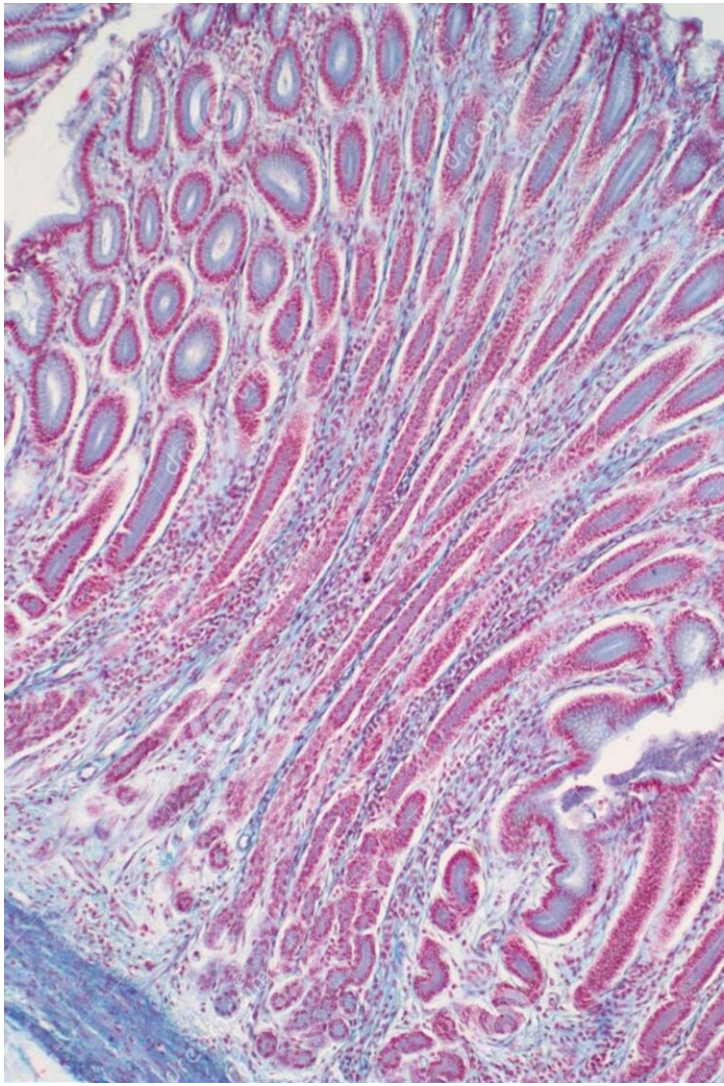
Microscopic Colitis:
A brief Update!

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Overview



REVIEW THE CLINICAL FEATURES AND EPIDEMIOLOGY OF MICROSCOPIC COLITIS



DIAGNOSTIC ISSUES



TREATMENT

Case presentation

- 65 F with chief complaint diarrhea
- Onset 10 wk ago, slowly progressive
- 3-5 watery BM/d, 1-2 over night
- Mild pain relieved after BM, mucus but no blood
- Has lost 4 kg

