Bacterial & parasitic infections

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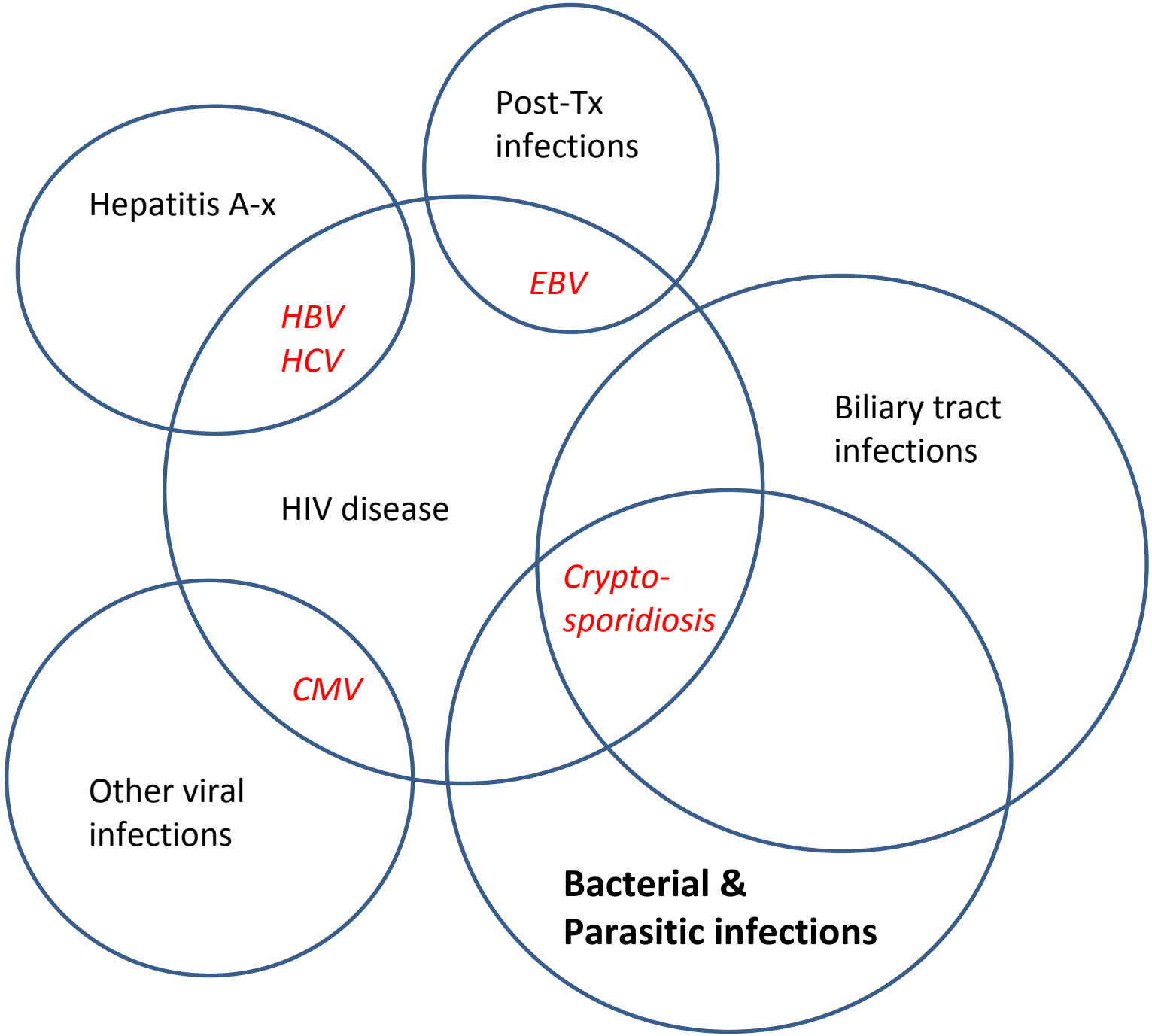

Post-Tx infections
Hepatitis A-x
EBV
HBV
HCV
Biliary tract infections
HIV disease
Crypto-sporidiosis
CMV
Other viral infections
Bacterial & Parasitic infections

Hepatobiliary parasites

Liver

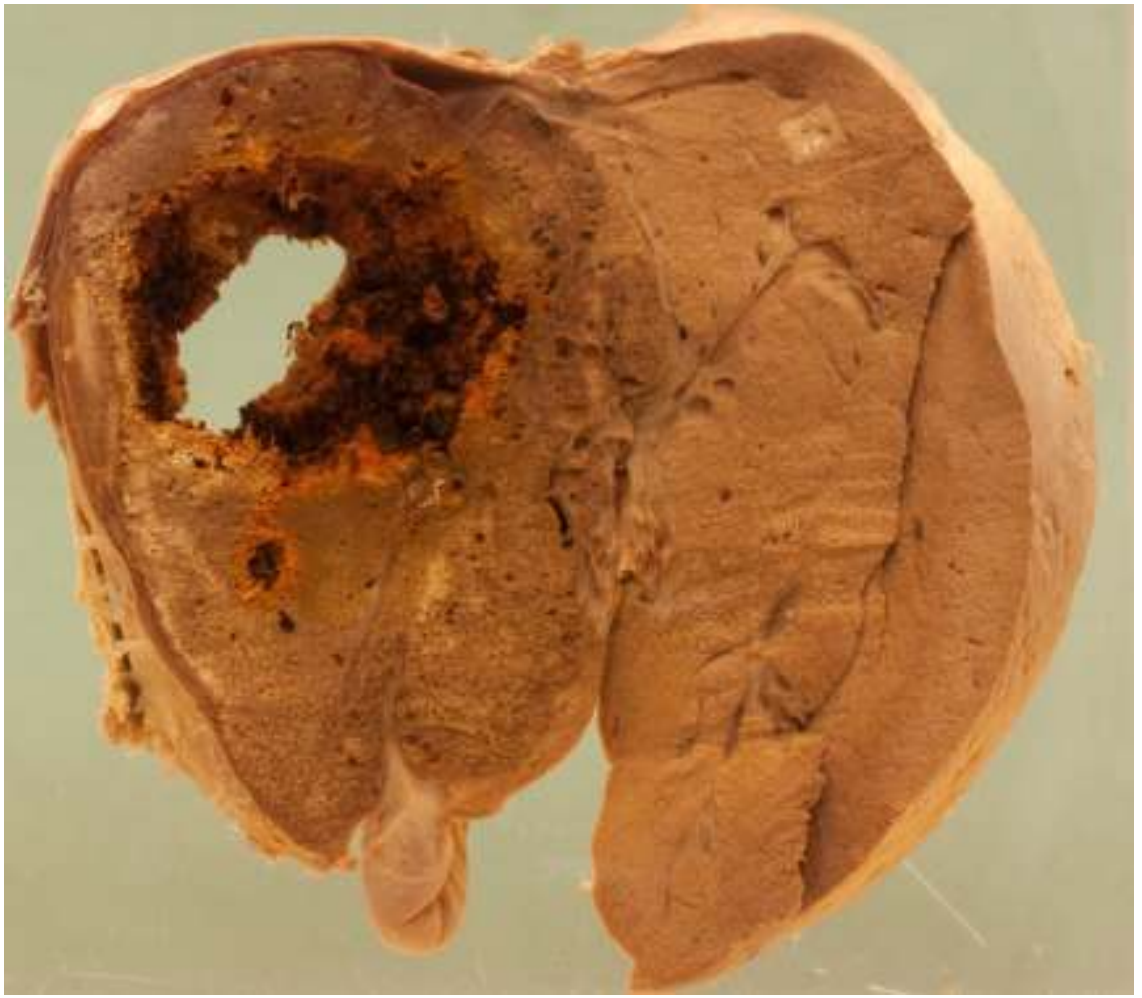
- Leishmania spp
- Trypanosoma cruzi
- Entamoeba histolytica
- Toxoplasma gondii
- Plasmodium falciparum
- Balantidium coli
- Strongyloides stercoralis
- Angiostrongylus spp
- Enterobius vermicularis
- Ascaris lumbricoides
- Baylisascaris
- Toxocara canis
- Gnathostoma spp
- Capillaria hepatica
- Schistosoma spp
- Echinococcus granulosus & multilocularis
- pentasomes

Biliary tree & GB

- microsporidia spp
- Cryptosporidium spp
- Ascaris
- Fasciola hepatica
- Clonorchis sinensis
- Opisthorcis viverrini
- Dicrocoelium
- Echinococcus granulosus

Gutierrez: 'Diagnostic Pathology of Parasitic Infections', Oxford, 2000

What is this?
Both are the same parasite



What is this?
Both are the same parasite

Echinococcus multilocularis

Bacterial infections of liver and biliary tree

- Chlamydia trachomatis
- Gram-ve rods
- Neisseria meningitidis
- Yersina pestis
- Streptococcus milleri
- Salmonella spp
- Burkholderia pseudomallei
- Listeria monocytogenes
- Brucella spp
- Bartonella spp
- Actinomycetes

- Treponema pallidum
- Borrelia spp
- Leptospira spp
- Mycobacterium spp
  - tuberculosis
  - avium-intracellulare
  - leprae

In 'MacSween'

2 manifestations of a classic bacterial infection

Bacteria & parasites

3 case studies

- Problem solving
- What it is
- What is the treatment

What you need to know

- What can happen
  - differential diagnosis
- How it can look pathologically
- What can be done to prove or exclude the infection
- Who you can ask for help

Summary

- Anything can happen
  - International travel
    - *'Unde venis?'*
  - Immunosuppression
    - Acquired
    - Iatrogenic
- Increasing reliance on molecular diagnostics
- Close collaboration with microbiologists and ID clinicians

Case 1

F20

Daughter of UK farmer

No travel abroad

Acute lymphoblastic leukaemia @ 12 years

2 months post haemopoietic stem cell transplant

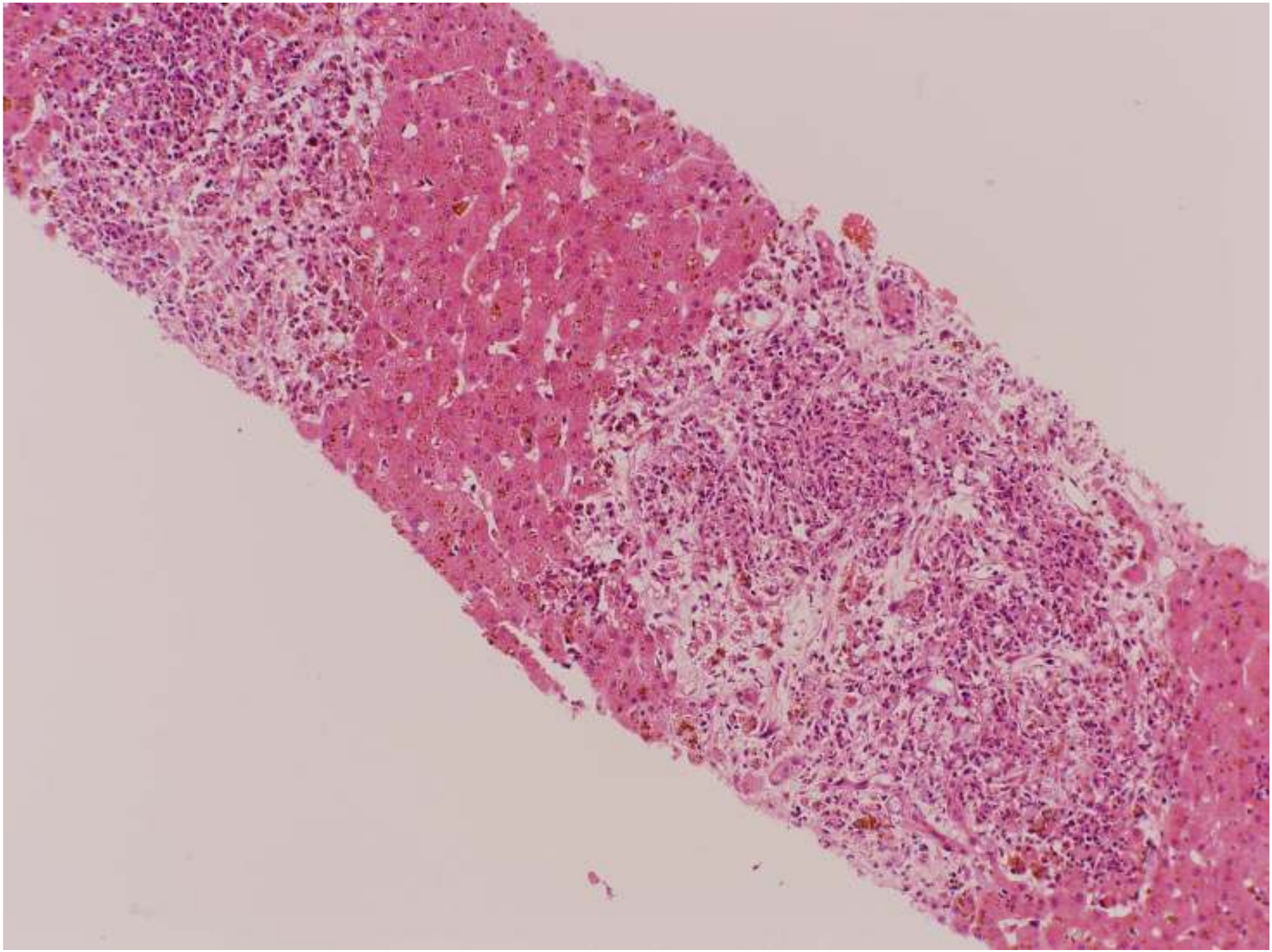
Total colectomy for mucormycosis

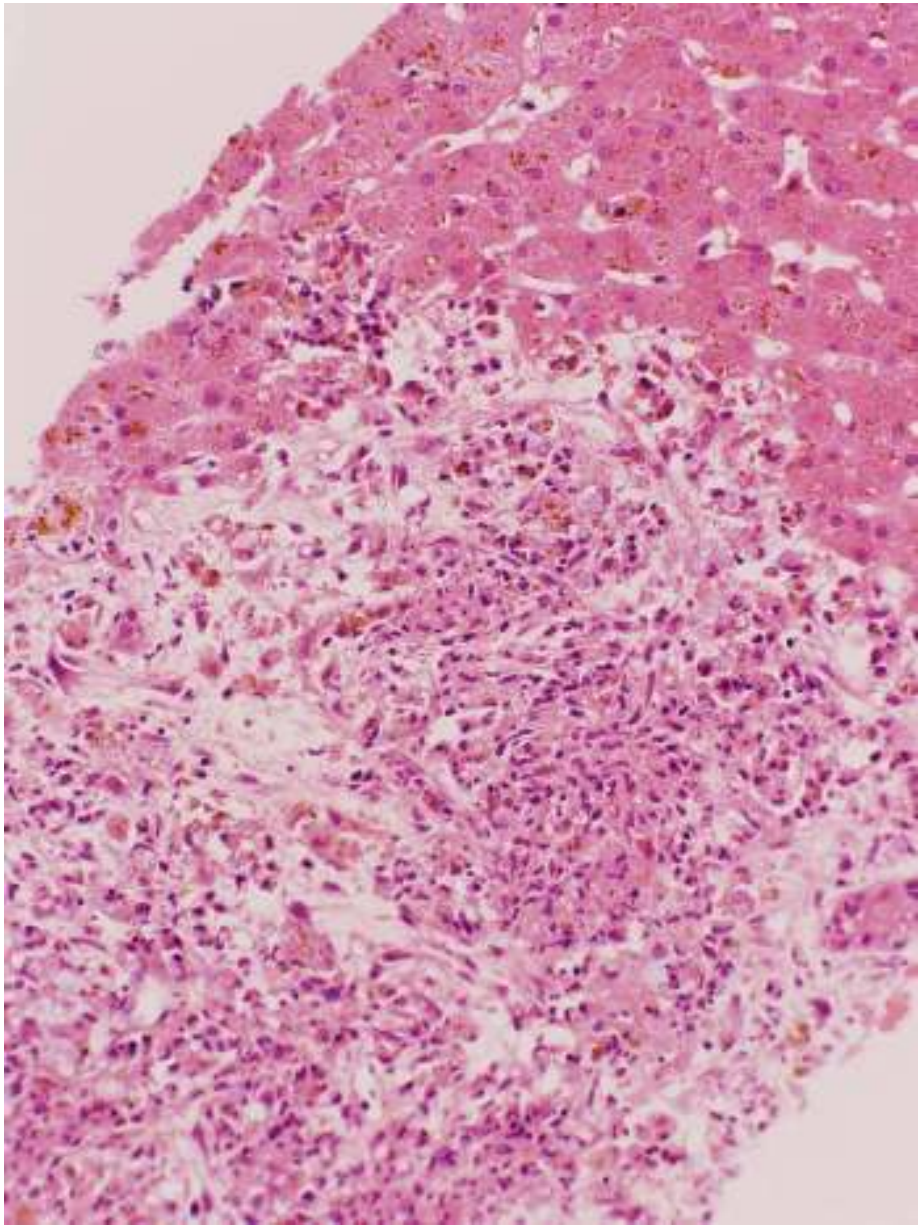
Not on steroids or cyclosporin

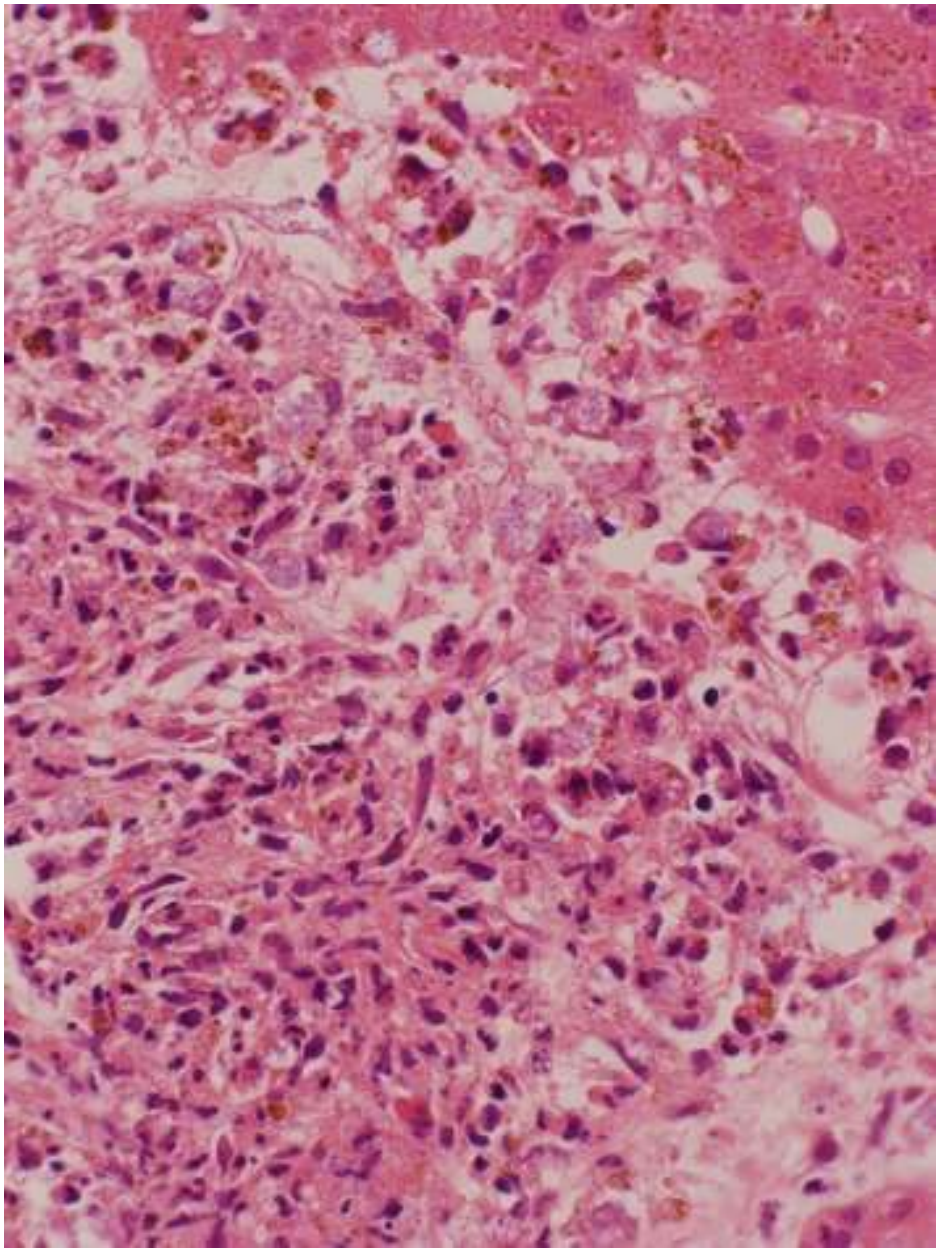
Fever; liver failure

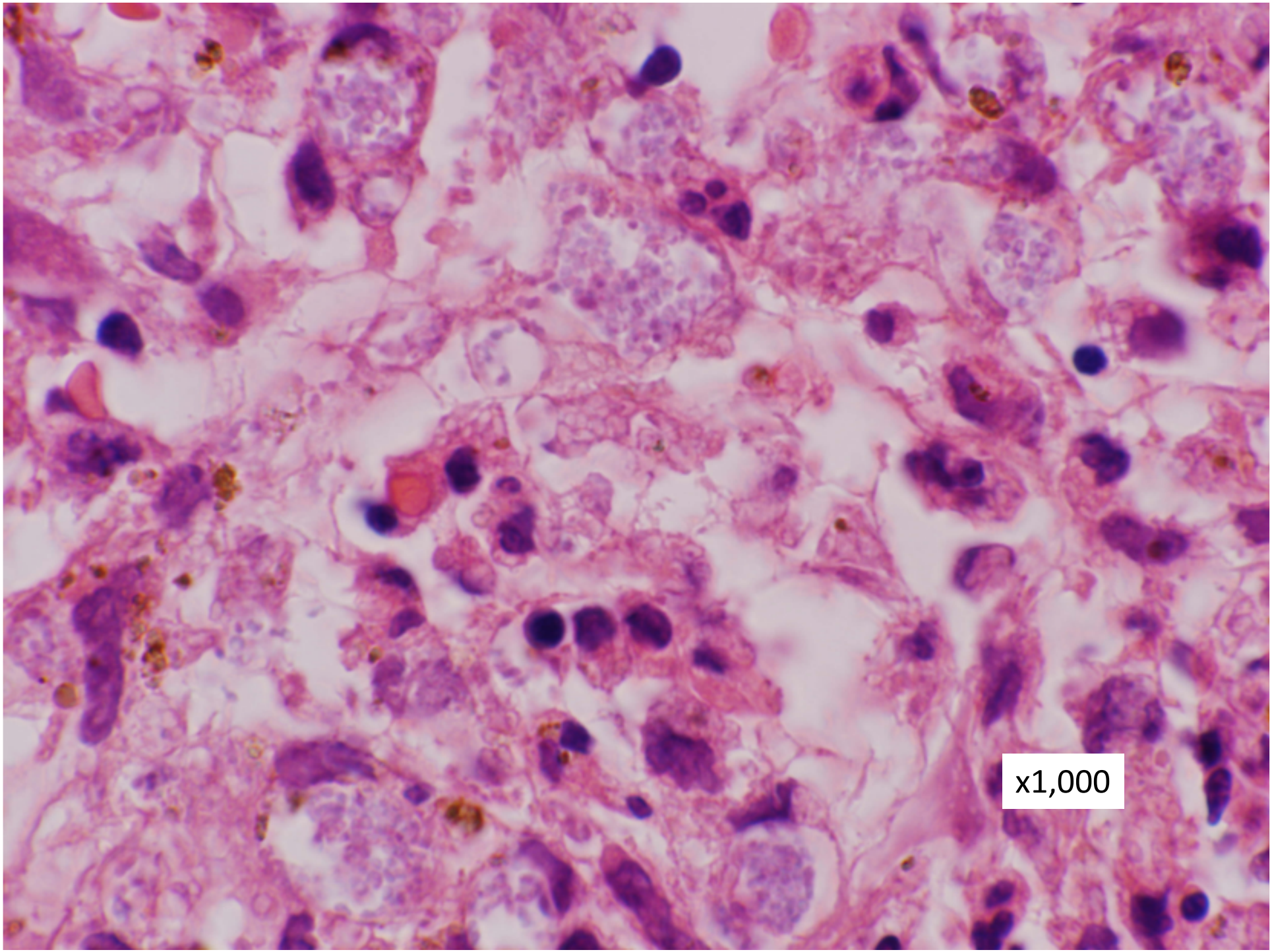
Liver biopsy

“Is this toxoplasmosis?”







