Inflammatory Bowel Disease: A Case Study

Winde Chambers, APRN, FNP
Practicum II- Spring 2011

Patient Profile

- This case study describes the care provided for a 21 year old white female who presented to the gastroenterology (GI) practice for management of Crohn's disease which was confirmed histologically from surgical intervention.

Reason for selecting case

- This case was chosen due to the significant impact Crohn's disease can make on a patient's quality of life and the diligent medical management required to maintain remission of this disease

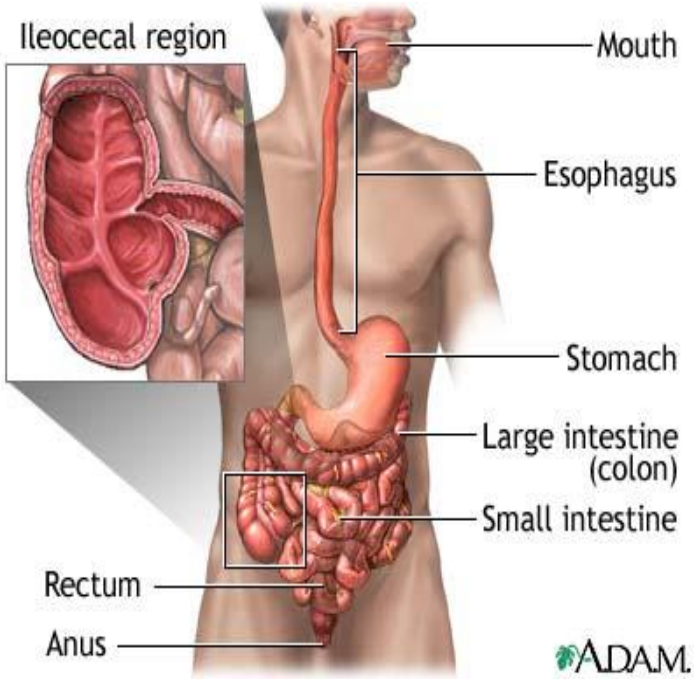
Clinical Site

- Private gastroenterology practice
- 9- Gastroenterologist, 3- NPs, 3-PAs
- Practice serves as a primary source for endoscopic services and specialty care for adults with gastrointestinal disorders located in a metropolitan area with a population of 350,471

(United States Census Bureau, 2011)

Crohn's Disease

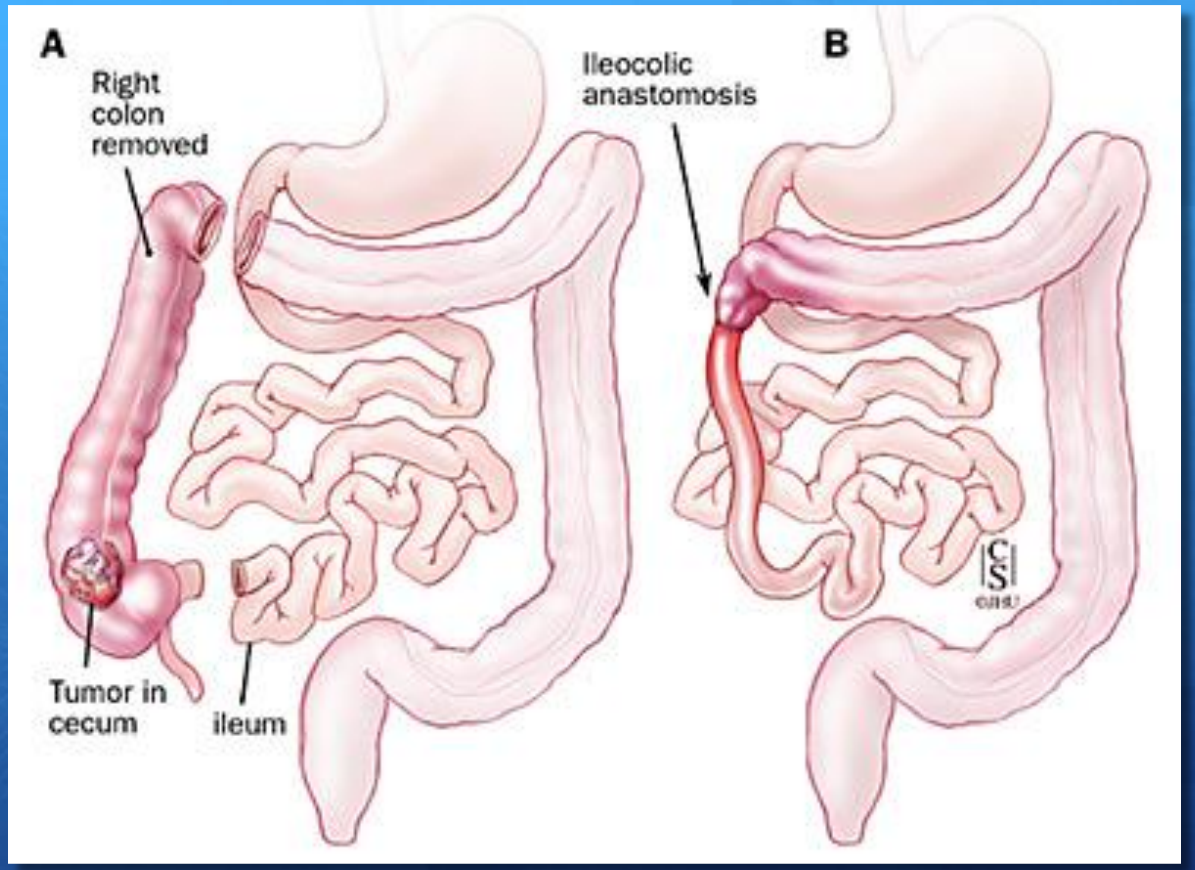
- *Transmural inflammation*
- *Skipped or cobblestone pattern*
- *Crohn's disease has an estimated annual incidence of 7 per 100,000 with a prevalence of 130 per 100,000*



