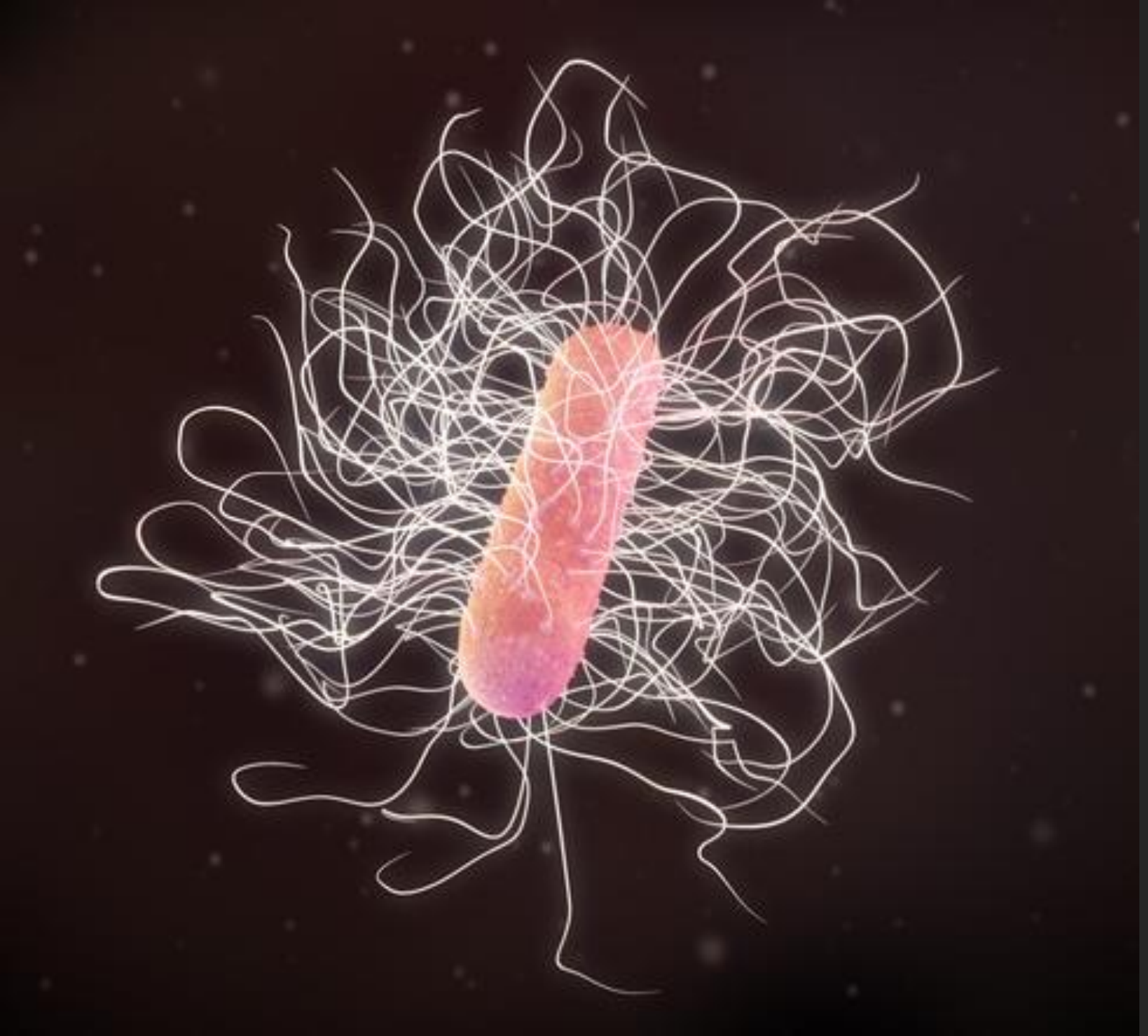


APPROACH TO INFECTIOUS COLITIS

Nasief van der Schyff
UCT/GSH
14 November 2024

OUTLINE OF PRESENTATION

1. EPIDEMIOLOGY
2. DIFFERENTIAL DIAGNOSIS
3. FOCUS ON MOST COMMON PATHOGENS
4. CLINICAL APPROACH TO INFECTIOUS COLITIS
5. INVESTIGATIONS
6. TREATMENT OVERVIEW
7. ALGORITHM

EPIDEMIOLOGY

- Diarrhoea caused by enteric infections is a global issue
- Major cause of morbidity and mortality throughout the world
  - Esp children < 5 years old
- 2-4 billion episode of infectious diarrhoea occur annually in developing countries
- IMBALANCE OF PROTECTIVE HOST FACTORS + MICROBIAL VIRULENCE

ACQUISITION OF ENTERIC INFECTION

EPIDEMIOLOGY

- **INFECTIOUS COLITIS = INFLAMMATION OF COLONIC MUCOSA CAUSED BY AN INFLAMMATORY PATHOGEN**
  - Invasive or non-invasive
  - 10% of all causes of diarrhoea
  - Infectious colitis should be actively sought in acutely patients
  - Cardinal symptoms:
    - Abdominal cramps/pain
    - Diarrhoea
    - Dysentery
    - Tenesmus
    - urgency

ACUTE ≤ 14 Days
- Infectious cause
- Esp Bacterial cause

CHRONIC > 14 Days
- IBD vs TB
- Recurrent C.Diff

INFECTIOUS COLITIS : AETIOLOGY

BACTERIA
Campylobacter
Salmonella
Shigella
E.Coli
Clostridioides Difficile
Mycobacterium TB
Yersinia Enterocolitica

INFECTIOUS COLITIS : AETIOLOGY

BACTERIA	VIRUSES
Campylobacter	**HIV**
Salmonella	**CMV**
Shigella	Norovirus
E.Coli	Rotavirus
Clostridioides Difficile	Adenovirus
Mycobacterium TB Yersinia Enterocolitica	

INFECTIOUS COLITIS : AETIOLOGY

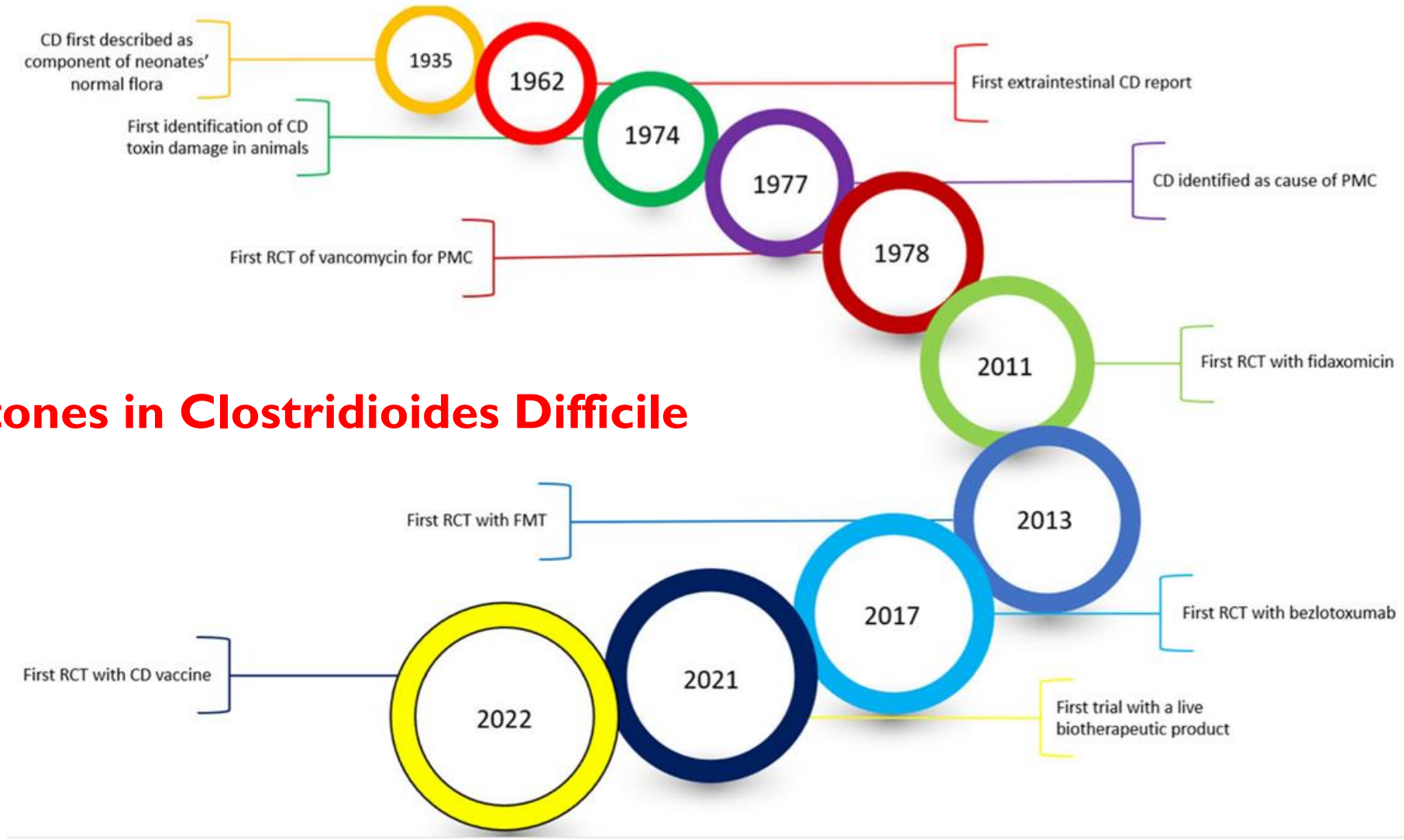
BACTERIA	VIRUSES	PARASITES
Campylobacter	**HIV**	**Entamoeba histolytica**
Salmonella	**CMV**	Strongyloides Stercoralis
Shigella	Norovirus	
E.Coli	Rotavirus	
Clostridioides Difficile	Adenovirus	
Mycobacterium TB Yersinia Enterocolitica		

INFECTIOUS COLITIS :AETIOLOGY

BACTERIA	VIRUSES	PARASITES	SEXUALLY TRANSMITTED PATHOGENS
Campylobacter	**HIV**	**Entamoeba histolytica**	Neisseria
Salmonella	**CMV**	Strongyloides Stercoralis	Chlamydia Trachomatis
Shigella	Norovirus		Treponema Pallidum
E.Coli	Rotavirus		**Herpes Simplex I & 2**
Clostridioides Difficile	Adenovirus		
Mycobacterium TB Yersinia Enterocolitica			

BACTERIAL COLITIS

Milestones in Clostridioides Difficile



C. difficile infection: a burdensome disease

29000
deaths/year

$5
billion/year

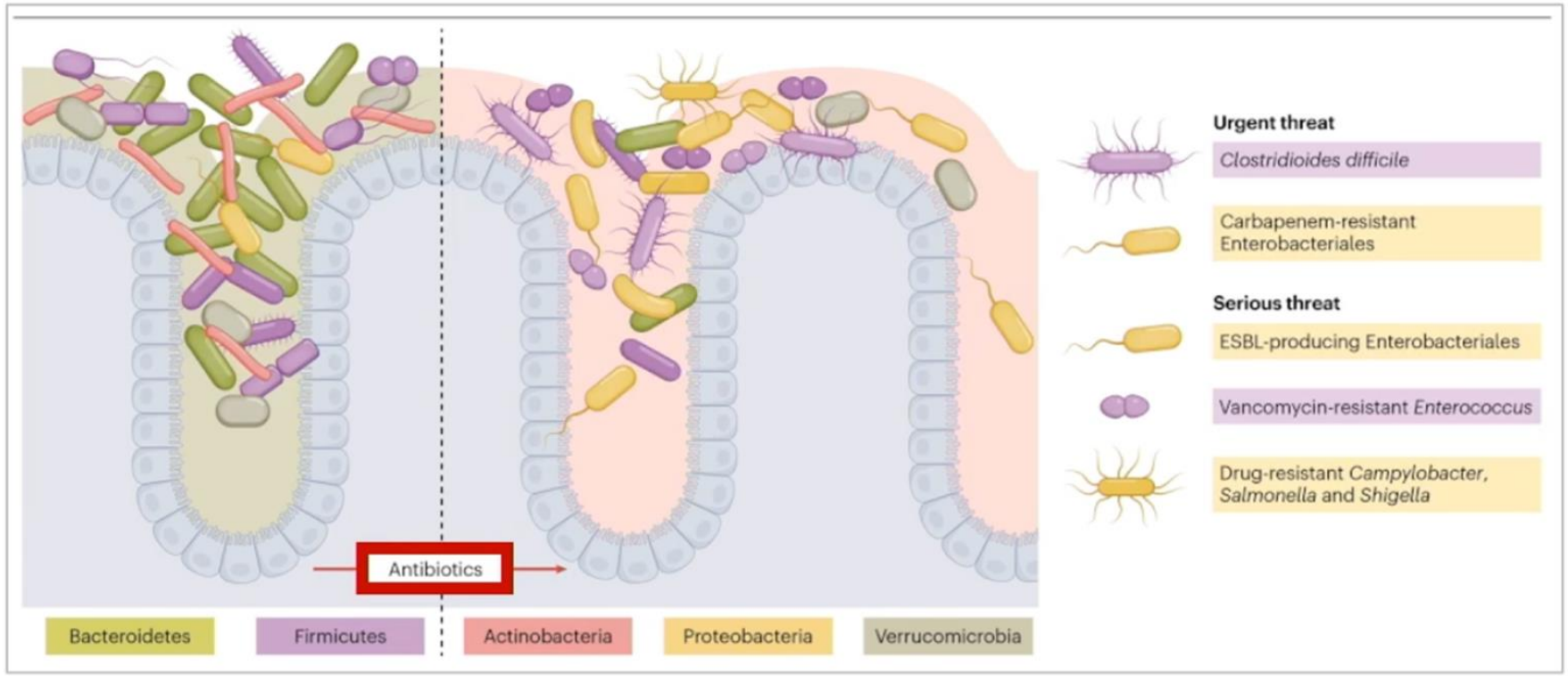
+42.7%
CDI incidence

+188.8%
rCDI incidence

Due to its resistance to antibiotics, **recurrent CDI is more likely to present with a severe clinical picture**, which increases the risk of life-threatening complications (i.e. toxic megacolon, sepsis) and death

Ma et al – Ann Intern Med 2017; Miller BA et al - Infect Cont Hosp Epidemiol 2011; Dubberke ER et al – Clin Infect Dis. 2012

Antibiotic-Mediated Destruction of the Gut Microbiome Opens an Opportunistic Niche



Fishbein SRS, et al., Nat Rev Microbiol. 2023;21:772-788

The clinical relevance of decreased microbiome diversity

The road to inflammation

Antibiotics can drive to decreased microbiome diversity transient alteration of healthy microbiota can drive to long-lasting effects, including **higher risk of VEO-IBD and overweight/obesity**

