Inflammatory Bowel Diseases

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Inflammatory Bowel Disease

- Total number of cases
  - Approx 1.4 million cases estimated in the United States
    - Ulcerative colitis (UC): ~50%
    - Crohn's disease (CD): ~50%
  - Males and females equally affected; mainly 15–35 yrs for CD (5–10 years later for UC)
  - Genes, environment, race and ethnicity are factors
- Disease course
  - Chronic, lifelong disease without medical cure (CD)
  - Surgical intervention ~2/3 CD patients

## Epidemiology of IBD in North America

- **Incidence (per 100,000 person-years)**
  - UC: 2.2 to 14.3 cases
  - CD: 3.1 to 14.6 cases

- **Prevalence (per 100,000 persons)**
  - UC: 37 to 246 cases
  - CD: 26 to 199 cases

- **New diagnoses (per year)**
  - UC: 7,000 to 46,000 cases
  - CD: 10,000 to 47,000 cases

- **Population experiencing IBD**
  - UC: ~780,000
  - CD: ~630,000


## Demographic Features of IBD in North America

- **Slight male predominance in UC**
  - Incidence of UC seems to have stabilized overall but continues to rise in males

- **Slight female predominance in CD**
  - Especially in late adolescence and early adulthood
  - Hormonal factors might play a part

- **Mean age at diagnosis**
  - UC: 5 to 10 years after that of CD
  - CD: 33.4 to 45 years

- **Late onset IBD**
  - Males more frequently diagnosed than females in fifth and sixth decade of life

Familial Patterns of Inheritance in IBD

- Relative risk 14 to 15 times higher among first-degree relatives than the general population
  - Prevalence in family members:
    - 4.6% parents
    - 2.6% siblings
    - 1.9% children

- Concordance in affected parent-child pairs:
  - 75% disease type
  - 63% extent
  - 70% extraintestinal manifestations
  - 85% smoking history


Worldwide Geographical Prevalence of IBD

Normal Intestine vs. Intestine With IBD

Environmental triggers (medications, infections, diet?)

Normally: inflammation is down-regulated

IBD: failure to down-regulate inflammation

Chronic uncontrolled inflammation = IBD


Overactive Mucosal Immune System in IBD

Failure to downregulate

Secretion of cytokines and other products from activated immune cells → injury to the colon

Activation of T cells results in increased immune response

 Trafficking to the colon of leukocytes, which are capable of cytokine production

Environmental Triggers

IBD Onset and Reactivation

- Antibiotics
- Acute infections
- NSAIDs (Non-steroidal anti-inflammatory drugs)
- Smoking
- Diet
- Stress
- Altered flora
- Altered barrier function

Bacteria as an Environmental Trigger for IBD

- IBD involves a loss of tolerance for normal gastrointestinal microflora
- IBD patients have altered composition of commensal enteric bacteria:
  - Decreased Bifidobacterium and Lactobacillus species, increased Bacteroides, adherent/invasive E. coli, Enterococci
- Genetic factors and environmental triggers must be present to cause inflammation
- Evidence from animal models
  - Genetically engineered models of IBD do not manifest IBD phenotype when raised germ-free

Sartor RB. Gastroenterology. 2004;126:1520

Farrell JJ, Sands BE. Etiology and pathogenesis of inflammatory bowel disease. In Colten RD, ed. Inflammatory Bowel Disease: Diagnosis and Therapeutics. 2003, Humana Press Inc, Totowa, NJ.
Potential Risk Factors Associated With IBD

Risk Factors With IBD Association

- Cigarette smoking
  - + risk factor for CD
  - - risk factor for UC

- Appendectomy
  - + risk factor for CD
  - - risk factor for UC

- Oral contraceptives
  - Weak association with IBD

- Diet
  - Increased sugar intake associated with IBD, especially CD

Risk Factors With Questionable IBD Association

- Perinatal and childhood factors

- Measles infection or vaccination

- Mycobacterial infection


Smoking and Ulcerative Colitis

- Cigarette smoking
  - Has protective effect on development and course of UC, including extraintestinal and postsurgical events
  - Nicotine therapy (gum, patch, enema) has mixed results
  - Restart smoking in severe or refractory colitis?

