Psychiatric Disorders in Gastrointestinal Disease

September, 2026

BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

Disclosures

- I have no conflicts of interest to disclose

Objectives

- Describe the intestinal microbiome and the gut-brain-microbiome axis and their role in the pathogenesis of psychiatric disorders in gastrointestinal disease
- Discuss psychiatric disorders in common disorders of gut brain interaction (DGBI- formerly functional disorders) and Inflammatory Bowel Disease (IBD)
- Consider treatment approaches and areas of emerging research for patients with gastrointestinal and psychiatric disorders

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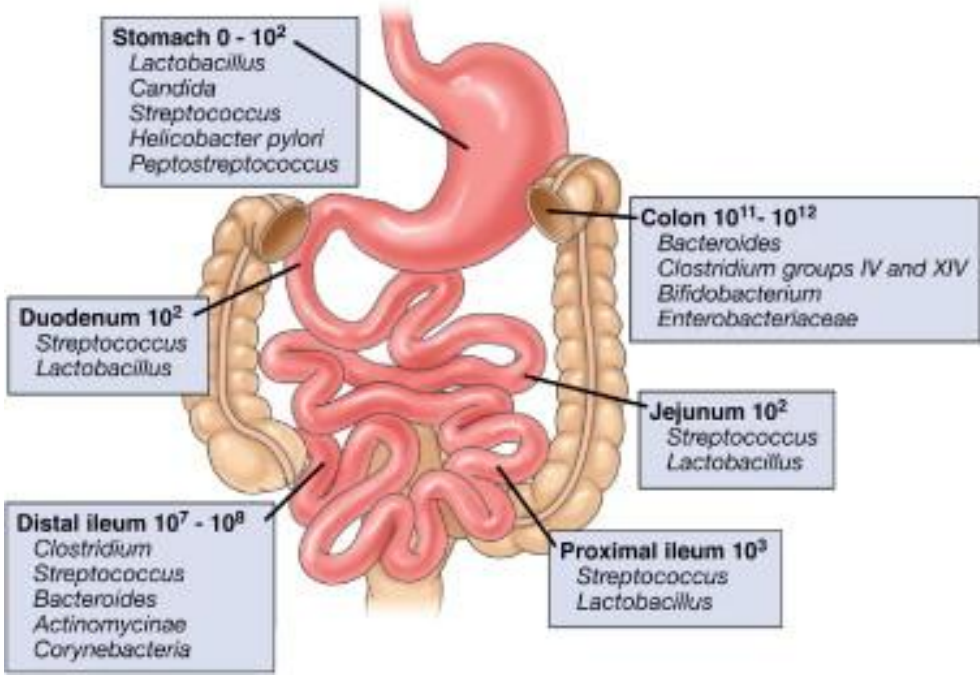
- Research focus: Psychiatric disorders in IBD, healthcare worker burnout, digital health

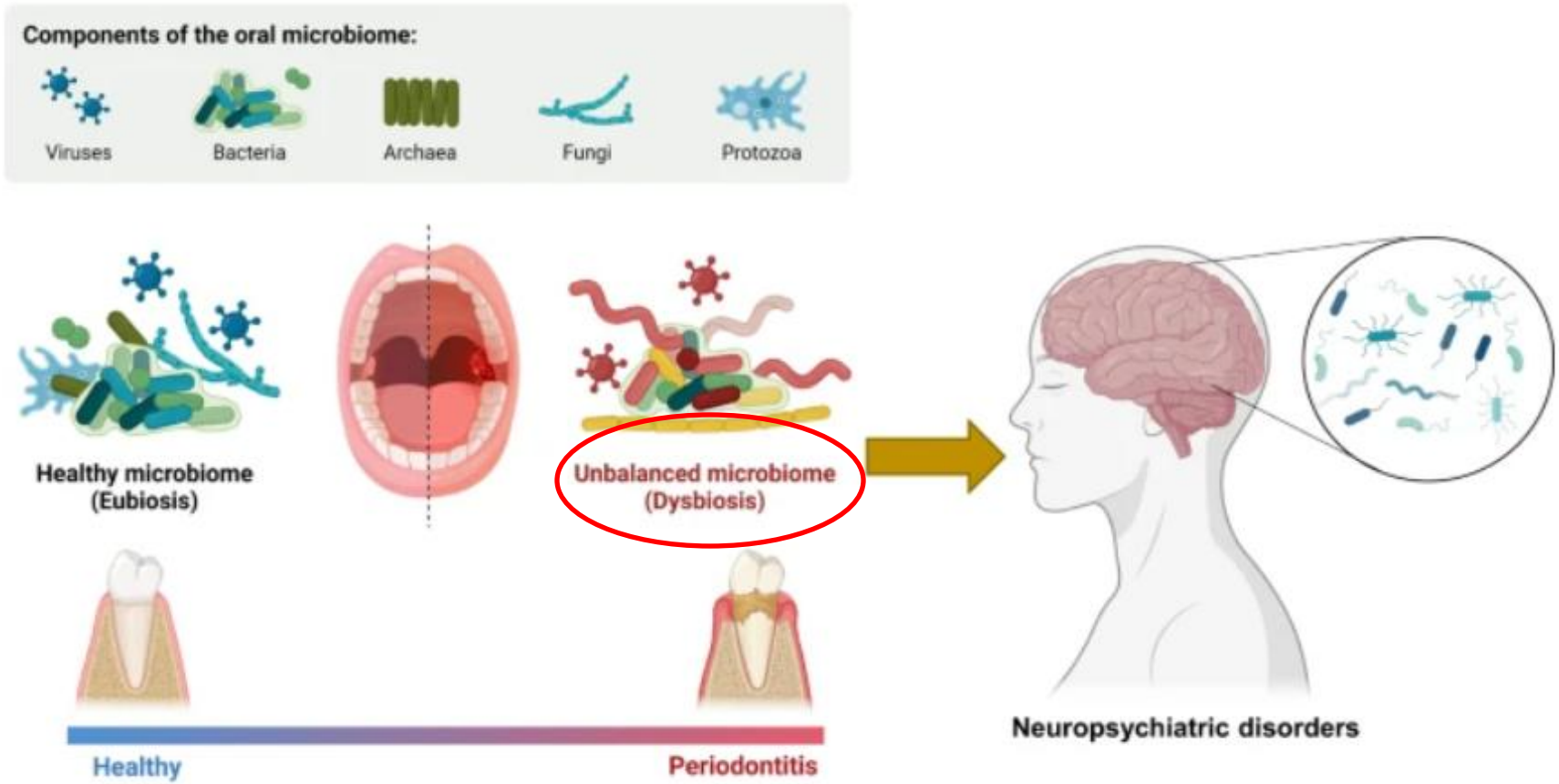
Intestinal Microbiome

- Bacteria colonize the gut in early post-natum
- Affect the immune system, key nutrients and energy metabolism
- Change in response to environmental and developmental factors in disease



