

# Inflammatory Bowel Disease: What You Need to Know

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## Disclosure:

- 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

## Crohn's Disease may be distinguished from Ulcerative Colitis by:

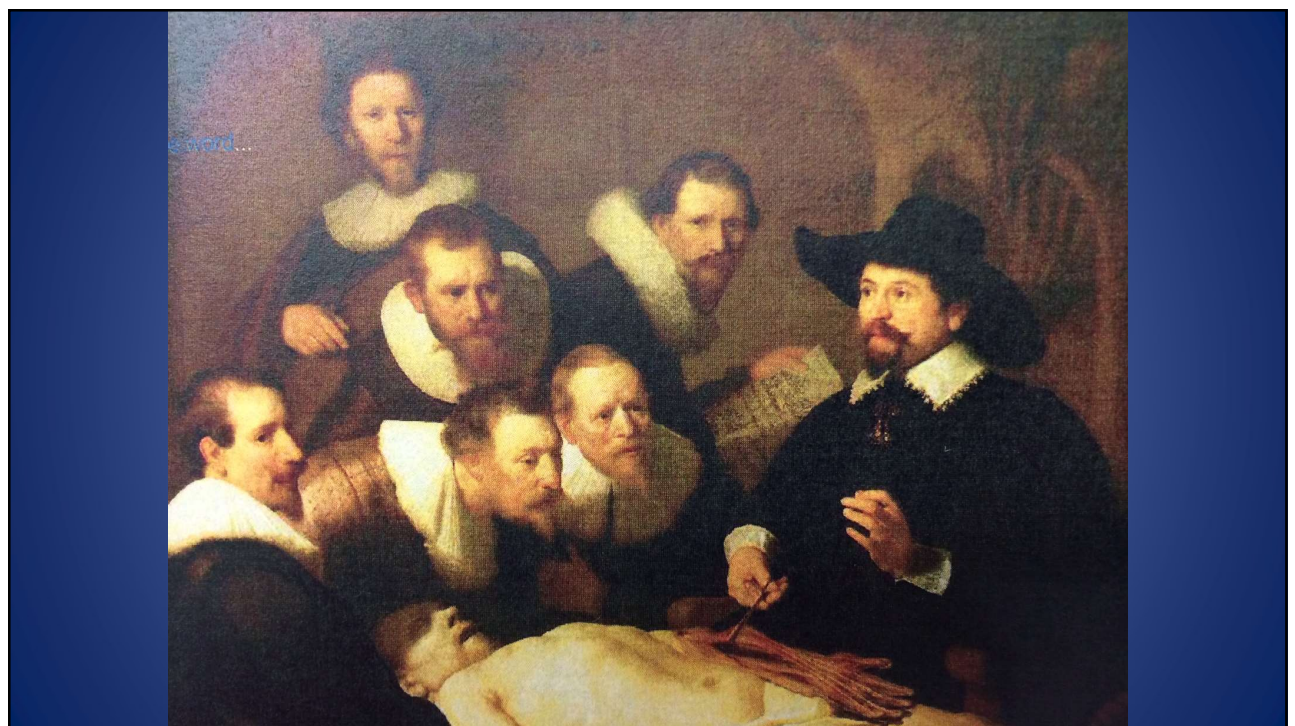
1. Extra intestinal manifestations
2. Rectal bleeding
3. The fact that Crohn's may involve the entire GI track while Ulcerative Colitis is confined to the colon
4. There is always more abdominal pain with Ulcerative Colitis

