A Review of the Large Intestine

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Contents

- Vasculature
- Function
  - Absorption
  - Motility
  - Neural reflexes and Control
- Colitis
- Malignancy
Section 1. Vasculature
Vasculature

- Superior Mesenteric Artery
- Inferior Mesenteric Artery
- Internal Iliac Arteries

Superior Mesenteric Artery (SMA)
- Supplies blood flow from the jejunum distally to the splenic flexure
  - Middle colic artery
  - Right colic artery
  - Ileo-colic artery

Inferior Mesenteric Artery
- Supplies blood flow from the splenic flexure to the rectum
  - Left colic artery
  - Marginal artery
  - Sigmoid artery
  - Superior rectal artery
Dual Blood Supply of the Rectum

- Inferior Mesenteric Artery
  - Superior Rectal Artery

- Internal Iliac Arteries
  - Middle Rectal
  - Inferior Rectal
Ischemic Colitis

- Most common ischemic injury to the GI tract
- 1 in 1000 hospitalizations est.
  - Underestimated
- Occlusive vs Non-occlusive
- Variable presentation
  - Transient
  - Gangrene

Ischemic Colitis

- Perfusion
  - Decreased systemic circulation vs changes to local mesenteric vasculature
  - Occlusive vs Non-occlusive
  - Hypoperfusion
    - Shock/Sepsis
    - Peri-operative period
    - Strenuous Physical Exercise
    - Constipation
    - Medications
Ischemic Colitis

- Risks
  - Age: 90% cases occur in pts > 60 yrs old
  - Medications
  - Hypercoagulable State
    - Factor V Leiden
    - Protein C/S
  - Idiopathic
    - Younger pts
    - Estrogens, cocaine and meth, sickle cell disease

Endoscopic Clue: Anti-Mesenteric Stripe
Ischemic Colitis

- Severity
  - 80-85% classified as non-gangrenous
  - Majority resolves 24-48 hrs, endoscopic resolution w/in 2 wks
  - Supportive care, resuscitation, antibiotics
  - Can be acute or chronic
    - Chronic -> recurrent segmental colitis or stricture
- Gangrenous
  - Peritonitis, septic shock, free air on radiographic studies
  - Laparotomy with resection of diseased colon

Ischemic Colitis

- Diagnosis
  - History and Physical (diarrhea, pain, bleeding, fever)
  - Imaging
    - XR abdomen
    - CT abdomen/pelvis
    - Mesenteric Angiography
      - Reserved for R colon involvement
  - Colonoscopy
Ischemic Colitis

Section 2. Function
Functions of the Large Intestine

- Absorb water and electrolytes
  - Proximal half of the colon resp for absorption
  - 1.5-2L of fluid pass into the colon daily
  - Can maximally absorb up to 5-8 L fluid
- Store and concentrate feces
  - Electrolytes/ions absorbed with water, 100 mL left to be excreted
- Role of colonic bacteria
  - Formation of vitamin K, thiamin, riboflavin

Function of the Large Intestine: Secretion

- Mucus Secetion
  - Crypts of Lieberkuhn are lined with mucus producing cells
  - Controlled by
    - Direct, tactile stimulation on surface of the mucosa
    - Intense irritants can lead to additional secretion of fluid and electrolytes (bacterial or viral enteritis), diluting the irritant
    - By neural reflexes
      - Parasympathetic stimulation increases mucus secretion
        - Also increases motility, causing mucoid diarrhea
Neural Control of the Large Intestine

- Enteric Nervous System
  - Lies entirely within the wall of the gut
  - Two nerve plexuses
    - Myenteric plexus (btw the two outer muscle layers)
      - Gastrointestinal movements (both inhibitory and excitatory neurons)
    - Submucosal plexus
      - Sensory signals
      - Local blood flow
      - Gastrointestinal secretion

Neural Control of the Large Intestine

- Neurotransmitters
  - Acetylcholine
  - Norepinephrine
  - Serotonin
  - Dopamine
  - VIP

- Sympathetic vs Parasympathetic Control
Functional Gastrointestinal Disorder (FGID)

- Irritable Bowel Syndrome
- Functional Diarrhea
- Chronic Idiopathic Constipation

