Inflammatory Bowel Disease
What You Need to Know

Peter Buch, MD, FACG, AGAF, FACP
Associate Professor
University of Connecticut School of Medicine
University of New England College of Osteopathic Medicine
Frank H. Netter MD School of Medicine

Conflicts

- None

Objectives

- To learn how to distinguish Inflammatory Bowel Disease (IBD) from Irritable Bowel Syndrome (IBS)
- To become familiar with the workup of IBD
- To become familiar with the various treatments for IBD
- To become aware of the controversies surrounding IBD

How do we distinguish Irritable Bowel Syndrome from Inflammatory Bowel Disease?

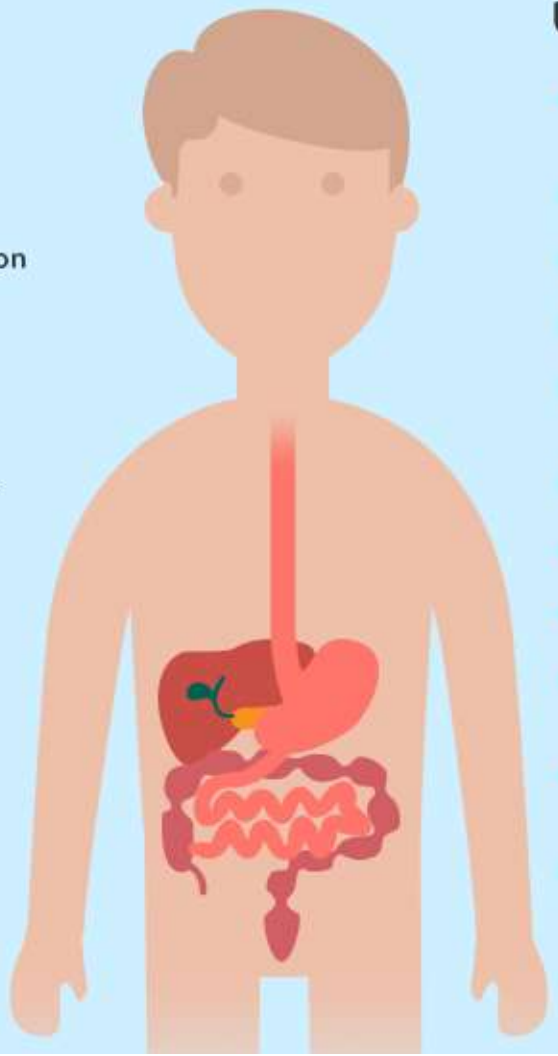
Making the Distinction

- No inflammation in Irritable Bowel Syndrome (IBS)
- No “Alarm Symptoms”
  - Rectal bleeding
  - Anemia
  - Weight loss
  - Fevers

How do we distinguish Crohn’s Disease from Ulcerative Colitis?

Crohn's

- Inflammation tends to occur in patches
- Can affect any part of the GI tract, from the anus to the oesophagus
- Blood and mucus in the stools not as common
- Can also cause nausea and vomiting
- Abdominal pain may be more severe or continuous
- Inflammation present in mucosa and muscle tissue
- Granulomas (specific cell formations developed by the immune system to isolate threats to the body) usually present
- More likely to cause fistulae (small tunnels), fissures (tears) or strictures (narrowings) in the bowel
- More commonly seen in smokers
- Treated with steroids, immunosuppressant medication and biologics, but 5-ASAs not usually as effective
- Surgery may not eliminate the disease



Ulcerative colitis

- Inflammation is more likely to be uniform or continuous
- Localised to the rectum and large bowel
- Blood and mucus in the stools more common
- Nausea and vomiting not usually seen
- Pain is more likely to be intermittent and experienced with bowel movements
- Typically inflammation is confined to mucosa
- Not as likely to cause granulomas
- Fistulae, fissures and strictures less common
- More commonly associated with non- or ex-smokers
- Treated with steroids, 5-ASAs, immunosuppressant medication and biologics
- Surgery to the colon (where required) resolves the disease

Between Crohn's Disease and Ulcerative Colitis

- Which is curable?
- Which is treatable?

Which is Curable/Which is Treatable

- Ulcerative Colitis is curable

  When the colon is removed, it's cured

- Crohn's Disease is treatable

  After surgery, high likelihood of recurrence

Describe How These Are Related to Inflammatory Bowel Disease

Food

Stress

Familial history

Relationships to IBD

- Food: exacerbates pre-existing disease/ NOT the cause
- Stress: exacerbates pre-existing disease/ NOT the cause
- Family History: 15% of patients with IBD have a familial history

Describe the relationship of smoking to:

- Crohn's
- Ulcerative Colitis

Describe the relationship of smoking to:

- Crohn's worsens
- Ulcerative Colitis improves

What percentage of Crohn's patients will have an exacerbation if they continue to smoke?

1. 25%
2. 50%
3. 75%

Nunes T et al
Impact of smoking cessation on the clinical course of Crohn's Disease under current therapeutic algorithms: a multicenter prospective study
Am J Gastroenterol 2016:111;411

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Can Inflammatory Bowel Disease and Irritable Bowel Disease Co Exist?

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YES

What Are the Clinical Features of Crohn's?

