

i. Partial-thickness laceration: simple closure

ii. Full-thickness perforation, <50% of the circumference involved: primary transverse closure in two layers

iii. 50-100% circumferential laceration of D1, D3 or D4 or 50-75% injury to D2:

a. Two-layer closure if lumen not compromised

b. Close distal duodenum; proximal Roux-en-Y duodenojejunostomy

c. Buttressing the duodenal repair with on-lay omental or serosal patch.

iv. 75-100% laceration of D2 at ampulla or bile duct:

a. When transmural injury is not severe, anastomosis of ampulla to duodenum

b. Pancreaticoduodenectomy (Whipple procedure)

c. Complex duodenal injury +/- pancreatic injury (controversial):

a. Primary repair with duodenal decompression and drain

b. Duodenal diverticulization (Berne procedure)

c. Pyloric exclusion (Jordan procedure)

d. Debridement of duodenal injury with on-lay patch of omentum or jejunum.

v. Duodenal hematoma: intramural hematoma that results in partial or complete duodenal obstruction. The second and third portions of the duodenum are the most commonly involved sites. Symptoms of abdominal pain and bilious vomiting. Diagnosis can be suspected on CT scan, but is usually confirmed by UGI (coil-spring sign). Therapy: observation for 3 weeks with NG suction and TPN; resolution of hematoma in most patients with 1-3 weeks.

C. Complications: (1/3 of patients)

i. Anastomotic breakdown, leak, or fistula formation (3-12% incidence)--maintain appropriate fluid & electrolyte balance; many respond to drainage, NG suction, TPN; sinogram should be considered when persistent.

ii. Late obstruction: usually at suture line; initial treatment of observation for 1-2 weeks; UGI can aide with assessment of the degree of obstruction; when persistent, surgical options include duodenojejunostomy or gastrojejunostomy.
Abscess formation is also a common complication. Usually managed by percutaneous drainage.

II. Pancreatic Injuries
A. Diagnosis: Clinical findings after blunt injury are minimal during first 2-3 hours, especially in patients with compromised mental status (CHI, alcohol, drugs). Hyperamylasemia is nonspecific (false negative 30-50%; false positive 20%), but helpful in conjunction with exam findings. DPL is non reliable, USG is not accurate yet, CT with contrast remains the diagnostic test of choice, ERCP to assess ductal integrity is rarely used in acute settings. When a ductal injury is suspected upon exploration, then an intraoperative pancreatography should be performed.

B. Treatment: In order to avoid missed injuries, exploration must be done in a careful, systematic manner: Kocher maneuver, exposure of anterior surface via lesser sac, evaluation of tail of pancreas by mobilizing spleen. Particular attention to identify and explore subcapsular, parenchymal hematoma, disruption, pancreatic drainage (clear fluid) and fat saponification. Specific treatment of pancreatic injuries depends primarily on two factors: integrity of pancreatic duct and location pancreatic injury.

i. Minor contusion or tear without ductal injury: hemostasis, closed-suction drainage (JP)

ii. Major contusion or tear (>3cm) without ductal injury: repair of tear and drainage

iii. Distal transection or tear with ductal injury: distal pancreatectomy +/- splenectomy

iv. Proximal transection or tear with ductal injury:
   a. Oversewing of proximal pancreatic head, distal pancreatectomy, drain
   b. Oversewing of proximal pancreatic head, Roux-en-Y distal pancreateojejunostomy, drain (intra op pancreatography to determine the presence or absence of ductal injury is maybe considered but not necessary; also consider postop ERCP)

v. Disruption of pancreatic head, pancreaticoduodenal disruption:
   a. Nonviable tissues: Whipple (but reserved as the last option)
   b. Hemodynamic instability: temporary packing and return in 24h
   c. Viable tissues with relative hemodynamic stability: primary repair, duodenal diversion (Berne or Jordan procedure), drain
   d. Duodenal diverticulization (Berne): antrectomy, closure of duodenal stump, tube duodenostomy, gastrojejunostomy, drain
   e. Pyloric exclusion (Jordan): closure of pylorus with staple or suture, tube duodenostomy, gastrojejunostomy, drain

C. Complications:

i. Fistula: incidence 10-40%, diagnosed by output volume and amylase concentration of the fluid; treated conservatively as most heal spontaneously, monitor fluid and electrolytes; Somatostatin and jejunal elemental feeding considered; when refractory, ERCP with pancreatic duct sphincterotomy with stent considered

ii. Pseudocysts as a result of trauma comprise 5% of all pancreatic pseudocysts; internal surgical drainage; percutaneous drainage can be considered.

iii. Pancreatitis is a common complication of trauma.

iv. Exocrine/endocrine insufficiency: extremely rare unless >90% pancreas removed; preservation of pancreatic tissue is the best approach to prevent these potential complications.
Bawduniak, MD

A. Diagnosis
   a. Usually unsuspected without hematuria
   b. Dx often delayed because associated life-threatening injuries
   c. Urologic likely with crush injury of upper abdomen/pelvis, direct blow to flank, severe accelerating/decelerating injury
   d. Signs: femur fx, pelvic fx, crush injury chest, abd bruising, severe head trauma
   e. Specific signs upper urologic tract: gross/microscopic hematuria, lower rib fx, lumbar fx process
   f. Signs lower urinary tract injury: blood at meatus, highriding prostate(urethral transection), urinary retention, bladder distension, inability to void.

B. Initial Evaluation
   a. Immediate urine specimen (no catheter if blood at meatus or resistance)
   b. If requires emergent operation- one shot pyelogram (ER or OR)
      i. Presence/absence functioning kidneys
      ii. May fail to identify renal outline
      iii. Extremely limited
      iv. Mark entry/exit penetrating wounds with steel clips
   c. crush injuries/bld at meatus- get retrograde cystourethrogram
   d. cystography- fill bladder 200-300cc, films when distended/emptied
   e. most difficult- recognize renal pedicle injury
      i. evaluate all gross hematuria, microscopic hematuria with associated injuries, shock, consistent mechanism, penetrating to GU
   f. IVP or CT with contrast

C. Kidney
   a. Penetrating injury usually not life threatening
   b. Debridement, primary repair
   c. Preop arteriography to define vascular disruption, embolization
      i. Often too unstable for this time-consuming procedure
   d. Proximal control renal pedicle prior to opening Gerota’s fascia
   e. Injury to collecting system- débride, suture watertight
   f. Preserve as much parenchyma as possible
   g. Many blunt kidney injuries can be managed nonoperatively
      i. 85% have minor injuries- manage expectantly
      ii. 5% have intermediate injuries- surgical or nonsurgical
         1. major cortical laceration with undisplaced fragments held in place by intact capsule
         2. often have hypertension as sequelae later
      iii. 10% life threatening (pedicle injury, shattered kidney, extensive laceration)
         1. 15% of these have significant injury to other viscera
h. Classification system
   i. I- renal pedicle injury
   ii. II- deep parenchymal injury with intact capsule
   iii. III- deep parenchymal injury with disrupted capsule
   iv. IV- shattered kidney with intact capsule
   v. V- shattered kidney with disrupted capsule
   vi. VI- ureteral or renal pelvis injury

D. Bladder
   a. Most commonly injured organ with pelvic fractures (72%)
   b. Bladder may be contused, penetrated, ruptured (intra/extraperitoneal)
   c. Large defects can have negative cystogram (clot, peritoneal contents, tissue can fill the defect)
   d. Post-evacuation cystogram always obtained- show extravasation in oblique or lateral view
   e. CT cystogram for more subtle injuries
   f. Treatment:
      i. Isolated extraperitoneal rupture- 10 days Foley
         1. most extraperitoneal ruptures associated with pelvic fx where bone has penetrated bladder wall
         2. fx should be reduced/stabilized, bladder wound débrided and closed in 2 layers
         3. then filled with 400cc saline to test if watertight
         4. if adequate closure, foley drainage
   g. intraperitoneal injury occurs with abdominal compression injury with a full bladder, or penetrating injury
   h. develop edge of wound to mobilize peritoneum off of ragged bladder tear, 3-layer closure
      i. inspect for watertightness, foley or suprapubic
SECTION 6

CHAPTER 20

BURN
Fluid Resuscitation for Burned Patients
Tammy Lee, MD

The immediate cardiovascular response to a significant burn injury is a decrease in cardiac output. The reduction in cardiac output is caused primarily by

- increased vascular permeability with a resultant shift of intravascular fluid to the interstitial space
- decreased systemic vascular resistance (potentiated by neurogenic or humoral factors)
- direct myocardial depressant factors.

As the process continues, compensation for the decrease in cardiac output fails, and, if untreated, these patients may go into "burn shock."

- Fluid resuscitation must begin as rapidly as possible to prevent shock and further physiologic derangement.
- Several fluid protocols or formulas exist that require the use of crystalloid, colloid, or a combination of both, based on the weight of the patient and the percentage of TBSA.

The most commonly used formula is the Parkland formula, which resuscitates with lactated Ringer's, 2 to 4 mL/kg/%TBSA in the first 24 hours. Half is given in the first 8 hours post-burn, and the other half over the next 16 hours. The resuscitation is titrated to maintain adequate, but not excessive, urine output.
The management of burn wounds relies on the daily appearance of the wound and varies with the degree & depth of the burn injury.

Topical burn treatments, including burn dressings, protect the burn wound from bacterial colonization, prevent heat loss and metabolic disturbances, and provide a dressing for protection and comfort.

**TOPICAL ANTIMICROBIALS:** with a daily debridement regimen, topical antimicrobials help to delay and minimize bacterial colonization.

**Offending microbes:**
- *S. Epidermidis*  
- *S. Aureus*  
- *Pseudomonas*  
- *Klebsiella*  
- *Clostridium*  
- *Candida*  
- *Proteus*  
- *S. Aureus*  
- *Enterococcus spp.*

1) **Silver Sulfadiazine (Silvadene):** most commonly used; silver ions kill microbes by poisoning microbe cellular respiration pathway; kills on contact.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ broad spectrum coverage</td>
<td>→ poor eschar penetration</td>
</tr>
<tr>
<td>→ painless application</td>
<td>→ transient leukopenia (5-15% of pt.’s &amp; resolves without complications)</td>
</tr>
<tr>
<td></td>
<td>→ forms “pseudoeschar”</td>
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2) **Mafenide Acetate (Sulfamylon):**

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ good eschar penetration</td>
<td>→ painful on sensate burn wounds</td>
</tr>
<tr>
<td>→ provides broad coverage (esp. against resistant <em>Pseudomonas</em> &amp; <em>Enterococcus spp.</em>)</td>
<td>→ limited <em>Staph</em> coverage (esp. MRSA)</td>
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<tr>
<td></td>
<td>→ inhibits carbonic anhydrase (results in metabolic acidosis when applied over large surfaces)</td>
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3) **Polymyxin B, Neomycin, Bacitracin:** used for facial burns, graft sites, healing donor sites, and small partial thickness burns (see Townsend, p.354)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ easy to use</td>
<td>→ limited antimicrobial coverage</td>
</tr>
<tr>
<td>→ painless application</td>
<td>→ limited eschar penetration</td>
</tr>
</tbody>
</table>

**Mupirocin (Bactroban)** has better activity against gram positives, including MRSA and some gram-negatives, but is expensive.
Nystatin ointment provides added coverage against fungal microbes and may be used in combination with other topical agents. **Nystatin plus Sulfamylon**, however, inactivate each other and should **not** be used together.

4) **Dakin’s Solution (Sodium Hypochlorite solution):** Used as a soak

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ good antimicrobial coverage</td>
<td>→ requires regular dressing changes</td>
</tr>
<tr>
<td></td>
<td>→ cytotoxic effects on healing cells at higher concentrations</td>
</tr>
</tbody>
</table>

**Sulfamylon soaks** offer same profile as Sulfamylon salve; **Silver nitrate soaks** fraught with possible electrolyte disturbances, staining of wound surfaces, and methemoglobinemia (replaced by Acticoat). **Acticoat** is a silver-releasing system which releases silver ions when moistened; provides all the advantages of silver nitrate soaks without side effects and dressing changes.

**SYNTHETIC & BIOLOGIC DRESSINGS:** applied within 24 hrs. of injury on partial-thickness burn wounds. As an alternative to topical antimicrobials, these dressings avoid painful dressing changes and do not inhibit epithelialization.