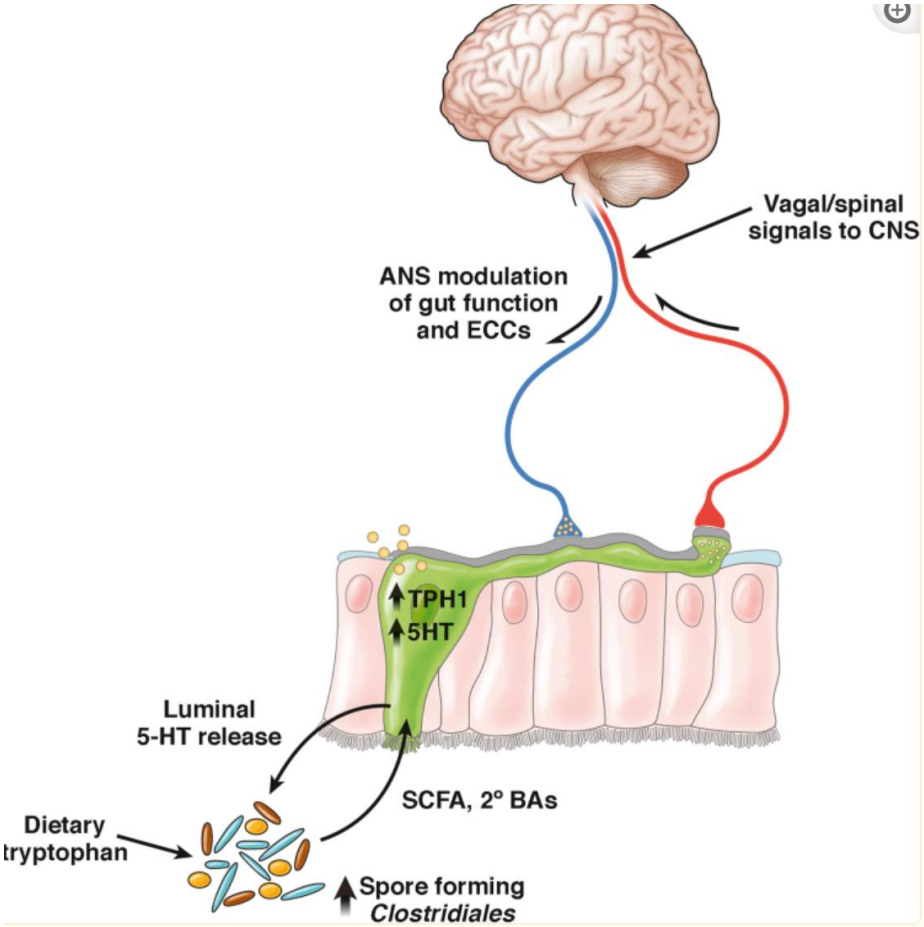
Abraham and Cho, 2009; Xavier and Podolsky, 2007; Korzenik and Podolsky, 2006