What Are the Clinical Features of Crohn's

- Diarrhea
- Pain
- Wt loss
- Fever
- Palpable RLQ mass

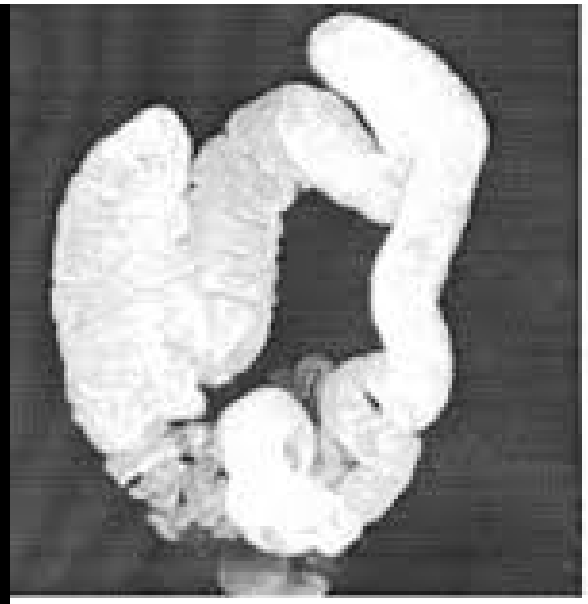
What is the differential diagnosis of Crohn's Disease?