1) **Biobrane:** silicone and collagen matrix, used on partial-thickness wounds.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ avoid dressing changes</td>
<td>→ exudate may collect and become infected</td>
</tr>
<tr>
<td>→ easily removed once healed</td>
<td>→ no antimicrobial properties</td>
</tr>
</tbody>
</table>

2) **Transcyte:** Biobrane + growth factors; stimulates wound healing

3) **Integra:** collagen matrix + silicone outer layer.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ closes full-thickness burns</td>
<td>→ no antimicrobial properties</td>
</tr>
<tr>
<td>→ dermal equivalent (lessens scarring)</td>
<td>→ expensive</td>
</tr>
</tbody>
</table>

**Xenografts** (i.e., pig skin) and **homografts** (cadaver skin) function like normal skin and are used optimally for large partial-thickness wounds. Disadvantages include the risk of viral transmission or residual “mesh” appearance if meshed allograft becomes engrafted.
POST BURN CATABOLISM
Carlos Rosales MD

I. Metabolic Response to Burn Injury
- Characterized by tachycardia, increased cardiac output, elevated energy expenditure, increased O2 consumption, proteolysis, lipolysis, and severe nitrogen losses.
- This response is sustained for 9 months after a burn injury

II. Eiology
- This response is due to catabolic hormones and futile substrate cycling
  A. Catecholamines
     - action through alpha and beta adrenergic receptors on hepatocytes and lipoocytes directly and indirectly through stimulation of adrenergic receptors in the pancreas
     - Increase glucose by gluconeogenesis and glycogenolysis
     - Increase fatty acid availability through peripheral lipolysis
     - Also leads to increase of net release of glucagon vs insuling
  B. Glucocorticoids
     - Released by hypothalmic-pituitary-adrenal axis
     - Induce insulin resistance adding to the hyperglycemia

III. Nitrogen Losses
- Excretion increase due to peripheral muscle breakdown during production of gluconeogenic amino acids
- Etiology is from increases in protein synthesis and breakdown of skeletal muscle, with greater increases in breakdown.

III. Possible treatments (catabolic modulators)
Oxandralone/testosterone
Beta-blockers
Insulin
IGF/IGFBP3
Growth hormone
Management of Electrical Burns
Chris T. Stephens, MD

Background/Introduction
- 3-5% of all burn pts admitted have electrical injuries
- visible areas of tissue necrosis represent only a fraction of the burned tissue
- electrical current enters the body typically through fingers or hand and travels through the tissues with the lowest resistance – generally nerves, blood vessels, and muscles
- current then leaves body at region of “grounded” area – typically the feet
- heat generated by transfer of electrical current and passage of current then damages the tissues – the resulting damage to blood vessels can cause thrombosis and resultant deep tissue injury
- injuries divided into high and low voltage injuries

Low-voltage Injuries
- similar to thermal injuries without penetration to deeper tissues – zones of injury from the surface can extend into the tissues
- most household currents (110 – 220 volts) produce this type of injury
- causes only local damage to tissues
- worst type in this class is burn to the edge of the mouth (oral commissure) – see with children gnawing on electrical cords

High-voltage Injuries
- described as a syndrome – consists of various degrees of cutaneous burns at the entry and exit sites, combined with hidden destruction of deeper tissues as the current travels along the bone
- many pts also have cutaneous burns from ignition of clothing secondary to discharge of current
- look for ventricular fibrillation in pts presenting with cardiac arrest – initiate defibrillation/CPR immediately
- continuous telemetry is necessary if pt presents with abnormal ECG on initial presentation or cardiac arrest after electrical burn with pharmacological Tx of any dysrhythmias

Management
- pts are also at risk for other trauma from being thrown from electrical source, falls, as well as the violent tetanic contractions of the muscles resulting from the alternating current sources - cause fractures and dislocations
- key to management lies in treatment of the wound – remember that most significant injury is within the deep tissue and subsequent edema can lead to vascular compromise to any distal tissue region. Watch for compartment syndrome.
- initial assessment always involves airway, breathing, circulation, and a thorough physical exam – as well as an electrocardiogram
- assessment should include circulation to distal vascular beds to determine perfusion patency and the need for escharotomy and fasciotomy – if muscle compartment is extensively injured and necrotic, early amputation may be necessary
- early exploration of muscle beds is important and debridement of devitalized tissues with care/attention given to deeper periosteal planes (tissues with potential for continued damage from heated bone source)
- fasciotomies should be complete and may require nerve decompressions such as carpal tunnel and Guyon canal releases
- if tissues have questionable viability – re-exploration in 48 hrs should be done – may require multiple re-explorations to ensure viability of remaining tissues and complete debridement
- after debridement – closure of wounds is important – grafts and/or flaps may be required
Other considerations

• Muscle damage results in release of hemochromogens (myoglobin) – filtered in the glomeruli and may result in obstructive nephropathy – aggressive hydration is of paramount importance to prevent renal failure – also IV administration of sodium bicarbonate (5% continuous infusion) and mannitol (25 g q 6 hrs) allows solubilizing of myoglobin and maintenance of urine output (maintain at 2 cc/kg/hr)

• Beware of delayed effects such as neurologic defects – serial neurologic evaluations should be performed after admission to determine any late neuropathology – pathology includes cortical encephalopathy, hemiplegia, aphasia, brain stem dysfunction have been reported up to 9 months post injury – cataracts have also been noted in victims of high – voltage injuries (up to 30% of patients – pts should be alerted to this possibility)
TEN (Toxic Epidermal Necrolysis)
Angela K. Champion, MD

**Definition**
Severe skin disorder characterized by blistering and peeling of epidermis

**Frequency**
Approximately 1/100,000 cases
Usually adults

**Clinical Features**
Painful localized area of skin erythema
Rapidly disseminates resulting in patches of loose skin
Patches may separate with slight pressure (Nikolsky sign) in sheets/layers
Fever, malaise, chills, myalgias
Scalded or raw areas of skin
Spread to eyes, mouth and genitalia

**Etiology**
Drugs—penicillin’s, sulfa, tetracycline’s, NSAIDS, anticonvulsants
Idiopathic
Radiotherapy
Chemical agents
Blood transfusion
Recent infection

**Diagnosis**
Rapid diagnosis based on clinical judgement
Biopsy skin lesion to determine level of dermal/epidermal separation to differentiate TEN from staphylococcal scalded skin syndrome

**Pathophysiology**
Theorized immune complex deposition at the dermal epidermal junction
Separation occurs between the dermis and epidermis
Unlike staphylococcal scalded skin syndrome, which separates within the epidermis.

**Mortality**
Approximately 40%
Secondary to sepsis, fluid/electrolyte imbalance, pneumonia, GI bleeds
Poor prognosis in elderly

**Treatment**
Burn unit management
Wound coverage, usually with homograft
Aggressive fluid hydration & diphenhydramine infusion
Debridement, local wound care, topical antibiotics
Discontinue any suspected medications
Consult ophthalmology for evaluation for conjunctivitis or corneal damage
Controversial: Corticosteroids probably worsen outcome
SECTION 6

CHAPTER 21

CRITICAL CARE
As hemoglobin becomes more saturated, the affinity of hemoglobin for oxygen also increases. This is reflected in the sigmoid shape of the curve, which indicates that a decrease in $P_aO_2$ makes considerably more oxygen available to the tissues. Thus, the sigmoid shape of the curve implies greater efficiency of blood transportation of oxygen from the lungs to tissues.

Shifts in the oxygen dissociation curve are quantitated by the $P_{50}$ - the partial pressure of oxygen at which hemoglobin is half saturated with oxygen at 37°C and pH 7.4.

A low $P_{50}$ indicates a left shift in the oxygen-dissociation curve and an increased affinity of hemoglobin for oxygen; in other words, the left shift of the curve indicates that a lower-than-normal oxygen tension saturates hemoglobin in the lung and the subsequent release of oxygen to the tissues occurs at a lower than normal capillary oxygen tension.
Lung Volumes
Chance L. Irwin, MD

I. Tidal Volume (TV)
   - the amount of air that moves into the lungs with each inspiration or the amount of air that moves out of the lungs with each expiration

II. Inspiratory Reserve Volume (IRV)
   - air inspired with a maximal inspiratory effort or the volume of air that can be exchanged from maximal TV to maximal vital capacity (VC).

III. Expiratory Reserve Volume (ERV)
   - volume expelled by an active expiratory effort after passive expiration

IV. Residual Volume (RV)
   - air left in the lungs after maximal expiratory effort

V. Vital Capacity (VC)
   - the largest amount of air that can be expired after a maximal inspiratory effort; frequently measured clinically as an index of pulmonary function; it gives useful information about the strength of the respiratory muscles

VI. Respiratory Dead Space
   - the space in the conducting zone of the airways occupied by gas that does not exchange with blood in the pulmonary vessels

VII. Forced Vital Capacity (FVC)
   - amount of gas exhaled following maximal inspiration and expiration

VIII. Forced Expiratory Volume (FEV)
   - normal value in an adult is 5-7 liters
   1. FEV1- the fraction of the VC expired during the first second of forced expiration with maximal effort
      a. Usually 80% of total FEV
      b. Restrictive disease- FEV1 and FVC are both restricted but the ratio is normal or slightly elevated (sarcoid, idiopathic pulmonary fibrosis, pneumoconiosis, interstitial lung disease, neuromuscular problems, and chest wall disease)
      c. Obstructive disease- both FEV1 and FVC are reduced and the ratio is 30-40% of the normal value (asthma, COPD, bronchiectasis, CF, and bronchiolitis)
   2. FEV25-75%- measure of average flow rate over the middle portion of expiration

IX. Functional Residual Capacity (FRC)
   - the amount of gas contained in the lung at the end of quiet or normal expiration (FRC=RV+ERV)
   - major reservoir for oxygen in the body second only to hemoglobin
   1. Closing Capacity (CC)
      - lung volume at which the airways begin to close
      - if FRC falls below CC then atelectasis occurs leading to hypoxemia
      - FRC falls with obesity, upper abdominal surgery, ARDS, pulmonary edema, pregnancy, supine position, and general anesthesia
      - FRC increases with COPD and PEEP
      - CC increases with advancing age, smoking, chronic bronchitis, and pulmonary edema

X. Minute Ventilation
   - amount of air inspired per minute which is normally about 6 liters (500ml/breath X 12 breaths/minute)

XI. High Operative Risk Patients
   - FVC <50% predicted
   - FEV1 <50% of FVC, greatest risk if <500ml
- FVC < 2 liters
- maximal voluntary ventilation (largest amount of gas that can be moved into and out of the lungs in 1 minute by voluntary effort- normal is 125-170 L/minute) < 50% predicted
- ratio of RV to TLC > 50%
- diffusing capacity < 50% predicted

XII. **Low Risk Operative Patients**
- mean pulmonary artery pressure on balloon occlusion and exercise < 35mmHg
- systemic PaO2 value on balloon and exercise > 45mmHg
- predicted post pneumonectomy FEV1 value > 0.8 liters
Description
- allows measurement of RA, RV, and PCWP
- allows calculation of cardiac output and other hemodynamic parameters via thermodilution
- allows sampling of pulmonary arterial (mixed venous) and right atrial blood
- lumens may allow measure of PAP, PCWP and obtaining mixed venous blood
- proximal (RA) lumen allows measure of RAP or CVP
- balloon lumen, when inflated assists with floating catheter through chambers into pulmonary artery
- thermistor lumen is used to calculate cardiac output by thermodilution

Waveform in Relation to Catheter Position
- superior vena cava/right atria pressure = 1-6 Hg
- right ventricle pressure = diastolic 1-6 Hg, systolic 15-30 Hg
- pulmonary artery pressure = diastolic 6-12 Hg, systolic 15-30 Hg
- pulmonary capillary wedge pressure = 6-12 Hg

Hemodynamic Measurements in Specific Disease States
- septic shock
  - early: ↓PCWP, ↓SVR, ↑CO
  - late: ↓PCWP, ↑SVR, ↓CO
- neurogenic shock: ↓PCWP, ↓SVR, NL/↓CO
- cardiogenic shock: ↑PCWP, ↑PADP, ↓CO, ↑SVR
- hypovolemic shock: ↓PCWP, ↓CO, ↑SVR
- pulmonary emboli: NL PCWP, ↑PADP, ↓CO
- cardiac tamponade: ↑PCWP, ↑SVR, ↓CO

Data Interpretation

<table>
<thead>
<tr>
<th>Hemodynamic Measurement</th>
<th>Normal Value</th>
<th>Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAP</td>
<td>1-6 Hg</td>
<td>↑RV failure, PE, tamponade</td>
</tr>
<tr>
<td>PAP</td>
<td>6-12 Hg (dia.)</td>
<td>↑PE, chronic lung disease, VSD</td>
</tr>
<tr>
<td></td>
<td>15-30 Hg (sys.)</td>
<td></td>
</tr>
<tr>
<td>PCWP</td>
<td>6-12 Hg</td>
<td>↑LV failure, acute mitral insuff., tamponade, decrease compliance, mitral stenosis</td>
</tr>
<tr>
<td>CO</td>
<td>3.5-7 L/min</td>
<td>↓dsyrhythmias, MI, ishcemia, VSD</td>
</tr>
<tr>
<td>SVR</td>
<td>900-1300</td>
<td>↑hypovolemic vasoconstriction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓septic shock</td>
</tr>
<tr>
<td>PVR</td>
<td>155-255</td>
<td>↑cor pulmonale, PE, valvular disease</td>
</tr>
</tbody>
</table>
I. Conventional Mechanical Ventilation refers to the delivery of full or partial ventilatory support by a volume-cycled mechanical ventilator or by pressure support. It can also include the maintenance of positive airway pressure at the end of exhalation (PEEP). Mechanical ventilation has two benefits: 1. It improves gas exchange and 2. It decreases the work of breathing. The application of PEEP to the respiratory system can improve V/Q matching and decrease intrapulmonary shunting, both of which relieve hypoxemia and diminish hypercapnia.

