INFLAMMATORY BOWEL DISEASES

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BUMCP

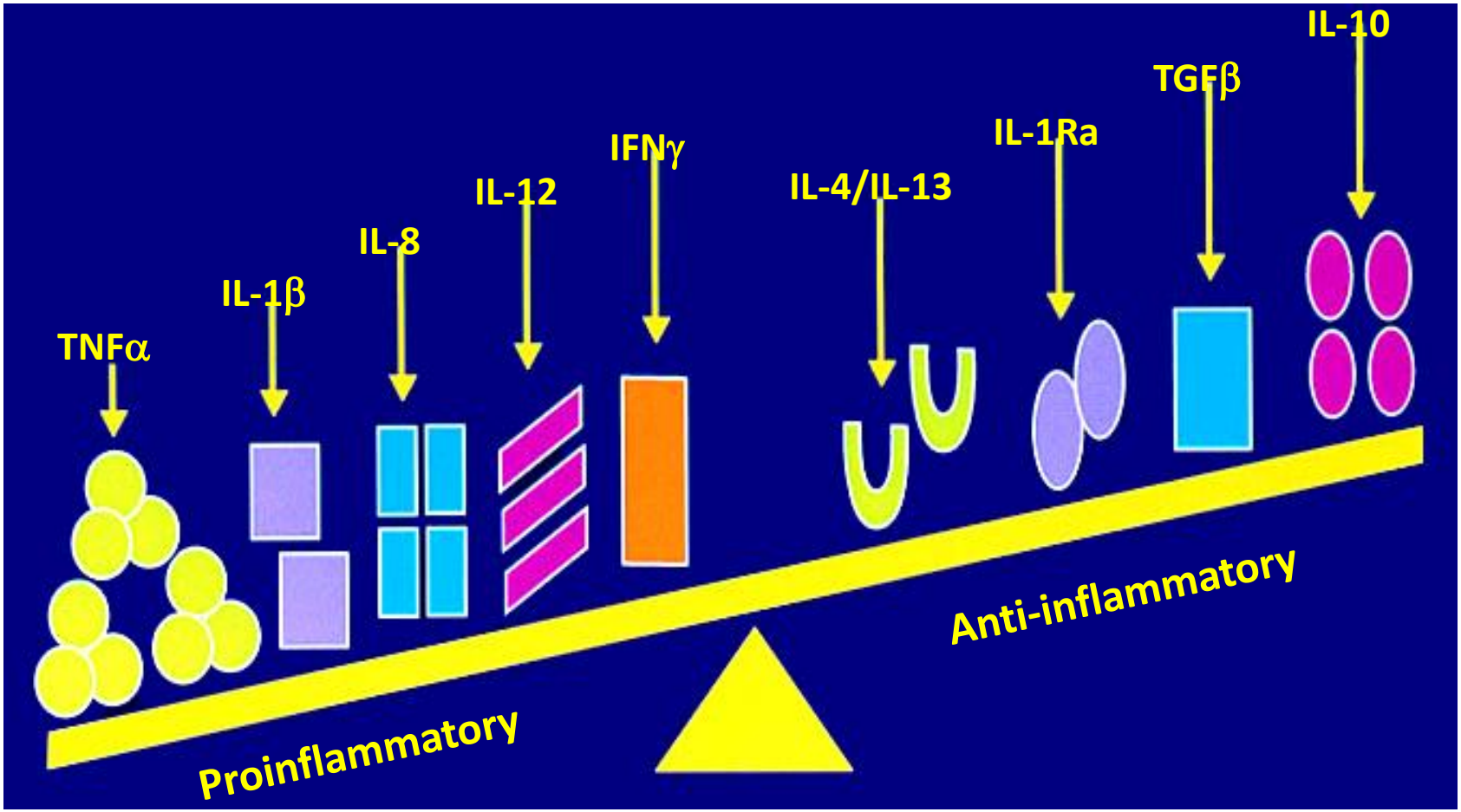
LEARNING POINTS

- Basics of IBD
- Identifying differences in UC and CD
- Current treatments in IBD
- Newer therapies in IBD

INFLAMMATORY BOWEL DISEASE (IBD)

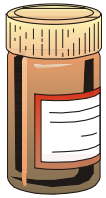
- A group of chronic diseases that causes inflammation in the large intestines (colon) and/or small intestines
- Periods of relapses and remissions
- Symptoms vary widely based on disease location and severity of inflammation