- Ex-smokers more likely to develop extensive UC (second age peak > 40 years)


Mortality and IBD

- IBD patients have an elevated mortality rate of 0.5% per year
- Extensive colitis and higher age (> 50 years) at diagnosis increase the risk for a fatal outcome in UC
- Greatest hazard ratio (HR)
  - UC – age group 40 to 59 years (HR 1.79)
  - CD – age group 20 to 39 years (HR 3.82)
- IBD is associated with an overall small increase in mortality rate greatest in relative terms in younger subjects but in absolute terms in the elderly


Inflammatory Bowel Diseases (IBDs)

INFLAMMATORY BOWEL DISEASE

Ulcerative Colitis (UC)  Crohn’s Disease (CD)

Mucosal Ulceration in Colon  Transmural Inflammation

Proctitis  Left-sided Colitis  Extensive Colitis

Upper Small Bowel Colonic Anorectal Gastrointestinal

Inflammatory Bowel Disease

Crohn's Disease
- Patchy inflammation
- Mouth to anus involvement
- Transmural inflammation
- Fistulas and strictures common
- Risk of cancer
- Extraintestinal manifestations
- Higher risk for smokers
- Can have granulomas (50%)

Ulcerative Colitis
- Continuous inflammation
- Generally affects the colon
- Mucosal inflammation
- Fistulas and strictures seldom
- Risk of colorectal cancer
- Extraintestinal manifestations
- Lower risk for smokers
- Granulomas extremely rare

IBD Related Complications

Complications of Crohn’s Disease
- Fistulas
- Abscesses
- Intestinal blockage
- Extraintestinal disorders
- Malnutrition
- Colon or rectal cancer
- Growth failure in children

Complications of Ulcerative Colitis
- Severe inflammation
- Perforation
- Megacolon
- Extraintestinal disorders
- Colon or rectal cancer
Fistula: Definition

• A communication between two epithelial-lined organs.
• Lifetime risk of fistula in CD: 30%

Percentage of Fistulae by Type

Perianal Fistulae: Parks’ Classification System

A Superficial fistula
B Intersphincteric fistula
C Transphincteric fistula
D Suprasphincteric fistula
E Extrasphincteric fistula

**Fistula**

- **Diagnostic evaluation**
- **Fistula type**
  - Not superficial
    - Seton
    - Antibiotics
    - 6-MP/AZA ± infliximab
    - Maintain 6-MP/AZA and/or infliximab
  - Superficial
    - Antibiotics
    - Consider fistulotomy
    - Observe
  - Definitive surgery
  - Tacrolimus
  - Failure

- Failure

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**Extraintestinal Manifestations of IBD**

- **Peripheral arthritis**
  - Arthralgia more prevalent in subjects with CD
- **Axial arthritis**
  - Ankylosing spondylitis more prevalent in subjects with UC
- **Osteoporosis**
  - Risk is greater in subjects with CD
- **Renal**
- **Dermatological**
- **Eye**
- **Thromboembolic**
- **Hepatic complications**

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Rheumatologic manifestations

• Axial arthritis
  – Ankylosing spondylitis
    • 18-20% of patients with IBD, more common in males
    • clinical course independent of bowel disease
    • associated with HLA-B27 haplotype
    • “bamboo” spine on plain x-rays
  – Sacroilitis
    • independent of bowel disease
    • associated with HLA-B27 haplotype
    • plain films show obliteration of sacroiliac joint space

• Peripheral arthritis
  – Activity parallels bowel disease activity
  – Peripheral arthritis in IBD is mono-articular (affects large joints such as knee, wrist, ankles), asymmetric, migratory, seronegative, and is not associated with deformity or erosive changes.
Putative Etiologies of Low Bone Density in Inflammatory Bowel Disease

- Inflammatory mediators
- Calcium and vitamin D malabsorption
- Medications
- Smoking (Crohn’s)
- Hypogonadism
- Physical activity

Buchman AL. Inflamm Bowel Dis. 1999;5:212.