II. Indications for Mechanical Ventilation
1. Loss of Ventilatory Reserve
   - RR greater than 35, TV less than 5ml/kg, VC less than 10 ml/kg, minute ventilation greater than 10 L/min, rise in PCO2 greater than 10mm Hg
2. Refractory Hypoxemia
   - Alveolar-arterial gradient greater than 450 at an FiO2 of 1, PaO2/PAO2 less than 0.15, PaO2 with supplemental O2 less than 55 mm HG
3. Protection of Airway secondary to impaired airway patency

III. Modes of Ventilation
1. CMV controlled mechanical ventilation
   - a tidal volume and rate are set on the ventilator and minute ventilation is completely dependent on those parameters.
   - Useful for patients that are making no respiratory effort.
2. AC assist controlled mech vent.
   - an inspiratory effort by the patient triggers the delivery of a pre-set tidal volume. Therefore, patient work is required to trigger the ventilator.
   - A safety back-up rate is set on the ventilator to prevent hypoventilation.
3. IMV intermittent mandatory mech vent
   - A combination of spontaneous breaths with machine breaths. The ventilator delivers a breath with the pre-set tidal volume at a pre-set intervals. The patient is also able to breathe spontaneously through the ventilator.
   - SIMV synchronized the patient’s inspiratory effort with the ventilator and eliminates random delivery of machine breaths, if enough breaths are initiated by the patient.
4. Pressure Support Ventilation
   - tends to be a more comfortable ventilatory option for the patient as he/she has greater control over the flow rates and ventilator cycle.
   - The ventilator delivers a pre-set pressure with each breath until the inspiratory flow stops.
   - The drawback to this setting is that neither the tidal volume nor the minute ventilation is predetermined. Therefore, close monitoring is a essential.
   - A combination of PS and IMV will give the benefit of a pre-set TV and minute ventilation (IMV) and a pressure support of any spontaneous breaths taken by the patient.
5. Pressure Control Ventilation
   - this setting is used in patients where barotrauma may become an issue. Its purpose is to control peak airway pressures.
   - This setting is sometimes used with inverse I/E ratios (prolonging inspiration which increases gas distribution and shortening expiration which decreases alveolar collapse). Potential problems with inverse I/E ratios include air trapping secondary to a shortened expiratory interval and respiratory acidosis from CO2 retention.

IV. PEEP
1. Definition – an elevation of alveolar pressure above atmospheric pressure at the end of exhalation.
2. Obstructive Lung Disease
   - Auto PEEP, persistent exhalation at the time of the next breath, is common in these patients. This increases the airway pressure the patient must generate in order to trigger a breath. PEEP can counteract this and decrease the amount of negative
pressure the patient must generate to trigger the ventilator (decreasing the work of breathing).

- It is recommended that PEEP should be less than the amount of auto PEEP. Otherwise, air trapping can result and lead to barotrauma.

3. PEEP and ARDS
   - The theory is that PEEP can help increase hemoglobin saturation, and decrease the amount of FiO2 needed for adequate oxygenation by increasing alveolar recruitment. This should result in an increase in functional residual capacity and improve V/Q mismatching.

4. PEEP and Cardiac Disease
   - Some studies have shown that patients in cardiogenic pulmonary edema may avoid subsequent need for intubation with the addition of PEEP.
   - The etiology of the cardiomyopathy may influence the hemodynamic response to PEEP. One study showed that patients with idiopathic dilated cardiomyopathy benefited more from PEEP than patients with ischemic cardiomyopathy.

5. Contraindications to PEEP
   - No absolute contraindications
   - Relative contraindications include elevated peak and mean airway pressures, elevated intracranial pressure, pulmonary embolism, unilateral lung disease and bronchopleural fistula.
Nitric Oxide
Mechanisms of Action & Uses
Nicole L. Nemeth, MD

NO Synthase Synthase

\[
\text{L-Arginine} + \text{NADPH} + \text{H}^+ + \text{O}_2 \quad \rightarrow \quad \text{L-Citrulline} + \text{NADP}^+ + \text{NO}
\]

- \(\text{NO} \equiv \text{EDRF}\) (endothelial derived relaxing factor)
- \(T_{1/2}\) only a few seconds, \(\therefore\) paracrine mediator
- Relaxes smooth muscle (of vascular and GI systems)
- Inhibits platelet aggregation
- Coordinates tumoricidal & bactericidal actions of macrophages
- Functions as a signal transduction molecule (regulates guanylyl cyclase which catalyzes \(\text{GMP} \rightarrow \text{GTP}\))

USES:

1) ARDS→
   - Characterized by pulmonary hypertension and intrapulmonary shunting
   - Inhaled NO (NO) relaxes muscular arteries and veins via guanylate cyclase (\(\uparrow\text{cGMP}\))
   - NO works locally without dilating the systemic circulation (NO binds to Hgb rapidly as is thus quickly inactivated)
   - NO shown to improve the perfusion of ventilated regions of lung in ARDS, thereby reducing the mean pulmonary-artery pressure, decreasing intrapulmonary shunting (\(\downarrow\text{V/Q}\) mismatch), and improving the \(\text{PaO}_2 / \text{FiO}_2\) ratio, without any change on the mean arterial pressure or cardiac output (versus IV prostacyclins)
     (N Engl J Med 1993; 328: 399-405)

2) Persistent Pulmonary Hypertension of the Newborn (PPHN)→
   - Only FDA approved use of NO
   - For >34 weeks gestation neonates with hypoxic respiratory failure associated with pulmonary HTN (sepsis and hypoxia in neonate can maintain \(\uparrow\) pulmonary artery pressure and patent ductus arteriosus \(\rightarrow\) persistent fetal circulation and pulmonary HTN)
   - Effective in reversal of PPHN (~20 ppm)

3) Sepsis→
   - NO known to be released in response to sepsis, evidenced by \(\uparrow\uparrow\) urinary and plasma nitrate levels in septic patients (NO + HgB \(\rightarrow\) nitrate)
   - Nitric oxide synthase (NOS) inhibitors function by competing with L-arginine for both entry into cells and substrate-binding sites on the enzyme
♦ NOS inhibitors (N(G)-methyl-L-arginine hydrochloride, for example) have been shown to maintain blood pressure and decrease the need for pressors (such as norepinephrine) in patients in septic shock
♦ NOS inhibitors and methylene blue are currently only in investigational use for treatment of the low SVR in adult sepsis, and their use has not been shown to improve mortality
♦ Detrimental effects from systemic administration may result from the inhibition of both the constitutive and inducible forms of NOS, disrupting microvascular flow (stimulating platelet aggregation & adherence), decreasing C.O., and ↑ pulmonary artery pressure

4) Liver Failure→
Hepatopulmonary Syndromes = alcoholic liver disease, dyspnea, and hypoxemia
Hypoxemia may be a result of pulmonary vasculature aberrations, either vasodilation and V/Q mismatch or vascular wall thickening & occlusion
Increased concentration of NO in the exhaled breath of patients with severe liver cirrhosis
∴ NOS inhibitors may improve hypoxemia if pulmonary dilation predominates
Portopulmonary Syndrome hypoxemia likely due to pulmonary vascular HTN
NO has been shown to improve hypoxemia in these subsets of patients
Respiratory Quotient
Chance L. Irwin, MD

I. Respiratory quotient (RQ) or respiratory exchange ratio (RER) is the ratio of the rate of carbon dioxide produced to the rate of oxygen uptake. In other words,

\[ RQ = \frac{VCO_2}{VO_2} \]

II. The respiratory quotient is a valuable indicator of substrate oxidation, that is the relative amounts of carbohydrate and fat being oxidized for energy production.

III. When oxygen is being combined with pure carbohydrate, energy is released at the rate of 5.1 kcal per liter of oxygen and a volume of carbon dioxide is produced equal to the volume of oxygen consumed, or

\[ VCO_2 = VO_2 \]
\[ RQ = 1.0 \]

IV. When oxygen is being combined with pure free fatty acid (FFA), energy is released at the rate of 4.7 kcal per liter of oxygen and carbon dioxide is produced at a rate that is 70% that of the rate of oxygen consumption, that is

\[ VCO_2 = 0.70 \times VO_2 \]
\[ RQ = 0.7 \]

V. During steady-state exercise, the average RQ will be between 0.7 and 1.0 (it will never be 0.7, some carbohydrate is always metabolized). The lower the RQ is, the more relative contribution fat is making to the energy demand of the exercise, and the higher the RQ, the higher relative contribution being made by carbohydrate.

**TYPICAL RQ Values**

- 1.3 Lipogenesis
- 1.0 Carbohydrate oxidation
- 0.8 Mixed fuel use
- 0.7 Fat oxidation
FRANK-STARLING LAW OF THE HEART
Ricki Y. Fram, MD

First, Basic Concepts:
- **Preload**: The degree of tension on the muscle when it begins to contract; also called the pressure during filling of the ventricle.
- **Afterload**: The load against which the muscle exerts its contractile force; also the arterial pressure against which the ventricle must contract.

Frank-Starling Mechanism
- Intrinsic ability of the heart to adapt to changing volumes of inflowing blood.
- The greater the heart is stretched during filling, the greater will be the force of contraction, and the greater will be the quantity of blood pumped into the aorta.
- When an extra amount of blood flows into the ventricles, the cardiac muscle itself is stretched to a greater length.
- This, in turn, causes the muscle to contract with increased force because the actin and myosin filaments are then brought to a more nearly optimal degree of interdigitation for force generation.
- The ventricle automatically pumps the extra blood into the arteries.
- This ability of stretched muscle, up to an optimal length, to contract with increased force is characteristic of all striated muscle.
SEPTIC SHOCK
John J. Bawduniak, MD

A Etiology
1. gram(-) bacilli- (E coli, Pseudomonas, Proteus, Klebsiella, Enterobacter, Serratia, Meningococcus)
2. Gram(+) - (S aureus, Pneumococcus, Streptococci)
3. fungal infections

B. Sites of Infection
1. GU, GI tract, respiratory, wound/infected IV, meningitis

C. Predisposing Factors
1. Malnutrition
2. Instrumentation
3. Advanced age
4. Immunosuppressive therapy
5. Neoplastic/chronic disease

D. Clinical Manifestations
1. Early Phase- fever, chills, leukocytosis with left shift, hyperventilation, tachycardia, hypotension, decreased PCWP and SVR, increased cardiac output
2. Late Phase- significant hypotension, skin cool and clammy, oliguria, metabolic acidosis (lactic acidosis), DIC, LFT abnormalities, renal failure, hypoglycemia, decreased PCWP, decreased cardiac output, increased SVR