EARLY ANTIBIOTICS

MICROBIOTA DISRUPTION

Reduced diversity
Reduced richness
Delayed maturation
Altered functions

IMMUNE CHANGES

+ 93% risk of IBD

Ortqvist et al – Gut 2019

METABOLIC CHANGES

+ 11%-57% risk of OBESITY & OVERWEIGHT

Jess T- Sci Rep 2019
Ajslev TA- Int J Obes 2011

Rasmussen et al – Diab Obes Met 2018
Korpela et al – Microbiome 2017

The knowledge of gut microbiome has changed our view of antibiotics

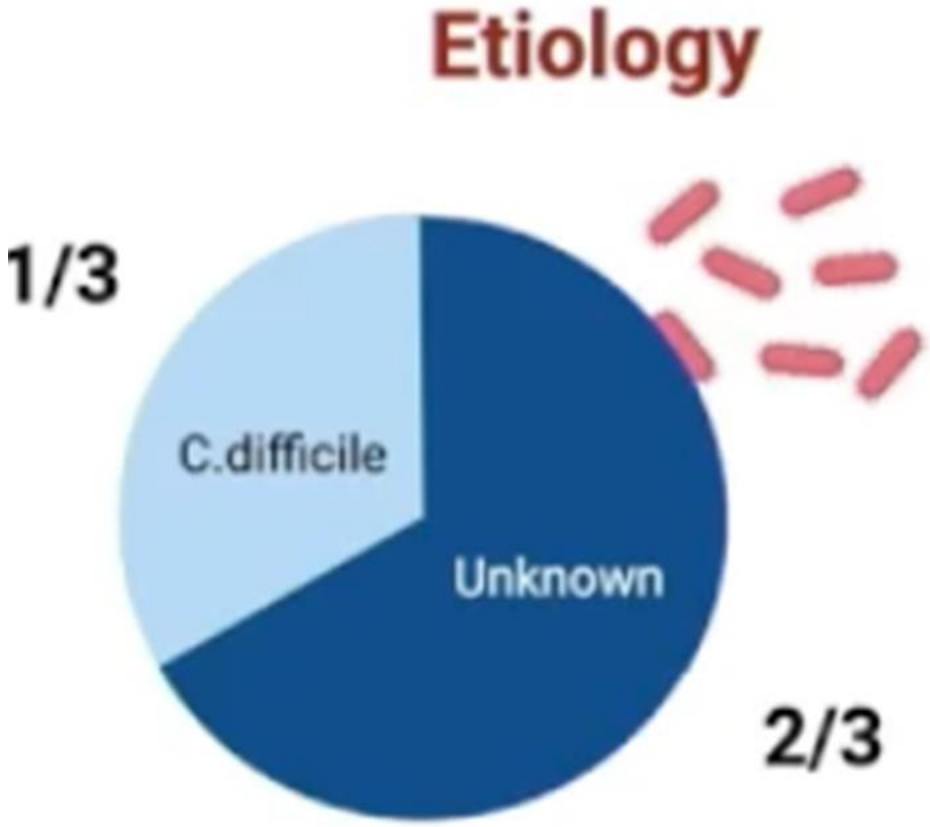
Antibiotics are no longer considered only beneficial, but also potentially harmful agents

Antibiotics overexposure may lead to the development of **genotypic antibiotic resistance** in the resident microbiota and potential transfer to pathogenic bacteria

Antibiotic overuse is associated with the development of many disorders associated with the **alteration of gut microbiota**

ANTIBIOTIC ASSOCIATED DIARRHOEA

- **Diarrhoea** (at least 3 watery stools/day) associated with antibiotic exposure either while on antibiotics or up to **8 weeks** after treatment

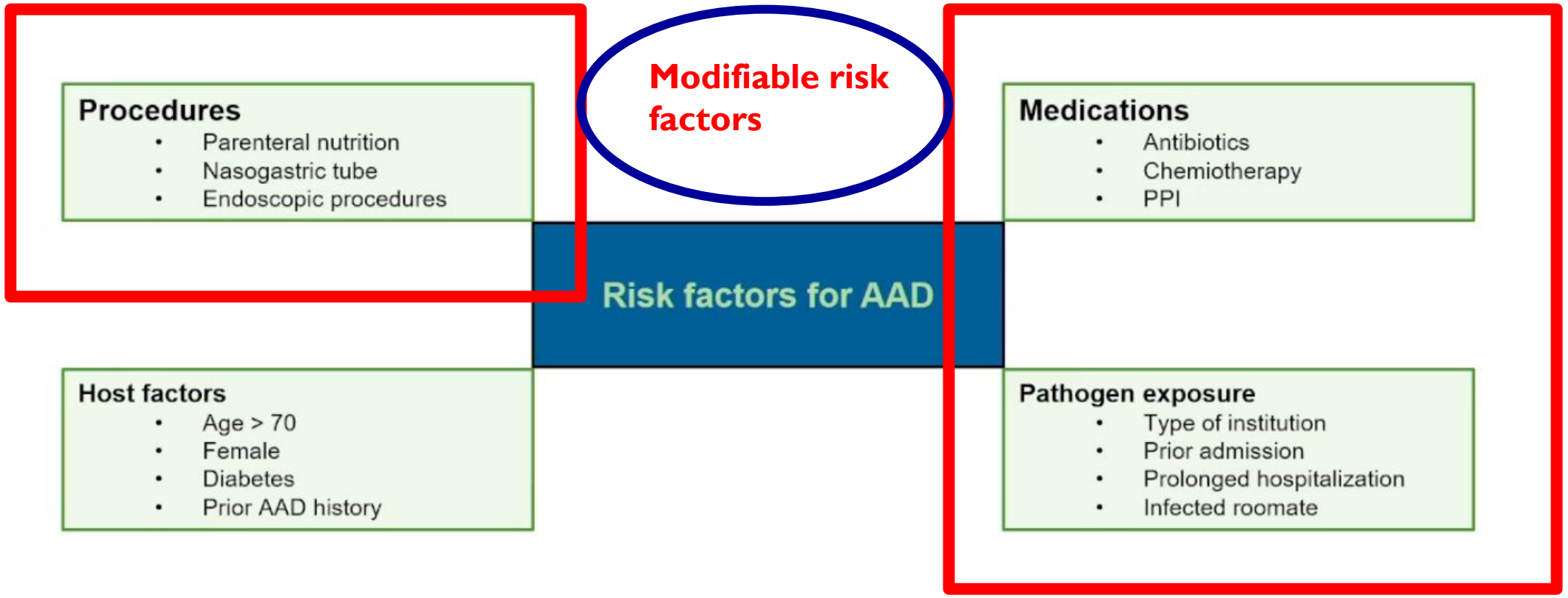


Risk Factors for Antibiotic-Associated Diarrhea

Recent history of CDI strongest risk factor for another episode of cdi

McFarland L.V.; Future Microbiol. 2008;3:563-78
Elseviers M.M. et al.; BMC Infect Dis. 2015;15:129

Risk Factors for Antibiotic-Associated Diarrhea



McFarland L.V.; Future Microbiol. 2008;3:563-78
Elseviers M.M. et al.; BMC Infect Dis. 2015;15:129

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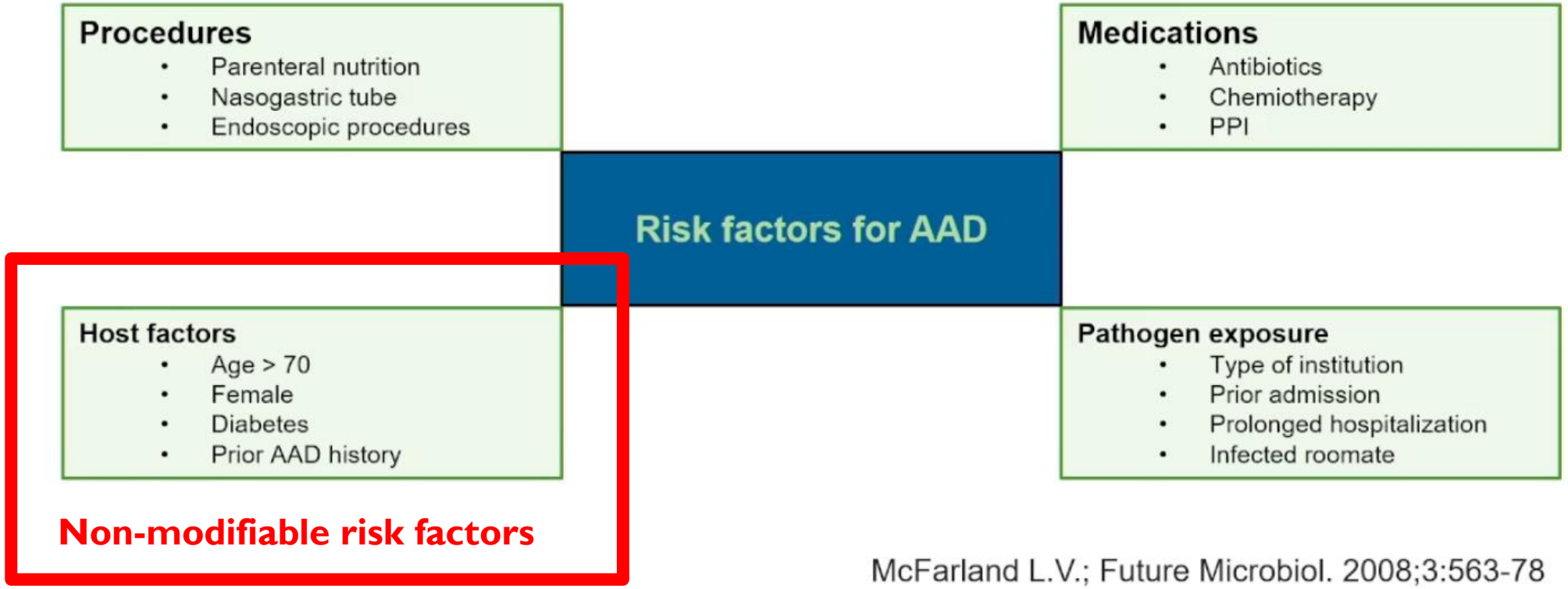
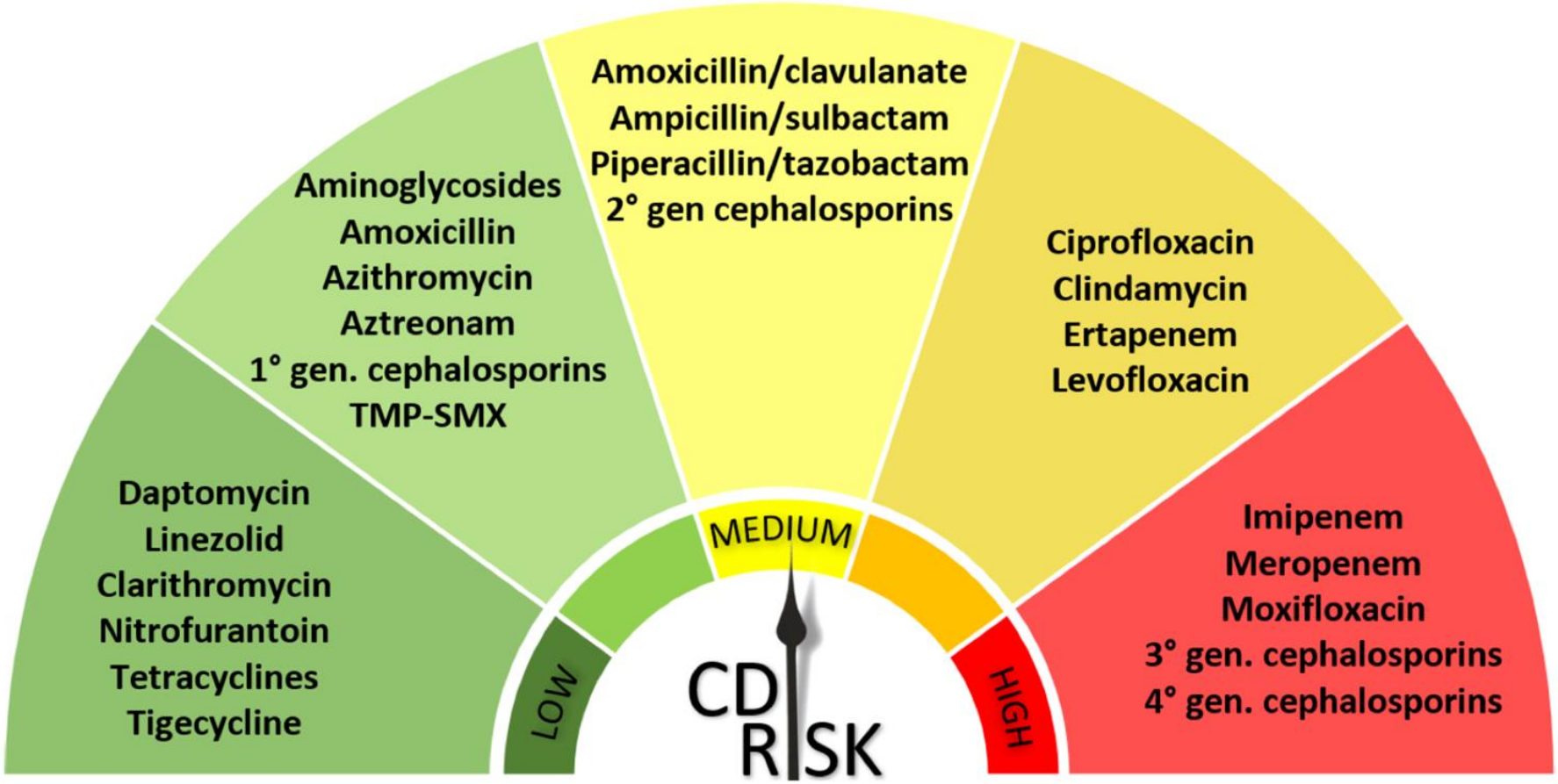


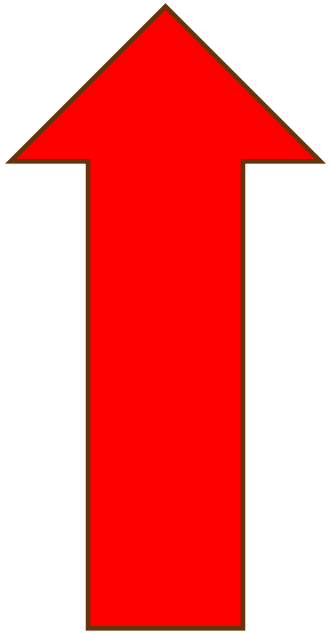
McFarland L.V.; Future Microbiol. 2008;3:563-78
Elseviers M.M. et al.; BMC Infect Dis. 2015;15:129

ANTIBIOTIC RISK FOR CDI



Approximate risk of CDI development according to different antimicrobials (65, 73–77).

INFLAMMATORY BOWEL DISEASE AND CDI



CDI COLONIZATION

SEVERITY

LENGTH OF HOSPITAL STAY

ADVERSE OUTCOMES

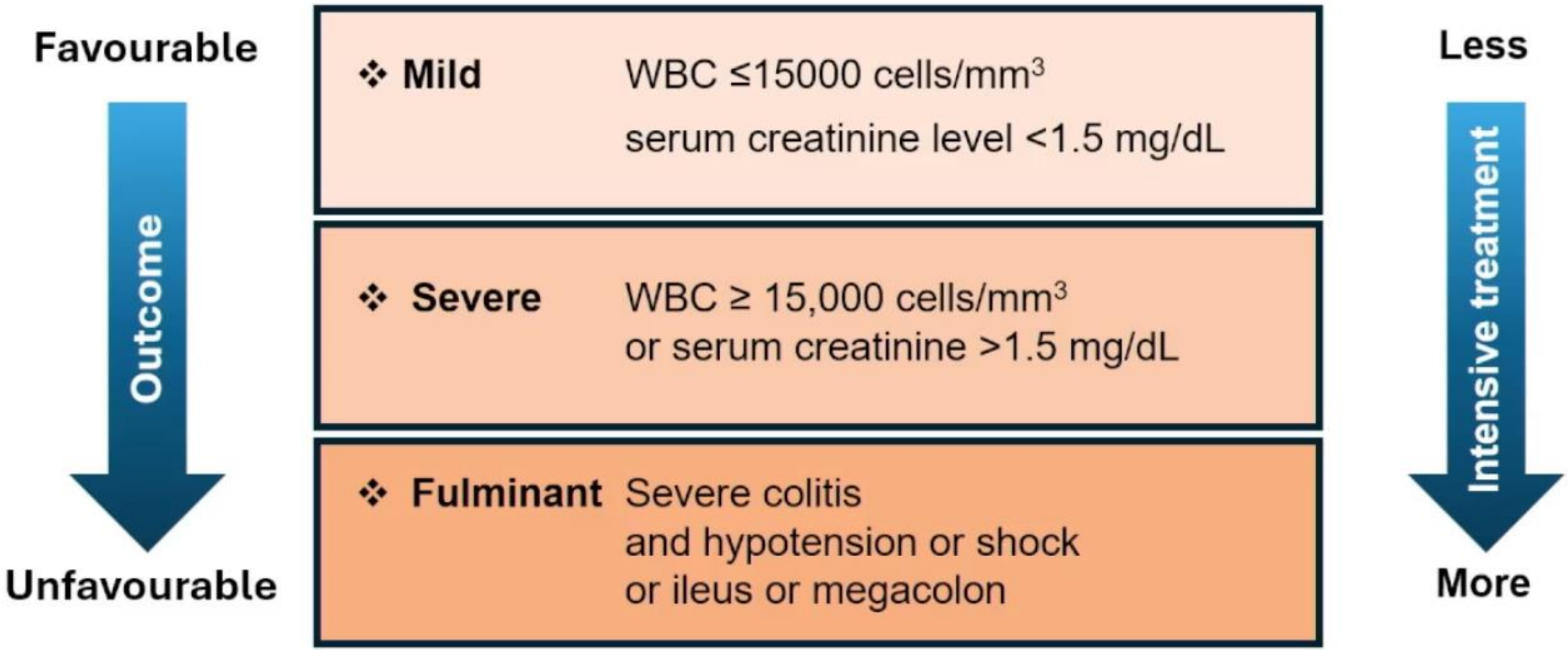
POOR RESPONSE TO MEDICAL THERAPY

COLECTOMY AND GI SURGERY RATES

MORTALITY (4X)

