

Inflammatory Bowel Disease

Ulcerative Colitis, Crohn's

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Inflammatory Bowel Disease

- Ulcerative colitis - nonspecific inflammatory bowel disease of unknown etiology that effects the mucosa of the colon and rectum
- Crohn's disease - nonspecific inflammatory bowel disease that may affect any segment of the gastrointestinal tract
- Indeterminate colitis
 - 15% patients with IBD impossible to differentiate

Ulcerative Colitis

Epidemiology

- 8-15 per 100,000 in US and Northern Europe where incidence is greatest
- 7,000 to 46,000 new cases in US each year
- Peak incidence 3rd (20's), 7th (60's) decades
- Slight male predominance
- Crohn's disease - nonspecific inflammatory bowel disease that may affect any segment of the gastrointestinal tract

Risk Factors for UC

- Diet, oral contraceptive use, breastfeeding, measles infection/vaccination and other widely discussed factors are not yet proven
- Cigarette smoking
 - Smokers are 40% as likely as non-smokers to develop UC; primarily sclerosing cholangitis and pouchitis are both also decreased in smokers
 - Active smokers are half as likely to be hospitalized as nonsmokers, and former smokers are 50% more likely to be hospitalized and twice as likely as current smokers or those who have never smoked to require colectomy
- Appendectomy
 - Protective effect of nearly 70% of appendectomy for the development of UC
 - Pts who developed UC after appendectomy were less likely to develop recurrent sx than those with colitis and an intact appendix and less likely to require colectomy
- Genetics
 - 5-10% of those affected have positive family hx
 - pANCA -> UC; ASCA, OmpC, Cbir1 -> Crohn's (Prometheus labs)

UC Pathology

- Macroscopic Appearance
 - Limited to mucosa and submucosa of rectum (nearly always) and colon
 - Starts distally, continuous involvement of varied amount of colon proximally
 - Pancolitis may include backwash ileitis (10%) - notably the ileum will appear dilated on radiography as opposed to the frequently narrow, fibrosed ileum in Crohn's disease
 - Confluence of numerous ulcers w/ heaped up regenerating mucosa-> "pseudopolyps", superficial fissures, loss of normally visualized endoscopic vascular pattern
- Microscopic Appearance
 - PMNs infiltrate crypts of Lieberkuhn at mucosal base to form crypt abscesses -> superficial desquamation of overlying epithelium leads to ulcer formation-> cryptitis undermines the adjacent mucosa which becomes edematous-> muscularis propria may undergo myocytolysis causing hyperemia and wall thinning

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UC Clinical Features

- Majority (80%) - mild, predominantly distal disease
 - Proctitis (40%)
 - Left-sided colitis (35%) - disease distal to splenic flexure
 - *Urgency, frequency, tenesmus; unremarkable abd exam; blood and mucus on DRE; inflamed mucosa on anoproctoscopy*
 - Progression to pancolitis 10%
- Minority (20%) - pancolitis
 - *Anemia, fatigue, anorexia, weight loss*
 - Chronic colitis-> loss of mucosal folds, haustra: lead pipe appearance on radiograph
 - ☐ Toxic megacolon: fever, abd pain, tachycardia, focal tenderness, leukocytosis, radiographic dilatation >6cm t-colon; risk of gangrene, perforation

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Extraintestinal manifestations

(that improve or resolve s/p colectomy)

- Arthritis (20%)
 - knees, ankles, hips, shoulders
 - typically in association with increased activity of intestinal disease
- Ankylosing spondylitis (3-5%)
 - HLA-B27+ or FamHx of AS
- Erythema nodosum (10-15%)
 - Often in conjunction with arthropathy
- Pyoderma gangrenosum (rare)
 - PG is associated with IBD in 50% of cases

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Extraintestinal manifestation

(does NOT resolve s/p colectomy)

- Primary Sclerosing Cholangitis (5-8%)
 - Men, younger than 40
 - HLA-B8 or HLA DR3
10x more likely to develop PSC
 - Colitis often more quiescent
 - Risk of colon CA increased 5x compared to UC alone
 - Liver transplantation needed for cure

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UC Diagnosis

- Rule out infectious causes
 - Fecal leukocytes
 - Confirm inflammatory origin to diarrhea, urgency etc
 - Stool cultures, Ova & Parasites
 - Campylobacter, Salmonella, Shigella, C. diff ...
- Proctosigmoidoscopy
 - Diffuse, confluent disease from dentate line proximally
- Rule out Crohn's
 - Small bowel follow-through
 - Prometheus panel
- *Indeterminate Colitis*
 - Treat as UC until/if declares itself Crohn's

