Enteric clostridial diseases

Francisco A. Uzal

California Animal Health and Food Safety Laboratory
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Lake Arrowhead
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Big Bear Lake
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Lytle Creek
Keenbrook
Scotland
Running Springs
Seven Oaks
Pinezanita
Heart Bar Campground
Angelus Oaks
Nealeys Corner
DEL ROSA
Muscoy
SIERRA LAKES
Highland
Rialto
San Bernardino
Kaiser
Fontana
Mountain Home Village
Forest Falls
Bloomington
Colton
Mentone
Redlands
Loma Linda
Oak Glen
Declezville
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Highgrove
GLEN AVON
Calimesa
Jurupa Valley
RUBIDOUX
MIRA LOMA
Box Springs Mountain Reserve Park
Riverside
El Casco
Moonlight Rim
Cherry Valley
Hinda
MORONGO RESERVATION
MAGNOLIA CENTER
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Norco
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Cabazon
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FIRE
FIRE


WEST


FIRE MANAGEMENT
VOLUNTEER

Second major earthquake rattles Southern California in two days

Updated 6:20 AM; Posted Jul 5, 10:56 PM

Breaking news from The Oregonian/OregonLive

Southern California reels from magnitude 7.1 quake

By JOHN ANTCZAK, ASSOCIATED PRESS LOS ANGELES — Jul 6, 2019, 4:05 AM ET

Some shelves are nearly empty as volunteers assist with cleanup at the Ridgecrest, Calif., branch of the Kern County Library on Friday, July 5, 2019, following... more +


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CAHFS Mission

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UCDAVIS VETERINARY MEDICINE
California Animal Health and Food Safety Laboratory System

Public Health


By Robert Hanashiro, USA TODAY

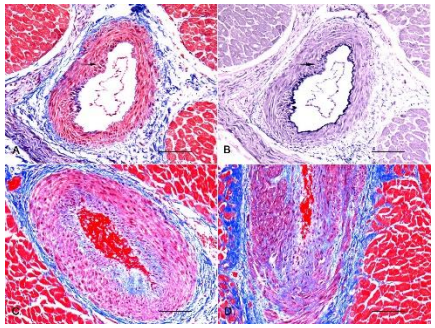
One bacteria, 30,000 deaths

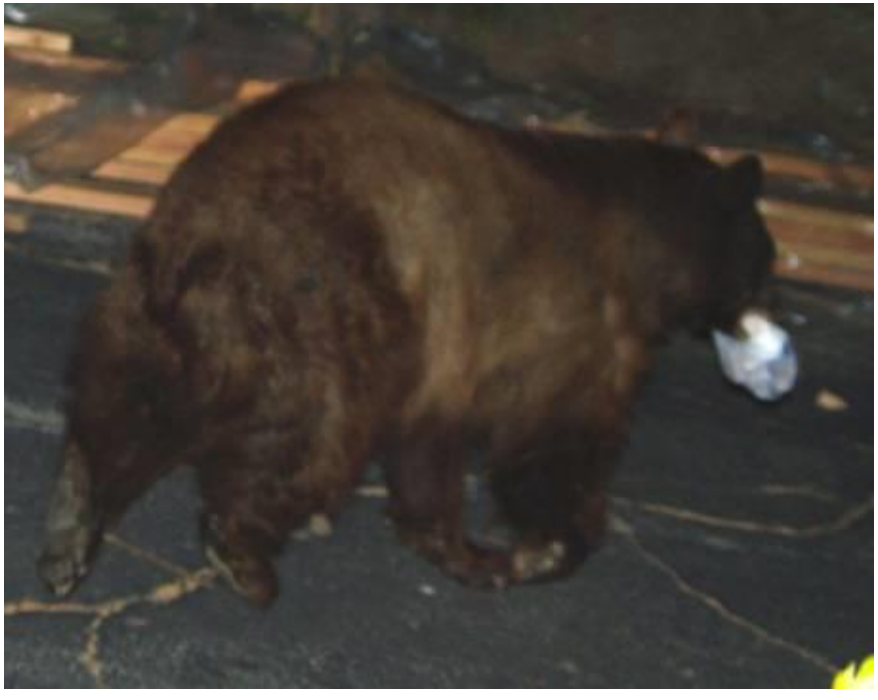
Survivor: Bailey, now 16, contracted C. diff after brain surgery.

An infection called C. diff is wreaking havoc in the USA's hospitals, nursing homes and other medical facilities — and officials could be doing far more to stop it

Equine Health

New Knowledge



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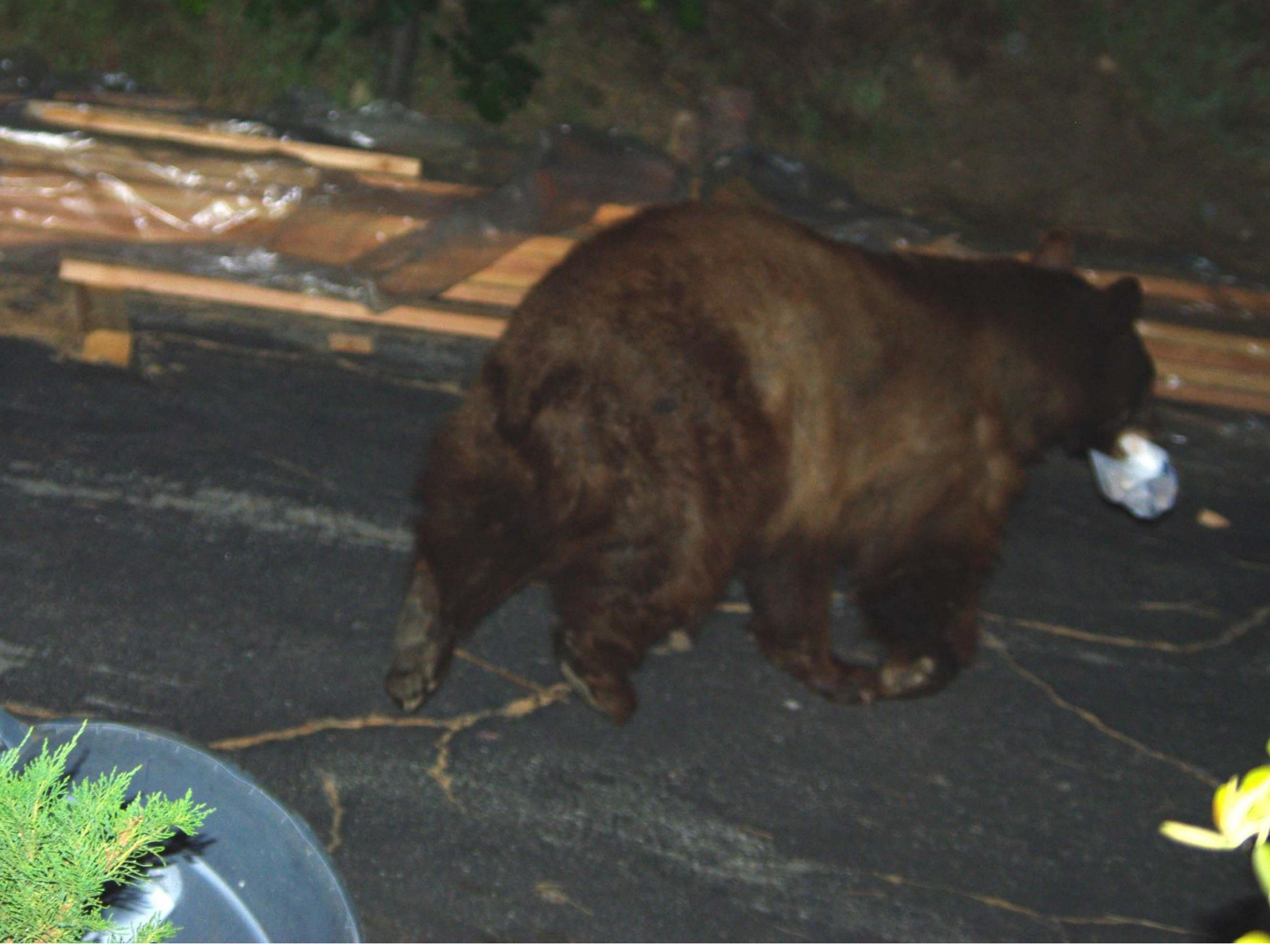
300
350
400
500
PUSH TO TURN
MED
REAR



The genus *Clostridium*

***Anaerobic (more or less strict)**

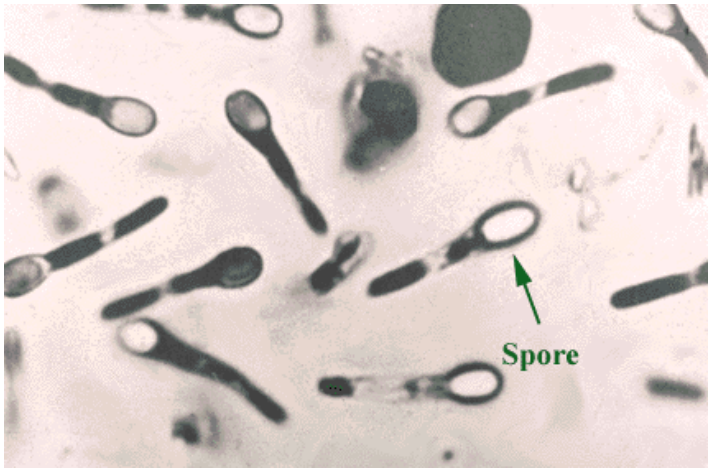
***Gram positive (most of them; exception?)**

***Rods**

***Sporulated (heat resistant endospores)**

***Ubiquitous (some of them)**

***Pathogenesis involves toxins**



***Clostridium tetani* spores – J.G. Songer**

GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric				
Histotoxic				
Neurotoxic				

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

GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric	**Enterotoxemias/ enteritis**	*C. perfringens*	✓	✓
		C. difficile	✓	✓
		C. piliforme	--	✓
		C. sordellii	--	✓
		C. colinum	--	✓
		C. spiroforme	--	✓
Histotoxic				
Neurotoxic				

GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric	Enterotoxemias/ enteritis	*C. perfringens*	✓	✓
Histotoxic				
Neurotoxic				

Enterotoxemia:

toxins generated in intestine

↓

absorbed to circulation; act in distant organs

Take-home message!!!

Up to 20 toxins

* “major” (typing) toxins
* beta2
* delta
* lamda
* NetF
* Tpel
* etc.

The classic toxinotyping of *C. perfringens*

Toxinotype	α-toxin (CPA)	β-toxin (CPB)	ε-toxin (ETX)	ι-toxin (ITX)
A	+	-	-	-
B	+	+	+	-
C	+	+	-	-
D	+	-	+	-
E	+	-	-	+

The 2018 *C. perfringens* toxin-based typing scheme

Toxinotype	α-toxin (CPA)	β-toxin (CPB)	ε-toxin (ETX)	ι-toxin (ITX)	enterot (CPE)	NetB
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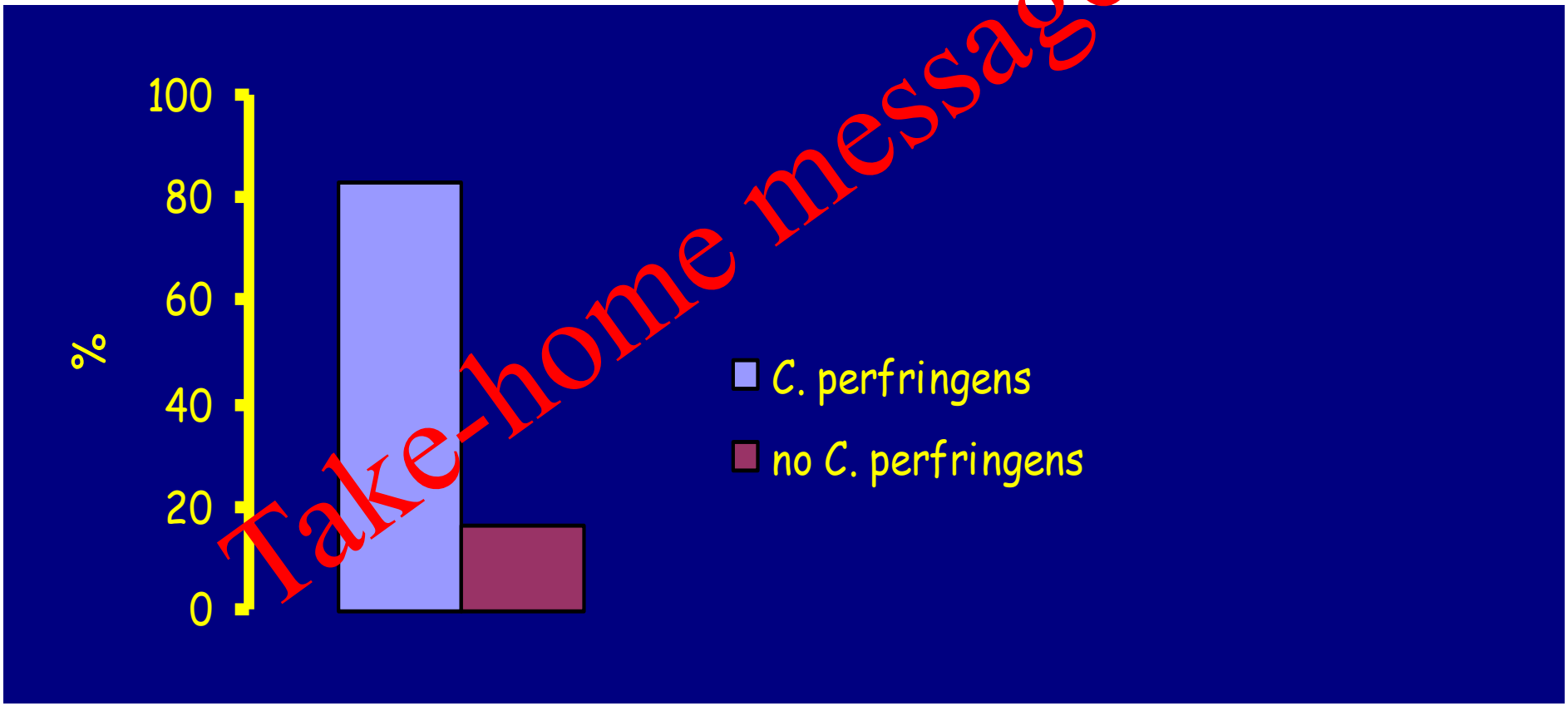
C	+	+	-	-	+/-	-
D	+	-	+	-	+/-	-
E	+	-	-	+	+/-	-
F	+	-	-	-	+	-
G	+	-	-	-	-	+

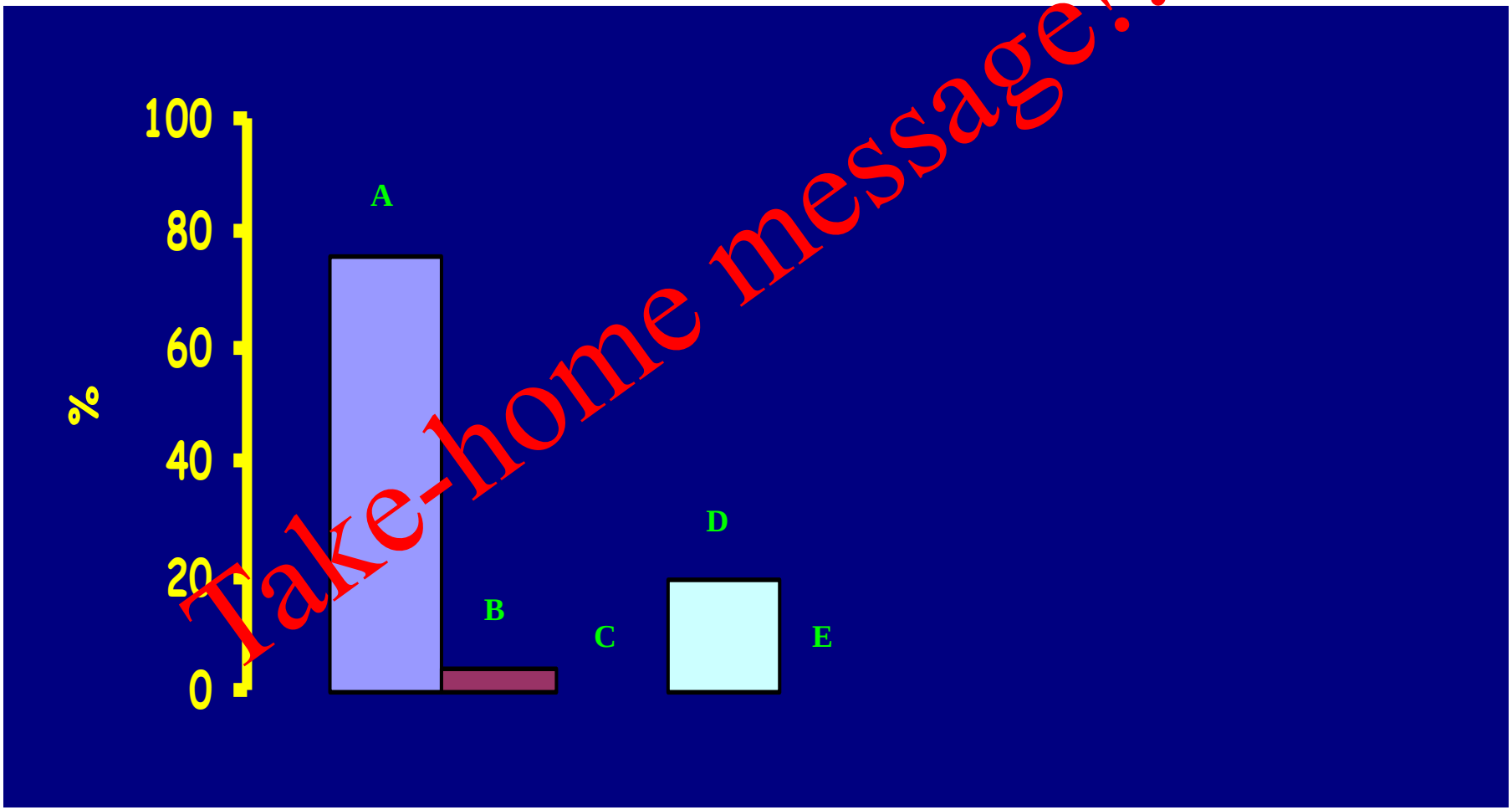
Rood et al, Anaerobe 2018

C. perfringens in s.i. of healthy sheep (lambs and adults) n=113



Take-home message!!!

C. perfringens in s.i.of healthy sheep (lambs and adults) n=113



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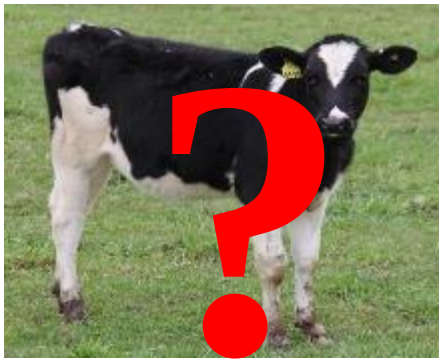
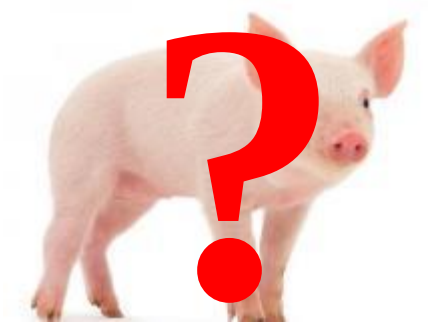
D	+	-	+	-	+/-	-
E	+	-	-	+	+/-	-
F	+	-	-	-	+	-
G	+	-	-	-	-	+

Rood et al, Anaerobe 2018

Yellow lamb disease





Etiology

C. perfringens type A

(high CPA-producing strains)

Pathogenesis

CPA: highly hemolytic

Pathogenesis:

High CPA expression

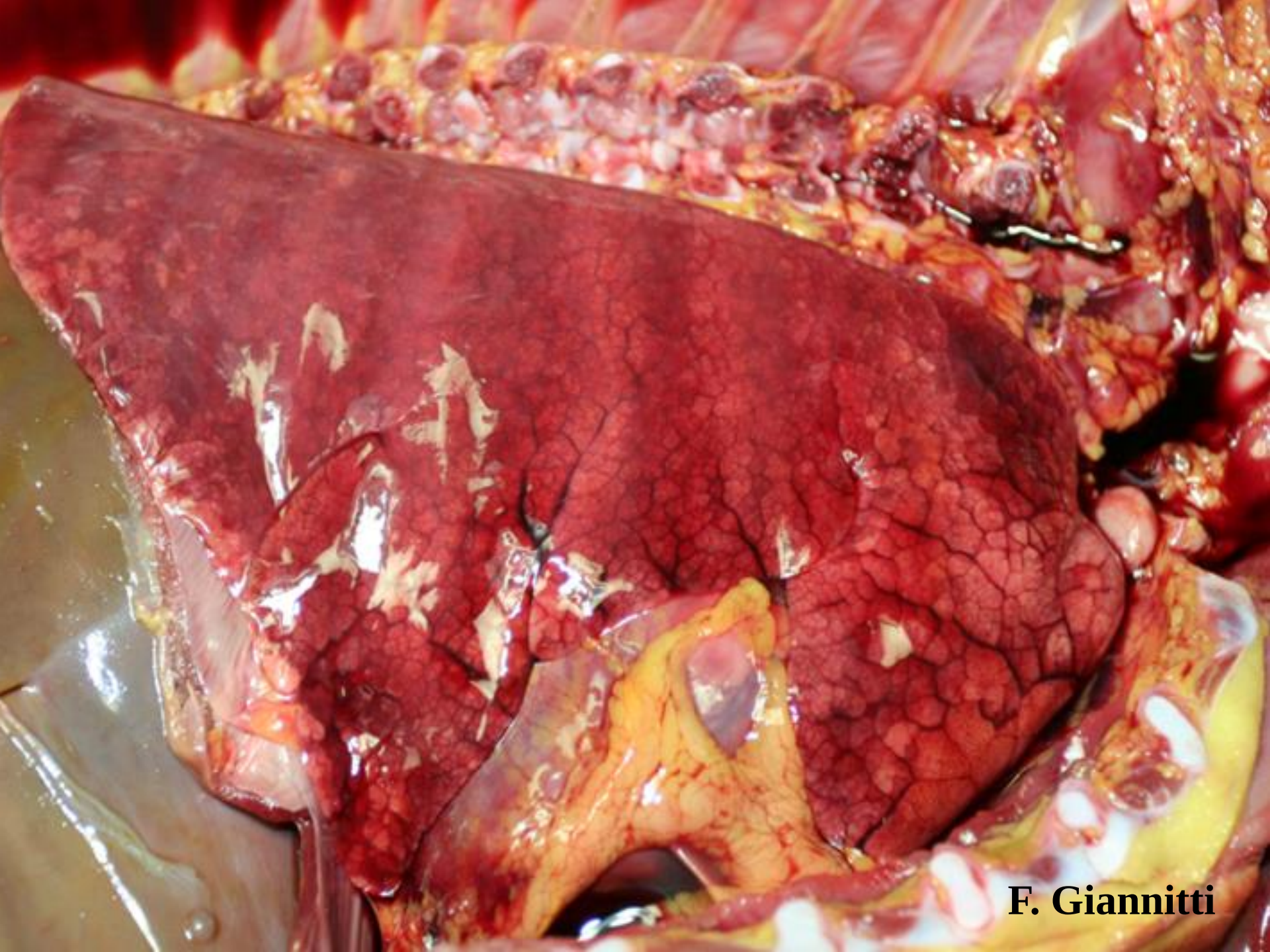
intravascular hemolysis

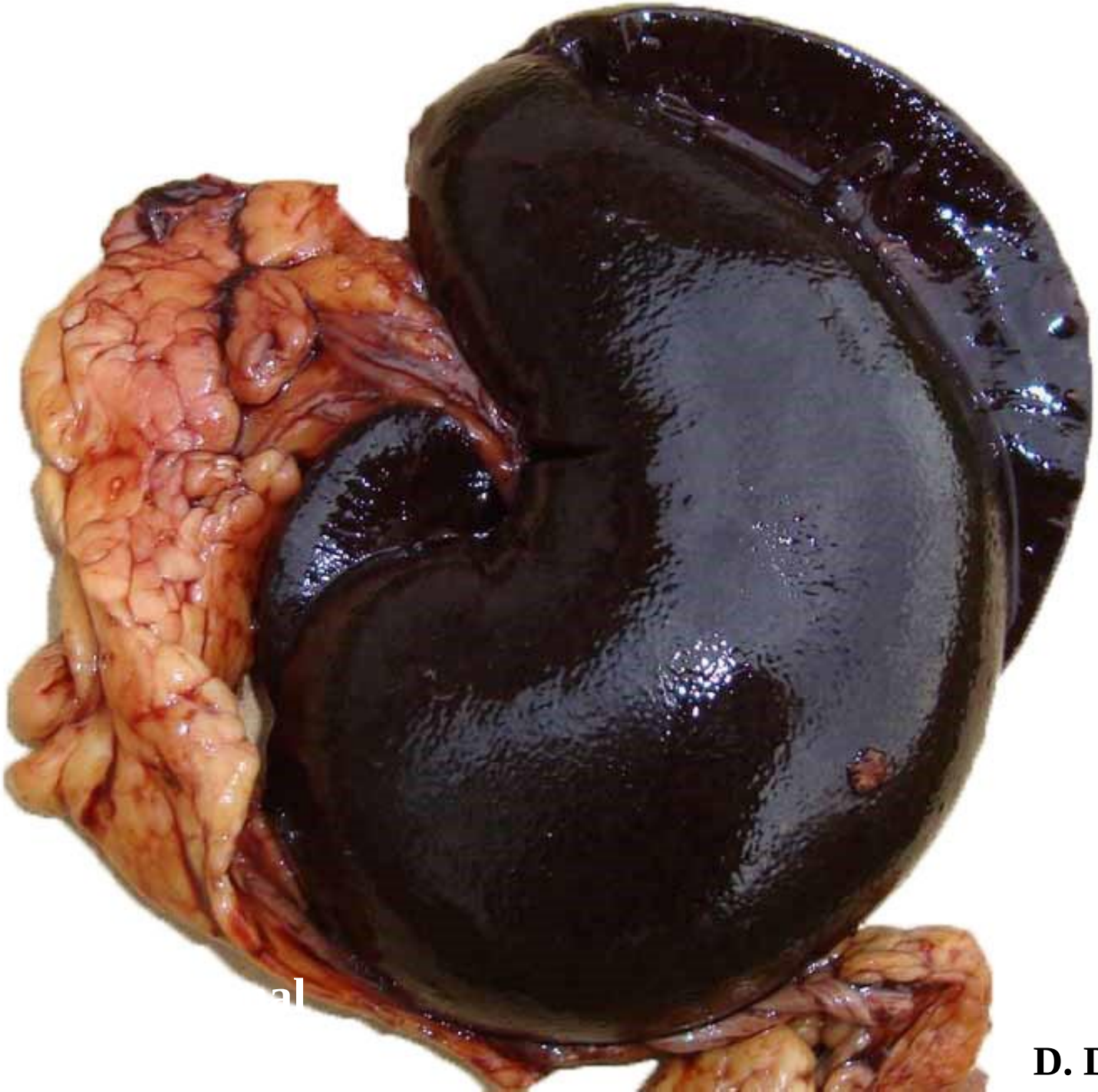
1-Anemia → **Hypoxia** → **Hepatic necrosis**

2-Free hemoglobin: → **Nephrosis, icterus**

Clinical signs

Depression
Anemia
Icterus
Diarrhea
Sudden death


F. Giannitti



D. Dinev

Diagnostic criteria

1-Clinics/gross

2-Histo

} **Suggestive**

3-Ancillary: **Culture (+ typing)**
(colony count)

} **Confirmatory?**

> 10^6/gr

Differential diagnoses

* Copper intoxication
* Hemoparasites
* Leptospirosis
* Oak intoxication
* Others….

