UTAH SOCIETY OF
HEALTH-SYSTEM PHARMACISTS

Fall CE Series
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What's the Scoop on the Poop?

Inflammatory Bowel Disease Update

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Disclosure

- Relevant Financial Conflicts of Interest
  - CE Presenter, Sabrina Sherwood
    - None
  - CE Mentor, Kami Roake
    - None

Off-Label Use of Medications

- None

Abbreviations

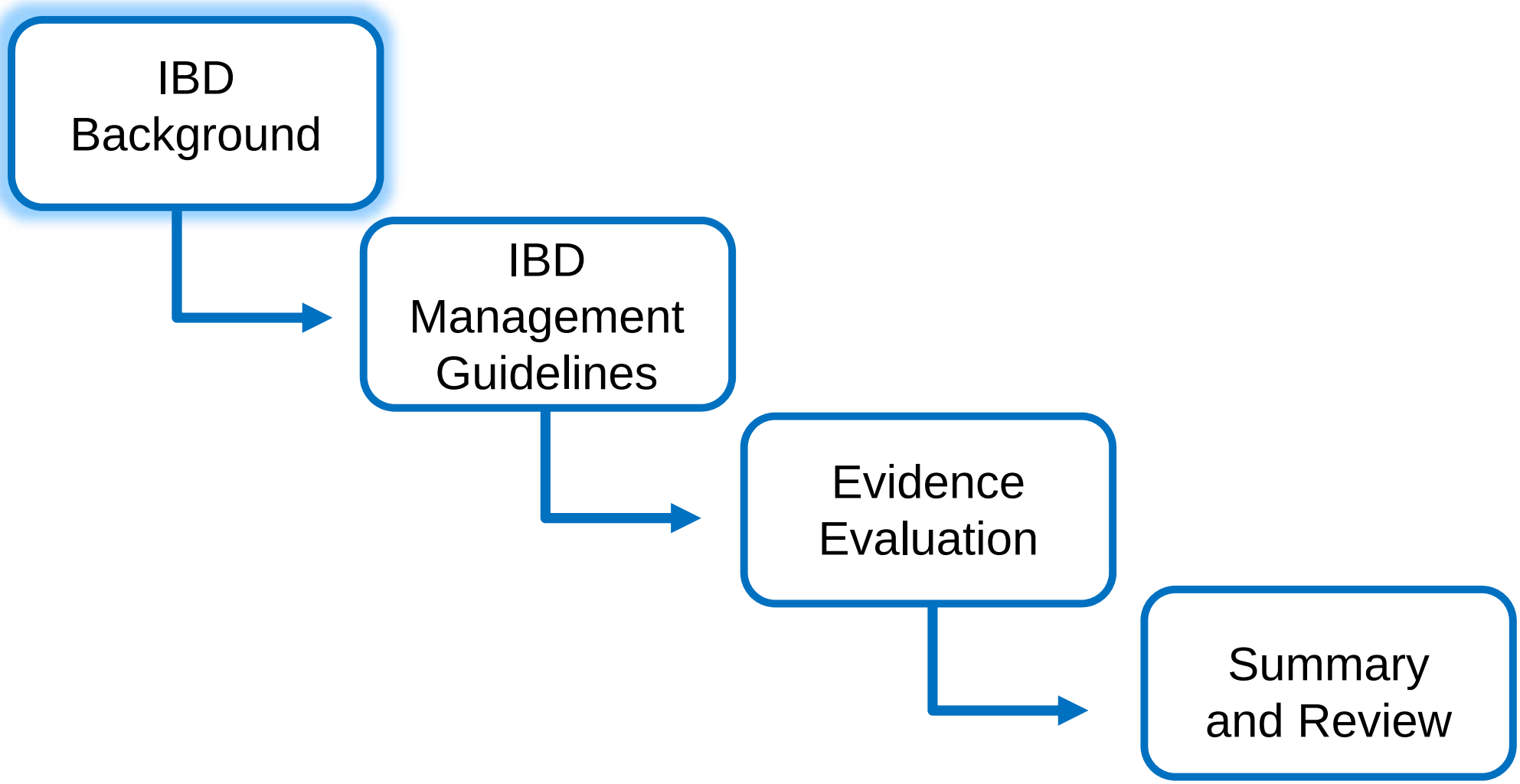
- 5-ASA: Aminosalicylates
- 6-MP: 6-mercaptopurine
- AGA: American Gastroenterological Association
- Anti-IL: Anti-interleukin
- BID: Twice daily
- CBC: Complete blood cell count
- CDC: Centers for Disease Control
- CRP: C-reactive protein
- ESR: Erythrocyte sedimentation rate
- HBV: Hepatitis B Virus
- Hs-CRP: High-sensitivity C-reactive protein
- IBD: Inflammatory bowel disease
- IBS: Irritable bowel syndrome
- IL: Interleukin
- JAK: Janus kinase
- LFT: Liver function test
- OR: Odds ratio
- PFT: Pulmonary function test
- PML: Progressive multifocal leukoencephalopathy
- STD: Standard deviation
- TB: Tuberculosis
- TNF-α: Tumor necrosis factor alpha
- UC: Ulcerative colitis
- WBC: White blood cell

Pharmacist Learning Objectives

- Analyze expert guidelines for Crohn's Disease and Ulcerative Colitis management
- Recall the pharmacology of agents used in IBD therapy management
- Evaluate supportive evidence for IBD therapy management recommendations
- Construct a therapeutic regimen and monitoring plan for a patient with IBD

Technician Learning Objectives

- Outline the signs and symptoms of IBD
- Identify both the brand, generic, and biosimilar names for commonly used IBD medications
- Demonstrate how to assist patients in gaining accessibility to and financial assistance for IBD medications


IBD Background
IBD Management Guidelines
Evidence Evaluation
Summary and Review

Patient Case

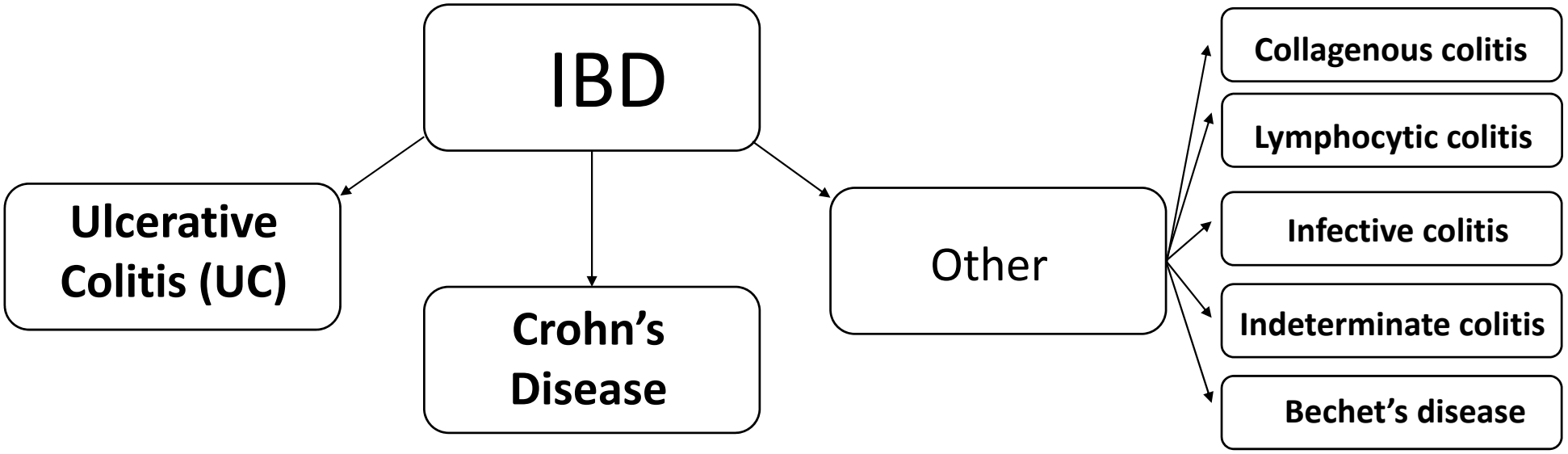
KS, a 26 year old male, presents to his primary care physician with complaints of fatigue, frequent bowel movements (10-15 times per day) with urgency and blood in his stool. He reports a 15 lb. weight loss over the last 2 months, which is approximately when the symptoms started. He complains of arthralgia and painful red nodules on his legs. He has no past medical history and is not taking any medications.

