Diagnosis and Preventive Care for Patients with Inflammatory Bowel Disease

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The University of Oklahoma Health Sciences Center
Conflicts of Interest

Speaker’s Bureau: AbbVie, Bristol Myers Squibb (BMS), Pfizer, Takeda.

Advisory Board: AbbVie, Pfizer
Learning Objectives

• Describe the natural history of inflammatory bowel disease.

• Outline the patients’ expectations during a clinic visit.

• Summarize the approach of diagnosis and management.

• Review the FDA-approved biologic and small-molecule agents for management of IBD.

• Identify the role of Primary Care Clinicians in the care for patients with IBD
  • Preventive care in IBD.
Anatomy of GI Tract

Colon:
- 5-6 feet long
- Water resorption
- Formation of solid waste.

Small Intestine:
- Duodenum, jejunum, ileum
- 20-25 feet long
- Digestion
- Absorption
Inflammatory Bowel Disease
Inflammatory Bowel Disease

Inflammatory Bowel Disease (IBD)

- Crohn's disease
- Ulcerative colitis
- Indeterminate colitis
Inflammatory Bowel Disease
Extra Intestinal Manifestation

- **Eyes**
  - Episcleritis
  - Uveitis

- **Kidneys**
  - Stones (nephrolithiasis)
  - Hydronephrosis
  - Fistulae
  - Urinary tract infection

- **Skin**
  - Erythema nodosum
  - Pyoderma gangrenosum

- **Liver**
  - Steatosis

- **Biliary tract**
  - Gallstones
  - Sclerosing cholangitis

- **Joints**
  - Spondylitis
  - Sacroiliitis
  - Peripheral arthritis

- **Circulation**
  - Phlebitis

- **Mouth**
  - Stomatitis
  - Aphthous ulcers
Inflammatory Bowel Disease
Pathogenesis

Genetics

Environment

Immune System
Inflammatory Bowel Disease
Pathogenesis

Immune System

Genetics

Environment

+200 loci

+30 CD-specific loci

+23 UC-specific loci

110 common IBD loci

CD genes

UC genes

NOD2 PTPN22

MHC ECM1

110 common IBD loci
Inflammatory Bowel Disease
Genes Don’t Explain It All

Genetics

Environment

Immune System

CD genes

-30 CD-specific loci

+23 UC-specific loci

+200 loci

NOD2
PTPN22

MHC
ECM1

110 common IBD loci
Inflammatory Bowel Disease
Diet

Crohn’s recommendations:
- Vegetables
- Fruits
- Saturated and trans fat
- Emulsifiers
- Carrageenans
- Artificial sweeteners
- Maltodextrins
- Titanium dioxide

Ulcerative colitis recommendations:
- Omega 3 oils from fish and food
- Red meat, processed meats
- Dairy fat, palm and coconut oil
- Saturated and trans fat
- Emulsifiers
- Carrageenans
- Artificial sweeteners
- Maltodextrins
- Titanium dioxide
Inflammatory Bowel Disease
Data and Statistics

• It is estimated that 1.3% of US adults (3 million) reported being diagnosed with IBD in 2015.

• Incidence (new cases):
  • CD: 10.7 per 100k (~33,000 new cases per year)
  • UC: 12.2 per 100k (~38,000 new cases per year)

Shivashankar R, et al. *CGH.* 2017
Inflammatory Bowel Disease
Data and Statistics

Trends in Age- and Sex-Adjusted Incidence Rate of Crohn's Disease (CD) and Ulcerative Colitis (UC):
Olmsted County, Minnesota, 1970-2011

Shivashankar R, et al. CGH. 2017
Inflammatory Bowel Disease
Data and Statistics – Age and Gender

<table>
<thead>
<tr>
<th></th>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>29.5 years</td>
<td>34.9 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Women ~&gt; Men</td>
<td>Men &gt; Women</td>
</tr>
</tbody>
</table>

Inflammatory Bowel Disease Data and Statistics – Race

Inflammatory Bowel Disease
Data and Statistics – Region

U.S. Geographic Region

<table>
<thead>
<tr>
<th>Region</th>
<th>IBD Prevalence (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>West</td>
<td>705</td>
</tr>
<tr>
<td>South</td>
<td>696</td>
</tr>
<tr>
<td>Midwest</td>
<td>1154</td>
</tr>
<tr>
<td>Northeast</td>
<td>1174</td>
</tr>
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</table>

Inflammatory Bowel Disease
Ulcerative Colitis

- Chronic, immune-mediated inflammatory condition of the large intestine.
  - Absence of rectal involvement ~ 5% (adults), 33% in pediatric-onset colitis.