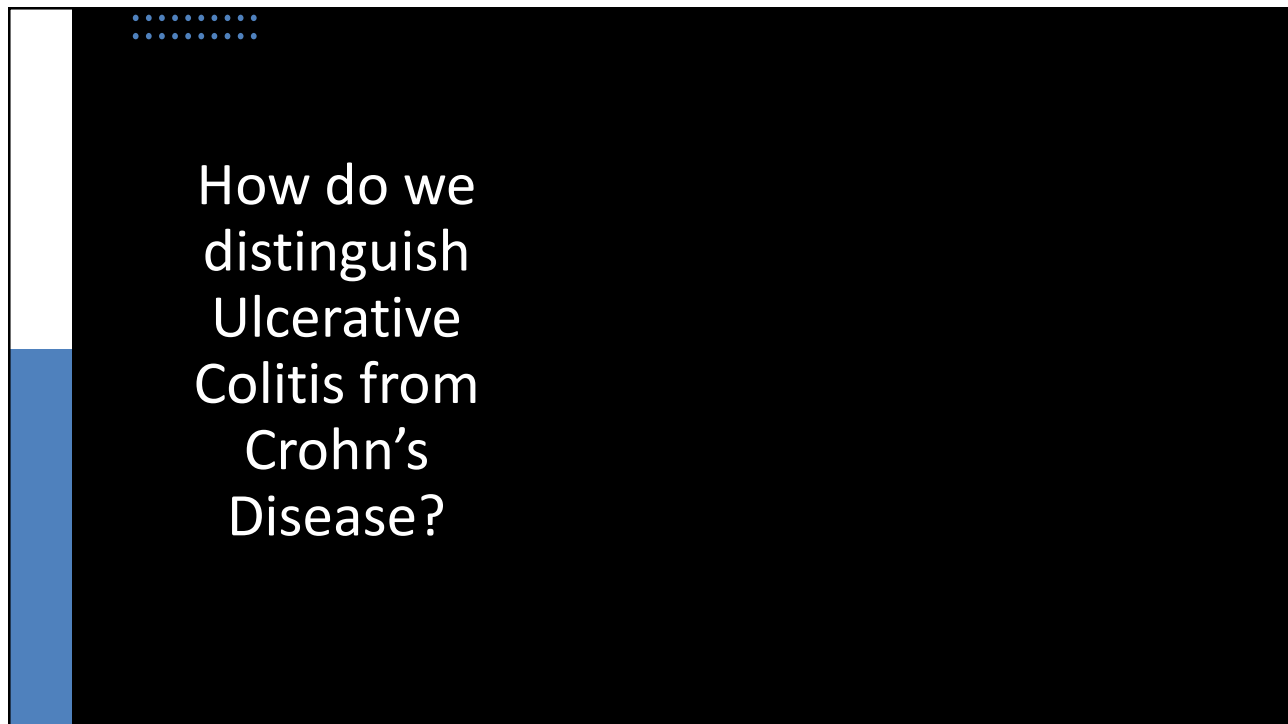
The advantage of non systemic  
steroids (Budesonide) in Inflammatory  
Bowel Disease is:

1. They are more effective
2. They have fewer side effects
3. They are much easier to taper
4. They can safely be used long term

When considering the use of anti TNFs like Adalimumab or Infliximab in the treatment of Inflammatory Bowel Disease, which of the following is true?

1. All anti TNFs have the potential to cause infections and lymphomas
2. Adalimumab (Humira) is equally effective with Infliximab (Remicade) in double blinded controlled studies
3. There is no concern for cancer reactivation
4. Anti TNFs will remain effective for 20 years or more in the majority of IBD patients





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



	Ulcerative Colitis	Crohn's Disease
Area of Involvement	Rectum +/- colon	Mouth to anus
Type of lesion	Continuous	Skip
Blood in stool	Yes	Occasional
Abd Pain	Yes	Occasional
Abd mass	Rarely	Yes
Systemic Symptoms	Occasional	Frequently

Between  
Crohn's  
Disease  
and  
Ulcerative  
Colitis

Which is  
curable?

Which is  
treatable?

Can Inflammatory Bowel Disease  
and Irritable Bowel Syndrome  
Co Exist?

Describe how  
these are  
related to  
Inflammatory  
Bowel  
Disease:

Food


Stress

Family History

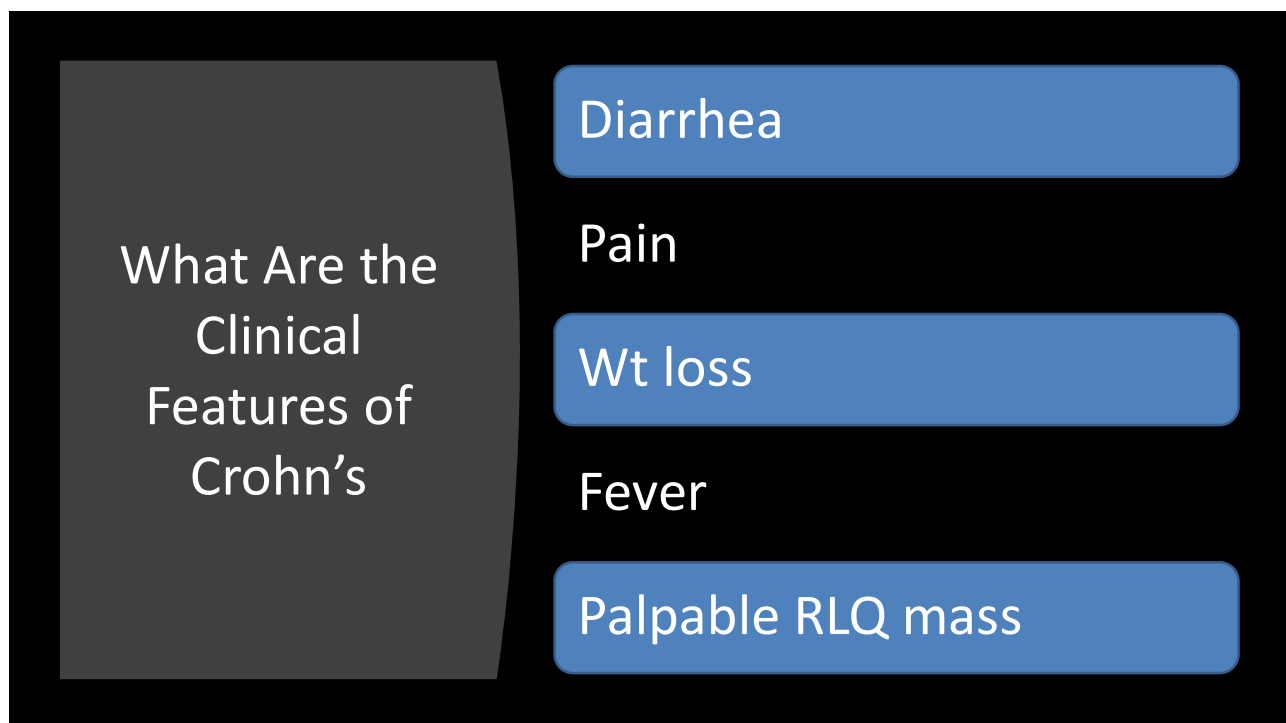
Describe  
the  
relationship  
of smoking  
to:

Crohn's

Ulcerative  
Colitis



What Are the Clinical Features of Crohn's







## Ddf

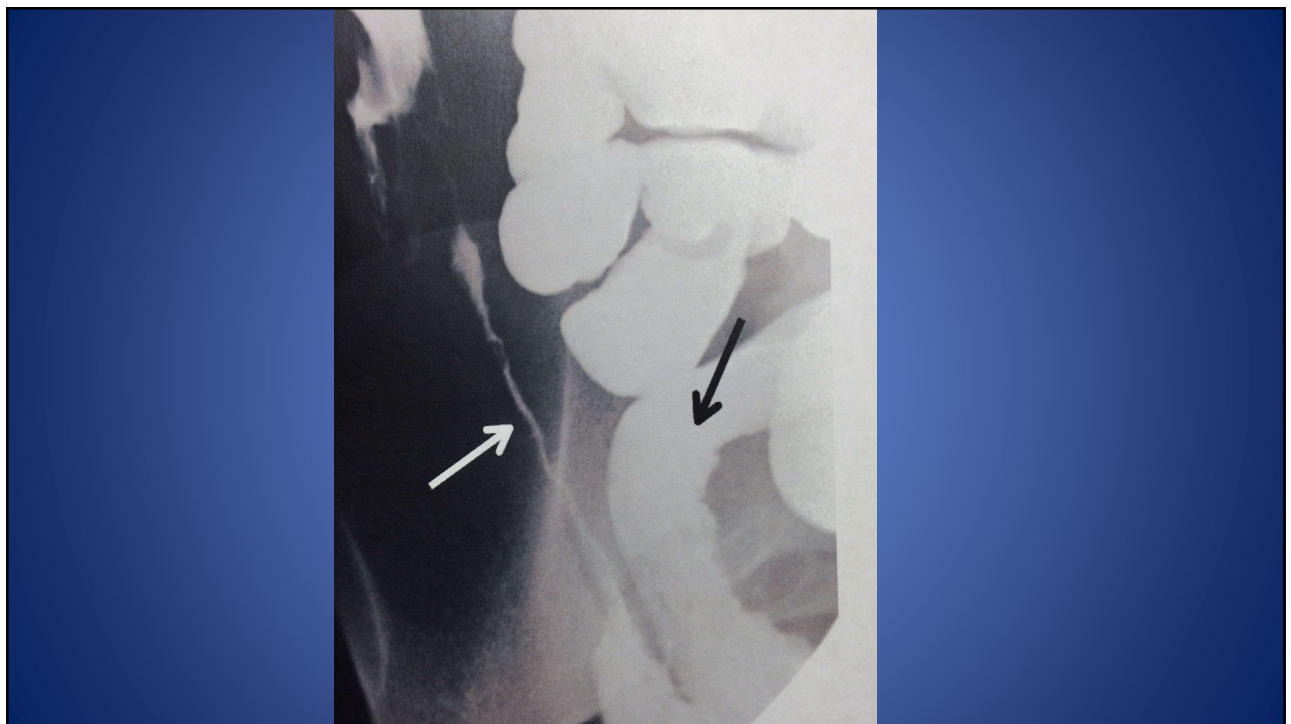
- Irritable bowel syndrome
- Ischemic bowel disease
- Ca
- NSAID use
- Celiac Disease
- Infectious colitis
- Ulcerative Colitis
- Etc

