TROPICAL GASTROINTESTINAL PATHOLOGY

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AGPS - 5th Annual Scientific Meeting – Adelaide; 25-26 of October ,2019

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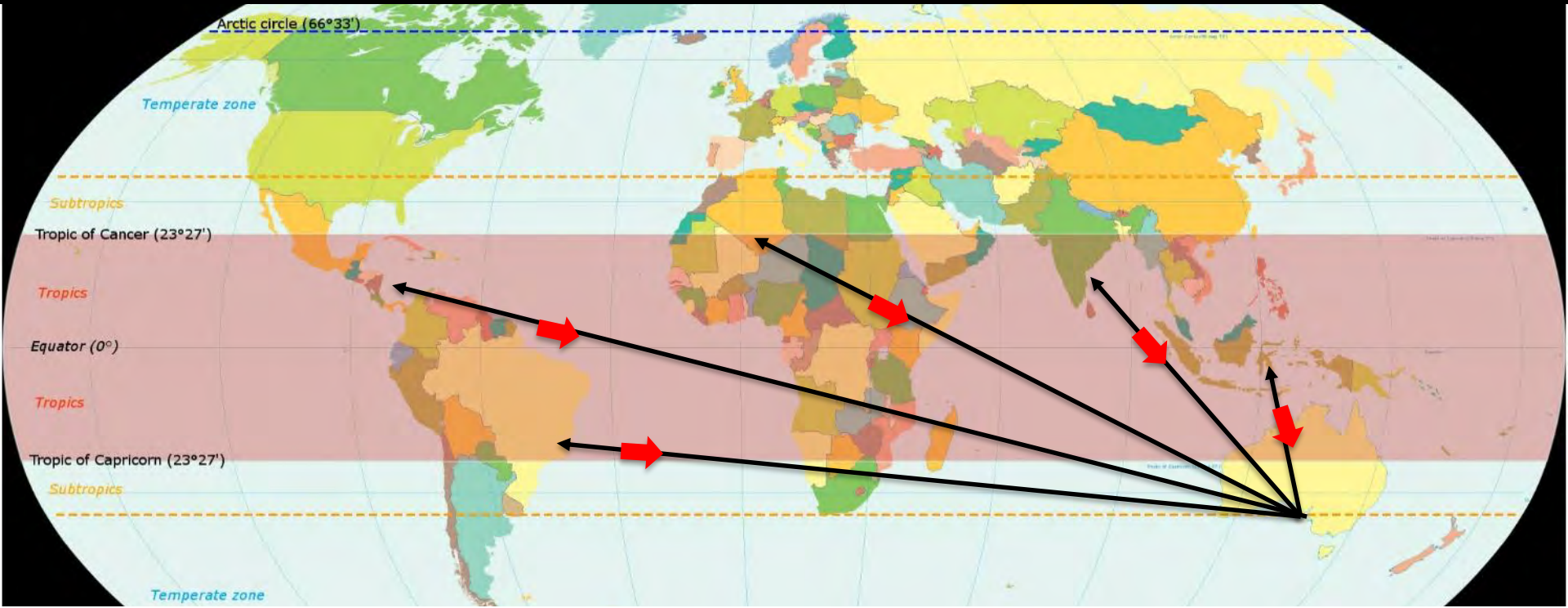
- **Last few decades have seen:**
  - **Increase international travels (tropics)**
  - **Global human migration**



- Hot & humid tropical/subtropical regions expose travelers to a wide spectrum of infectious diseases.
- Countries may have limited infrastructure, minimal amenities and poor sanitation.

GIT: a common primary site of tropical infections

(particularly lower GIT)

- Direct fecal-oral route of pathogen transmission related to ingestion of contaminated water, food, soil or organic material.

- Skin exposure is less frequent.
  - Relates to specific stage of a pathogen's lifecycle in water or soil with secondary gut involvement [e.g.,*Schistosomiasis*].

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Travelers to developing countries are 9–151 times more likely to develop diarrhea*

*when compared to the developed world

- Acute or chronic watery, mucoid or bloody.
  - *+/- cramping / abd. pain, N/V , malabsorption, wt loss, hemorrhage & tenesmus.*
  - *Constipation, obstruction & bowel perforation are also reported.*
- Fever - if present - indicates invasive infection or systemic dissemination.
- Infections such as *helminthiases* may take months/years before clinical presentation because of long incubation (up to 12 wks in schistosomiasis).

Etiologic considerations

- Bacteria & parasites [depending on series~2/3 cases each]
- Viruses [<15% of the pathogens]

➢*Infections are mostly only of a few days duration.*

Chronic infections leading to mucosal inflammation lasting > 2–4 wks resulting in evidence of chronicity

Distinction from IBD can be close to impossible

- *clinical >endoscopy>serology>microbiology together w/ follow-up, may be required for a definitive diagnosis.*

Etiologies:

- Helminthiases (e.g. schistosomiasis and strongyloidiasis),
- Late stage of bacterial dysentery (e.g.,Shigella and non-typhi Salmonella spp)
- Intestinal yersiniosis; less often, amoebiasis and coccidiosis, as well as some cases of typhoid fever.

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Normal or near normal mucosa

- viral infection
- cholera
- *E. coli* infection (enterotoxigenic, enteroadherent)
- giardiasis
- some helminth infections (especially cestodes, nematodes)

** exclude non-GIT pathology as cause of symptoms*

Chronic non destructive infla[tion] with/without intraepithelial lymphocytes

- viral infection
- tropical sprue
- giardiasis
- coccidiosis

** exclude non-infectious pathology (coeliac disease, protein hypersensitivity, drugs)*

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Tropical viral infections

[small intestine]

Tropical viral infections

[small intestine]

- Rotavirus,
- Adenovirus,
- Enterovirus,
- Norwalk virus (norovirus)
- Coronavirus.

- Acute watery, non-bloody diarrhea
- Mild symptomatology
- Self-limiting nature (exception is cholera)
- Rare endoscopy
- DX:
  - stool culture/immunoassay
  - PCR

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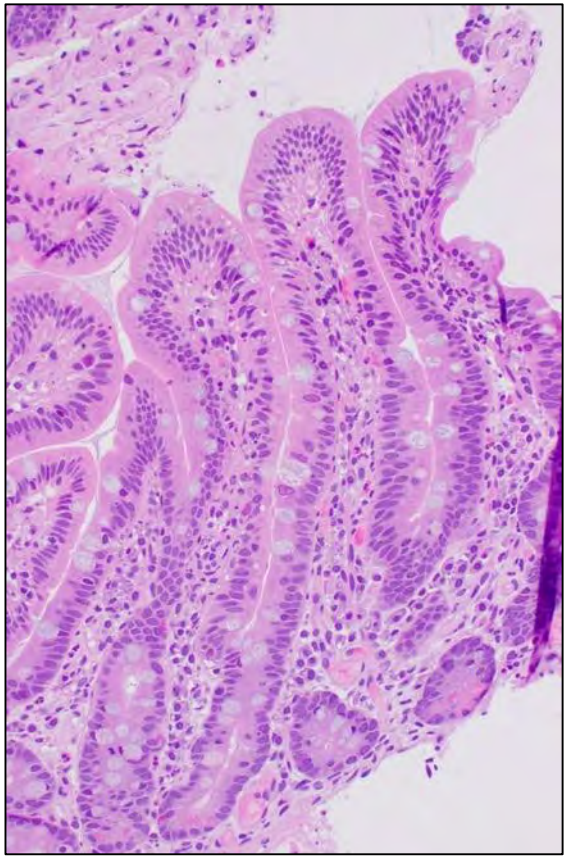
❖ ***Rotavirus diminished over the last decade due immunization in many developed countries***

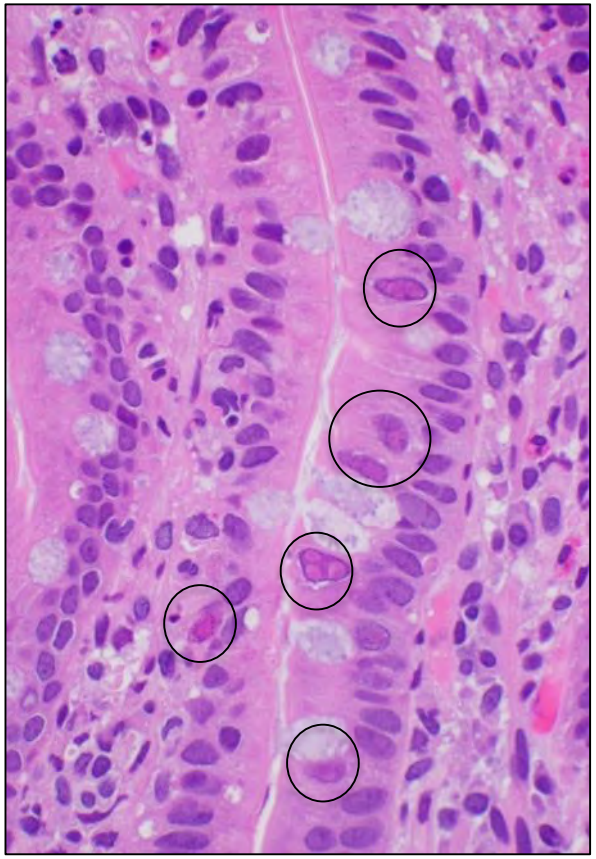
New bathing suit line……

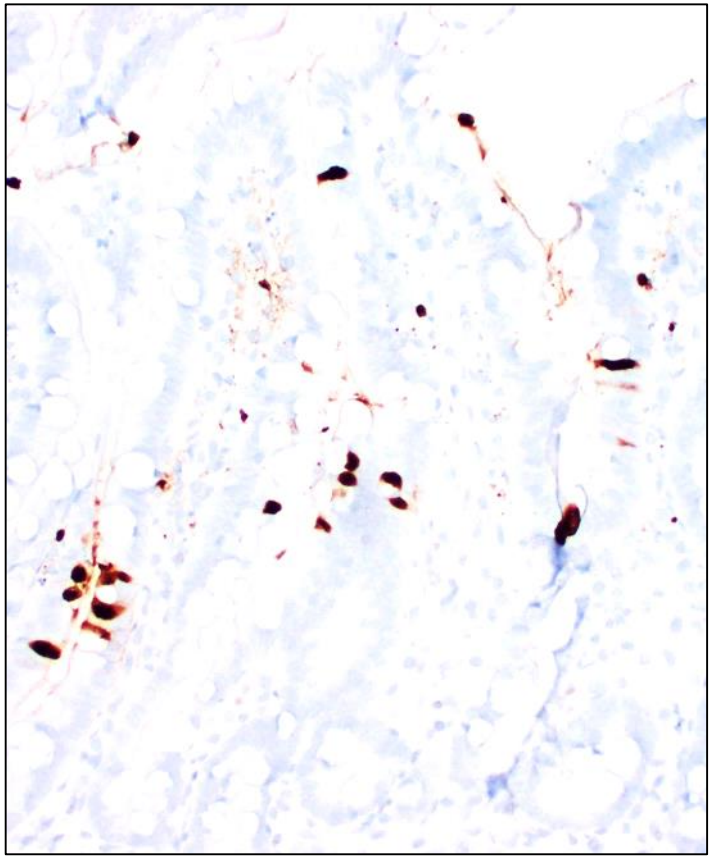
Histopathology of tropical viral infections

- usually no significant histologic changes,
- In some cases….
  - Villous blunting / broadening,
  - No crypt hyperplasia
  - Surface epithelial vacuolization, disarray, apoptosis
  - Increase in LP chronic inflammation and lymphoid hyperplasia can be seen.

Adenovirus





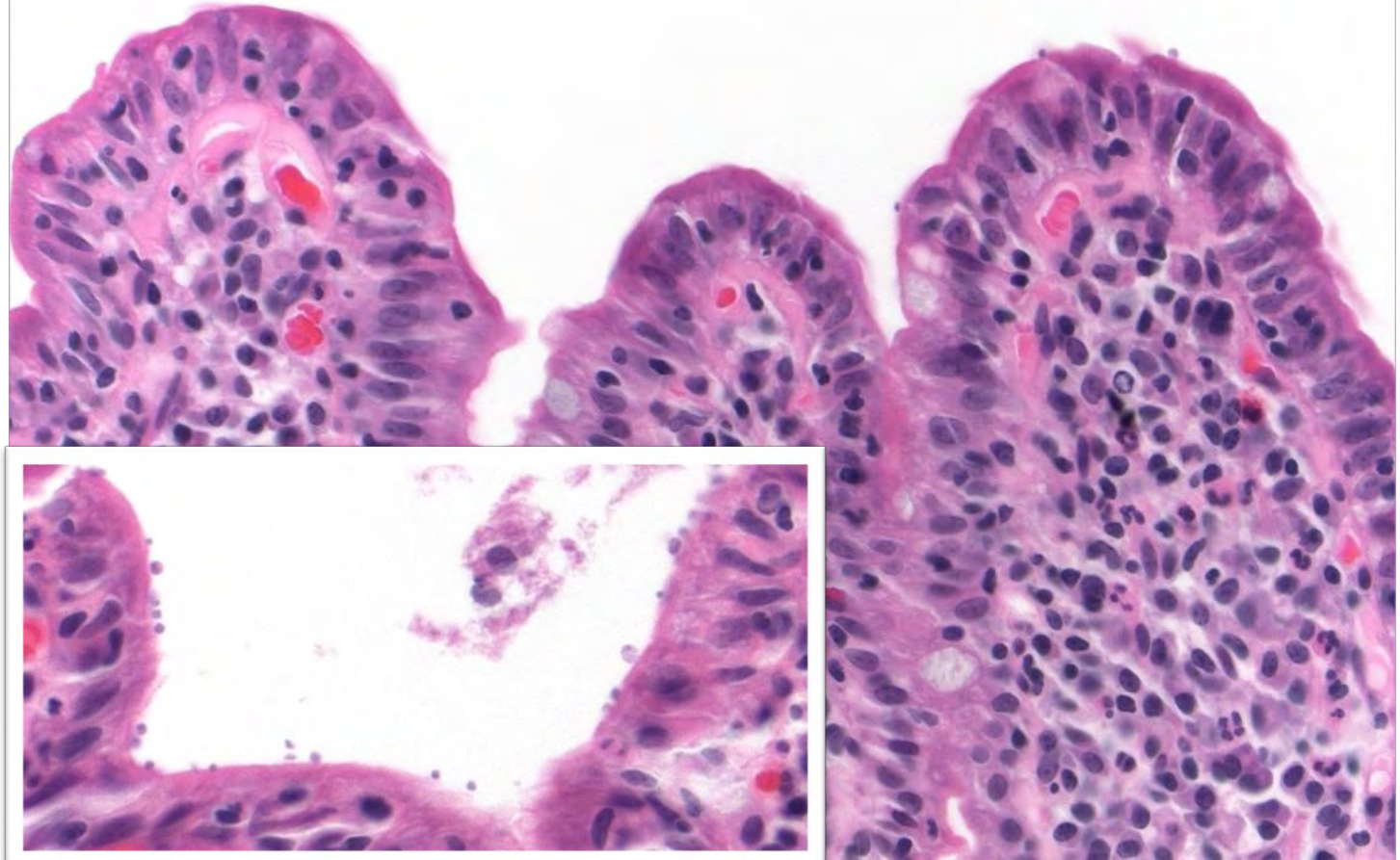


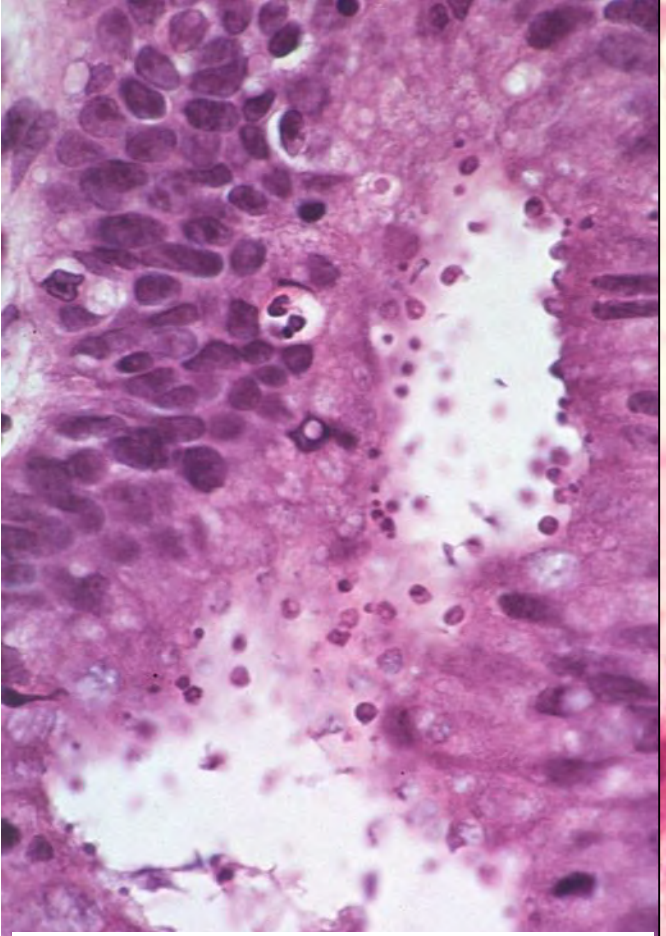
Focal epithelial apoptosis, nucleomegaly and nuclear inclusions-initially eosinophilic and later basophilic with ‘smudged’ nuclei—