E. Management
1. Treat hypotension with saline, aggressive volume resuscitation, hemodynamic monitoring critical, titrate volume PCWP of 15-18mmHg
2. Colloid/crystalloid may be necessary in some pts
3. Vasopressors indicated only when other measures fail to correct hypotension and PCWP has been raised to 15-18mmHg.
4. Broad Abx after cultures sent
5. Monitor with PA cath and arterial line
6. Drain any infectious foci
7. Monitor blood gases, electrolytes, renal function
8. Measure UOP hourly
9. Correct acid-base/electrolyte/hypoxia
10. IV hydrocortisone if adrenal insufficiency is suspected
11. Correct platelets, coags (FFP)
12. Intubate if PaO2<60mmHg with FIO2>.6 or resp rate >35
13. PA catheter may be required.
Inotropic Drugs
Farin W. Smith, MD

These are adrenergic agents that act at the neurosynaptic junction. As a review, antagonists of the receptors have the following effects:

\( \alpha_1 \) receptors are located at postsynaptic membrane of end organs and involve smooth muscle constriction.
- **Effects:** vasoconstriction, ↑ PVR, ↑ BP, mydriasis, ↑ tone of internal bladder sphincter

\( \alpha_2 \) receptors are located in presynaptic nerve endings and inhibit \( \alpha_1 \).
- **Effects:** Inhibits Norepi release, inhibits insulin release

\( \beta_1 \) receptors predominate in cardiac muscle and cause increase in HR and contractility.
- **Effects:** Tachycardia, ↑ lipolysis, ↑ myocardial contractility

\( \beta_2 \) receptors predominate in the skeletal muscle vasculature.
- **Effects:** Vasodilation, slight ↓ PVR, bronchodilation, ↑ glucagon release, relaxed uterine smooth muscle

<table>
<thead>
<tr>
<th>Drug</th>
<th>Use</th>
<th>Contract</th>
<th>HR</th>
<th>SVR</th>
<th>MAP</th>
<th>CO</th>
<th>Vasodilate</th>
<th>Arrhythmia</th>
<th>Renal Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digitalis</td>
<td>LV diastolic dysfunction</td>
<td>↑↑↑</td>
<td>↓</td>
<td>↓</td>
<td>0</td>
<td>↑</td>
<td>↑</td>
<td>↑↑</td>
<td>↑/↓</td>
</tr>
<tr>
<td>Dopamine</td>
<td>cardiac failure, sepsis, shock</td>
<td>↑↑↑</td>
<td>↑</td>
<td>↑</td>
<td>↑↑↑</td>
<td>0</td>
<td>↑</td>
<td>↑↑</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>Acute or congestive heart failure</td>
<td>↑↑↑</td>
<td>↑</td>
<td>0</td>
<td>↑↑↑</td>
<td>0 to ↑</td>
<td>↑</td>
<td>↑/↓</td>
<td>↑↑</td>
</tr>
<tr>
<td>Nor-Epi</td>
<td>High o/p cardiac failure, sepsis</td>
<td>↑↑</td>
<td>↓</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>↓</td>
<td>↓↓↓</td>
<td>↑</td>
<td>↓↓</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>shock</td>
<td>0</td>
<td>↓</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>0</td>
<td>↓↓↓</td>
<td>↑</td>
<td>↓↓</td>
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<tr>
<td>Epinephrine</td>
<td>Cardiac arrest, anaphylaxis, asthma</td>
<td>↑↑↑</td>
<td>↑↑</td>
<td>↑/↓</td>
<td>↑</td>
<td>↑↑</td>
<td>↑↑↑</td>
<td>↑↑</td>
<td>↓</td>
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<tr>
<td>Isoproterenol</td>
<td>Arrhythmia, bradycardia</td>
<td>↑↑↑</td>
<td>↓</td>
<td>↑↑↑</td>
<td>↓</td>
<td>↑↑</td>
<td>↓↑</td>
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<td>↓</td>
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<tr>
<td>Milirinone</td>
<td>CHF</td>
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<td>0</td>
<td>↓↓↓</td>
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<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
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</tbody>
</table>

The chart above has all the drugs and all the effects that that they have. But the chart below is what you really need to know when thinking inotropic drug therapy in the acute setting.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>BP</th>
<th>HR</th>
<th>PVR</th>
<th>OTHER</th>
</tr>
</thead>
<tbody>
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<td>↓</td>
<td>↑</td>
<td>↓ renal flow</td>
</tr>
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<td>Phenylephrine</td>
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<td>↓</td>
<td>↑</td>
<td>↓ renal flow</td>
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<tr>
<td>Dopamine</td>
<td>↑</td>
<td>↑</td>
<td>↑/↓</td>
<td>↑↑ renal flow</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>↑</td>
<td>0</td>
<td>0</td>
<td>arrhythmia</td>
</tr>
</tbody>
</table>
Glutamine Uses and Function
Chris T. Stephens, MD

- Primary metabolic fuel within the small intestine – 40% of available glutamine taken up by the gut from the general circulation (increased uptake by liver during sepsis) and directly from the gut lumen

- Enterocytes most likely take most of the glutamine (lymphocytes and macrophages may contribute to the uptake process) – glutamine taken up from both the basolateral membrane and gut luminal membrane (via brush border glutamine transporter)

- Gut is an efficient utilizer of glutamine and it strives to maintain its own concentration of it – when internal concentration decreases, glutamine synthetase increases (producing glutamine from glutamate and ammonium)

- Glutamine produced by muscle and lung can be taken up by the intestine and broken down into ammonium and glutamate – ammonium transported to the liver via portal circulation to be converted into urea while glutamate is broken down into alpha ketogluterate, citrulline, or alanine which can be utilized as fuels

- Addition of glutamine to the parenteral nutrition of patients may prevent gut atrophy that occurs during TPN administration – investigators have demonstrated this protective mechanism in laboratory animals by seeing improvements in villus heights and DNA content of intestine luminal cells – additionally glutamine has been shown to improve mucosal morphology in animals – however, conclusive benefits to humans after administration of glutamine during stress/illness has been lacking

- Glutamine is the preferred energy source of the small intestine during both stress and non-stress states – during simple surgical stress, synthesis of glutamine increases in other tissues such as muscle and lung and uptake increases in the small intestine – net result is a decrease in the amount of circulating glutamine. Sepsis – production of glutamine increased as well; however, liver uptake exceeds small intestine – therefore, during sepsis, glutamine levels increase and the decrease in small bowel uptake is believed to be the cause of mucosal barrier breakdown, increased permeability, translocation, and bacteremia

- Post major stress/injury – skeletal muscle catabolism and negative nitrogen balance occurs with an increased release in glutamine and alanine – mechanism allows for increased production of glutamine to compensate for increased need for glutamine during stress
Local Anesthetics
Carlos A. Murillo, MD

Local Anesthetics
- Cause reversible interruption of the conduction of impulses in peripheral nerves
- Cause a local decrease in the rate and degree of depolarization of the nerve membrane
- Effects are due to the blockade of sodium channels
- May be influenced by the local availability of the free base (B), as only the unionized portion can diffuse through the neural membrane
- Relatively inactive when injected into tissues with an acid pH (i.e. pyogenic abscess) which is presumably due to reduced release of free base
- Traction on certain tissues, particularly the peritoneum, is still uncomfortable
- Clinically, the order of loss of nerve function is as follows:
  - Temperature,
  - Touch,
  - Proprioception, and
  - Skeletal muscle tone

Signs of CNS toxicity:
  Early – tinnitus, lightheadedness, confusion, numbness
  Middle – shivering, muscle twitching, tremors, tonic-clonic seizures
  Late – loss of consciousness, CNS depression, respiratory arrest

Signs of cardiovascular toxicity:
  Early – hypertension, tachycardia
  Middle – myocardial depression, decreased cardiac output, mild to moderate hypotension
  Late – peripheral vasodilation, sinus bradycardia, conduction defects, arrhythmias, CV collapse

Types (amides):
  Bupivacaine (Marcaine): half-life 28 minutes, elimination half-life 3.5 hours
    Maximum dose 2 mg/kg with or without epi; sensory block longer than motor block
  Lidocaine (lignocaine): half-life 30 minutes; elimination half-life 100 minutes;
    Maximum dose 4.5-5 mg/kg without, 7 mg/kg with epinephrine

Management of Acute Toxicity

1) Maintain airway (supplemental oxygen, ventilation for apnea)
2) Seizures should be treated with anticonvulsant drugs such as thiopentone (150-250 mg I.V.) or diazepam (10-20 mg I.V.), repeat as necessary
3) Profound hypotension and brady-arrhythmias should be treated with intravenous atropine (0.5-1.5 mg) and colloid or crystalloid infusion
4) CPR should be continued for at least 60 minutes in case of bupivacaine toxicity
SECTION 7

CHAPTER 22

TRANSPLANTATION
Allorecognition

**Direct Pathway**—T cells recognize the MHC-peptide complex as foreign

**Indirect Pathway**—T cells recognize the peptide presented by MHC by a “self” cell as foreign

**Major Histocompatibility Complex, Class I (MHC-I)**

A.k.a. Human Leukocyte Antigen (HLA) –A, -B, -C

Found on all cells that are not in immunologically privileged sites

Two chains: $\alpha$-chain and $\beta_2$-microglobulin

The first two segments of the $\alpha$-chain form a groove for an 8-12 residue peptide, which jointly binds the T cell receptor (TCR)

$\alpha_3$-chain segment binds CD8 (cytotoxic T cells), giving specificity

**Major Histocompatibility Complex, Class II (MHC-II)**

A.k.a. Human Leukocyte Antigen (HLA) –DR, -DQ, -DP

Found on antigen presenting cells

- Macrophages/monocytes
- Dendritic cells
- Endothelial cells
- Thymic epithelial cells
- B cells

Two chains: $\alpha$-chain and $\beta$-chain

$\alpha_1$-chain and $\beta_1$-chain segments form groove for a 10-30 residue peptide, which jointly binds the TCR

$\beta_2$-chain segment binds CD4 (helper T cells), giving specificity

MHC-II mismatches result in increased immunological responsiveness when compared to Class I mismatches

**Minor Histocompatibility Antigens (MiHA)**

Relatively little contribution in transplant settings, unless HLA matched

**HLA Matching**

- Kidneys—0 antigen mismatch with improved graft function & survival
- Livers—HLA matching not as important
- Hearts—usually just ABO matched

**Panel Reactive Antibody (PRA)**

Serum from patient is incubated with complement and with B and T cells from a panel of donors that represent common HLA types

PRA value is the percent of lysed B or T cells

Higher PRA patients have higher positive crossmatch rates
Crossmatching (XM)
  Patient’s serum tested directly against donor cells
  Positive crossmatch associated with hyperacute rejection
Flow cytometry crossmatches (FCXM)
  Detects very low levels of circulating anti-HLA antibody
  Associated with higher rates of early acute rejection
Immunosuppressive agents
Carlos A. Murillo, MD

A. Immunosuppressive agents
   a. Essential for graft survival
   b. Common side effects
      i. Increased susceptibility to infection
      ii. Reactivation of previous infections, i.e. CMV
          Increased period 6-12 weeks after transplantation and during treatments for rejection
      iii. Increase risk for some malignancies
          i.e. In situ carcinomas of the cervix and low-grade skin tumors
      iv. Increased risk for virus-mediated tumors
          i.e. Lymphomas from EBV
   c. Increased risk for cardiovascular disease

B. Two main types: Induction and Maintenance Therapy

   **Induction Therapy**
   - Used for rejection therapy as well
   - Antibody preparation targeted towards lymphocyte depletion of IL-2 receptor inhibition
   a. Lymphocyte Depletion Measures
      1. Antithymocyte Globulin (ATG)
         a. Polyclonal sera produced when human lymphocytes are injected into animals of a different species
         b. Action targeted towards T-cells.
         c. **Lymphocytes coated with ATG are lysed or cleared by the reticuloendothelial cells in the liver and spleen.**
         d. Two types: Horse (hALG) and rabbit antisera (rATG) (rabbit > horse in potency)
         e. Results depend on potency and length of administration rather than a single dose.
         f. Toxicity depends on cross-reactivity to other tissues and ability of patient to produce Ab towards foreign proteins; results in thrombocytopenia and anemia
         g. Most common complication is allergic response to antisera: urticaria, serum sickness, anaphylaxis
      2. Monoclonal Antibody
         a. Monoclonal antibodies targeted towards T-cells in general (OKT3, anti-CD3)
         b. Others have been made: OKT4, OKT8
         c. Used to treat acute rejections for renal, heart, heart-lung, and liver
         d. Binds to the TCR (CD3) and functions to modulate the receptor and inactivate the T-cell
            i. Blocks naïve and established T-cells
            ii. TCR-OKT3 complex internalized and the cell is removed by the reticuloendothelial system.
            iii. T-cell #’s drop within 30-60 minutes, and return quickly after OKT3 is stopped.
            iv. Limitations are that it is immunogenic (becomes less effective with each dose) and can cause over immunosuppression (Tx<2 weeks)
      3. IL-2 Receptor Inhibitors (anti-CD25, basiliximab and daclizumab)
         a. IL-2R is a complex of proteins: $\alpha$(CD75), $\beta$, $\gamma$.
            i. $\alpha$ chain is only present on activated T-cells, and some activated B-cells and APC
            ii. **Action is based on the blockage of the IL-2R, leaving no free receptors to be used by the cell.**
            iii. Immunogenicity of basiliximab (chimeric) and Daclizumab (humanized) is reduced from the murine anti-CD25
            iv. Decrease in acute rejection rates, without an increase in infections or malignancies.
b. Adrenal Corticosteroids