Renal Manifestations

- Nephrolithiasis
  - Urate stones associated with ulcerative colitis
  - Oxate stones associated with Crohn’s disease
- Obstructive hydronephritis
  - Associated with Crohn’s disease but not UC
  - Caused by local extension of bowel inflammation to ureters
- Pyelonephritis
Dermatologic manifestations

• Erythema nodosum
  – most common skin manifestation of IBD
  – occurs in 9% of UC, 15% of CD
  – directly related to bowel disease activity and resolves with control of the disease
  – erythema nodosum is non-specific for IBD

• Pyoderma gangrenosum
  – occurs in 2-5% UC, 1-2% of CD
  – clinical course is independent of bowel disease
  – treatment with intralesional / systemic steroids

ERYTHEMA NODOSUM

Figure 3: Multiple erythematous plaques on the gastroin
Ocular Manifestations

• Uveitis
  – *Clinical course is independent of bowel disease activity*
  – Associated with HLA-B27 haplotype
  – *Clinical presentation is painful, injected eye with synechiae and opacity in the anterior chamber.*

• Episcleritis
Hepatobiliary Manifestations

- **Primary sclerosing cholangitis**
  - 4-6% of patients with UC
  - 70% of patients with PSC have UC
  - associated with DRW-52A haplotype
  - clinical course is independent of bowel disease
  - diagnosis made by ERCP; suggested by liver biopsy
  - cholangiocarcinoma is a complication of PSC

- **Pericholangitis**

- **Cholelithiasis**
  - cholesterol stones may occur in CD patients with terminal ileal involvement
  - Occurs in 15-30% of patients with small bowel CD
  - Resection or disruption of ileal absorptive surface causes alteration of enterohepatic circulation and bile salt depletion

- **Chronic active hepatitis**
### Ulcerative Colitis:
**Defining Extent of Disease**

- Ulcerative proctitis (rectum only)
- Left-sided Colitis (extends to splenic flexure)
- Extensive Colitis (beyond splenic flexure)

Adapted from Orangio GR. Surgical Therapy for IBD. In: Stein SH, Rood RP, eds. *Inflammatory Bowel Disease*. Philadelphia, PA: Lippincott-Raven; 1999:155(Fig 10).


### The Location and Extent of Ulcerative Colitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Occurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proctitis alone</td>
<td>~30%</td>
</tr>
<tr>
<td>Proctosigmoiditis</td>
<td>~20%</td>
</tr>
<tr>
<td>Distal/Left-sided Colitis</td>
<td>~30%</td>
</tr>
<tr>
<td>Extensive Colitis</td>
<td>~20%</td>
</tr>
</tbody>
</table>

Adapted from Orangio GR. Surgical Therapy for IBD. In: Stein SH, Rood RP, eds. *Inflammatory Bowel Disease*. Philadelphia, PA: Lippincott-Raven; 1999:155(Fig 10).

### Colitis Activity Assessment

<table>
<thead>
<tr>
<th>Mild Activity</th>
<th>Severe Activity</th>
<th>Fulminant Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 stools daily</td>
<td>&gt;6 stools daily</td>
<td>&gt;10 stools daily</td>
</tr>
</tbody>
</table>

- **Blood in stool**: Intermittent, Frequent, Continuous
- **Temperature (C)**: Normal, > 37.5, > 37.5
- **Pulse**: Normal, > 90, > 90
- **Hemoglobin**: Normal, <75% of normal, Transfusion required
- **ESR**: < 30, > 30, > 30

