DISCLOSURE

Financial: None

Thanks: Randy Pellish MD
        Ben Hyatt MD
for allowing me to use several of their slides
Outline of Talk

1. Pathophysiology Update
2. Diagnosis Update
3. Treatment Overview
4. Best Practices
5. Quality Indicators of Patient Care
**IBD: Epidemiology**

- **Epidemiology**
  - In the West, incidence rising over the last 50 years
  - Most data from population based studies in Scandinavia and Olmsted County MN 1950-1970’s
  - Estimated **1.4 Million Americans** affected by IBD
  - Health Care Costs associated with IBD: $6.3 billion

- **Crohn’s Disease**
  - Incidence: 8-14/100,000
  - Prevalence: 120-200/100,000

- **Ulcerative Colitis**
  - Incidence: 6-15/100,000
  - Prevalence: 50-200/100,000

*Incidence: number of new cases per population in a given time period (risk of contracting disease)*

*Prevalance: total number of cases of disease in a population (how widespread disease is)*

Kappelman et al Gastro. 2008
Cosnes et al. Gastro 2011
What are the potential causes of IBD?

**Genetic Predisposition**
20%–25% of patients have a close relative with IBD

**Immune System Abnormalities**
An inappropriate reaction by the body’s immune system

**Environmental Factors**
Infections, antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDS), diet, smoking
Inflammatory Bowel Disease
Pathophysiological Definition

An inappropriate, immune-mediated, chronic, inflammatory response to intestinal bacteria in a genetically susceptible person following exposure to an environmental agent.
Observations suggesting genetic link in IBD:

1) First-degree relatives found to have 10-fold increase risk of UC or CD (Orholm et al. NEJM 1991)

2) Children who have both parents with IBD have a 33% risk of developing IBD by age 28 (Laharie et al. Gastro 2001)

3) Concordance in 2 family members for CD type and site
   - CD Type (stricturing vs. fistulizing): 86% concordance
   - CD Site: 82% concordance (Bayless et al. Gastro 1996)
IBD Genetics

- **NOD2 and increased risk of CD:**
  - Heterozygosity increases risk by factor of 1.75 to 4
  - Homozygosity increases risk by factor of 11 to 27

- **NOD2 carriers more likely to have:**
  - Ileal involvement
  - Fibrostenosis
  - Surgical resection

*NOD2 only represents one of more than 100 susceptibility loci identified for IBD* (Abraham et al. NEJM 2009)
Bacterial Influence


IBD - Pathogenesis

Role of Bacteria

- No bacteria: No immune activation, No colitis
- Resident bacteria: Macrophage and TH\(_1\) immune activation, Colitis

Mice
- IL-2\(^{K0}\)
- IL-10\(^{K0}\)
- TCR\(\alpha\)^{K0}
- CD\(_3\)E\(_{26}\) TG
- SAMP1/Yit
- DSS
- CD\(_{45}\)RB\(_{hi}\) SCID

Rats
- HLA-B27 TG
- Indomethacin
- Guinea pigs
- Carrageenan

Non-human primate
- Cotton top tamarin
What is the intestinal Microbiome?

- Bacteria living in gastrointestinal tract, predominantly colon
- Colonization begins at birth
- Estimated >1 trillion organisms of >500 species
- A symbiotic, balanced relationship

- $10^2 = 100$
- $10^3 = 1000$
- $10^{4-5} = 10000 – 100,000$
- $10^7 = 10,000,000$
- $10^9 = 1,000,000,000$
- $10^{12} = 1,000,000,000,000$
T Helper Cell Activity

Normal: TR1/TH3

Crohn’s Disease: TH1/TH17

Ulcerative Colitis: TH2/TH17
Pathogenesis of IBD

1. Antigen and Antigen Presentation

Macrophage

Activated Macrophage

Activated CD4+ T Cell

IL-12

TNF

IFN-γ

2. T Cell Activation and Differentiation

CD4+ T Cell

Activated CD4+ T Cell

IL-4

Th1

Th2

IL-10

Th3

TGFβ

3. Cytokine mediated response amplification

4. Adhesion and recruitment

Bacteria

Intestinal Epithelial Cell

5. Restitution and Repair

Fibroblast

IL-10

Prostaglandins

Leukotrienes

Proteases

ROM

NO

After Sands B., 2003

Endothelium

Granulocyte

MAdCAM

ICAM-1

Mononuclear Cell

After Sands B., 2003
IBD Diagnostics

- **Diagnosis of IBD is made clinically:**
  - Various studies used including: history/physical, labs, radiology, and endoscopy, histopathology