- Symptoms.

- Risk of colon cancer.

- Colectomy.
Inflammatory Bowel Disease
Ulcerative Colitis

Proctitis

30–60% of patients
Symptoms
Rectal bleeding, tenesmus, urgency

Left-sided colitis

16–45% of patients
Symptoms
Proctitis plus diarrhoea, abdominal cramping

Extensive colitis

15–35% of patients
Symptoms
Left-sided colitis plus constitutional symptoms, fatigue, and fever

Ungaro R, et al. The Lancet. 2017
Inflammatory Bowel Disease
Ulcerative Colitis

Safroneeva E, et al.  AP&T.  2015
Inflammatory Bowel Disease
Crohn’s Disease

• Chronic inflammatory condition that can affect the entire GI tract.
  • Majority of the time: progressive, destructive disease if left untreated.

• 10-year risk of abdominal surgery: 30% (decreased from 50%)

• 25% will have perianal disease.

• Hallmark symptoms: abdominal pain, diarrhea, fatigue, weight loss.
Inflammatory Bowel Disease
Crohn’s Disease

Perianal disease
(up to 25%)

Inflammatory Bowel Disease
Crohn’s Disease

- Diarrhoea
- Abdominal pain
- Weight loss
- Low-grade fever
- Fatigue
- Growth retardation in children
- Malnourishment

- Postprandial pain
- Bloating
- Nausea and vomiting
- Occlusion or sub-occlusion

Symptoms depend on the location of fistula:
- Enterosigmoid fistula: diarrhea, pneumaturia, and recurrent UTI
- Rectovaginal fistula: dyspareunia and stool discharge through the vagina
- Enterocutaneous fistula: asymptomatic and abdominal abscesses

Torres J, et al. The Lancet. 2017
Inflammatory Bowel Disease
Crohn’s Disease – Disease Progression

Kennedy NA, et al. CGH. 2019
Inflammatory Bowel Disease Diagnosis

• Clinical Diagnosis.
  • Constellation of
    1. Symptoms (subjective), and
    2. Evidence of inflammation (objective).
      a. Blood work.
      b. Endoscopy + capsule video exam.
      c. Sampling and reviewing under microscope (histology)
      d. Radiology (changes found on CT scan or MRI scan)

• Goals –
  1. Diagnosis
  2. Stratify disease severity ⇒ dictates management
Inflammatory Bowel Disease Clinic Visit

- History and physical exam.
Inflammatory Bowel Disease
Clinic Visit

• History and physical exam.

• Blood/stool work up.
  • CBC (anemia, infection)
  • Chemistry (liver abnormalities, albumin, electrolyte abnormalities)
  • Vitamin panel (Vit D, Vit B12, folic acid)
  • Iron panel (chronic blood loss → iron deficiency)
  • Inflammatory markers (C-reactive protein, fecal calprotectin, albumin).
  • Pre-treatment (biologics) blood tests.
  • Stool tests – infection and inflammation.
Inflammatory Bowel Disease Clinic Visit

• History and physical exam.

• Blood/stool work up.

• Decide on:
  1. Modality of obtaining samples for diagnosis (endoscopy),
  2. Disease extension (CT-scan, MRI scan).
Inflammatory Bowel Disease
Colonoscopy

What to Expect During a Colonoscopy

1. 24 hours before test: Clear out bowels with laxatives, enema, all-liquid diet
2. Lie on left side while IV is administered to help you relax
3. Colonoscope inserted into rectum
4. Colonoscope transmits images as it passes through length of colon

https://www.verywellhealth.com/colonoscopy-4014117
## Endoscopic Assessment of Disease Activity

<table>
<thead>
<tr>
<th>Endoscopic Features</th>
<th>UCEIS Score</th>
<th>Mayo Score</th>
<th>Endoscopic Features</th>
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</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td>Erythema, decreased vascular pattern, mild friability</td>
<td>1-3</td>
<td>1</td>
<td>Erythema, decreased vascular pattern, mild friability</td>
</tr>
<tr>
<td>Marked erythema, absent vascular pattern, friability, erosions</td>
<td>4-6</td>
<td>2</td>
<td>Marked erythema, absent vascular pattern, friability, erosions</td>
</tr>
<tr>
<td>Spontaneous bleeding, ulceration</td>
<td>7-8</td>
<td>3</td>
<td>Spontaneous bleeding, ulceration</td>
</tr>
</tbody>
</table>