Truelove / Witts criteria

### UC: Natural History

**Disease Severity at Presentation**

- **Mild Activity**: < 4 stools daily, No systemic disturbance, ESR: NI
- **Moderate Activity**: > 4 stools daily, Minimal systemic effects
- **Severe Activity**: > 6 stools daily, Bloody stools, Fever, Tachycardia, Anemia, ESR > 30 mm/hr

Hendriksen C, Kreiner S, Binder V. Gut 1985;26:158-163
Clinical Presentation of Ulcerative Colitis

- Diarrhea, typically bloody and with mucus
- Abdominal pain and tenderness
- Loss of appetite and weight
- Fever
- Fatigue
- Urgency for bowel movement
- Children: growth and developmental failure

Exclusion of Infectious Colitis

- Exclusion of infectious colitis may be clinically, endoscopically, and histologically indistinguishable from IBD.
  - stool for ova and parasites
  - stool cultures for enteric pathogens
- Patients with proctitis
  - exclude STDs if there is a history of anal intercourse
- Patients with diarrhea and recent antibiotic use
  - exclude pseudomembranous colitis
  - check stools for C. difficile toxin
Ulcerative Colitis

**Flexible sigmoidoscopy:**
- Assess disease activity in acute UC
- Mucosal involvement is continuous and non-segmented
- Mucosa is granular / friable with discrete ulcerations

**Colonoscopy:**
- relatively contraindicated in acute UC due to increased risk of perforation.
- useful in chronic UC to evaluate disease extent, evaluate strictures, and surveillance for colonic CA

**Plain films of abdomen**

**Barium enema:**
- contraindicated in acute UC
- useful in chronic UC – “lead pipe” colon
- colonic strictures should be considered malignant until proven otherwise

Antibody Testing in IBD

**IBD vs. non-IBD controls**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCA+</td>
<td>60%</td>
<td>91%</td>
<td>88%</td>
</tr>
<tr>
<td>pANCA+</td>
<td>50%</td>
<td>95%</td>
<td>69%</td>
</tr>
<tr>
<td>ASCA+/pANCA-</td>
<td>56%</td>
<td>94%</td>
<td>91%</td>
</tr>
<tr>
<td>pANCA+/ASCA-</td>
<td>44%</td>
<td>97%</td>
<td>78%</td>
</tr>
</tbody>
</table>

ASCA = Anti-saccharomyces cervisiae antibodies
pANCA = perinuclear antineutrophil cytoplasmic antibodies

AmJGastro 2001; 96 : 730
Endoscopic Severity Index for Ulcerative Colitis

Mild
- Granular mucosa
- Edematous
- Loss of normal vascular pattern

Moderate
- Coarsely granular
- Small ulcerations
- Friable

Severe
- Frank ulcerations
- Spontaneous hemorrhage

Images courtesy of R. Cohen MD.

Histology of Ulcerative Colitis

Quiescent
- Crypt distortion
- No active inflammation

Active
- Crypt distortion
- Inflammation infiltrates
- Crypt abscesses

Images courtesy of John Hart, MD.
Therapeutic Pyramid for Active UC

Ulcerative Colitis: Induction of Remission

- **Mild disease**
  - *Aminosalicylate*
    - Topical therapy (distal disease)
    - Oral therapy (extensive disease)
Oral 5-ASA Release Sites

- **Stomach**
- **Small Intestine**
- **Large Intestine**

**Azo bond**

**Mesalamine in microgranules**

**Pentasa®**

**Asacol®**

**AZO-COMPOUNDS**

5-ASA Delivery Systems

- **PENTASA®**
- **ASACOL®**
- **SASP/OLS/BALS**
- **ENEMA**
- **SUPP**

**JEJUNUM / ILEUM / ASC / DES / SIG / RECT**
Ulcerative Colitis: Mild to Moderate

- Acute flare
- Exclude enteric pathogen
- Patient unwilling to take rectal therapy
  - Oral 5-ASA
    - Response adequate
      - Maintain
    - Response inadequate
      - Consider rectal therapy (5-ASA and/or steroid)
  - Patient willing to take rectal therapy
  - Extensive
    - Oral 5-ASA
      - Response adequate
        - Maintain oral 5-ASA
      - Response inadequate
        - Consider increased dose
      - Oral steroid