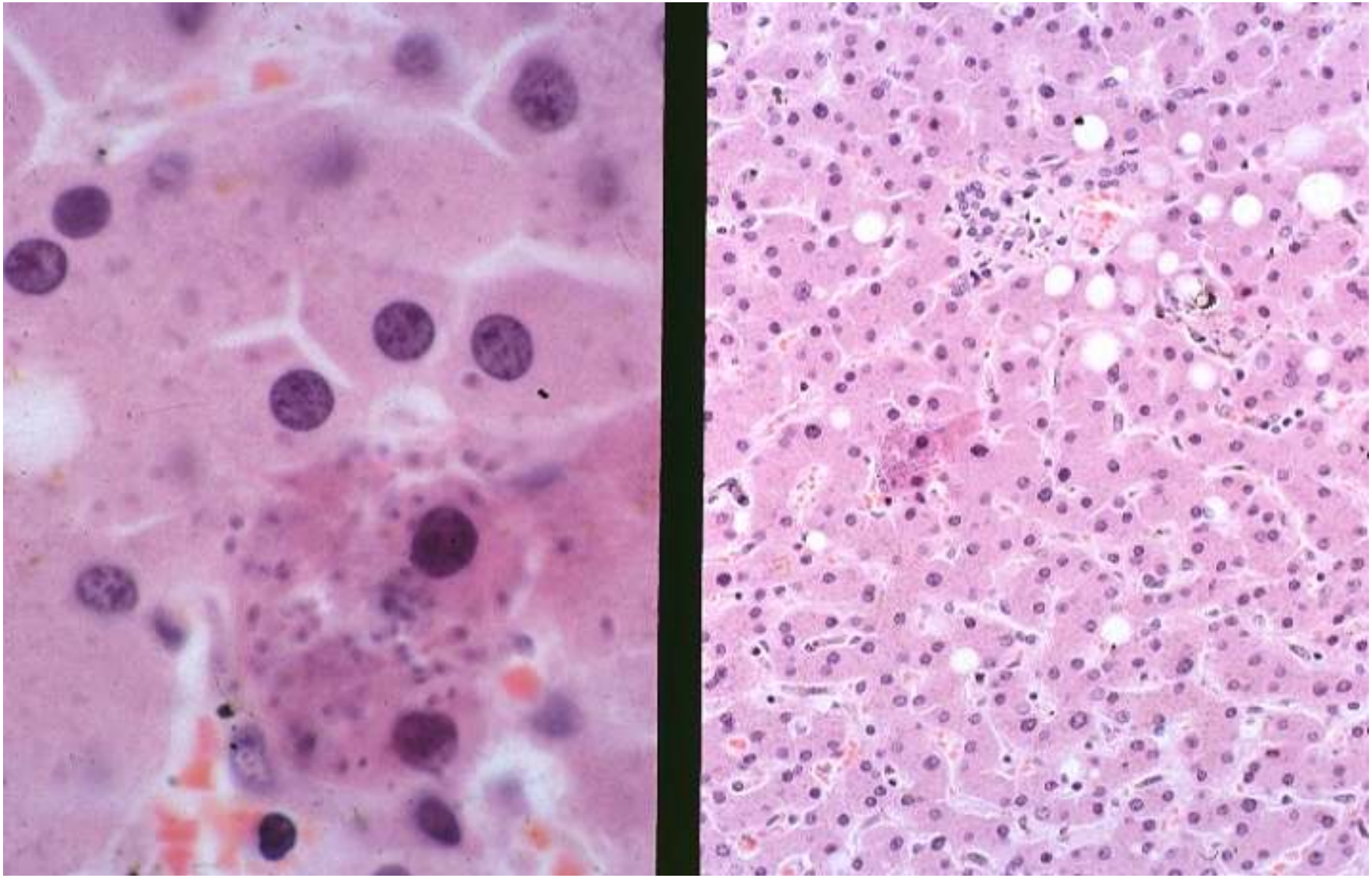

x1,000

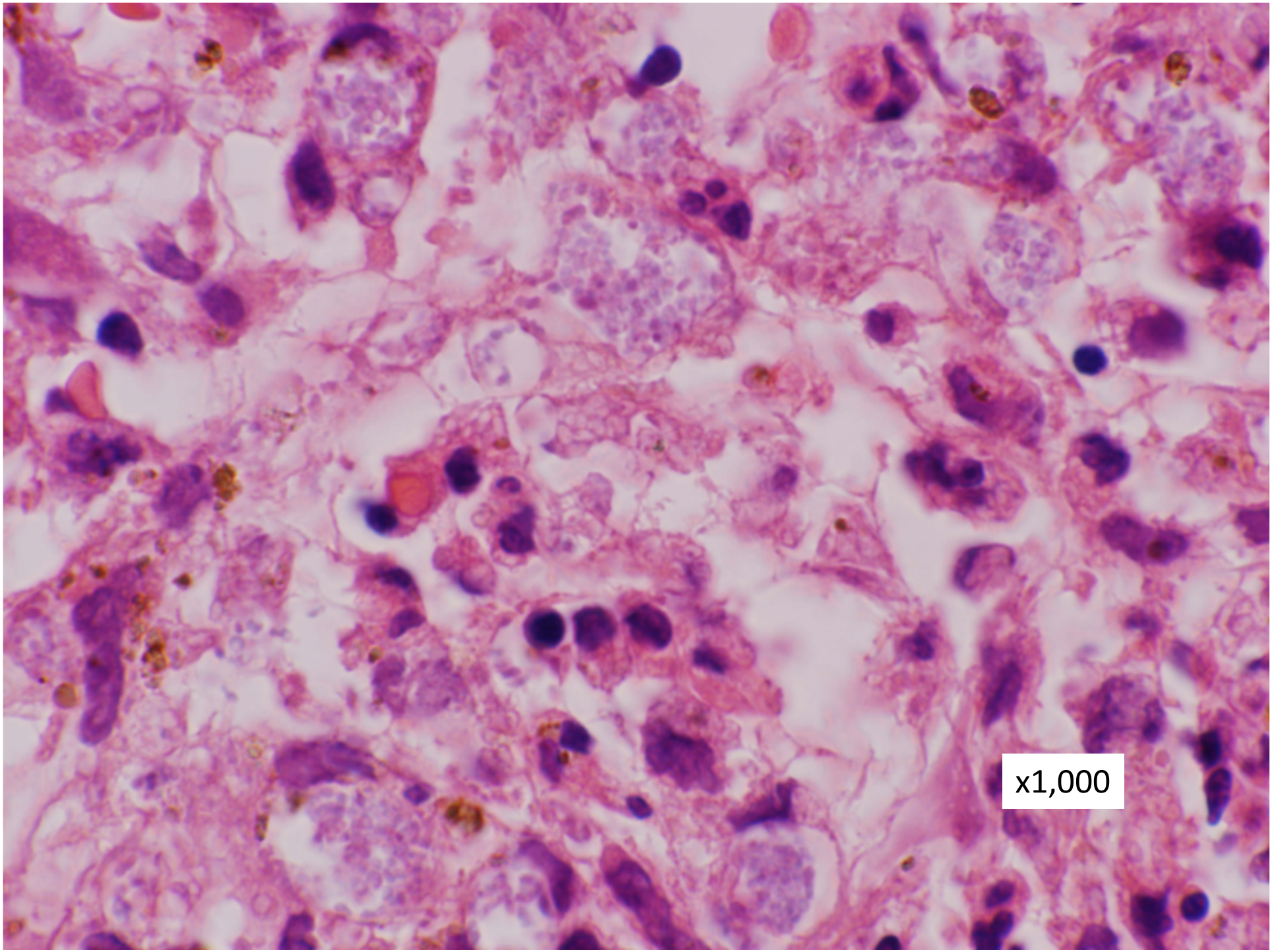
Small blue dots

- Toxoplasma
- Trypanosoma cruzi
- Leishmania
- Cryptosporidium
- microsporidia

- Bacterial cocci
  - Staphylococcus
- Fungi
  - Histoplasma capsulatum
  - Candida spp
  - Penicillium marneffei

Toxoplasma gondii

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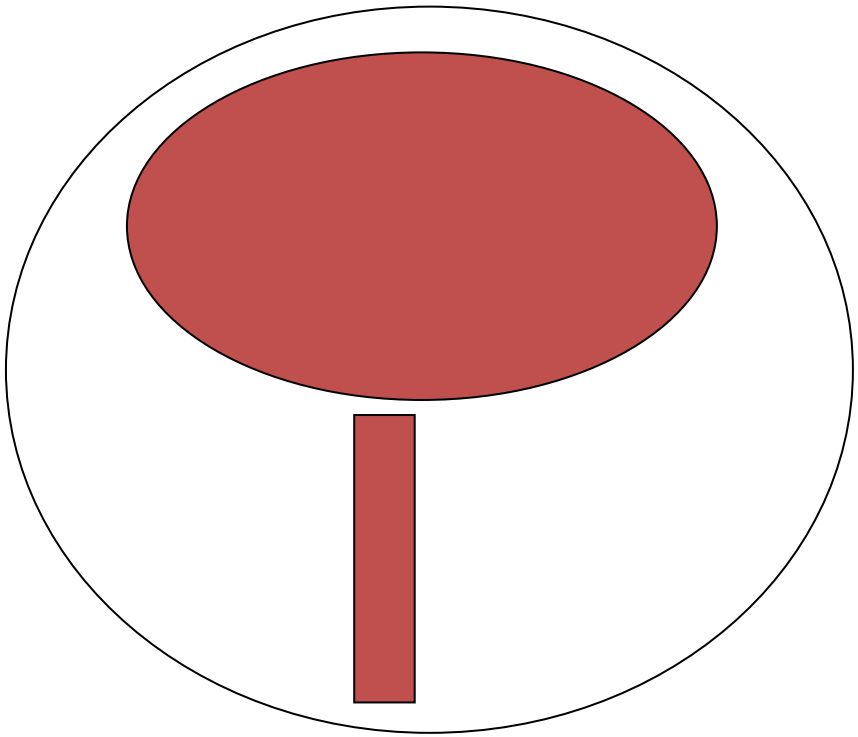
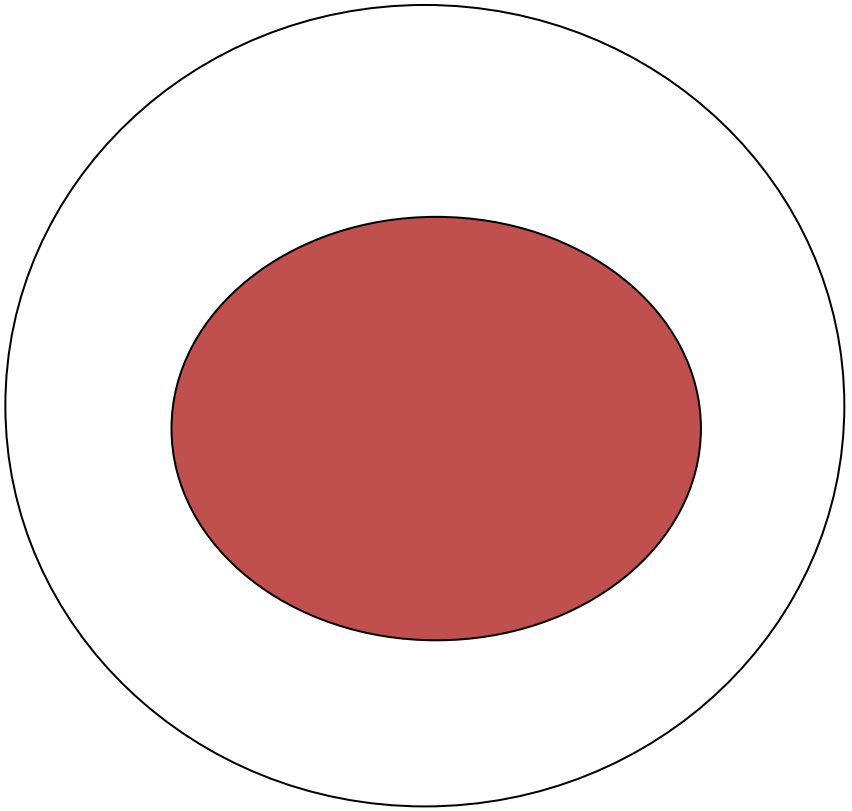
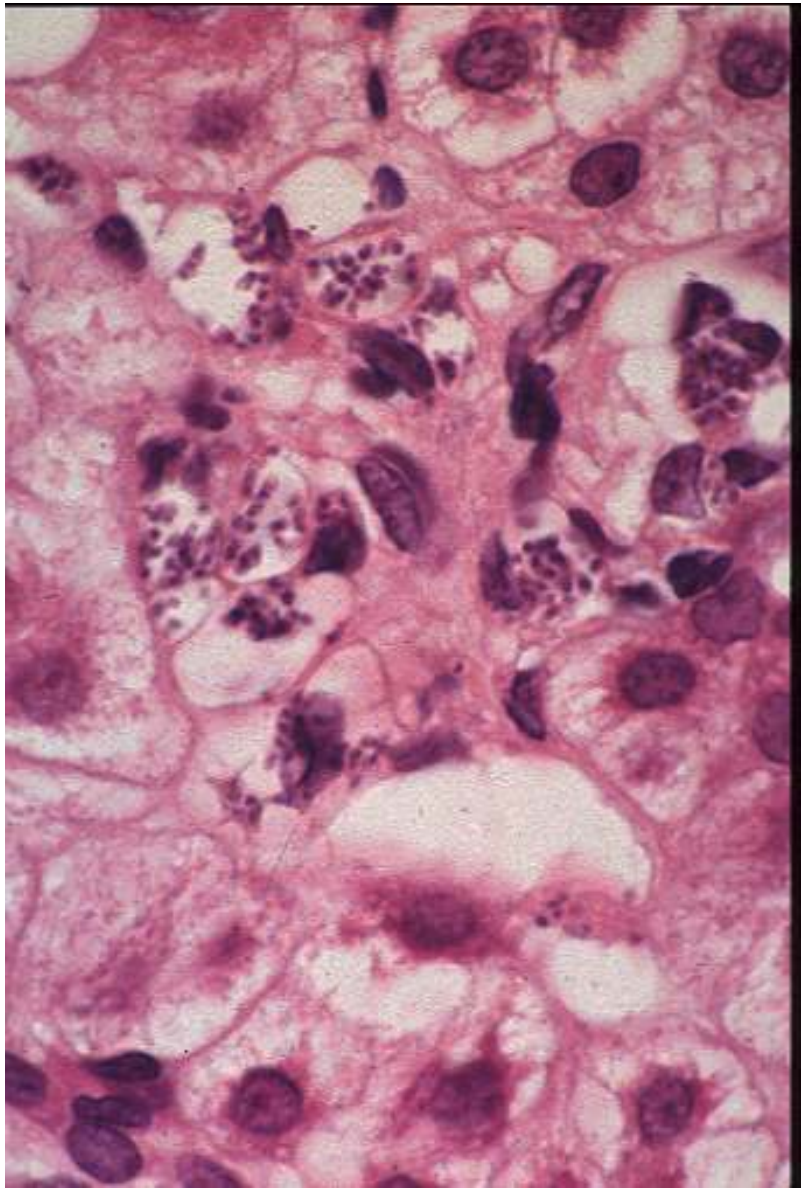
Leish vs Histo