Canine hemorrhagic gastroenteritis
Necrotizing enteritis of foals

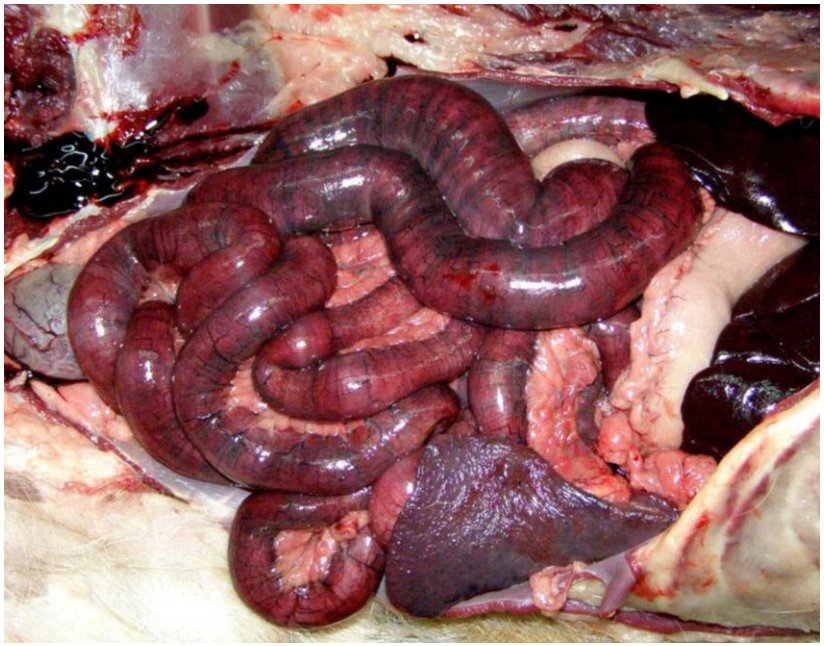
C. perfringens type A NetF + isolates

High correlation isolation/disease

A novel pore-forming toxin in type A *Clostridium perfringens* is associated with both fatal canine hemorrhagic gastroenteritis and fatal foal necrotizing enterocolitis. Mehdizadeh Gohari I, Parreira VR, Nowell VJ, Nicholson VM, Oliphant K, Prescott JF. PLoS One. 2015 Apr 8;10(4):e0122684

Necrotizing enteritis of foals
Canine hemorrhagic gastroenteritis

Gohari et al, 2016



L. Minatel

C. perfringens type A frequently blamed for enteritis, abomasitis and/or enterotoxemia in cattle

* *C. perfringens* type A in intestinal content of healthy cattle (Uzal et al, 2006; Uzal et al, 2016; many more….)

* Isolation of *C. perfrinngens* type A from intestinal content of sick animals:

no diagnostic relevance

* Large amounts of CPA in feces of healthy cattle (Niilo et al, 1963; Timoney et al,1988; Uzal et al, 2016)

Detection of alpha toxin in intestinal content of sick animals:

no diagnostic relevance

Role of *C. perfringens* type A in enteric disease of cattle:

*** No Koch postulates fullfilled**
*** No disease definition**
*** No diagnostic criteria**

The 2018 *C. perfringens* toxin-based typing scheme

Toxinotype	α-toxin (CPA)	β-toxin (CPB)	ε-toxin (ETX)	ι-toxin (ITX)	enterot (CPE)	NetB
A	+	-	-	-	-	-
B	+	+	+	-	-	-
C	+	+	-	-	+/-	-
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E	+	-	-	+	+/-	-
F	+	-	-	-	+	-
G	+	-	-	-	-	+

Rood et al, Anaerobe 2018

***C. perfringens* type B**

Rare: Mostly Middle East

Pathogenesis

CPB: necrotizing
ETX: neurotoxin

Take-home message!!!

The 2018 *C. perfringens* toxin-based typing scheme

Toxinotype	α-toxin (CPA)	β-toxin (CPB)	ε-toxin (ETX)	ι-toxin (ITX)	enterot (CPE)	NetB
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E	+	-	-	+	+/-	-
F	+	-	-	-	+	-
G	+	-	-	-	-	+

Rood et al, Anaerobe 2018

Beta toxin (CPB)

* 35 kDa

* pore-forming

* necrotizing

* trypsin-sensitive

Due to this……

1-Intestinal trypsin: natural defense against type C disease

2-Type C disease:

-neonates

-pancreatic disease

-trypsin inhibitors (sweet potato; soybean)

Clostridium perfringens type C

1-enteritis necroticans: humans
2-enterotoxemias: animals

Clostridium perfringens type C

1-enteritis necroticans: humans

2-enterotoxemias: animals

The pigbel story……, 1960s……

Photo: Greg Lawrance

Photo Greg Lawrance

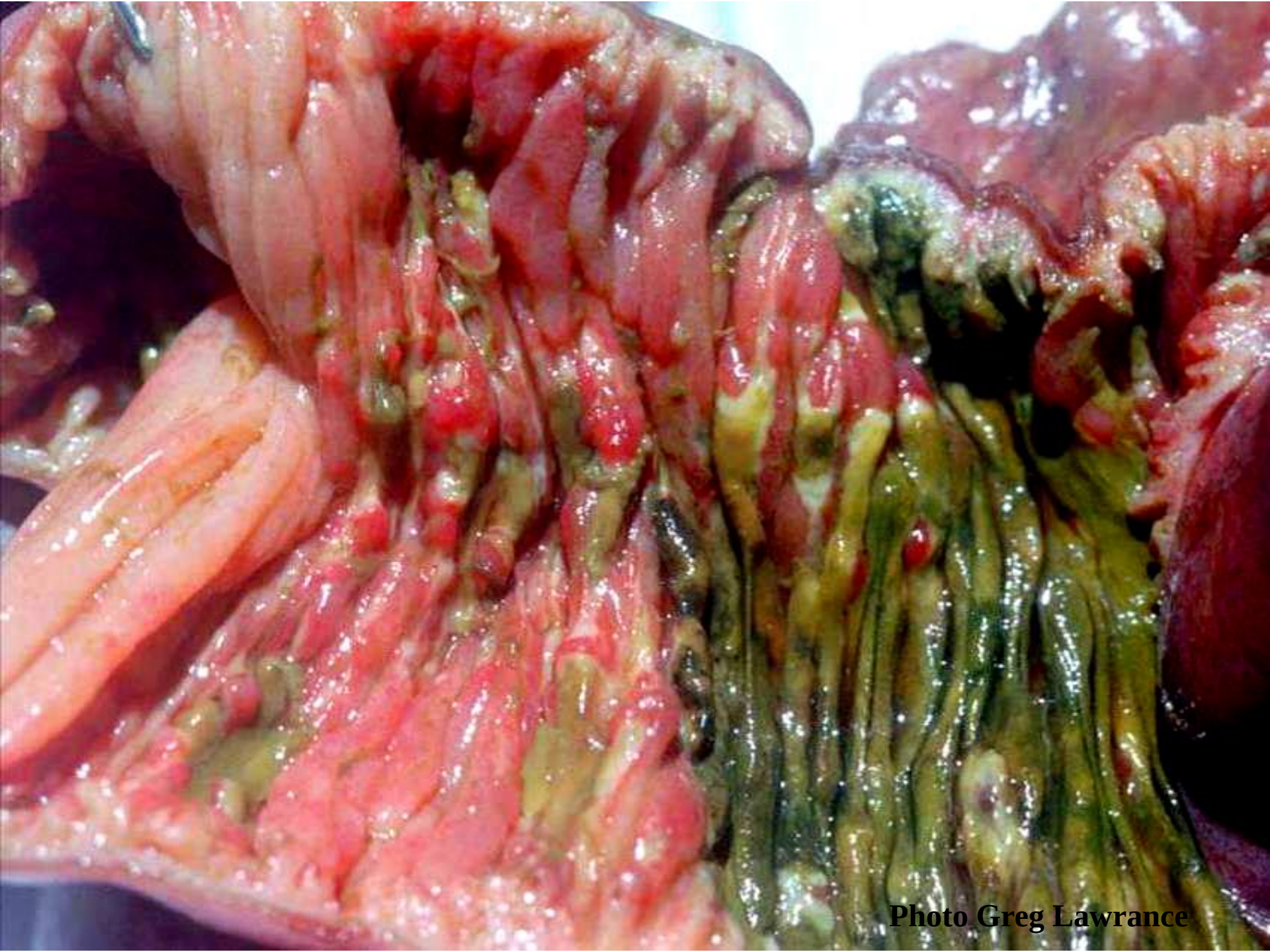


Photo Greg Lawrance

Frequent carrier of
C. perfringens type C

Photo Greg Lawrance

Fecal contamination of meat


Sweet potatoes:
Trypsin inhibitor!!!!
Photo Greg Lawrance

Photo Greg Lawrance

Clostridium perfringens type C

1-enteritis necroticans: humans

2-enterotoxemias: animals

Clinical signs

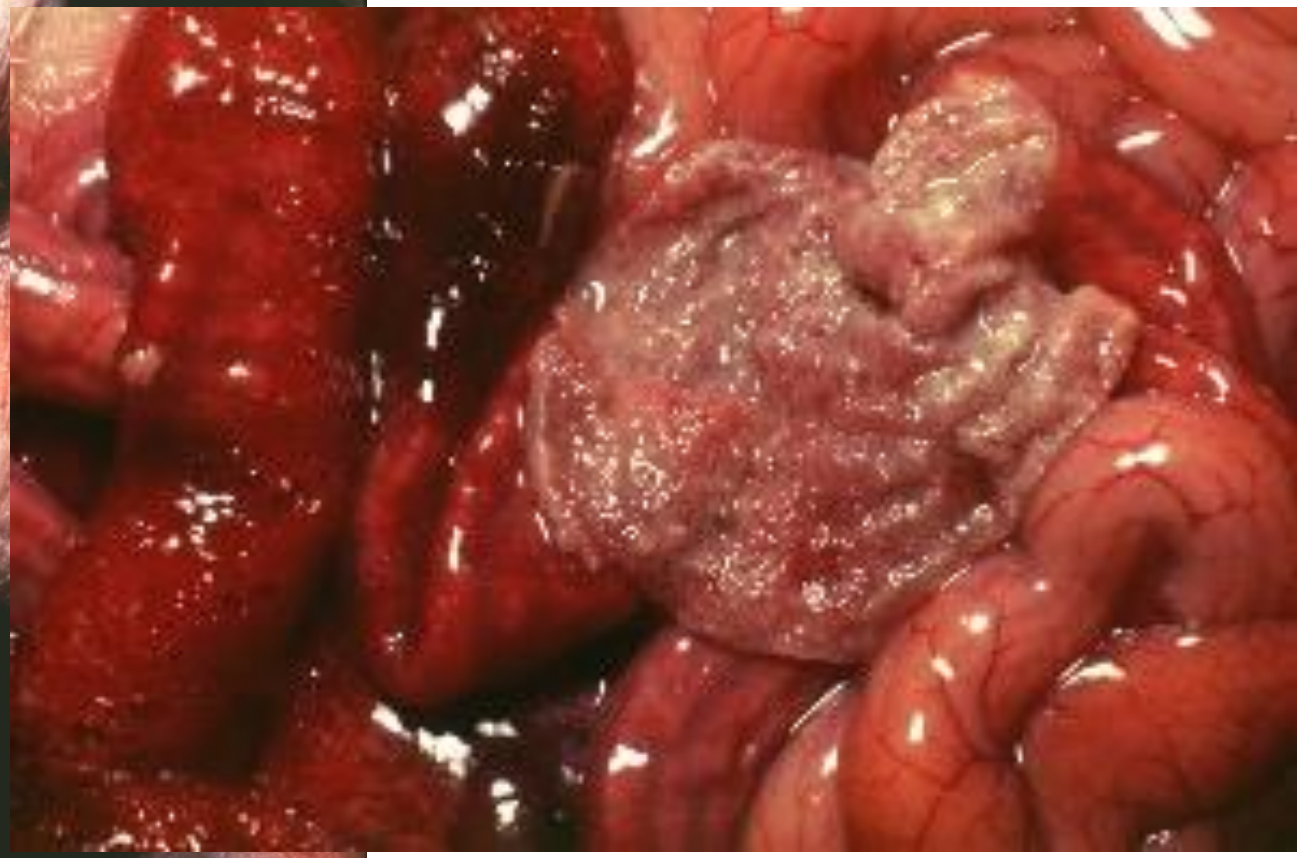
NEONATES

hemorrhagic diarrhea

neurologic signs

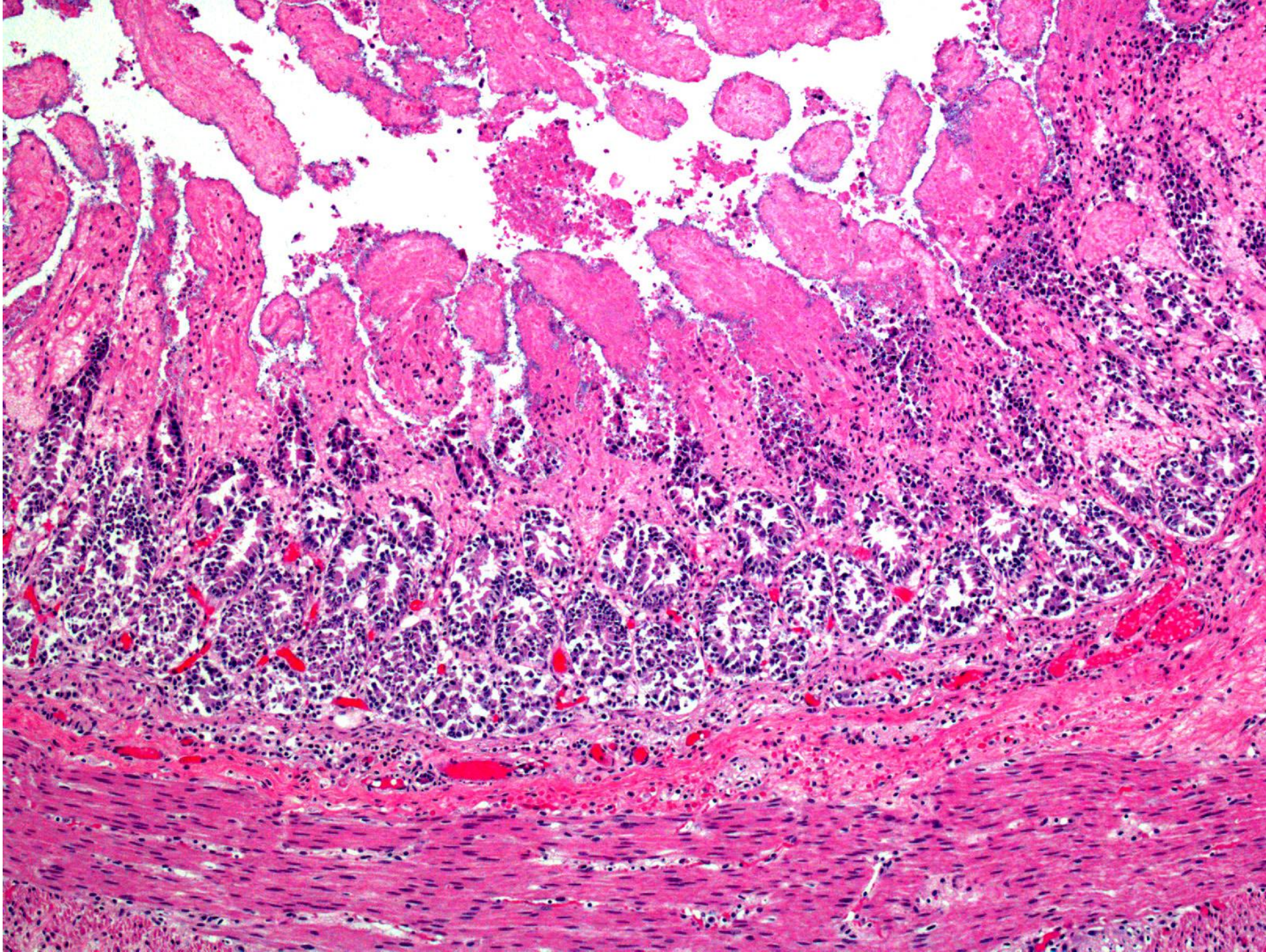
sudden death

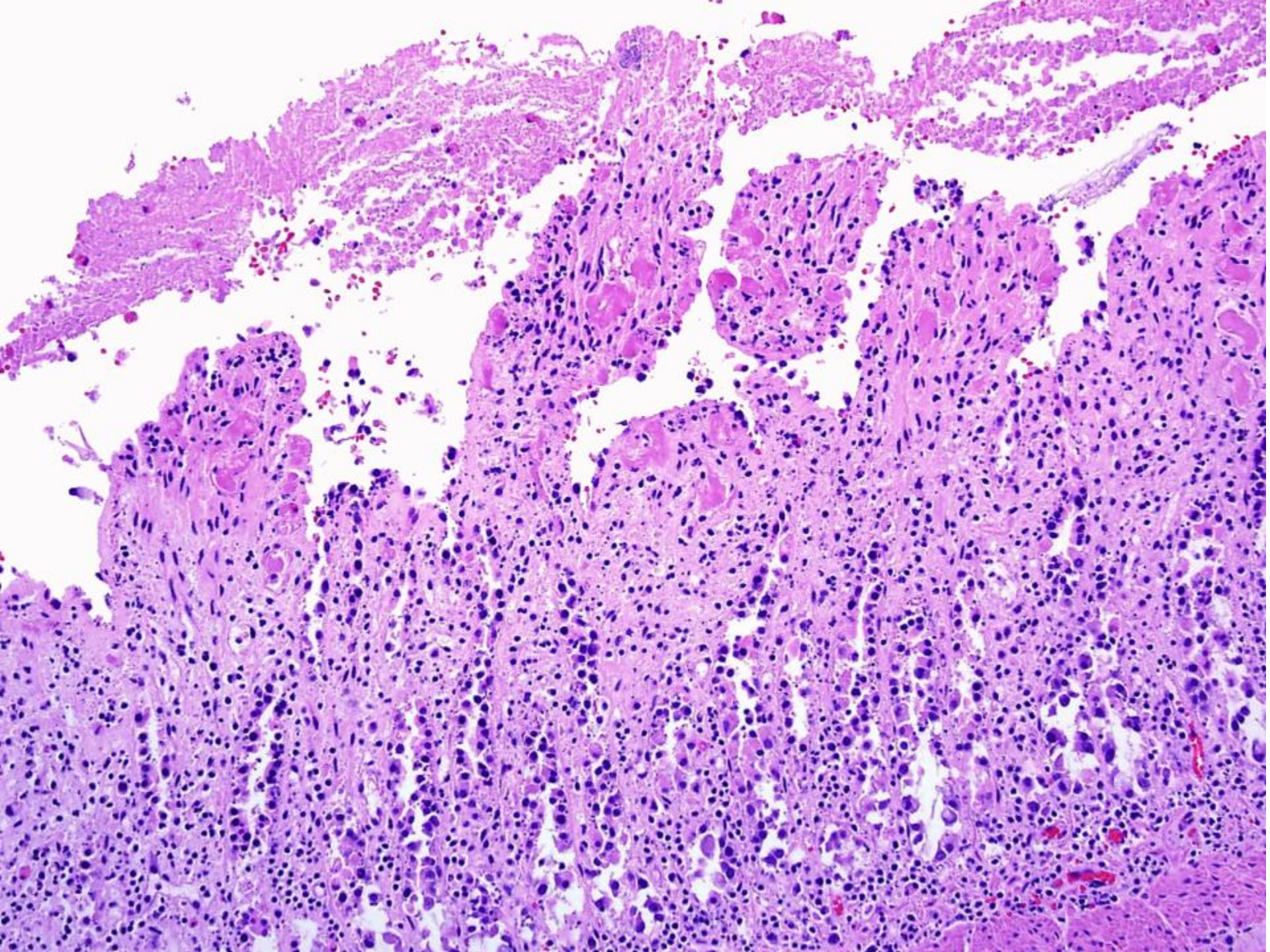
Take-home message!!!



G. Stevenson


D. O’Toole





Diagnostic criteria

1-Clinics/Gross

2-Histo

} **Suggestive**

3-Ancillary: Culture (+ typing)

} **Suggestive +**

CPB toxin
(intestinal content)

} **Confirmatory**

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F	+	-	-	-	+	-
G	+	-	-	-	-	+

Rood et al, Anaerobe 2018

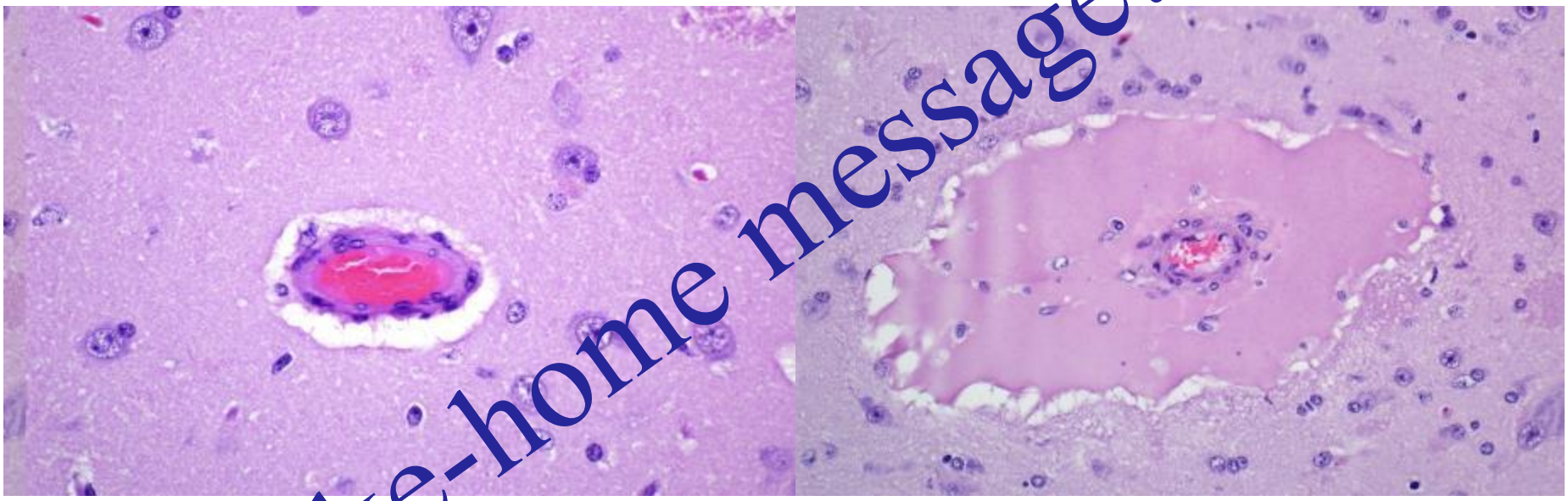
Epsilon toxin (ETX)

* 30 KD toxin ~~(USDA/CDC list B select agent)~~

* pore forming

* neurotoxin

* trypsin-activation required



Take-home message!!!!

HE

Photo Jorge Garcia

epsilon toxin

vascular permeability

Take-home message!!!

Epsilon toxin

*** *Clostridium perfringens* types B and D**

*** Enterotoxemia of sheep, goats and cattle**

*** Human disease: multiple sclerosis association suggested**

OPEN ACCESS Freely available online

PLOS ONE

Isolation of *Clostridium perfringens* Type B in an Individual at First Clinical Presentation of Multiple Sclerosis Provides Clues for Environmental Triggers of the Disease

Kareem Rashid Rumah[1,2,3], Jennifer Linden[2], Vincent A. Fischetti[3], Timothy Vartanian[2]*

1 Tri-Institutional M.D.-Ph.D. Program of Weill Cornell Medical College, Rockefeller University and Memorial Sloan-Kettering Hospital, New York, New York, United States of America, **2** The Brain and Mind Research Institute and the Department of Neurology, Weill Cornell Medical College, New York, New York, United States of America, **3** The Laboratory of Bacterial Pathogenesis and Immunology, Rockefeller University, New York, New York, United States of America

Abstract

We have isolated *Clostridium perfringens* type B, an epsilon toxin-secreting bacillus, from a young woman at clinical presentation of Multiple Sclerosis (MS) with actively enhancing lesions on brain MRI. This finding represents the first time that *C. perfringens* type B has been detected in a human. Epsilon toxin's tropism for the blood-brain barrier (BBB) and binding to oligodendrocytes/myelin makes it a provocative candidate for nascent lesion formation in MS. We examined a well-characterized population of MS patients and healthy controls for carriage of *C. perfringens* toxinotypes in the

MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Evidence of *Clostridium perfringens* epsilon toxin associated with multiple sclerosis

Sariqa Wagley, Monika Bokori-Brown, Helen Morcrette, Andrea Malaspina, Caroline D'Arcy, Sharmilee Gnanapavan, Nicholas Lewis, Michel R Popoff, Dominika Raciborska, Richard Nicholas, Ben Turner and Richard W Titball

Multiple Sclerosis Journal

1–8

DOI: 10.1177/1352458518767327

Correspondence to:
RW Titball
College of Life and Environmental Sciences, University of Exeter, Exeter EX4 4QD, Devon, UK.

Abstract

Background: It was recently reported that, using Western blotting, some multiple sclerosis (MS) patients in the United States had antibodies against epsilon toxin (Etx) from *Clostridium perfringens*, suggesting that the toxin may play a role in the disease.

Type D disease

Natural hosts

* Sheep
* Goats
* Cattle
* May be others….

Type D disease

Natural hosts

* Sheep
* Goats
* Cattle
* May be others….