Intestinal Microbiome-
Practical Applications



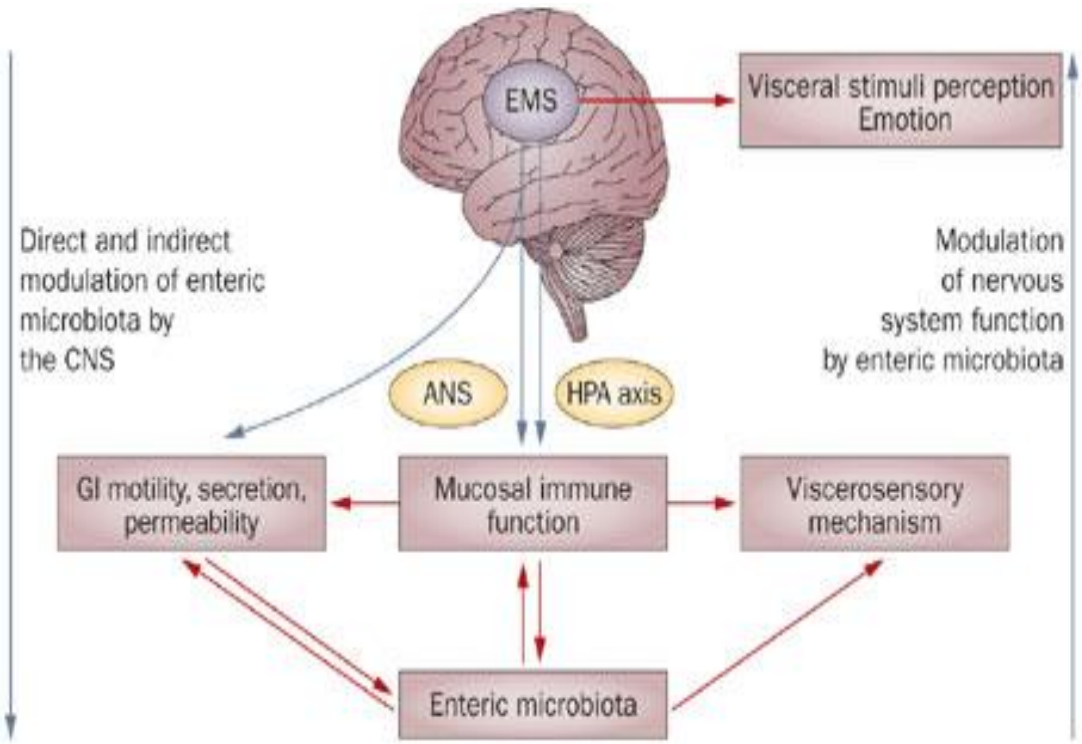
Brain-Gut-Microbiota Axis Mechanisms

- Extrinsic plexus modulates the intrinsic plexus



Keefer and Kane, 2017;
Martin et al, 2018

Brain-Gut-Microbiota Axis Mechanisms

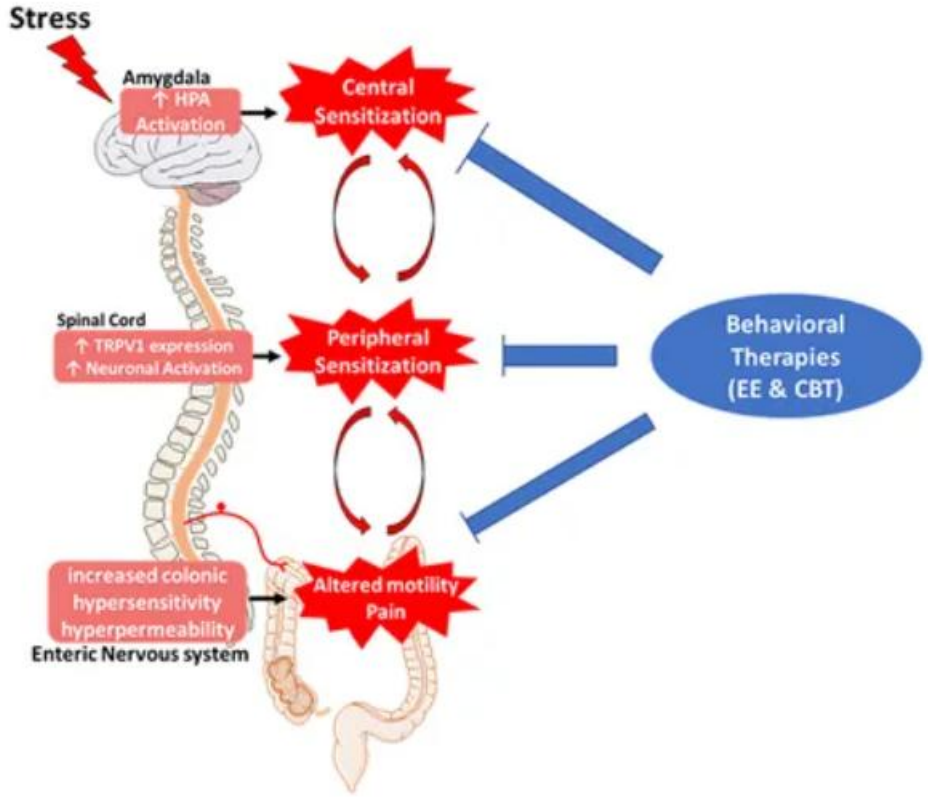


- Neuroanatomical pathways such as vagus nerve (VN) or spinal cord
- Neuroendocrine system such as the hypothalamic-pituitary-adrenal axis (HPA axis)
- Immune links mediated by cytokines
- Direct or indirect chemical pathways that may involve microbial metabolites and some specific neurotransmitters
- ***Stress changes intestinal permeability***

Keefer and Kane, 2017

Brain-Gut-Microbiome in Psychiatric Disorders in GI Disease

Figure 1



- Dysregulation of the brain gut axis
- Stress → HPA axis activation, in turn causing CNS and ENS afferent sensitization, with increased pain and changes in motility

Orack, 2021

Case

- A 29 y/o woman with a medical history notable for migraines, functional dyspepsia and episodic use of cannabis is admitted to the hospital for intractable vomiting. She reports she is unable to tolerate PO content. She has not recently used cannabis. She explains that she experiences intermittent episodes of vomiting which last 5 days at a time. She is insisting the medical team prescribe Ativan which they do not wish to prescribe. They consult you for help in managing her case.

Disorders of Gut Brain Interaction (DGBI): IBS

- Recurrent abdominal pain, altered bowel habits and often bloating

- Recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with **two or more** of the following criteria:

- Related to defecation
- Associated with a change in frequency of stool
- Associated with a change in form (appearance) of stool

- Symptom duration 3 months, symptom onset at least 6 months prior to diagnosis

IBS and Psychiatric Disorders

- **MDD:** Prevalence 27-47% - 3x higher rate, severe GI sx, risk factor for IBS, low energy, difficulty sleeping, headaches, back and joint pain
- **GAD:** Prevalence 32% -anticipatory worries, avoidance, rumination about GI sx
- **PTSD:** 36% - close association with physical and sexual trauma; increased risk among female veterans
- **Panic d/o:** 44% - symptoms of nausea, diarrhea and abdominal discomfort

Treatment Approach: TIC

Safety	Choice	Collaboration	Trustworthiness	Empowerment
Definitions				
Ensuring physical and emotional safety	Individual has choice and control	Making decisions with the individual and sharing power	Task clarity, consistency, and Interpersonal Boundaries	Prioritizing empowerment and skill building
Principles in Practice				
Common areas are welcoming and privacy is respected	Individuals are provided a clear and appropriate message about their rights and responsibilities	Individuals are provided a significant role in planning and evaluating services	Respectful and professional boundaries are maintained	Providing an atmosphere that allows individuals to feel validated and affirmed with each and every contact at the agency

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Institute on Trauma and Trauma-Informed Care, 2015

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Treatment

- Integrated approach: Team communication
- Psychotropic approach:

→Visceral hypersensitivity: TCAs, SNRIs

→Nausea/appetite/satiety: Mirtazipine

→Bloating/epigastric discomfort: Buspar, Venlafaxine

→Motility/bloating: SSRIs – Citalopram, Paroxetine

→Refractory symptoms: Quetiapine, Olanzapine

- CBT

IBS-D vs IBS-C

Drug Name	Symptoms Targeted	Type of IBS
Amitriptyline/Nortriptyline	Pain/Loose Stools/Incomplete Defecation	IBS-D
Duloxetine/Venlafaxine	Pain/Loose Stools/Mood	IBS-D
Escitalopram/Citalopram/ Fluoxetine/Sertraline	Bloating/Pain/ Frequency/Mood	IBS-C

DGBI:
Functional Dyspepsia

1. *One or more* of the following:
   1. Bothersome postprandial fullness
   2. Bothersome early satiation
   3. Bothersome epigastric pain
   4. Bothersome epigastric burning

   AND

2. No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms

- Symptoms symptom duration 3 months, symptom onset 6 months

Functional Dyspepsia and Psychiatric Disorders

- Significant association with both **anxiety** (26%) and **depressive disorder** (34%), particularly in tx refractory patients (65%)
- High incidence of physical and sexual **trauma** (one study reported at high as 67%)
- Emotional distress in FD related to inability to achieve adequate food and drink intake

Assessment and Treatment

- Assess target symptoms for psychotropic usage:
  - -Appetite changes
  - -Weight fluctuation
  - -Nausea/vomiting
  - -Pain
  - -Insomnia
- Literature focus on TCAs, some reports on Mirtazipine
- CBT

DGBI: CVS

1. Stereotypical episodes of vomiting regarding onset (*acute*) and duration (*less than 1 week*)
2. At least three discrete episodes in the prior year and two episodes in the past 6 months, occurring at least 1 week apart
3. Absence of vomiting between episodes, but other milder symptoms can be present between cycles

- Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Cycle of CVS

- **Inter-episodic phase:** Symptom free
- **Pre-emesis phase:** Approach of an episode, nausea varies, can still retain PO meds
- **Emetic phase:** Intense, persistent nausea, vomiting and other symptoms
- **Recovery period:** Hunger, tolerance of oral intake and vigor return to normal

CVS versus CHES

Cyclical Vomiting Syndrome	Cannabinoid Hyperemesis Syndrome
Intractable vomiting with periods of being well relieved by hot showers	Intractable vomiting with periods of being well relieved by hot showers
No clear pattern of relationship	Prolonged, excessive use of cannabis with symptoms < 24 hours of last use
No clear pattern of relationship though use of cannabis can also provide relief	Complete and sustained cessation produces remission though use of cannabis can also provide relief
Rapid gastric emptying	Delayed gastric emptying
Family history of migraines	Variable history
Odansetron (Zofran) can help	Hallmark of odansetron not helping

* Cannabis withdrawal symptoms – like CHES, relief with cannabis usage, but symptoms typically begin >24 hours (1-10 days) after last use and no relief with hot showers