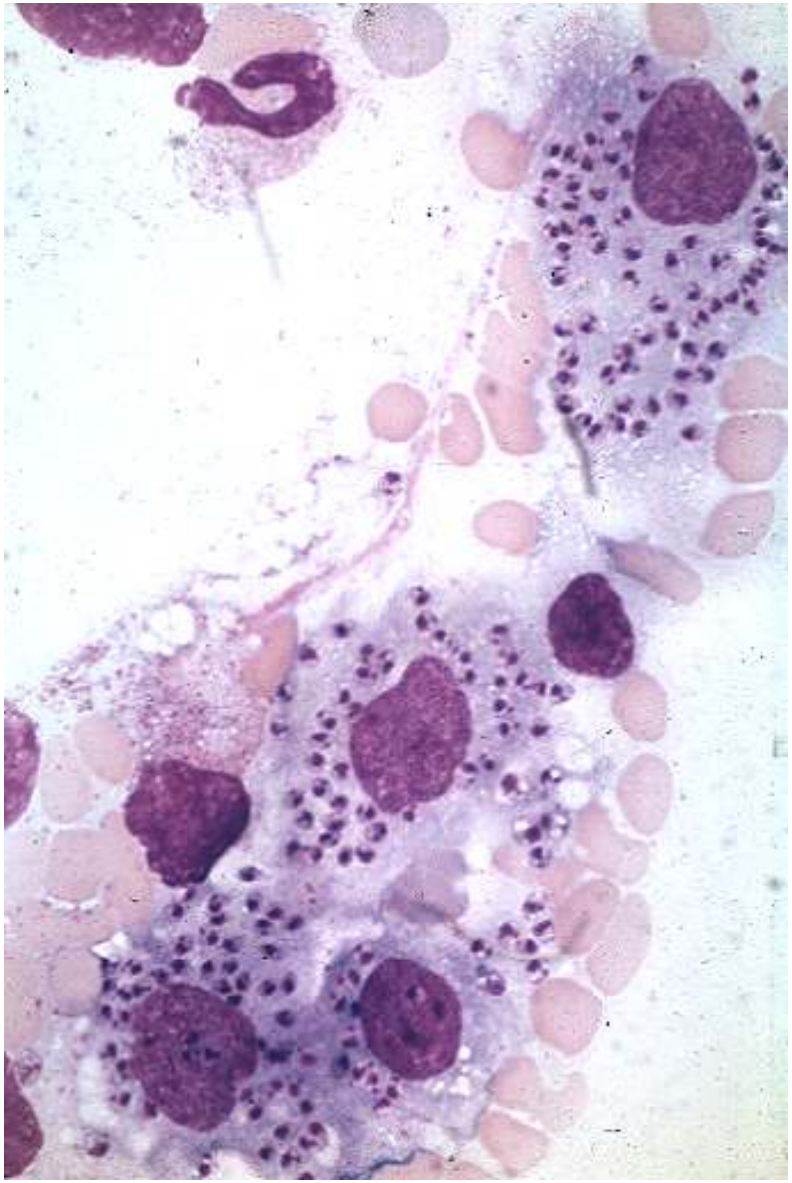


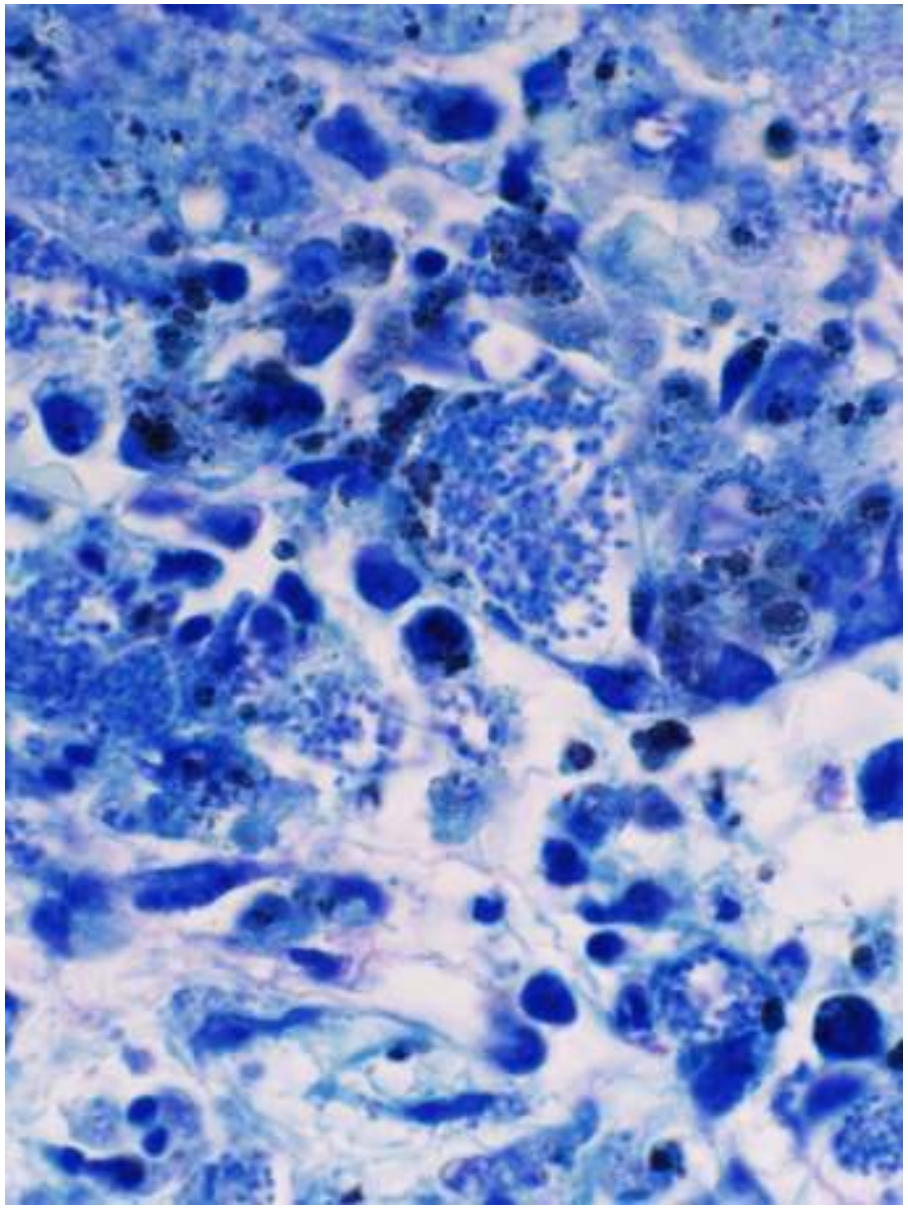
kinetoplast

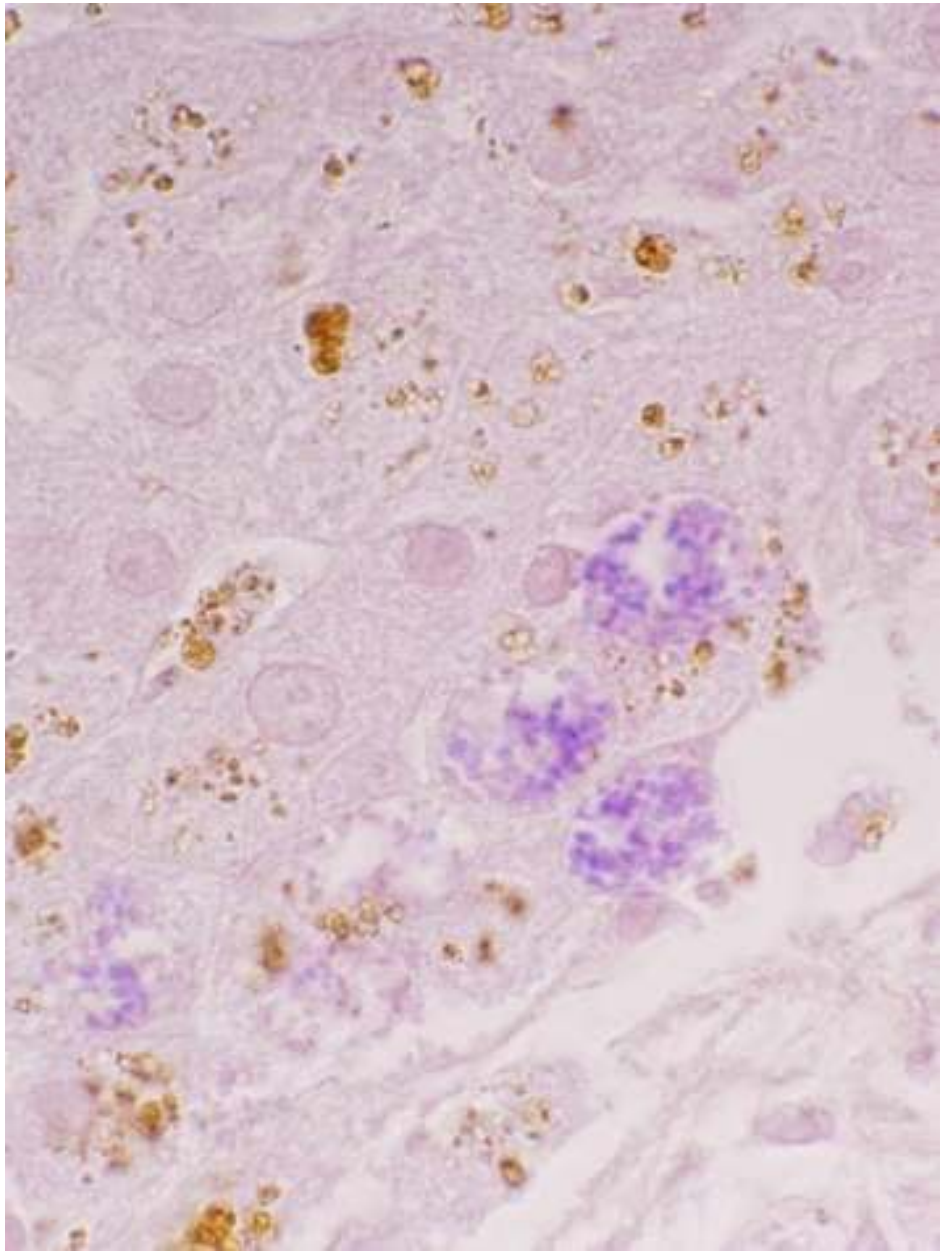


Leish histo & cyto

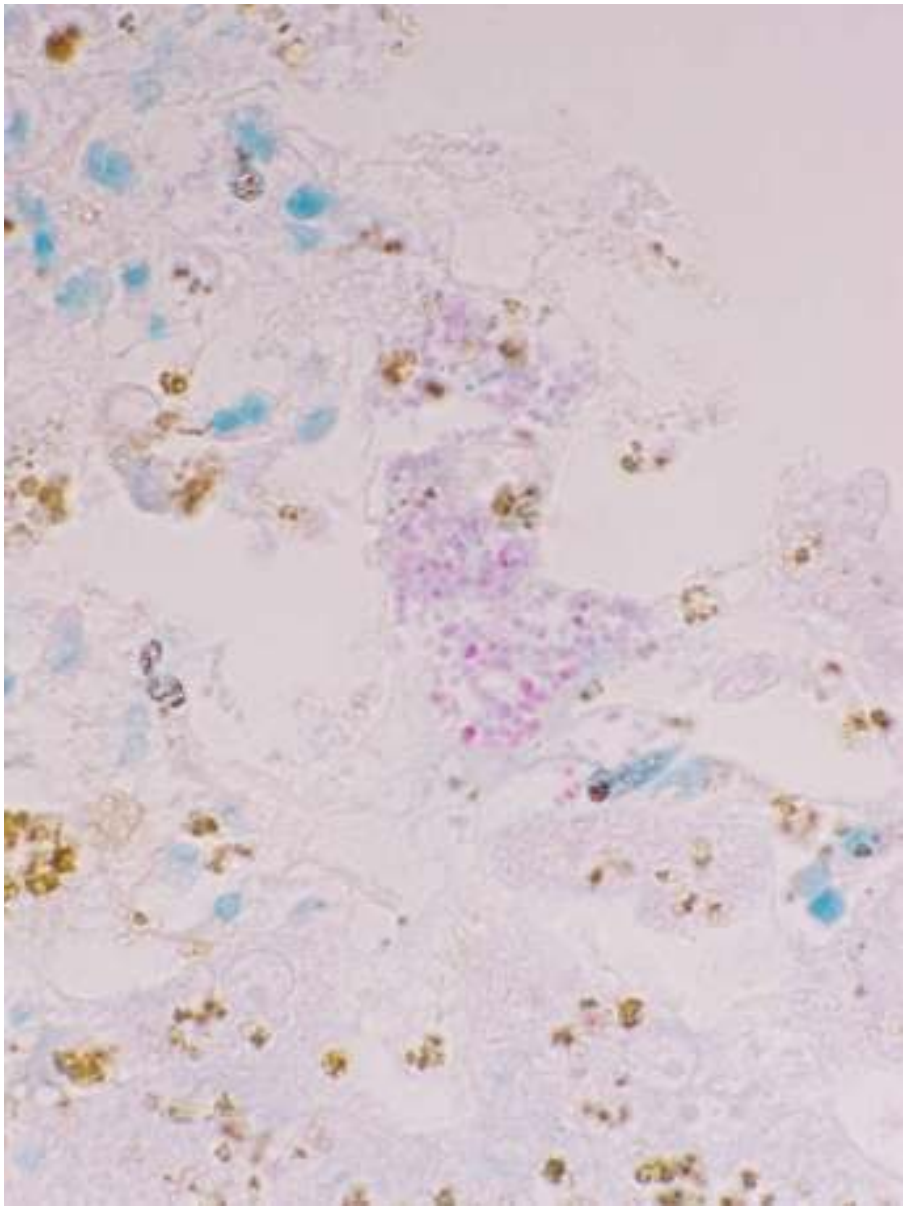


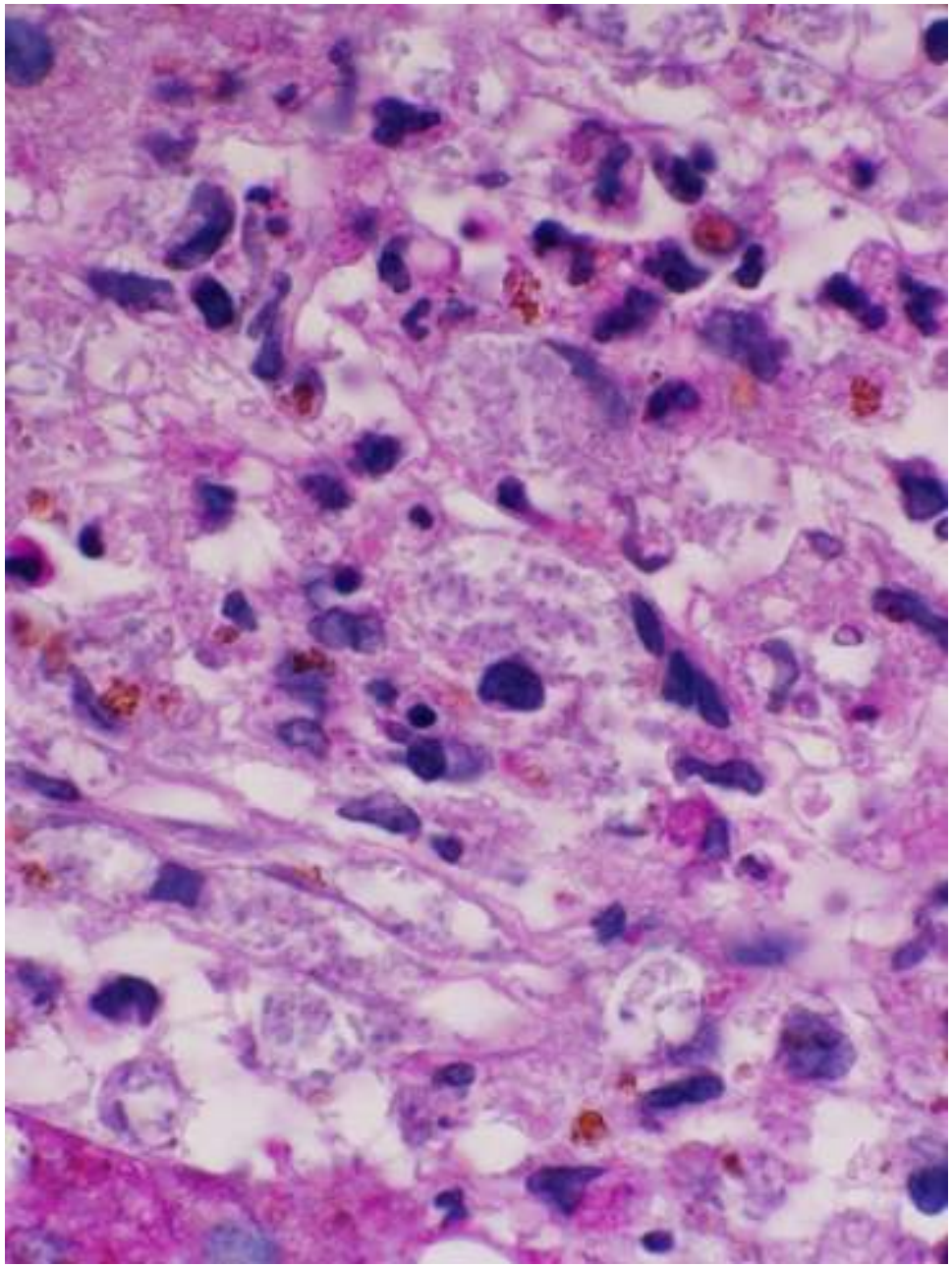






Giemsa & Gram = protozoa, eccentric nucleus gram+





ZN (carbol fuchsin)+ and PAS+ polar dots

Case

- Not fungi
- Not bacterial
- Protozoa
  - Not leishmania or toxoplasma

- Microsporidia
  - Encephalitozoon sp
  - Pleistophora sp

How to confirm microsporidia?

Electron microscopy

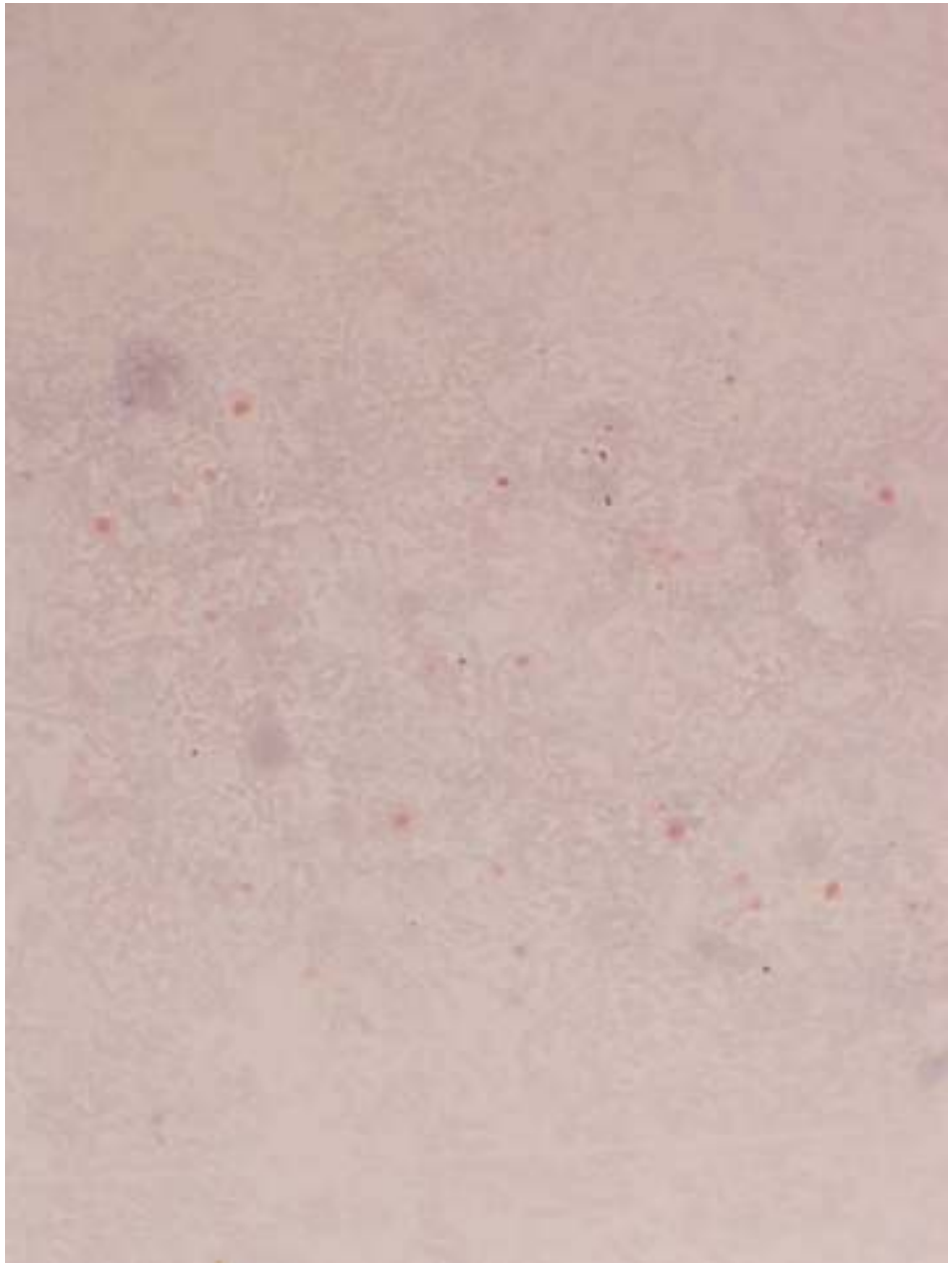
Faecal analysis (acid fast stain)

PCR on tissue or faeces

[no tissue remained in the biopsy block]

PCR = *Encephalitozoon cuniculi*

Patient died despite therapy



EM identification

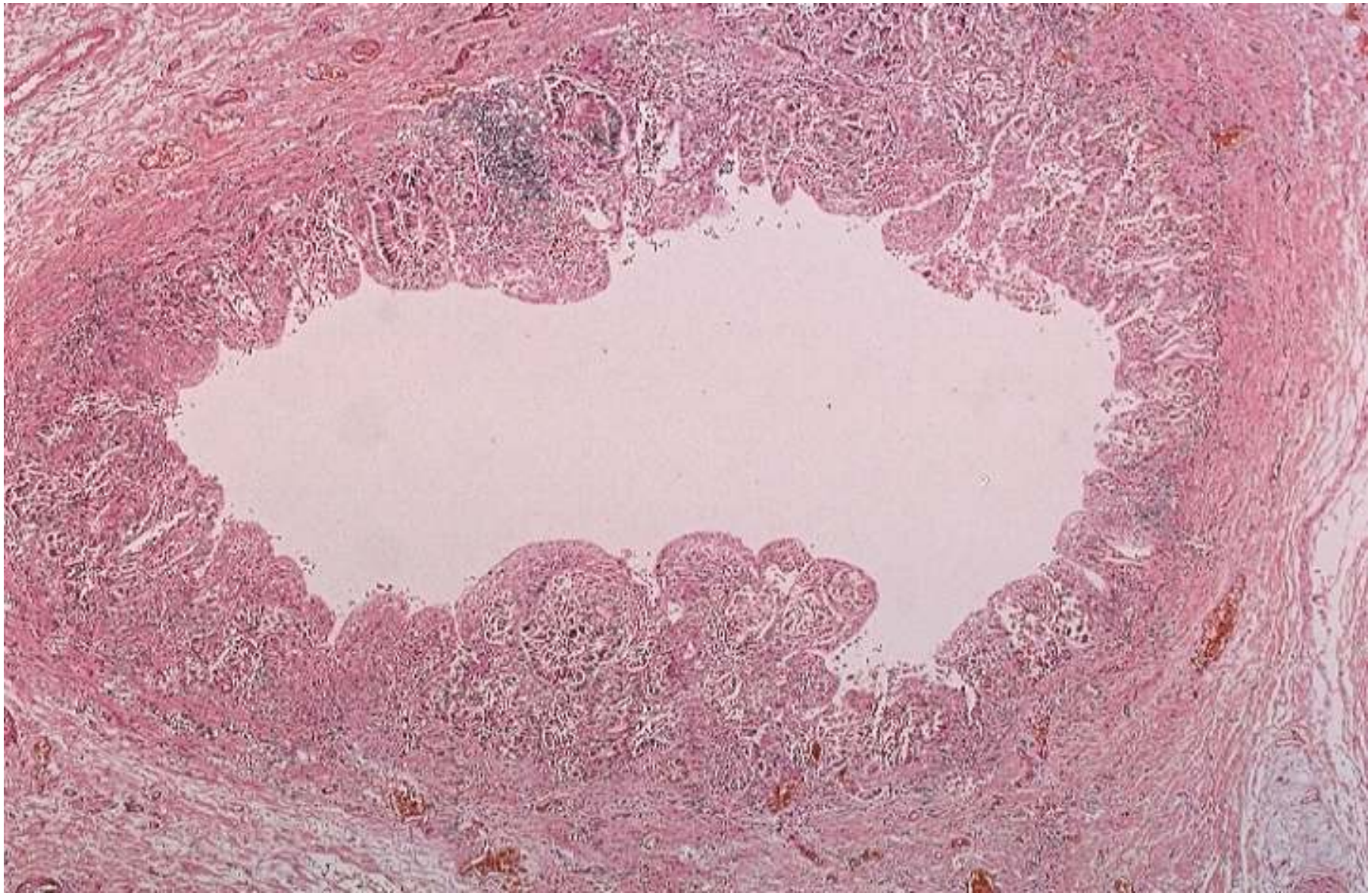
EM (thanks to Alan Curry, Manchester HPA)

Microsporidia

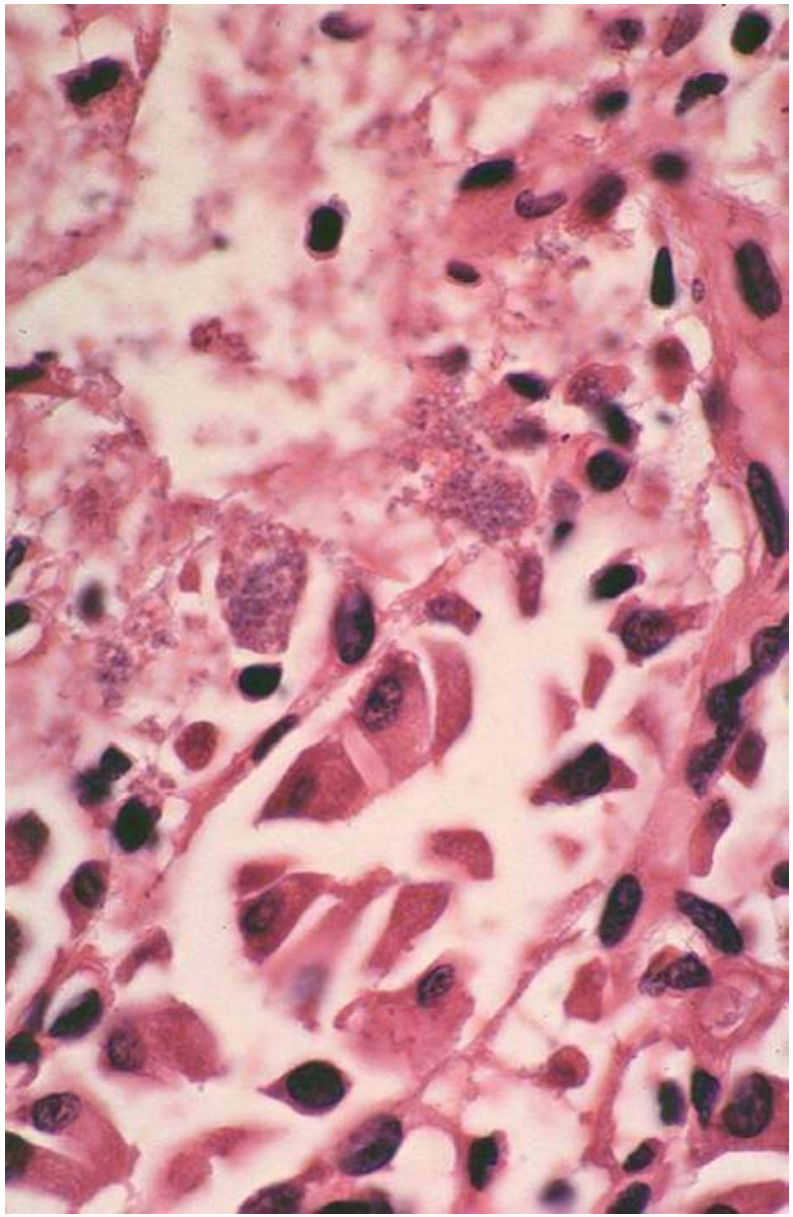
- Parasitic protozoa of invertebrates & vertebrates
- Well known to vet pathologists
- Virtually unknown to human pathology until HIV/AIDS
- 1985: *Enterocytozoon bieneusi* – gut
- 1987: *Encephalitozoon intestinalis* – gut, systemic infection
- et seq: many other species - *Pleistophora, E.cuniculi*

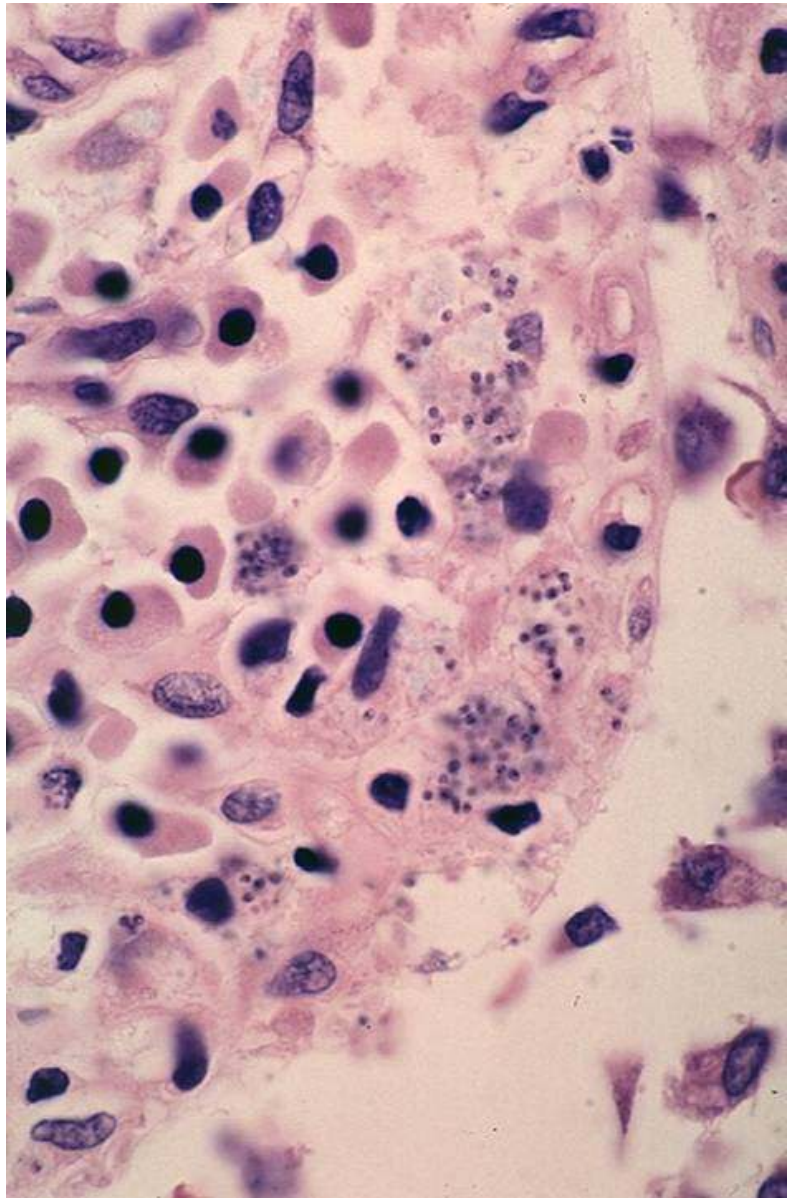
- Treatment? albendazole + intraconazole

An autopsy case - cholangitis

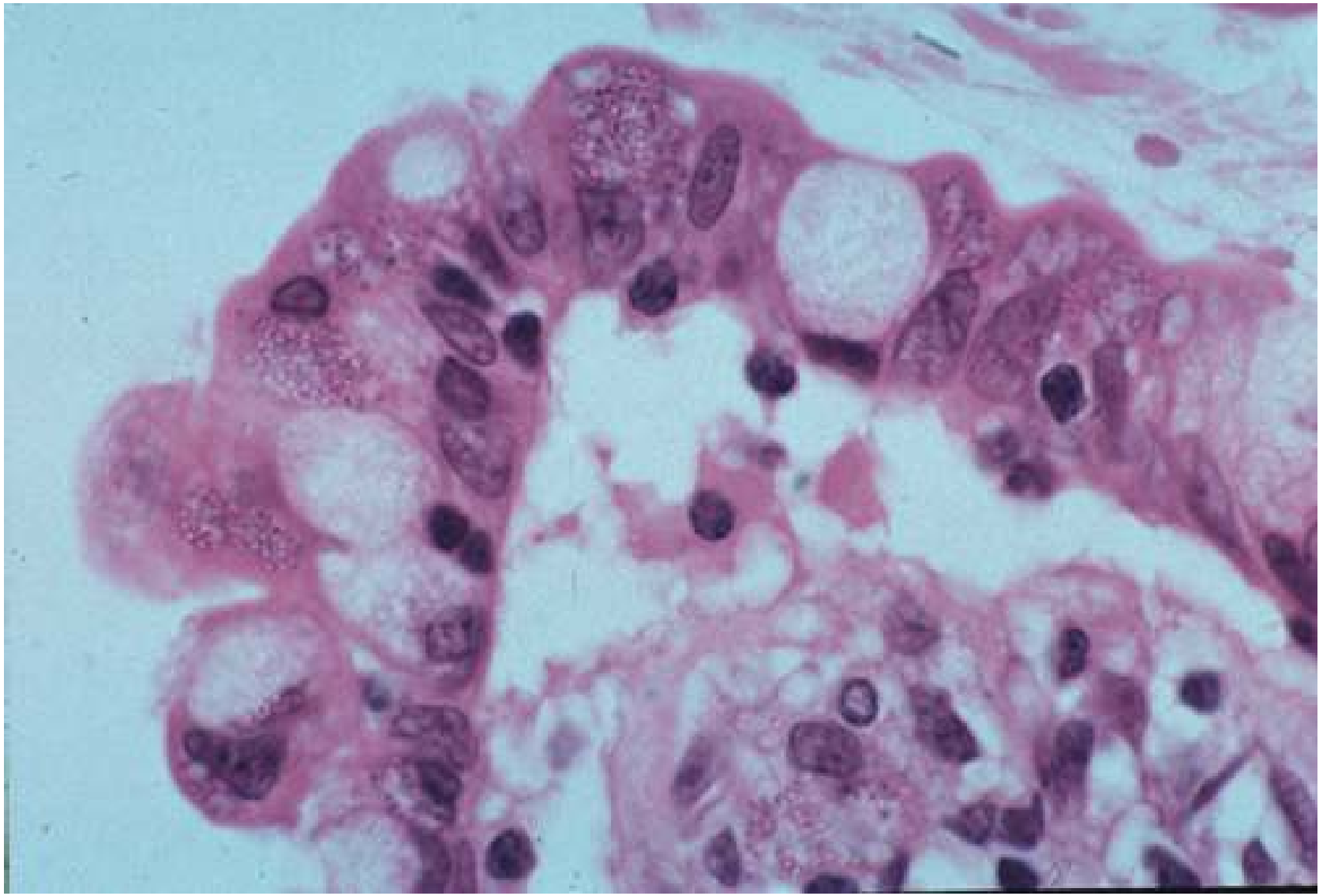


Autopsy case of disseminated microsporidiosis





microsporidiosis



Case solved

- H&E histopathology
  - Supportive special stains
- Exclusion of alternatives (special stain)
- Examination of corroborative material
- Molecular diagnostics
- Electron microscopy

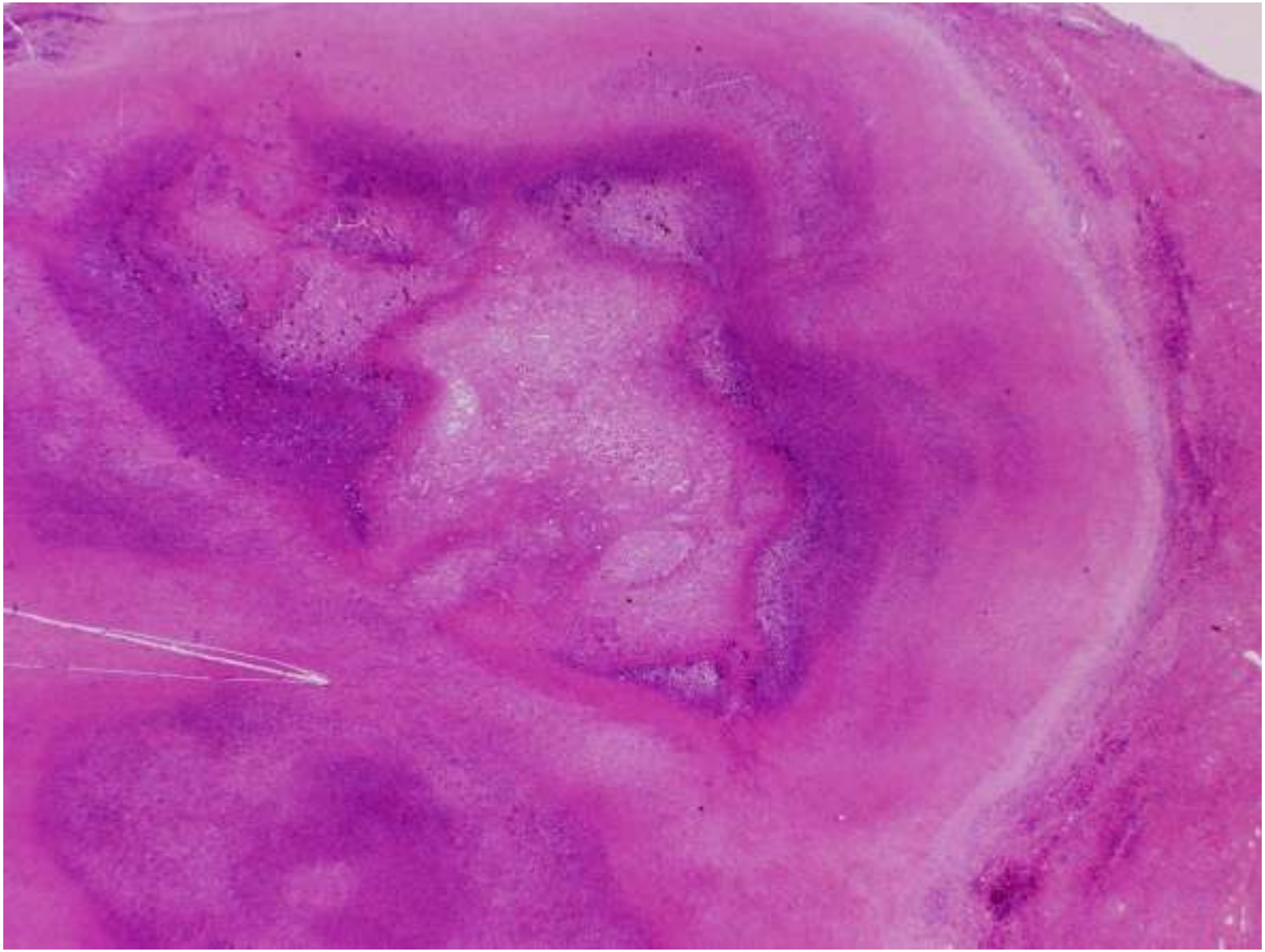
- In the meantime, treatment started
  - albendazole + itraconazole