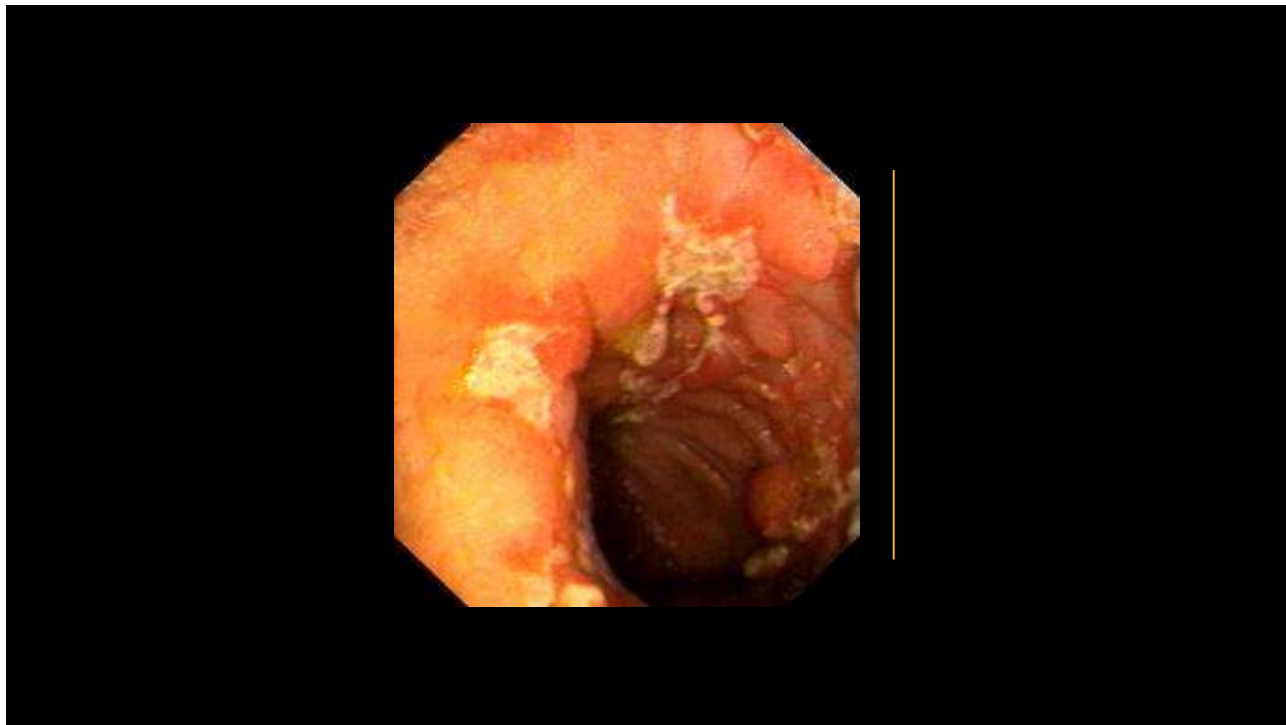


## Evaluation for Crohn's

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





20

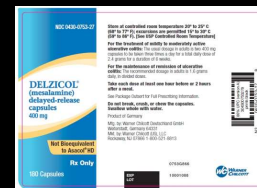
## Capsule Questions:

- What is the accuracy of a capsule study in making a Crohn's dx?
- When should we not do a capsule study?



