



UC DAVIS

VETERINARY MEDICINE

California Animal Health and
Food Safety Laboratory System



Histo and neurotoxic clostridial diseases

Part A

F.A. Uzal

**California Animal Health and Food Safety Laboratory, School of
Veterinary Medicine, University of California, Davis, USA**

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

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				

Black leg

Bovine

Ovine (very rare)

Endogenous

No wounds

Muscle

Gas gangrene

Ovine

caprine Bovine/

equine

Exogenous

Wounds

SQ tissue

Black leg

Etiology: *Clostridium chauvoei*



Pathogenia

Spores in soil →

ingested → absorbed in intestine →

macrophages →

spores latent in muscle →

reduction O_2 → germination → toxins →

muscular necrosis → toxemia → shock

Most common predisposing factors:

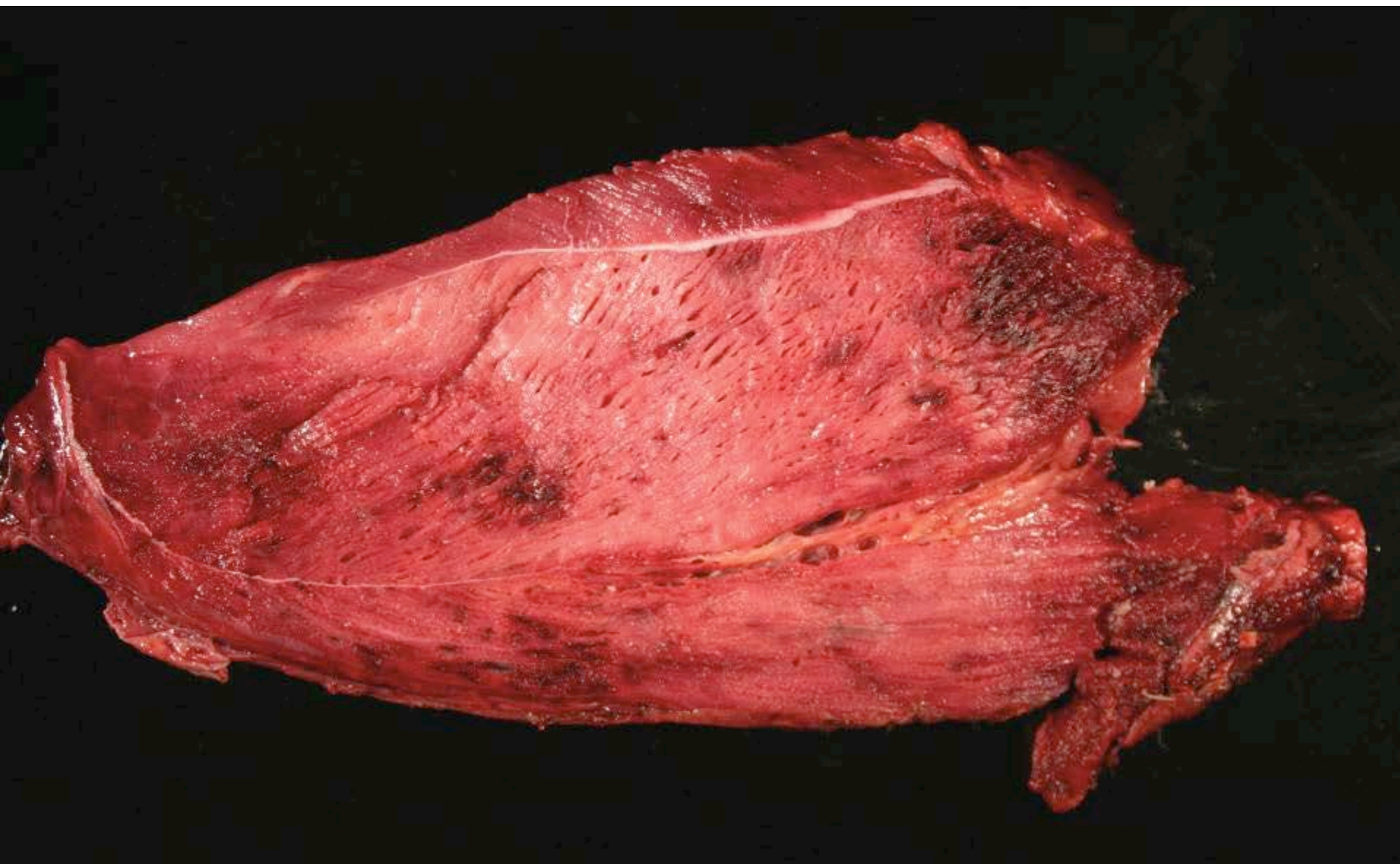
- * trauma (no skin/mucosa laceration)
- * toxic substances (blackleg of the heart)?