Case 2

- Female Briton age 74
- Scan of liver shows a mass
- ? Tumour

- Partial liver resection 17 x 13 x 7cm
- Well circumscribed mass comprising two adjacent nodules 2m diameter

Liver resection – H&E

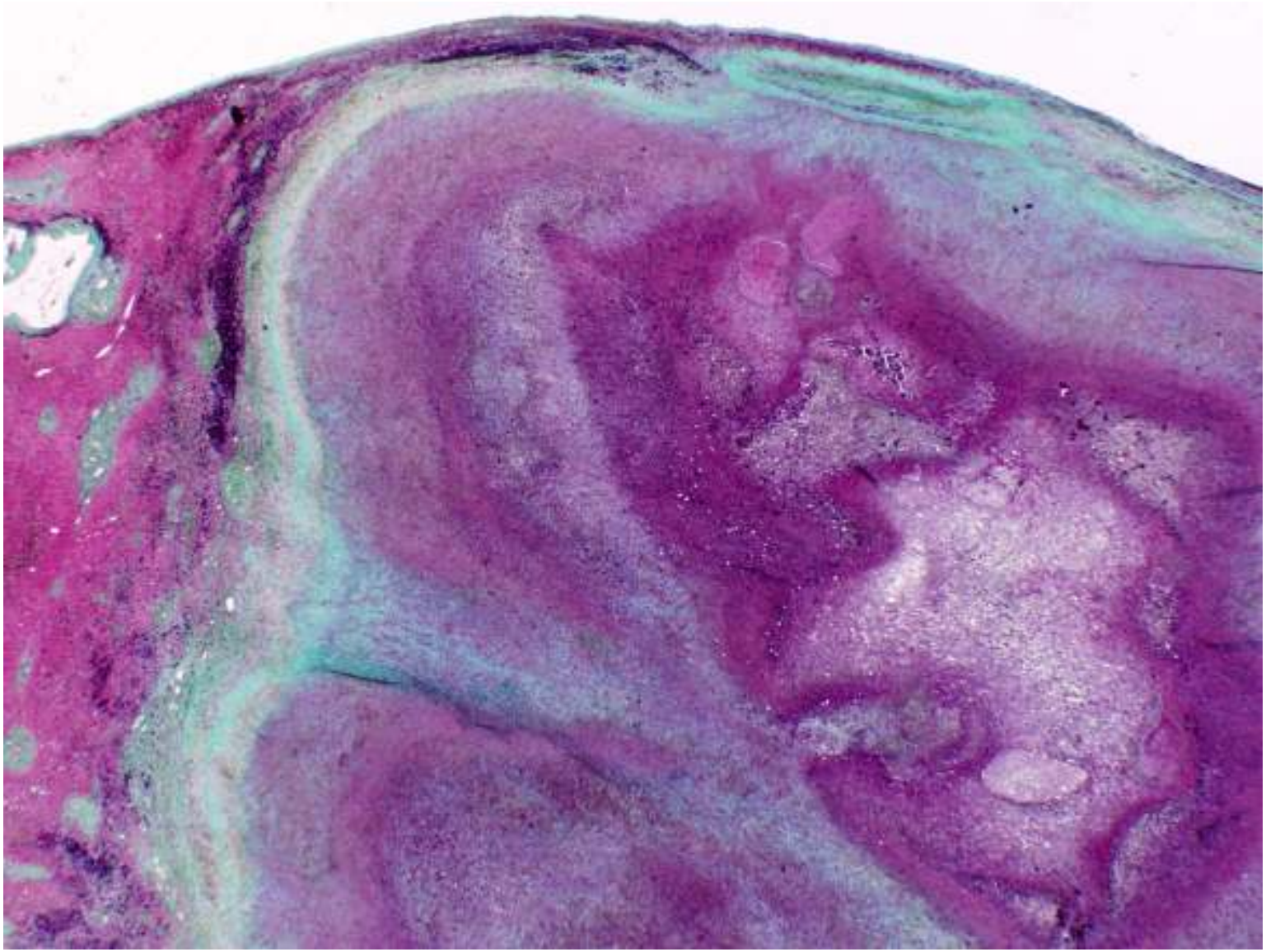


Eosinophilic necrotic nodules (liver, lymph node, spleen)

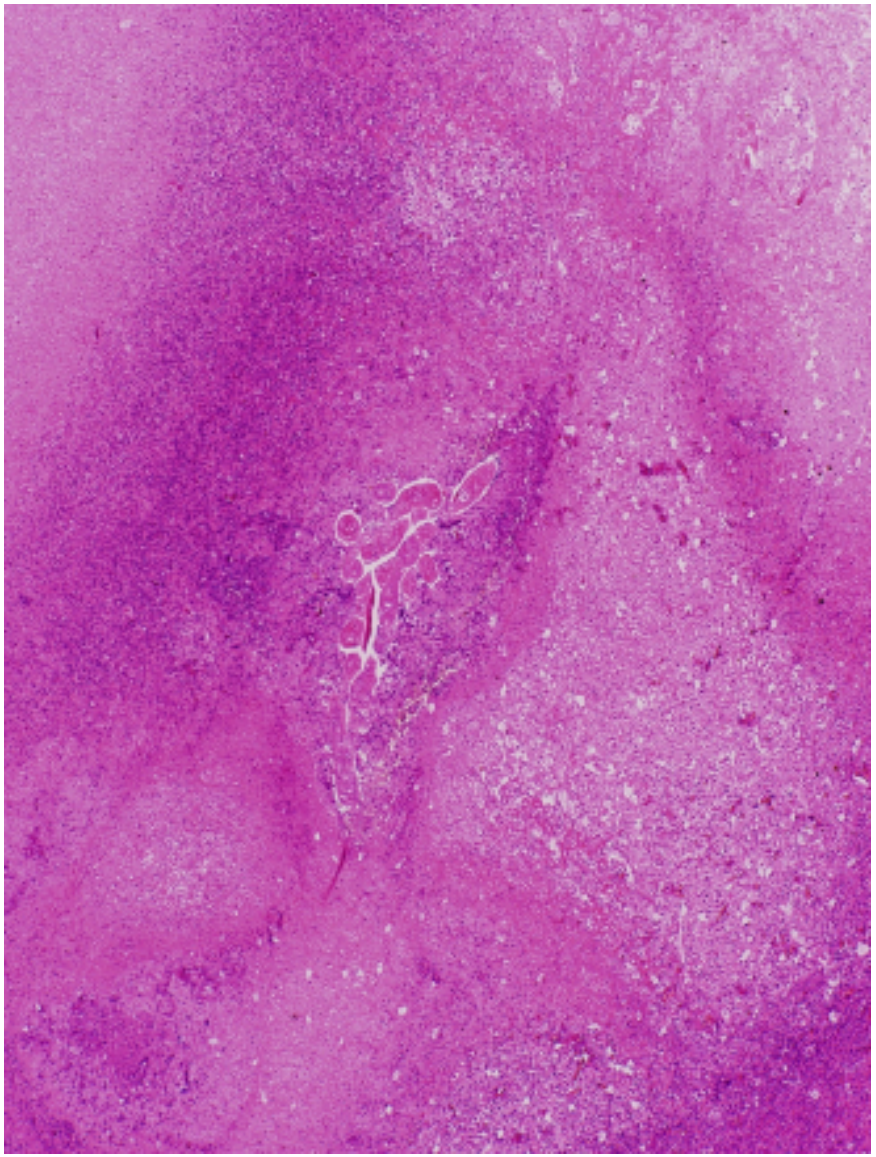
- Worm infections
- Tumour
  - Hodgkin disease
- Drug reaction
- Idiopathic allergy / immunopathology

- NB: no useful published literature
  - *'Focal eosinophilic necrosis' (FEN) mentioned in the radiological imaging literature from Asia*

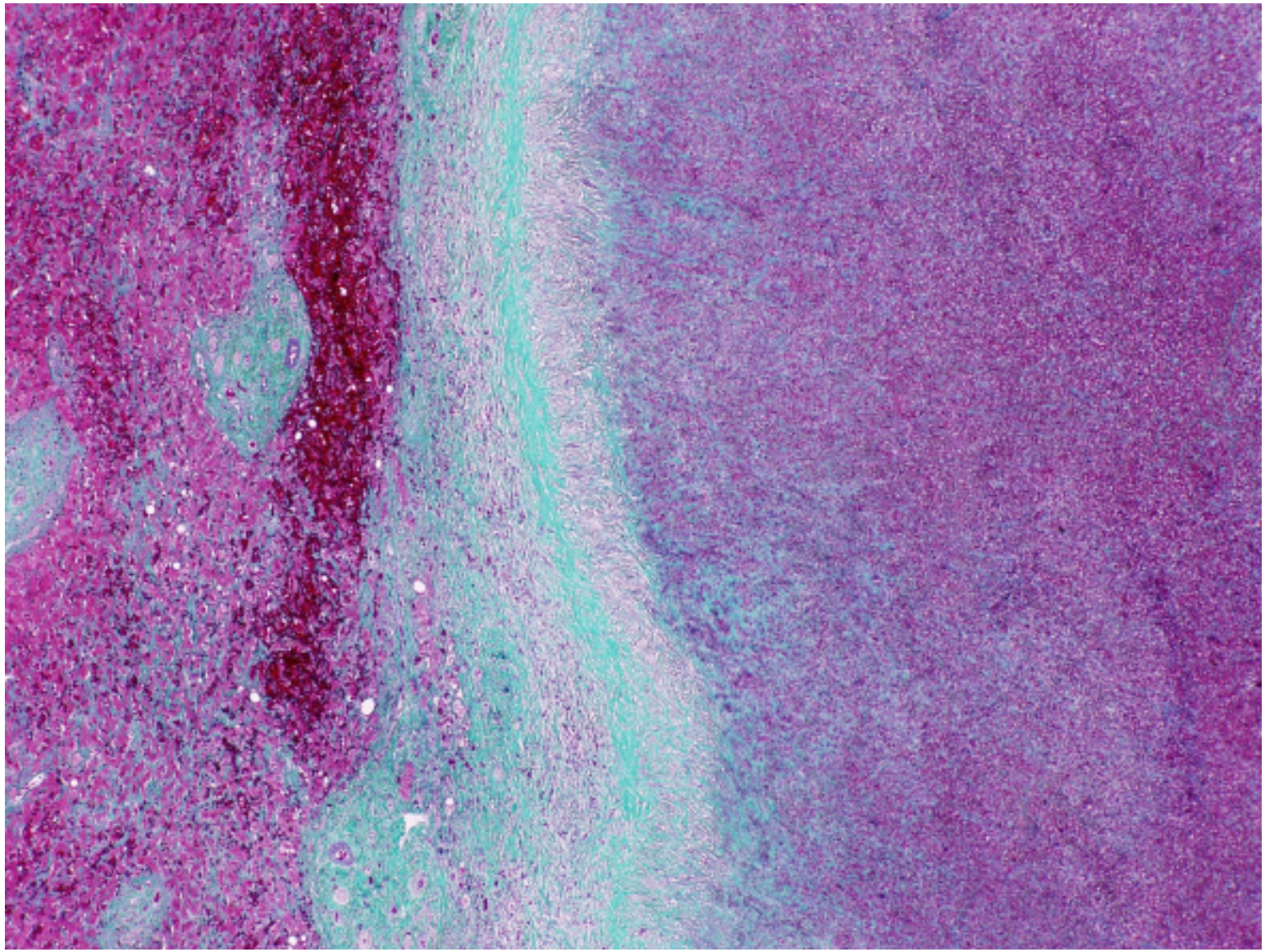
Liver resection



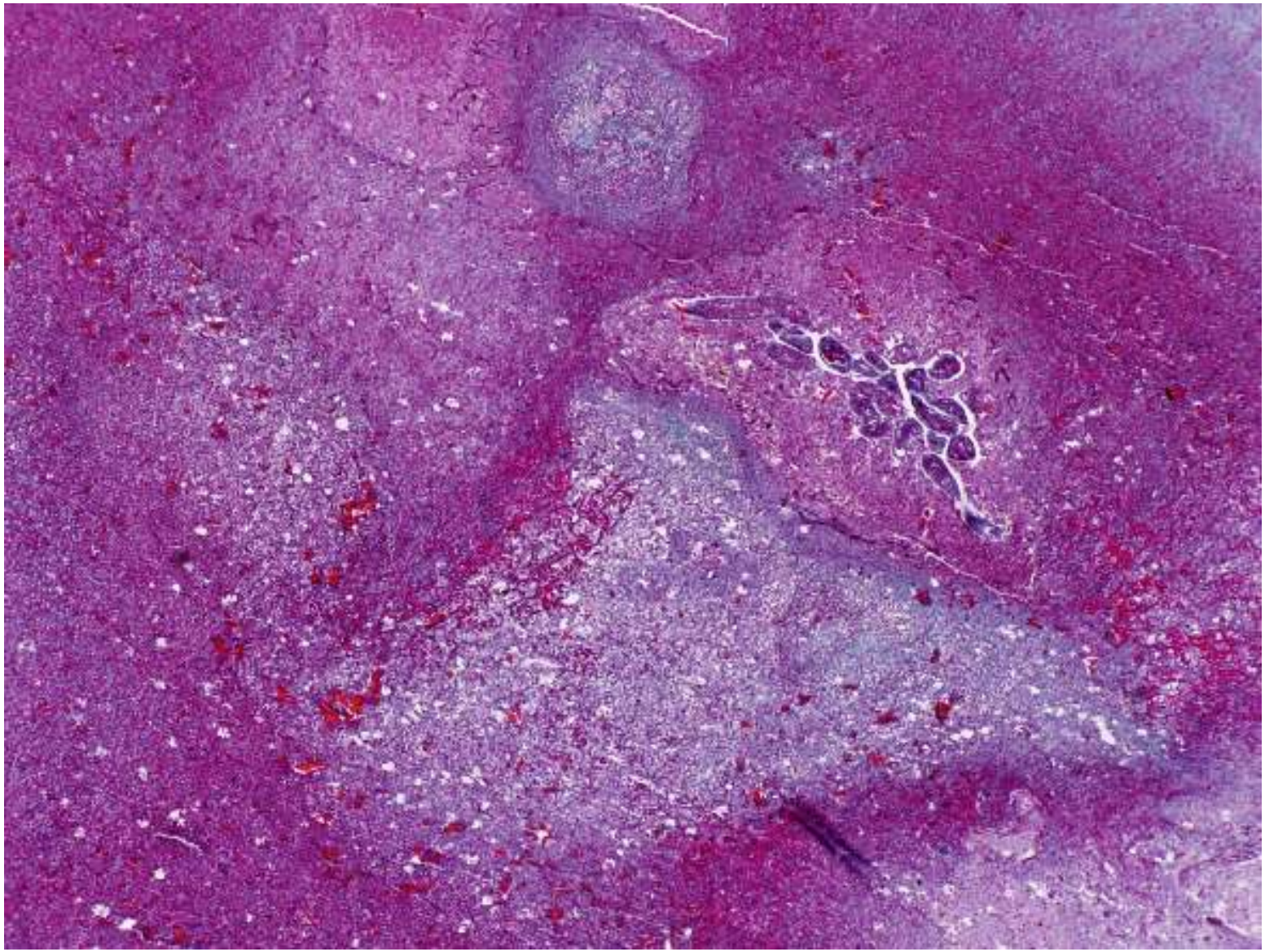
Liver resection – H&E



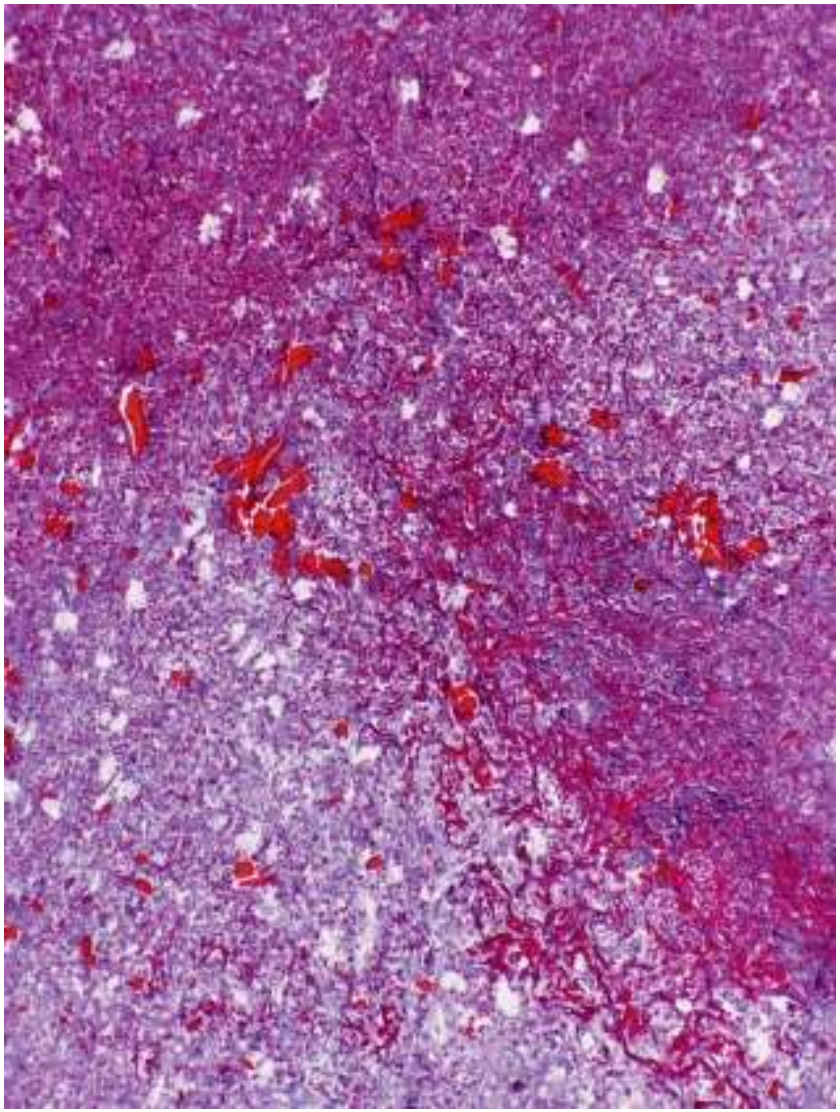
Liver resection

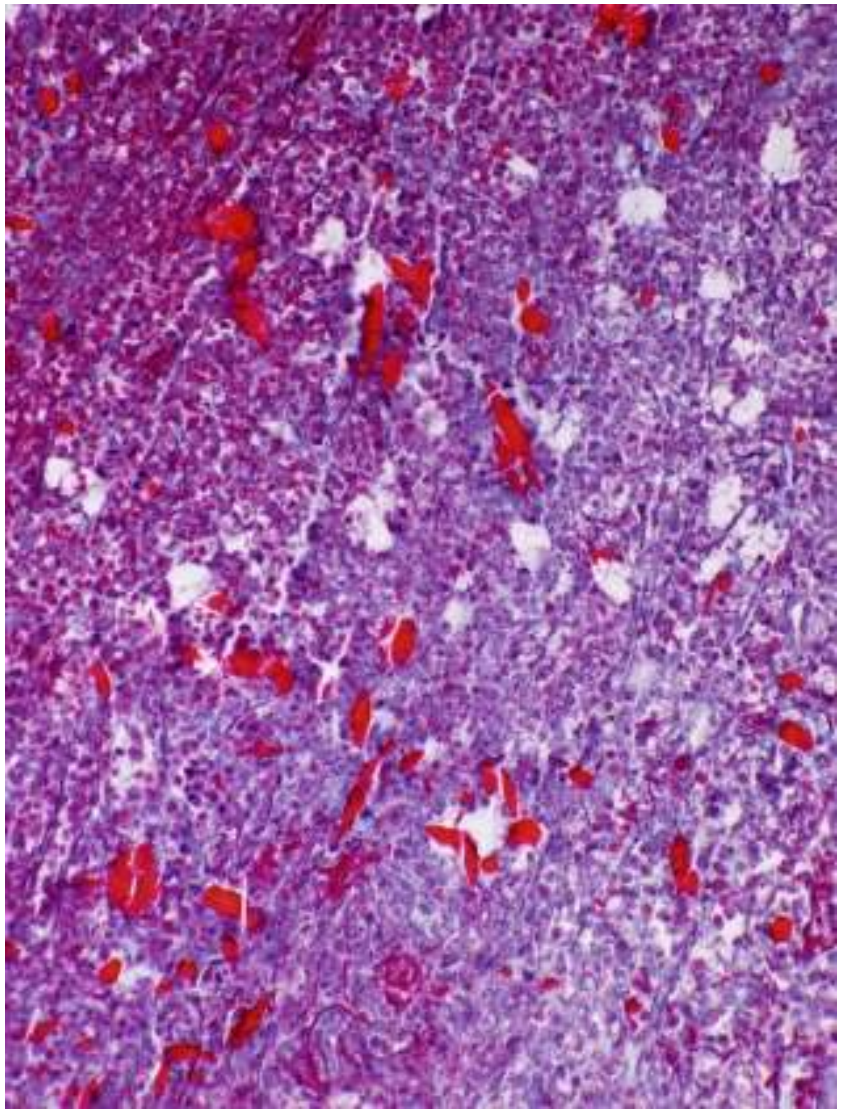


Liver resection

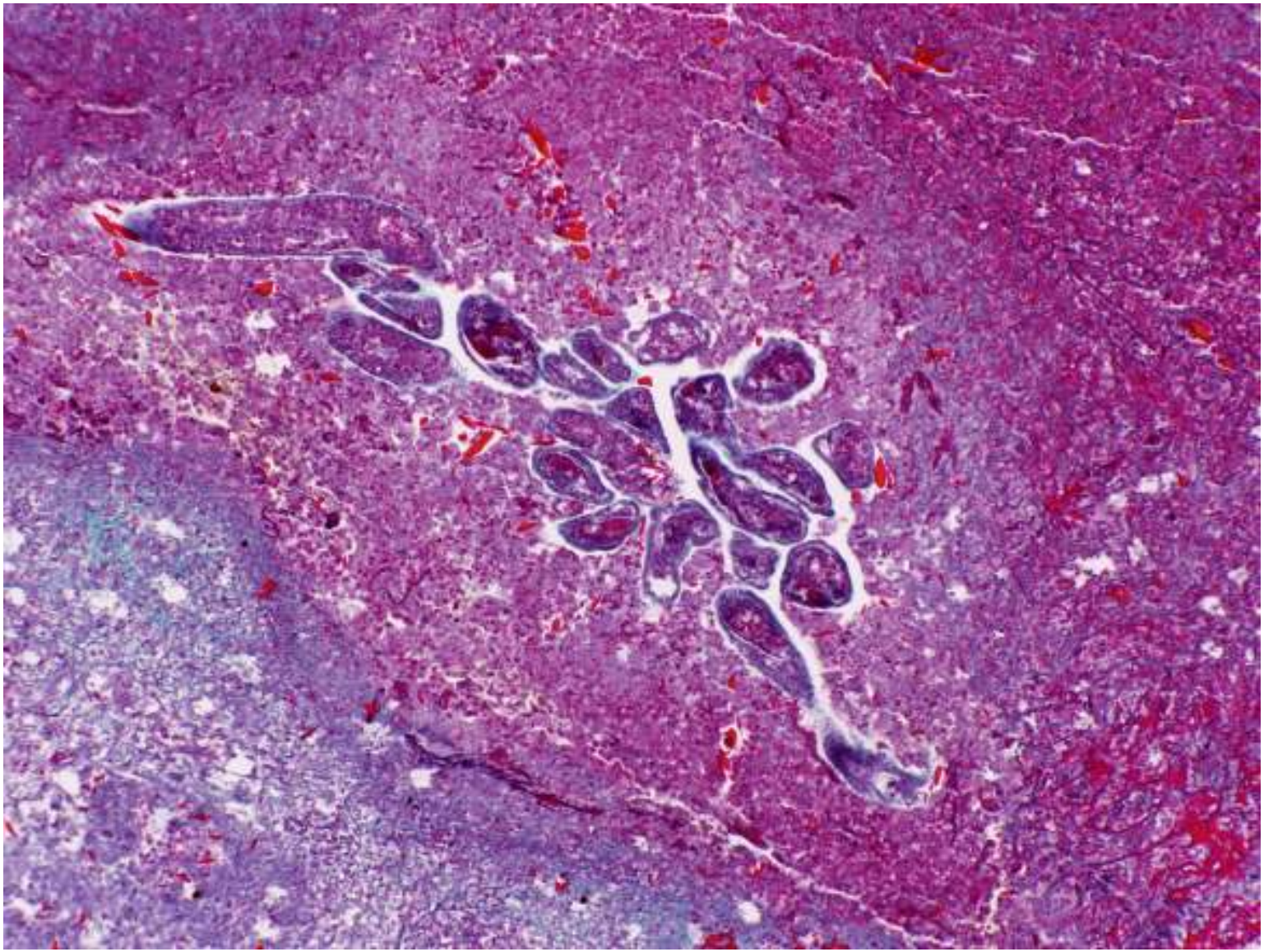


Liver resection – Charcot-Leyden crystals





Liver resection – what is this?