- Differentiating between IBD flare and active CDI challenging
- Immunosuppression can exacerbate infections but required to treat IBD flare

Stratification by Severity of *C. difficile* Infection

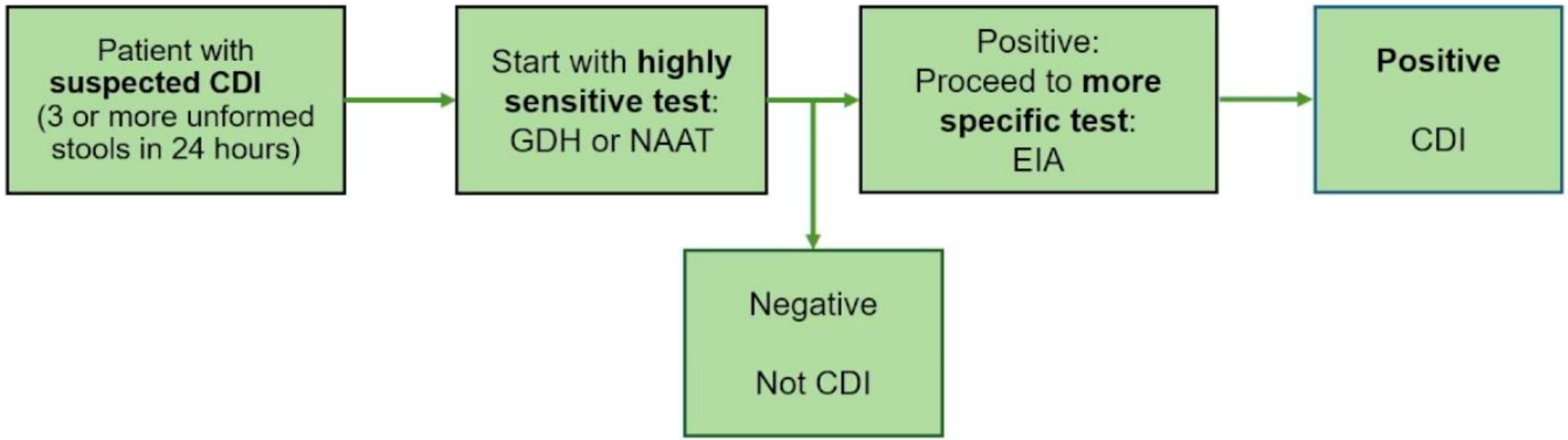


McDonald LC et al., Clin Infect Dis 2018;56:e00782-18
Kelly CR et al., Am J Gastroenterol 2021;116:1124-1147

CDI TESTING

- **GLUTAMATE DEHYDROGENASE (GDH) - Antigen**
  - Antigen (enzyme)used to diagnose presence of CDI
  - High sensitivity, low specificity
- **Ezyme Immunoassay (EIA) for Toxin A/B**
  - Indicates active CDI infection
- **Nucleic Acid Amplification Test (NAAT)**
  - PCR
  - High sensitivity and specificity
  - Does **NOT** test for toxin

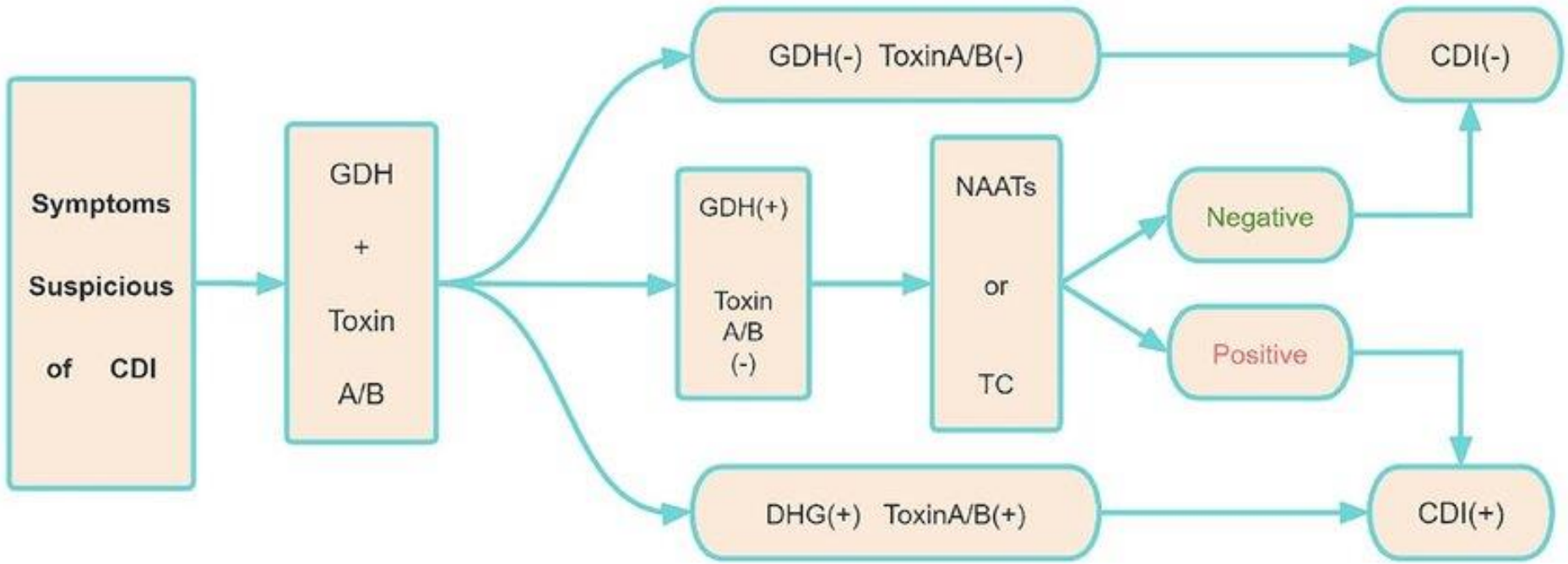
C. difficile Testing Algorithm



EIA, enzyme immunoassay; GDH, glutamate dehydrogenase; NAAT, nucleic acid amplification testing; PCR, polymerase chain reaction: CDI: Clostridiodes difficile

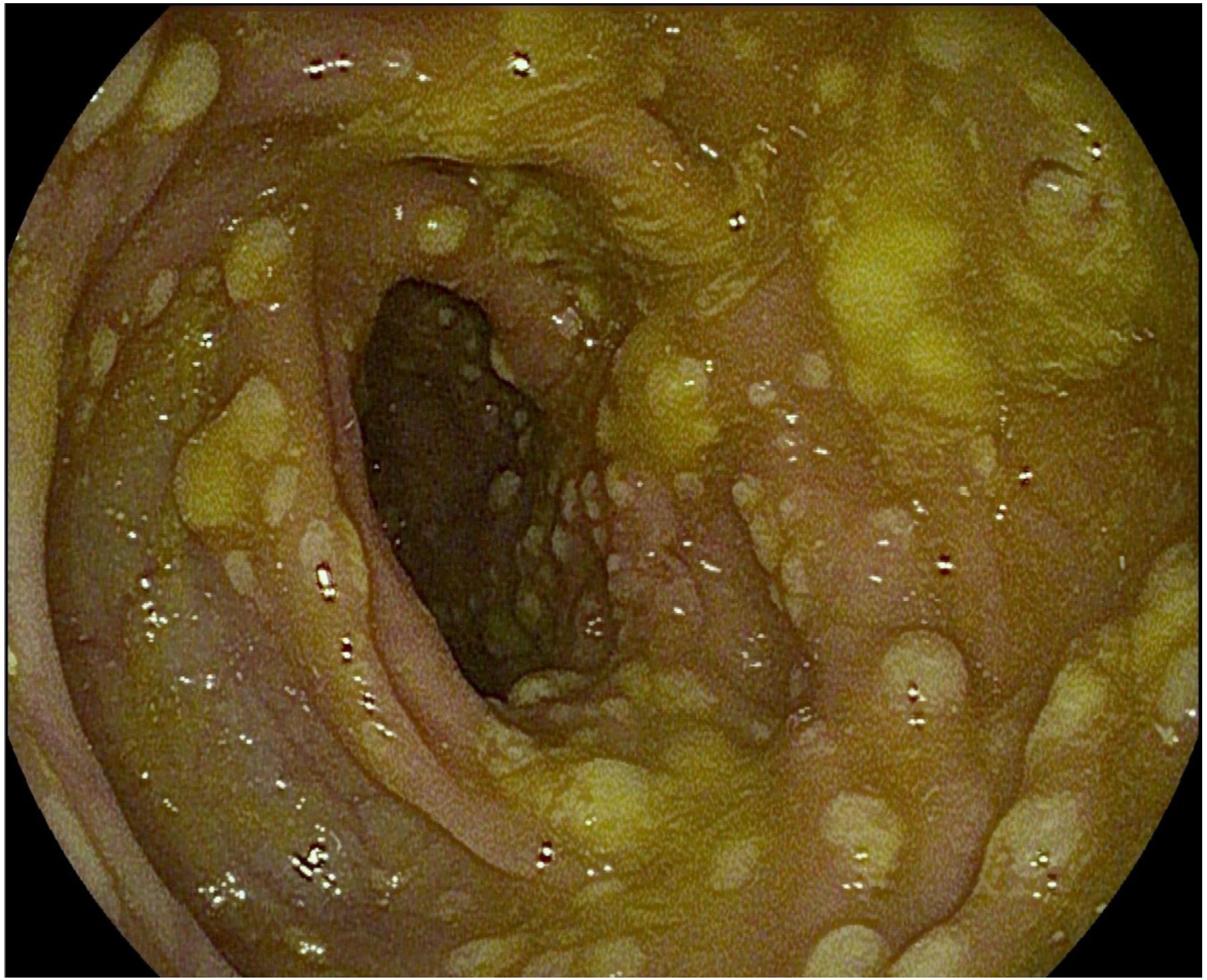
Kelly CR, et al., Am J Gastroenterol 2021;116:1124-1147

CDI TESTING INTERPRETATION



PSEUDOMEMBRANES IN CDI (40-60% PTS)

- 1/3 in **RIGHT COLON**
- Differential Diagnosis
- Bacterial infections
- CMV Colitis
- Parasitic (Amoeba/Schisto)
- Non-infectious
  - Ischaemic colitis
  - IBD
  - Behcet Disease



IMAGING

- Imaging crucial when suspecting complication
- **Abdominal X-Ray**
  - Colon dilatation
  - Nodular haustral thickening
  - Thumbprinting
  - Ascites
  - Fulminant – Toxic megacolon
  - Perforation (free air)

CONTRAST-ENHANCED CT SCAN

- Colon wall thickening
- Pancolitis
- Right sided involvement (30-40%)
- Nodularity
- Dilatation
- Accordion sign (trapped positive contrast between inflamed mucosal folds)
- Double halo/ Target sign

Five parameter CT scale predicting surgery

- Cecal wall thickness >3mm
- TV colon wall thickness >3mm
- Sigmoid wall thickness >3mm
- Pancolitis
- Bowel dilatation

TREATMENT OF CDI (NON-FULMINANT)

INITIAL EPISODE

VANCOMYCIN 125mg QID for 10days

or

FIDAXOMYCIN 200mg BD for 10days

Severe disease/IBD : 14-day duration

ALTERNATIVE IF BOTH UNAVAILABLE

METRONIDAZOLE (ORAL) 400mg TDS for 10-14 days

RECURRENT EPISODES

- Option between oral vancomycin or Fidaxomycin depending on initial choice
- Consider PULSE and TAPERING regimen

FIDAXOMYCIN 200mg BD for 5days, then daily on alternate day for days

HIGH RISK FOR FUTURE RECURRENCE

BEZLOTOXUMAB **10mg/kg STAT**

TREATMENT OF FULMINANT CDI

- **ABSENCE OF ILEUS**: Enteric vancomycin *PLUS* IV Metronidazole

VANCOMYCIN 500mg orally or NGT QID

METRONIDAZOLE 500mg IV 8hourly

- **ILEUS PRESENT:** consider adding **RECTAL VANCOMYCIN every 6 hours**

INTESTINAL TUBERCULOSIS

- Isolated colonic TB is rare
  - 2-3% with abdominal TB have isolated colonic involvement
- Most affected site is the **ileocecal region**
- Clinical features may be non-specific
- May cause significant diagnostic dilemma – **TB vs Crohn's disease**