Assessment and Treatment

- Lorazepam/Antiemetics/ Triptans abortive
- *Strong:* TCAs (Amitryptiline) 100mg dosage in 10mg increments po QHS can produce remission
- *Conditional:* Topomax 50mg BID in 25mg increments
- Sleep and stress management (meditation/biofeedback, healthy diet)

Case

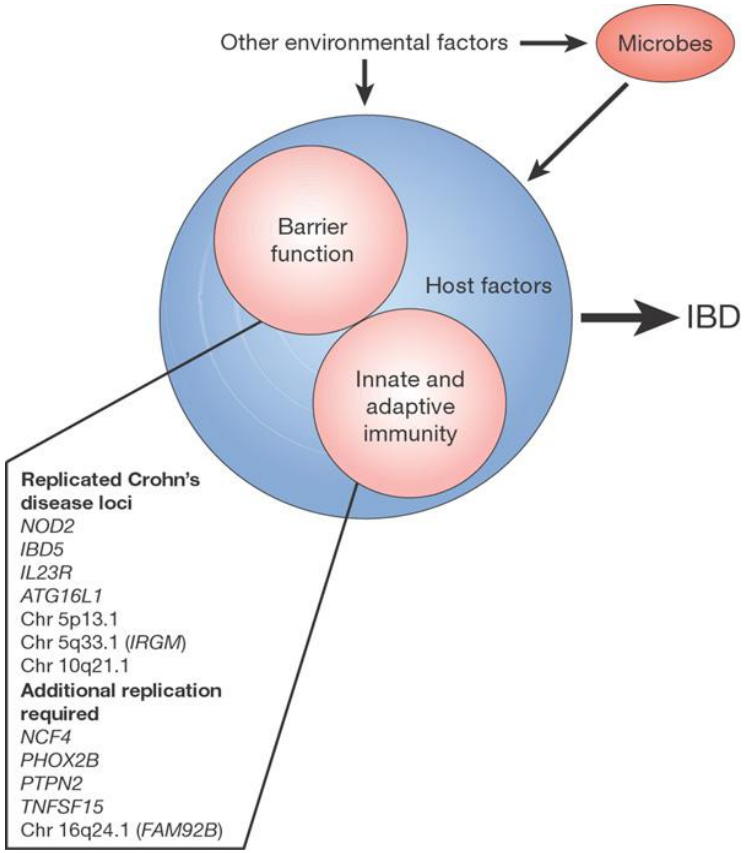
- 42 y/old woman with ileocolonic Crohn's first dx 19 years ago. Has had multiple resection surgeries (ileo-cecal, mid-jejunum, ileal) with 80 cm of small bowel remaining. Current ostomy.
- As many as 10 hospitalizations per year for fatigue, abdominal pain and diarrhea – usually placed on fluids and TPN. Dysmenorrhea correlates with Crohn's flares. **She's been hospitalized again, and you get called to address her existing depression and consult on how to decrease future ED visits.**
- Prior trials of Ustekinumab (Stelara) and Natalizumab (Tysabri). Psychiatric history of depression, anxiety and PTSD due to childhood emotional and sexual abuse. On Valium, Mirtazipine, Celexa, and Trazodone.
- Family history of Crohn's and Hodgkins. Married to a policeman with 2 children; supportive family. Got her GED and completed nursing school; on SSDI for past 5 years.
- Complains of sx of gastroparesis, pain, anxiety, insomnia and tends to catastrophize. Smokes 0.5 ppd.

Inflammatory bowel disease

- 3.1 million Americans
- Peak onset 15 to 30 years
- Interaction of genetic and nongenetic factors –

  -Twin studies indicate 5-fold risk with one relative

  -Diet, antibiotic usage, intestinal colonization have a role



Abraham and Cho, 2009; Xavier and Podolsky, 2007; Korzenik and Podolsky, 2006

IBS vs IBD

IBS

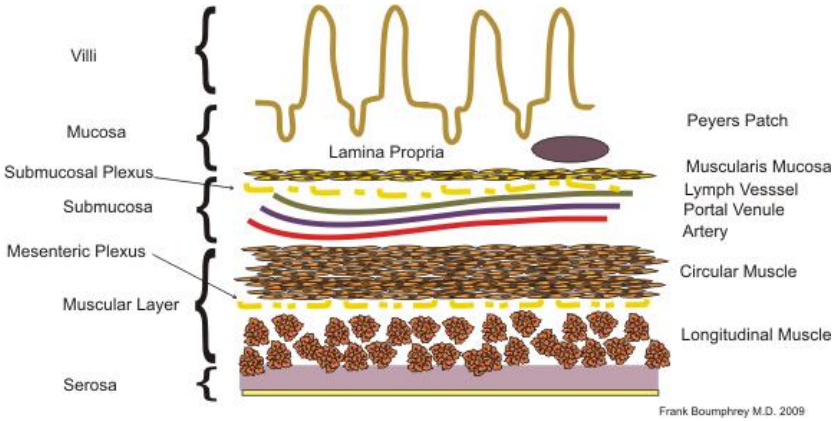
- Functional
- Syndrome
- No inflammation
- No permanent harm to intestines
- Higher current, lifetime mood d/o prevalence

IBD

- Structural
- Genetic ←→ environment
- Disease
- Inflammation on scope
- Intestinal bleeds, elevated colon cancer risks

