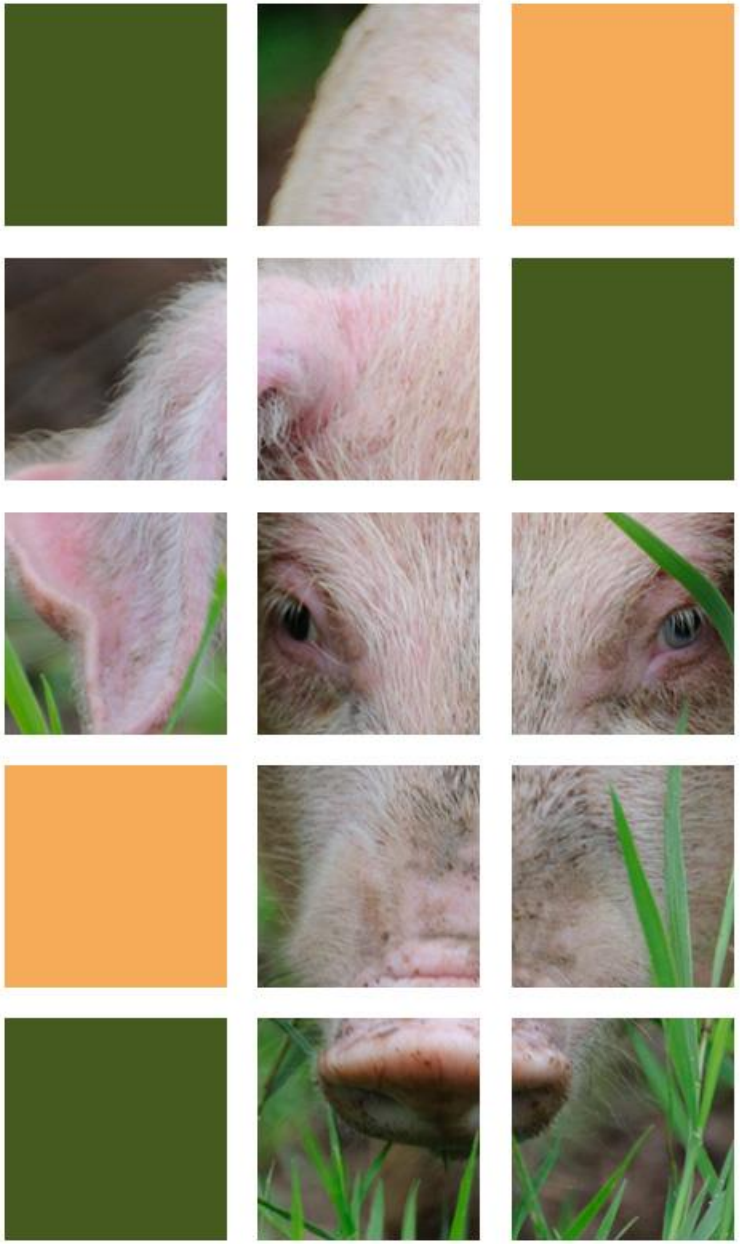

Herd diagnosis devil's advocate: what do you have, what do you think you have and what do you not have!

Joaquim Segalés

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IRTA

“A diagnosis is a matter of facts; it is not a matter of opinion”

Steve Henry, AASV 2003

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“For each mistake we make by not knowing, we will make ten mistakes by not looking”

Steve Henry, AASV 2003

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Diagnosis

Identification of the nature of anything, either by analytical methods or processes of elimination

In (veterinary) medicine, diagnosis includes to determine the causes of symptoms, mitigations for problems, or solutions to medical issues

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Essential components of the diagnostic procedure

Clinical investigation ("the visit" – but much more…) – INDUCTIVE STAGE:

- **Anamnesis – clinical history**
- **Clinical signs**
- **Epidemiology**
- **Gross pathology**
- **So far implemented actions**

"What, Who has what, Where, When, Since when, How many and How"

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Essential components of the diagnostic procedure

"What, Who has what, Where, When, Since when, How many and How"

From perceptions, impressions, subjective conclusions… to facts!!