(Bernstein et al., 2009)

Subjective Data

- CC: Recent diagnosis of Crohn's disease
- HPI: 21 year old white female who presented to the ER February with RLQ pain. CT scan showed lower abdominal mass felt to be ovarian mass. Laparoscopic exploration was performed and initially thought to have appendicitis. General surgeon was called to the OR and was found to have a large phlegmonous mass surrounding the cecum. She underwent right hemicolectomy with ileocolonic side to side anastomosis. She was also found to have a left ovarian cyst which was a hemorrhagic corpus luteum cyst.



Right hemicolectomy with ileocolonic anastamosis

Pathology report: diffuse active ileocolitis with transmural inflammation and stricture formation consistent with inflammatory bowel disease favoring Crohn's disease.

Subjective Data

- HPI cont..
  - Prior to admission, she had a chronic history of diarrhea with 5-6 loose stools daily since early teenage years. She denies any recent rectal bleeding or extraintestinal symptoms such as arthropathy, rashes, skin lesions, changes in vision or eye problems. She has regained 13 pounds of a 15 pounds weight loss.
- PMH: Recent diagnosis of Crohn's disease, otherwise negative
- PSH: Right hemicolectomy and resection of hemorrhagic corpus leteum cyst

Subjective Data

- FH: No family history of GI, hepatobiliary, pancreatic malignancy or disease. No history of IBD.
- SH: No history of alcohol, tobacco or drug use.

Subjective Data

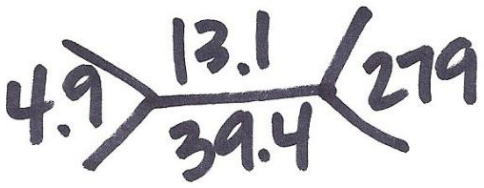
- Review of Systems
  - Constitutional: No fever, fatigue, night sweats, weight loss. Positive for weight gain.
  - HEENT: No vision changes, headaches, hearing loss.
  - Respiratory: Denies cough, wheezing or SOB.
  - Cardiovascular: No chest pain or palpitations.
  - Gastrointestinal: See HPI.
  - Genitourinary: No dysuria or hematuria.
  - Neuro/Psychiatric: No dizziness, no emotional disturbances.
  - Dermatologic: No unusual rashes or lesions.
  - Musculoskeletal: No joint pain or swelling; no weakness.
  - Hematology: No bruising or bleeding.

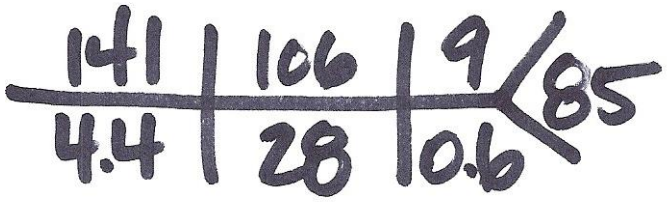
Objective Data

- Physical Exam
  - Vitals: BP 120/83, HR 76, Temp 98.0, Weight 131, BMI 23.9
  - Constitutional: No apparent distress, Well nourished and well developed.
  - HEENT: No nasal deformity, mucous membranes normal. Tongue and throat appear normal without mucosal lesions.
  - Respiratory: Symmetric chest, Lungs clear to auscultation.
  - Cardiovascular: Regular rate and rhythm without murmur.
  - Abdomen: Soft, non-tender, non-distended without masses or organomegaly. Bowel sounds present.
  - Integumentary: No rashes or lesions.
  - Rectal exam: Perianal exam normal. No masses palpated.