Case 2

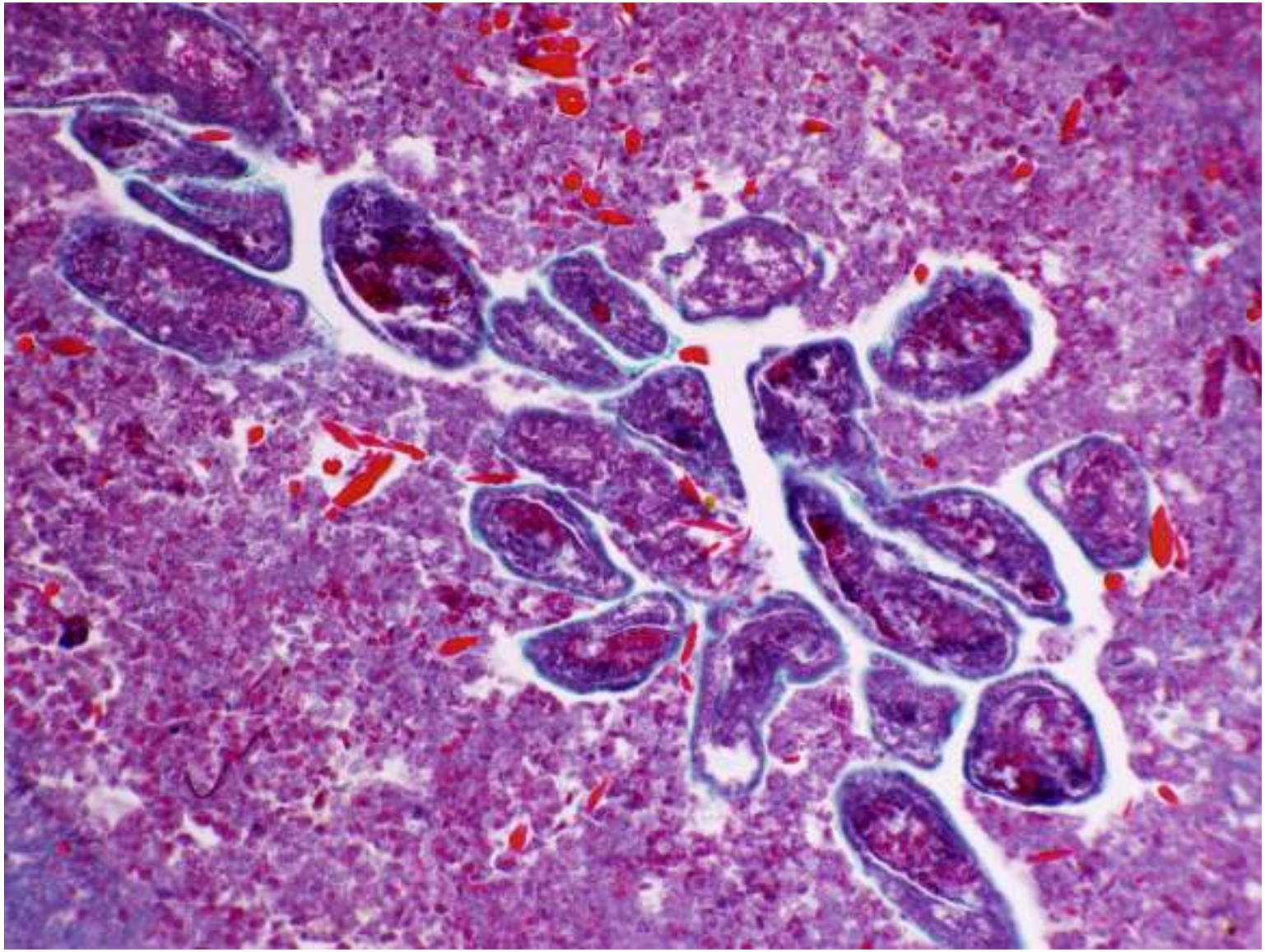
- Original diagnosis
  - Hydatid cyst
- …but hydatid serology negative
- Review of biopsy……

Your [Swiss path soc] diagnoses

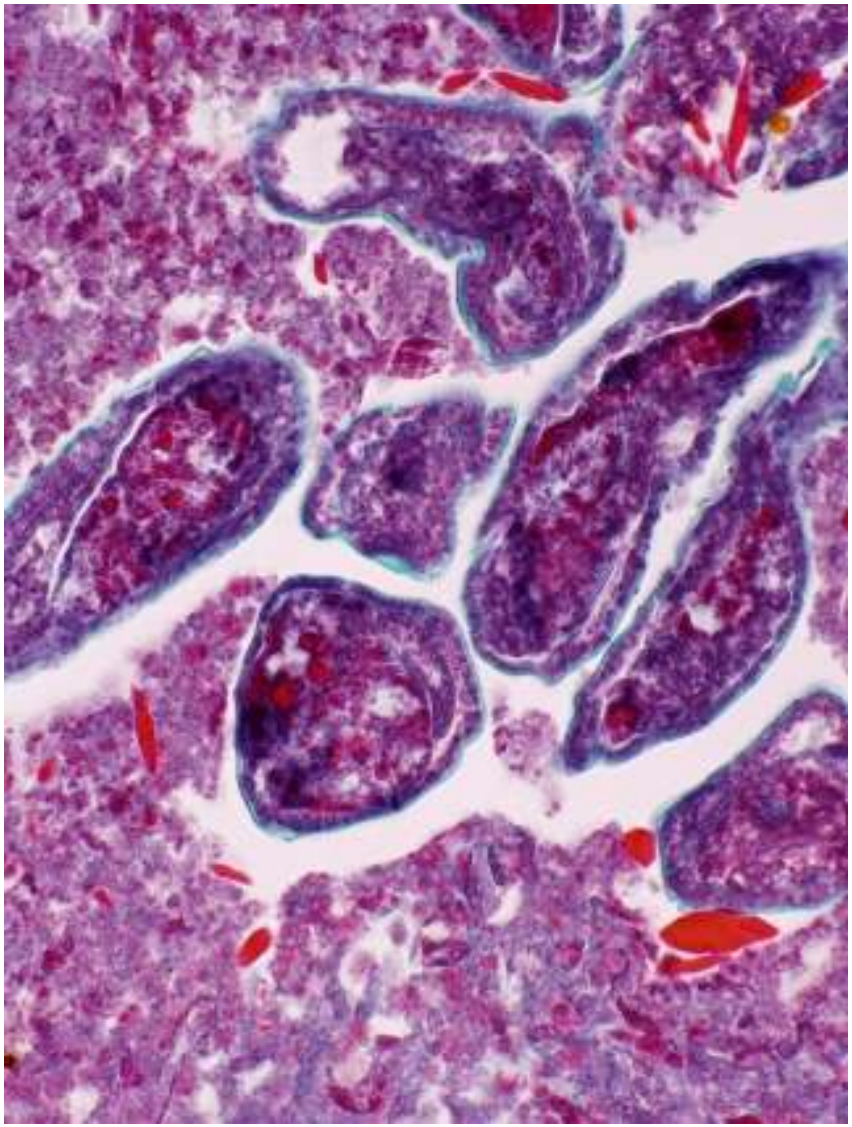
- Amoebic abscess 14
- Fungal abscess 3

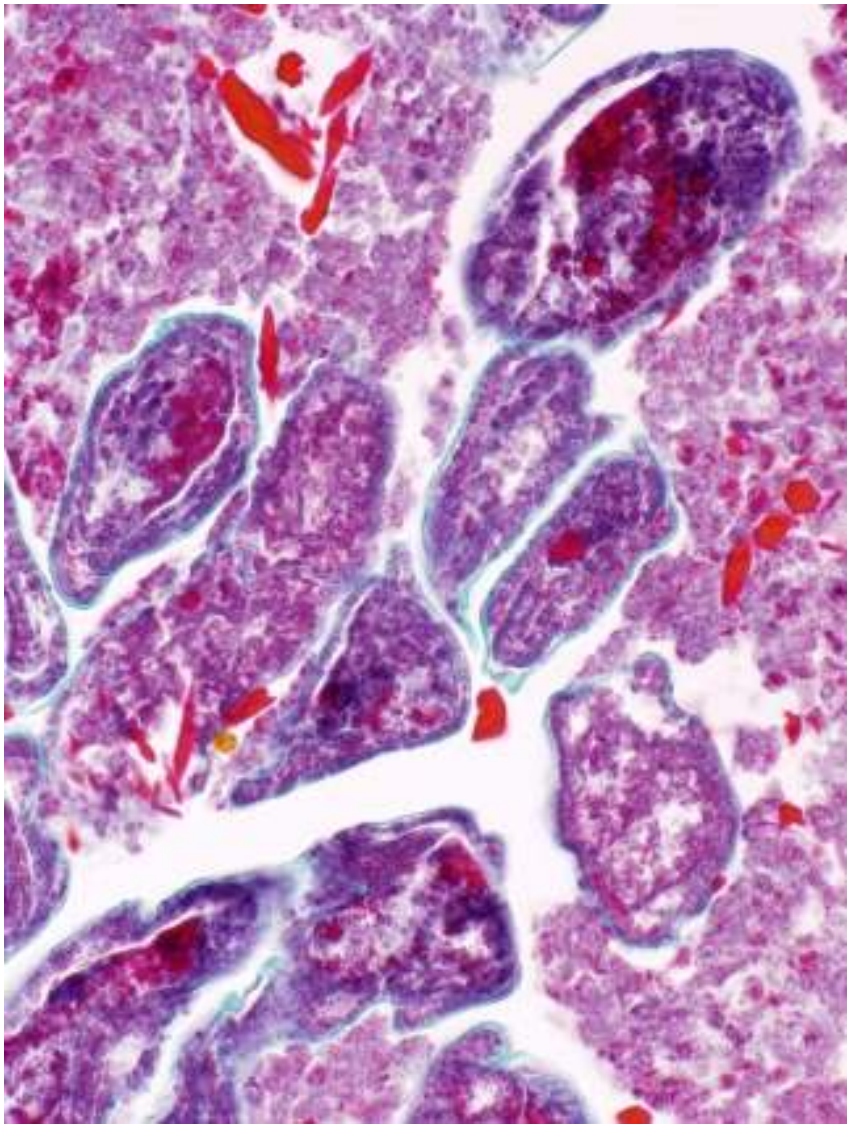
- Worm
  - Hydatid 9
  - Enterobius 7
  - Schistosomiasis 4
  - Onchocerca 1
  - Fasciola 1
  - Dicrocoelium 1

Liver resection

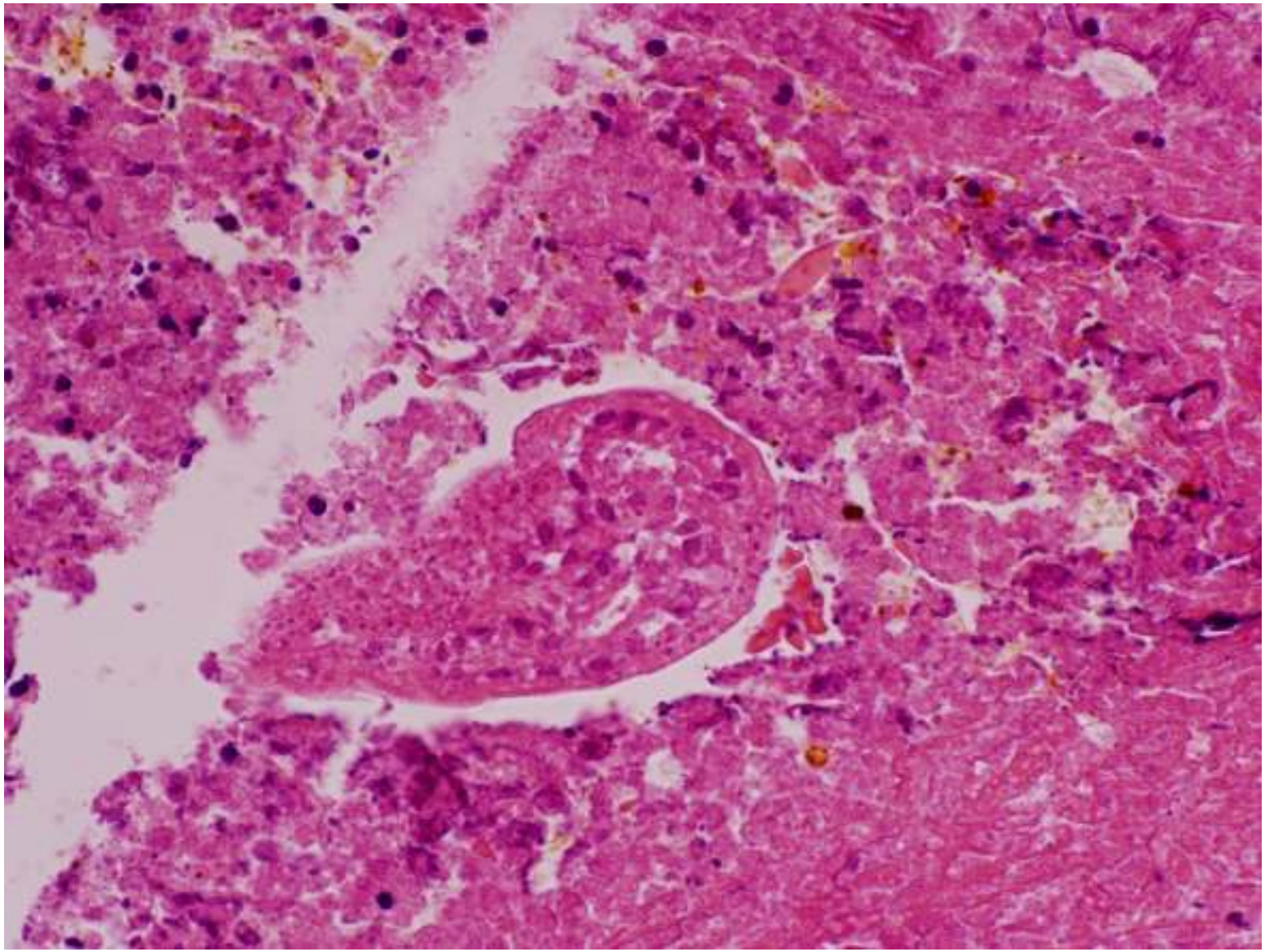


Liver resection – necrotic worm

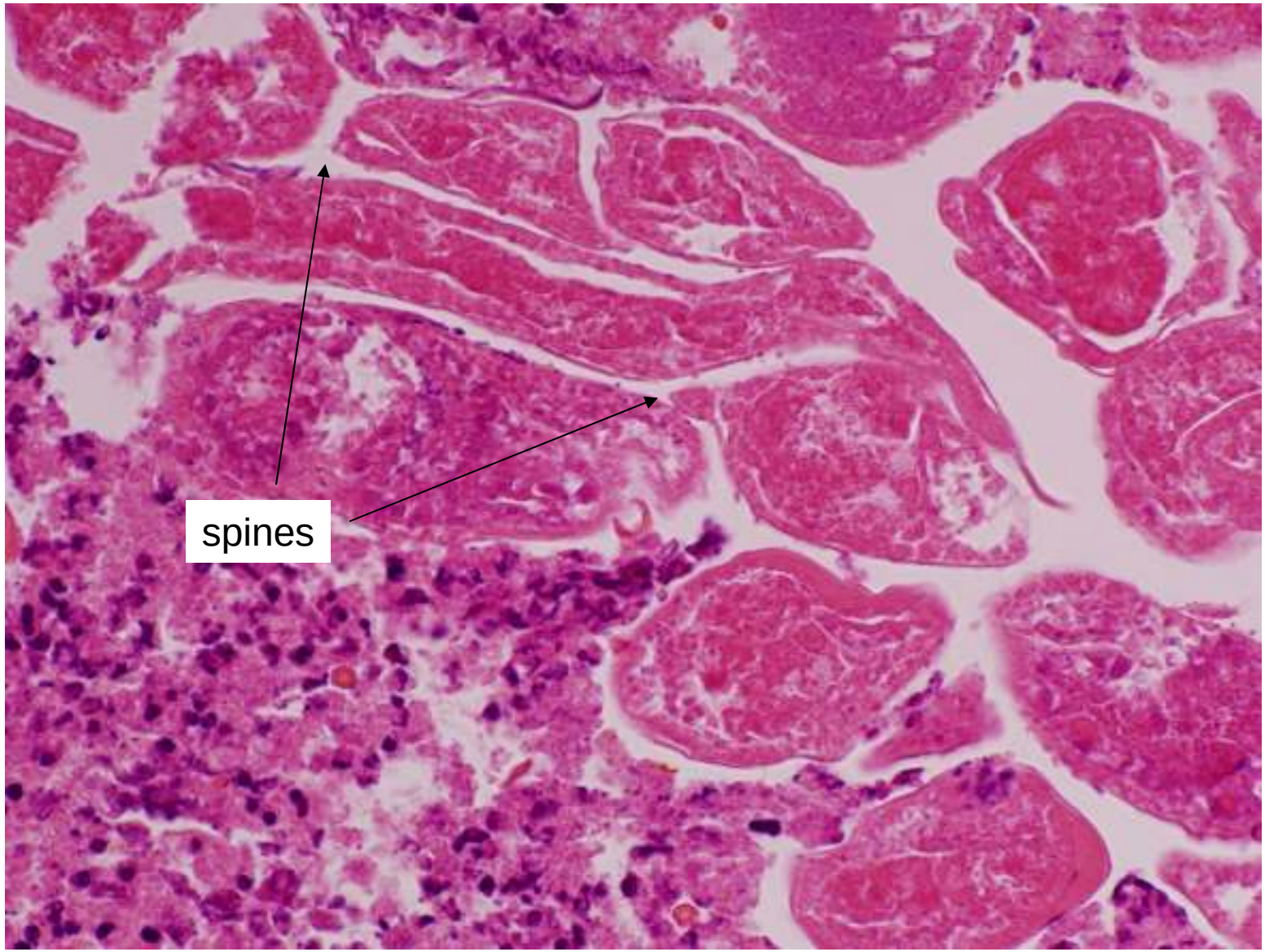




Liver resection - ?testis

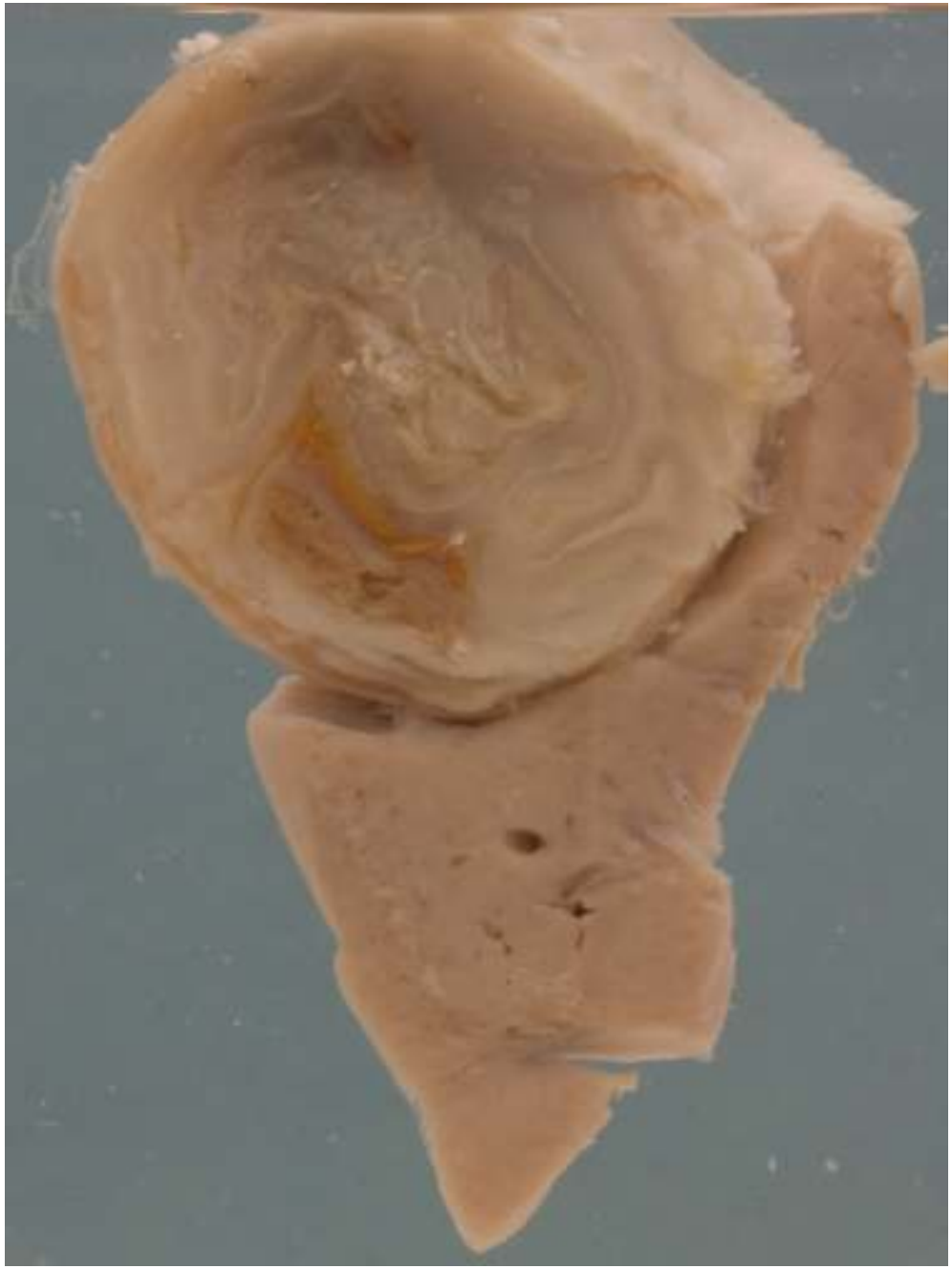


Liver resection

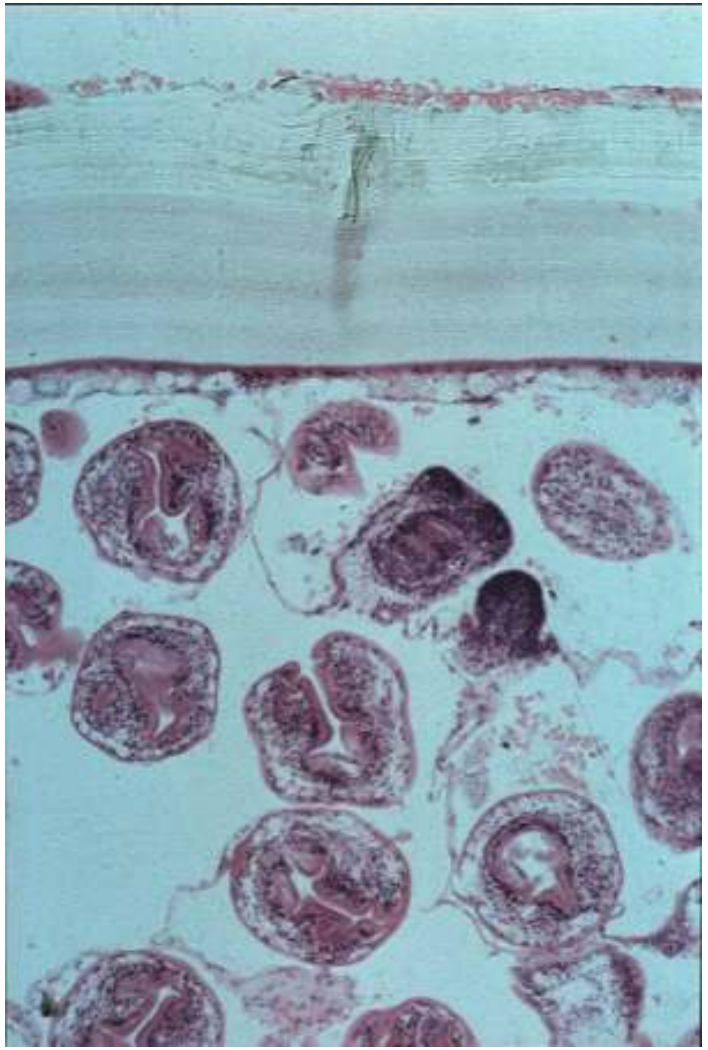


Case 2

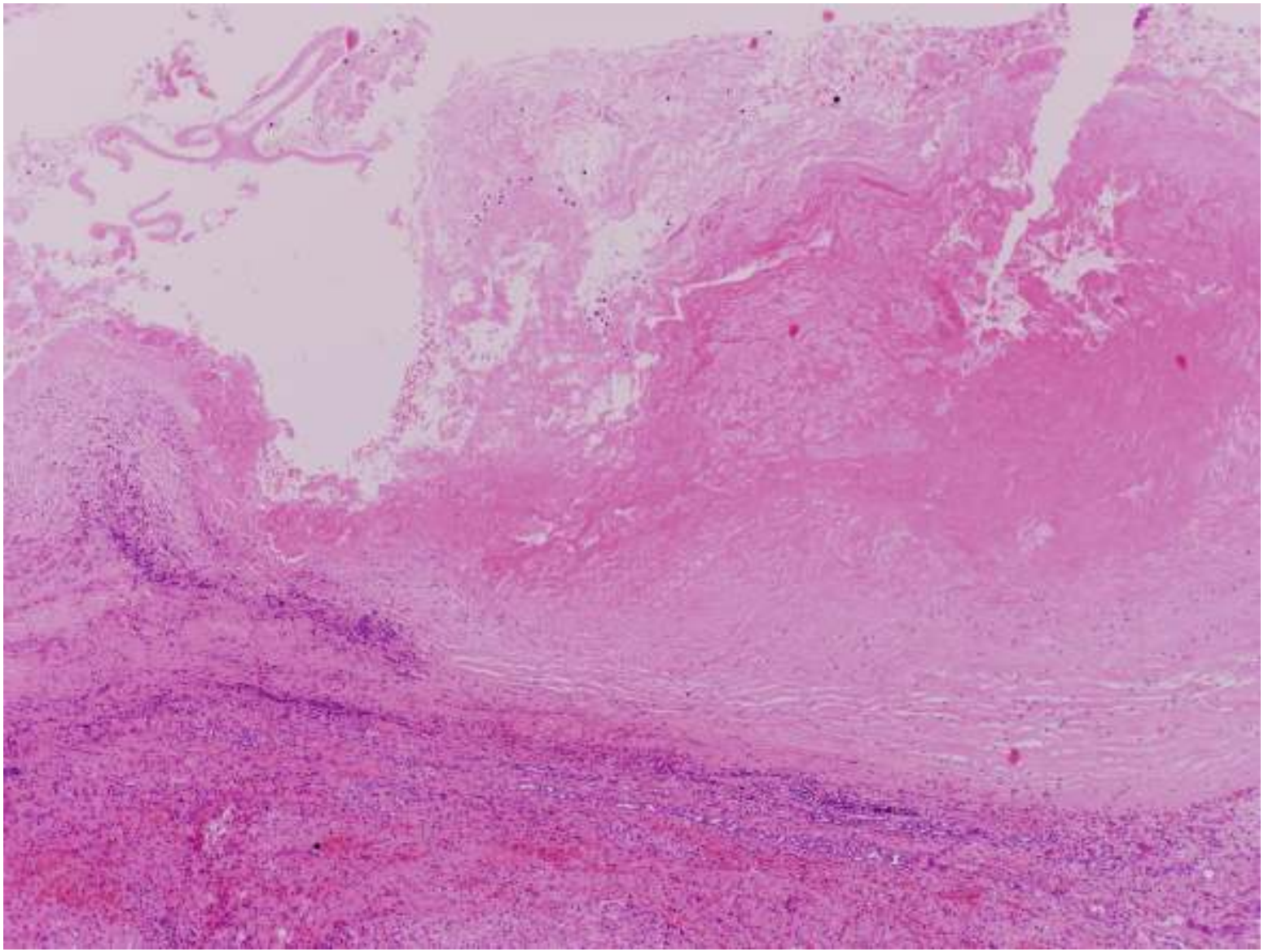
- Parasites most often seen in liver
  - Hydatid cyst
  - Schistosomiasis
  - *Enterobius vermicularis* (pinworm)
  - Visceral larva migrans
  - *Fasciola hepatica*
  - *Clonorchis sinensis*