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Risk for carcinoma in UC

- Disease duration
 - 25% at 25 yrs, 35% at 30 yrs, 45% at 35 yrs, and 65% at 40 yrs
- Pancolonic disease
 - Left-sided only pts less likely to develop cancer than pancolitis pts
- Continuously active disease
- Severity of Inflammation
 - Colonic stricture must be considered to be cancer until proven otherwise

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IBD Cancer detection

- ACS Colonoscopy Surveillance guidelines:
 - q1-2y beginning 8 yr after onset pancolitis, or 12-15y after onset of left-sided colitis
 - based on the premise that a dysplastic lesion can be detected endoscopically before invasive carcinoma has developed
 - debate on number of biopsies, 10-30 bx
- Dysplasia surveillance versus prophylactic colectomy
 - carcinoma found in 10% of colons displaying low-grade dysplasia, in 30% to 40% with high-grade dysplasia, and in more than 50% of colons with dysplasia associated with a lesion or mass (DALM)
 - 25% of carcinomas in patients with ulcerative colitis are not associated with dysplasia elsewhere in the colon

UC Medical Therapy

- Aminosalicylates (e.g. sulfasalazine, mesalamine)
 - Block cyclooxygenase, lipoxygenase pathways of arachadonic acid metabolism, scavage free-radicals
 - Toxicity: nausea, H/A, agranulocytosis (sulfasalazine)
- Corticosteroids (e.g. prednisone, budesonide)
 - Block phospholipase A2, thereby decreasing prostaglandins and leukotrienes
 - PR administration effective in rectal and left-sided disease with fewer adverse systemic effects
- Immunomodulatory agents
 - 6-MP, Azathioprine - inhibit proliferation of T>B lymphocytes
 - Toxicity: reversible BM suppression, pancreatitis
 - Cyclosporine - inhibits IL-2 gene transcription
 - Toxicity: nephro/hepatotoxicity, sz, lymphoprolif. disease

Indications for Surgery

- Intractability (most common indication)
 - Debilitating symptoms, complications of steroid therapy, extracolonic manifestations
- Dysplasia-Carcinoma
- Massive colonic bleeding
 - Uncommon event, representing <5% of pts requiring operation
 - Subtotal colectomy usually suffices, proctectomy only if bleeding refractory
- Toxic megacolon
 - IVF, NGT, stress-dose steroids, broad-spectrum antibiotics
 - Deterioration or lack of improvement w/in 24-28h->OR
 - Total abdominal colectomy w/ ileostomy
 - Mucus fistula vs Hartmann's pouch

Operations

- Segmental colectomy
 - *Contraindicated*: due to recurrence in remnant colon
- Abdominal colectomy with ileorectal anastomosis
 - *Contraindicated*: rectal sparing UC is exceedingly rare; often postoperatively the retained, inflamed rectum causes intractable diarrhea
 - if truly rectal sparing consider Crohn's dx
- Total proctocolectomy with end ileostomy
- Total proctocolectomy with continent ileostomy
- Total proctocolectomy with ileal pouch-anal anastomosis

Total proctocolectomy with end ileostomy

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- Advantage: removing all diseased mucosa, prevents further inflammation and progression dysplasia/carcinoma
- Major disadvantage: need for a permanent ileostomy
- Morbidity: perineal wound healing, adhesions, the ileostomy, and complications of pelvic dissection
- Intersphincteric proctectomy may reduce perineal wound problems by preserving the external sphincter and levator ani for a more secure perineal wound closure
- Candidates: Elderly patients, those with poor sphincter function, and patients with carcinomas in the distal rectum

Total proctocolectomy with continent ileostomy

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- Introduced by Kock in 1969; popular in the 1970s because it offered control of evacuations
- A single-chambered reservoir is fashioned by suturing several limbs of ileum together after the antimesenteric border has been divided
- The outflow tract is intussuscepted into the reservoir to create a valve that provides obstruction to the pouch contents
- As the pouch distends, pressure over the valve causes it close and retain stool, permitting patients to wear a simple bandage over a skin-level stoma
- 2-4x/d, the patient introduces a tube through the valve to evacuate the pouch
- Nearly 50% reoperation rate:
 - Slipped valve is most common complication
 - inflammation of the ileal pouch mucosa (“pouchitis”) in 15% to 30% of cases, fistula formation (10%), and stoma stricture (10%)

Total proctocolectomy with ileal pouch-anal anastomosis (IPAA or J-pouch)

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- Near-total proctocolectomy with preservation of the anal sphincter complex
- A single-chambered pouch is fashioned from the distal 30 cm of the ileum (Fig. 50-33) and sutured to the anus using a double-stapled technique

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Total proctocolectomy with ileal pouch-anal anastomosis (IPAA)

