When the flasks shatter

22 September 2020
Interhospital Meeting
Speaker: Dr. Clement LEUNG
Chairperson: Dr. Michele TANG

Our Case…

- M/31y
- No known drug allergy
- Non-smoker, non-drinker
- International school teacher

- Past medical history:
  - OSA previously on CPAP
  - Substance abuser (methamphetamine)
  - Adjustment disorder
  - History of Shigella dysentry in 5/2018

Presentation

- Watery diarrhoea for 10 days
- BO >10 times per day
- Watery, brownish stool
- One episode of PR bleeding
- Associated with abdominal pain
- Fever and chills
- TOCC negative
- No documented weight loss

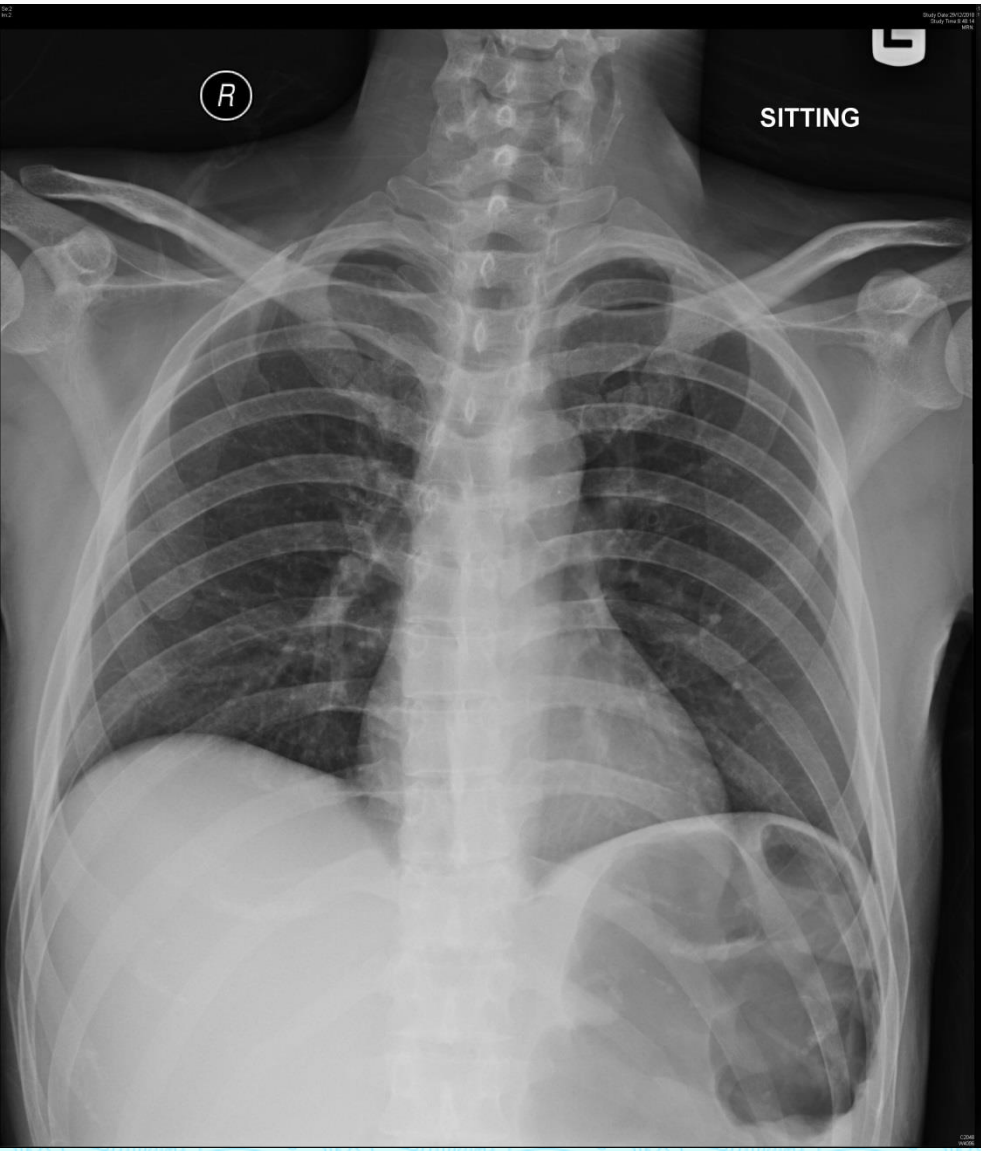
Examination

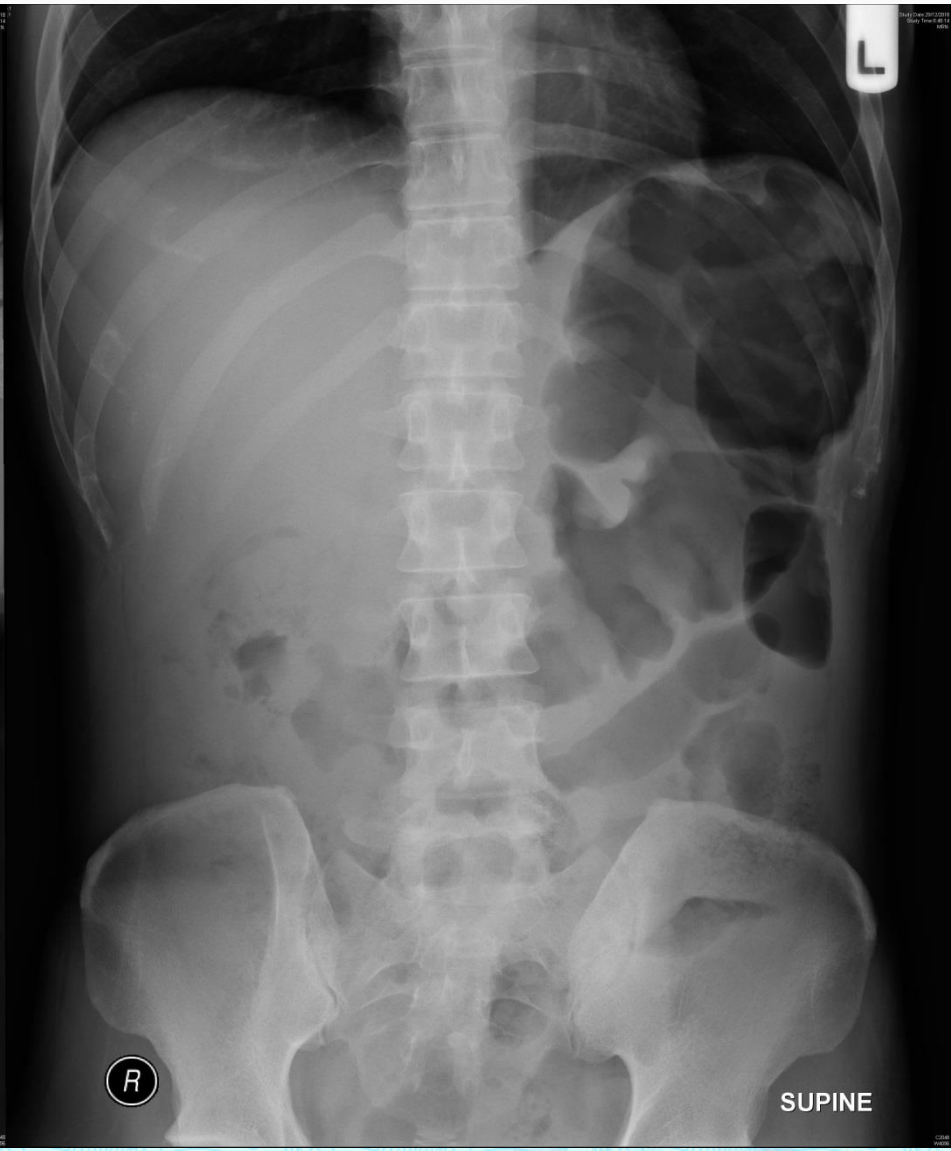
- Upon admission:
  - Alert and conscious
  - Very dehydrated
  - BP 150/70 mmHg, Pulse 133/min, sinus
  - Temp 38.1°C
  - Chest clear
  - HS dual, no murmur
  - Abdomen soft, tenderness+ over lower abdomen, no organomegaly
  - No enlarged palpable lymph nodes
  - No joint swelling or rash

Investigations

- Bloods on admission:
  - CBC:
    - Hb 13 (normocytic, normochromic)
    - WCC 22.22 (neutrophilic)
  - RFT:
    - Na 122, K 3.1, Cr 57, Urea 3.9
  - LFT:
    - ALT 20, ALP 104, Albumin 18, bilirubin 13
  - Amylase 13
  - VBG:
    - pH 7.53, pCO2 4.10, pO2 6.49, HCO3 25.7, BE 3.6

CXR/AXR





Progress

- Admitted to CMC MED on 29 December 2018
- Working Dx: severe gastroenteritis

- Initial management by medical:
  - NPO
  - Intravenous fluid NS Q6H
  - IV Augmentin 1.2g STAT + Q8H
  - Later stepped up to IV Tazocin and Ciprofloxacin in view of swinging fever and elevated WCC

Investigations

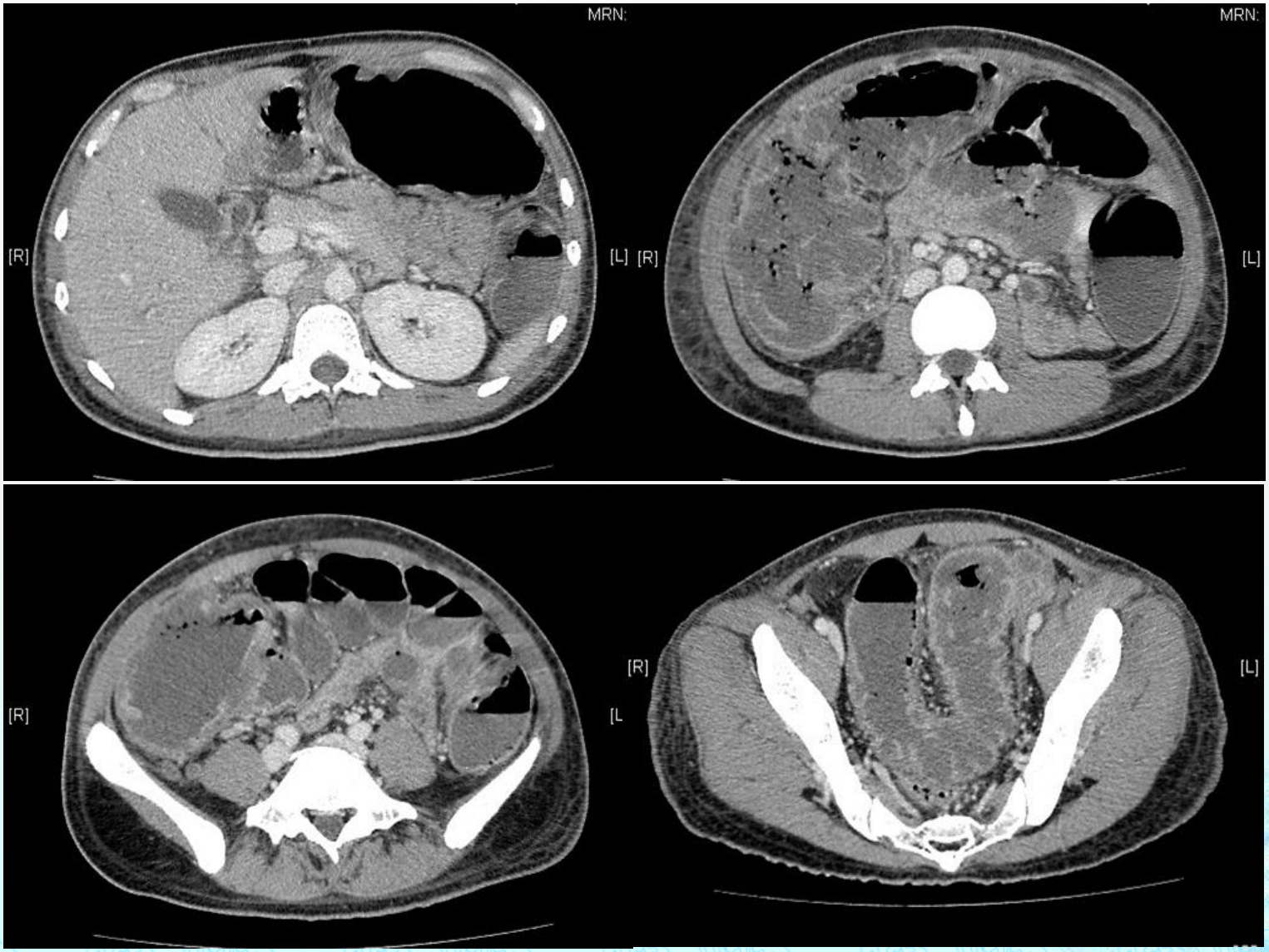
- Further workup:
  - Bloods:
    - Culture negative (29/12/2018)
    - Anti-HIV Ab negative (31/12/2018)
  - Stool:
    - Norovirus – negative (30/12/2018)
    - Rotavirus – negative (30/12/2018)
    - Ova and cyst – negative (30/12/2018)

Investigations

1 January 2019

- 1st CT abdomen + pelvis with contrast
  - Large bowel and distal small bowel are grossly distended, associated with prominent enhancement, mural edema and multiple air-fluid levels. No definite transitional zone / site of obstruction seen in the small bowel. ? extensive colitis including possibility of pseudomembranous colitis.
  - Multiple prominent lymph nodes found in the mesentery and para-aortic region
  - No free gas nor loculated collection
  - The superior and inferior mesenteric arteries are patent.