Case study

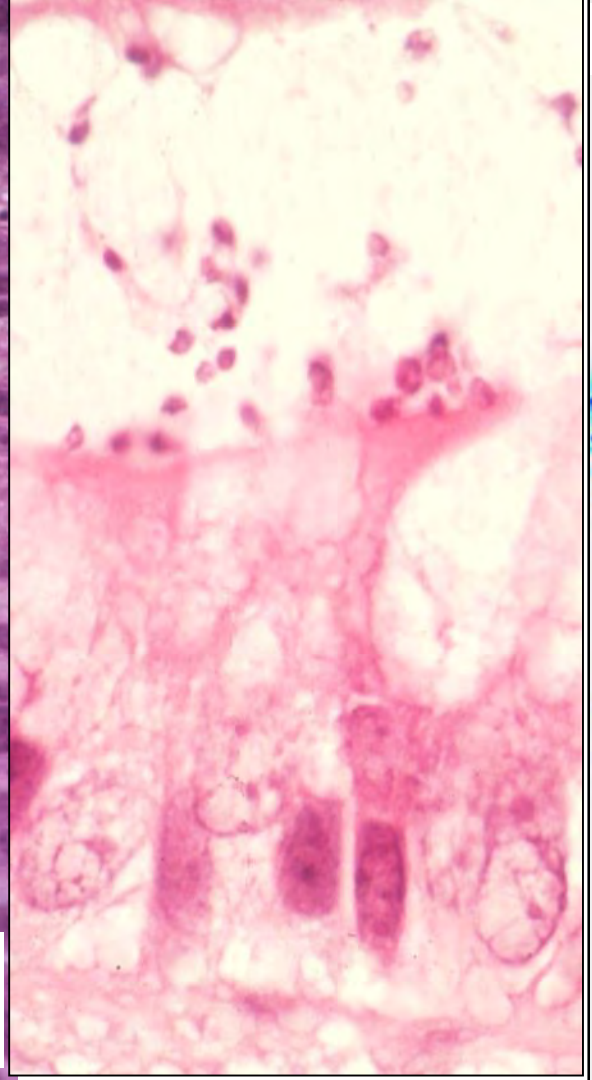
- 13 y/o male went on a photo safari with his parents in South Africa
- History of diarrhea x 1 month
- D2 mild scalloping
- Provisional diagnosis - Celiac disease

Cryptosporidia *Cryptosporidium parvum*

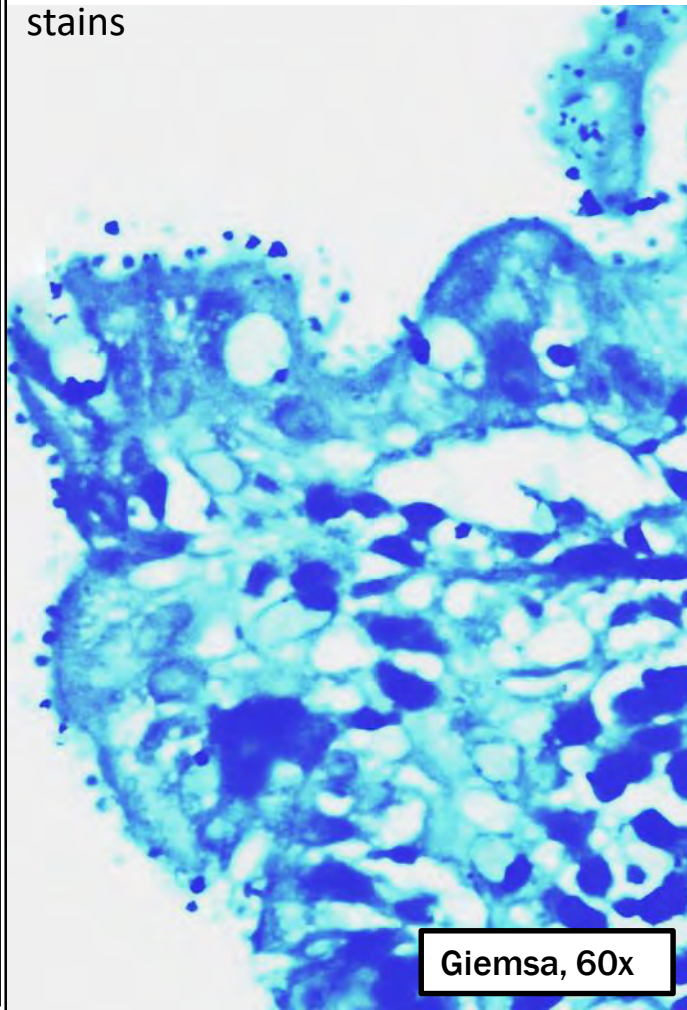




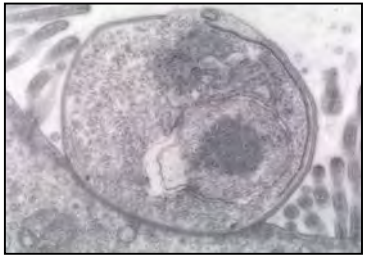
2-5-um basophilic spheres on the epithelial apical



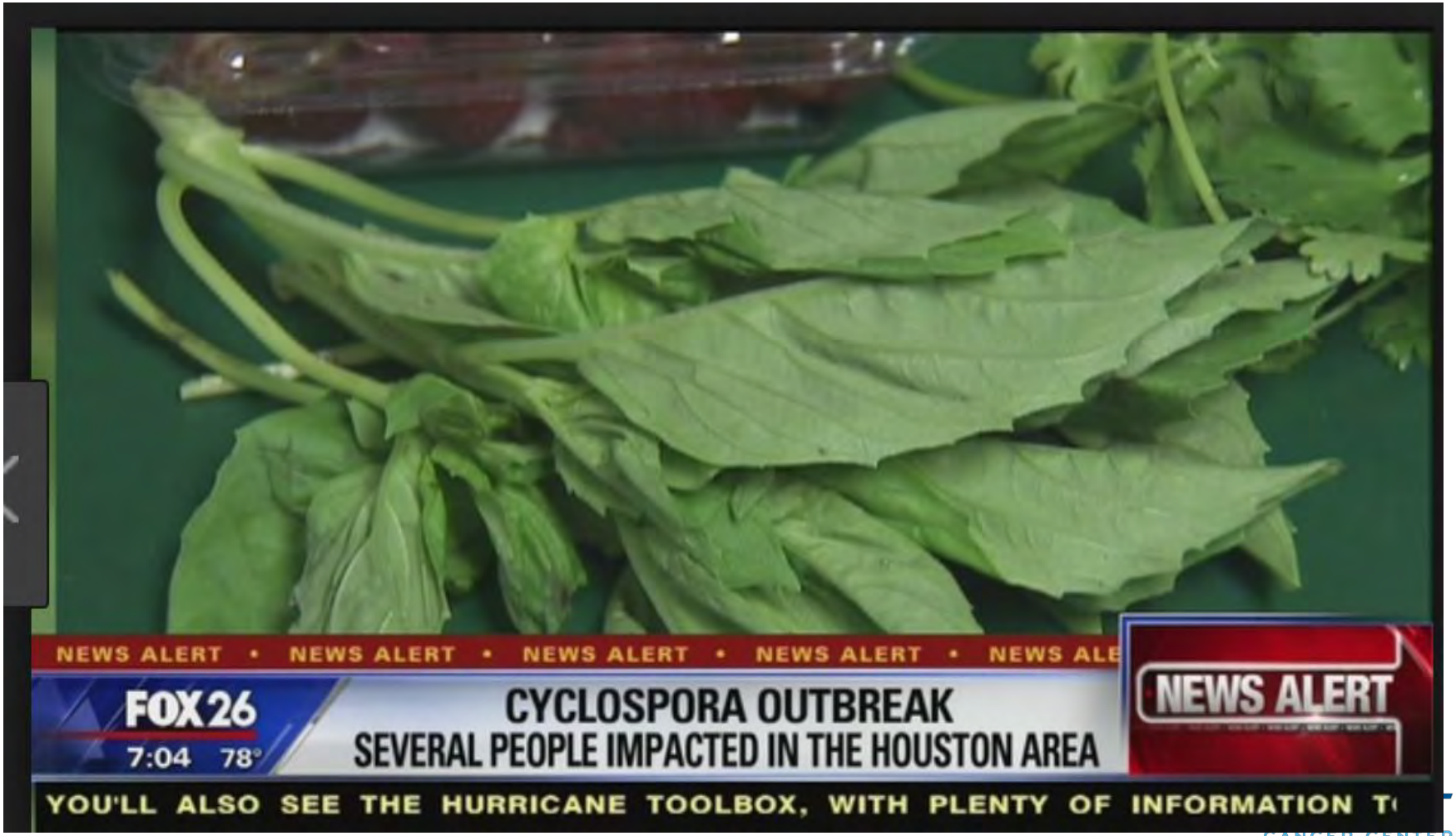
[+] Warthin-Starry, Giemsa & Gram stains



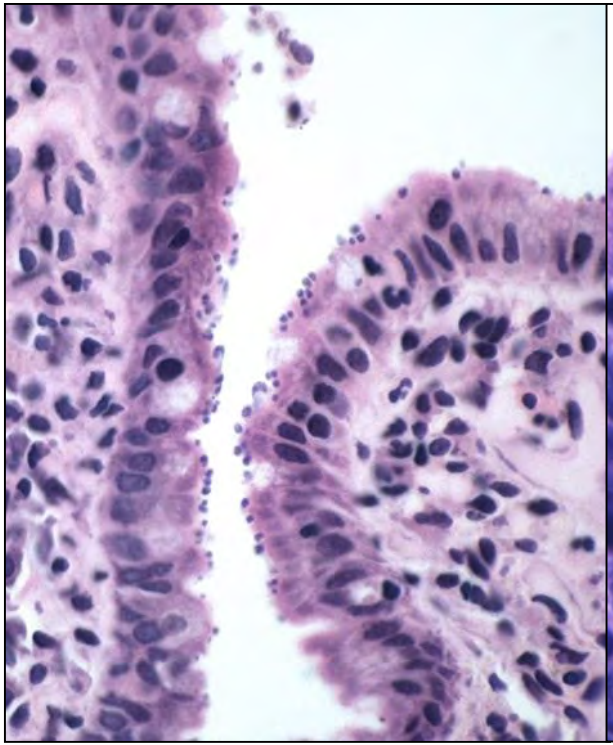
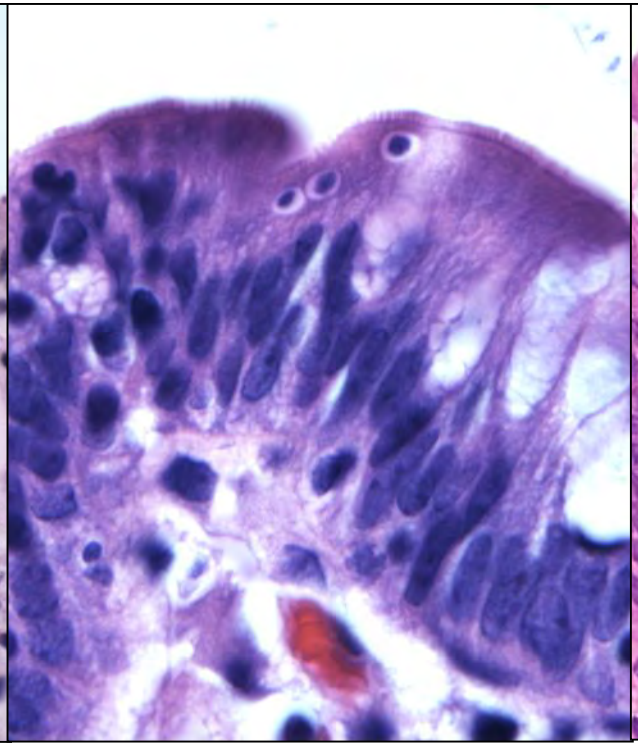
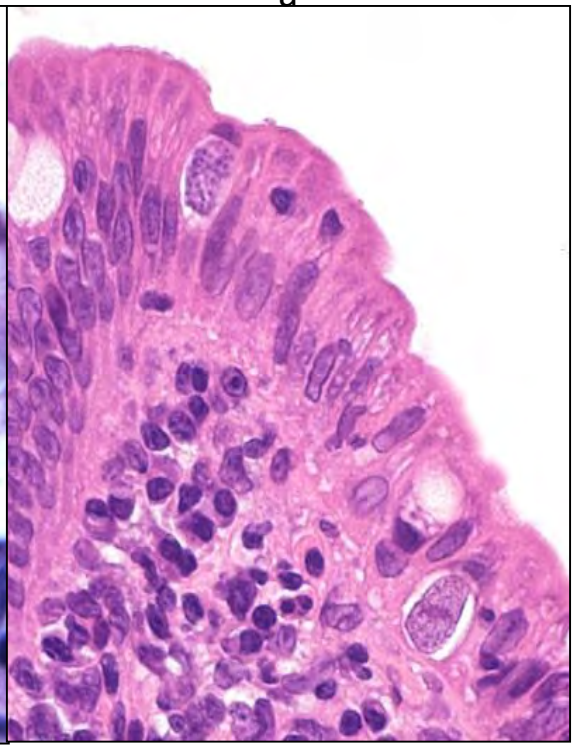
Cryptosporidia *Cryptosporidium parvum*



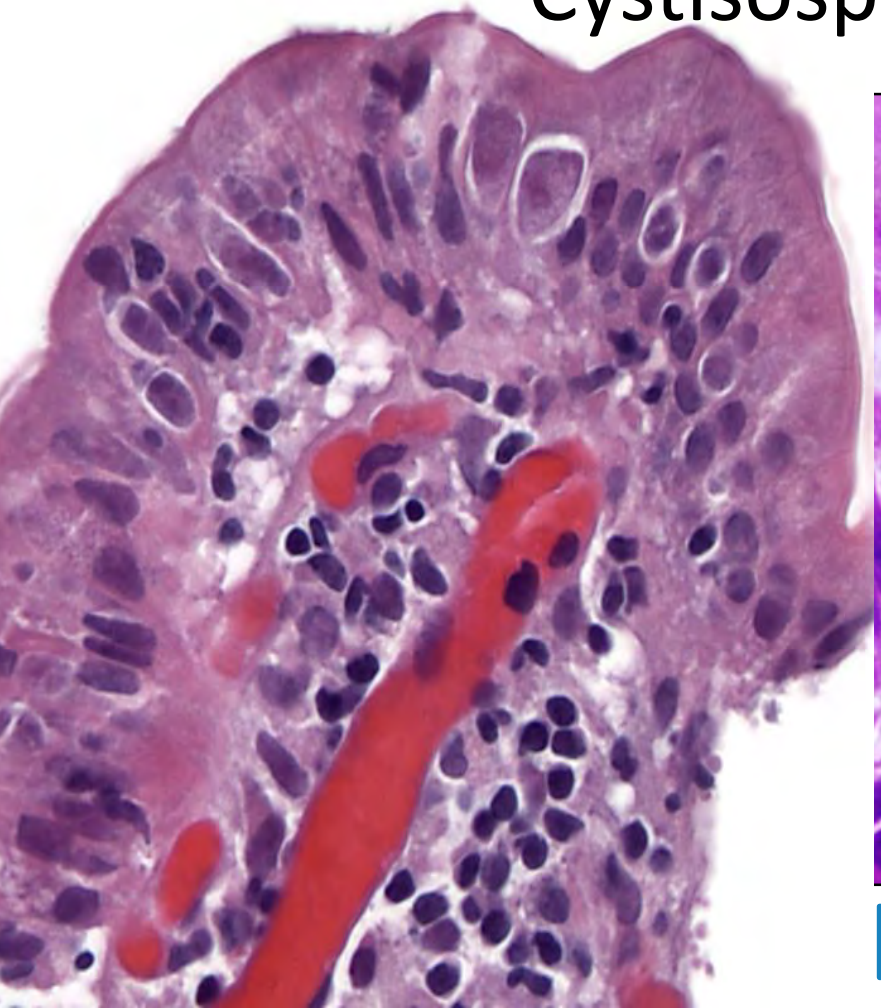
- Tropical/ subtropical countries with a high HIV burden
- *Increasing cause of traveler's diarrhea*.
- Immunocompetent pts: usually asymptomatic or mild and self-limiting.
- Chronic diarrhea, malabsorption immunodeficient pts
- Endoscopy: mucosal erythema, erosion, granularity
- Demonstration of the parasite [bx, stool, ELISA, IHC, EM]

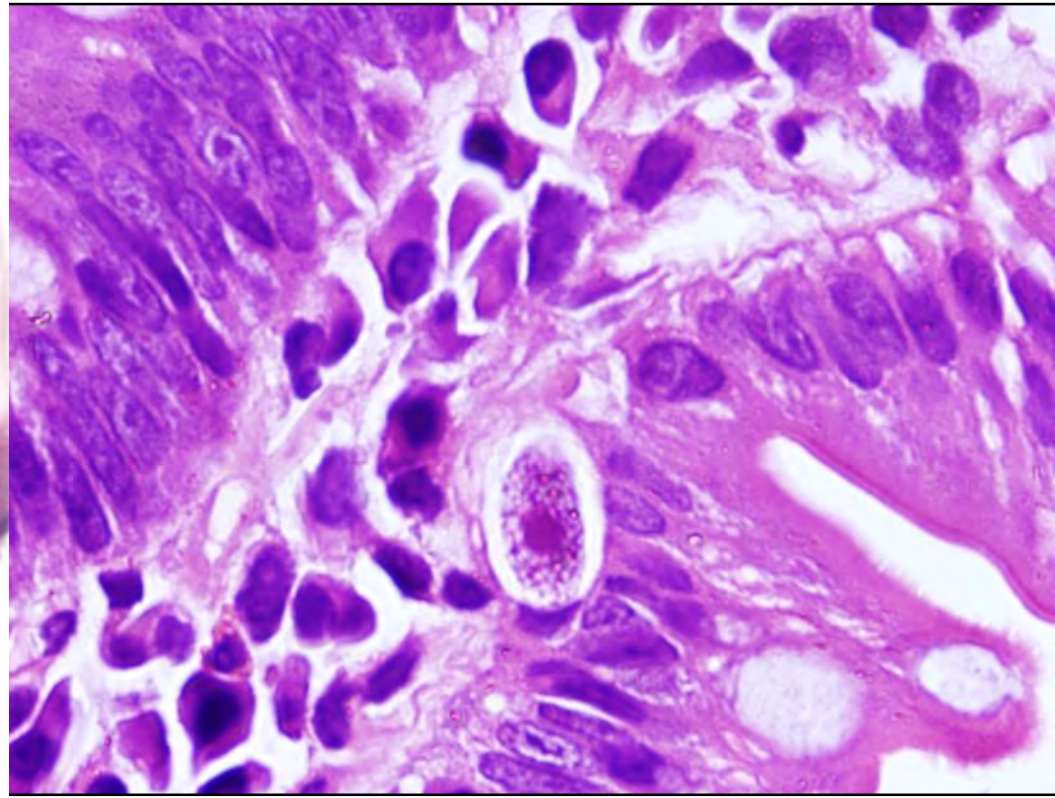


organism	characteristics	stains
Cryptosporidium parvum	2- 5 µm basophilic spheres protruding from apex of enterocytes.	[+] Warthin-Starry, Giemsa and Gram stains
Cystisospora belli	20 µm ovoid enterocyte inclusions [perinuclear & subnuclear]. Rarely in Lamina Propria or macrophages. Parasitophorous vacuoles [EM] at some stages	[+] GMS, Giemsa & periodic acid-Schiff (PAS) stains
Cyclospora cayetanensis	8- 10 µm round or crescentic located in parasitophorous vacuoles in the upper part of enterocytes. Can be present on the cell surface	[-]PAS, GMS and Gram stains. [+] Auramine, acid fast (modified Kinyoun)
Sarcocystis hominis [rare]	not well documented; small intestinal biopsy may show macrogametocyte and sporocyst parasitic forms	
Microsporidia: *Enterocytozoon bieneusi and*	2- 3 µm apical inclusions [spores] in the enterocytes which are difficult to identify	[+] Modified trichrome, Warthin-Starry, Gram and Giemsa