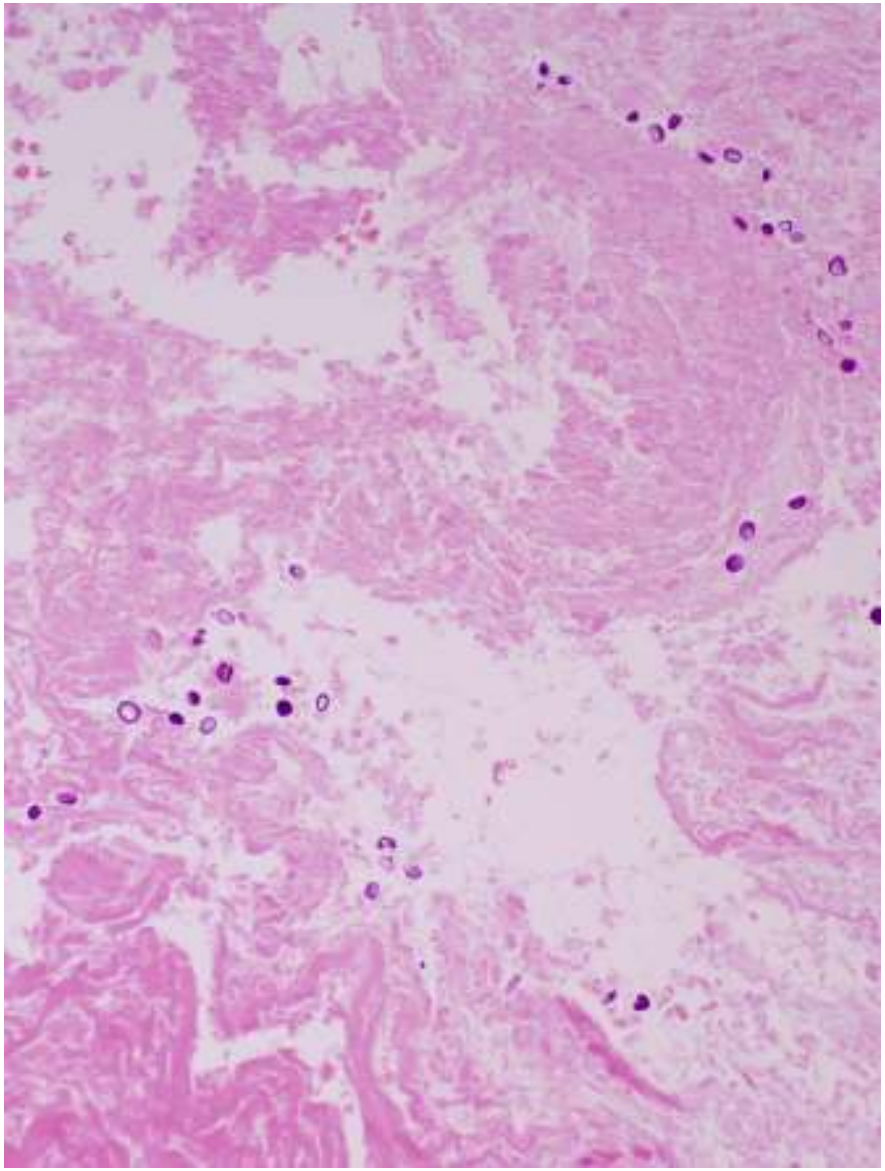
Hydatid cyst

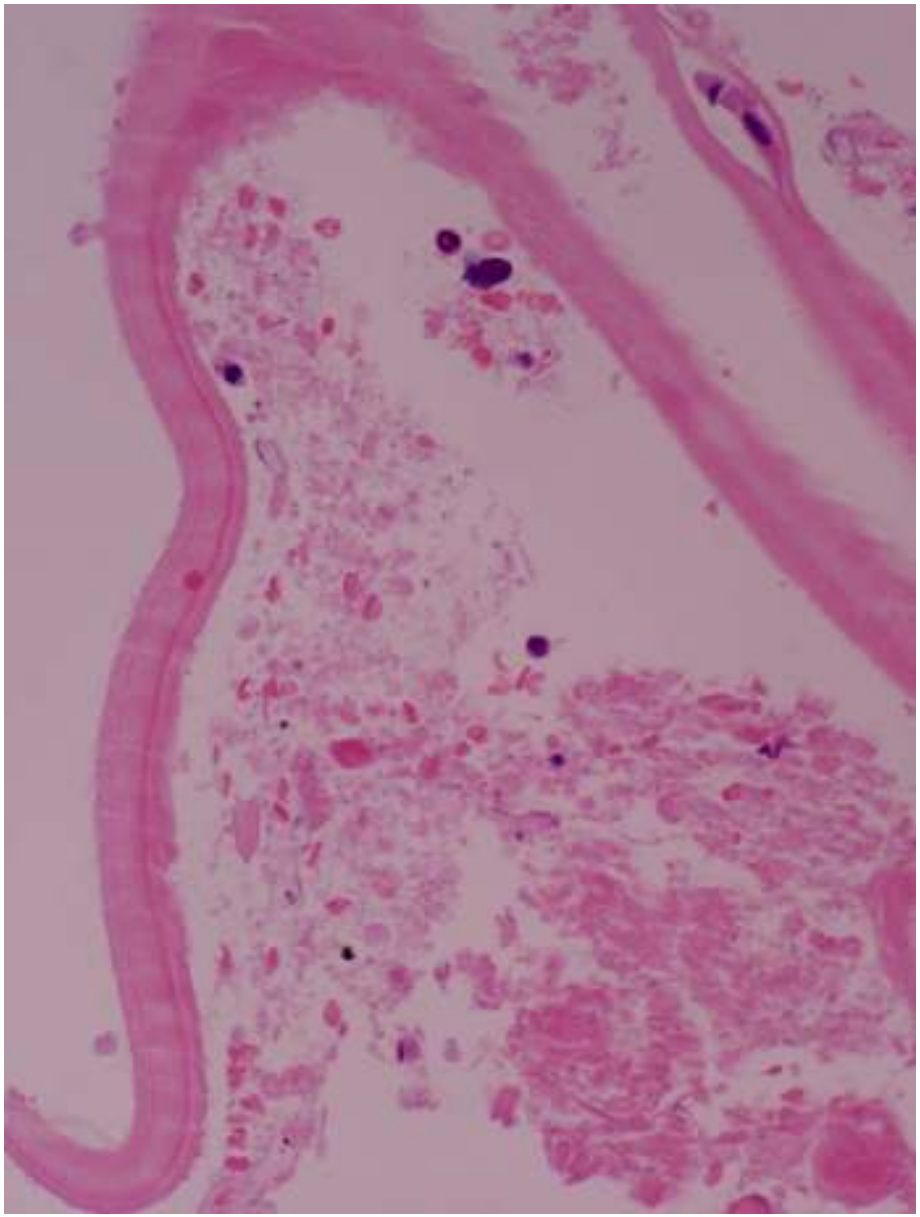


Old hydatid cyst in liver



Calcareous corpuscles & laminated membrane





Observations

- PRESENT
- Worm fragments
  - Not scolices
- ?testis present
- Small cuticle spines

- ABSENT
- Laminated hydatid membrane
- Ova
- Small larvae
- Intestine visible
- Calcareous corpuscles (cestode)

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  - Visceral larva migrans
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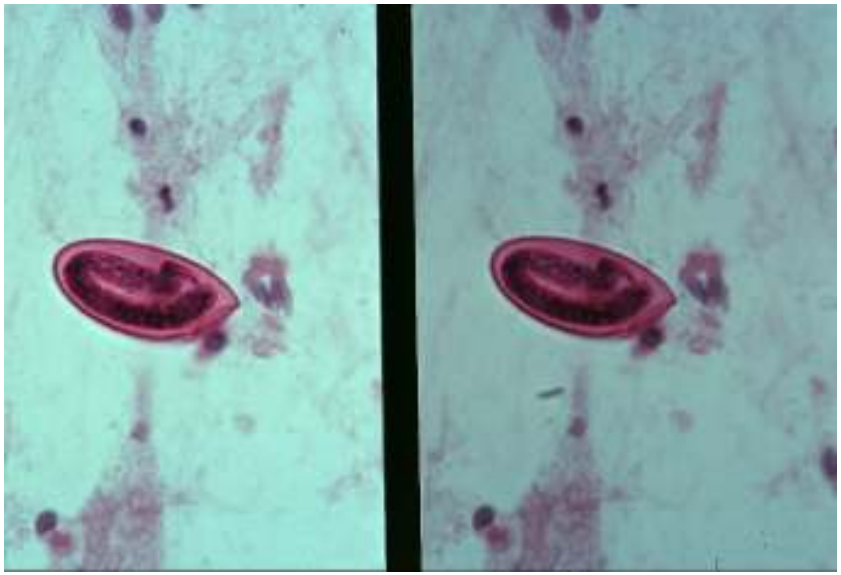
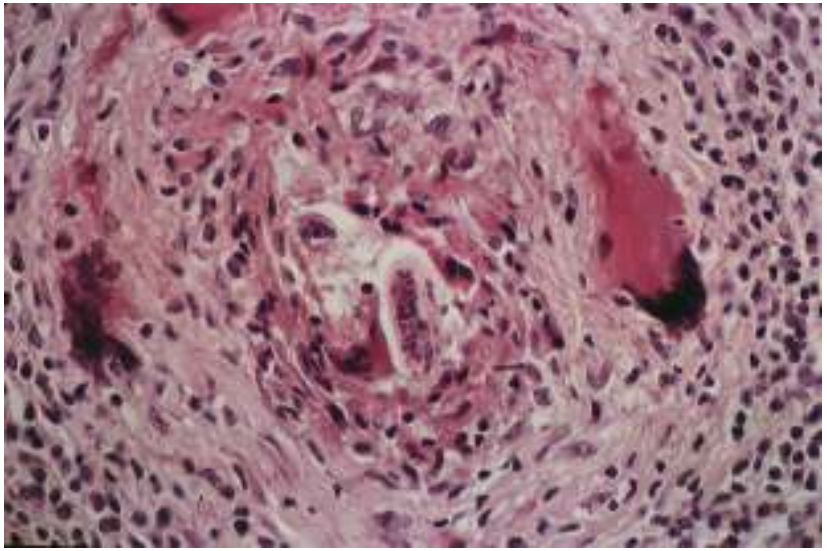
Enterobius – simulating a liver metastasis