CHRONIC INFLAMMATION



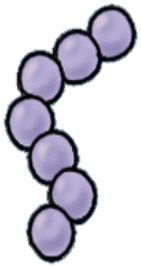
“On” **“Off”**

Environmental Triggers of IBD



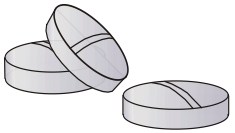
Antibiotics

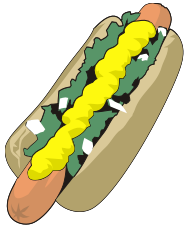
Acute infections



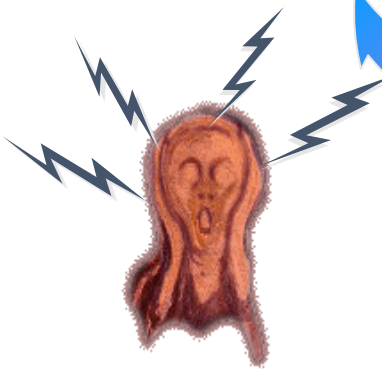
IBD
Onset and
Reactivation

NSAIDs

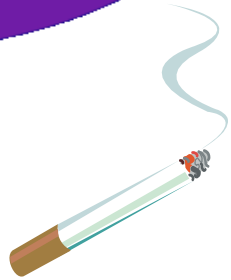




Diet

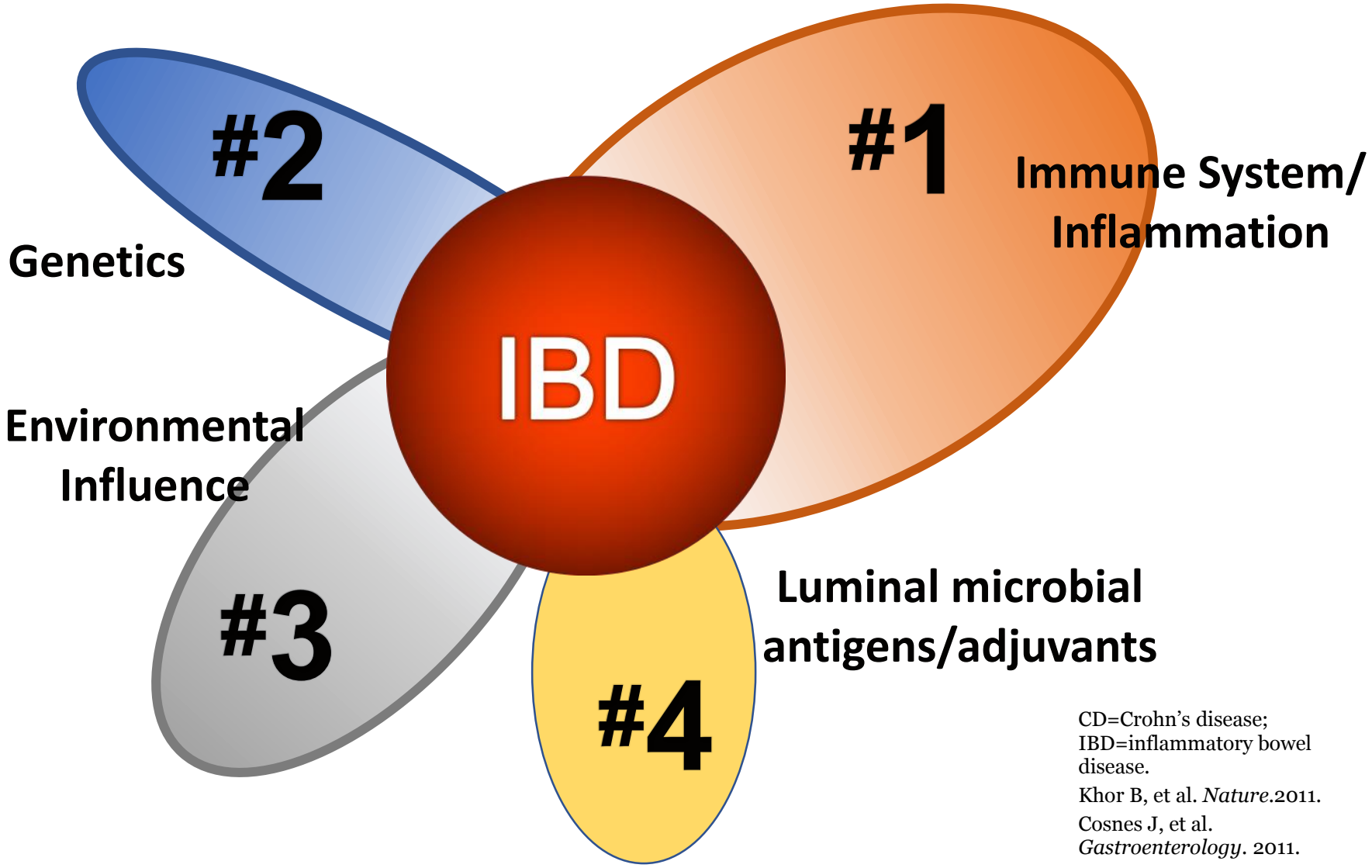


Stress



Smoking

EXACT ETIOLOGY UNKNOWN: INAPPROPRIATE IMMUNE RESPONSE



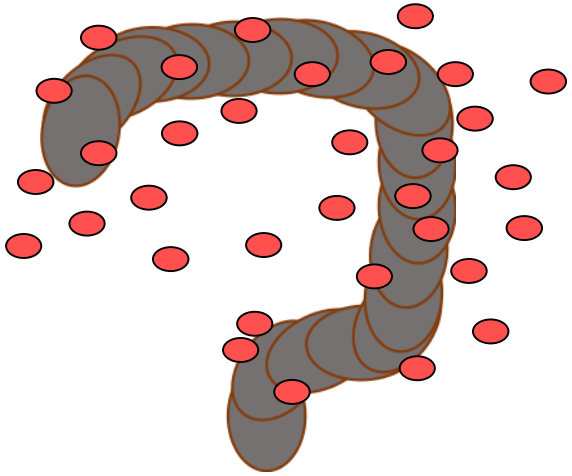
CD=Crohn's disease; IBD=inflammatory bowel disease.

Khor B, et al. *Nature*.2011.

Cosnes J, et al. *Gastroenterology*. 2011.