CT abdomen + pelvis (1/1/2019)



Progress

- Severe sepsis: persistent swinging fever and tachycardia
- ICU was consulted on 2/1/2019

- Taken over and transferred to ICU
  - Febrile
  - Sinus tachycardia ~ 130/min
  - Complained of persistent severe abdominal pain
  - Distended abdomen with voluntary guarding

- Ddx:
  - Pseudomembranous colitis
  - Inflammatory bowel disease
  - Ischemic colitis
  - Vasculitis induced colitis

Investigations

2 January 2019

- 2nd CT abdomen + pelvis with contrast
  - Grossly distended large bowel and distal small bowel
  - Prominent enhancement, mural edema and multiple air-fluid levels
  - No definite transitional zone / site of obstruction seen in the small bowel
  - Multiple prominent lymph nodes found in the mesentery and para-aortic region
  - No gross free gas. Small amount of ascites.

- Imp: extensive colitis, possibility of pseudomembranous colitis

Progress

- Remained febrile and tachycardic
- Frequent watery diarrhoea
- Occasional PR bleeding

- Consulted surgical team -> colitis, suggested antibiotic treatment, no surgical intervention

- Consulted GI team -> suggested enteral vancomycin for suspected pseudomembranous colitis
  - Enteral vancomycin via RT given
  - Continue Tazocin IV

Progress

- 3/1/2019: Urine toxicology : Methamphetamine, Midazolam metabolite, Haloperidol metabolite, Tramadol
- 5/1/2019: Stool CD Toxin: negative

- Patient condition:
  - Abdominal pain and hydration improved
  - Abdomen less tense, no peritoneal sign, BS +ve, passed loose stool
  - WCC normalised, no acidosis
  - Remained febrile and tachycardic

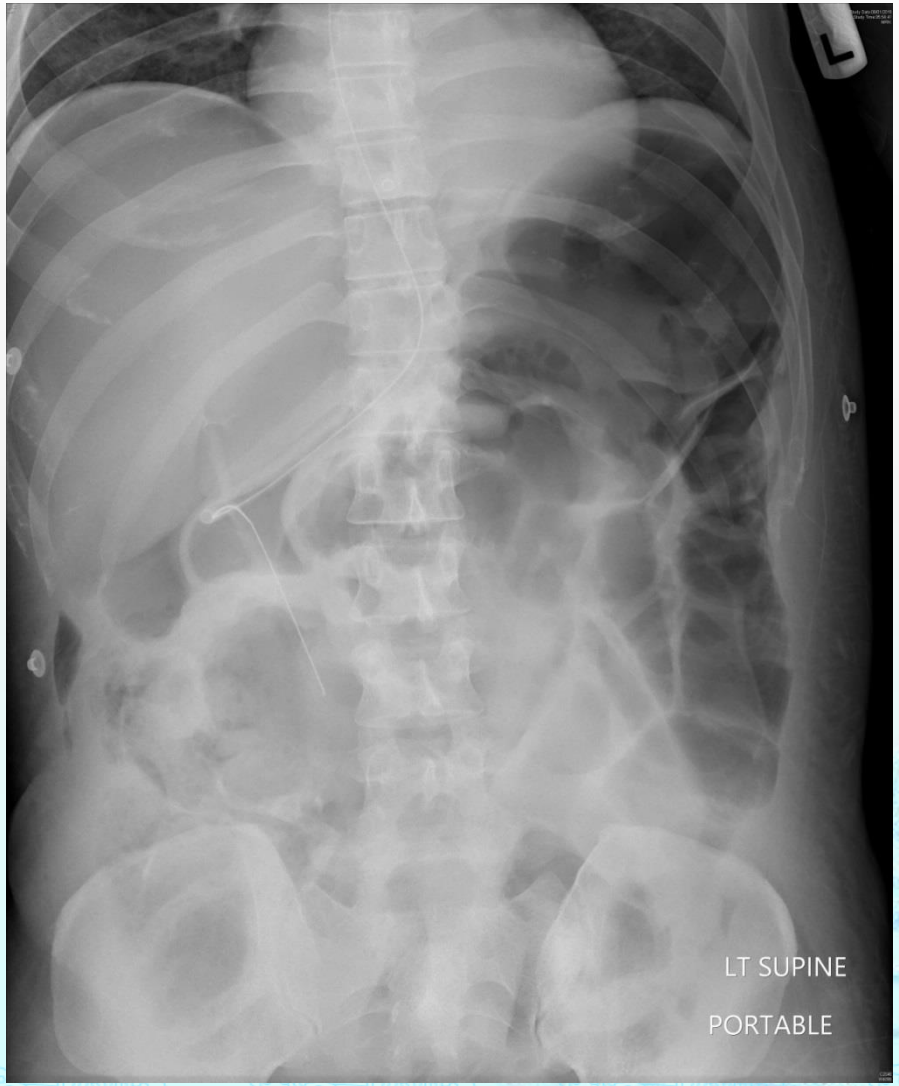
- Consulted GI team and suggested sigmoidoscopy
  - For diagnostic purpose, to rule out inflammatory bowel disease
  - Attempt to “decompress the large bowel”

Progress

- Sigmoidoscopy:
  - Large amount of exudates and yellowish feces
  - Mucosa looks more inflammed with large amount of mucus / exudates
  - Ulcers at sigmoid and mucosa looks less inflammed and smaller amount of mucous / exudates and ulcers at rectum
  - 1st degree piles
  - Biopsy taken
- Post-procedure uneventful, no immediate adverse effect

Progress

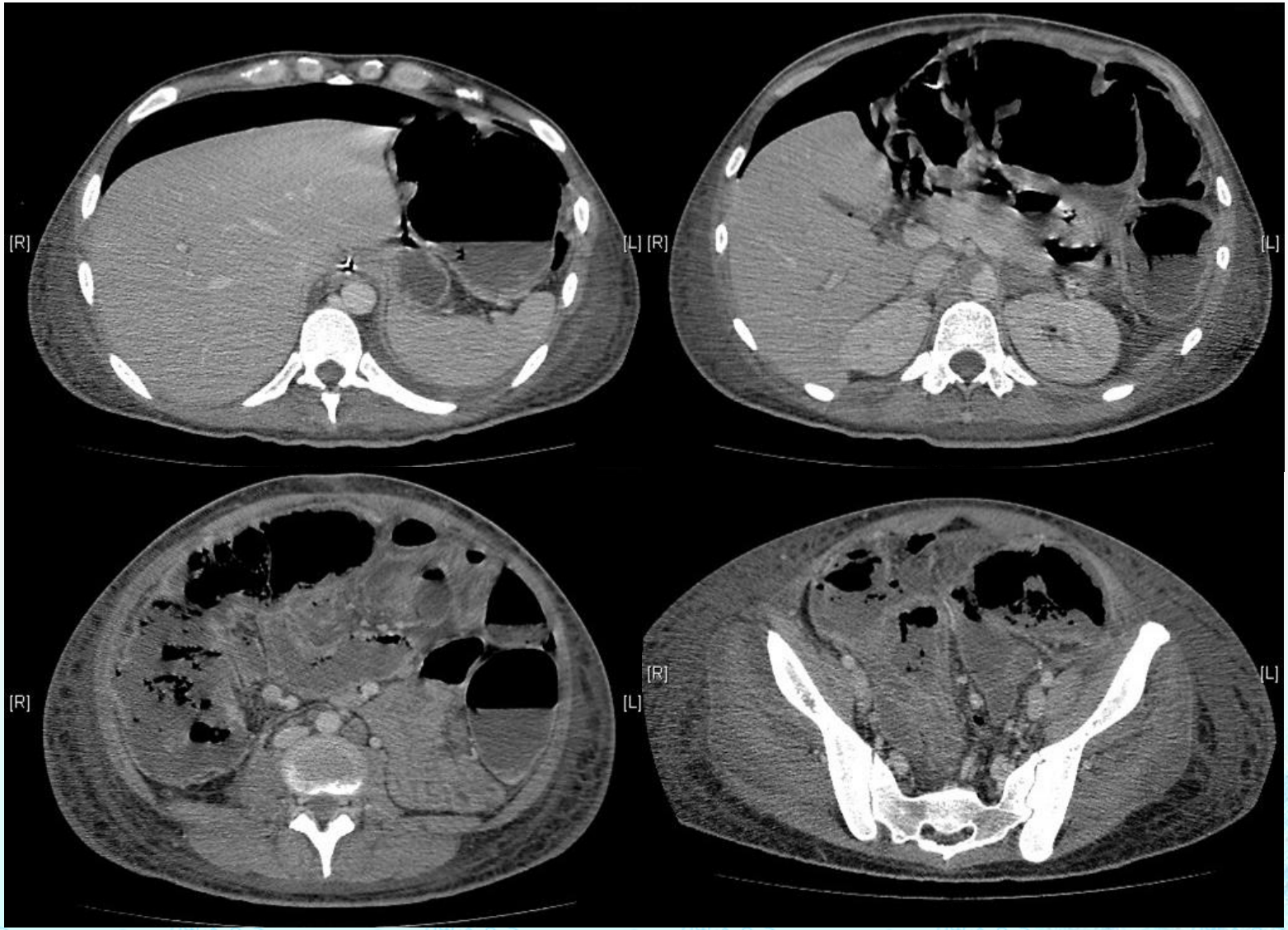
- 8/1/2019:
  - Noted abdomen distended and tense
  - Lower abdomen rebound +ve
  - Temp 39’C
  - HR 140bpm
  - AXR: dilated bowels, hyperlucency at RUQ



Progress

- 8/1/2019:
  - 3rd CT abdomen + pelvis with contrast
    - Newly seen pneumoperitoneum
    - Grossly dilated large bowel with mural edema noted,
    - Distension up to 10cm at transverse colon, compatible with toxic megacolon
    - Terminal/ distal ileum are similarly distended and edematous
    - Multiple prominent mesenteric and paraaortic nodes similarly noted

CT abdomen + pelvis (8/1/2019)



Progress

- 8/1/2019:
  - EOT - laparotomy & drainage, ileostomy
  - OT findings:
    - Generalized faecal peritonitis
    - Whole colon necrosed and communicating into peritoneal cavity
    - Edematous small bowel with no perforation
  - Post-op back to ICU:
    - In severe inflammatory response and shock
    - Not reversed on ventilatory support
    - High dose vasopressor infusion
    - Metabolic acidosis HCO3 15.7 put on CVVH (Oxiris)

Progress

- 9/1/2019:

  Message from microbiologist:

  - Stool x Entamoeba histolytica antigen: positive
  - Stool x amoeba microscopy:
    - Entamoeba histolytica/Entamoeba dispar complex
  - → Started on IV flagyl 750mg Q8H, continue Tazocin

  - Blood procalcitonin (8/1/2019): 17

  - Clinical condition improved and able to gradually wean off vasopressor

Progress

- 10/1/2019:
  - Second EOT findings:
    - old blood stained fluid in side the peritoneal cavity
    - residual necrotic unhealthy bowel wall including ascending colon, descending colon and sigmoid colon
    - inflammed mesenteric tissue
  - Residual bowel wall at ascending colon, descending and sigmoid colon resected