## Medications

- What does the literature say about 5 ASA use in Crohn's?
- What is the common practice?
- Does QD dosing really matter?
- What are important side effects of 5 ASAs?



Antibiotics


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Old meds still effective

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

# Steroids



The image contains three icons arranged horizontally. The first icon is a red rounded square with a black silhouette of a pill bottle and a pill. The second icon is a green rounded square with a black stopwatch icon. The third icon is a purple rounded square with a black silhouette of two champagne glasses clinking.

DOSE?

DURATION

TRICKS OF THE TAPER



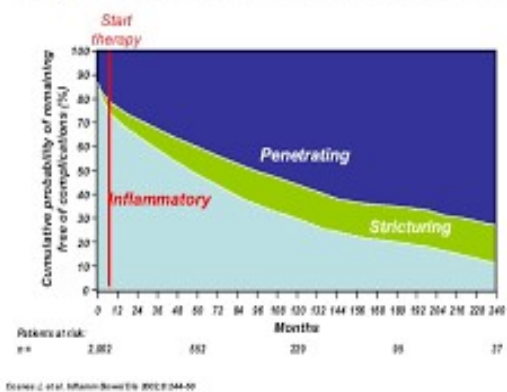
Is There Any Benefit to Giving More Than  
60 mg of Prednisone to an IBD Pt?

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## 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



## Use of Non Systemic Steroids (Budesonide) “Entocort” or “Uceris” in IBD



WHY USE THEM?



EFFECTIVENESS



TAPER??

Antimetabolites  
such as Azathioprine (Imuran)  
6 Mercaptopurine (Purinthol)  
Methotrexate (various names)



Controversies over dose



TPMT



How do we monitor antimetabolites over time?

## Antimetabolites and Lymphoma

- Use of antimetabolites increases the risk of lymphoma by a factor of 4
- Stopping antimetabolites reduces lymphoma 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
  - Lymphoma
  - 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
- 50% of patients lose response in 1 year

Gisbert J and Panes J  
Loss of response and requirement of infliximab dose intensification in Crohn's Disease: a review  
Am J Gastroenterol 2009;104:760

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



## 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?
- Is there a benefit to using a combination of antimetabolites and anti TNFs?\*

\*Columbel JF et al  
Infliximab, Azathioprine or combination therapy for Crohn's Disease  
NEJM 2010;362:1383

## More anti TNF Questions

- Why do anti TNFs lose effectiveness?
- How do we prevent this?
- What is Hepato Splenic T cell lymphoma?
- Can/should we ever stop anti TNFs?\*

\*Torres J et al

Systematic review of effects of withdrawal of immunomodulators or biological agents from patients with Inflammatory Bowel Disease  
Gastroenterology 2015;149:1716

## Even More Questions

- Are there peri operative risks in using anti TNFs?
- Should we use anti TNFs in the post op Crohn's pt?\*

\*Yamamoto T et al

Impact of infliximab therapy after early endoscopic recurrence following ileo colonic resection of Crohn's Disease: a prospective study  
Inflamm Bowel Dis 2009;15:1460

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







## Ulcerative Colitis

- Clinical Features
- Differential dx
- Testing



CS 73



## How Would the Treatment Vary for:

- Pan colitis
- Proctitis



## Ulcerative Colitis Therapies

- 5 ASA
- Mesalamine suppositories
- Steroid enemas
- Budesonide MMX
- Oral steroids
- Antimetabolites
- Anti TNFs
- Vedolizumab (Entyvio)
- Tofacitinib (Xeljanz)

