Understanding
Inflammatory Bowel Diseases: What Every Patient Needs to Know

An educational program for patients, families and caregivers living with Crohn’s disease and ulcerative colitis.

Dr. William Holderman
Washington Gastroenterology, Digestive Health Specialists Division
Tacoma, WA
Today’s Objectives

Define IBD, its potential causes and diagnosis

- Discuss management and treatment
- Highlight special populations
- Answer questions
INFLAMMATORY BOWEL DISEASE

ULCERATIVE COLITIS
Mucosal Ulceration in Colon

CROHN’S DISEASE
Transmural Inflammation
Ileitis
Ileocolitis
Colitis
IBD vs. IBS

- **IBD = Inflammatory Bowel Disease**
  - Chronic intestinal inflammation
  - Crohn’s disease, ulcerative colitis

- **IBS = Irritable Bowel Syndrome**
  - No findings on labs or exams
    - Bowel hypersensitivity
    - Change in bowel habits
    - Pain relieved with defecation
IBD CHARACTERIZED BY CHRONIC INFLAMMATION IN THE GUT

Dysregulation of the immune system
What is the Immune System?

- Cells (T cells, B cells, macrophages) that defend the body against attack from infections
- To eradicate infection, the immune system turns on, causes inflammation
- Once an infection is eliminated, the immune system knows how to turn itself off

Photo courtesy of Scott Plevy, MD
Dysregulated Immune System

- In IBD, the “off” switch is broken
- Inflammation is a Key Aspect of IBD
CHRONIC INFLAMMATION:
PROTEINS CALLED CYTOKINES ARE THE LIGHT SWITCH

“On”

“Off”
U.S. Incidence and Prevalence

- Approximately 1.5 million Americans suffer from IBD
- Prevalence ~1/200 people have IBD in the U.S.
- 15-20,000 Individuals in Greater Puget Sound Region living with IBD
- 400 New Cases/year in GPSR
- Men and women are affected equally
- Bimodal distribution: 20-30 and ≥ 60 years
- Increase among different race/ethnic groups (HMC)
Inflammatory Bowel Disease – Age of Onset
Ulcerative colitis

Proctitis  Left-sided Colitis  Total Colitis

Small Intestine Not Involved
Ileocolonoscopy

Normal findings of terminal ileum and colon
UC Spectrum of Disease

Normal

Mild

Moderate

Severe
Crohn’s Disease Anatomic Distribution

- Colon alone (20%)
- Small bowel alone (33%)
- Ileocolic (45%)
CD Spectrum of Disease
Understanding Complications of Crohn’s Disease

- Intestinal obstruction
- Abscess
- Fistula
- Stricture
- Colorectal cancer
Understanding Complications of Ulcerative Colitis

- Anemia from blood loss
- Perforation (rupture) of the bowel
- Colorectal cancer
- Toxic megacolon
What are the Potential Causes of IBD?

**Genetic Disposition**
- 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
Environmental Triggers of IBD

- Antibiotics
- Acute Infections
- NSAIDS
- Diet
- IBD Onset and Reactivation
- Stress
- Smoking
Clinical Features of IBD

<table>
<thead>
<tr>
<th>Typical Symptoms</th>
<th>Common Physical Examination Findings</th>
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<tbody>
<tr>
<td>Abdominal Pain</td>
<td>Abdominal tenderness</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Palpable mass</td>
</tr>
<tr>
<td>Fever</td>
<td>Perianal disease</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Extra-intestinal manifestations:</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>• Mouth</td>
</tr>
<tr>
<td>Weight loss</td>
<td>• Skin</td>
</tr>
<tr>
<td>Anorexia</td>
<td>• Eyes</td>
</tr>
<tr>
<td>Nausea</td>
<td>• Joints</td>
</tr>
<tr>
<td></td>
<td>• Liver</td>
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Common Laboratory & Radiographic Findings

- Anemia
- Leukocytosis
- Elevated EST/CRP**
- Guaiac-positive stool
- Small bowel disease
- Fistulas
- Strictures

CRP = C-reactive protein
EST = erythrocyte sedimentation rate
## Impact of IBD

### Medical Impact
- 85% of patients suffer from diarrhea
- 51% of patients were hospitalized in the last 3 years
- 64% required surgery
- ~90% of CD will have surgery in their lifetime

### Work Disability Impact
- 55% missed work due to disease in the past year
- 5.3% become permanently work disabled

### Emotional Impact
- 70% of patients report anxiety or depression, compared with 30% of population norms

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Smoking in IBD

- **Ulcerative Colitis**
  - Smoking can protect against UC
  - Ex-smokers are more likely to develop UC