Objective Data

- Laboratory Data





ALP 53
ALT 24
AST 26
TBIL 0.23

CRP <0.29

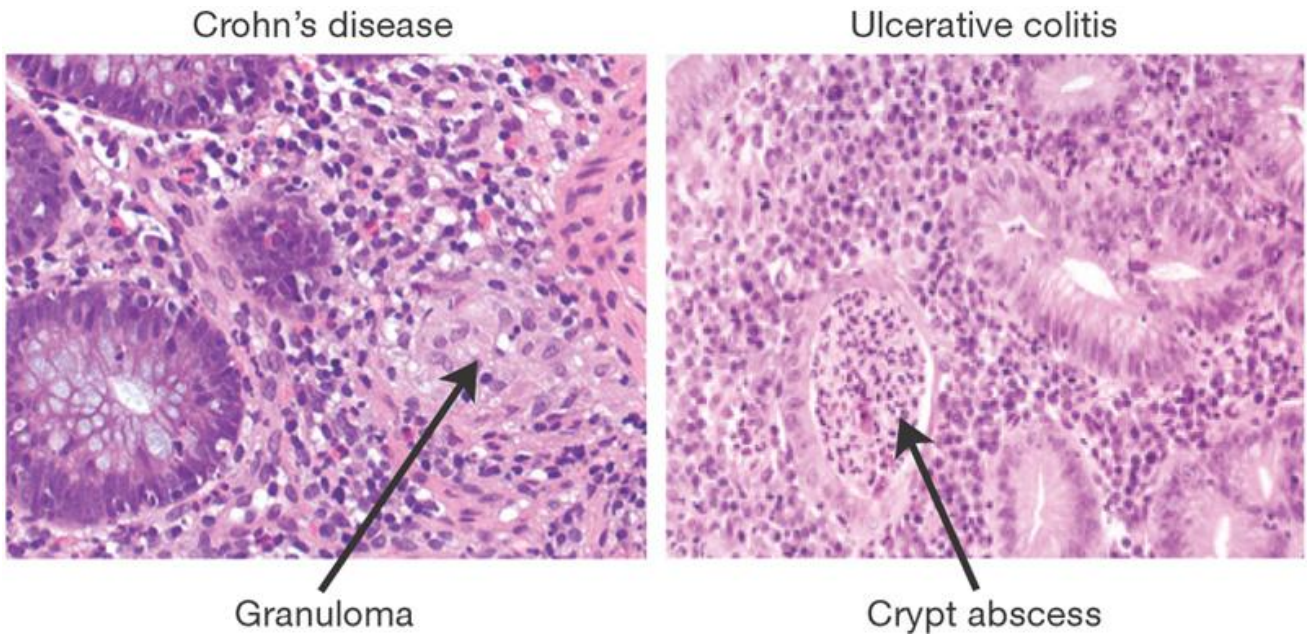
Objective Data

- Diagnostic Test
  - Colonoscopy- to terminal ileum
    - Evidence of Crohn's disease with ileitis and stricture of the distal ileum. Findings were described as diffuse moderate inflammation characterized by congestion, erosions, erythema, granularity and confluent ulcerations in the distal ileum. There was notation of a patent end-to-side ileocolonic anastomosis

Endoscopic evaluation allows for assessment of disease location and further pathological evaluation. In addition, evaluation of the surgical anastomoses allows for prediction of clinical relapse and response to therapy (Lichtenstein, Hanauer & Sandborn, 2009).

Objective Data

- Pathology- sections reveal moderately acute and chronic inflammation with eosinophils, early granuloma formation and mucosal erosion.



Assessment

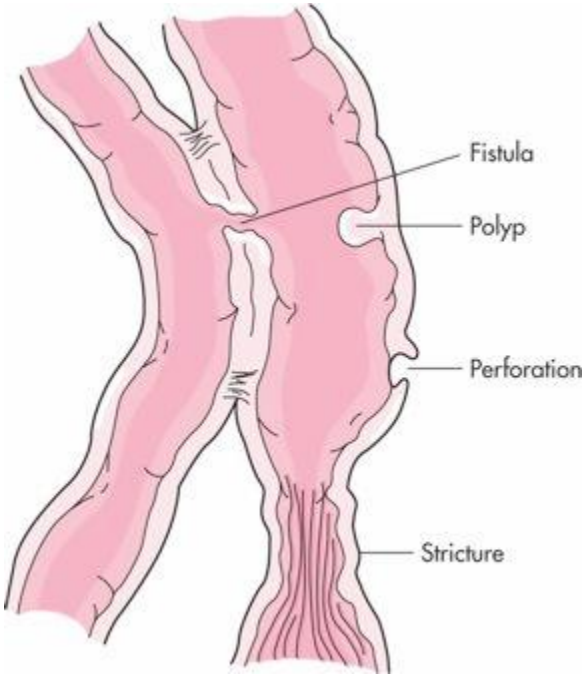
- Crohn's disease status post right hemicolectomy secondary to phlegmonous cecal mass
- Differential diagnosis:
  - Ulcerative colitis
  - Lymphomas of the bowel
  - Tuberculosis of the bowel
  - Chronic *Yersinia* infection

(Floch et al., 2005)

Crohns's vs. Ulcerative colitis

Characteristic	Ulcerative Colitis	Crohn's Disease
Usual area affected	Left colon, rectum	Distal ileum, right colon
		Can occur anywhere in gastrointestinal tract
Extent of involvement	Diffuse areas, contiguous	Segmental areas, noncontiguous
Inflammation	Mostly mucosal	Transmural
Mucosal appearance	Shallow mucosal ulcerations, edematous, superficial bleeding	Cobblestone effect, granulomas
		Thickened walls, narrowed lumen
Complications	Loss of absorption and elasticity	Fistulas
	Replacement of mucosa by scar tissue	Perianal disease
		Strictures
	Development of pseudopolyps that may become malignant	Abscesses
	Toxic megacolon	Perforation
	Hemorrhoids	Anemia
	Bleeding	Malabsorption of fat and fat-soluble vitamins