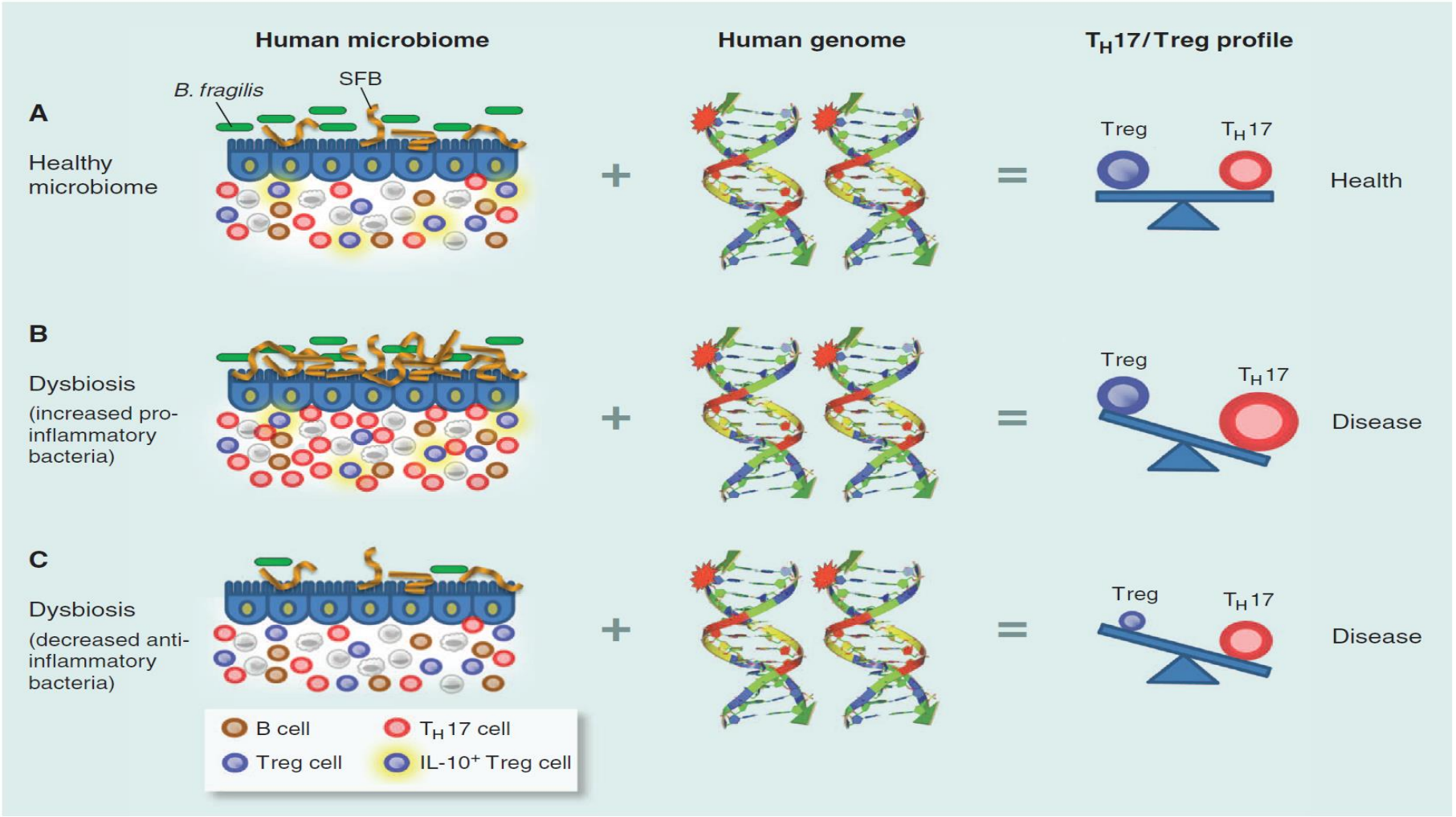
You Are Only 10% Human

= 10^{12} to 10^{13} Cells



= 10^{13} to 10^{14} Intestinal Bacteria

Proposed Model Leading to IBD:
Interaction of Genes and Environment

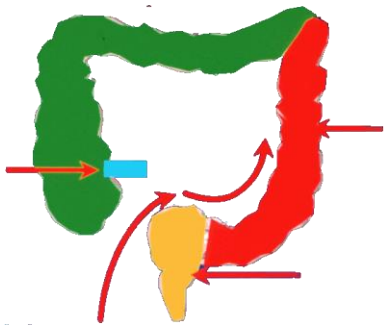


Lee YK and Mazmanian SK. Science 2010

TWO MAIN TYPES

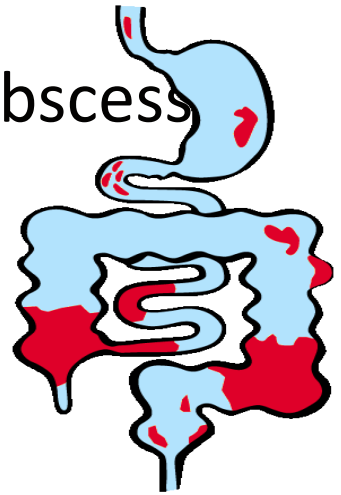
Ulcerative Colitis

- Contiguous & circumferential, superficial inflammation
- Erythema, Edema
- Loss of vascular pattern
- Friability
- Granularity

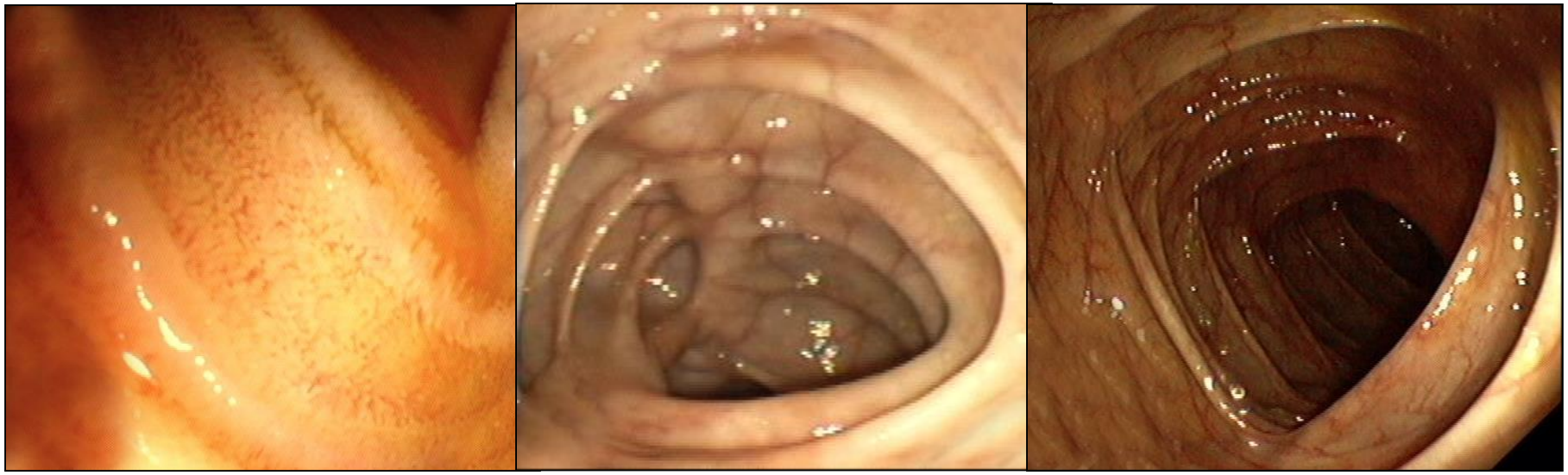


Crohn's Disease

- Discontinuous, patchy, full-thickness inflammation
- Mouth-to-anus involvement
- Strictures
- Fistulas and abscess