[Images of CD (ileoscopy) and UC (colonoscopy)]
IBD Diagnostics

- **Fecal Calprotectin:**
  - Calcium binding protein representing 60% of cytosolic proteins in neutrophils
    - Stable in stool for up to 7 days at room temp
  - Concentration in the stool is an indirect measure of neutrophil infiltrate in bowel mucosa (thus active IBD)
  - Fecal calprotectin levels correlate with degree of mucosal inflammation
    - Levels normalize with histologic mucosal healing

IBD Diagnostics

Fecal Calprotectin:

- Calprotectin used to determine active CD vs. IBS
  - One study showed 100% Sensitivity and 97% Specificity

- Calprotectin to predict relapse in Quiescent IBD
  - Meta-analysis showed pooled Sn 78% and Sp 73%

- Calprotectin may be a useful screening tool to assess for active disease in IBD
  - Cut down on unnecessary endoscopic procedures

Judd et al. JGH 2011.
Mao et al. IBD 2012
CT enterography

- New standard in CT imaging of small bowel in CD
- Developed in 1997 as alternative to CT enteroclysis

**Technique:**
- Small bowel distension with neutral/low-density oral contrast
  - 1.5-2L oral contrast over 45-60min
- IV contrast then CT imaging during the enteric phase

IBD Diagnostics

- **CT enterography (CTE)**
  - Normal CTE
  - CTE: distal ileal inflammation in active CD
  - CTE: enlarged vasa recta in neo-TI in active CD (comb sign)

IBD Diagnostics

- MR enterography (MRE)
  - Similar concept to CTE with MR modality

Strictures in CD
Wall Thickening in CD

IBD Diagnostics

- **MRE vs. CTE**
  - **MRE Advantages**
    - Lack of ionizing radiation
      - Important given most patients with CD are young and are at increased risk for cumulative radiation over time
    - Ability to perform real-time functional imaging
    - Improved tissue contrast via variety of pulse sequences
    - Ability to distinguish inflammatory vs. fibrotic strictures
      - Due to differential water content in the two tissue types
  - **CTE Advantages**
    - Less expensive, shorter exam, no issue claustrophobia

IBD Diagnostics

- Endoscopy is still the Gold Standard.

CD (ileoscopy) | UC (colonoscopy)
IBD Diagnostics

- Capsule Endoscopy:
  - Pill camera (26x11mm)
  - Pill swallowed, transmits pictures via wireless signal to data recorder
  - 50,000-60,000 images over 8 hours
  - Useful in evaluation of suspected CD or follow up of established CD
  - Primary risk is capsule retention
    - Risk is < 1% if no known CD (about 4-5% if CD)
    - Patency Capsule can be used first in patients with CD, known SB stricture, previous SB surgery, or prior radiation
IBD Diagnostics

- Capsule Endoscopy (CE) Examples:
  
  Normal
  
  Active CD
IBD Diagnostics

- **Serology in IBD:**
  - Distinguishing IBD vs. non-IBD
    - Low Sensitivity of serology for determining IBD vs. non-IBD
    - Should not be used for screening the general population
    - Should not be used alone for diagnosis
      - May be helpful as an adjunct to other diagnostic tests

<table>
<thead>
<tr>
<th>TABLE 2. IBD Versus Non-IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Inflammatory bowel disease subjects versus healthy subjects</td>
</tr>
<tr>
<td>ASCA</td>
</tr>
<tr>
<td>pANCA</td>
</tr>
<tr>
<td>Anti-OmpC</td>
</tr>
<tr>
<td>ACCA</td>
</tr>
<tr>
<td>ALCA</td>
</tr>
<tr>
<td>AMCA</td>
</tr>
<tr>
<td>Anti-C</td>
</tr>
<tr>
<td>Anti-L</td>
</tr>
</tbody>
</table>

Prideaux et al. IBD 2012
IBD Diagnostics

Summary: Serology in IBD

Helpful for the following:

1. Differentiating between CD and UC
2. Pre-operative evaluation for indeterminate colitis prior to colectomy with pouch
3. Predicting IBD disease progression

Not Helpful for the following:

1. Primary diagnostic tool
2. Predict responses to treatment
IBD: Disease Activity

Indices: UC: Truelove + Witts; Mayo
Crohn’s: CDAI, Harvey Bradshaw Index (HBI)