His laboratory work is notable for the following:

Hemoglobin	Platelets	CRP	Temperature
9.0 g/dL	700 cells/mm^3	17 mmol/L	100.1º Fahrenheit

Inflammatory Bowel Disease

- Group of chronic disorders that cause inflammation or ulceration in large and small intestines



Bernstein CN, Fried M, Krabshuis JH, et al. World Gastroenterology Organization Practice Guidelines for the diagnosis and management of IBD in 2010.Inflamm Bowel Dis. 2010 Jan;16(1):112-24.

Irritable Bowel Syndrome (IBS)	Inflammatory Bowel Disease (IBD)
No intestinal inflammation, ulcers, or bowel damage	Associated with inflammation, ulcers, and bowel damage
Laboratory markers and intestinal pathology commonly normal	Laboratory markers and intestinal pathology abnormal with disease flare
Characterized by abdominal pain, discomfort, disturbed defecation	Commonly characterized by blood in stool, joint pain, weight loss, or dermatologic problems

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IBD Epidemiology

- Affects 1 million people in the United States
- Prevalence
  - Ulcerative colitis
    - 238 cases per 100,000 adults
  - Crohn's disease
    - 201 cases per 100,000 adults
- Incidence is higher in higher socioeconomic classes
  - Hygiene hypothesis

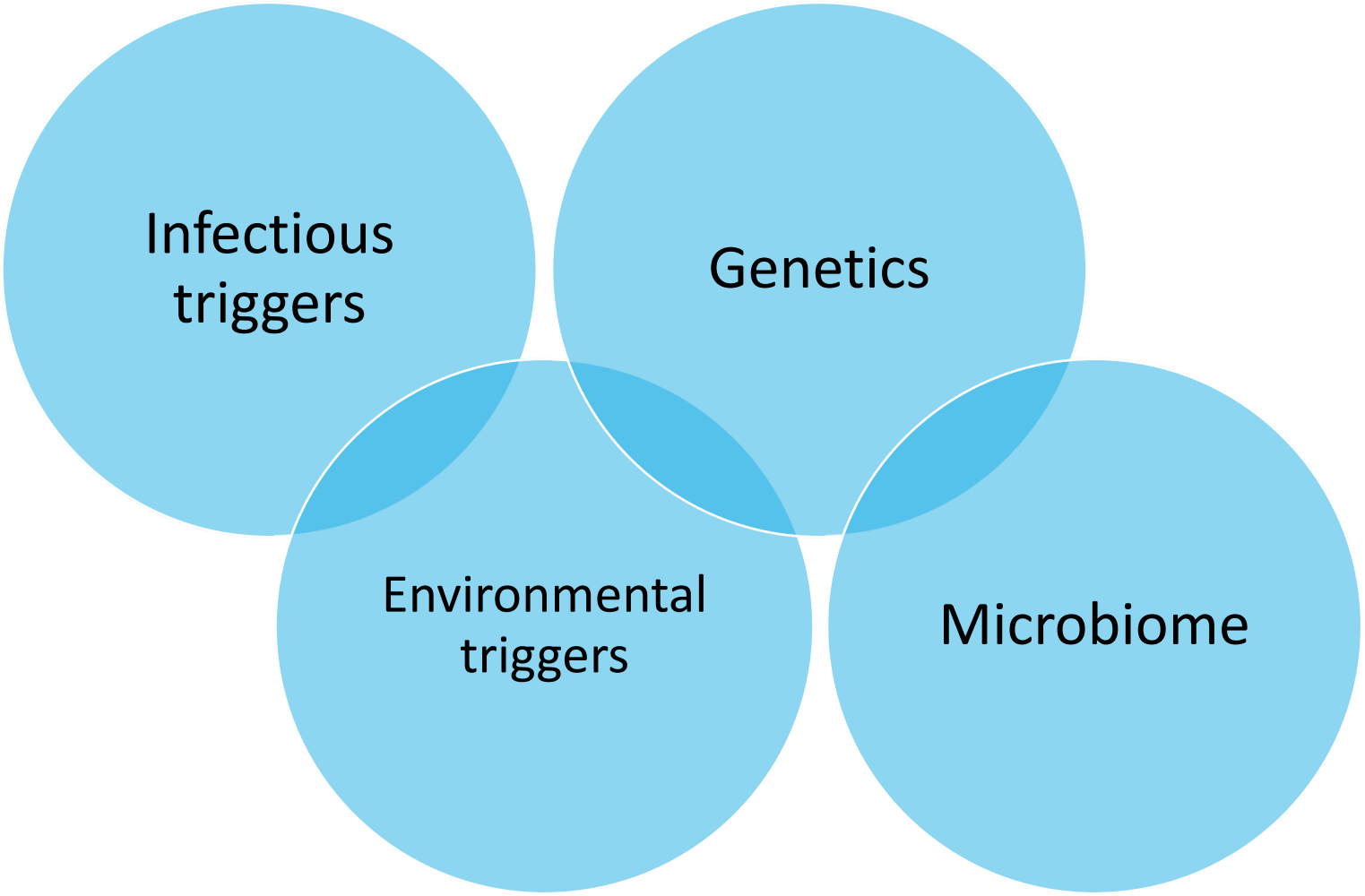
Bernstein CN, Fried M, Krabshuis JH, et al. World Gastroenterology Organization Practice Guidelines for the diagnosis and management of IBD in 2010.Inflamm Bowel Dis. 2010 Jan;16(1):112-24.
Kappelman MD, Rifas-Shiman SL, Kleinman K, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol.* 2007; 5:1424-9.
Bernstein CN, Kraut A, Blanchard JF, Rawsthorne P, Yu N, Walld R. The relationship between inflammatory bowel disease and socioeconomic variables. *Am J Gastroenterol* 2001;96(7):2117–25.

IBD Epidemiology Continued

- **Sex**
  - Ulcerative colitis is more common in males
  - Crohn's disease is more common in females
- **Ethnicity**
  - Most common in Caucasians
- **Environmental**
  - Ulcerative colitis is more common among ex-smokers and nonsmokers
  - Crohn's disease is more common among smokers

Kappelman MD, Rifas-Shiman SL, Kleinman K, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol.* 2007; 5:1424-9.
Bernstein CN, Kraut A, Blanchard JF, Rawsthorne P, Yu N, Walld R. The relationship between inflammatory bowel disease and socioeconomic variables. *Am J Gastroenterol* 2001;96(7):2117–25.

Etiology



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The Burden of IBD Annually

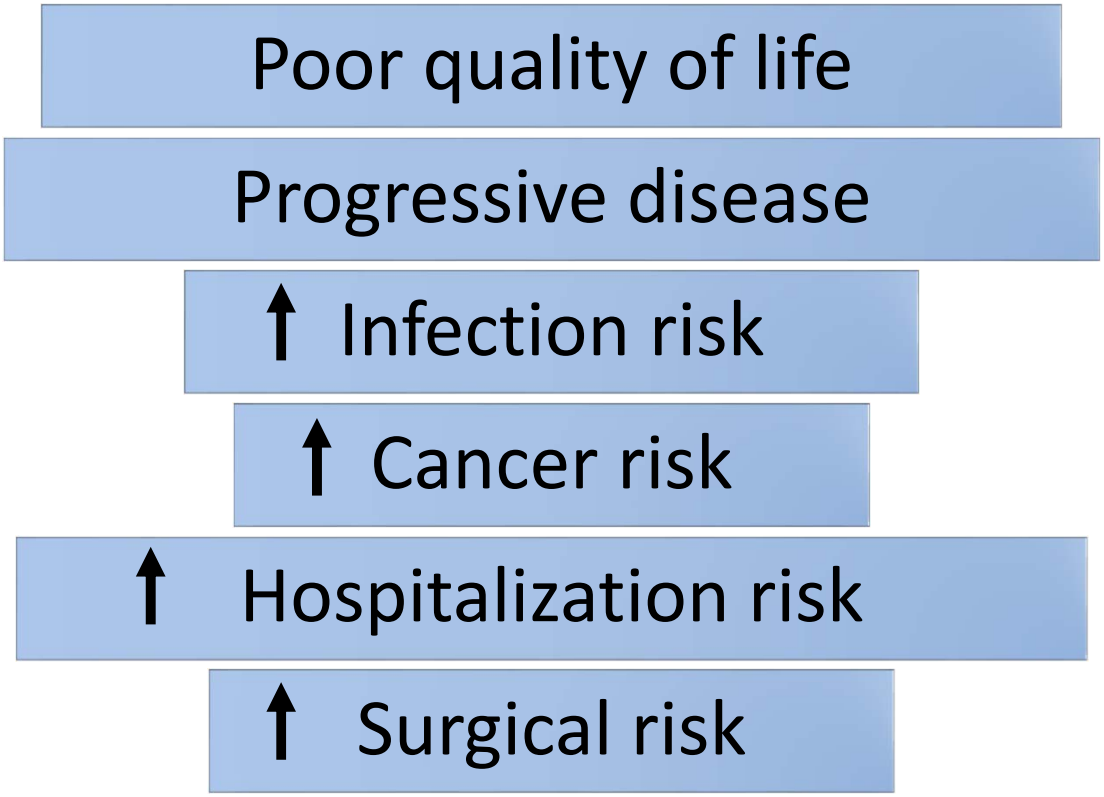
100,000 hospitalizations

> 700,000 physician visits

$4,000,000,000 in direct costs

Kappelman MD, Rifas-Shiman SL, Porter CQ, et al. Direct health care costs of Crohn's disease and ulcerative colitis in US children and adults. *Gastroenterology*. 2008;135(6):1907-1913
Hospital Image. Bing Creative Commons. Accessed September 2018. Image available at: https://binged.it/2NnRi0h
Provider Image. Bing Creative Commons September 2018. Image available at: https://binged.it/2NkZk9Z
Money Image. Bing Creative Commons. Accessed September 2018. Image available at: https://binged.it/2xq36nR