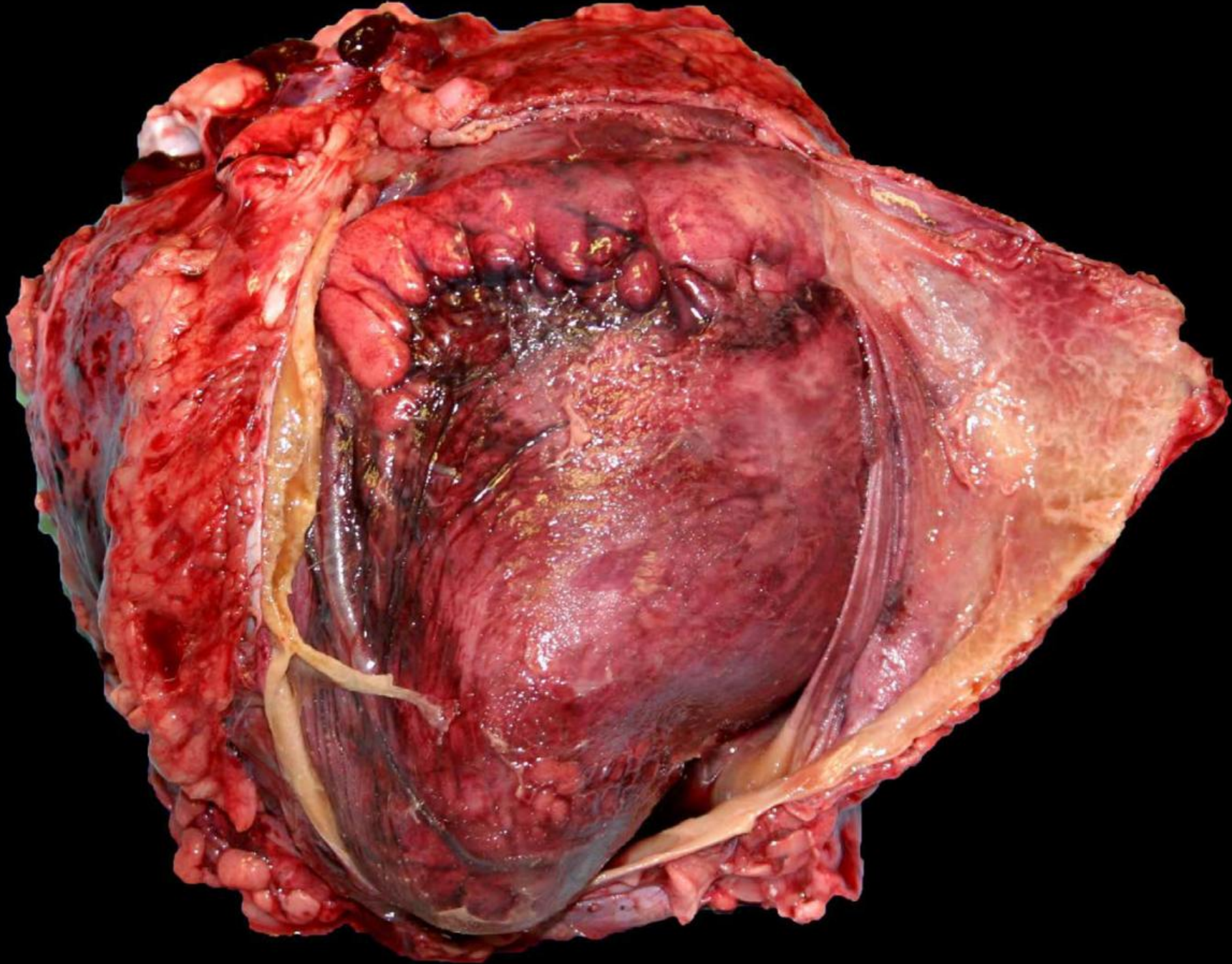
Main virulence factors

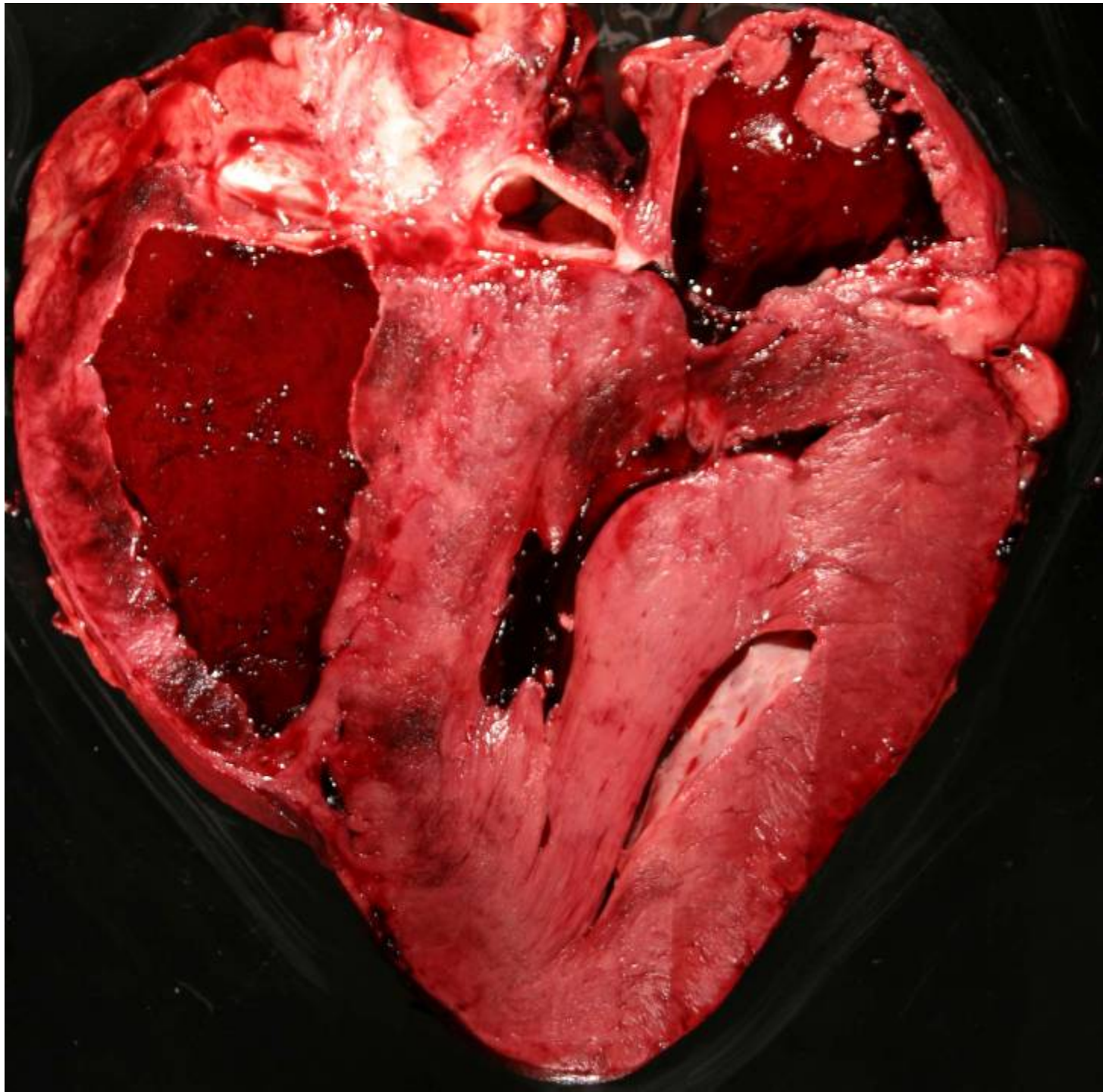
CctA: β -PFT; cell necrosis/hemolysis

Chauveolysisn, neuraminidase, DNase,
hyaluronidase



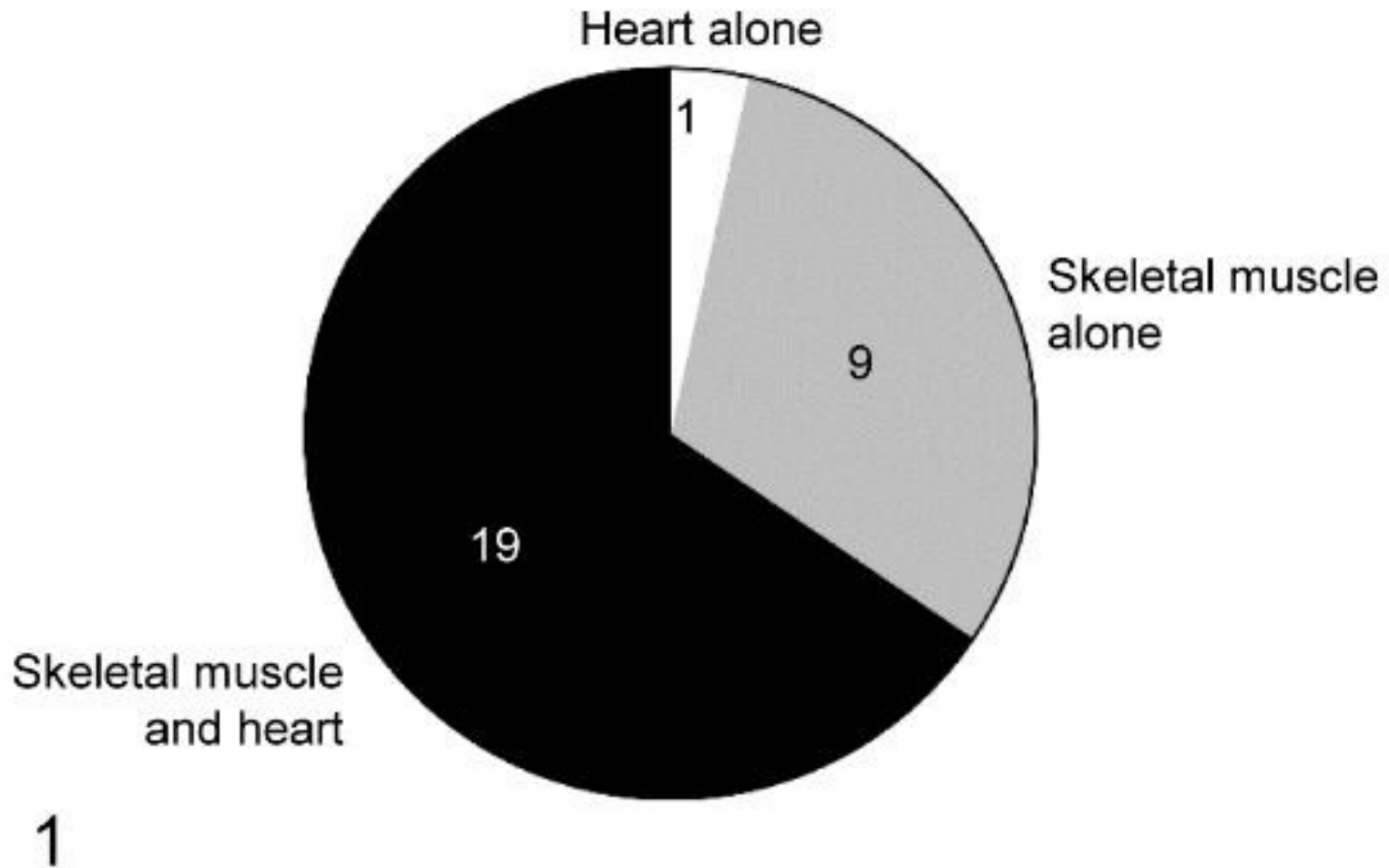


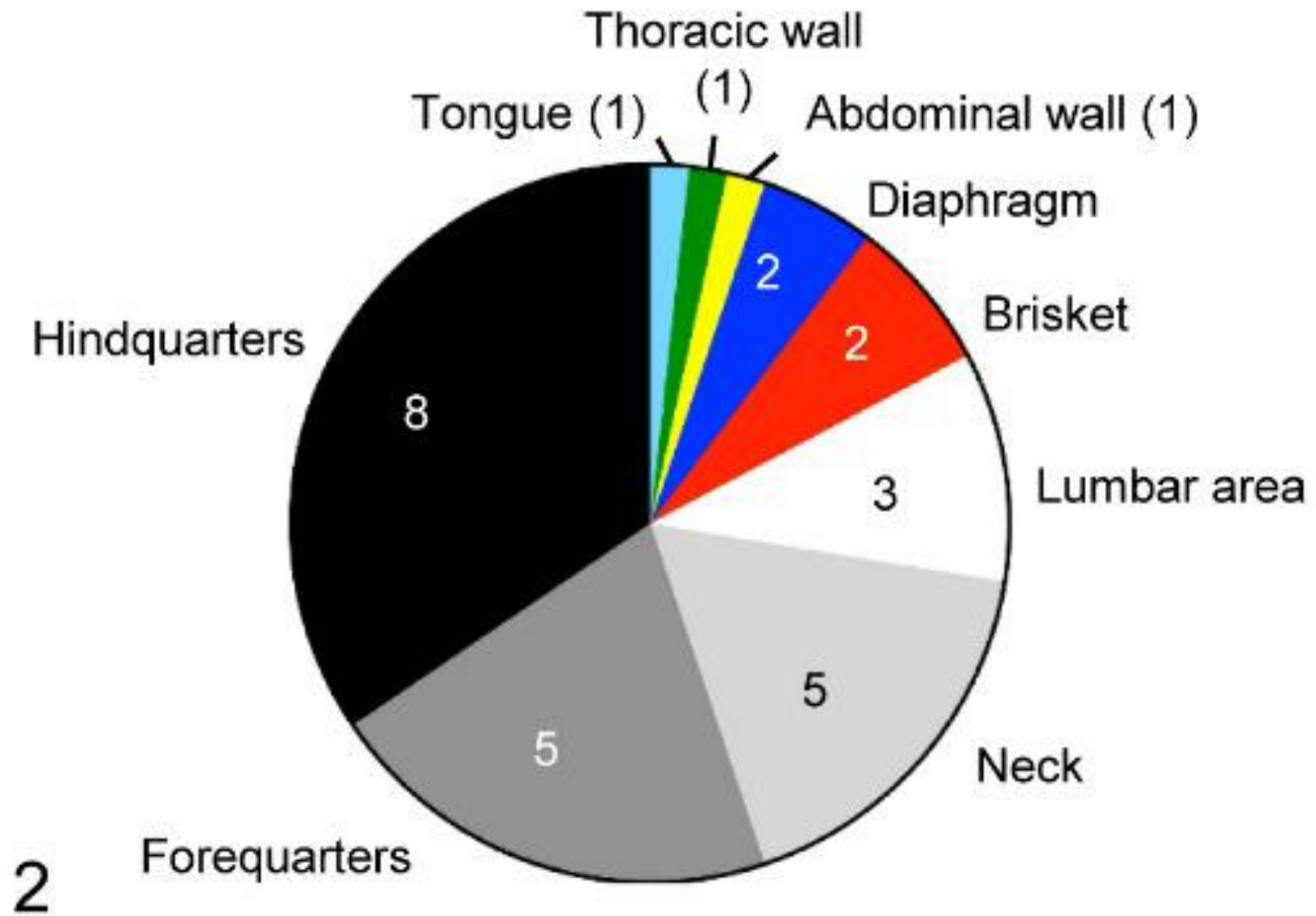


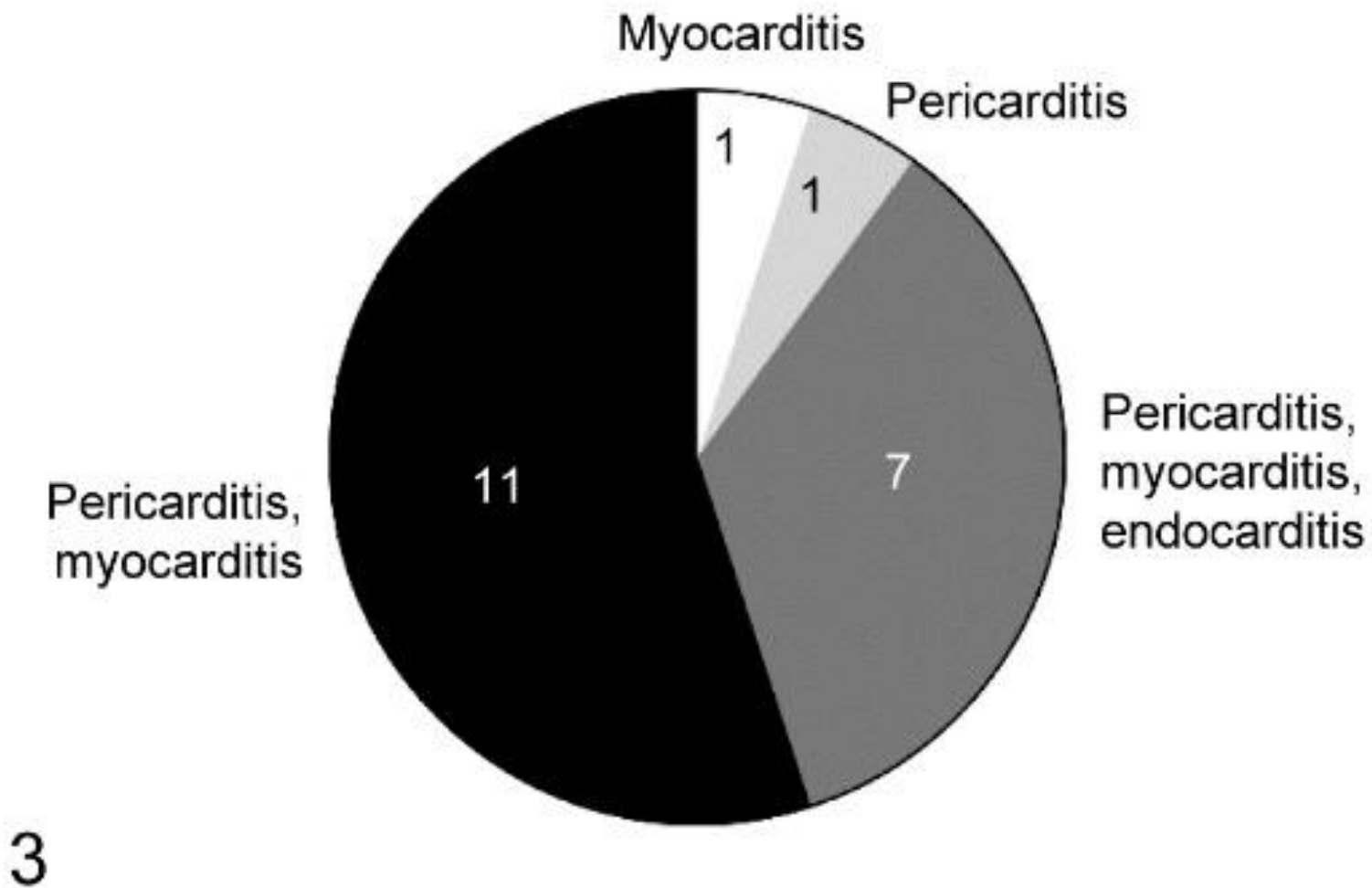


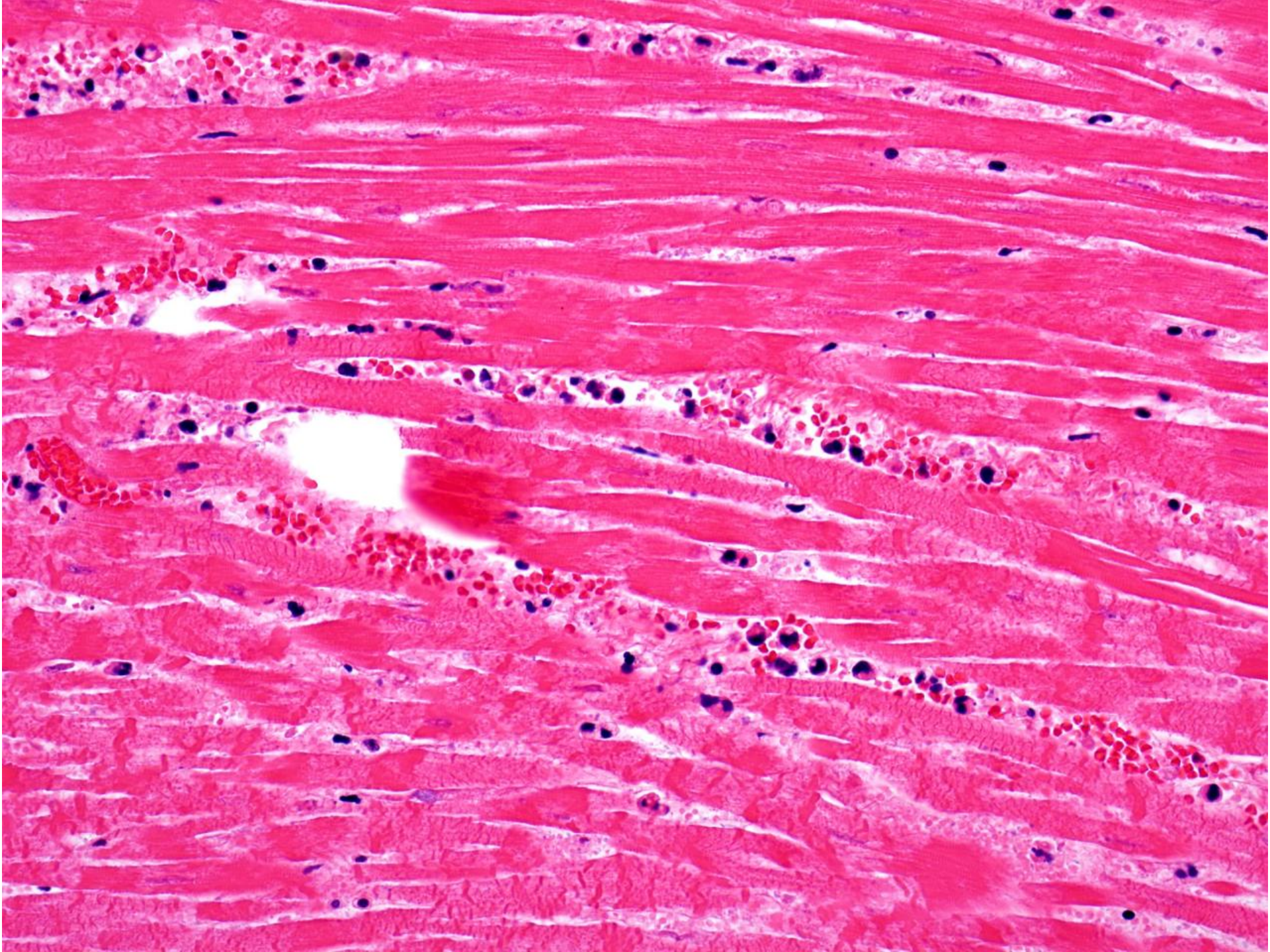
**Simultaneous skeletal and cardiac
muscle disease:**