Tests: CBC, CRP, ESR, fecal calprotectin

Endoscopy: colonoscopy, video capsule endoscopy

Radiology: enterography (CTE, MRE)

IBDQ: Inflammatory Bowel Disease Questionnaire
## Colitis Activity Assessment: TWI

### Table

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Severe</th>
<th>Fulminant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stools</td>
<td>&lt; 4</td>
<td>&gt; 6</td>
<td>&gt; 10</td>
</tr>
<tr>
<td>Blood</td>
<td>Intermitt.</td>
<td>Freq.</td>
<td>Continuous</td>
</tr>
<tr>
<td>Temp</td>
<td>NL</td>
<td>&gt; 37.6</td>
<td>&gt; 37.6</td>
</tr>
<tr>
<td>Pulse</td>
<td>NL</td>
<td>&gt; 90</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>Hgb</td>
<td>NL</td>
<td>&lt; 75% of NL</td>
<td>Transfusion required</td>
</tr>
<tr>
<td>ESR</td>
<td>&lt; 30</td>
<td>&gt; 30</td>
<td>&gt; 30</td>
</tr>
</tbody>
</table>
## Colitis Activity Assessment: TWI

<table>
<thead>
<tr>
<th>Stools</th>
<th>&lt; 4</th>
<th>&gt; 6</th>
<th>➚ 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Intermitt.</td>
<td>Freq.</td>
<td>Continuous</td>
</tr>
</tbody>
</table>

- **MILD**
- **SEVERE**
- **FULMINANT**
# Ulcerative colitis – Mayo Score

<table>
<thead>
<tr>
<th>Items</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freq</td>
<td>NL</td>
<td>1-2</td>
<td>3-4</td>
<td>5 or more</td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>-</td>
<td>Streaks</td>
<td>Obvious</td>
<td>Mostly</td>
<td></td>
</tr>
<tr>
<td>Mucosa</td>
<td>NL</td>
<td>Granular</td>
<td>Friable</td>
<td>Spont. bleeding</td>
<td>Ulcerated</td>
</tr>
<tr>
<td>MD rating</td>
<td>NL</td>
<td>Mild</td>
<td>Mod</td>
<td>Severe</td>
<td></td>
</tr>
</tbody>
</table>

0-2: Remission
3-5: Mild
6-10: Moderate
11-13: Severe

Response: 3 point drop
0-1 bleed score
# Crohn’s Disease Activity Index

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multiplication factor</th>
</tr>
</thead>
<tbody>
<tr>
<td># of liquid stool/d x 7d</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal pain (0 to 3) x 7d</td>
<td>5</td>
</tr>
<tr>
<td>General well being (0 to 4) x 7d</td>
<td>7</td>
</tr>
<tr>
<td>Complications</td>
<td>20</td>
</tr>
<tr>
<td>Use of opiates for diarrhea</td>
<td>30</td>
</tr>
<tr>
<td>Abdominal mass (0,2,5)</td>
<td>10</td>
</tr>
<tr>
<td>Hematocrit deviation (from 47%, 42%)</td>
<td>6</td>
</tr>
<tr>
<td>% deviation from standard weight</td>
<td>1</td>
</tr>
</tbody>
</table>

| Remission                                        | <150                  |
| Severe                                           | >450                  |
| Response                                         | 70-100 decrease.      |
Harvey-Bradshaw Index (HBI)

___ General Well Being: (0=well; 1=below average; 2=poor;
3=very poor; 4=terrible)

___ Abdominal pain: (0=none; 1=mild; 2=moderate; 3=severe)

___ # of Liquid Stools: (0=0-1; 1=2-3; 2=4-5; 3=6-7; 4=8-9;
5=10+ stools)

___ Abd. Mass: (0=none; 1=dubious; 2=definite; 3=tender)

___ Complications: arthralgia, uveitis, erythema nodosa, apthous,
ulcers, pyoderma gangrenosum, anal fissures, new fistula, abscess
(1 point for each)

Remission: < 3 Total: 0-16
Relapse: > 7
Current Approach – IBD Pyramid:

- “Step-Up” therapy

- Surgery
- Anti-TNF
  - Infliximab
  - Adalimumab
  - Certulizumab (CD only)
- TP: 6-MP/AZA, Steroids
- 5-ASA, Antibiotics, Budesonide
IBD Therapeutics

- New Approach – Flipping the CD Pyramid:
  - “Top-Down” Strategy – in severe disease