Cryptosporidia	Cyclospora	Cystisospora
		
2- 5 µm	8- 10 µm	20 µm

Cystisospora belli





GMS, Giemsa & PAS stains

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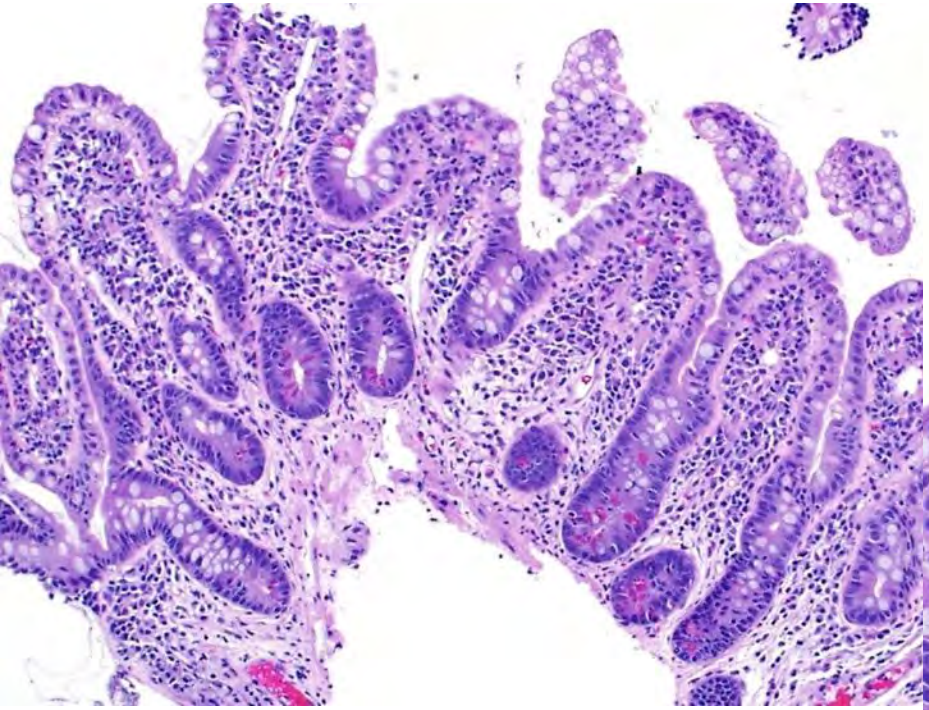
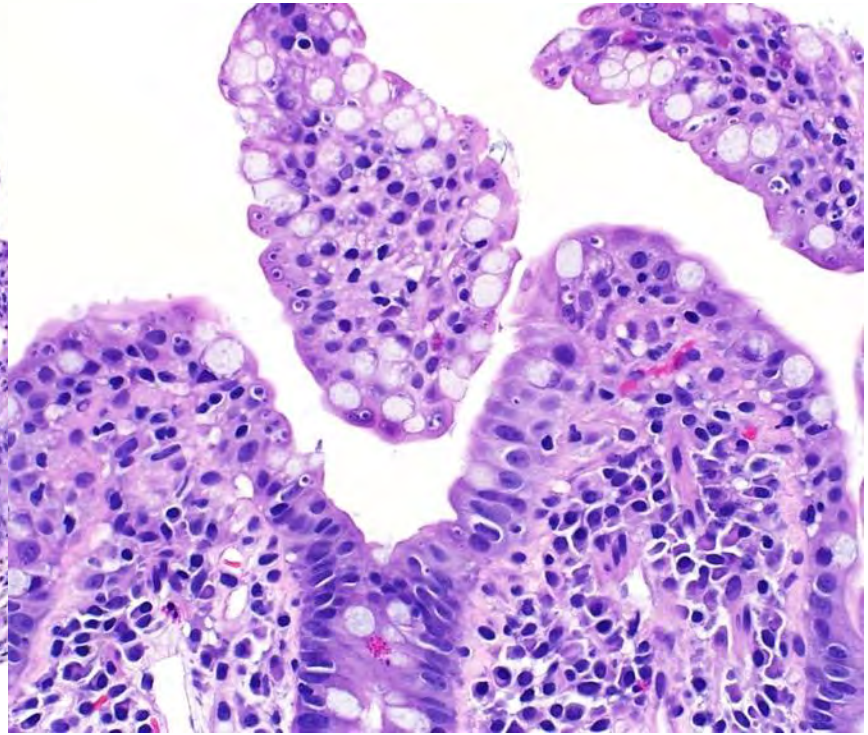
Cyclospora cayetanensis



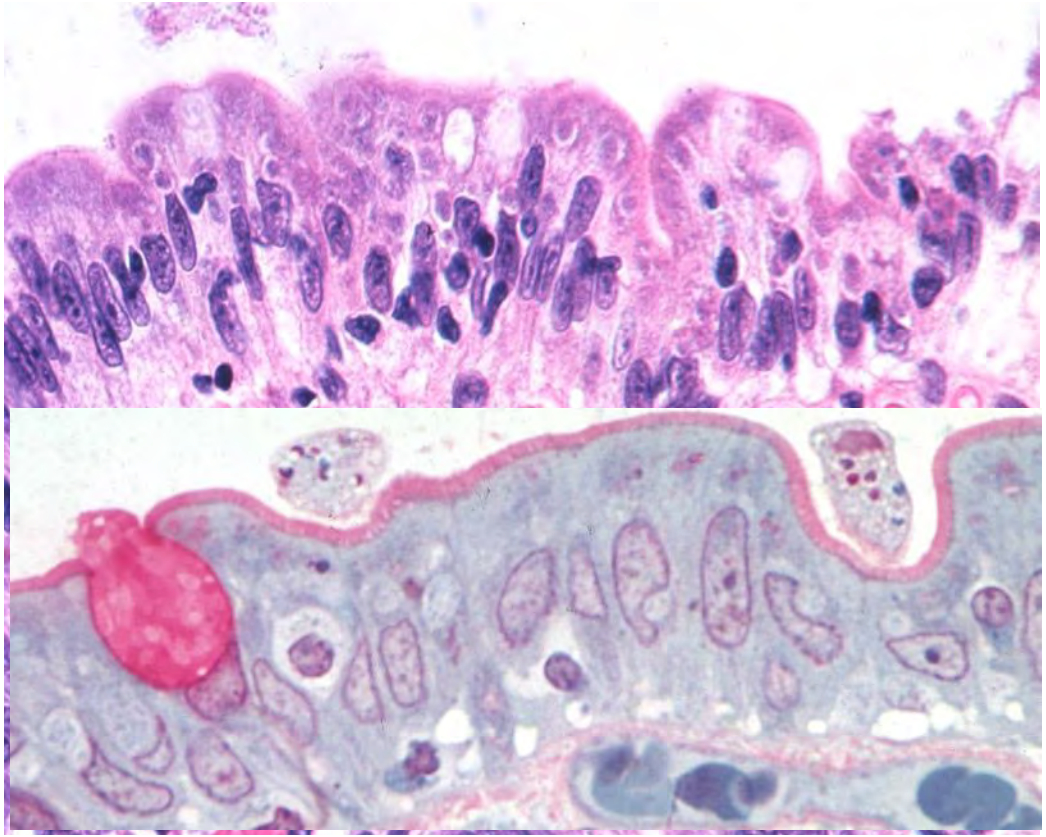


- ‘90s US outbreak in US due to raspberries from Central America with diarrhea, nausea, vomiting, cramps but also fevers, chills, myalgias

Auramine, acid fast (modified Kinyoun)

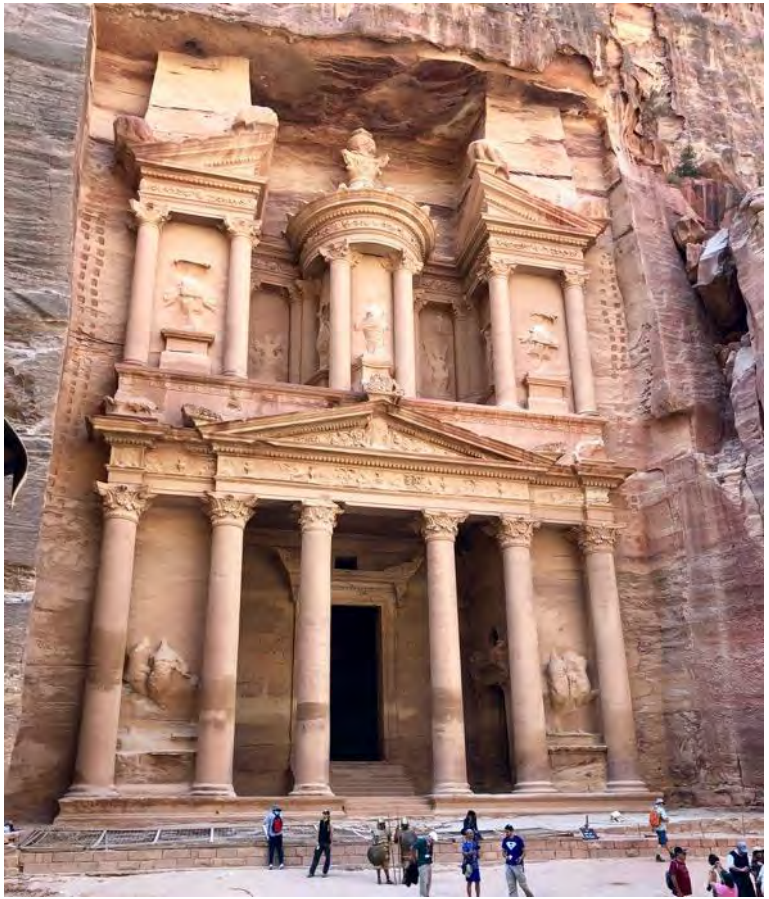
Microsporidia *Enterocytozoon bieneusi*

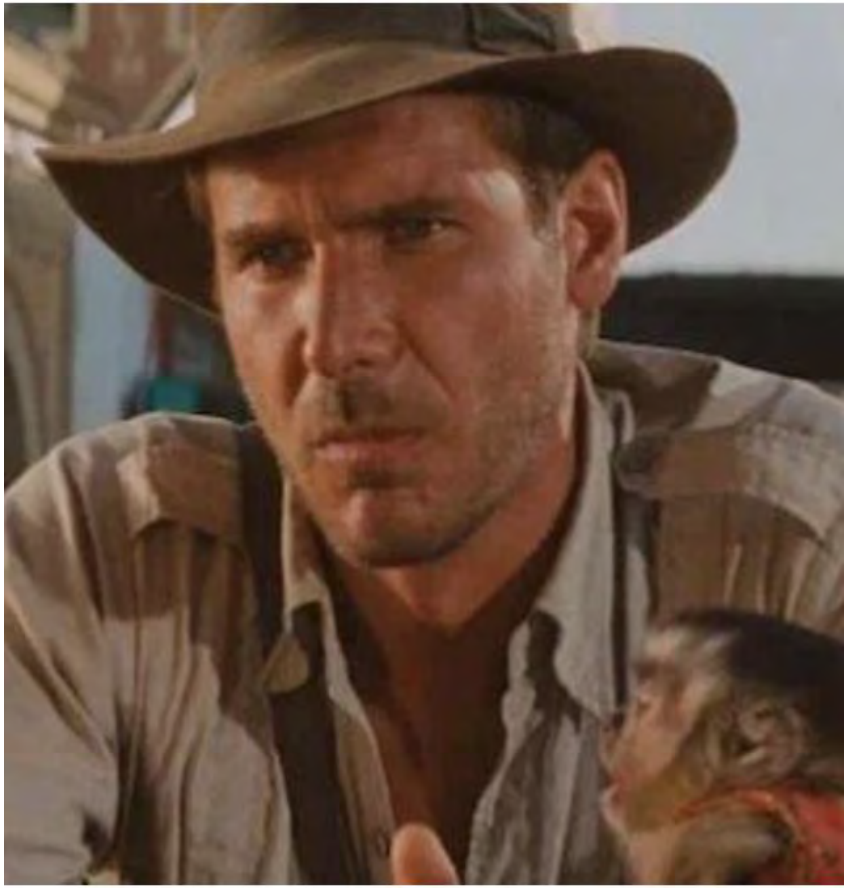
- small bowel, but can be seen in colon & bile duct
- Profound watery diarrhea
- sclerosing cholangitis like illness (*AIDS cholangiopathy*)



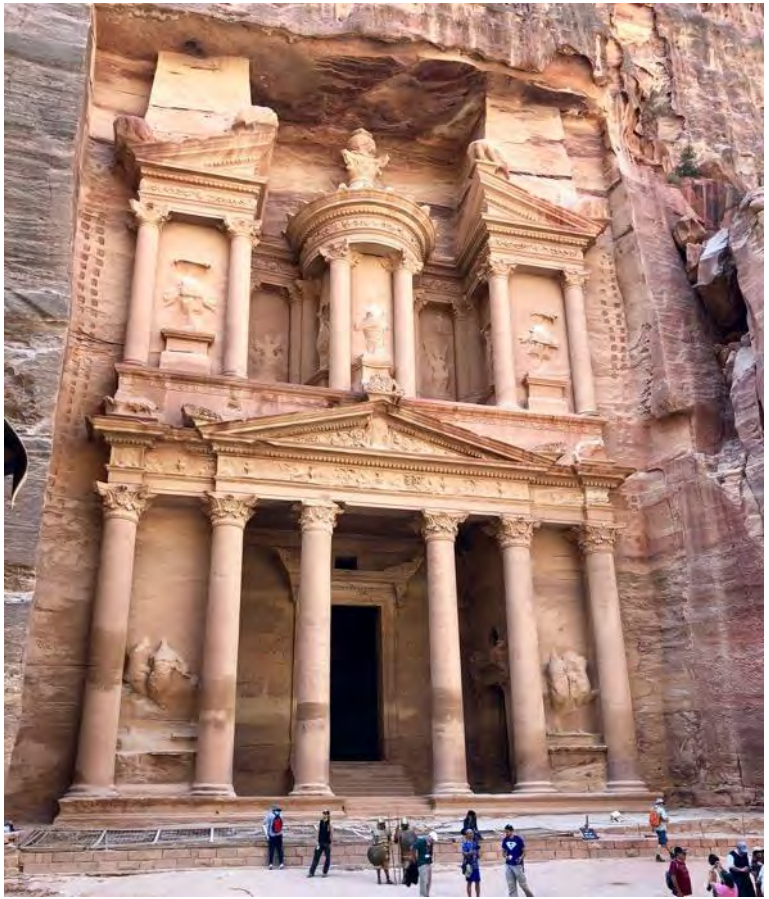
Modified trichrome, Warthin-Starry, Gram and