Ulcerative Colitis: Moderate to Severe

- Moderate
  - Oral steroid
    - Inadequate response
      - Taper
    - Adequate response
      - Maintain on 5-ASA and observe
  - IV Steroid
    - Inadequate response
      - 6MP/AZA
        - Response
          - Failure
            - Colectomy
          - No response
        - Success
          - Maintain 6-MP/AZA
          - Infliximab
            - Maintain infliximab
        - No response
          - Consider CyA
  - Consider CyA
    - Inadequate response
      - No response
Maintenance Therapies for Ulcerative Colitis

- Aminosalicylates
- Azathioprine / 6-MP
- Biologic therapy (anti-TNF vs anti-integrin vs Jak inhibitor)

Norwegian inception cohort data suggest lower colecotmy rates – 7.5% at 5 years

Meta regression of 32 studies (1991pts) – short-term colectomy rate still 27% over last 30 years despite therapy advances

Henriksen 2006; Turner 2007

Ulcerative Colitis

Indications for Surgery

Absolute
- Exsanguinating hemorrhage
- Perforation
- Cancer or dysplasia
- Unresponsive acute disease

Relative
- Chronic intractability
- Steroid dependency
- Growth retardation
- Systemic complications
Colectomy in Ulcerative Colitis

Cumulative probability for colectomy at initial diagnosis of UC

Years of follow-up after UC diagnosis

Colectomy %

0 5 10 15 20 25 30 35

0 20 40 60 80 100

Pancolitis
Substantial Colitis
Proctitis


Surgical Options

Ulcerative Colitis

Conventional ileostomy (Brooke)

Continent ileostomy (Kock pouch)

Ileal pouch-anal anastomosis

Ileorectal anastomosis
Complications of UC Surgery

- Mortality (<0.5%)\textsuperscript{1}
- 3-10 stools/24 hrs so bowel pattern not normal\textsuperscript{1}
- Impotence (1.5%)\textsuperscript{2}
- Pouchitis (10-60%)\textsuperscript{1}
- Small bowel obstruction (20%)\textsuperscript{1}
- Decrease in female fertility (56-98%)\textsuperscript{3-5}
- Pouch-vaginal fistula (4%)\textsuperscript{1}

\textsuperscript{1}Sagar PM, Pemberton JH. In Satsangi J, Sutherland L, et al, eds. Inflammatory Bowel Diseases. Spain: Elsevier Limited; 2003:491 511.

Crohn’s Disease: Anatomic Distribution

- Small bowel alone (33%)
- Ileocolic (45%)
- Colon alone (20%)

Freq of involvement

Most
Least
**Locations in the GI Tract Most Often Affected by Crohn’s Disease**

![Bar chart showing the percentage of occurrence in different parts of the GI tract.]

- **Small intestine**: 30%
- **Large intestine**: 20%-25%
- **Small and large intestine**: ~50%


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**Clinical Presentation of Crohn’s Disease**

- **PEDIATRIC**
  - Abdominal pain
  - Diarrhea
  - Weight loss
  - Anorexia
  - Vomiting
  - Rectal bleeding
  - Stunted growth
  - Fevers

- **ADULT**
  - Similar presentation
  - Growth and development issues less apparent
  - Often had silent disease as child / teen


Endoscopic Appearance of Crohn’s Colitis

Normal
- Loss of normal vascular pattern
- Edema

Mild Colitis
- Deep, linear, “bear-claw” ulcers

Severe Colitis

Histology of Crohn’s Ileitis

Crohn’s Ileitis
Distorted villous architecture

Images courtesy of R. Cohen, MD.

Image courtesy of John Hart, MD.
**Histology of Crohn’s Colitis**

![Image of Crohn’s Colitis](Image courtesy of John Hart, MD.)