Pathology

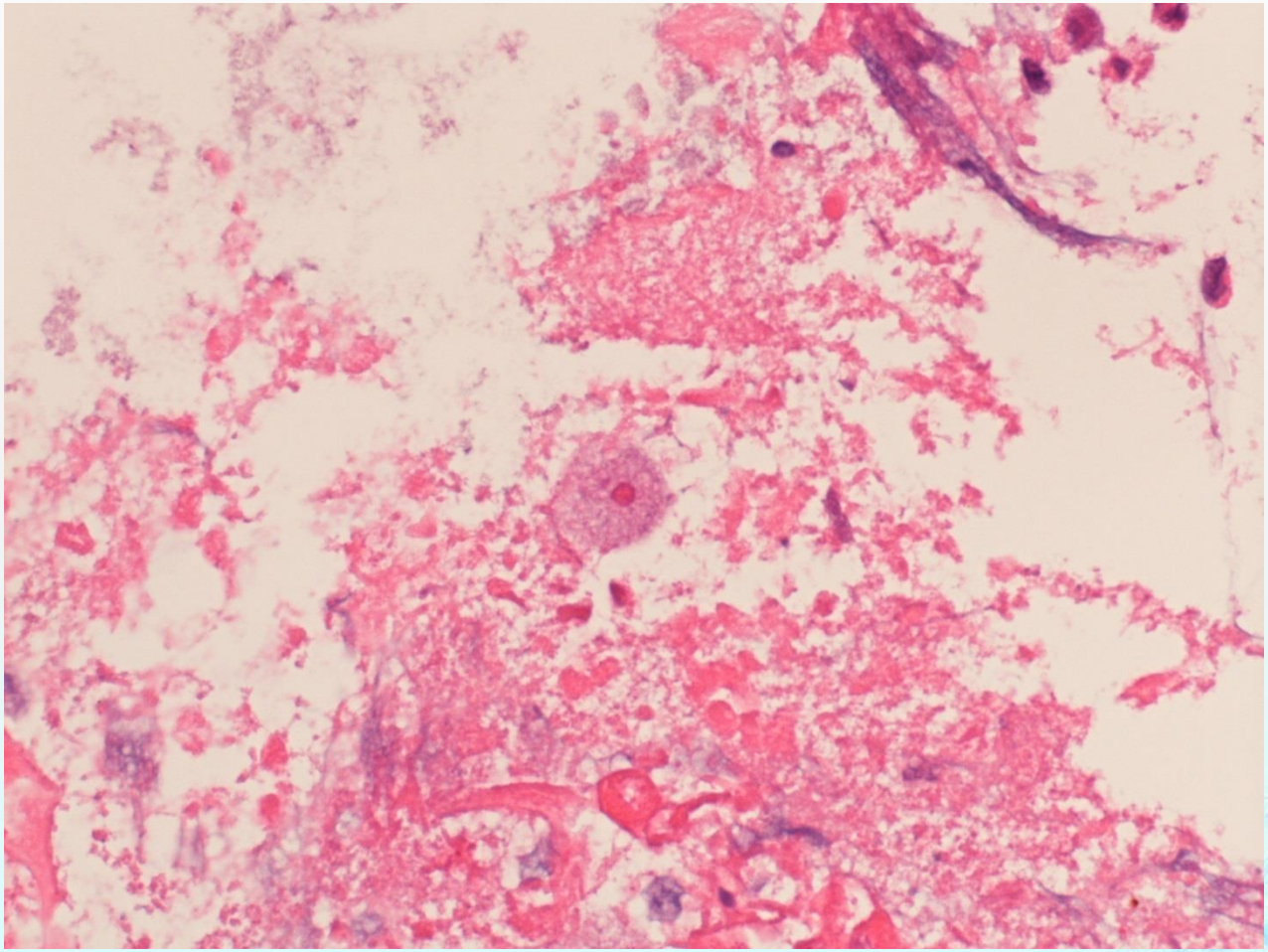
- Colonic biopsy (7/1/2019) from sigmoidoscopy:
  - Necrotic tissue and amorphous eosinophilic debris with no viable tissue
  - Presence of micro-organism, featuring distinct cell membrane, foamy cytoplasm and round, eccentric located nuclei. Stain positive for PAS

  → confirming presence of Entamoeba Histolytica

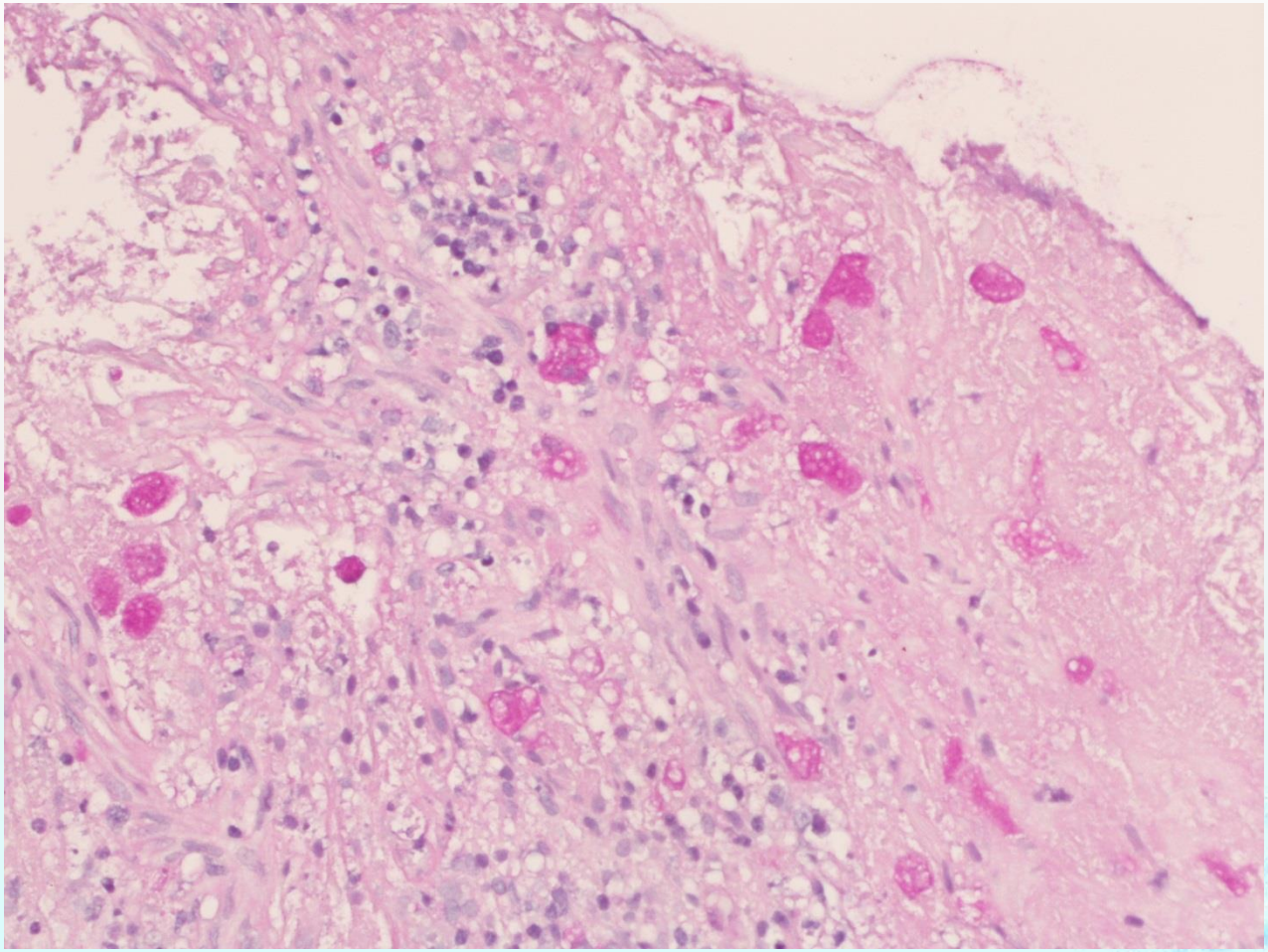
Pathology

- Large Bowel specimen (8/1/2019) from 1st EOT
  - Macroscopic
    - Serosa was covered by inflammatory exudate
    - Multiple **perforations** were found
    - Multiple **ulcers** adjacent to the perforations
    - The remaining tissue were necrotic looking with dull greyish to greenish color and thin
    - No tumor was found
  - Microscopic
    - Transmural necrosis
    - Abundant necrotic debris
    - Microorganisms consistent with trophozoites of Entamoeba histolytica (PAS positive) are found in the lumina surface and in the debris
- Diagnosis :
  - AMEBIASIS with PERFORATION and NECROSIS