The curse of the explorers

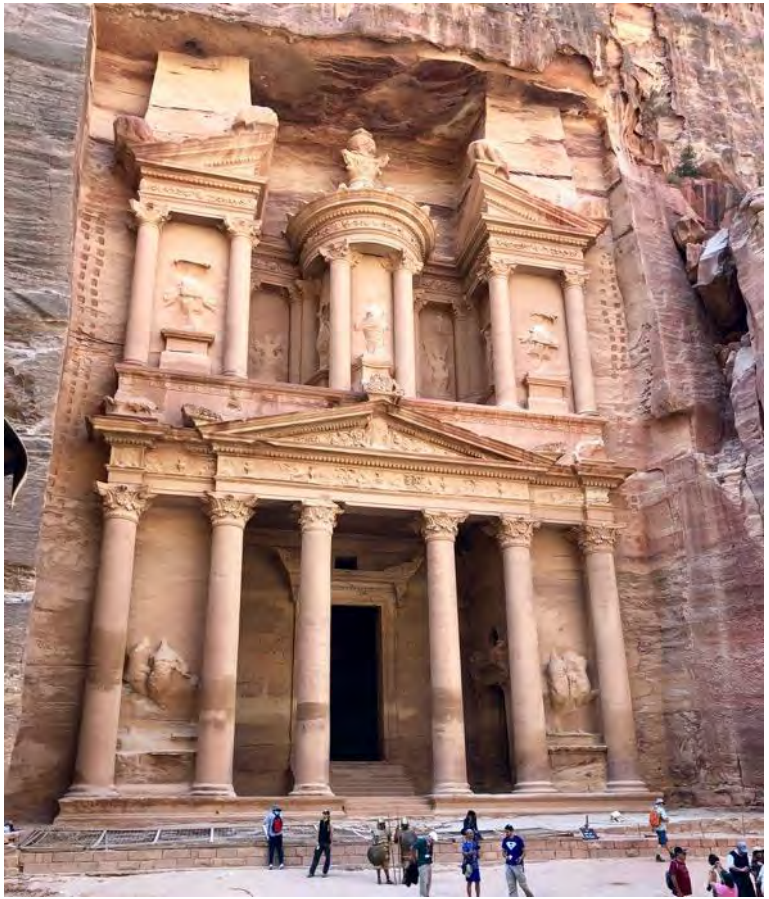




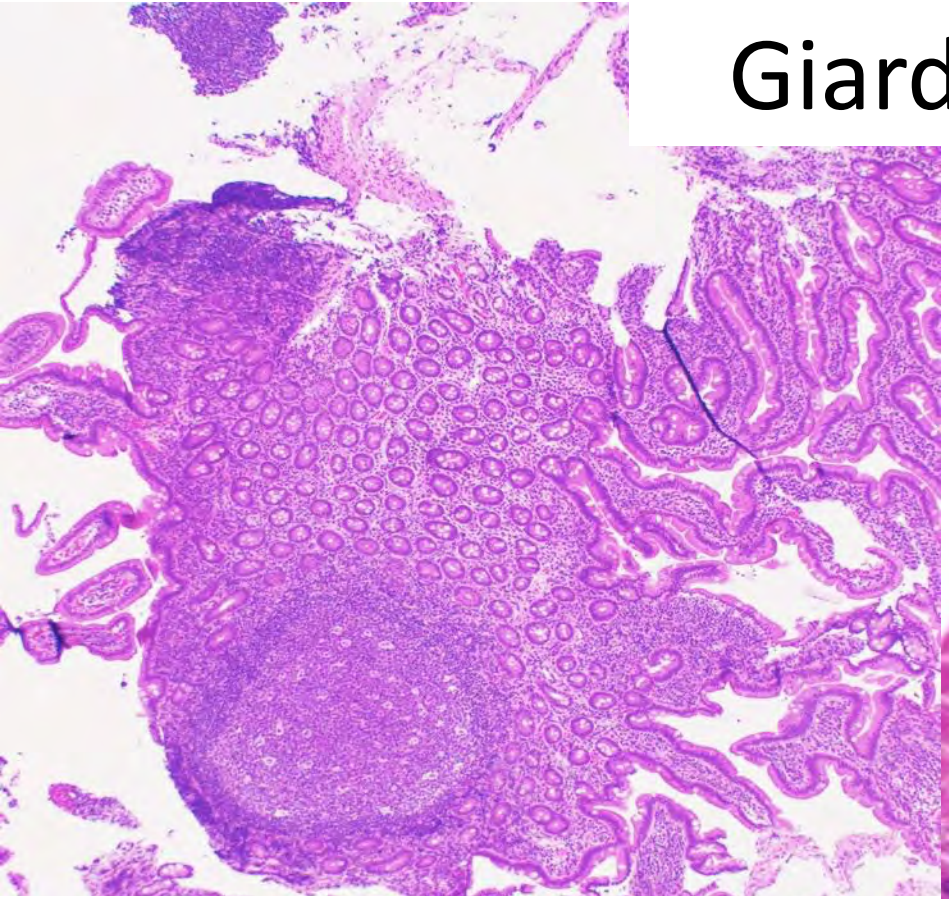
The curse of the explorers

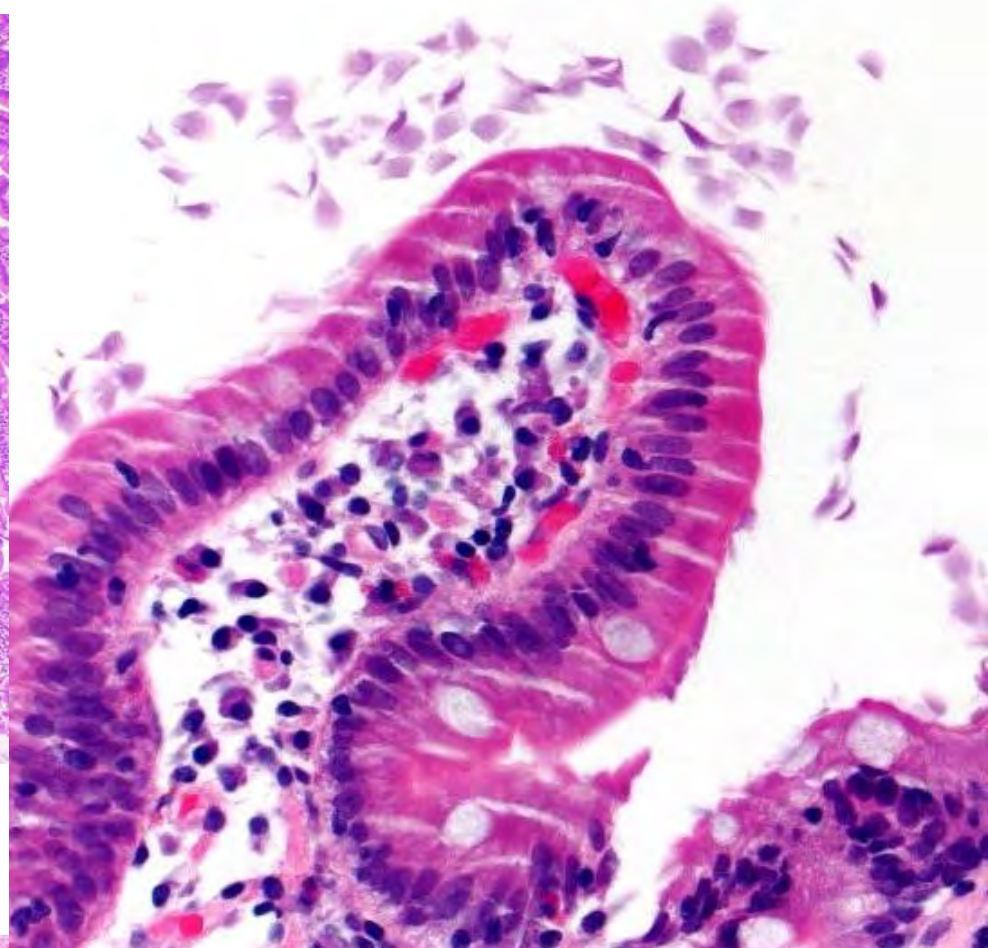


The curse of the explorers



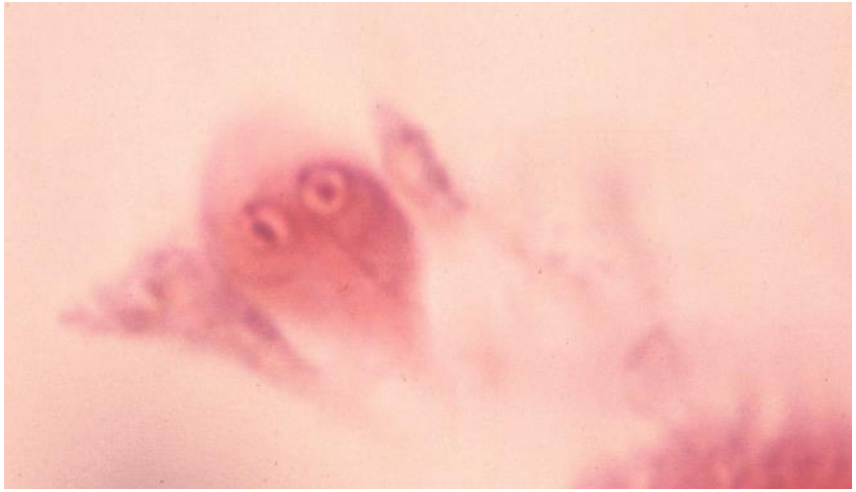
Giardiasis





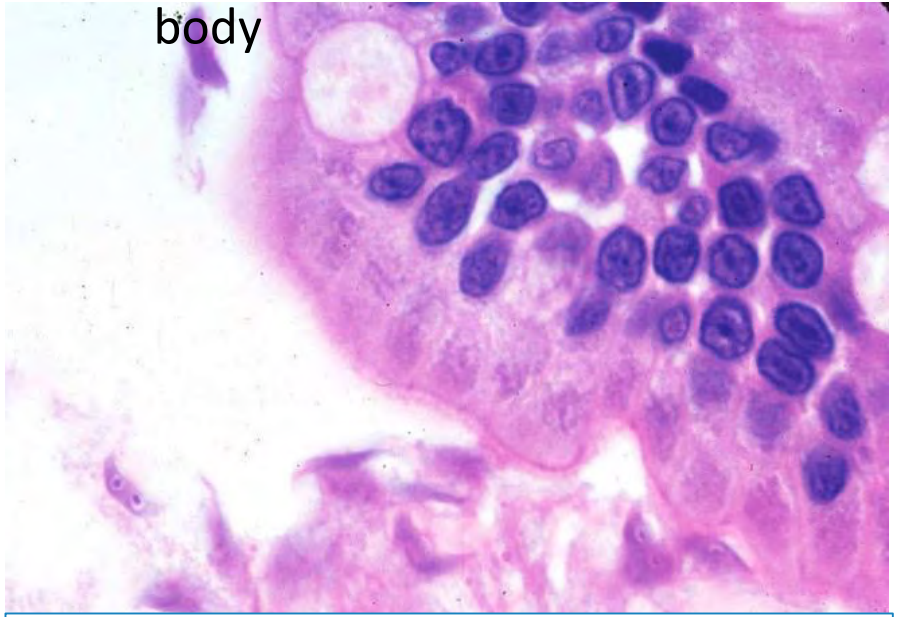
- Organisms best found in distal duod. or prox. jejunal bx

Ventral view: pear shaped body with 2 nuclei



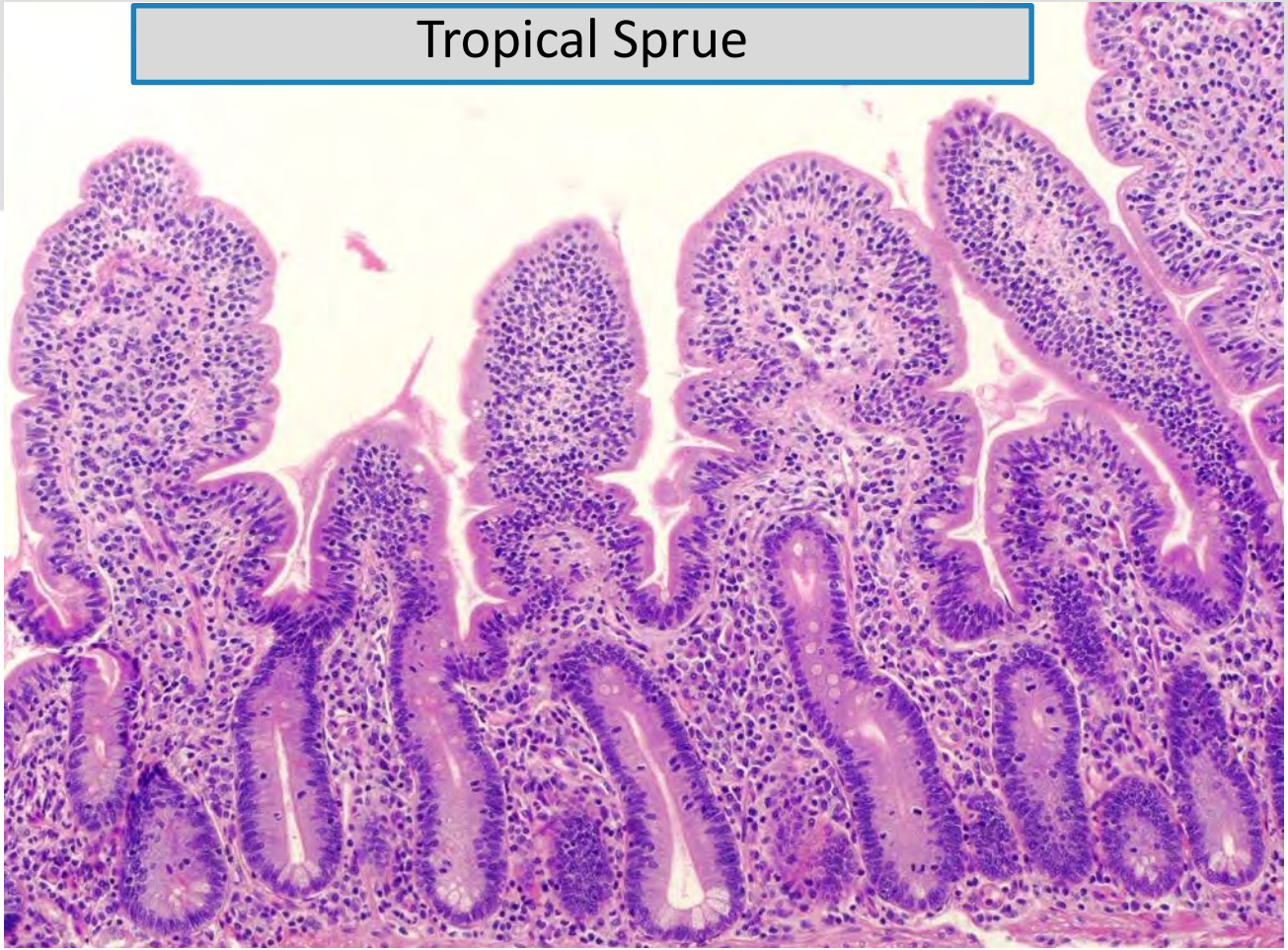
- Duod. fluid aspirate or String test may have better yield
- Cysts may be identified in stool exam (cysts and trophs i if diarrhea is severe)
- Stool antigen test available

-Lateral view: Sickle shaped body



- Trichrome, Giemsa, PTAH or PAS –D may help bring out details of organism
- Touch preps of biopsy may also help

Tropical Sprue



- villous blunting, crypt hyperplasia, increased mucosal chronic inflammatory cells and IELs.

Tropical Sprue vs Gluten Sensitive Enteropathy

- Eosinophilia
- Deep (crypt) IEL
- Rare total villous atrophy
- Diffuse [& relatively uniform] w/ ileal involvement more sev

- Malabsorption
- Dx in pts from developing countries or migrants
- [-] serological tests for celiac antibodies
- Respond to antibiotic and folate therapy

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ACTIVE INFLAMMATION

Neutrophils predominant

- **bacterial dysentery**
- **amoebiasis**
- **coccidiosis**

** exclude non-infectious pathology (idiopathic inflammatory bowel disease, drugs)*

- Various bacterial pathogens:
  - Shigella and non-typhi Salmonella spp. (50% of cases),
  - Campylobacter spp .
  - Yersinia spp. (especially Y.enterocolitica)
  - Others

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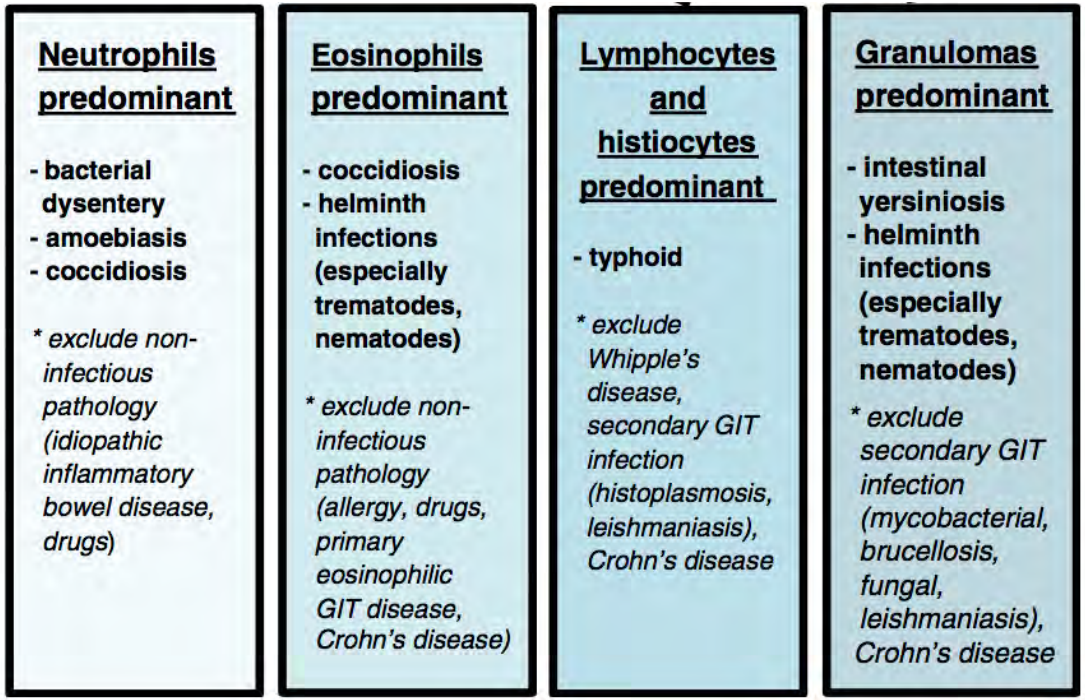
'Bacterial dysentery'

- Acute bloody diarrhea abundant leukocytes.
- First 2 weeks, neutrophil infiltrate w/ acute self-limited/infectious-type colitis features.
- Later, superficial mucosal involvement, w/ patchy lamina propria neutrophilic clustering, cryptitis w/ epithelial degeneration, erosion & ulceration