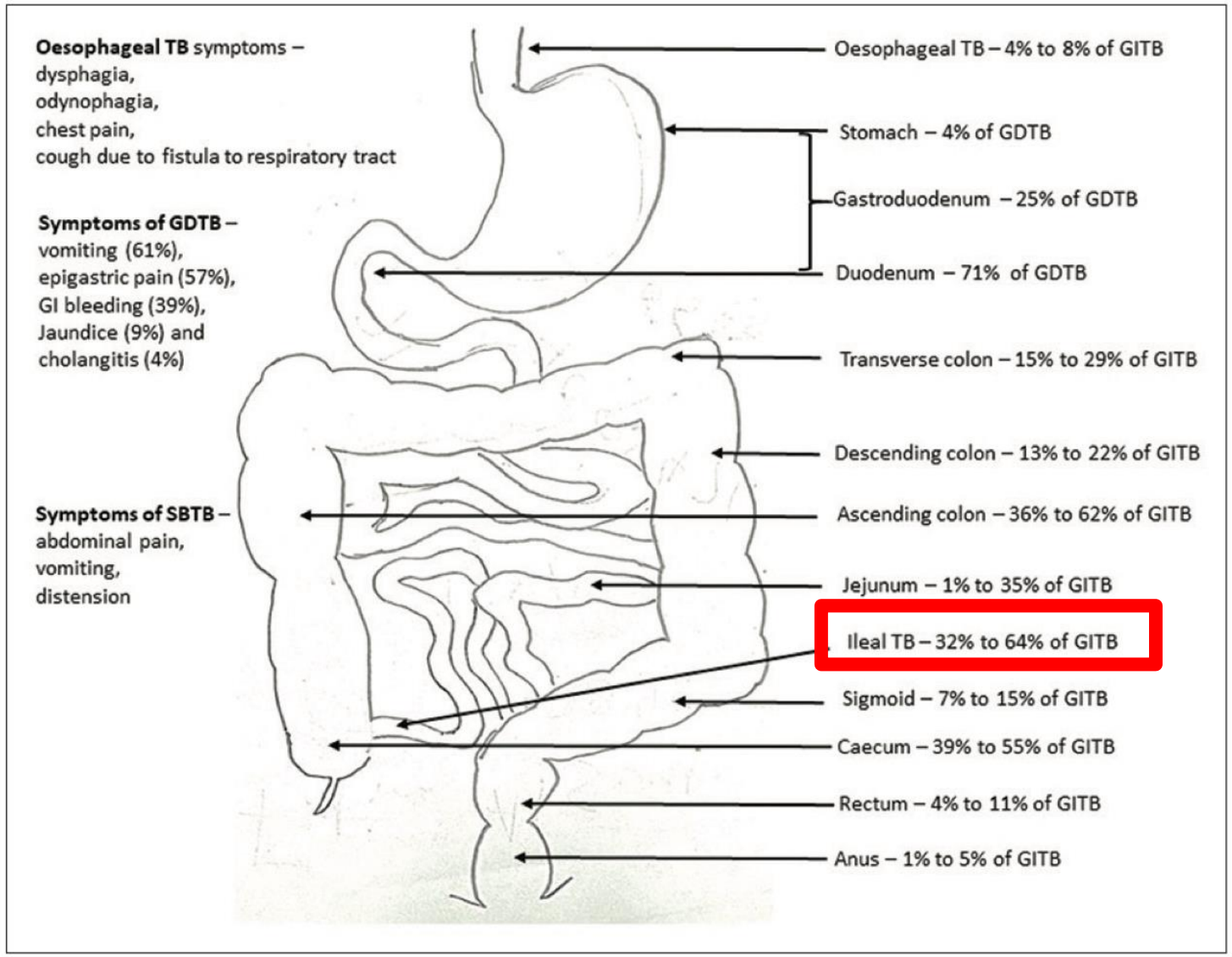
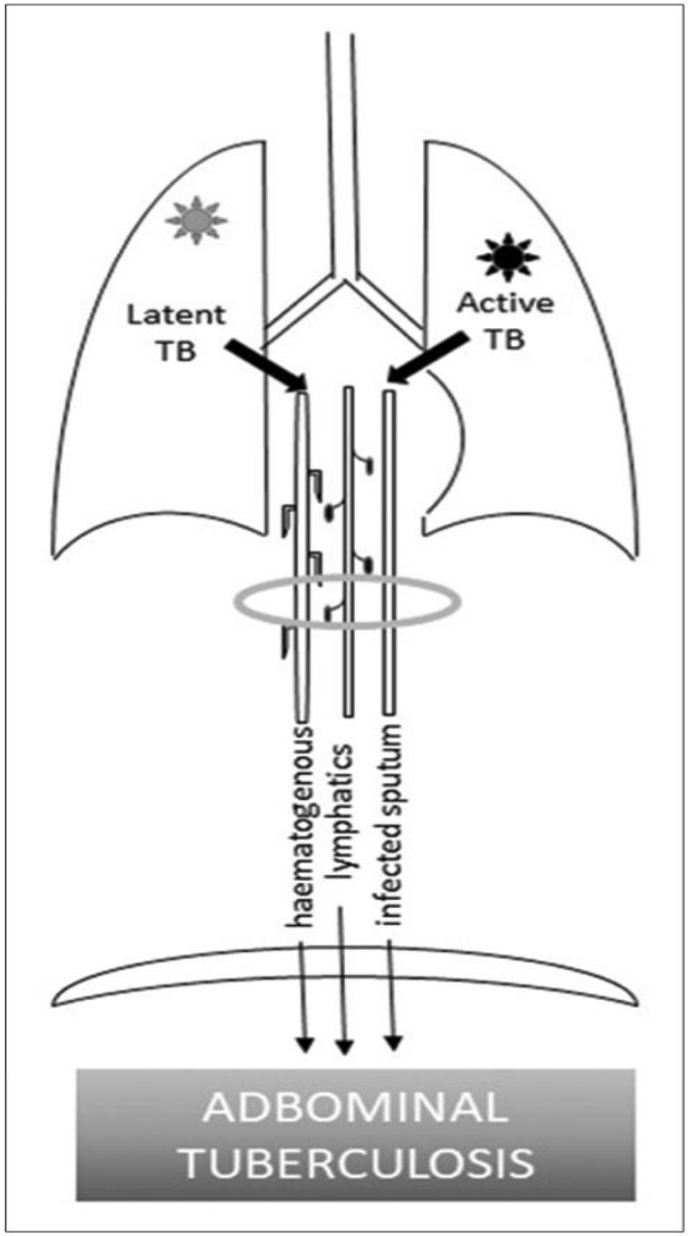


Figure 4: Different sites involved in GITB with associated symptoms

TERMINAL ILEUM AND ILEOCECAL VALVE MOST COMMON SITE

- Narrow lumen
- Relatively increased physiological stasis (absorption of organism)
- Minimal digestive activity
- Presence of M cells in lymphatic tissue that can take up tubercle bacilli



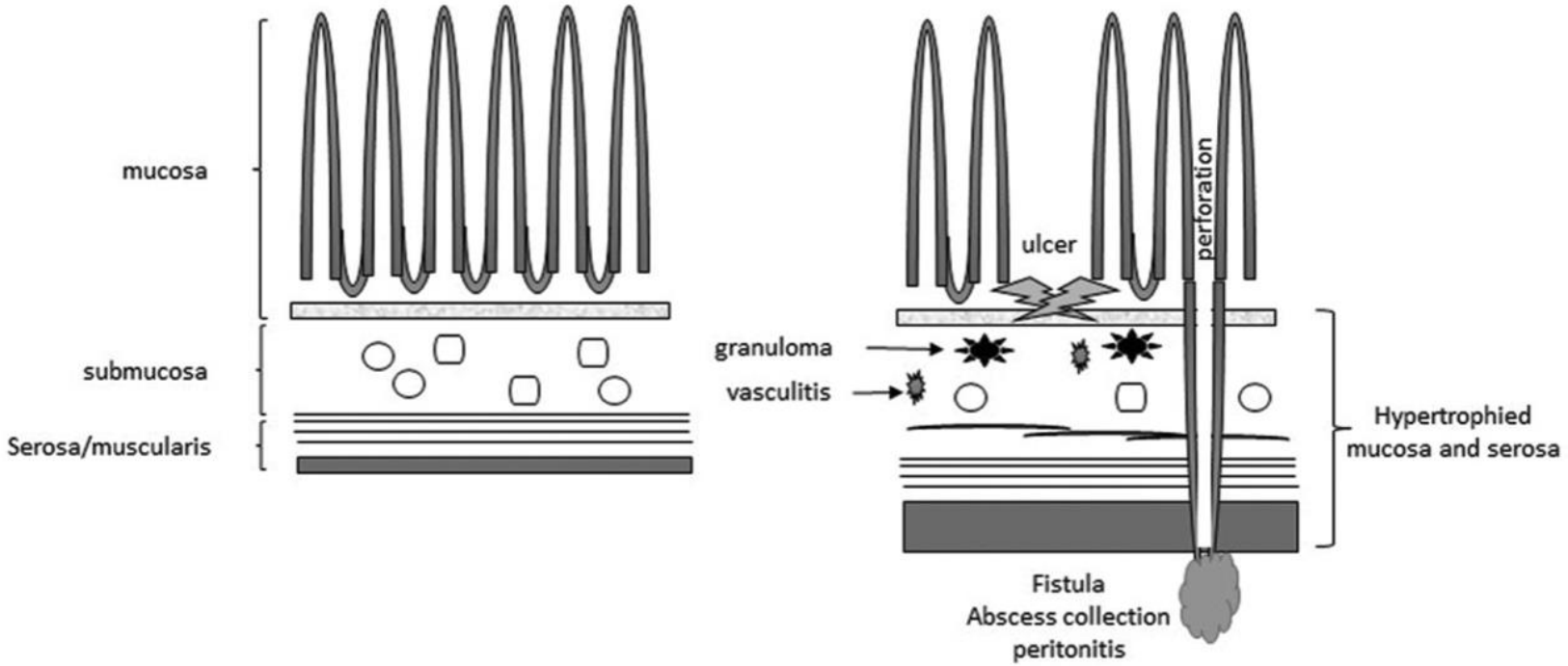
SPREAD TO GASTROINTESTINAL TRACT

Mycobacterium invades

SUBMUCOSA

- GRANULOMAS
- VASCULITIS
- HYPERTROPHY

- ULCERS
- FISTULA
- ABSCESS
- PERFORATION



4 MAJOR SUBTYPES IDENTIFIED IN GI TRACT

- **Ulcerative :**

✓ the most common form
✓ Usually presents with superficial transverse ulcers
✓ It is more likely to be seen in the small intestine

- **Hypertrophic :**

✓ occurs as a hyperplastic reaction around the ulcer, producing an inflammatory mass
✓ It is more likely to be seen in the cecum

- **Ulcero-hypertrophic :**

✓ a combination of ulcerative and hypertrophic forms

may occur

- **Fibrous stricturing :**

✓ may lead to fibrosis and stricture formation, resulting in intestinal obstruction

CLINICAL FEATURES

- In 2/3 of patients, **no** evidence of PULMONARY TB
- May be indistinguishable from **IBD (CD)**

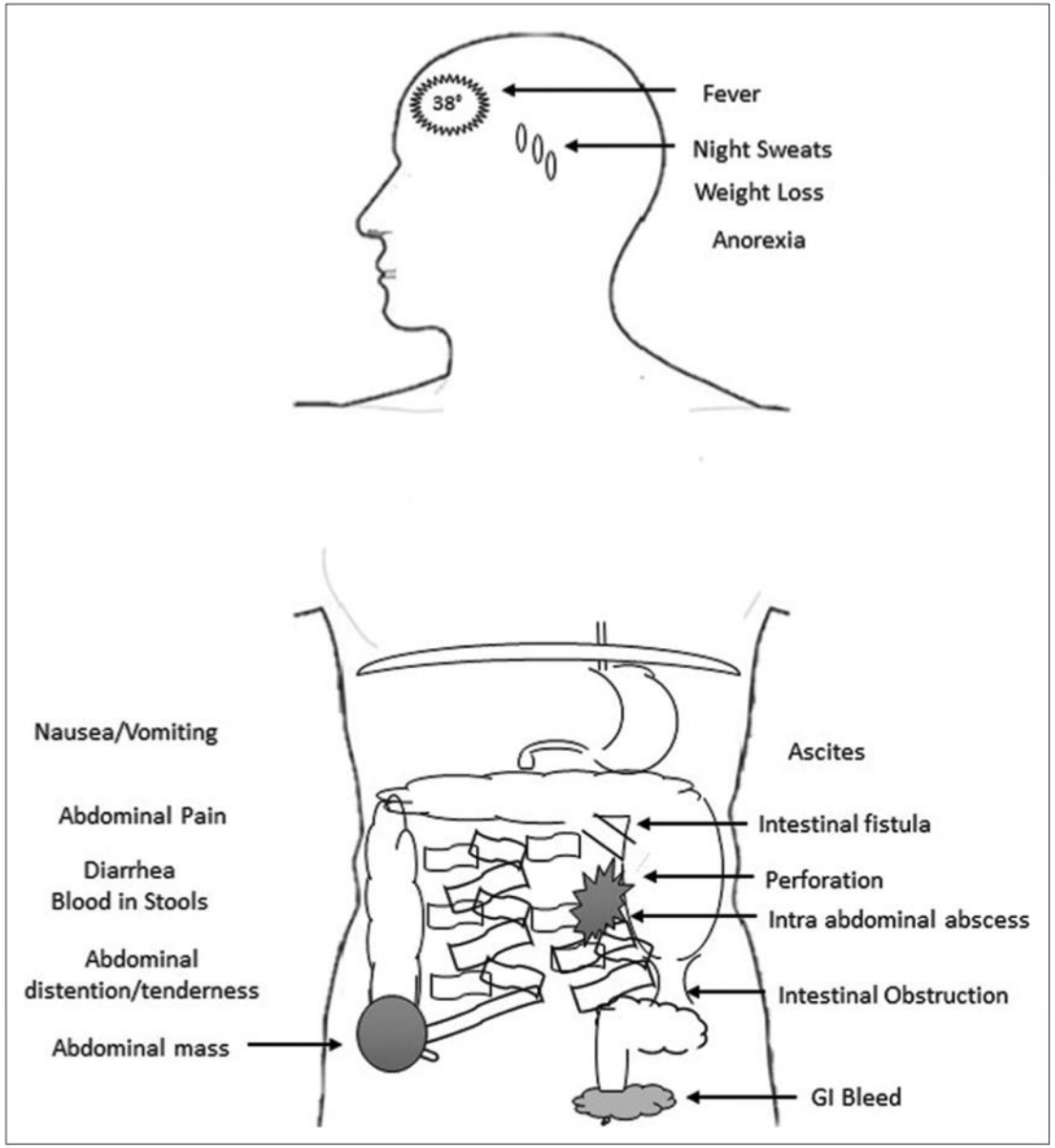
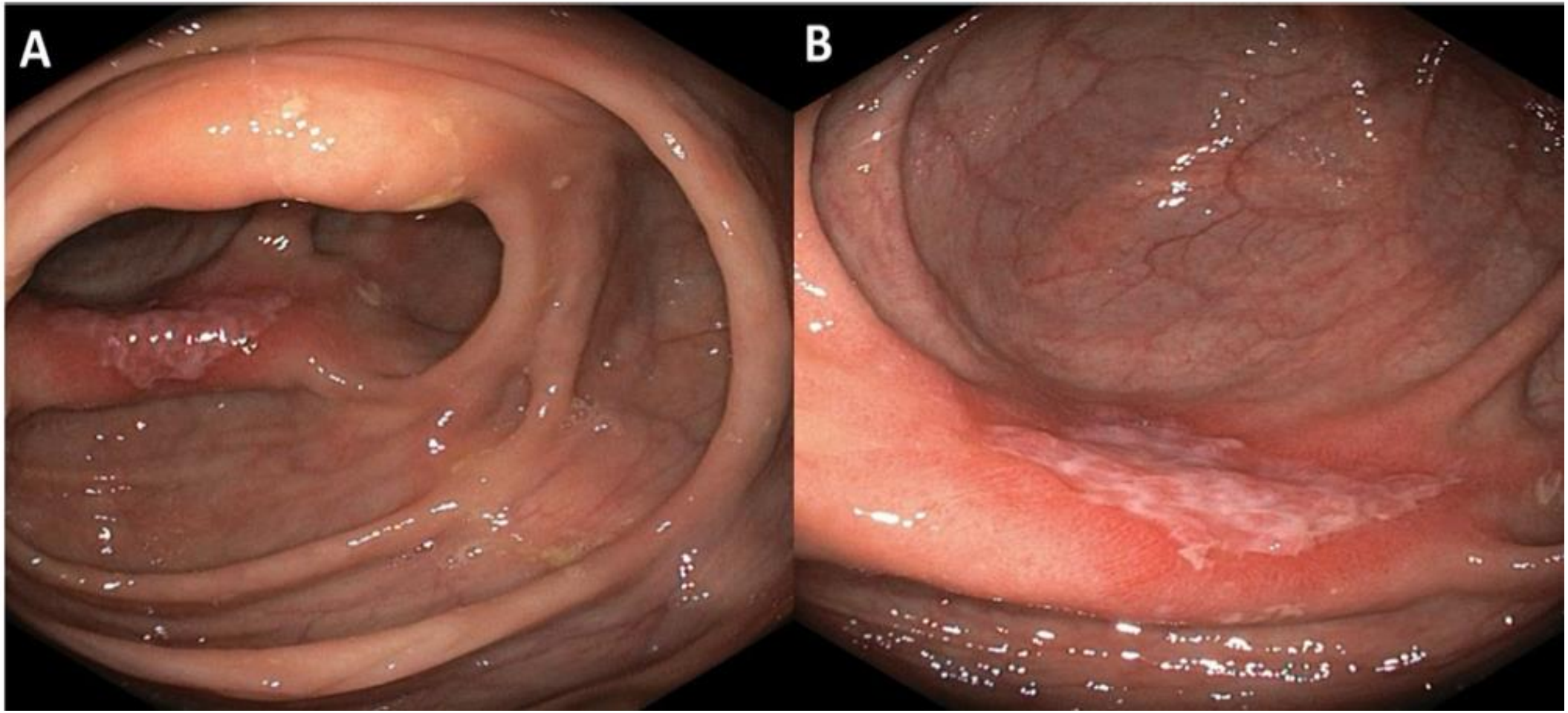
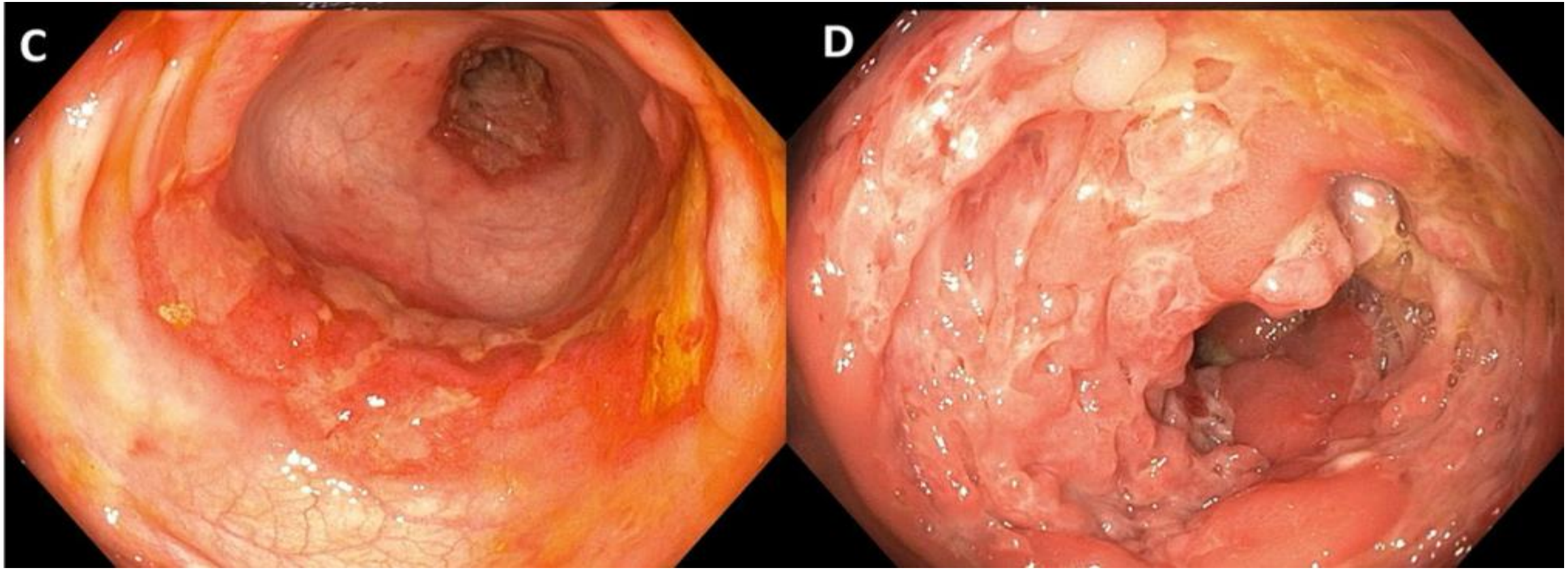