1. Diverse anti-inflammatory effects
2. Decreases the pool of circulating lymphocytes with in 6 hours of administration
3. **Causes the T-cells and B-cell to relocate to lymphoid compartments**
   a. Believed to be due to surface changes promoting cell adhesion to endothelial tissues.
4. **Affects cytokine transcription and response (i.e. IL-1, IL-6, TNF, and IL-2) and prostaglandin production.**
5. Used in treatment of ongoing rejection, preventing rejection
6. Side effects include HTN, osteoporosis, hyperglycemia, GI bleeding an ulcer formation, etc.
7. Increased susceptibility to pyogenic and opportunistic infections

b. Antiproliferative Agents

1. Azathioprine
   a. Is 6-mercaptopurine with a side chain to protect the sulfhydryl group.
   b. Structurally similar to Inosine-MP
   c. **Produces a feedback inhibition to the Purine Biosynthetic Pathway to decrease AMP and GMP production, halting DNA and RNA production.**
   d. Given after cells are first stimulated; blocks humoral and cellular immunity
   e. Toxicity develops from anti-metabolite effects: bone marrow suppression and leukopenia
2. Mycophenolate Mofetil
   a. Inhibits purine metabolism by inhibiting **inosine monophosphate dehydrogenase** and blocks the proliferation of lymphocytes. Lymphocytes lack the salvage pathway.
   b. Decreased rejection rates compared to azathioprine with at least 2g per day.
   c. Side effects include diarrhea and leukopenia

3. T-Cell Directed Immunosuppressants

1. Cyclosporine
   a. Fungal metabolite from *Tolypocladium inflatum*
   b. Selectively inhibits TCR-mediated activation events without general myelosuppression
      i. **Inhibits IL-2-producing and cytotoxic T-cells**
      ii. **Inhibits IL-2 gene expression in activated lymphocytes**
      iii. **No inhibition of activated T-cells in response to exogenous IL-2**
      iv. **Inhibition of IL-1 Production**
      v. **Inhibition of resting T-cell activation**
   c. Metabolized by liver cytochrome P450; has a narrow therapeutic window
   d. Side effects include nephrotoxicity, HTN, hyperkalemia, hirsutism, and gingival hyperplasia, and hepatotoxicity
2. Tacrolimus (FK506)
   a. From soil fungus *Streptomyces tsukubaensis*
   b. Forms a complex with FK506 binding protein that **blocks the phosphatase activity of calcineurin that is important in IL-2 transcription**
   c. Similar functions as cyclosporine, only 100 more potent
   d. Used with cardiac, renal, bowel, and hepatic transplants; liver rejection, and some efficacy in rescue therapy for recurrent acute rejection
   e. Similar side effects without hirsutism and gum hyperplasia; increased alopecia and posttransplant diabetes.
3. Sirolimus (Rapamycin)
   a. Has a close structural analogue to tacrolimus and binds to the same FKBP.
   b. Does not block T-cell cytokine expression; **inhibits the transduction of signals from the IL-2R to nucleus**
   c. Acts synergistically with cyclosporine and serves to prevent graft vessel disease in rat transplant models.
   d. Not nephrotoxic; does increase triglycerides and decreases platelets
Clinical Rejection Syndromes
Robert P. Thomas, MD

- Rejection has been classified into three groups:
  1. Hyperacute
  2. Acute
  3. Chronic
- Of these, only acute can be successfully reversed
- Hyperacute is most preventable
- Chronic rejection remains the most difficult

Hyper Acute Rejection
- Caused by presentation of the recipient to an antigen expressed by donor; preformed cytotoxic antibodies against donor HLA I antigens (prior exposure from transfusion, pregnancy, or transplantation)
- Develops in minutes to hours
- Proper crossmatching helps eliminate (99.5%): ABO typing and lymphocytotoxic crossmatch- donor non-activated T cells mixed with serum from recipient in the presence of complement
- Pathological hallmarks: leukocyte clumping in glomerular capillaries, intravascular coagulation, and thrombosis
- Inflammation from this event can cause severe local pain and systemic effects:
  - fever, malaise, arthralgias, nausea, vomiting, wheezing, bronchospasm, hemolysis, platelet consumption, and pulmonary edema (even rupture of kidney/organ)
- Immediate plasmapheresis has had limited success
- Hyperacutely rejected organ should be removed or replaced

Acute Rejection
- Caused by T cells/ evolves over a period of days to weeks (most common in 1st 6 mo.)
- T cells bind antigen via TCR (T cell receptor) or after phagocytosis of donor tissue and re-presentation of MHC peptides
- Infiltration of graft with T cells (activated)
- Usually asymptomatic, can cause fever, graft dysfunction (oliguria), hypertension, graft swelling, pain
- 70% of cellular rejection episodes can be treated with high-dose steroids
- Antithymocyte globulin (ATG) also used

Chronic Rejection
- Poorly understood
- Insidious onset: months to years
- Histology: replacement of parenchyma with fibrosis and vascular fibromuscular hyperplasia
- Not direct cell-mediated tissue destruction
- Cumulative effects of mild subclinical immune recognition, by several arms of the immune system and the resulting exposure to fibrogenic cytokines, damages epithelium and vascular endothelium
Posttransplant Tumors
M. Joseph Elieson, MD

• There is a 3-4 fold increased incidence of cancer in transplant patients compared to age-matched controls in the general population.

• These cancers frequently demonstrate a more aggressive nature than do tumors in patients that have not undergone transplantation.

• There is no increase in the incidence of neoplasms that are commonly observed in the general population (lung, breast, prostate, colon, & uterine).

• Most common tumors were those of the skin and lips, lymphoma, Kaposi’s sarcoma, renal carcinomas, vulvar / perineal carcinoma, hepatobiliary carcinomas, and sarcomas.

• Many Cancers are associated with viral infections

• The incidence of cancer increases with the length of follow-up after transplantation.
  Percent probability of developing cancer following renal transplantation at 24 yrs was 72% (66% for skin cancers, 27% for non-skin cancers) in one study.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Increased Incidence</th>
<th>Average Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>4-21x</td>
<td>75 mo</td>
</tr>
<tr>
<td>Lips</td>
<td>29x</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>28-49x</td>
<td>34 mo</td>
</tr>
<tr>
<td>Kaposi’s Sarcoma</td>
<td>400-500x</td>
<td>21 mo</td>
</tr>
<tr>
<td>Vulvar / Perineal Carcinoma</td>
<td>100x</td>
<td>115 mo</td>
</tr>
<tr>
<td>Hepatobiliary Carcinomas</td>
<td>20-38x</td>
<td></td>
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</table>

• Skin Cancers are 4-21 times more common in transplant patients than the general population.
  • Basal cell carcinomas outnumber squamous cell carcinomas in the general population 5:1
  The opposite is true in transplant recipients in whom SCCs out number BCCs by 1.8:1
  • SCCs occur mostly in people in their 60’s and 70’s in the general population
  SCCs occur 30 years younger in transplant recipients.

• Posttransplant lymphoproliferative disease (PTLD) is a term used to express the different characteristics of lymphomas and lymphoproliferations in transplant patients. It encompasses a broad spectrum of disorders ranging from benign hyperplasias to frank malignant lymphoma.
  • Lymphomas in the general population frequently involve lymph nodes, 70% of PTLDs occurred in extranodal sites (liver-25%, lungs-21%, CNS-21%, intestines-19%, kidneys-18%, spleen-12%)
  • Of those with CNS involvement, 54% were limited to the CNS, whereas in the general population cerebral lymphomas are frequently associated with lesions in other organs, and only 1% of lymphomas are confined to the CNS.
  • The transplanted organ was involved in 23% of PTLD.
  • Lymphoma in transplant patients is associated with EBV infection.

• Kaposi’s sarcoma (KS) is four to five hundred times more common in renal transplant patients than the general population in the US.
  • The number of transplant patients with KS exceeds those with carcinomas of the Colorectum or breast or prostate.
  • Apart from individuals with AIDS, there is no other group in which the number of KS’s exceed these common cancers.
  • KS affects transplanted patients in a 3:1 male to female ratio which is far lower than the 9–15:1 ratio seen in the general population.
• Renal Tumors have a 30-40 increased frequency in renal transplant patients.
  • This is thought to be due more in part to the patient’s underlying kidney disease than as a complication of immunosuppressive therapy.

• Cancers of the vulva, perineum, scrotum, penis, perianal skin, or anus are increased 100x in transplant patients over the general population.
  • Females outnumber males by 2.6:1 in contrast with most other post transplant cancers where males outnumber females by more than 2:1.
  • Transplant patients developed these cancers at much a younger age (avg. 42 yrs) than the general population (50-70 yrs).

• Hepatobiliary tumors are increased 20-38x in transplant patients.
  Most are hepatomas and a substantial number have a history of Hepatitis B or C infection.

Lifetime follow up and surveillance for cancer is critical in transplant patients. A high percentage of posttransplant tumors are low-grade malignancies that are readily amenable to treatment.
SECTION 7

CHAPTER 23

INFECTIOUS DISEASES & WOUND HEALING
Collagen as a fibrous protein—

- Made in fibroblasts (osteoblasts, chondroblasts)
- Triple-helix structure, consisting of 3 α chains
- Polytripeptide sequence (Gly – Leu – Hyp – Gly – X – Y)n
- Y = proline or lysine, which are then hydroxylated
- O₂ and Vitamin C (ascorbic acid) are necessary substrates for hydroxylation
- Hydroxylation enables collagen fibrils to cross-link
- Cross-linking is essential for the stability and tensile strength properties of collagen

\[\text{Prolyl} \xrightarrow{\text{Prolyl Hydroxylase}} \text{Hydroxyprolyl}\]

Types of Collagen—

<table>
<thead>
<tr>
<th>Type</th>
<th>Tissues</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Skin, bone, tendon, blood vessels, cornea</td>
</tr>
<tr>
<td>II</td>
<td>Cartilage, intervertebral disk, vitreous body</td>
</tr>
<tr>
<td>III</td>
<td>Blood vessels, fetal skin</td>
</tr>
<tr>
<td>IV</td>
<td>Basement membrane</td>
</tr>
<tr>
<td>V</td>
<td>Smooth muscle</td>
</tr>
<tr>
<td>XII</td>
<td>Tendons, ligaments, periosteum, skin, cartilage</td>
</tr>
<tr>
<td>XVI</td>
<td>Placenta, fibroblasts, smooth muscle cells</td>
</tr>
<tr>
<td>XIX</td>
<td>Vascular, neuronal</td>
</tr>
<tr>
<td></td>
<td>basement membrane zone</td>
</tr>
</tbody>
</table>

Collagen in wound healing—

1) Proliferating epithelial &/or endothelial cells produce pericellular & basement membrane collagens

2) Fibrillar collagens (Types III and V) + single interspersed Type-I derived fibers are deposited

3) More fibrous and dense scar tissue forms, consisting primarily of Type-I collagen.

Perturbations in normal wound healing— (ref. Townsend 16/e, Table 7-4)

- Infection
- Diabetes Mellitus
- Ischemia
- Radiation
- Advanced Age
- **Vitamin C deficiency**
- Glucocorticosteroids
Agents of Insult:

Oxygen - Oxidative burst after periods of ischemia can result in cell injury and death. Reduced oxygen free radicals degrade collagen and hyaluronic acid; disrupt organelles and protein systems as it destroys cell membranes. Free radicals can be created from radiation, chemical insult, ischemia reperfusion injury, and inflammation.

