



# **Histo and neurotoxic clostridial diseases**

**Part B**

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# Infectious necrotic hepatitis

**Etiology: *Clostridium novyi* type B**



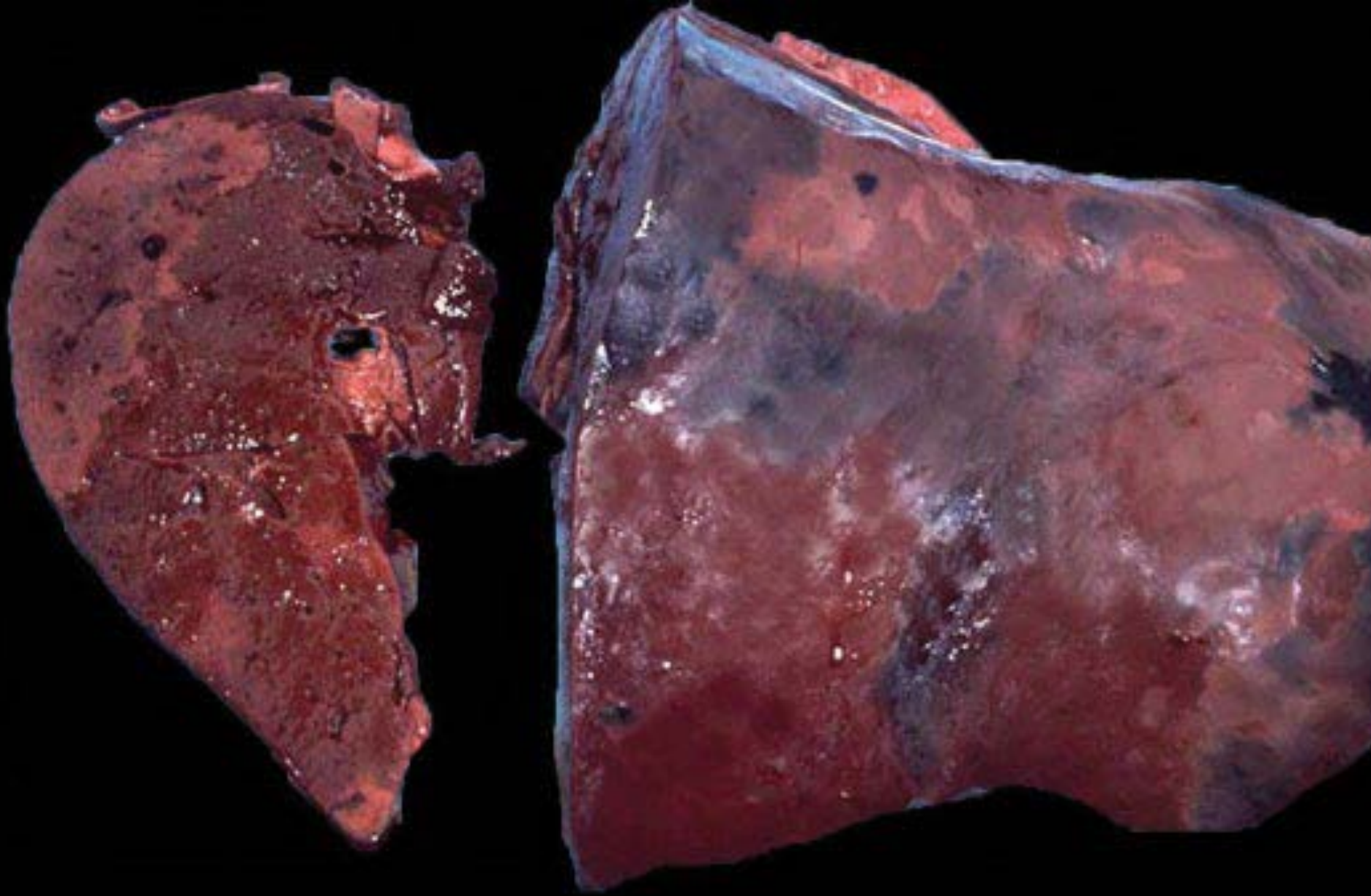
Tissue damage (*F. hepatica*, others) → Hypoxia →