Predictors of MC vs. IBS

Older age

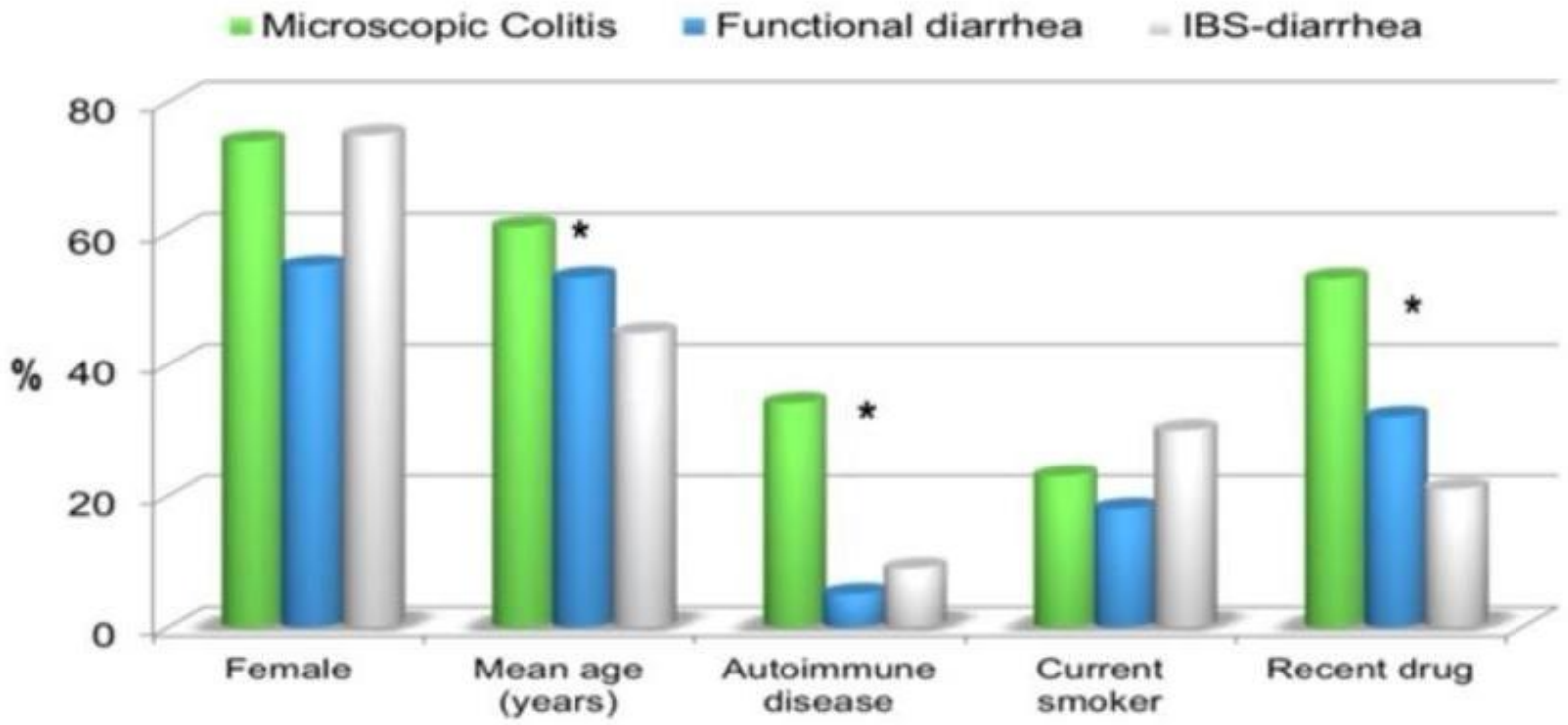
Female gender

Shorter duration of diarrhea

- 44-46% of patients with MC had less than 12 weeks of symptoms

1) Limsui IBD 2007 2) Abboud IBD 2013

Microscopic Colitis vs. Functional Diarrhea or IBS



Macaigne G, Am J Gastro 2014

In patients who have a colonoscopy for chronic diarrhea, 15%–30% will be diagnosed with MC.

EPIDEMIOLOGY

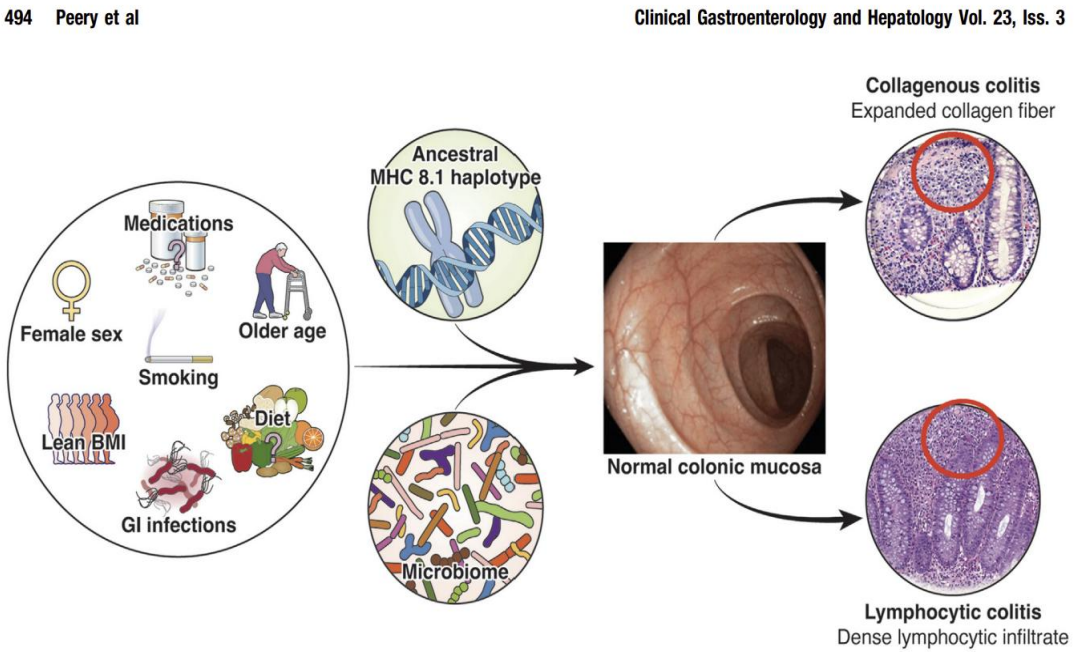
Incidence, Prevalence & Trends

25.8	246.2	0.9%
Per 100,000 person-years	Per 100,000 persons	Lifetime risk — women
Incidence (Europe & select US populations) populations)	Prevalence	Sweden; men: 0.4%

Incidence rose 1985–2001 (Olmsted County), then stabilized through 2019. Corroborated by European cohorts.

PATHOPHYSIOLOGY

Aberrant Immune Response in a Susceptible Host



Immune Cell Expansion

CD8+ infiltration; Th1/Th17 cells in lamina lamina propria; local lymphocyte proliferation proliferation (Ki67+, reduced TREC)