**Crohn’s Colitis**

Arrows indicate granulomas

**Evolution of Crohn's Disease Behavior Over Time**

![Graph showing cumulative probability of Crohn's disease behavior](Image courtesy of John Hart, MD.)

Established percentage of CD patients remaining free of penetrating complications (upper curve) and free of stricturing and/or penetrating complication (lower curve) in 2002 patients with Crohn's disease since onset (diagnosis) of the disease.

Adapted from Cosnes J, et al. *Inflammatory Bowel Dis.* 2000;8:244.
CT Enterography

Normal Terminal Ileum

Active Disease
CT Enterography

- CTE compared to operative findings in 36 CD patients
- CTE correctly identified
  - 100% strictures (83% accuracy)
  - 100% abscesses
  - 94% fistulae (86% accuracy for # fistulae)
  - 97% inflammatory mass
- Overestimated or underestimated disease extent in 31%
  - Stricture, fistula, inflammatory mass, abscess counts
# Goals of Therapy for IBD/CD

- Inducing remission
- Maintaining remission
- Restoring and maintaining nutrition
- Maintaining patient’s quality of life
- Surgical intervention (selection of optimal time for surgery)

## Inductive Therapies for Crohn’s Disease

- Aminosalicylates
- Antibiotics
- Corticosteroids
- Immunomodulators
- Biologics
Therapeutic Pyramid for Crohn’s Disease

- Severe-Fulminant
  - Surgery
  - Bowel rest
  - Cyclosporine
  - Tacrolimus
  - TNF antagonist etc.
- Moderate-Severe
  - Azathioprine
  - 6-mercaptopurine
  - Methotrexate
  - Prednisone
  - Budesonide
  - TNF antagonist etc.
- Mild-Moderate
  - Aminosalicylate (mesalamine or sulfasalazine)
  - Antibiotics
  - Budesonide


The Adaptive Immune System in IBD-Cytokines in T-cell Activation

- CD4+ T cells and T-helper subsets
- Th1, Th2, Th3
- CD40L
- IL-17, IL-2, IL-4, IL-10
- Th17
- T helper cells
- B cell
- Adhesion and recruitment

Key Actions Attributed to TNF-α

- Proinflammatory cytokines
- Chemokines
- Macrophages
- Increased inflammation
- Increased cell infiltration
- Endothelium
- Increased adhesion molecules
- Fibroblasts
- Increased CRP in serum
- Epithelium
- Compromised barrier function
- Metalloproteinase synthesis
- Tissue remodeling
- Acute phase response


Anti-TNF-alpha Adverse Effects

- Infusion reactions (infliximab)
- Drug-induced lupus
- Injection site reactions (adalimumab & certolizumab)
- Non-Hodgkin’s lymphoma (T-cell type) 1/500-1000
- Serious infections (~ 3%)
- Opportunistic infections (TB, histoplasmosis & coccidiomycosis)
- Demyelination
- Skin reactions
- Immunogenicity
Healing of Colonic Ulceration with Infliximab


Pretreatment

4 weeks post-treatment

Maintenance Therapy for Crohn’s Disease: Issues

- **Definition of remission**
  - Clinical, endoscopic, radiologic, laboratory
- **Induction therapy**
  - 5-ASA, steroids, antibiotics, immunomodulators, anti-TNF
  - Surgery
- **Disease location**
- **Disease behavior**
  - Inflammatory, fibrostenotic, fistulizing
- **Smoking**
Cumulative Probability of Surgical Intervention in CD


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Adapted from Cosnes J, et al. Inflammatory Bowel Dis. 2000;8:244.
Unmet Needs in Crohn’s Disease Management

- No defining diagnostic marker¹
- Loss of response to therapy²
- Recurrent surgical intervention³

Cumulative probability* of surgery in Crohn’s disease³

*Kaplan-Meier analysis

Ulcerative Colitis and Increased Risk of Colorectal Cancer

- Overall prevalence of CRC in any UC patient is 3.7%

Who’s At Risk?
Risks of Dysplasia or CRC in UC

- Longer duration of disease
- Greater extent of disease
- Family history of CRC\(^1,2\)
- Primary sclerosing cholangitis\(^3\)
- Younger age of diagnosis (?)
- Backwash ileitis (?)
- Increased activity of disease\(^4,5,6\) (!)