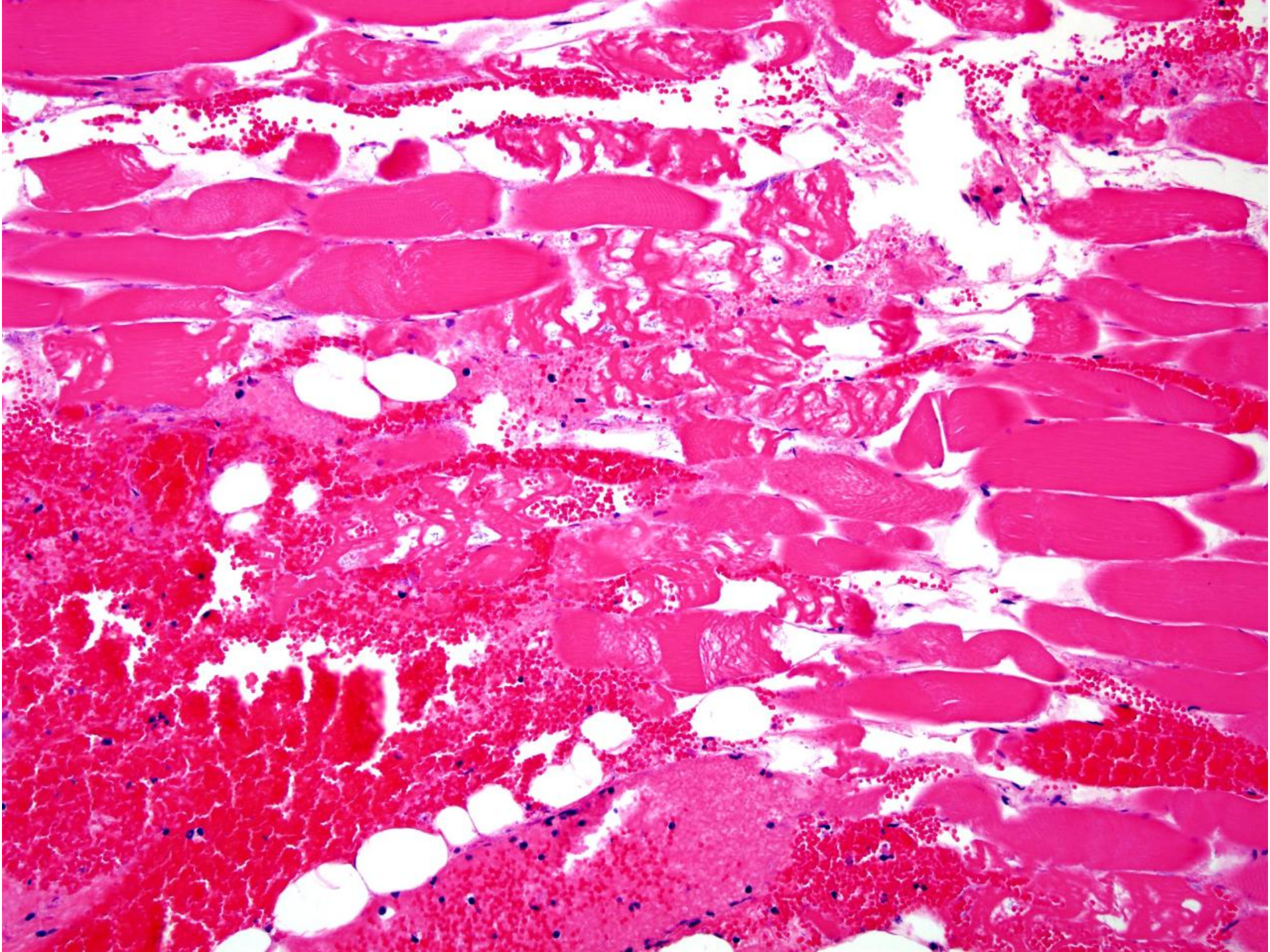
frequent

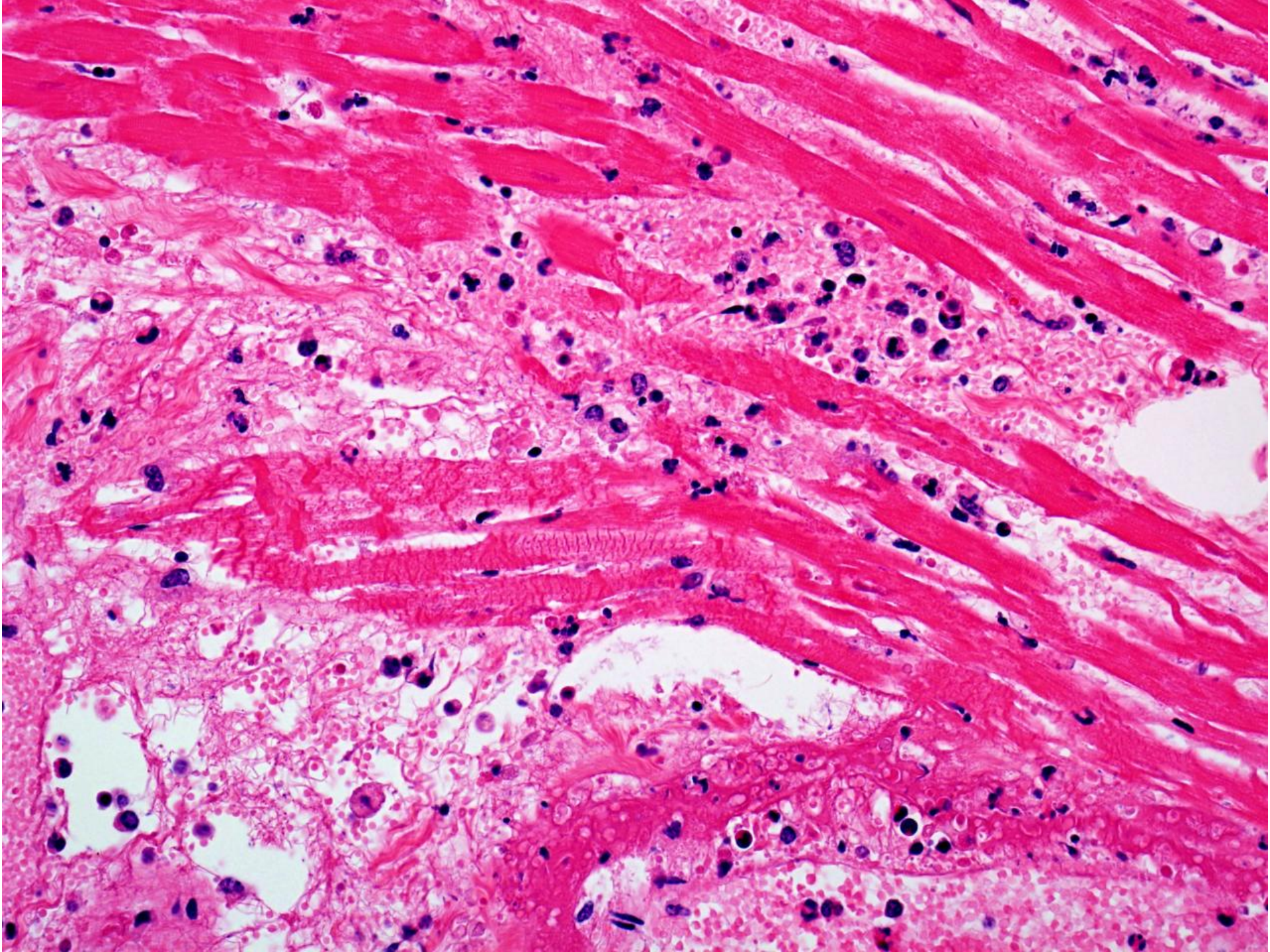


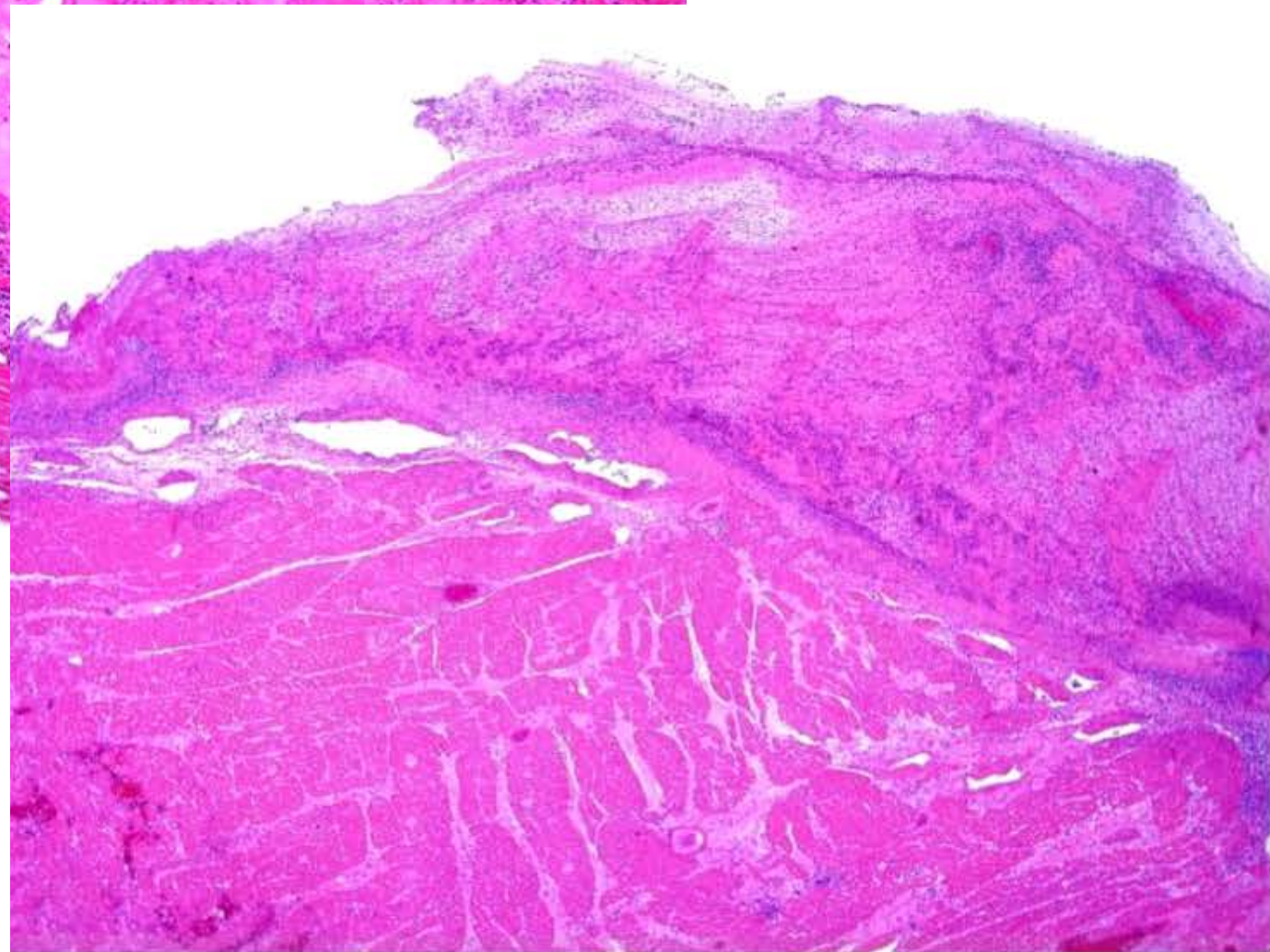
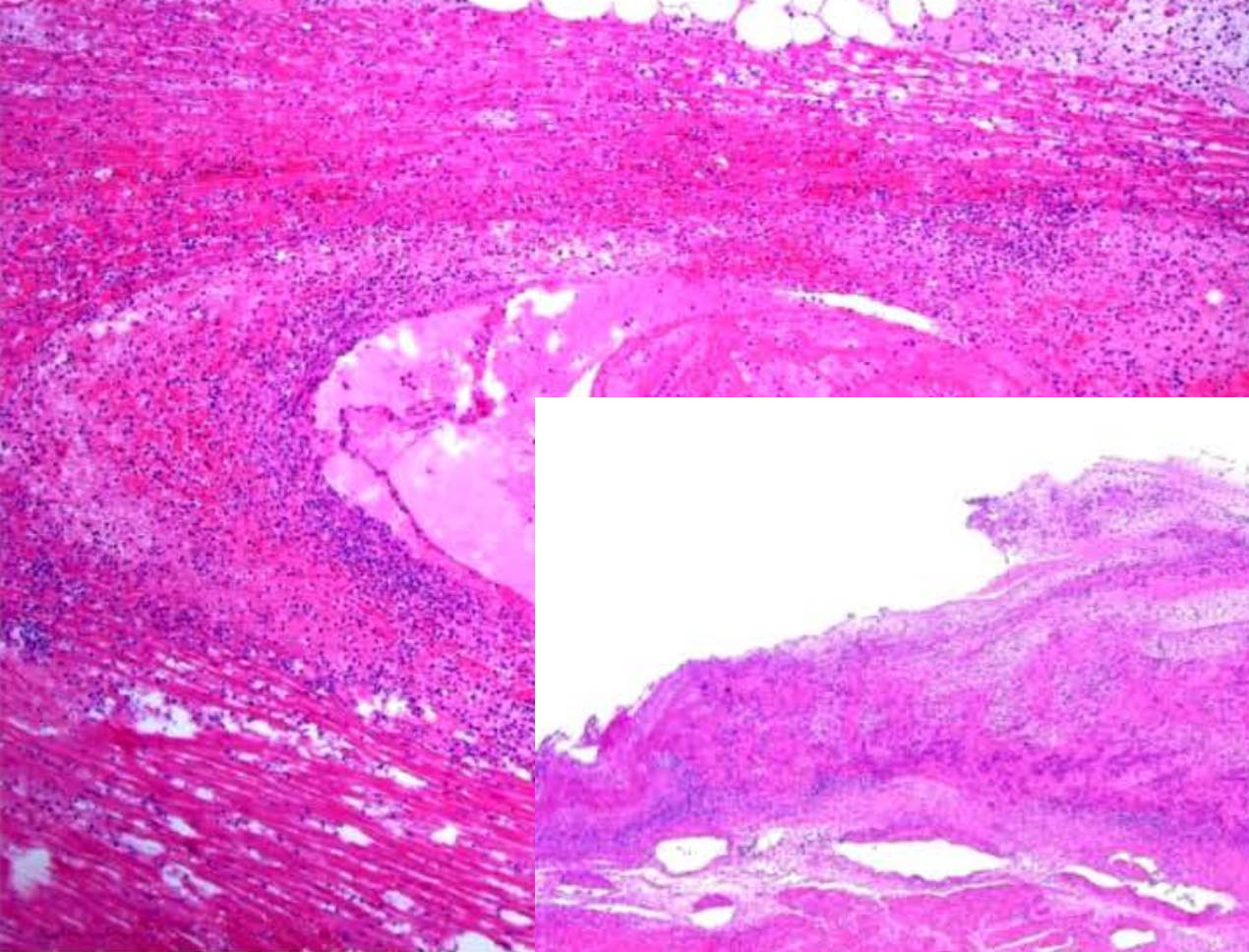