Inflammatory Bowel Disease

CT scan

What to Expect During a CT Scan

1. You may need a contrast agent to help images appear

2. Lie on table outside of scanner

3. Table slides into scanner

4. Scanner spins around taking x-rays

https://www.verywellhealth.com/what-is-a-cat-scan-189603
Inflammatory Bowel Disease
MRI scan

What to Expect During an MRI

1. You may need a contrast agent to help images appear
2. Lie on table outside of scanner
3. Table slides into scanner
4. Scans taken for 15-60 minutes

https://www.verywellhealth.com/mri-for-multiple-sclerosis-2440713
Inflammatory Bowel Disease
Management of IBD

• Goals.
  • Patient goals vs provider goals.
The Life of a Patient with IBD

- Will I be fired for missing work because of doctor’s appointments?
- Will I be able to make it through my commute without a bathroom?
- How do I talk with my friends and family about my condition?
- Will my symptoms get worse over time?
- Could the food I eat trigger my condition?

Inflammatory Bowel Disease
Management of IBD

• Goals.
  • Patient goals vs provider goals.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leave the house</td>
<td>Stop diarrhea</td>
</tr>
<tr>
<td>Eat what I want</td>
<td>Prevent disease progression</td>
</tr>
<tr>
<td>Go to school/work</td>
<td>Optimize bowel function</td>
</tr>
<tr>
<td>Go hiking/camping</td>
<td>Give vaccinations to prevent infections</td>
</tr>
<tr>
<td>Go out on a date</td>
<td>Treat skin conditions (PAF)</td>
</tr>
<tr>
<td>Reassure spouse</td>
<td>Simplify medications/limit toxicity</td>
</tr>
<tr>
<td>Avoid the “bag”</td>
<td>Prevent disease-related complications</td>
</tr>
<tr>
<td>Back to “normal”</td>
<td>Heal the colon and/or small bowel</td>
</tr>
<tr>
<td>Stop medications</td>
<td>Lowest effective dose, prevent flares</td>
</tr>
</tbody>
</table>
Inflammatory Bowel Disease
Management of IBD

• Goals.
  • Patient goals vs provider goals.

• Treatment options –
  • Medical management (pills, injectables)
    • Decisions.
  • Surgery
  • Endoscopy (narrowing)
  • Stem-cell transplant (perianal fistula)
## Timeline of Approvals of Biologics and Small Molecules in the United States

<table>
<thead>
<tr>
<th>CD</th>
<th>CDf</th>
<th>IFX (ACCENT)</th>
<th>ADM (CHARM)</th>
<th>CZP (PRECiSE)</th>
<th>VDZ (G2)</th>
<th>UST (UNITI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC</td>
<td>IFX (ACT)</td>
<td>IFX (ACCENT)</td>
<td>ADM (ULTRA)</td>
<td>GOL (PERSUIT) (G1)</td>
<td>VDZ</td>
<td>TOF (OCTAVE)</td>
</tr>
</tbody>
</table>

- **IFX**: infliximab
- **ADM**: adalimumab
- **CZP**: certolizumab pegol
- **GOL**: golimumab
- **VDZ**: vedolizumab
- **UST**: Ustekinumab
- **TOF**: tofacitinib
- **OZD**: ozanimod

- 1998
- 2002
- 2005
- 2007
- 2008
- 2012
- 2013
- 2014
- 2016
- 2018
- 2019
- 2021

www.accessdata.fda.gov/scripts/cder

Last accessed Sep, 22\textsuperscript{nd} 2021
Inflammatory Bowel Disease
Management of IBD

- Options for medical management of ulcerative colitis

<table>
<thead>
<tr>
<th>Pills</th>
<th>Rectal therapy</th>
<th>Infusion</th>
<th>Subcutaneous injection</th>
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</thead>
<tbody>
<tr>
<td>Mesalamine</td>
<td>Mesalamine</td>
<td>Remicade (Infliximab)</td>
<td>Humira (Adalimumab)</td>
</tr>
<tr>
<td>Azathioprine/6-MP/cyclosporine</td>
<td>Budesonide</td>
<td>Entyvio (Vedolizumab)</td>
<td>Simponi (Golimumab)</td>
</tr>
<tr>
<td>Prednisone</td>
<td>Tacrolimus (OL)</td>
<td></td>
<td>Stelara (Ustekinumab)</td>
</tr>
<tr>
<td>Budesonide</td>
<td></td>
<td></td>
<td>Entyvio/CTP-13 *</td>
</tr>
<tr>
<td>Xeljanz (Tofacitinib)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zeposia (Ozanimod)</td>
<td></td>
<td></td>
<td></td>
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Inflammatory Bowel Disease
Management of IBD