Figure 3: Constitutional and local symptoms/signs due to GITB

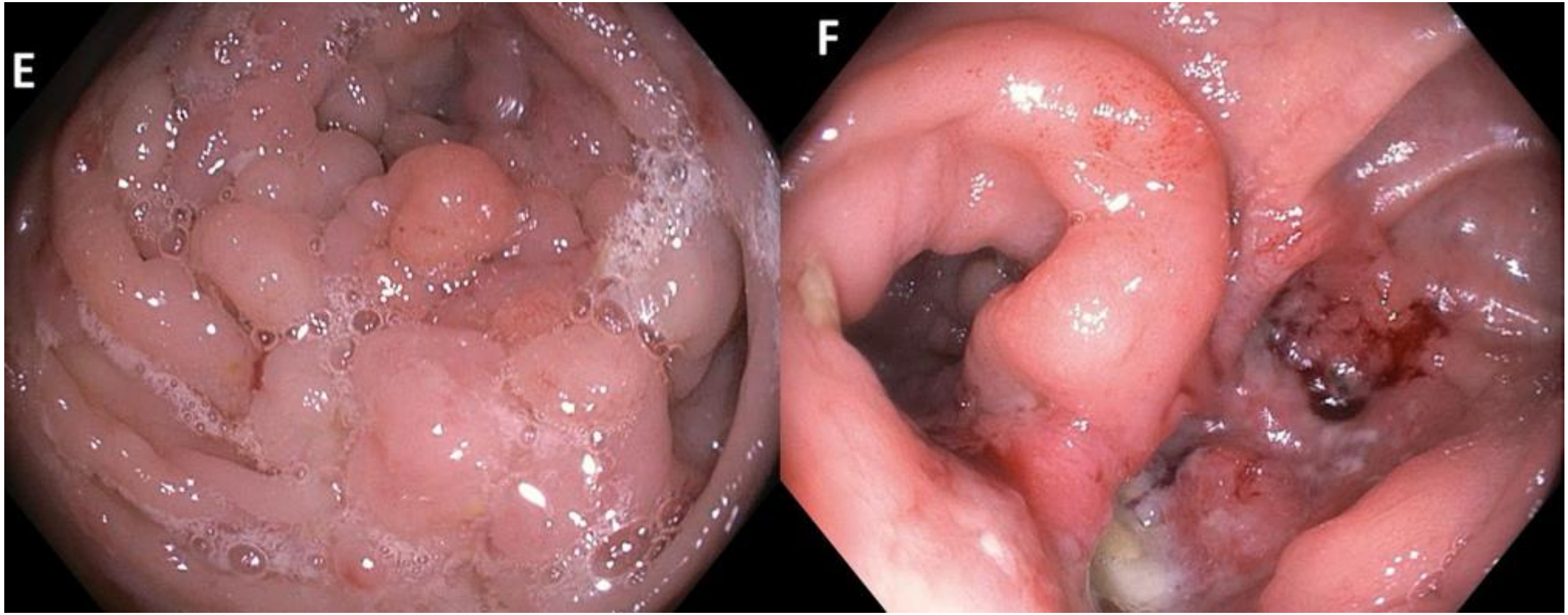
A & B: CAECAL AND AC ULCER





C. **Transverse ulcer in AC**
Skip lesion with distorted, ulcerated and narrowed caecum

D. **Ulcerations and pseudopolyp** like lesions in the caecum



E. Multiple pseudopolyps and narrowing requiring surgery

F. Distorted, narrowed and ulcerated caecum with gaping ileocecal valve

Table 3 Sensitivity of various tests for diagnosis of gastrointestinal tuberculosis and peritoneal tuberculosis

Test	Gastrointestinal tuberculosis	Peritoneal tuberculosis
AFB stain	<5%	3%
Xpert MTB/RIF	23% against a composite reference	30% against a composite reference 60% against culture
Adenosine deaminase	Not applicable	93% to 100%
MTB PCR (IS6110)	47%	25% to 80% (usually around 50%)
Multiplex PCR	75%	89%
Cultures	7% to 80% (usually around 40)	35%
Histology		NA
Confluent granuloma	38%	
Caseation	21%	
Ulcers lined by epithelioid histiocytes	41%	

AFB acid fast bacilli, *MTB PCR* Mycobacterium tuberculosis-polymerase chain reaction test, *NA* not applicable

IMAGING

CXR/AXR

- 25% of patients with Intestinal TB may have past or present features of PTB
- Normal CXR – Consider **HRCT chest** if constitutional symptoms or high pretest probability of PTB
  - *Tree-in-bud appearance*
  - Mediastinal/hilar lymph nodes
- AXR useful for complications/emergencies
  - Intestinal obstruction
  - Perforation

ULTRASOUND

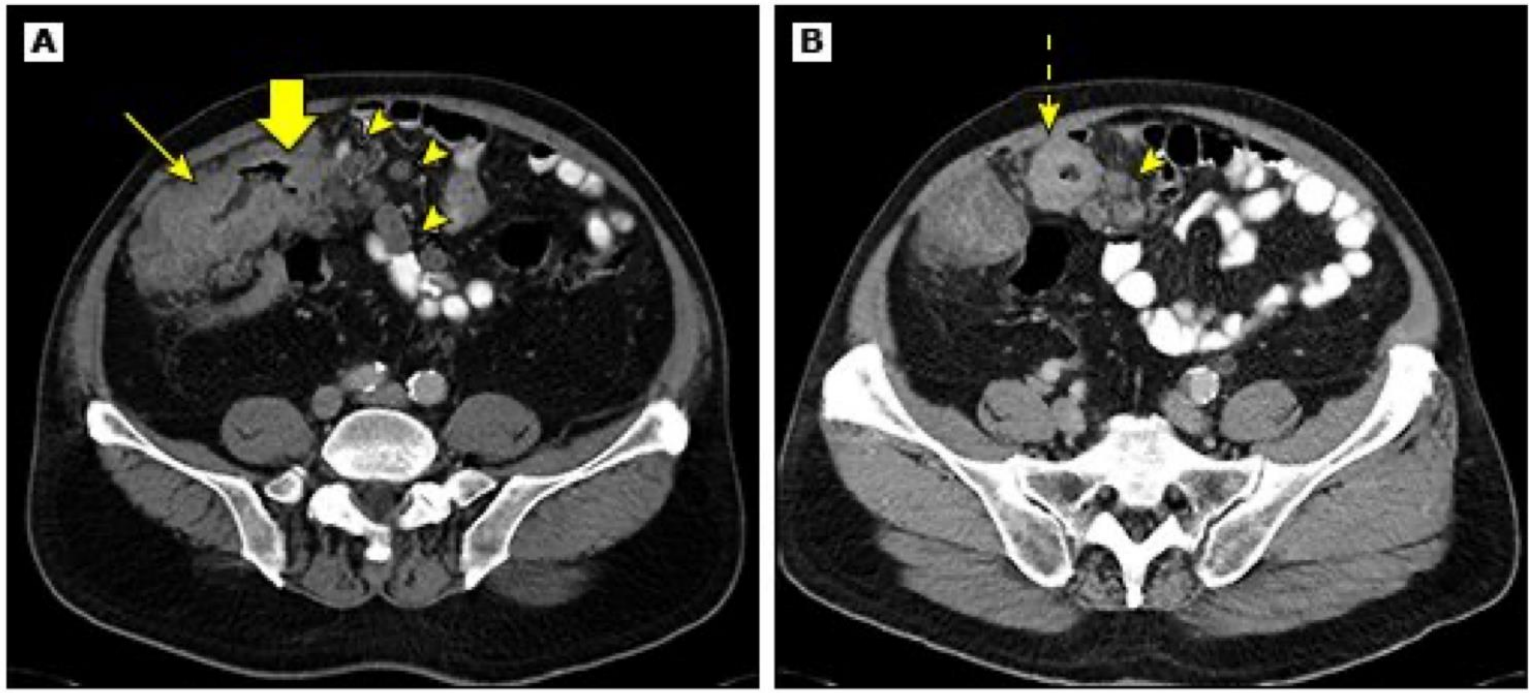
- Bowel thickening (incl ileocecal region)'
- Abdominal LN
- Presence of ascites
- Omental or peritoneal changes

Potential for fine needle aspiration or core biopsy

CONTRAST-ENHANCED CT ABDOMEN – INTESTINAL TB

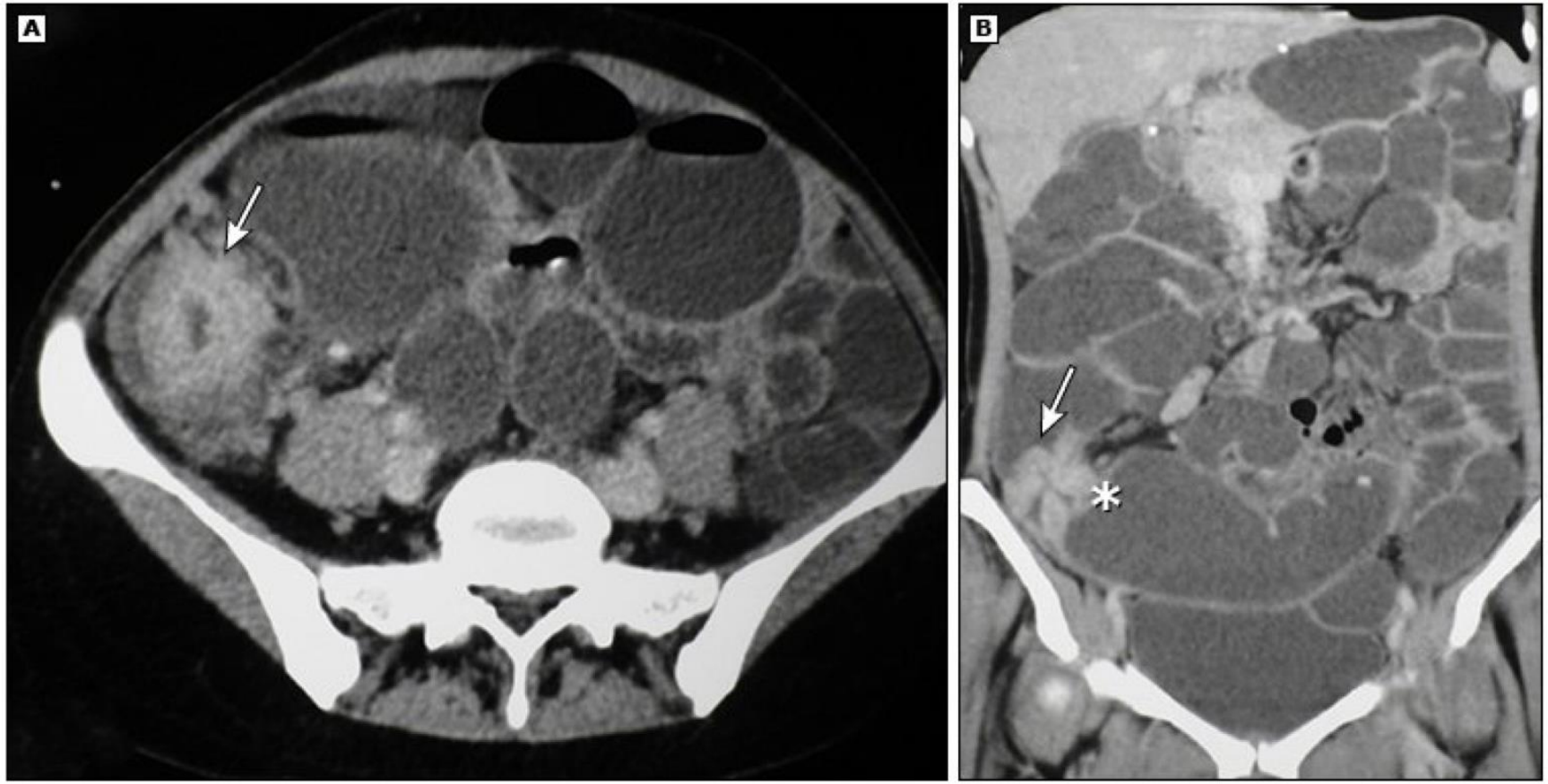
- Evaluate intestinal and extra-intestinal lesions
- Circumferential wall thickening and mucosal enhancement in terminal ileum and ileocecal regions
- Fibrostenotic strictures
- **Extra-intestinal features**
  - Mesenteric and retroperitoneal LN (esp necrotic LN)
  - Ascites
  - Omental or peritoneal thickening
  - Abdominal cocoon (fibrous sac around the small intestine)
  - Liver or splenic involvement

Tuberculous enteritis – Computed tomography



Contrast-enhanced computed tomography of histologically proven ileocecal tuberculosis showing thickened terminal ileum (arrow), ileocecal valve (thick arrow), and cecum (dashed arrow) with enlarged necrotic ileocecal lymph nodes (arrowheads).

Intestinal tuberculosis – CT enteroclysis II



Axial (A) and coronal reformatted (B) images demonstrate short segment annular terminal ileal stricture (arrow) with contiguous ileocecal involvement (asterisk).