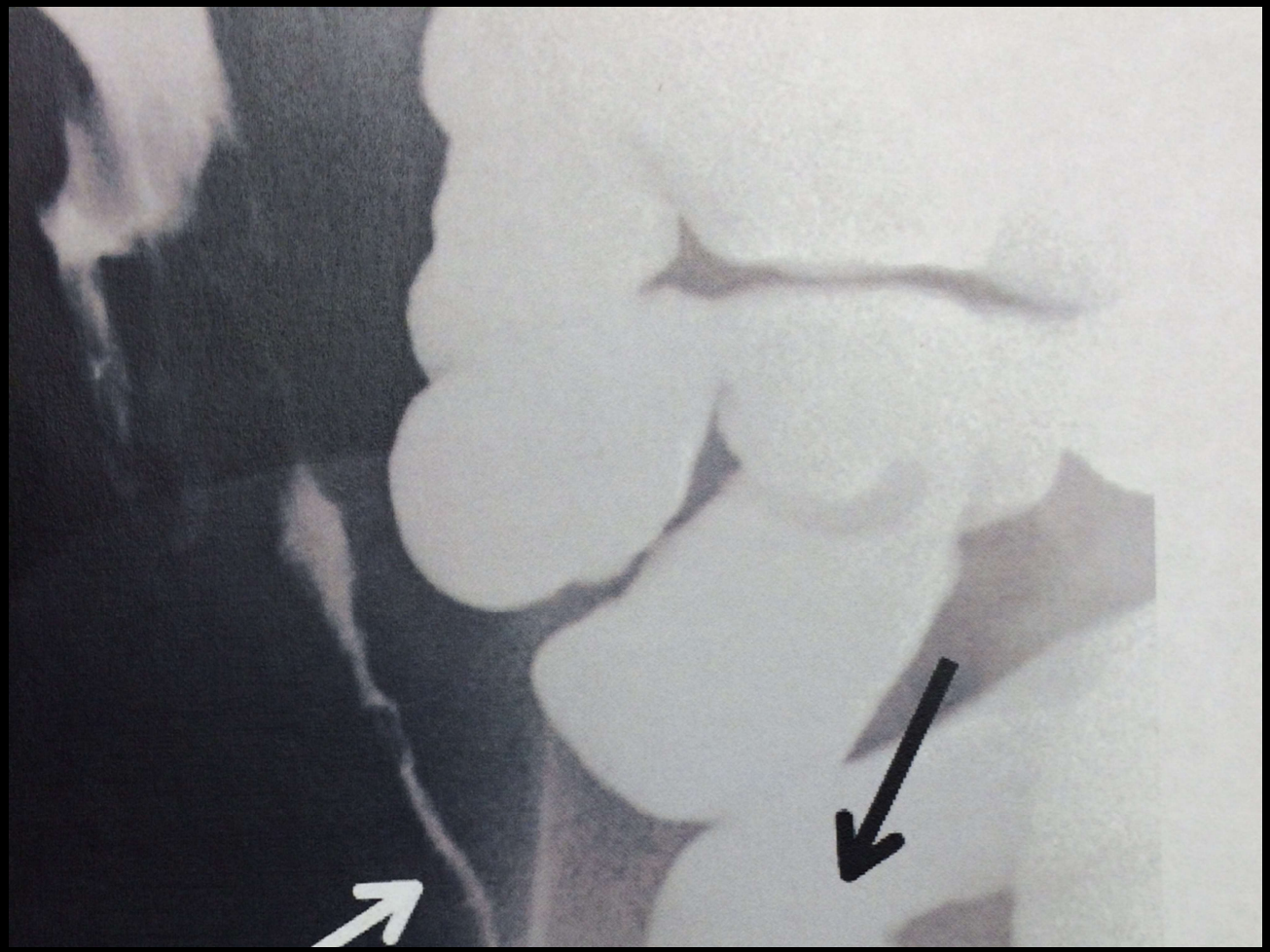
Ddf

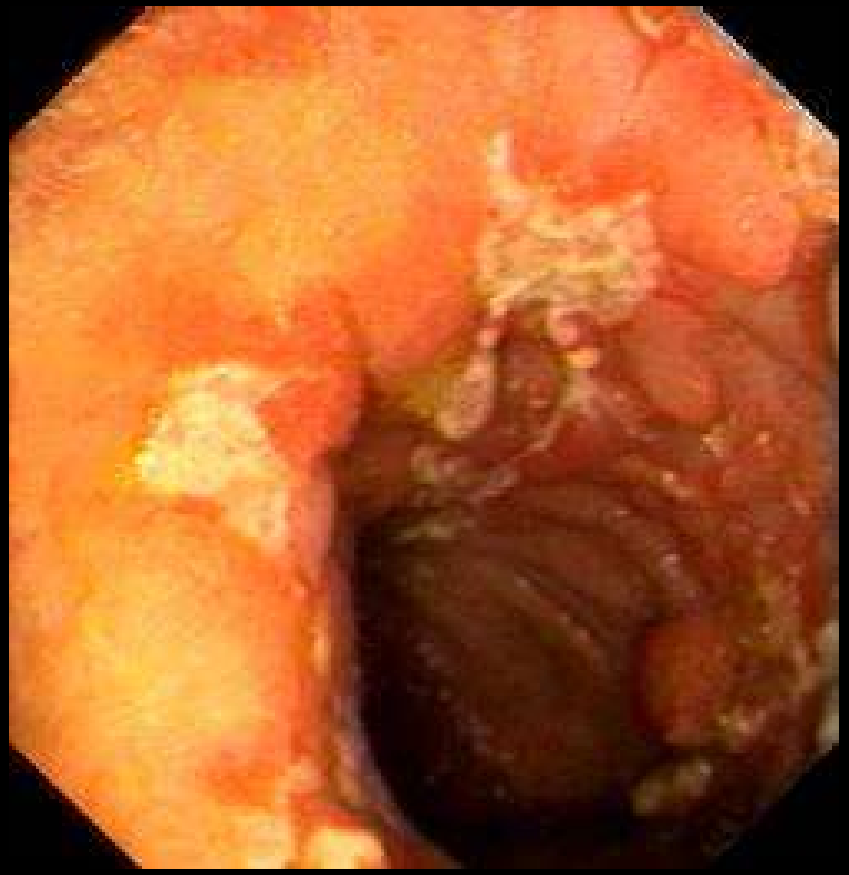
- Irritable bowel syndrome
- Ischemic bowel disease
- Ca
- TB of small bowel (3rd world countries)
- NSAID use
- Celiac Disease

Evaluation for Crohn's

- CBC
- CRP
- Endoscopy/colonoscopy
- CT
- MRI
- Enteroscopy
- Capsule







Capsule Questions:

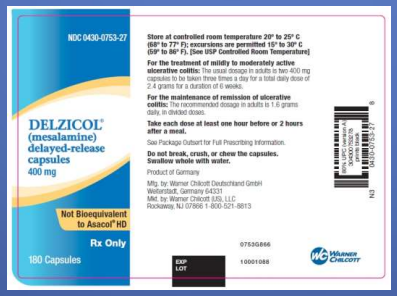
- When should we **not** do a capsule study?

Capsule Questions:

- When should we **not** do a capsule study?