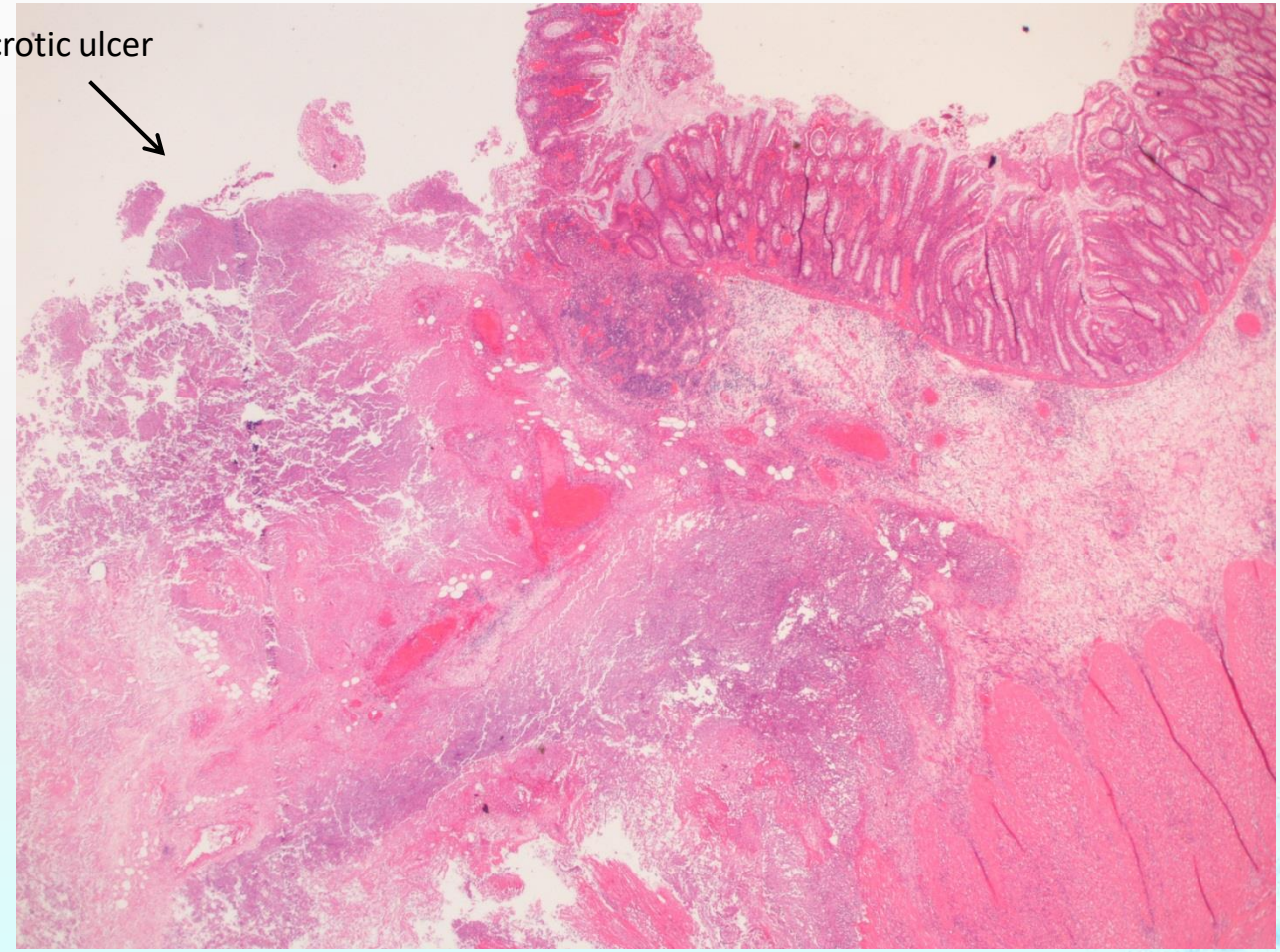
Colonic biopsy (7/1/2019) x 400



Colonic biopsy (7/1/2019) x 200
PAS stain



Large bowel excision (8/1/2019) x 10



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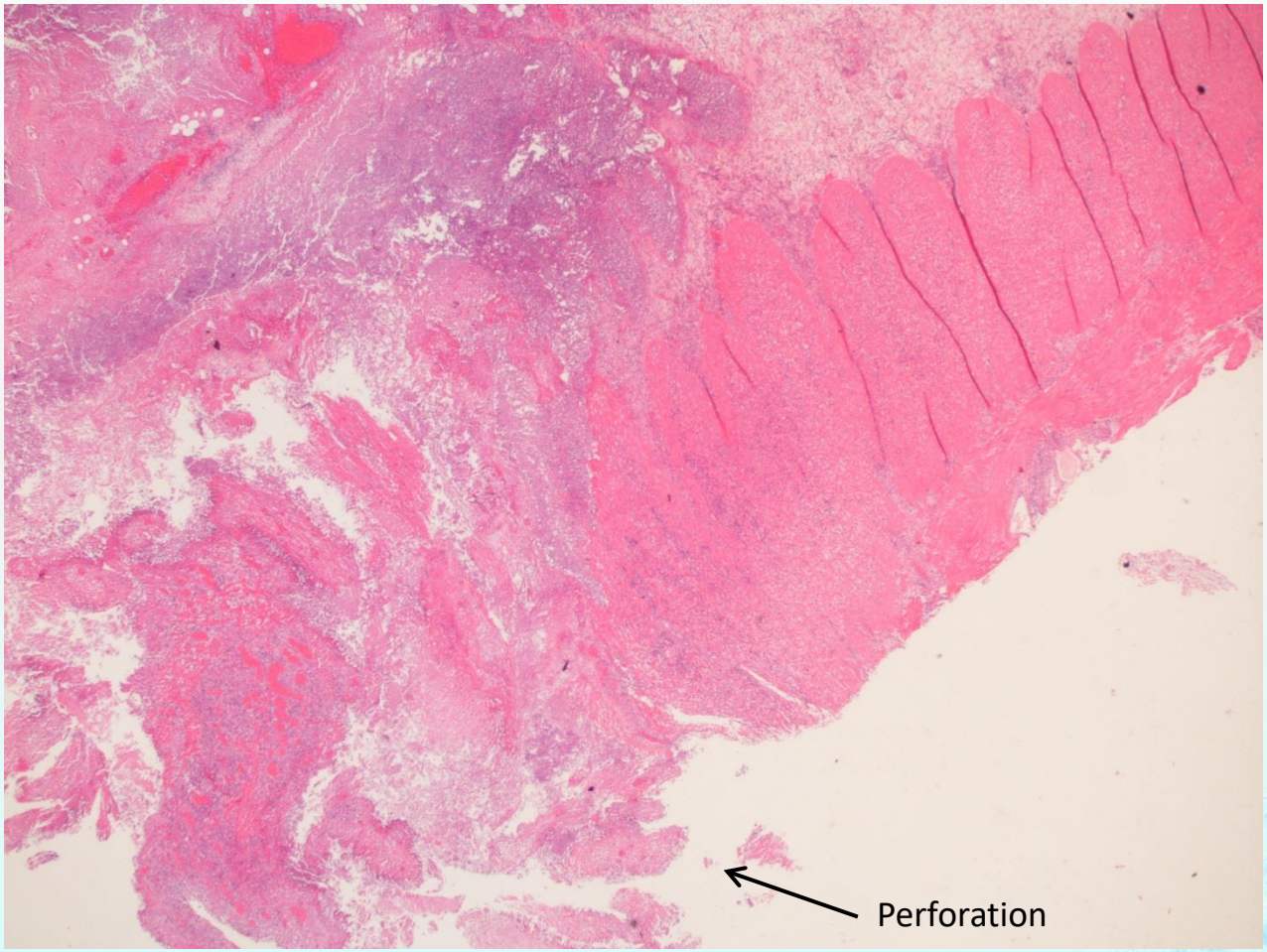
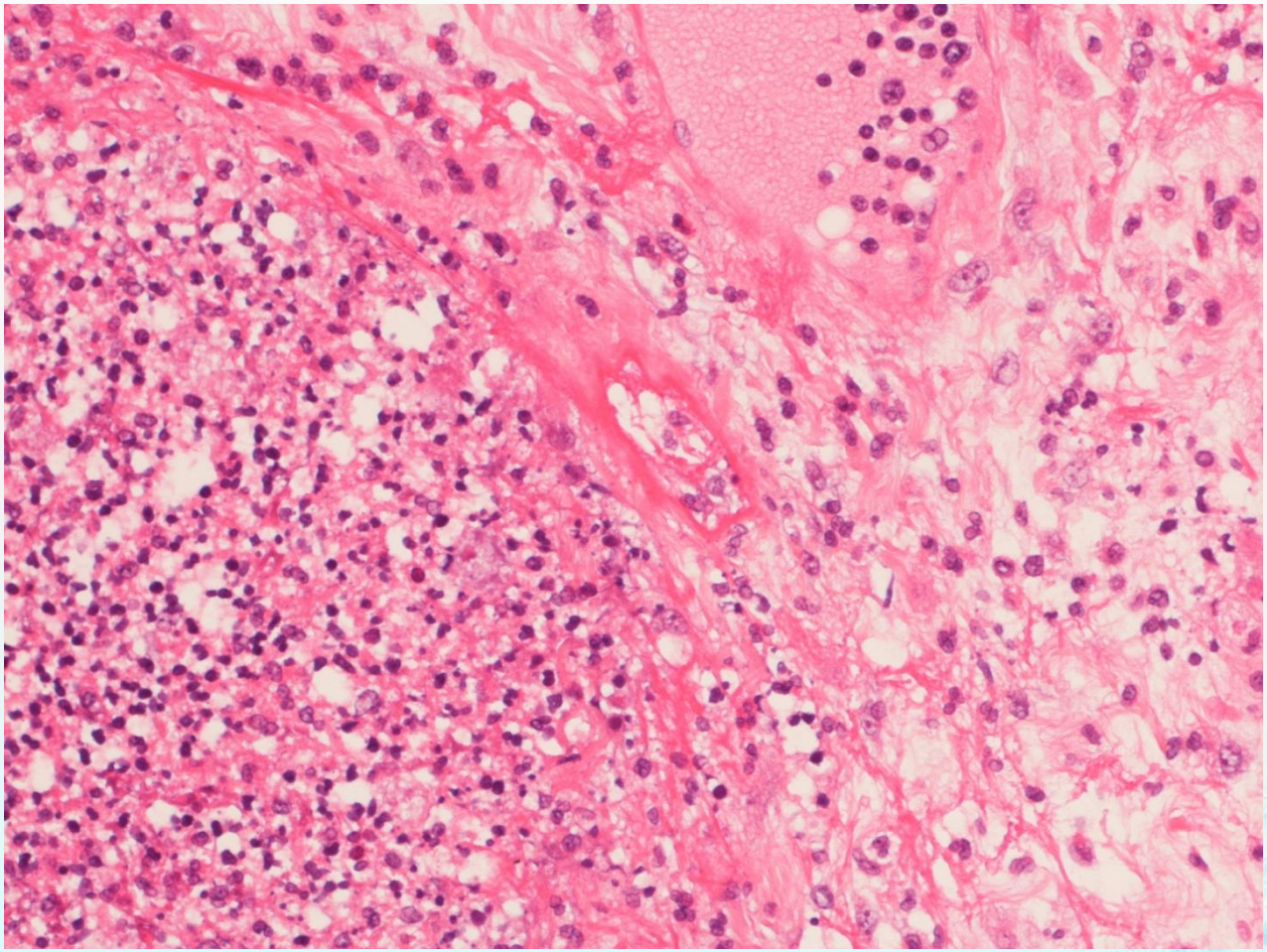