Relevant vs. irrelevant/confusing

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With this first stage we must establish:

WHAT DO WE THINK WE HAVE

Which might be your degree of certainty?

Essential components of the diagnostic procedure (cont.)

Clinical investigation ("the visit" – but much more…) – DEDUCTIVE STAGE:

- Scientific-technical knowledge
  - Veterinary degree
  - Post-graduate training
  - Continuous education
  - Scientific-technical literature:
    - Peer-reviewed articles
    - Conference abstracts
    - Non-peer reviewed articles

- Experience
- Logic sense

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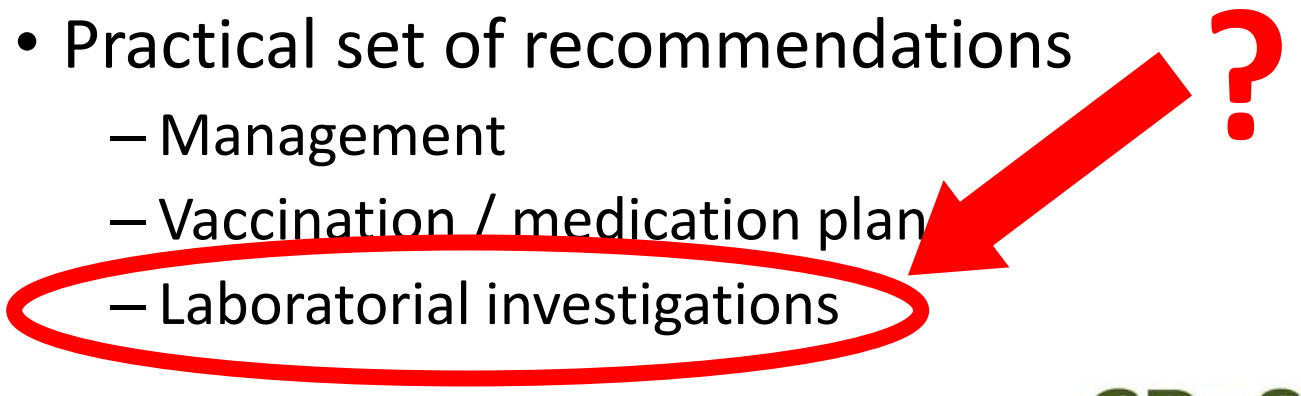
Essential components of the diagnostic procedure (cont.)

Clinical investigation ("the visit" – but much more…) should end with the:

- CLINICAL INVESTIGATION REPORT
  - Facts
  - Methodology used
  - Pedagogical material (for producers, technicians)
  - Practical set of recommendations
    - Management
    - Vaccination / medication plan
    - Laboratorial investigations



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The myth…
Diagnoses vs. Analyses

“Field veterinarians rely their diagnosis mainly (or sometimes almost exclusively) on the results obtained after analysis given by a Veterinary Diagnostic Laboratory”

Guy P. Martineau, 2005

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The truth…
Diagnoses vs. Analyses

"Even diagnostic laboratories can help identifying agents potentially involved in a environmental factors must be determined by the submitting veterinarian"

The pig veterinarian working under field conditions represents, in essence, a diagnostician!!

Gardner and Blanchard, 2006

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A criticism: are we, pig veterinarians, too sharply "microbiologistics"?

Pig medicine → **Population diagnostic approach**

↳ **Infectious/contagious diseases are perceived as the most important ones**

↳ **Usual first question in front of a given disease problem is: "Which is the causal pathogen?"**

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Issues to take into account…

Pathogen participation is very frequently present in disease problems, but…

…a number of times the infectious agent reflects an added factor to a non-infectious primary cause or triggering factor

- **To counteract such non-infectious primary cause or triggering event may represent the solution of the disease scenario**
- **The specific control of the found pathogen might represent only a temporary solution**

In such scenario, which would be the "key" question?

What do I want to know?

Is the agent present?

Is the agent present and causing problems?

Is the agent really absent?

Is it the only agent present?

Which other agents are present?

Which is the most important agent in regards the clinical problem?

Combination of above?

Other?