Clinical signs

Neurological disease

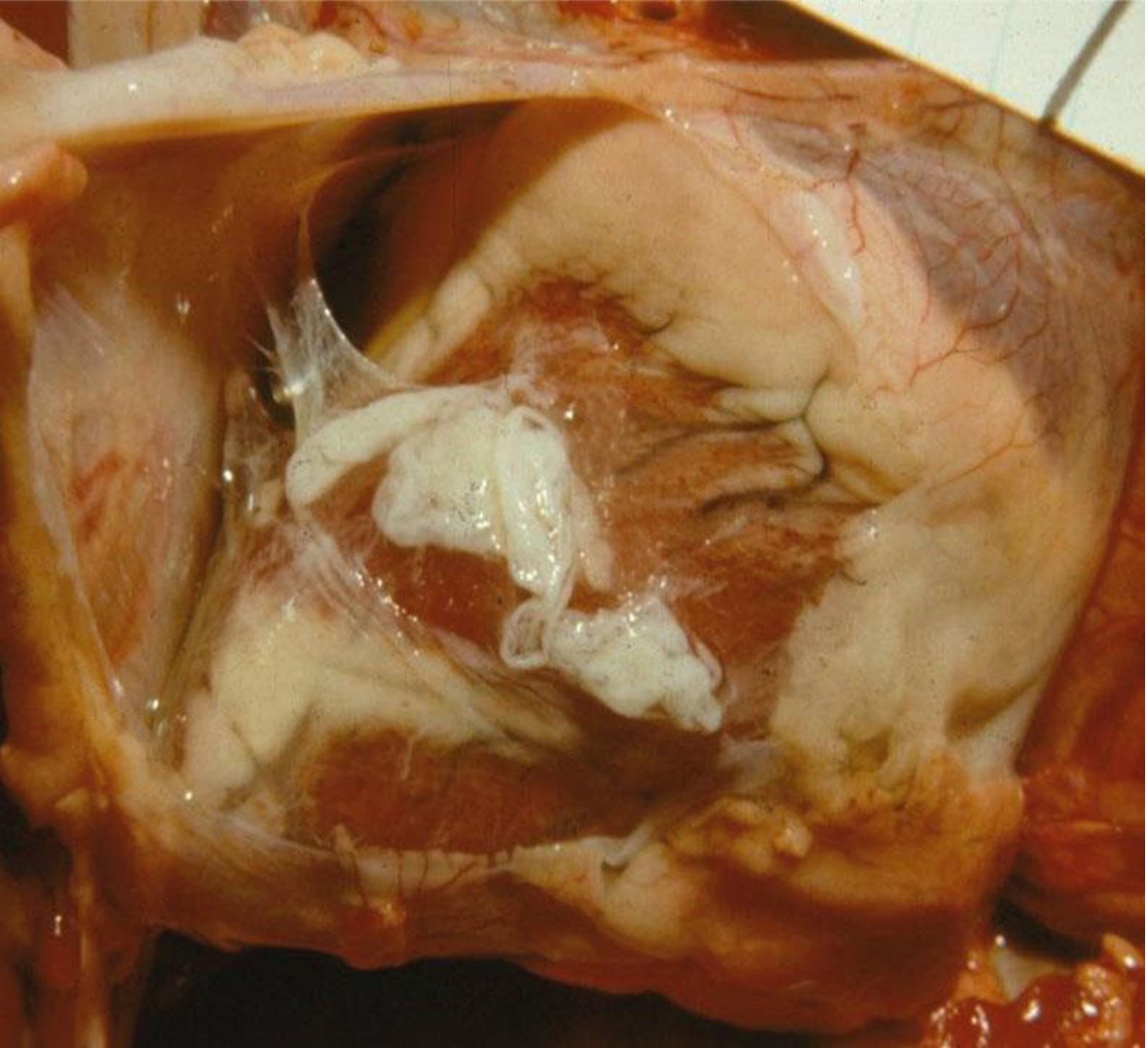
(leaky disease)

Respiratory difficulty

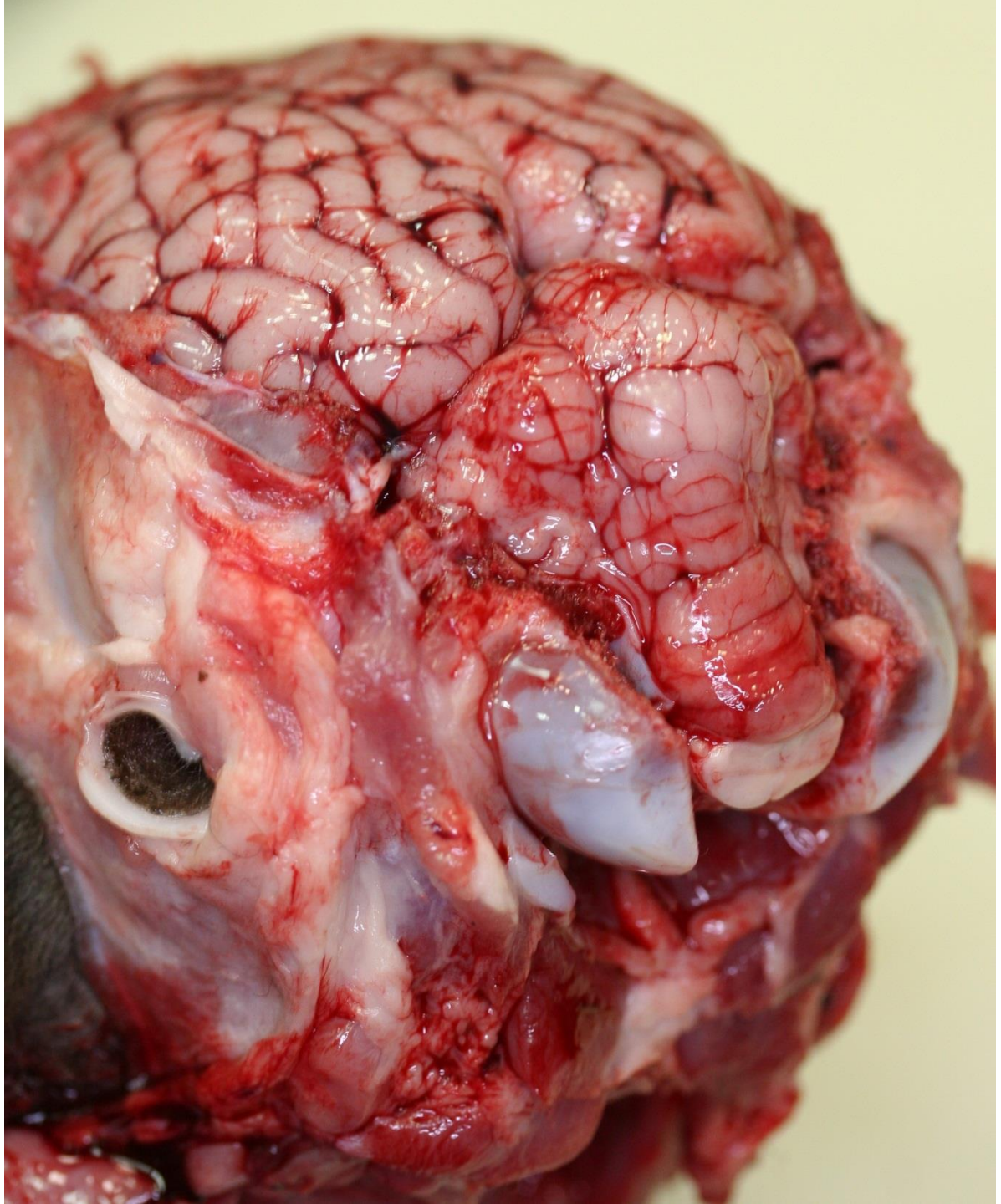
Sudden death

NO DIARRHEA (usually)

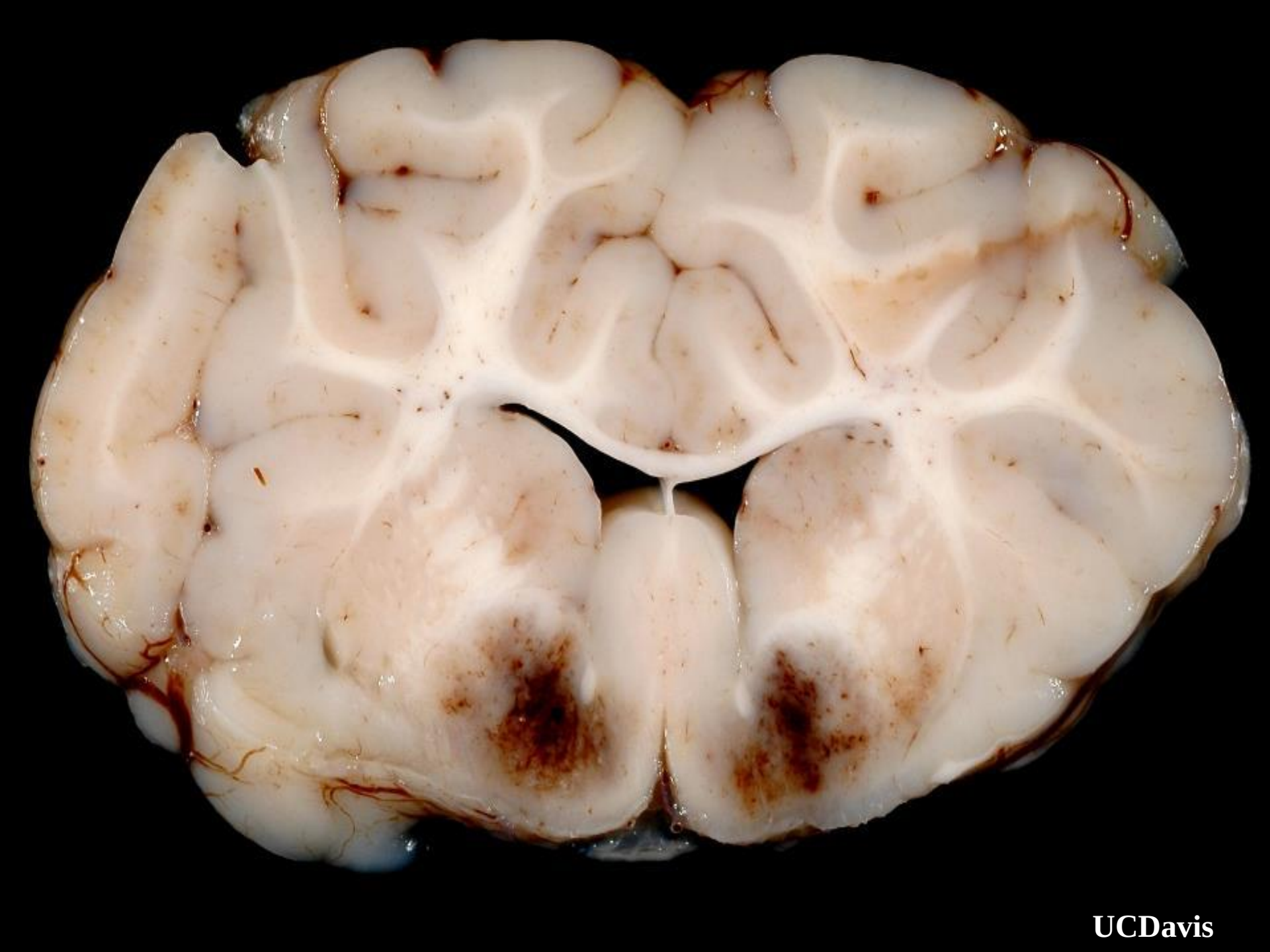
Take-home message!!!