- When we suspect a small bowel obstruction

Medications

- Are 5 ASAs very effective for Crohn's?
- What is the common practice?
- Are there clinical differences in brands?
- Does QD dosing really matter?
- What are important side effects of 5 ASAs?



Antibiotics

Old meds still effective

Are best for patients with active colonic and peri anal Crohn’s

Steroids

- Dose?
- Duration
- Tricks of the taper

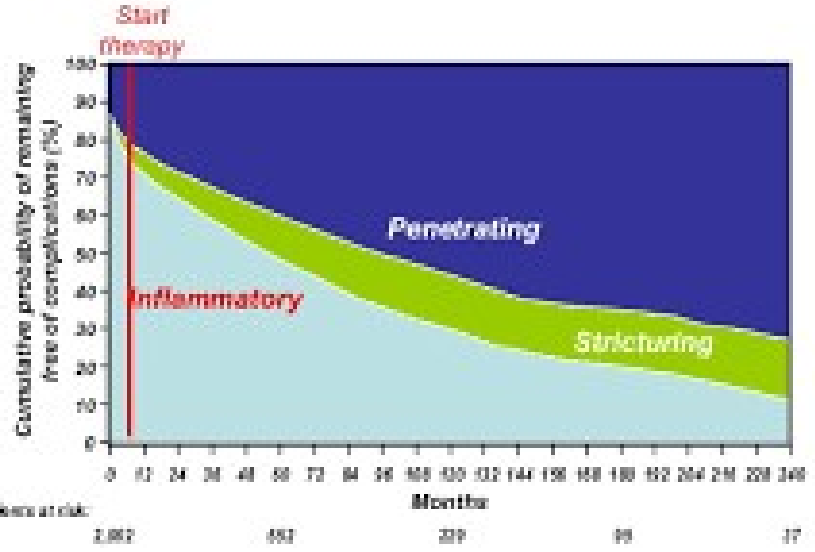
Is There Any Benefit to Giving More Than 60 mg of Prednisone to an IBD Pt?