Irritable Bowel Syndrome: Rome Criteria
Irritable Bowel Syndrome: Rome Criteria IV

- May 2016
- Shift from Functional to Disorders of the Brain-Gut Interaction
  - Avoid stigma
  - Focus on alterations in gut bacteria, alterations in gut permeability, CNS role
- Diagnosis
  - Abdominal pain (discomfort removed) with two or more features of:
    - Related to defecation
    - Assoc w/ change in frequency of defecation
    - Assoc w/ change in appearance of stool
    - Symptoms present at least 1 day per week for the last month
    - Symptoms present > 6 months total

Irritable Bowel Syndrome

- Testing
  - Labs and stool studies
  - +/- Colonoscopy and EGD based on symptoms
  - Hydrogen Glucose Breath Testing

- Inflammatory vs Non-inflammatory
Irritable Bowel Syndrome

- Disruption of bi-directional brain-gut communication (neural and hormonal mediated)
  - Visceral hypersensitivity
  - Alters digestive secretion and motility
- Decreased integrity of the intestinal barrier
  - Caused by changes to composition of gut microbiota, psychological stress
    - Activates mast cells -> increases intestinal permeability
    - Antigens cross epithelial barrier and trigger immune response, abnormal neuronal behavior

Irritable Bowel Syndrome

- Treatment
  - Anti-spasmodics
    - Dicyclomine (Bentyl)
    - Hyoscyamine (Levsin)
  - Motility
    - Loperamide
  - Antidepressants (focus treatment on neurotransmitters, visceral or neuropathic, pain, alteration of motility)
    - Selective Serotonin Reuptake Inhibitors (SSRI)
    - Serotonin-Norepinephrine Reuptake Inhibitor (SNRI)
  - Tri-Cyclic Antidepressants
  - Hypnotherapy, Biofeedback
Chronic Idiopathic Constipation

- No single “definition”, subjective

Causes
- Normal-transit
- Slow-transit
- Disorders of rectal evacuation

Chronic Idiopathic Constipation

- Normal transit
  - Most common
  - Perceived difficulty and hard stools, often with bloating/discomfort
  - Often improves with hydration and fiber or other osmotic laxatives
  - Lack of improvement raises possibility of either of the other two causes

- Slow transit
  - Young women, often starts at puberty
  - Lack of defecatory urge, presence of abd pain + bloating
  - Often poor response to increased fiber
  - Caused by decreased emptying of the proximal colon and decrease in high amplitude post-prandial peristalsis
Chronic Idiopathic Constipation

- Slow transit constipation pathology
  - Myenteric plexus neurons and neurotransmitters
    - Excitatory: Substance P
    - Inhibitory: Vasoactive Intestinal Peptide (VIP) and nitric oxide
    - Interstitial Cells of Cajal (regular GI motility)
- Diseases related to slow transit
  - Hirschsprung’s disease
    - Ganglion cells absent (developmental arrest)
    - Narrowing of affected segments of bowel
    - Most often diagnosed in infancy or childhood
  - Colonic Inertia
    - Severe absence of motor activity after meals and no response to muscle stimulants (bisacodyl, anticholinesterase such as neostigmine)

Chronic Idiopathic Constipation

- Continence
  - Normal rectal sensation
  - Tonic contraction of the internal anal sphincter
  - Tonic contraction of the puborectalis muscle (creates the ano-rectal angle as it wraps behind the ano-rectum)

- Defecation
  - The pelvic floor muscles relax, allowing descent of the perineum (1.0-3.5 cm)
  - Puborectalis muscle relaxes, straightening the ano-rectal angle
  - Relaxation of the external anal sphincter
Chronic Idiopathic Constipation

- Defecatory Disorders
  - Diagnosed with defecography or ano-rectal motility or balloon expulsion
  - Reduced descent of the perineum and/or reduced change in the ano-rectal angle during straining
  - Caused by:
    - reduced rectal sensation
    - disorder of the anal sphincter
    - injury to the pelvic floor
    - paradoxical contractions of the pelvic floor during defecation
    - prolonged avoidance of anal pain from hard, large stools
Chronic Idiopathic Constipation