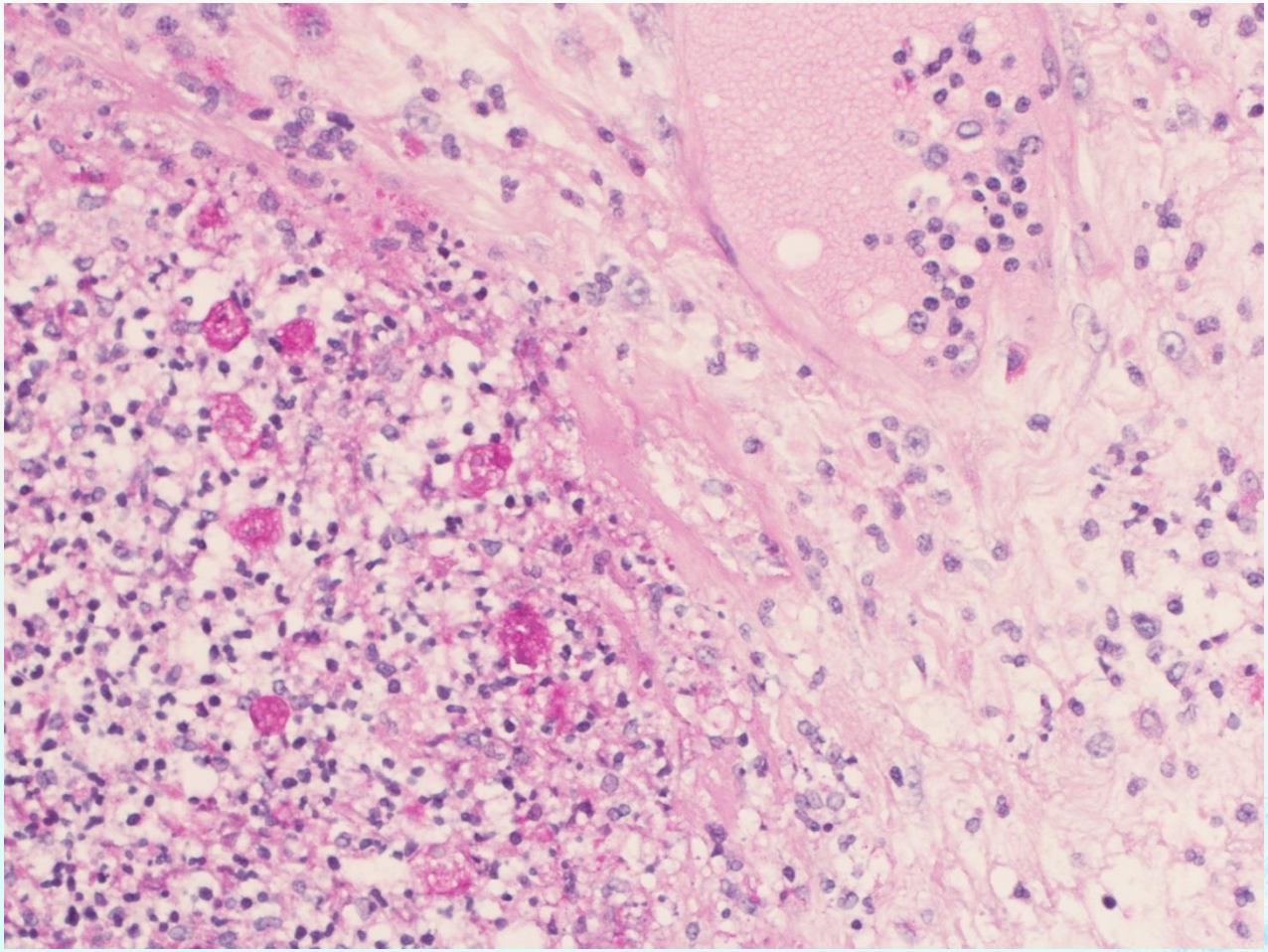
Large bowel excision (8/1/2019) x 200



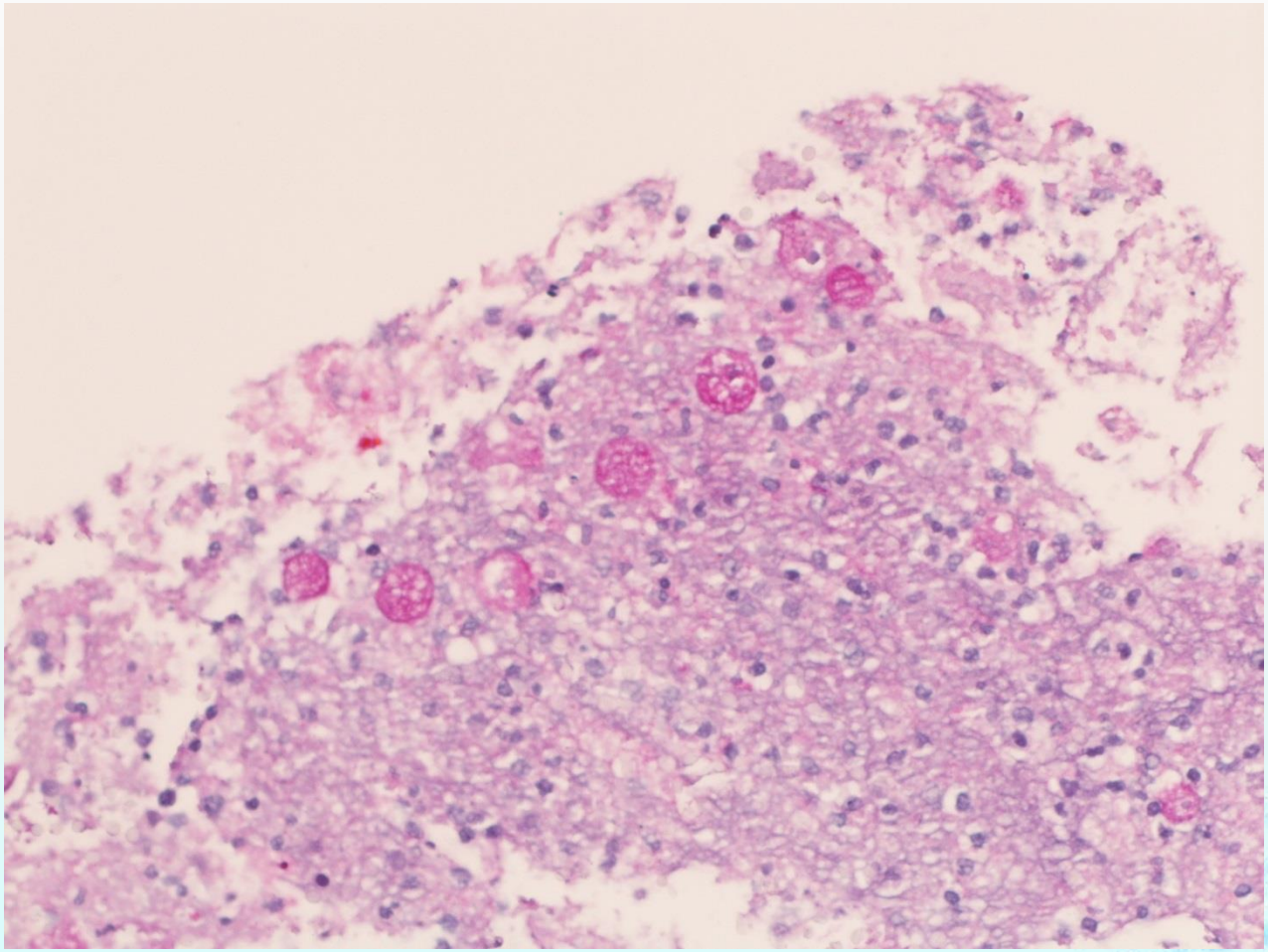
Ulcer debris

Submucosa

Large bowel excision (8/1/2019) x 200 PAS stain



Large bowel excision (8/1/2019) x 200 PAS stain



Back to our case…

12/1/2019 Extubated

Peripheral parenteral nutrition (PPN) support

Fever down
HR improving…

15/1/2019 Fever and tachycardia again…

4th CT abdomen and pelvis with contrast:
A large intra-abdominal collection with rim enhancement at right abdomen

USG guided aspiration of abdominal collection

Progress

- Slowly improving

17/1/2019	Resumed enteral feeding
23/1/2019	5th CT abdomen + pelvis: Left abdominal collection
24/1/2019	USG guided drainage to Left abdominal collection
1/2/2019	Revision of Left abdominal collection
2/2/2019	6th CT abdomen: Interval reduction in size of collection
11/2/2019	Discharged from ICU **(ICU Day 41)**

Case summary

- Presented with severe gastroenteritis symptoms - Watery diarrhoea and PR bleeding
- Methamphetamine abuser and homosexuality (history was only reviewed later by patient)
- CT showed extensive colitis
- Perforations of large bowel with fecal peritonitis
- Histological and microbiological investigations suggested amoebic infection

- Diagnosis:
  - Amoebiasis – Amoebic colitis

Amoebiasis

- Infection caused by any of the amoebae of the *Entamoeba* group
- Most commonly due to *Entamoeba histolytica*

Cyst of *E. histolytica/E. dispar* stained with trichrome

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

(courtesy of the Centers for Disease Control and Prevention)

Amoebiasis

Amoebiasis (ICD-10)

Incl.: infection due to Entamoeba histolytica

Excl.: other protozoal intestinal diseases (A07.-)

A06.0 Acute amoebic dysentery

Acute amoebiasis

Intestinal amoebiasis NOS

A06.1 Chronic intestinal amoebiasis

A06.2 Amoebic nondysenteric colitis

A06.3 Amoeboma of intestine

Amoeboma NOS

A06.4 Amoebic liver abscess (K77.0)

Hepatic amoebiasis

A06.5 Amoebic lung abscess (J99.8)

Amoebic abscess of lung (and liver)

A06.6 Amoebic brain abscess (G07)

Amoebic abscess of brain (and liver)(and lung)

A06.7 Cutaneous amoebiasis

A06.8 Amoebic infection of other sites

Amoebic:

- appendicitis
- balanitis (N51.2)

A06.9 Amoebiasis, unspecified

Amoeba

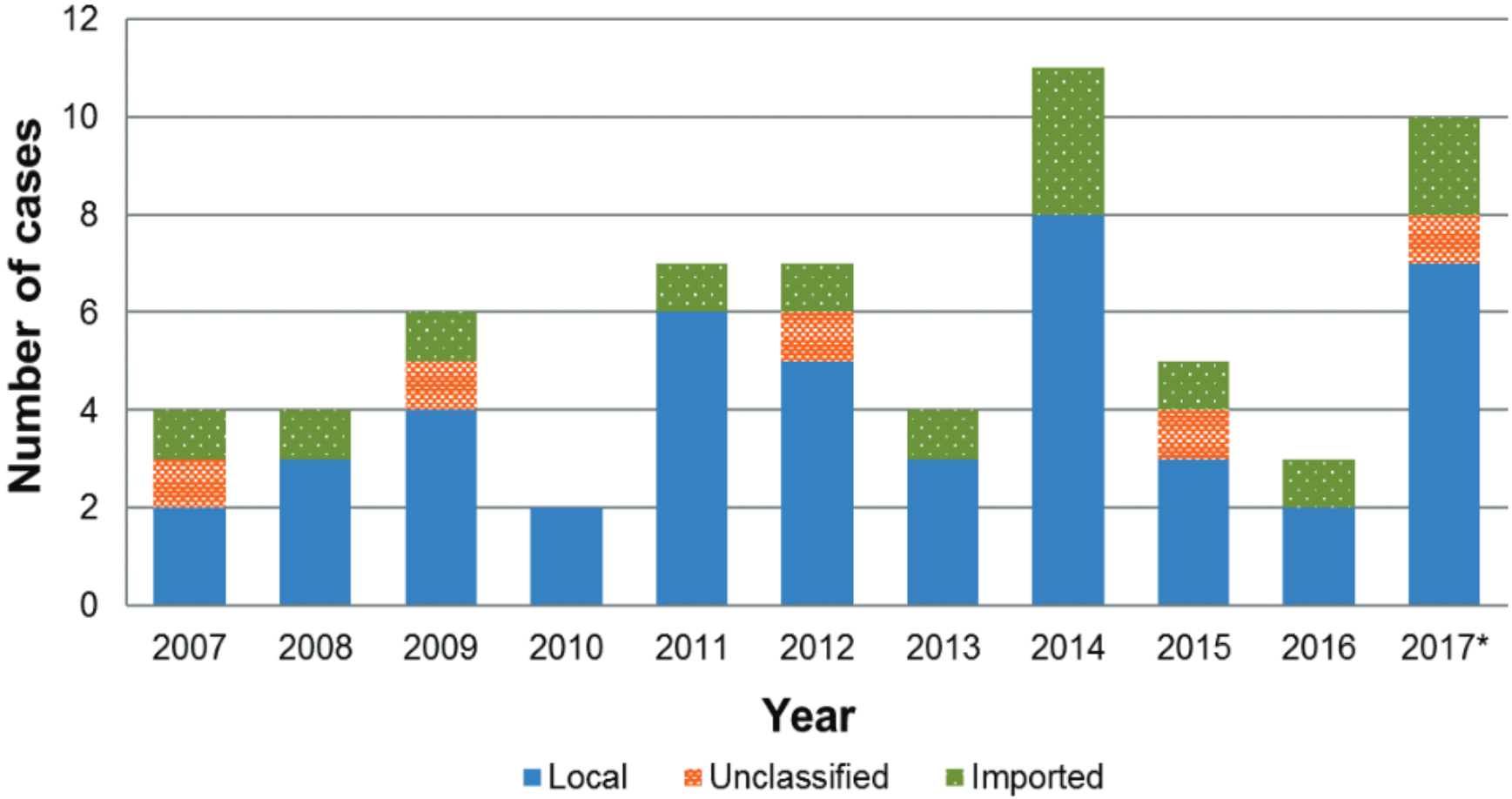
- 4 types of intestinal amoebae
  - ***Entamoeba histolytica***
  - ***Entamoeba dispar***
  - *Entamoeba moshkovskii*
  - *Entamoeba bangladeshi*

Epidemiology

- Over 100,000 deaths worldwide annually due to amoebiasis [1]
- Higher risks in homosexual, bisexual men, and other men who have sex with men (MSM) [2,3]
- Endemic in developing parts of Central and South America, Africa, and Asia

1. Bercu TE, Petri WA, Behm JW. Amebic colitis: new insights into pathogenesis and treatment. *Curr Gastroenterol Rep*. 2007;9(5):429-433. doi:10.1007/s11894-007-0054-8
2. Hung CC, Ji DD, Sun HY, et al. Increased risk for Entamoeba histolytica infection and invasive amebiasis in HIV seropositive men who have sex with men in Taiwan. *PLoS Negl Trop Dis*. 2008;2(2):e175. Published 2008 Feb 27. doi:10.1371/journal.pntd.0000175
3. Watanabe K, Aoki T, Nagata N, et al. Clinical significance of high anti-entamoeba histolytica antibody titer in asymptomatic HIV-1-infected individuals. *J Infect Dis*. 2014;209(11):1801-1807. doi:10.1093/infdis/jit815

Amoebiasis in Hong Kong

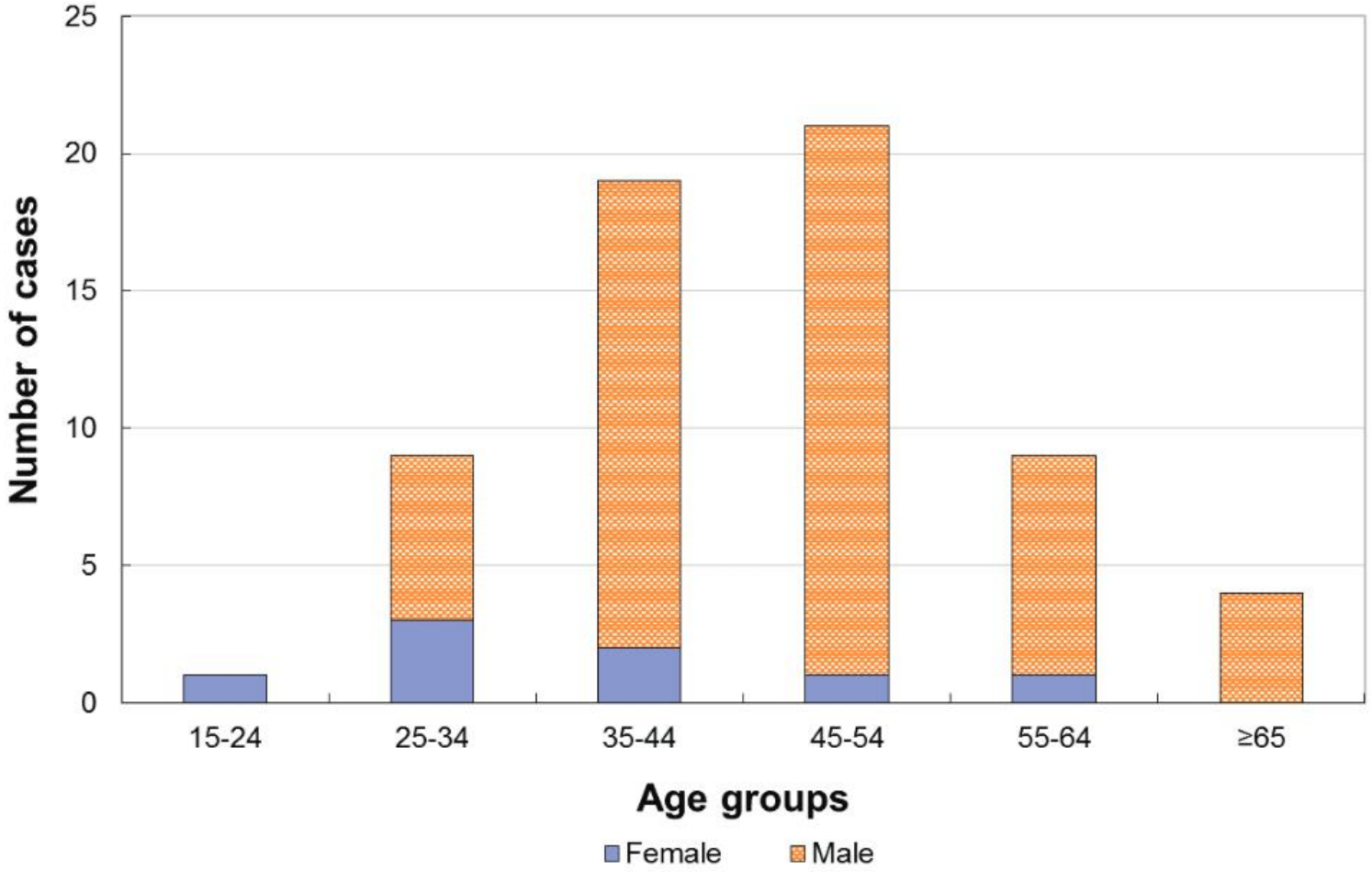


*Annual number and importation status of amoebic dysentery, 2007 to 2017 (*as of July 31, 2017) (n=63)*

Update on amoebic dysentery in Hong Kong, 2007-2017

Reported by Ms Doris CHOI, Scientific Officer, Enteric and Vector-borne Disease Office, Surveillance and Epidemiology Branch, CHP.