Steroids - Commonly inducing wound-healing delay, steroids stabilize macrophages inhibiting fibrogenesis, angiogenesis, and wound contraction. Steroids stabilize lysosomal membrane to inhibit the wound healing capabilities of the macrophage.

Smoking - Decreases oxygen delivery through nicotine induced vasoconstriction and left hemoglobin dissociation curve shift from increased levels of carbon monoxide.

HIV - Decreased CD4 counts place the patient at potential risk for postoperative infection in the immunocompromised host.

Age - Results in generalized slowing of the wound healing phases. A topic of much debate, some suggest that age results in poor tolerance to ischemia.

Denervation - No effects on wound contraction or epithelialization. Ulcerations result from tissue susceptibility to temperature changes as well as vulnerability of anesthetized tissue to pressure.

Infection - Prolongation of inflammatory phase to delay and inhibit the phases of wound healing. Results from decrease in pO2 and toxic byproducts.

Chemotherapy - Decrease fibroblast proliferation and wound contraction. When started at least fifteen days postop, few long-term effects are noted on wound healing.

Radiation Therapy - Occlusion of small vessels to result in decreased collagen deposition and tensile strength. Radiation can result in irreversible injury with potential for progressive disease. Induces most significant wound healing impairment when given preoperatively within three weeks.

Diabetes Mellitus - Thickened capillary membranes decreased transport of oxygen to impair the entire wound healing process. Glycosylated collagen is more brittle.

Inherited Disorders - Pseudoxanthoma Elasticum, Ehlers-Danlos syndrome, and epidermolysis bullosa. All impair wound healing.
Promoters of Healing:

Oxygen- One of many critical nutrients, oxygen concentration determines the healing rate of many wounds. A tissue PO2 greater than 40 mmHg is required to sustain fibroblast replication with collagen production, myofibroblast stimulation, as well as hydroxylation of proline and lysine in collagen cross linking.

Vitamin A- By destabilizing the lysosomal membrane vitamin A restores the inflammatory effects of monocytes impaired by steroids. Vitamin A administration has been shown to reverse the detrimental effects of steroids, increase breaking strength with oral ingestion, and accelerate wound reepithelialization. Vitamin A deficiency impairs the normal phases of wound healing.

Vitamin C: Essential for the production of collagen.

Vitamin E: Reported to increase tensile strength in tissue exposed to preoperative radiation. Acts through antioxidant neutralization of lipid peroxidation a product resulting from radiation. Such antioxidant properties result in decreased free radicals and peroxidases. Excess of vitamin E has been found to decrease wound strength.

Zinc: Cofactor for many enzymes responsible for epithelialization and fibroplasias, sufficient zinc concentrations are required for normal wound healing. Only enhances wound healing in the zinc deficient state.

Tissue Adhesives (fibrin glue)- The use of artificial fibrin deposition to bond tissues has been found to enhance breaking strength.

Nutrition- Results in decreased tensile strength when deficient with the amino acid methionine being key to fibroplasias.

Hydration- Provides environment to enhance wound healing as seen that moist wounds heal faster than dry wounds.

References: Townsend, Textbook of Surgery; Selected Readings in Plastic Surgery v9, number 3
**Clostridial Infections**  
David B. Loran, MD

- Normally found in GI and female genital tracts  
- 30 species of Clostridium identified  
- Diseases caused by Clostridium:  
  - Intestinal syndromes: food poisoning, enteritis, colitis  
  - Deep tissue infections  
  - Soft tissue infections: spectrum from simple contamination to myonecrosis  
  - Bacteremia: transient or sepsis

- Botulism  
  - Food-borne: incubation 18-36h, causes cranial nerve paralysis then descending paralysis from neck to legs  
  - Wound-borne: incubation period 10 days, similar symptoms  
  - Treatment: supportive and anti-toxin

- Tetanus  
  - Causes blockage of inhibitory neurotransmitter at presynaptic junctions  
  - Symptoms: within 3-14d, increased masseter tone then descending stiffness  
  - Treatment: anti-toxin for symptomatic or severely contaminated wounds and muscle relaxants/benzodiazepines/paralytics to control spasm

- Deep tissue and soft tissue infections  
  - Treatment: Pen G and clindamycin +/- debridement

- Clostridium difficile  
  - Most frequently associated with Clindamycin but can be ANY antibiotic  
  - Symptoms: presents 1-2 weeks after initiating antibiotic therapy  
    - Watery diarrhea, abdm cramps, low-grade fever  
    - Toxic megacolon or generalized peritonitis 1 – 3 %  
  - Pathophysiology  
    - Non-invasive infection which alters gut flora allowing proliferation of C. diff. and production of toxin  
  - Treatment  
    - Stop antibiotic  
    - Flagyl PO and Vancomycin PO have equal efficacy (10-14 day treatment). Vancomycin may predispose to VRE, so Flagyl should be utilized first.  
    - Cholestyramine – binds toxin to control symptoms, poor for eradication of C. diff.  
    - Recurrent infection – re-treat with Flagyl or Vancomycin 95% cure rate  
  - Indication for surgical treatment  
    - Perforation  
    - Toxic megacolon  
    - Sepsis
Mechanisms of Antimicrobial Resistance
Katherine M. Trahan, MD

I. Mechanisms of Developing Resistance
   a. Plasmids-produces drug destroying enzymes (most common)
   b. Mutations-alters cell permeability, alters target sites, efflux of drug, alteration or substitution of metabolic pathways
   c. Transposable Elements

II. Acquisition of Mechanisms-transfer of mechanisms
   a. Transduction-carriage of non-phage DNA between bacteria by phage coat and injected into cell
   b. Conjugation-(most common) direct contact between cells
   c. Transformation-uptake of DNA followed by recombination

III. Drug Specifics
   a. Lactams
      A. Mechanisms of Action (MOA): inhibits cell wall crosslinking
      B. Resistance-drug inactivation (betalactamase), insensitive target (altered binding protein), decreased permeability, active efflux
   b. Vancomycin
      A. MOA-interferes w/new cell wall unit additions
      B. Resistance-altered target
   c. Bacitracin
      A. MOA-prevents addition of new cell units by inhibits membrane lipid carrier
      B. Resistance-unknown
   d. Macrolides
      A. MOA-bind to 50s ribosomal subunit
      B. Resistance-alters target, active efflux
   e. Chloramphenicol
      A. MOA-binds to 50s ribosomal subunit
      B. Resistance-drug inactivation, active efflux
   f. Tetracycline
      A. MOA-binds to 30s ribosomal subunit
      B. Resistance-active efflux, insensitive target
   g. Aminoglycoside
      A. MOA-bind to 30S ribosomal subunit
      B. Resistance-drug inactivation, decreased permeability in gram neg, active efflux
   h. Sulfonamides/TMP
      A. MOA-inhibits enzymes at two levels in folic acid synthesis
      B. Resistance-production of insensitive targets and creates dihydrofolate reductase that bypass metabolic block
   i. Rifampin
      A. MOA-inhibits DNA dependent RNA polymerase
      B. Resistance-insensitive target (mutates polymerase gene)
   j. Metronidazole
      A. MOA-unknown
      B. Resistance-unknown
   k. Quinolone
      A. MOA-inhibits DNA gyrase and topoisomerase
      B. Resistance-insensitive target, active efflux
SECTION 7

CHAPTER 24

HEMATOLOGY
VITAMIN K; VON WILLEBRAND’S FACTOR (vWF)
Michael K. Obeng, MD

Vitamin K:
- Fat soluble vitamin found in 2 natural forms K1 (phylloquinone) and K2 (menaquinone)
- K1 is found in plants and green vegetables, while K2 is found in animals.
- A synthetic form K3 (menadione) exist.
- It functions as a coenzyme for vitamin K – dependent gamma carboxylation of glutamic acid moieties on factors II, VII, IX, X, proteins C, and S in order for calcium to effectively bind for effective coagulation.
- Deficiencies occur as a result of inadequate dietary intake, malabsorption, lack of bile salts, obstructive jaundice, biliary fistula and broad-spectrum antibiotic usage.
- It is recycled because of its limited storage capabilities.
- Warfarin prevents the recycling of vitamin K by inhibiting carboxylation
- Toxicities include interference with glutathione function resulting in oxidative damages to cell membrane, also flushing, sweating, jaundice and anemia.
- Deficiencies can be corrected by administering vit. K (menadione) parenterally, subcutaneously, and intramuscularly.
  1. up to 5 mg iv can be given slowly as an initial dose
  2. parenteral administration corrects clotting times within 6-12 hours
  3. 10 – 25 mg SQ/IM per day X 3 days allow total body repletion
  4. FFP with vit. K rapidly corrects coagulation deficits in ongoing bleeding

von Willebrand factor and disease:
- vWF is a heterogenous glycoprotein found in plasma, platelets and endothelial cells.
- It aids in platelet aggregation at the site of injury and also serves as a principal carrier for circulating factor VIII.
- Deficiency or abnormalities in this protein results in von Willebrand’s disease.
- vW disease is the most common congenital bleeding disorder. (Affects 1-2% of pop.)
- Symptoms are milder than hemophilia (mucosal bleeding, petechiae, epistaxis, menorrhagia).
- Mode of inheritance varies from autosomal dominant to recessive.
- Several subtypes exist, but the 3 most common ones are:
  Type I: autosomal dominant inheritance, most common and mildest form, levels of vWF and VIII:C are slightly lower than normal, normal PT and platelet count, mildly prolonged PTT, and bleeding time is abnormal.
  Type II: variable inheritance, qualitative defect in vWF, depressed ristocetin assay. May be classified as IIa. (quantitative decrease and qualitative defect in vWF) or IIb (qualitative defect with increase ability of platelet aggregation.
  Type III: autosomal recessive, most severe form, patient may have total absence of vWF and less than 10 % of VIII. PTT is markedly prolonged, abnormal bleeding time, and low platelet counts.
  Pseudo (or platelet-type) von Willebrand’s disease
  - resemble Type IIb vW disease with the defect in the platelets. Very large platelets that aggregate in the presence of cryoprecipitate.

Rx:
1. Desmopressin acetate (DDAVP) intranasally for mild disease or 0.3ug/kg to shorten bleeding time and normalize factor VIII.
2. Alphanate, Humate-P (viral inactivated factor VIII)
3. FFP
I. Administration
A. Administered as the sodium salt and has 100% bioavailability
B. 99% of racemic warfarin is bound to plasma albumin
   1. Contributes to small volume of distribution
   2. Long half life in plasma - 36 hours
   3. Lack of urinary excretion of unchanged drug

II. Mechanism of Action
A. Blocks the gamma-carboxylation of several glutamate residues in prothrombin
   and factors VII, IX, and X as well as the endogenous anticoagulants proteins
   C and S
B. Results in incomplete molecules that are biologically inactive in coagulation
C. The protein carboxylation is physiologically coupled with the oxidative
deactivation of vitamin K
D. Prevents reductive metabolism of the inactive vitamin K epoxide back to its
   active hydroquinone form
E. Mutational change of the responsible enzyme, vitamin K epoxide reductase,
can give rise to genetic resistance
F. 8-12 hour delay in the action of warfarin
G. The anticoagulant effect results from a balance between partially inhibited
   synthesis and unaltered degradation of the 4 vitamin K-dependent clotting
   factors
H. Half lives are 6, 24, 40, and 60 hours for factors VII, IX, X, and II,
   respectively
I. Larger initial doses up 0.75mg/kg will hasten the onset of anticoagulation with
   no increased effect beyond that dose

III. Toxicity
A. Crosses the placenta readily, leading to hemorrhagic disorders in the fetus
B. Fetal proteins with gamma-carboxyglutamate residues in bone and blood may
   be affected
C. Cutaneous necrosis with reduced activity of protein C sometimes occurs
   during the first weeks of therapy. This is prevented by prior heparinization.
D. Rarely the same process causes frank infarction of breast, fatty tissues,
   intestine, and extremities- the pathologic lesion associated with hemorrhagic
   infarction is venous thrombosis due to warfarin-induced depression of protein
   C synthesis