	Favors Gastrointestinal Tuberculosis	Do not favor a particular diagnosis	Favors Crohn's Disease
Clinical Presentation	Shorter History (< 6 months) **Pulmonary symptoms (Cough, hemoptysis)** **Peritoneal involvement (Ascites)** Abdominal lump **+ve TB contact**	Abdominal Pain Intestinal Obstruction	Chronic diarrhea Hematochezia Perianal symptoms Extraintestinal manifestations
Imaging findings	**Necrotic lymph node** Patulous ileo-cecal valve Short strictures Asymmetric mural thickening Ascites, peritoneal or omental involvement Pulmonary lesions	Mural thickening Strictures Lymph nodes	Mural stratification Fibrofatty proliferation Comb sign Skip lesions Long segment involvement (> 3cm)
Colonoscopic findings	Patulous Ileo-cecal valve Circumferential or transverse ulcers **Caecum > ileum**	Ulcers Pseudopolyps Strictures Ulcerated narrowing	Aphthous ulcers Longitudinal ulcers Serpiginous ulcers Cobblestoning Skip lesions **ileum > caecum**
Histopathology	Large granuloma **Confluent granuloma** **Caseating granuloma** **Ulcer lined by histiocytes**	Granuloma Chronic inflammation including distorted architecture Paneth cell metaplasia	Focally enhanced colitis Microgranuloma Sparse granuloma

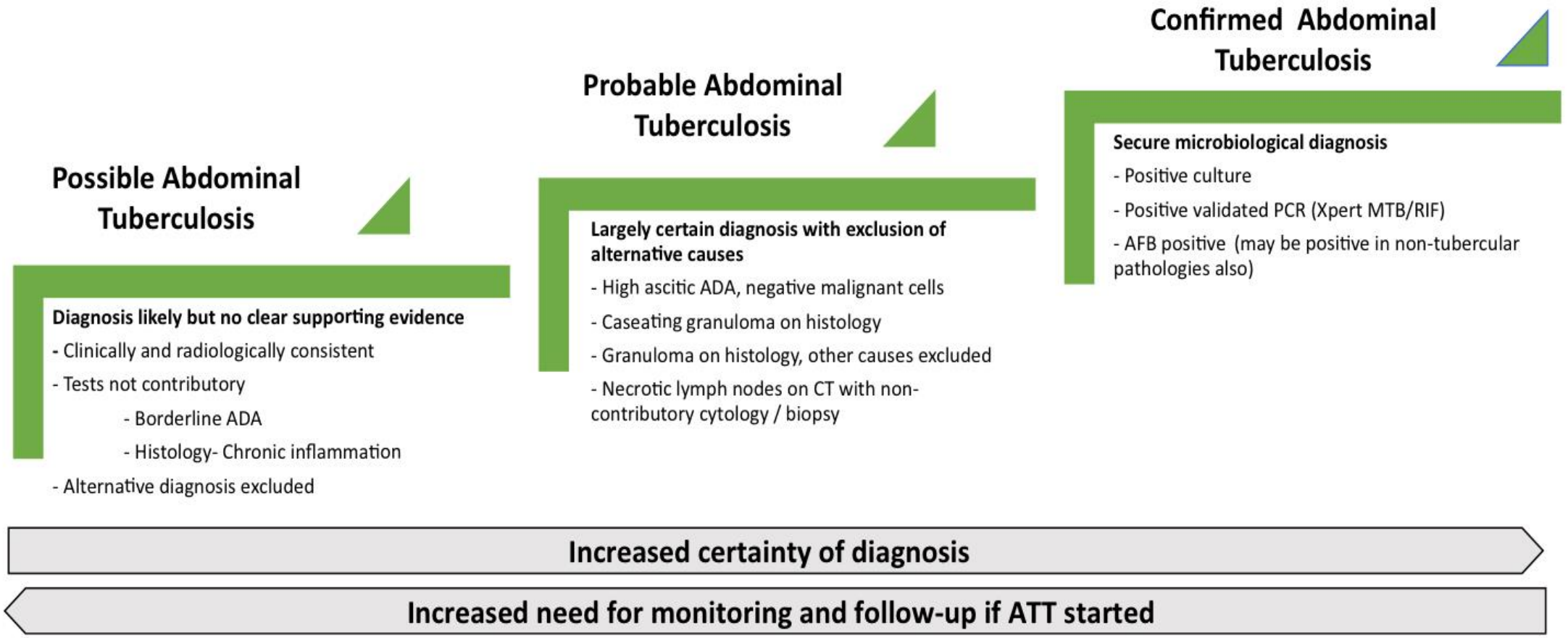


Fig. 1 Summary of case definitions and a hierarchical approach to defining an abdominal tuberculosis case. *ADA* adenosine deaminase, *CT* computed tomography, *PCR* polymerase chain reaction, *AFB* acid-fast bacilli

INFECTIOUS COLITIS : AETIOLOGY

BACTERIA	VIRUSES
Campylobacter	**HIV**
Salmonella	**CMV**
Shigella	Norovirus
E.Coli	Rotavirus
Clostridioides Difficile	Adenovirus
Mycobacterium TB Yersinia Enterocolitica	

VIRAL COLITIS

- Norovirus, Rotavirus & Adenovirus common in infants and young children
- **CMV colitis** more common adults > children
  - Prevalence of CMV infections 12%-34%
  - Esp IBD (mainly UC) in immunocompetent patients
    - Prevalence 4.5% - 16%
    - **Classic presentation: Steroid refractory colitis (typically ASUC) in immunosuppressed patient**
      - **Ulcers usually present**
      - **Require colonic biopsies and immunohistochemistry**
      - **CMV virema in only 30%**
    - > 25% require colectomy
  - HIV positive pts – CD4< 50, usually associated CMV retinitis

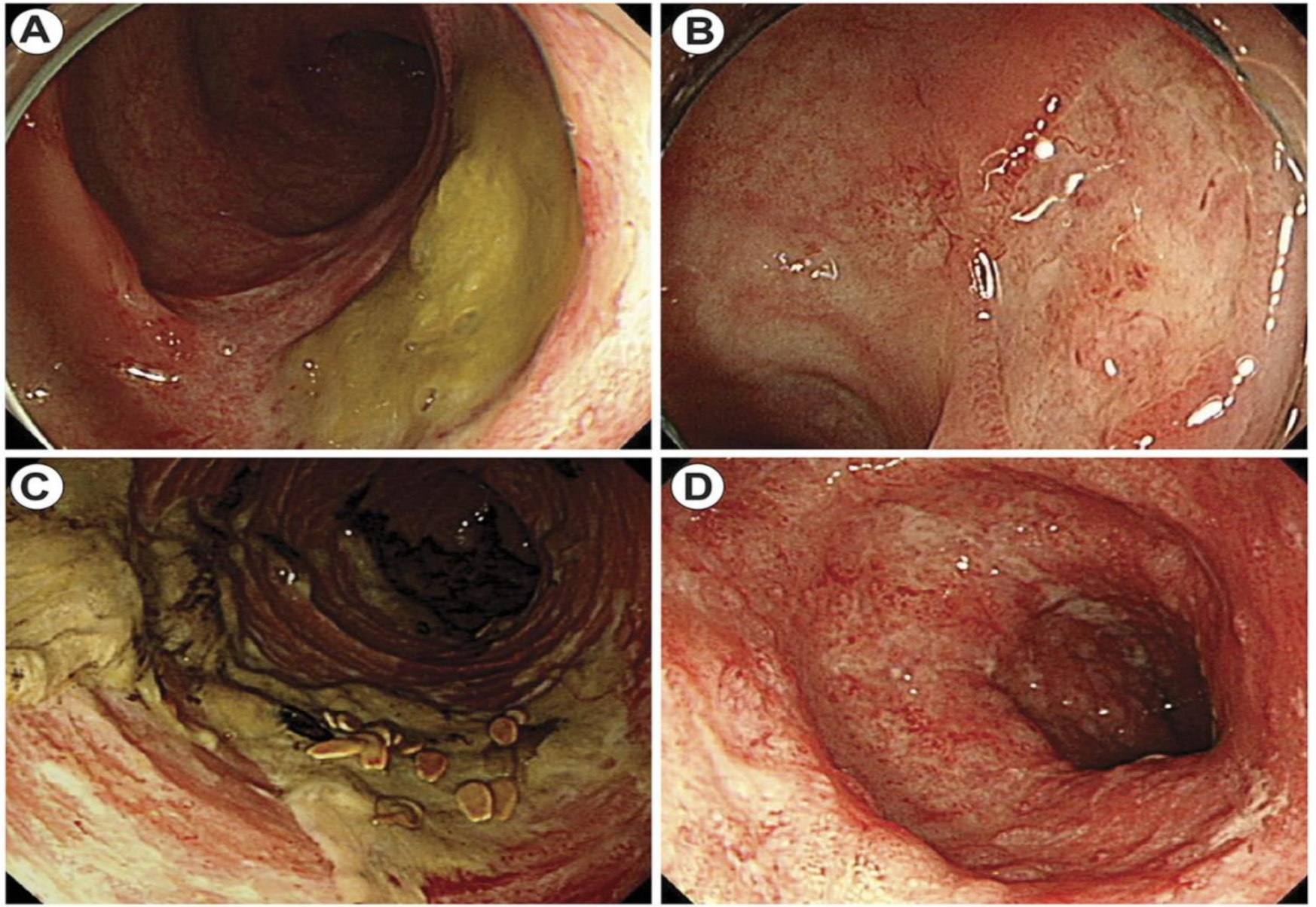


Figure 2. Endoscopic types according to gross features. (**A**) Discrete ulcerative type with exudate. (**B**) Discrete ulcerative type without exudate. (**C**) Diffuse erythematous type with exudate. (**D**) Diffuse erythematous type without exudate. All images (**A**–**D**) are cytomegalovirus colitis.

DIAGNOSTIC TESTS FOR CMV COLITIS

SEROLOGY – IgM

- 4x IGG

Quantitative PCR on Blood – Viral DNA (viral load)

ANTIGEN – pp65 Antigen

Tissue invasive disease – Colonic biopsies demonstrating:

- CMV inclusions
- positive CMV-specific immunohistochemistry staining on histopathology

Diagnostic tests for cytomegalovirus*

	Serology	Quantitative PCR¶	Antigenemia△	Culture	Histopathology◇	Resistance testing
Immunocompetent						
Acute or recent infection	IgM or fourfold increase of IgG	Plasma or whole blood				
Past infection	IgG					
Critically ill		Plasma or whole blood; consider BAL				
Immunocompromised						
Assessing risk of CMV disease	IgG					
Diagnosis of disease						
Viral syndrome		Plasma or whole blood	PBMCs			
Pneumonitis		Plasma or whole blood; consider BAL	PBMCs	BAL or lung tissue	BAL or lung tissue	
Gastrointestinal disease		Plasma or whole blood§	PBMCs§	Tissue	Tissue	

CMV INFECTION AND DISEASE

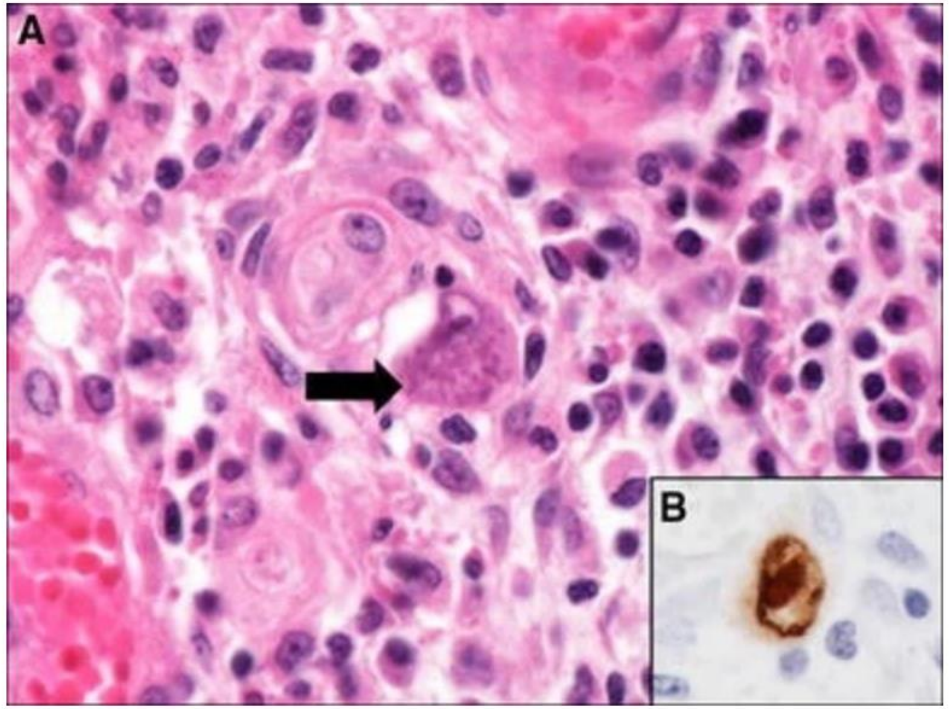
CMV INFECTION

- virus isolation or detection of viral proteins (antigens) in any body fluid or tissue specimen **regardless of symptoms or signs**
- Seroconversion with the appearance of anti-CMV IgM antibodies
- 4X increase anti-CMV IgG titres
- Detection of CMV antigens in infected cells
- CMV-PCR testing dominant technique at present

CMV DISEASE

- **evidence of CMV infection with attributable symptoms or signs**
- Transplant patients: CMV viral load of DNA >500 copies/ugram of Total DNA in peripheral blood had clinical evidence of disease

CMV INFECTION IN PATIENT WITH TOXIC MEGACOLON/ STEROID REFRACTORY UC



Histological diagnosis of cytomegalovirus. **a** Microphotograph (H&E, ×40) of colonic tissue showing eosinophilic intranuclear and cytoplasmatic inclusions (*arrow*). **b** Positive immunohistochemical staining for CMV (×40)

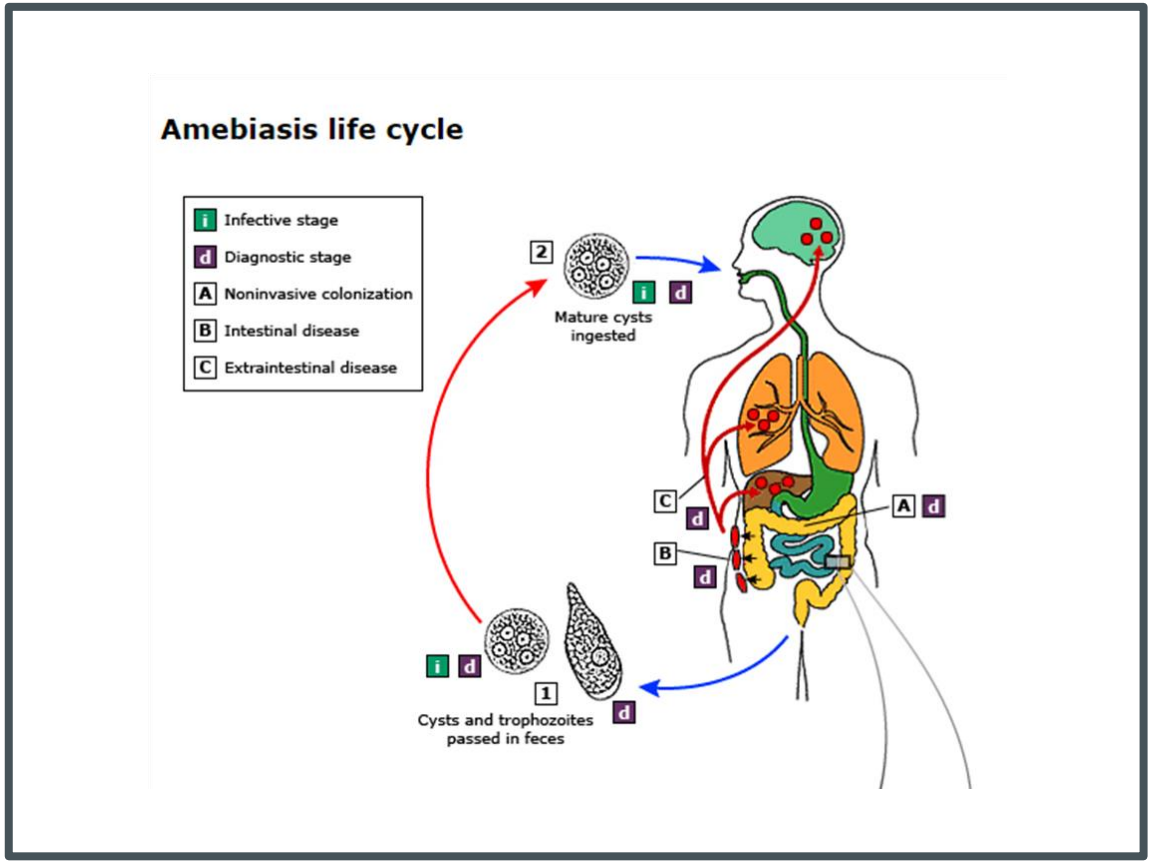
TREATMENT OF CMV COLITIS

- Selection of antiviral treatment is determined by:
  - **severity of illness, initial viral load**
  - **ability to tolerate oral vs IV medication**
- Continue current immunosuppression (GSH practice)
- Severe disease (tissue invasive disease): **IV GANCICLOVIR 5mg/kg BD**
- Mild to moderate disease: **oral valganciclovir 450mg BD**
- **Duration of treatment – until symptoms and viremia disappears**
  - Usually IV treatment for 7 days, followed by oral treatment (900mg OD) for 14 days (1-3 months in literature)
- Monitor response with Viral load and Antigen (weekly)

