This Presentation Includes a Live Interactive Case

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Inflammatory Bowel Diseases for the General Internist
When to Consider and How to Optimize Care?

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I have no conflicts of interest to disclose in relation to this presentation
Objectives

At the conclusion of this presentation, participants will be able to

1. Recognize the signs and symptoms of inflammatory bowel diseases and identify candidates for endoscopic evaluation and gastroenterology referral
2. Recognize disease and treatment complications and coordinate care with managing gastroenterologist
3. Promote appropriate preventive health services for IBD population
4. Answer common IBD patient questions in the primary care setting
A 26-year-old female has small and large bowel Crohn’s disease diagnosed 5 years ago. She has required multiple courses of steroids and a distal ileum stricture resection in the past but has done better since starting therapy with azathioprine and infliximab 2 years ago.

She reports occasional bloating and mild abdominal cramping relieved by passing stool. Otherwise she feels well.

Colonoscopy one month ago showed scattered aphthae in the terminal ileum and a small ulcer in the ascending colon. Overall this represents a marked improvement compared to prior exams. Her blood work is unremarkable.

She is concerned about the long-term health impact of current immunosuppressants and would like to discuss her options.
Which of the following management decisions is correct?

- A “drug holiday” with close monitoring is safe given sustained clinical remission for over one year
- Should patient plan to get pregnant, stop both medications and switch to oral mesalamine to reduce risk of congenital malformations
- Continue both azathioprine and infliximab and optimize therapy
- Influenza and pneumococcal vaccines are contraindicated in the setting of anti-TNF use but can be used with azathioprine
Disease Burden

0.5-1% of population suffer from IBD in the US

Loftus et al. Gastroenterology 2004
Cosnes et al. Gastro 2011
Why Me?

Intestinal Dysbiosis
Genetically Susceptible Host
Inappropriate chronic inflammatory response

Hygiene Hypothesis

Summers et al. Gut 2005
Lashner et al. AJG 2008
Schölmerich et al. JCC 2017
Disease Distribution

Crohn’s Disease

Ungaro et al. Lancet 2017

Ulcerative Colitis

Think Systemic Disorders

- Extraintestinal manifestations may precede diagnosis
- Most mirror intestinal disease activity
- Some ophthalmologic manifestations are medical emergencies
Approach to Diagnosis

- CD and UC have overlapping features with other GI disorders

- **No single test is accurate enough to diagnose IBD**
  - Diagnosis relies on a combination of clinical features, laboratory, endoscopy and imaging tests

- Right demographic
  - Peak age for CD is 20–30 years and for UC 30–40 years
Inflammatory vs Functional?

~40% of IBD patients meet IBS Criteria

IBS-IBD Overlap

IBD Population

Population Prevalence

IBS

IBD

Halpin et al. Am J Gastroenterol 2012
Clinical Pearls

Chronic Diarrhea with Inflammatory Features
- Nighttime occurrence
- Fecal urgency and tenesmus
- Blood mixed in stool
- Lack of specific food triggers

Chronic Abdominal Pain
- Nighttime occurrence
- Worse after eating
- Not relieved by moving bowels

Systemic Symptoms

Family History of IBD

Concomitant Autoimmune Disorders
- AS, celiac disease, Psoriasis, SLE, RA, MS
Laboratory (Alarm) Features

- Iron deficiency anemia
- Vitamin B12 and folic acid deficiencies (CD)
- Hypoalbuminemia
- Elevated inflammatory markers
  - Can be used to screen patients with suspected functional diarrhea for IBD

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
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</thead>
<tbody>
<tr>
<td>CRP</td>
<td>49%</td>
<td>92%</td>
</tr>
<tr>
<td>Fecal Calprotectin</td>
<td>88%</td>
<td>73%</td>
</tr>
<tr>
<td>Stool Lactoferrin</td>
<td>82%</td>
<td>79%</td>
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</table>

Table. Diagnostic accuracy for assessment of endoscopic disease activity in IBD

Mosli et al. Am J Gastroenterol 2015
Smaalley et al. Gastro 2019
IBD Serology Panels