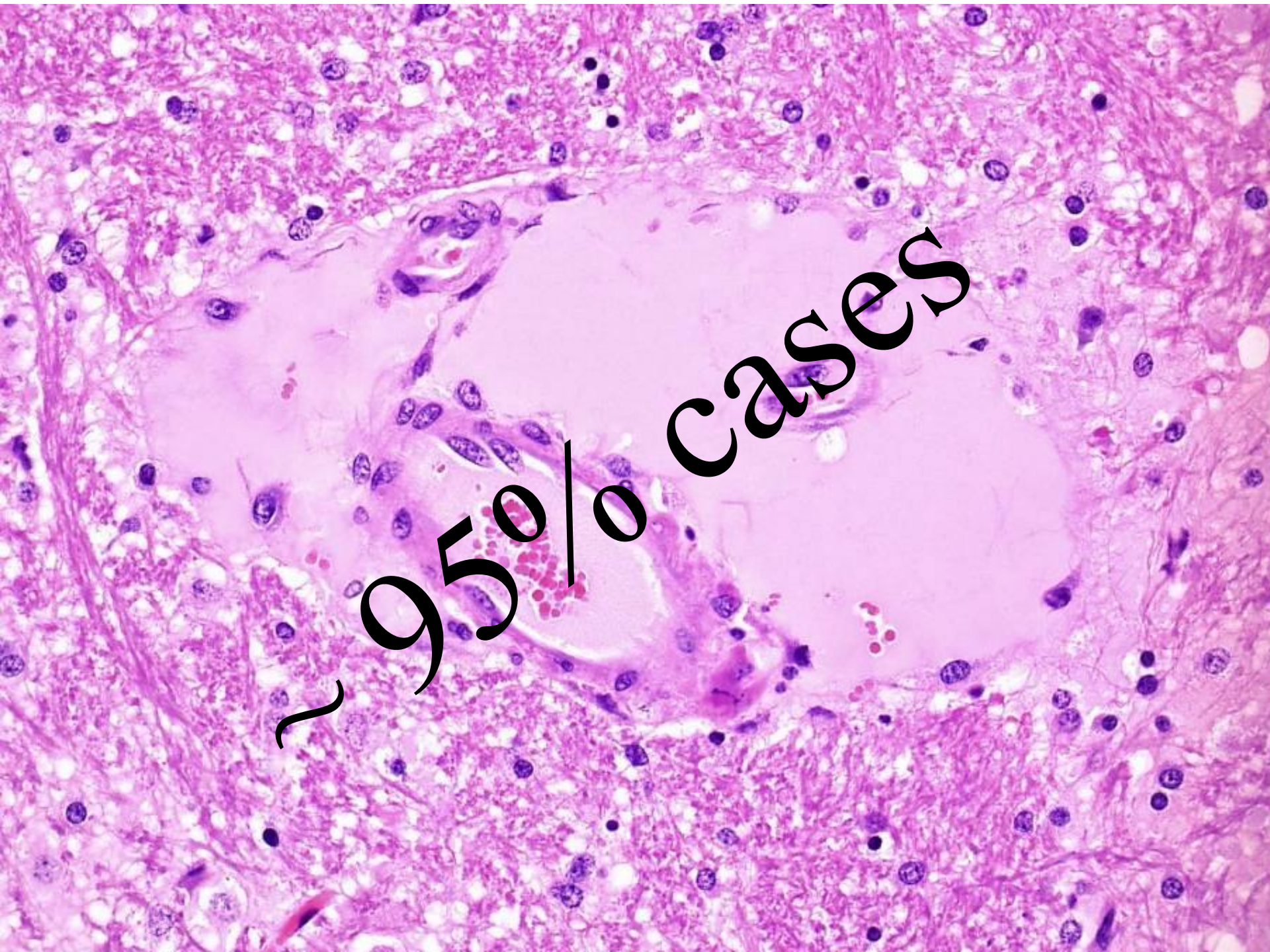


Bill Hartley

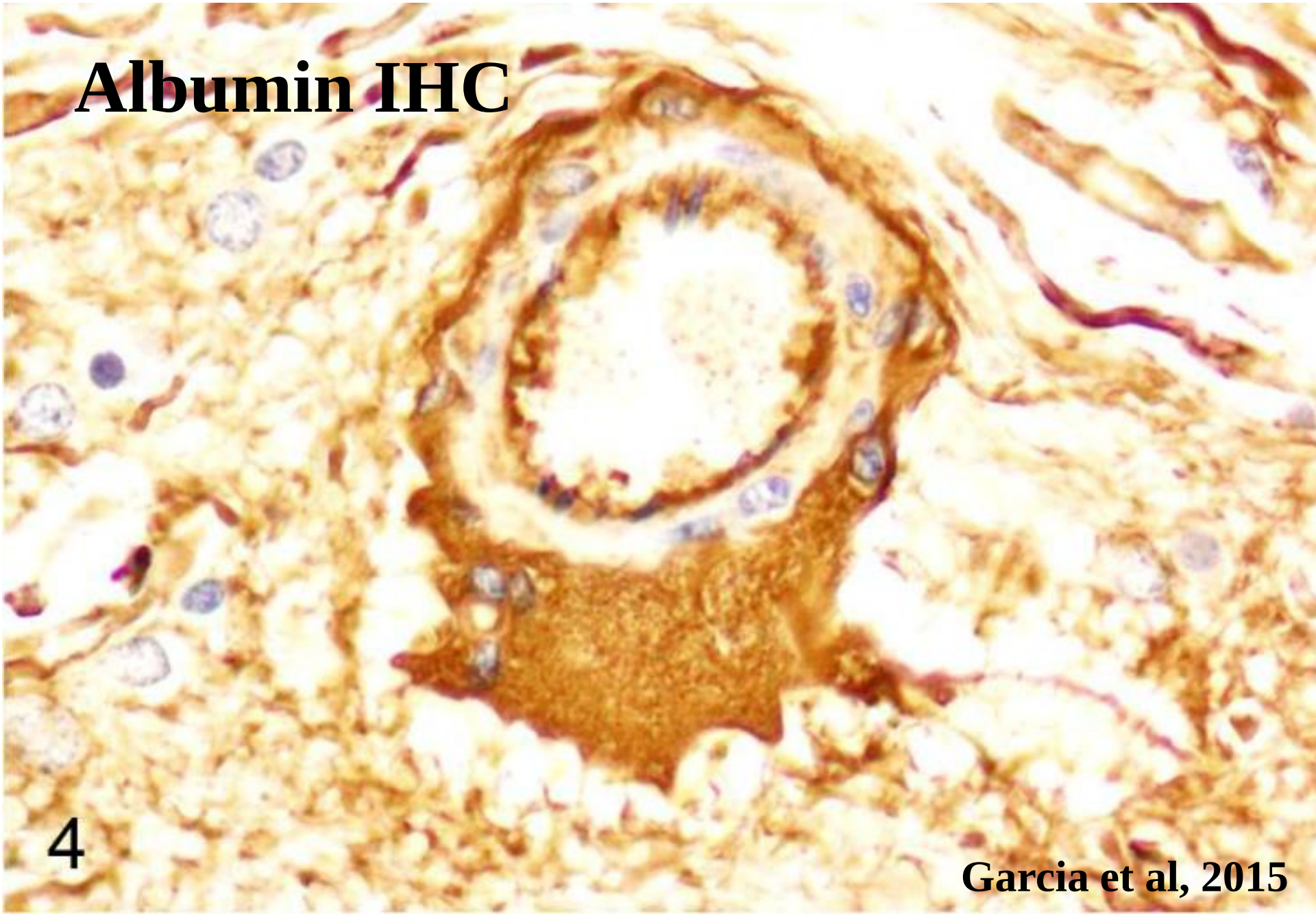


Bradd Barr


UCDavis

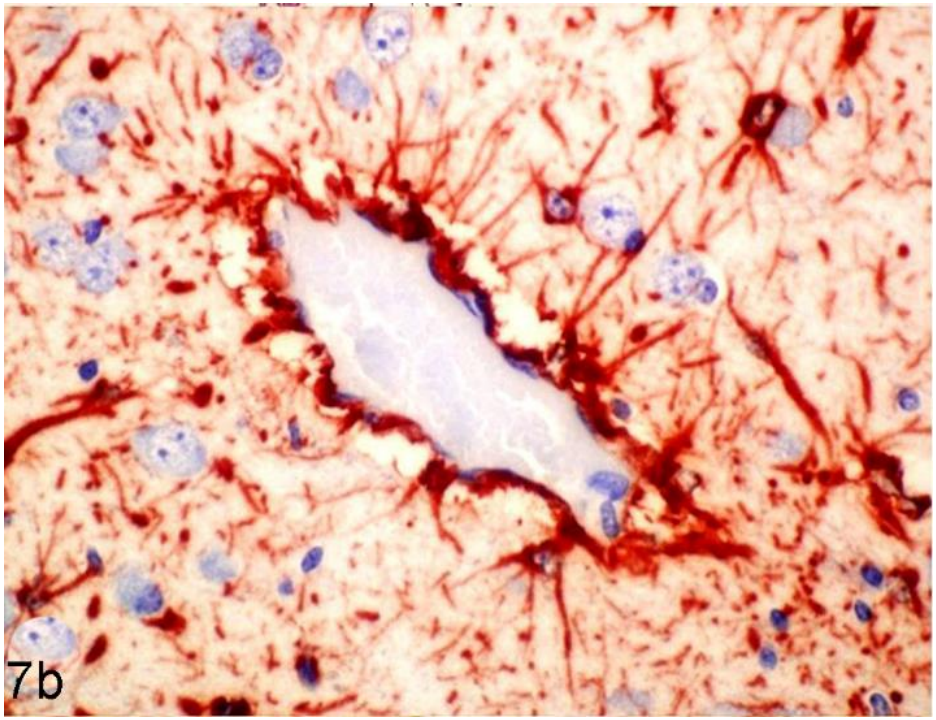

~ 95% cases

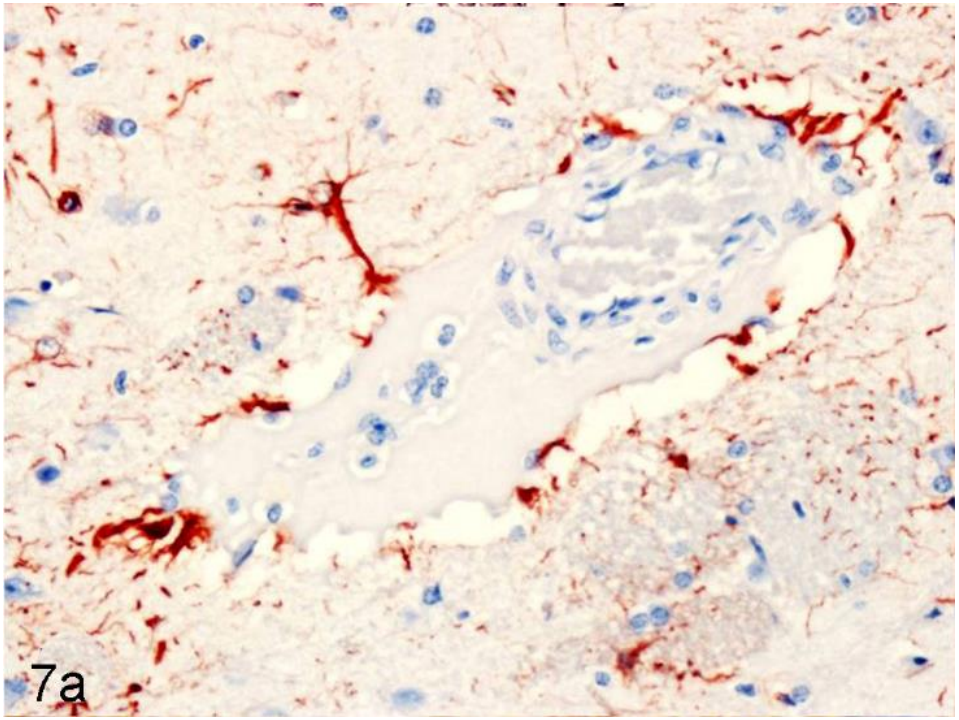
Albumin IHC



Garcia et al, 2015

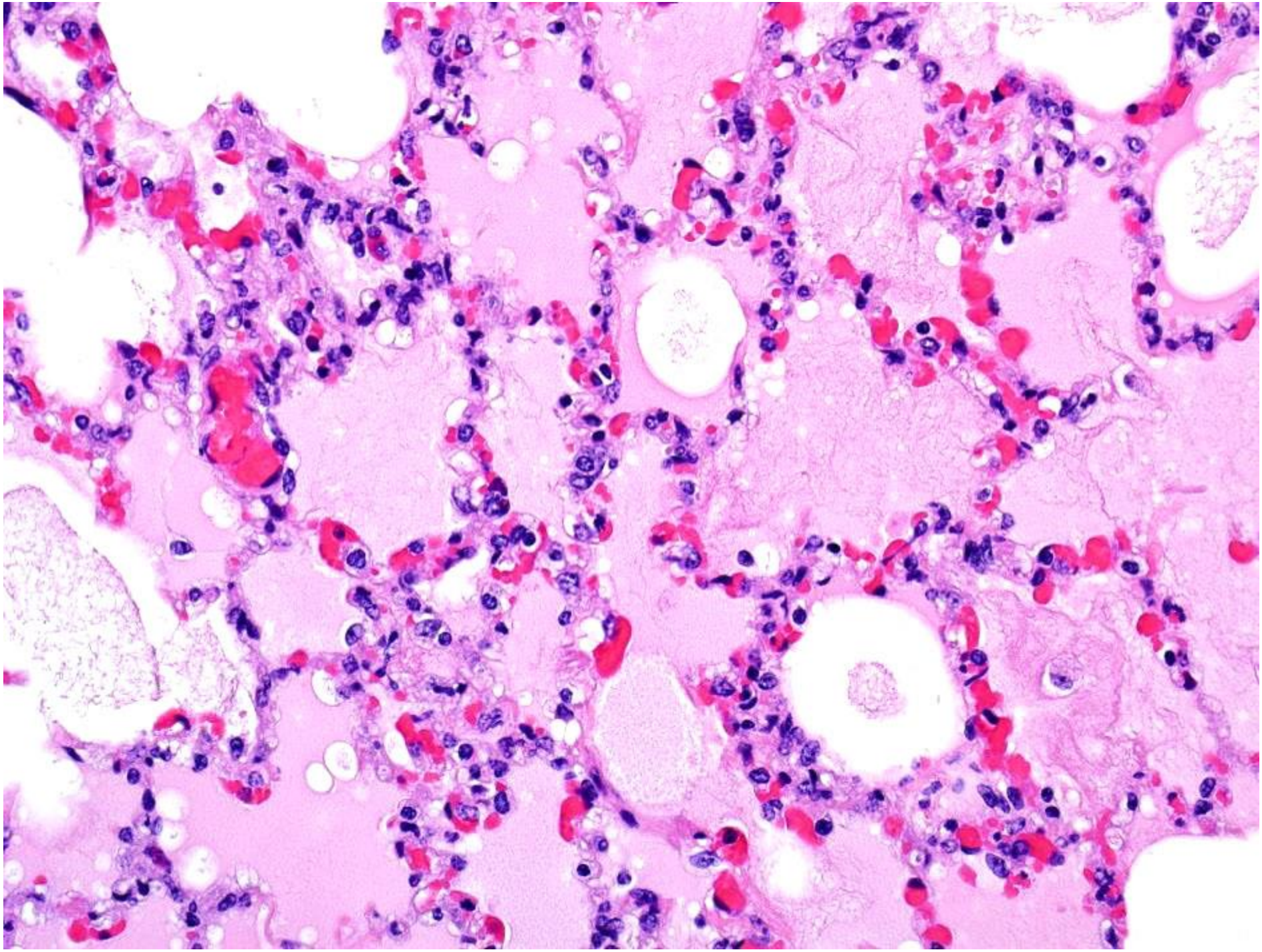
GFAP

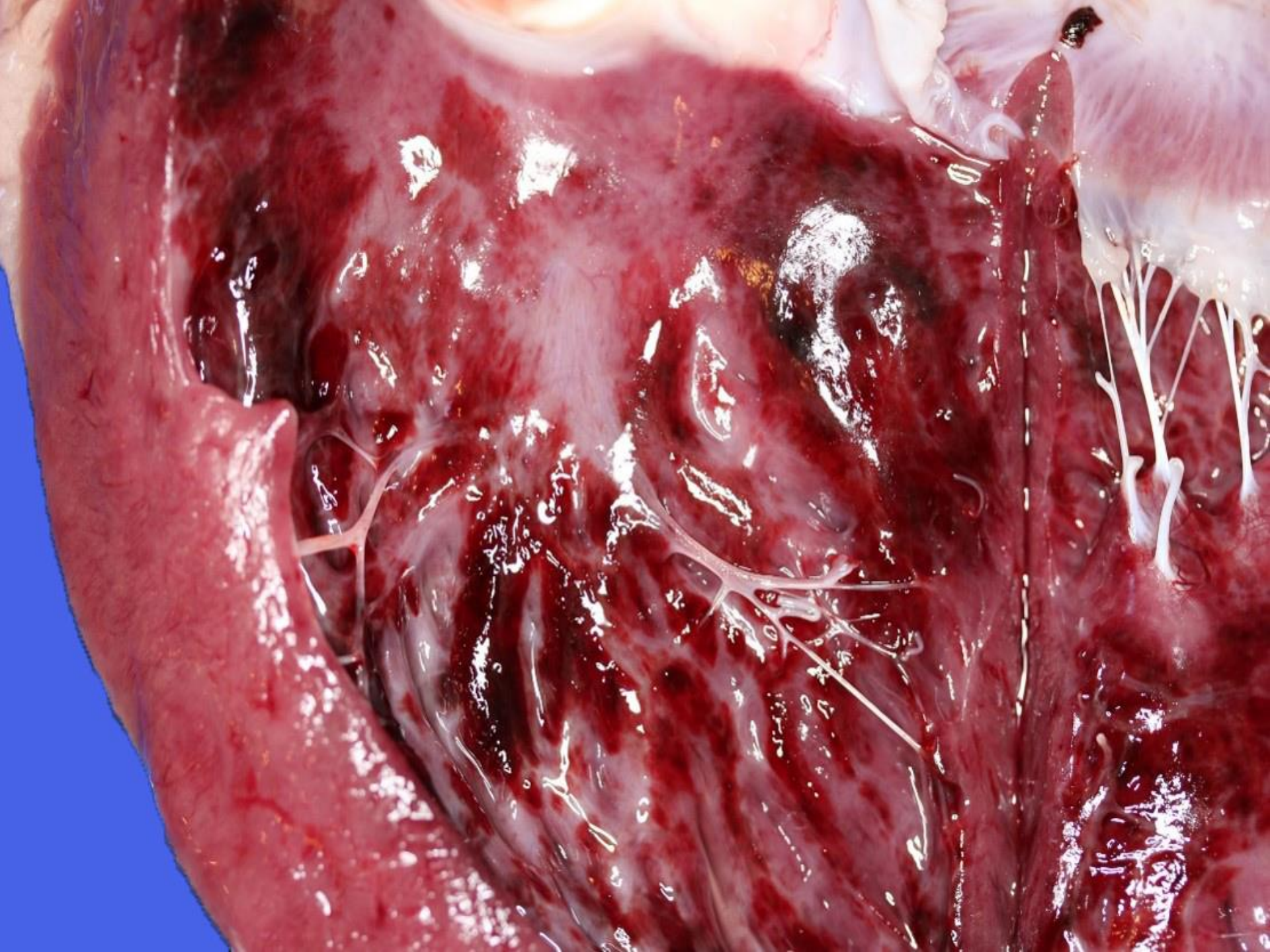


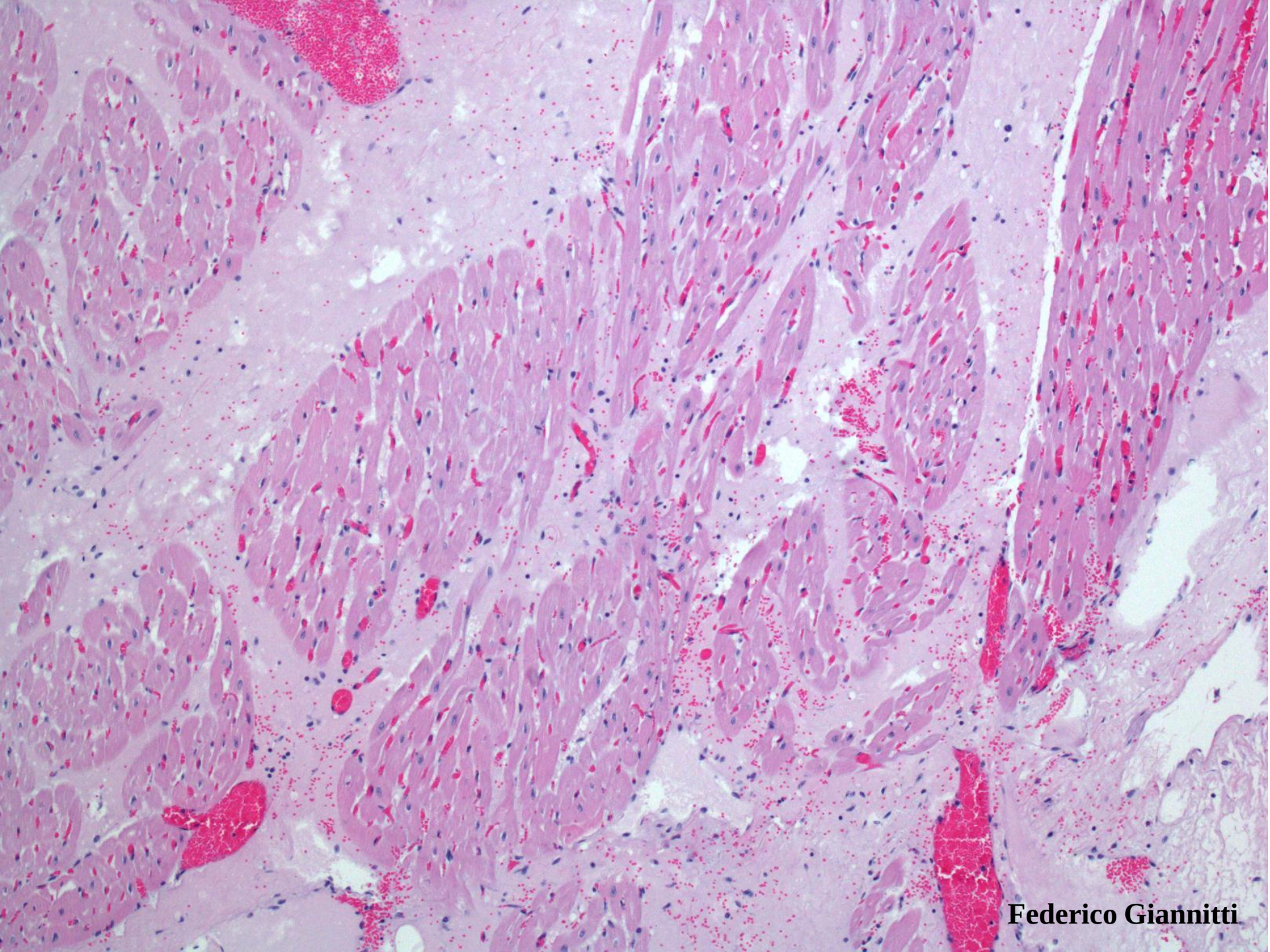


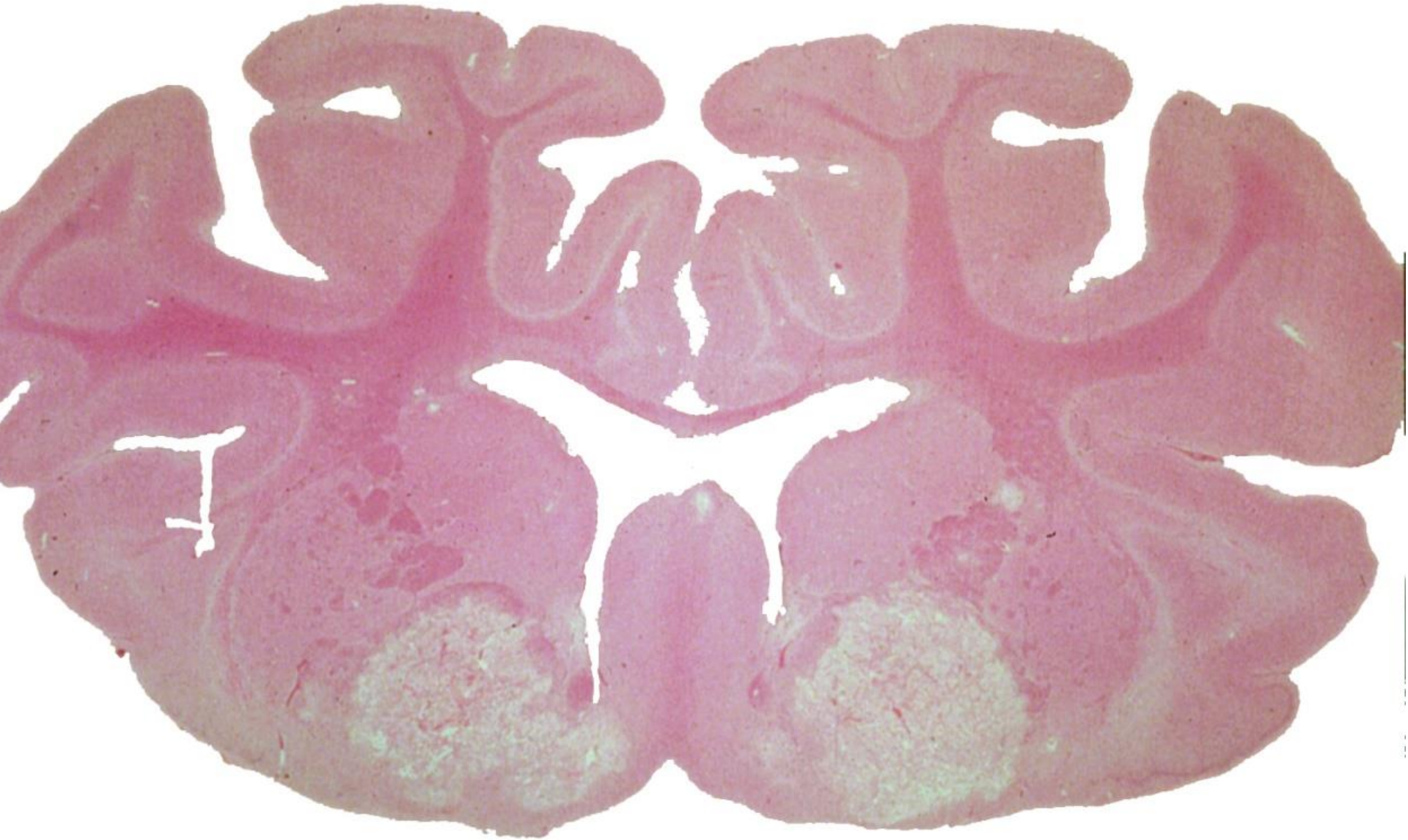
Control **ETX**

Garcia et al, 2015

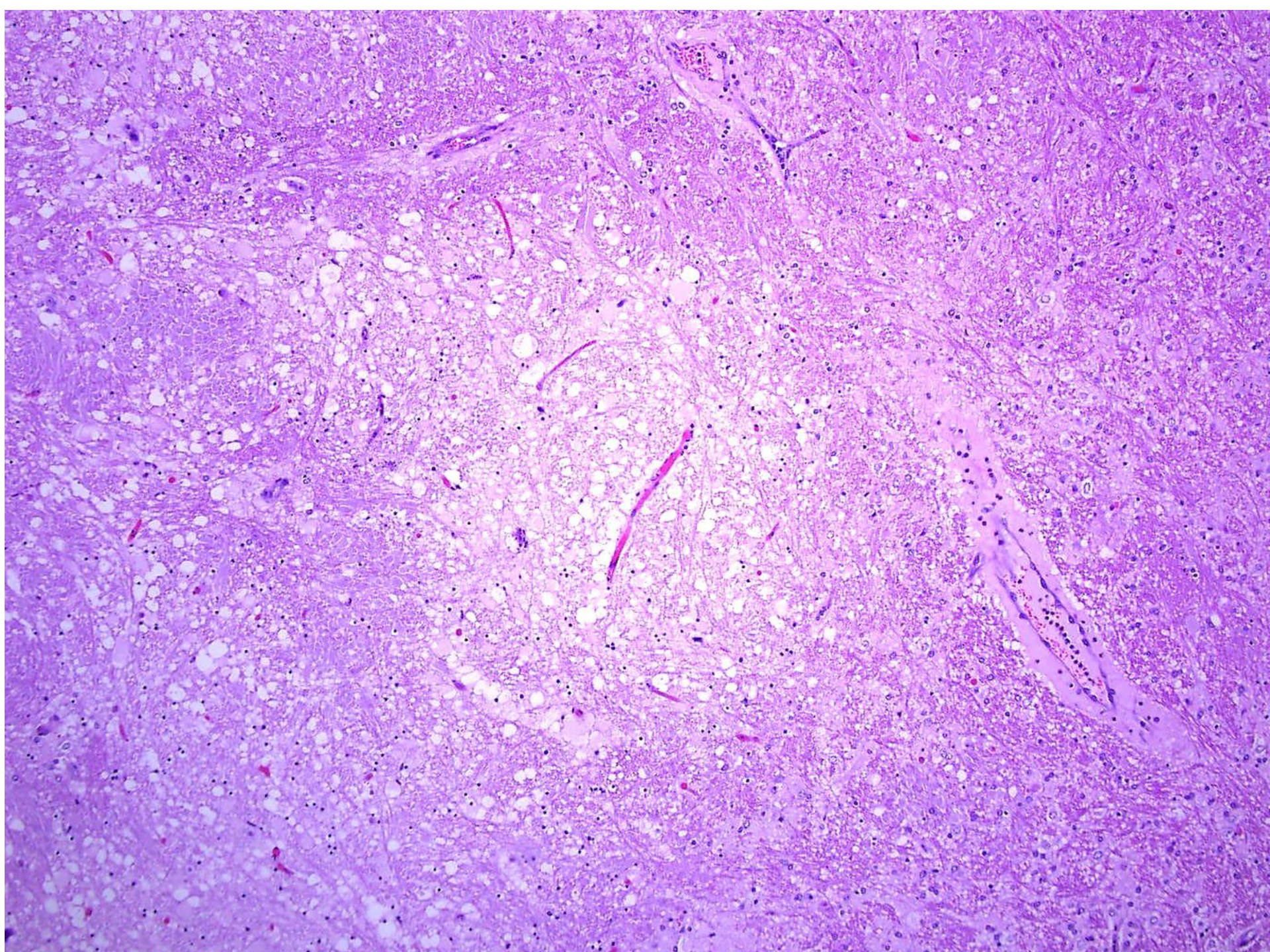


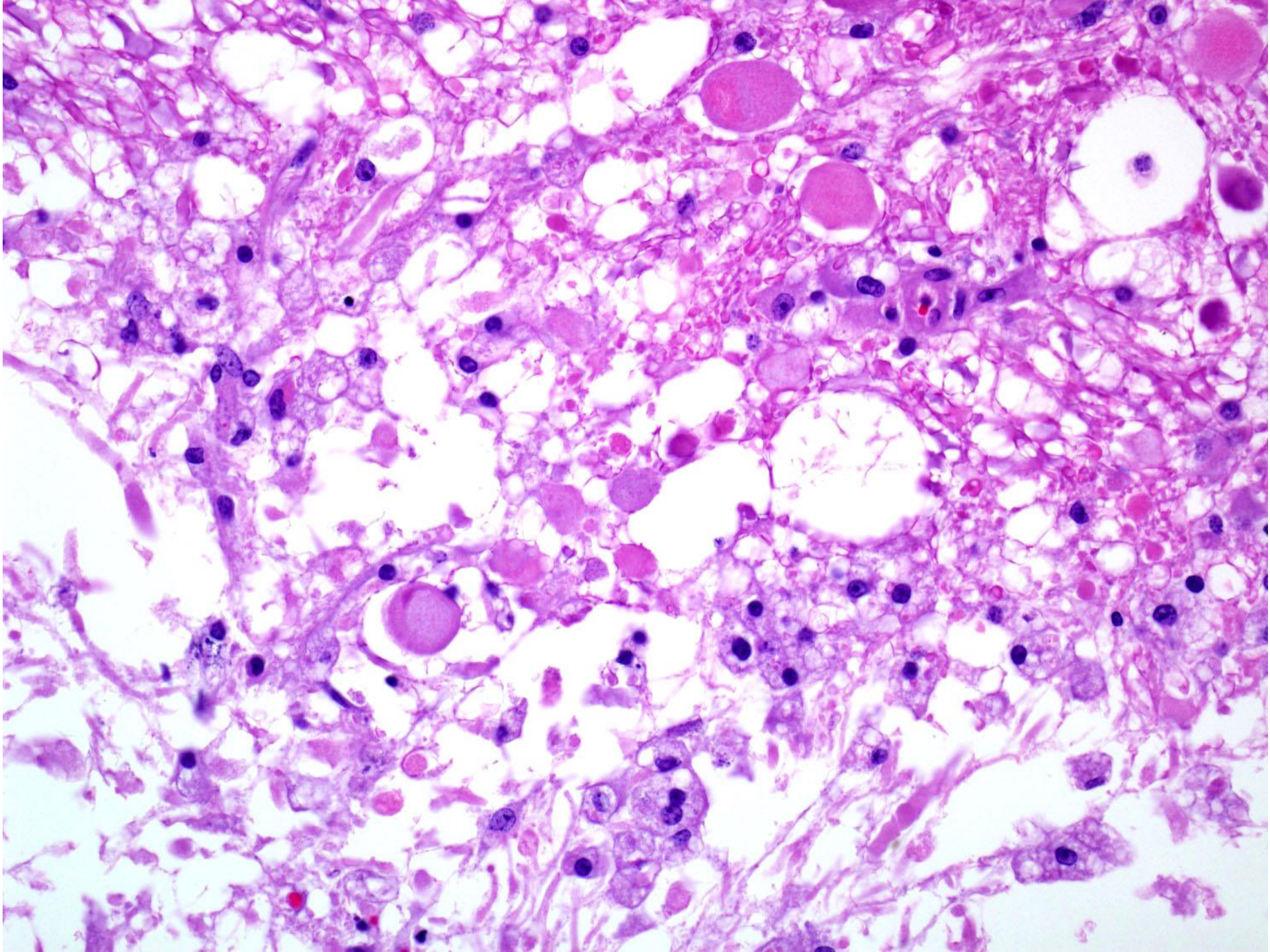



Federico Giannitti



Bill Hartley

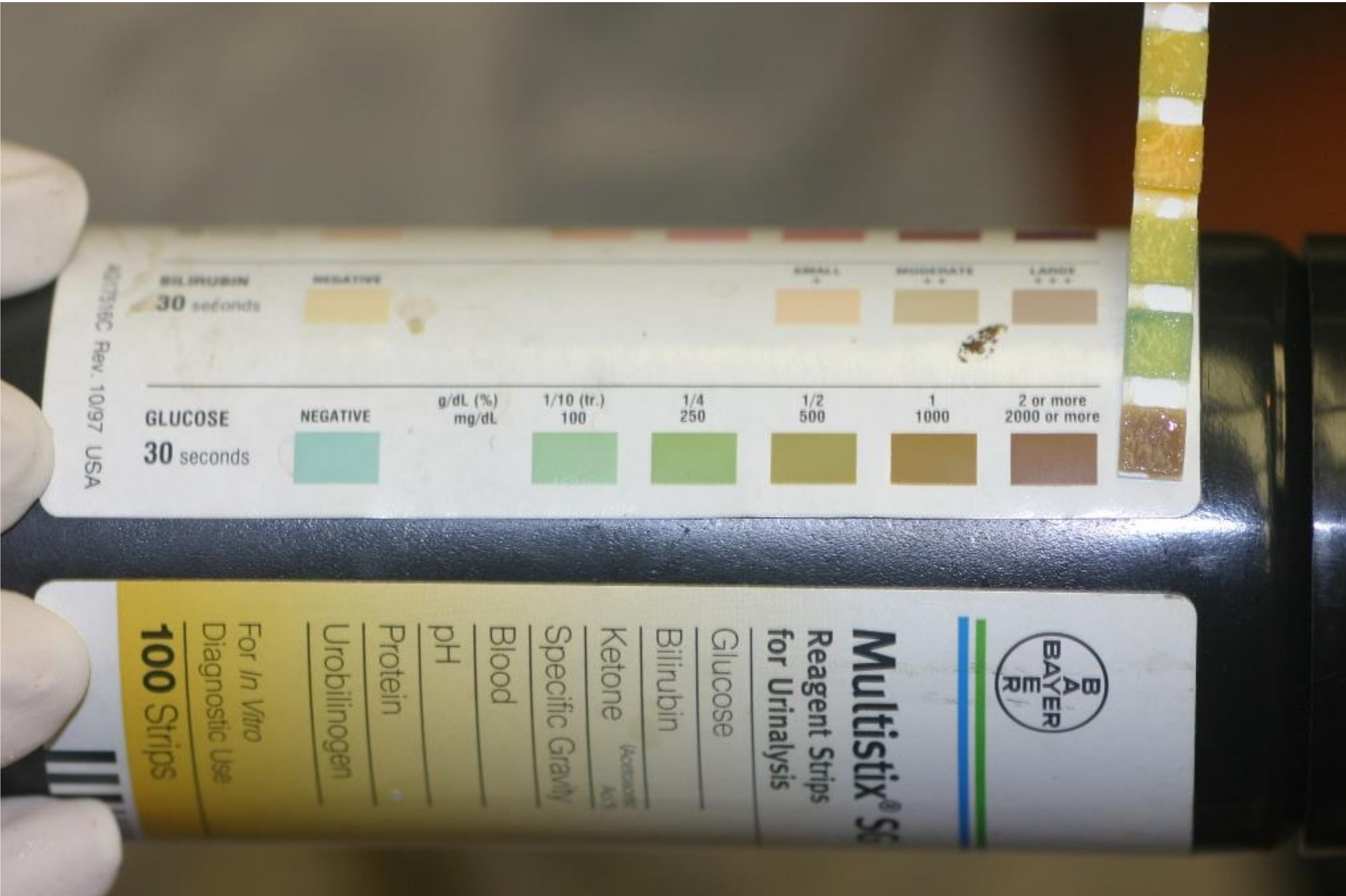




Diagnostic criteria

1-Clinics/gross		**Suggestive/confir.***
2-Histology		**Confirmatory***
3-Ancillary:	Culture (+ typing)	**Suggestive**
4-Ancillary:	Epsilon toxin	**Confirmatory**

Other practical diagnostic tools

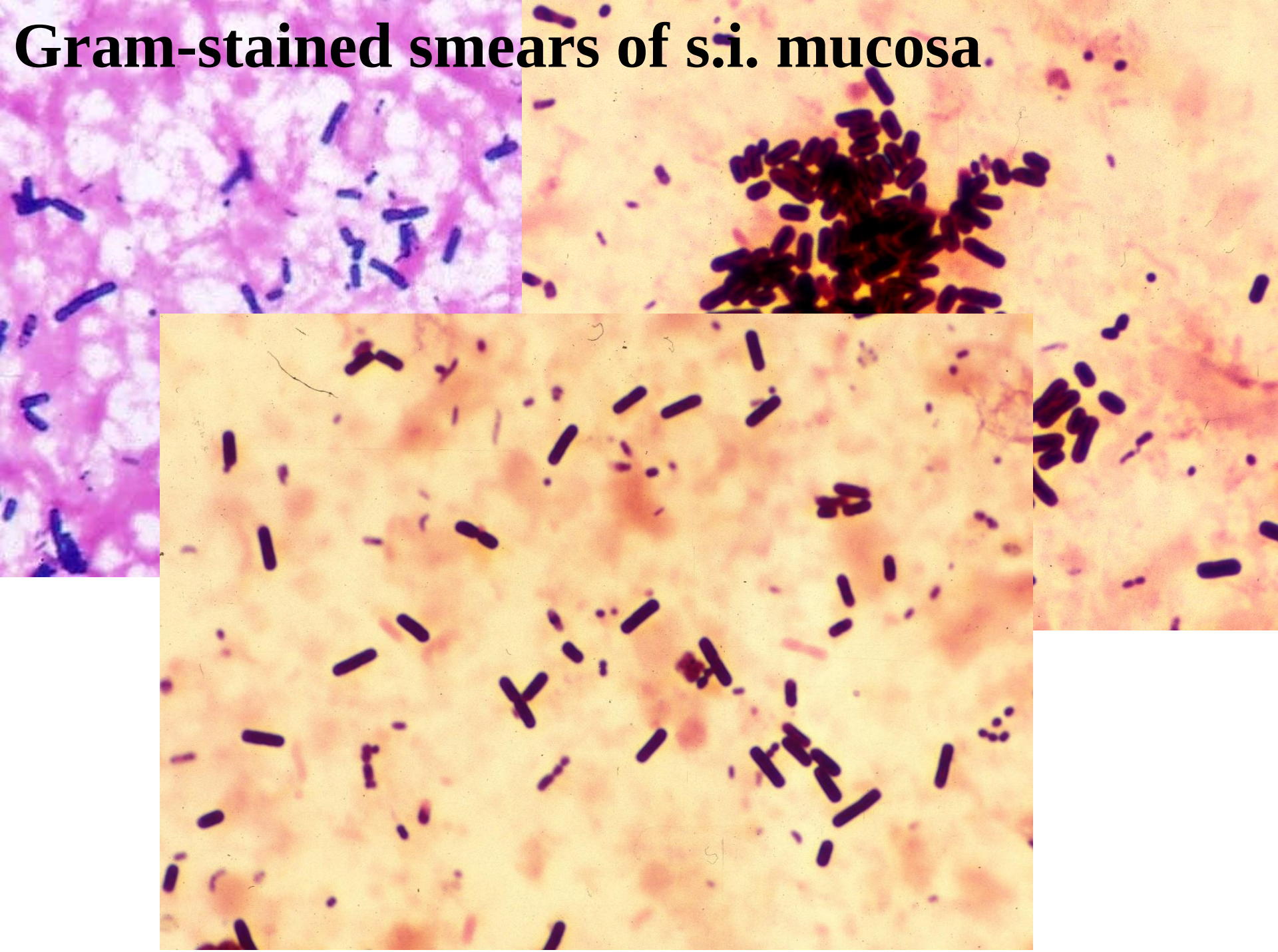


BILIRUBIN
30 seconds
GLUCOSE
30 seconds
NEGATIVE
g/dL (%)
mg/dL
1/10 (tr.)
100
1/4
250
1/2
500
1
1000
2 or more
2000 or more
Rev. 10/97 USA
BAYER
Multistix®
Reagent Strips
for Urinalysis
Glucose
Bilirubin
Ketone
Specific Gravity
Blood
pH
Protein
Urobilinogen
For In Vitro
Diagnostic Use
100 Strips

Glucosuria:

Helpful but rare
Treatment complicates

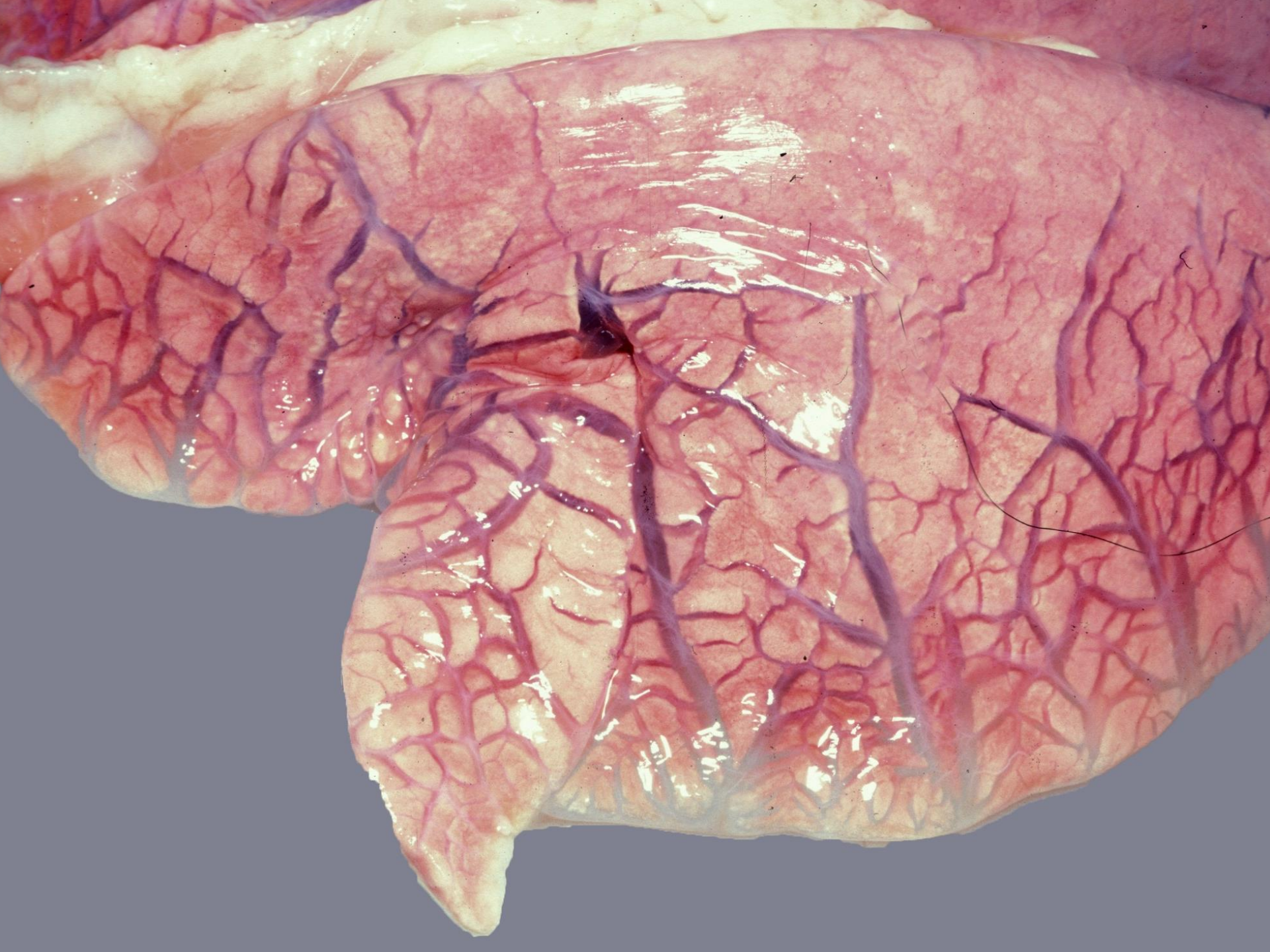
Gram-stained smears of s.i. mucosa

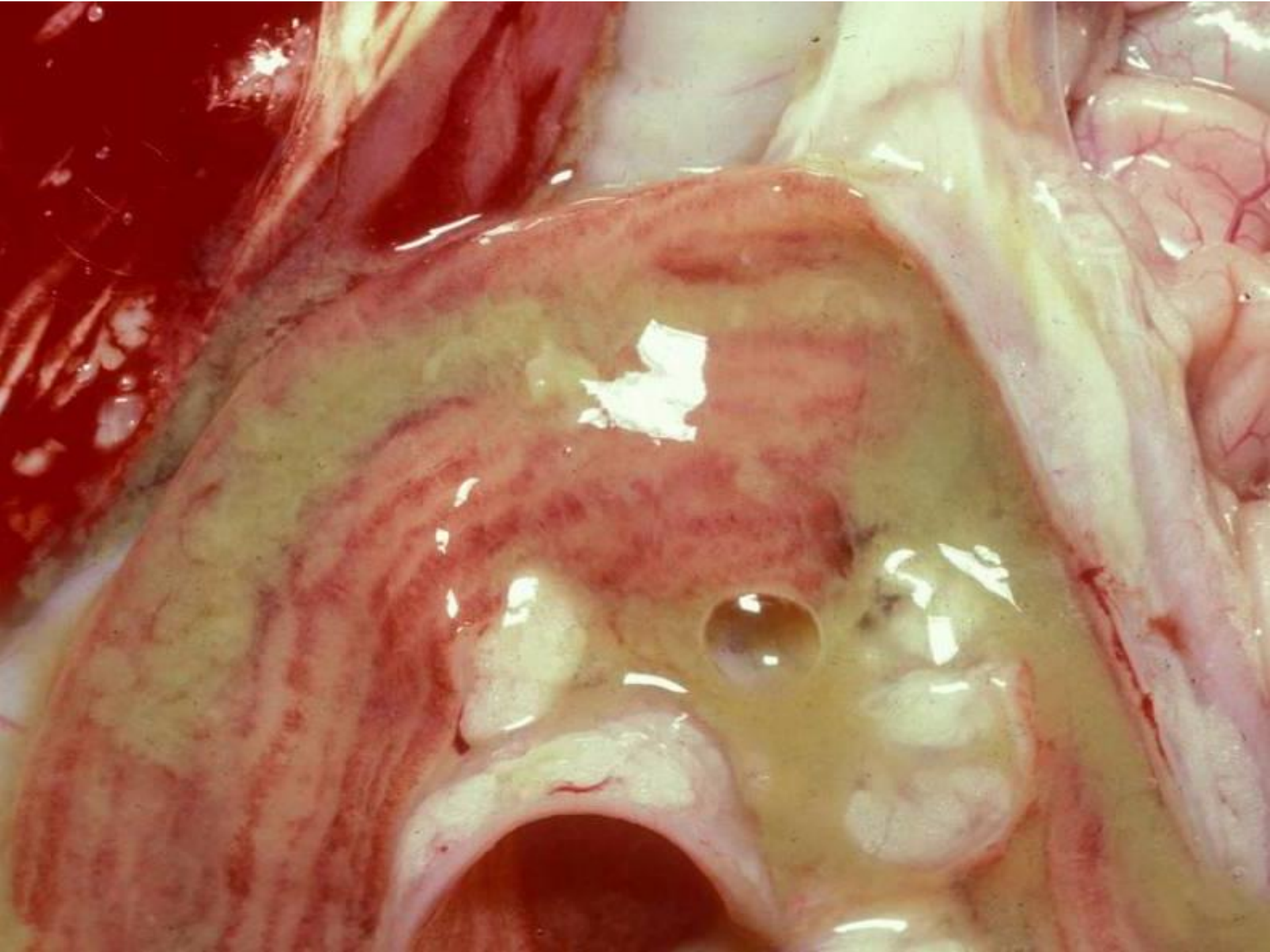


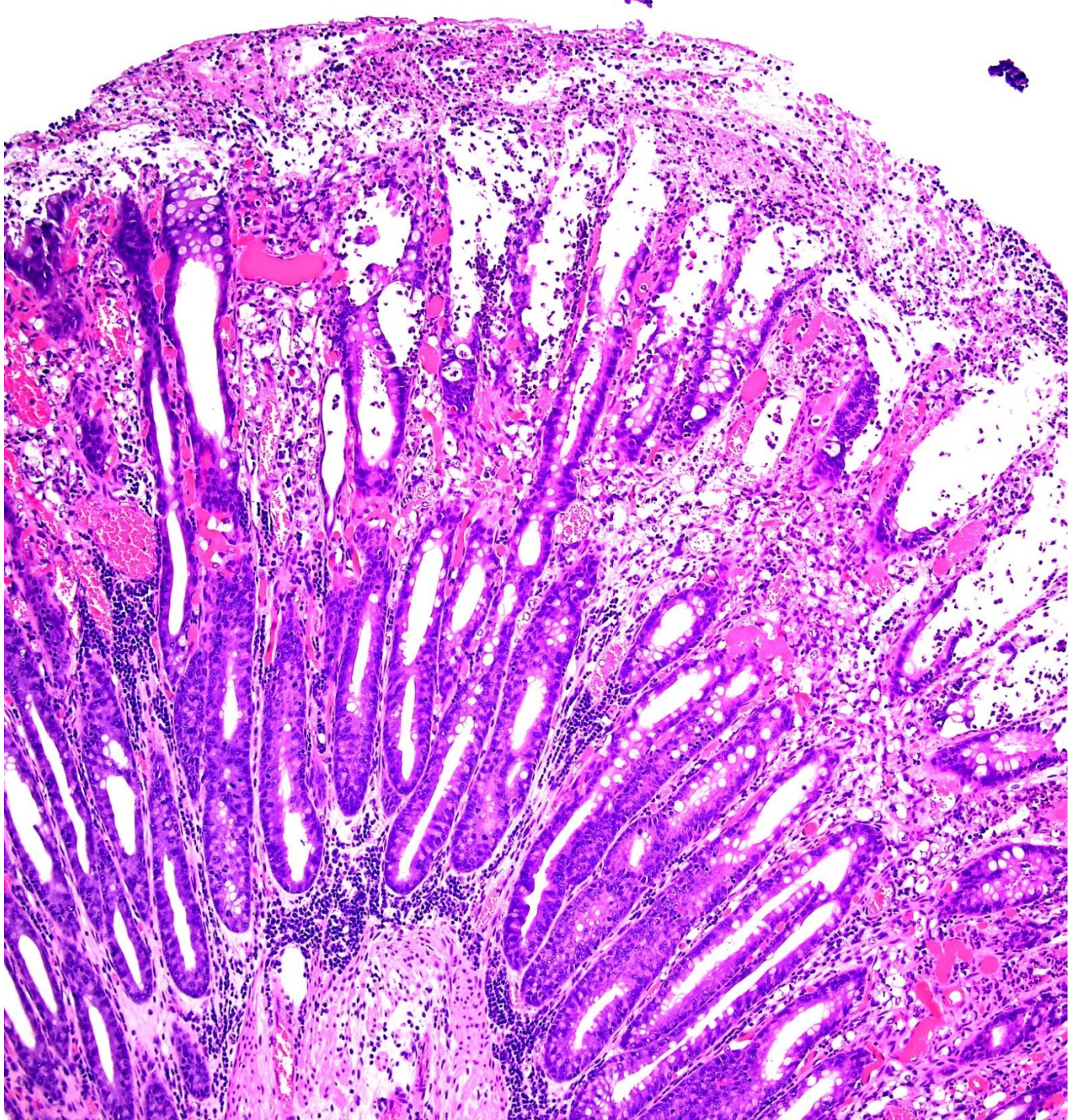
Natural hosts

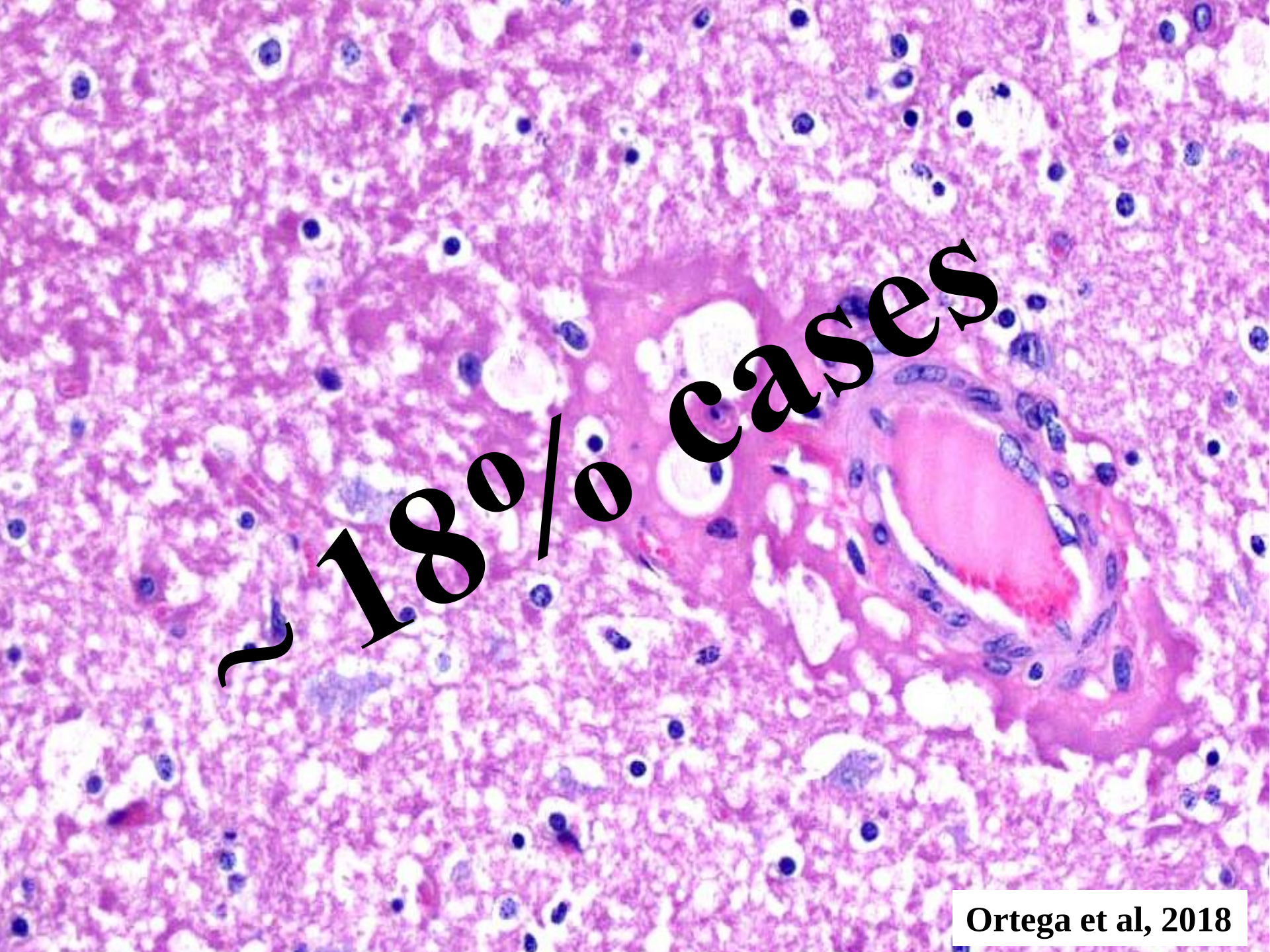
* Sheep
* **Goats**
* Cattle
* May be others….

- **Acute** } **Neurologic**
- **Sub-acute** } **Neurologic or Neurologic + colitis**








~ 18% cases
Ortega et al, 2018

Clinical signs

- Acute } Neurologic
- Sub-acute } Neurologic or Neurologic + colitis
- **Chronic** } Colitis

≠

Take home message

Natural hosts

* Sheep
* Goats
* **Cattle**
* May be others….


8210

Brain lesions similar to those produced in sheep by *C. perfringens* type D

Buxton et al, 1981; Jeffrey, 1992; Fairley 2005


FSE
Photo Rob Fairley

No causal relationship

between *C. perfringens* type D

and

these lesions

Enterotoxemia type D in cattle

1-Experimental disease: Yes!!!

2-Natural disease: very rare?

Enterotoxemia type D in cattle

1-Experimental disease: Yes!!!

2-Natural disease: very rare?

J. Comp. Path. 2002, Vol. 126, 71–75
doi:10.1053/jcpa.2001.0514, available online at http://www.idealibrary.com on IDEAL®

SHORT PAPER

Effects of Intravenous Injection of *Clostridium perfringens* Type D Epsilon Toxin in Calves

F. A. Uzal, W. R. Kelly*, W. E. Morris and R. A. Assis†

Vet Pathol 46:1213–1220 (2009)
DOI: 10.1354/vp.08-VP-0304-U-FL

Clinicopathologic Features of Experimental *Clostridium perfringens* Type D Enterotoxemia in Cattle

E. J. F. Filho, A. U. Carvalho, R. A. Assis, F. F. Lobato, M. A. Rachid, A. A. Carvalho, P. M. Ferreira, R. A. Nascimento, A. A. Fernandes, J. E. Vidal, and F. A. Uzal

Department of Veterinary Clinics and Surgery (EJFF, AUC, MAR, PMF) and Department of Preventive Veterinary Medicine (FFL, AAF), Veterinary School, Federal University of Minas Gerais, Belo Horizonte, Brazil; LANAGRO, Ministry of Agriculture and Provisioning, Pedro Leopoldo, Minas Gerais, Brazil (RAA, AAC, RAN); Department of Microbiology and Molecular Genetics, University of Pittsburgh, School of Medicine, Pittsburgh, PA (JEV); and California Animal Health and Food Safety Laboratory, San Bernardino Branch, University of California, Davis, Davis, CA (FAU)

Enterotoxemia type D in cattle

1-Experimental disease: Yes!!!

2-Natural disease: very rare?

Clostridium perfringens type D epsilon one-day-

P. J. Watson, S. F. I

Clostridium perfringens t
is a very common caus
numerous scientific pu
enterotoxaemia in she
type D enterotoxaemia
reports of naturally occ
and others 1981, Fairle
cases of C *perfringens* ty
that was notable for the
tion of both character
in the intestinal conte

The affected calves
hill sheep farm in the I
housed in traditional s
in February while the c
February 28, 2004, in t
born unassisted in the
and was seen to feed
discovered 'flat out' in
21.30 on the same day.

The carcase was su
(VLA) – Penrith for di
weighed 38 kg and was

Domestic Mammal Disease

Veterinary Pathology
50(5) 765-768

DOI: 10.1177/0300985813476058
vet.sagepub.com

Brain Lesions Associated With *Clostridium perfringens* Type D Epsilon Toxin in a Holstein Heifer Calf

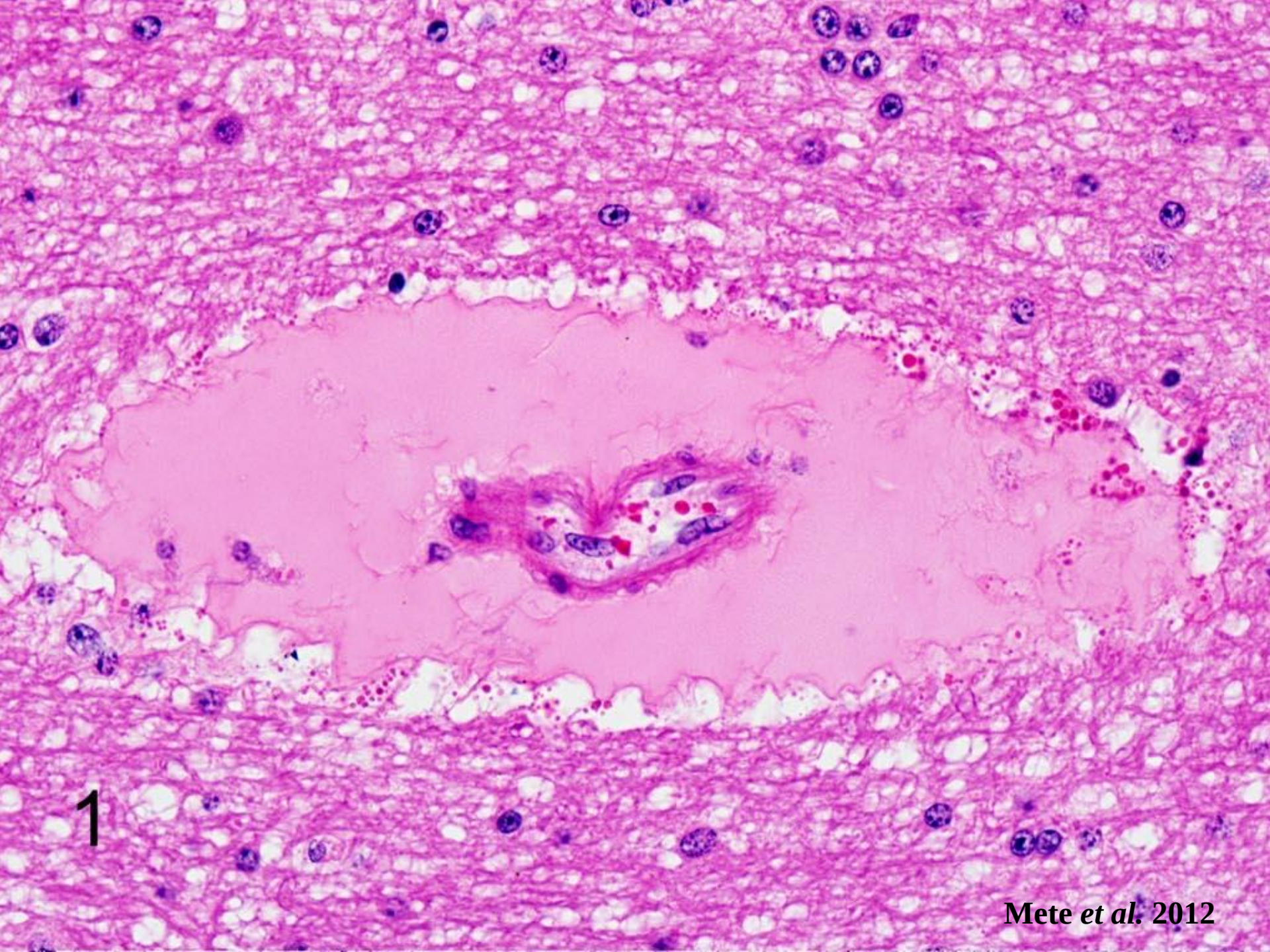
A. Mete[1], J. Garcia[2], J. Ortega[3], M. Lane[4], S. Scholes[5], and F. A. Uzal[2]

Abstract

A 6-month-old dairy heifer calf with no premonitory signs was acutely down after the morning feeding and could not rise. On presentation, the heifer was in right lateral recumbency and moribund with opisthotonus and left hind limb paddling. Following euthanasia, gross examination of the brain revealed multifocal loss of gray-white matter distinction and extensive petechiae throughout the brainstem. On histopathological examination, there was striking white matter edema and marked perivascular proteinaceous edema surrounding many arterioles and venules (microangiopathy), mainly in the white matter of the internal capsule, thalamus, midbrain, cerebellum, and cerebellar peduncles. The perivascular neuropil was strongly positive for Alzheimer precursor protein A4. *Clostridium perfringens* epsilon toxin was detected in the intestinal contents. This is the first report of microangiopathy in postneonatal cattle associated with the detection of epsilon toxin in the intestinal contents.

Keywords

brain, cattle, *Clostridium perfringens*, enterotoxemia, epsilon toxin, ETX, microangiopathy, Alzheimer precursor protein, APP



Mete *et al.* 2012

The 2018 *C. perfringens* toxin-based typing scheme

Toxinotype	α-toxin	β-toxin	ε-toxin	ι-toxin	CPE	NetB
A	+	-	-	-	-	-
B	+	+	+	-	-	-
C	+	+	-	-	+/-	-
D	+	-	+	-	+/-	-
E	+	-	-	+	+/-	-
F	+	-	-	-	+	-
G	+	-	-	-	-	+

Rood et al, Anaerobe 2018

Main virulence factors

Alpha toxin
Iota toxin

Iota toxin:

Cross reaction: *C. spiroforme* toxin

Cases published in……

diagnoses mostly based on isolation……

ELSEVIER

Anaerobe 10 (2004) 239–242

Anaerobe

www.elsevier.com/locate/anaerobe

Veterinary anaerobes and diseases

Clostridium perfringens type E enteritis in calves: two cases and a brief review of the literature

J. Glenn Songer[a,*], Dale W. Miskimmins[b]

[a] *Department of Veterinary Science and Microbiology, The University of Arizona, Tucson, AZ 85721, USA*
[b] *Department of Veterinary Science, South Dakota State University, Brookings, SD 57007, USA*

Received 5 April 2004; accepted 5 May 2004

The 2018 *C. perfringens* toxin-based typing scheme

Toxinotype	α-toxin	β-toxin	ε-toxin	ι-toxin	CPE	NetB
A	+	-	-	-	-	-
B	+	+	+	-	-	-
C	+	+	-	-	+/-	-
D	+	-	+	-	+/-	-
E	+	-	-	+	+/-	-
F	+	-	-	-	+	-
G	+	-	-	-	-	+

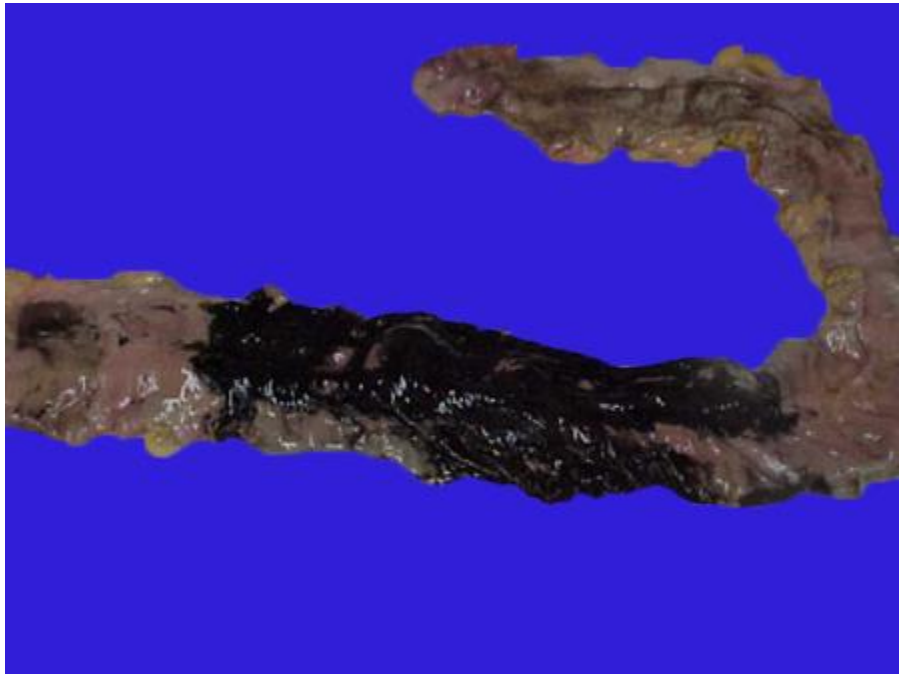
Rood et al, Anaerobe 2018

Enterotoxin of *C. perfringens* (CPE)

C. perfringens type F

Humans: **Food poisoning/ATB associated**

Animals: **Enteritis (?)**



C. perfringens type F food poisoning

- **Second most common cause of bacterial food poisoning (USA: ~400,000/year).**

- **Fourth most common cause of deaths from bacterial food poisoning in the USA (elderly or debilitated).**