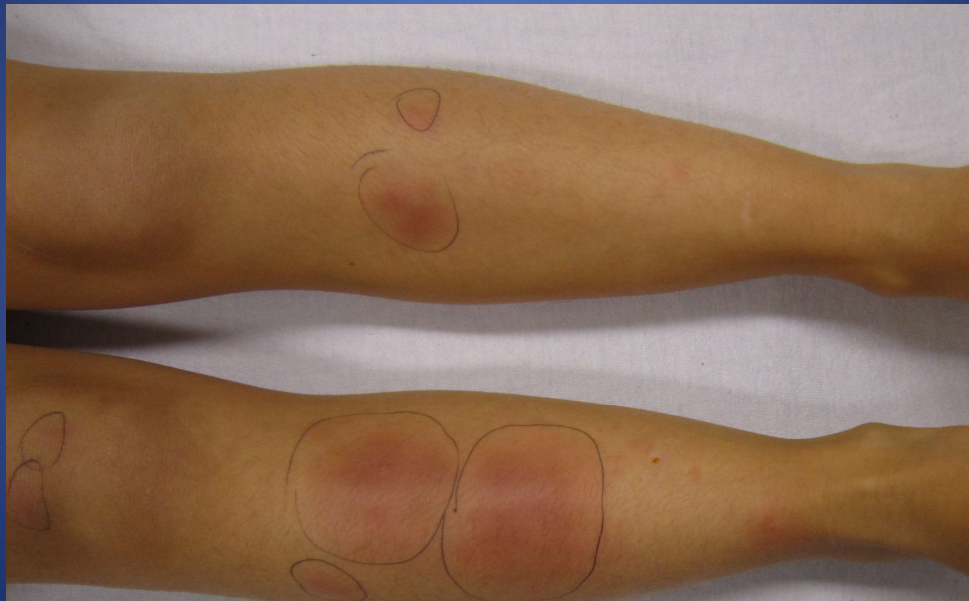


Can Extra Intestinal Manifestations  
Precede Bowel Symptoms in  
Inflammatory Bowel Disease?