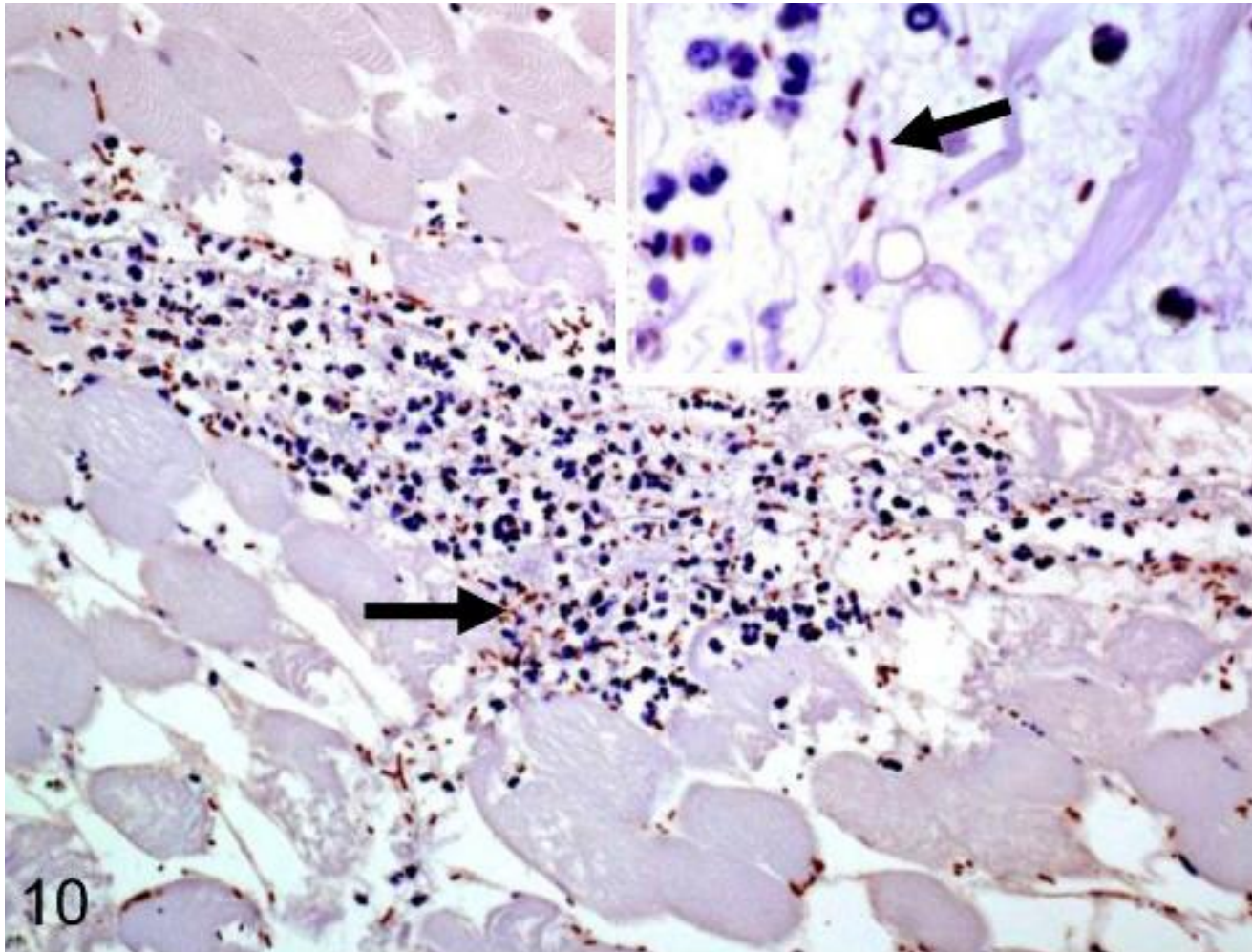


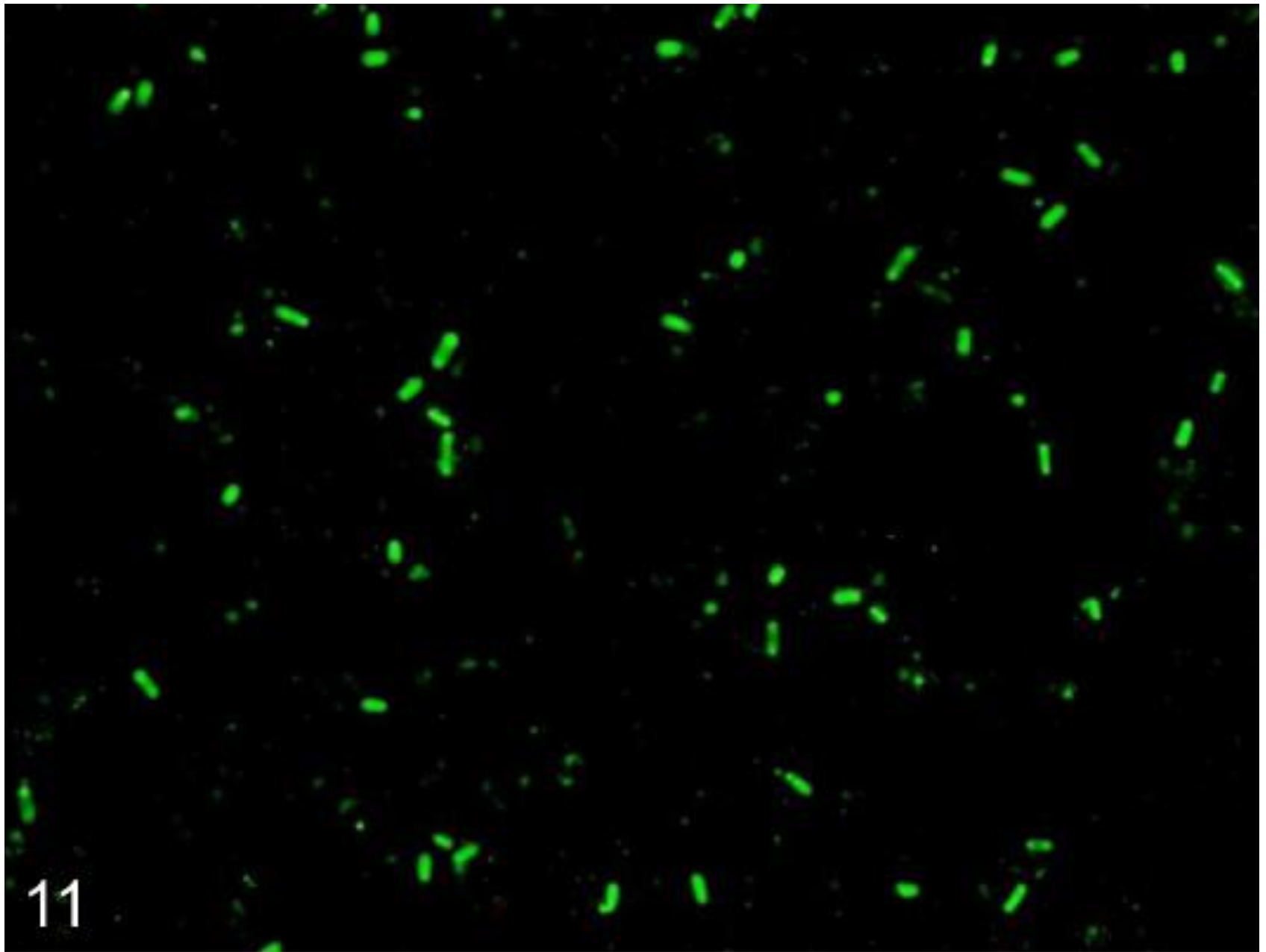


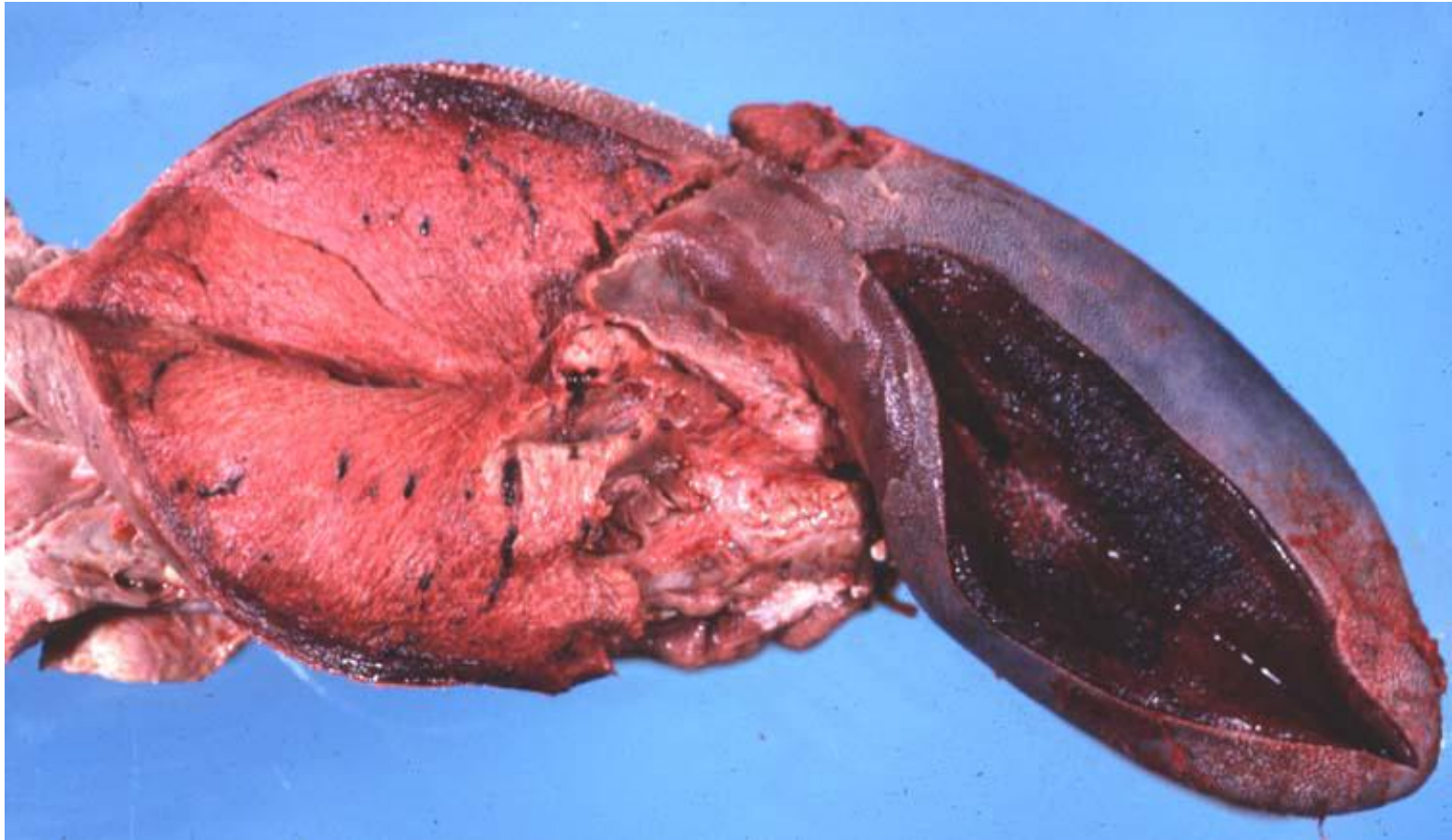












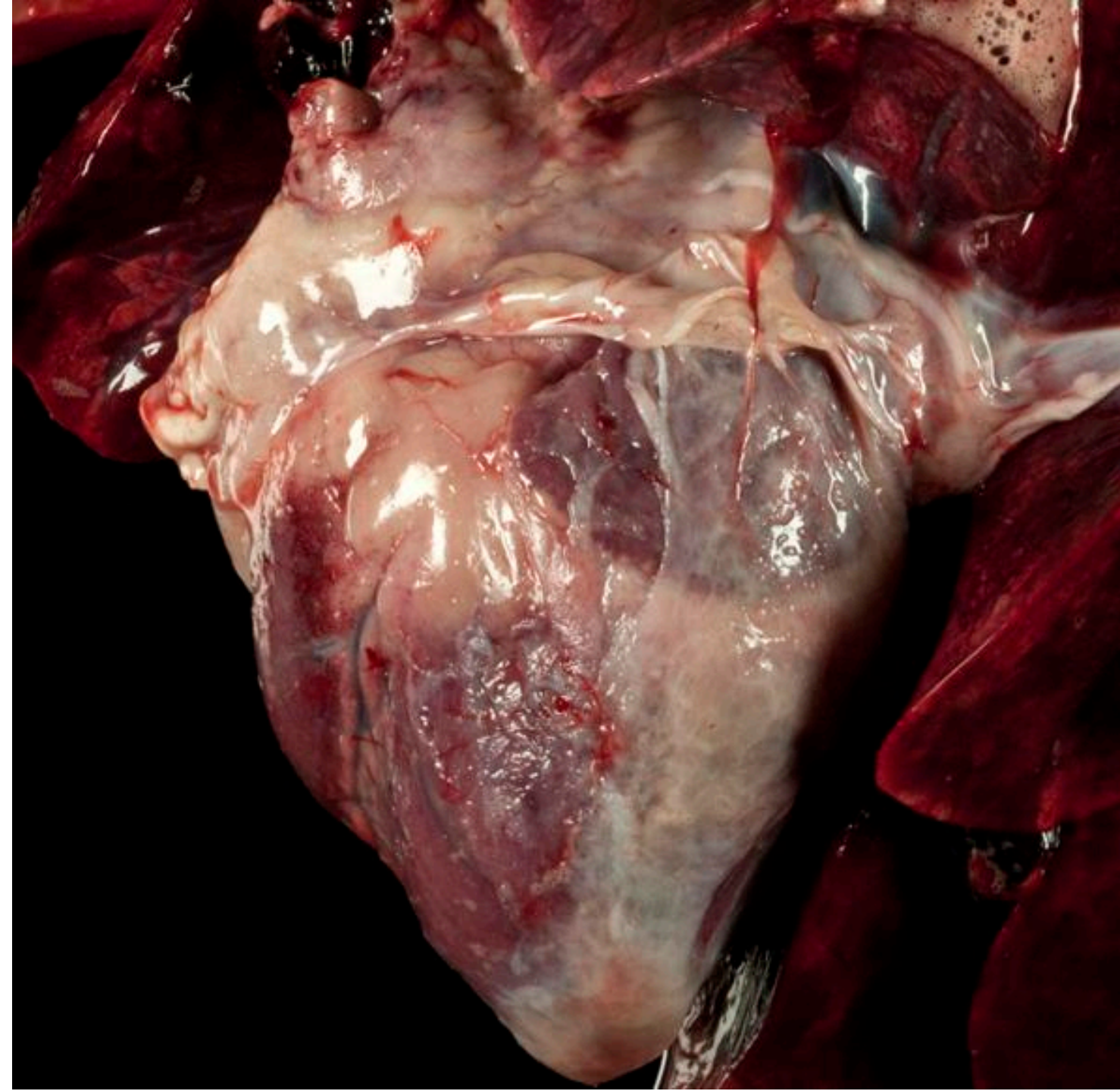


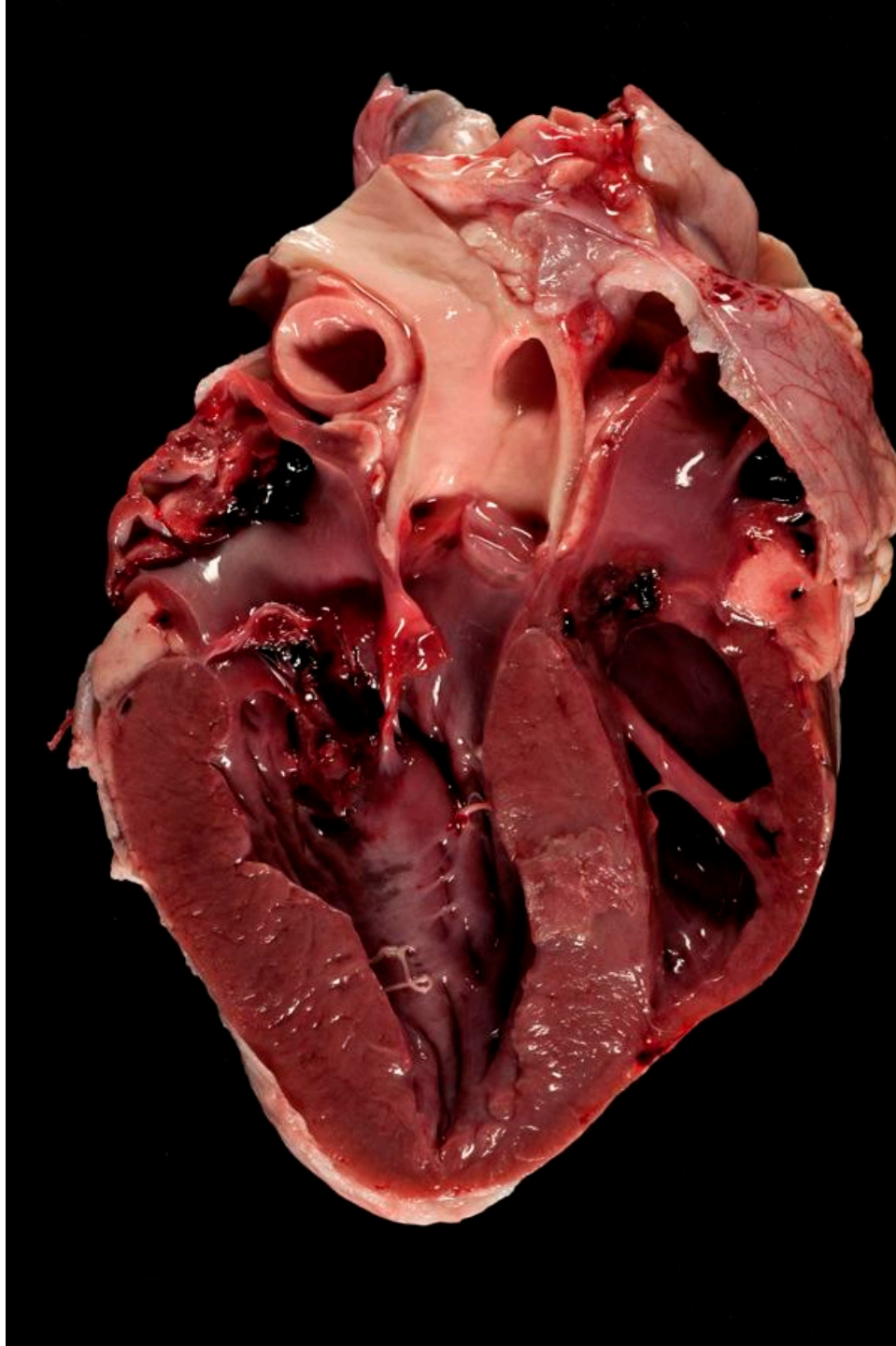
F. Dutra











Sheep:

Blackleg or gas gangrene.....?

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>	✓	✓
	Hepatitis			

Human gas gangrene



Human gas gangrene

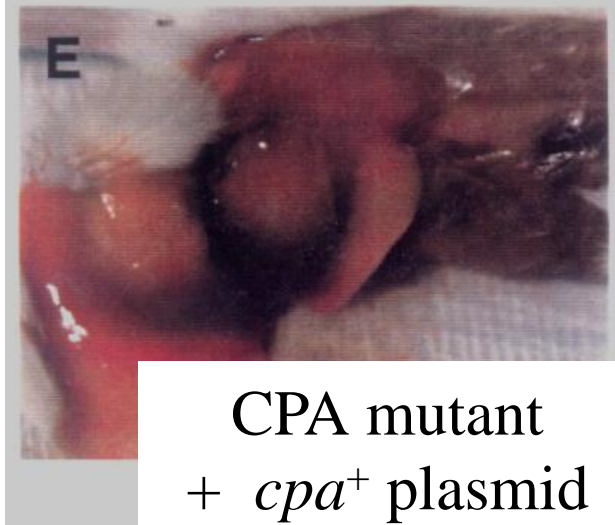
MAIN VIRULENCE FACTORS



* Alpha toxin

* Perfringolysin (synergism)

Alpha toxin is essential for virulence



Animal gas gangrene

Etiology:

Clostridium septicum

Clostridium chauvoei

Clostridium novyi

Clostridium sordellii

Clostridium perfringens

Take-home message!!!



Clostridium septicum

Main virulence factors

- * Alpha toxin: β -PFT; cell necrosis
- * Septicolysis: cell necrosis/hemolysis

Pathogenesis

Spores/bacteria in soil →

contaminated wounds →

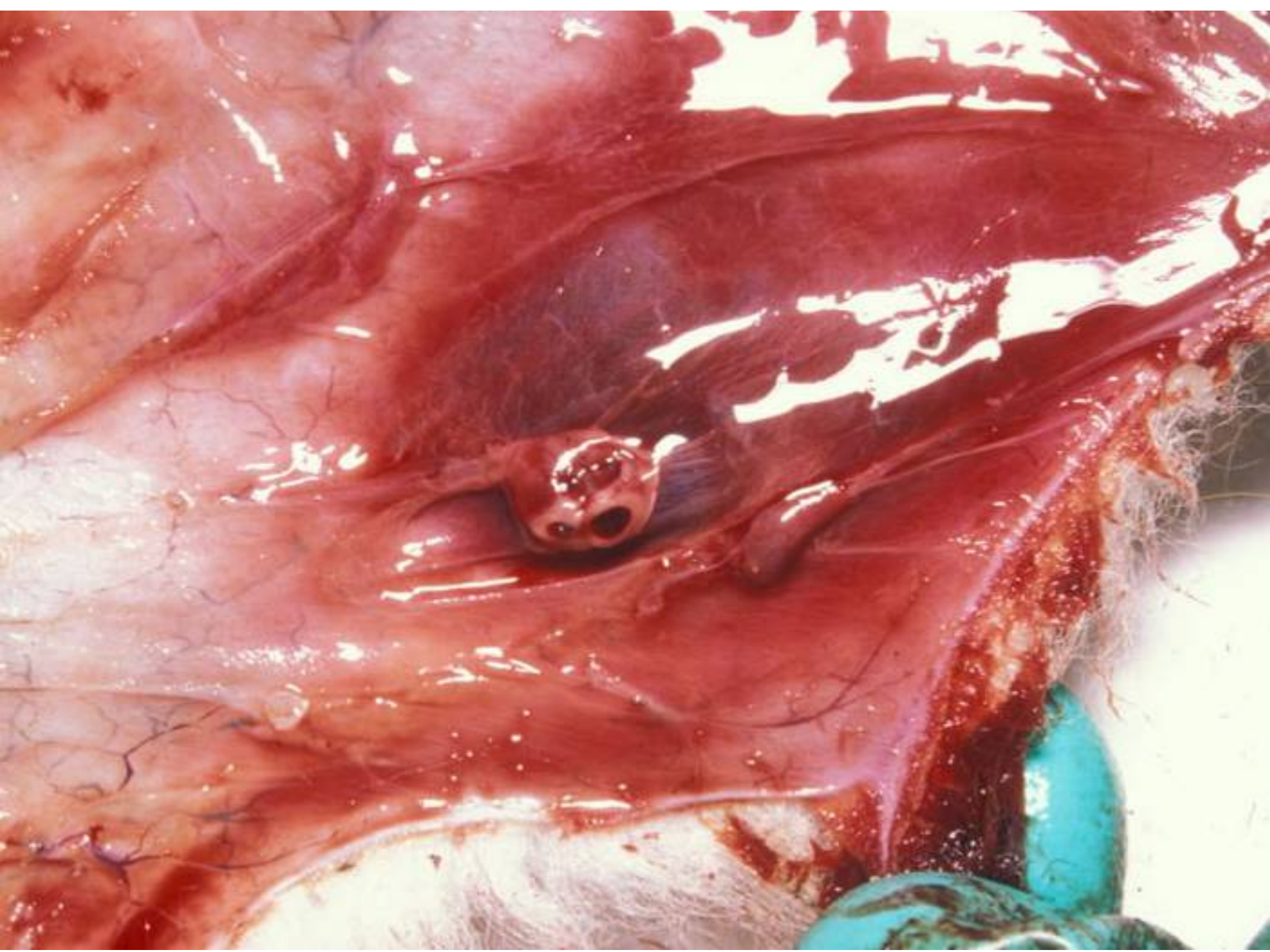
reduction O_2 → germination → toxins →

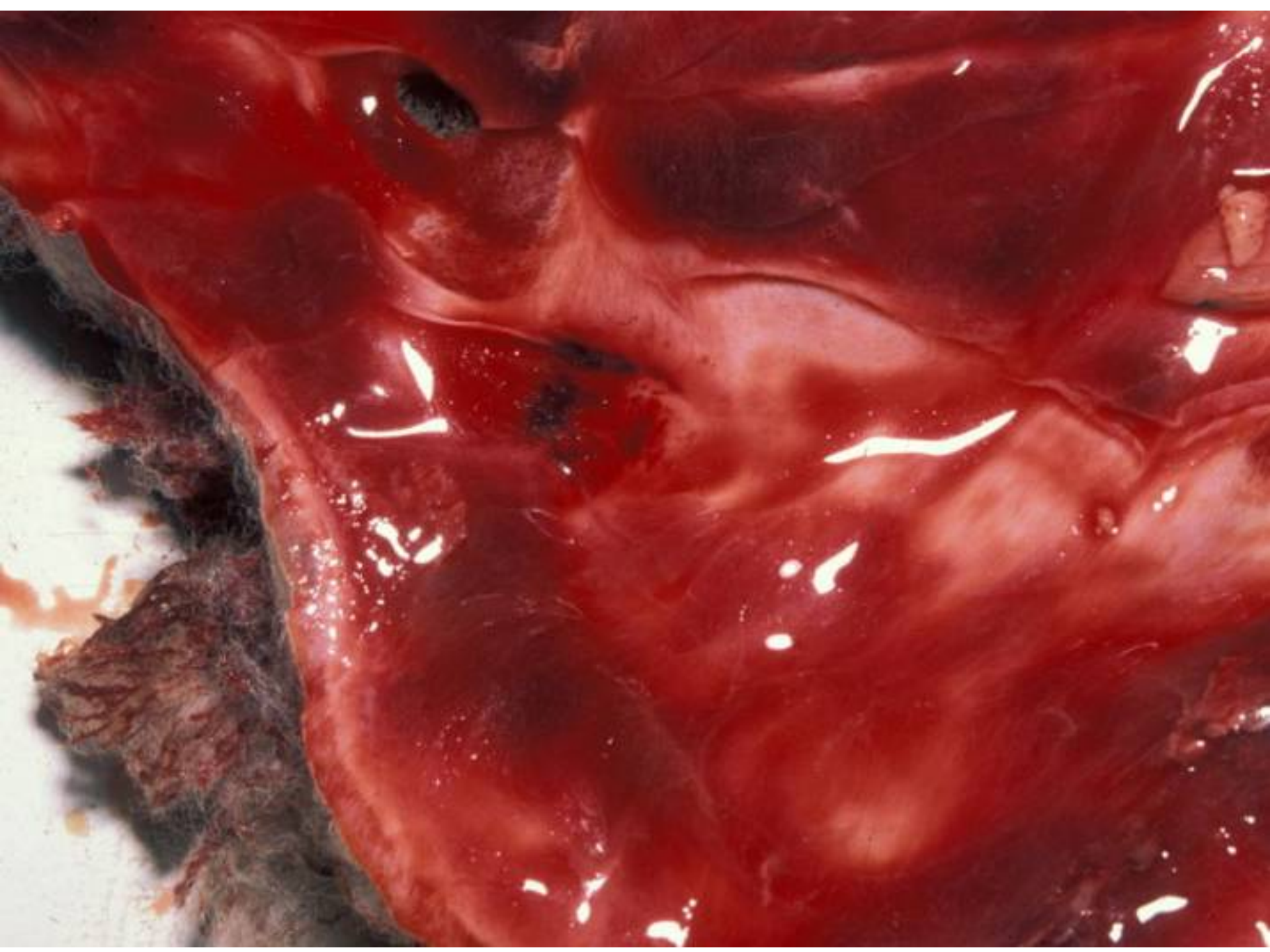
SQ/muscular necrosis → toxemia → shock

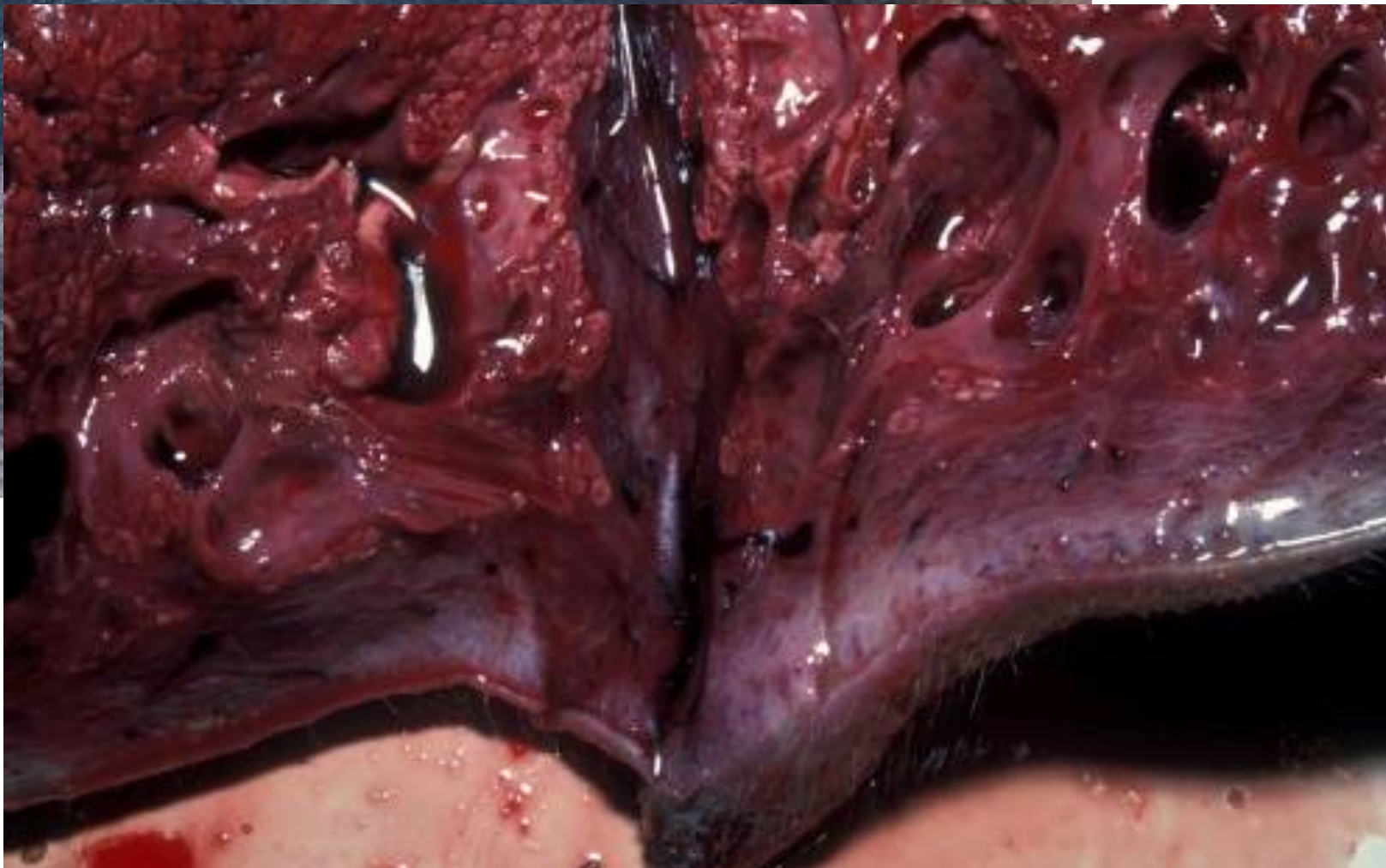
Skin/mucosa wounds necessary:

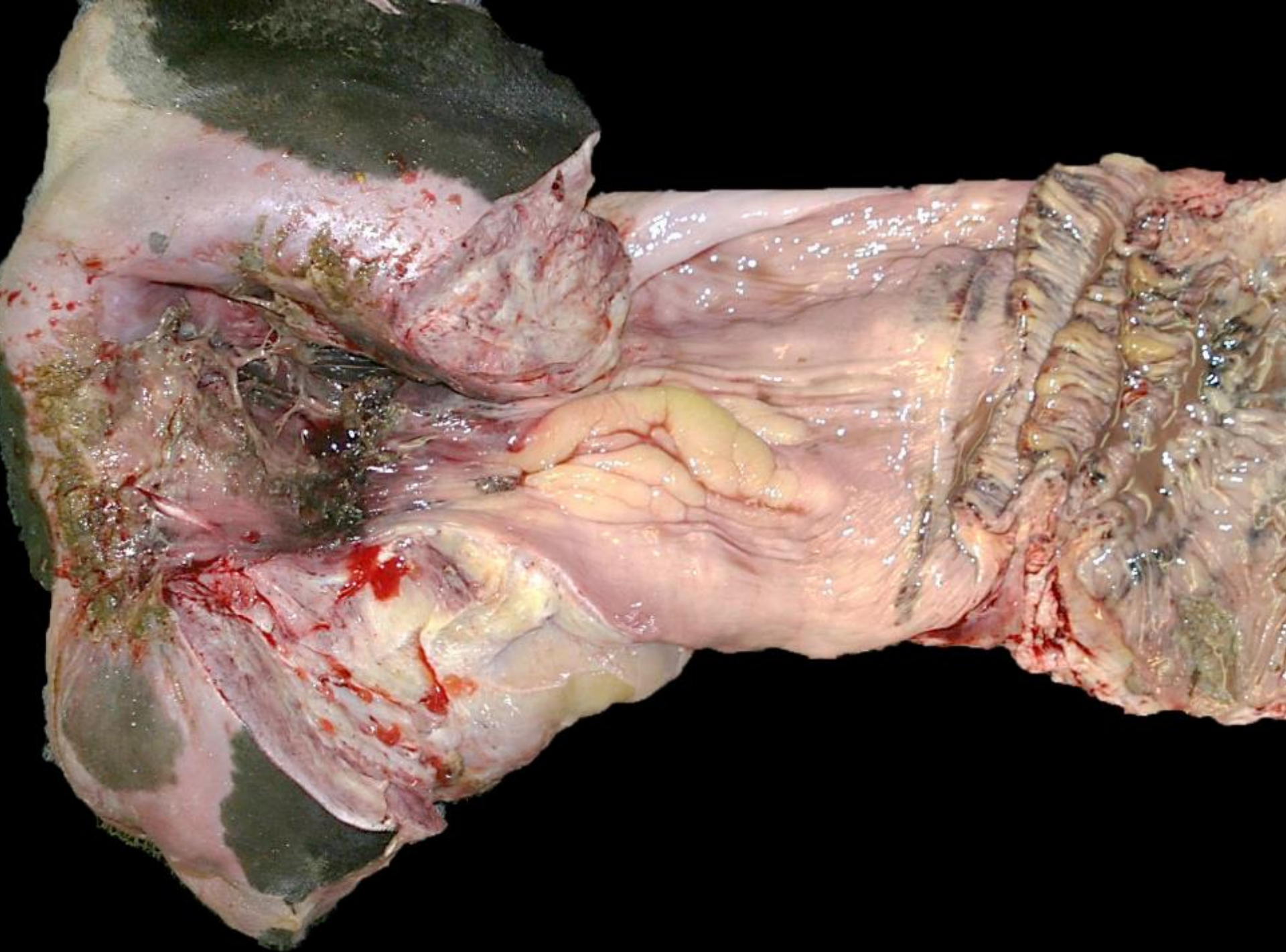
- * vaccination**
- * castration**
- * dehorning**
- * sharp elements in feed**
- * parturition**
- * blood sampling**



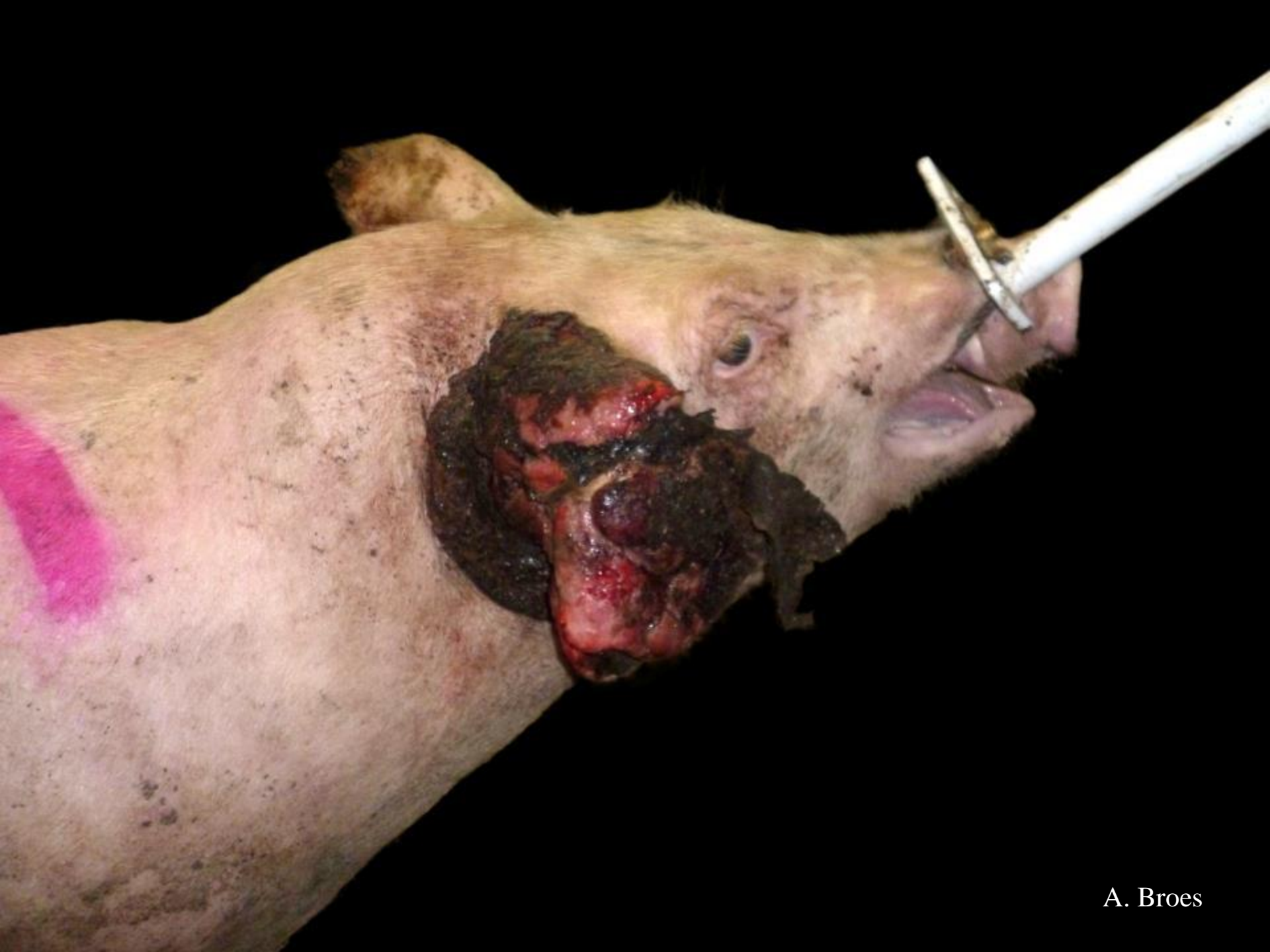






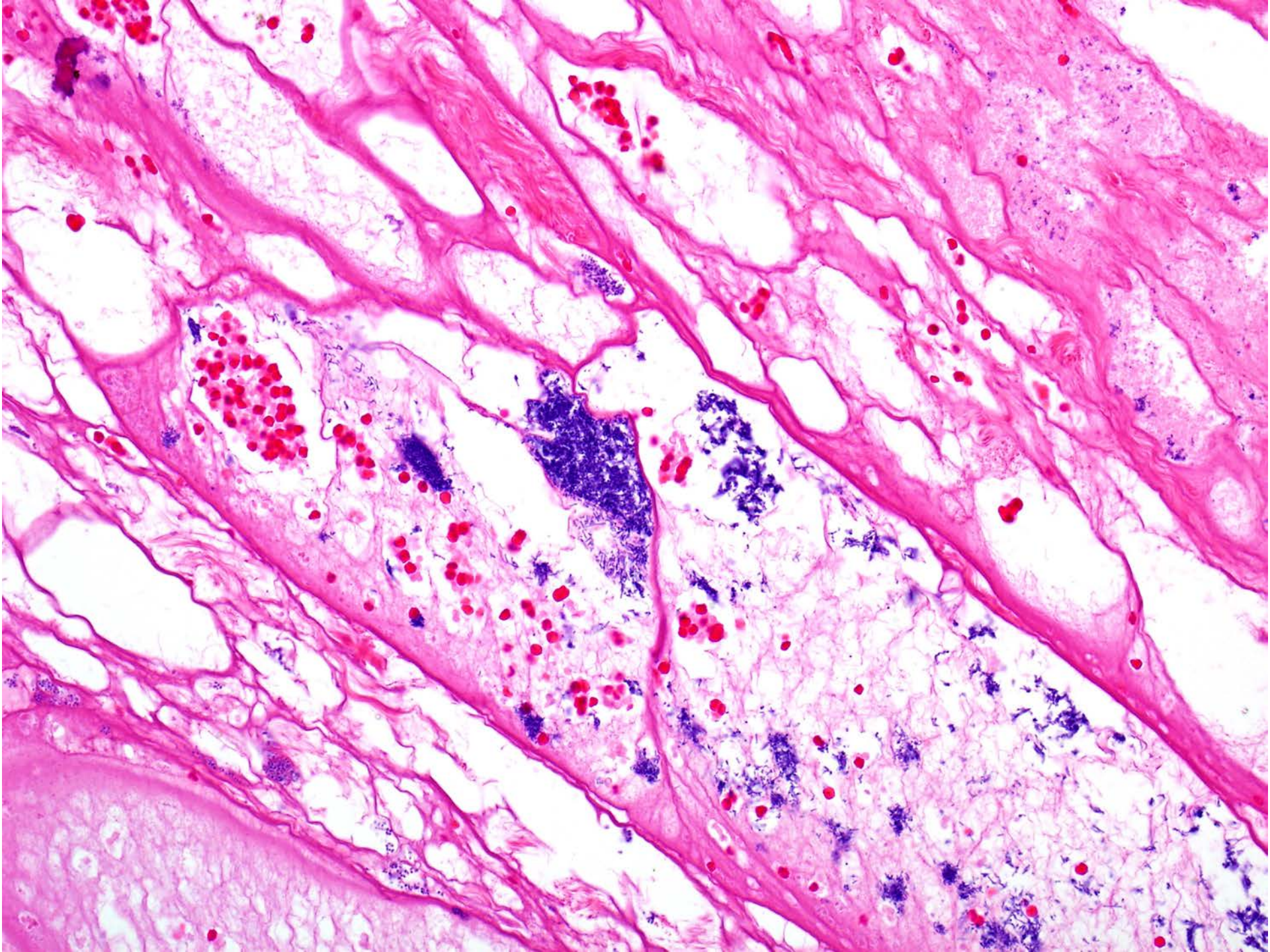


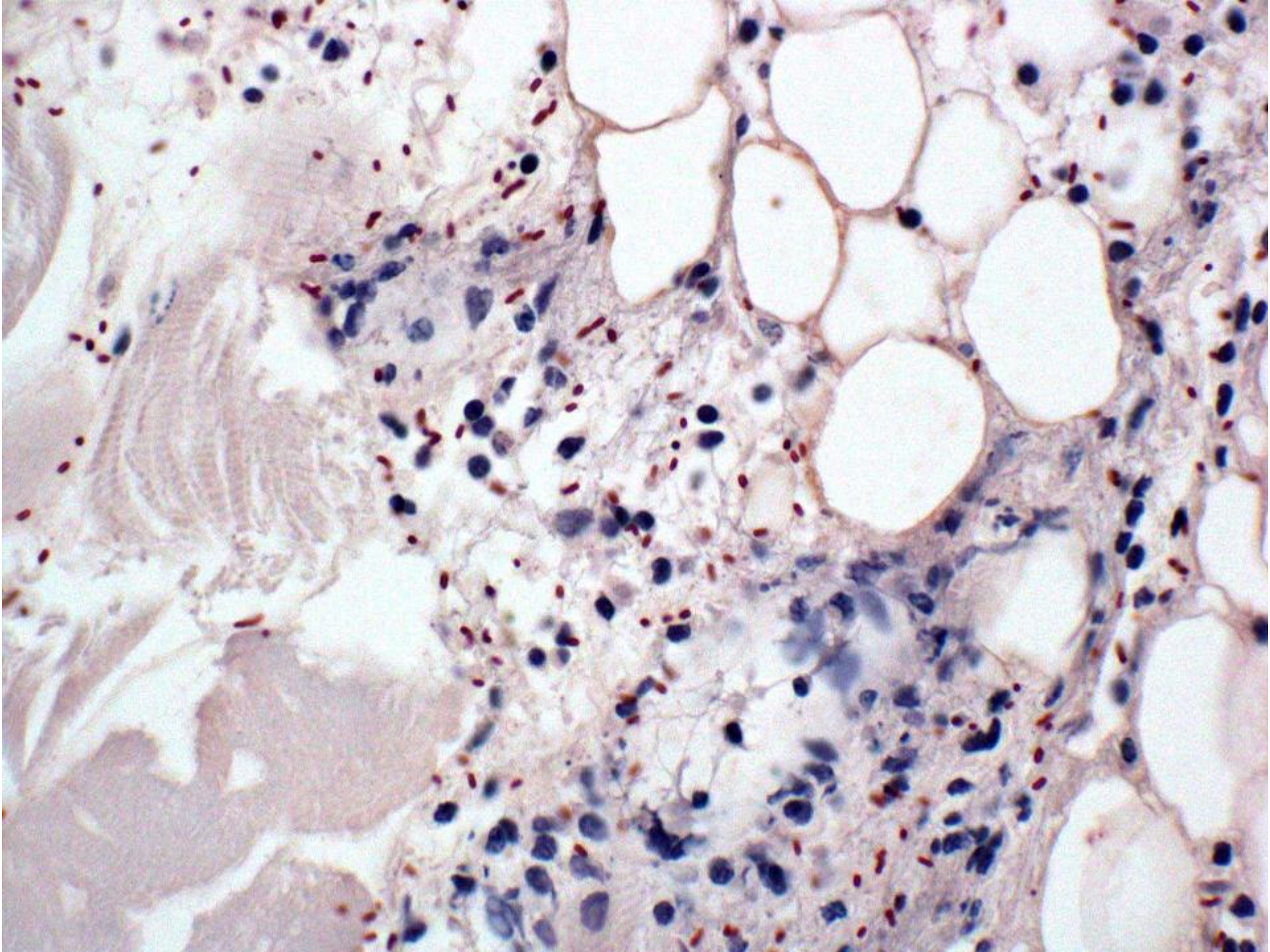






A. Broes







Most prevalent causes:

C. perfringens type A

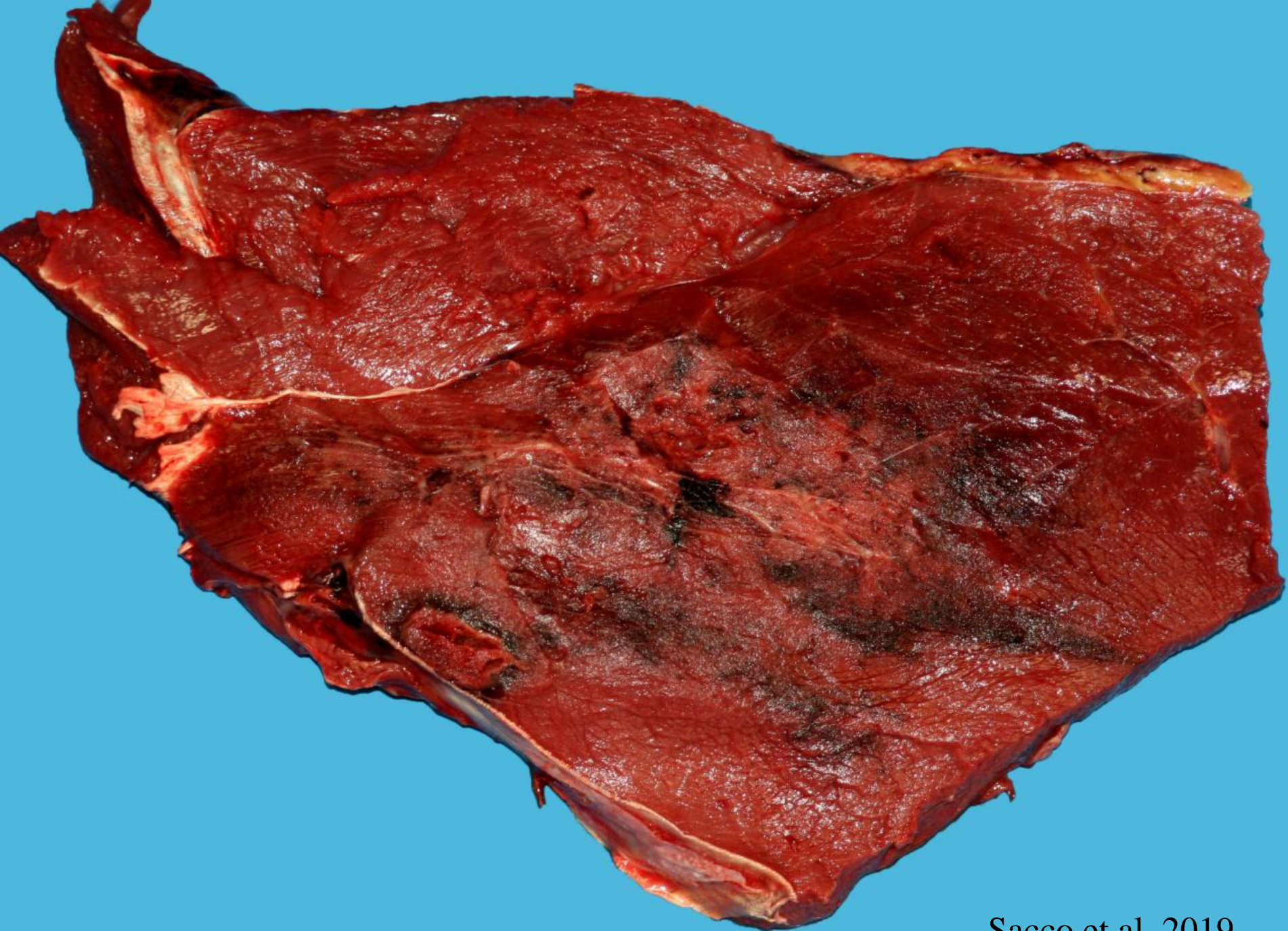
C. sordellii

Pathogenesis

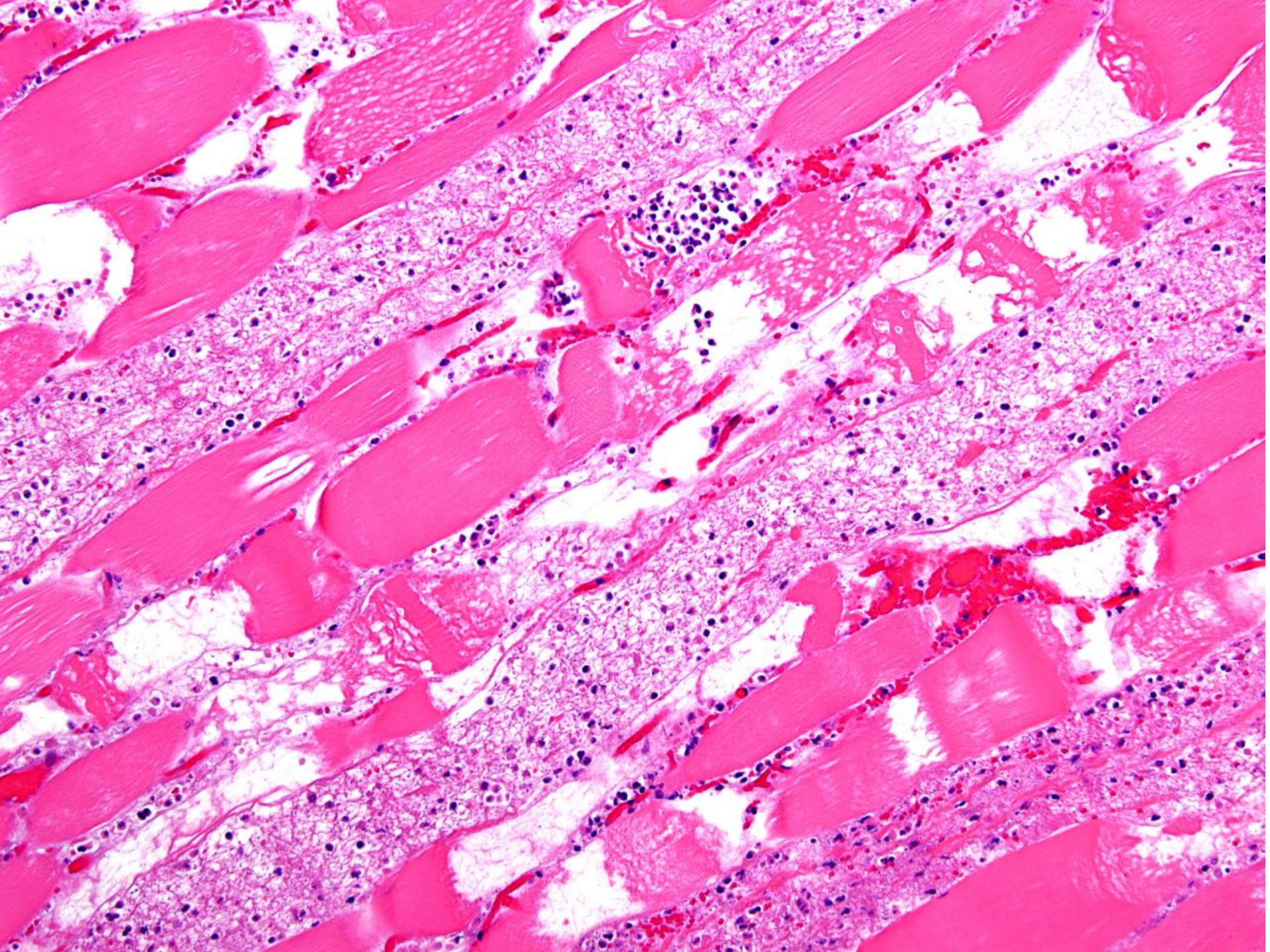
- * wounds
- * omphalitis

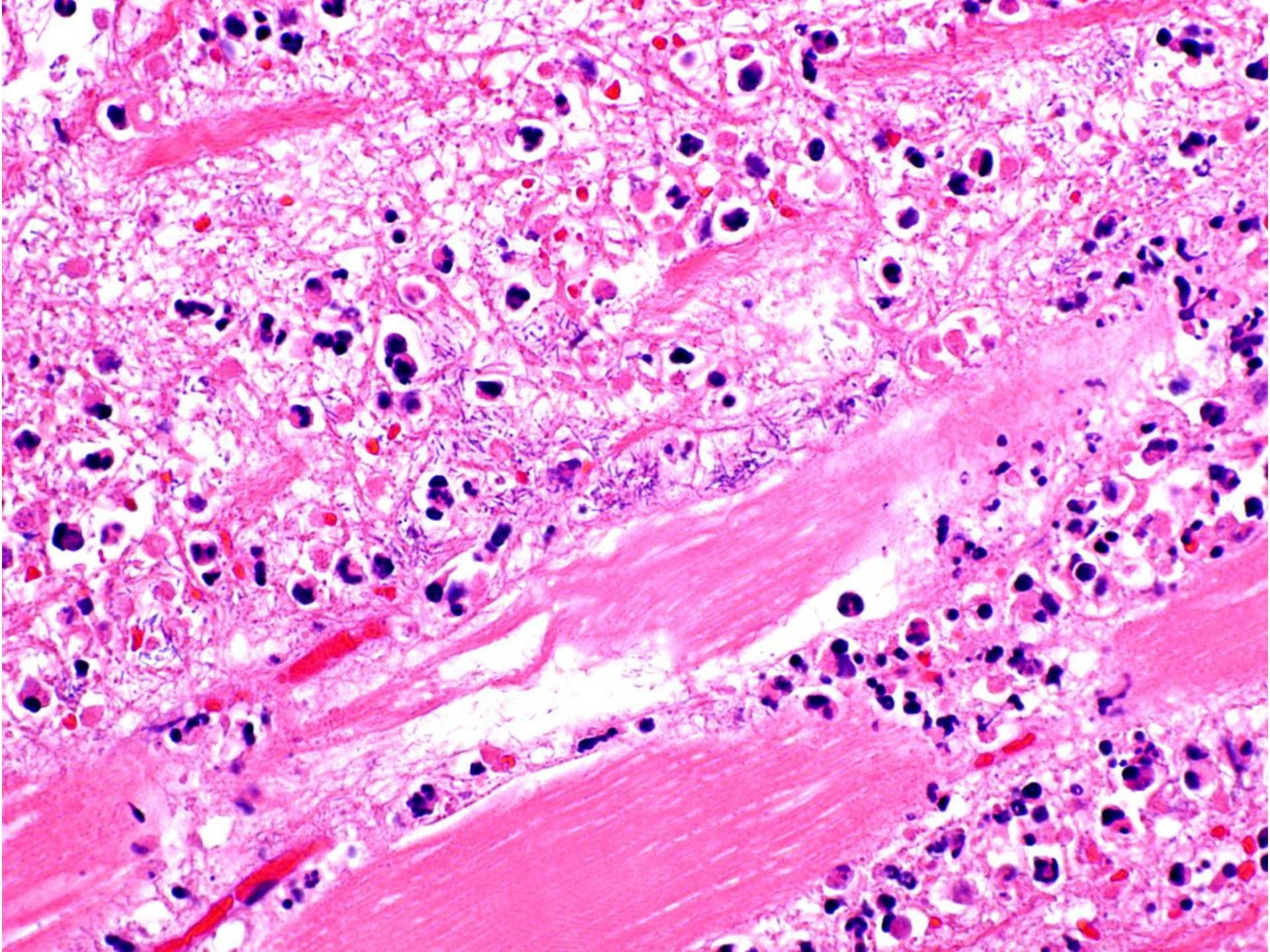


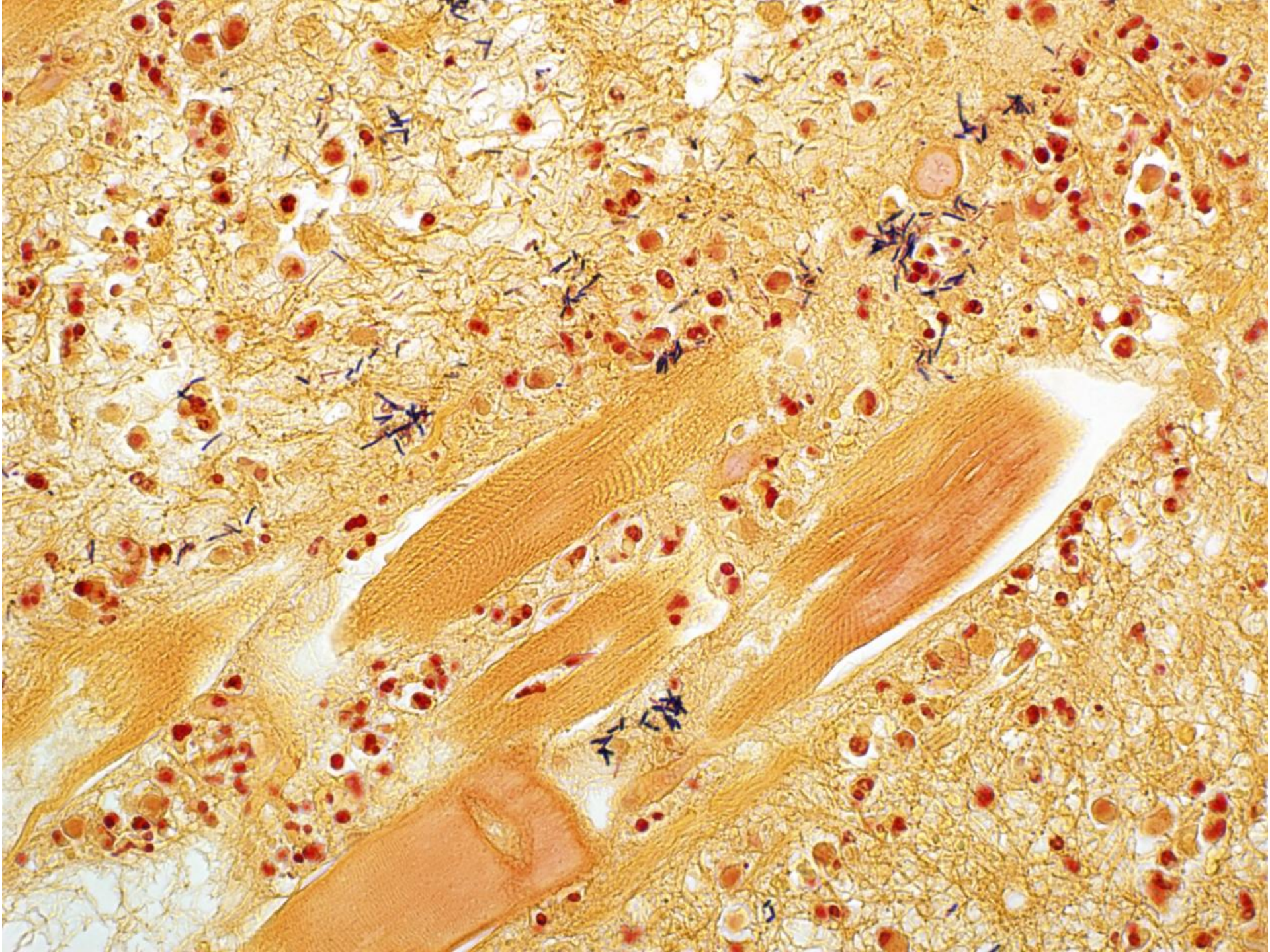
Sacco et al, 2019

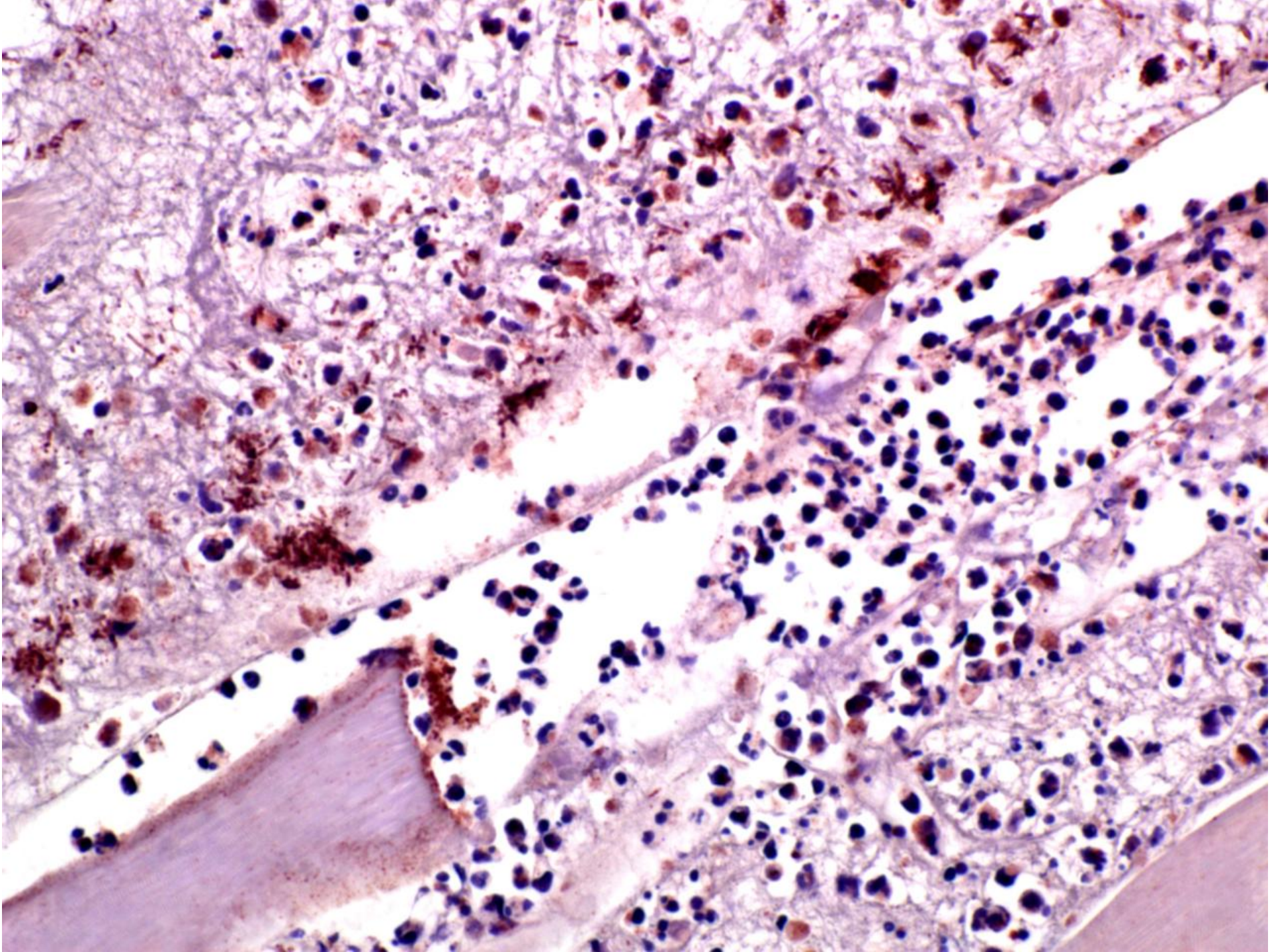


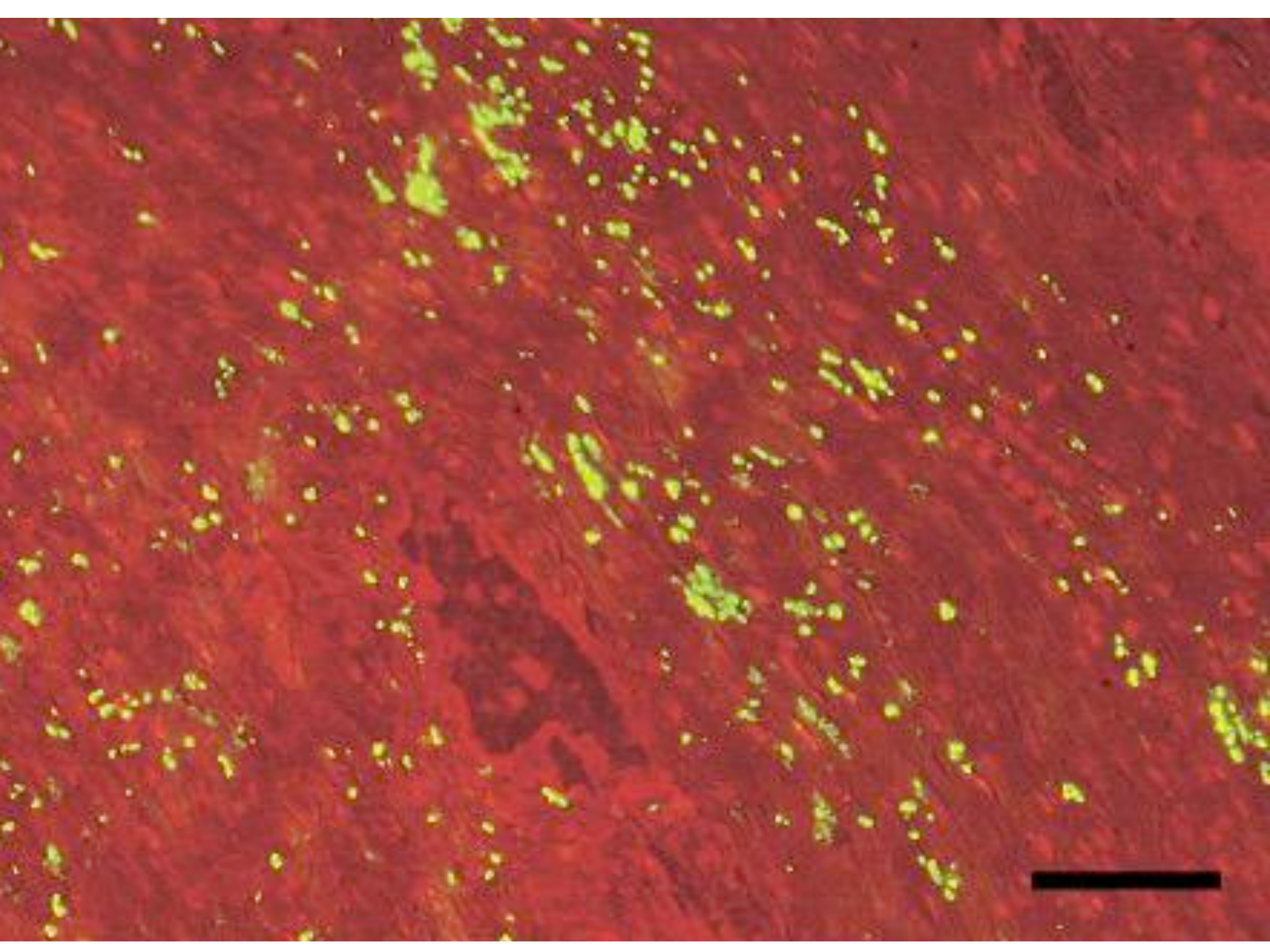
Sacco et al, 2019