ACTIVE INFLAMMATION



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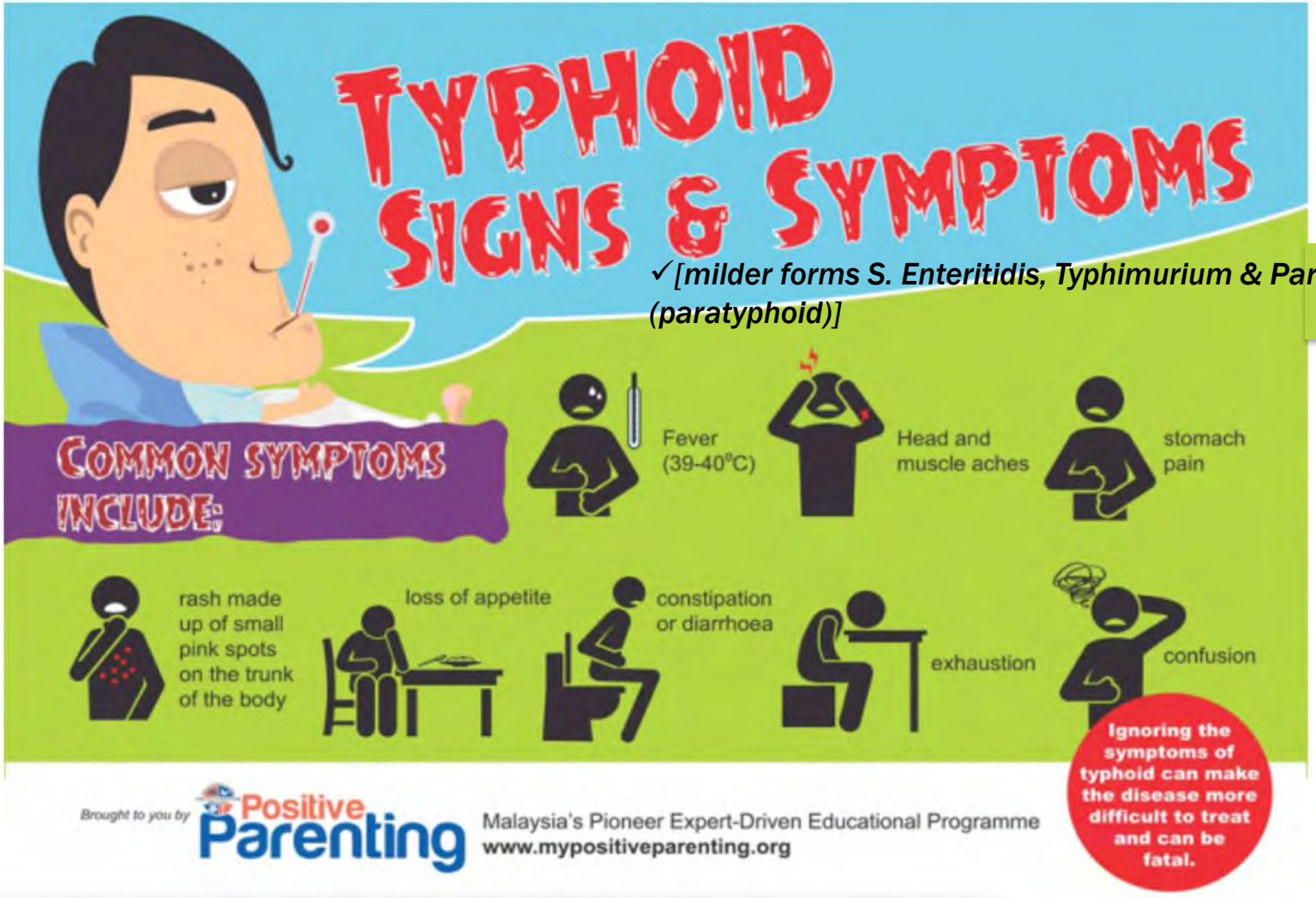
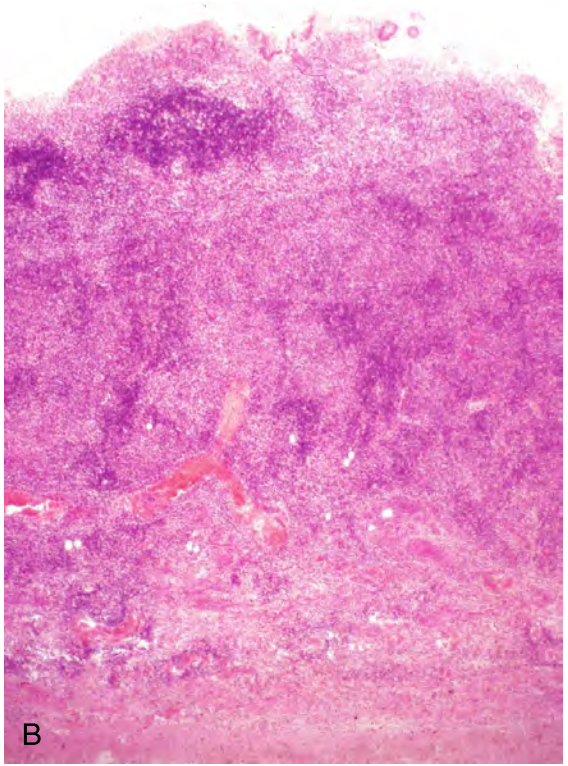


✓*[milder forms S. Enteritidis, Typhimurium & Paratyphi (paratyphoid)]*

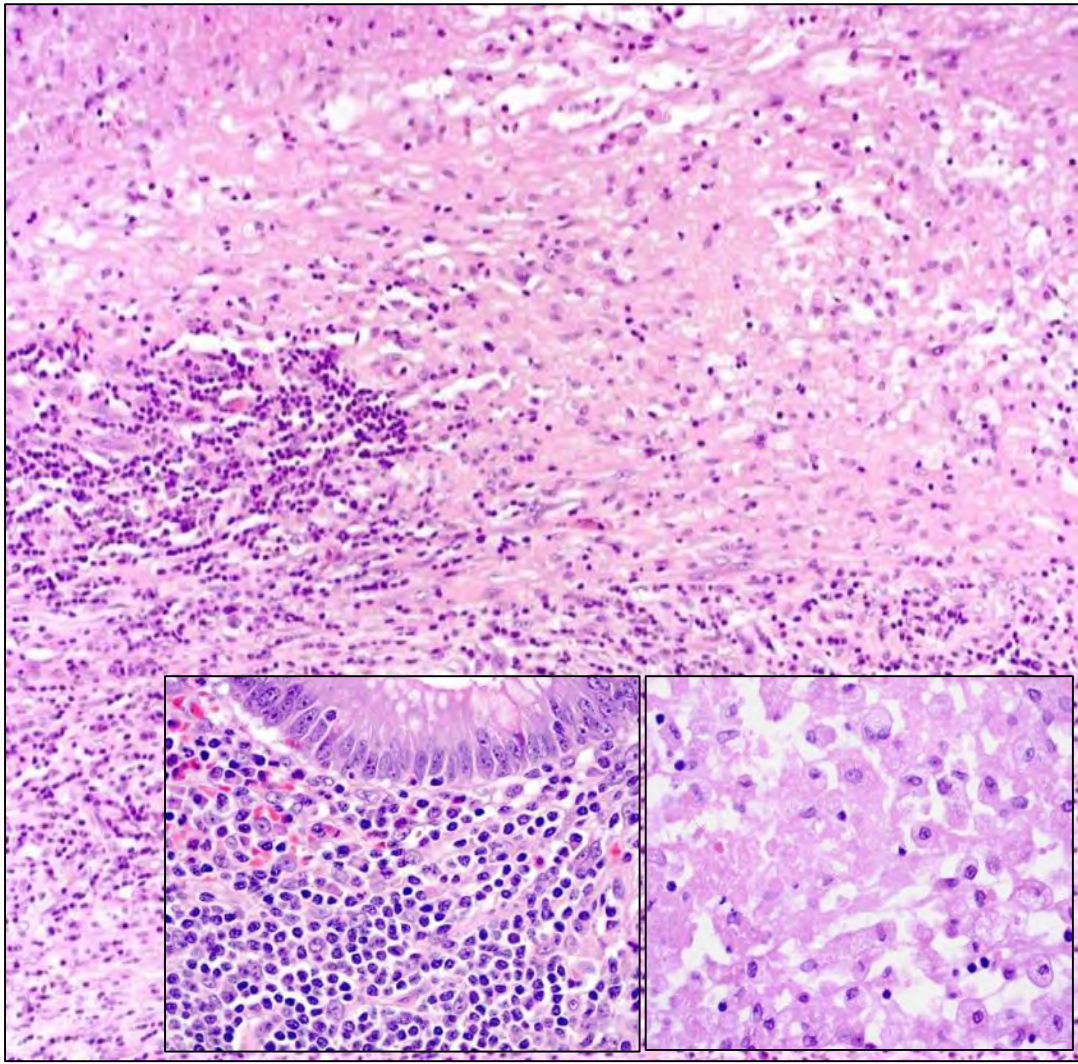
Typhoid (enteric) fever

Ulceration, along ileal Peyer's patches.

Ileum, appendix right colon are preferentially involved



- Necrosis:
  - mixed lymphoplasmacytic infiltrate w/ abundant histiocytes
  - Few neutrophils [asso^{ciated} neutropenia}.
  - Phagocytosis of RBCs lymphocytes & typhoid bacilli *[Mallory cells]* in macrophages
  - Crohn's disease may be considered, but 1] necrosis, 2] abundance of histiocytes, 3] scant neutrophils & 4] absence of granulomas rule out the diagnosis.



E. histolytica

- Infects 10% of world population
- Presentation ranges from asymptomatic to have mild and non-specific symptoms to fulminant colitis with severe bloody diarrhea (*amebic dysentery*)
  - ***E. dispar* may also be pathogenic**
- In industrialized countries, associated with homosexual population and unsanitized water

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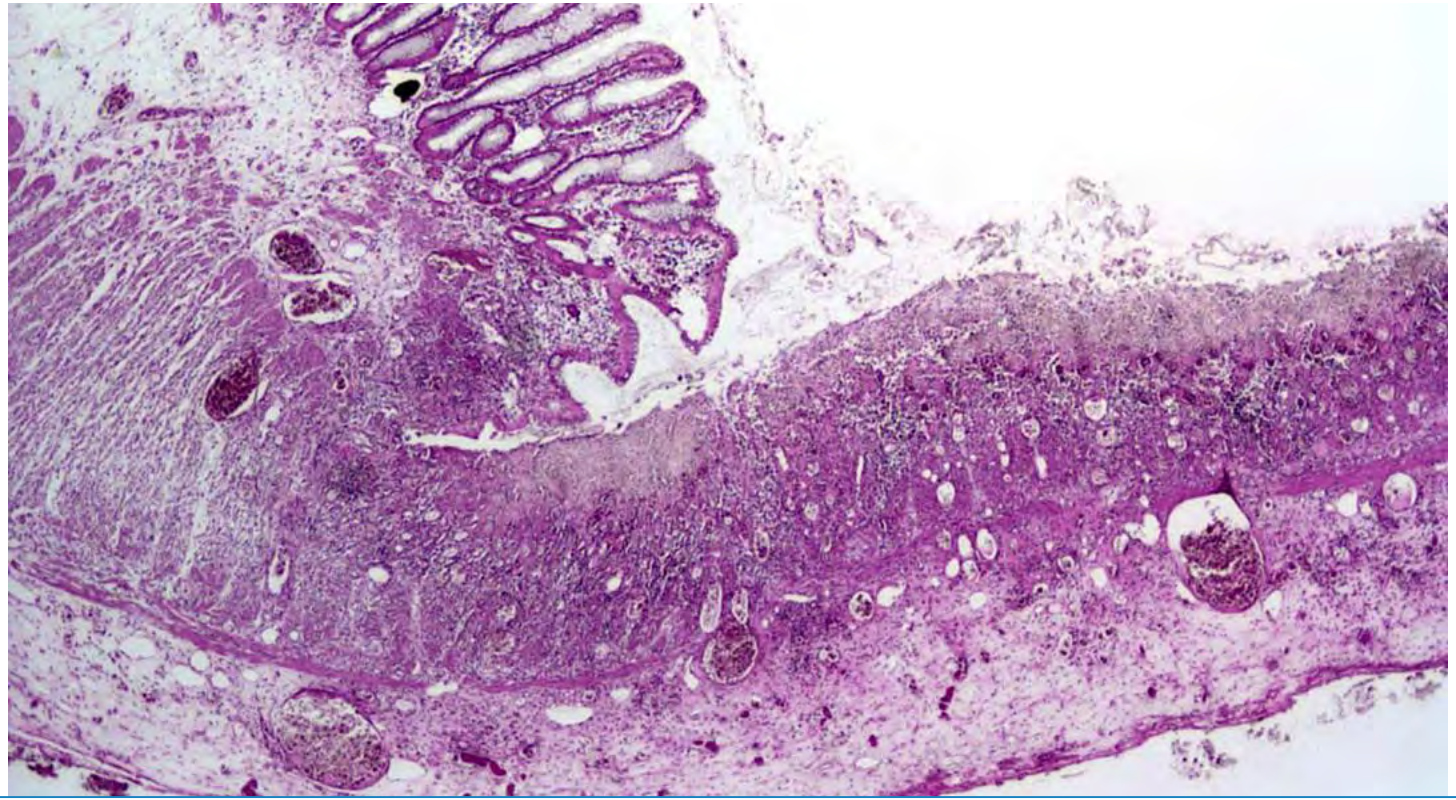
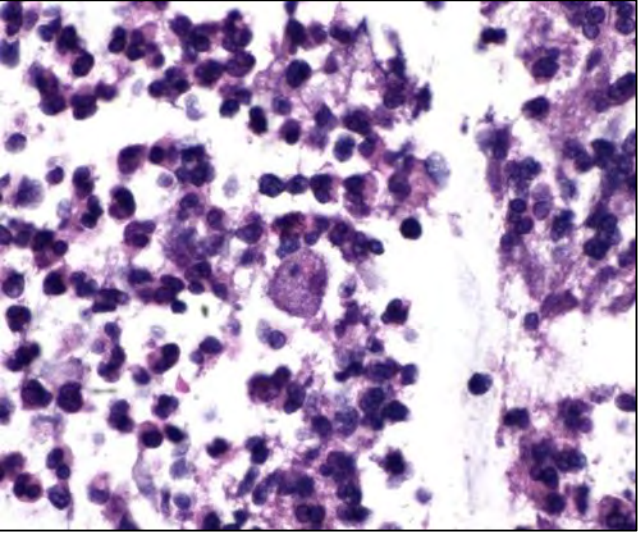
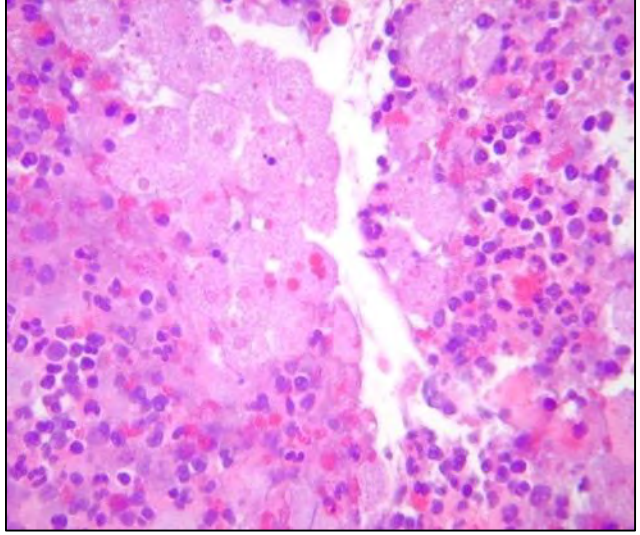
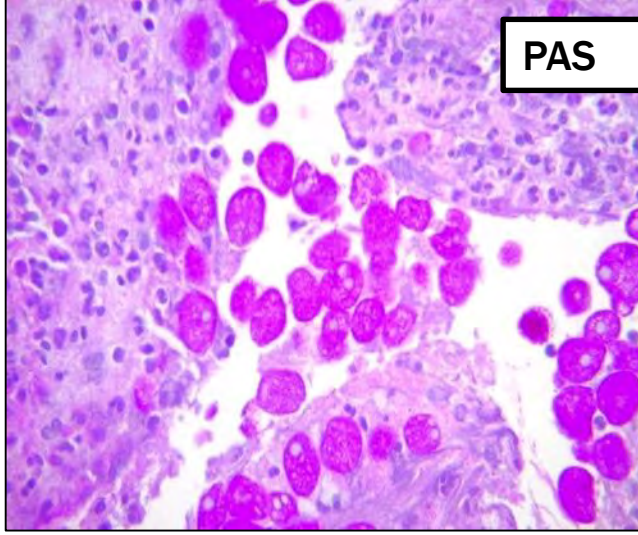
- Acute necrotizing inflammation / degree of necrosis often disproportionate to the intensity of inflammation, and deep, frequently undermining (‘flask-shaped) ulcers.