C. perfringens type F food poisoning

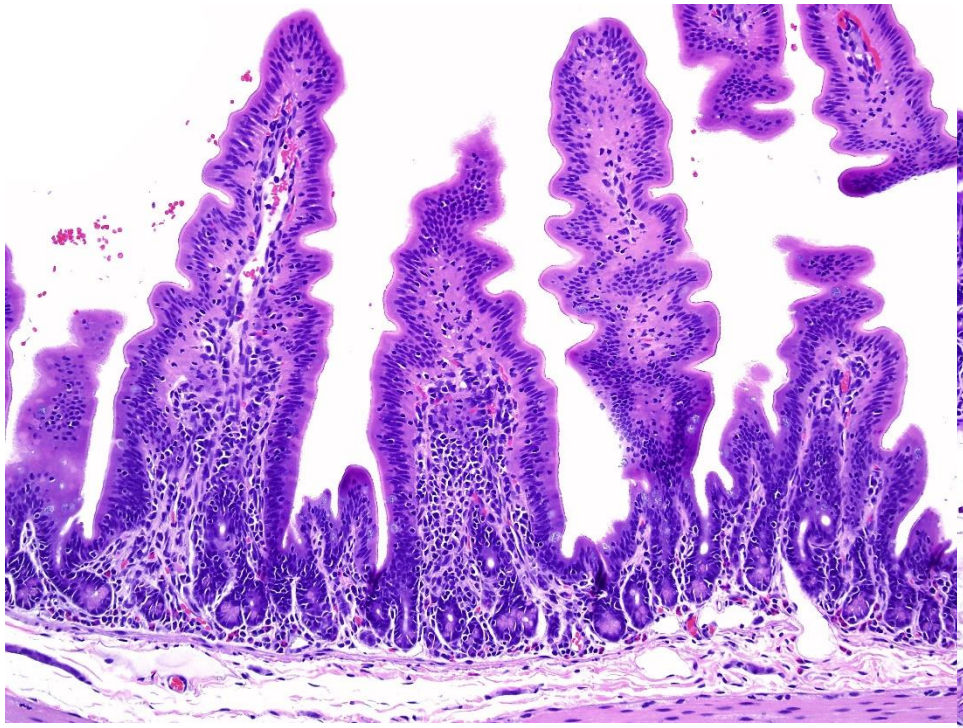
- **~12 hour incubation, illness 12-24 hours**
- **Diarrhea and abdominal cramps**

Clostridium perfringens food poisoning

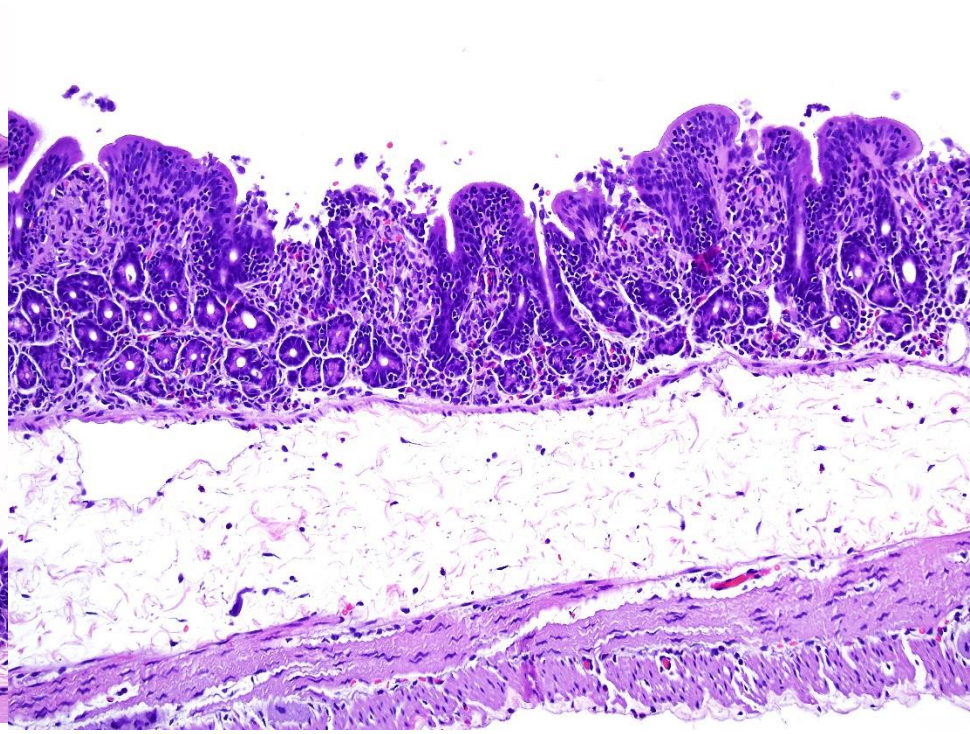
CPE: sporulation sub-product

Rabbit intestinal loops 6 hours

Buffer



CPE



The 2018 *C. perfringens* toxin-based typing scheme

Toxinotype	α-toxin	β-toxin	ε-toxin	ι-toxin	CPE	NetB
A	+	-	-	-	-	-
B	+	+	+	-	-	-
C	+	+	-	-	+/-	-
D	+	-	+	-	+/-	-
E	+	-	-	+	+/-	-
F	+	-	-	-	+	-
G	+	-	-	-	-	+

Rood et al, Anaerobe 2018

Necrotic enteritis

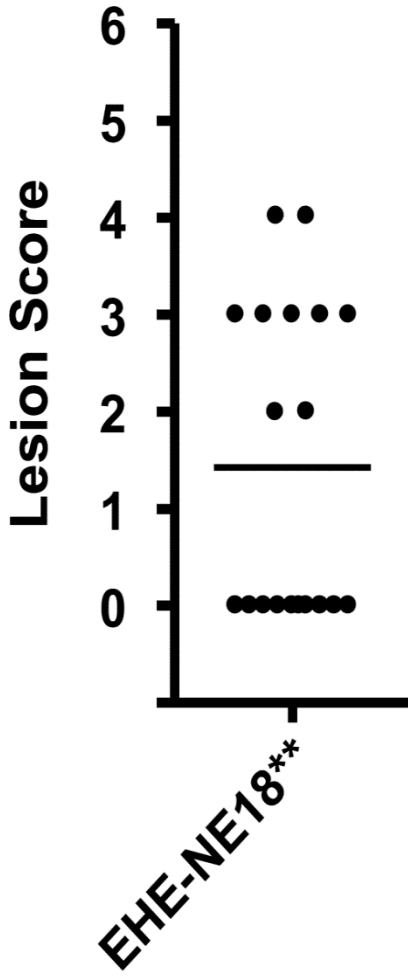
Virulence factors

NetB

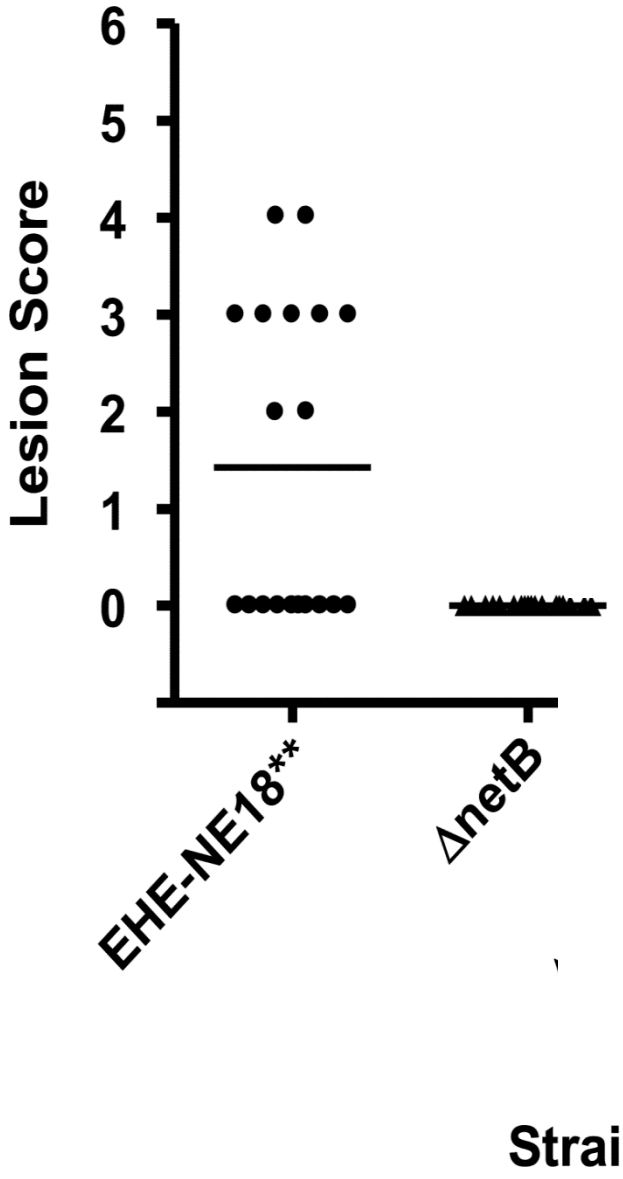
Alpha?

Others?

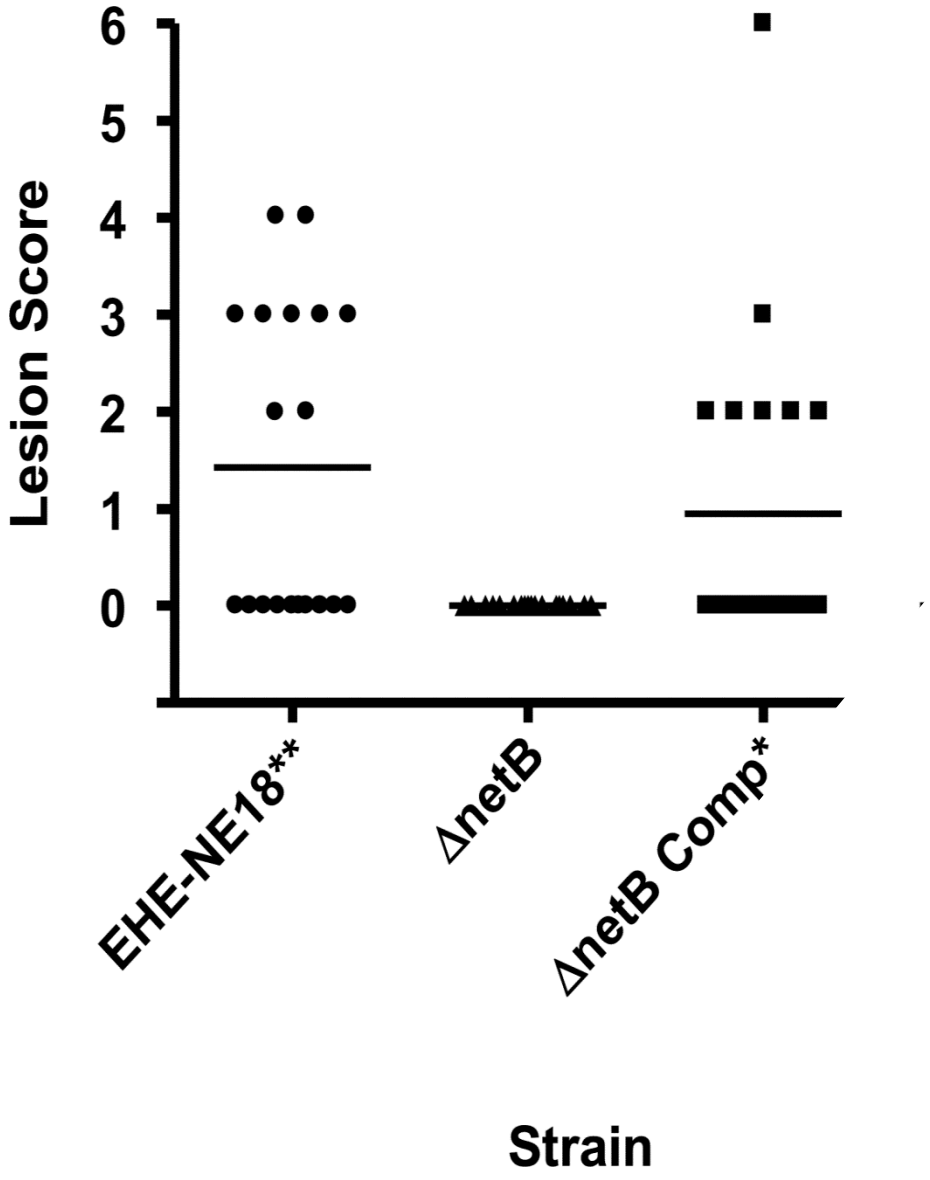
Take-home message!!!!



Keyburn et al , 2008



Keyburn et al , 2008



Keyburn et al , 2008

Re-emerging disease

* Restrictive use of antibiotics

* High-density housing

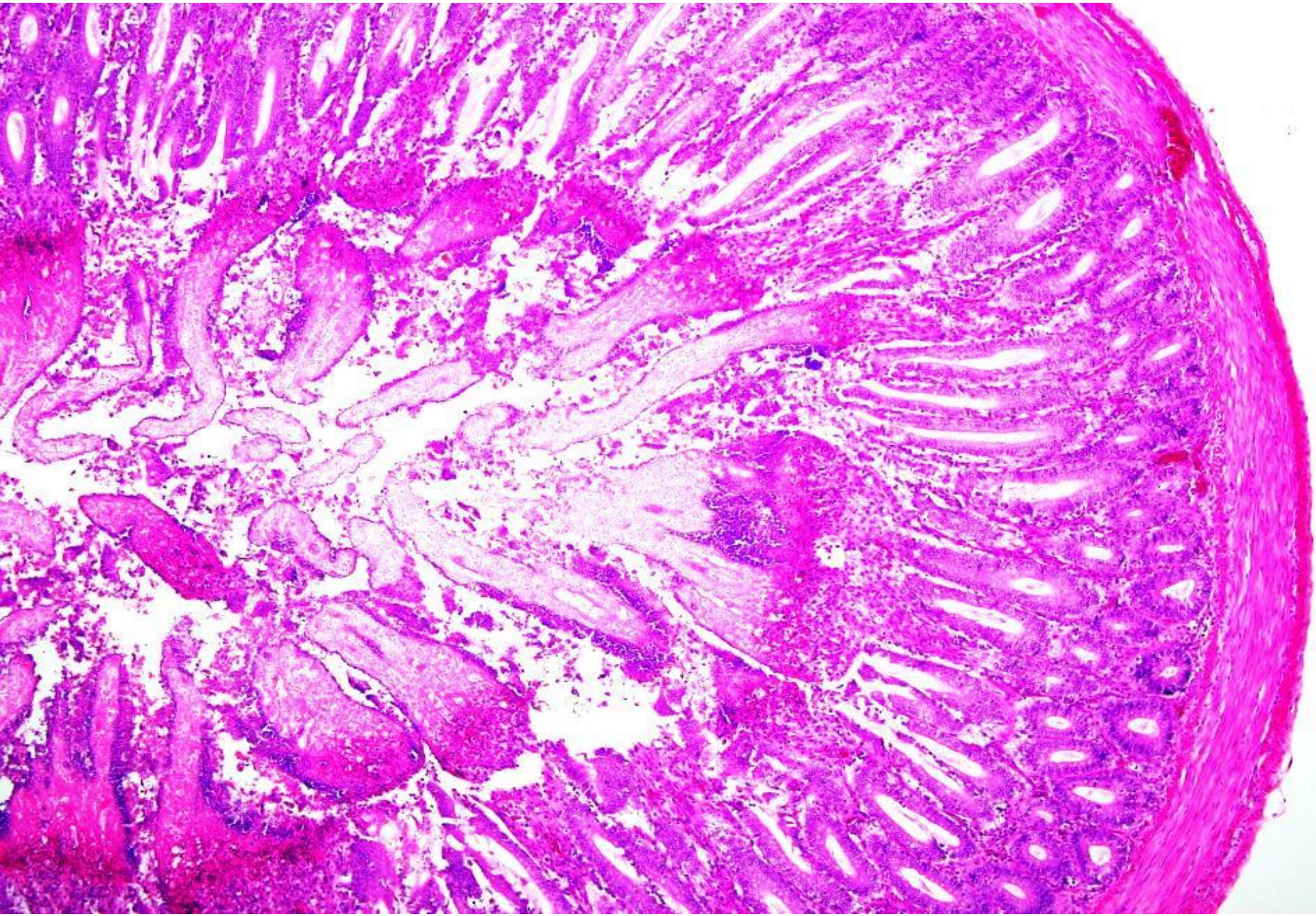
* Re-use of litter

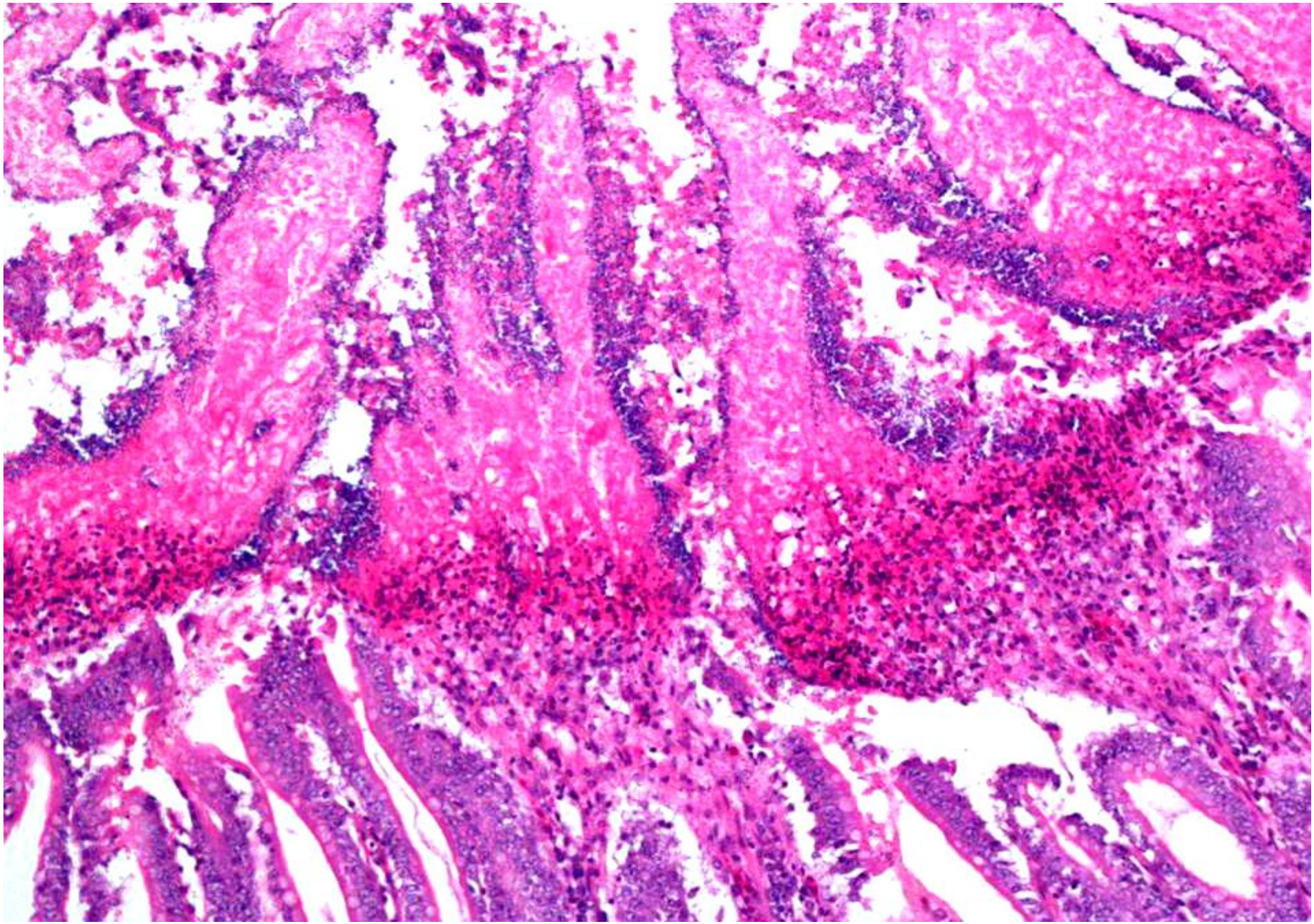
Main predisposing factor: *Eimeria spp.*

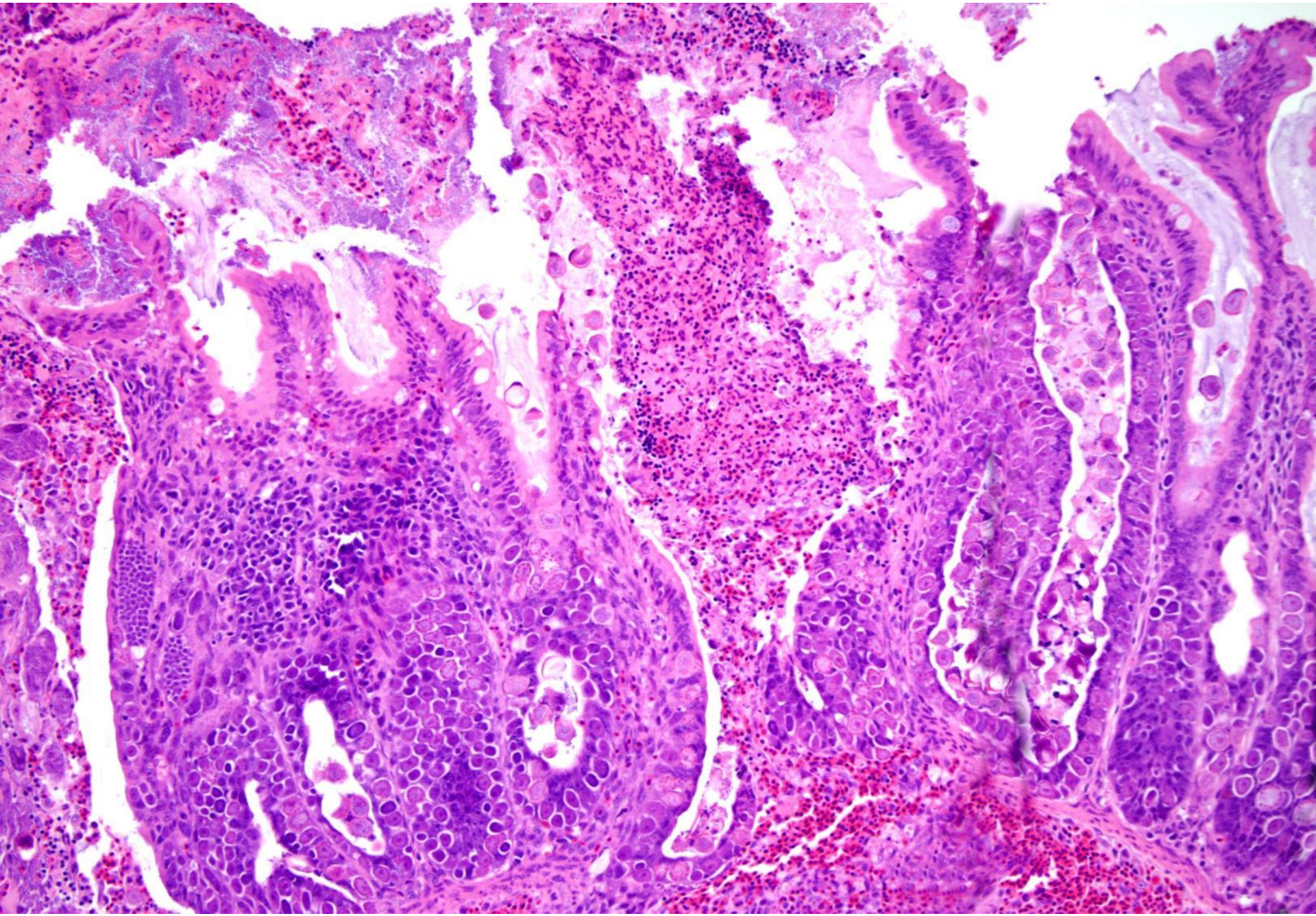
Take-home message!!!

* **Clinical**

* **Sub-clinical**







Diagnostic criteria

1-Clinics/gross

2-Histo

3-Ancillary: **Culture (+ typing)**

} **Suggestive**

4- 1+2+3

} **Confirmatory?**

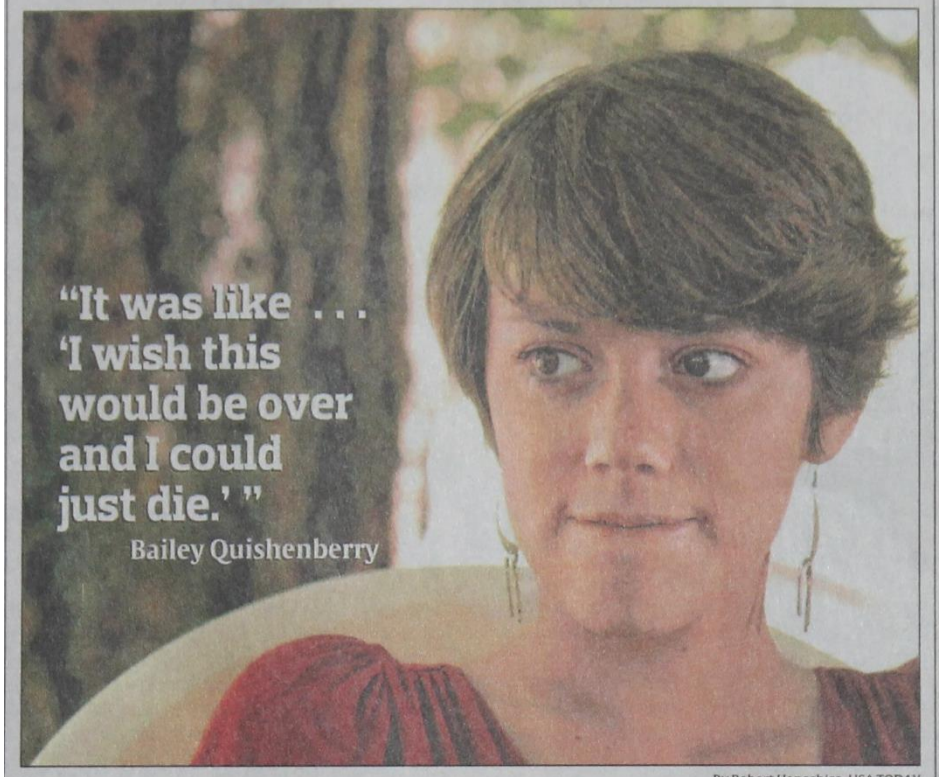
GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric	Enterotoxemias/ enteritis	*C. perfringens*	✓	✓
		C. difficile	✓	✓
Histotoxic				
Neurotoxic				

Clostridium difficile

Main cause of ATB associated diarrhea in humans and animals

NOT ATB IN PIGS or FOALS!!!!

A USA TODAY INVESTIGATION



By Robert Hanashiro, USA TODAY

Survivor: Bailey, now 16, contracted C. diff after brain surgery.