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The “key” question

DO NOT ASK TO THE LABORATORY WHATEVER THAT CANNOT BE ANSWERED!!! – Big source of confusion, frustration and loss of money/confidence/ productivity

Do not ask for a test that you know in advance you will not be able to interpret adequately

- Serology to PCV2 for diagnosing PCV2-SD
- Serology to a certain infectious agent of a single pig
- PCR of a single pig
- Others…

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The “key” question

ARE YOU SURE THAT YOU NEED LABORATORY ANALYSES IN ORDER TO ANSWER PROPERLY YOUR “KEY” QUESTION?

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“The diagnostic chain”

Pathological situation suspicion (⇒farmer)

Visual confirmation of the suspicion in farm (⇒ veterinarian)

On-farm veterinarian actions ⇒diagnostic approach!!:

- Available diagnostic tools:
  - Clinical history / previous farm knowledge
  - Clinical signs and epidemiology (⇒CLINICAL DIAGNOSIS)
  - NECROPSIES (⇒PATHOLOGICAL DIAGNOSIS)

Establishment of the treatment we **believe/feel** it will work (“TO-DO-SOMETHING STRATEGY!!!”)

If the situation is complex enough and the veterinarian **believe/feel** that more analyses are needed, then, to take samples and send them to the corresponding laboratory is needed