Complications- Crohn's



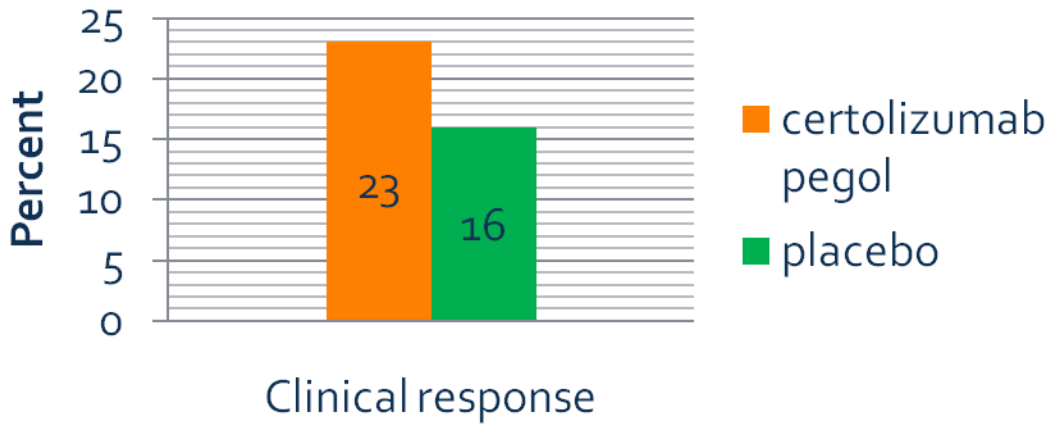
Plan- Pharmacological

- Start certolizumab pegol 400 mg SQ at week 0, 2, 4 then 400 mg SQ every 4 weeks

GOAL- MUCOSAL HEALING

Evidence based practice

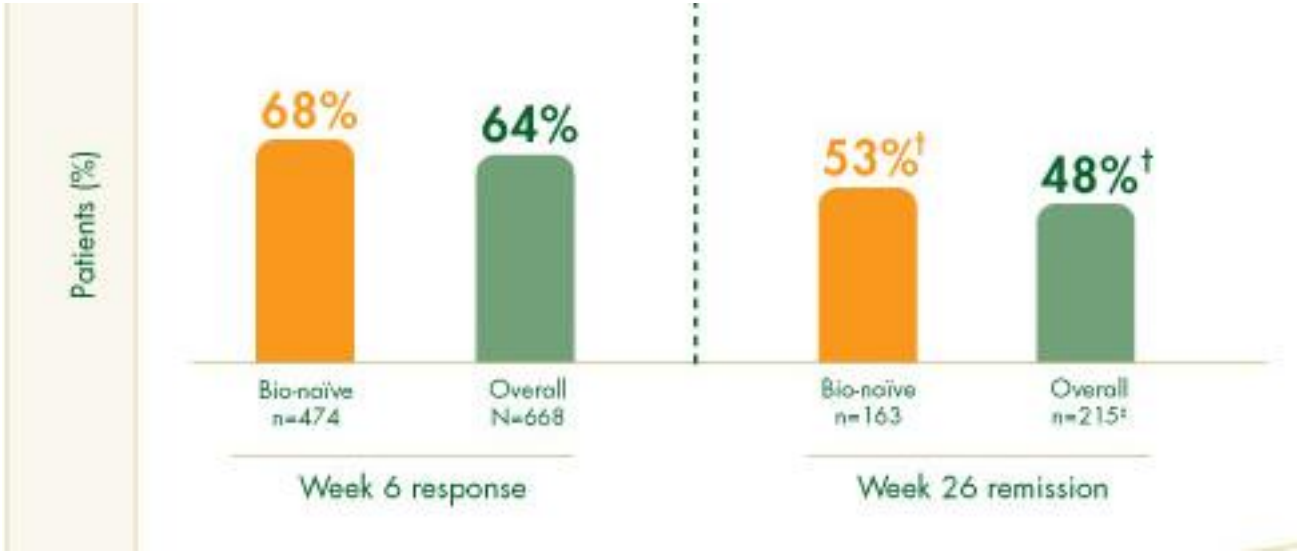
- PRECISE 1 TRIAL
  - *Randomized double-blind, placebo-controlled trial evaluating the efficacy of certolizumab pegol in severe Crohn's disease*
  - *Inclusion- Active Crohn's disease for at least three months with a CDAI greater than 450*
  - *331 patients-certolizumab pegol 329 patients- placebo*
  - AT 26 weeks-



(Sandborn, 2007)

Evidence based practice

- PRECISE 2 TRIAL



(Schreiber, 2007)

Evidence based practice

- *Rutgeerts, Schreiber, Feagan, Keininger, O'Neil, and Fedorak (2008) conducted a randomized double blind placebo controlled trial that **assessed health related quality of life** in patients that received certolizumab pegol for the treatment of moderate to severe Crohn's disease*
- *A health care quality of life questionnaire was administered at baseline and every 2 weeks which assessed bowel and systemic systems, emotional and social function*
- *The researchers found…patients that received certolizumab pegol had improvement overtime…patients that received 400 mg every 4 weeks had a statistically significant improvement in health related quality of life*

Other therapies available

- Anti-TNF agents
  - Infliximab
  - Adalimumab
  - Certolizumab pegol
- Immunomodulators
  - Azathioprine
  - 6-mercaptopurine
  - Methotrexate
- Corticosteroids
- Aminosalicylates (5-aminosalicylates (ASA))
  - Mesalamine

(AGA, 2006; Floch et al., 2005)

Plan- Labs

- Hepatitis panel - negative
- PPD - negative

With Anti-TNF α agents, there is an increased risk of reactivation of latent tuberculosis as well as hepatitis B (Bernstein, et al., 2009).