Germination and multiplication of *C. haemolyticum* →

Release of **alpha toxin** (PLC) →

Necrotizing →

# Infectious necrotic hepatitis

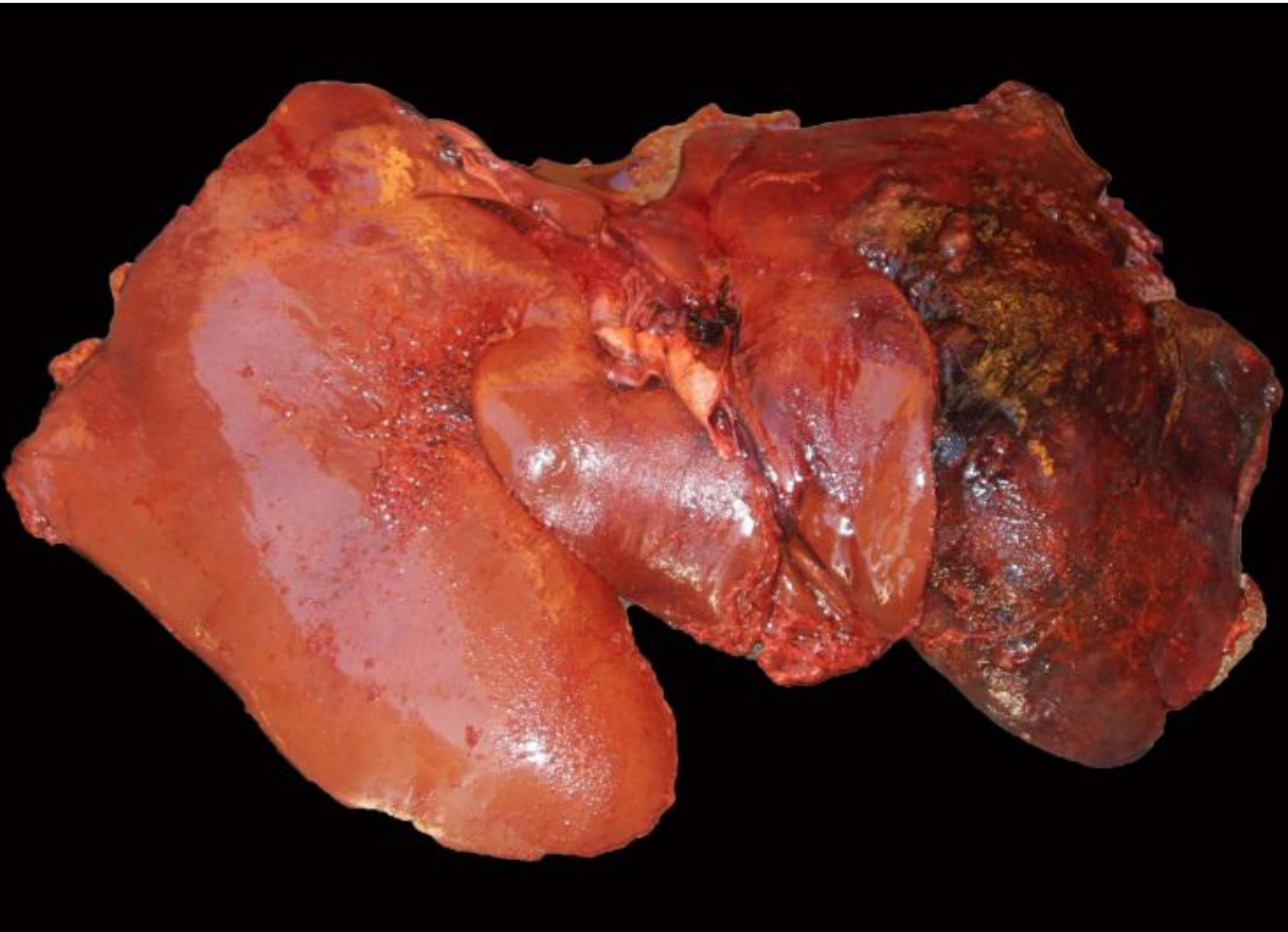


Usually multifocal hepatic lesions



*C. haemolyticum*  
*C. novyi* type B









Lisa Whitfield

# MAIN VIRULENCE FACTORS

*C. haemolyticum*

alpha, **beta**

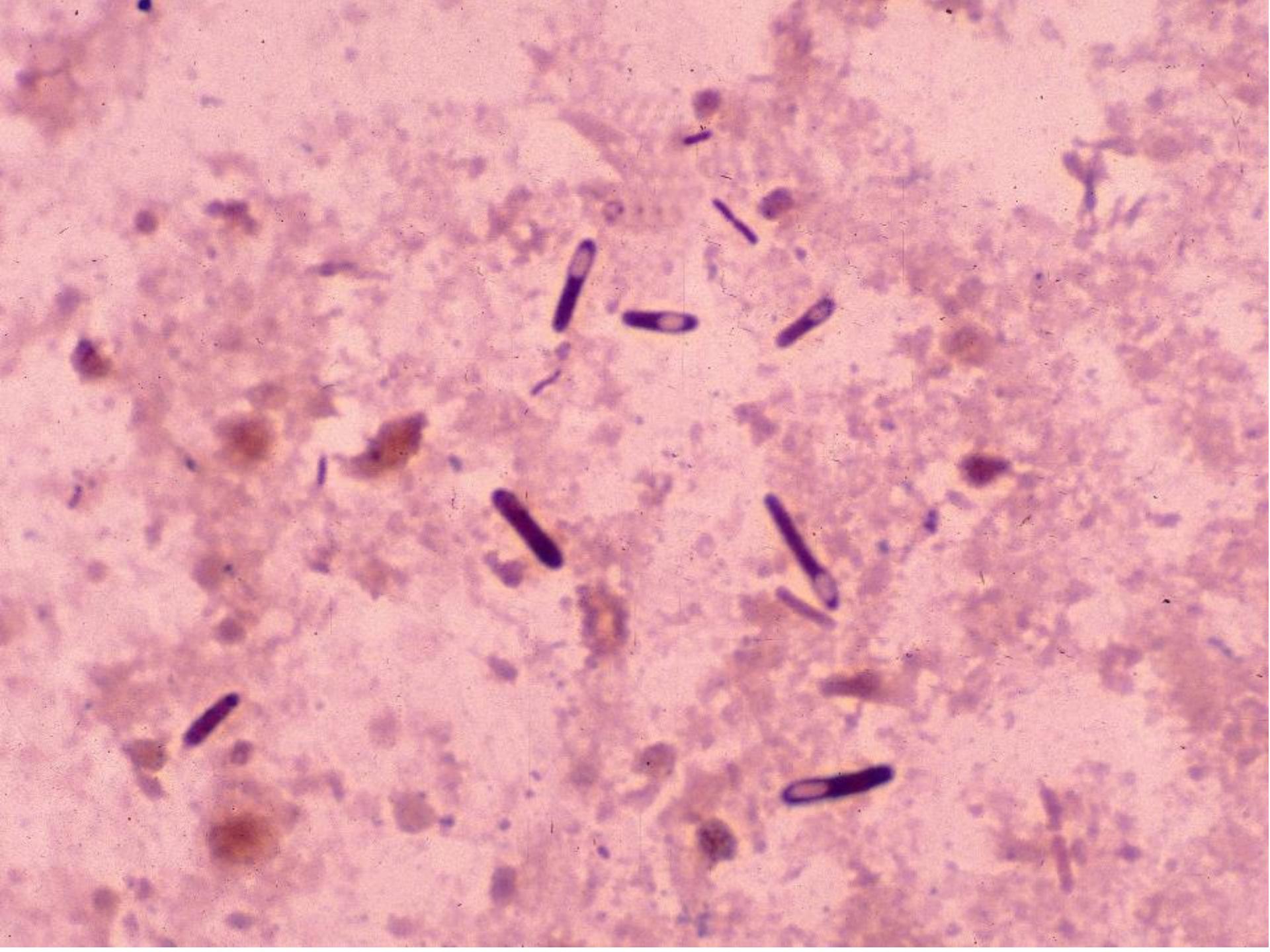
*C. novyi* type B

**alpha**, beta

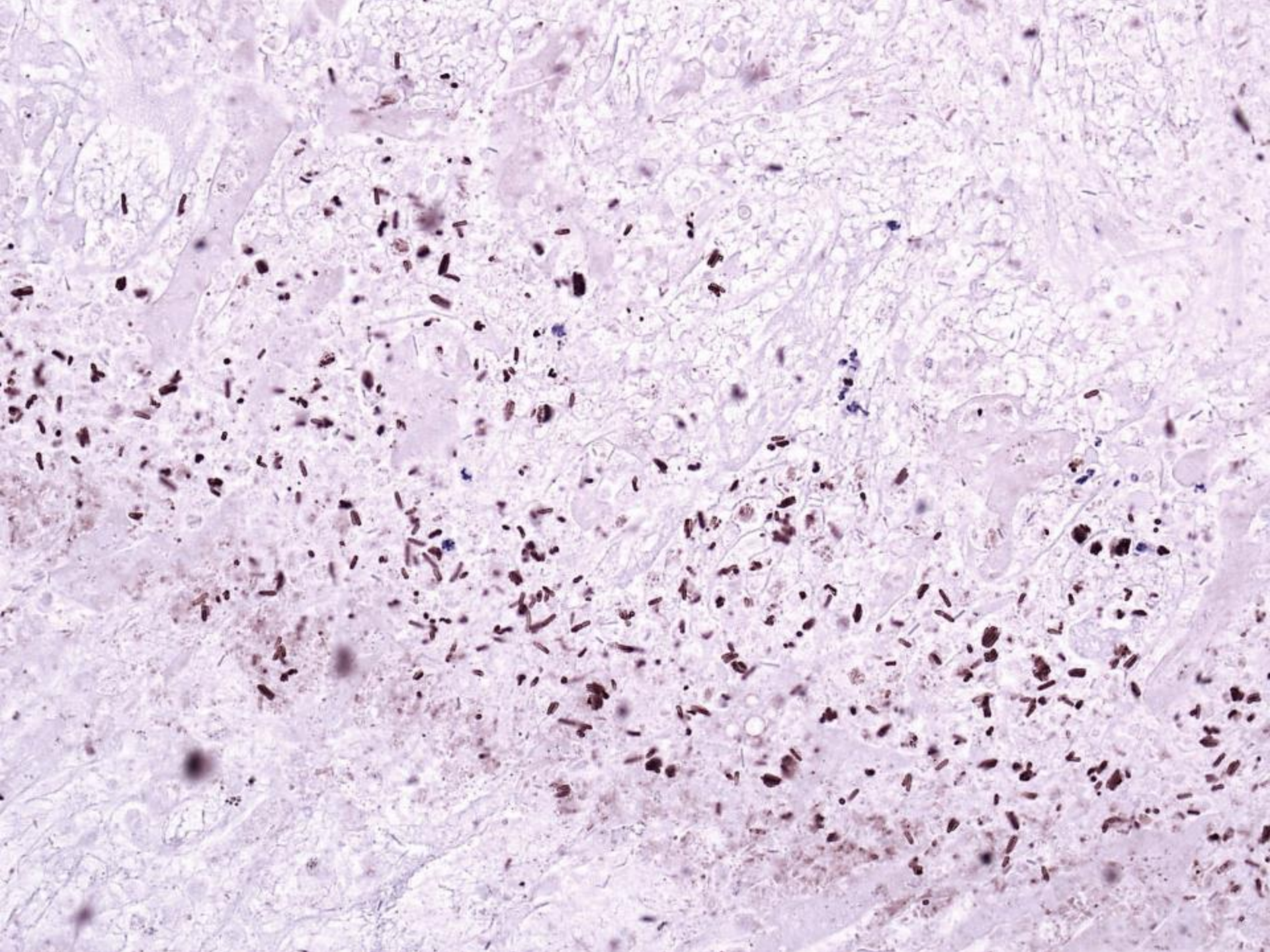


# Diagnostic criteria

- 1-Necropsy } Suggestive +
- 2-Histopathology; smears; FAT; IHC } Suggestive +



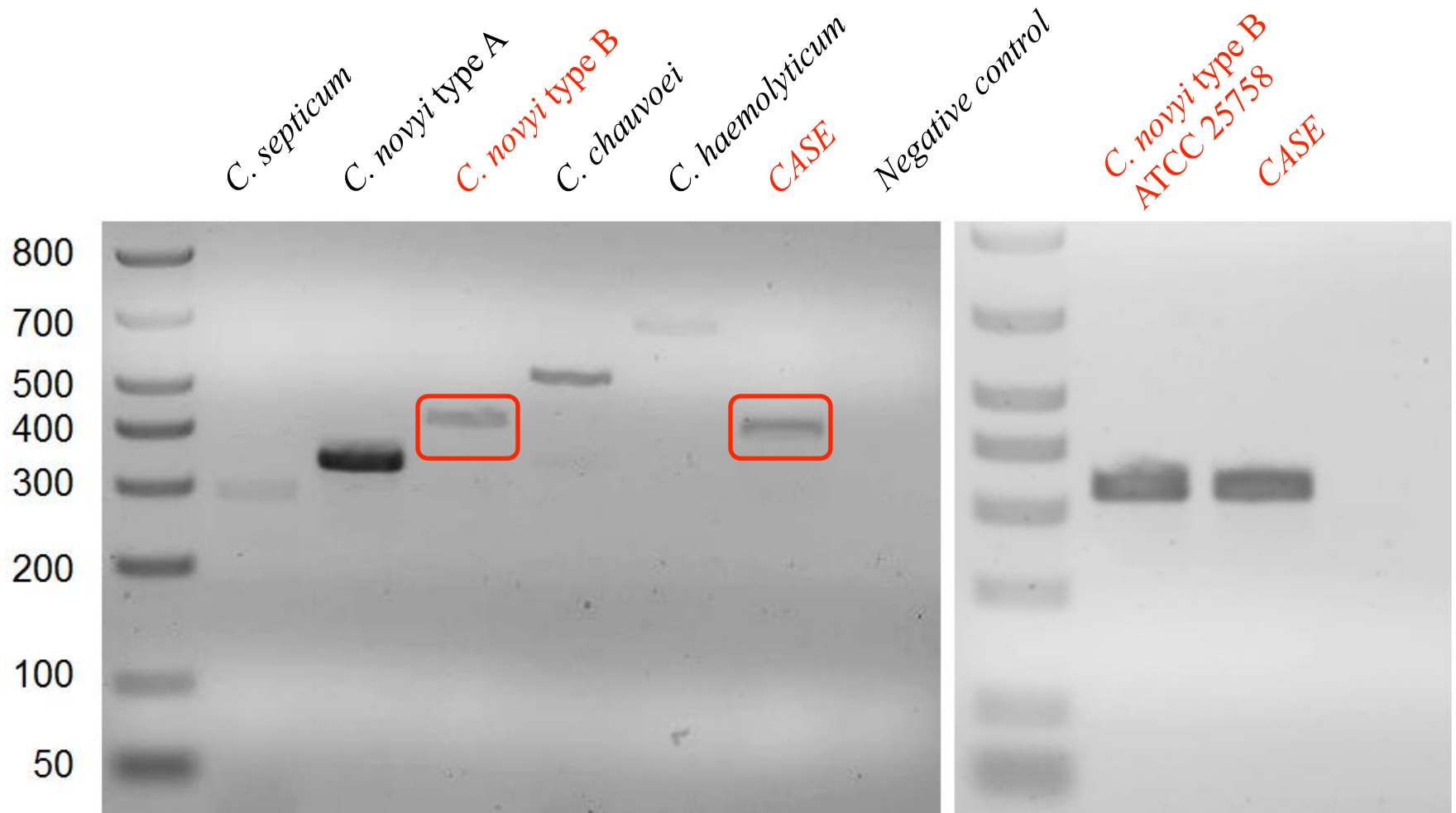






# Diagnostic criteria

- 1-Necropsy } **Suggestive +**
- 2-Histopathology; smears; FAT; IHC } **Suggestive +**
- 3-Ancillary tests: Culture/PCR } **Confirmatory**



PCR for *fliC* gene of  
histotoxic clostridia

*C. novyi* type  
B  $\alpha$ -toxin  
gene





GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric				
Histotoxic	Black leg	<i>C. chauvoei</i>	--	✓
		<i>C. septicum</i>	✓	✓
		<i>C. chauvoei</i>	--	✓
	Gas gangrene	<i>C. perfringens</i>	✓	✓
		<i>C. sordellii</i>	✓	✓
		<i>C. novyi</i>	✓	✓
		<i>C. novyi</i>	--	✓
	Hepatitis	<i>C. haemolyticum</i>	--	✓
		<i>C. piliforme</i>	--	✓
Neurotoxic	Tetanus			
	Botulism			

Tyzzer's disease

- \* Pathogenesis poorly understood (no known virulence factors)
- \* Fecal-oral transmission
- \* *C. piliforme* proliferates in the intestinal mucosa (ileum, colon and cecum) → Necrosis of enterocytes
- \* Entry to portal circulation
- \* Dissemination to the liver and other organs (heart)