Consequences of Untreated Disease



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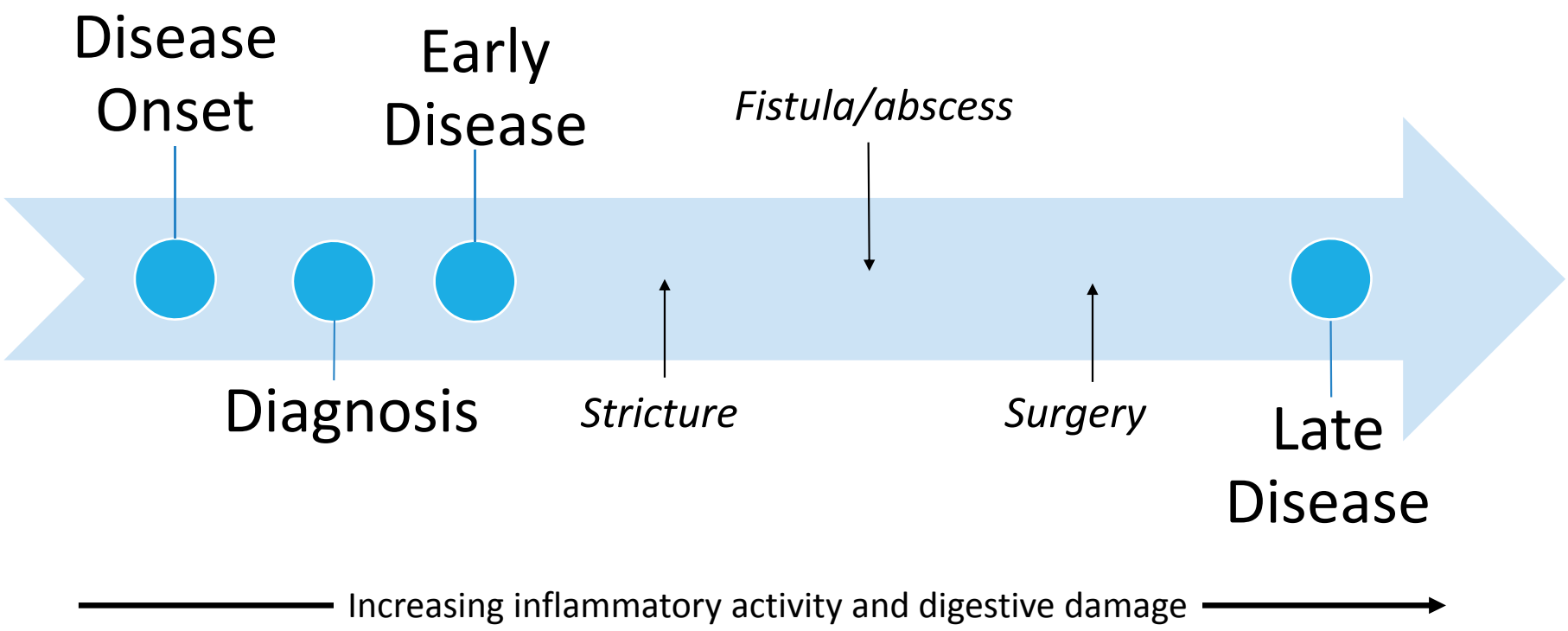
Progression of Disease (IBD)



Pariente B, Cosnes J, Danese S, et al. Development of the Crohn's disease digestive damage score, the Lémann score. Inflamm Bowel Dis. 2011 Jun;17(6):1415-22.

Symptoms of IBD

- Diarrhea
  - Stool may contain blood or mucus
  - Incontinence
  - Nocturnal awakenings
- Constipation
- Pain or rectal bleeding with bowel movement
- Severe bowel movement urgency
- Tenesmus

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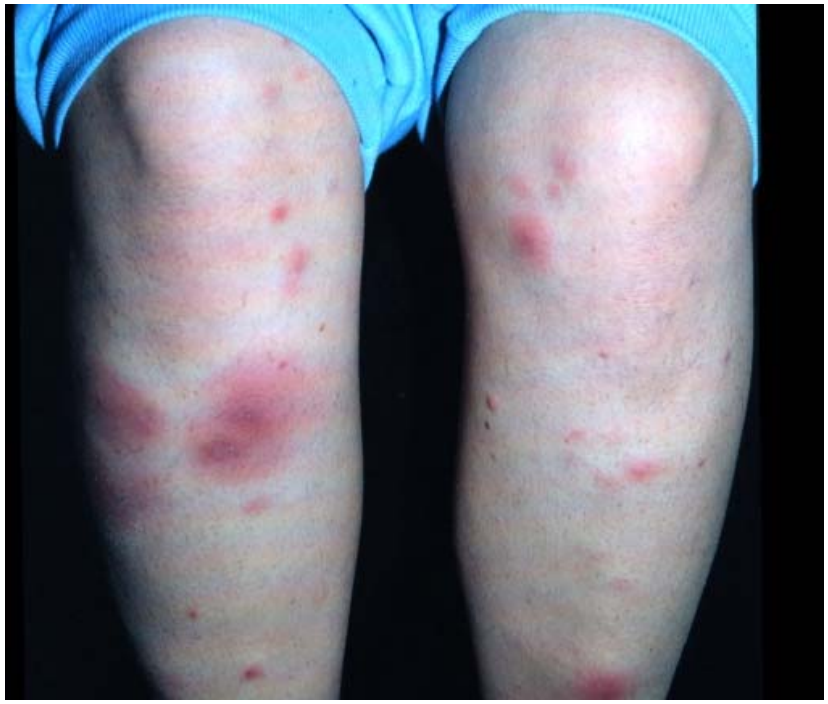
Signs and Symptoms Continued

- Fever
- Weight loss
- Loss of appetite
- Fatigue
- Extra-intestinal manifestations
  - Dermatologic disease
  - Ocular disease
  - Arthralgia



Erythema Nodosum

Bernstein CN, Fried M, Krabshuis JH, et al. World Gastroenterology Organization Practice Guidelines for the diagnosis and management of IBD in 2010.Inflamm Bowel Dis. 2010 Jan;16(1):112-24.

Laboratory Findings

Routine testing in IBD patients or those with concerning symptoms	Common findings in a disease flare
Complete Blood Count	↑ Platelets ↑ WBC ↓ Hemoglobin
Inflammatory markers	↑ ESR ↑ CRP/hs-CRP
Stool examination	Infectious diseases negative ↑ Calprotectin
Indicators for malabsorption	↓ Albumin ↓ Vitamin D ↓ Vitamin B12

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Clinical Characteristics

Characteristics	Crohn's Disease	Ulcerative Colitis
Location of bowel involvement	Mouth to anus	Rectum/Colon
Inflammation pattern	Patchy	Continuous
Depth of disease	Submucosa or deeper	Superficial mucosa
Histology	Granulomas	Crypt abscesses
Stricture, fistula, perforation	Yes	No
Colorectal cancer	Uncommon	Yes

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His laboratory work is notable for the following:

Hemoglobin	Platelets	CRP	Temperature
9.0 g/dL	700 cells/mm^3	17 mmol/L	100.1^o Fahrenheit

This patient is referred to a gastroenterologist. Which clinical findings would you expect to find upon further workup?