Relative Risk of Colorectal Cancer Based on Extent of Ulcerative Colitis

Risk of Colon Cancer in Patients With Crohn’s Disease
Surveillance Guidelines
(Secondary Prevention)

- Who: all patients with left-sided or pan-UC more than 8-10 years (exception: PSC and UC- start immediately)
- Technique: 4-quadrant biopsies every 10 cm of mucosa; at least 33 biopsies; extra focus on nodules, masses, strictures
- How often: based on duration, extent, age, PSC and family history of colorectal cancer (q 6 months-2 years)
- Outcome (reviewed by second pathologist):
  - High-grade dysplasia: colectomy
  - Low-grade dysplasia: “prompt consideration of colectomy”
  - Indefinite dysplasia: increase surveillance?
  - Atypia or indeterminate: treatment of active disease, repeat colonoscopy and biopsies


Suggested Approach to Dysplasia

Dysplasia

Endoscopic appearance
- Flat
- Polyp

Grade?
- High
- Low

Multifocal?
- Yes
- No

Active disease?
- No
- Favor positive?
  - Yes
  - No

Treat inflammatory activity

Indefinite for dysplasia?
- Yes
- No

Colectomy
- Yes
- No

Colectomy vs aggressive follow-up
- Yes
- No

Coloscopy ≤6 months
- Yes
- No

Colonoscopy 1-2 years
- Yes
- No

Colonoscopy 6-12 months
- Yes
- No

Colonoscopy 3-6 months
- Yes
- No

Cancer in IBD: Natural History and Prevention Opportunities

**Future Trends**

- Refining genetic categories
  - Pharmacogenetics?
  - Colon cancer risk?
- Expand understanding of environmental stimuli
- “Revolution” of biological therapies
- Improving detection of precancerous lesions of the colon
- Minimally invasive surgery and other advances in operative approaches
- Vaccines?
Disease flare in 19% of CD pregnancies
Disease flare in 30% of UC pregnancies

- IBD flare occurred in 21.2% of the IBD pregnancies
- IBD flare occurred most commonly during the first trimester (63.6% of flares)
  - IBD maintenance therapy had been discontinued in 43% of patients experiencing first trimester flare.

IBD post-partum flares

- 13.7% of IBD patients post-partum flare
- 57% of post partum flares occurred within the 1st month of delivery
- Post-partum flare was associated with drug cessation in 28.6% of patients
IBD Obstetrical Complications

29.3% of IBD patients

- Spontaneous abortions in 11.8% of IBD patients
  - Pre-eclampsia in 7.8% of IBD patients
  - Gestational diabetes in 2% of IBD patients

Predictors of Poor Outcome

- Active Disease (UC and CD)
- Activity at conception => Fetal loss
- Activity during pregnancy => LBW
- Independent of medication use
  - Ileal Crohn’s Disease (p = 0.035) Moser
  - (Not consistently found in other studies)
- Previous bowel resection (p = 0.065) Moser
Summary: IBD and pregnancy

- **Fertility**
  - IPAA Surgery clearly reduces fertility rates in women
  - Role of medications in fertility unclear

- **Pregnancy Outcomes**
  - Complicated pregnancies occur in majority of patients
  - Increased rates Preterm birth, SA, LBW
  - No increase in congenital anomalies
  - Aggressive management of IBD flare during pregnancy with medications is warranted

- **Medications**
  - Yes: 5-ASA, Steroids, 6MP/AZA, Infliximab
  - No: MTX, Thalidomide