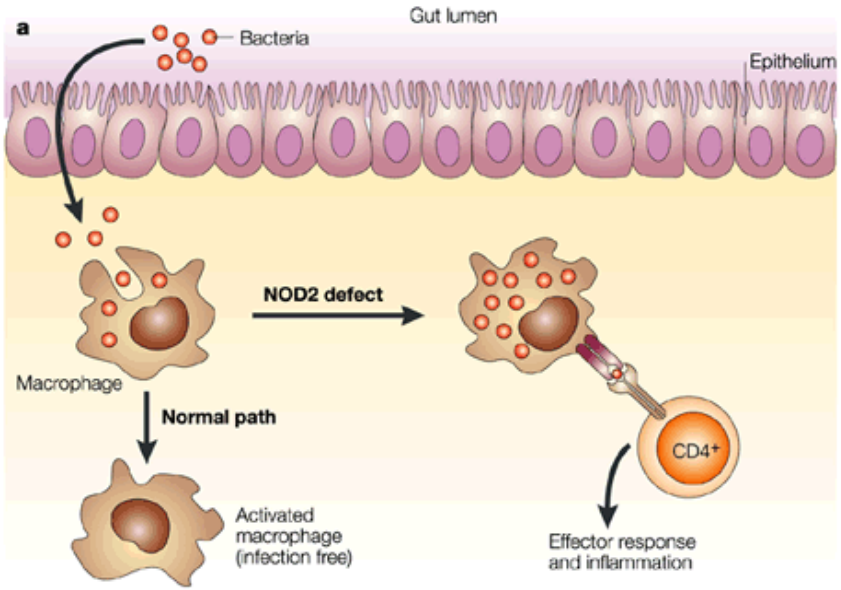
Inflammatory Response

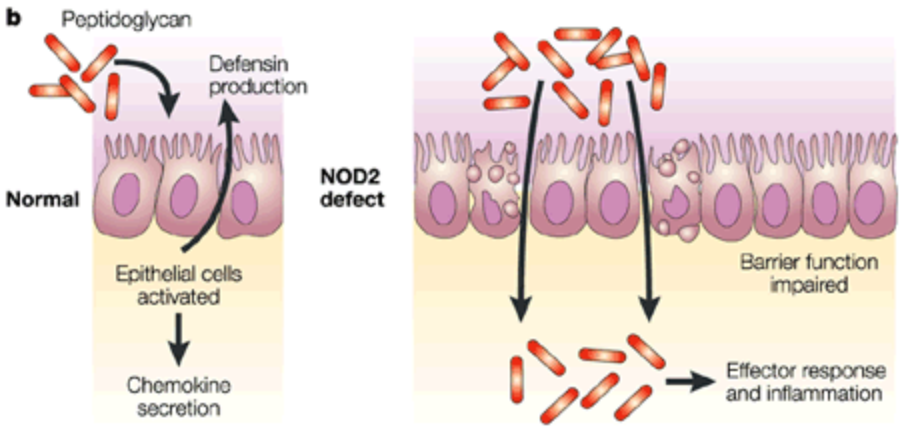
- Hallmark of active IBD is activation of innate immune cells (neutrophils, macrophages, natural killer T cells) and adaptive immune cells (B and T cells) in the intestinal mucosa
- Activation of these cells activate inflammatory markers like TNF-a, interleukin 1-B, interferon-y and cytokines of the interleukin-23-Th17 pathway



Turner, 2009

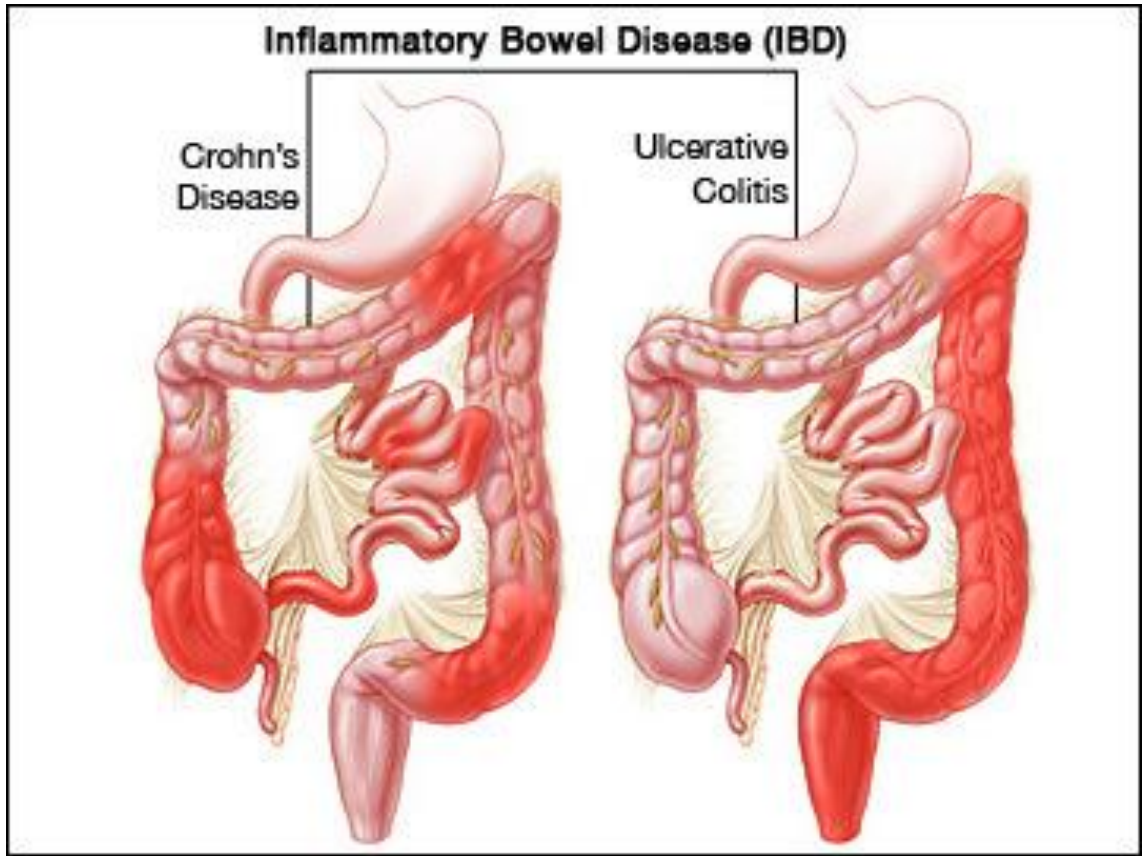
IBD pathophysiology





Abraham and Cho, 2009; Xavier and Podolsky, 2007; Korzenik and Podolsky, 2006

Crohn's vs Ulcerative Colitis



Abraham and Cho, 2009; Xavier and Podolsky, 2007; Korzenik and Podolsky, 2006

Treatment

- Monoclonal antibodies against TNF-a and interleukin-23
- Infliximab (Remicade), Vedolizumab (Entyvio), Nataluzimab (Tysabri), Adalimubab (Humira)
- Aminosalicylates, corticosteroids, antibiotics reduce inflammation and promote mucosal healing

Mood Disorders in IBD

- Depression and/or anxiety

-30-35% in remission

-80% during relapse

- IBD patients twice as likely to experience depressive disorder compared to general population
- Risk factors

-Severe and active disease

-Corticosteroid usage

Mood Disorders in IBD

Depression

- More frequent IBD relapse
- Earlier IBD relapse
- Increased disease activity
- Interference with remission from Infliximab
- Reduced med adherence in geriatric patients

IBD ←→ Depression

The bi-directional association between IBD and depression

Risk of New-Onset Depression by IBD status

Group	Adjusted OR for Depression[a]
IBD patients	9.43 (95% CI, 6.43–13.81; *P* <.001)
Unaffected siblings	1.82 (95% CI, 1.14–2.91; *P* =.013)
Control group	Reference

OR, odds ratio; IBD, inflammatory bowel disease

[a]Adjusted for age, sex, monthly income, urbanization, Charlson comorbidity index, medical comorbidities, and all-cause clinical visits.