A. Colonoscopy will show no inflammation, pathology will be normal, markers of malabsorption will be normal

B. Colonoscopy will show inflammation, pathology will be normal, markers of malabsorption will be normal

C. Colonoscopy will show inflammation, pathology will show evidence of disease, fecal calprotectin will be elevated, markers of malabsorption will be low

D. Colonoscopy will show no inflammation, infectious workup will be positive for CMV colitis

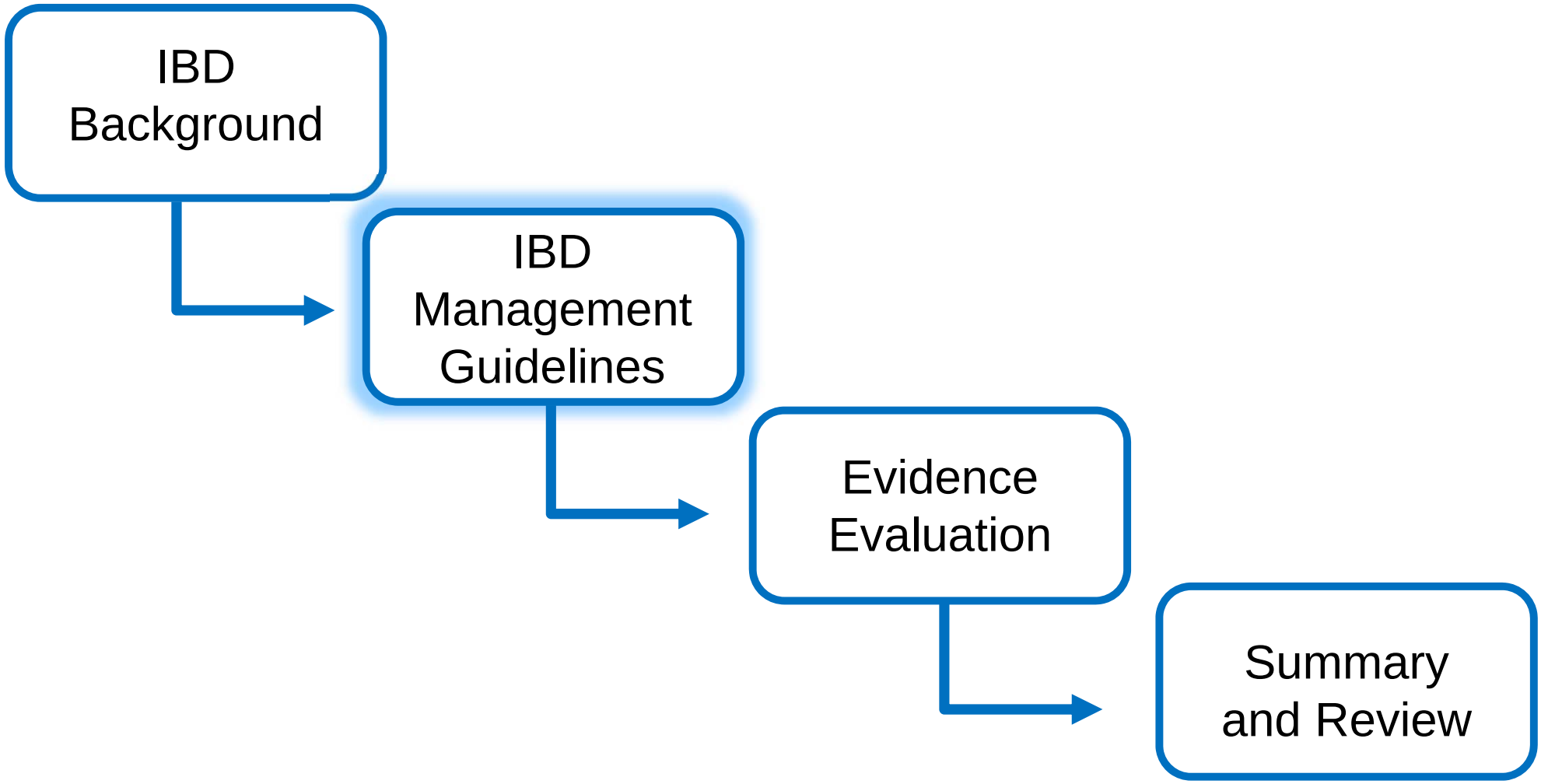
Which signs and symptoms does KS exhibit that are concerning for IBD rather than IBS?

A. Fatigue, weight gain, increased number of bowel movements

B. Erythema nodosum, blood in stool, weight loss, and arthralgia

C. Normal temperature, fatigue, increased number of bowel movements

D. Increased number of bowel movements, bowel movement urgency and fatigue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IBD Guidelines

- American College of Gastroenterology
  - Management of Crohn's Disease in Adults (2018)
  - Ulcerative Colitis in Adults (2010)
  - Preventative Care in Inflammatory Bowel Disease (2017)
- American Gastroenterological Association
  - Therapeutic Drug Monitoring 2017
- World Gastroenterology Organization Guidelines 2010

Gary R. Lichtenstein, Edward V. Loftus, Kim L. Isaacs, et al. American College of Gastroenterology. Management of Crohn's Disease in Adults. *Am J Gastroenterol* 2018; 113:481–517
Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010 Mar;105(3).
Feuerstein JD, Nguyen GC, Kupfer SS, et al; American Gastroenterological Association Institute Clinical Guidelines Committee. AGA Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroenterology. 2017 Sep;153(3):827-834.

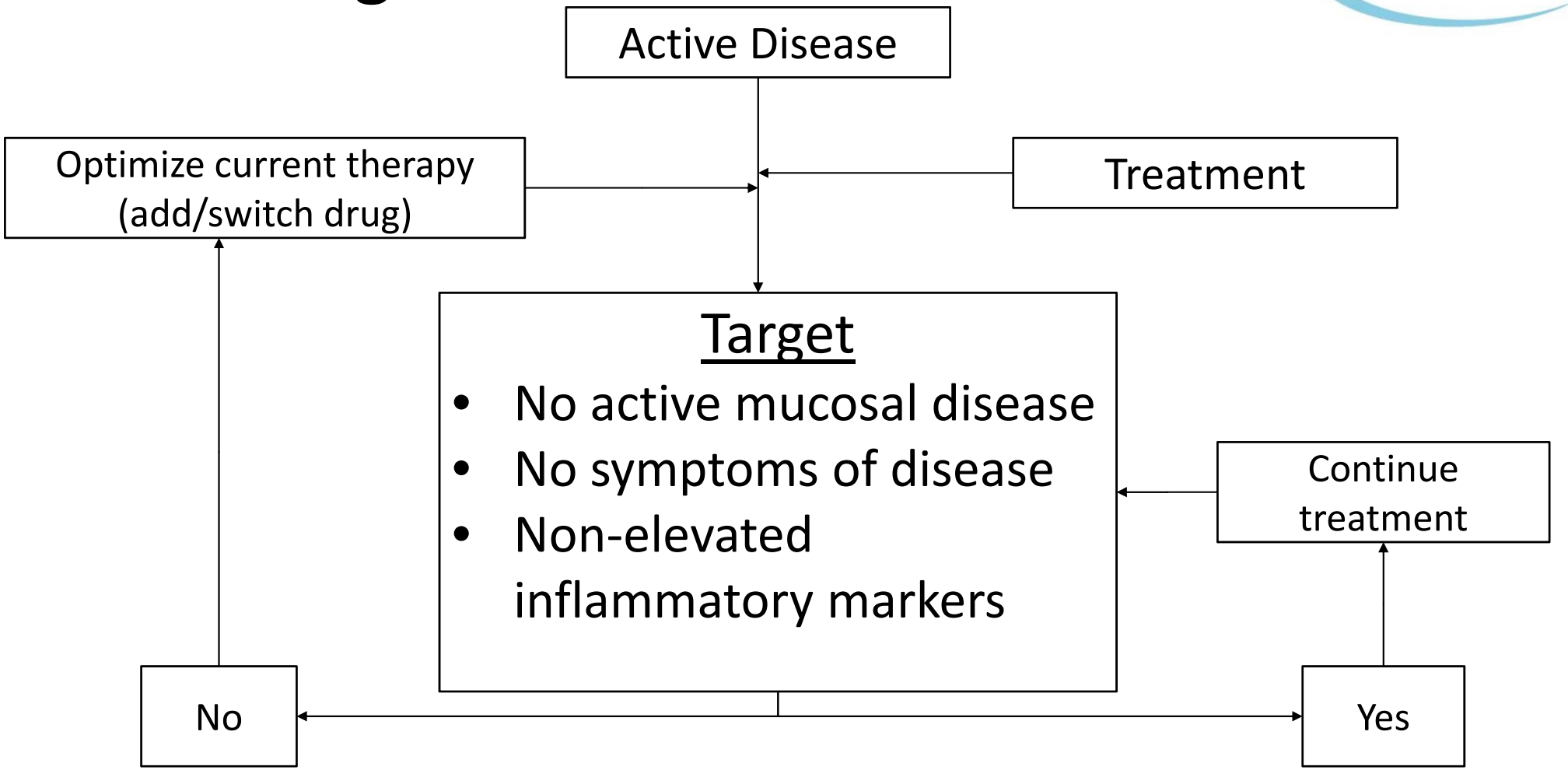
Goals of Therapy

Treat to Target

- Optimize quality of life
- Treat acute disease & obtain mucosal healing
- Maintain steroid free remissions
- Prevent hospitalizations and surgery
- Maintain adequate nutritional status