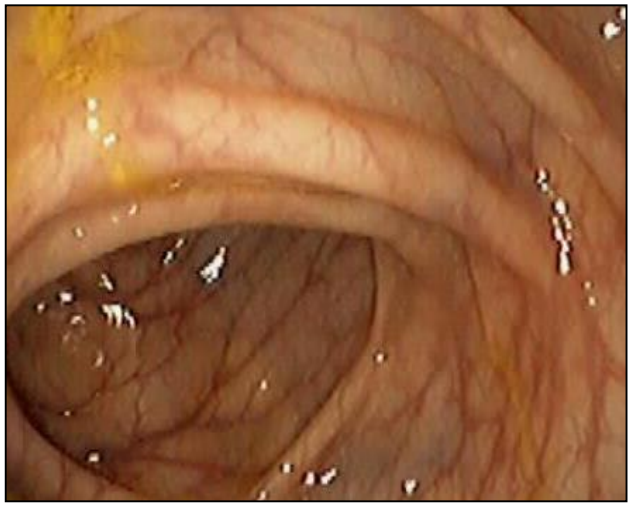
ILEOCOLONOSCOPY

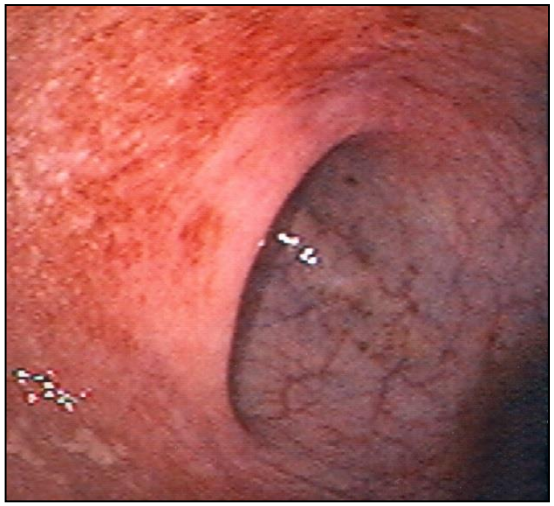


- Normal findings of terminal ileum and colon

UC
Spectrum of Disease

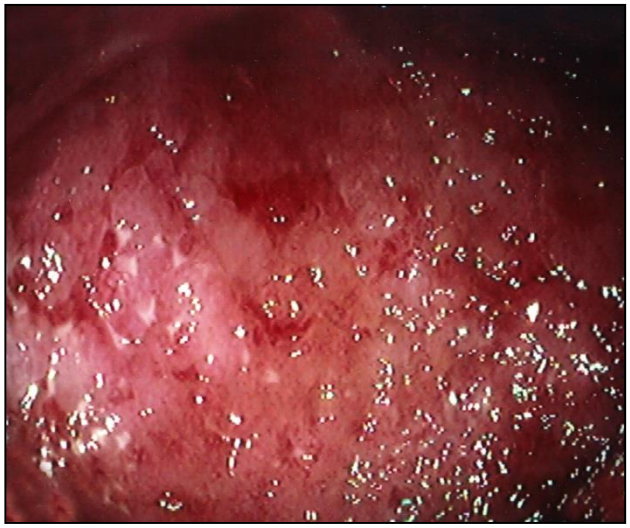
Normal

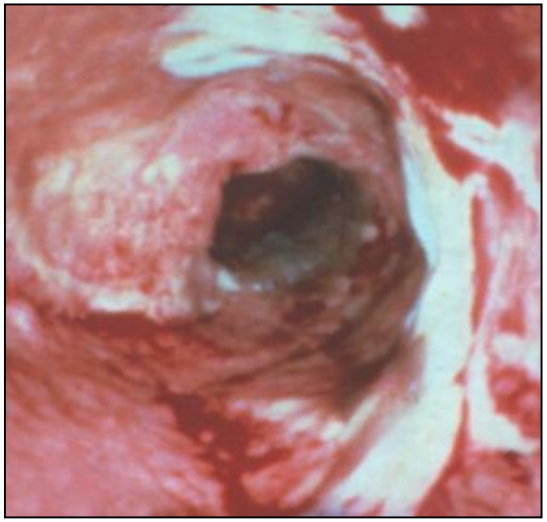




Mild

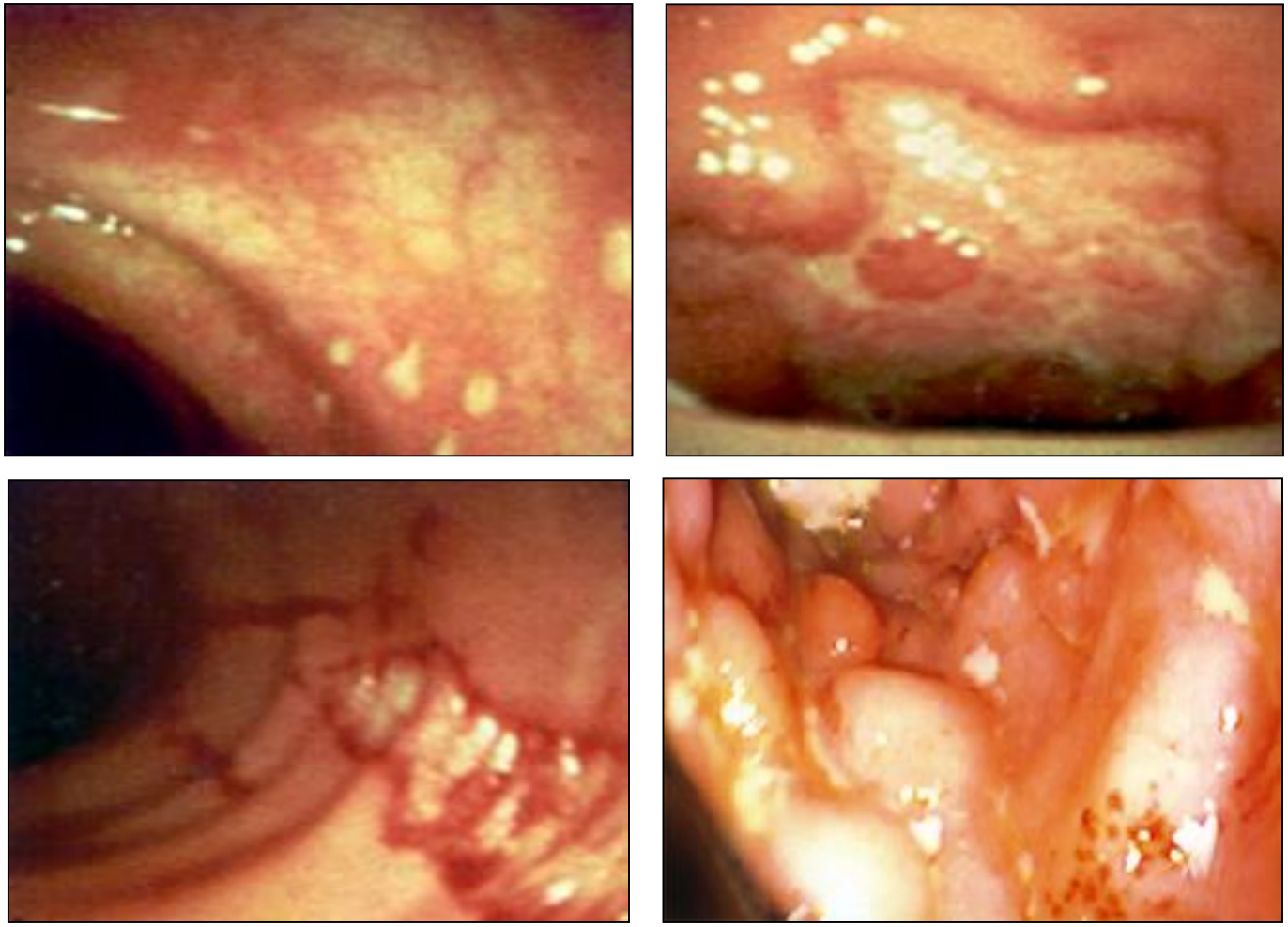
Moderate





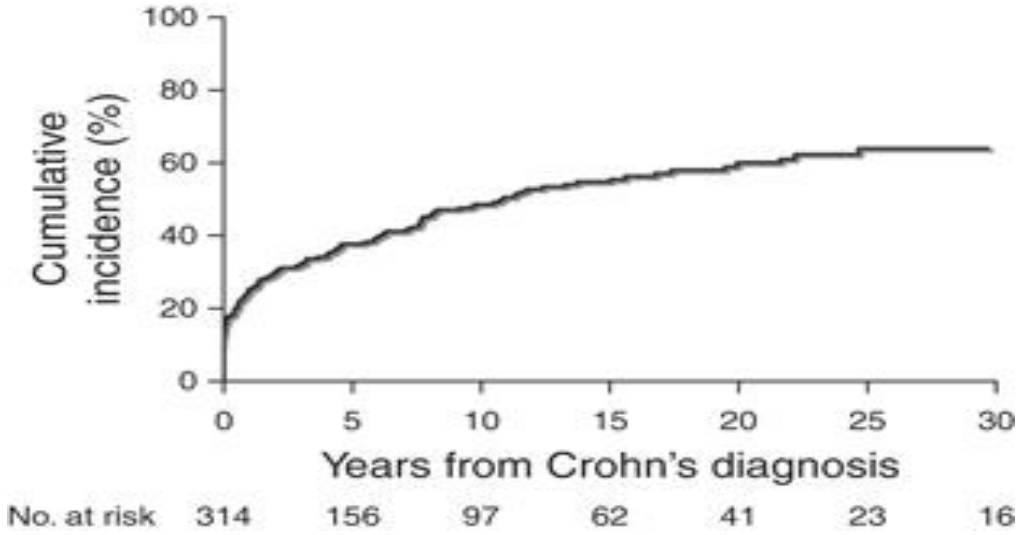
Severe

CD
Spectrum of Disease



Crohn's Disease

- Characterized by flares alternating with remission
  - <20% unremitting
  - 10% prolonged remission
- More than 80% lifetime risk of surgery