INFECTIOUS COLITIS : AETIOLOGY

BACTERIA	VIRUSES	PARASITES
Campylobacter	**HIV**	**Entamoeba histolytica**
Salmonella	**CMV**	Strongyloides Stercoralis
Shigella	Norovirus	
E.Coli	Rotavirus	
Clostridioides Difficile	Adenovirus	
Mycobacterium TB Yersinia Enterocolitica		

AMOEBIASIS



- **4 different species -** E. histolytica, E. dispar, E. moshkovskii, E. Bangladeshi
- Intestinal amoebiasis caused by **Entamoeba histolytica**
- parasite exists in two forms:
  - **Cyst stage** (the infective form)
  - **Trophozoite stage** (the form that causes invasive disease)
- Infection occurs following ingestion of **amoebic cysts**
  - usually via contaminated food or water
  - Cysts can remain viable in the environment for weeks to months
  - ingestion of a single cyst is sufficient to cause disease

RISK FACTORS FOR SEVERE AMOEBIASIS

- young age
- Pregnancy
- Malignancy
- Malnutrition
- Alcoholism
- **Corticosteroid treatment**
  - Rapid deterioration for incorrect steroid usage for misdiagnosed colitis – 25%mortality

CLINICAL PRESENTATION - AMOEBIASIS

- Subacute onset (1-3 weeks)
- **Chronic non-dysenteric colitis** - most frequent form of amoebiasis in people of all ages
- Symptoms range from mild diarrhea to severe dysentery:
  - ✓ abdominal pain (12 to 80 percent)
  - ✓ diarrhea (94 to 100 percent)
  - ✓ Bloody stools (94 to 100 percent)

  hematophagous trophozoites (trophozoites with ingested red blood cells) in stools –

  INVASIVE INTESTINAL AMOEBIASIS

- ✓ Weight loss (50%)
- ✓ Fever (38%)
- ✓ fulminant amebic colitis

Acute fulminant necrotizing amebic colitis presents with life-threatening lower gastrointestinal bleeding without diarrhea

FULMINANT AMOEBIC COLITIS

Fulminant amoebic colitis with bowel necrosis

↓

Peritonitis

Toxic megacolon

↓

PERFORATION (0.5%)

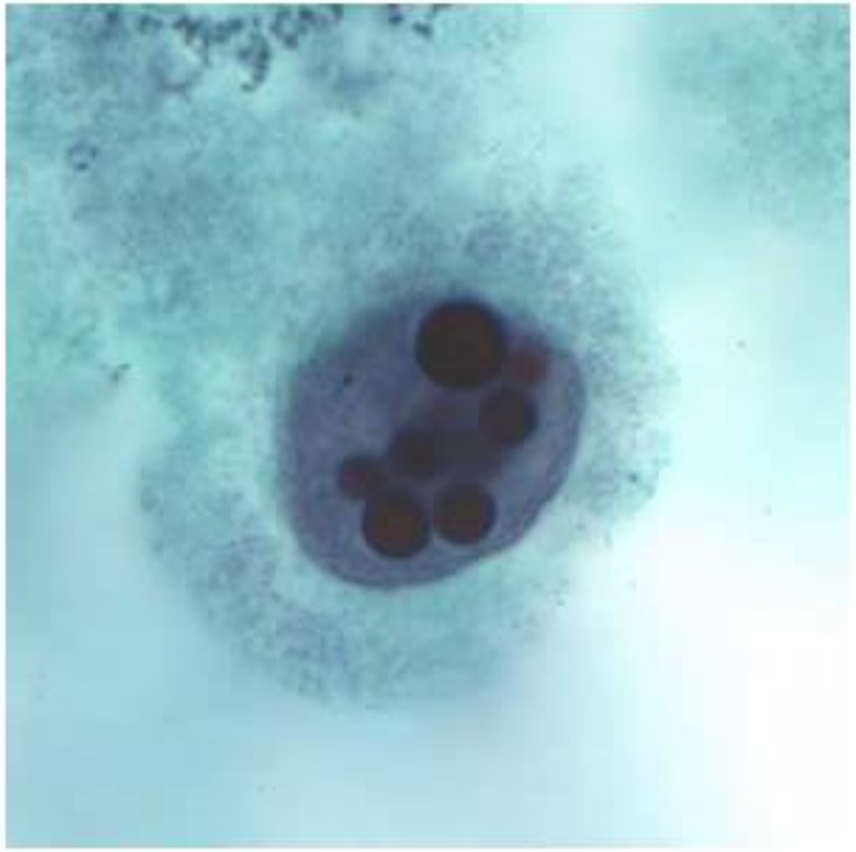
Mortality = 40%

DIAGNOSIS - AMOEBIASIS

- **Stool evaluation: 3 samples on 3days**
  - **Microscopy** - demonstration of cysts or trophozoites
  - **Stool antigen** - sensitive, specific, rapid, easy to perform
    - Sensitivity 87% specificity >90%
  - **Stool PCR** – **Preferred**
    - High sensitivity and specificity >> Stool antigen
    - Differentiate between different strains of Entamoeba

Serology is not very helpful in endemic areas as antibodies can persist for years after infection

Entamoeba histolytica trophozoite: Microscopy



Trophozoites of *E. histolytica* with ingested erythrocytes stained with trichrome.

DIAGNOSIS - SEROLOGY

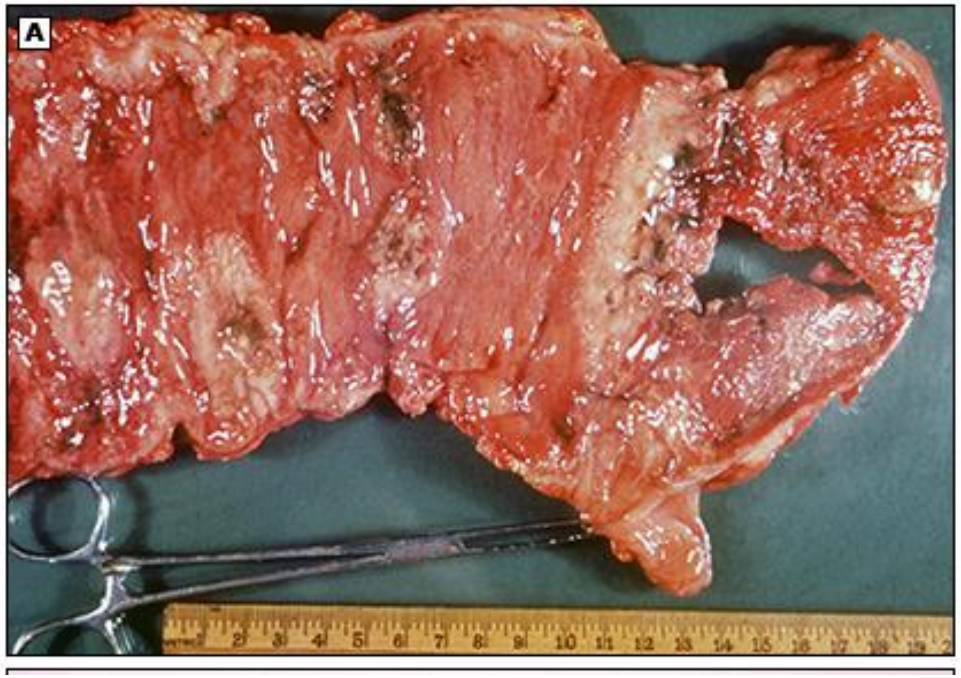
- **Antibodies** are detectable **5-7 days** of acute infection
  - may persist for years
  - **Indirect hemagglutination (IHA)** is the most sensitive serologic assay >90% symptomatic pts

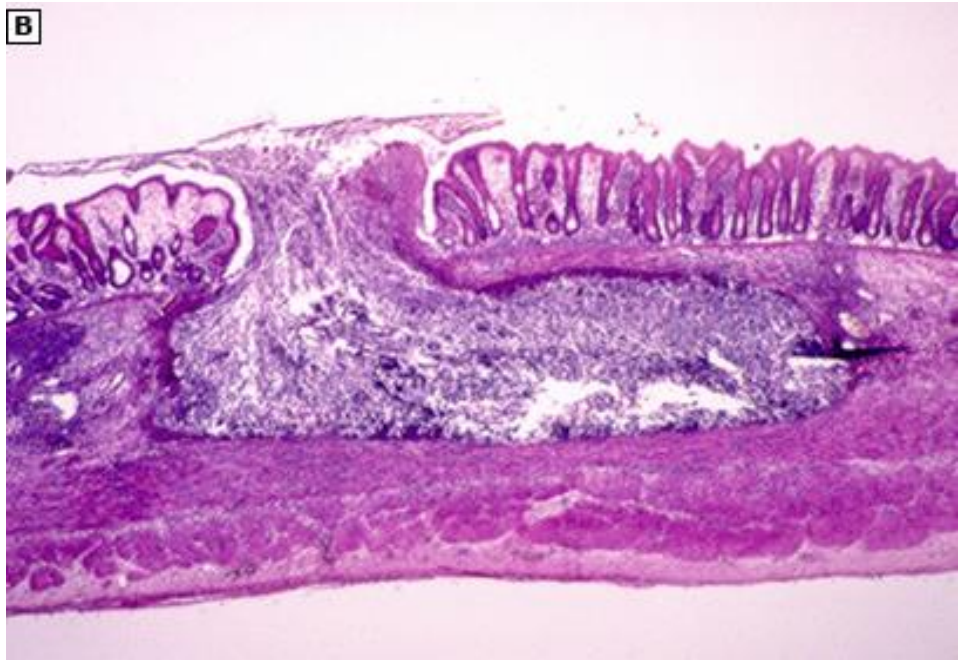
- **NEGATIVE** serology **EXCLUDES** the disease
- **POSITIVE** serology = **acute and previous infection** (esp in endemic areas)
  - 10 -35 percent of uninfected individuals in endemic areas have antibodies due to previous infection with *E. histolytica*

DIAGNOSIS - ENDOSCOPY

- **Sigmoidoscopy/ colonoscopy** useful for :
  - diagnosing amoebiasis
  - exclude other causes of symptoms
- **Increased risk of perforation**
  - Air insufflation in the presence of amebic ulcerations
- Typical findings : diffuse wall thickening, skip lesions or pancolitis
- **Colonic biopsies** from the edge of ulcers:
  - may be positive for cysts or trophozoites on microscopy
  - Antigen testing for *E. histolytica* may be positive
- **Histology:** range from nonspecific mucosal thickening and inflammation to classic **flask-shaped amebic ulcers**

Ulceration in amebic colitis





Multiple ulcers in post-op specimen

- **Classic flask-shaped ulcer**
- **Mucosal ulceration with submucosal invasion**

TREATMENT OF INTESTINAL AMOEBIASIS

- All patients should be treated (incl asymptomatic)
- Mild -moderate disease: oral metronidazole for 10 days
- **Fulminant colitis/peritonitis/toxic megacolon:** IV Metronidazole plus treatment for gram-negative enteric organism (IV Ceftriaxone)

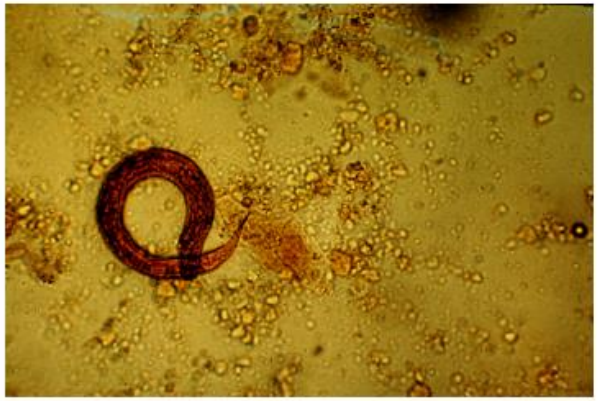
STRONGYLOIDES STERCORALIS COLITIS (ROUND WORM)

STRONGYLOIDES HYPERINFECTION SYNDROME

catastrophic complication precipitated by usage of **STEROIDS** and immunosuppression in a patient with Strongyloides infection

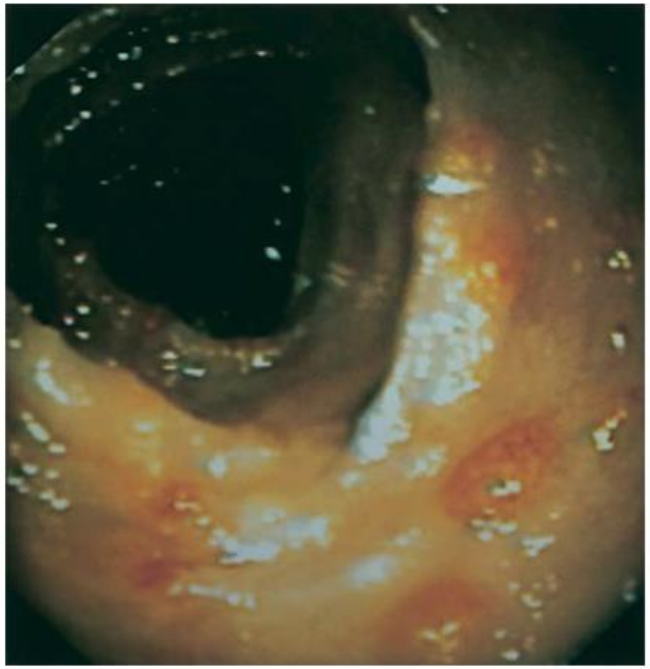
- Accelerated autoinfection and disseminated Strongyloides infection
- Initially misdiagnosed and treated as **IBD**
- **Mortality 77-100%**

Strongyloides stercoralis



Wet mount of stool (x100) shows the diagnostic rhabditiform larval form of *Strongyloides stercoralis*.

Endoscopy - strongyloidiasis



Colonoscopic view of multiple 2 mm diameter nodules with surrounding erythema.

INFECTIOUS COLITIS :AETIOLOGY

BACTERIA	VIRUSES	PARASITES	SEXUALLY TRANSMITTED PATHOGENS
Campylobacter	**HIV**	**Entamoeba histolytica**	Neisseria
Salmonella	**CMV**	Strongyloides Stercoralis	Chlamydia Trachomatis
Shigella	Norovirus		Treponema Pallidum
E.Coli	Rotavirus		**Herpes Simplex I & 2**
Clostridioides Difficile	Adenovirus		
Mycobacterium TB Yersinia Enterocolitica			

DIARRHOEA IN HIV PATIENT

Enteric pathogens

Pathogen	Small bowel	Colon
Bacteria	*Salmonella**	*Campylobacter**
	Escherichia coli¶	*Shigella*
	Clostridium perfringens	*Clostridioides difficile*
	Staphylococcus aureus	*Yersinia*
	Aeromonas hydrophila	*Vibrio parahaemolyticus*
	Bacillus cereus	Enteroinvasive *E. coli*
	Vibrio cholerae	*Plesiomonas shigelloides*
		Klebsiella oxytoca (rare)
Virus	Rotavirus	Cytomegalovirus*
	Norovirus	Adenovirus
	Astrovirus	Herpes simplex virus
Protozoa	*Cryptosporidium**	*Entamoeba histolytica*
	*Microsporidium**	
	Cystoisospora	
	Cyclospora	
	Giardia lamblia	

* Can involve both the small and large bowel, but are most likely to occur as listed.