Test Results

Assay Name	Result	Reference Range
PROMETHEUS TPMT Genetics	TPMT*1/TPMT*1	TPMT*1/TPMT*1

Alleles present are associated with NORMAL ENZYME ACTIVITY.

Report Reviewed by the Laboratory Medical Director.

PROMETHEUS TPMT Genetics is an analysis to determine an ability to produce thiopurine methyltransferase (TPMT) activity. It is a method to identify patients at risk for acute toxicity from 6-MP or azathioprine. This profile provides a breakdown of a patient's genetics. The distribution of TPMT activity is trimodal: homozygous normal (89%), heterozygous (11%) and homozygous recessive (0.3%) (1). Approximately 1 in 1213 individuals may have a low TPMT enzyme activity (homozygous low) resulting from known and theoretical mutations that are not included in this panel.

Notes: Genetic testing results are reported above as the individual allele present on each chromosome for three different polymorphisms: G238C, G460A, and A719G within the TPMT gene on chromosome 6. The alleles are numbered based on order of discovery.

A combination of Cepheid Smart Mix Reagents with ABI (Applied Biosystems Sequence Detection System) Prism 7000 allelic discrimination was used in determining the presence or absence of 3 polymorphisms of the TPMT gene located on chromosome 6. Included are 3 separate PCR reactions, 3 different sets of probes and primers. This test was developed and its performance characteristics determined by Prometheus Laboratories Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing.

The homozygous recessive genotype predicts a deficient capacity to produce TPMT enzyme activity. TPMT enzyme activity is essential for normal metabolism of azathioprine or 6-mercaptopurine (2).

Our genotyping procedures will not distinguish between TPMT*1/TPMT*3A from the rare TPMT*3B/TPMT*3C which has a frequency of 1:120,890. This rare genotype is associated with low enzyme activity. Enzyme activity evaluation or sequencing is necessary to definitively identify this rare genotype.

US Patent No. 5,856,095

References:
(1) Lennard, L. et al., "The Clinical Pharmacology of 6-Mercaptopurine", European Journal of Clinical Pharmacology, Vol.43, 1992, p 329-339.
(2) Charles R. Yates et al., "Molecular Diagnosis of Thiopurine S-Methyltransferase Deficiency: Genetic Basis for Azathioprine and Mercaptopurine Intolerance", Annals of Internal Medicine, Vol. 126, No. 8, April 1997, p 608-614.

PROMETHEUS TPMT

Informed Consent for Anti-TNF Treatment
(Remicade, Humira and Cimzia)

PROCEDURE: Treatment of Inflammatory Bowel Disease with an Anti-TNF (tumor necrosis factor) agent.

DECSRIPTION: Treatment with an Anti-TNF agent is indicated for reducing signs and symptoms of Crohn's disease Chronic Ulcerative Colitis (CUC) and maintaining clinical response in adult patients with moderately to severely active disease that have had inadequate response to other therapy.

WARNINGS and PRECAUTIONS:
Anti-TNF therapy may result in the formation of antibodies and, rarely, in the development of lupus-like syndrome. In clinical trials, patients who develop symptoms suggestive of a lupus-like syndrome have had resolution of symptoms after the medication was discontinued.
There is the rare potential for serious adverse reactions, possibly even death, which may occur after any medications or intravenous infusion of foreign proteins.
Anti-TNF therapy reduces inflammation and modulates cellular immune response; therefore, the possibility exists for anti-TNF therapies to affect normal immune responses.
Patients with a long duration of Crohn's Disease and chronic exposure to immunosuppressant therapies are more prone to develop lymphomas and infections. Potential long term side effects such as lymphoma, other tumors, or other serious infections can not be predicted. Symptoms of immune reactions include shortness of breath, joint pain, or a rash on the cheeks or arms that worsen with sun exposure.

Serious Infections: Serious infections, sepsis, and cases of opportunistic infections, including fatalities, have been reported in patients receiving TNF blockers. Many of the serious infections occurred in patients on multiple immunosuppressive therapies that, in addition to their Crohn's disease, could predispose them to infections. Infections have been observed with various pathogens including viral, bacterial, fungal and protozoal organisms.
Anti-TNF therapy should not be started on patients with active infections, including chronic or localized infections. Patients who develop a new infection while undergoing treatment should be monitored closely and treatment may need to be discontinued.

Tuberculosis: Tuberculosis associated with the administration of anti-TNF therapies has been reported, including fatalities. Some patients who have previously received treatment for latent or active tuberculosis have developed active tuberculosis while being treated with TNF blockers. Patients should seek medical advice if signs/symptoms (e.g., persistent cough, wasting, weight loss, low grade fever) suggestive of tuberculosis infection occur.

Hepatitis B Reactivation: Use of TNF blockers may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. In some instances, HBV reactivation occurring in conjunction with TNF blocker therapy has been fatal. The majority of reports have occurred in patients receiving multiple medications that suppress the immune system, which may also contribute to HBV reactivation.