Risks of Steroids (in Crohn's)

- Failure to achieve mucosal healing
- The above allows for stricture formation
- High relapse after withdrawal
- Steroid use and CV complications

- Wei, L et al
- Taking glucocorticoids by prescription is associated with subsequent cardiovascular disease
- Annals of Internal Medicine 2004;141; 764-70

Long-term evolution of Crohn's disease behaviour



Graham J. et al. Inflamm Bowel Dis. 2002;8:244-50

Use of Non Systemic Steroids in Crohn's

- Why use them?
- Effectiveness

Antimetabolites

(Azathioprine, 6 Mercaptopurine, Methotrexate)

- Controversies over dose
- TPMT (thiopurine methyl transferase)
- Risks/benefits
- How do we monitor antimetabolites over time?
- Lymphoma facts

Antimetabolites and Lymphoma

- Use of antimetabolites increases the risk of lymphoma by a factor of 4
- Lymphoma risk related to duration of antimetabolite
- Stopping antimetabolites reduces the risk to 0

Kandiel A et al
Increased risk of lymphoma among inflammatory bowel disease patients treated with azathioprine and 6 mercaptopurine
Gut 2004:54;1121

Anti TNFs: What We Know

- Indications
- Benefits
- Risks
- CHF
- Non melanoma skin cancer
- Infections
- TB (let's talk about Quantiferon/CXR)
- Fungal Infections
- Hepatitis B and C

Anti TNF **Limitations** in Crohn's

- With current anti TNF medications

70% respond
30% do not respond (primary non response)

50% of patients lose response over 1 year
(secondary non response)

Siegel CA
What options do we have for the induction therapy for Crohn's Disease
Dig Dis 2010:28;543

Preventive Care in IBD

- IBD patients do not receive adequate preventive services
- Issue: Who is in charge?
  GI or Primary Care
- Needs
  Vaccination
  Screening for osteoporosis
  Cancer screening
  Screening for depression
  Smoking cessation

Vaccination Recommendations in IBD

- Hepatitis A/B
- Pneumococcus
- Influenza
- Tdap (tetanus, diphtheria, acellular pertussis)

Reich J et al
Vaccinating patients with inflammatory bowel disease
Gastroenterology and Hepatology 2016:12;540

Vaccination: special circumstances

- Human papilloma virus (age 9 – 26)
- Zoster (after age 50) especially prior to Tofacitinib
- Meningococcus (at risk pts)

Reich J et al
Vaccinating patients with inflammatory bowel disease
Gastroenterology and Hepatology 2016:12;540

Anti TNF questions

Would you recommend an anti TNF to a tb pt treated for a month?

Would you use an anti TNF in a patient with a remote hx of breast Ca?

Your elderly pt on an anti TNF is bringing in their grandchild for an MMR. Is there any concern?

More anti TNF Questions

- Why do anti TNFs lose effectiveness?
- How do we prevent this?
- When should we switch anti TNFs?

Even More Questions

- Can anti TNFs be given intermittently?
- What is Hepato Splenic T cell lymphoma?
- How can we minimize it?
- Can/should we ever stop anti TNFs?

Poor prognostic features in Crohn's

- Admission with intestinal obstruction
- Severe peri anal/fistulizing disease
- Age below 40
- Need for steroids
- Extensive disease

Poor Prognostic Features in Ulcerative Colitis

- Young age
- Non smoker
- Anemia
- Extensive disease

Case 1

- John R is a 56 year old lawyer with a 40 year hx of Crohn's disease. 10 years ago he had an ileo rt colectomy. Despite recent therapy, he has recently had an additional segment of ileum removed and now feels well. Pathology shows a clean margin
- What should we do?

1. Wait and see
2. Colonoscopy
3. Meds
4. Send him far away

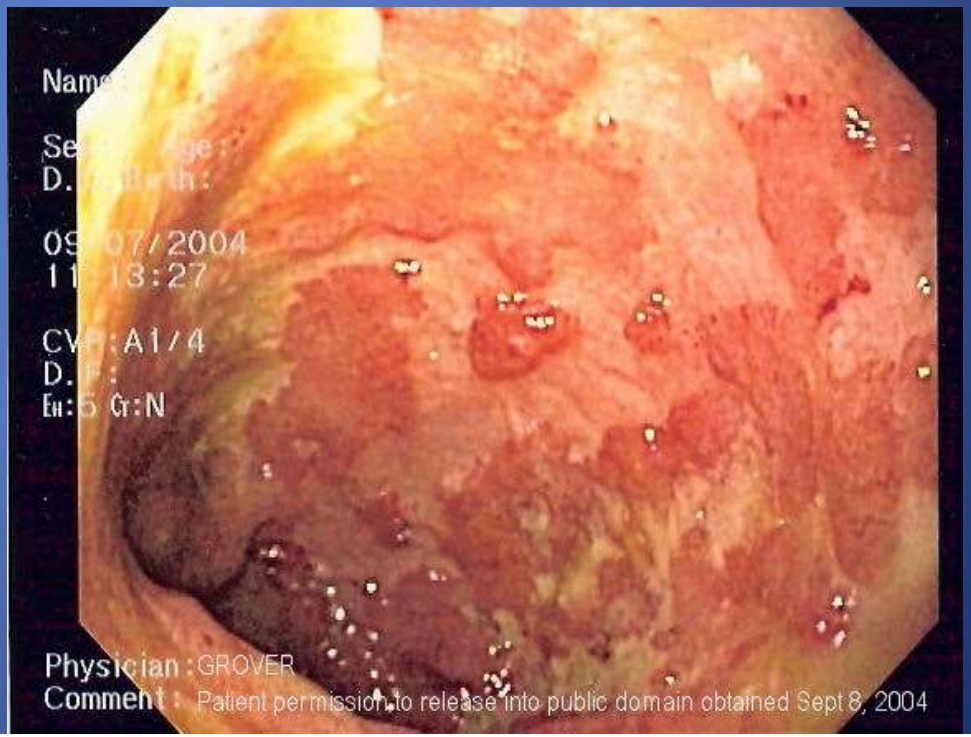
What are the risk factors for recurrence after Crohn's surgery?