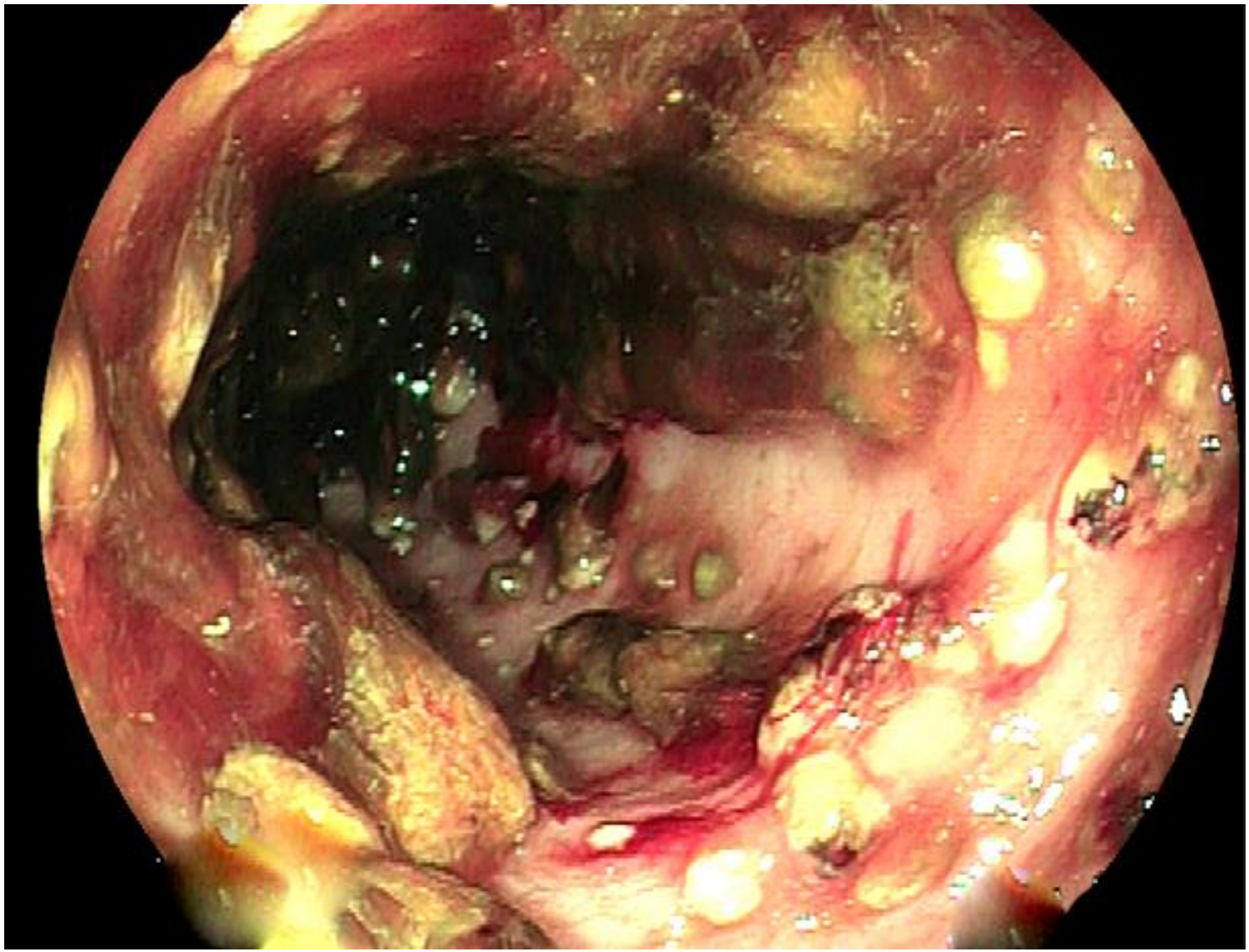
One bacteria, 30,000 deaths

An infection called C. diff is wreaking havoc in the USA's hospitals, nursing homes and other medical facilities — and officials could be doing far more to stop it

By Peter Eisler
USA TODAY

WHEN

8/16/2012



Stephen Sontag

Predisposing factors:

* antibiotic therapy (virtually any antibiotic)

* hospitalization

Take-home message!!!

Sturdy environmental contaminant

UBIQUITOUS:

- Hospitals, households, etc.
- Intestinal content and feces
- Meat and vegetables


VICTORIAN
FARMSTEAD
MEAT COMPANY
"Life's Too Short To Eat Crappy Meat"
Vegetarians warning

C. difficile detected in:

*** Ready to eat organic/nonorganic salads**

*** Lettuce, green peppers and eggplant**

(overall prevalence in vegetables: up to 7.5%)

INITIALLY

TcdA: key virulence factor

TcdB: no effect

LETTER

doi:10.1038/nature09397

The role of toxin A and toxin B in *Clostridium difficile* infection

Sarah A. Kuehne[1]*, Stephen T. Cartman[1]*, John T. Heap[1], Michelle L. Kelly[1], Alan Cockayne[1] & Nigel P. Minton[1]

7 OCTOBER 2010 | VOL 467 | NATURE | 711

Toxin B is essential for virulence of *Clostridium difficile*

Dena Lyras[1], Jennifer R. O'Connor[1,3], Pauline M. Howarth[1], Susan P. Sambol[3], Glen P. Carter[1], Tongted Phumoonna[1], Rachael Poon[1,2], Vicki Adams[1], Gayatri Vedantam[3], Stuart Johnson[3], Dale N. Gerding[3], and Julian I. Rood[1,2,†]

[1]Australian Bacterial Pathogenesis Program, Monash University, VIC 3800, Australia

[2]Australian Research Council Centre of Excellence in Structural and Functional Microbial Genomics, Department of Microbiology, Monash University, VIC 3800, Australia

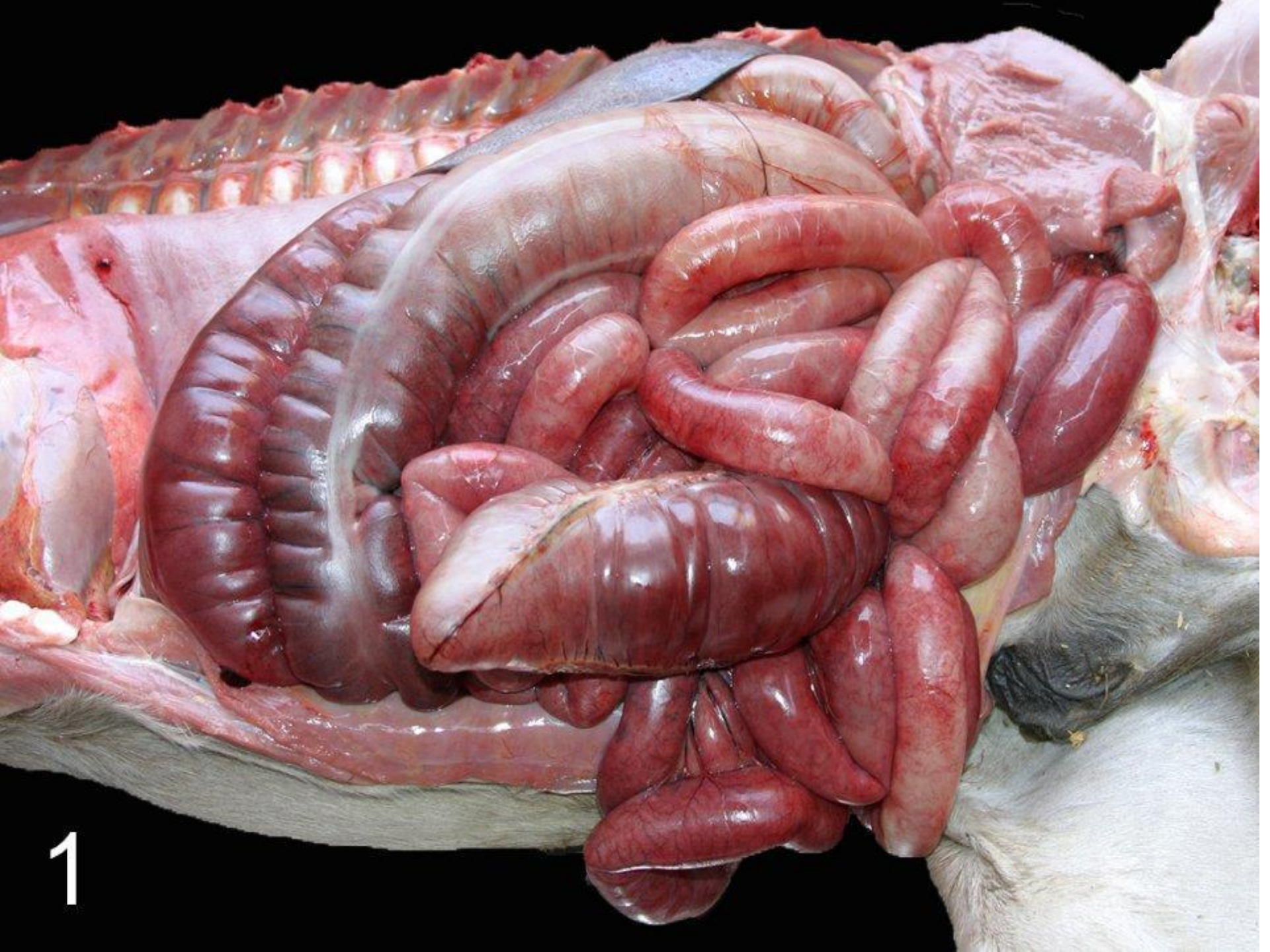
[3]Medical Service and Research Service, Hines VA Hospital, Hines, IL, U.S.A. and Infectious Disease Section, Stritch School of Medicine, Loyola University Chicago, Maywood, IL, U.S.A.

Published in final edited form as:

Nature. 2009 April 30; 458(7242): 1176–1179. doi:10.1038/nature07822.

CURRENTLY

TcdA and TcdB might act synergistically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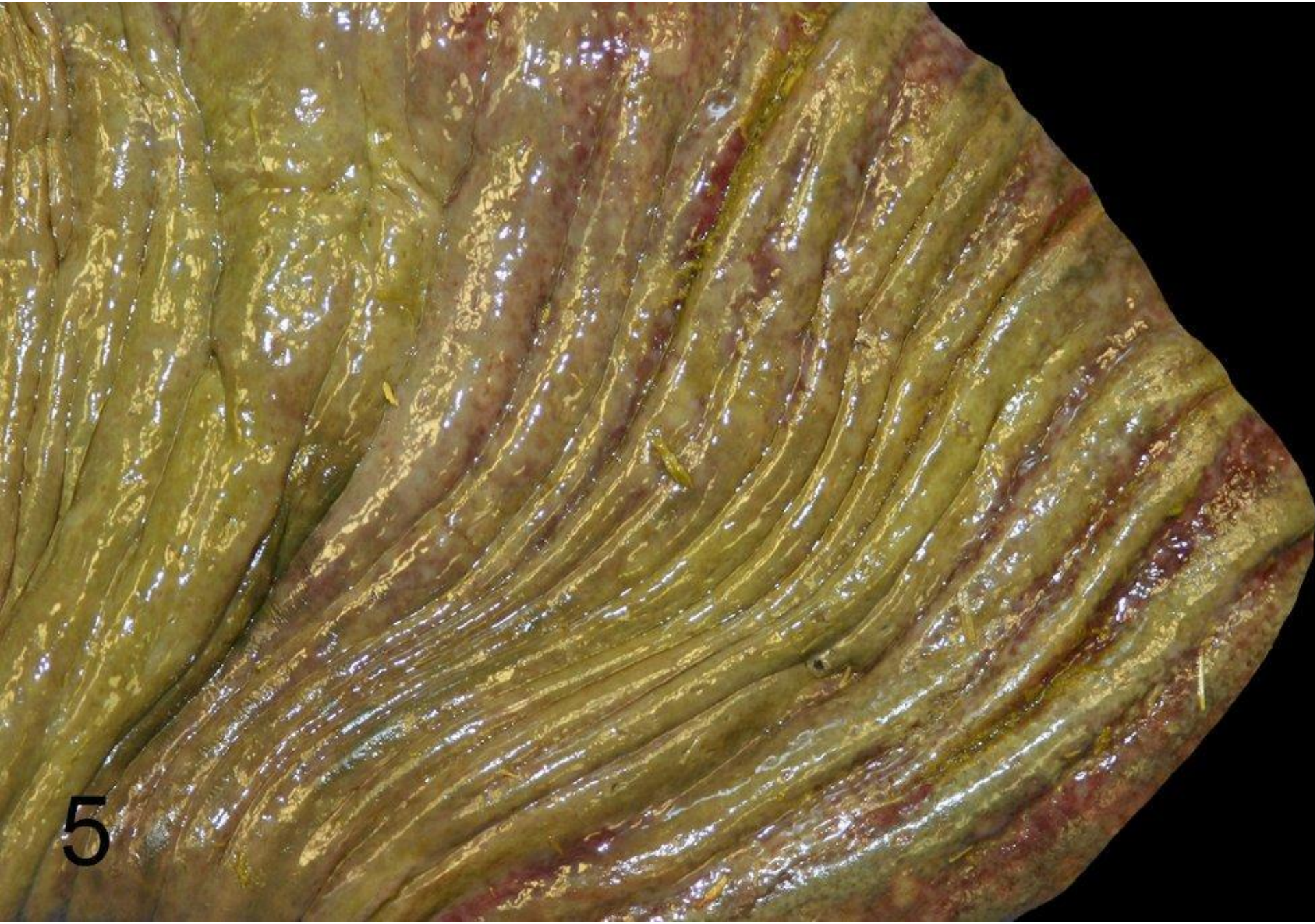
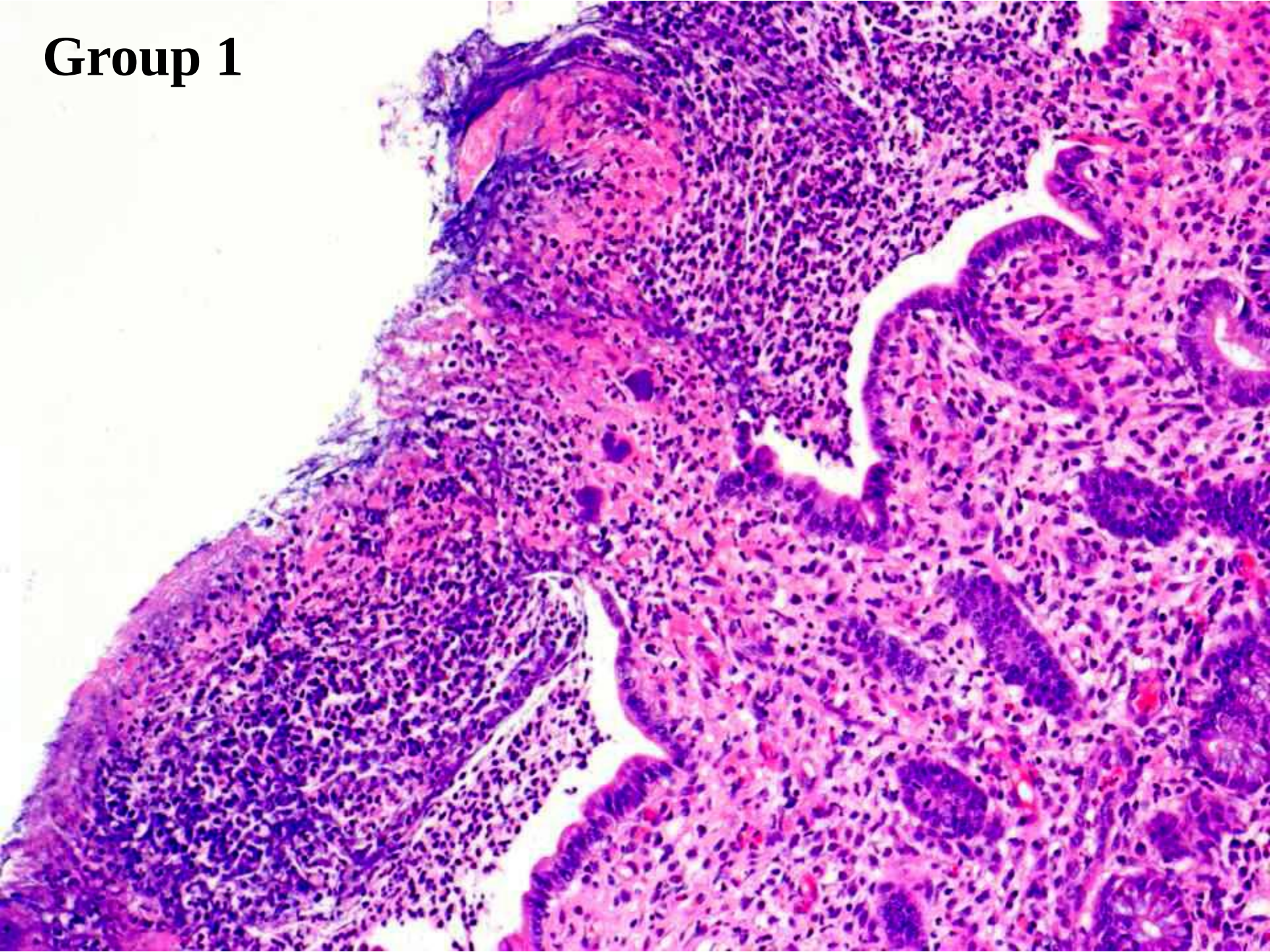
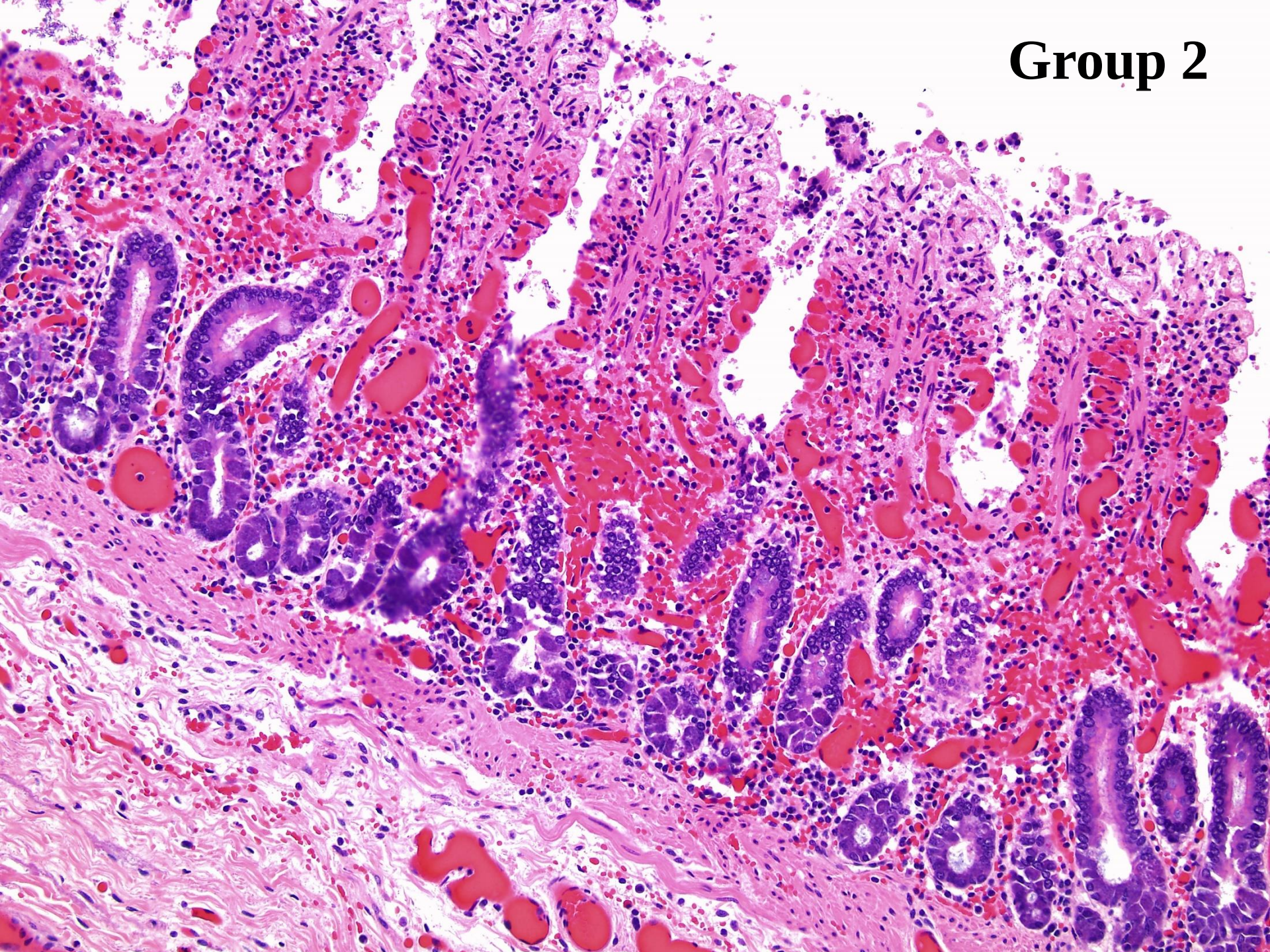

5

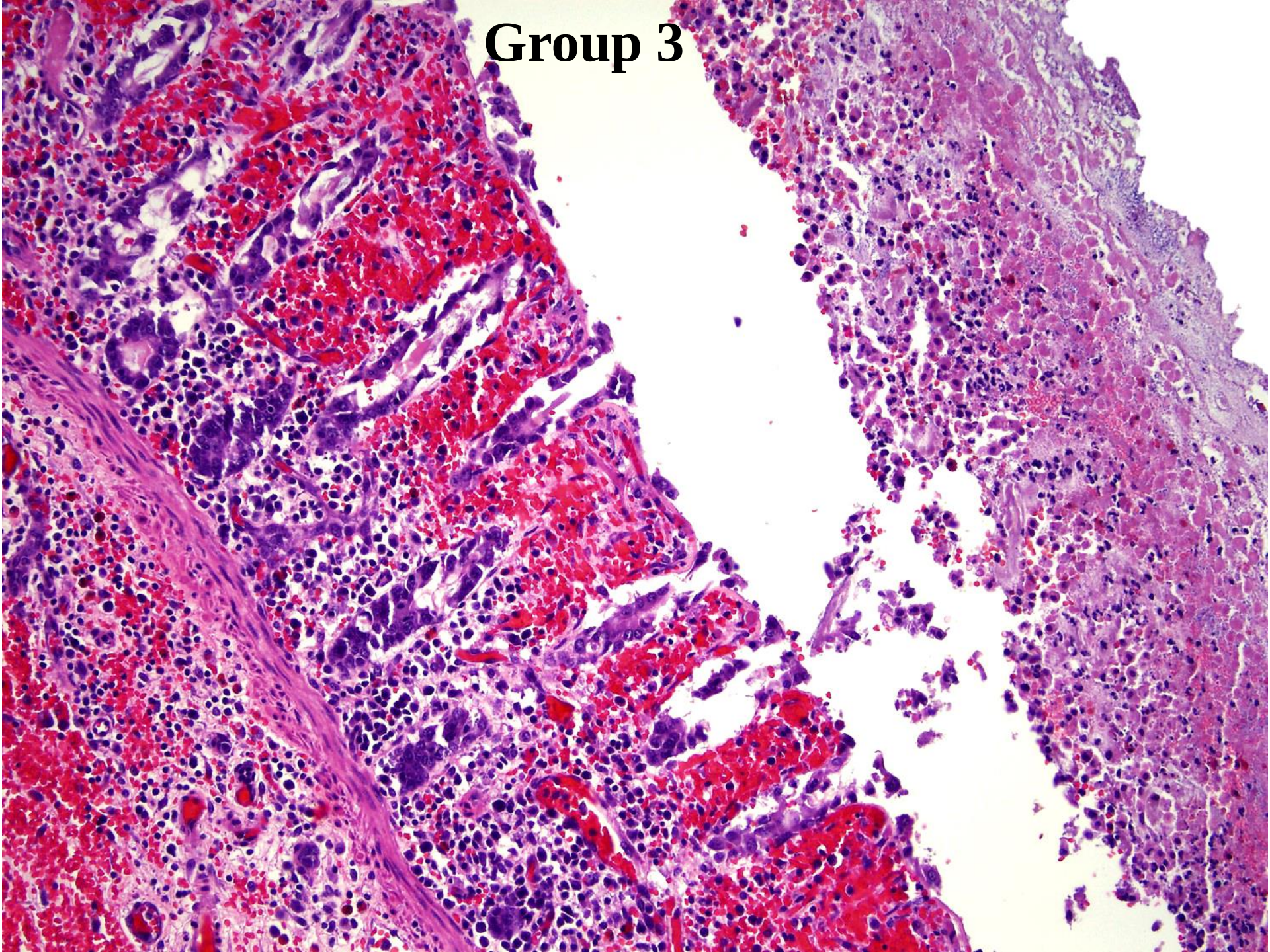
Histology

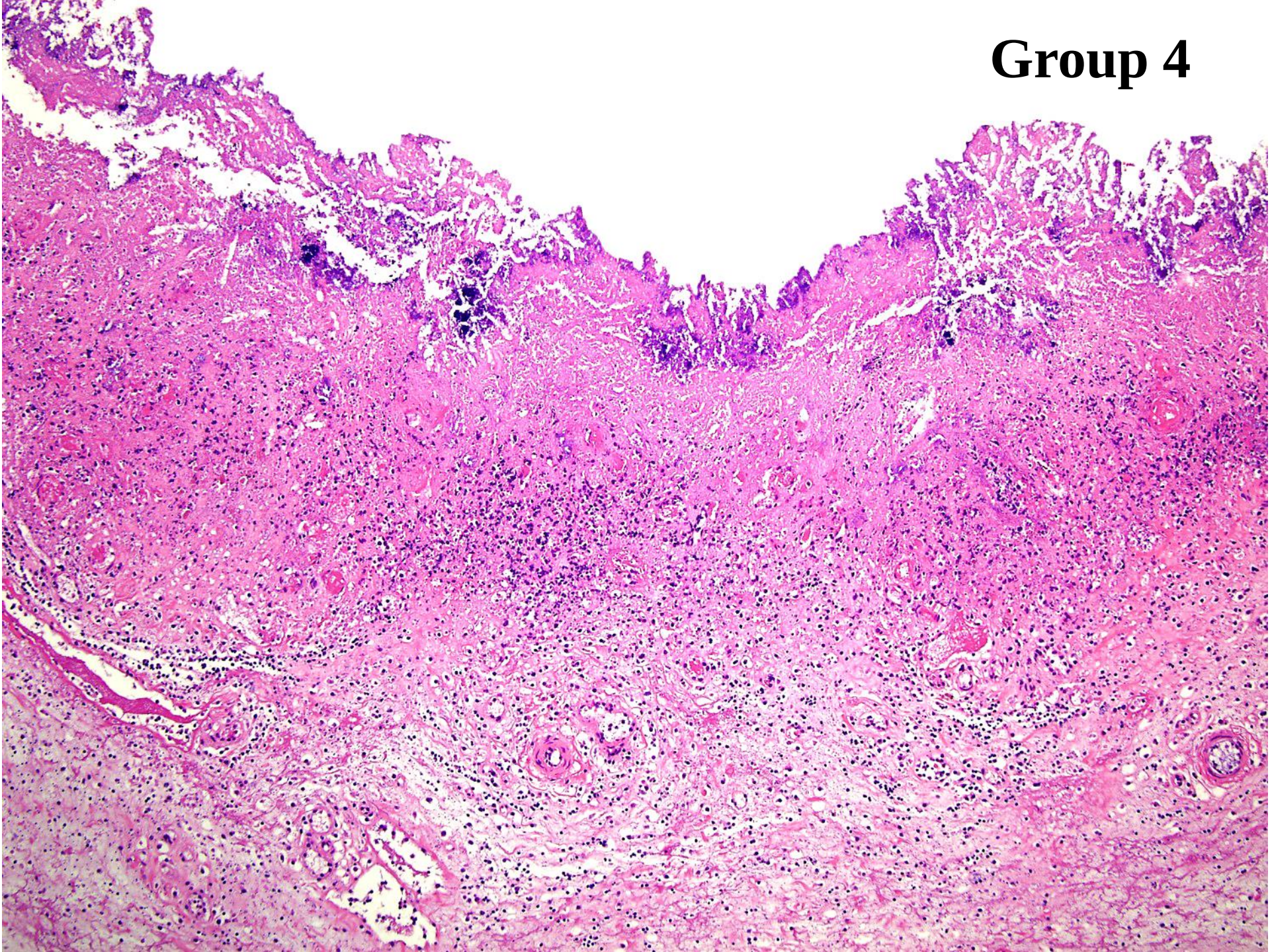
4 main groups
(~ 25% each)

Group 1




Group 2


Group 3


Group 4


Mesocolonic edema
Take-home message!!!!