Malignancies: In controlled portions of clinical studies of some TNF blockers, more cases of malignancies have been observed among patients receiving TNF blockers compared to control patients. Patients with Crohn's disease or other diseases that require chronic exposure to immunosuppressive therapies may be at a higher risk than the general population for the development of lymphoma, even in the absence of TNF blocker therapy. The potential role of TNF blocker therapy in the development of malignancy is not known.

Neurologic Reactions: Use of TNF blockers has been associated with rare cases of new onset or exacerbation of neurological disorders, including seizure disorder, optic neuritis (inflammation of the nerves of the eyes) and peripheral neuropathy and other nervous system problems such as Multiple Sclerosis. Symptoms include dizziness, numbness or tingling, problems with your vision, and weakness in your arms and legs.

Hematological Reactions: Rare reports of pancytopenia, including aplastic anemia have been reported with TNF blockers. Exercise caution in patients being treated with TNF blockers who have ongoing, or a history of, significant hematologic abnormalities. Patients should seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever, bruising, bleeding, pallor). Discontinuation of therapy will be considered in patients with confirmed significant hematologic abnormalities.

Heart Failure: Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. Extreme caution should be exercised when using TNF blockers in patients who have heart failure and they should be monitored closely. Symptoms include shortness of breath, or swelling of your ankles or feet.

Immunosuppression: TNF blockers may lower the ability of the immune system to fight infections. Patients should contact their physician immediately if they develop symptoms of infection including fever, cough, flu-like symptoms or have any open cuts or sores on their body.

Allergic Reaction: Signs of an allergic reaction include a skin rash, swollen face, or trouble breathing.

Common side effects (may or may not occur)**:** Headache, nausea, upper respiratory tract infections (cold, flu, etc.), abdominal pain, fatigue, fever, pharyngitis, vomiting, pain, dizziness, brohchitis, rash, rhinitis, chest pain, coughing, pruritis, sinusitis, myalgia, back pain and moniliasis.

My signature below means that I have read this informed consent and/or the meaning has been explained to me. I am also stating that I have been given the opportunity to ask any questions about the medication that I have been prescribed. By signing this consent, I have not given up any of my legal rights.

I, hereby, authorize and direct Dr. _____ and/or associates to

administer/begin my treatment with _____, which in his judgment is advisable for my well being, and to provide additional services, as he may deem appropriate.

_____	_____	_____
Patient Name (printed)	Patient Signature	Date
_____	_____	_____
Witness Name (printed)	Witness Signature	Date
_____		_____
Physician Signature		Date

Anti-TNF Pre-Treatment Worksheet
(Remicade, Humira and Cimzia)

PATIENT NAME:_____ **ACCOUNT #** _____

Have you ever been exposed to TB? _____ Have you ever been treated for TB? _____

Have you ever been given an immunization (BCG) to prevent TB? _____

Have you had recent close contact with a known or suspected TB patient? _____

When was your last TB skin test? _____ Results:_____*

Are you currently being treated for any condition that is associated with immune suppression? _____

Do you have any medical procedures/surgeries scheduled in the next 30 days?_____
(If patient answers yes, please check with physician to see if Remicade infusion recommended)

Do you have the following symptoms/complaints: (check all the apply)
☐Productive Cough ☐Hemoptysis ☐Fever ☐Night Sweats

Have you ever received Hepatitis B vaccination? _____ If yes, when?_____**

Have you ever been treated with Remicade? _____ If yes, when was your last infusion?_____

Date of Hepatitis B Surface Ag/Hepatitis B Core Ab Total:_____ **Pt. must have this BEFORE starting Anti-TNF Treatment.**

Patient Signature: _____ **Date:**_____

Nurse Signature:_____ **Date:**_____

Physician Signature:_____ **Date:**_____

*** If patient has ever had a positive skin test or received the immunization BCG, then a CXR will be ordered in lieu of the skin test. All other patients must have a PPD with controls prior to beginning treatment.**

**** Patient who have never received the vaccine must begin the Hep B vaccine series – patients may start the vaccine at the time of their first treatment.**

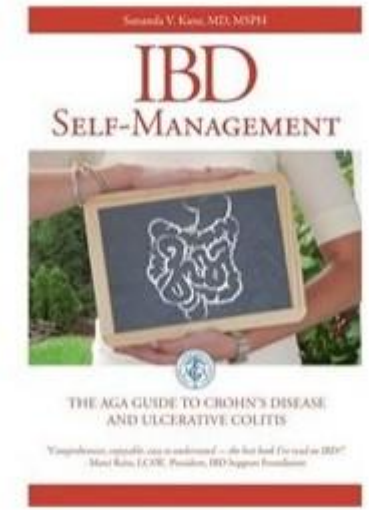
Additional Orders:_____

_____

Physician Signature:_____

Plan- Education

- Pathophysiology of Crohn's disease
- Treatment options
- Anti-TNF agents
  - Common side effects
  - Adverse effects
    - Lymphoma
    - Increase risk of infections
    - Heart failure
    - Neurological
    - Hematological