- High Risk Factors:
  - Smokers
  - Penetrating Disease
  - Previous surgeries

Lichtenstein GR et al
ACG Clinical Guideline: Management of Crohn's Disease in Adults
Am J Gastroenterol 2018:113;481

Ulcerative Colitis

- Clinical Features
- Differential dx
- Testing



In Ulcerative Colitis, symptom severity tends to correlate with disease severity:

True

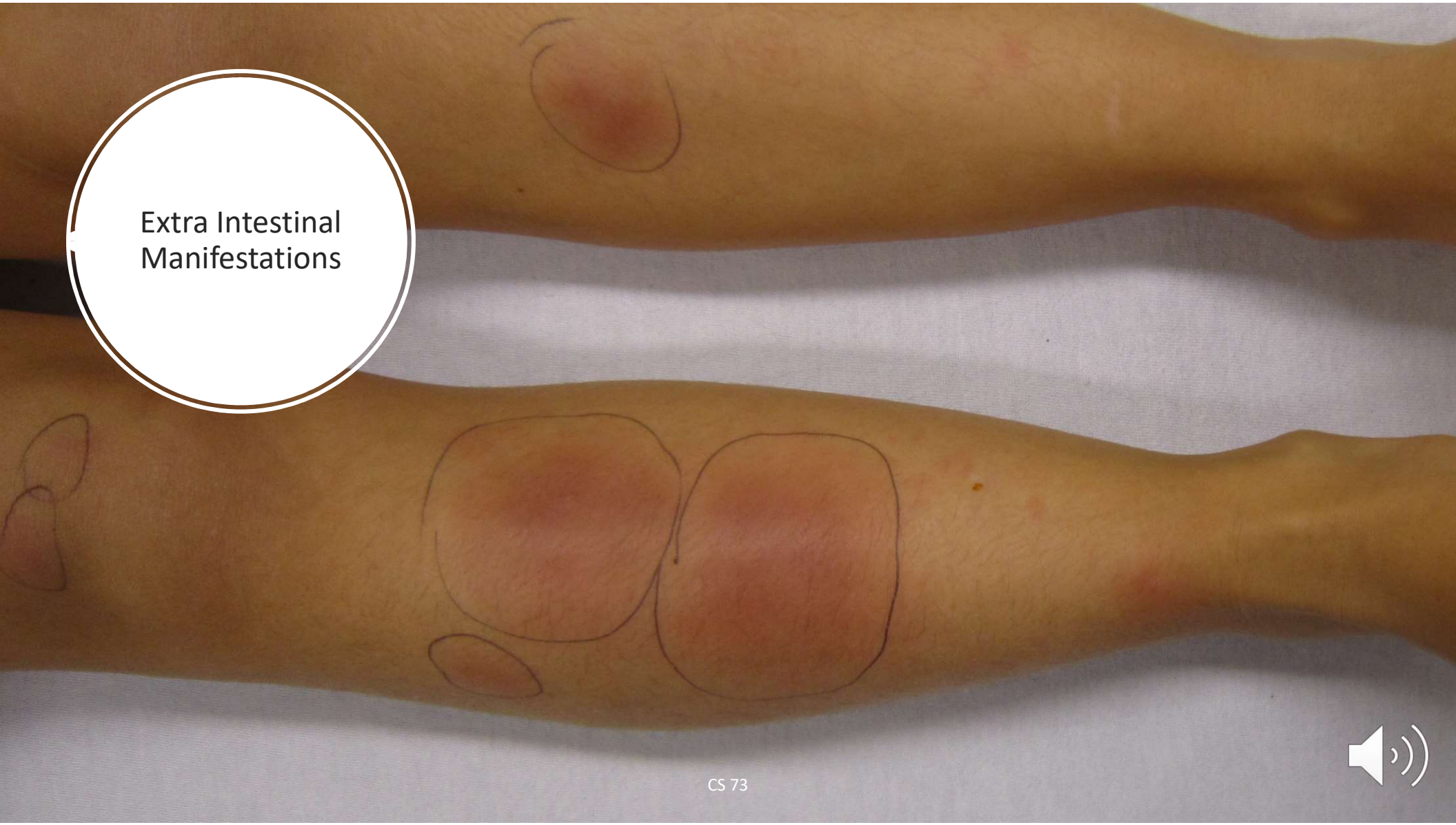
False

Ulcerative Colitis Therapies

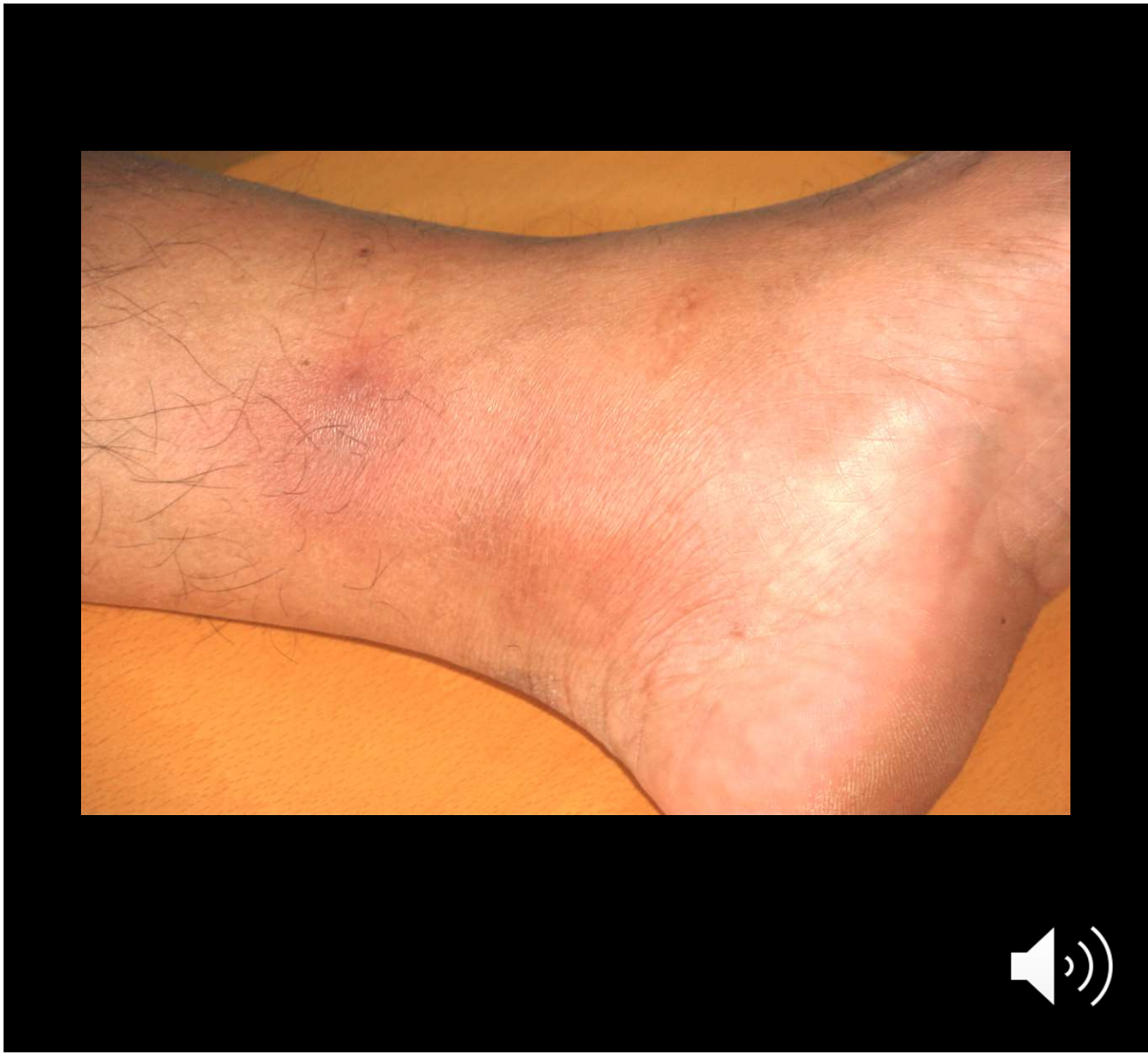
- 5 ASA
- Mesalamine suppositories
- Steroid enemas
- Budesonide MMX
- Oral steroids
- Antimetabolites
- Anti TNFs
- Vedolizumab (Monoclonal Ab)
- Ustekinumab
- Tofacitinib (JAK inhibitor)