Genetic Susceptibility

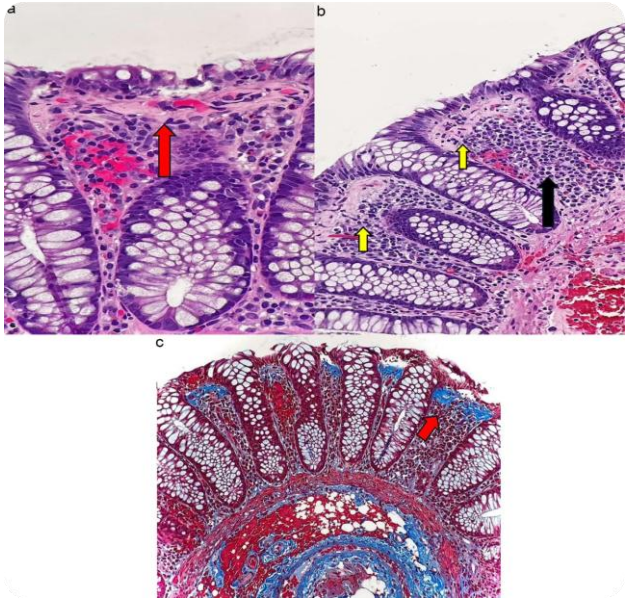
HLA Ancestral Haplotype 8.1 → collagenous colitis; polygenic pleiotropy with IBD

Microbiome & Bile Acids

Fecal stream diversion induces remission; FXR receptor downregulated; bile acid malabsorption in ~60%

OVERVIEW

What Is Microscopic Colitis?



- Very similar clinically and histologically
- Unclear if distinct or parts of a spectrum

Lymphocytic Colitis

≥20 intraepithelial lymphocytes / 100 epithelial cells

Collagenous Colitis

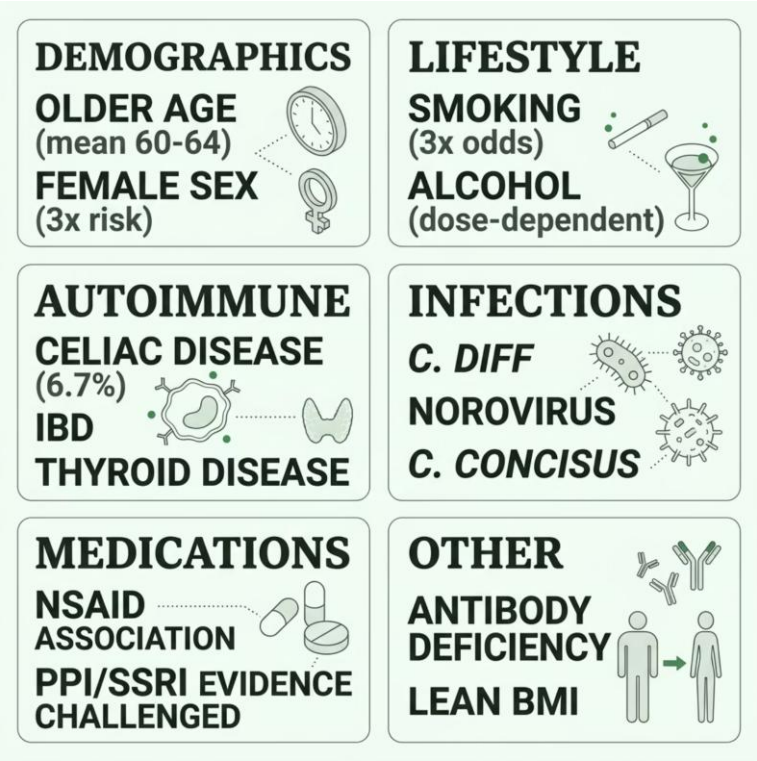
Subepithelial collagen band >10 µm

Key Symptoms

Chronic watery diarrhea, urgency, nocturnal BMs, incontinence, abdominal pain

RISK FACTORS

Who Develops Microscopic Colitis?



Key Epidemiologic Insights

- **Female sex:** 3× higher risk
- **Smoking:** 3× odds vs. non-smokers
- **Celiac disease:** 6.7% develop MC
- **GI infections:** Risk peaks Year 1, persists for years
- **Medications:** NSAID link retained; PPI/SSRI evidence challenged by recent controlled studies

checkpoint inhibitor–induced enterocolitis

Drug-induced Microscopic colitis

- High level evidence
  - acarbose, aspirin, NSAIDs, PPI, SSRI, ticlopidine
- Intermediate level evidence
  - carbamazepine, flutamide, lisinopril, simvastatin

Beaugerie and Pardi APT 2005

Drug-induced Microscopic colitis

- PPI + NSAID may increase risk even further

- Diarrhea persisting >3 mo after d/c or beginning after being on a drug for 1 year not likely due to that drug

Verhaegh, APT 2016

Clinical Features of Microscopic Colitis

- Chronic watery diarrhea
- Fecal urgency (93%)
- Fecal incontinence (68%)
- weight loss (65%), mild
- Nocturnal bowel movements (62%)
- Abdominal pain (52%)
- Fatigue is often reported and may be caused by sleep disturbance from nocturnal bowel movements.

1) Limsui IBD 2007 2) Madish World J Gastro 2005

Predicting MC in Chronic Diarrhea

- Age >50, female, PPI and NSAID use, weight loss, mild abdomen pain all a/w likelihood of MC on bx
  - High sensitivity but only modest specificity
- Clinical features alone cannot reliably distinguish MC from other causes of diarrhea

1) Kane Clin Gastro Hep 2015

The Natural History?

Promising.....significant risk for chronic symptoms.

40% of patients with MC had a relapsing or chronic disease course 5 years after diagnosis.

Slightly increased risk of death because of a greater burden of comorbidities.