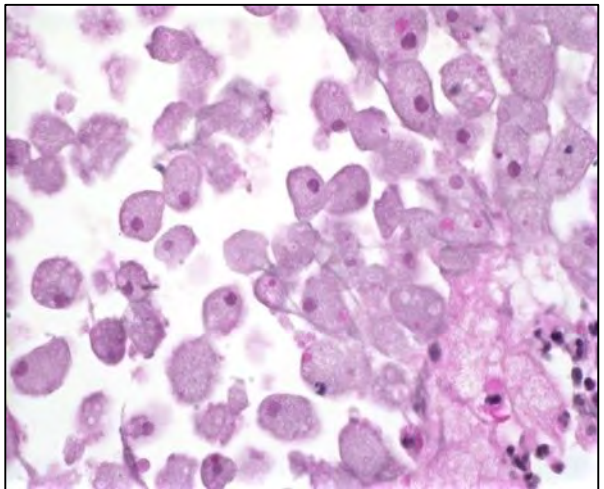
- Typical: Right side involvement ---Involvement of rest of the colorectum, appendix & small bowel, as well rupture with peritonitis, dissemination & metastatic

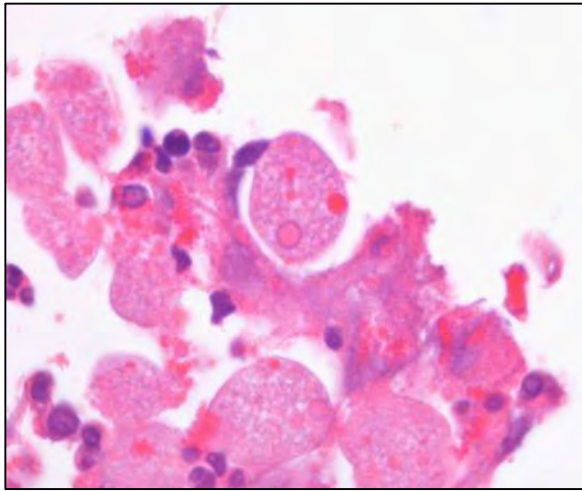


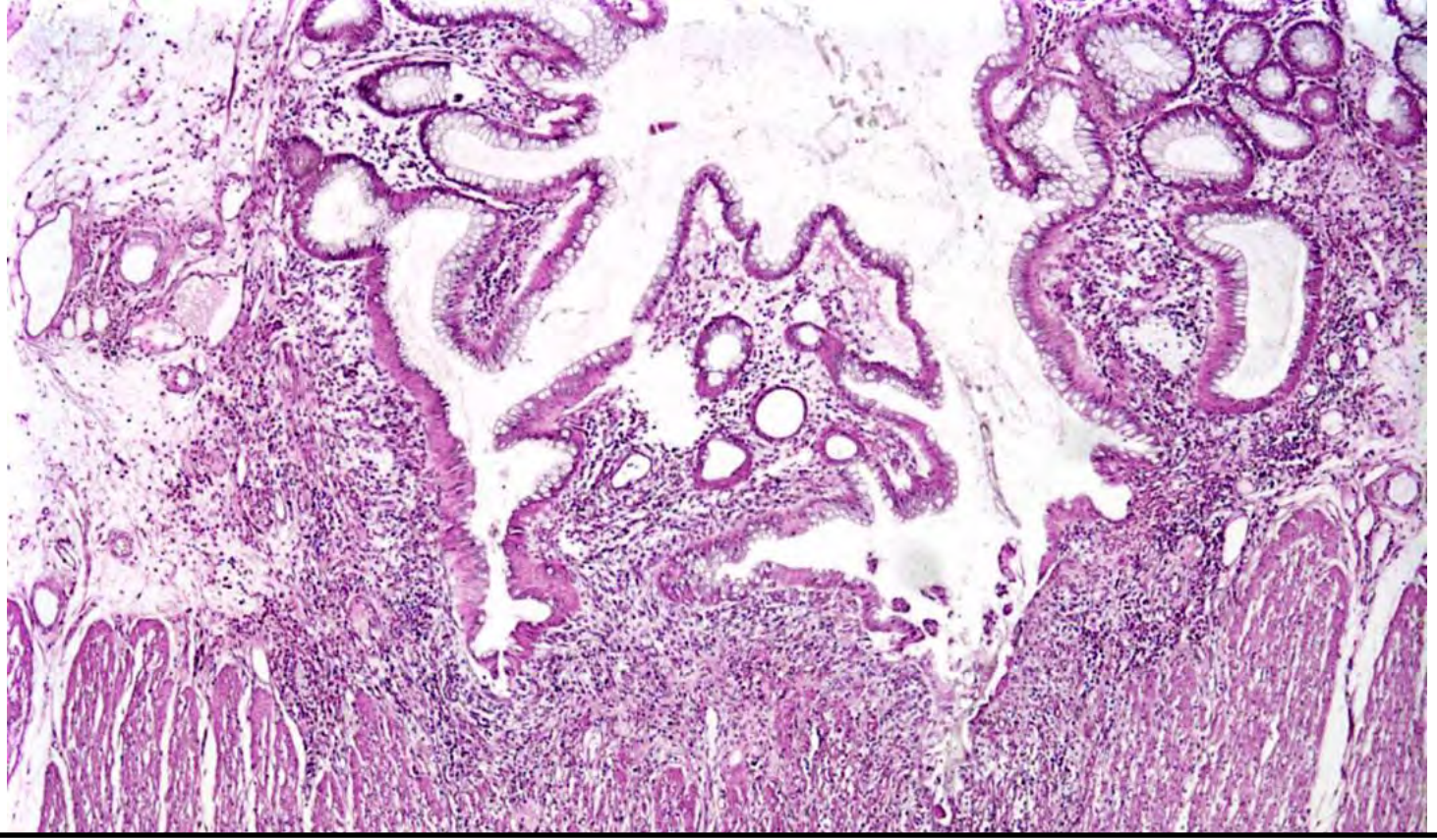




- Pale foamy cytoplasm
- Round, eccentric nuclei
- Ingested red cells



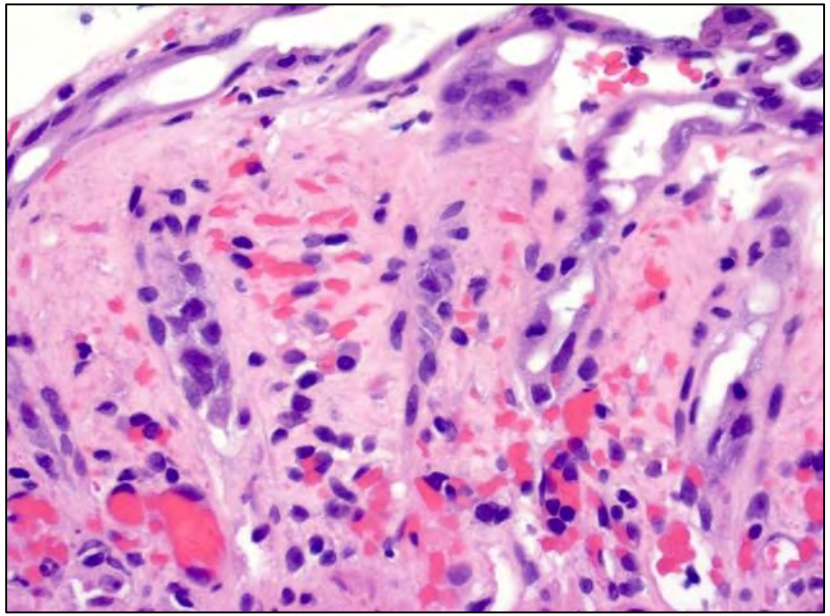




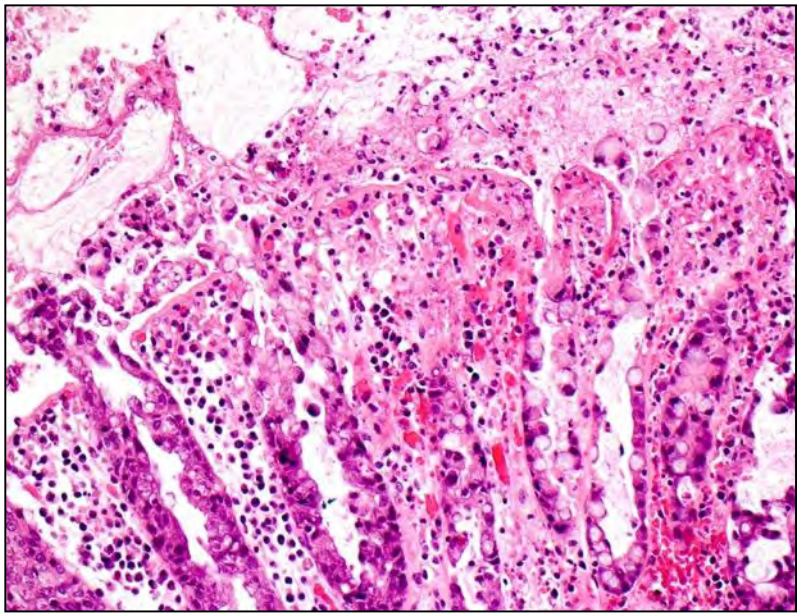
- Atypical
  - Crohns-like w/ skip lesions
  - Pseudomembranes / Toxic megacolon

Courtesy Dr. David Owen

Acute ischemic or pseudomembranous changes



EHEC (*enterohaemorrhagic E. coli*), strain O157:H7



EHEC O157:H7, *Clostridium Difficile*, *Klebsiella oxytoca*

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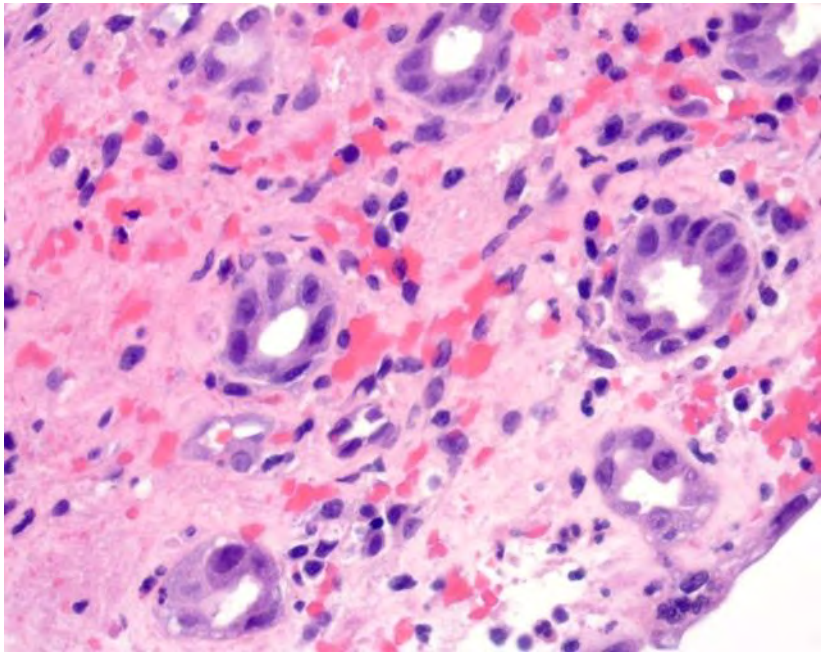
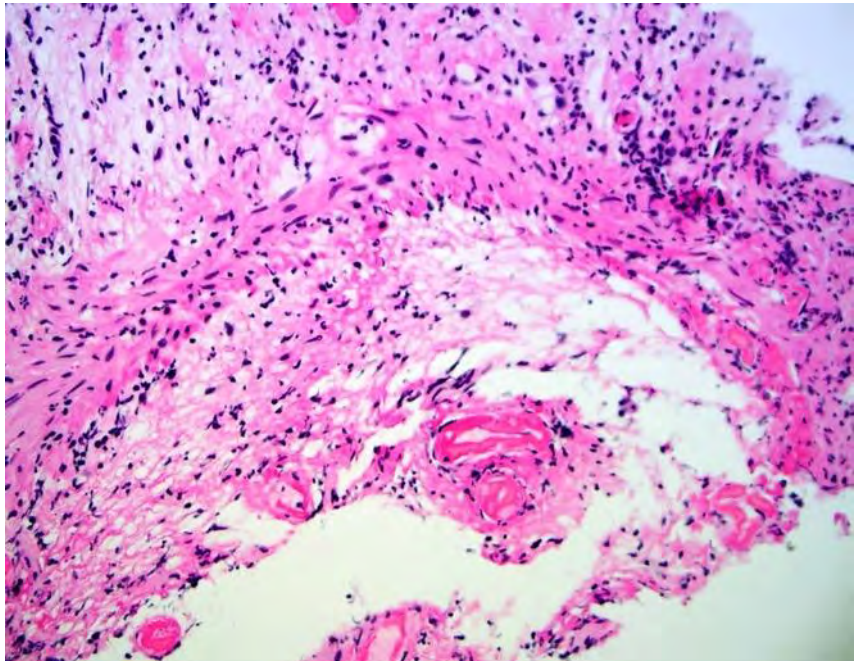
EHEC O157:H7 >> bloody diarrhea and can lead to the hemolytic-uremic sd & thrombotic thrombocytopenic purpura [right-sided colonic involvement ++].





crypt withering, lamina propria hyalinization, capillary microthrombi and associated acute inflammatory exudates

Active inflammation, eosinophils predominant

- Parasitic worms (helminths), less frequently, coccidians
- Helminths:
  - **Cestodes: rarely cause any histologic abnormalities,**
  - **Trematodes: usually assoc^{iated} w/ pronounced infl.^{tion}**
  - **Nematodes: invasive infections elicit eosinophila [deep in the mucosa w/ extensive degranulation]**
- Frequent chronic mucosal injury and prominent fibrosis

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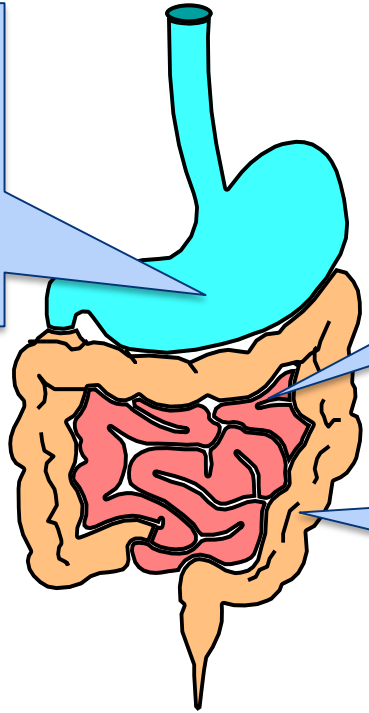
Preferred sites of infections of helminths

Stomach:
Strongyloides stercoralis,
Schistosomiasis,
Anisakiasis



Small Intestine:
Ascariasis, Trichuriasis, Hookworm infection, Strongyloidiasis
Schistosomiasis

Colon:
Enterobiasis - Trichuriasis

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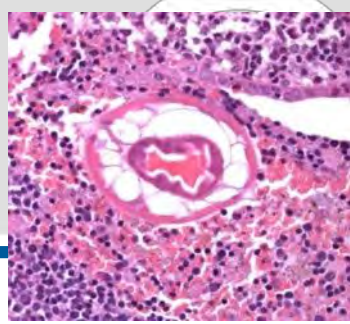
Nematodes



- Commonest: ascariasis, trichuriasis, hookworm infection and enterobiasis (enterobius vermicularis).
- Often discovered incidentally during workup for anemia or malabsorption.
- If no mucosal invasion: no abnormalities or minimal inflammation and villous blunting.

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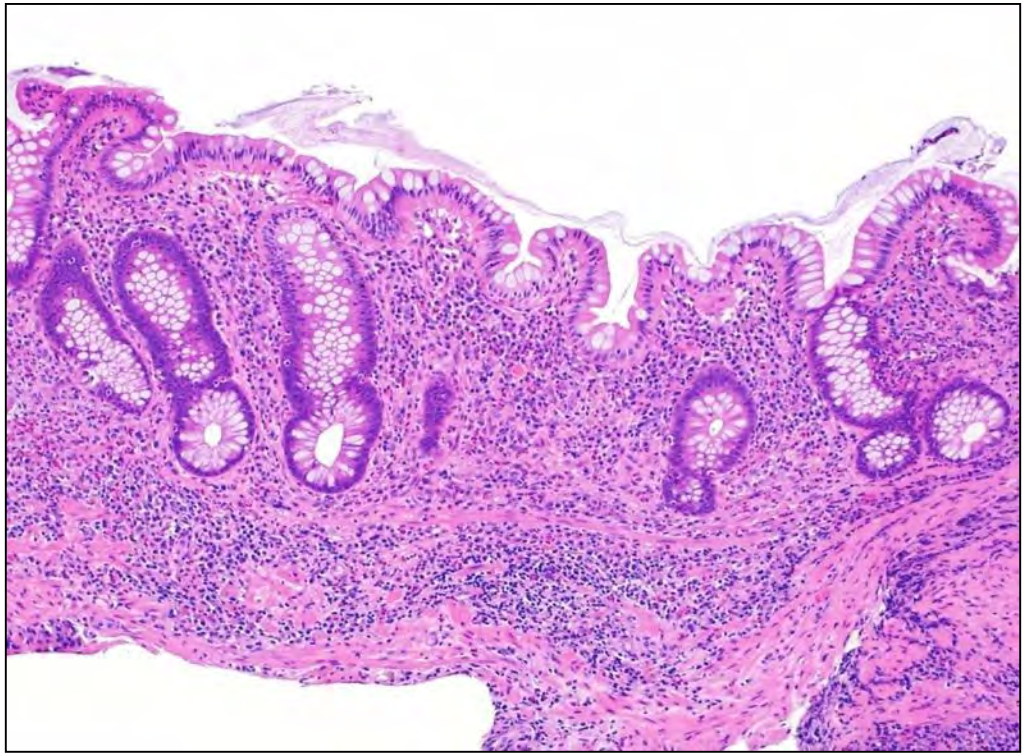
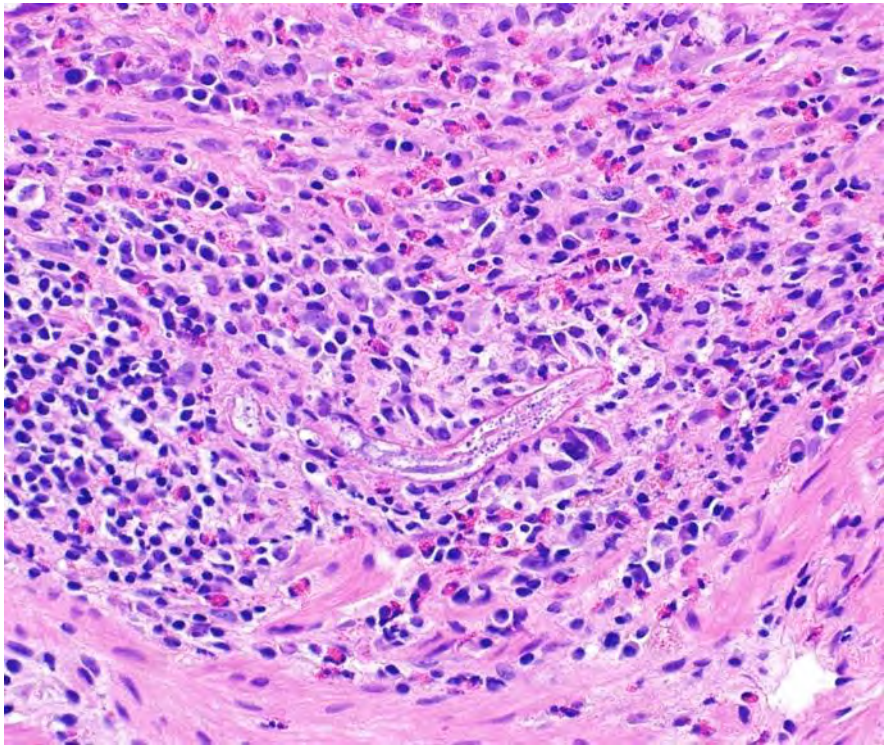
Strongyloidiasis





Strongyloides Stercoralis

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Strongyloides Colitis

- Can be right-sided, patchy and spare the rectum
  - pancolitis in 53%
- Eosinophilic microabscesses [30%]
- Granulomas [44%]
- Few crypt abscesses but frequent ulcers
- 52% initially misdiagnosed, 38.5% were called UC
- Fatality rate of 39% (may be as high as 90%)

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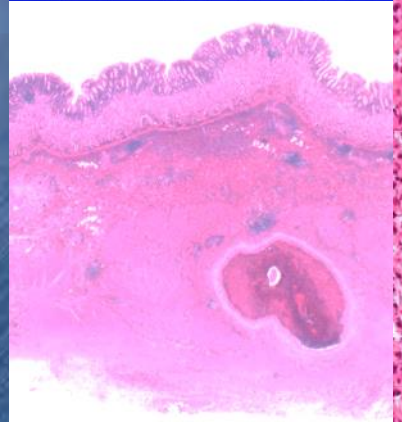
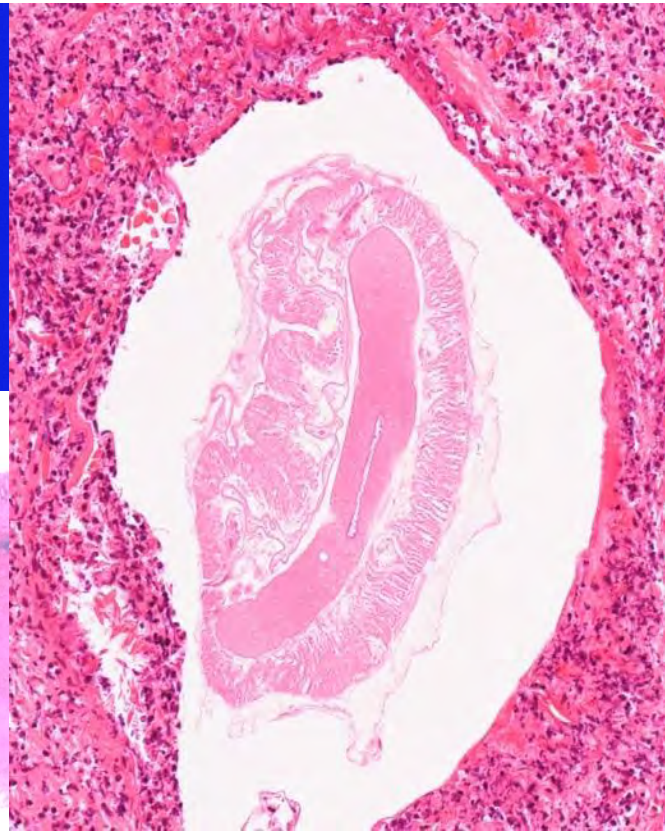
Qu et al, Human Pathology 2009 40:572-7.