- Early
- Late
**IBD Therapeutics**

- **“Top-Down” Strategy in CD:**
  - **SONIC Trial:** (Study of Biologic and Immunomodulator Naïve Patients in Crohn’s Disease)
    - Patients with mod-severe CD randomly assigned to receive:
      - Azathioprine 2.5mg/kg + Placebo Infusion
      - Infliximab 5mg/kg + Placebo Capsules
      - Infliximab 5mg/kg + Azathioprine 2.5mg/kg
  - Patients naïve to immunomodulators and biologics
  - **Primary Endpoint:** Steroid free remission at week 26
  - **Secondary Endpoint:** Mucosal healing at week 26

Coloumbel et al. NEJM. 2010
“Top-Down” Strategy in CD:

SONIC Trial: (Study of Biologic and Immunomodulator Naïve Patients in Crohn’s Disease)

Coloumbel et al. NEJM. 2010
IBD Therapeutics

Discussion Safety of therapy with IBD Patients:

- Treatments very effective but have risk

- Risk must be communicated effectively with patients
  - Challenging: Lack of resources/time, misinformation online
  - Often an emotional topic for patients

- By discussing risks effectively, we can make pts. less fearful and more comfortable with IBD therapies

Siegel CA, IBD 2010;16:2168-72
Treatment Algorithm Pyramid – Where do probiotics fit in a treatment strategy?

- Induction
- Maintenance
- Treatment
- Progression

Probiotics

- Biologics
- Surgery
- Immunomodulators
- Corticosteroids
- Aminosalicylates (Oral and Topical)
- Antibiotics
How might a probiotic help in IBD?

Probiotic Mechanisms in IBD

1. **Lumen**
   - Antimicrobial Activity
   - Stimulation of an immune response

2. **Enhanced Barrier Integrity**
   - Increase mucus secretion
   - Enhance tight junctions

3. **Lamina Propria**
   - Immunomodulatory actions
     - Decrease TNFα and IFNγ secretion
     - Increase IL-10 and TGFβ secretion
     - Induce T(reg) cells
     - Induce T cell apoptosis
     - Dendritic cell modulation

4. Competitive Exclusion of Bacterial Adhesion/Translocation

Common Probiotics

- Lactobacillus
  - Lactobacillus acidophilus
The which, what, how, when questions when considering probiotics

- Which organism to take?
- Which product to buy?
- What dose is ideal?
- How long to take?
- What, if any, are side effects?
- What is the cost?
Expert Recommendations

- Probiotics lack evidence to support use in Crohn’s disease (6 studies, 341 pts.)
- Probiotic E. coli Nissle 1917 has evidence for maintenance of remission in ulcerative colitis (10 studies, 861 pts.)
- Probiotic mixture (VSL#3) has evidence for prevention and maintenance of remission in pouchitis

IBD: ? Dietary Rx.

Traditional Advice:
- “Avoid foods that bother you.”
- Avoid lactose containing foods, if ? of lactase def.
- Avoid osmotically active foods: fruit juices, soda
- Eat turkey, chicken, fish, eggs, rice, clear soups

New Consideration:
- Specific Carbohydrate Diet:
  Restricts complex carbohydrates: refined sugars, grains, and starch from the diet.
Specific Carbohydrate Diet (SCD)

No evidence based data (controlled trials) to recommend (SCD).

UMMHC experience: 10pts; 7 CD, 3 UC;
6 pts: 1 or more drug treatment failures; all on Rx.
Rx: SCD for 6 months
Result: all patients had less symptoms and BMs.
4 patients had IBD medications stopped or reduced.

Olendzki et al: abstract CCFA Meeting 2011
Pt. A.B. 30y.o. female; CD, Dx: 2006

**Past Surgical History:**
- a. I&D perirectal abscess, Seton placement 10/07
- b. Removal of seton 8/2008
- c. Fistulotomy, 10/10

**Extent of Disease:** distal ileum + perirectal disease by C/D 2006, and MRI 2010

**Complications:**
- a. Perianal disease, resolved 2010
- b. Anemia (chronic inflammation); resolved 1/13
- c. Adverse reaction to AZA 2007

**Previous Treatment:**
- a. Infliximab: 11/07 to 12/12
IBD Visit Checklist
Best Practices

CLINICAL ASSESSMENT:

Disease Activity Index: HBI; TWI, Mayo

Complications: hospitalization, surgery, work history, quality of life.