Case…

- PMH: HTN, ↑cholesterol, GERD
- Meds: Olmesartan, simvastatin, omeprazole
- Denies aspirin, NSAID use
- FHx: No IBD, celiac , colon cancer

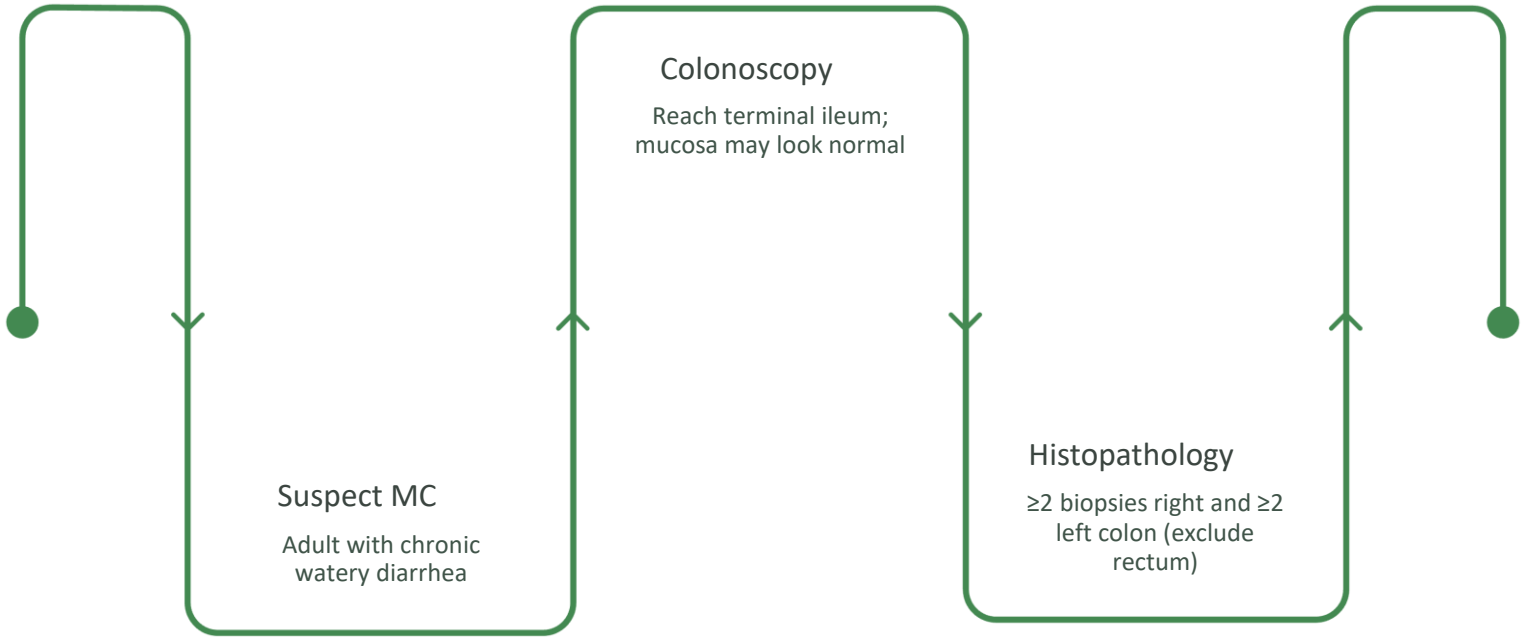
Case …

- Medications stopped for 6 weeks, no better
- Does she need a colonoscopy?
- Where to biopsy? How many biopsies?
- Right and left colon in separate bottles?

Diagnosis

DIAGNOSIS

Diagnosing Microscopic Colitis



No reliable blood or fecal biomarkers, including fecal calprotectin, to screen for MC.