Anisakiasis

No! Sushi – the parasitic nightmare in your lunchbox

Don't fancy a worm with your nigiri? Freezing or cooking the fish is the answer





Case Report

Human infection by acanthocephalan parasites belonging to the genus *Corynosoma* found from small bowel endoscopy

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ARTICLE INFO

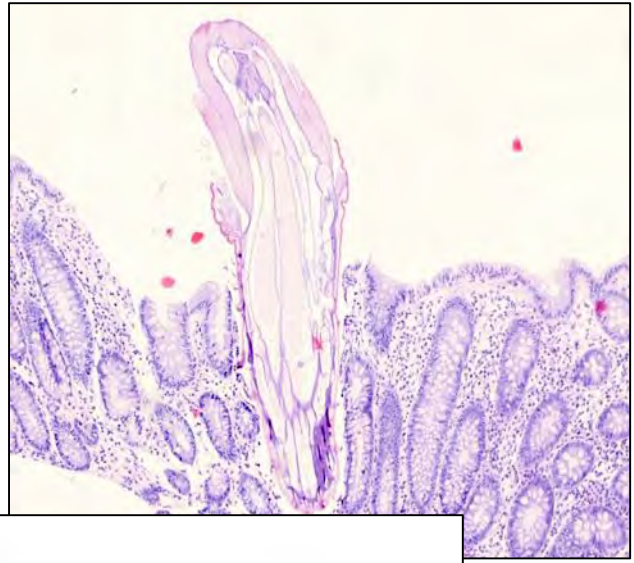
Artide history:
Received 26 March 2016
Received in revised form 28 June 2016
Accepted 5 July 2016
Available online 7 July 2016

Keywords:
Acanthocephala
Human infection
Small intestine
Ileus
Corynosoma

ABSTRACT

A 73-year-old man with a suspected ileus in January 2013 and subsequently suffered melena in February 2014 was endoscopically examined. As a result of the examinations, unidentified species of *Corynosoma* sp. and *Corynosoma villosum* were recovered from the small intestine, further endoscopic diagnosis suggested relevance between abdominal pain and the present infections in the small intestine. The recovered worms were composed of gravid females with developed eggs, suggesting that these parasites can survive for a long time in the intestine after infection. In this case, the short interval between infections appears to be due to the individual's eating habits which consist of regularly consuming uncooked seafood.

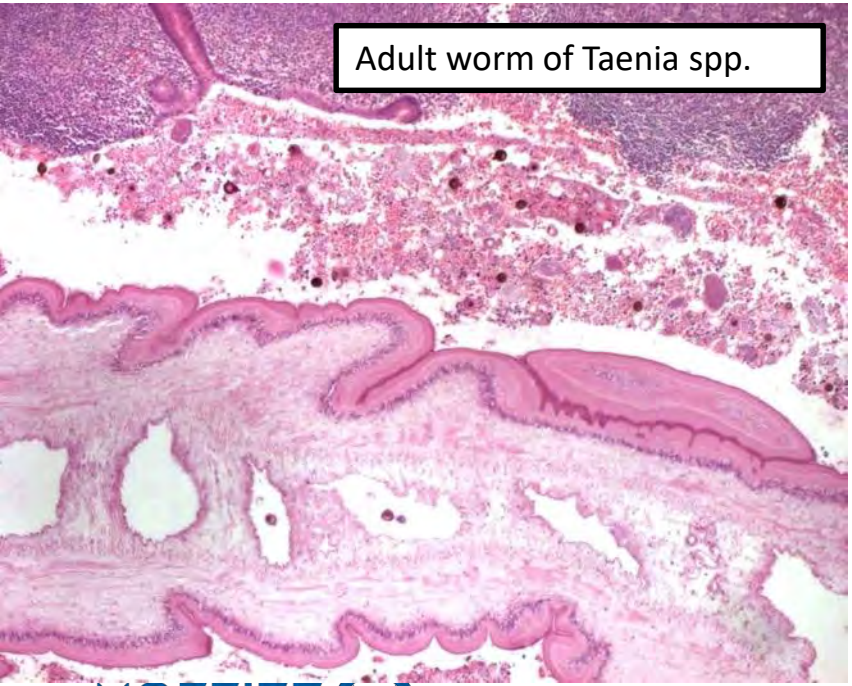
spiny/thorny headed worm!!



ABSTRACT

A 73-year-old man with a suspected ileus in January 2013 and subsequently suffered melena in February 2014 was endoscopically examined. As a result of the examinations, unidentified species of *Corynosoma* sp. and *Corynosoma villosum* were recovered from the small intestine, further endoscopic diagnosis suggested relevance between abdominal pain and the present infections in the small intestine. The recovered worms were composed of gravid females with developed eggs, suggesting that these parasites can survive for a long time in the intestine after infection. In this case, the short interval between infections appears to be due to the individual's eating habits which consist of regularly consuming uncooked seafood.

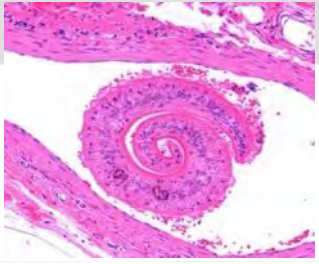
Cestodes



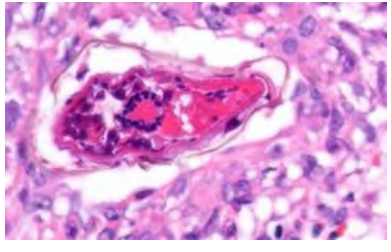
- May evoke mucosal eosinophilia (attachment site of the worm).
- Humans can become an accidental intermediate host for *Taenia solium* following ingestion of parasitic ova or gravid proglottids w/ cysticercosis, the development of parasitic cysts at numerous extra-GIT sites (e.g.,skeletal muscle and brain)

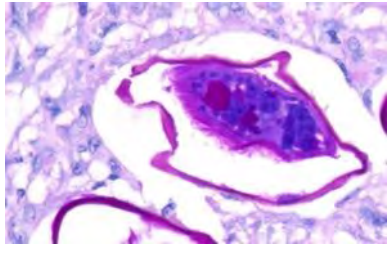
Schistosomiasis: most common trematode infection

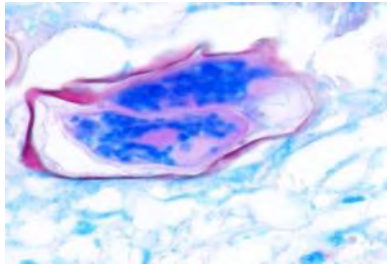
- Adult worms reside in intestinal veins >>>>



	Geographic distribution	Size	Shape	Spine
S. guineensis and related S. *intercalatum*	West and Central Africa	140–240 × 50–85 μm	Elongated	Terminal
S. haematobium	Africa, Madagascar and Middle East	110–170 × 40–70 μm	Elongated	Terminal
S. japonicum	China, East Asia and Philippines	55–85 × 40–60 μm	Oval	Small lateral knob
S. mansoni	Africa, Middle East, parts of South America and Caribbean	115–175 × 45–70 μm	Elongated	Lateral
S. mekongi	Southeast Asia, especially Mekong delta	50–65 × 30–55 μm	Oval	Small lateral knob







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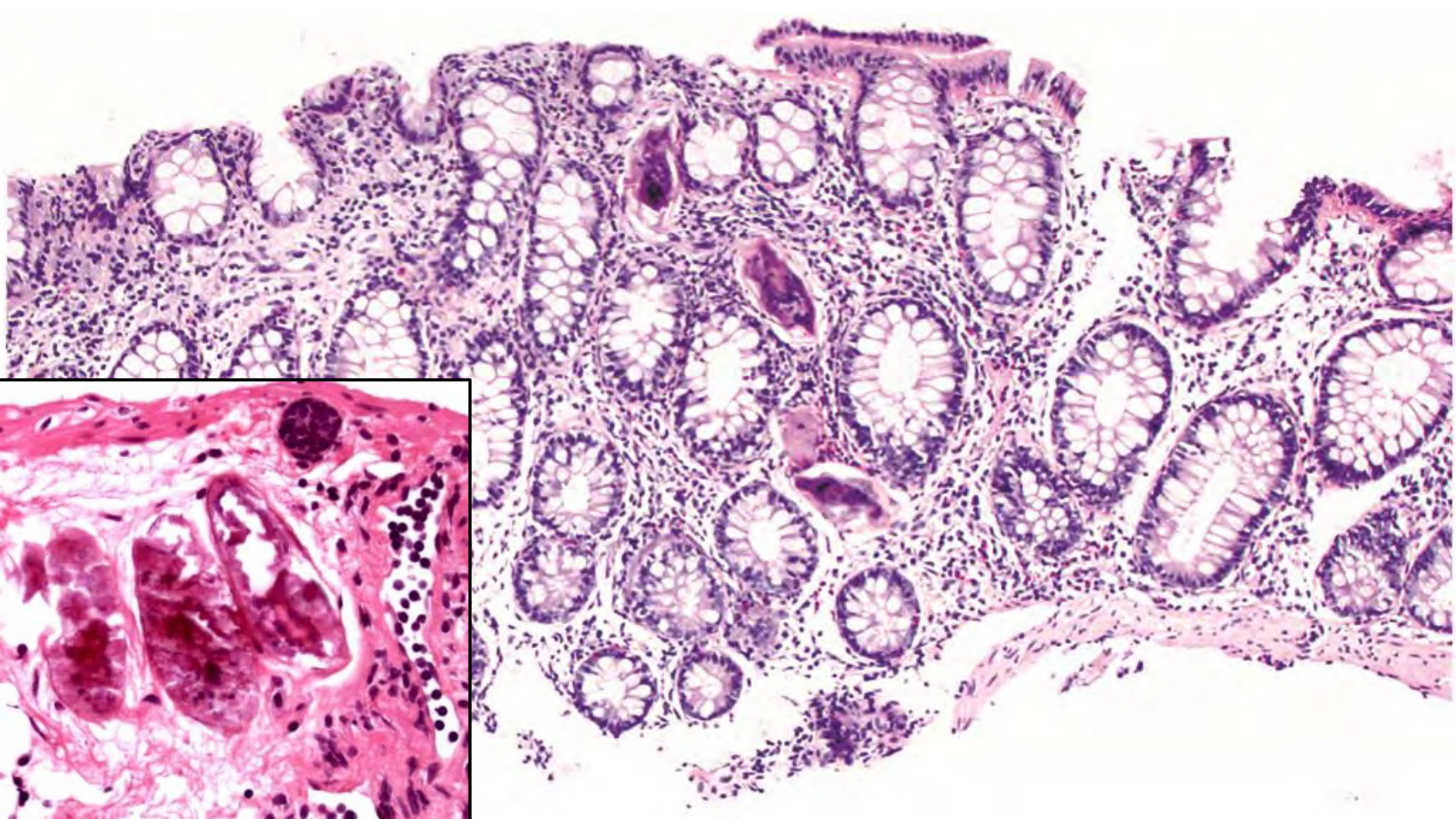
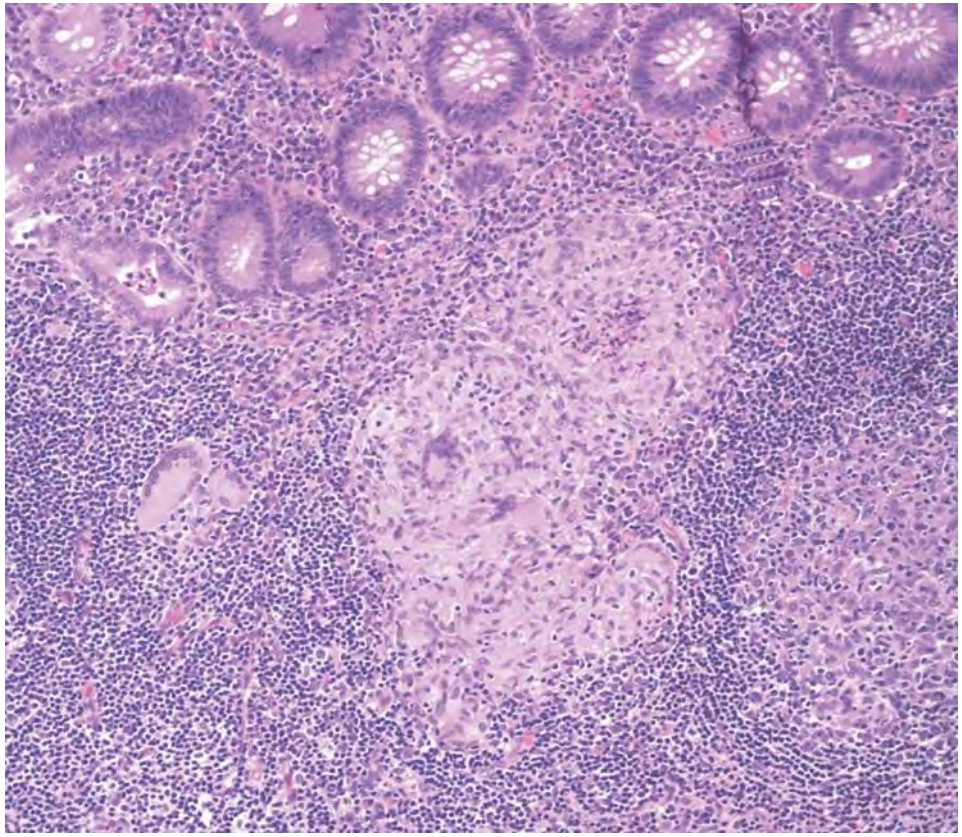


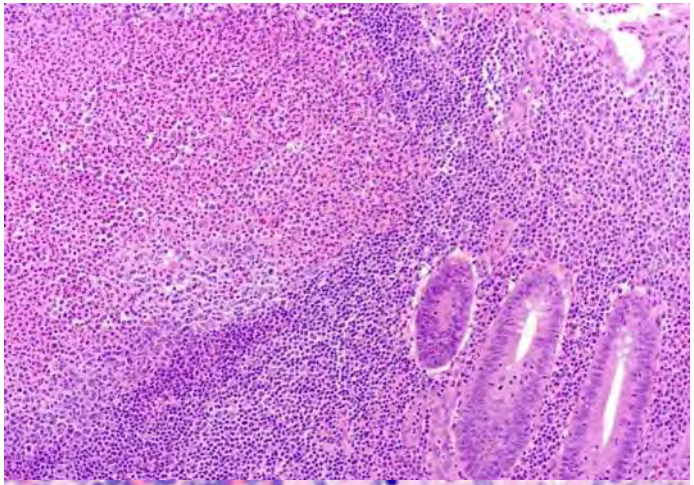
Active inflammation, granulomas predominant

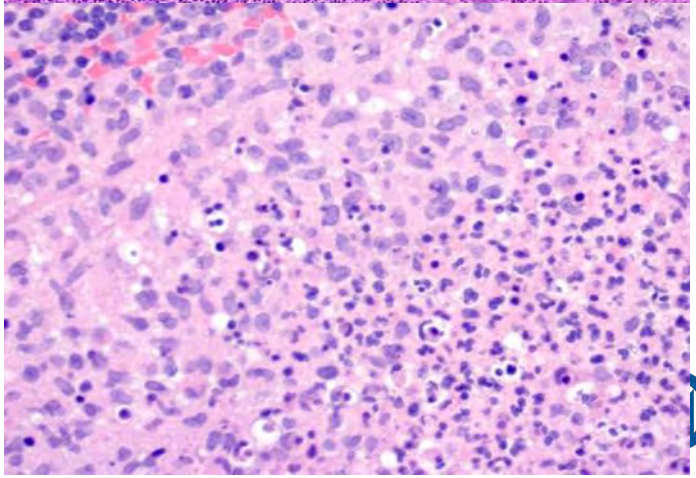
- *Yersinia enterocolitica* and *Y. pseudotuberculosis*
- [some helminthiases w/ prominence of eosinophils]

- Intestinal yersiniosis is an uncommon cause of traveler's diarrhea, but increased risk for infection exists in pts w/ iron overload.
  - predilection for the ileum, right colon and appendix.
  - Granulomatous inflammation often accompanied by suppurative changes.