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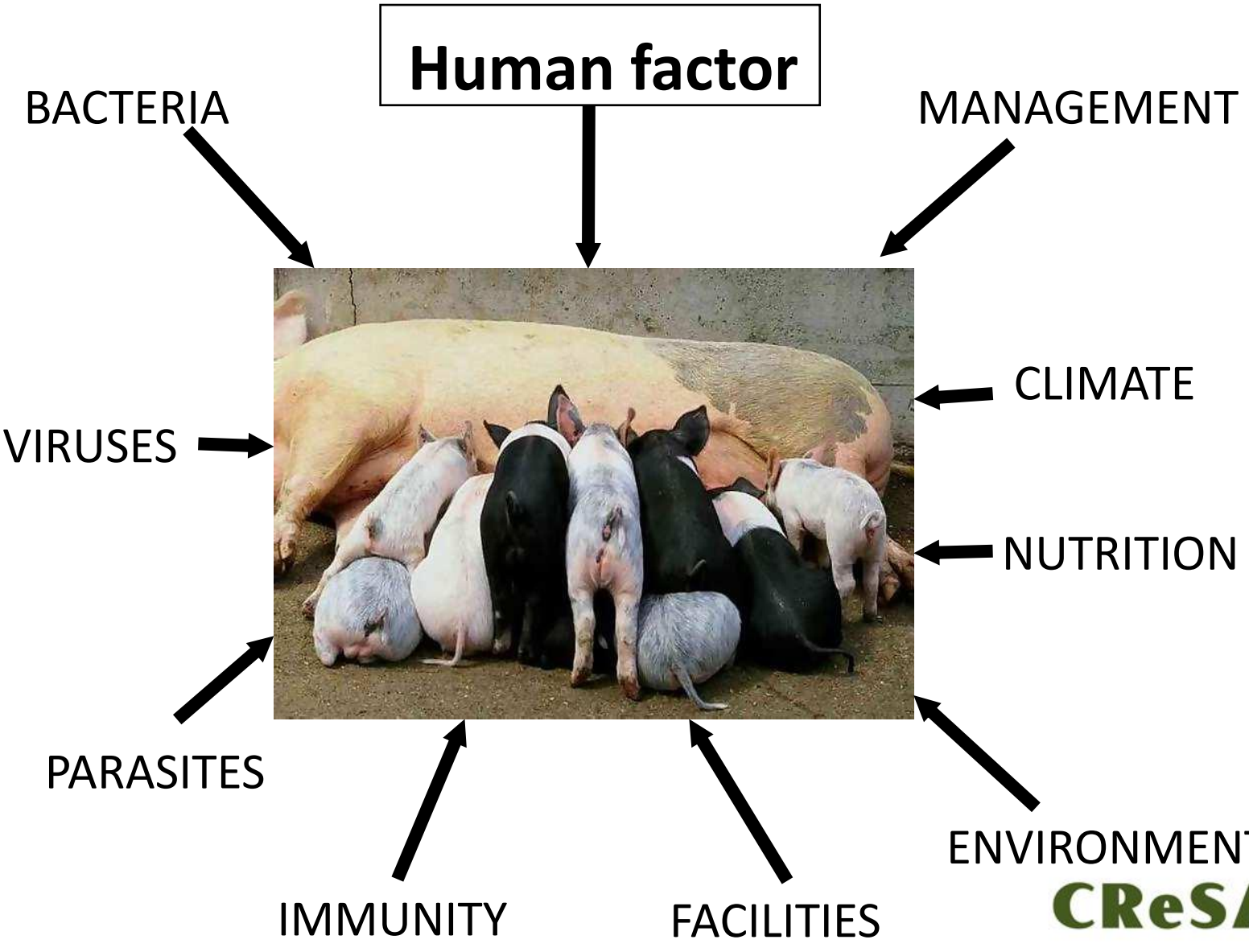
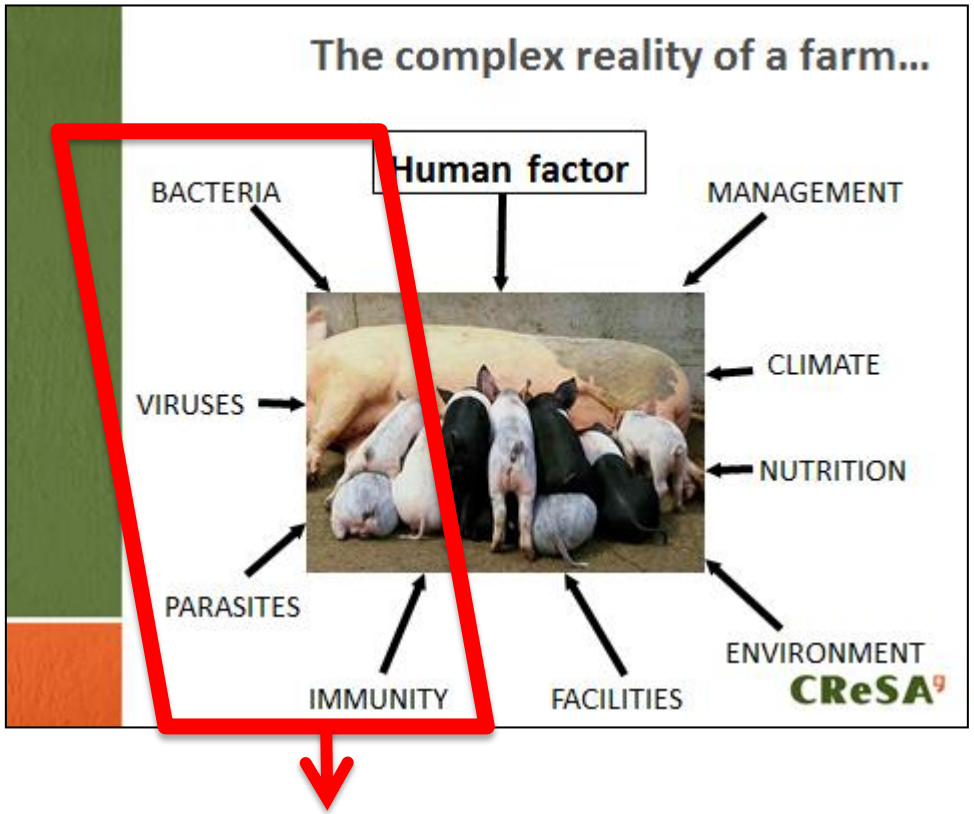
The complex reality of a farm…



The herd diagnosis…

Find out the maximum from all these issues that affect the fine balance of a well-performing farm



UNBALANCE OF THE SYSTEM

=

DISEASE OR POOR PRODUCTION PROBLEM

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The usual usefulness of laboratory tests

- Detect pathogens or toxins that are responsible (or not) for disease outbreaks or suboptimal production
- Evaluate the infection/exposure status of individual pigs
- Determine if a herd was infected with or exposed to a pathogen and, if so, which age or production groups were affected
- Estimate the percentage of herd or pigs with antibodies to an infectious agent
- Monitor a herd's serological response to vaccination
- Monitor the progress and success of disease control or eradication programs

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Do you really know how to properly interpret laboratory analyses?