- **Crohn’s Disease**
  - Two-fold risk in current smokers
  - Smokers are less responsive to treatment
  - Smokers are more likely to develop recurrence of disease after surgery
Crohn’s Disease is Characterized by Flare-ups Alternating with Periods of Remission
Diagnosing IBD
Diagnosing IBD

Normal colon on colonoscopy

UC on colonoscopy

CD on colonoscopy
Recognizing Symptoms of IBD Flares

- Diarrhea
  - Often increased from usual course of disease
  - Rectal bleeding
- Abdominal pain or cramping
- Low-grade fever
- Fatigue

- Extraintestinal manifestations
  - Joint pain/swelling
  - Eye inflammation
  - Skin lesions
  - Mouth ulcers
C-difficile in IBD Patients

![Graphs showing in-hospital mortality, bowel surgery, and emergency readmissions in IBD patients compared to IBD alone and IBD-CDAD-HAI from 2002 to 2007.](image)

Source: Aliment Pharmacol Ther © 2011 Blackwell Publishing
Management & Treatment of IBD
Comprehensive IBD Management

IBD Management Goals

- Control symptoms
- Treat inflammation
- Treat complications
- Minimize treatment toxicity
- Replenish nutritional deficits
- Improve quality of life
- Prevent cancer
- Provide emotional support
- Maintain Steroid Free Remission

Maintain Steroid Free Remission
Understanding Treatment Options

- Over-the-counter agents
- Prescription medications
- Complimentary and alternative therapies
- Surgery
IBD Medicine Cabinet

Over-the-Counter

Antibiotics

5-Aminosalicylates/Mesalamine

Corticosteroids, Budesonide

Immunomodulators – AZA/6MP, MTX
### Prescription Medications

<table>
<thead>
<tr>
<th>Class</th>
<th>Agents</th>
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</thead>
</table>
| 5-ASA Agents| - Balsalazide (Colazal®)  
- Mesalamine formulations  
  - Delayed release tablets (Lialda®, Asacol®, Asacol HD®)  
  - Controlled release tablets (Pentasa®)  
  - Extended release capsules (Apriso™)  
  - Rectal suspension (Rowasa®)  
  - Rectal suppository (Canasa®)  
- Olsalazine (Dipentum®); Sulfasalazine (Azulfidine®) |
| Corticosteroids | - Adrenocorticotropic hormone  
- Budesonide (Entocort®); MMX (Uceris)  
- Hydrocortisone (Cortenema®, Cortifoam®)  
- Methylprednisolone (Medrol®)  
- Prednisone |
| Antibiotics  | - Ciprofloxacin (Cipro®)  
- Metronidazole (Flagyl®)  
- Rifaximin (Xifaxin®) |
## Prescription Medications

<table>
<thead>
<tr>
<th>Class</th>
<th>Agents</th>
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<tbody>
<tr>
<td>Immunologic Agents</td>
<td>- Azathioprine (Imuran®, Azasan®)</td>
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<tr>
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<td>- Cyclosporine (Neoral®)</td>
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<tr>
<td></td>
<td>- 6-Mercaptopurine (Purinethol®)</td>
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<td>- Methotrexate</td>
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<td>- Tacrolimus (Prograf®)</td>
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<tr>
<td></td>
<td>- Xeljanz (Tofacitinib) Summer 2018</td>
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<tr>
<td>Biologic Agents</td>
<td>- Infliximab (Remicade®) 1998</td>
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<tr>
<td></td>
<td>- Adalimumab (Humira®) 2004</td>
</tr>
<tr>
<td></td>
<td>- Certolizumab pegol (Cimzia®) 2008</td>
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<tr>
<td></td>
<td>- Natalizumab (Tysabri®) 2008</td>
</tr>
<tr>
<td></td>
<td>- Vedolizumab (Entyvio) 2014</td>
</tr>
<tr>
<td></td>
<td>- Ustekinumab (Stelara) 2017</td>
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</table>
The Role of Pro-Inflammatory Cytokines in IBD
5-ASA Release Sites

- **Stomach**
  - Pentasa®
  - Asacol®
  - Azulfidine®
  - Dipentum®
  - Colazal®

- **Small Intestine**
  - Mesalamine in microgranules
  - Mesalamine w/ eudragit-S

- **Large Intestine**
  - Azo bond
  - Rowasa®
  - Canasa®
Immune-Modulators
Imuran® (azathioprine) & Purinetheol ® (6-MP)

**Myths**
- Dangerous drugs used to treat cancer
- Cause cancer
- Should not be used longer than 3 years
- If they don’t work over 3-6 months, they will not work
- Must be stopped before or during pregnancy

**Facts**
- Very slight increased risk of lymphoma
- Can be used for more than 3 years
- If they don’t seem to work at first does, the dose needs to be reassessed
- Can be used during pregnancy – must be monitored
Corticosteroids

Benefits
- Induces remissions in UC and CD
- Quick fix
- Inexpensive
- Oral or rectal

Risks
- No long term benefits
- Numerous side effects
  - Cushingoid changes
  - Hypertension
  - Diabetes
  - Osteoporosis
  - Acne
  - Cataracts
  - Depression
  - Growth retardation
We Don’t See the Deformities of the Intestines until Complication
Can Treatment Alter the Natural History of CD and UC?