¶ EPEC, EAggEC, EHEC, ETEC may all contribute; routine laboratories and cultures will not differentiate these from E. coli which are normal flora.

UpToDate®

Gut neoplasms
Lymphoma
Kaposi's sarcoma
Pancreatic insufficiency

APPROACH TO INFECTIOUS COLITIS

- **Thorough history and physical examination is crucial**
- Aim is to identify patients who may be at **risk of severe illness** or susceptible to **complications**

INITIAL DIAGNOSTIC WORK-UP

Bloods:

- FBC and Diff (esp Eosinophil)
- U&E
- INFLAMMTORY MARKERS – CRP ± ESR
- LFT and ALBUMIN
- ARTERIAL BLOOD GAS
- Blood cultures
- HIV

Stool:

- MC&S
- CDI Antigen and toxin

Sputum for GXP if TB is considered

IMAGING

- Plain radiographs: **CXR and AXR**
- **Abdominal and Pelvis CT (contrasted)**
  - Useful for differentiating infectious vs non-infectious colitis
  - 5 Radiological signs for bacterial colitis
    - Continuous distribution
    - Empty colon
    - Absence of fat stranding
    - Absence of "comb" sign
    - Absence of enlarged lymph nodes

ENDOSCOPY – SIGMOIDOSCOPY/COLONOSCOPY

INDICATION

- If work-up has not confirmed a diagnosis
- Identify PMC in CDI
- Evaluate proctitis, tenesmus or STD
- Evaluate underlying IBD (if known or suspected)

CONTRA-INDICATIONS

- **Absolute:**
  - Proven or suspected perforations
  - Major comorbidities
- **Relative:**
  - Acute, fulminant colitis
  - Toxic megacolon

Performed early on, preferably within 4-5 days after initiation of symptoms

- Lesions tend to **migrate distally** and coalesce with time
- Rectum may be **intact** early in the course of infectious colitis, but severely infected in later stages
- **patchy lesions may become confluent**

General tips

- Unprepared colon, fleet enemas may be used
- Use very minimal air to lower perforation risk
- Describe nature, severity and distribution of lesions
- Biopsy normal and abnormal areas

General complications

C. difficile	*Salmonella*	*Shigella*	*C. jejuni*	CMV	Rotavirus	Enteroinvasive *E. coli*	Enterohaemorrhagic *E. Coli*	*Y. enterocolitica*
•Toxic megacolon	•Toxic megacolon	•Toxic megacolon	•Toxic megacolon	•Toxic megacolon	•Toxic megacolon			
•Septic shock and death		•Septic shock and death						
		•Haemolytic-uraemic syndrome	•Haemolytic-uraemic syndrome				•Haemolytic-uraemic syndrome	
		•Reactive arthritis	•Reactive arthritis					•Reactive arthritis
			•Guillain-Barré syndrome (serotype HS:19)	•Guillain-Barré syndrome				
						•Haemorrhagic colitis	•Haemorrhagic colitis	
•Pseudo-membrane formation	•Elevated serum pancreatic enzymes without clinical pancreatitis	•Encephalitis and seizure	•Pancreatitis, cholecystitis, meningitis, purulent arthritis	•If complicating IBD, severe haemorrhage, megacolon, fulminant colitis, or colon perforation				•Erythema nodosum
•Renal failure and shock		•Hypoglycaemia and hyponatremia						

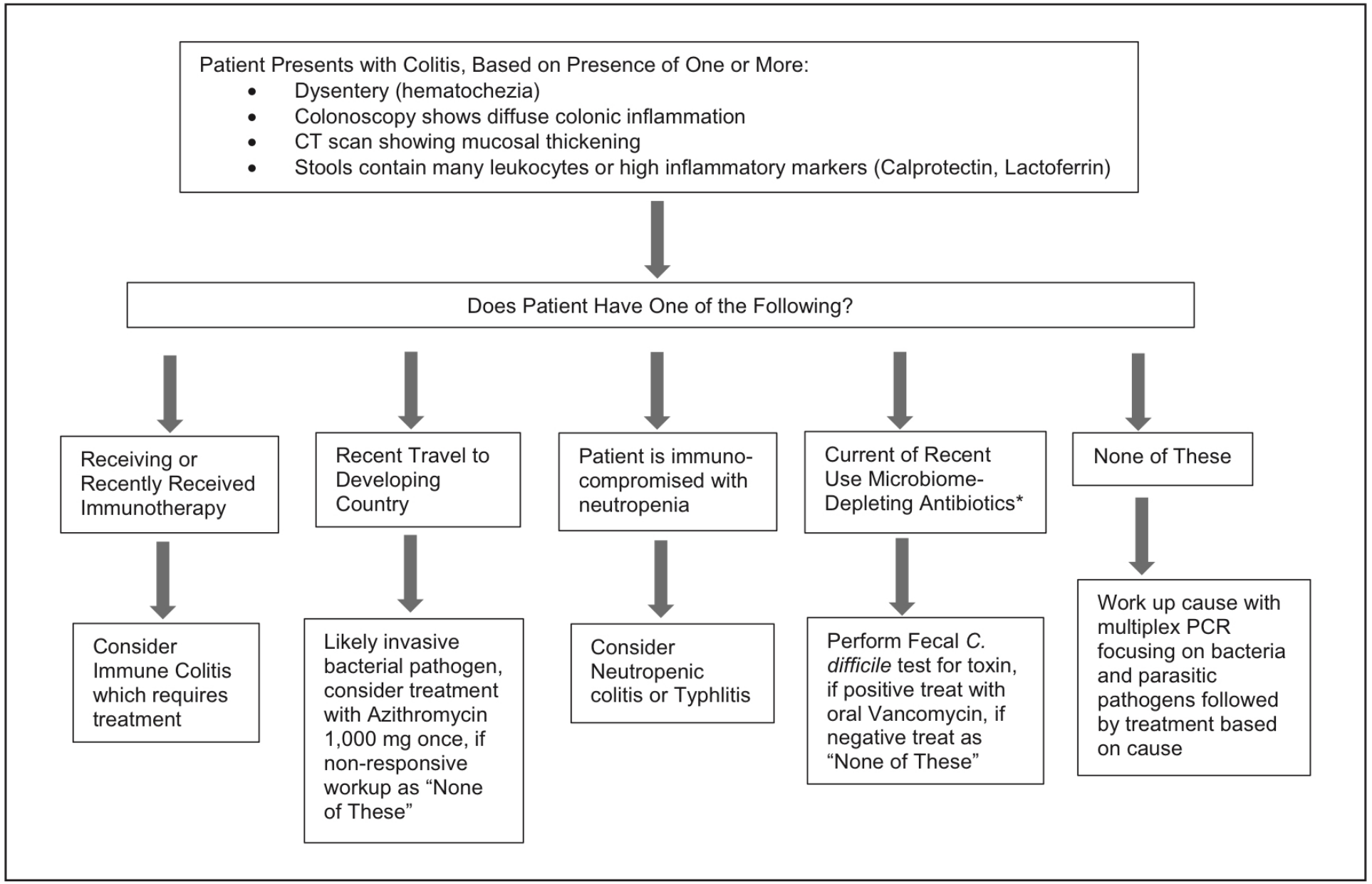
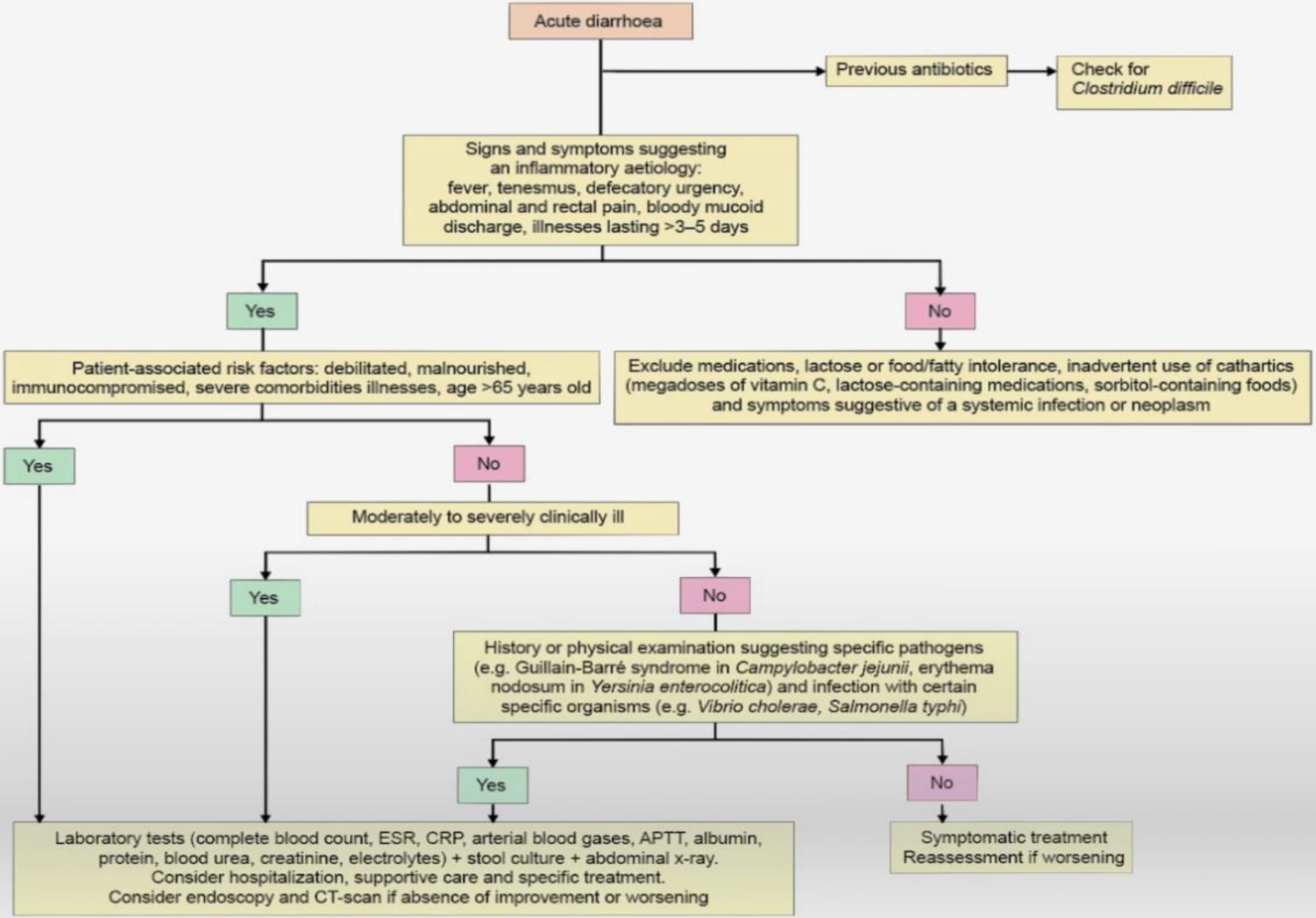

Patient Presents with Colitis, Based on Presence of One or More:
• Dysentery (hematochezia)
• Colonoscopy shows diffuse colonic inflammation
• CT scan showing mucosal thickening
• Stools contain many leukocytes or high inflammatory markers (Calprotectin, Lactoferrin)
Does Patient Have One of the Following?
Receiving or Recently Received Immunotherapy
Consider Immune Colitis which requires treatment
Recent Travel to Developing Country
Likely invasive bacterial pathogen, consider treatment with Azithromycin 1,000 mg once, if non-responsive workup as "None of These"
Patient is immuno-compromised with neutropenia
Consider Neutropenic colitis or Typhlitis
Current of Recent Use Microbiome-Depleting Antibiotics*
Perform Fecal C. difficile test for toxin, if positive treat with oral Vancomycin, if negative treat as "None of These"
None of These
Work up cause with multiplex PCR focusing on bacteria and parasitic pathogens followed by treatment based on cause

Table 2. Therapy of infectious colitis determined by cause

Infectious etiology	Recommended therapy	Alternate therapy
Campylobacter spp.	Azithromycin 500 mg once a day for 3–5 days	Erythromycin 500 mg QID for 3–5 days. For bacteremia or resistant cases, Meropenem 1 g IV for 3 days
Nontyphoidal *Salmonella spp.*	Ciprofloxacin or Levofloxacin 500 mg once a day for 7 or 14 days in immunosuppressed patients	Azithromycin 500 mg once a day for 3–5 days. For bacteremia, Cefixime 200 mg BID for 7 days or IV Ceftriaxone 1–2 g once a day for 7–10 days
Shigella spp.	Ciprofloxacin 500 mg BID for 3 days	Azithromycin 500 mg once a day for 3 days. Cefixime 400 mg once a day or IV Ceftriaxone 1 g once a day for 3 days
Shiga-Toxin producing *E. coli* (O157:H7 and non-O157 strains)	Antibiotics are not recommended	None
Clostridioides difficile	Vancomycin 125 mg QID for 10–14 days or fidaxomicin 200 mg BID for 10 days. For complicated CDI, IV metronidazole (500 mg every 8 h) or vancomycin retention enema. For recurrence, oral vancomycin 125 mg QID for 14 days followed by tapered doses of vancomycin for 3–5 weeks.	Fidaxomicin 200 mg BID for 5 days, followed by extended-pulsed doses once a day on alternating days 7–25. FMT if $\geq$3 bouts nonresponsive to standard antibiotics. Bezlotoxumab 10 mg/kg single IV infusion as adjunct to standard antibiotic for prevention of recurrence
Enteroinvasive E. coli	Same as Shigella	Same as Shigella
Yersinia enterocolitica	Same as Shigella	Same as Shigella
Aeromonas spp.	Same as Shigella	Same as Shigella
Pleisomonas shigelloides	Same as Shigella	Same as Shigella
Noncholera *Vibrio spp. (parahemolyticus)*	Doxycycline 100 mg BID for 5 days or Ciprofloxacin 750 mg BID for 3 days	For sepsis, Doxycycline or Ciprofloxacin plus add Cefotaxime 2 g IV TID or Ceftriaxone 1–2 g IV daily for 7–10 days
Entamoeba histolytica	Metronidazole 750 mg TID for 5 days followed by a luminal agent (Diloxanide furoate 500 mg TID for 10 days or Paromomycin 25–35 mg/kg divided in 3 doses for 5–10 days)	Tinidazole 2g QD for 3 days or Nitazoxanide 500 mg BID for 3 days followed by a luminal agent
Schistosoma mansoni	Praziquantil 40 mg/kg body weight, single dose	Praziquantil plus Artemether 6 mg/kg body weight may prevent re-infection in endemic regions
Cytomegalovirus	Ganciclovir 5 mg/kg IV BID for 14 days or oral Valganciclovir 900 mg BID for 21 days	Foscarnet 90 mg/kg IV BID in resistant cases. Letermovir 480 mg/day only for CMV prophylaxis in HSCT recipients

Algorithm


Acute diarrhoea
Previous antibiotics
Check for *Clostridium difficile*
Signs and symptoms suggesting an inflammatory aetiology: fever, tenesmus, defecatory urgency, abdominal and rectal pain, bloody mucoid discharge, illnesses lasting >3–5 days
Yes
No
Patient-associated risk factors: debilitated, malnourished, immunocompromised, severe comorbidities illnesses, age >65 years old
Exclude medications, lactose or food/fatty intolerance, inadvertent use of cathartics (megadoses of vitamin C, lactose-containing medications, sorbitol-containing foods) and symptoms suggestive of a systemic infection or neoplasm
Yes
No
Moderately to severely clinically ill
Yes
No
History or physical examination suggesting specific pathogens (e.g. Guillain-Barré syndrome in *Campylobacter jejunii*, erythema nodosum in *Yersinia enterocolitica*) and infection with certain specific organisms (e.g. *Vibrio cholerae, Salmonella typhi*)
Yes
No
Laboratory tests (complete blood count, ESR, CRP, arterial blood gases, APTT, albumin, protein, blood urea, creatinine, electrolytes) + stool culture + abdominal x-ray.
Consider hospitalization, supportive care and specific treatment.
Consider endoscopy and CT-scan if absence of improvement or worsening
Symptomatic treatment
Reassessment if worsening

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