And, more importantly, do you know what to ask for to laboratories?

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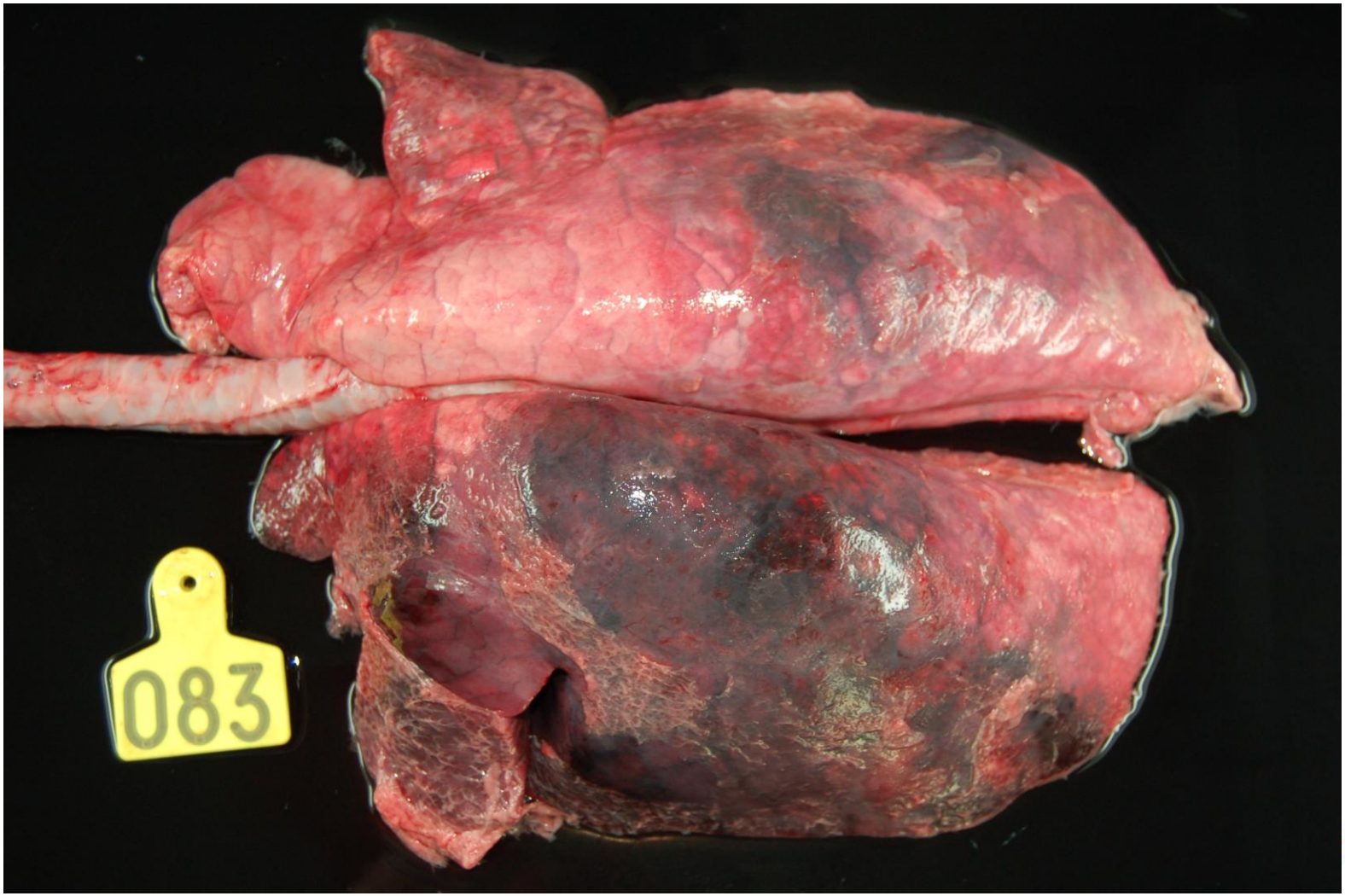
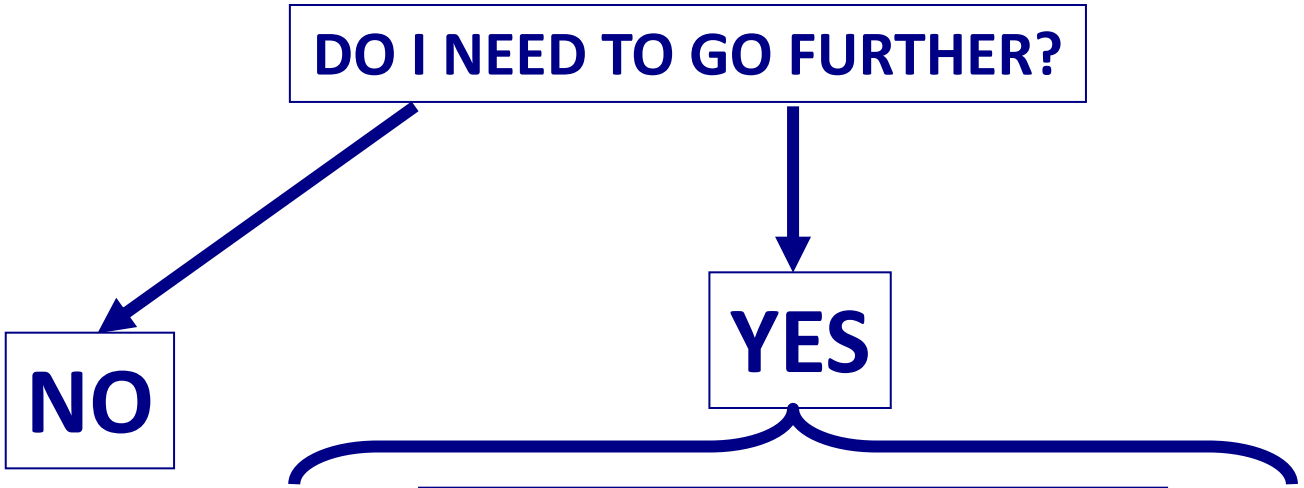
The real world… some examples