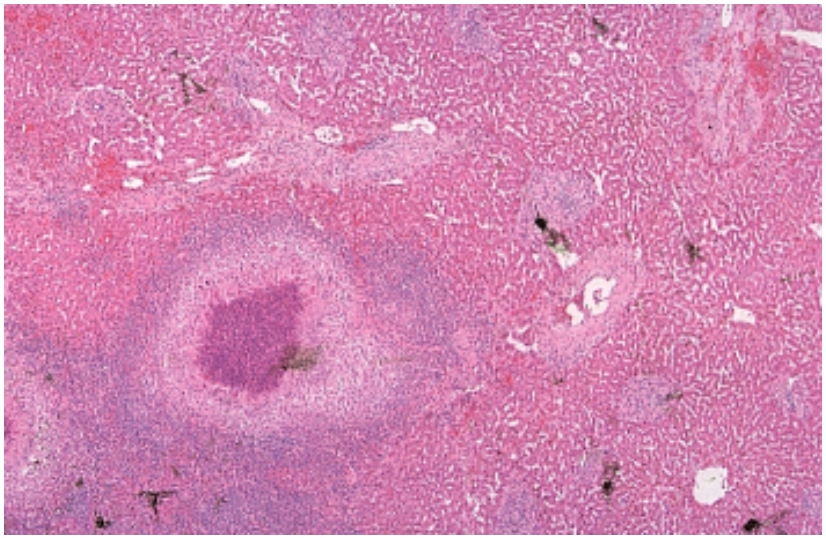
Enterobius vermicularis

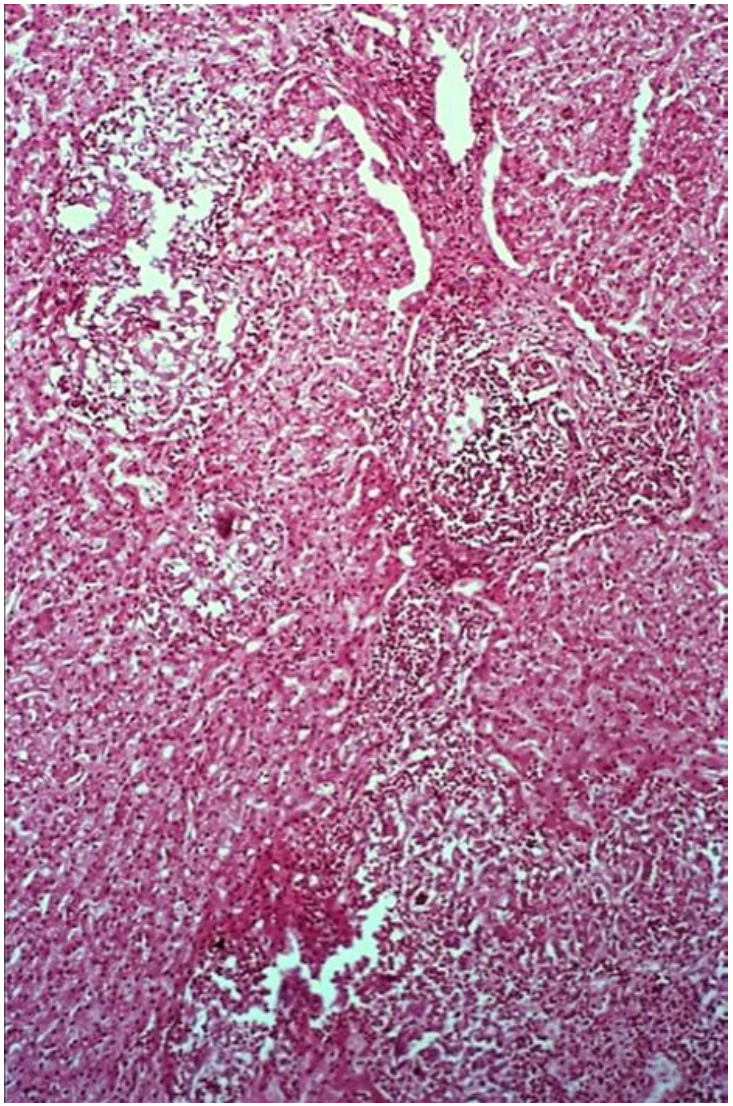


Visceral larva migrans

Toxocara canis

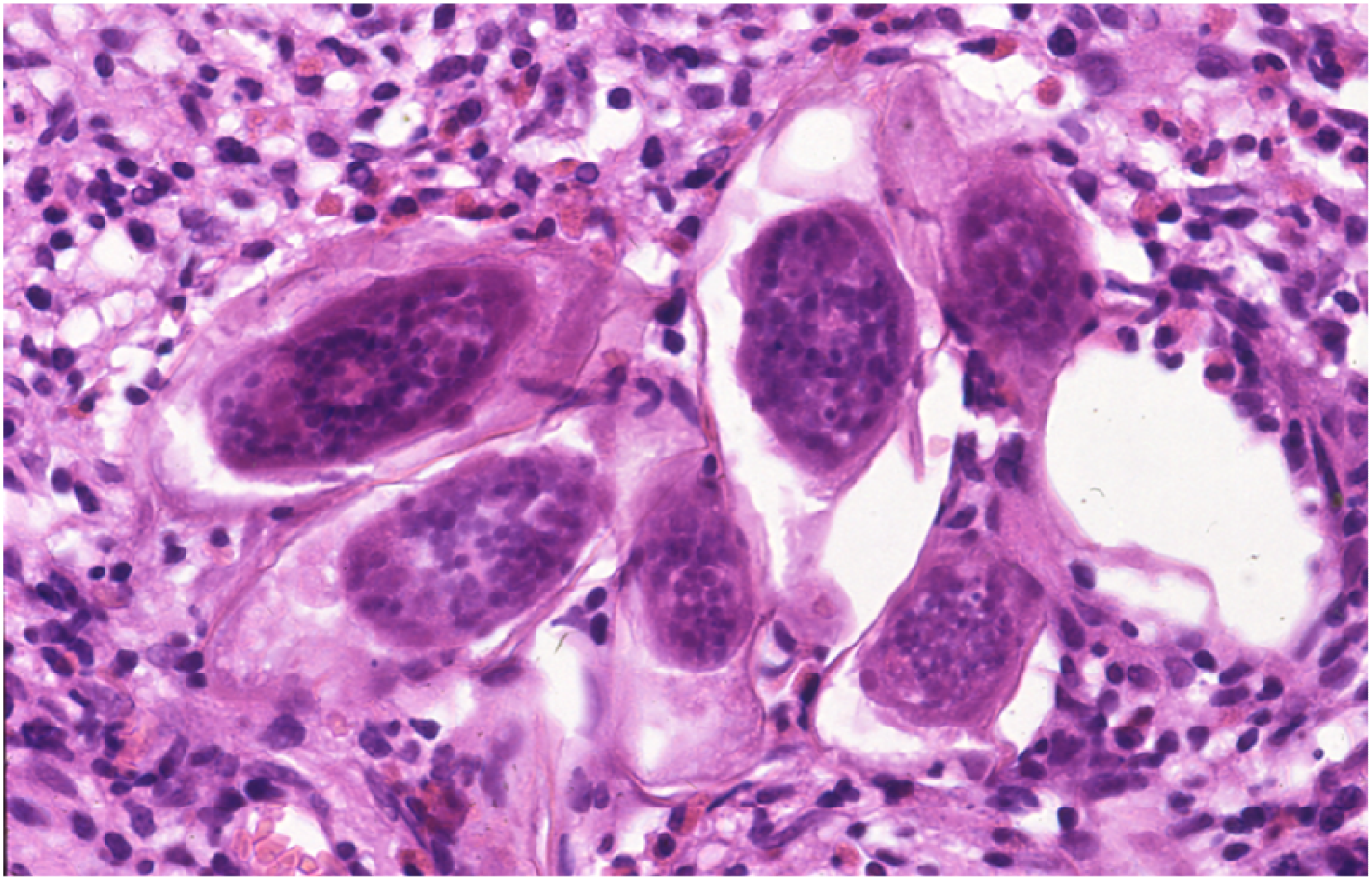




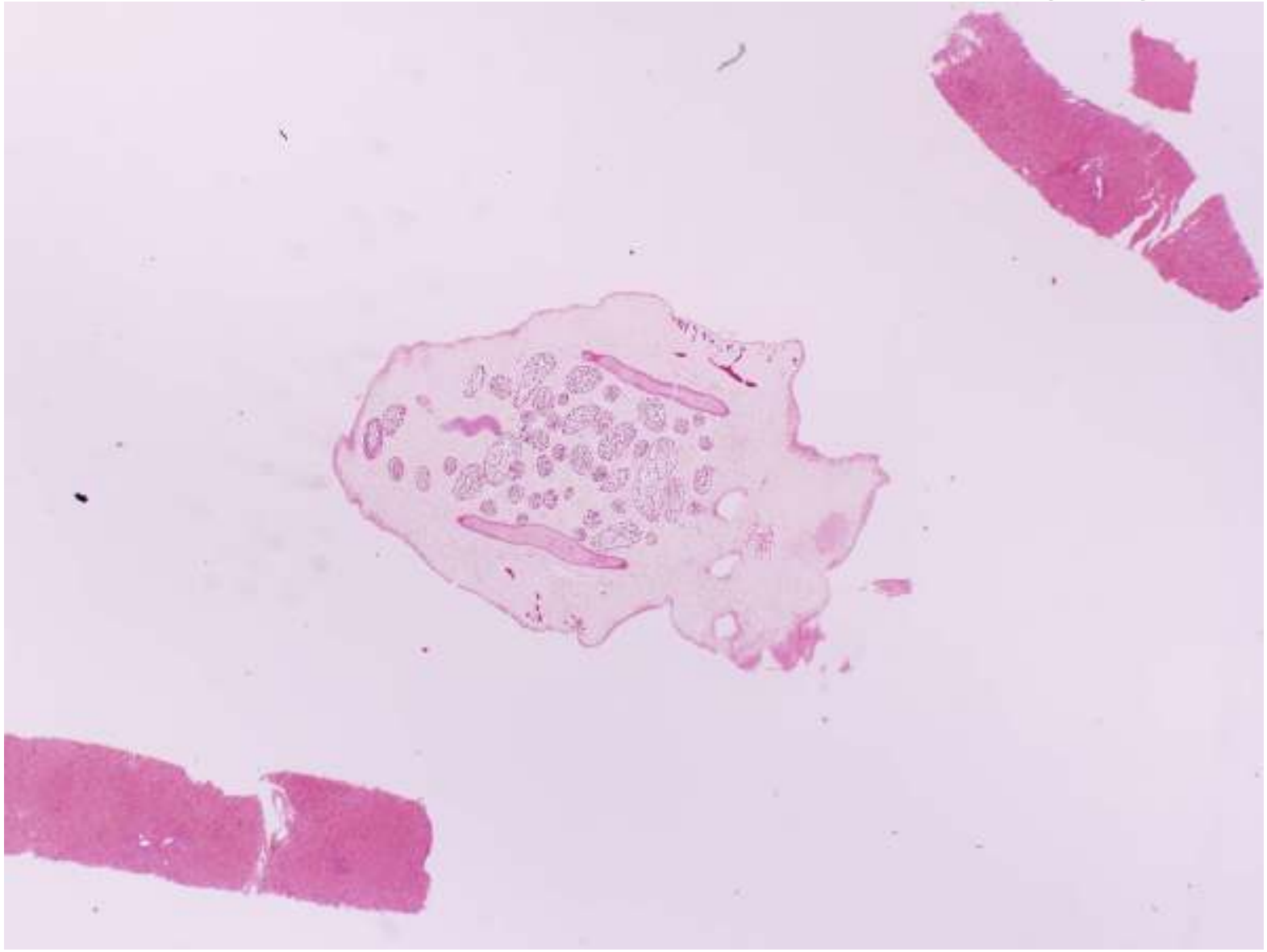


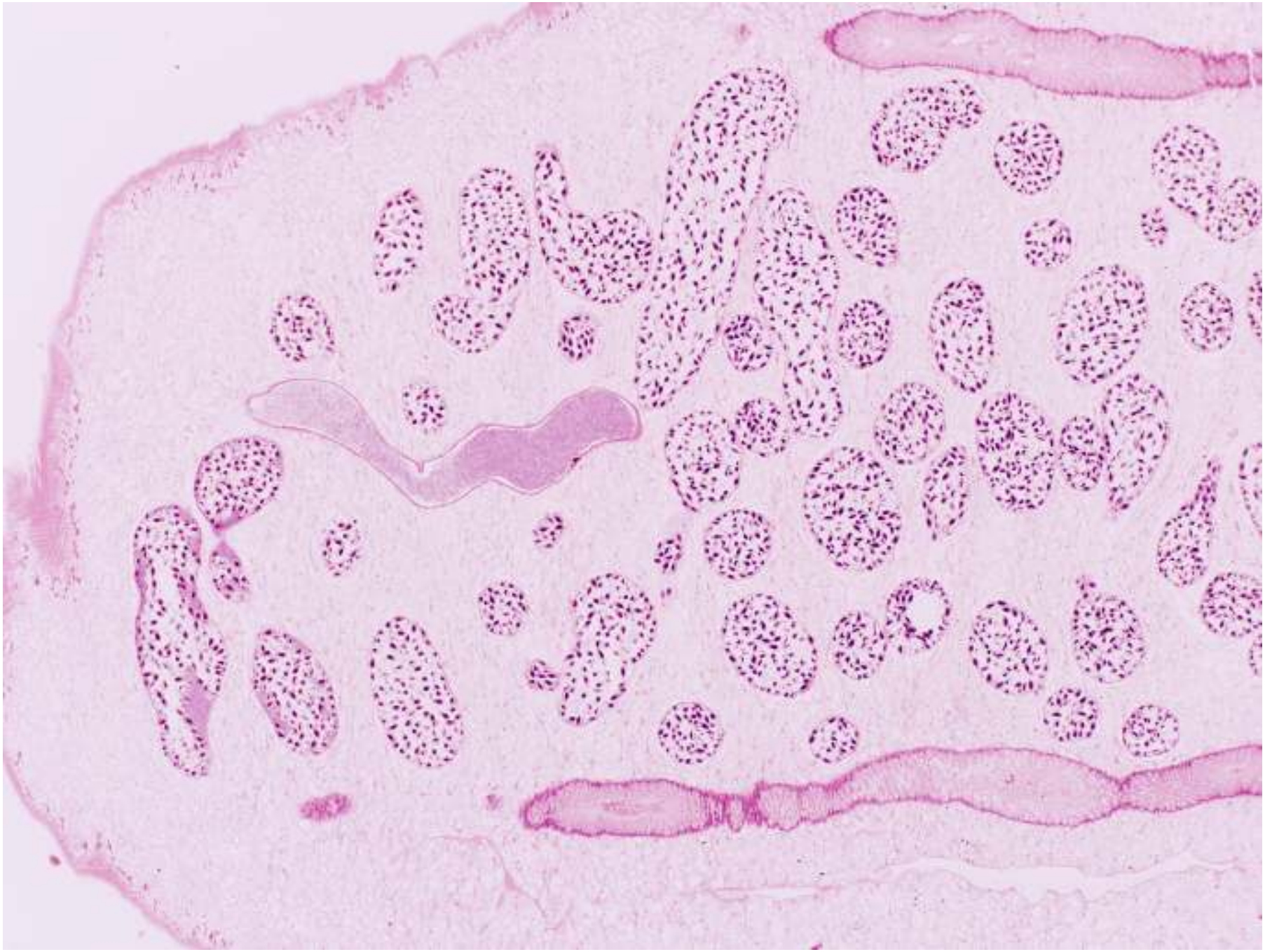
Schistosome pair in a liver biopsy

Schistosome eggs



Clonorchis in a liver biopsy





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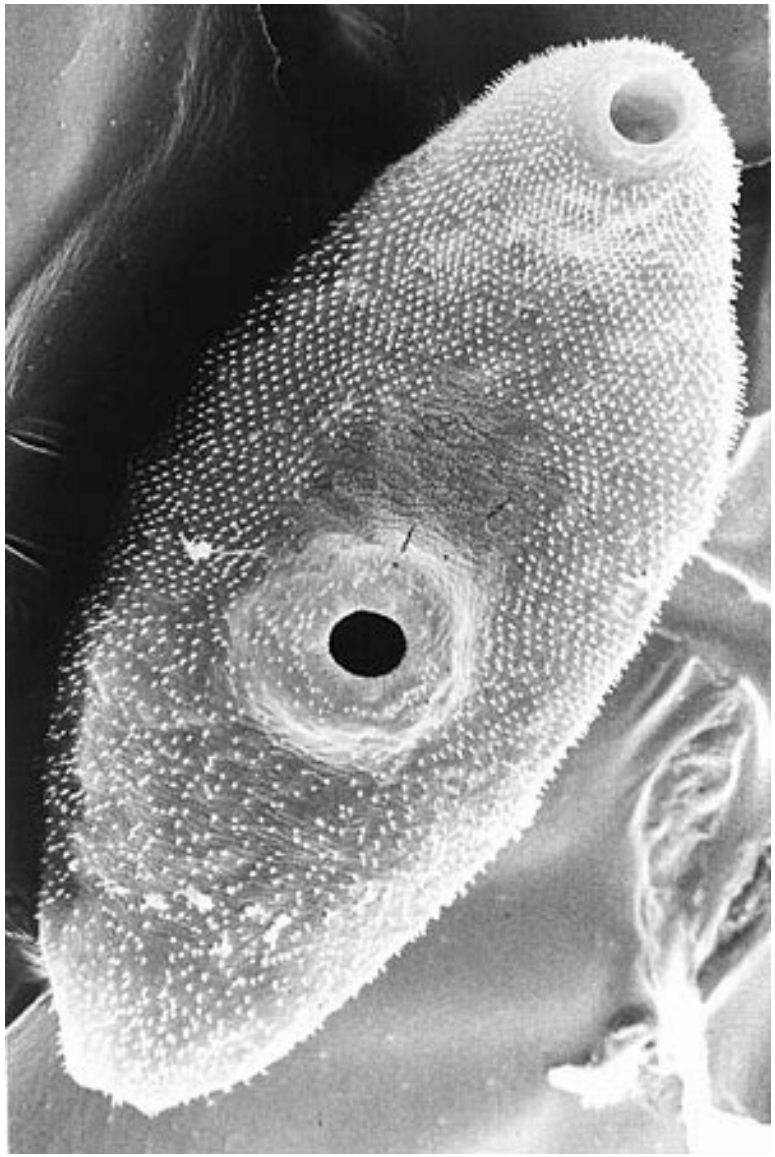
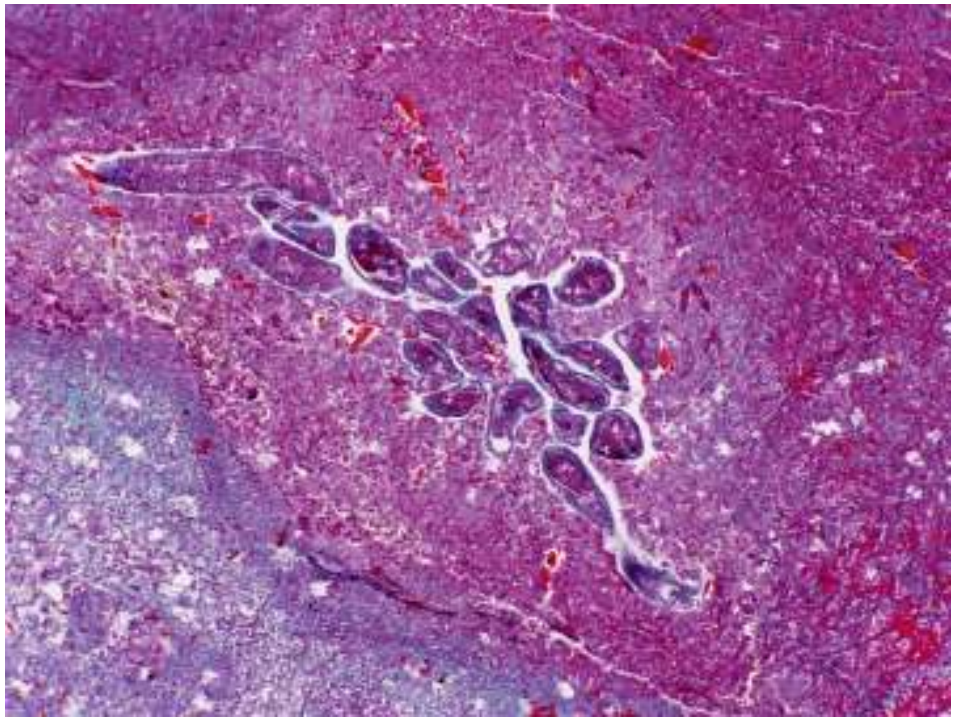
  - *Clonorchis sinensis*

Fasciola hepatica

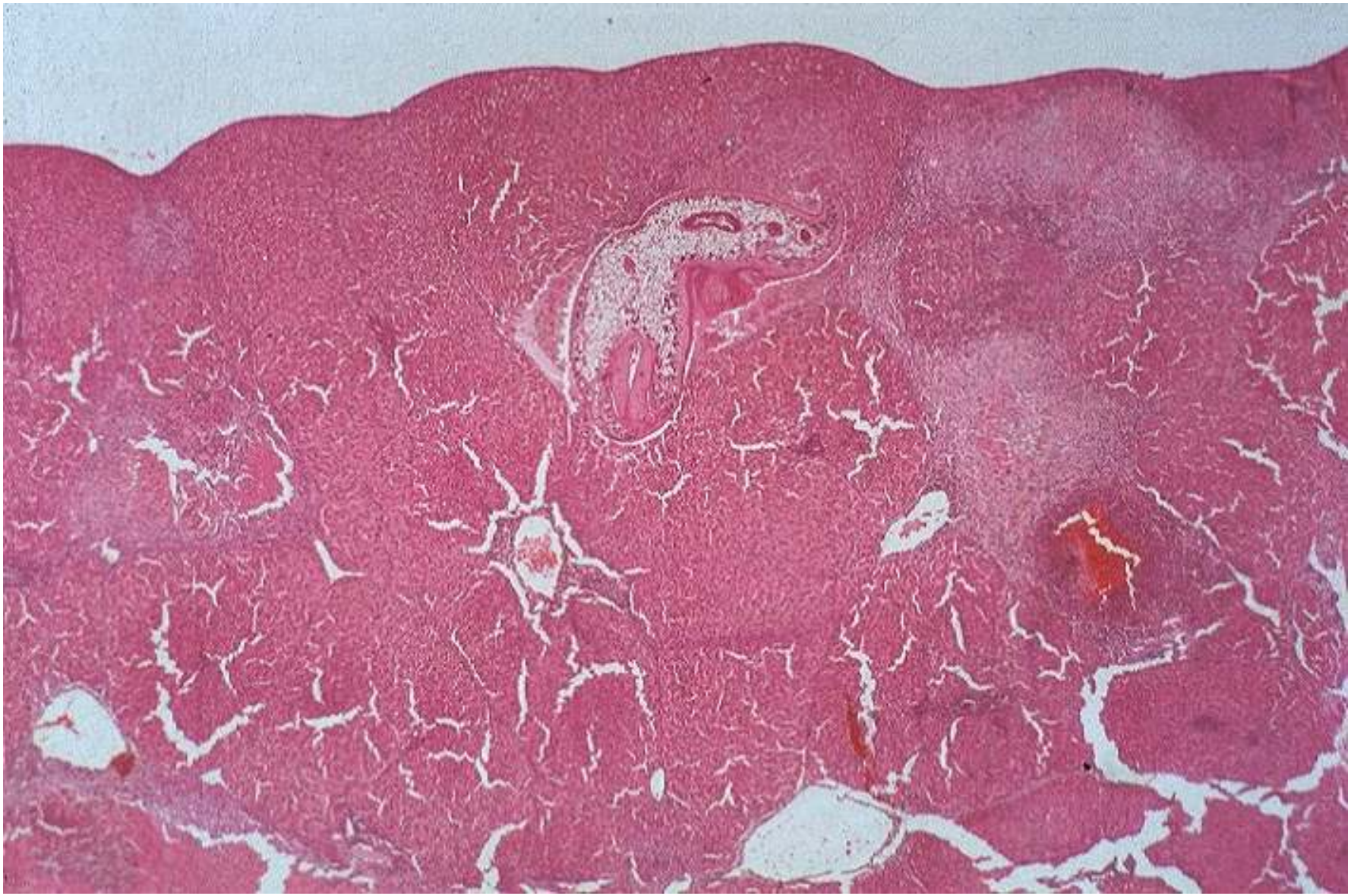


- Patient had never left England

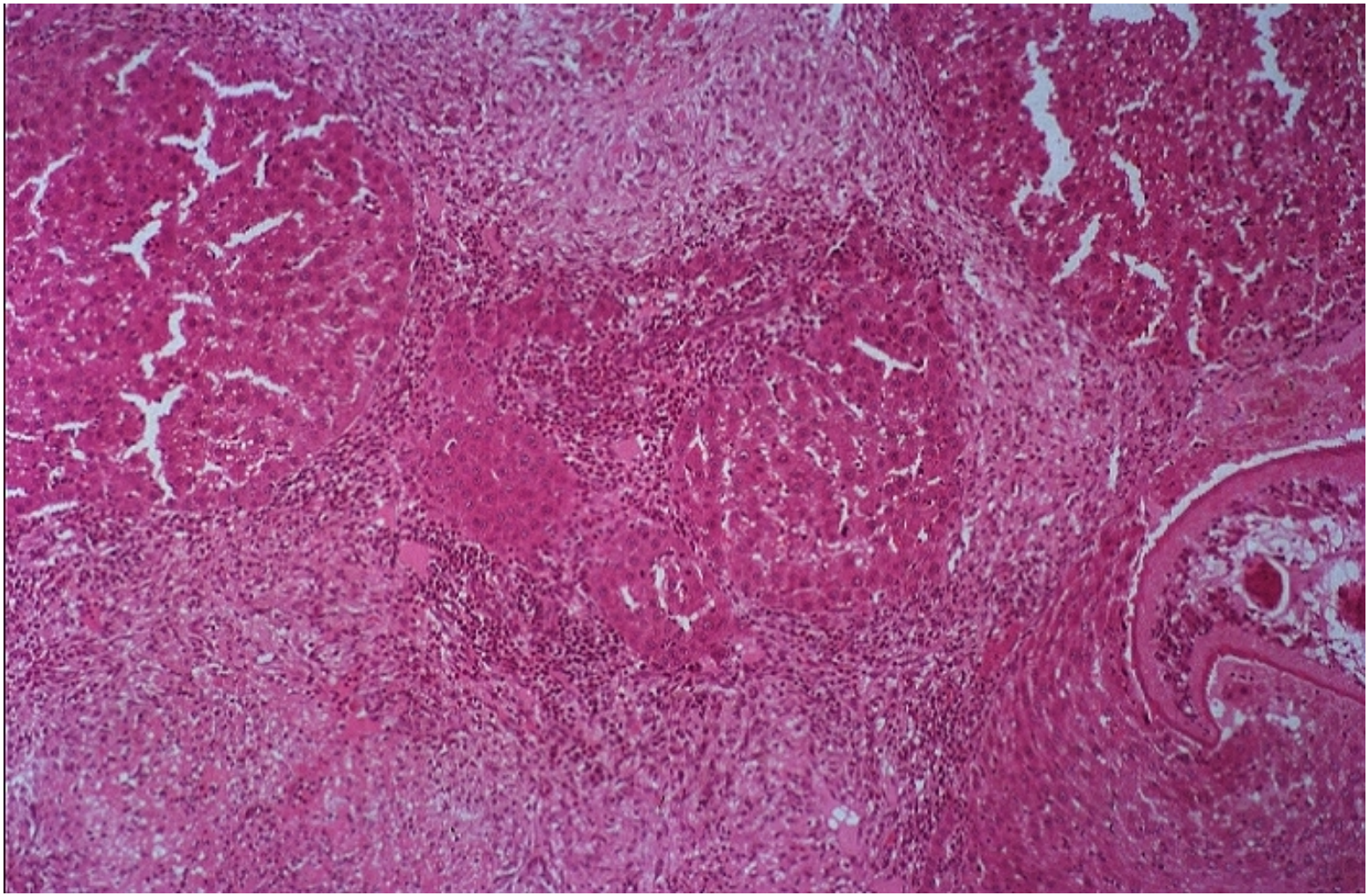


Fasciola hepatica

Fasciola invading liver



Fasciola



Serology

Hydatid –ve

Fasciola –ve

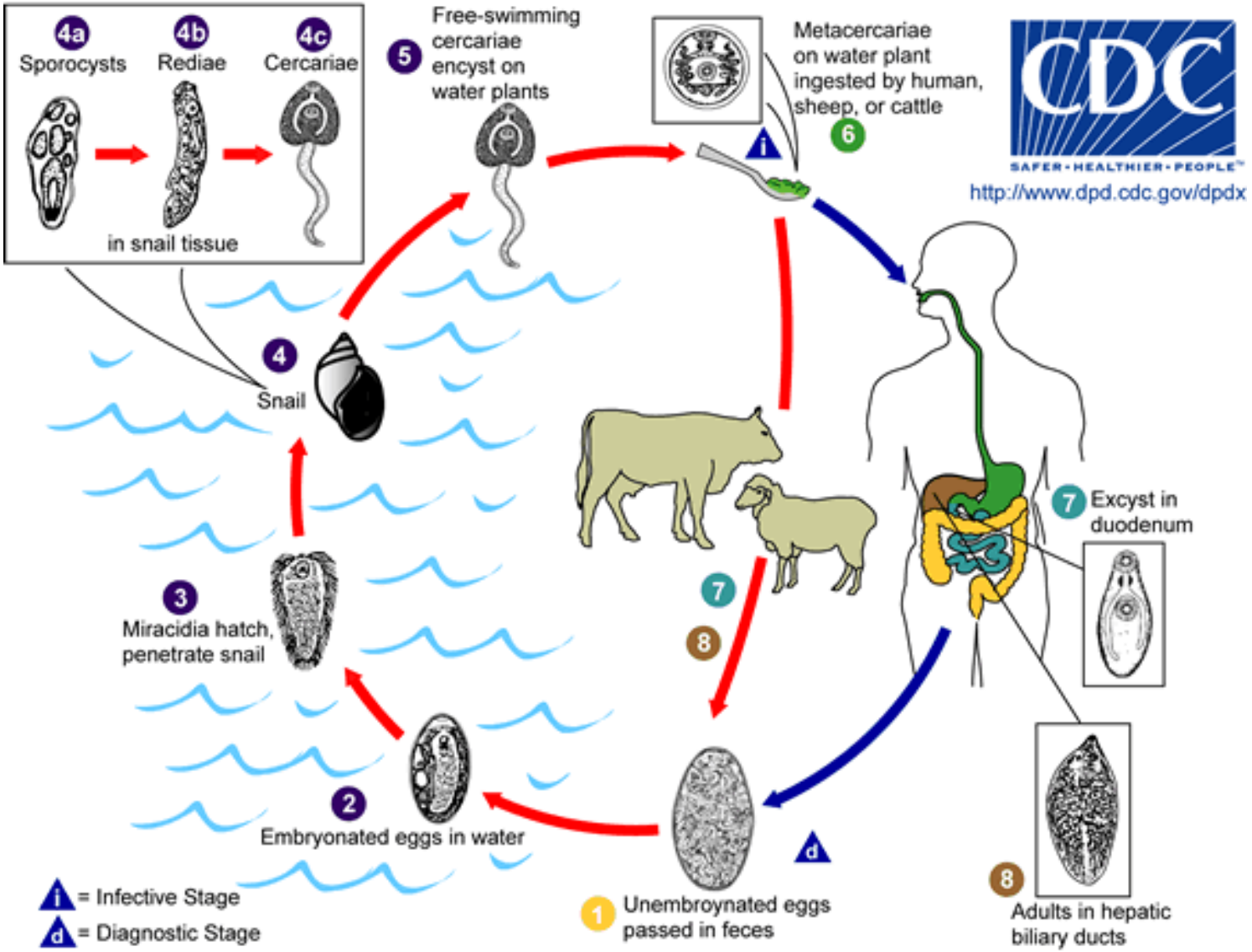
(but may be negative if infection is dead)

Our diagnosis

[Swiss vet pathologist agreed]

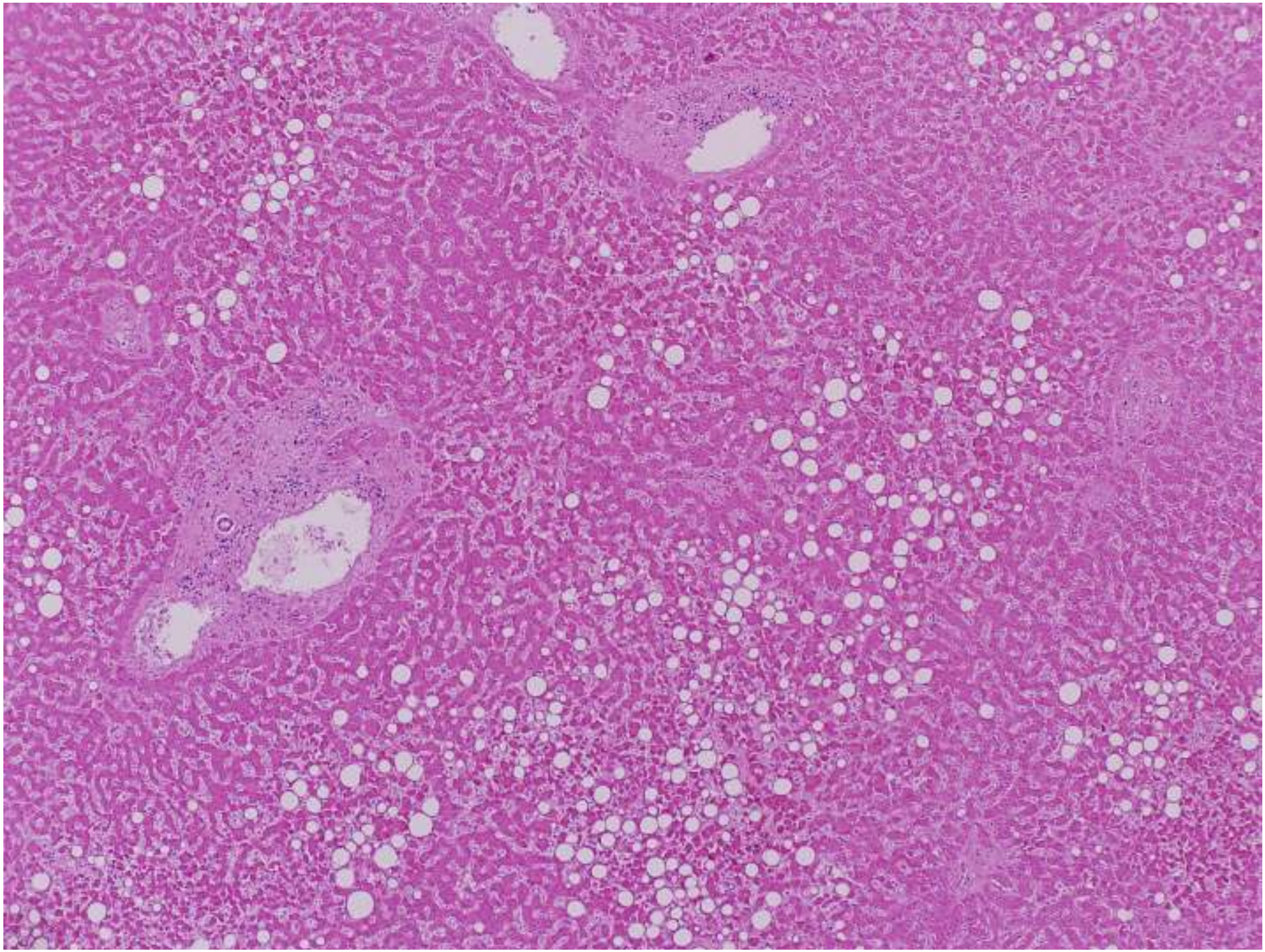
Degenerate *Fasciola hepatica* worm

Life cycle of *Fasciola hepatica*



Case 3

Dangers of exotic holidays



Case 3

- Male 59 years
- British caucasian
- No previous travel history

- Jamaica 2-week holiday
- In second week, felt unwell
- One week after return, very ill

Case 3

- On admission
- Renal failure
- Liver failure
  - Bilirubin up to 448

- Diagnosis: septic shock
- Much serology, blood culture (all -ve)

Case 3

- Intensive Care
- Support for lungs, liver and kidney
- Antibiotics

- WBC rose to 25,000
- Diagnosis: ?chronic myelomonocytic leukaemia

Case 3

- Died one week after admission
- = 3 weeks after starting illness

- Tests results available
  - HIV, HAV, HBV, HCV – negative
- Awaited
  - dengue, yellow fever, CMV, EBV