# Clinical signs

Depression

Icterus

Neurologic signs

Sudden death

# Pathology

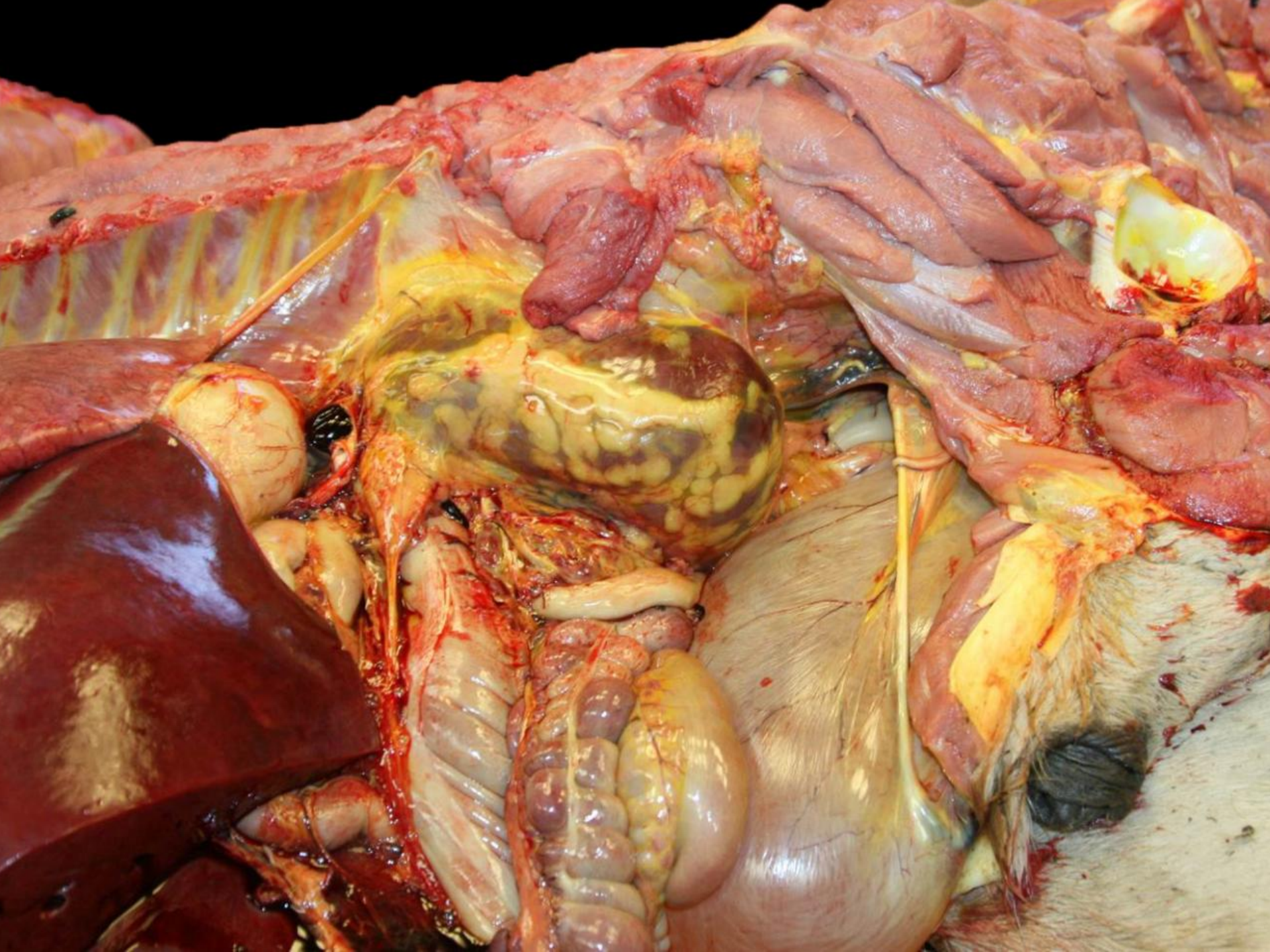
(triad of lesions)

1-Colitis

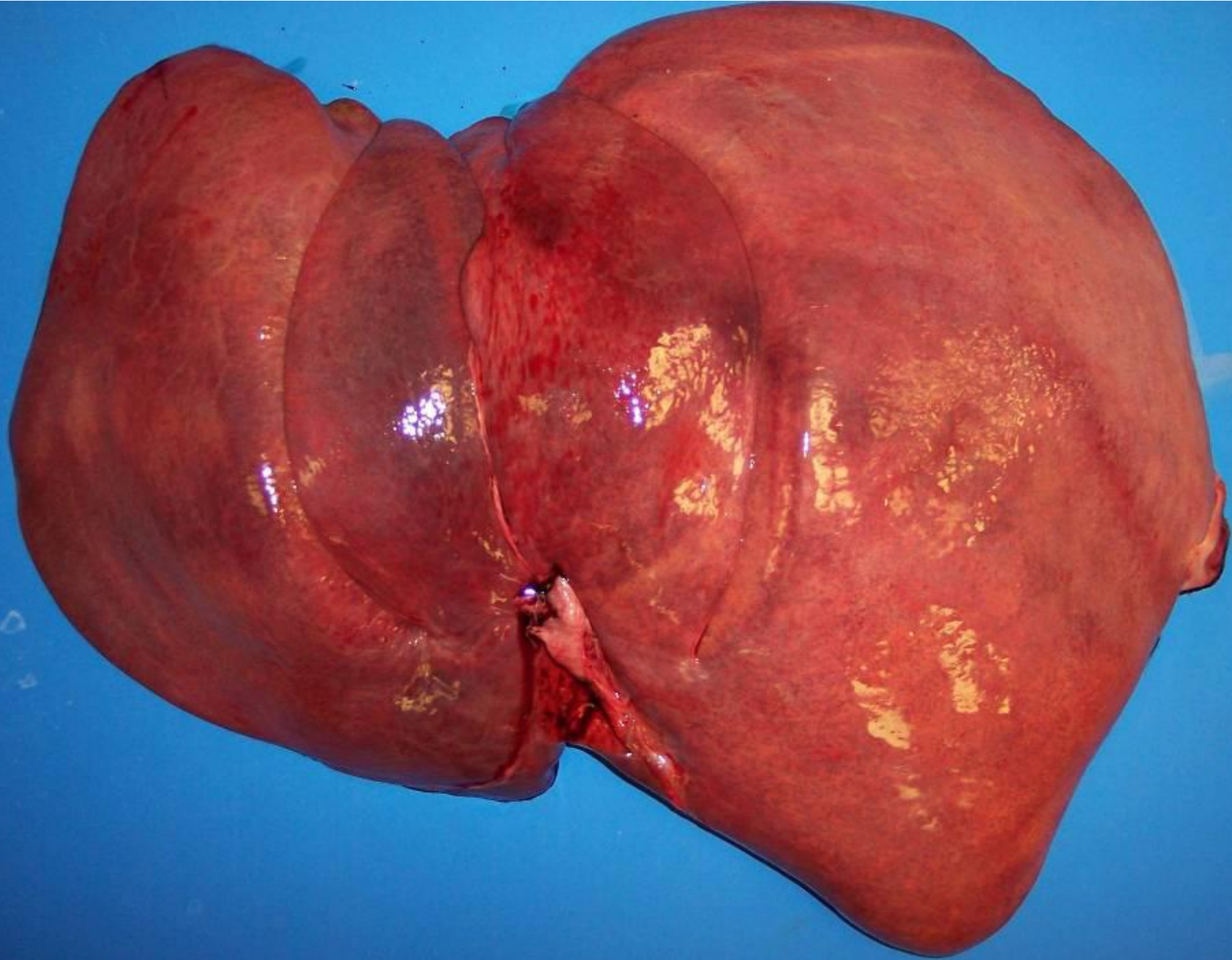
2-Hepatitis

3-Myocarditis

Take-home message!!!!