Vermeire et al APT 2007; 25:3-12
Peyrin-Biroulet et al AJG 2010; 105: 289-297
Dhillon et al. AJG 2005; 100: S305

CLINICAL FEATURES IN IBD

Typical Symptoms

- Abdominal pain
- Diarrhea
- Fever
- Fatigue
- Rectal bleeding
- Weight loss
- Anorexia
- Nausea

Common Physical Examination Findings

- Abdominal tenderness
- Palpable mass
- Perianal disease
- Extra-intestinal manifestations:
  - Mouth
  - Skin
  - Eyes
  - Joints
  - Liver

Common Laboratory & Radiographic Findings

- Anemia
- Leukocytosis
- Elevated ESR/CRP**
- Guaiac-positive stool
- Small bowel disease
- Fistulas
- Strictures

CRP = C-reactive protein
ESR = erythrocyte sedimentation rate
Podolsky DK. *N Engl J Med*. 2002

WHEN IS IT NOT Crohn's Disease

Infections:

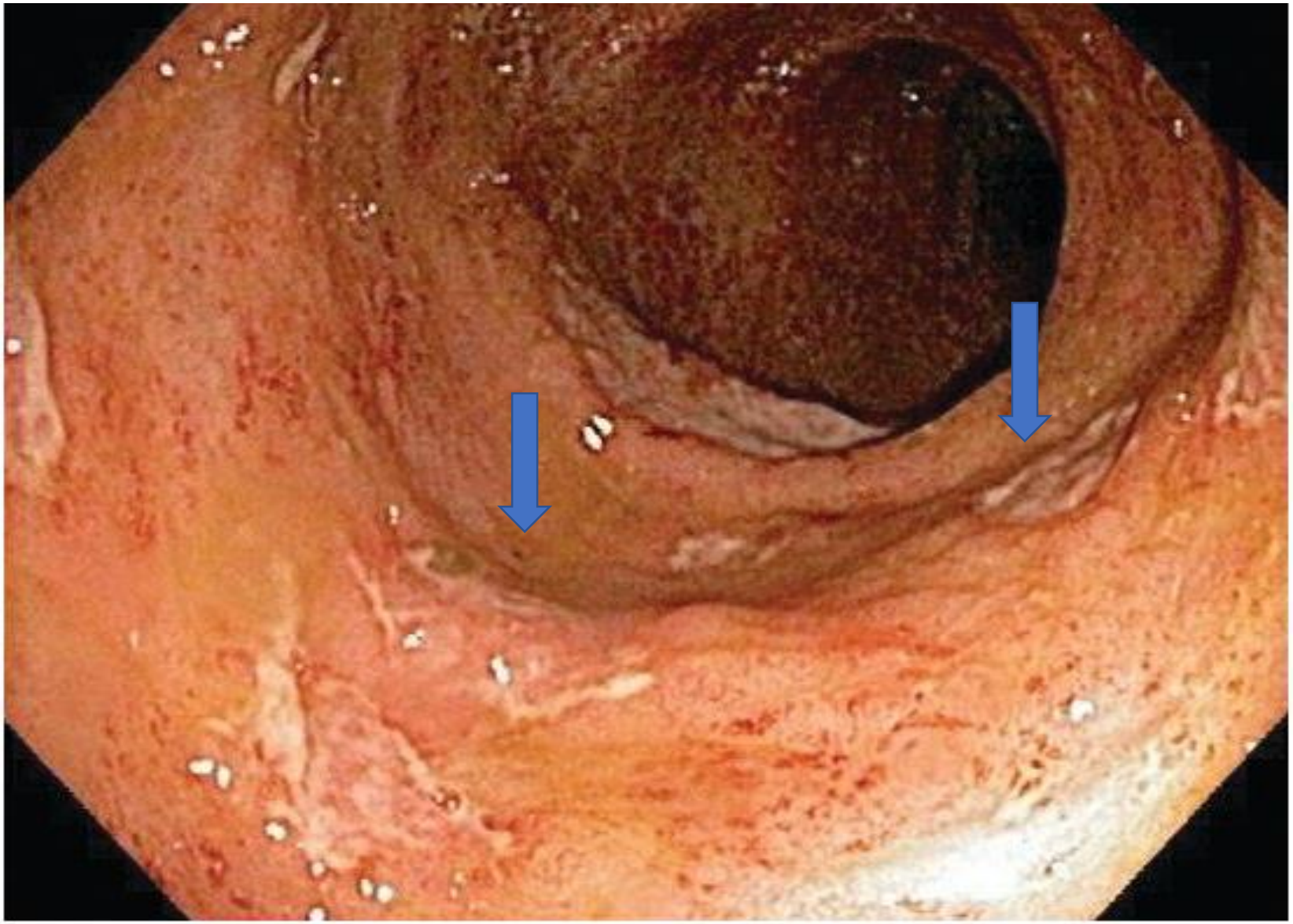
C diff
Salmonella
Yersinia
Shigella
Campylobacter
MTB
CMV

Medications:

NSAID
KCL

Others:

Ileitis Associated with spondyloarthropathies
Vasculitis
Ischemia
Small bowel Neoplasm



Which of the following is the most likely diagnosis?

A. Collagenous Colitis
B. Crohn's Disease
C. Ischemic Colitis
D. Ulcerative colitis

Wound Measuring Guide
Discard after single use.
Wound Measuring Guic
Discard after single use.
Name/Nom

Which of the following is the most likely cause of this patient's skin findings?

A. Acrodermatitis enteropathica

B. Erythema nodosum

C. Pyoderma gangrenosum

D. Squamous cell carcinoma

IBD Treatment Goals

- Induce and maintain response/remission
- Mucosal healing
- Improve/maintain quality of life
- Limit surgery
- Prevent complications
  - Disease related
  - Therapy related

Principles of Treatment

- Treatment of active disease followed by maintenance of remission
- One size does not fit all
- Risks vs benefits

Treatment Overview

- Induction
  - ***Steroids***
  - Sulfasalazine
  - Mesalamine
  - Azathioprine/6-MP
  - Methotrexate
  - Biologics
- Maintenance
  - Sulfasalazine
  - Mesalamine
  - Azathioprine/6-MP
  - Methotrexate
  - Biologics

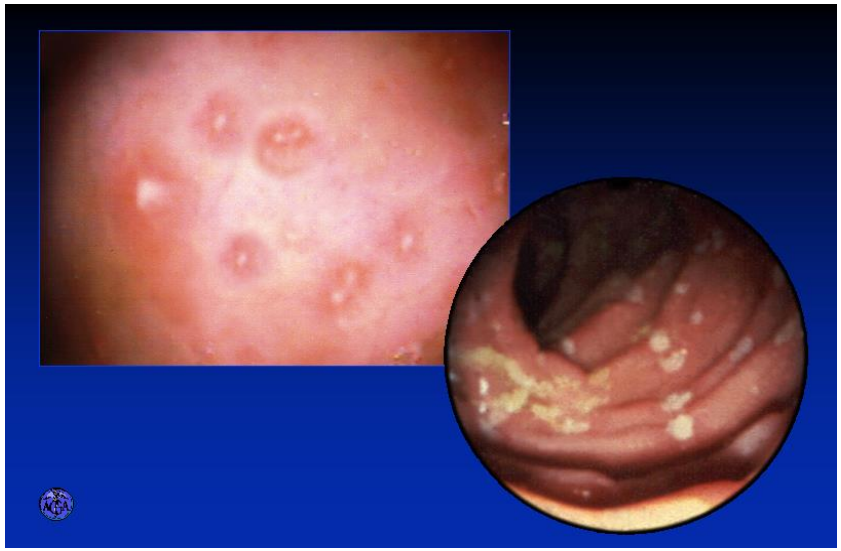
IBD ‘MEDICINE CABINET’