Gary R. Lichtenstein, Edward V. Loftus, Kim L. Isaacs, et al. American College of Gastroenterology. Management of Crohn's Disease in Adults. *Am J Gastroenterol* 2018; 113:481–517
Bouguen G, Levesque BG, Pola S, et al. Endoscopic assessment and treating to target increase the likelihood of mucosal healing in patients with Crohn's disease. Clin Gastroenterol Hepatol. 2014 Jun;12(6):978-85.

Treat to Target



Bouguen G, Levesque BG, Pola S, et al. Endoscopic assessment and treating to target increase the likelihood of mucosal healing in patients with Crohn's disease. Clin Gastroenterol Hepatol. 2014 Jun;12(6):978-85.

Treat to Target

How might the goals of therapy be different for these two patients?

Considerations for Therapy Management

- Severity of disease
- Location of disease
- Comorbidities
- Medication specific considerations
  - Onset of action
  - Efficacy
  - Adverse effects
  - Formulation (Topical, Parenteral, Oral)
  - Cost

Gary R. Lichtenstein, Edward V. Loftus, Kim L. Isaacs, et al. American College of Gastroenterology. Management of Crohn's Disease in Adults. *Am J Gastroenterol* 2018; 113:481–517
Hemstreet, BA .Chapter 21. Inflammatory Bowel Disease. In: DiPiro J.T., Talbert R.L., Yee G.C., Matzke G.R., Wells B.G., Posey L Eds. *Pharmacotherapy: A Pathophysiologic Approach, 9e* New York, NY: McGraw-Hill; 2014.

Drug Therapies

- Corticosteroids
- Aminosalicylates
- Immunomodulators
- Biologics
- Small molecule

Hemstreet, BA .Chapter 21. Inflammatory Bowel Disease. In: DiPiro J.T., Talbert R.L., Yee G.C., Matzke G.R., Wells B.G., Posey L Eds. *Pharmacotherapy: A Pathophysiologic Approach, 9e* New York, NY: McGraw-Hill; 2014.

Mild to Moderate Disease Severity

Crohn's Disease

- Aminosalicylate
  - Topical and oral (if disease involves the colon or distal ileum)
- Corticosteroids
  - Budesonide
  - Prednisone
- Antibiotics

Ulcerative Colitis

- Aminosalicylate
  - Topical and oral
- Corticosteroids
  - Budesonide or hydrocortisone enema
  - Prednisone

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Moderate to Severe Disease Severity

Crohn's Disease

- Oral corticosteroid, IV corticosteroid
- Thiopurine/Methotrexate
- Biologic therapy
- Surgery

Ulcerative Colitis

- Oral corticosteroid, IV corticosteroid
- Thiopurine
- Biologic therapy
- Small molecule therapy
- Surgery

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Corticosteroids

- Anti-inflammatory
- Used for induction of remission, not for maintenance
- Common adverse effects
  - Osteoporosis, infection, hyperglycemia, weight gain, etc.

Oral Formulations	**Rectal Formulations (foam, enema, suppository)**
Prednisone, prednisolone, dexamethasone, budesonide (Entocort, Uceris)	Suppository: Hydrocortisone Enema: Hydrocortisone Rectal foam: Hydrocortisone

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Aminosalicylates (5-ASA)

- Mechanism:
  - Largely unknown
  - Free radical scavenger
  - Inhibitor of tumor necrosis factor (TNF)
- Used as both maintenance and induction therapy
- Combination therapy (topical plus oral) is more effective than topical or oral monotherapy

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Aminosalicylates (5-ASA)

- Formulations:
  - Oral, suppository, and enema
- Adverse effects:
  - Headache, diarrhea, interstitial nephritis, rash, pancreatitis
- Monitoring:
  - Renal function, CBC

Hemstreet, BA .Chapter 21. Inflammatory Bowel Disease. In: DiPiro J.T., Talbert R.L., Yee G.C., Matzke G.R., Wells B.G., Posey L Eds. *Pharmacotherapy: A Pathophysiologic Approach, 9e* New York, NY: McGraw-Hill; 2014.

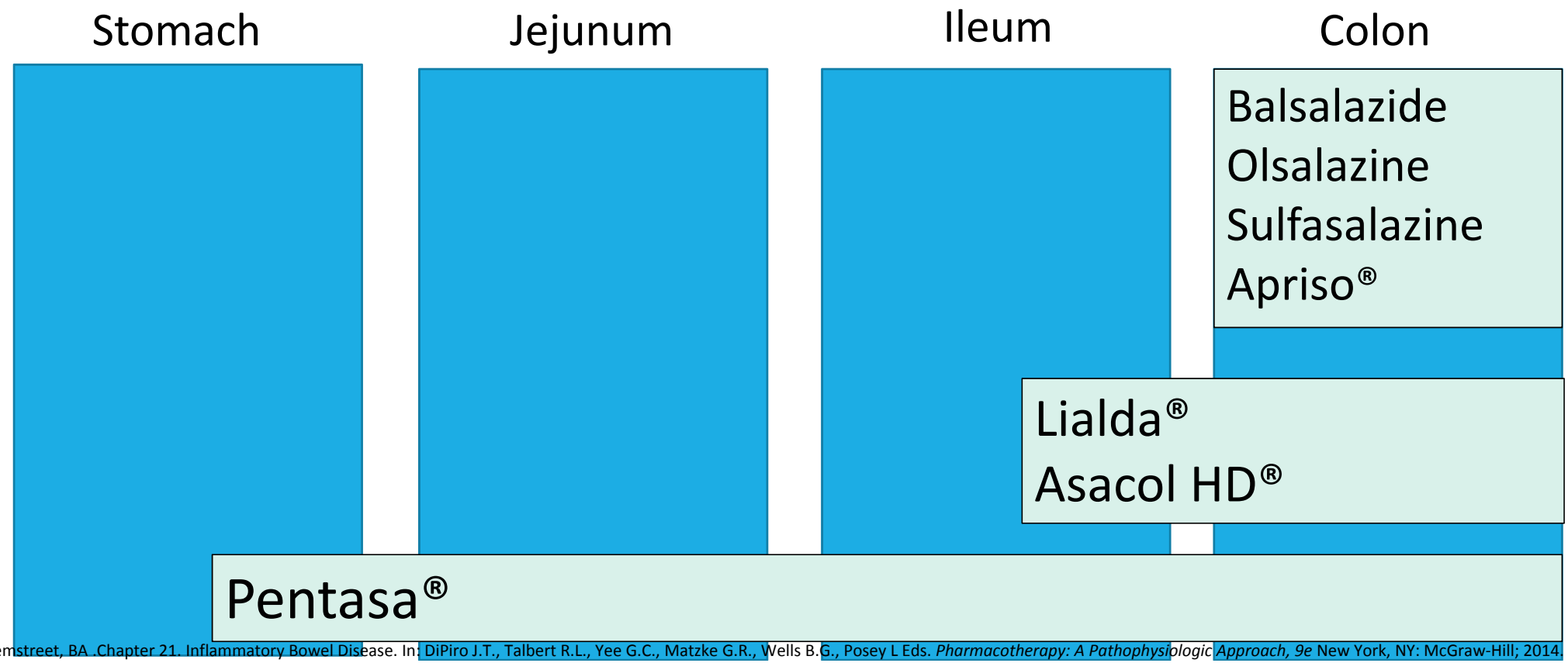
Aminosalicylates (5-ASA)

Mesalamine, Balsalazide, Sulfasalazine, Olsalazine

Azulfidine®	Apriso®	Asacol®	Asacol HD®	Colazal®
Dipentum®	Lialda®	Pentasa®	Rowasa® Enema	Canasa® Suppository

Hemstreet, BA .Chapter 21. Inflammatory Bowel Disease. In: DiPiro J.T., Talbert R.L., Yee G.C., Matzke G.R., Wells B.G., Posey L Eds. *Pharmacotherapy: A Pathophysiologic Approach, 9e* New York, NY: McGraw-Hill; 2014.