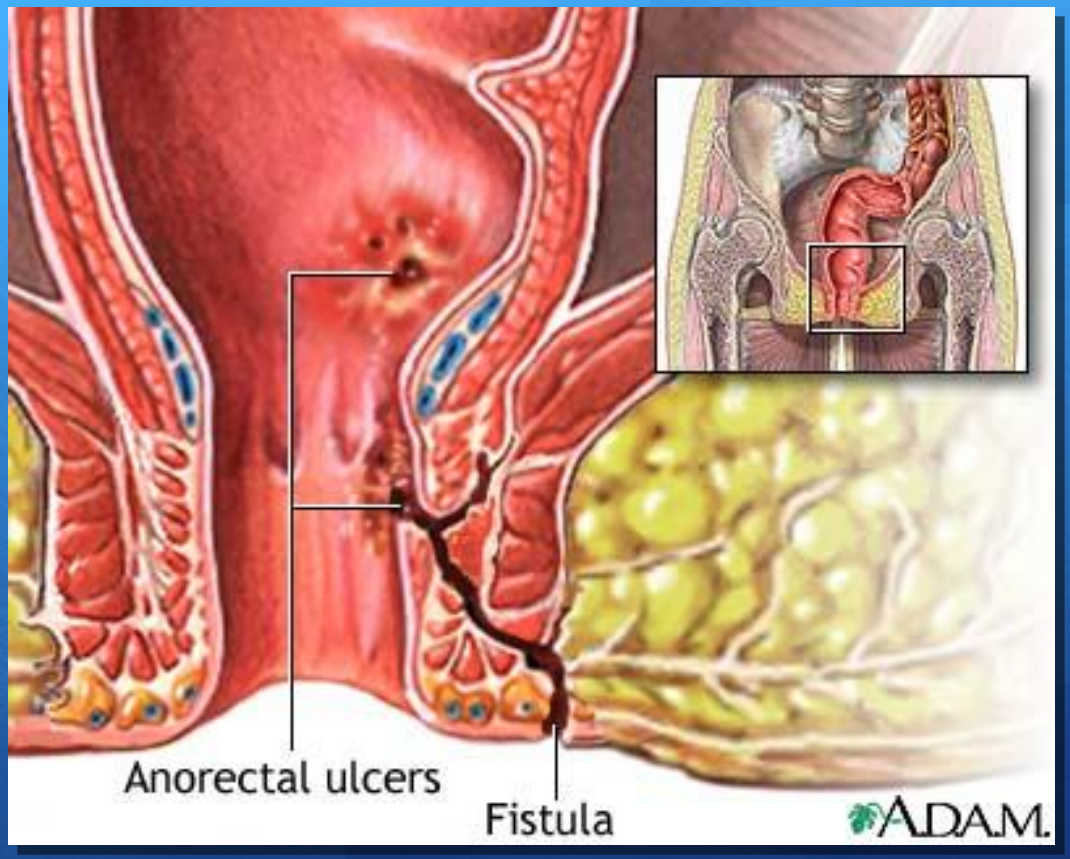


(Baker, 2008)

Plan- Follow-up

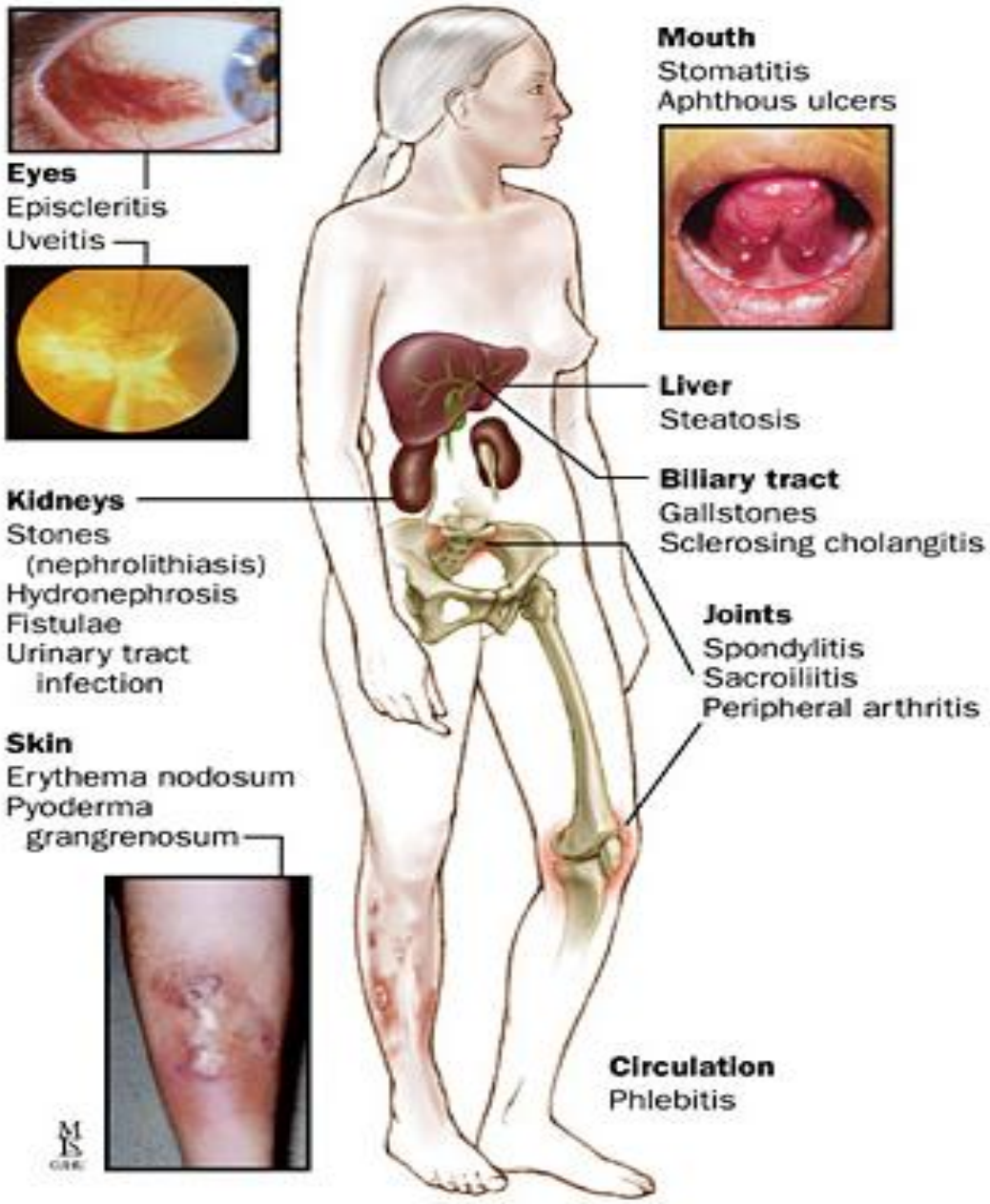
- Three months following the initiation of Cimzia
- She is having 3-4 loose stools per day without rectal bleeding or abdominal pain. She has gained approximately 22 pounds since initial consultation.
- Continue Cimzia
- Return to the clinic in 6 months for follow-up visit or sooner if needed.