- Over-the-Counter
- Antibiotics
- 5-Aminosalicylates/Mesalamine
- Corticosteroids, Budesonide
- Immunomodulators – AZA/6MP, MTX
- Biologics - Target Protein Specific

Case Presentation

- 22 yo M
  - 4 week history bloody diarrhea (3-4/day)
  - Mild abdominal pain
- Colonoscopy and biopsies
  - Mild Crohn's colitis

Recommend oral 5-ASA



Anti-Inflammatory Drugs

- 5-aminosalicylate (5-ASA)
  - Sulfasalazine: 3-6 g/day
  - Mesalamine: 4g/day

5-ASA Side Effects

- Sulfasalazine
  - Headache
  - Nausea/vomiting
  - Rash
  - Folate malabsorption
  - Reversible oligospermia
  - Pancreatitis
  - Bone marrow suppression
  - Paradoxical exacerbation
  - **Interstitial nephritis**

- Mesalamine
  - Headache
  - Nausea
  - Rash
  - Pancreatitis
  - Paradoxical exacerbation
  - **Interstitial nephritis**

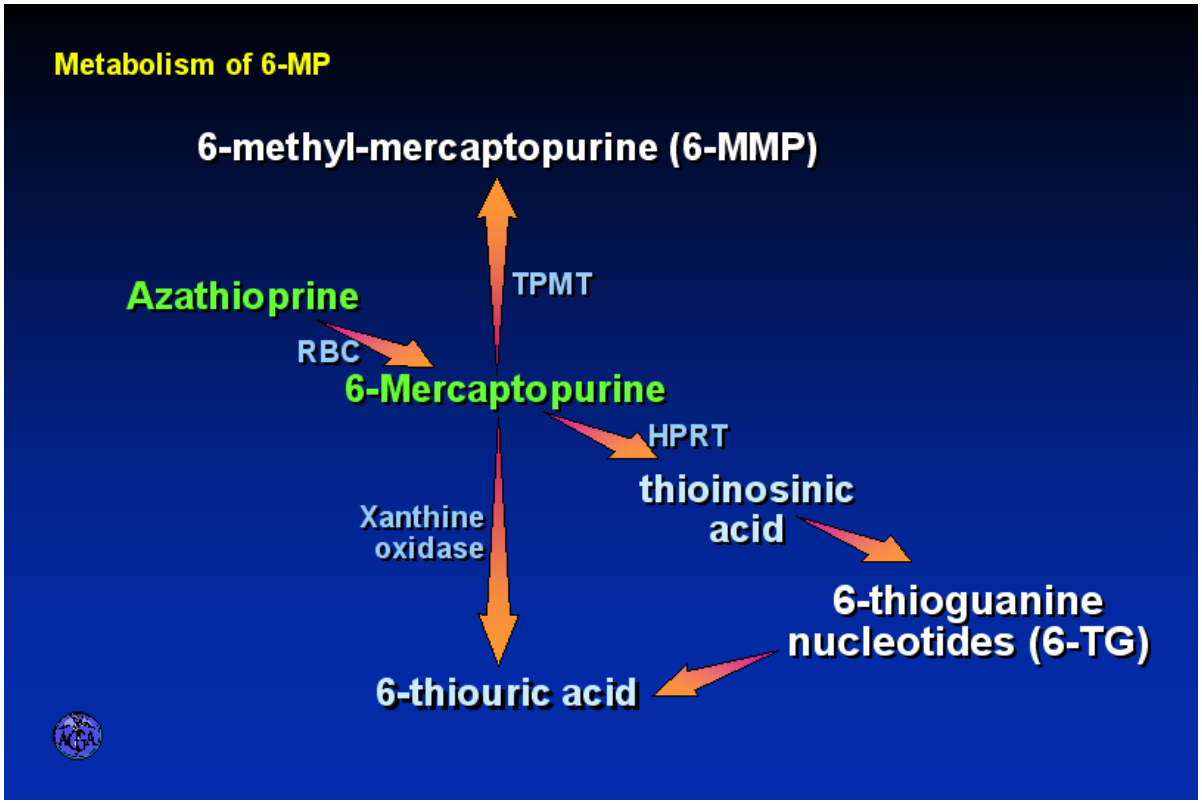
Case Presentation

- 33 y/o M with 1 yearr hx Crohn's Disease
  - Previously treated with steroids and mesalamine
  - Abdominal pain, diarrhea controlled on steroids
- Colonoscopy
  - Inflammation and ulcers in TI and colon
  - Biopsies with ileo-colonic Crohn's
- MR Enterography
  - No stricture/fistula/abscess

Recommend azathioprine

Immunomodulator Drugs

- Azathioprine/6-MP



Azathioprine Risks

- BM – Leukopenia (2-5%)
- Hepatotoxicity (rare)
- Pancreatitis (3%)
- Drug intolerance (10-15%)
  - Fatigue
  - Nausea
  - Flu-like
  - Hypersensitivity rxn
- Infection (2-3:1)
  - Viral- HSV, CMV, EBV
- Lymphoma (~4x)

Corticosteroids

- IV: hydrocortisone, methylprednisolone
- Oral: prednisolone, prednisone, budesonide
- Budesonide
  - Topically active glucocorticoid
  - Limited systemic bioavailability
  - Less toxicity

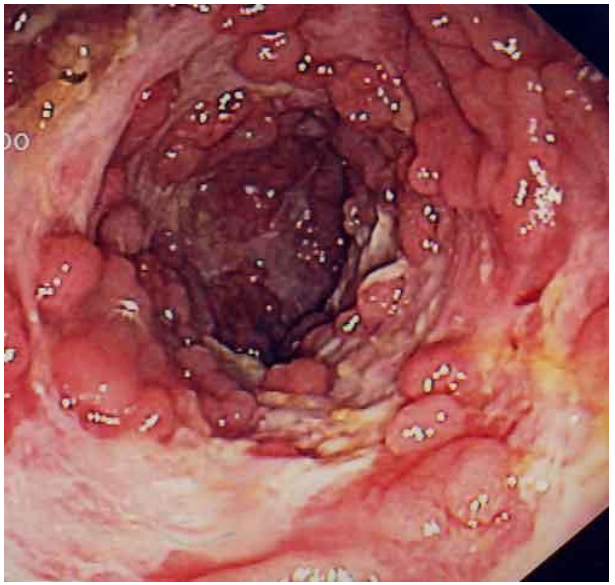
Seow et al Cochrane Database of Systematic Reviews 2005

Corticosteroids Side Effects

- Cataracts
- Glaucoma
- Diabetes
- Weight gain
- Hypertension
- Osteopenia/Osteoporosis
- Acne
- Mood/sleep disturbances
- Infection