Aminosalicylates & Sites of Action



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Immunomodulators

- Thiopurines
  - Azathioprine, 6-mercaptopurine (6-MP)
- Methotrexate
- Calcineurin inhibitors

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Thiopurines (Azathioprine, 6-MP)

- Inhibit purine nucleotide synthesis and metabolism → suppresses T-cell activity
- Used as maintenance therapy
  - Onset 2 to 3 months
- Adverse effects:
  - Nausea, vomiting, leukopenia, thrombocytopenia, rash, arthralgia, non-melanoma skin cancer

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Methotrexate (MTX)

- Anti-folate → immune modulating and anti-inflammatory activity
- Dosing: Inject 25 mg by subcutaneous route once **weekly**
- Folic acid 1-2 mg/day should be administered in conjunction

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Methotrexate (MTX)

- Adverse effects:
  - Nausea, vomiting, thrombocytopenia, anorexia, headache/mind "fogginess", stomatitis, infection, methotrexate pneumonitis
- Monitoring:
  - CBC, renal function, LFTs (baseline, monthly, then every 2 to 3 months)
  - Chest X-ray, PFTs at baseline, then as clinically indicated (consider)

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Biologic Agents

Anti-TNFα agents

Infliximab (Remicade®)

Adalimumab (Humira®)

Certolizumab (Cimzia®)

Golimumab (Simponi®)

Anti-alpha 4- integrin

Natalizumab (Tysabri®)

Vedolizumab (Entyvio®)

Anti-IL 12, IL 23

Ustekinumab (Stelara®)

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Anti-TNF α agents – Maintenance Dosing

- Infliximab (Remicade®)
  - Infusion dosed every 8 weeks
- Adalimumab (Humira®)
  - Prefilled syringe and pen dosed every 2 weeks
- Certolizumab (Cimzia®)
  - Crohn's only
  - Prefilled syringe or vial for SQ administration dosed every 2 to 4 weeks
- Golimumab (Simponi®)
  - Ulcerative colitis only
  - Prefilled syringe, pen, and IV solution dosed every 4 weeks

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Anti-TNFα agents

- Mechanism: Reduce inflammatory response due to TNFα by inducing apoptosis of TNFα containing cells
- Adverse effects:
  - Increase risk of infection (screen for TB and viral hepatitis)
  - Increase risk of heart failure and/or exacerbation
  - Antibody formation and infusion reactions (infliximab)
- Onset of action: Days to weeks

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Anti-TNF α agents – Therapeutic Drug Monitoring

- Immunogenicity
  - Infliximab > adalimumab > golimumab > certolizumab
  - Prevention:
    - SONIC and COMMIT studies
    - Combine therapy with azathioprine, mercaptopurine, or methotrexate
- Proactive vs reactive therapeutic drug monitoring
  - AGA Therapeutic Drug Monitoring Guidelines (2017) currently prefers reactive monitoring

Feuerstein JD, Nguyen GC, Kupfer SS, et al; American Gastroenterological Association Institute Clinical Guidelines Committee. AGA Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroenterology. 2017 Sep;153(3):827-834

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Anti-TNF α agents – Therapeutic Drug Monitoring

Drug	Suggested trough concentration mcg/mL
Infliximab	≥5
Adalimumab	≥7.5
Certolizumab	≥20
Golimumab	Unknown

Anti-alpha 4- integrin

- Vedolizumab (Entyvio®)
  - Given as an infusion every 8 weeks (maintenance dosing)
  - Adverse effects
    - Nausea, arthralgia, anaphylaxis, hepatitis, tuberculosis
  - Onset of action: 3 to 6 months
  - Monitoring: HBV and TB screening prior to initiation, signs of progressive multifocal leukoencephalopathy (PML) or infection
- Natalizumab (Tysabri®)
  - Used rarely due to higher risk of PML

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Biosimilar Agents

- Similar in molecular structure, but not an exact match with the original reference product
- Biosimilar agents are not interchangeable
- FDA approved biosimilar agents:
  - Infliximab-**dyyb** (Inflectra®)
  - Adalimumab-**atto** (Amjevita®)

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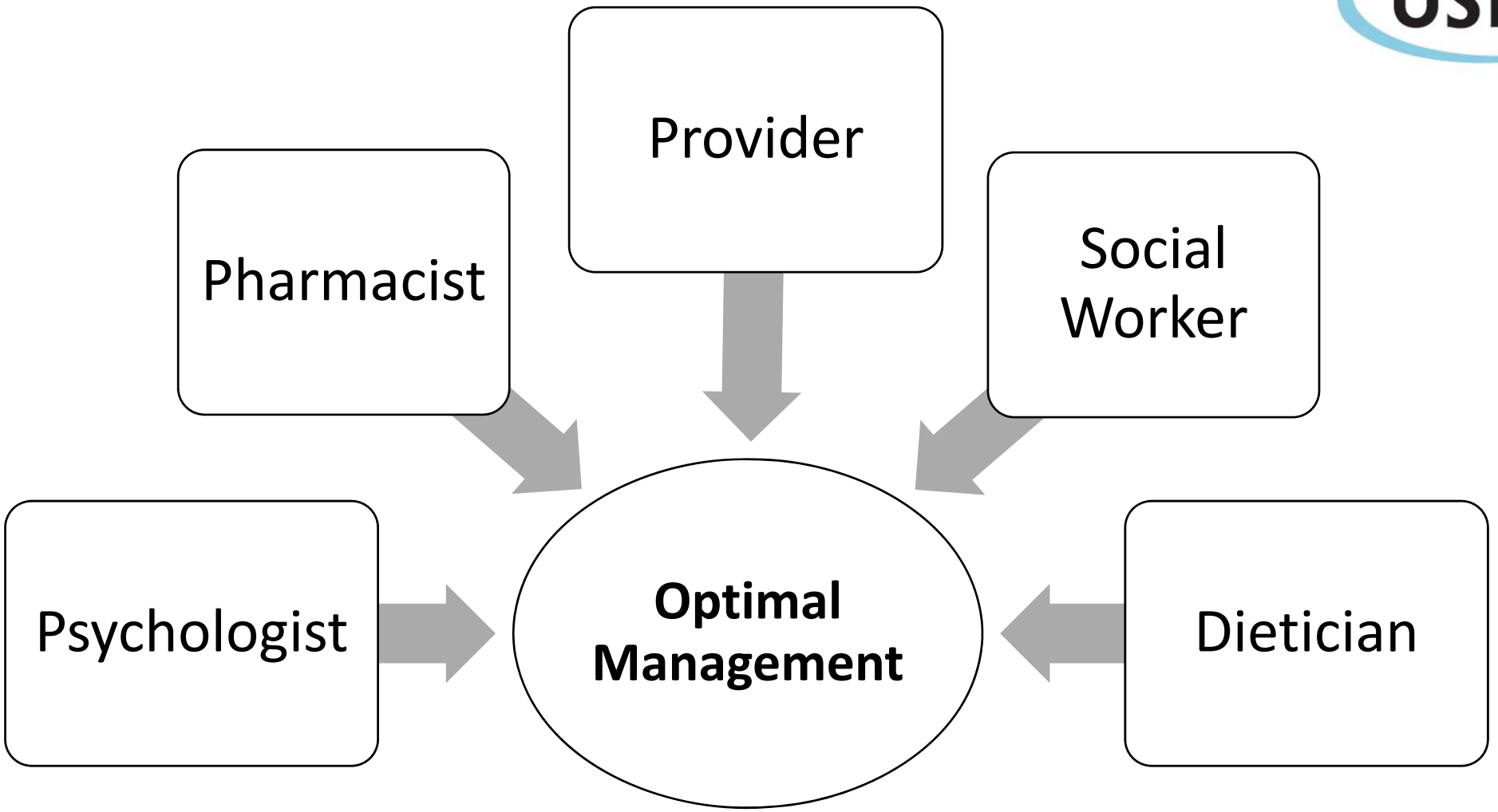
Small molecule – Tofacitinib (Xeljanz®)

- Mechanism: Inhibits Janus kinase (JAK) enzymes, preventing cytokine expression and immune cell activity
- Dose: 10 mg PO twice daily for ≥8 weeks followed by 5 or 10 mg twice daily
- Adverse effects: Infection, hypertension, rash, diarrhea, herpes zoster, lymphocytopenia, anemia, transaminitis, non-melanoma skin cancer
- Monitoring: CBC, LFTs, viral hepatitis, skin examination



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Optimal Management

- Smoking cessation
  - Crohn's disease: Beneficial for disease state
  - Ulcerative colitis: Associated with disease flare, but still recommended
- Vaccination
  - Some patients eligible for vaccines given to those receiving "iatrogenic immunosuppression" per CDC recommendations
  - Give prior to immunosuppressive therapies if possible

Medication Access

- Financial
  - Patient assistance programs: www.needymeds.org
  - Copay cards from the manufacturer
  - Websites such as GoodRx.com
- Access
  - Help facilitate delivery of specialty medications
  - Help patients maintain adherence to therapies to continue eligibility for medication coverage

Which of the following therapies reduces inflammation by inhibiting the activity of TNF- α?