Discussion



Clinical Question?

What are the extraintestinal manifestations of IBD?


Eyes
Episcleritis
Uveitis
Mouth
Stomatitis
Aphthous ulcers
Liver
Steatosis
Biliary tract
Gallstones
Sclerosing cholangitis
Kidneys
Stones
(nephrolithiasis)
Hydronephrosis
Fistulae
Urinary tract
infection
Joints
Spondylitis
Sacroiliitis
Peripheral arthritis
Skin
Erythema nodosum
Pyoderma
gangrenosum
Circulation
Phlebitis

Clinical Question?

What treatments are safe for my pregnant patient with IBD?

Pregnancy & IBD

Safety of IBD medications during pregnancy

Category B	Category C	Category D	Category X
Loperamide	Ciprofloxacin	Azathioprine	Methotrexate
Mesalamine	Cyclosporine	6-MP	Thalidomide
Balsalazide	Diphenoxylate		
Corticosteroids	Olsalazine		
Sulfalazine	Tacrolimus		
Anti-TNF agents	Natalizumab		
Metronidazole			

(PDR)

Pregnancy & IBD

- Key Points
  - Disease control at conception improves pregnancy outcomes
  - Thiopurines and anti-TNF agents are safe during pregnancy
  - Infliximab and adalimumab do cross the placenta in the third trimester…preliminary evidence suggest that certolizumab does not cross but further evidence is needed

(Cornerstones IBD Roundtable)

Questions?

References

American Gastroenterological Association Institute. (2006). American Gastroenterological Association Institute medical position statement on corticosteroids, immunomodulators, and infliximb in inflammatory bowel disease. Gastroenterology, 130, 935-939. doi: 10.1053/j.gastro.2006.01.047.

Baker, D. (2008). Certolizumab pegol: A polyethylene glycolated fab' fragment of humanized anti-tumor necrosis factor alpha monoclonal antibody for the treatment of Crohn's disease. *Reviews in Gastroenterological Disorders, 8*(4), 240-253.

Bernstein, C., Fried, M., Krabshuis, J., Cohen, H., Eliakim, R., Fedail, S.,...Watermeyer, G. (2009). Inflammatory bowel disease: a global perspective. Retrieved from http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/21_inflammatory_bowel_disease.pdf

Floch, M., Floch, N., Kowley, K., Pitchumoni, C., Rosenthal, R. & Scolapio, J. (Eds.). (2005). Netter's Gastroenterology. Icon Learning Systems, Carlstadt: New Jersey.

References

Lichtenstein, G., Hanauer, S., & Sandborn, W. (2009). Management of Crohn's disease in adults. The American Journal of Gastroenterology. doi:10.1038/ajg.2008.168

Rutgeerts, P., Schreiber, S., Feagan, B., Keininger, D., O'Neil, L., & Fedorak, R. (2008). certolizumab pegol, a monthly subcutaneously administered Fc-free anti- TNF α, improves health-related quality of life in patients with moderate to severe Crohn's disease. International Journal of Colorectal Diseases, 23, 289-296. doi: 10.1007/s003484-007-0395-7.

Sanborn, W., Feagan, B., Stoinov, S., Mason, D., Bloomfield, R., & Schreiber, S. (2007). Certolizumab pegol for the treatment of Crohn's disease. *New England Journal of Medicine, 357*, 228-238.

Schreiber, S., Kareemi., M., Lawrence, I., Thomsen, O., Hanauer, S., McColm, J., Bloonfield, R., & Sandborn, W. (2007). Maintenance therapy with certolizumab pegol for Crohn's disease. *New England Journal of Medicine, 357,* 239-250.