Systemic Symptoms: weight loss, fatigue

Extraintestinal Manifestations: eye, skin, joint

Note: fatigue +/or joint pain may be the only symptom of active Crohn’s disease.
Harvey-Bradshaw Index (HBI)

___ General Well Being: (0=well; 1=below average; 2=poor; 3=very poor; 4=terrible)

___ Abdominal pain: (0=none; 1=mild; 2=moderate; 3=severe)

___ # of Liquid Stools: (0=0-1; 1=2-3; 2=4-5; 3=6-7; 4=8-9; 5=10+ stools)

___ Abd. Mass: (0=none; 1=dubious; 2=definite; 3=tender)

___ Complications: arthralgia, uveitis, erythema nodosa, apthous, ulcers, pyoderma gangrenosa, anal fissures, new fistula, abscess (1 point for each)

Remission: < 3 Total: 0-16

Relapse: > 7
IBD Visit Checklist
Best Practices

Laboratory:

1. **Disease Activity:** CBC, ESR, CRP, Fecal calprotectin
2. **If worsening diarrhea:** C. difficile PCR
3. **If considering AZA, 6-MP Rx.**: TPMT (thiopurine methyltransferase)
4. **If on AZA, or 6-MP:** CBC, ALT, 3x/year
5. **If active disease or on steroids:** watch Vitamin D level
6. **If ileal disease:** check Vitamin B12 level
7. **Before anti-TNF Rx.:** PPD, Chest x-ray; HBsAg.
8. **If on 5-ASA:** creatinine yearly
IBD Visit Checklist
Best Practices

GENERAL HEALTH MAINTENANCE:

- Gynecologic exam (annual if immunosuppressed)
- Assessment of smoking status
- Depression check
- PPD/chest x-ray (annual if on an anti-TNF)
- IBD patients should avoid NSAIDS.
- Metabolic bone disease screen (Vitamin D level, bone density.) - 18-42% osteoporosis; 22-77% osteopenia

Gastroenterology 2003;124:795
IBD Visit Checklist
Best Practices

SURVEILLANCE:

. Dermatologic examination (if on chronic immunomodulator Rx.)

. Ophthalmologic examination (annual)

. Colonic dysplasia screening (q1-3 years if > 8 yrs of extensive Ulcerative Colitis or Crohn’s Disease)
VACCINATIONS:

. Initial visit vaccinations: (HAV: 2 doses; HBV; HPV: 3 doses)

. Subsequent vaccinations: (influenza: annual; Td/Tdap: every 10 years; pneumococcal: 1-time revaccination in immunosuppressed patients; HAV booster after 10 years)
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Check titer before vaccination?</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Td/Tdap</td>
<td>No</td>
<td>Administer the vaccine if it has not been given over the past 10 years, or give Tdap if Td was administered ≥2 years ago.</td>
</tr>
<tr>
<td>HPV</td>
<td>No</td>
<td>3 doses at 0, 2, and 6 months in females 9–26 years of age and in males 11–26 years of age</td>
</tr>
<tr>
<td>Influenza</td>
<td>No</td>
<td>Administer annually. Use trivalent inactivated influenza vaccine. Avoid live attenuated influenza vaccine.</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>No</td>
<td>Vaccinate if no vaccine has been given previously. 1-time revaccination after 5 years if the patient is immunosuppressed.</td>
</tr>
<tr>
<td>Hepatitis A virus</td>
<td>Yes</td>
<td>2 doses at 0 and 6–12 months or 0 and 6–18 months. Booster given &gt;10 years.</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>Yes</td>
<td>3 doses at 1, 1–2, and 4–6 months. Check postvaccination titers 1 month after finishing last dose. If there is no response, revaccinate with a double dose.</td>
</tr>
<tr>
<td>Combination hepatitis A/B virus</td>
<td>Yes</td>
<td>May be given instead of individual hepatitis A virus vaccine and hepatitis B virus vaccine, particularly in individuals who do not respond to hepatitis B virus vaccination.</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>No</td>
<td>Vaccinate at-risk patients if no vaccine has been given previously.</td>
</tr>
</tbody>
</table>

HPV = human papillomavirus; Td = tetanus and diphtheria; Tdap = tetanus, diphtheria, and pertussis.

Modified from Wasan SK. et al14 and Advisory Committee on Immunization Practices.15
IBD and Pregnancy
The Essential Facts

IBD patients with quiescent disease have normal fertility.

Infertility may result in patients with active IBD.

Ileal Pouch Anal Anastomosis is associated with reduced fertility.