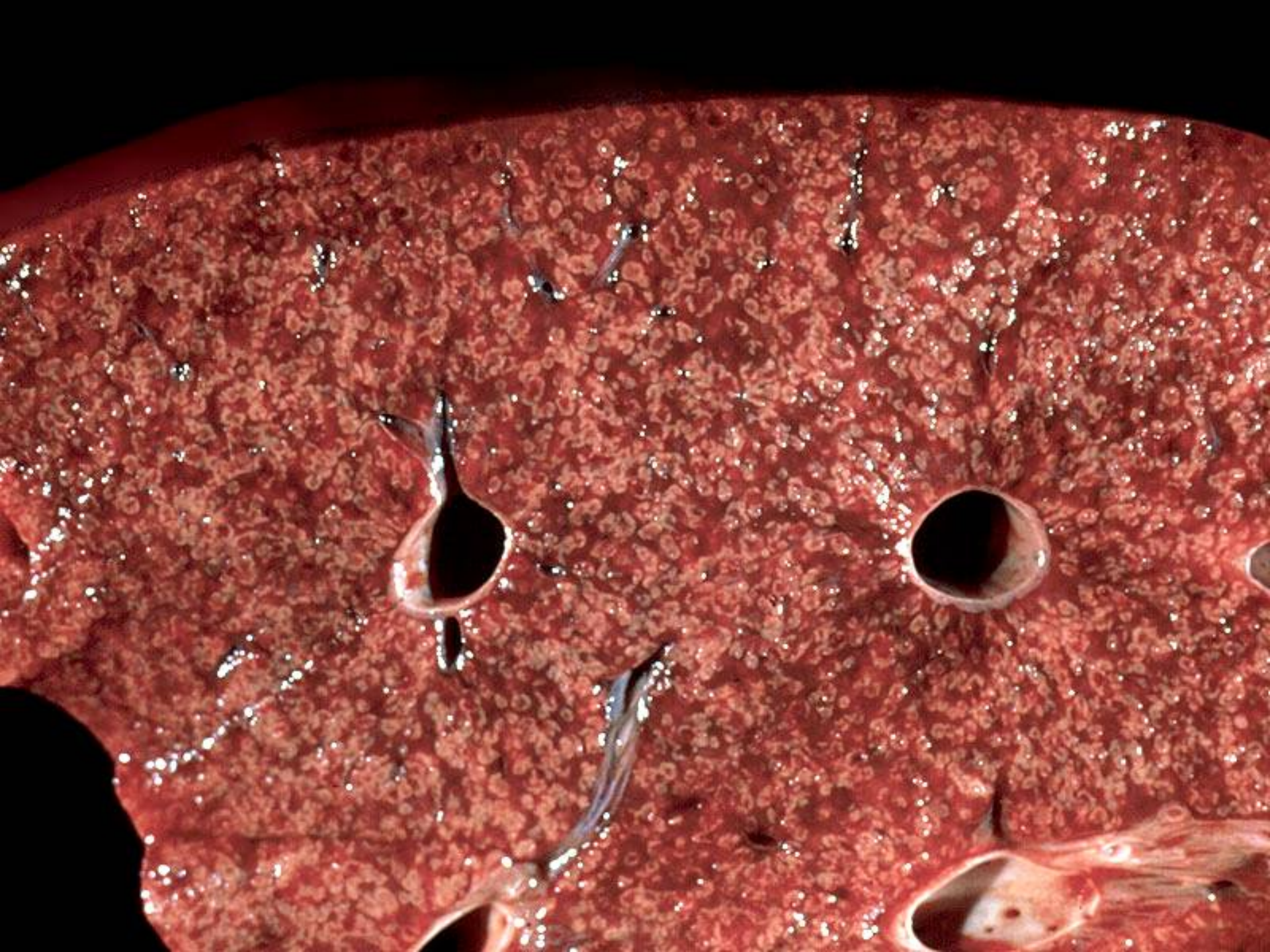








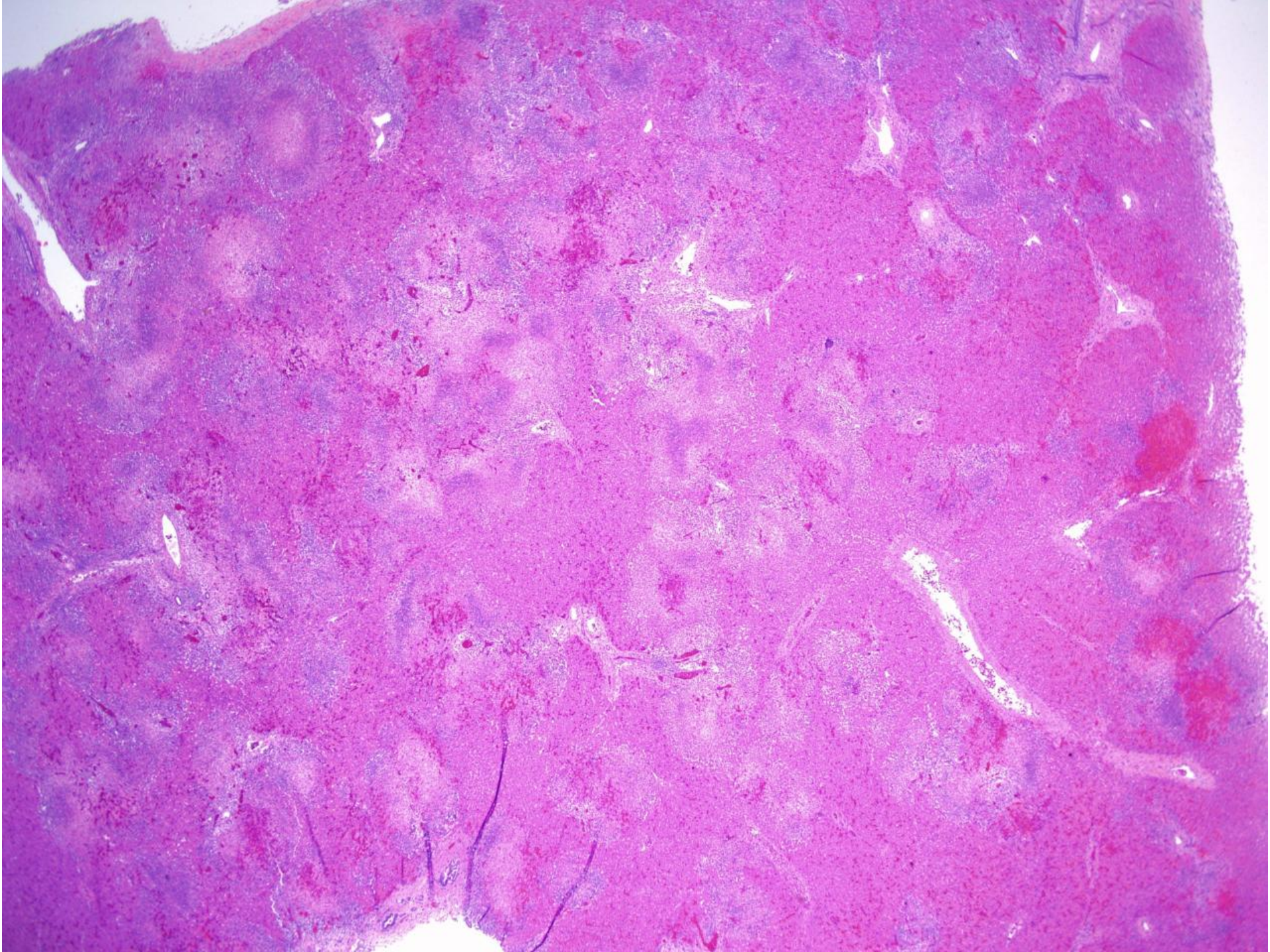




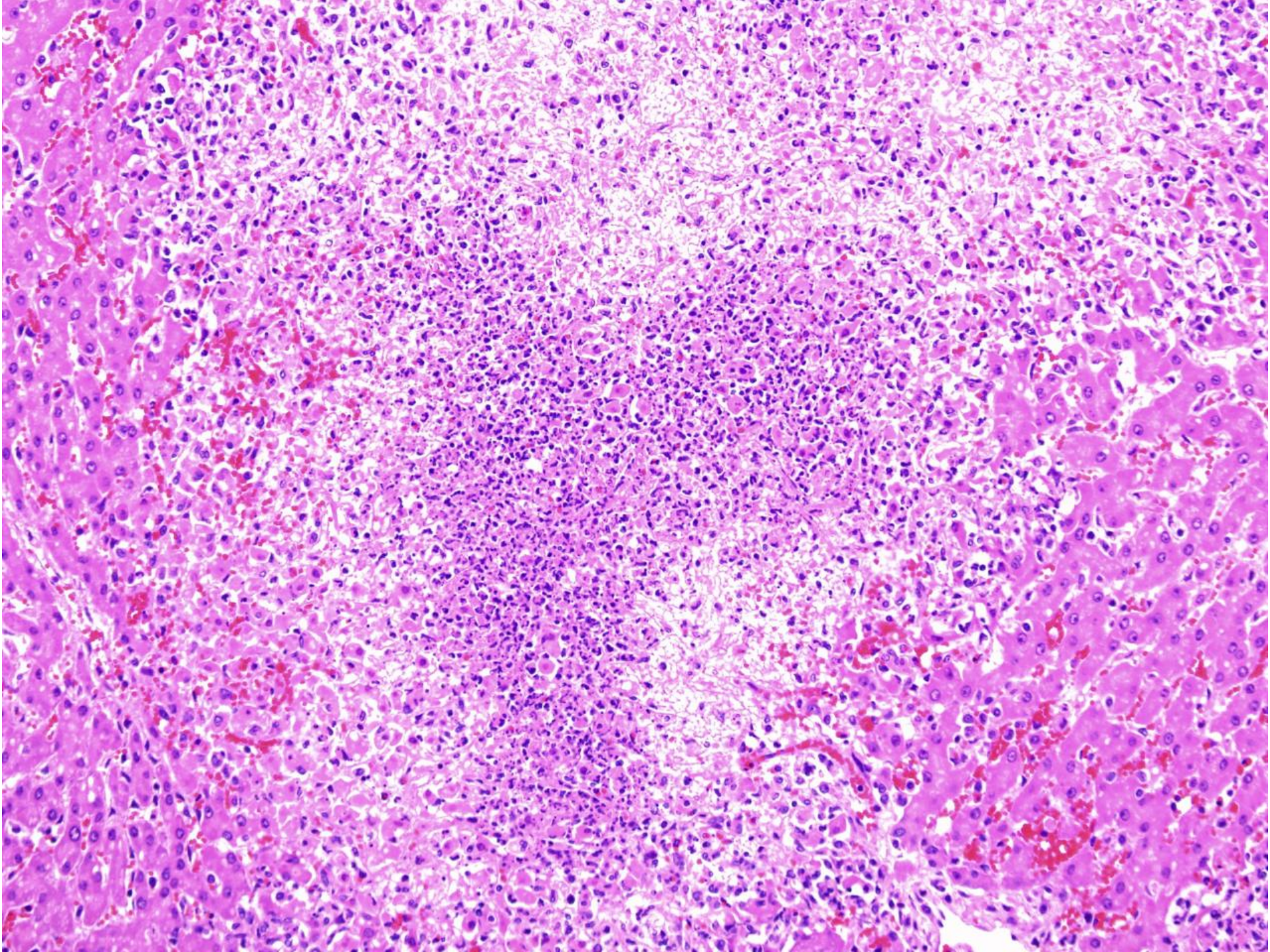




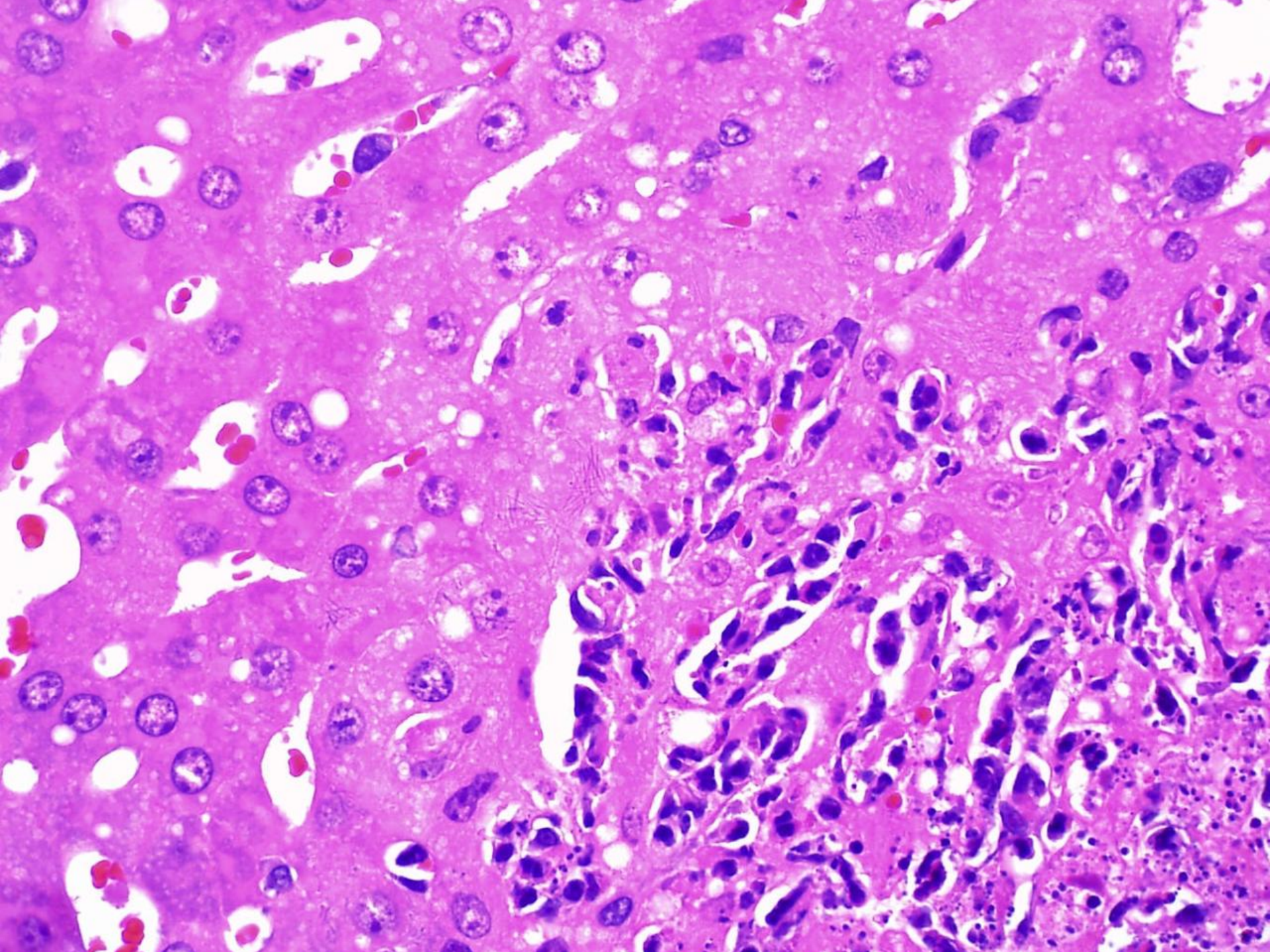




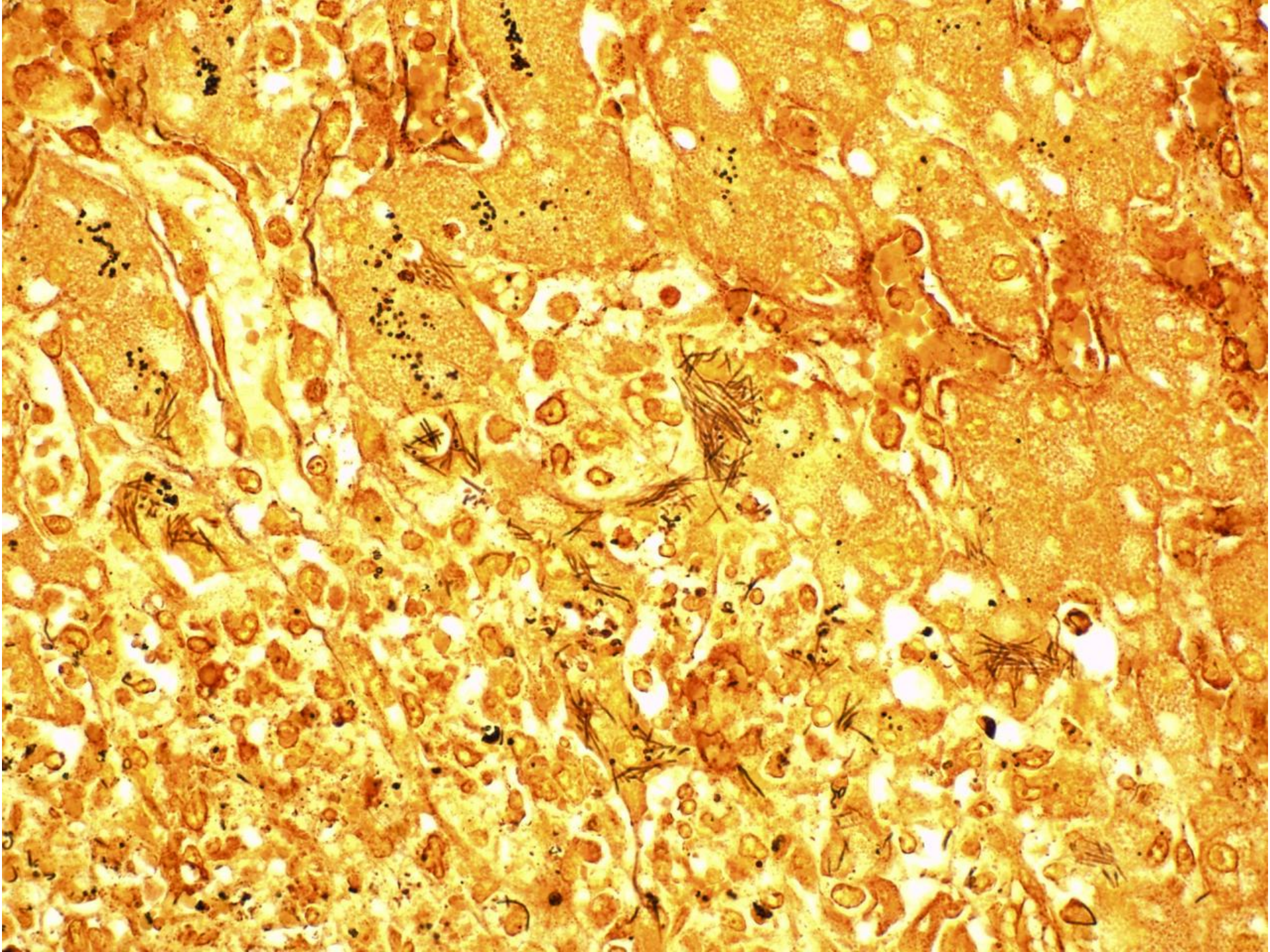




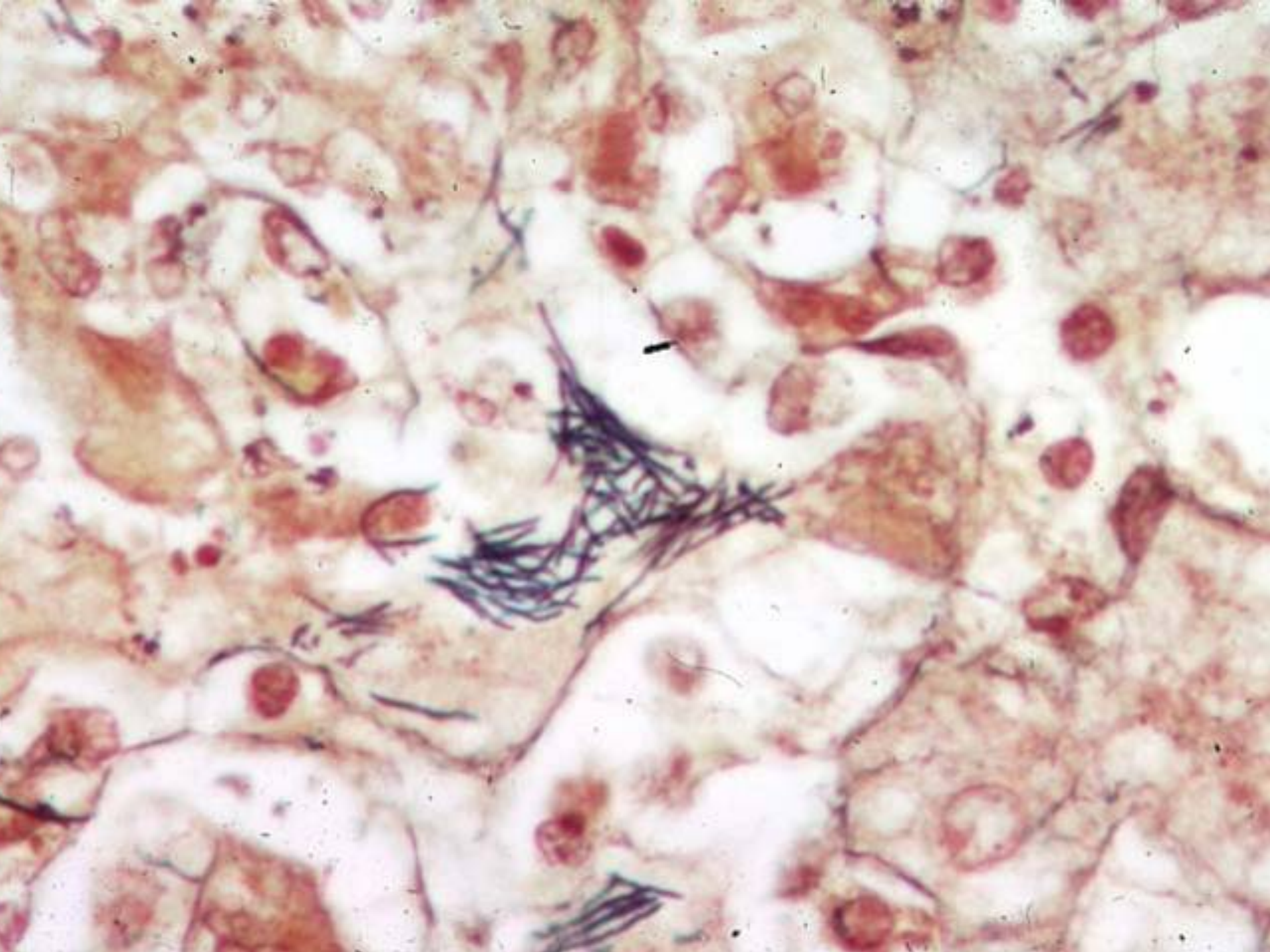






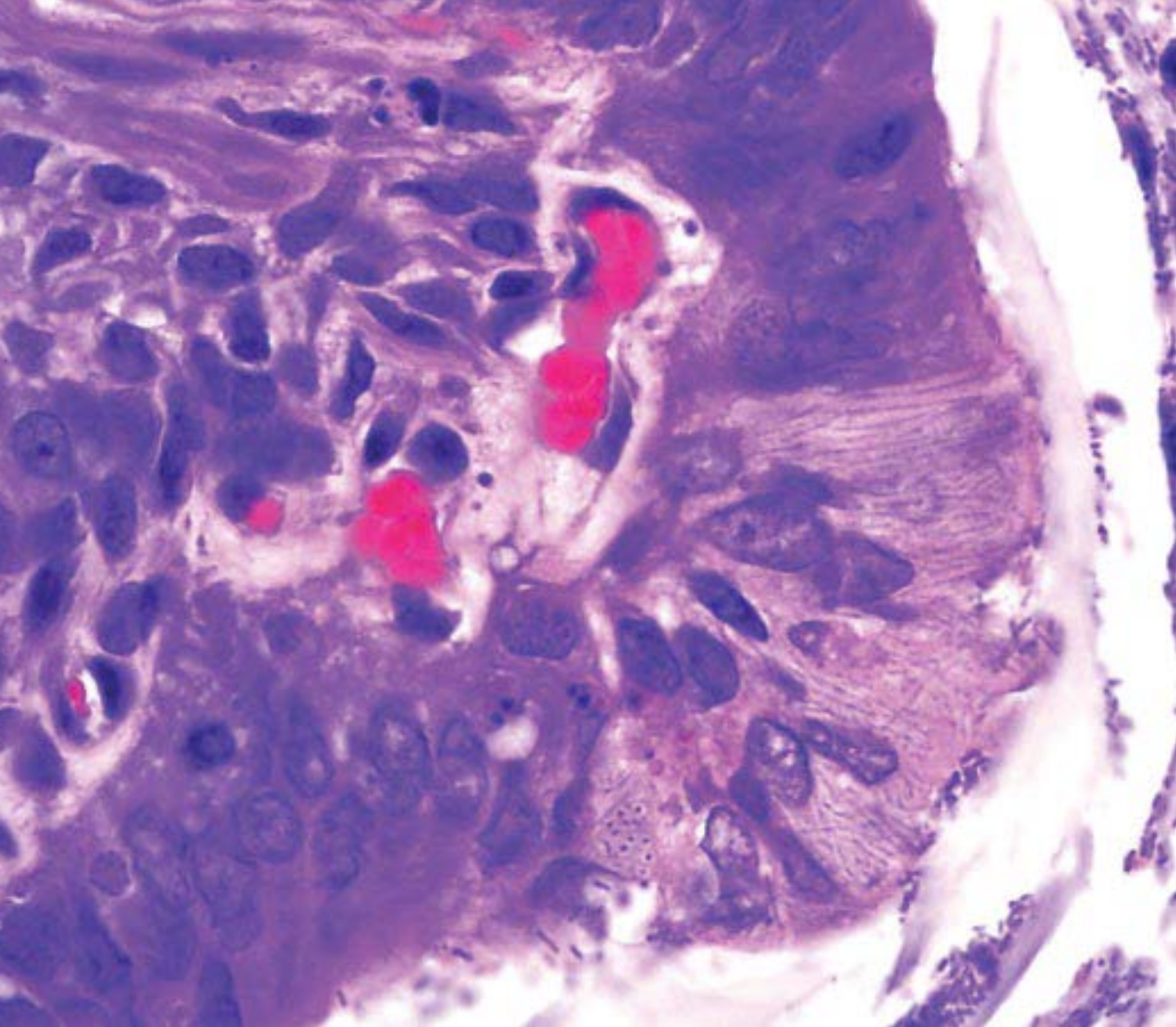






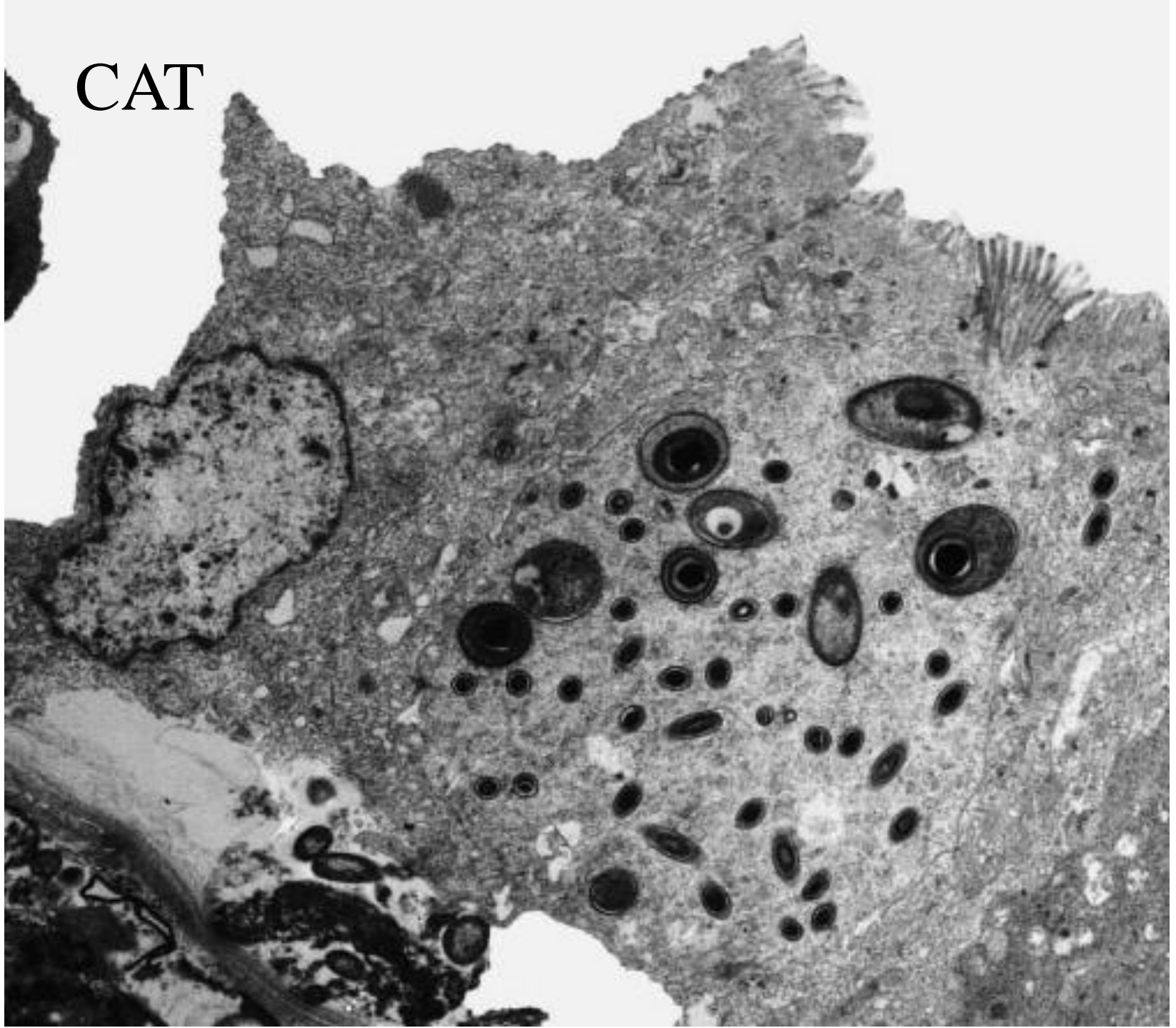