Causes of mesocolonic edema in pigs:

1-*C. difficile*
2-*E. coli* (edema disease)
3-PCV-2
4-PRSS virus

CATTLE

C. difficile

potential role in neonatal calf diarrhea

C. difficile prevalence (calves):

1-Rodriguez-Palacios et al. (2006)

Culture:

*** diarrheic calves:** **7.6% (11/144)**

*** control calves:** **15% (20/134)**

Toxins:

*** diarrheic calves:** **39.6% (57/144)**

*** control calves:** **20.9% (28/134)**

C. difficile prevalence (calves):

2-Hammitt et al. (2008):

Culture

* Diarrheic: 25.3% (64/253)
* Control: 13% (7/53)

Toxin

* Diarrheic: 22.9% (58/253)
* Controls: 30.2% (16/53)

C. difficile in calves

*** Accompanying BCV, BRV, Crypto, Salmonella, AEEC, others**

*** role in diarrhea: not fully determined**

SHEEP AND GOATS

Prevalence: 0–8.5%

(Knight and Riley, 2013; Avbersˇek et al., 2015; Rodriguez et al., 2016)

No evidence of role in disease

Diagnostic criteria

1-Clinics/gross } **Suggestive**

2-Histology } **Suggestive**

3-Ancillary: Culture (+ typing) } **Suggestive ++**

4-Ancillary: Toxins A/B } **Confirmatory**

GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric	**Enterotoxemias/ enteritis**	*C. perfringens*	✓	✓
		C. difficile	✓	✓
		C. piliforme	--	✓
Histotoxic				
Neurotoxic				

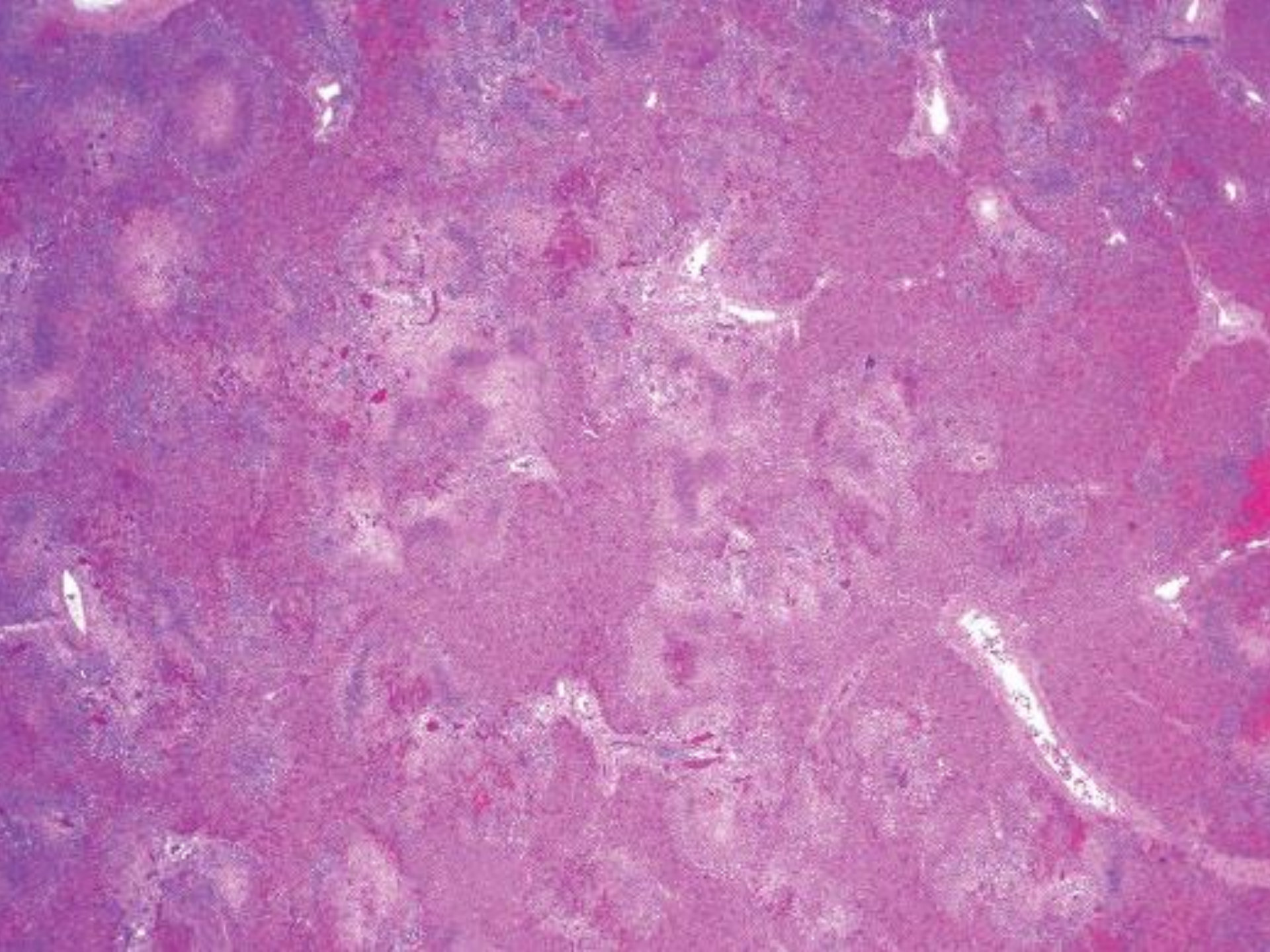
Tizzer’s disease

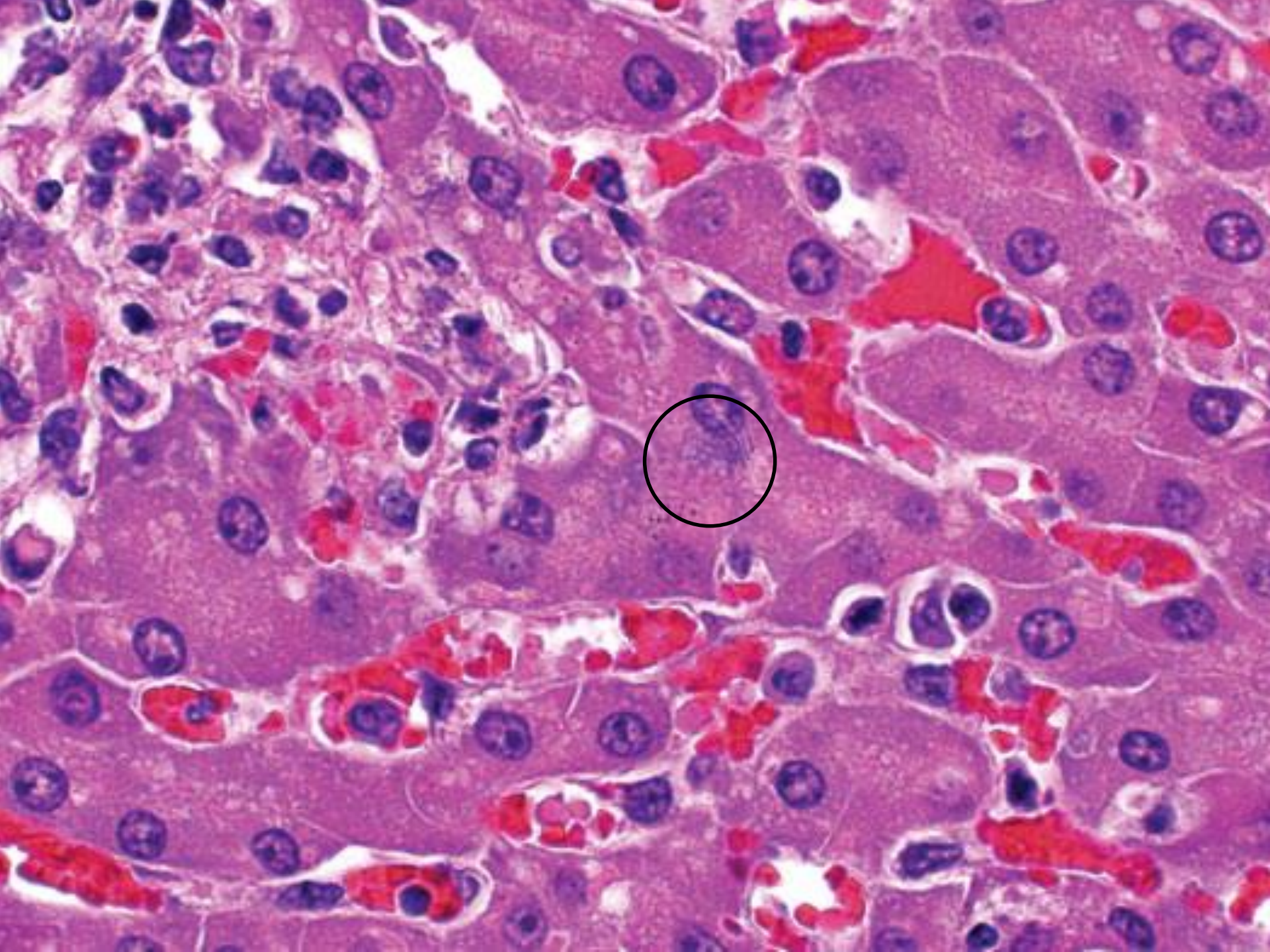
Horse
Rabbit
Rat
Hamster
Cats
Others

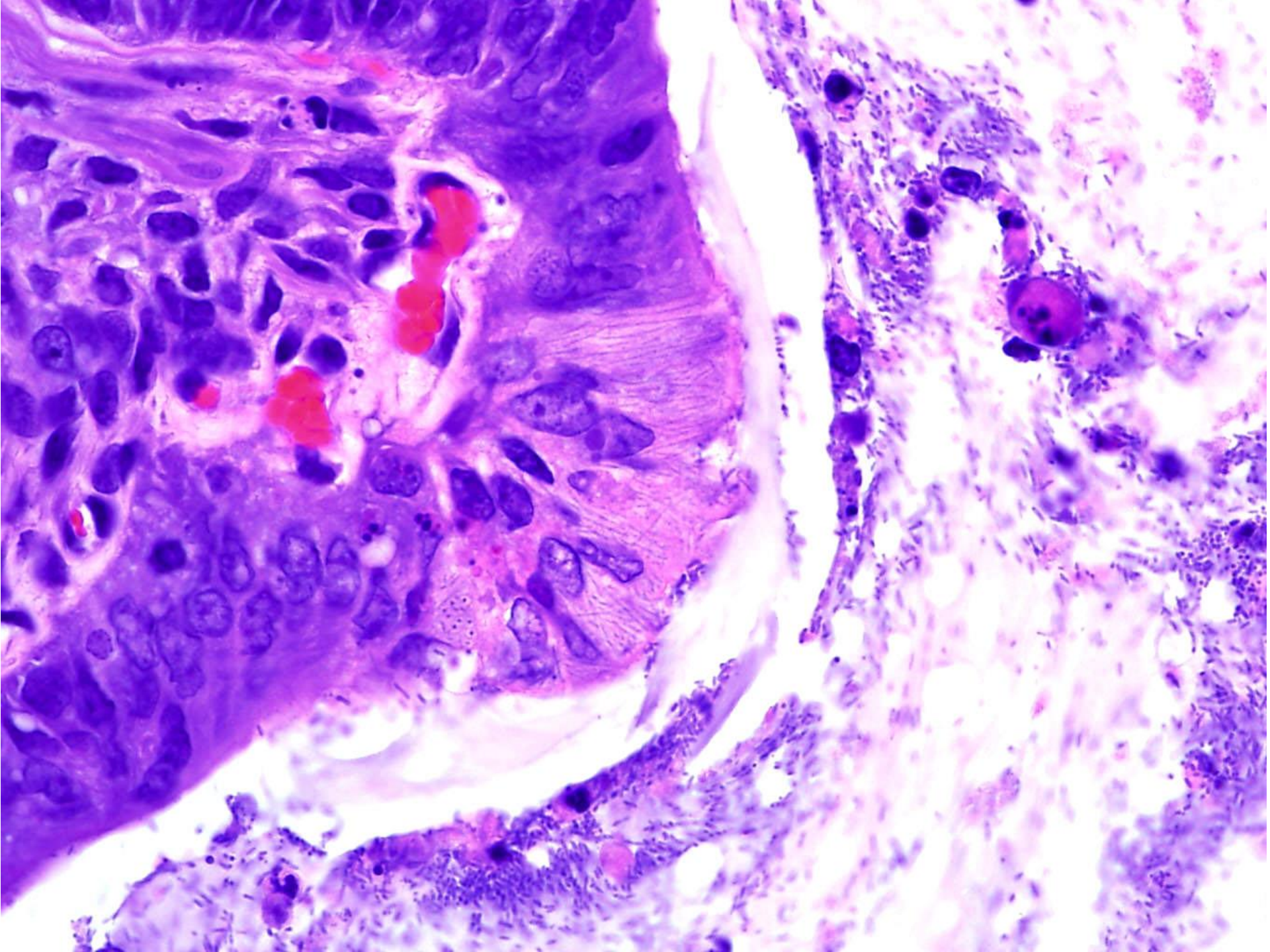
Triad of lesions

Hepatitis
Colitis
Myocarditis

Take-home message!!!







Diagnosis:

1-Histology (HE; silver; Giemsa)

2-PCR

3-Culture (embryonated egg only)

GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric	**Enterotoxemias/ enteritis**	*C. perfringens*	✓	✓
		C. difficile	✓	✓
		C. piliforme	--	✓
		C. sordellii	--	✓
Histotoxic				
Neurotoxic				

GI disease in animals:

AVIAN DISEASES 59:447–451, 2015

Case Report——

Necrotic Enteritis in Chickens Associated with *Clostridium sordellii*

Guillermo Rimoldi,[AE] Francisco Uzal,[B] R. P. Chin,[A] Enzo A. Palombo,[C] Milena Awad,[D] Dena Lyras,[D] and H. L. Shivaprasad[A]

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Received 7 April 2015; Accepted 22 April 2015; Published ahead of print 20 May 2015

AVIAN DISEASES 57:698–702, 2013

Case Report—

Ulcerative Enteritis-like Disease Associated with *Clostridium sordellii* in Quail

Rocio Crespo,[AD] Monique Franca,[B] and H. L. Shivaprasad[C]

[A]Avian Health and Food Safety Laboratory, Washington Animal Disease Diagnostic Laboratory, Washington State University, 2607 West Pioneer, Puyallup, WA 98371
[B]Poultry Diagnostic and Research Center, College of Veterinary Medicine, University of Georgia, 501 D.W. Brooks Drive, Athens, GA 30602
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Received 17 January 2013; Accepted 27 March 2013; Published ahead of print 9 April 2013

Clostridium sordellii in Lambs with Abomasal Bloat, Haemorrhage and Ulcers

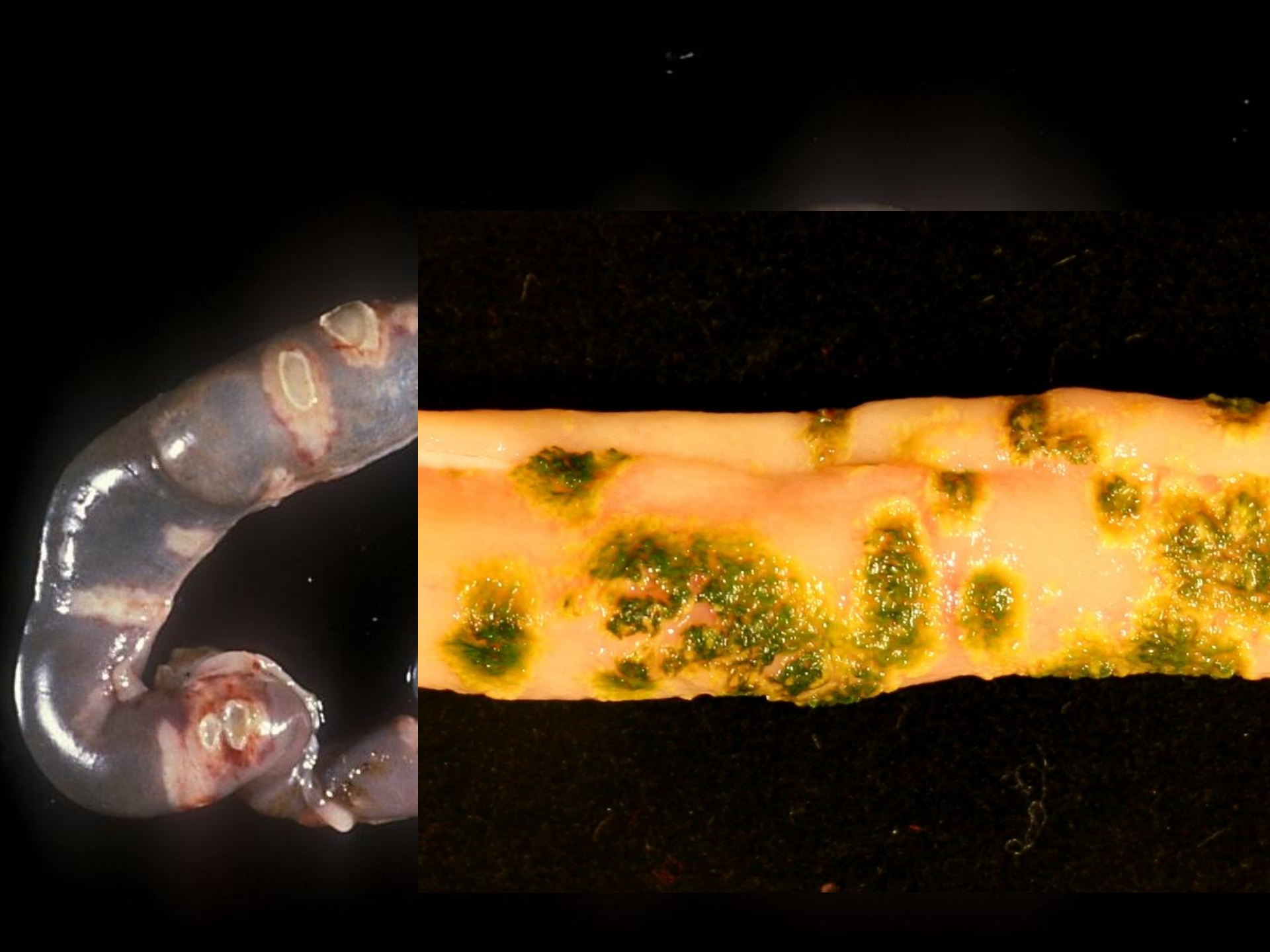
S. Vatn [a], M.A. Tranulis [a], M. Hofshagen [b]

⊞ Show more

https://doi.org/10.1053/jcpa.1999.0363

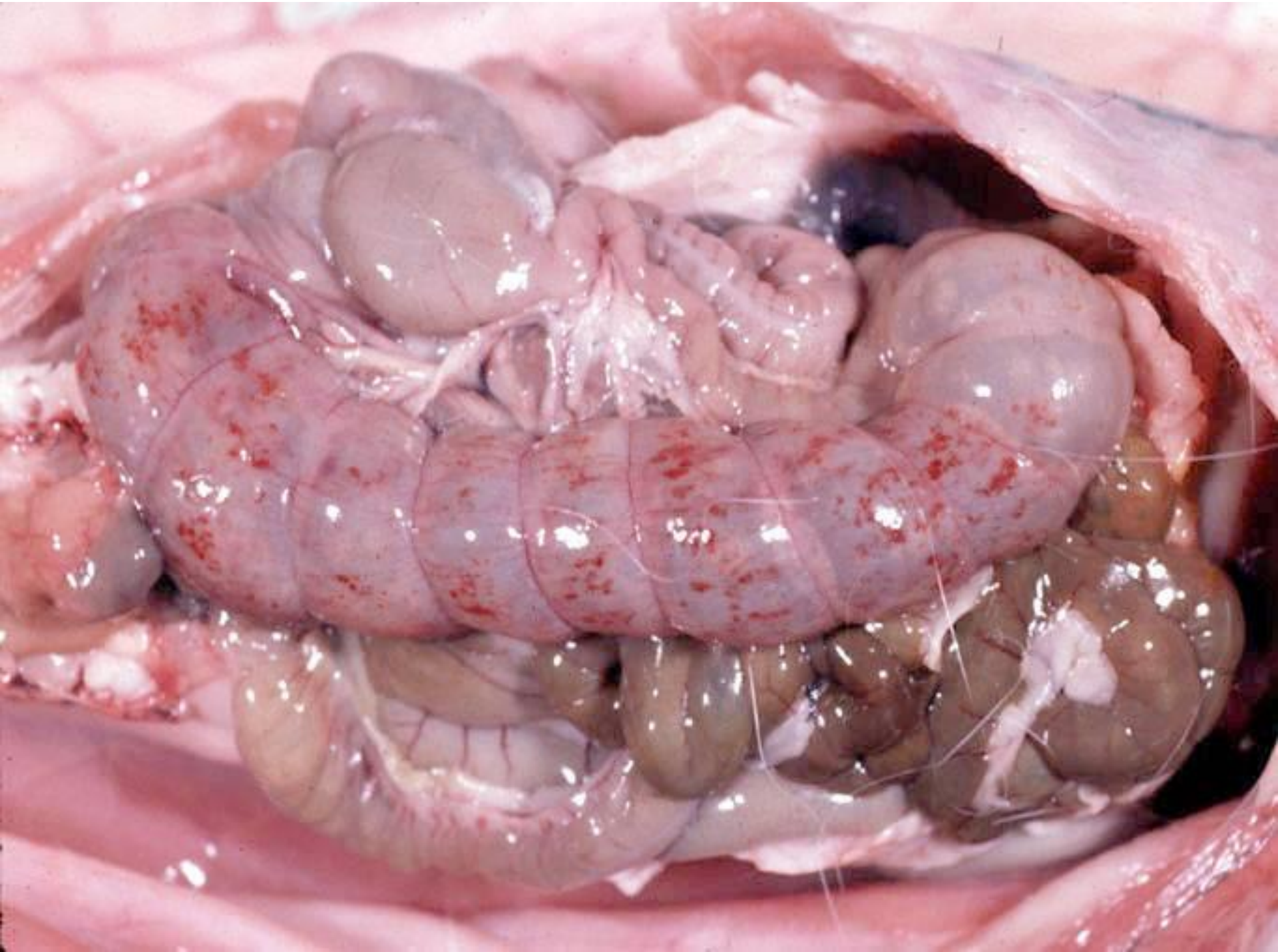
GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric	**Enterotoxemias/ enteritis**	*C. perfringens*	✓	✓
		C. difficile	✓	✓
		C. piliforme	--	✓
		C. sordellii	--	✓
		C. colinum	--	✓
Histotoxic				
Neurotoxic				

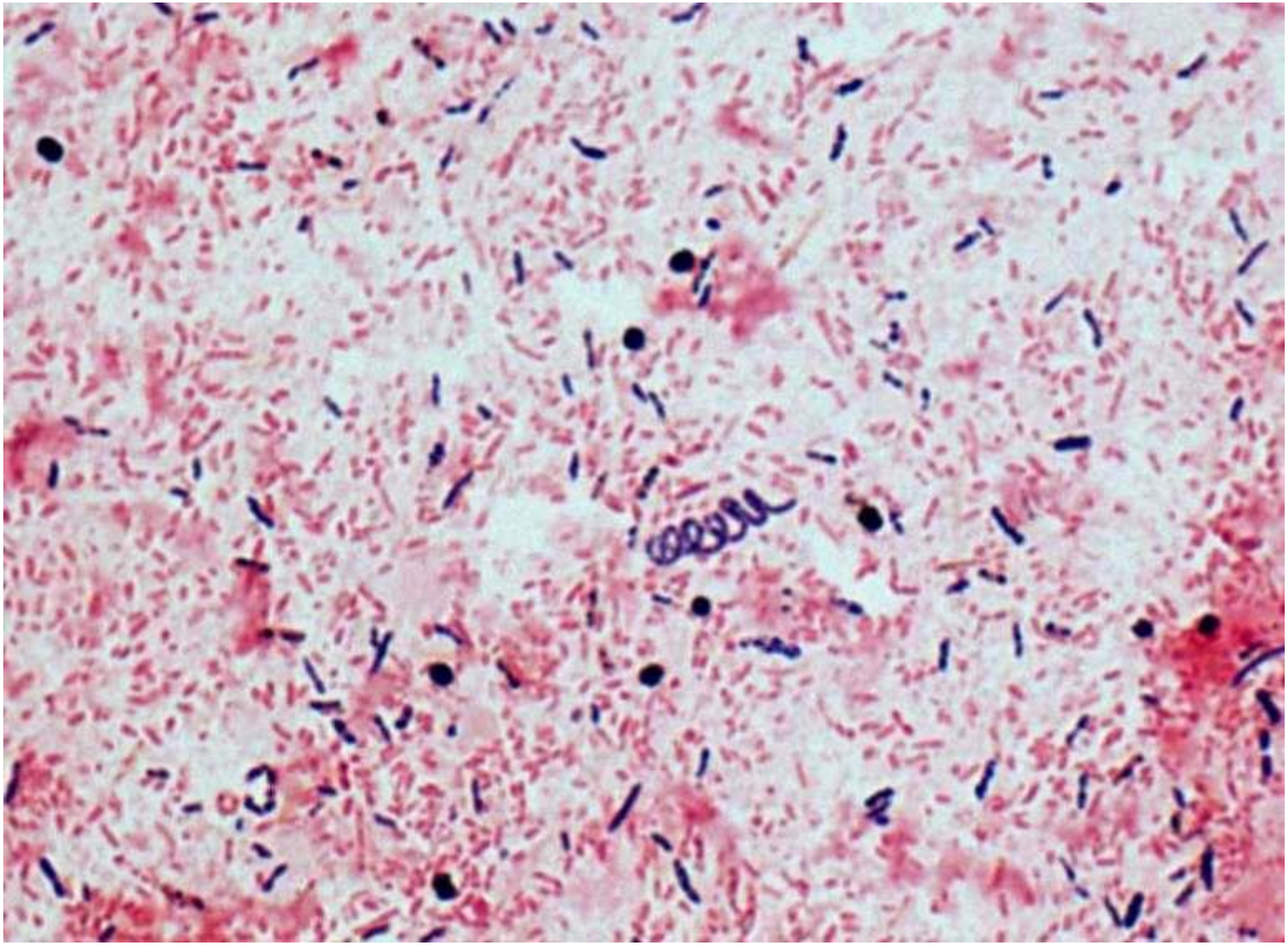
“Quail disease”



GROUP	DISEASE	ORGANISM	HUMANS	OTHER ANIMALS
Enteric	**Enterotoxemias/ enteritis**	*C. perfringens*	✓	✓
		C. difficile	✓	✓
		C. piliforme	--	✓
		C. sordellii	--	✓
		C. colinum	--	✓
		C. spiroforme	--	✓
Histotoxic				
Neurotoxic				

“Rabbit enterotoxemia”





Thank you!!!

Diseases that look clostridial

Undetermined etiology

Jejunal hematoma

Adult dairy cows


Photo Rob Moeller