**IBD Questions**

A 25 y/o WM with 2 month hx of UC presents to the ER with fatigue, abdominal pain, hematochezia & diarrhea. Since the time of his dx with UC, he has been treated with prednisone 40 mg/day & mesalamine 4 gms/day. For the last week he has had approx. 10 BMs/day and cramping abdominal pain. He is admitted to the hospital, where hydration & parenteral corticosteroids are given. Over the ensuing 12 hrs, his abdominal pain becomes worse, he develops abdominal distention & obstipation. On PE – he has a temp of 38.6 °C, pulse – 120/min, & his abdomen is distended & diffusely tender with rebound. He had an AXR that showed a dilated transverse colon to 8 cm with thumb-printing. No free intraperitoneal air was observed. At this point in time, the most appropriate therapy for this patient is:

A. Oral high-dose Mesalamine
B. Intravenous cyclosporine
C. 6-mercaptopurine or azathioprine
D. Intramuscular methotrexate
E. Urgent subtotal colectomy
IBD Questions

A 25 y/o WM with 2 month hx of UC presents to the ER with fatigue, abdominal pain, hematochezia & diarrhea. Since the time of his dx with UC, he has been treated with prednisone 40 mg/day & mesalamine 4 gms/day. For the last week he has had approx. 10 BMs/day and cramping abdominal pain. He is admitted to the hospital, where hydration & parenteral corticosteroids are given. Over the ensuing 12 hrs, his abdominal pain becomes worse, he develops abdominal distention & obstipation. On PE – he has a temp of 38.6 °C, pulse – 120/min, & his abdomen is distended & diffusely tender with rebound. He had an AXR that showed a dilated transverse colon to 8 cm with thumb-printing. No free intraperitoneal air was observed. At this point in time, the most appropriate therapy for this patient is:

A. Oral high-dose Mesalamine
B. Intravenous cyclosporine
C. 6-mercaptopurine or azathioprine
D. Intramuscular methotrexate
E. Urgent subtotal colectomy

IBD Questions

MJ, a 24 y/o FP resident has had UC since childhood involving his rectum (proctitis). He presents to you for evaluation of his risk for development of colorectal carcinoma. He was recently discovered to have low-grade dysplasia in 2 bx of the rectal area in the absence of inflammation. He has recently had routine lab tests performed & was found to have cholestatic liver chemistries with alkaline phosphatase of 6 x NL, NL aminotransferases, & a Total Bili was 3 x NL. He undergoes MRCP exam & a liver bx & is diagnosed with primary sclerosing cholangitis. He relates that his father developed a colorectal carcinoma of the sigmoid colon @ the age of 45 yrs.

All of the following are independent risk factors for the development of colorectal cancer in this patient with UC except:

A. Rectal involvement (proctitis)
B. Prolonged duration of disease (UC > 10 years’ duration)
C. The presence of low-grade dysplasia on biopsy
D. A family history of colon cancer in a first-degree relative
E. The concomitant presence of primary sclerosing cholangitis
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Which of the following medications have been demonstrated in randomized controlled trials to be effective for induction of remission in patients with UC but not effective to maintain remission in this population cohort?

A. Oral 5-ASA (mesalamine) such as Asacol & Pentasa
B. Corticosteroids (oral or topical)
C. Azathioprine (Imuran) or 6-mercaptopurine (Purinethol)
D. Topical mesalamine (enemas/Rowasa or suppositories/Canasa)
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IBD Questions

When counseling a patient regarding the risks & benefits of using infliximab (anti-TNF agents), a discussion regarding safety is merited. All of the following side effects have been directly attributed to the use of infliximab and may be encountered except which of the following?

A. Infection such as sinusitis
B. Active tuberculosis from reactivation of old TB
C. Arthralgias in the presence of a newly positive antinuclear antibody (ANA) & a newly positive anti-double stranded DNA antibody
D. Rash, myalgias, & fever occurring 2 to 12 days post-infliximab infusion in a patient previously exposed to infliximab with a long hiatus between infusions
E. Oral squamous cell cancers
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