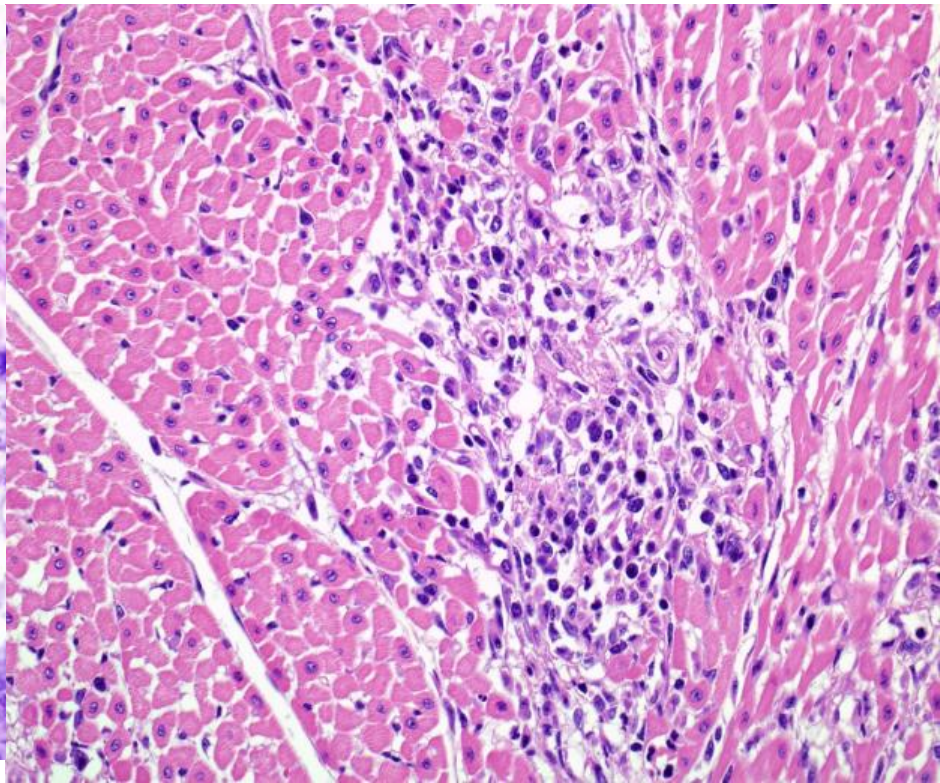
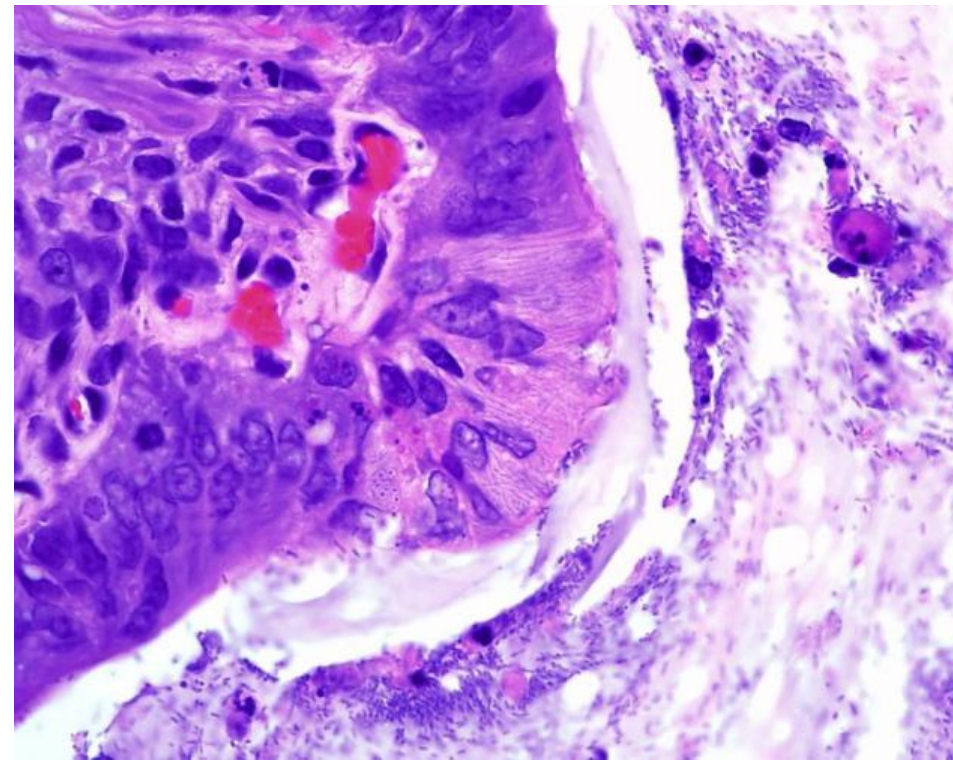




CAT







Intestinal and cardiac lesions rare in horses

# Diagnosis:

- 1-Histology (HE; silver; Giemsa)
- 2-TEM
- 3-PCR
- 4-Culture (embryonated egg only)

Take-home message!!!!







GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric				
Histotoxic				
Neurotoxic	Tetanus	<i>C. tetani</i>	✓	✓