- Options for medical management of Crohn’s disease

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<th>Pills</th>
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<th>Subcutaneous injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfasalazine</td>
<td>Remicade (Infliximab)</td>
<td>Humira (Adalimumab)</td>
</tr>
<tr>
<td>Azathioprine/6-MP/MTX</td>
<td>Entyvio (Vedolizumab)</td>
<td>Cimzia (Certolizumab pegol)</td>
</tr>
<tr>
<td>Prednisone</td>
<td></td>
<td>Stelara (Ustekinumab)</td>
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Inflammatory Bowel Disease
Healthcare maintenance in IBD

• Physical exams
• Smoking cessation (CD/UC)
• Serial labs (disease related vs medication related)
• Skin exams
• Anxiety/depression
• Cancer prevention (colon, skin, cervical)
• Vaccination
  • Flu
  • Pneumonia
  • Hep A/B
  • Herpes Zoster
  • HPV
Inflammatory Bowel Disease

Healthcare maintenance in IBD

• Physical exams
• Smoking cessation (CD/UC)
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• Skin exams
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• Cancer prevention (colon, skin, cervical)
• Vaccination
  • Flu
  • Pneumonia
  • Hep A/B
  • Herpes Zoster
  • HPV

COVID-19!
Inflammatory Bowel Disease
Healthcare maintenance in IBD

• Vaccination:
  • Influenza (killed): annually
  • HPV: 3 doses (9-26)
  • Pneumonia:
    • Immune-suppressed: PCV13→PSV23
    • Not immune-suppressed: PSV 23
  • Hepatitis B
    • May need to check titers and re-vaccinate (TNFa-i)
  • Shingrex.
    • Age 50+, JAK-I.

• Bone health.
  • Steroid use +3 months, post-menop.

• Cancer prevention
  • Colon cancer
  • Cervical cancer
    • Annual if immune-suppressed
  • Prostate cancer
  • Skin cancer (M/NMSC)
    • Annual full-skin exam by derm. (regardless to Rx)

• Misc.:
  • Smoking status. (CD vs UC)
  • Nutritional status
    • B12/folate/iron/25-OH vitD
  • Behavioral
    • Depression (35%)
  • Fatigue
    • Disease vs others
  • Sleep disorders
    • Disease vs others
  • Bone health.
  • Steroid use +3 months, post-menop.
  • Cancer prevention
  • Colon cancer
  • Cervical cancer
    • Annual if immune-suppressed
  • Prostate cancer
  • Skin cancer (M/NMSC)
    • Annual full-skin exam by derm. (regardless to Rx)
Inflammatory Bowel Disease
Summary

• Inflammatory bowel diseases affect ~ 1% of general population.
• It is a treatable, **not curable**, condition.
• Appropriate diagnosis is key for management.
  • Hematochezia, diarrhea, weight loss, nocturnal symptoms.
  • Family history of IBD.
  • Anemia, low albumin, inflammatory markers (CRP, fecal calprotectin).
  • Sometimes over-diagnosed (Crohn’s disease).
• Different agents are available to manage inflammation. More in the pipeline.
• Healthcare maintenance is key!
Crohn’s and Colitis Center – OU Edmond

• Gastroenterologist
• Colorectal surgeons
• Primary care providers
  • Radiologists
  • Infusion clinic
  • Social worker
  • IBD Nurse

• Endoscopy suite/imaging
  • Psychologist
  • Dietician
  • Ostomy nurse
• Clinical trial unit (downtown)
  • IBD Support Group
Crohn’s and Colitis Center – OU Physicians

**Clinic**
OU Physicians Fountain Lake
14101 N. Eastern Avenue, Edmond, OK 73013
Phone: (405) 271-8423
Fax: (405) 271-4239

**Endoscopy**
OU Medical Center - Edmond
1 South Bryant, Edmond, OK 73034
Ambulatory Care Pavilion, 1st floor
Ambulatory Care Unit  (405) 359-5512