- Contain autoantibodies and antimicrobial antibodies
  - *IBDsgi diagnostic* assay adds several genetic risk markers (Prometheus Laboratories)

- **One stop test to diagnose IBD? NO**
  - Variable component sensitivities
  - Low disease prevalence limits positive predictive value
  - 2018 and 2019 ACG CD and UC clinical guidelines recommend against use

Sands et al. CGH 2018
Ileo-Colonoscopy: Gold Standard

- Normal Colon Wall
- Ulcerative Colitis: Usually affects only the inner layer of the bowel wall.
- Crohn Disease: May affect all layers of the bowel wall.
Shifting Treatment Paradigms

**Traditional Approach**

1. Steroid Free Clinical Remission
2. Mucosal Healing
3. Deep Remission
4. Change Disease Course

**Therapeutic Targets**

- Treat Early (therapeutic window)
- Use Effective Therapy
- Optimize Therapy
- Prevent Complications and Avoid Surgery

- Attainable in some patients
- Attempt in all patients
Treatment Options

- 5-ASA (mesalamine): mild to moderate UC only
- Steroids (Conventional and Budesonide): induction of remission
- Immuno-modulators: Azathioprine/6-MP and Methotrexate
- Biologics
- JAK inhibitor (small molecule)
  - Tofacitinib (approved in 2018 for UC only)

<table>
<thead>
<tr>
<th>Biologic Drug</th>
<th>Commercial Name</th>
<th>FDA Approval</th>
<th>Indication</th>
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<tbody>
<tr>
<td>Infliximab</td>
<td>Remicade®</td>
<td>1998</td>
<td>CD and UC</td>
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<tr>
<td>Adalimumab</td>
<td>Humira®</td>
<td>2002</td>
<td>CD and UC</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>Cimzia®</td>
<td>2008</td>
<td>CD</td>
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<tr>
<td>Golimumab</td>
<td>Simponi®</td>
<td>2009</td>
<td>CD and UC</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>Entyvio®</td>
<td>2014</td>
<td>CD and UC</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>Stelara®</td>
<td>2016</td>
<td>CD</td>
</tr>
</tbody>
</table>
Safety
Increased risk of opportunistic infections and certain malignancies
Preventive Care
Smoking Cessation

- Crohn’s disease patients should be counselled to quit smoking
  - Inferior response to biologics
  - Higher risk of disease recurrence after surgery
  - Higher risk of stricturing disease and perianal disease complications

- Ulcerative Colitis
  - Smoking cessation is associated with worsening disease activity

Farraye et al. Am J Gastroenterol 2017
1.5-3 fold increase in incidence of influenza, pneumococcal disease and Zoster in IBD population

Risk increased by but not always related to immuno-suppressive medications

- 64% of GIs believed PCP should determine which vaccinations to give
- 83% believed PCP should administer the vaccines

- Only 37% of family practitioners felt comfortable providing primary care (including vaccines) across a range of IBD severity

Kants et al. Am J Gastroenterol 2015
Tinsley et al. Inflamm Bowel Dis 2018
Long et al. Aliment Pharmacol Ther 2013
Wasan et al. Inflamm Bowel Dis 2011
Selby et al. Dig Dis 2011
### Influenza Vaccination

**Recommendations**

1a. All adult patients with IBD should undergo annual vaccination against influenza with very low level of evidence.

1b. Those on immunosuppressive medications with high contacts should receive influenza vaccination. Contraindicated for live vaccine. Commercially available inactivated vaccine.

### Pneumococcal Vaccination

**Recommendation**

2. Adult patients with IBD receiving immunosuppressive therapy should receive pneumococcal vaccination with both the 23-valent and 7-valent pneumococcal vaccines. Contraindicated for 23-valent pneumococcal vaccine, uncertain for 7-valent pneumococcal vaccine. Guidelines agree with national guidelines. Contraindicated for 7-valent pneumococcal vaccine with very low level of evidence.