2/3s of patients with active disease will have continued or worsening of symptoms. (Corollary: don’t get pregnant if IBD is active.)

All IBD anti-inflammatory and immunosuppressive agents EXCEPT METHOTREXATE may be used safely during pregnancy and breast feeding. (Biologics may be stopped 8-10 weeks before delivery)

IBD patients with perineal disease, rectal Crohn’s disease, or IPAA should have a Cesarean section.

PeppercornM, 2013: UpToDate
<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IF a patient with IBD is initiating anti-tumor necrosis factor therapy,</td>
</tr>
<tr>
<td>THEN tuberculosis risk assessment should be documented, and tuberculin</td>
</tr>
<tr>
<td>skin testing or interferon gamma release assay should be performed</td>
</tr>
<tr>
<td>IF a patient with IBD is initiating therapy with anti-TNF, THEN risk</td>
</tr>
<tr>
<td>assessment for hepatitis B virus should be documented</td>
</tr>
<tr>
<td>IF a patient with IBD requires at least 10 mg prednisone (or equivalent)</td>
</tr>
<tr>
<td>for 16 weeks or longer, THEN an appropriately dosed steroid-sparing</td>
</tr>
<tr>
<td>agent or operation should be recommended</td>
</tr>
<tr>
<td>IF a hospitalized patient with severe colitis is not improving on</td>
</tr>
<tr>
<td>intravenous steroids within 3 days, THEN sigmoidoscopy with biopsy should</td>
</tr>
<tr>
<td>be performed to exclude cytomegalovirus, AND surgical consultation</td>
</tr>
<tr>
<td>should be obtained</td>
</tr>
<tr>
<td>IF a patient in whom a flare of IBD is suspected with new or worsening</td>
</tr>
<tr>
<td>diarrhea THEN the patient should undergo <em>Clostridium difficile</em> testing</td>
</tr>
<tr>
<td>at least once</td>
</tr>
<tr>
<td>IF a patient with IBD is initiating 6 MP/AZA, THEN TPMT testing should</td>
</tr>
<tr>
<td>be performed before starting therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IF a patient with ulcerative colitis is found to have confirmed low-grade</td>
</tr>
<tr>
<td>dysplasia in flat mucosa, THEN proctocolectomy or repeat surveillance</td>
</tr>
<tr>
<td>within 6 months should be offered</td>
</tr>
<tr>
<td>IF a patient with extensive ulcerative colitis or Crohn’s disease</td>
</tr>
<tr>
<td>involving the colon has had their disease for 8 to 10 years, THEN</td>
</tr>
<tr>
<td>surveillance colonoscopy should be performed every 1 to 3 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Health care maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IF a patient with IBD is on immunosuppressive therapy, THEN patients</td>
</tr>
<tr>
<td>should be educated about appropriate vaccinations, including (1) annual</td>
</tr>
<tr>
<td>inactivated influenza, (2) pneumococcal vaccination with a 5-year booster,</td>
</tr>
<tr>
<td>and (3) general avoidance of live virus vaccines</td>
</tr>
<tr>
<td>IF a patient with Crohn’s disease is an active tobacco smoker, THEN</td>
</tr>
<tr>
<td>smoking cessation should be recommended, and treatment should be offered</td>
</tr>
<tr>
<td>or suitable referral provided at least annually</td>
</tr>
</tbody>
</table>

6MP, 6-mercaptopurine; AZA, azathioprine; TPMT, thiopurine methyltransferase; PSC, primary sclerosing cholangitis.

*a* All measures had median ratings of 8 or higher on a 1 through 9 rating scale.

*b* 6-mercaptopurine, 1.0 to 1.5 mg/kg daily; azathioprine, 2.0 to 2.5 mg/kg daily (if normal TPMT metabolism); methotrexate 25 mg injected subcutaneously weekly, or appropriately dosed biological therapy.

*c* L-sided for ulcerative colitis, or 1/3 or more for Crohn’s disease.