Amoebiasis in Hong Kong



Number of cases of amoebic dysentery by gender and age groups of patients, 2007-2017 (*as of July 31, 2017) (n=63).*

Update on amoebic dysentery in Hong Kong, 2007-2017

Reported by Ms Doris CHOI, Scientific Officer, Enteric and Vector-borne Disease Office, Surveillance and Epidemiology Branch, CHP.

Recent Prevalence Estimates of *Entamoeba histolytica* Infection by World Regions

Country	f, %	Method	Study Characteristics
Durango, Mexico	42	AB	Cross-sectional serosurvey among rural communities
Beijing and Tianjin, China	41	AB	Cross-sectional serosurvey of men who have sex with men
Chinese Center of Disease Control and Prevention, China	11	AB	Cross-sectional serosurvey of the general population (7 provinces of China including Guangxi, Qinghai, Guizhou, Shanghai, Sichuan, Sinkiang, and Beijing)
Lahore, Pakistan	17	AG	Cross-sectional survey among 3 different socioeconomic strata
Northeast, India	14	PCR	Cross-sectional survey
Dhaka, Bangladesh	11	PCR	Prospective birth cohort study of infants followed for 1 year
Selangor, Malaysia	8	PCR	Cross-sectional survey of selected ethnic groups
Sydney, Australia	5	AB	Retrospective study of HIV-infected men who have sex with men
Mirzapur, Bangladesh	3	AG	Multinational case–control study of children <5 years with moderate to severe diarrhea
Turkey	32	AG	Prevalence study among patients presenting with ulcerative colitis
Jeddah, Saudi Arabia	20	AG	Cross-sectional study of children hospitalized with acute diarrhea
Yemen	20	PCR	Community-based cross-sectional survey
Cairo, Egypt	38	AG	Case–control study of patients presenting with acute diarrhea
Vhembe, South Africa	34	AB	Cross-sectional serosurvey
Giyani and Soshanguve, South Africa	9	PCR	Cross-sectional study of patients attending gastroenterology clinic

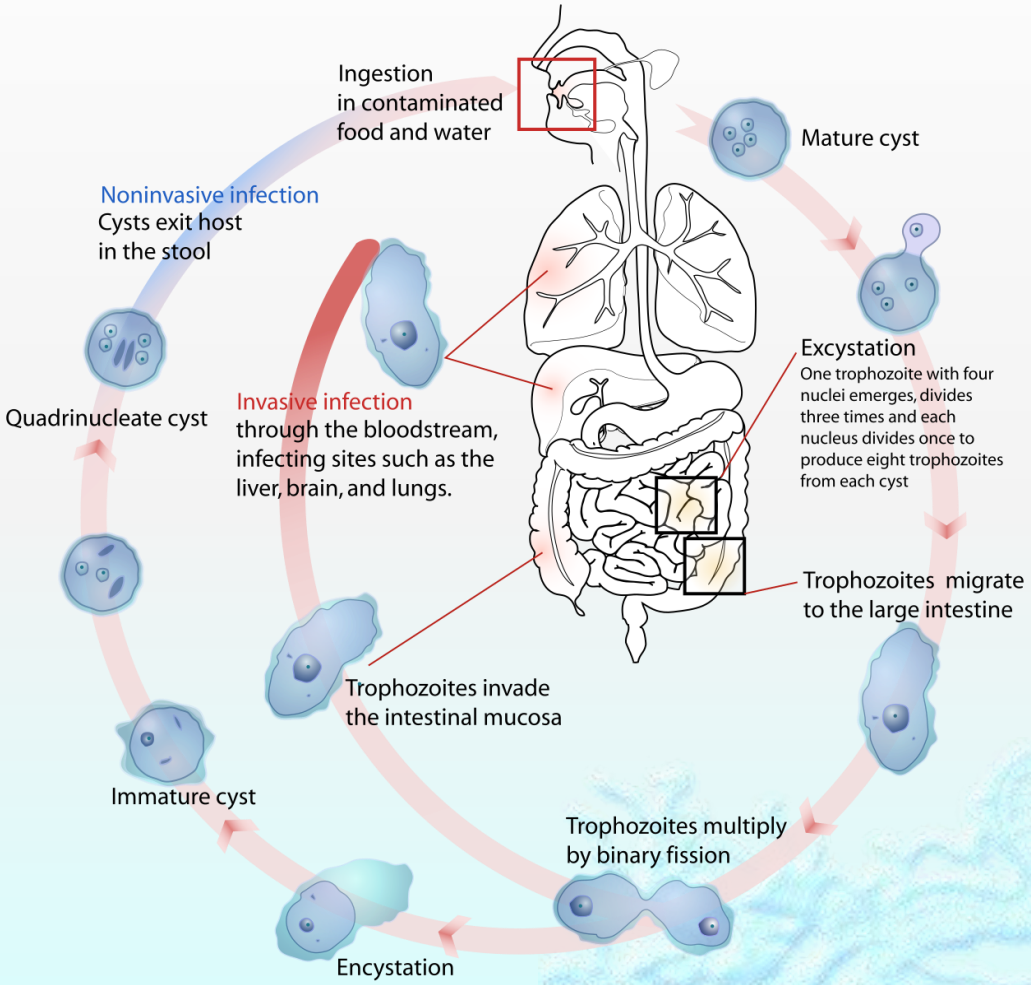
Shirley DT, Farr L, Watanabe K, Moonah S. A Review of the Global Burden, New Diagnostics, and Current Therapeutics for Amebiasis. *Open Forum Infect Dis*. 2018;5(7):ofy161. Published 2018 Jul 5. doi:10.1093/ofid/ofy161

Epidemiology

Transmission

- Faecal-oral route
  - Sexual transmission through fecal-oral contact
  - Indirectly by eating or drinking food or water contaminated with faecal matter

- Cysts and trophozoites are passed in stools
  - cyst can survive in the environment for weeks, whereas trophozoites do not survive
  - cysts are resistant to gastric acidity
  - cysts can be killed by boiling



Pathogenesis

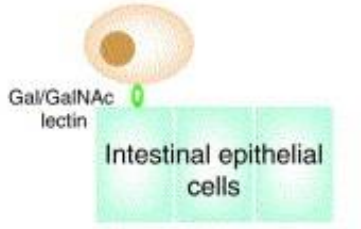
- Cysts ingested and excyst to form trophozoites in small intestine
- Invade and penetrate through the mucous layer of colon → colitis

Mechanisms

- Parasite invasion:
  - Secretion of proteinases by the trophozoites
- Direct cell killing:
  - Lysis of target cells via a contact-dependent mechanism
  - Killing of mammalian cells by apoptosis (programmed cell death)
  - Formation of amoebapores, a family of small peptides that can form pores in lipid bilayers, resulting in cytolysis of infected cells
- Inflammation:
  - Changes in intestinal permeability, disruption of tight-junction proteins

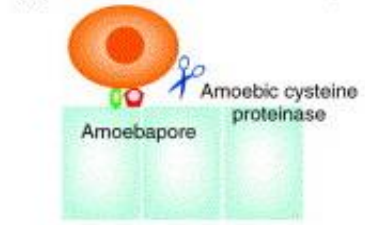
Pathogenesis

1) Amoebic adherence

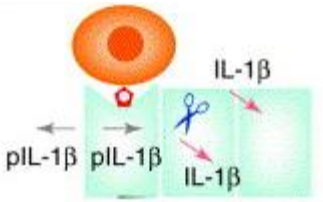


Adherence to colonic epithelial cells via a specific lectin (galactose-N-acetylgalactosamine lectin)

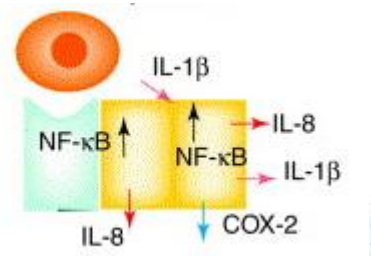
2) Activation of virulence program



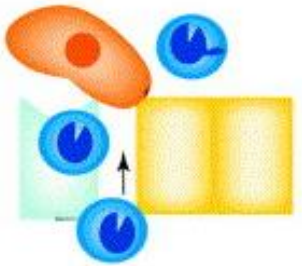
3) Cell damage with release of cytokines



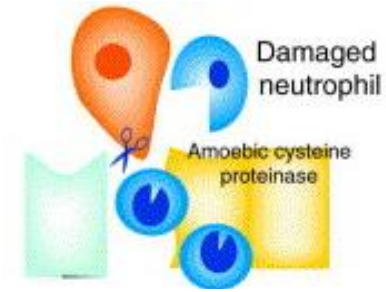
4) Cytokines and inflammatory mediators produced