Case Presentation 3

- 26 y/o F with 2 year hx Crohn's Disease
  - Previously treated with steroids and AZA
  - Abdominal pain, diarrhea, perianal fistula
- Colonoscopy
  - Inflammation and ulcers in colon and TI
- MRI-e
  - No stricture, no abscess



Recommend anti-TNF

Anti-TNFs in IBD- BIOLOGICS

Infliximab approved for CD 1998

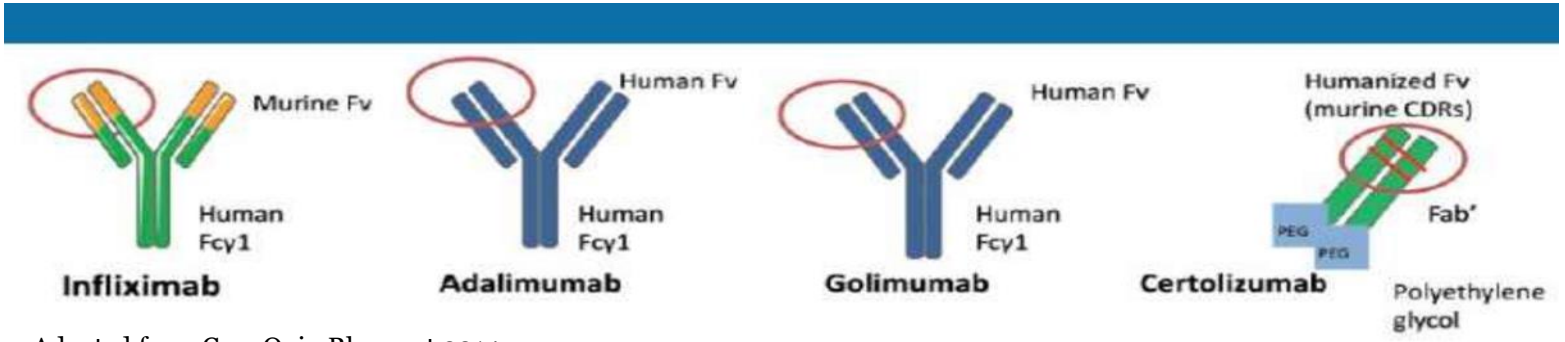
Adalimumab for CD 2002

Certolizumab pegol for CD 2008

Infliximab approved for UC 2005

Adalimumab for UC 2012

Golimumab for UC 2013



Adapted from Curr Opin Rheumat 2014

Fausel R & Afzali A. Ther Clin Risk Manag 2015

Benefits

- Steroid free remission
- Improved quality of life
- Decreased hospitalizations
- Decreased need for surgeries
- Improved mucosal healing

Lichtenstein et al Gastroenterology 2005; 128: 862-9

Risks of Anti-TNF's

- Infusion Reaction (5%)
- Infection
  - Reactivation TB, HBV
  - Sepsis
- Lymphoma
- Demyelinating diseases (rare)
- Hepatotoxicity (rare)
- Drug induced lupus (<1%)

Anti-TNF: Endoscopic Healing

QUESTION 3

A 38-year-old man is evaluated in follow-up after a diagnosis of **ulcerative colitis. Ten days ago he was started on prednisone, 60 mg/d, but his symptoms have not improved**. He has six to **nine bloody bowel movements per day and moderate abdominal pain**. He has decreased his oral intake because eating exacerbates his pain and diarrhea.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 110/56 mm Hg, and pulse rate is 96/min. He is pale but in no distress. The abdomen is diffusely tender without distention, guarding, or rebound.

Laboratory studies reveal **a hemoglobin level of 9.7 g/dL (97 g/L) and a leukocyte count of 6300/µL (6.3 × 10^9/L).**

Stool culture and *Clostridium difficile* assay are negative.

Which of the following is the most appropriate treatment?

A. Increase prednisone to 80 mg/d

B. Initiate adalimumab

C. Initiate ciprofloxacin and metronidazole

D. Initiate mesalamine

E. Initiate sulfasalazine

QUESTION 4

- A 38-year-old man is evaluated in follow-up after starting therapy for ulcerative colitis. A **colonoscopy performed 3 months ago showed moderate colitis extending from the rectum to the proximal transverse colon**. He was initially treated with **mesalamine without any improvement** in his symptoms. On prednisone, 40 mg/d, his symptoms have steadily improved, with cessation of bleeding and a decrease in diarrhea. The dose of prednisone has been tapered to 20 mg/d, and he is now having one to two mostly formed stools per day.
- On physical examination, vital signs are normal. Abdominal examination is unremarkable.
- Laboratory studies reveal a normal complete blood count, and the serum thiopurine methyltransferase level is undetectable

Which of the following is the most appropriate maintenance therapy?

A. Infliximab

B. Azathioprine

C. 6- MP

D. Methotrexate

E. Prednisone

QUESTION 5

- A 22-year-old woman is evaluated for a **flare of Crohn disease**. A **colonoscopy performed 6 months ago showed moderate, patchy, left-sided colitis extending from the descending colon to the splenic flexure.** She responded to therapy with prednisone but declined maintenance therapy in advance of conceiving. She is now **12 weeks pregnant and for the past 2 weeks** has experienced bloody diarrhea and left-sided abdominal pain.
- On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 110/66 mm Hg, and pulse rate is 76/min. Abdominal examination reveals left-sided abdominal tenderness without guarding or rebound.
- Flexible sigmoidoscopy shows recurrent left-sided patchy colitis, and stool studies are negative for *Clostridium difficile* infection.

Which of the following is the most appropriate treatment?

A. Certolizumab

B. Ciprofloxacin and metronidazole

C. Controlled ileal-release budesonide

D. Mesalamine

E. Methotrexate

QUESTION 6

- A 29-year-old man is evaluated during a routine examination. His medical history is significant for **ulcerative colitis** involving the entire colon, which was **diagnosed 4 years ago**. His symptoms responded to therapy with **mesalamine and have remained in remission on this medication.** His family history is significant for a maternal uncle who died of colon cancer at the age of 50 years.
- Physical examination is unremarkable.
- Serum alkaline phosphatase, alanine aminotransferase, and aspartate aminotransferase levels are normal.

Which of the following is the most appropriate interval at which to perform colonoscopy with biopsies in this patient?