IV. Administration and Dosage
A. Initiated with a small daily dose of 5-10 mg
B. Initial adjustment of prothrombin time takes about 1 week with a usual
   maintenance dose of 5-7 mg/day
C. PT time should be increased to a level representing 25% of normal activity
D. Therapeutic range is defined in terms of INR- usually adjusted to achieve INR
   of 2.5-3.5, depending on the condition
V. Drug Interactions
A. Pharmacokinetic- enzyme induction, enzyme inhibition, and reduced plasma protein binding
B. Pharmacodynamic- synergism (impaired hemostasis, reduced clotting factor synthesis), competitive antagonism (vitamin K), and an altered physiologic control loop for vitamin K (hereditary resistance to anticoagulants)
C. Most serious are those that increase the anticoagulant effect- most dangerous are interactions with pyrazoles such as phenylbutazone and sulfipyrazone- these drugs augment hypoprothrombinemia and also inhibit platelet function as well as induce peptic ulcer disease
D. Mechanism of hypoprothrombinemic interaction are a stereoselective inhibition of oxidative metabolic transformation of S-warfarin and displacement of albumin-bound warfarin increasing the free fraction
E. Metronidazole, fluconazole, and bactrim also stereoselectively inhibit the metabolic transformation of S-warfarin
F. Amiodarone, disulfiram, and cimetidine inhibit metabolism of both enantiomorphs of warfarin
G. Aspirin, hepatic disease, and hyperthyroidism augment warfarin pharmacodynamically- aspirin by its effect on platelet function and the latter two by increasing the turnover rate of clotting factors
H. Third generation cephalosporins eliminate the bacteria in the intestinal tract that produce vitamin K and, like warfarin, also inhibit vitamin K epoxide reductase
I. Barbiturates and rifampin cause a marked decrease of the anticoagulant effect by induction of the hepatic enzymes that transform racemic warfarin
J. Cholestyramine binds warfarin in the intestine and reduces its absorption and bioavailability
K. Pharmacodynamic reductions of anticoagulant effect occur with vitamin K (increased synthesis of clotting factors), the diuretics chlorthalidone and spironolactone (clotting factor concentration), hereditary resistance (mutation of vitamin K reactivation cycle molecules), and hypothyroidism (decreased turnover rate of clotting factors)
L. No effect on anticoagulant therapy- ethanol, phenothiazines, benzodiazepines, acetaminophen, narcotics, indomethacin, and most antibiotics

VI. Reversal of Action
A. Stop the drug
B. Vitamin K1 (phytonadione)
C. FFP or Factor IX concentrates like konyne 80 or proplex T
D. Serious bleeding requires large amounts of vitamin K1 IV in 50 mg infusions, Factor IX concentrates and sometimes transfusion of whole blood
HODGKIN’S DISEASE
Ricki Y. Fram, MD

Histologic Subtypes of the Rye Classification System

Nodular Sclerosis
- Findings include Reed-Sternberg cells, lacunar cells and interconnective broad sclerotic bands of collagenous connective tissue that divide the lymph node into cellular nodules.
- Most common histologic type occurring in 40 to 60% of all cases.
- Incidence peaks in adolescence and the early twenties but remains the most common subtype at all ages.
- Most frequently involves the mediastinum and supraclavicular areas.

Mixed Cellularity
- Lymph nodes comprise a mixture of normal histiocytes, neutrophils, eosinophils, plasma cells, lymphocytes and fibroblasts.
- There is also abundant Reed-Sternberg cells and diagnostic variants without fibrotic bands.
- Accounts for 15 to 30% of all cases.
- Most frequent histology found in HIV-infected individuals.
- Peak age incidence is 30 to 45 years and at 40 to 55 years.

Lymphocyte Predominant
- Characterized by sparse neoplastic cells and abundant lymphocytic and/or histiocytic stroma, few inflammatory cells, and no necrosis.
- There are two types, nodular and diffuse.
- Evenly distributed across all ages, from 20s to 60s.
- Has a tendency to run an indolent course, with an 80% 10-year survival.

Lymphocyte Depletion
- Reed-Sternberg cells are present in stroma profoundly depleted of lymphocytes and other reactive cells.
- There is a disorganized deposition of proteinaceous fibrillar matrix.
- Very uncommon, less than 5% of cases of Hodgkin’s Disease.

Clinical Manifestations
- Enlarged lymph nodes, particularly cervical adenopathy
- Mediastinal Mass
- Splenomegaly
- Abdominal Mass
- Fever, weight loss, night sweats
- Pruritus
- Bone pain
- Thrombocytosis, leukocytosis, eosinophilia
- Elevated ESR and alkaline phosphatase
Stage I
Stage I adult Hodgkin's lymphoma means the involvement of a single lymph node region (I) or localized involvement of a single extralymphatic organ or site (IE).

Stage II
Stage II adult Hodgkin's lymphoma means the involvement of 2 or more lymph node regions on the same side of the diaphragm (II) or localized involvement of a single associated extralymphatic organ or site and its regional lymph node(s) with or without involvement of other lymph node regions on the same side of the diaphragm (IIE). Note: The number of lymph node regions involved may be indicated by a subscript.

Stage III
Stage III adult Hodgkin's lymphoma means the involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of an associated extralymphatic organ or site (IIIE), by involvement of the spleen (IIIS), or by involvement of both (IIIE + S). Stage III disease may be subdivided by anatomic distribution of abdominal involvement or by extent of splenic involvement. Stage III(1) indicates involvement that is limited to the upper abdomen above the renal vein. Stage III(2) indicates involvement of pelvic and/or para-aortic nodes.

Stage IV
Stage IV adult Hodgkin's lymphoma means there is disseminated (multifocal) involvement of 1 or more extralymphatic organs, with or without associated lymph node involvement, or isolated extralymphatic organ involvement with distant (nonregional) nodal involvement.

Stages I, II, III, and IV adult Hodgkin's lymphoma can be subclassified into A and B categories: B for those with defined general symptoms and A for those without B symptoms. The B designation is given to patients with any of the following symptoms: Unexplained loss of more than 10% of body weight in the 6 months before diagnosis. Unexplained fever with temperatures above 38 degrees Celsius. Drenching night sweats.

Treatment

Early Stage
- Treatment of choice: radiation therapy
- Combination chemotherapy may be considered for stage II disease
  - ABVD is the treatment of choice if fertility is an issue
  - If fertility is not an issue, MOPP/ABVD or MOPP-ABV hybrid therapy

Advanced-Stage
- **MOPP:** nitrogen mustard, vincristine, procarbazine, prednisone
- **ABVD:** Doxorubicin, bleomycin, vinblastine, dacarbazine
- **MOPP/ABV:** nitrogen mustard, vincristine, procarbazine, prednisone, doxorubicin, vinblastine, bleomycin
Relapsed and Refractory Disease
- High-dose therapy with hematopoietic support
Uremic Coagulopathy – Use of DDAVP
Tammy Lee, MD

Uremic Coagulopathy
- Usually mucocutaneous signs
  - epistaxis, ecchymosis
- Occasionally cause GI bleed, hemopericardium, subdural hematoma
- Important to surgeons - Increased perioperative bleeding

Mechanisms
- Platelet count may be normal
- **Functional defect** between platelets and vWF leading to defects in platelet-platelet interactions and platelet-vessel wall interactions.
- Best test for platelet dysfunction is **bleeding time**
- BT > 10-15 min - high risk of hemorrhage

Correction of Uremic Coagulopathy
- DDAVP
- Cryoprecipitate
- Conjugated Estrogens
- Transfusion
- Dialysis

DDAVP
- 1 – deamino – 8 – D – arginine - vasopressin
- aka Desmopressin
- Synthetic derivative of ADH
- Causes release of **Factor VIII** and **vWF** from endothelium – improving platelet function
- Shortens PTT and BT
- 0.3 mcg/kg IV
- Give 1 hour before surgery
- Used to treat mild Hemophilia A and Type I vWD
Side Effects of Blood Product Administration
Farin W. Smith, MD

Transfusion Reactions: Can be scaled in severity from mild rash to frank shock

- **Shock** (most severe)
  - Complement mediated from ABO-incompatible transfusions. Leads to RBC destruction intravascularly
  - Activates clotting cascade → decreased renal blood flow, hypotension, DIC
  - Sx – chest tightness, f/c, pain/redness along vein, hematuria, hypotension
  - Most are from human errors
  - Treatment
    1. stop transfusion, check blood and send to blood bank for analysis
    2. fluid administration – to combat hypotension and incr. renal blood flow
    3. mannitol can be used in severe cases

- **Hemolytic rxn** – decreased Hct, fever, jaundice
  - Can occur hours or days after transfusion
  - Causes chills and fever
  - Pre-medicate with Tylenol

- **Non-hemolytic rxn**
  - Caused by antibodies against WBC’s or plasma proteins
  - Chills and fever – can lead to urticaria or anaphylaxis
  - Premedicate with Benadryl & Tylenol

Infectious Transmissions

- **Viral**: EBV, CMV, Hepatitis, HIV, HTLV
  - CMV – most common viral agent transmitted
  - HIV – latent period (45d) for antibody production after
    - Risk 1:2,000,000 to 1:200,000 per unit
    - High risk donors are screened out
  - HTLV – causes spastic paralysis, T-cell leukemia, myelopathy
    - Donors screened routinely since 1989
  - Hepatitis –
    - Blood is screened for Hep-BsAg, Hep-C virus, non-A/B Hep surrogate markers
    - Hep-B risk 1:30,000 to 1:250,000 per unit
    - Hep-C risk 1:30,000 to 1:150,000 per unit

- **Bacterial**: syphilis, malaria, *Yersinia, Trypanosoma cruzi* (overall risk 1:1 million transfusions)

Graft vs Host Disease:

- Usually in immunocompromised pts
- Lymphocyte mediated
- Sx: fever, chills, rash, nausea, vomiting, diarrhea, decr cell counts, and liver fx abnormalities,
- Irradiated blood decreases this risk
- 90% mortality
SECTION 7

CHAPTER 25

PEDIATRIC SURGERY
**Common Problems in Pediatric Surgery**
Robert P. Thomas, MD

I. Hernia

A. Inguinal
- Process vaginalis is present at 12 wks, peritoneal diverticulum that extends as testis descends in the 7th and 8th mo. of gestation
- Increase risk for premature and male children: Overall incidence, 1-5%; premature males, as high as 30%
- Associated disease/disorders: cystic fibrosis, connective tissue diseases [Ehler-Danlos, mucopolysaccharidosis], peritoneal dialysis, and ventriculoperitoneal shunts
- Risk of incarceration exceeds 60% in 1st 6 mo. Repair should be performed before infant discharge
- Direct/femoral- rare and up to 1/3 had prior indirect repair
- Bilateral incidence and treatment controversial topic- incidence depends on definition
- Age of presentation is important- in children less than 2 with finding of inguinal hernia as many a 63% have bilateral patent process vaginalis
- Females with hernia as many as 20-50% have bilateral disease- most recommend bilateral exploration
- For males, age and assoc. conditions factor in decision
- Data not complete, but use of laparoscopic exploration of contralateral side has been shown to alter exploration plans in 30-50% of cases

B. Umbilical
- Umbilical ring closes in all directions- cranial, caudal, and lateral, initiated after umbilical cord is ligated
- Predisposition: Race and prematurity- 10 times more common in Africa-American children, 75-84% in children < 1500 gm
- Associated diseases/disorders: Trisomy 21, cong. hypothyroidism, mucopolysaccharidosis, and exomphalos-macroglossia-gigantism
- Related symptoms rare (incarceration/strangulation)/ Hernia 1.5-2.0 cm unlikely to close
- If umbilical hernia present at 4-5 y.o. should be repaired
- Earlier repair considered if symptoms of incarceration or recurrent pain exist

II. Undescended testis (UDT)
- Descent of testis depends on complex interaction of endocrine, paracrine, and mechanical factors- incompletely understood
- Androgens: dihydrotestosterone and human chorionic gonadotropin (hCG)
- Growth factors:
  1. Epidermal growth factor –enhances gonadotropin release
  2. Descendin- androgen independent, effects gubernacular development
- Mechanical factors: increased intraabdominal pressure
- Lesser factors: Estrogen, Mullerian Inhibitory factor, calcitonin gene-related peptide
- Incidence: 3 % for term males, up to 33% in premature children
- Most testes will descend in one year; therefore, overall incidence is 1%
- Associated diseases/disorders: patent processus vaginalis, epididymal abnormalities, hypospadias, posterior urethral valves, and upper urinary tract abnormalities
- History and physical exam are keys to making diagnosis [MRI-limited, but favored imaging technique]
- 10,000 IU of hCG given over several weeks can lower a retractile testicle, but is ineffective in making true UDT descend
- hCG stimulation test- [2000 IU given for 3 days and testosterone level on the 6th] distinguish anorchia from bilateral UDT
- Bilateral UDT cuts fertility in half, while unilateral disease has little effect
- Carcinoma risk: risk of malignancy in UDT patient is high, even in unaffected testis
  Estimated 10-60 times greater [15-20% of disease found in unaffected testis]
Orchiopexy does not lower risk, facilitates detection
Most common tumor – nonseminomatous germ cell tumor
Pediatric Neck Masses
Dirk C. Johnson, MD