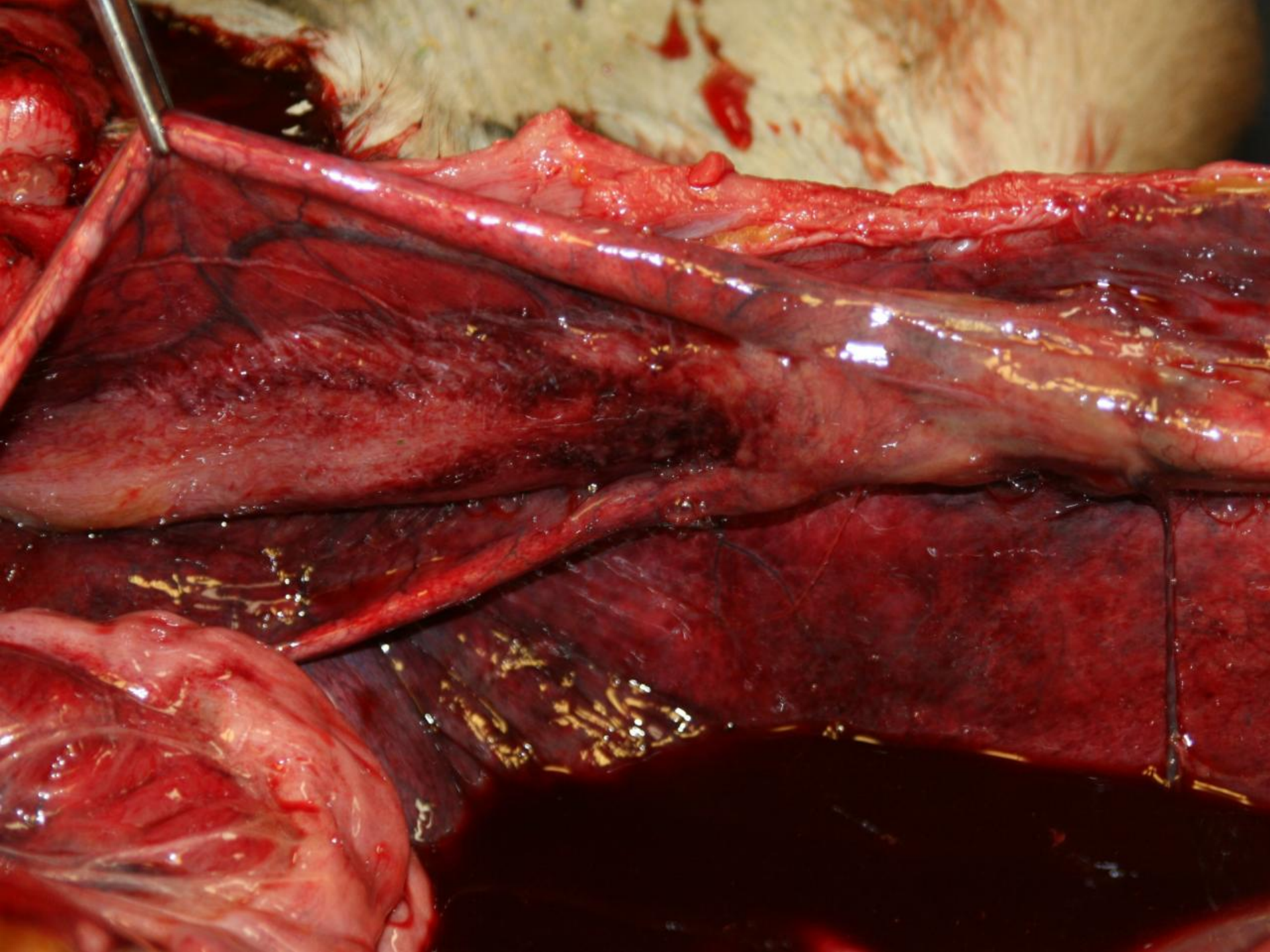






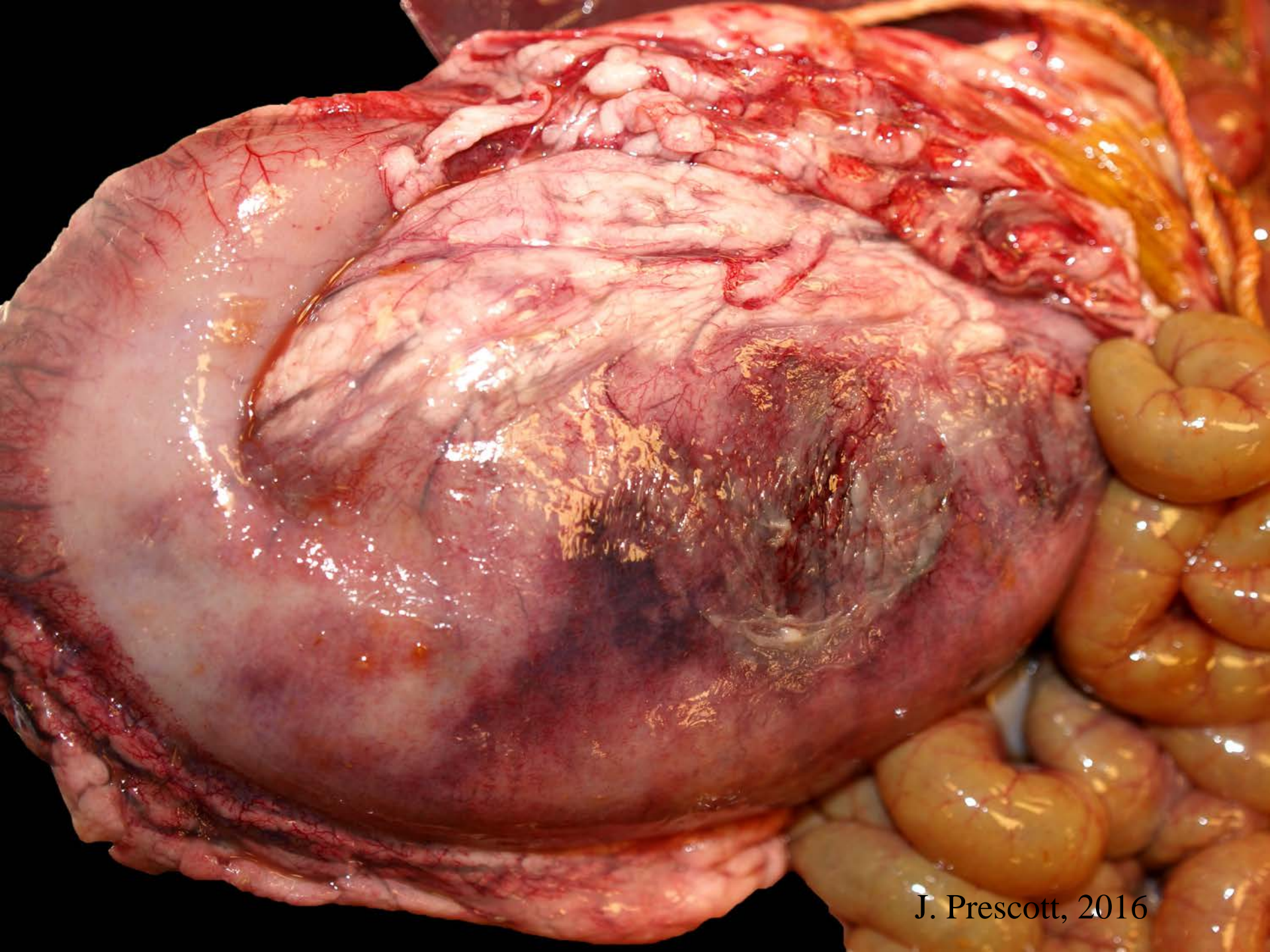




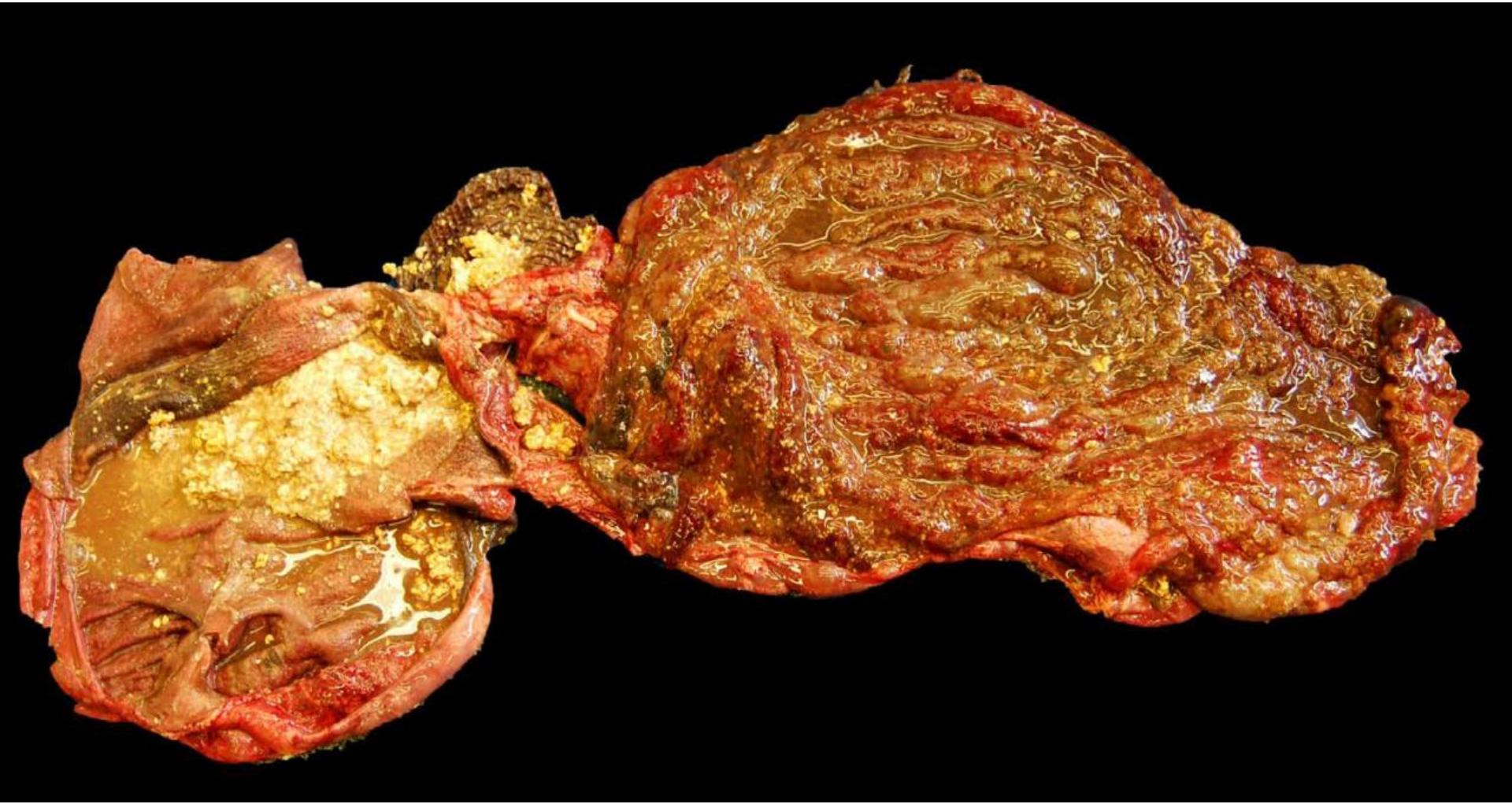


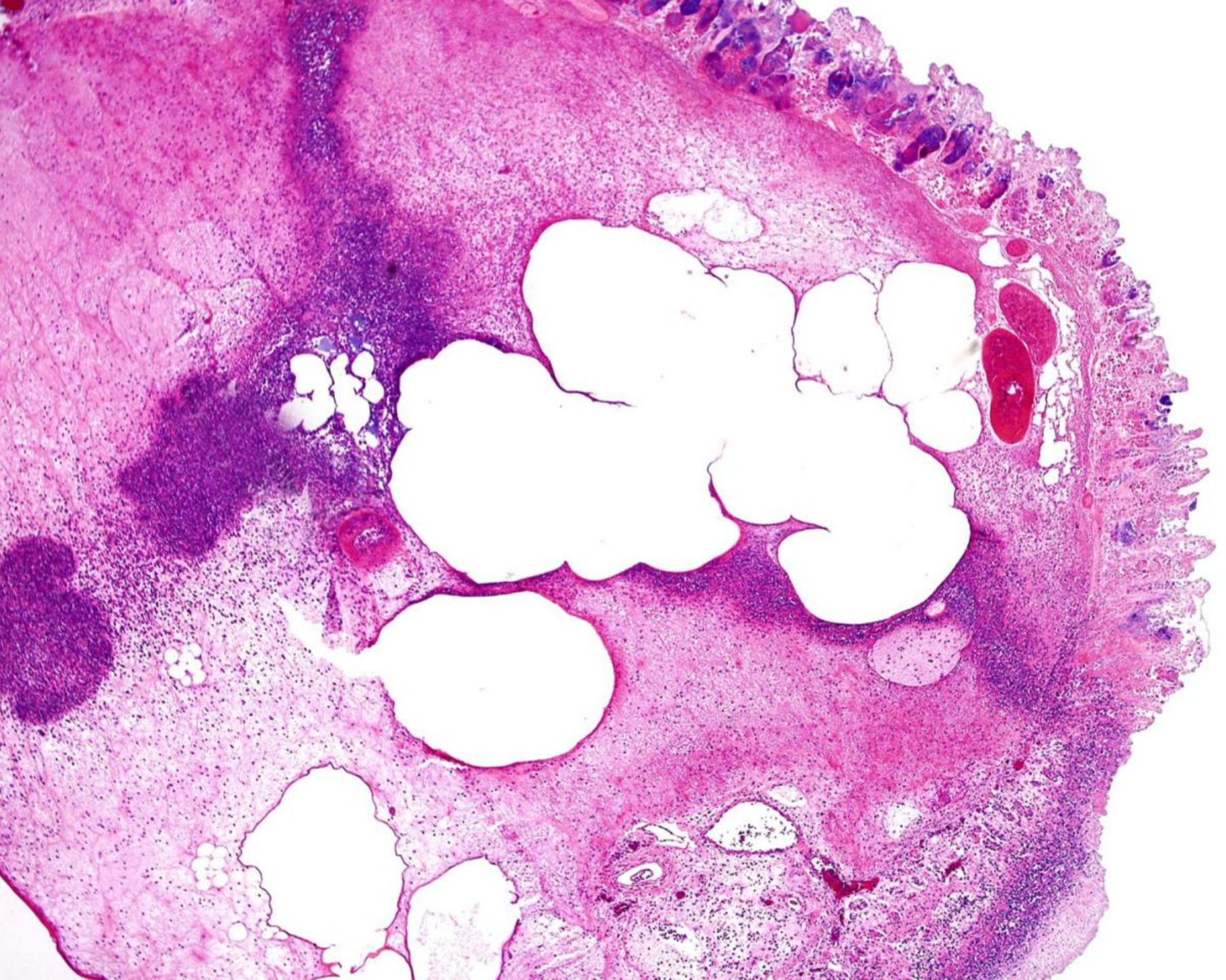
**Braxy (bradsot),
Necrotizing abomasitis
(*C. septicum*)**

sheep
cattle



J. Prescott, 2016





Pathogenesis

Frozen grass (really?)

Probably multifactorial: cold milk.....