A. Adalimumab

B. Vedolizumab

C. Ustekinumab

D. Methotrexate

Patient Case

KS, a 26 year old male, presents to his primary care physician with complaints of fatigue, frequent bowel movements (10-15 times per day) with urgency and blood in his stool. He reports a 15 lb. weight loss over the last 2 months, which is approximately when the symptoms started. He complains of arthralgia and painful red nodules on his legs. He has no past medical history and is not taking any medications.

His laboratory work is notable for the following:

Hemoglobin	Platelets	CRP	Temperature
9.0 g/dL	700 cells/mm^3	17 mmol/L	100.1^o Fahrenheit

Patient Case

KS undergoes colonoscopy and the following is noted on pathology:

- Severe active colitis with marked crypt distortion affecting the left colon, right colon, and terminal ileum
- Focal, superficial acute inflammation
- Occasional crypt abscesses
- Attenuated surface epithelium suggestive of re-epithelialization of previously ulcerated areas

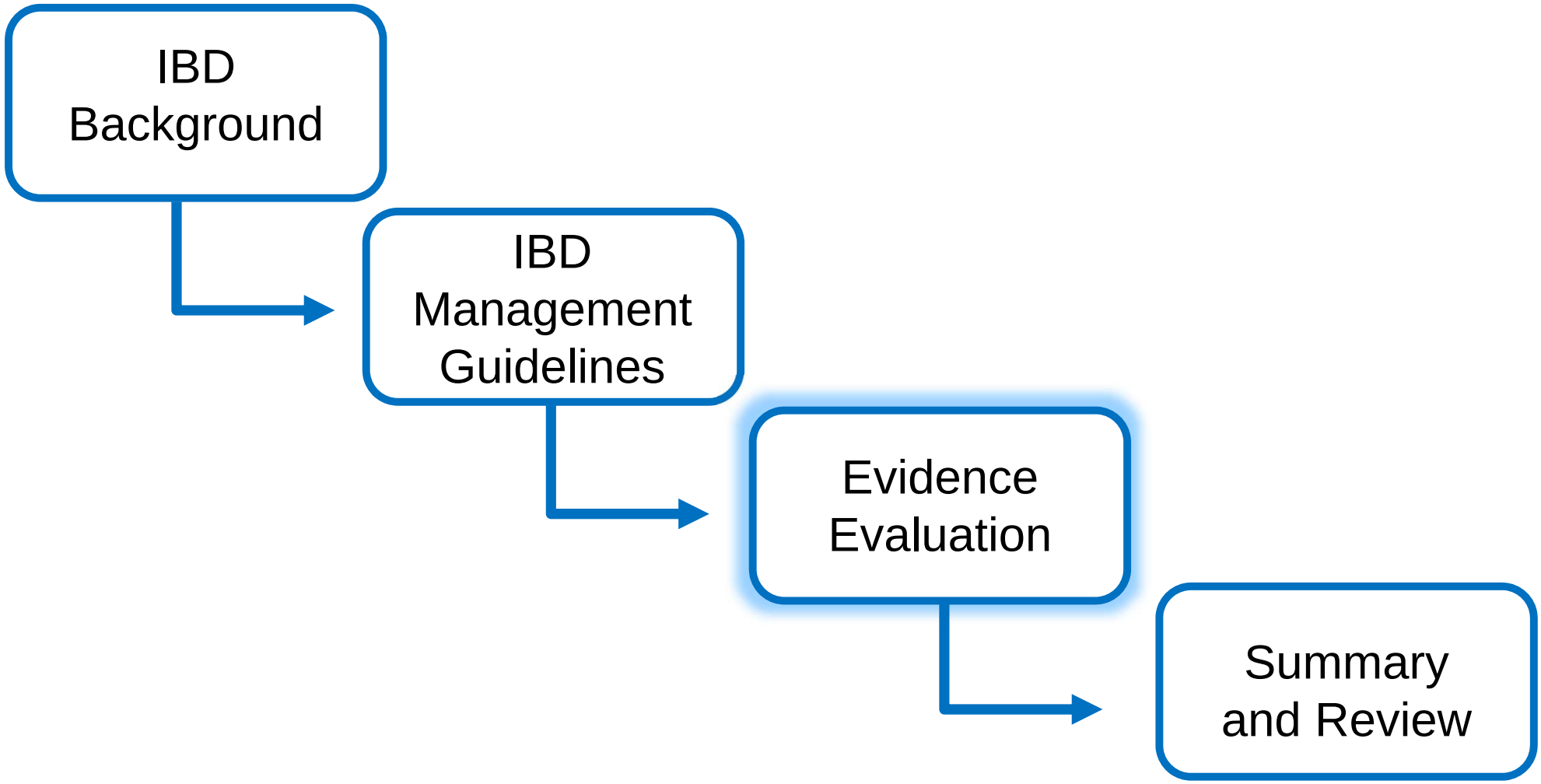
Which of the following therapy and monitoring plans would be appropriate for KS?

A. Azathioprine; CBC weekly for the first month

B. Infliximab plus oral prednisone; Rule out TB and HBV prior to initiation of infliximab

C. Oral prednisone plus rectal hydrocortisone; Blood glucose during therapy

D. Mesalamine (Pentasa®); CBC, Creatinine prior to and periodically during therapy


IBD Background
IBD Management Guidelines
Evidence Evaluation
Summary and Review

Tofacitinib (Xeljanz®) for Ulcerative Colitis

- Received FDA approval for moderate to severe ulcerative colitis on May 30, 2018
- Recommendation based on the OCTAVE studies
- First oral medication approved for use in moderate to severe active ulcerative colitis

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

Tofacitinib for Induction of Remission in Ulcerative Colitis: Systematic Review and Meta-Analysis

Annals of Gastroenterology. 2018 Sep-Oct; 31(5): 572–582.

Methods

- Systematic review and meta-analysis of randomized controlled trials
- Inclusion:
  - Mayo score 6 to 12
  - Endoscopic subscore $\geq$ 2 (moderate disease)
  - Previous therapy with mesalamine, corticosteroids, azathioprine/6-MP, or anti-TNF regimens
- Concomitant treatment allowed: Oral mesalamine and oral corticosteroids at a stable dose

Primary Outcome at 8 Weeks	Secondary Outcomes at 8 Weeks
Clinical remission: A total Mayo score of $\leq$2 points	Clinical response: A change in Mayo score from baseline $\geq$ 3 points & $\geq$ 30%)
	Mucosal healing
	Quality of life
	Safety endpoints

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

Mayo Score

- Range of score 0 to 12 (12 being most severe)
- All studies required a Mayo score of 6 to 12 on enrollment
- Clinical response defined based on a change in Mayo score from baseline of at least 3 points

Example of Mayo Score: Two Components

Stool Frequency	Rectal Bleeding
0 = Normal 1 = 1 to 2 stools/day more than normal 2 = 3 to 4 stools/day more than normal 3 = >4 stools/day more than normal	0 = None 1 = Visible blood with stool less than half the time 2 = Visible blood with stool half of the time or more 3 = Passing blood alone

Lewis JD, Chuai S, Nessel L, et al. Use of the Non-invasive Components of the Mayo Score to Assess Clinical Response in Ulcerative Colitis. *Inflammatory bowel diseases*. 2008;14(12):1660-1666. doi:10.1002/ibd.20520.