Granulomas are more frequently associated w/ *Y. pseudotuberculosis*







Lymphoid cuff / central neutrophil microabscesses

Yersiniosis & CD share transmural lymphoid aggregates, skip lesions fissuring ulcers

- ***In favor of yersiniosis.***
  - Prominent appendiceal involvement
  - *Absence of:*
    - Chronicity – local & distant - to the site of active inflammation [crypt distortion, thickening of M. mucosae, prominent neural hyperplasia]
    - Upper GI and extra-intestinal manifestations
    - Endoscopic mucosal cobblestoning

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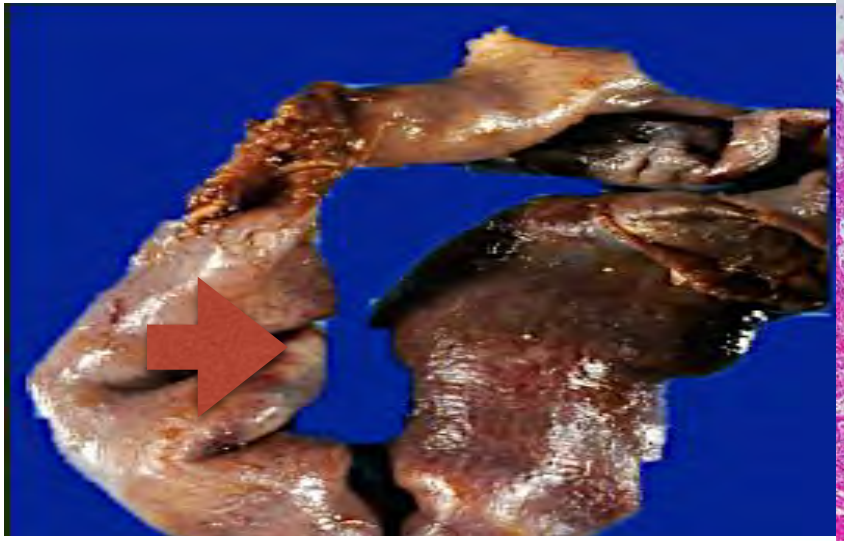
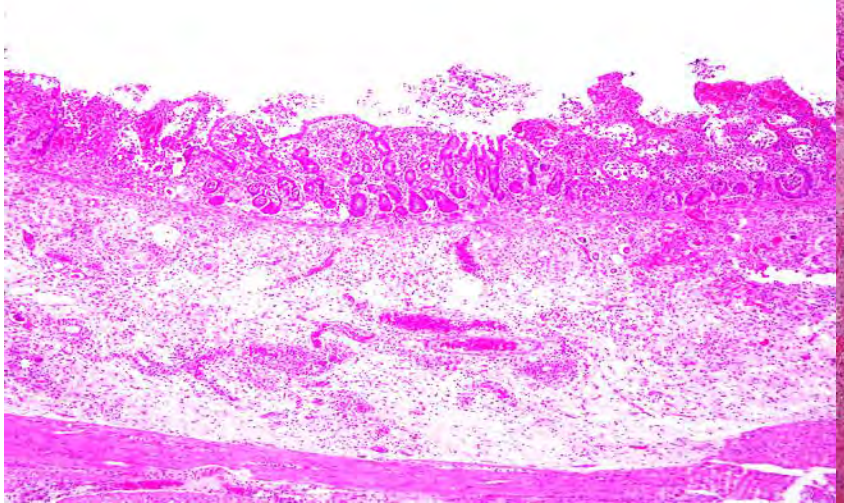
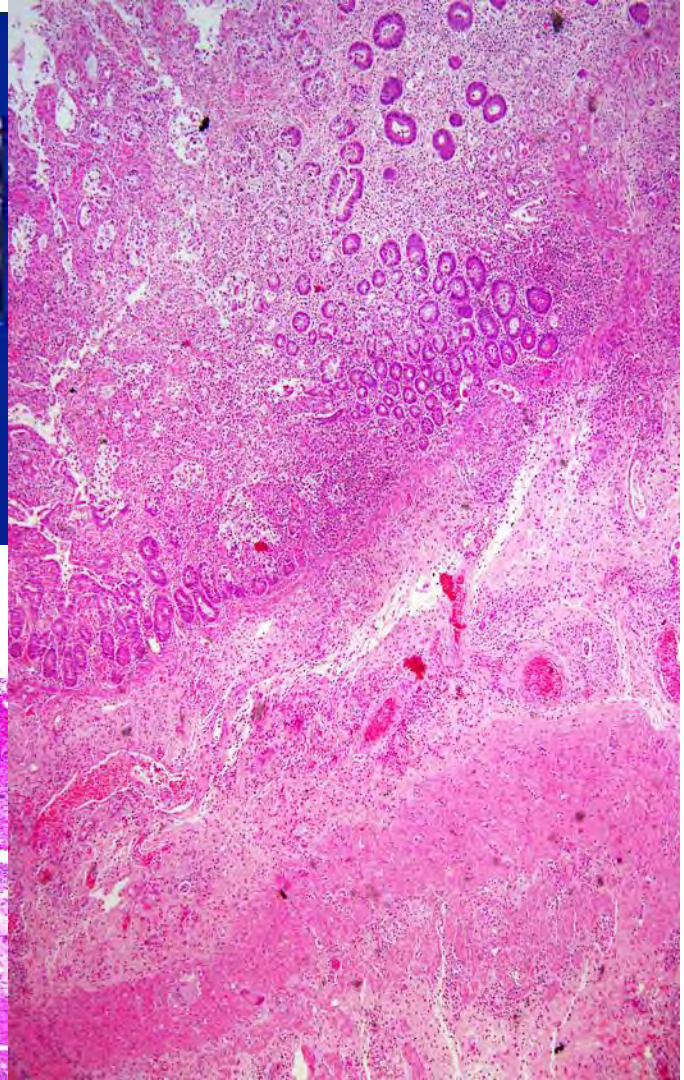
A case from Costa Rica.....

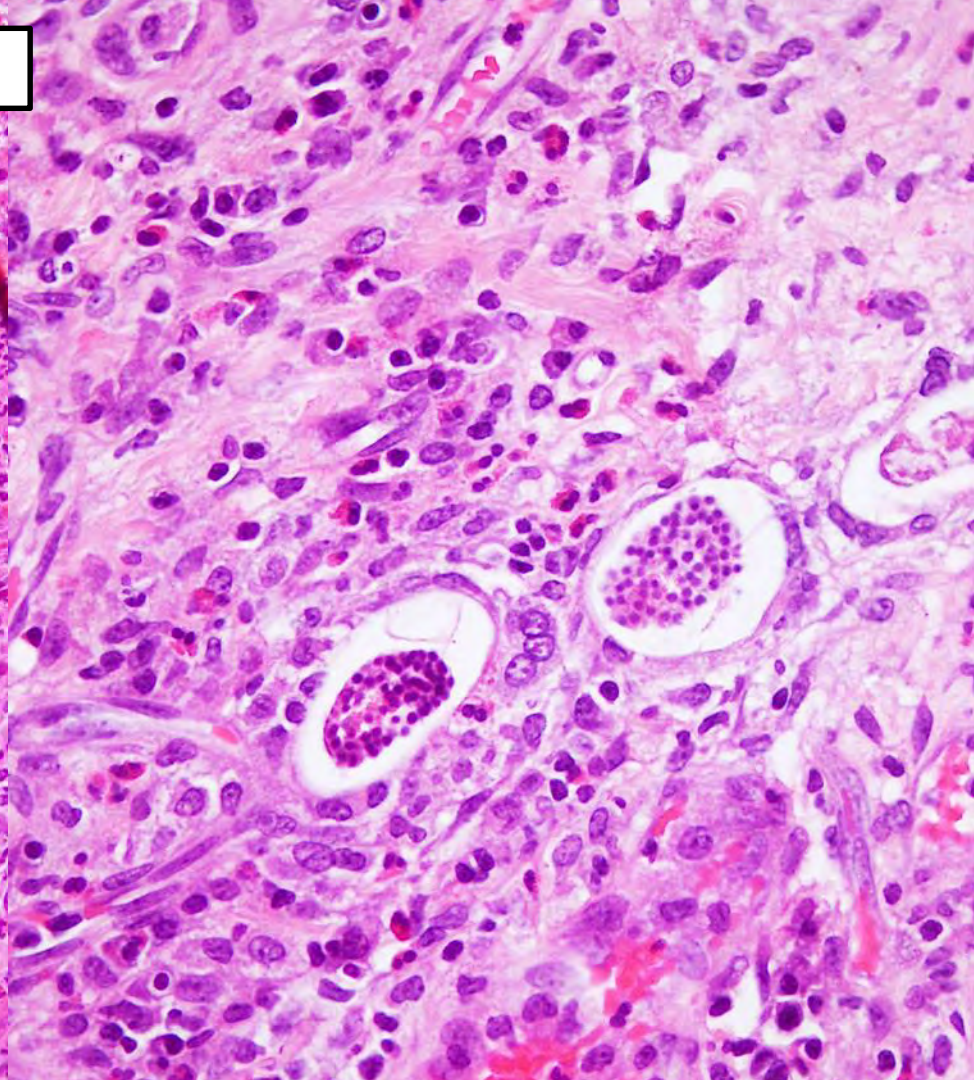
- Paciente femenina de 9 meses de edad.
- Ingresada por cuadro febril, anorexia, asociado a dolor abdominal, de 3 días de evolución y hypereosinophilia
- Es referida a infectología por persistencia del cuadro clínico



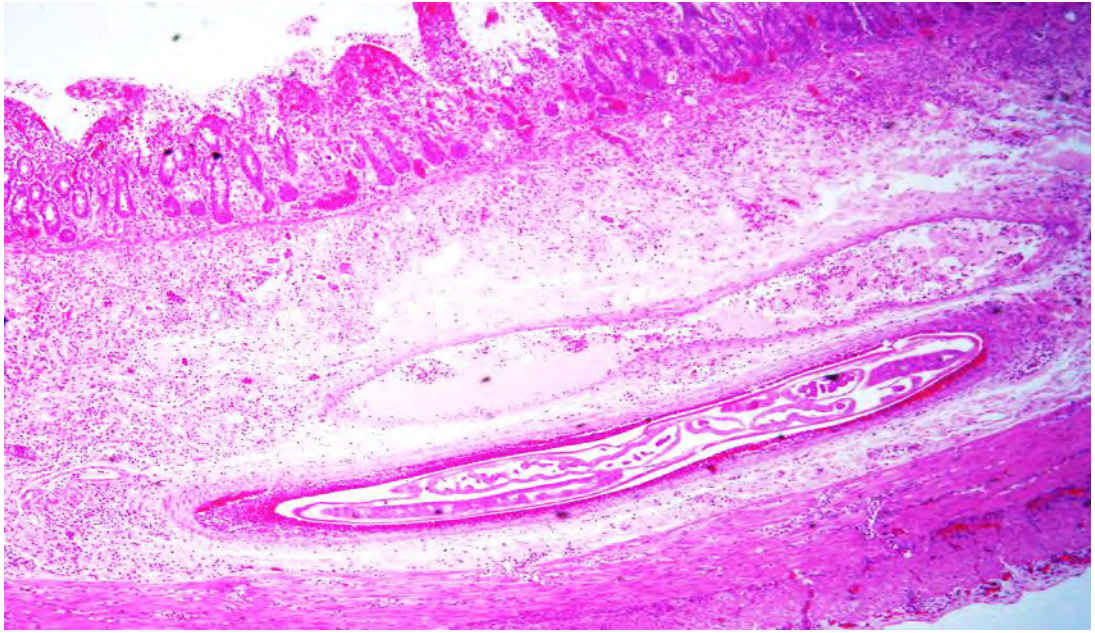


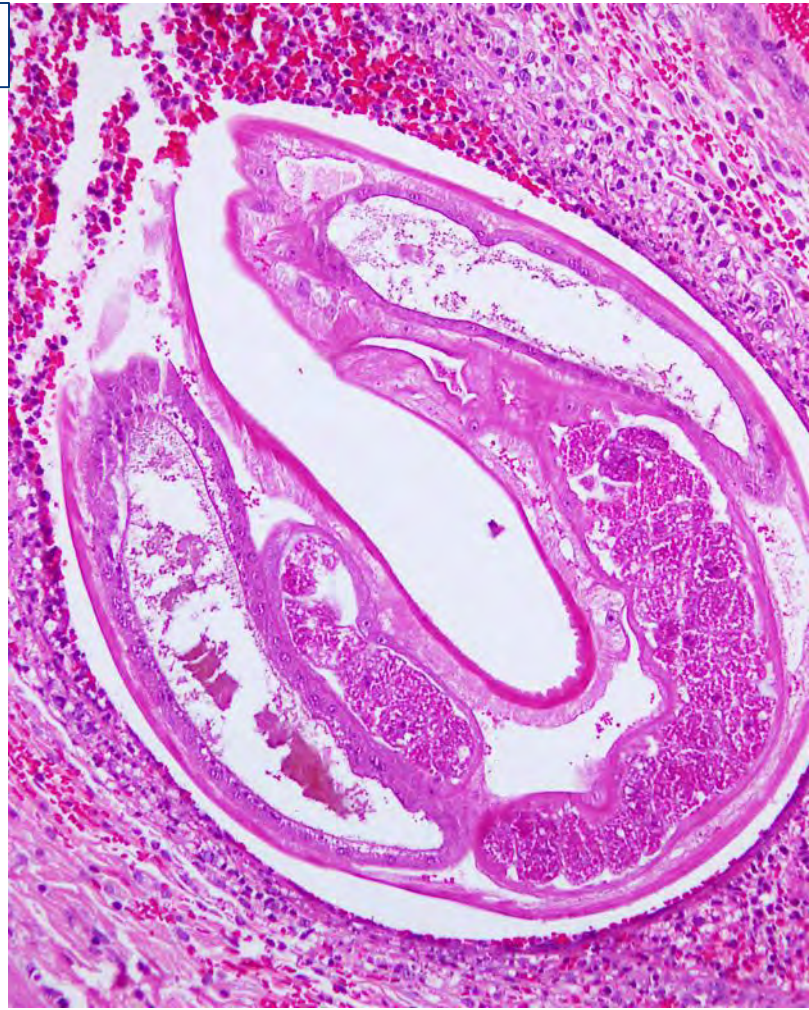


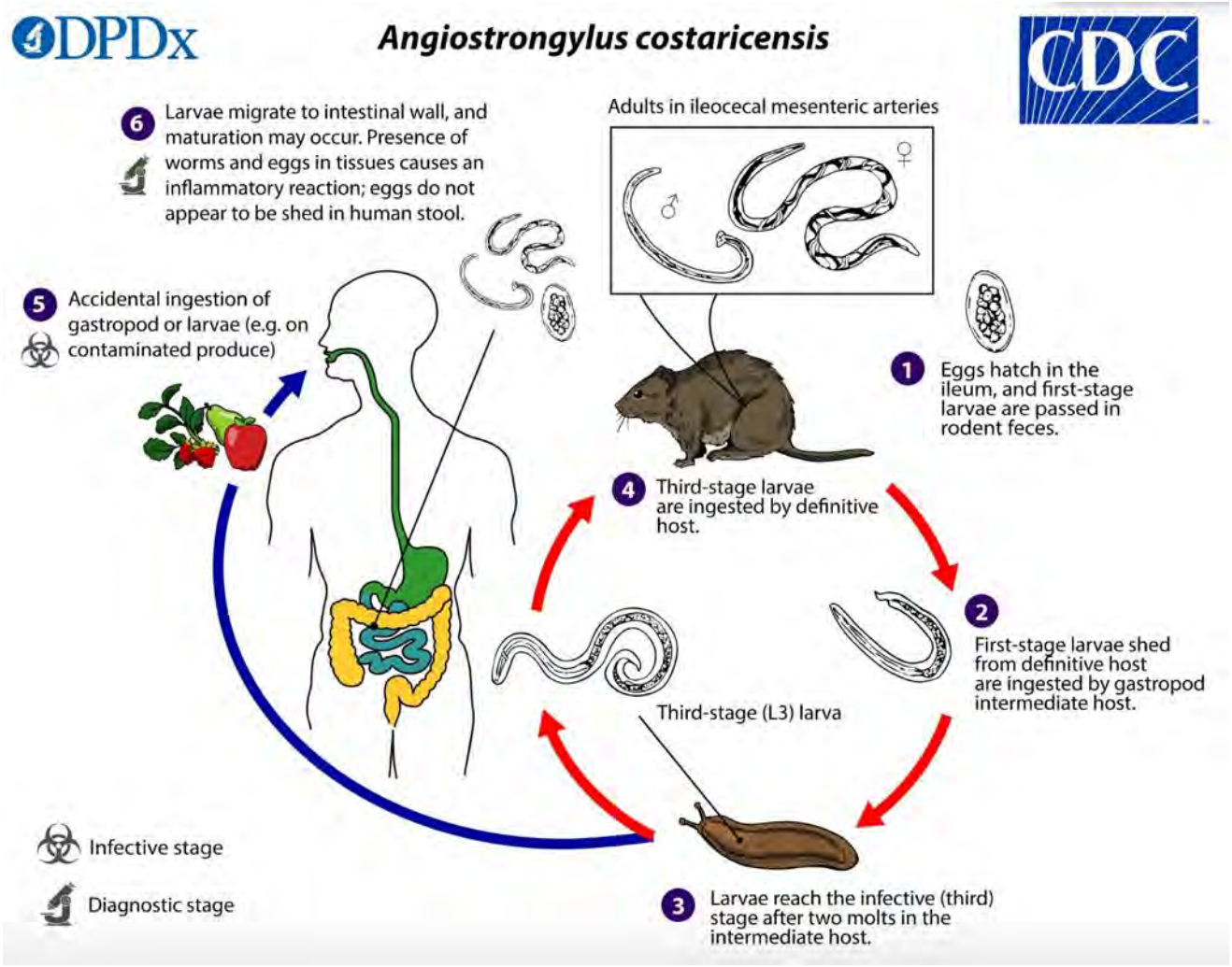
Parásito en Estadio de Huevos Embrionados



Angiostrongyliasis costaricensis [adult forms]







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Histology of ENDOSCOPIC INTESTINAL BIOPSY