- Alternatively, a hand-sewn anastomosis may be fashioned between the pouch and the anus after stripping the distal rectal mucosa from the internal anal sphincter (mucosectomy)
 - Mucosectomy has been complicated by cancer arising at the anastomosis and extraluminally in the pelvis, evidently from islands of glands that remained after the mucosa was incompletely removed.
 - The mucosectomy technique may conceal retained rectal mucosa in up to 20% of patients
 - Avoiding the mucosectomy preserves the anal transition zone, which contains nerve endings involved in differentiating liquid and solid stool from gas, and is thus thought to provide superior postoperative continence.
- Temporary fecal diversion (ie diverting loop ileostomy)
 - Recommended in high-risk patients, especially those taking steroids preoperatively

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Total proctocolectomy with ileal pouch-anal anastamosis (IPAA)

- Postoperatively pts typically have 5-8 bowel movements per day. Function continues to improve for 3-24 months after reestablishment of GI continuity
- Complications
 - Small bowel obstruction (up to 27%), often severe; requires surgery in 1/2 of cases
 - Up to 2/3 involve loop ileostomy; either at the loop or around it
 - Pelvic sepsis, from pouch leaks
 - Tx: diverting ileostomy, drainage of abscesses
 - *Pouchitis* (7-33%)
 - increased stool frequency, fever, bleeding, cramps, and dehydration
 - Tx: rehydration, PO abx (Cipro, Flagyl)

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Elective operations for ulcerative colitis

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Postoperative Care

- Nasogastric tubes are usually removed at the completion of the procedure
- Liquid diets are offered to patients in the early recovery period
- Diet is advanced with return of bowel function as evidenced by ileostomy function
- If a pelvic drain is used, it is typically removed after 48 to 72 hours
- Bladder catheters are typically left in place for 3 to 4 days depending on the difficulty of pelvic dissection
- A water-soluble contrast enema is performed about 10 weeks postoperatively to ensure an intact IPAA. If the enema shows a leak, the contrast examination is repeated in 6 weeks; *close to 95% of anastomotic leaks heal in the absence of pelvic sepsis*. If the radiograph shows no leak, the diverting ileostomy is closed.

Crohn's Disease

Focus on Crohn's Colitis

Epidemiology

- 1-5 per 100,000 US and Northern Europe where incidence is greatest
- Bimodal: 15-30yr, 55-60yr
- Whites>black>asians
 - Ashkenazi's 3-4x increased risk compared to non-Jewish whites
- Immigrants from low incidence countries show increase in risk for Crohn's disease to level of native population upon moving to country with greater risk, suggesting potent environmental influences

Etiology

- Three prevalent theories include:
 - response to a specific infectious agent
 - a defective mucosal barrier allowing an increased exposure to antigens
 - an abnormal host response to dietary antigens
- One infectious agent that has generated some interest is *Mycobacterium paratuberculosis*, isolated in up to 65% of tissue samples from Crohn's patients
- A statistically significant association between the onset of Crohn's disease and prior use of antibiotics has also been observed
- Smoking appears to be a risk factor for Crohn's disease, and after intestinal resection, the risk of recurrence is greatly increased in smokers

Pathology

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- Gross appearance
 - *Transmural*, predominantly submucosal inflammation characterized by a thickened colonic wall
 - *Cobblestone* appearance on endoscopy
 - The bowel wall may be entirely encased by *creeping fat* of the mesentery, and *strictures* may develop in the small and large intestine
 - The mucosa may demonstrate long, deep linear ulcers that appear like “railroad tracks” or “bear claws.”
 - Normal mucosa may intervene between areas of inflammation, causing “skip areas” characteristic of the disease
- Histologic
 - transmural inflammation, submucosal edema, lymphoid aggregation, and ultimately fibrosis
 - Pathognomonic: the *noncaseating granuloma*, a localized, well-formed aggregate of epithelioid histocytes surrounded by lymphocytes and giant cells; found in 50% of resected specimens

Clinical Presentation

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- Characteristic triad: abdominal pain, diarrhea, weight loss
 - Mimics viral gastroenteritis or IBS
 - Other sx: anorexia, fever, recurrent aphthous ulcers
- Patients with family history typically present with more extensive disease
- Only 1/2 of pts with Crohn's have rectal involvement; 2/3 have involvement of entire colon
- Anal disease (anal fistulas, fissures, strictures, edematous skin tags..) occurs in 30% of pts with terminal ileum disease, 50% of pts with colonic disease

Diagnosis

- Rule out infectious causes
- Differentiate from UC by extra-colonic involvement (e.g. oral, anal)
- Characteristic radiographic findings:
 - skip lesions, contour defects, *longitudinal* and transverse *ulcers*, a cobblestone-like mucosal pattern, *strictures*, thickening of the haustral margin, and irregular nodular defects