- Treatment
  - Pharmacologic
    - Biofeedback with physical therapy
      - Strengthen pelvic floor muscles
      - Retraining of the pelvic floor for pts with paradoxical sphincter contraction
    - Subjective Improvement
      - Increased freq, reduced bloating
      - Improvement in symptom driven anxiety, hostility, depression
    - Objective Improvement
      - ARM values

Section 3. Colitis
Inflammatory Bowel Disease

- Crohn’s disease
- Ulcerative Colitis
- Indeterminate Colitis

**Incidence**
- Highest in Northern Europe, U.K., N. America
  - UC rates stable or decreasing, CD continues to increase
  - Less common in Southeast and South Asia, but incidence is increasing
    - UC rises first, then CD

**Prevalence (N. America)**
- CD and UC: btw 50-200 per 100,000
- 1-2 of every 1,000 in developed countries

**Age (peak)**
- CD: 20-30 yrs of age
- UC: 30-40 yrs of age
- Pediatric IBD accts for 10-20% of cases
Inflammatory Bowel Disease

- Crohn's, anatomical
  - Any part of the GI tract
  - Most common: TI, colon
  - Only 10-15% have upper GI lesions
  - 15-20% have peri-anal fistula at time of presentation, up to 45% will by 20 yrs
    - Risk increased for patients with colitis vs risk in ileitis

- CD phenotypes
  - Inflammatory
  - Penetrating
  - Strictureing
  - Phenotypes = Spectrum
  - Post-operative model, disease progression
  - Role of Surgery in CD and UC
Inflammatory Bowel Disease

**Treatment, UC**
- **Induction**
  - Mild to moderate: 5-ASA products
  - Acute Severe: Steroids, Infliximab, Cyclosporine, Surgery
- **Maintenance**
  - Mild to moderate, 5-ASA products
  -取决于位置
  - Relapses despite treatment with 5-ASA product
  - Biologics > Thiopurines

**Treatment, CD**
- **Induction**
  - Mild to moderate: 5-ASA products have questionable efficacy
    - Steroids, Methotrexate, Budesonide
  - Acute Severe: Steroids, Infliximab, Surgery
- **Maintenance**
  - Smoking cessation
  - No role for mesalamine
  - Budesonide
  - Relapses or severe disease
    - Biologics + Thiopurines
  - Perianal disease
    - Antibiotics
Microscopic Colitis

- Common cause of watery diarrhea
  - 4-13% of cases of diarrhea
  - Female, 6th-7th decade, Caucasian
  - Increased incidence in patients with Celiac disease

- Diagnosis
  - Endoscopic appearance is normal
  - Pathology

- Pathophysiology
  - Collagenous and Lymphocytic subtypes
  - Pathophysiology

Microscopic Colitis: Treatment

- Stop offending drug
  - NSAIDs

- Anti-diarrheals

- Bismuth subsalicylate

- Steroids

- 5-ASA products

- Azathioprine/Mercaptopurine
Diverticular Disease

- Diverticulosis
- Diverticulitis
- Diverticular Hemorrhage

Diverticulosis

- Pseudo-diverticulum, herniation of the mucosa and submucosa only
  - Distal colon
- True diverticula, all three layers
  - Proximal colon
- Physiology
  - Low dietary fiber -> Smaller volume stools -> Exaggerated contractions creating high intra-luminal pressures
Diverticulosis

- Acute Diverticulitis
  - Fever, localized pain, leukocytosis
  - Diagnosis and severity: CT Scan
    - Bowel wall thickening, fat stranding, phlegmon, small abscess, frank perforation
  - Treatment with antibiotics, bowel rest, management of abscess, surgery
    - Aerobic and anaerobic Gram-negative coverage
  - Inpatient vs Outpatient management
    - Presence of complications
    - Ability to tolerate oral meds
    - Response to oral meds
  - Pathophysiology: Obstruction +/- alteration is local bacterial flora
Diverticulosis

- Chronic pain secondary to diverticulosis
  - Cause
    - Visceral hypersensitivity
      - Inflammation (chronic) alters nerve regeneration and transmitter release
    - Altered colonic motility
    - Low-grade mucosal inflammation
    - Must differentiate from IBS, as symptoms respond to surgical resection of diseased area
  - Treat with 5-ASA products, probiotics