### Herpes Zoster Vaccination

**Recommendation**

3. Adults with IBD over the age of 50 should consider vaccination against herpes zoster, including certain subgroups of immunosuppressed patients. **Strong recommendation, with low level of evidence.**

Live vaccines are contraindicated in patients on biologics, high dose steroids or high dose immunomodulators.
Osteoporosis

- Related to malabsorption, negative effects of pro-inflammatory cytokines and adverse reactions from medications (steroids)
- DXA screening for patients with one or more risk factors
  - Chronic corticosteroid therapy (>3 months)
  - Postmenopausal women
- Correct Vitamin D deficiency to >30 ng/ml (immunoregulatory effects)
Preventive Care-Other

- Skin cancer risk
  - Melanoma ~30% (with anti-TNF use)
  - Non-melanoma skin cancers 2 fold (with thiopurine use)
  - Screening dermatology visit: case-by-case surveillance strategy

- Cervical cancer
  - Women with IBD on immunosuppressive therapy should undergo annual cervical cancer screening

Farraye et al. Am J Gastroenterol 2017
What Should Patients with IBD be Eating?

- No special "anti-inflammatory diet" (Exclusive and partial enteral nutrition are used infrequently in adult patients with CD)
- Low fiber diet if stricture
- Low FODMAP and gluten free helpful for patients with concomitant IBS and celiac disease
Fecal Microbiota Transplantation

Magic Bullet?

- 2/3 RCTs on the use of FMT in UC achieved their primary end point of clinical remission
  - Remission rates 20-30%
- No RCTs in Crohn’s disease
- Currently, only accepted application is recurrent C. difficile colitis (investigational with IND enforcement discretion)

Narula et al. Inflamm Bowel Dis 2017
What about Supplements?

- **Omega-3 fatty acids** --- No
- **Curcumin** --- Maybe
  - Mild to moderate UC
  - Daily dose 2-3 g in addition to mesalamine
- **Cannabis** --- ??
  - Symptom improvement in Crohn’s disease but no evidence of objective improvement in bowel inflammation
  - Negative Study in UC
  - CBD vs THC? Oral vs smoked?

Quezada et al. Inflamm Bowel Dis 2016
And Probiotics?

- **Crohn's Disease**
  - No benefit in inducing or maintaining remission or in preventing relapse of CD after surgery

- **Ulcerative Colitis (mild to moderate)**
  - **VSL#3** may be effective in inducing remission
  - **E. coli Nissle 1917** may be as effective as 5-ASAs in preventing relapse

Derwa et al. Aliment Pharmacol Ther. 2017
NSAID Use

- Use common in IBD population
- Conflicting evidence but overall in favor of increased risk of disease activity with frequent NSAID use
- Avoid all NSAIDs if possible
  - Cox-2 blockers may be safer

Wallace et al. Gastro & Hepatology 2011
Narcotics

Use tripled over past 2 decades
- Presence of psychiatric illness and use of narcotics among top factors associated with high costs of IBD care

Use of strong opiates is associated with increased all-cause premature mortality

Reserve for acute pain only
- Tramadol and codeine may be safe

Burr et al. Clin Gastroenterol Hepatol 2018
Regueiro et al. Gastro 2017
Interrupting Biologic Therapy and “Drug Holidays”

- Interruption risks the formation of antibodies thus decreasing clinical efficacy
  - Elective surgeries can be scheduled at drug trough level
- Drug holidays only for patients in clinical (and preferably endoscopic) remission
  - 1 year relapse ~50%

Vermeire et al. Ther Adv Gastroenterol 2018
Vaughn et al. Inflamm Bowel Dis 2015
Louis et al. Gastro 2012
1. Preconception counseling critical to positive pregnancy outcomes
2. Anti-TNF and azathioprine are **safe** during pregnancy and breastfeeding
3. Avoid live vaccinations within the first 6 months for newborns exposed to maternal anti-TNFs
Take Home Messages

1. Inflammatory Bowel Diseases are chronic morbid GI conditions commonly affecting younger adults
2. Distinction from more common functional bowel disorders is essential for early diagnosis and treatment
3. Optimizing care goes beyond anti-inflammatory therapy and includes essential preventive services
4. Care of IBD patients is multidisciplinary which makes coordination between health services critical to good outcomes
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Questions?

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