	Botulism	<i>C. botulinum</i>	✓	✓

# Paralysis

**TETANUS**

**BOTULISM**

Spastic

Flacid



# Tetanus



A soldier dying from tetanus.  
Charles Bell. Royal College of Surgeons, Edinburgh

# Botulism

Rood et al, 1997





# Tetanus

*Clostridium tetani*

# Tetanus Neurotoxin (TeNT)

- “Tetanospasmin”
- Plasmid encoded

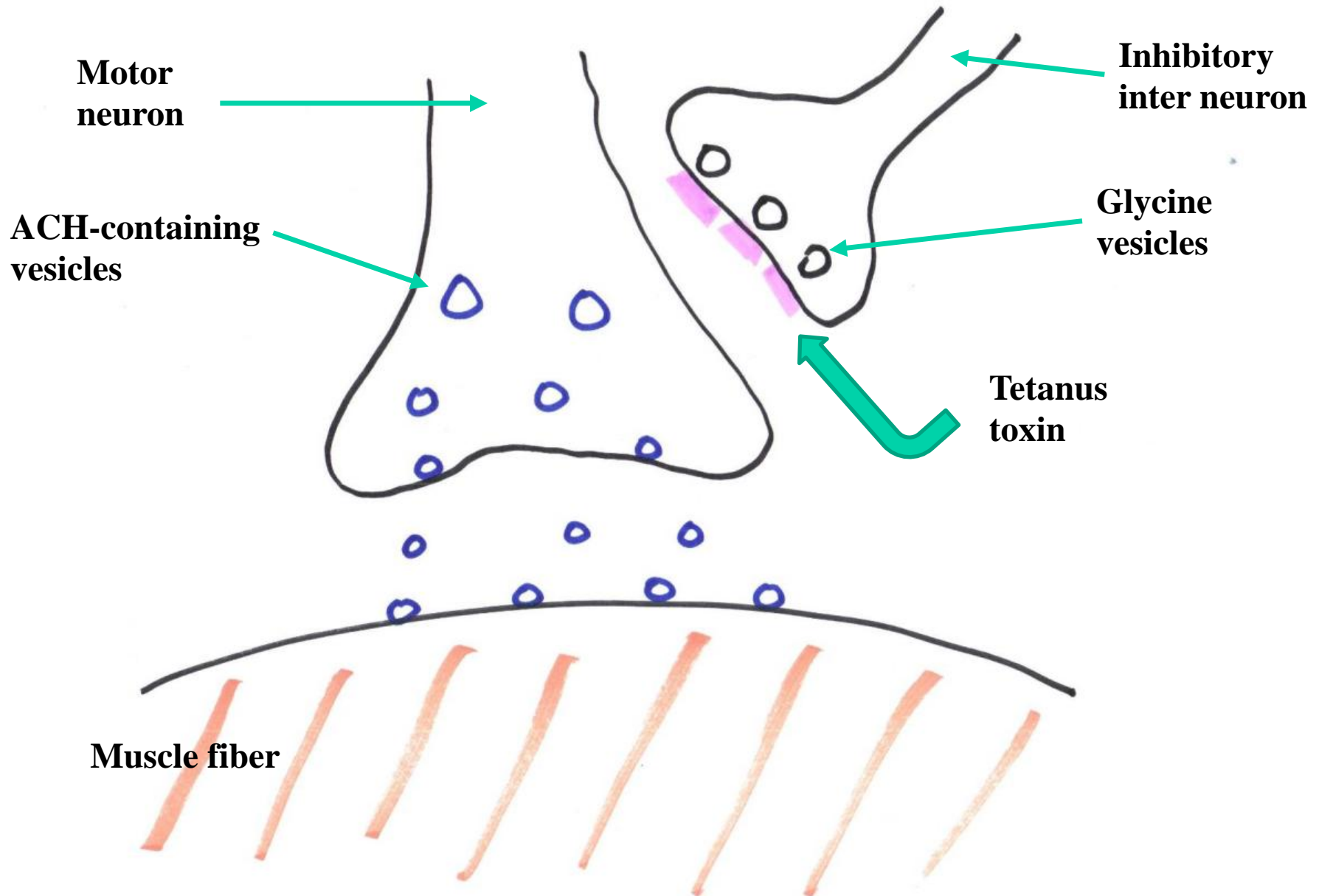
# Tetanus Neurotoxin (TeNT)