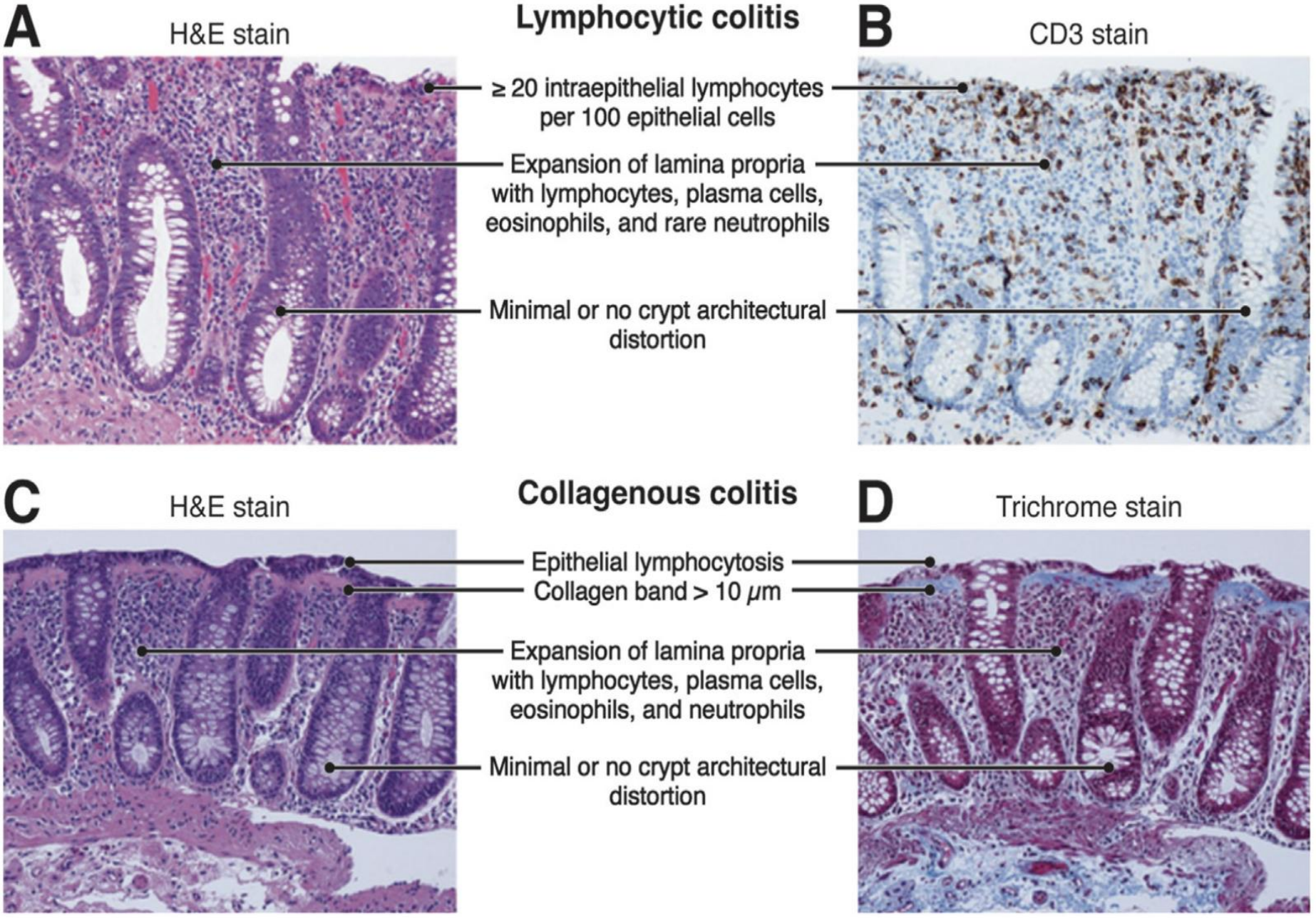
The colon mucosa most commonly appears normal;

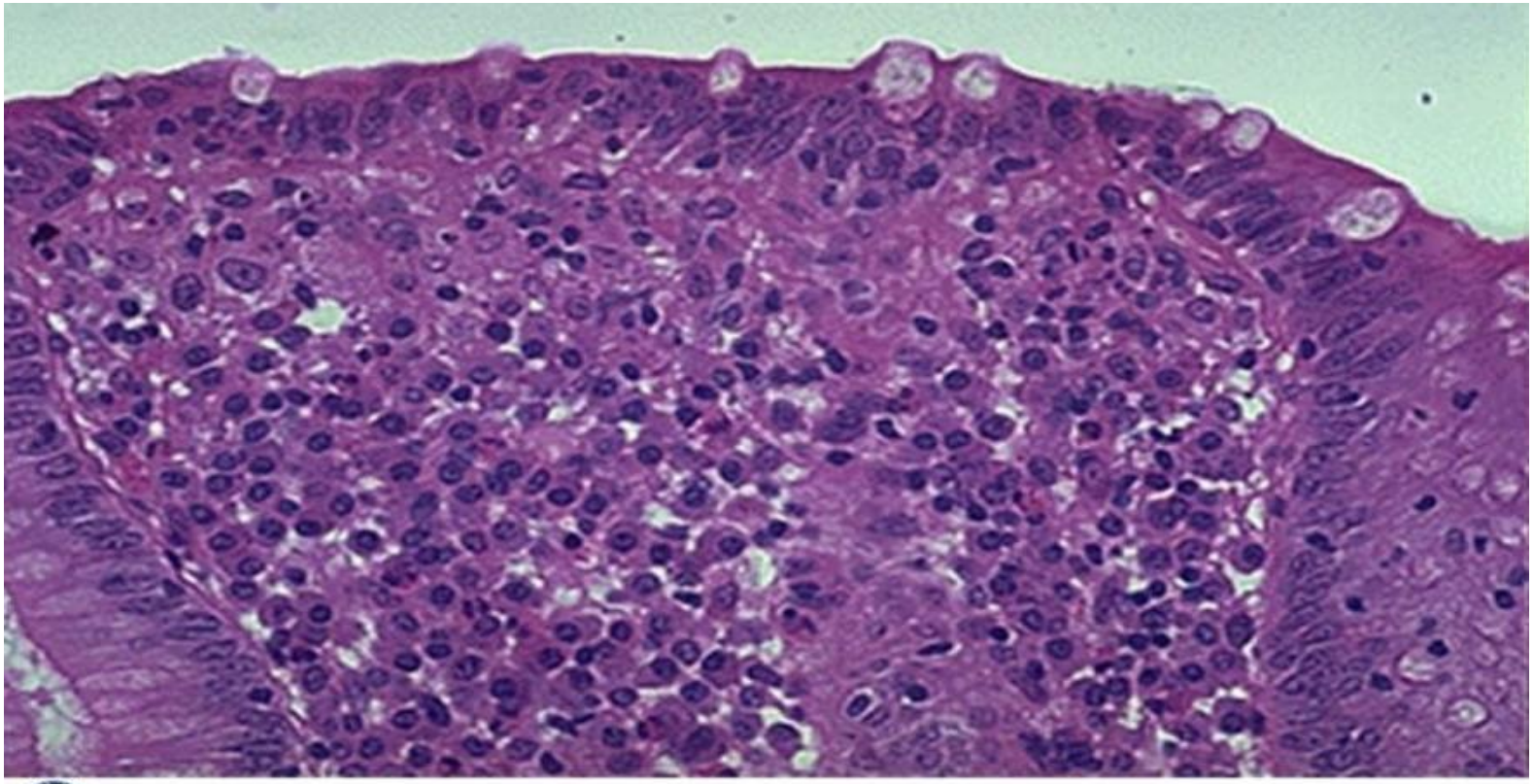
Macroscopic colonic findings can be seen in 17% of patients including erythema, erosions, scarring, and less commonly pseudo membranes, ulceration, or mucosal tears.