- Induce and maintain gastrointestinal healing
- Prevent strictures and penetrating complications
- Prevent extraintestinal complications
- Decrease hospitalization/surgery
- Decrease long-term cost of care
Anti-TNF: Endoscopic Healing
New Approaches to Therapeutic Intervention in Crohn’s Disease? The “Step-up” vs. “Top down” Trial

AZA, azathioprine; IFX, infliximab; MTX, methotrexate
Natural History – Most Crohn’s Patients Will Require Surgery

The Evolution of Crohn’s Disease: Inflammation Leads to Damage

Over a 20-year period, 88% risk of developing stricturing (18%) or penetrating (70%) disease

Cosnes J et al. Inflamm Bowel Dis. 2002
Natural History – Ulcerative Colitis

Risk of colectomy: 24% after 10 years
~ 30% after 20 years

Significant increased risk of cancer

Adapted from Langholz E, et al. Gastroenterology 1994
Over-the-Counter (OTC) Agents

- Address only specific symptoms
  - Antidiarrheal agents
  - Laxatives
  - Pain relievers
- Important to discuss with physician before taking any OTC medications
Complementary & Alternative Therapies: Probiotics

- “Good” bacteria that restores balance to the enteric microbiota—bacteria in the intestines
  - VSL #3
- May be helpful in aiding recovery of the intestine and maintaining remission
- Important to discuss with physician before initiating treatment
- Alternative therapies should not replace prescription medications
Surgery in IBD

Crohn’s Disease
- Stricturoplasty
- Resection of small intestinal segment
- Colectomy (partial or complete)
- Proctocolectomy
- Crohns cannot be cured with surgery

Ulcerative Colitis
- Proctocolectomy (removal of the colon and rectum)
  - With ileostomy
  - Restorative (ileoanal or J pouch)
- Disease is “cured” once colon is removed
Understanding the Importance of Diet and Nutrition in Managing IBD

- Causes of nutritional deficits
  - Decreased intake (no desire to eat)
  - Active disease
    - Protein and fluid loss
- Decreased absorption of nutrients (when small intestine is affected by CD)
  - Fat
  - Vitamins
Understanding the Importance of Diet and Nutrition in Managing IBD

- Create a food journal
- Eliminate problematic foods
- Strive for a well-balanced, healthy diet based on
  - Hydration
  - Electrolyte balance
  - Continual adequate nutrient intake
IBD in Special Populations
Understanding IBD in Children & Adolescents

- Special considerations
- Ability to swallow capsules or tablets
- Side effects of drug therapy
  - Risks of long-term corticosteroid use
  - Emotional/social concerns
- Adherence
- Growth failure and need for nutritional supplementation
- Emotional well-being
Understanding IBD in Pregnant Women

- Special considerations
- IBD should be controlled before considering pregnancy
- Remain on most prescribed medications
- Well-balanced diet with vitamins including folic acid
- Ongoing communication between obstetrician and gastroenterologist
Living Well with IBD

- Be adherent with medications
- Understand your disease and possible complications
- Schedule follow up appointments
- Maintain a well-balanced diet
- Establish a support system
- Empower yourself with information
- Follow “Helpful Tips” handout
Adherence Decreases Risk of Relapse

Vaccination Recommendations per Routine Guidelines

Regardless of immunosuppression
- Inactivated influenza (trivalent inactivated vaccine)
- Tetanus (as part of Td, Tdap or DTaP)
- HPV (quadrivalent vaccine against types 6, 11, 16 and 18)
- Meningococcus (MCV4 or MPSV-4)
- Hepatitis A (single-antigen vaccine or as part of Hepatitis A and B combination vaccine)
- Hepatitis B vaccine

Ideally before initiation of immunosuppression
- Pneumococcus (PCV13 or PPSV23)
- Pertussis (as part of Tdap or DtaP)
Vaccination Recommendations
Vaccines contraindicated ON Immunosuppression and Biologics

- Live, attenuated influenza (intranasal vaccine. Shots are OK)
- Varicella zoster vaccine
- Herpes zoster (live zoster vaccine. Shingrix® is OK)
- Yellow fever vaccine
- Measles-mumps-rubella vaccine

- Typhoid live oral vaccine
- Smallpox vaccine
- Tuberculosis Bacillus Calmette-Guérin vaccine
- Polio live oral vaccine
- Anthrax vaccine

“Live/attenuated virus vaccines”
Questions & Answers