Baseline Characteristics – Sandborn 2012

	Tofacitinib 10 mg BID	Placebo
Number of patients	33	48
Males	64%	48%
Age (mean)	43.2 years	42.5 years
% of anti-TNF naïve patients	70%	69%
% of patients with concomitant treatment with steroids	58%	27%
Disease severity, Mayo score (mean ± STD)	8 ± 1.7	8.2 ± 1.6
% of patients with extensive colitis/pancolitis at baseline	42%	43%

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

Baseline Characteristics – OCTAVE 1

	Tofacitinib 10 mg BID	Placebo
Number of patients	476	122
Males	58%	63%
Age (mean)	41.3 years	41.8 years
% of anti-TNF naïve patients	53.4%	53.3%
% of patients with concomitant treatment with steroids	45%	47.5%
Disease severity, Mayo score (mean ± STD)	9.0 ± 1.4	9.1 ± 1.4
% of patients with extensive colitis/pancolitis at baseline	53.1%	54.1%

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

Baseline Characteristics – OCTAVE 2

	Tofacitinib 10 mg BID	Placebo
Number of patients	429	112
Males	60%	49%
Age (mean)	41.1 years	40.4 years
% of anti-TNF naïve patients	54.5%	58%
% of patients with concomitant treatment with steroids	46.2%	49.1%
Disease severity, Mayo score (median)	6	6.2
% of patients with extensive colitis/pancolitis at baseline	49.3%	50.5%

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

Results

Primary Outcome

Tofacitinib > placebo in inducing **clinical remission**

- (OR 3.84, 95% CI 2.29-6.44, I^2 41%)

Select Secondary Outcomes

Tofacitinib > placebo in achieving **clinical response**

- (OR 2.95, 95% CI 2.21-3.95, I^2 0%)

Tofacitinib > placebo in achieving **mucosal healing**

- (OR 2.70, 95% CI 1.81-4.03, I^2 0%)

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

Results Continued

- No significant differences in the safety profile (incidence of serious adverse events) between tofacitinib and placebo
- Study withdrawal due to adverse events similar between tofacitinib and placebo (OR 0.93, 95% CI 0.68-1.28, I^2 0%)
  - Most common reason for discontinuation of therapy was worsening of ulcerative colitis

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

Conclusion

- Tofacitinib is the first orally administered therapy indicated for the treatment of moderate to severe active ulcerative colitis
- Data from 3 randomized controlled trials support the efficacy and safety of tofacitinib
- Consider short term treatment with tofacitinib in patients with moderate to severe active ulcerative colitis

Paschos P, Katsoula A, Giouleme O, et al. Tofacitinib for induction of remission in ulcerative colitis: systematic review and meta-analysis. Ann Gastroenterol. 2018 Sep-Oct;31(5):572-582.

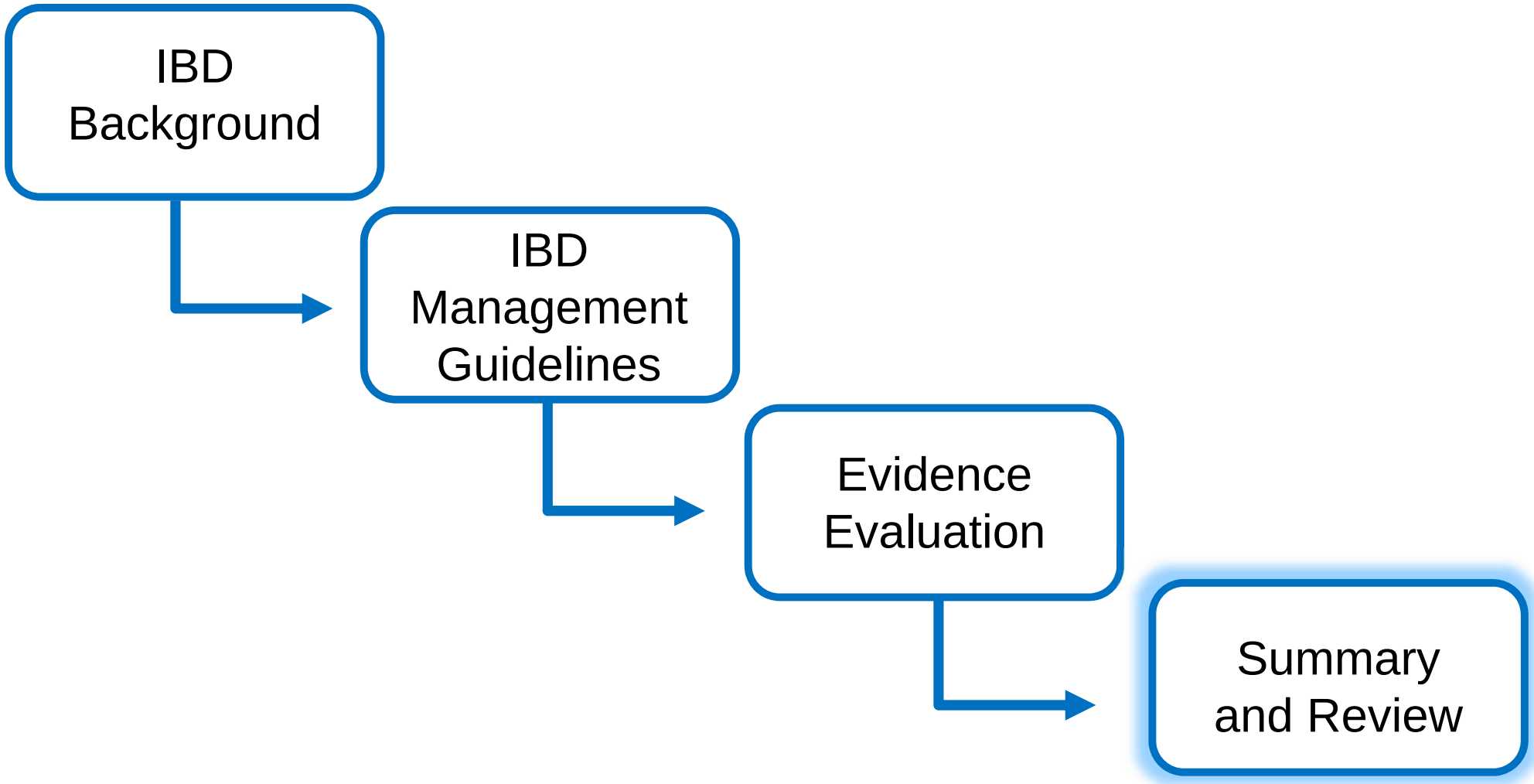
The systematic review and meta-analysis completed by Paschos and colleagues in 2018 enrolled patients with the following characteristics:

A. Crohn's disease, moderate to severe disease, with no history of TNF-α use

B. Ulcerative colitis, mild to moderate disease, with no history of corticosteroid use

C. Ulcerative colitis, moderate to severe disease, with Mayo scores of less than 6 at baseline

D. Ulcerative colitis, moderate to severe disease, with history of mesalamine, corticosteroids, azathioprine/6-MP, or anti-TNF regimens


IBD Background
IBD Management Guidelines
Evidence Evaluation
Summary and Review

Key Takeaways

- Multiple clinical guidelines are available for pharmacists to utilize when optimizing therapy for patients with IBD
- Pharmacologic agents used in the treatment of IBD often require close monitoring to ensure safe and effective therapy
- Pharmacists should work with the care team to create a patient specific “treat to target” plan in an effort to improve outcomes
- Both pharmacists and pharmacy technicians have a major role in ensuring accessibility and affordability of IBD therapies

What's the Scoop on the Poop?

Inflammatory Bowel Disease Update

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The World Gastroenterology Organization Practice Guidelines recommend which combination of therapies to prevent immunogenicity?

A. Tofacitinib plus methotrexate

B. Aminosalicylates plus oral corticosteroids

C. Infliximab plus azathioprine

D. Adalimumab plus topical corticosteroids

Which of the following is true?

A. Infliximab-dyyb (Remicade®) is the biosimilar to infliximab (Inflectra®)

B. Vedolizumab's brand name is Simponi®

C. Ustekinumab's brand name is Tysabri®

D. Adalimumab-atto (Amjevita®) is the biosimilar to adalimumab (Humira®)

A patient with IBD comes up to the pharmacy counter stating he is no longer able to afford his adalimumab (Humira®) due to losing his insurance coverage. He makes ~$30,000 per year. What is one suggestion you could make to help him overcome this financial barrier?

A. Connect the patient with a patient assistance program (if you have one). If not, ask the patient to follow up with his provider to apply for the Humira® patient assistance program found on www.needymeds.org.

B. Suggest that the patient receive adalimumab infusions via IV rather than injections

C. Give him a copay card to use for his next adalimumab refill

D. Suggest that the patient quit taking adalimumab since he is in remission

Patient Education Resources

- Crohn's Foundation: http://www.crohnscolitisfoundation.org/
- Mechanisms of Medicine: http://www.youandibd.com
- University of Michigan IBD School: http://www.med.umich.edu/ibd/school/index.html