Diagnostic Questions

- Where to biopsy?
  - Histology may be patchy
  - Proximal to distal gradient
  - Recommend biopsies from multiple areas
- How many biopsies?
- Right and left colon in separate bottles?

The diagnosis requires histopathologic analysis of 2 biopsies from the right colon and 2 biopsies from the left colon, rectum excluded.


A
H&E stain
Lymphocytic colitis
B
CD3 stain
≥ 20 intraepithelial lymphocytes per 100 epithelial cells
Expansion of lamina propria with lymphocytes, plasma cells, eosinophils, and rare neutrophils
Minimal or no crypt architectural distortion
C
H&E stain
Collagenous colitis
D
Trichrome stain
Epithelial lymphocytosis
Collagen band > 10 μm
Expansion of lamina propria with lymphocytes, plasma cells, eosinophils, and neutrophils
Minimal or no crypt architectural distortion



Management

There is no evidence to suggest that the management of collagenous and lymphocytic colitis should be different, so the treatment approach outlined here applies to both subtypes.

There is a temporal association between starting a medication and the onset of diarrhea.

The first step in management …stopping culprit medications (mainly proton pump inhibitors, nonsteroidal anti-inflammatory drugs, and selective serotonin reuptake inhibitors) if an association is identified.

Longstanding medications with no temporal association should not be discontinued.

In addition, there is an association between smoking and MC, so smokers should be encouraged to stop

Response to treatment should be patient centered and symptom-based.
Treatment should improve patient's symptoms and quality of life.

<3 stools per day and <1 watery stool per day

It is not necessary to confirm histologic response to treatment.

TREATMENT

Standard Therapy: Budesonide

Induction:

9 mg/day × 8 weeks

Maintenance

3–6 mg/day (or qod)

84% remission rate

Relapse Rate

50–80% after discontinuation

Key Evidence

- Superior to placebo in multiple RCTs & RCTs & population cohorts
- Low systemic bioavailability (first-pass hepatic metabolism)
- No increase in steroid-related AEs on maintenance doses
- AGA recommends for maintenance after relapse
- Taper?

Points to Consider

- What to monitor for on long term budesonide?
  - Steroid related side effects
- What dose do you use?
  - Lowest effective dose
- Any special instructions?
  - Avoid grapefruit, Echinacea, P450 drugs
- Alternative treatments?

In some cases based on
symptom severity and patient preferences, antidiarrheal
medications, such as loperamide or bismuth subsalicylate (3 of
262-mg tablets 3 times a day for 6–8 weeks),

Maintenance therapy with bismuth
subsalicylate is not recommended because of potential
toxicity.

Bile acid sequestrants

Evidence to suggest these medications are effective, either as monotherapy or in combination with budesonide to decrease budesonide dependence.

Not recommended:

Mesalamine (no better than placebo)