## 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

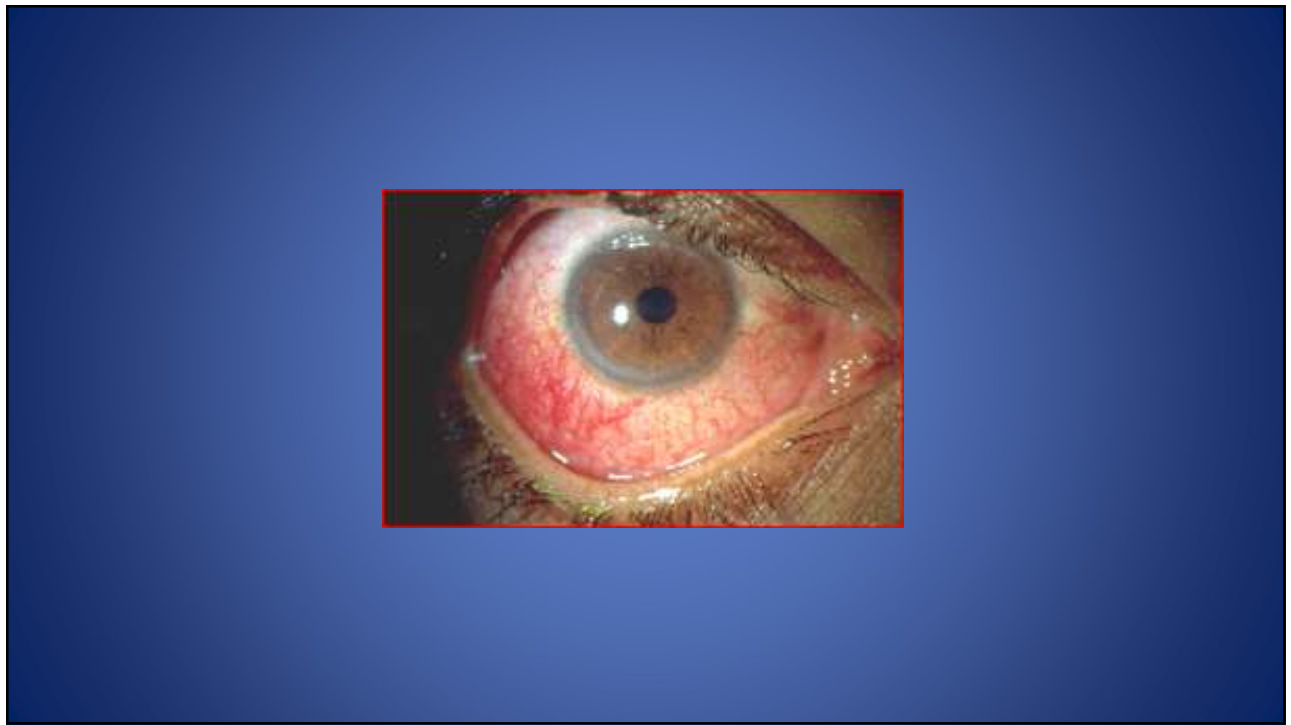


## Extra intestinal manifestations









## 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 might Jeff still be ill?

1. Use of NSAID meds
2. Poor compliance
3. CI difficile infection
4. All the above

What are  
the  
Limitations  
of anti  
TNFs?

Non responders

Loss of response

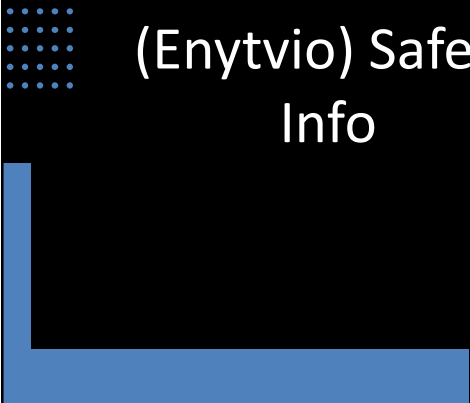
Infection

Lymphoma concerns



## Vedolizumab (Entyvio)

- Indicated for moderate to severe **Ulcerative Colitis** and **Crohn's** who have had an inadequate response with, lost response or were intolerant to TNF blocker or immunomodulators or inadequate response, were intolerant to or demonstrated dependence on steroids



## Vedolizumab (Enytvio) Safety Info


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

- **NO LYMPHOMAS TO DATE**
- Non Melanotic Skin Cancer reported





## Vedolizumab

- May be equally effective to anti TNFs with fewer side effects
- 

## Vedolizumab limitations in Crohn's

- Previous anti TNF exposure
  - Smoking
  - Perineal disease
  - Severe disease
- 
- All predictors of poor response

Dulai PS et al

The real world effectiveness and safety of vedolizumab for moderate-severe Crohn's Disease: results from the US Victory Consortium  
Am j Gastroenterol 2016;111;1147

# Ustekinumab (Stelara)

- Indicated for **Crohn's and U.C.**
- **NO LYMPHOMAS** reported to date
- Fewer infections than anti TNFs

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

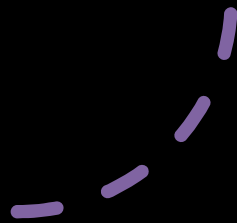
# Ustekinumab

2/3 of Crohn's Disease patients refractory to at least one anti TNF responded to Ustekinumab

Khorrani S et al  
Ustekinumab for the treatment of refractory Crohn's Disease; the Spanish experience in a large multicenter open-label cohort  
Inflamm Bowel dis 2016;22;1662



Tofacitinib  
(Xeljanz)

- ORAL MED
  - Indicated for the treatment of moderate to severe Ulcerative Colitis
  - Safety factors: infection  
lymphoma  
malignancy
- 



# Tofacitinib

- Anti TNF naive patients may respond better than anti TNF experienced

Sandborn WJ et al  
Efficacy and safety of oral tofacitinib as induction therapy in patients with moderate to severe ulcerative colitis: results from 2 phase 3 randomized controlled trials  
J Crohn's Colitis 2016;150:s157

## Tofacitinib Warning

- Black box warning
- 10mg bid dose
- Increased risk of pulmonary emboli and death

	U.C.	Crohn's
• Vedolizumab (Entyvio)	+	+
• Ustekinumab (Stelara)	+	+
• Tofacitinib (Xeljanz)	+	



## Tectonic Changes With Biosimilars

- Costs of biologics have been burdensome
- Will there be more immunogenicity when switching from the reference biologic to a biosimilar?