Diagnostic criteria

1-Clinics/Necropsy



Suggestive

2-Histopathology/smears



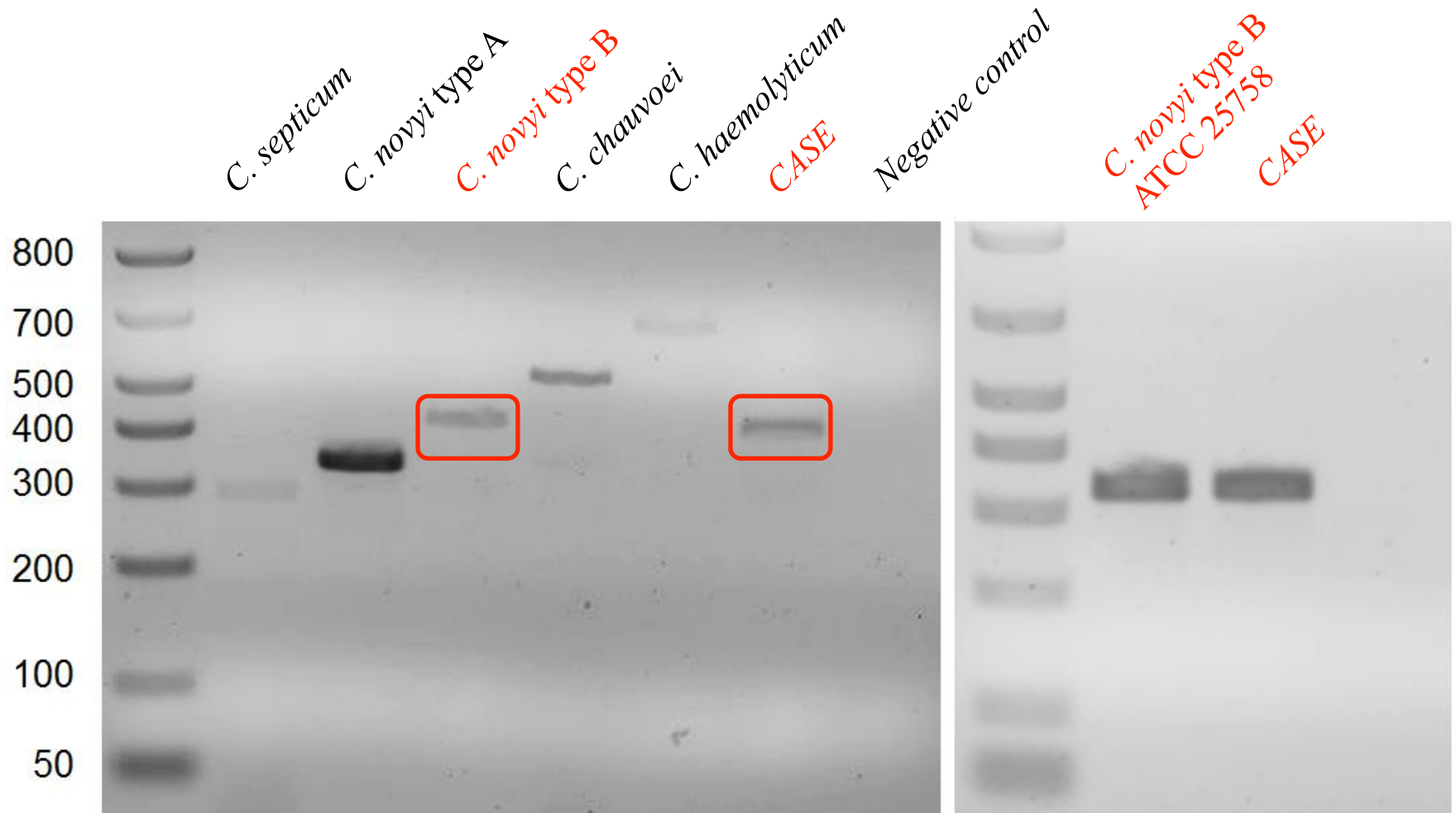
Suggestive

3-Ancillary: Culture/PCR
 FAT/IHC



Confirmatory





PCR for *fliC* gene of
histotoxic clostridia

C. novyi type
B α -toxin
gene

Other causes of
clostridial abomasitis?



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				

Clostridium novyi

- * **Type A:** gas gangrene (animal & human)
- * **Type B:** necrotic hepatitis (black disease)
- * **Type C:** non pathogenic
- * **Type D (*C. haemolyticum*):** bovine bacillary hemoglobinuria

**Infectious
necrotic
hepatitis**

**Bovine bacillary
hemoglobinuria**



Take-home message!!!

New Zealand Veterinary Journal

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/tnzv20>

Necrotic hepatitis associated with *Clostridium novyi* infection (black disease) in a horse in New Zealand

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Accepted author version posted online: 17 Oct 2014.

Brief Communication



Infectious necrotic hepatitis caused by *Clostridium novyi* type B in a horse: case report and review of the literature

Journal of Veterinary Diagnostic Investigation
2018, Vol. 30(2) 294–299

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DOI: 10.1177/1040638717737125

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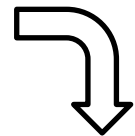
Akinyi C. Nyaoke,^{*} Mauricio A. Navarro,^{*} Juliann Beingesser, Francisco A. Uzal¹



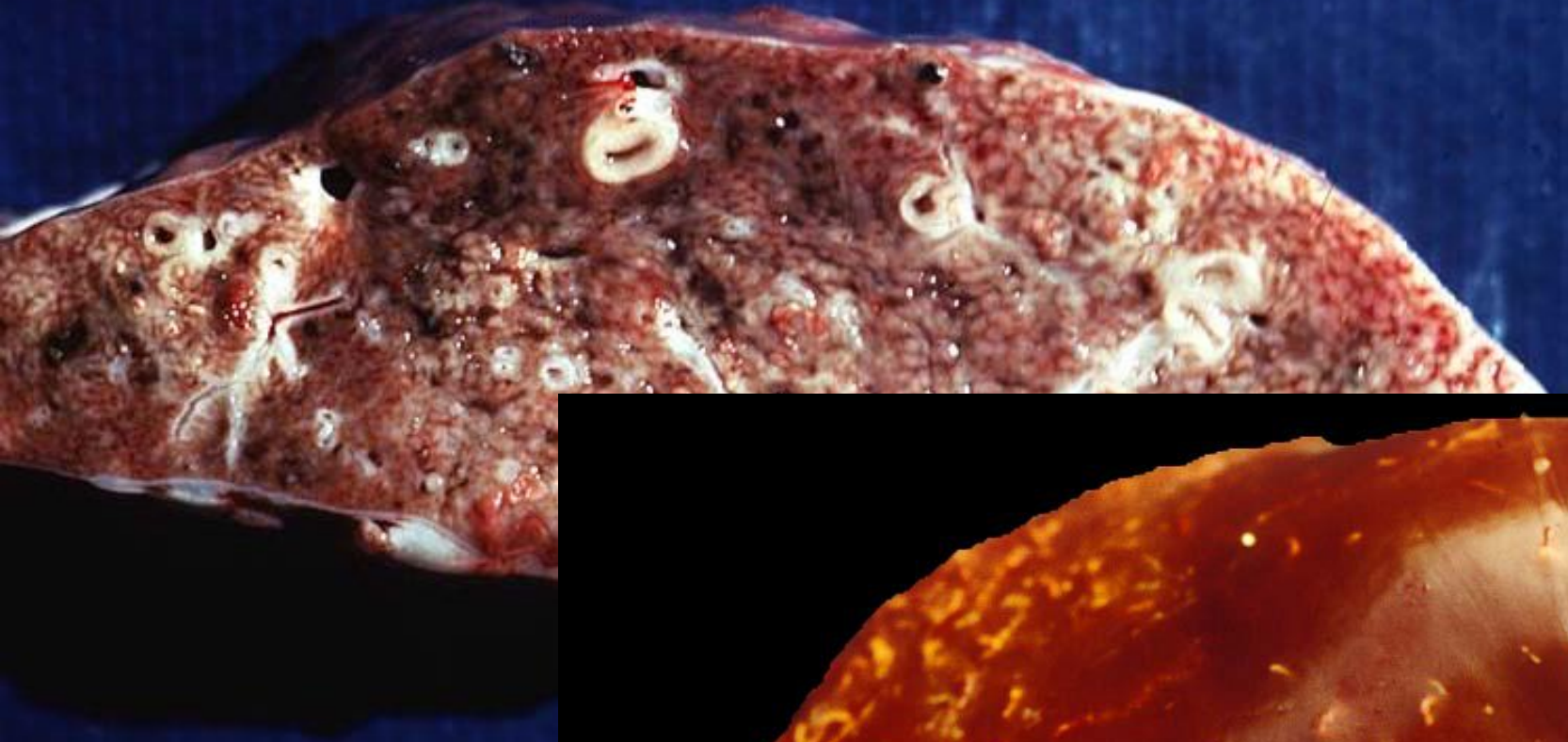
- Alkaline pH (8.0)
- Poorly drained pastures...

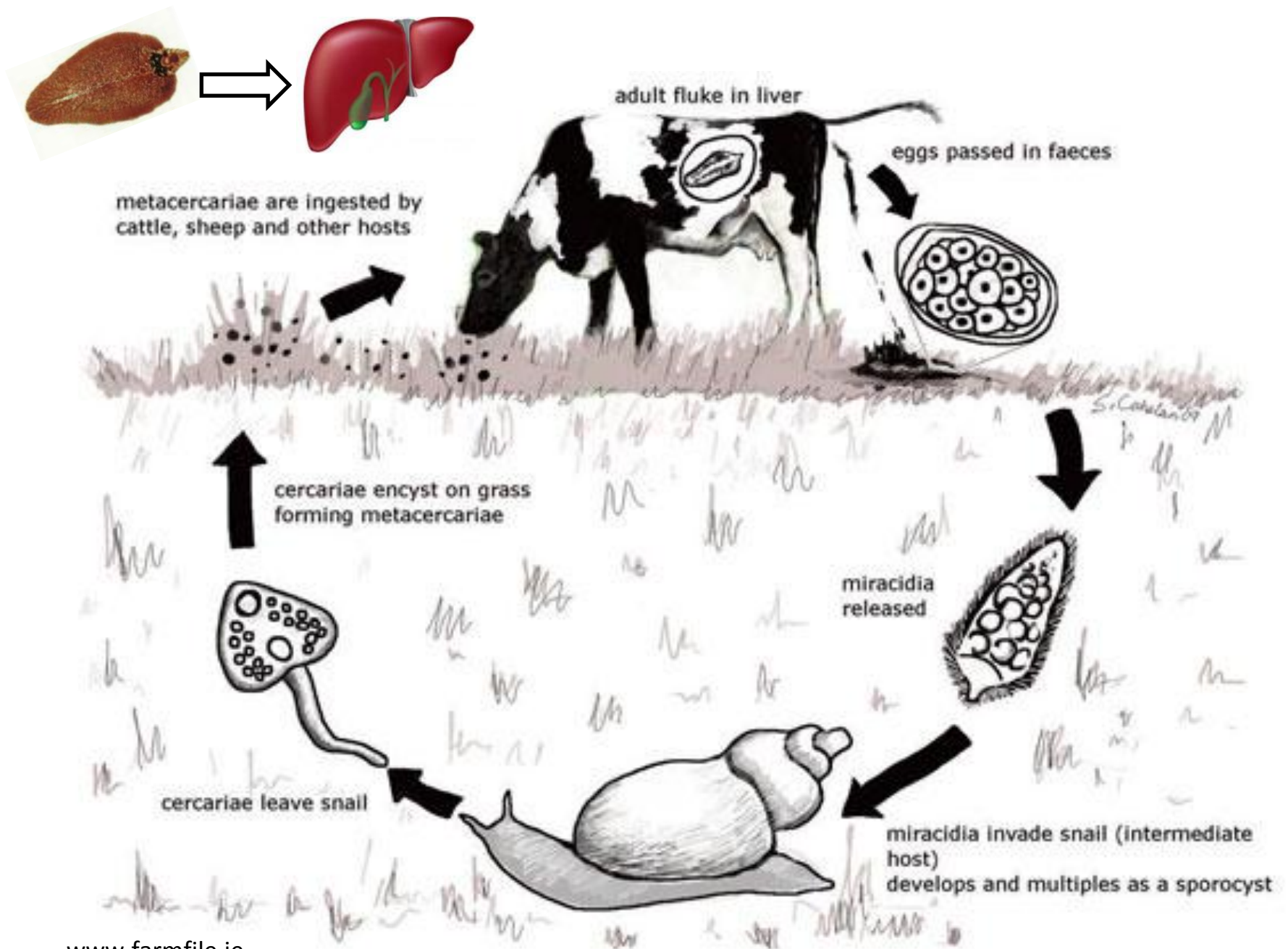


Lymnaea spp.



*Fasciola
hepatica*





Additional causes of initial liver damage

- * *Cysticercus spp.*
- * *Fascioloides magna*
- * *Dicroelium dendriticum*
- * *Fusobacterium necrophorum*
- * Pregnancy?
- * Toxicants?

Bacillary hemoglobinuria

Etiology: *Clostridium haemolyticum*
(*C. novyi* type D)



Pathology of Naturally Occurring Bacillary Hemoglobinuria in Cattle

Veterinary Pathology
2017, Vol. 54(3) 457-466
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DOI: 10.1177/0300985816688945
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J. C. Freedman⁴, E. Morrell¹, J. Beingesser¹, and F. A. Uzal¹

Abstract

Clostridium haemolyticum causes bacillary hemoglobinuria (BH), an infectious and usually fatal disease that occurs mostly in cattle, which is clinically characterized by jaundice, hemoglobinuria, and anemia. The trematode *Fasciola hepatica* has been commonly reported as the main predisposing factor that triggers this condition. The authors evaluated 20 naturally occurring cases of bovine BH to characterize the pathology and pathogenesis of the disease. Grossly, the most consistent finding was a large, frequently single focus of necrosis surrounded by a red to purple halo, observed most frequently on the parietal surface of the right and left hepatic lobes. Other findings were jaundice, dark-brown discoloration of kidneys, and red urine in the urinary bladder. Microscopically, characteristic lesions were locally extensive, necrotizing hepatitis with thrombosis and numerous intralesional Gram-positive rod-shaped bacteria, and acute renal tubular necrosis. By immunohistochemistry, many hepatocytes outside the necrotic focus in the liver were positive for activated caspase 3, suggesting that those cells were undergoing apoptosis. Ultrastructural evaluation revealed hepatocyte necrosis, hemolysis, and clumps of vegetative and sporulating bacilli within the liver. Polymerase chain reaction for the *C. haemolyticum* beta toxin gene was positive in randomly selected liver samples. No gross or microscopic lesions indicative of fascioliasis were detected in the liver of any animal, suggesting that other yet undetermined predisposing factors were associated with these cases of BH.

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

Germination and multiplication of *C. haemolyticum* →

Release of **beta toxin** (PLC) →

Hemolytic and necrotizing →

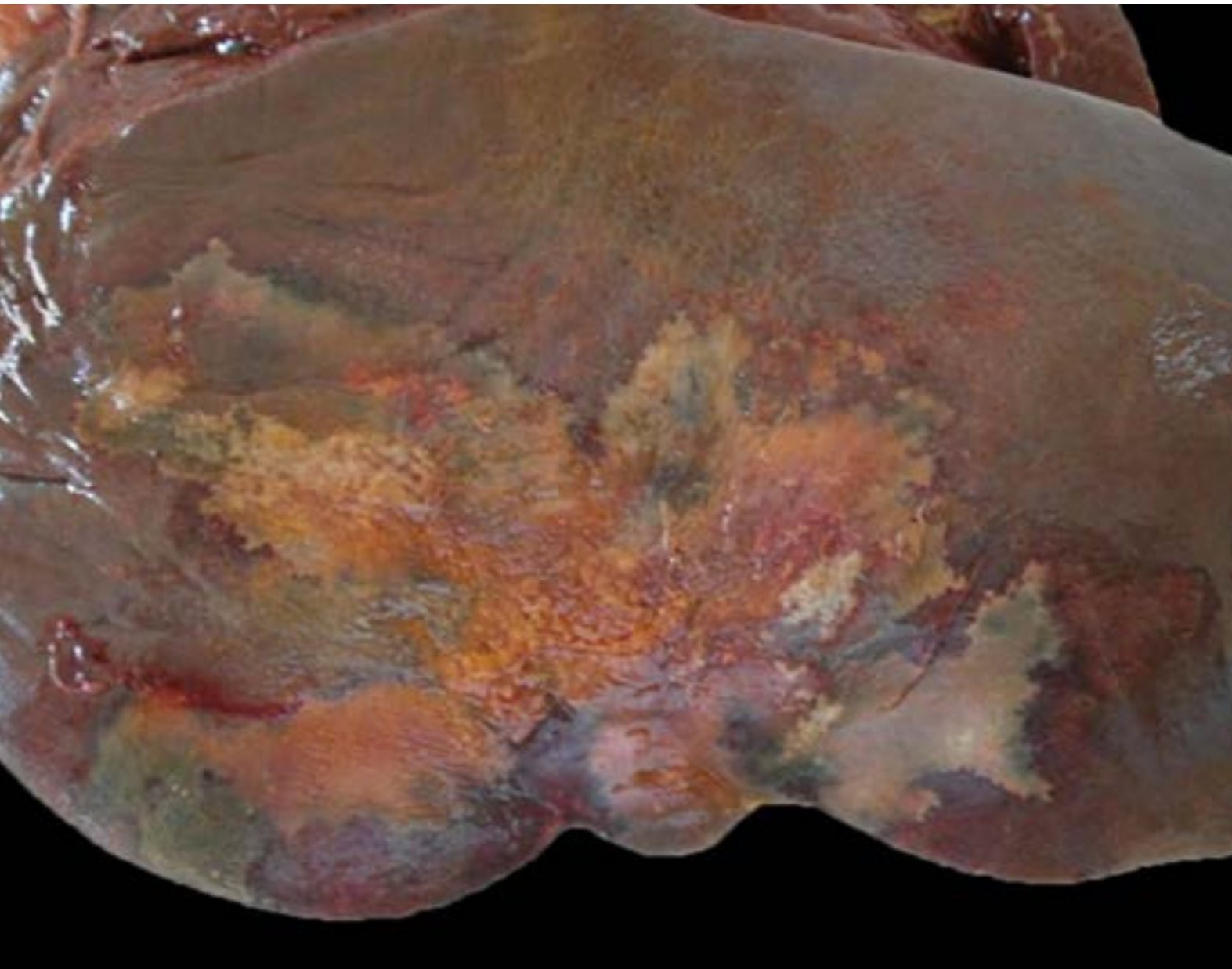
Bacillary hemoglobinuria











Lesions:

Single
75%

Multiple
(2 to 5)
25%