- Patients with depression were also at risk for IBD development

  25,552 patients with depression, 26,147 unaffected siblings, and 104, 588 healthy controls without depression.
- The adjusted odds ratio for IBD among patients with depression and their unaffected siblings were 1.87 (95% CI, 1.07–3.26; *P* =.028) and 1.69 (95% CI, 1.05–2.69; P = 0.029), respectively

Zhang et al, 2022

Controversies on Depression in IBD

- *Relapse or Remission?*
- *Crohns vs Colitis?*
- *Frequency higher than other medical illnesses?*
- *Before or after IBD dx?*

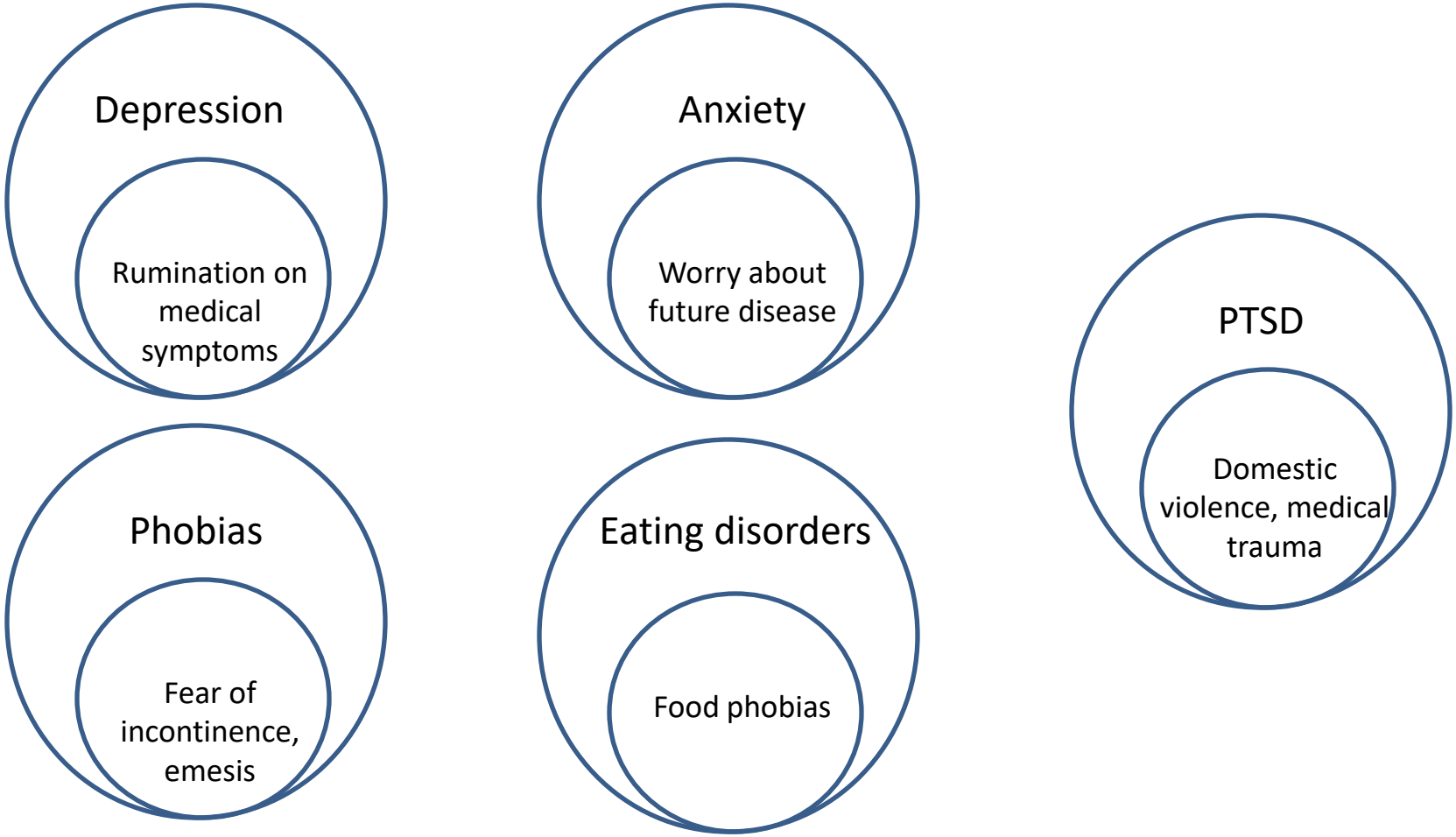
- Subset of patients with IBS-like sx have higher rates of depression during remission
- Higher rate of lifetime psychiatric illness in CD pts due to more severe somatic sx
- Frequency equal to other medical conditions (e.g. ~30%)
- Increasing evidence of a bidirectional relationship between depression and IBD

Depressive Subtypes

- 75%: Mild depression, with prominent symptoms being fatigue, irritability, and depressed feelings
- 20%: Somatic depression, with prominent features including anhedonia, change in appetite, fatigue, physical complaints, irritability, and depressed feelings
- 5%: Cognitive despair, morbid and suicidal ideation, weeping, hopelessness, fatigue, and feelings of sadness

Szigethy et al, 2014

Clinical Presentation



Other Pathologies

- PTSD (32%)
- Specific phobia
- Panic Disorder (8%)
- Social Anxiety Disorders (6%)
- Personality Types
- Substance Use Disorders

Treatment Approach

- Interview (IBS, visceral hypersensitivity, insomnia, fatigue, cognitive dysfunction)
- Psychoeducation
- Objective disease disproportionate to sx
- Treatment options (pharm and/or therapy)
- Malnutrition, anemia, vitamin def
- Smoking cessation

Psychopharmacology

- Differences in side effects guide choices
- E.g. Zoloft, Venlafaxine vs Paroxetine
- Bupropion in case studies
- SSRIs and GI bleeds
- Clonidine
- TCAs
- Psychotherapy

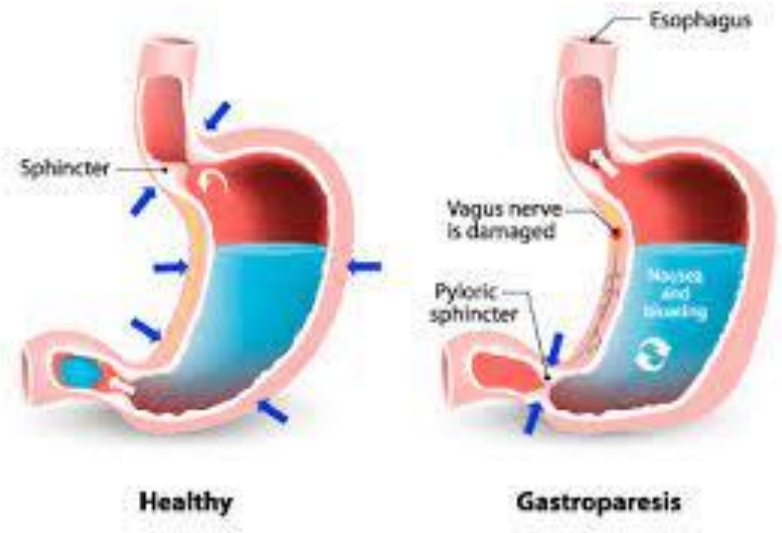
Psychopharmacology: Microscopic Colitis

- Collagenous vs lymphocytic
- Zoloft and Clozapine (higher risk)
- Duloxetine and Paroxetine (intermediate risk)
- Lexapro (lower risk)

Lucendo, 2017

Psychopharmacology: Gastroparesis

- Partial paralysis of the stomach
- Nausea, early satiety, reduced appetite
- Buspar, Mirtazipine



Psychopharmacology: Fatigue

Fatigue is common, treatable, and usually multifactorial—even when bowel symptoms look controlled.