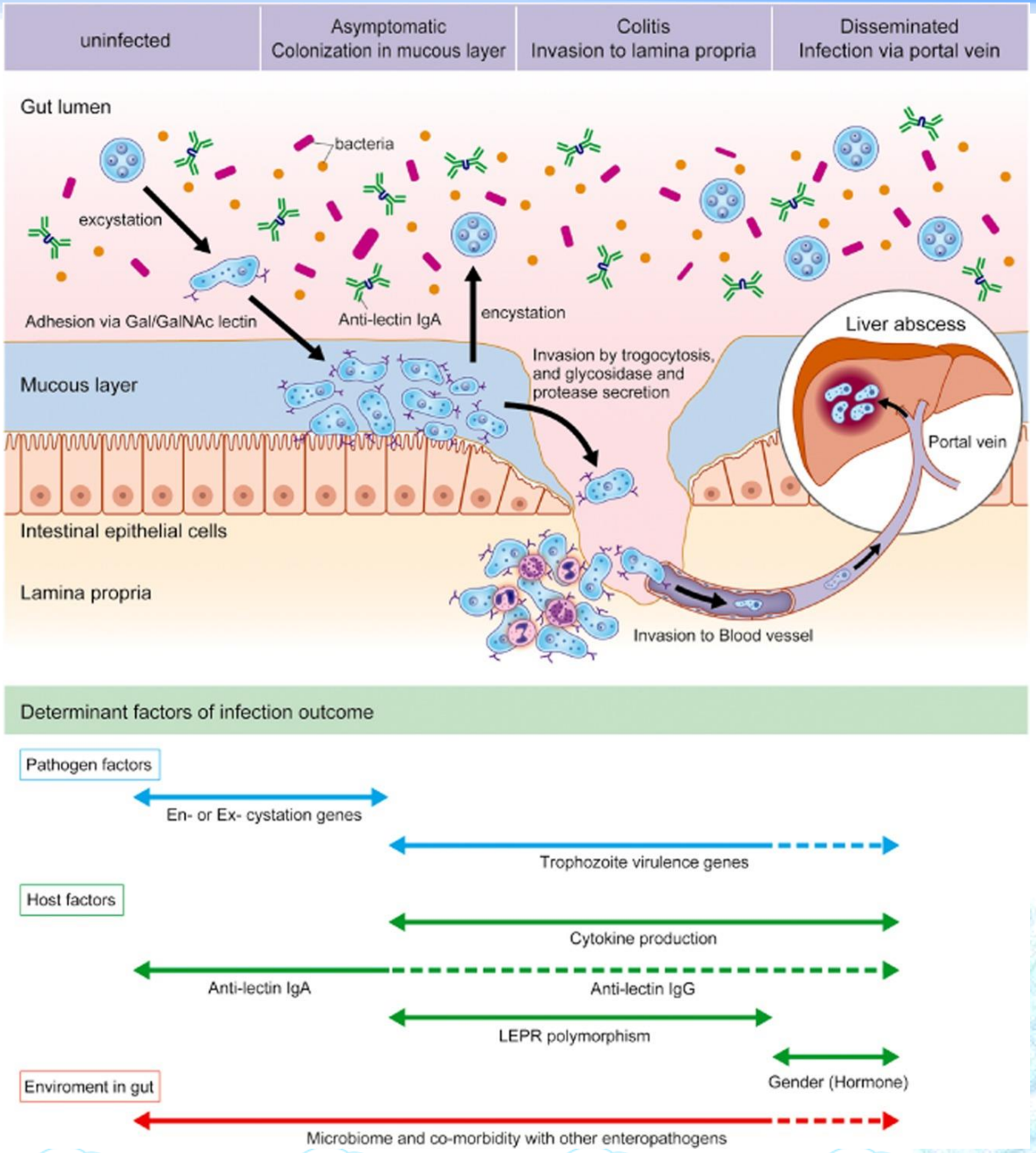
5) Neutrophil influx



6) Amoeba invasion

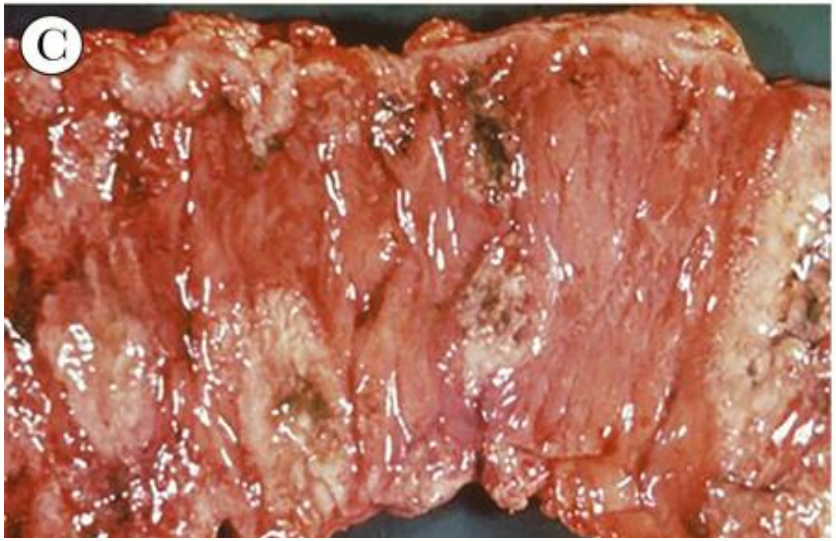


Pathophysiology of amoebiasis, Samuel LStanleyJr, Depts Medicine and Molecular Microbiology, Washington University School of Medicine, St Louis, MO 63110, USA, https://doi.org/10.1016/S1471-4922(01)01903-1

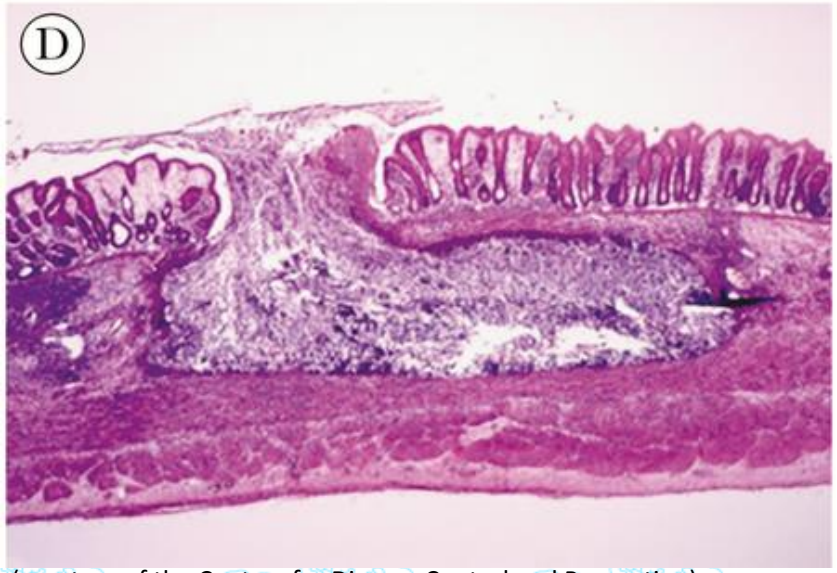


Molecular biology research to benefit patients with *Entamoeba histolytica* infection ; Koji Watanabe, William A. Petri Jr., https://doi.org/10.1111/mmi.13131

Pathogenesis



- Intestinal tissue with multiple ulcers



- Classical “flask-shaped” ulcers

(courtesy of the Centers for Disease Control and Prevention)

Clinical manifestations

- Asymptomatic (90%)

- Abdominal pain (12-80%)
- Diarrhea (94-100%)
- Bloody stools (94-100%)
- Weight loss (~50%)
- Fever (38%)
- Fulminant amoebic colitis (FAC) +/- peritonitis (0.5%)
  - mortality rate > 40%

Clinical manifestations in Hong Kong

- Common symptoms:
  - bloody diarrhoea (n=43, 68.3%)
  - non-bloody diarrhoea (n=40, 63.5%)
  - abdominal pain (n=37, 58.7%)
  - mucus in stool (n=33, 53.0%)
  - 1 case of gangrenous colitis followed by multiple organ failure and shock (n=1, 1.6%)
- Length of hospital stay:
  - 1 - 99 days (median=3.5 days)

Update on amoebic dysentery in Hong Kong, 2007-2017
Reported by Ms Doris CHOI, Scientific Officer, Enteric and Vector-borne Disease Office, Surveillance and Epidemiology Branch, CHP.

Fulminant amoebic colitis (FAC)

- A rare and grave complication of intestinal amoebiasis
- Prevalence: <0.5% of all cases of amoebiasis
- Mortality: 55% to 100%
  - 55%-85% in fulminant amoebic colitis
  - 75%-100% in cases with perforation and peritonitis

Beg MY, Bains L, Mahajan R, et al. Fulminant Necrotising Amoebic Colitis of Whole of Large Bowel: A Rare Complication of a Common Infectious Disease. *Case Rep Infect Dis*. 2020;2020:8845263. Published 2020 Aug 11. doi:10.1155/2020/8845263

Fulminant amoebic colitis (FAC)

- Observational retrospective analysis from 6/2007 – 12/2011 in India:
  - Adult patients underwent colonic resection with diagnosis of amoebic colitis based on histological examination
  - 30 patients included (18 men and 12 women) of mean age 50.1 years (range 21–89)
  - Diagnosis based on initial clinical-radiological examination:
    - 5 cases (16.7%) – amoebic aetiology
    - 7 cases (23.3%) – malignancy
    - 5 cases (16.7%) – acute appendicitis
    - 3 cases (10.0%) – tuberculosis
    - 3 cases (10.0%) – ischemic bowel
    - 7 cases (23.3%) – no specific pre-operative diagnosis…
  - Predominantly right-sided involvement
  - Mortality: 57% (17/30)

Chaturvedi R, Gupte PA, Joshi AS. Fulminant amoebic colitis: a clinicopathological study of 30 cases. *Postgrad Med J.* 2015;91(1074):200-205. doi:10.1136/postgradmedj-2014-132597

Fulminant amoebic colitis (FAC)

Mortality associated with comorbidities	21	14 (66.7%)
Immunosuppression	**16**	**9 (56.3%)**
Diabetes mellitus	7	4 (57.1%)
Debilitation from tuberculosis Treated pulmonary Concurrent abdominal	7 4 3	3 (42.9%) 2 (50%) 1 (33.3%)
HIV	1	0 (0)
Alcoholism	3	3 (100%)
On steroid therapy	2	0 (0)
Post-partum	1	1 (100%)
Other comorbidities	**11**	**9 (81.8%)**
Hypertension	10	8 (80%)
Hypothyroidism	1	1 (100%)
Leprosy	1	0 (0)
Tinea corporis	1	1 (100%)
Filariasis (lower limb)	1	1 (100%)
Hyperhomocysteinaemia	1	1 (100%)

Chaturvedi R, Gupte PA, Joshi AS. Fulminant amoebic colitis: a clinicopathological study of 30 cases. *Postgrad Med J.* 2015;91(1074):200-205. doi:10.1136/postgradmedj-2014-132597

Fulminant amoebic colitis (FAC)

- Mortality associated with extent of bowel involvement on gross examination
  - 15 out of 17 mortality cases: mortality increased with the extent of involvement beyond the caecum

Extent of bowel involvement on gross examination	Total no. of cases (N=30)	No. (%) of deaths (N=17)
Caecum	9	2 (30%)
Beyond caecum	21	15 (71.4)
Caecum to ascending colon	17	11 (65%)
Caecum to transverse colon	2	2 (100%)
Caecum to descending colon	2	2 (100%)

Chaturvedi R, Gupte PA, Joshi AS. Fulminant amoebic colitis: a clinicopathological study of 30 cases. *Postgrad Med J.* 2015;91(1074):200-205. doi:10.1136/postgradmedj-2014-132597

Fulminant amoebic colitis (FAC)

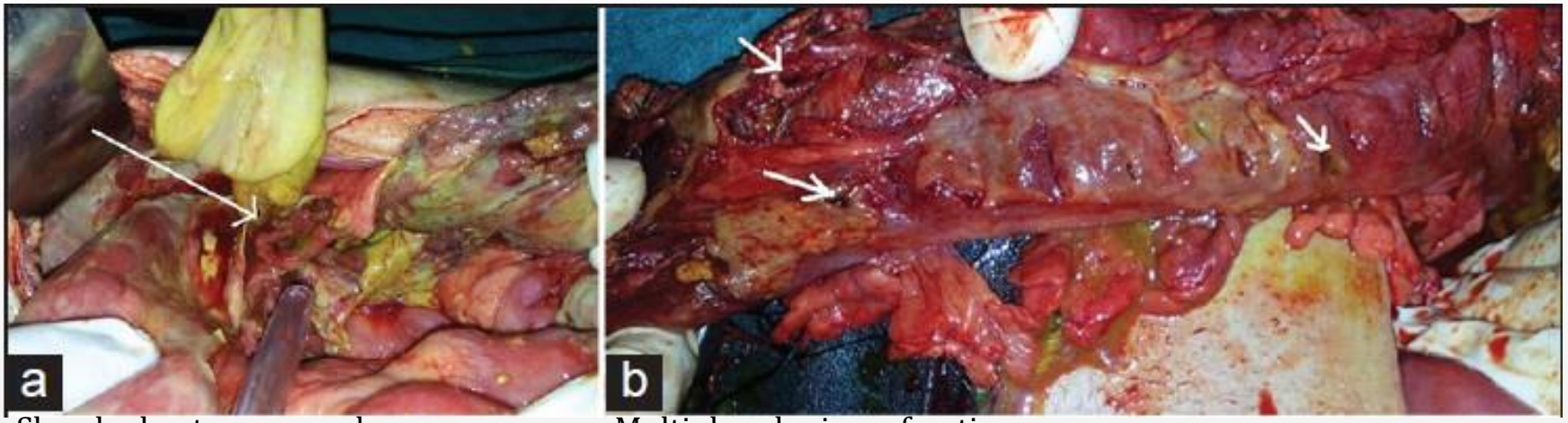
Why is FAC so deadly?