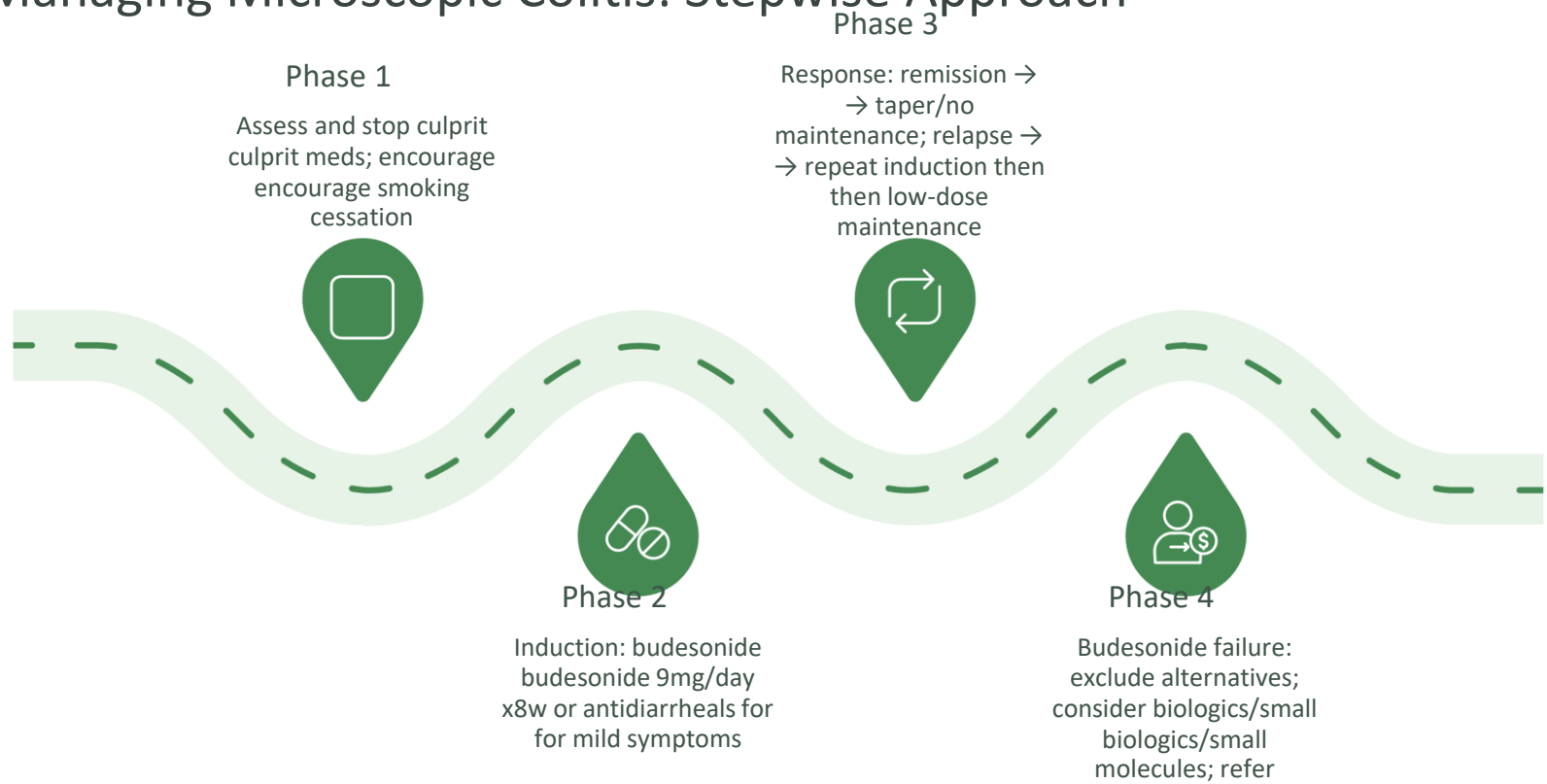
systemic corticosteroids (limited benefit, unfavorable risk)

Case ..

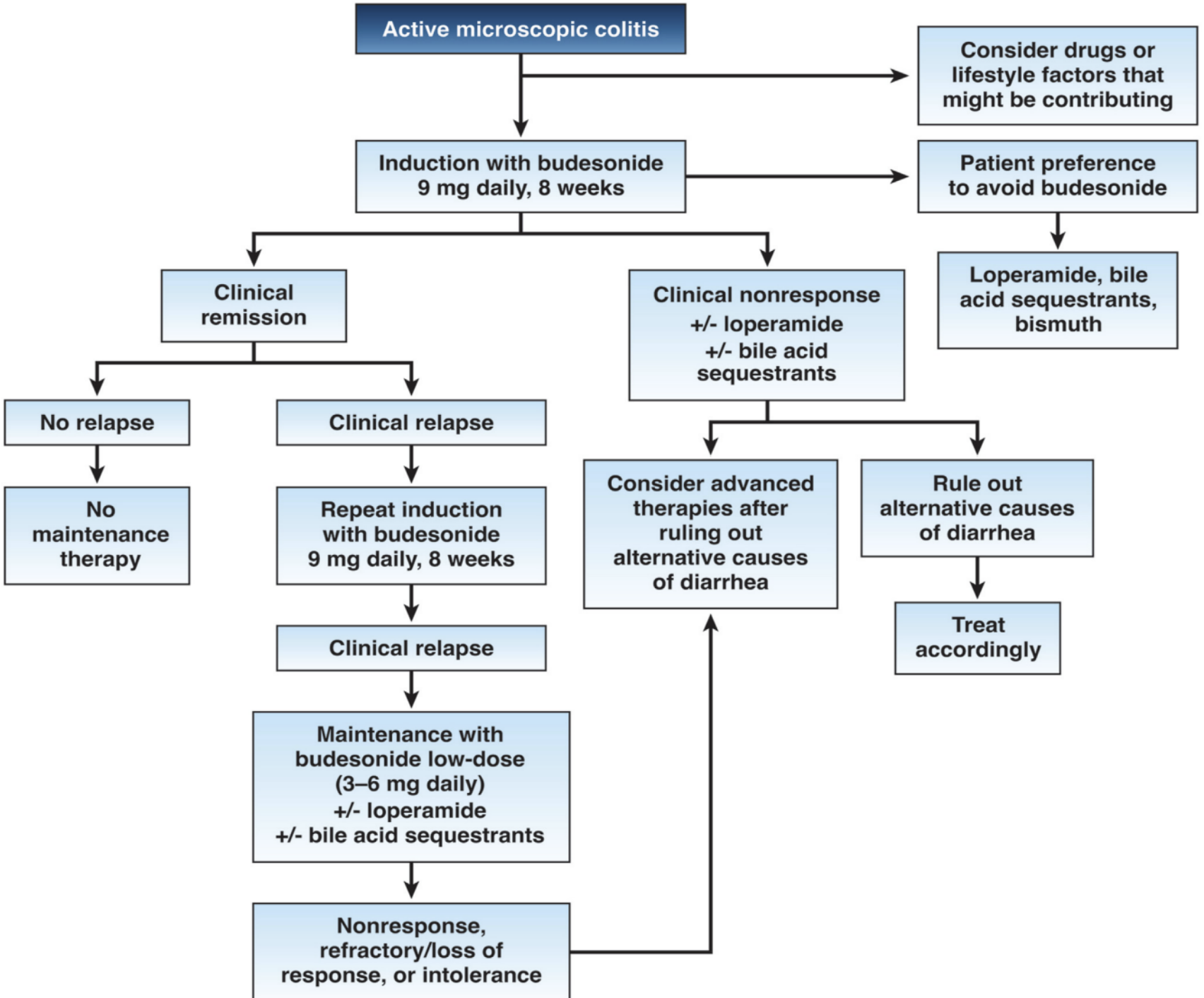
- Bismuth 3 TID for 6 weeks, no better
- Budesonide 9 mg/d, sx better after 4 days, resolved after 1 week
- D/C after 8 weeks
- 3 weeks later, symptoms return