A practical differential

Think in buckets, then match the workup to the patient's fatigue phenotype.

1 Inflammation

Active disease, cytokines, flare physiology, extraintestinal inflammation

2 Deficiency states

Iron deficiency/anemia, B12/folate, vitamin D, malnutrition, dehydration

3 Sleep + pain

Nocturnal stooling, abdominal pain, insomnia, nonrestorative sleep

IBD fatigue

Symptom burden + biology + behavior

Often persists after remission because drivers can shift from inflammatory to sleep, mood, nutrition, medications, or deconditioning.

Validate it. Screen for reversible causes. Then treat the subtype.

4 Medication effects

Steroids, sedatives, antihistamines, opioids, polypharmacy

5 Mood + stress load

Depression, anxiety, fear of flares, stigma, caregiving/work strain

6 Deconditioning

Reduced activity, muscle loss, autonomic symptoms, low reserve

D'Silva et al., Clin Gastroenterol Hepatol, 2022; Nocerino et al., Dig Dis Sci, 2020; Giri et al., World J Gastroenterol, 2025; Crohn's & Colitis Foundation.

Chart fatigue by phenotype → treat what is driving it

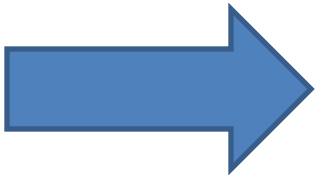
A useful clinic frame is physical, cognitive, and behavioral fatigue; patients often have more than one.

Dimension	What it sounds like	Check first	Treatment menu
Physical	"My body feels heavy." Low stamina; exertion wipes me out.	Inflammation; ferritin/CBC; B12/folate/D; thyroid; sleep/pain; meds.	Optimize IBD control; iron/nutrient repletion; sleep + pain care; medication review; paced movement/rehab.
Cognitive	"I have brain fog." Slowed thinking, attention, memory.	Sleep debt; anemia; active inflammation; depression/anxiety; sedating meds.	Treat reversible drivers; CBT-I/sleep regularity; mood treatment; accommodations.
Behavioral	"I stopped doing things." Avoidance, lost routines, low confidence.	Fear of symptoms; flare unpredictability; isolation; deconditioning; energy over/under-shooting.	behavioral activation; structured activity plan; CBT/ACT; nutrition/hydration routines;

Principle: Start with reversible medical drivers, but do not stop there — persistent fatigue often needs sleep, mood, activity, and coping interventions.

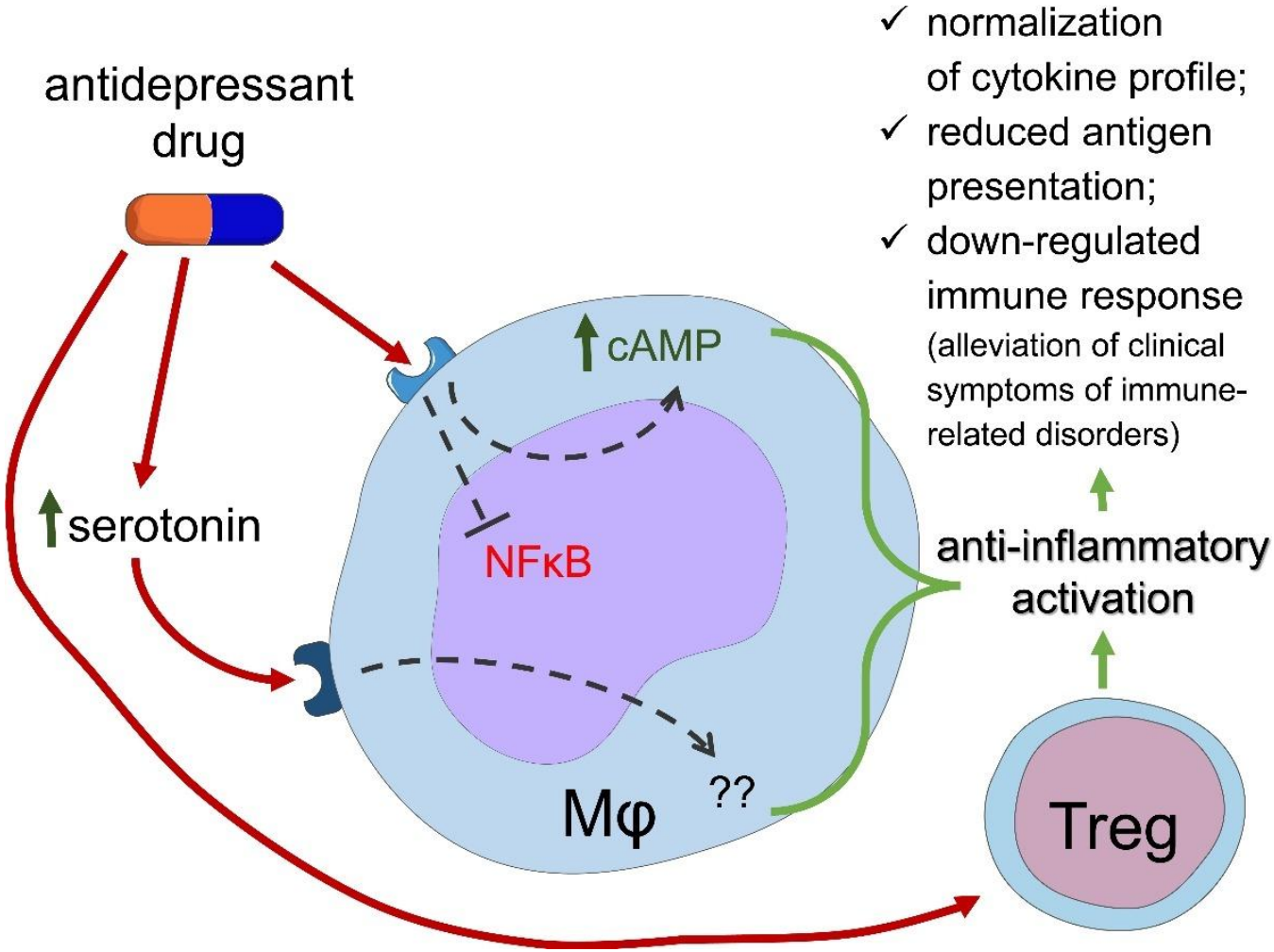
Psychiatric Treatment

Antidepressants
(SSRIs, SNRIs,
TCAs, Mirtazipine)



- Psychiatric diagnoses
- Inflammation
- Appetite
- Weight
- Pain
- Nausea
- Insomnia
- Fatigue
- Cognitive dysfunction
- IBS overlay