Case 3

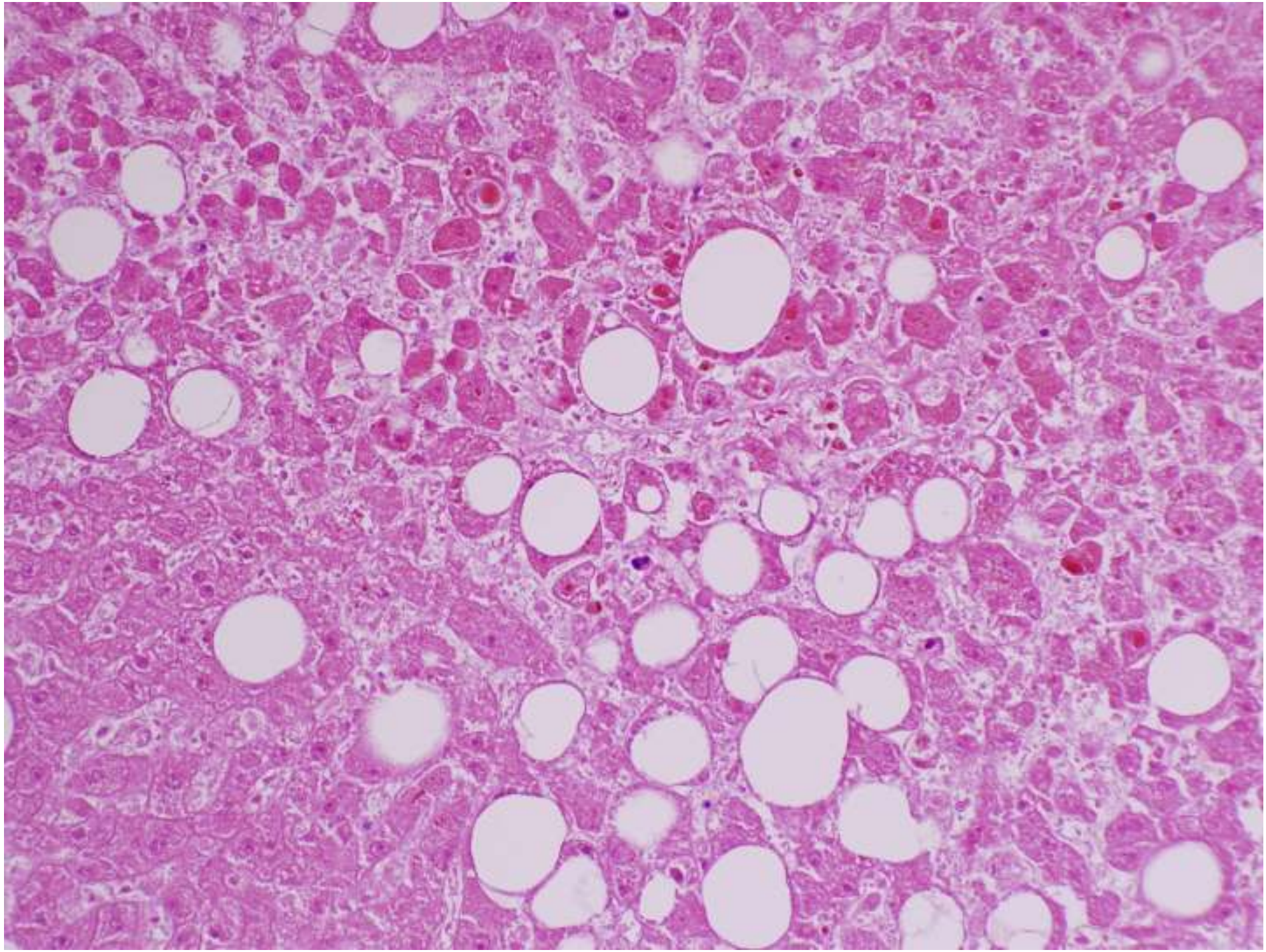
- Autopsy 5 days after death
  - Ht 198cm, Wt 94kg
- Jaundice & oedema
- Petechiae around skin punctures

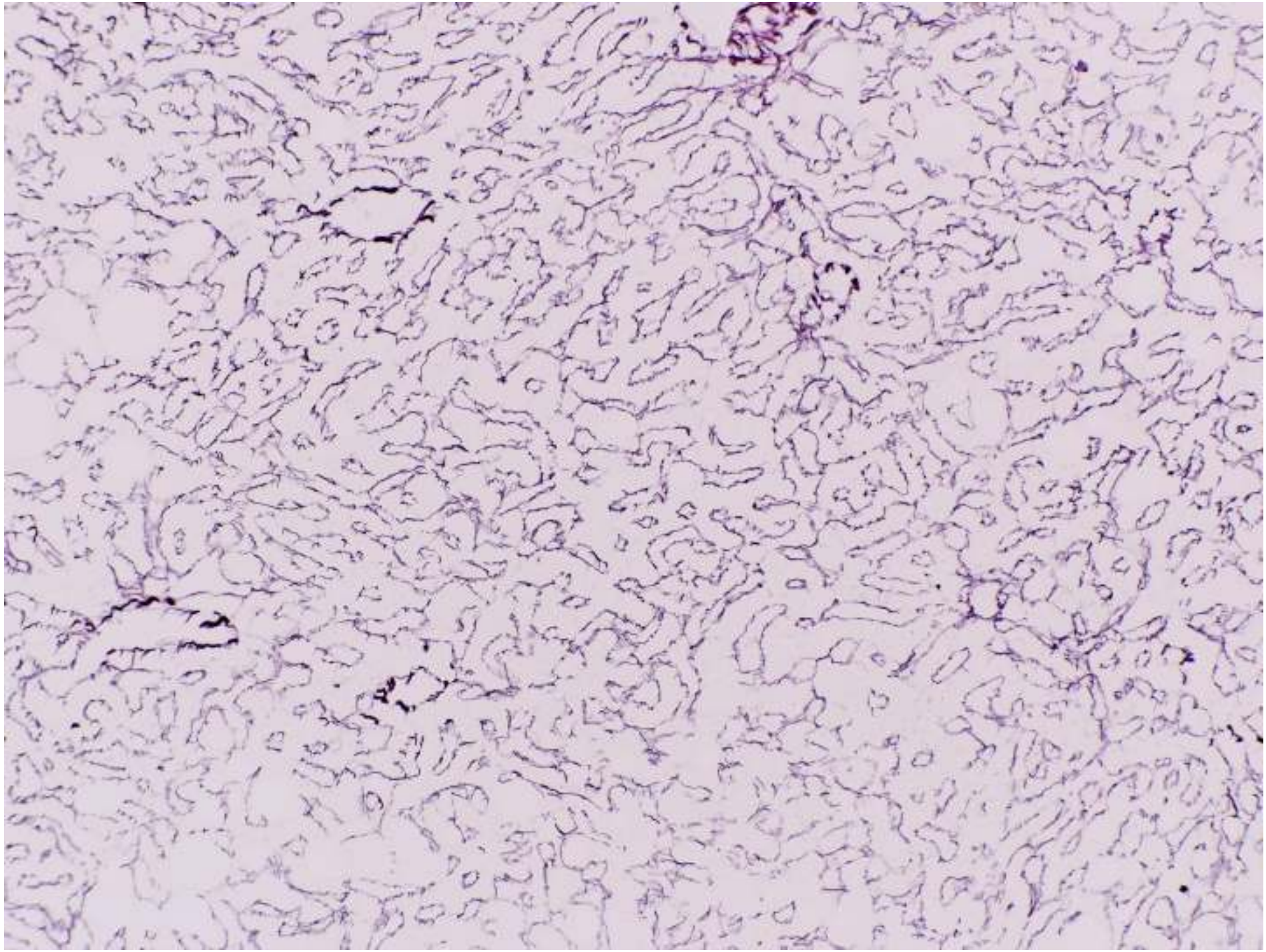
- Lungs – solid and red – ARDS
- Kidneys: 245 & 310gm – enlarged, soft, yellow, petechiae++
- Spleen 430gm - soft

Case 3

- Liver 1840gm
- Soft, yellow, not cirrhotic, no haemorrhages, no focal lesions, possibly collapsing

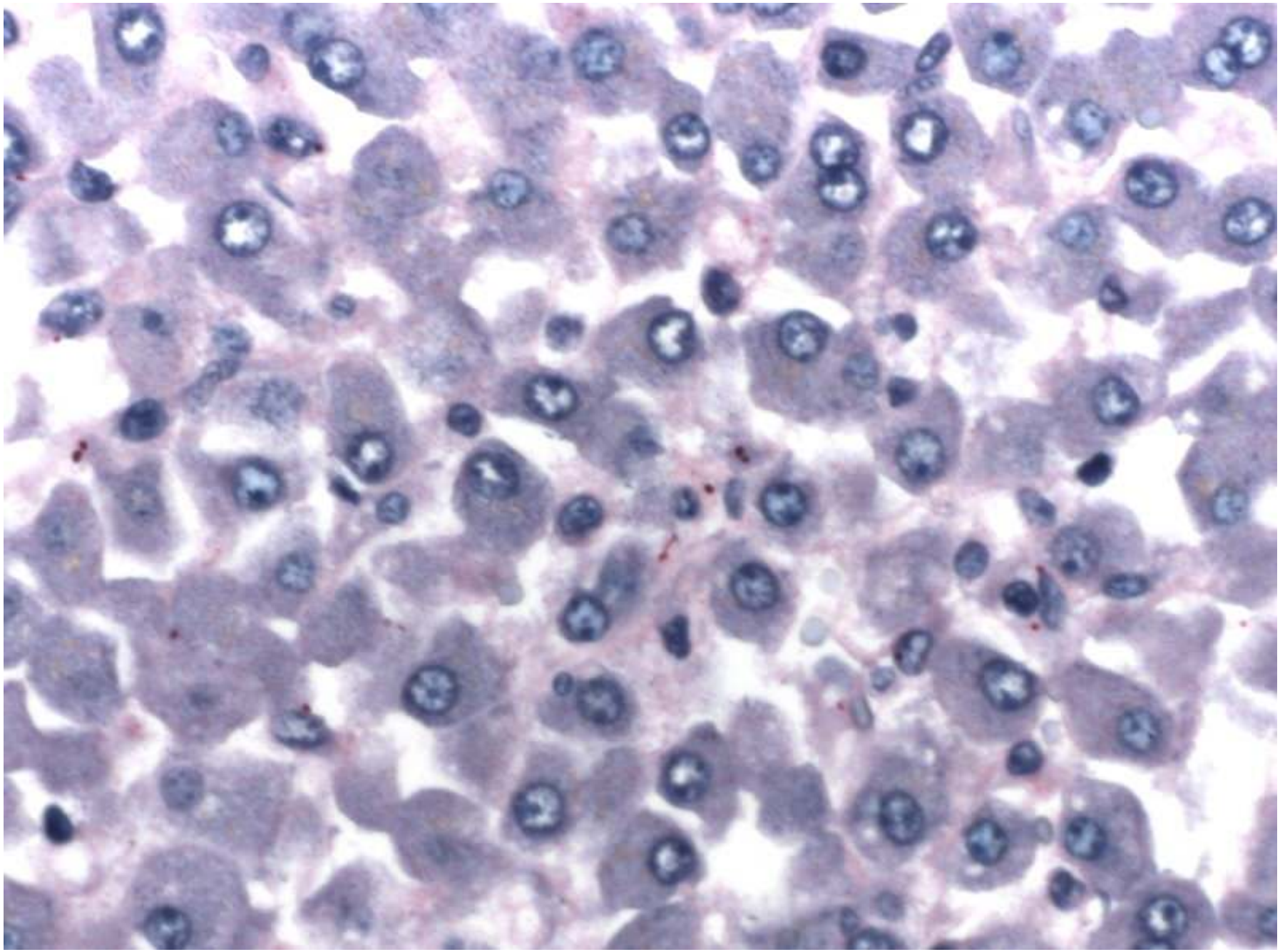
- Bile duct & gall bladder - normal





Case 3

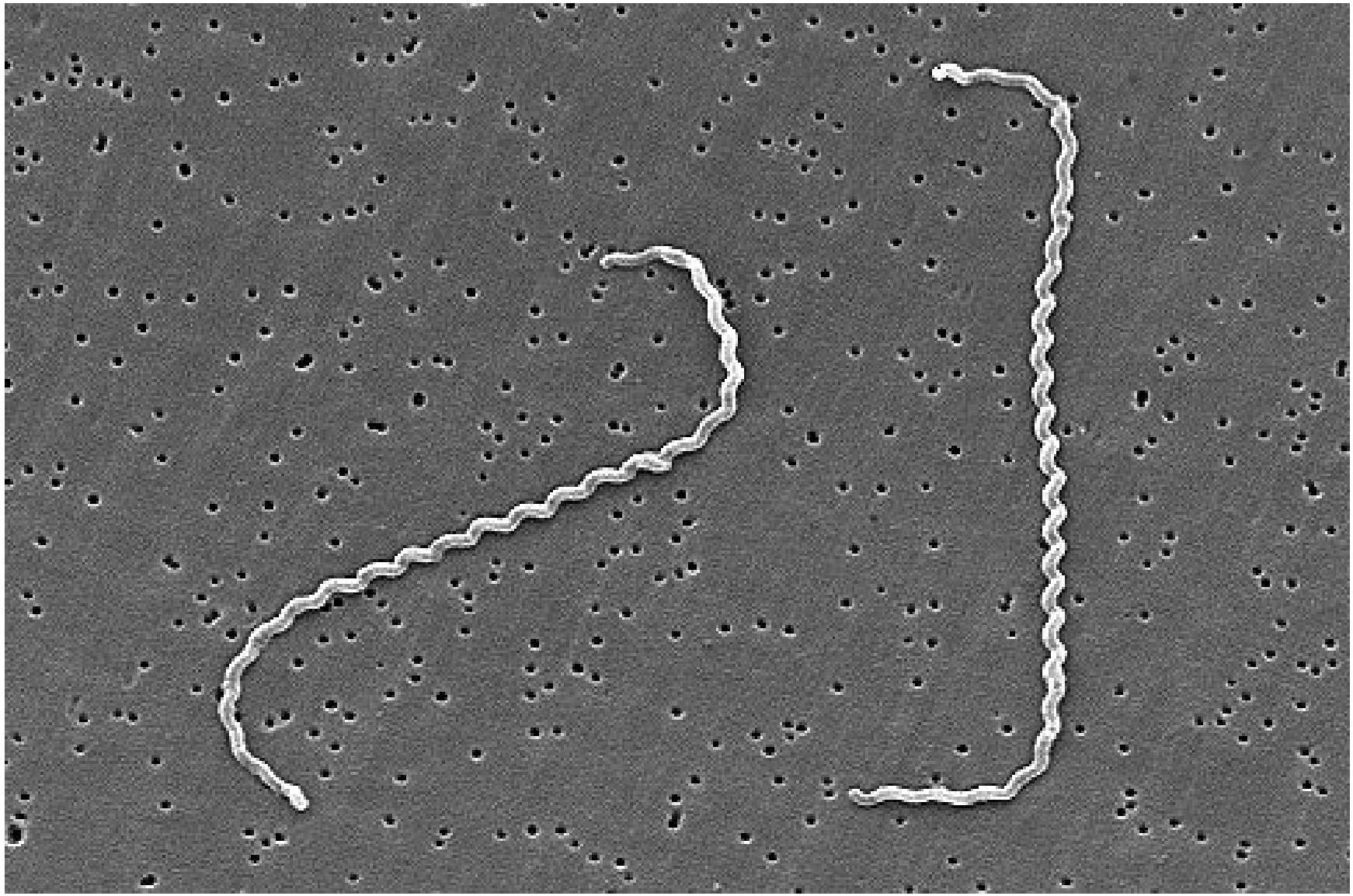
- Autopsy liver tissue and pre-mortem blood
- *Leptospira interrogans* DNA
  - (Micropathology Lab, Coventry, UK)
- IHC for *Leptospira* spp
  - Dr Sherif Zaki, CDC, Atlanta, USA



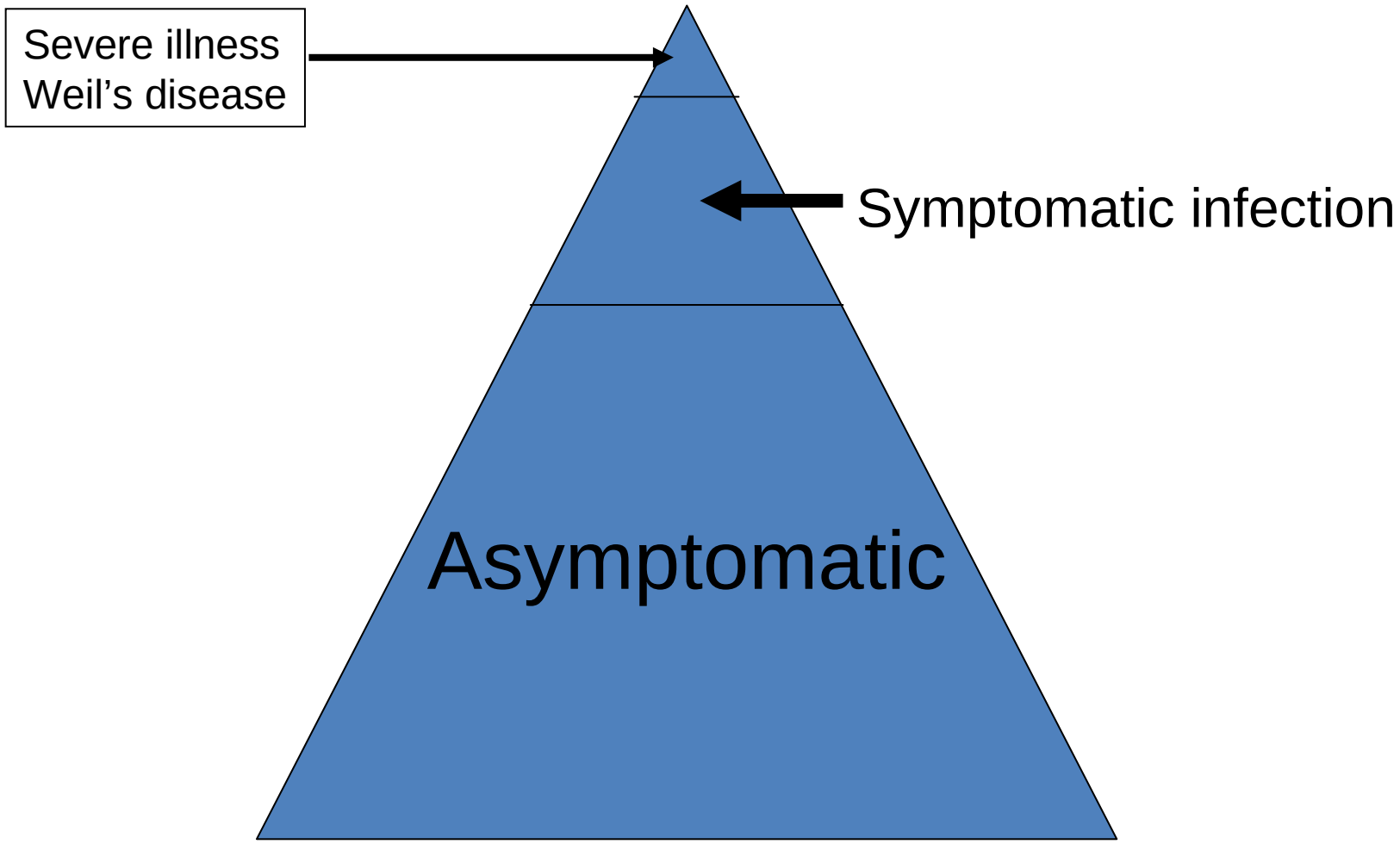
Leptospira taxonomy: determined by DNA reassociation 13 named species

Species	Selected serovars
L.interrogans	Icterohaemorrhagiae, Copenhageni, Australis, Caniola, etc
L.noguchi	Panama, Pomona
L.borgpetersenii	Ballum, Hardjo, Javanica
L.germospecies 1	Sichuan
L.germospecies 2-4	Non-pathogens
L.biflexa	Non-pathogens

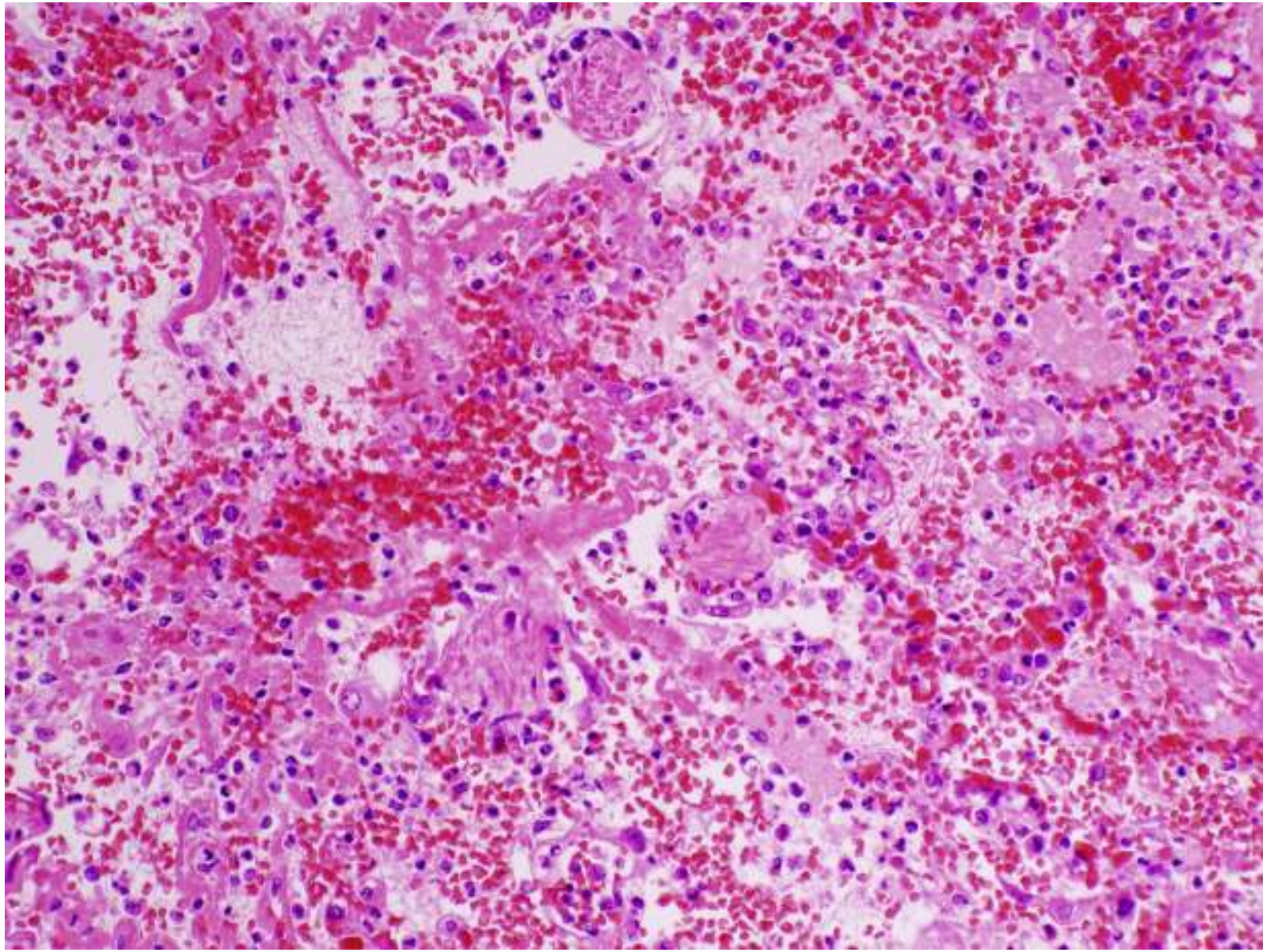
Leptospira scanning EM



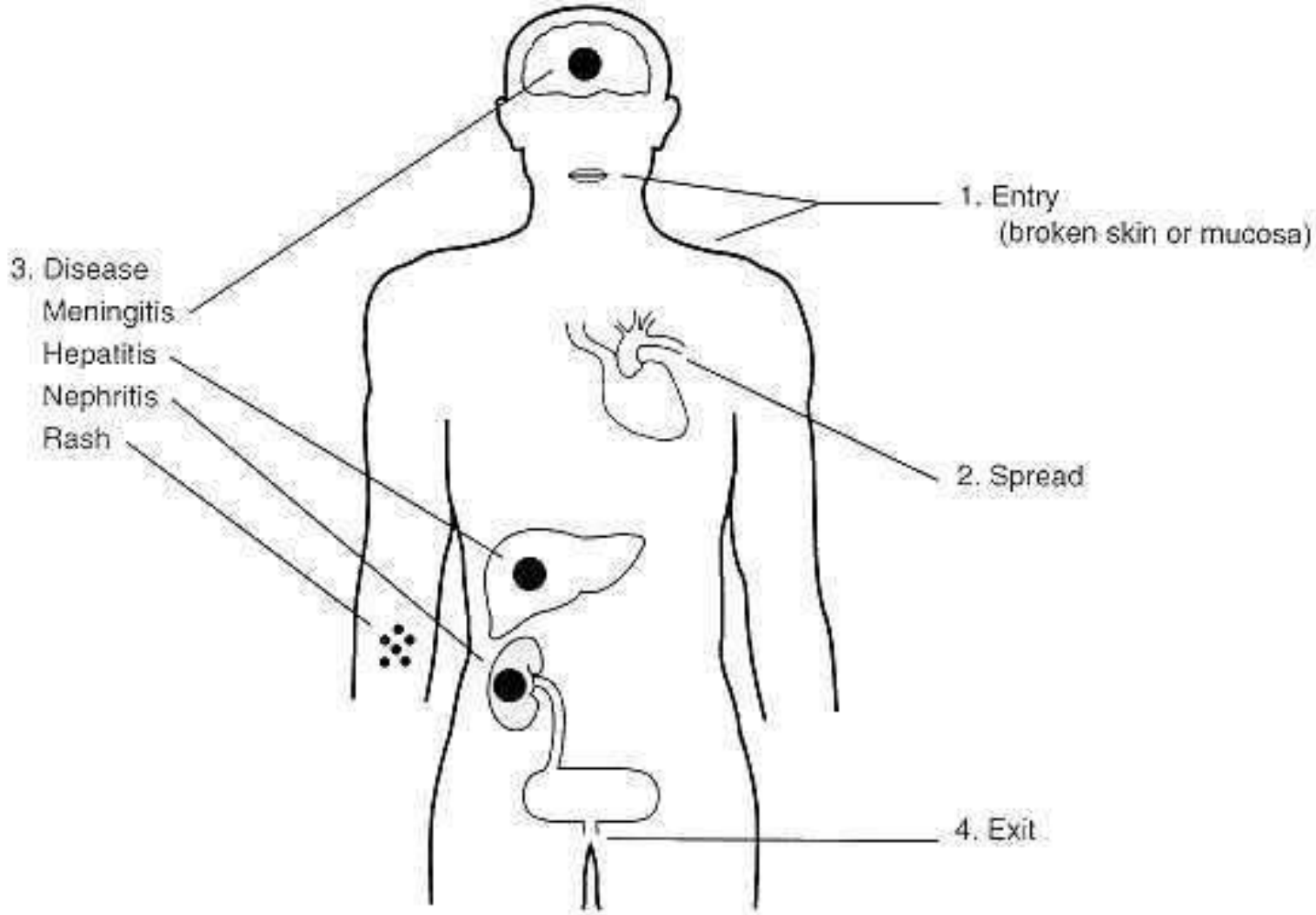
Tip of the iceberg



Case 3 Lung - ALI



Manifestation of leptospirosis



Summary

- Anything can happen
  - International travel
    - *'Unde venis?'*
  - Immunosuppression
    - Acquired
    - Iatrogenic
- Increasing reliance on molecular diagnostics
- Close collaboration with microbiologists and ID clinicians