Cohen HP et al  
Switching reference medicines to biosimilars: a systematic literature review of clinical outcomes  
Drugs 2018;78;463



## What are some unanswered questions in IBD?

- Which is the “BEST” medicine for an individual?
- Which patients receiving anti TNFs should also be on anti metabolites?
- Under what conditions should meds be stopped if a patient is doing well?

## Surgery Questions

- If a patient has severe ulcerative colitis of the L colon, can that area be removed and a transverse colon-rectal anastomosis be created?
- In Ulcerative Colitis, when is it time to give up on meds and do a colectomy?

## Our Future

### PERSONALIZED MEDICINE

To choose the

correct **drug**

correct **dose**

correct **patient**

correct **route**

correct **time**

In order to optimize efficacy and minimize side effects in a cost effective manner

## References

Ko CW et al

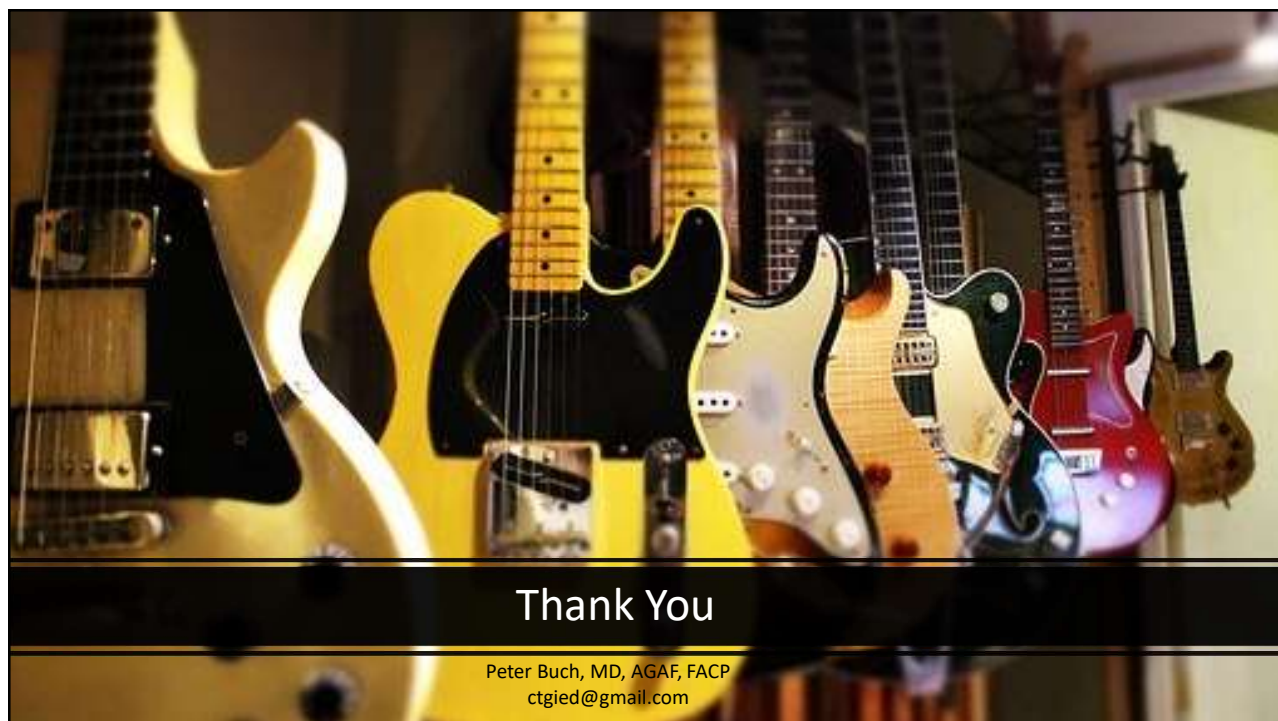
AGA clinical practice guidelines on the management of mild-to-moderate ulcerative colitis  
Gastroenterology 2019;156;748

Rubin DT et al

ACG clinical guideline: Ulcerative Colitis in adults  
Am J Gastroenterol 2019;114;384

Lichtenstein GR et al

ACG clinical guideline: management of Crohn's Disease in adults  
Am J Gastroenterol 2018;113;481



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