Psychiatric Treatment



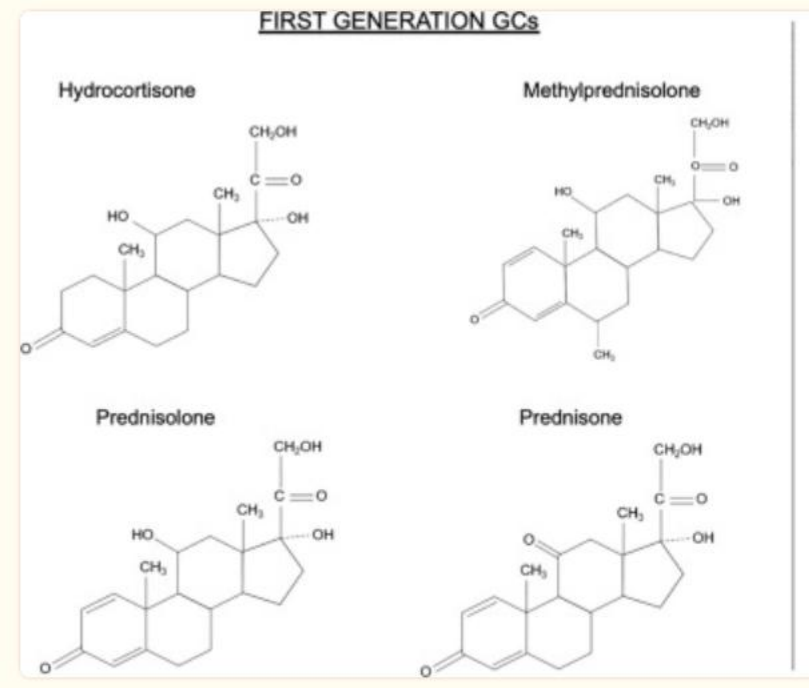
Nazimek et al, 2017

Adverse Effects of Glucocorticoids

- Possible neuropsychiatric effects include:
  - -Anxiety, depression
  - -Insomnia
  - -Mania, hypomania
  - -Psychosis
  - -Cognitive decline
- Dose dependent onset:
  - -Risk of development minimal (1.3%): < 40 mg
  - -Risk of development high (18.4%): > 80mg

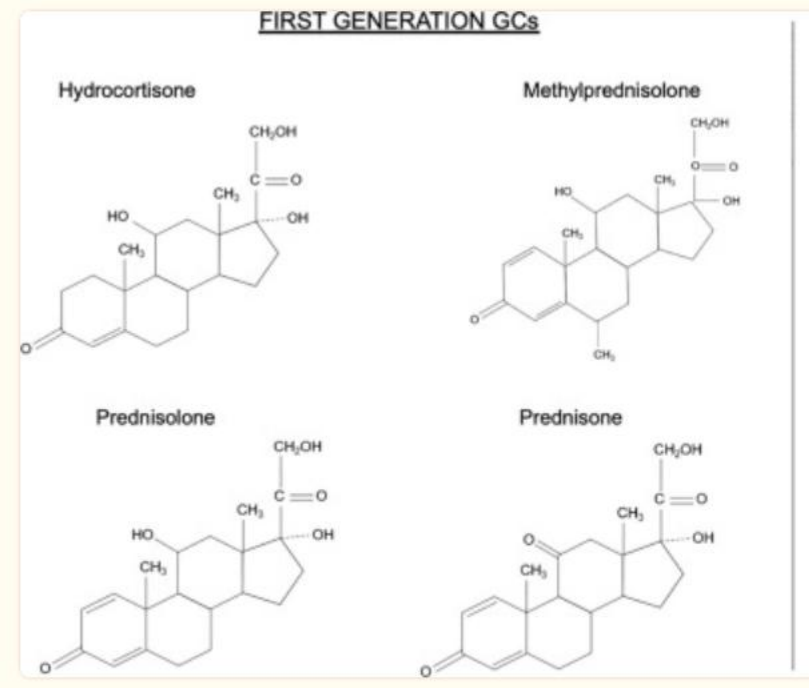
Adverse Effects of Glucocorticoids

- Cohort of 53 patients monitored with BDI
- 49% of IBD patients (26/53) prescribed a high dose of 40mg prednisone for 2 weeks or more experienced mood changes
- 25/26 cases experienced mania
- Symptoms included irritability, inability to focus and poor sleep quality, impulsivity, rapid thought process, over-activity, feeling “sped up” inside or restlessness



Adverse Effects of Glucocorticoids

- Onset 2-3 weeks after beginning prednisone
- Younger age and female gender associated with neuropsychiatric effects
- IBD diagnosis, presence of psychiatric condition, type of maintenance therapy, initial disease activity score, duration of prednisone before mood reassessment, and positive response to treatment not associated
- Tapering prednisone reduced symptoms without further psychiatric intervention



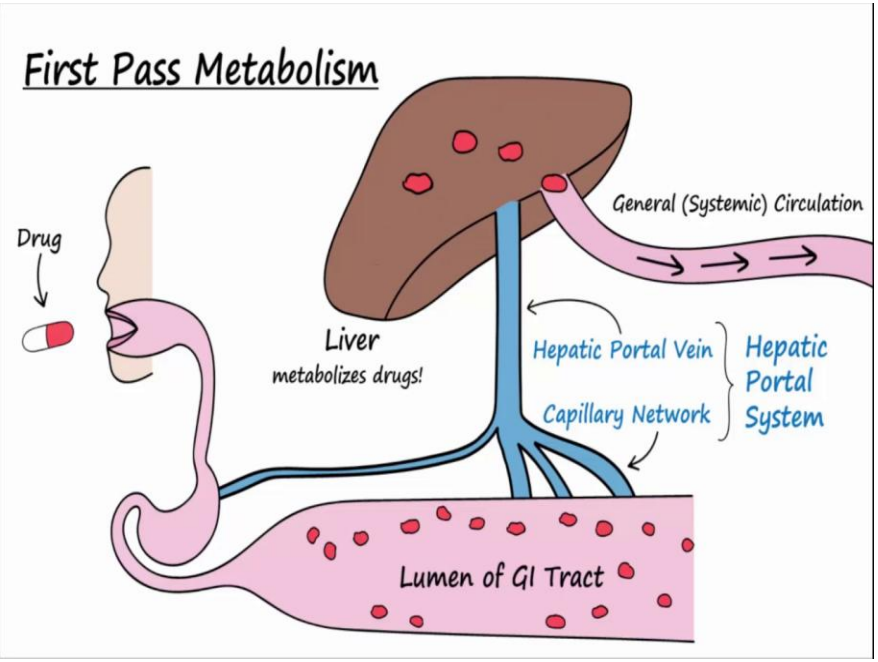
IBD medications and mental health

Corticosteroids

- 2nd generation corticosteroids (Budesonide)
  - high efficacy,
  - fewer adverse events

Biological agents

- Not associated with increased risk of anxiety, depression, psychiatric illness



Bruscoli et al, 2021; Mawdsley and Rampton, 2005

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