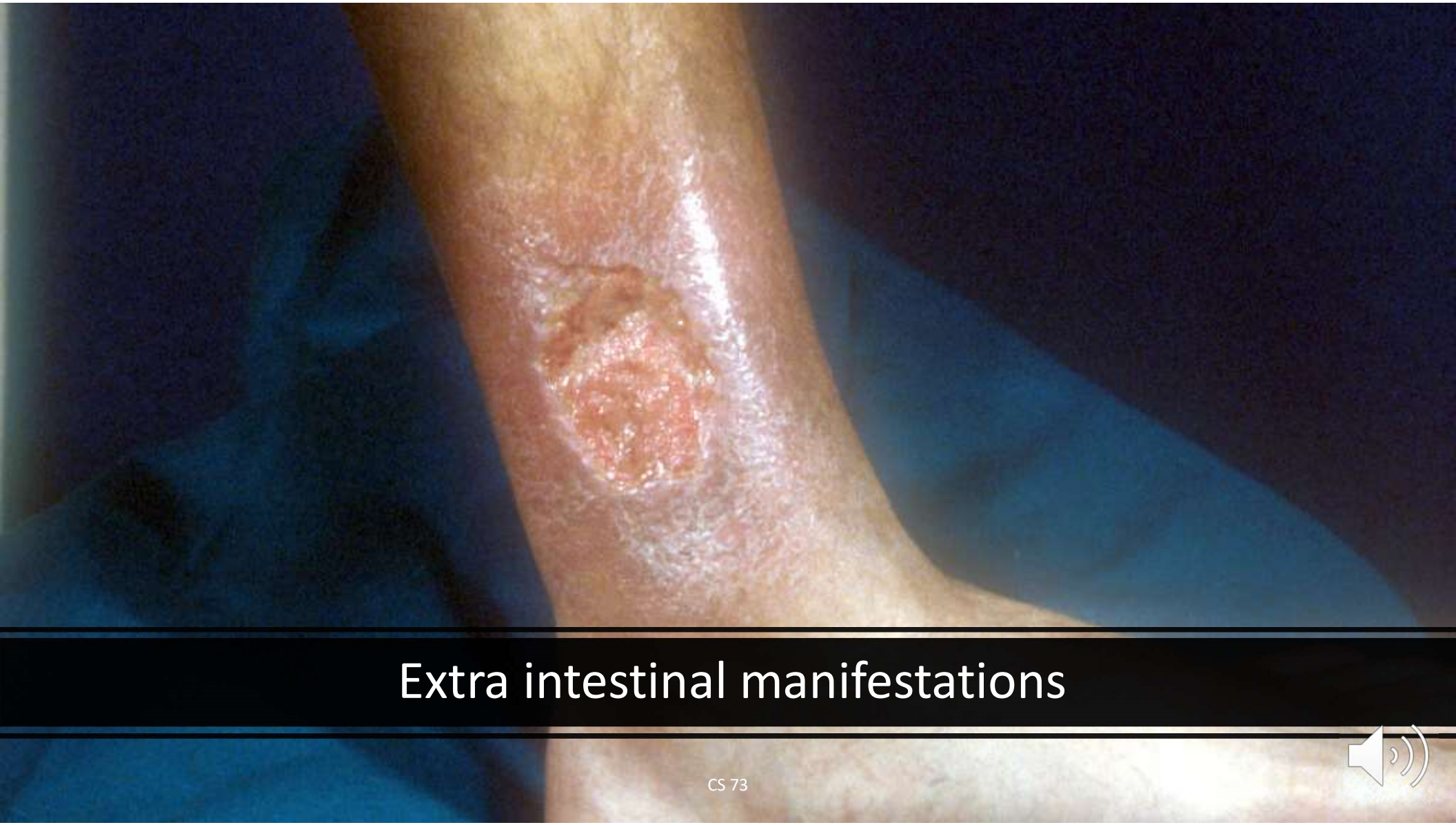
Extra Intestinal Manifestations May Precede Intestinal Disease in Inflammatory Bowel Disease

- Arthritis
- Hypercoagulable state
- Osteoporosis
- Anxiety/depression
- Gallstones (in Crohn's)
- Kidney stones

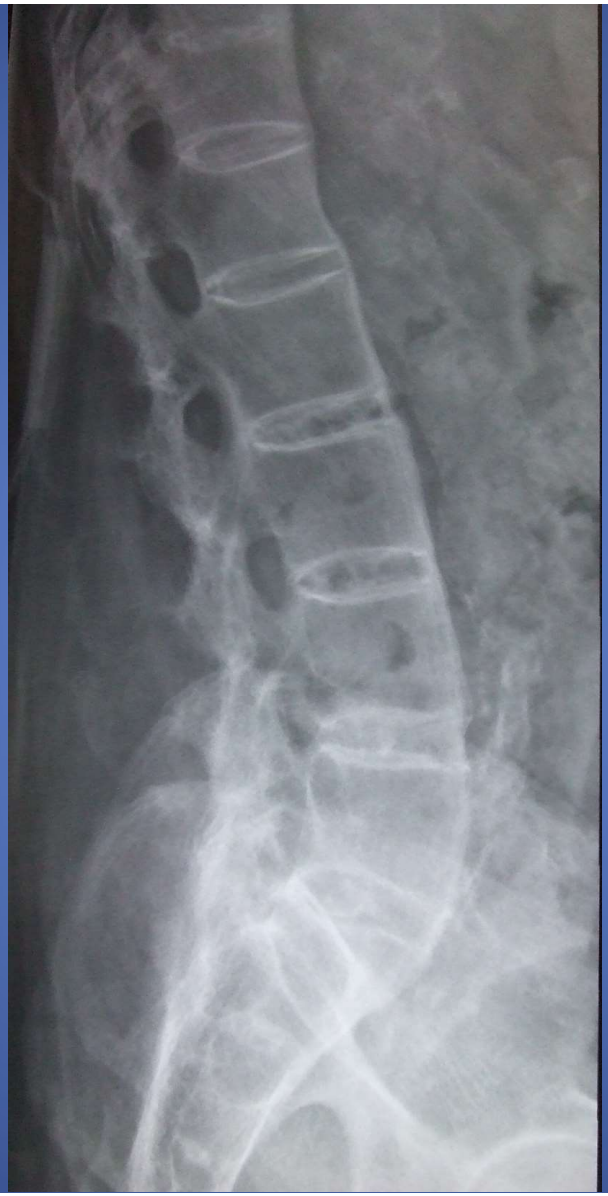

Extra Intestinal
Manifestations

Extra intestinal manifestations





Extra intestinal manifestations



Case 2: Jeff

- Is a 37 year old patient who has had Ulcerative Colitis for 20 years. Despite having been on maximum doses of Imuran and Adalimumab, he still has 6 bloody bowel movements a day