- *Actinobacillus pleuropneumoniae*:



The real world… some examples



► Bacterial isolation and antibiogram

I want to confirm the presence of the bacteria and know how it circulates

► Antibody profile - seroconversion

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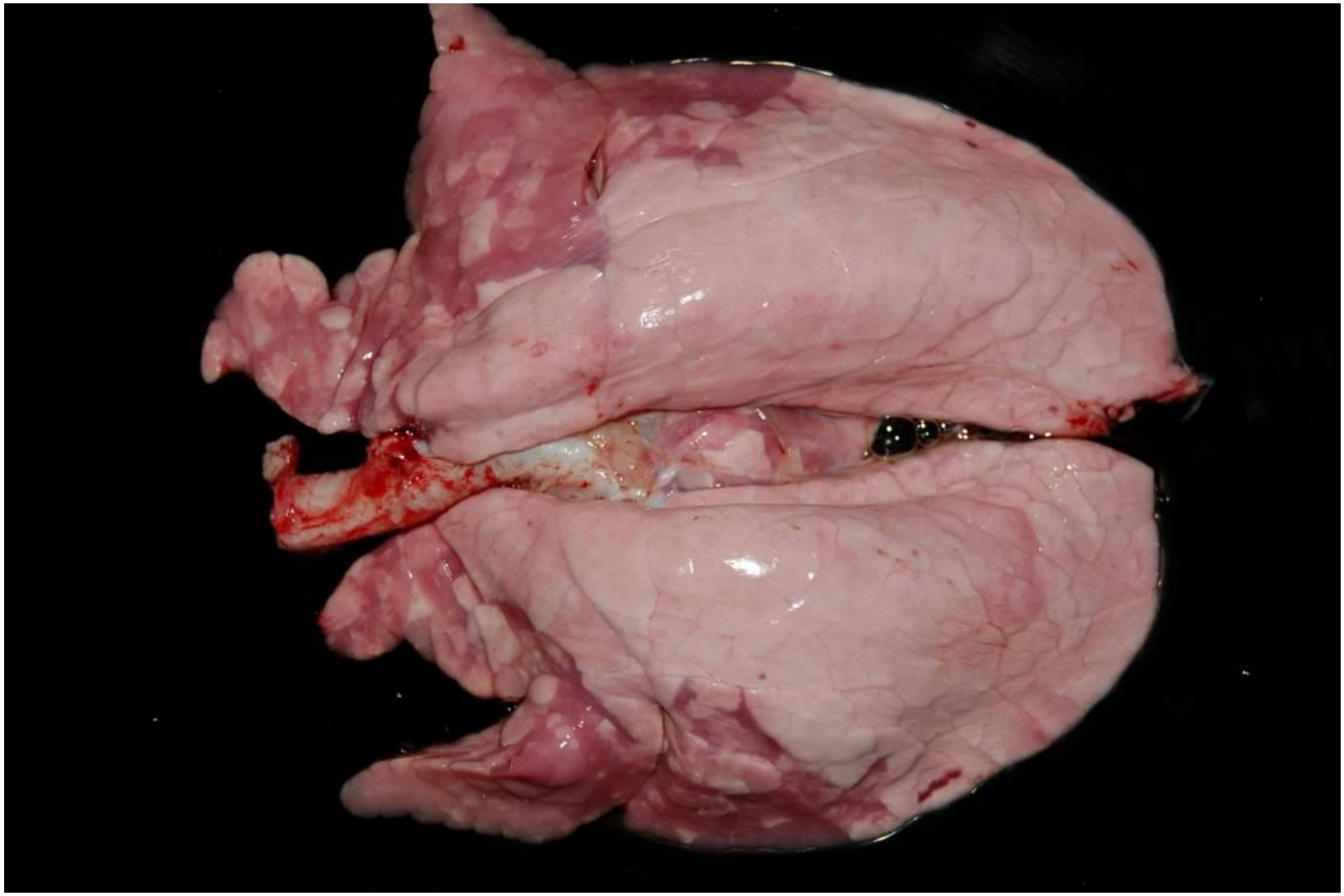
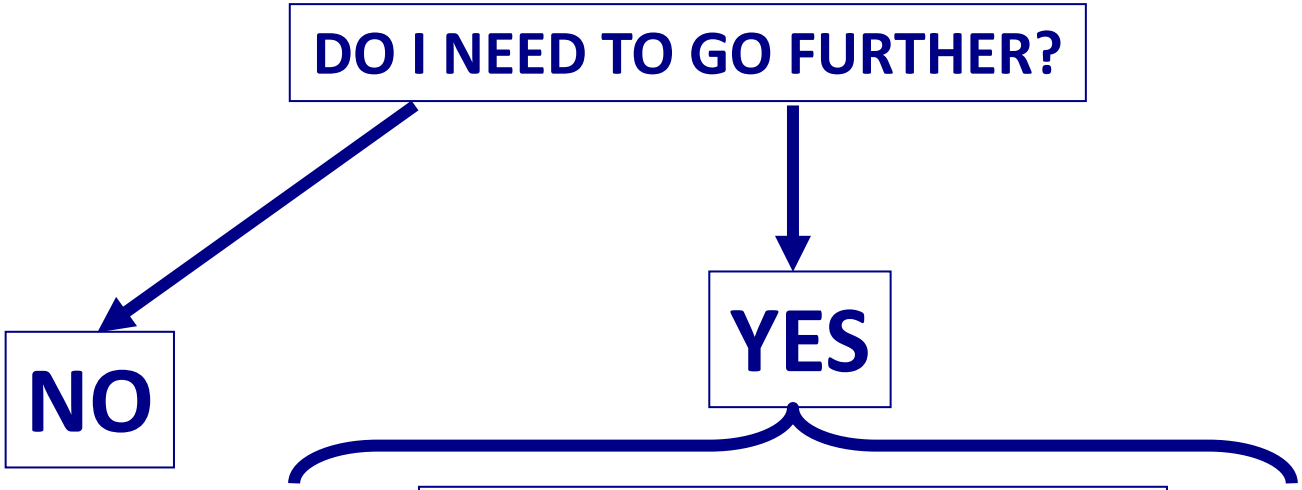
The real world… some examples

- *Mycoplasma hyopneumoniae*:



The real world… some examples



ARE YOU SURE???