TREATMENT ALGORITHM

Managing Microscopic Colitis: Stepwise Approach



Clinical remission target: **<3 stools/day and <1 watery stool/day** (Hjortswang criteria). Histologic confirmation of response is not required.


Active microscopic colitis
Consider drugs or lifestyle factors that might be contributing
Induction with budesonide 9 mg daily, 8 weeks
Patient preference to avoid budesonide
Loperamide, bile acid sequestrants, bismuth
Clinical remission
Clinical nonresponse +/- loperamide +/- bile acid sequestrants
No relapse
Clinical relapse
No maintenance therapy
Repeat induction with budesonide 9 mg daily, 8 weeks
Consider advanced therapies after ruling out alternative causes of diarrhea
Rule out alternative causes of diarrhea
Clinical relapse
Treat accordingly
Maintenance with budesonide low-dose (3–6 mg daily) +/- loperamide +/- bile acid sequestrants
Nonresponse, refractory/loss of response, or intolerance

ADVANCED THERAPIES

Budesonide-Refractory Disease

When to Escalate

Nonresponse

Persistent activity despite 9 mg induction

Refractory / Loss of Response

Activity on 3–6 mg maintenance

Intolerance

Unacceptable budesonide side effects

Biologic & Small Molecule Data

Agent	Induction Remission	Maintenance Remission
Vedolizumab	63.5%	65.9%
Infliximab	57.8%	45.3%
Adalimumab	39.3%	32.5%
JAK Inhibitors	Promising	–

Refer to IBD center for severe or refractory cases. Rule out celiac disease, IBD, and antibody deficiency first.

Points to Consider

- What is going on?
- Does she need repeat colonoscopy with biopsies?
- Treatment?

- Clinical response and normal QOL

Table 1. Key Considerations for Diagnosing and Managing Microscopic Colitis

Microscopic colitis should be considered in the differential for all adults with chronic, watery diarrhea.
Several autoimmune diseases and select gastrointestinal infections are risk factors for developing microscopic colitis.
Immune checkpoint inhibitors can induce a type of microscopic colitis that may be more severe and may require different treatment.
Microscopic colitis can be misdiagnosed as irritable bowel syndrome.
Microscopic colitis cannot be ruled out with blood or fecal biomarkers, including fecal calprotectin.
The diagnosis requires histopathologic analysis of $\geq$ 2 biopsies from the right colon and $\geq$ 2 biopsies from the left colon, rectum excluded.
Smoking cessation should be encouraged.
Stop a medication only if a clear temporal relationship with medication exposure and diarrhea onset. Long-standing medications with no association should not be discontinued.
In patients who report experiencing subjectively mild symptoms, antidiarrheal medications, such as loperamide, bismuth subsalicylate, or bile acid sequestrants, may be sufficient.

Mesalamine and systemic corticosteroids are not recommended as a treatment in microscopic colitis.
The primary treatment for inducing clinical remission in microscopic colitis is budesonide.
Maintenance therapy is often necessary for microscopic colitis.
After induction, most patients can be maintained on lower doses of budesonide, often as low as 3 mg per day or every other day.
To decrease budesonide dependence, loperamide or bile acid sequestrants can be used as adjuvant therapy.
Maintenance therapy with bismuth subsalicylate is not recommended.
Treatment should improve patient's symptoms and quality of life. Some have suggested that clinical remission be defined as a mean of <3 stools per day and <1 watery stool per day.
Budesonide failure is uncommon and requires further investigation. In cases with a remote diagnosis, repeat colonoscopy should be performed to confirm the diagnosis. Alternative diagnoses (celiac disease, ulcerative colitis, and Crohn's disease) should be ruled out. Antibody deficiency should be considered in younger patients.
Therapies reserved for ulcerative colitis and Crohn's disease (biologics and small molecules) are a treatment option for patients who fail budesonide. Consultation with an inflammatory bowel disease center is advised for patients who fail budesonide.

CONCLUSIONS

Key Takeaways & Unmet Needs



Noninvasive Biomarkers

No validated blood or fecal marker — unmet diagnostic need



Pathophysiology

Immune-microbiome interactions remain poorly defined



Budesonide-Refractory MC

Novel therapies needed; biologics show promise but lack approval



Patient-Centered Goals

Treat to symptom relief and quality of life — not histology