- **Lymphadenitis**
  - Enlarged lymph node
  - Can progress to supportive lymphadenites, which require incision and drainage

- **Peritonsillar abscess**
  - Complication of tonsillitis, pharyngitis, or dental infection
  - Presents as hoarse voice, medial displacement of tonsils, edematous deviated uvula, inflamed soft palate, fever, chills
  - If abscess present requires drainage by needle or incision
  - Pathogen is usually B-hemolytic streptococcus

- **Thyroglossal duct abnormalities**
  - Midline fluctuant cystic mass superior to the thyroid
    - May enlarge in size
    - Mass is mobile, painless, and move with swallowing
  - Treatment is surgical excision
    - Requires excision of central portion of the hyoid (Sistrunk Procedure)
    - May need Methylene blue to identify entire tract
    - Complete dissection goes to base of the tongue
    - Antibiotics (if no abscess can treat with antibiotics alone)
    - Recurrent abscess is indication for tonsillectomy

- **Branchial cleft anomalies**
  - Develop from remnants of branchial clefts and pouches
  - Present as cysts, sinuses, cartilaginous nests in lateral neck
  - Can be as high as periauricular
  - First cleft anomalies are suprahyoid
  - Second cleft anomalies (most common) lie along anterior sternocleidomastoid (SCM)
  - Third cleft anomalies connect with the piriform sinus
  - Treatment is complete excision

- **Cystic hygroma**
  - Lymphangioma derived from primitive embryonic jugular venolymphatic sacs
  - Detected by ultrasound
  - Can extend into the axilla or chest (10%)
  - Treatment is complete excision
  - Can recur
  - No cyst wall, can involve nerves (should not sacrifice nerves because lesion is benign)

- **Torticollis**
  - Hard mass in SCM in first 2-4 weeks of life
  - Associated with breech delivery, vertebral anomalies,
  - Treatment is surgical division of SCM and fascia
Lymphatic Malformations of the Skin
Kenneth J. Woodside, MD

**General Lymphatic Characteristics**
Lymphatics function to drain protein rich fluids from the extracellular and extravascular space that leaks from the capillaries and return the fluid to the central circulation. Movement of the lymph is dependent on intrinsic pumping, valves, and extrinsic pressures such as muscle contractions.

Four layers of lymphatics:
- **Superficial primary lymphatics**
  - No valves
  - Form a capillary lymphatic network

- **Subdermal lymphatics (secondary lymphatics)**
  - Has valves
  - Drain the superficial lymphatics

- **Tertiary lymphatics**
  - Drain upper systems
  - Have valves and muscular wall

- **Intramuscular lymphatics**
  - Independent of superficial dermal system

**Drainage**
- Right lymphatic trunk drains the right side of the head and neck, the right arm, and the right chest.
  - This trunk drains into the right jugular-subclavian junction.
- The abdominal organs and other extremities drain into the cisterna chyli and thoracic duct, which, in turn, drains into the left jugular-subclavian junction.

**Capillary Lymphangioma**

**General**
- No communication between normal lymphatics and lymphangioma
- Complications include pain, recurrent infections, annoying exudate, and poor cosmesis

**Lymphangioma simplex**
- Superficial, elevated, clear smooth papules versus wart like vesicles
- Histologically with thin, dilated lymphatic channels in the dermis and epidermis
- Single or multiple
- Often on the tongue, oropharynx, or genitals
- Responds well to treatment of surgical excision, cryotherapy, laser tx, or electrocoagulation

**Lymphangioma circumscriptum**
- Similar to lymphangioma simplex, but with deeper subcutaneous components
- Can involve the face, chest, or extremities
- Similar treatment as simplex version, but the deeper components must be removed.

**Cavernous Lymphangioma**

**General**
- Characterized by superficial and deep small lymphatic spaces, dilated lymph channels, and endothelial lining, possibly with smooth muscle in the vessel wall
- May be anywhere on the body and in the retroperitoneum and tongue
- Usually occur at birth or during infancy
- May extend deep into the muscles and surrounding tissue, and often enlarge after infection or trauma

**Complications**
- Infection
- Anatomic interference from pressure on adjacent tissues
- Poor cosmesis and exudative fluid

**Treatment**
- Spontaneous resolution is possible, so expectant treatment is acceptable in asymptomatic patients
Surgical excision
If the lesion is in the oropharynx and is present with macroglossia, rigorous airway management is required. Infections must be vigorously suppressed.

CO2 laser has been used for head, neck, and airway lesions

Cystic Hygroma

General
Large, soft, cystic, transilluminating mass that often distorts the nearby anatomy
Multiloculated cystic spaces lined by endothelial cells
Loculations separated by smooth muscle cells and fibrous tissues
Do not connect to the normal drainage system
Incidence of 1/12,000 births, with 50-65% appearing at birth and 80-90% by the 2nd year
3/4 in the neck (mostly on the left in the posterior triangle), with 1/5 in the axilla and the balance in the mediastinum, retroperitoneum, pelvis, and groin
Nuchal or posterior cervical lesions are associated with congenital anomalies (esp. chromosomal abnormalities). If such a lesions are seen on prenatal US, further prenatal work up is required. These lesions carry a high mortality rate.

Diagnosis
Physical exam
US can be helpful, although US is less useful for deeper lesions
MRI often used for orbital lymphangiomas or other such questionable lesions to demonstrate the relationship of the lesion to the soft tissue and vasculature

Complications
Most grow in proportion to normal growth
Can increase rapidly in response to trauma, infection, or bleeding into the cystic space
Respiratory obstruction can occur if the lesion is in the airway, especially as 3-5% extend into the mediastinum. Dysphagia can also occur.
Infection, inflammation, and hemorrhage causing pain and anatomic compression

Treatment
Meticulous excision if possible
Surgical mortality of 2-6%
Often exceedingly difficult
Timing of excision is controversial, but should not be delayed if the lesion is enlarging and symptoms are progressing.
Not a neoplasm, so radial resection with removal of major vessels or nerves is not indicated
Sclerotherapy with bleomycin, OK-432, doxycycline, or fibrin glue is an alternative to surgery
Swelling of the lesion post injection can bring serious risks
XRT can be used as a last resort

Intraabdominal Lymphangioma
Rare and usually incidentally found
Appear early in infancy, with 90% detection of significant lesions by 2 years of age
A palpable soft mass may be found on abdominal exam
Presentation is based on anatomic location and complications (e.g. hemorrhage or infection)
Tx by excision, marsupialization, or argon beam ablation.

References
Cotran RS, et al., Robbins Pathologic Basis of Disease, 5/e.
Goldsmith LA, et al., Adult and Pediatric Dermatology: A Color Guide to Diagnosis and Treatment, 1/e.
SECTION 7

CHAPTER 26

HERNIAS
Layers of the abdominal wall in the inguinal region:
- Skin
- Subcutaneous fat
- Camper’s & Scarpa’s fascia
- External abdominal oblique aponeurosis
- Spermatic cord
- Transversus Abdominous aponeurosis
- Transversalis fascia
- Preperitoneal tissues
- Peritoneum

Inguinal Ligament – thickened lower portion of the external oblique aponeurosis
- Laterally: anterior superior iliac spine
- Medially: superior pubic ramus & pubic tubercle

Hasselbach’s Triangle
- Superior: inferior epigastric vessels
- Medial: rectus sheath
- Lateroinferior: inguinal ligament

Boundaries of the inguinal canal
- Anterior: aponeurosis of the external abdominal oblique muscle
- Posterior: aponeurosis of the transverse abdominal muscle fused with the transversalis fascia
- Superior: lower edge of the internal abdominal oblique muscle
- Inferior: inguinal ligament
- Upper end: internal inguinal ring
- Lower end: external inguinal ring

Contents of the male inguinal canal:
- Arteries: Testicular artery
  - Artery of the ductus deferens
  - Cremasteric artery
    - Anastomosis between the first two exists in all patients
    - Anastomosis between the all three exists in 2/3 of patients
- Veins: Pampiniform plexis (10-12 veins) coalesce to become the testicular veins
  - Right drains into the inferior vena cava, left drains into the left renal vein
- Nerves: Genital branch of the genital femoral nerve (L1 & L3) innervates the cremasteric muscle
  - Ilioinguinal nerve (L1) innervates the skin of the penile root and upper scrotum
- Fasciae: External spermatic fascia - continuation of the external abdominal oblique aponeurosis
  - Cremasteric fascia - from the internal abdominal oblique & transversus abdominous
  - Internal spermatic fascia - extension of transversalis fascia
- Cremasteric Muscle
- Vas Deferens
  - (In the female, the canal is occupied by the round ligament of the uterus)
Femoral Hernias
Kenneth J. Woodside, MD

Incidence
Approximately 5% of all hernias
Over 3/4 are in women (although inguinal hernias are more common in women)
Incarceration or strangulation rate is 2-3 times higher than inguinal hernias
(20-30%)

Hernia anatomy & boundaries (Townsend Figures 40-1 and 40-2)
Superior  Iliopubic tract
Inferior  Cooper’s ligament
Lateral  Femoral vein
Medial  Insertion of the iliopubic tract into the Cooper’s ligament

Variations
Sac protrudes lateral to the femoral vessels (Hesselbach’s hernia)
Sac protrudes into the aponeurosis of the pectineus (Cloquet’s hernia)
Sac protrudes posteriorly to the vessels (Serafini’s hernia)
Sac protrudes between the femoral vessels

Presentation & Diagnosis
Symptoms and complaints include a groin mass that may be reducible and may be painful
or tender. As with any hernia, symptoms of a bowel obstruction may be present.

On physical examination, the sac may be felt in the upper thigh. However, it can also
curve superiorly over the inguinal region, causing misdiagnosis as an inguinal
hernia. It may reduce manually or spontaneously.

Treatment
As there is a significant rate of incarceration and strangulation, all femoral hernias should
be operatively repaired. If signs or symptoms of small bowel obstruction are
present, therapy should include NG suction, IV fluids, etc.

Operative approaches
Any bowel in the sac must be assessed for necrosis or damage.
Cooper’s ligament (McVay) repair (Townsend Figure 40-4)
Conjoined tendon sutured to Cooper’s ligament from
the pubic tubercle laterally to the femoral canal.
Preperitoneal approach (Townsend Figure 40-9)
Laparoscopic approach

Postoperative complications
Similar to other groin hernias
Recurrence rate and complications dependent on the repair type
Wound infection (2%), testicular atrophy (1.8%), hydrocele (0.5%)
ilioinguinal neuritis (0.3%), divided vas deferens (0.3%)

References
Townsend et al. Textbook of Surgery, 16/e.
Complications of hernia repair
Buckminster J. Farrow, MD

1. Recurrence
   a. Factors
      i. Tension in repair
      ii. Failure to repair entire aponeurotic/fascial defect
      iii. Poor tensile strength of tissue repair
      iv. Infection (1-5% incidence)
      v. Wound healing abnormalities
      vi. Sudden increases in intraabdominal pressure (COPD, etc.)

2. Nerve Injury
   a. Iliohypogastric- transected with elevation of external oblique aponeurosis
   b. Ilioinguinal- torn with cord mobilization
   c. Genital branch of genitofemoral nerve- damaged during cremasteric dissection
   d. Sensory deficits usually cause minimal patient complaints and largely resolve over months
   e. Pain also usually resolves, but may persist if nerve is entrapped in sutures; use local blocks to diagnose the nerve involved- may need to excise

3. Injury to Adjacent structures
   a. Vascular (rare)- femoral vein, femoral artery, require immediate repair
   b. Bladder- during sac dissection with direct or large indirect; treatment is 2-layer closure of defect and Foley x 7 days
   c. Bowel- injury from high sac ligation or improper dissection of sac

4. Testicular and spermatic cord complications
   a. Atrophy- most commonly from damage to testicular veins/lymphatics (not the artery)
   b. Swelling/atrophy may occur if closure around the cord is too tight
   c. Scrotal hematoma- usually absorbs rapidly, rarely becomes infected/requires drainage

Ref: Greenfield’s textbook, Townsend’s textbook, Maingot’s Abdominal Operations