Diverticulosis

- Segmental colitis associated with diverticulosis (SCAD)
  - Pain and rectal bleeding
  - Friability in region of diverticuli (absence of ulcers)
  - Pathophysiology unknown; linked to IBD
  - Treatment: 5-ASA products and antibiotics

- Recurrent Diverticulitis
  - 25% of patients with acute diverticulitis will suffer a recurrence
  - No increase in morbidity or mortality with recurrent attacks
    - Changes surgical guidance
    - Consider age and utilize probiotics
Section 4: Colorectal Cancer

Colorectal Cancer

- 3rd most commonly Dx’ed cancer worldwide
  - 3rd highest incidence in males (lung, prostate)
  - 2nd highest incidence in females (breast)
- Global variation
  - Australia/NZ (m = 45/100,000), Europe, N. America
  - Lowest incidence in W. Africa (m = 3/100,000)
- US trend
  - Decreasing incidence since mid 80’s, when CRC screening widely implemented
  - Increasing incidence in patients btw 40-45 (l)
Colorectal Cancer: Risk Factors

- Increased genetic susceptibility
  - Hereditary colorectal cancer syndromes
  - 10% of CRC cases
  - Hereditary non-polyposis colon cancer most common
- Family history of colon cancer
  - Potentially 2-3x greater lifetime risk when 1st degree family member has CRC
- Environmental / Acquired
  - IBD
  - Cigarette smoking
  - Obesity
  - “Western” diet
    - High in red meat
    - Low in fiber
  - EtOH – moderate to heavy

Colorectal Cancer: Progression of Adenoma
Colorectal Cancer

Colorectal Cancer: Screening Tools

- Stool Testing
  - Guaiac-based FOBT: Hemoglobin catalyzes reaction between hydrogen peroxide and guaiac
    - Subjective
    - False positives (high meat content diet -> animal heme)
    - False negatives (Vitamin C, lack of sensitivity requires 3 consecutive samples)
  - Fecal Immunochromatographic Testing
    - Uses specific Ab to human Hgb (removes subjectivity and dietary influence)
    - Still limited to detecting bleeding cancers (misses non-bleeding polyps)
    - Limits on specificity
  - Molecular stool testing
    - Cologuard (multi-target stool DNA test) every 3 yrs
    - Common mutations found in colon cancer
    - Highly specific
Colorectal Cancer: Screening Tools

- Imaging
  - Double-Contrast Barium Enema
    - Sensitivity for large polyps > 10 mm is ~ 50%
    - Requires bowel prep
  - CT Colonography
    - Sensitivity for colorectal cancer approaching rates with colonoscopy
    - No sedation, but still requires prep
    - Extra-colonic findings (good or bad?)

Colorectal Cancer: Screening

- Colonoscopy
  - Gold standard
  - Rate of complication (major) 0.1-0.2%
  - Bowel prep and sedation
Colorectal Cancer

- Staging
  - Surgical
  - Radiographical
  - TNM
    - T: depth of invasion within the wall, relation to structures beyond the colon
    - N: number of nodes
    - M: presence of mets

Colorectal Cancer: Prognosis

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis only</td>
<td>100%</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1-T2 only</td>
<td>93%</td>
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<tr>
<td>Stage II-A</td>
<td>T3 only</td>
<td>85%</td>
</tr>
<tr>
<td>Stage III-A</td>
<td>T1-2 with LN mets &lt; 7 or deposits into mesentery or pericolic tissue w/out LN</td>
<td>83%</td>
</tr>
<tr>
<td>Stage II-A,B</td>
<td>T4 lesion w/out LN or mets</td>
<td>72%</td>
</tr>
<tr>
<td>Stage III-B,C</td>
<td>T4 lesion with LN, no mets</td>
<td>44-64%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any mets</td>
<td>8%</td>
</tr>
</tbody>
</table>
Colorectal Cancer

- Treatment Strategies
  - Chemotherapy
  - Radiation
  - Surgical Resection

Questions?