A. Begin now and repeat annually

B. Begin in 4 years and repeat every 1-2 years

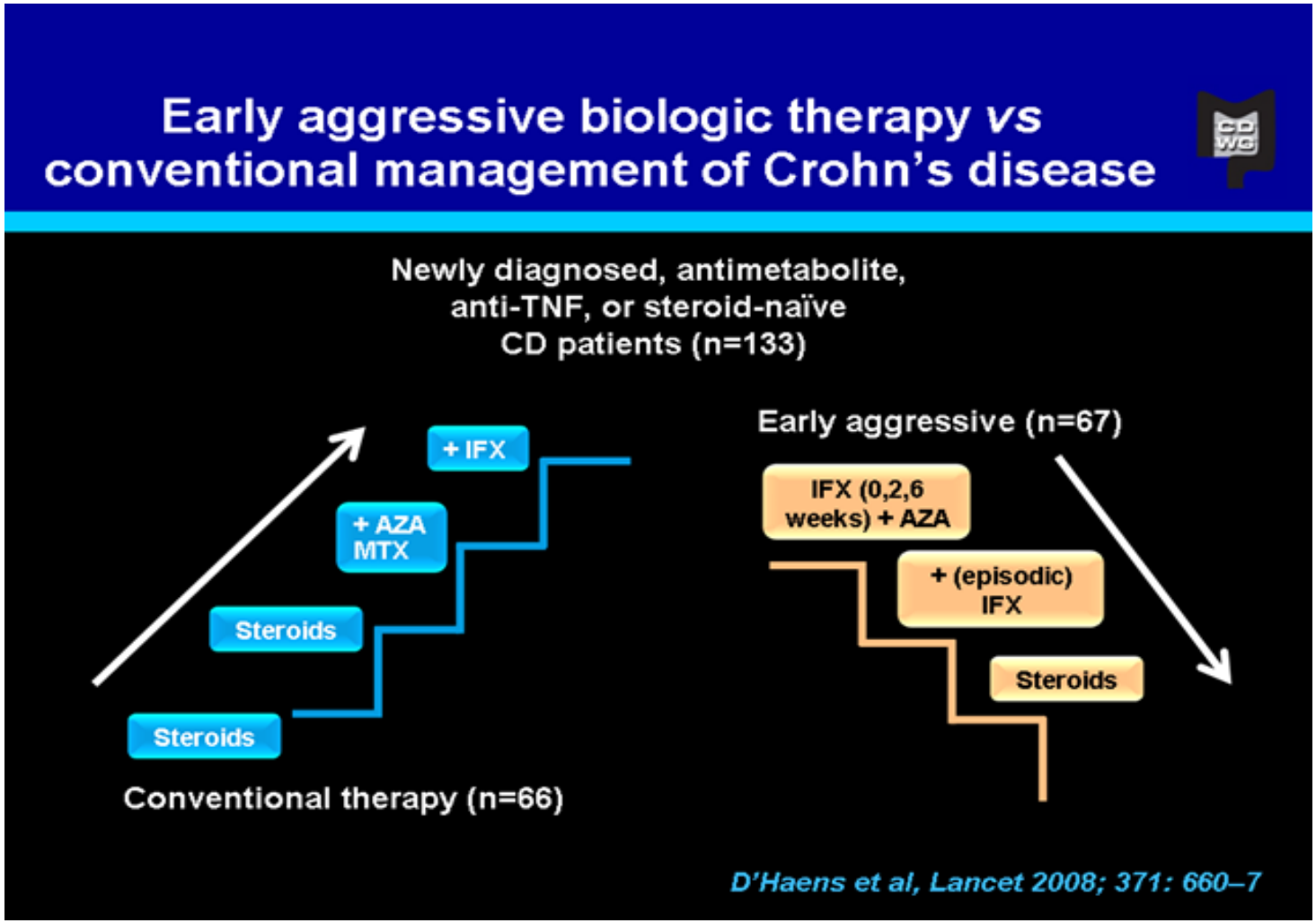
C. Begin in 4 years and repeat every 10 years

D. Begin at 40 years and repeat every 5 years

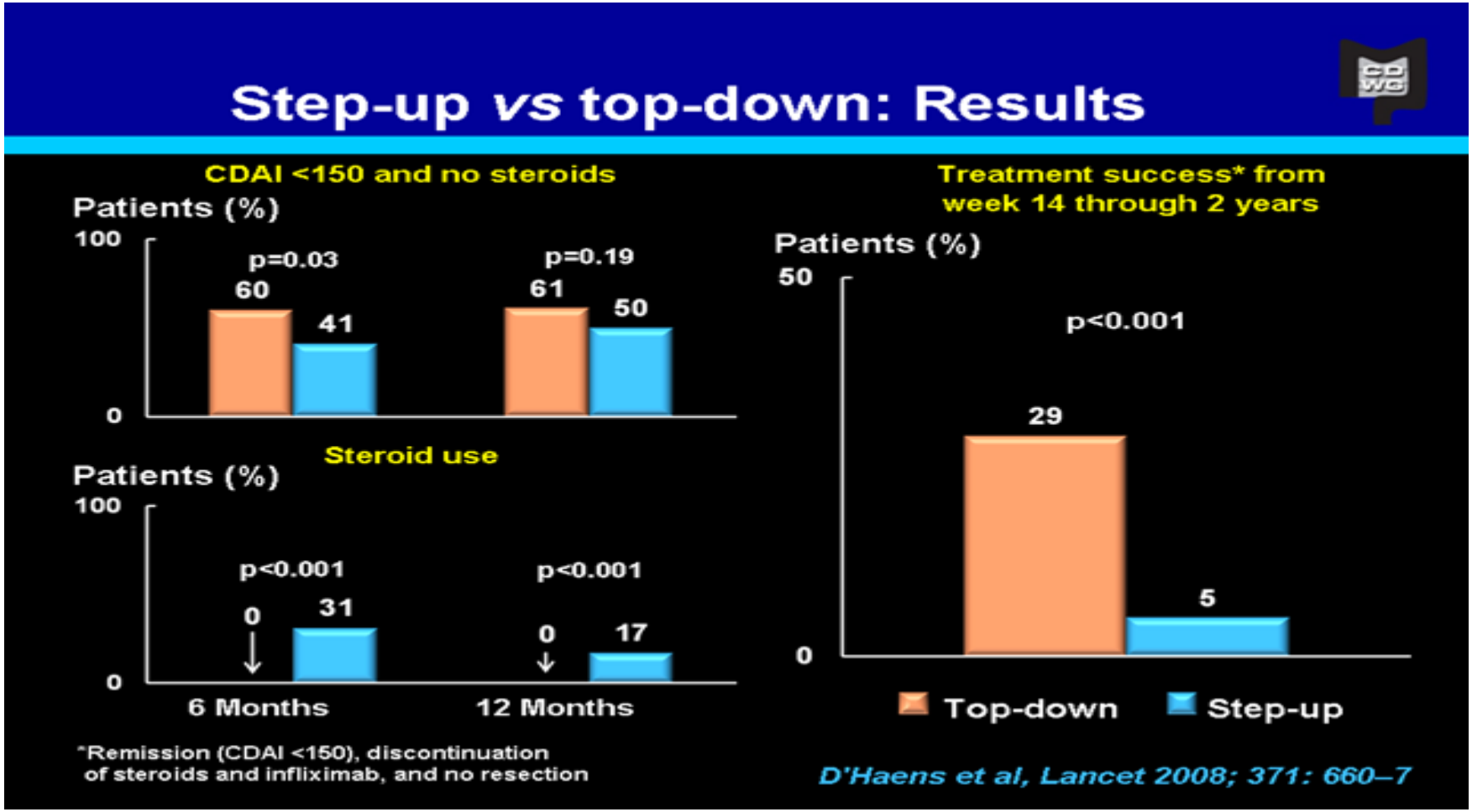
Current Questions

- Step Up vs Top Down
- Mucosal Healing
- Combination vs Monotherapy

Step up vs Top Down



Step up vs Top Down



QUESTIONS