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Medical Therapy

- Aminosalicylates (sulfasalazine, mesalamine)
- Corticosteroids (prednisone, budesonide)
- Immunomodulatory agents (azathioprine, 6-MP, cyclosporine)
 - Infliximab - monoclonal anti-tumor necrosis factor- α (anti-TNF- α) antibody
 - Blocks TNF- α receptor in an effort to decrease inflammation
 - Intravenous infusion to treat Crohn's disease in steroid-dependent or intractable patients, also patients with chronic draining fistulas
 - Adverse effects include potentially increased rates of lymphoma

Indications for Surgery

- **Intractability**
 - For patients with debilitating disease refractory to medical treatment
 - Like for UC, this is the most common indication
- **Intestinal obstruction**
 - Causes: active inflammation, a fibrotic stricture from chronic disease, an abscess or phlegmon causing a mass effect or adhesions from previous abdominal operation(s)
 - Administer steroids in addition to bowel rest, decompression, hydration
 - Endoscopic balloon dilation may treat anastamotic strictures
- **Intra-abdominal abscess**
 - Results from intestinal perforation caused by transmural inflammation
 - Ex-lap if IR drainage not possible or disease refractory to percutaneous management
- **Fistulas**
 - Up to 35% of patients develop fistulas, most involving small intestine
 - Ileosigmoid fistula is common; SBR w/ primary sigmoid repair is sometimes possible
 - Enterocutaneous fistulas develop spontaneously (typically ileal disease) or as the result of postoperative anastamotic breakdown
- **Fulminant Colitis and Toxic Megacolon**
 - Because the pathologic process in Crohn's disease involves inflammation of the entire bowel wall, the colonic dilation characteristic of toxic megacolon may not occur in patients with Crohn's disease, but the toxicity of the colitis may be no less severe
 - Similar to the case of toxic megacolon in UC, treatment is subtotal colectomy with end ileostomy

Indications for Surgery

- Massive bleeding
 - Less common than in UC; up to 13% in some series
 - Terminal ileum most common site
 - If disease is colonic and ileum is spared, rectal source for bleeding should be ruled out with flexible sigmoidoscopy
 - Tx: Abdominal colectomy with end ileostomy or ileorectal anastomosis if rectum is not inflamed; additional proctectomy if significant rectal bleeding
- Cancer
 - increased risk for the development of adenocarcinoma of the colon and small intestine
 - observed prevalence of 0.3% for small bowel adenocarcinoma and 1.8% for large-intestinal adenocarcinoma
 - Nonfunctional bowel that has been excluded from the fecal stream seems to be at particular risk for malignancy
 - Surveillance practices for severe, prolonged colonic involvement in Crohn's mirror those for UC
 - q1-2y colonoscopy 8y after onset pancolitis, 12-15y after onset left-sided colitis
- Growth Retardation
 - Young patients may have impaired growth and mental development due to prolonged inadequate caloric intake
 - Resection of severely diseased segments may eliminate growth retardation and guard against premature closure of bone epiphyses

Elective Operations

(unique to Crohn's)

- Ileocecal resection
 - Indicated in patients with several disease of the terminal ileum resulting in obstruction or perforation
 - Typically involves resection of ~6-12 in of the terminal ileum and cecum, with an anastomosis created between the ileum and ascending colon.
 - The terminal ileum is transected 2 cm proximal to the grossly apparent Crohn's disease
 - The recurrence rate of Crohn's disease requiring re-resection in patients who have undergone ileocolic resection is roughly 50% in 10 years

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Elective Operations

(unique to Crohn's)

- Total abdominal colectomy with ileorectal anastomosis
 - Indicated in patients with Crohn's colitis with sparing of the rectum and anus
 - Offers the best functional results in patients who wish to maintain intestinal continuity
 - Postoperatively, patients may expect to have between four and six bowel movements per day
 - The major disadvantage of the operation is the high likelihood of recurrence requiring completion proctectomy and ileostomy; roughly 50% of patients require proctectomy within 10 years
- Total proctectomy with IPAA
 - Controversial; potential for ileal disease increases risk for pouch complications/loss

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Elective Operations

(unique to Crohn's)

- Segmental colon resections
 - May be indicated in the 10-20% of patients with Crohn's limited to a segment of colon (stricture or obstruction)
 - It is contraindicated in patients with severe rectal or anal disease
 - Within 5 years, recurrence % and 50%, with 60% of patients requiring reoperation by 10 years.
 - Despite these high recurrence rates, segmental colectomy may be a good option in patients with limited disease who wish to avoid an ostomy.

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