*d* If a patient with ulcerative colitis has co-existing PSC (of any duration), THEN surveillance colonoscopy should be performed every 1 to 3 years.
**TABLE 2. Ten Most Highly Rated Outcome Measures**

<table>
<thead>
<tr>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid Use</td>
</tr>
<tr>
<td>Proportion of patients with steroid-free clinical remission for &gt; 12 month period</td>
</tr>
<tr>
<td>Proportion of patients currently taking prednisone (excluding those diagnosed within the last 112 days)</td>
</tr>
<tr>
<td>Number of days per month/year lost from school/work attributable to IBD</td>
</tr>
<tr>
<td>Number of days per year in the hospital attributable to IBD</td>
</tr>
<tr>
<td>Number of emergency room visits per year for IBD</td>
</tr>
<tr>
<td>Proportion of patients with malnutrition</td>
</tr>
<tr>
<td>Proportion of patients with anemia</td>
</tr>
<tr>
<td>Proportion of patients with normal disease-targeted health-related quality of life</td>
</tr>
<tr>
<td>Proportion of patients currently taking narcotic analgesics</td>
</tr>
<tr>
<td>Proportion of patients with nighttime BM’s or leakage</td>
</tr>
<tr>
<td>Proportion of patients with incontinence in the last month</td>
</tr>
</tbody>
</table>

\(^a\)All measures had median ratings of 8 or higher on a 1 through 9 rating scale.
AGA IBD QUALITY INDICATORS

The patient’s IBD type, anatomic location, and disease activity assessed within the past year.

The patient has been on corticosteroids $\geq 10$mg prednisone for 60 or more days in past year.

The patient has received an influenza vaccination within the past year.
AGA IBD QUALITY INDICATORS

Patient has received a pneumococcal immunization at any point in his/her life.

Plan to initiate anti-TNF therapy for this patient for the first time ever in his/her life.

I have assessed this patient’s tobacco use status within the past year.


IBD For Primary Care Physicians

John K Zawacki MD
April 10, 2013
The Intestinal Immune System

IBD Burden

Healthcare Costs Associated with IBD

- Estimated annual disease-attributable direct costs in US (Extrapolated based on prevalence and cost data)

$3.6 billion for CD

$2.7 billion for UC

$6.3 billion total

Indirect costs not included here: Transportation, productivity costs due to missed work, etc

Kappelman et al. Gastro 2008
IBD: History

- Age of onset
- Previous surgery
- Location of disease
- Previous treatments
- Hospitalizations for IBD
- Extraintestinal disease (skin, joint, eye)
- Family History of IBD
- History of smoking, NSAIDs
- Pregnancies
- Work history, quality of life
IBD: Physical Exam

HEENT: eye inflammation; conjunctiva; mouth ulcers

ABDOMEN: ? Palpable mass or bowel loop in RLQ
If mass or bowel loop palpable, ? Tender

RECTAL: skin tag, fissure, swelling, tenderness, fistulous opening, anal canal stricture
Intestinal Flora

Complex: 3,000 – 5,000 species

Numerous: $10^{14}$ bacteria cc/stool
Genetic Predisposition

Presently > 100 genes on 10 chromosomes are implicated in the pathogenesis of IBD

**The majority of the genes implicated affect how the intestinal immune system interacts with intestinal bacteria.**
<table>
<thead>
<tr>
<th><strong>Table 4. Harvey-Bradshaw Index (HBI)</strong></th>
</tr>
</thead>
</table>
| **General well being**  
(0=very well; 1=slightly below average; 2=poor; 3=very poor; 4=terrible) |
| **Abdominal pain**  
(0=none; 1=mild; 2=moderate; 3=severe) |
| **Number of liquid stools per day**  
(0=0–1 stools; 1=2–3 stools; 2=4–5 stools; 3=6–7 stools; 4=8–9 stools; 5=10+ stools) |
| **Abdominal mass**  
(0=none; 1=dubious; 2=definite; 3=tender) |
| **Complications**  
Arthralgia, uveitis, erythema nodosum, aphthous ulcers, pyoderma gangrenosum, anal fissures, new fistulas, abscesses (1 point for each) |
| **Total score** |

Remission: HBI score <3 points.  
Relapse: HBI score >7 points.  
Modified from Vermeire S, et al.⁵
<table>
<thead>
<tr>
<th>1. Clinical status assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Indices (CDAI* or HBI; IBDQ) or thorough review of systems</td>
</tr>
<tr>
<td>- Weight loss</td>
</tr>
<tr>
<td>- Complications (hospitalizations, surgeries, work history, quality of life)</td>
</tr>
<tr>
<td>- Extraintestinal manifestations (eye, skin, joint)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Vaccinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Initial visit vaccinations, with all doses completed (HAV: 2 doses; HBV, HPV: 3 doses**)</td>
</tr>
<tr>
<td>- Subsequent vaccinations (including influenza: annual; Td/Tdap: every 10 years; pneumococcal: 1-time revaccination in immunosuppressed patients; HAV: booster after 10 years)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. General health maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Gynecologic examination (annual)*</td>
</tr>
<tr>
<td>- Assessment of smoking status</td>
</tr>
<tr>
<td>- PPD/chest radiograph (annual)**</td>
</tr>
<tr>
<td>- Metabolic bone disease screening (including vitamin D levels, bone density testing**)</td>
</tr>
<tr>
<td>- Depression screening</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Dermatologic examination*</td>
</tr>
<tr>
<td>- Ophthalmologic examination (annual)</td>
</tr>
<tr>
<td>- Colonic dysplasia screening</td>
</tr>
</tbody>
</table>