1. Colonic perforation
   - Main cause of death: perforation peritonitis → septicemia
   - Colonic perforation present in 30.4% of autopsies in FAC according to a study [1]

2. High chance of misdiagnosis: [2]
   - Easily mimics idiopathic IBD: similar clinical presentations, laboratory studies, X-ray findings and culture results
   - Erroneous administration of steroids for IBD
   - Delayed anti-amoebic treatments or surgery

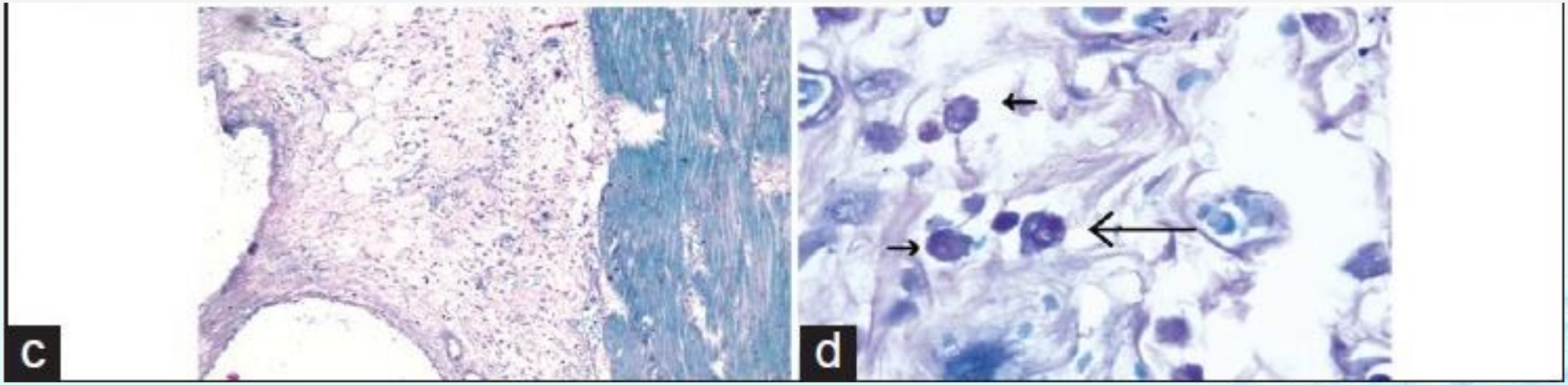
1. Chen WJ, Chen KM, Lin M. Colon perforation in amebiasis. Arch Surg 1971;103:676-80.
2. Suhani, Ali S, Thomas S, Aggarwal L. Fulminant necrotizing colitis: A rare complication of a common entity. Ann Trop Med Public Health 2013;6:661-3

Fulminant amoebic colitis (FAC)



Sloughed out cecum and ascending colon

Multiple colonic perforations



Periodic-acid Schiff (PAS) positive amebic trophozoites in the mucosa and muscularis layer

PAS positive trophozoites with erythrophagocytosis

1. Suhani, Ali S, Thomas S, Aggarwal L. Fulminant necrotizing colitis: A rare complication of a common entity. Ann Trop Med Public Health 2013;6:661-3

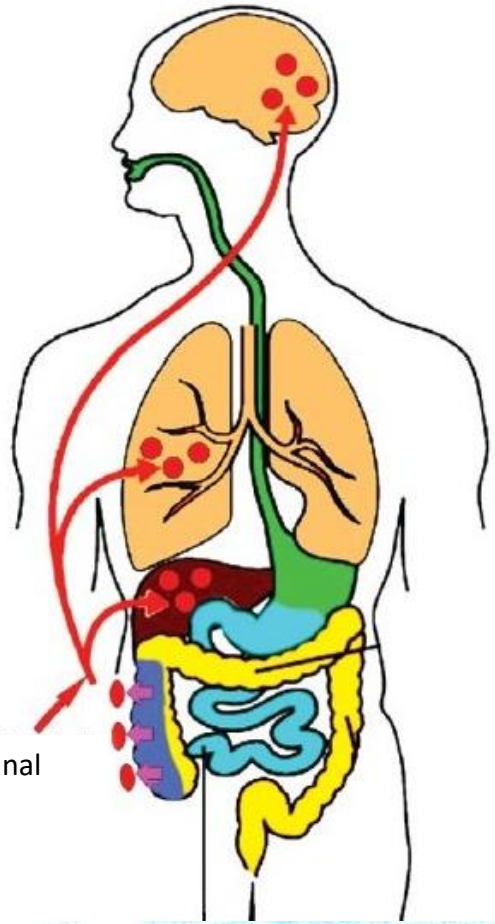
Fulminant amoebic colitis (FAC)

- Risk factors:
  - male gender
  - extremes of age (>60 years and <10 years)
  - tropical climate
  - associated liver abscess
  - persistent abdominal pain
  - poor nutrition
  - immunocompromised state / immunosuppressants
  - the presence of peritonitis / pancolitis
  - hypoalbuminemia
  - electrolyte imbalance (hyponatremia, hypokalemia, and hypocalcemia)

- Beg MY, Bains L, Mahajan R, et al. Fulminant Necrotising Amoebic Colitis of Whole of Large Bowel: A Rare Complication of a Common Infectious Disease. *Case Rep Infect Dis*. 2020;2020:8845263. Published 2020 Aug 11. doi:10.1155/2020/8845263
- Gupta R, Riyaz S, Soni N. Acute fulminant necrotizing amoebic pancolitis: A lethal entity in children. Med J DY Patil Vidyapeeth 2018;11:338-41

Extraintestinal manifestations

- Amoebic liver abscess (most common)
- Other extraintestinal sites
  - Pleuropulmonary infection
  - Cardiac infection
  - Brain abscess
  - Cutaneous infection



Extraintestinal invasion

Novelties on amoebiasis: A neglected tropical disease
Ximénez Cecilia, Morán Patricia, Rojas Liliana, Valadez Alicia, Gómez Alejandro, Ramiro Manuel, Cerritos René, González Enrique, Hernández Eric, Oswaldo Partida

Amoebic liver abscess

- The most common extra-intestinal manifestation of amoebiasis
- Epidemiology
  - Most frequently in patients aged 40-50
  - Male to female: 7-10:1

- "anchovy paste“ upon drainage
- 70-80% solitary
- Tissue agent and luminal agent
- Drainage if impending rupture or >10cm

- Complications:
  - Bronchohepatic fistula (rare):
    - Right lobe → Right pleural effusion / empyema / lung abscess
    - Left lobe → Left pleuropulmonary / pericardial invasion
  - Peritonitis

- Salles JM, Salles MJ, Moraes LA, Silva MC. Invasive amebiasis: an update on diagnosis and management. *Expert Rev Anti Infect Ther*. 2007;5(5):893-901. doi:10.1586/14787210.5.5.893
- Lyche KD, Jensen WA. Pleuropulmonary amebiasis. *Semin Respir Infect*. 1997;12(2):106-112.

Pleuropulmonary amoebiasis

- Epidemiology
  - Mainly occurs in patients aged 20-40
  - Male to female = 10:1
- Risk factors:
  - Low socioeconomic conditions
  - Malnutrition
  - Chronic alcoholism
  - Atrial septal defect with left to right shunt
- Can be associated with amoebic liver abscess by bronchohepatic fistula rarely

- Shamsuzzaman SM, Hashiguchi Y. Thoracic amebiasis. *Clin Chest Med*. 2002;23(2):479-492. doi:10.1016/s0272-5231(01)00008-9
- Lyche KD, Jensen WA. Pleuropulmonary amebiasis. *Semin Respir Infect*. 1997;12(2):106-112.

Diagnosis

- **Microscopy**
- **Antigen detection**
- **Molecular tests (e.g. PCR)**
- **Serology**

- Endoscopic biopsy
- Imaging
  - For amoebic liver abscesses and other extraintestinal manifestations

Comparison of Laboratory Diagnostic Tests for Amebiasis

Method	Sensitivity	Specificity	Advantages	Disadvantages
Microscopy	<60%	-	Widely available	1. Poor sensitivity and specificity 2. Cannot differentiate from other *Entamoeba* spp.
			Screens for other parasites	Multiple stools need to be submitted
			Minimal equipment and reagents required	1. Skilled observer required 2. Time-consuming
Serology	65%–92%	>90%	High sensitivity and specificity, useful adjunct to stool studies	Serology remains positive for years after resolution of infection → Cannot differentiate acute from previous infections
			Rapid turnaround	Antibody response is often detectable by the time of presentation

Debbie-Ann T Shirley, Laura Farr, Koji Watanabe, Shannon Moonah, A Review of the Global Burden, New Diagnostics, and Current Therapeutics for Amebiasis, *Open Forum Infectious Diseases*, Volume 5, Issue 7, July 2018, ofy161, https://doi.org/10.1093/ofid/ofy161

Comparison of Laboratory Diagnostic Tests for Amebiasis

Method	Sensitivity	Specificity	Advantages	Disadvantages
Stool antigen detection	0%–88%	>80%	High sensitivity in endemic areas but reduced sensitivity in nonendemic areas	Poor sensitivity for amebic liver abscess
			Can differentiate E. dispar vs histolytica	
			Commercially available combined tests exist: 1. simple to perform 2. rapid turnaround time 3. detect several enteroparasites	Requires fresh, not fixative preserved stool for analysis
PCR	92%–100%	89%–100%	Gold standard; high sensitivity and specificity	Expensive
			Can differentiate different Entamoeba species	
			Rapid turnaround time	Requires analysis instruments, kits, and skilled technician
			Can be combined with multiplex panels to detect multiple enteric pathogens at a time	

Debbie-Ann T Shirley, Laura Farr, Koji Watanabe, Shannon Moonah, A Review of the Global Burden, New Diagnostics, and Current Therapeutics for Amebiasis, *Open Forum Infectious Diseases*, Volume 5, Issue 7, July 2018, ofy161, https://doi.org/10.1093/ofid/ofy161

Treatment

- No vaccines available
- Prevention and hygiene is important!!!

- Medications:

1. Initiate treatment with tissue-active agents for eliminating the invading trophozoites and eradicating intestinal carriage of the organism
2. Followed by subsequent intraluminal agents to eliminate intraluminal cysts

(1) Tissue-active agents:

- Metronidazole - 750 mg po TDS (35–50 mg/ kg/d divided TDS)
  - Amoebic colitis: 5-10 days
  - Amebic liver abscess /disseminated amebic disease: 10 days
- Tinidazole - 2 g po once daily (50 mg/kg once daily)
  - Amoebic colitis: 3-5 days
  - Amebic liver abscess /disseminated amebic disease: 5 days

(2) Luminal agents:

- Paromomycin (25–35 mg/kg/d po divided TDS for 7 days)
- Iodoquinol (650 mg po TDS for 20 days)
- Diloxanide (500 mg po TDS for 10 days)

Treatment

- Auranofin
  - Initially approved by the FDA in 1985 for treatment of rheumatoid arthritis
  - Currently still a novel drug under study for parasitic infections
  - Mechanism: Gold targeting the oxidant protective system of parasitic infection
  - Phase I Clinical Trial in 2016 (15 subjects x 7 days)
    - Generally well tolerated in the healthy-subject population studies
    - 3 (20%) reported GI symptoms
    - 2 (15%) had mildly decreased levels of platelets
    - No significant adverse events or deaths

Capparelli EV, Bricker-Ford R, Rogers MJ, McKerrow JH, Reed SL. Phase I Clinical Trial Results of Auranofin, a Novel Antiparasitic Agent. *Antimicrob Agents Chemother*. 2016;61(1):e01947-16. Published 2016 Dec 27. doi:10.1128/AAC.01947-16

Treatment

- For asymptomatic carriers:
  - All carriers should be treated:
    - Risks of developing invasive disease
    - Risks of spreading to close family members
  - Asymptomatic patients with *E. histolytica* should be treated with an intraluminal agent alone
  - 4–10% develop invasive disease within a year if left untreated [1]

1. Stanley S. L., Jr Amoebiasis. *The Lancet*. 2003;361(9362):1025–103410

Treatment for FAC

- Patients with fulminant amebic colitis
  - fluid resuscitation
  - intensive supportive care
  - broad-spectrum antimicrobial therapy for peritonitis
  - surgical intervention for bowel perforation and bowel necrosis
  - colectomy for development of toxic megacolon or extensive bowel necrosis

Surgical intervention for FAC

- Resection and anastomosis during the first surgery should always be discouraged
  1. Chances of an anastomotic leak are very high due to inflamed and friable bowel.
  2. Ulcers in the distal segment may slough off leading to leaking.
- A staged surgery in the form of exteriorization of the proximal and distal transected ends as stoma, and bowel reconstruction 3–6 months later, is highly recommended

- Ellyson JH, Bezmalinovic Z, Parks SN, Lewis FR Jr. Necrotizing amebic colitis: a frequently fatal complication. Am J Surg. 1986 Jul;152(1):21-6. doi: 10.1016/0002-9610(86)90131-5. PMID: 3728812.
- Beg MY, Bains L, Mahajan R, et al. Fulminant Necrotising Amoebic Colitis of Whole of Large Bowel: A Rare Complication of a Common Infectious Disease. *Case Rep Infect Dis*. 2020;2020:8845263. Published 2020 Aug 11. doi:10.1155/2020/8845263

Take home messages

- Fulminant amoebic colitis is a rare but deadly complication of amoebiasis
- Consider amoebic colitis as possible differential diagnosis in patients presenting with colitis, especially those with risk factors
- Importance of early anti-amoebic treatment with urgent surgical intervention in reducing mortality