- Cleavage of neuron-specific soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins
  - Vesicle-associated membrane protein 2 (VAMP2, *aka* synaptobrevin 2)
- Prevents release of inhibitory neurotransmitters
  - Such as  $\gamma$ -aminobutyric acid (GABA) & glycine in spinal cord



# Tetanus Neurotoxin (TeNT)

Prevents release of *inhibitory* neurotransmitters



# Tetanus (human)

- Soil/fecal organism
- 700,000-1,000,000 human cases/yr globally
- Contaminated wounds infected
  - Older adults (gardening) & injection drug users
- Neurotoxin causes muscle excitation (spasms)
- 100% vaccine preventable





# **Main predisposing factors**

## **(animals)**

- \*Puncturing wounds
- \*Obstetric interventions
- \*Surgery (dehorning, castration, tail removal, hoof, shearing)





# Clinical signs in horses

Colic

Stiffness and lameness

Generalized spasticity (hypertonia)

Lips retracted

Ears pulled down

Tail elevated

Trismus

Spasms by auditory, ocular or tactile stimulation

Third eyelid flashing

Respiratory difficulty: hypoxia

















# Diagnostic criteria

1-Clinics

}

Confirmatory?







# Diagnostic criteria

1-Clinics

}

Confirmatory?

2-Necropsy

}

Suggestive

Typical example of negative necropsy  
(except for wounds)



# Diagnostic criteria

1-Clinics

}

Confirmatory?