*A CDAI calculator is available at http://www.ibdjohn.com/cdai/.
**See text for details. *In patients on immunomodulator therapy.

CDAI=Crohn’s Disease Activity Index; HAV=hepatitis A virus; HBI=Harvey-Bradshaw Index; HBV=hepatitis B virus; HPV=human papillomavirus; IBDQ=Inflammatory Bowel Disease Questionnaire; PPD=purified protein derivative; Td/Tdap=tetanus, diphtheria, and pertussis.
<table>
<thead>
<tr>
<th>Participants</th>
<th>Probiotic</th>
<th>Study Duration</th>
<th>Study Design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>32 adults</td>
<td>Saccharomyces boulardii</td>
<td>6 months</td>
<td>R</td>
<td>Maintenance of remission minimal</td>
</tr>
<tr>
<td>55 adults</td>
<td>Lactobacillus GG</td>
<td>12 months</td>
<td>R, PC</td>
<td>No effect preventing recurrence after surgery</td>
</tr>
<tr>
<td>11 adults</td>
<td>Lactobacillus GG</td>
<td>6 months</td>
<td>R, PC</td>
<td>No effect on disease activity</td>
</tr>
<tr>
<td>75 children</td>
<td>Lactobacillus GG</td>
<td>2 years</td>
<td>R, PC</td>
<td>No effect preventing relapse</td>
</tr>
<tr>
<td>98 adults</td>
<td>Lactobacillus johnsonii</td>
<td>6 months</td>
<td>R, PC</td>
<td>No effect preventing recurrence after surgery</td>
</tr>
<tr>
<td>70 adults</td>
<td>Lactobacillus johnsonii</td>
<td>1 year</td>
<td>R, PC</td>
<td>No effect preventing recurrence after surgery</td>
</tr>
<tr>
<td>Participants</td>
<td>Probiotic</td>
<td>Study Duration</td>
<td>Study Design</td>
<td>Outcome</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------------------</td>
<td>----------------</td>
<td>--------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>116 adults</td>
<td>E. coli Nissle 1917</td>
<td>12 months</td>
<td>R, PC</td>
<td>Maintenance of remission</td>
</tr>
<tr>
<td>20 adults</td>
<td>Mixture 8 strains</td>
<td>12 months</td>
<td></td>
<td>Maintenance of remission</td>
</tr>
<tr>
<td>21 adults</td>
<td>Bifidobacterium, Lactobacillus</td>
<td>12 months</td>
<td>R</td>
<td>Maintenance of remission</td>
</tr>
<tr>
<td>327 children</td>
<td>E. coli Nissle 1917</td>
<td>12 months</td>
<td>R</td>
<td>Maintenance of remission</td>
</tr>
<tr>
<td>30 adults</td>
<td>Mixture 3 strains</td>
<td>8 weeks</td>
<td>R, PC</td>
<td>Maintenance of remission</td>
</tr>
<tr>
<td>20 adults</td>
<td>Bifidobacterium, Lactobacillus</td>
<td>12 weeks</td>
<td>R, PC</td>
<td>Clinical, endoscopic improvement</td>
</tr>
<tr>
<td>90 adults</td>
<td>Mixture 8 strains</td>
<td>8 weeks</td>
<td>R</td>
<td>Maintenance of remission</td>
</tr>
<tr>
<td>18 adults</td>
<td>Bifidobacterium longum</td>
<td>4 weeks</td>
<td>R, PC</td>
<td>Improved inflammation</td>
</tr>
<tr>
<td>32 adults</td>
<td>Mixture 8 strains</td>
<td>6 weeks</td>
<td>R</td>
<td>Induction of remission</td>
</tr>
<tr>
<td>187 adults</td>
<td>Lactobacillus GG</td>
<td>12 months</td>
<td>R</td>
<td>Maintenance of remission</td>
</tr>
</tbody>
</table>