Jeff

- PE unremarkable

- Labs: WBC 12,200 shift to L
- H/H 11/33.1
- MCV 22
- CRP 7 mg/dl
- colonoscopy: moderate pan colitis

Why may the symptoms be continuing?

(more than 1 answer is possible)

1. Cl diff
2. NSAID use
3. Compliance
4. Worsening of the Ulcerative Colitis

Newer concepts in IBD

- Mucosal healing rather than symptom based
- Deep remission:
  - Clinical & Endoscopic Remission
- Does treatment for ulcerative colitis prevent colon cancer?
- When withdrawing meds, we don't want to wait until symptoms appear

Vedolizumab (Entyvio) A Monoclonal Antibody

- Indicated for moderate to severe Ulcerative Colitis and Crohn's

Vedolizumab Safety Info

- Infusion Rx (there is an Ab)
- .7% chance for serious infections

- NO LYMPHOMAS to date
- Non Melanoma Skin Cancer reported

Ustekinumab (Stelara)

- Indicated for Crohn's and U.C.
- Potential for infections
- No lymphomas reported to date

Feagan B et al
Ustekinumab as induction and maintenance therapy for Crohn's disease
NEJM 2016:375;1946

Tofacitinib (Xeljanz) a JAK inhibitor

- Indicated for treatment of moderate to severe Ulcerative Colitis, not Crohn's
- Safety factors: infections
  lymphoma
  malignancies
- FDA Warning: only to be used after anti TNF failure

Feuerstein JD et al
AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis
Gastroenterology 2020:158;1450

Tofacitinib WARNING

- Black Box Warning
- 10 mg twice a day dose
- Increased risk of pulmonary emboli and death

Tectonic Changes With Biosimilars

Costs of biologics have been burdensome

The manufacture process of biologics has changed since approval, promoting the concept that these “ORIGINALS” may indeed already be BIOSIMILARS

What is the “best” medicine for an individual with IBD

- May be governed by third party players!

IBD and COVID-19

- Having IBD does not increase the risk of getting COVID-19
- Steroids are the only single agent that has been associated with increased poor outcome with COVID-19

D'Amico F et al
Inflammatory Bowel Disease Management During the COVID 19 Outbreak: A Survey from the European Crohn's and Colitis Organization
Gastroenterology 2020:159;14

Joint Society Recommendations (AASLD, ACG,AGA,ASGE

- Patients on immunosuppressive drugs for IBD should continue taking their medications in the absence of COVID-19 symptoms
- The risk of flares outweighs the chance of contracting COVID-19
- Reduce dose or stop steroids if possible

Rubin DT et al
AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic: Expert Opinion
Gastroenterology 2020:159;350

IBD with suspected or known COVID-19

- Individualized therapy
- Weigh risks/benefits of medications

IBD Medication Use With COVID-19 Infection

Safe

- Budesonide
- 5 ASAs
- Antibiotics

Need Adjustment*

- Steroids
- Immunomodulators:
  - Azathioprine
  - 6 Mercaptopurine
  - Methotrexate
- Biologics:
  - anti TNFs
  - Ustekinumab
  - Vedolizumab
- Tofacitinib

Additional IBD COVID-19 References

- Crohn's and Colitis Foundation COVID-19 Resource
  https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwiK58zVmc7uAhXpEVkFHVD6Bm8QFjABegQICRAC&url=https%3A%2F%2Fwww.crohnscolitisfoundation.org%2Fcoronavirus%2Fprofessional-resources&usg=AOvVaw1fPldX_inAHO0t_lDrSxLT

- Secure IBD https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwir0NCsgtHuAhUqm-AKHVE4BKAQFjAAegQIAhAD&url=https%3A%2F%2Fcovidibd.org%2F&usg=AOvVaw3zKJfBn-OrKbyQmt5PW42f

- AGA Decision Tool - Algorithm
  https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&cad=rja&uact=8&ved=2ahUKEwj1ofy6g9HuAhVwQt8KHU-HCzwQFjAAegQIBxAC&url=https%3A%2F%2Fwww.gastrojournal.org%2Farticle%2FS0016-5085(20)30482-0%2Ffulltext&usg=AOvVaw3loLEEOr23IsszgWVZwQGi

Summary

- Irritable Bowel Syndrome can be distinguished from Inflammatory Bowel Disease by lack of alarm symptoms
- Ulcerative Colitis is “curable” Crohn’s Disease is “treatable”
- Smoking is a significant independent risk factor in IBD
- Make sure your IBD patients receive appropriate vaccinations
- Delay of diagnosis in IBD is directly related to a worse prognosis


Thank you!
Peter Buch, MD ctgied@gmail.com