2-Necropsy

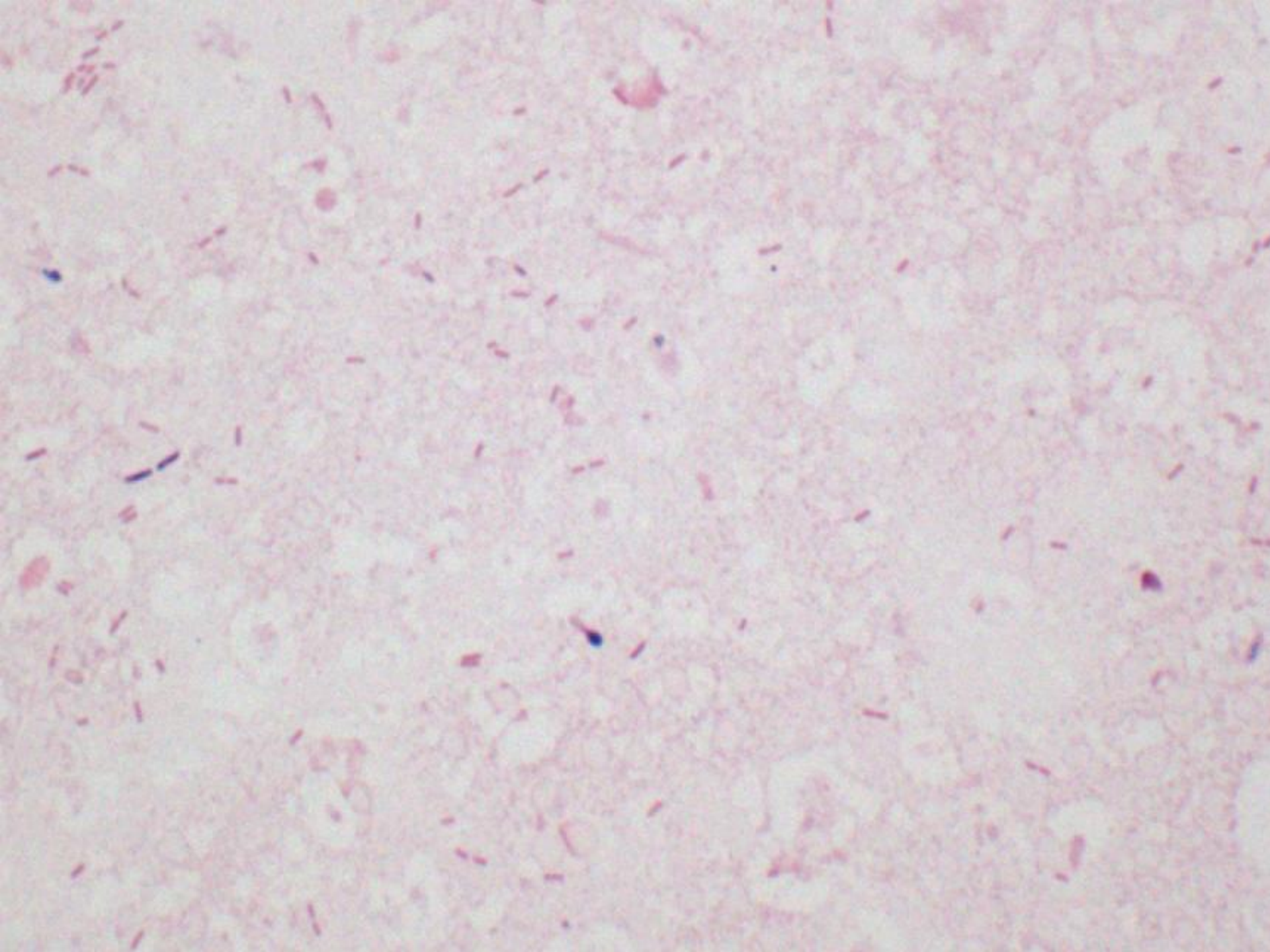
}

Suggestive

3-Ancillary: Culture; smears

}

Suggestive+







Currently no commercial tests  
available for toxin detection



# **Botulism**

*Clostridium botulinum*

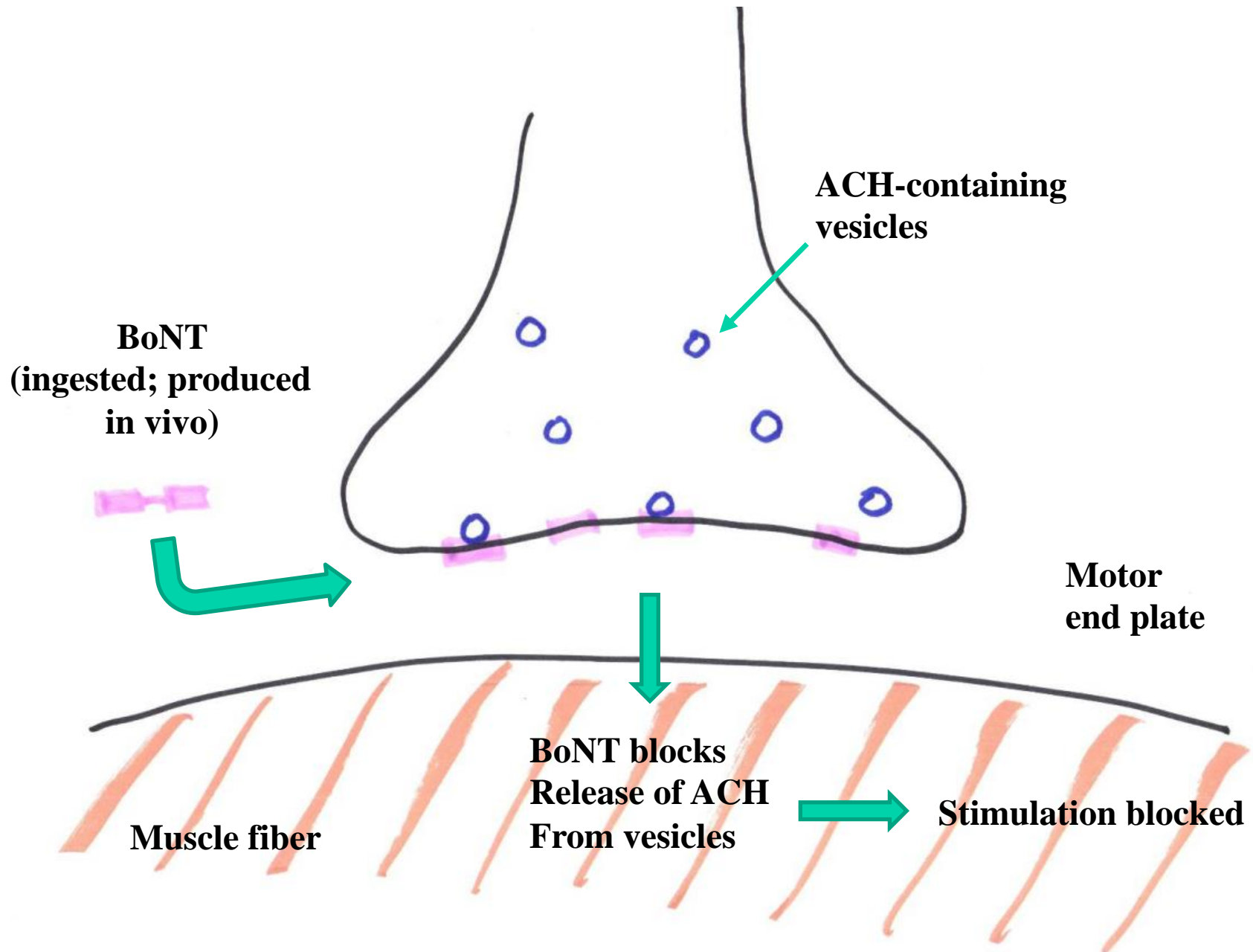


# **Triad of symptoms (humans)**

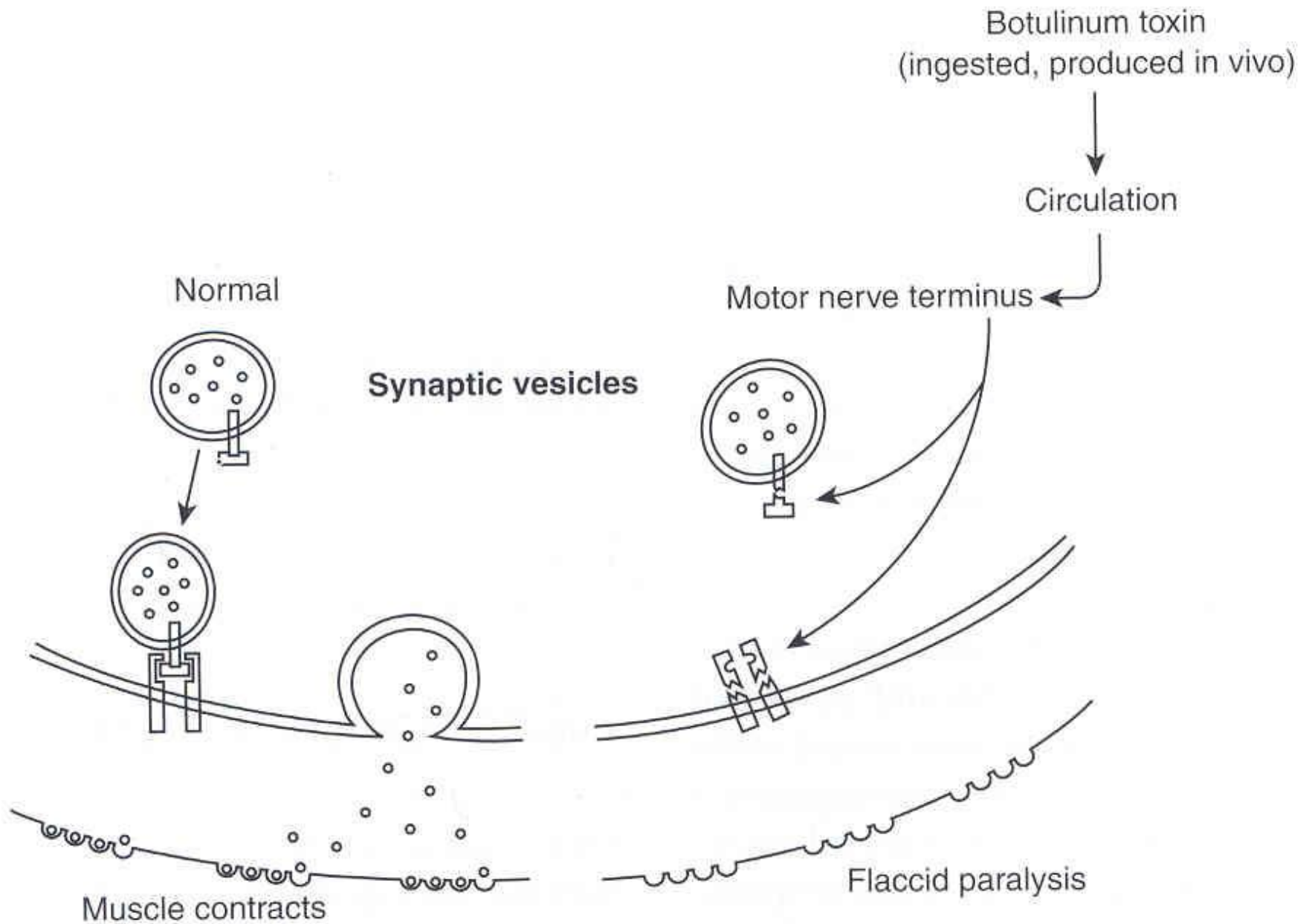
- \* No fever
- \* Symmetrical descending paralysis & bulbar palsy
- \* Clear sensorium (humans might have communication difficulty)

# 8 BoNT: A-H

- \* Bi-valent toxins
- \* A& B: therapeutic







# **Clinical forms of human botulism in US (in decreasing order of occurrence)**

- \* Infant**
- \* Wound**
- \* Foodborne**
- \* Physician-associated**
- \* Inhalation**





# Types C and D (less A)

- \* Pica

- \* Contaminated feed

- \* Water (cadavers)

# Forms

- \* Food poisoning

- \* Wound botulism

- \* Toxicoinfectious (???)







Dr I. Dutra







Photo: I. Dutra





# Clinical signs (adult horses)

Generalized muscle weakness (myasthenia)

Dysphagia

Slight depression

Decreased exercise tolerance

Slowness to eat

Colic

Decreased eyelid and tail tone

Shuffling gait

Exaggerated expiratory effort

# Clinical signs (foals)

Generalized muscle weakness (myasthenia)

Dysphagia

Recumbency

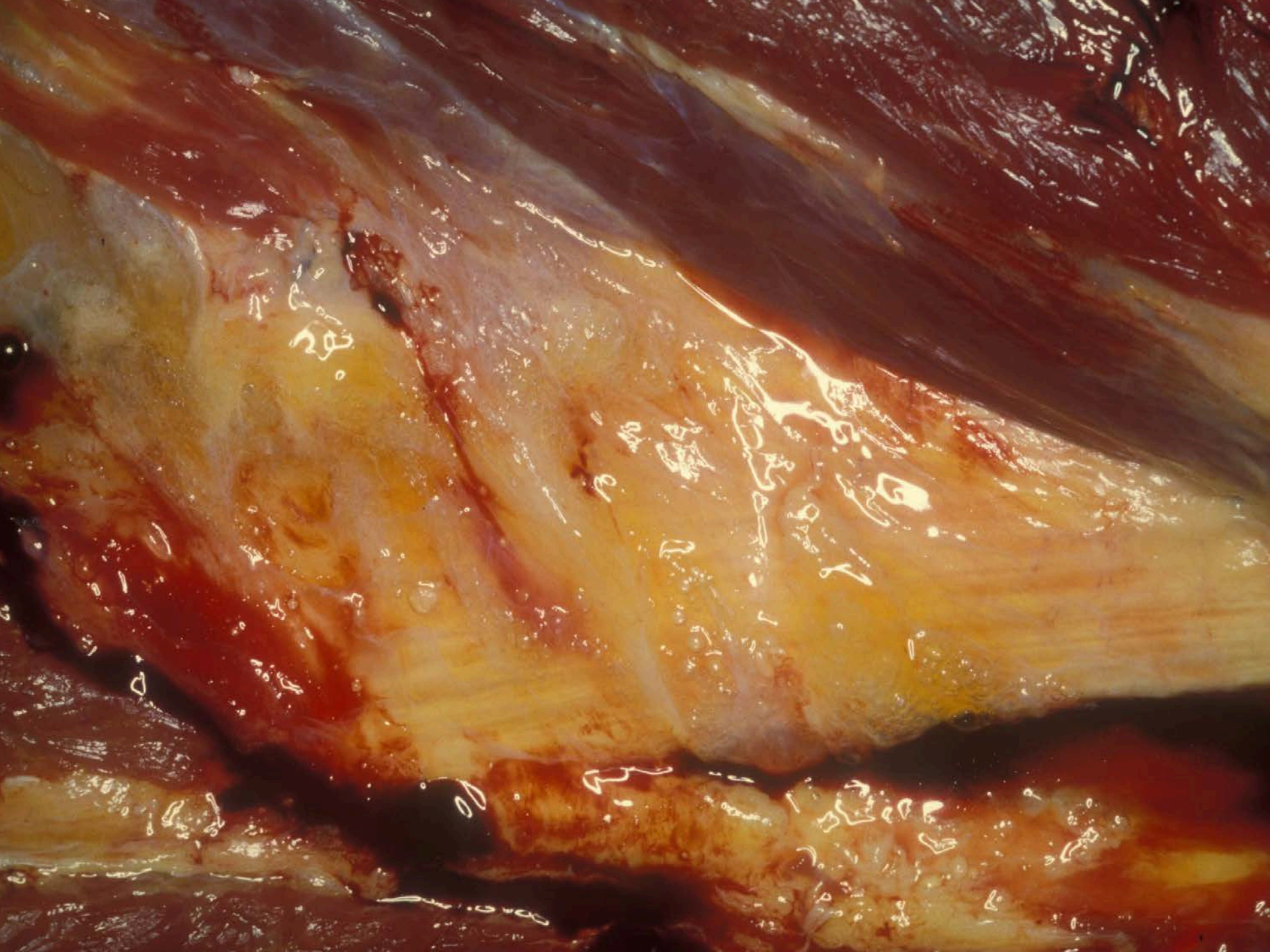
Decreased tongue tone

Mydriasis and weak eyelid tone

Constipation and ileus



Typical example of negative necropsy;  
except.....



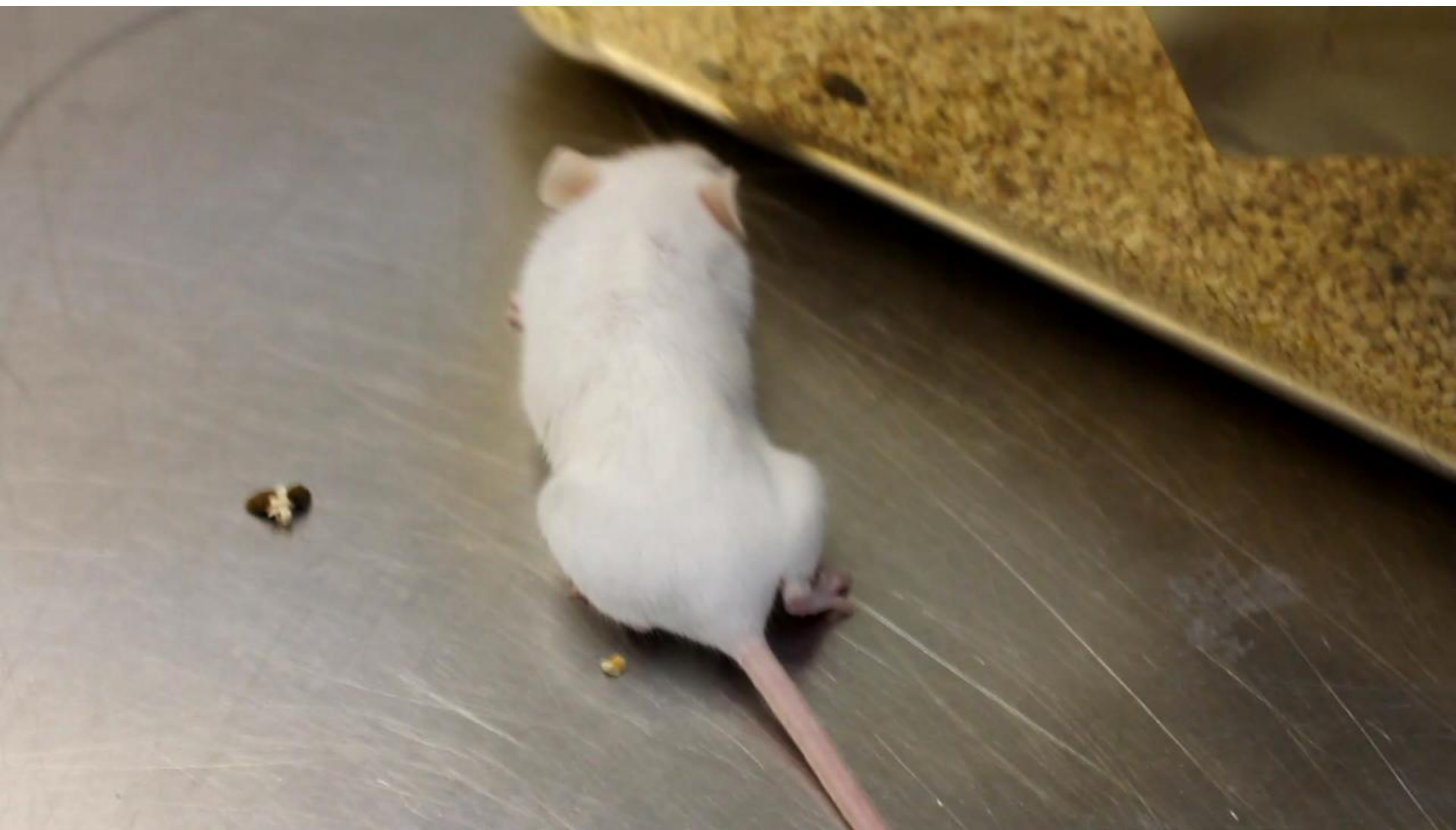






# Type C (less A and D)

- \* Low water level reservoirs
- \* Contaminated feed
- \* Re-used litter



# Diagnostic criteria

1-Clinica/Necropsy

}

Suggestive +

2-Histopathology

}

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3-Ancillary tests:

mouse test

}

Confirmatory



**THANK YOU!!!!**