► PCR, IF, IHC,…

► Antibody/PCR profiles - seroconversion

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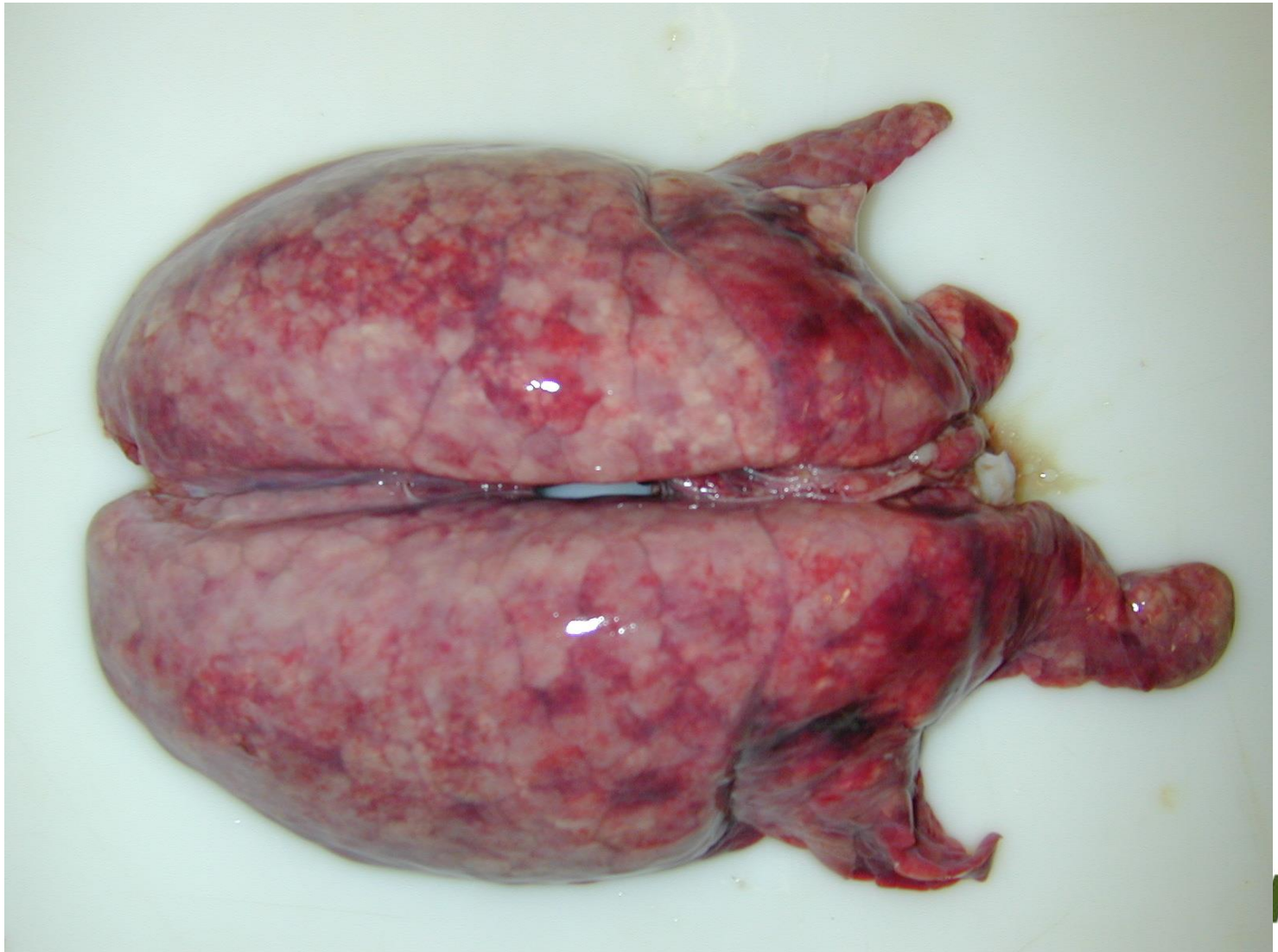
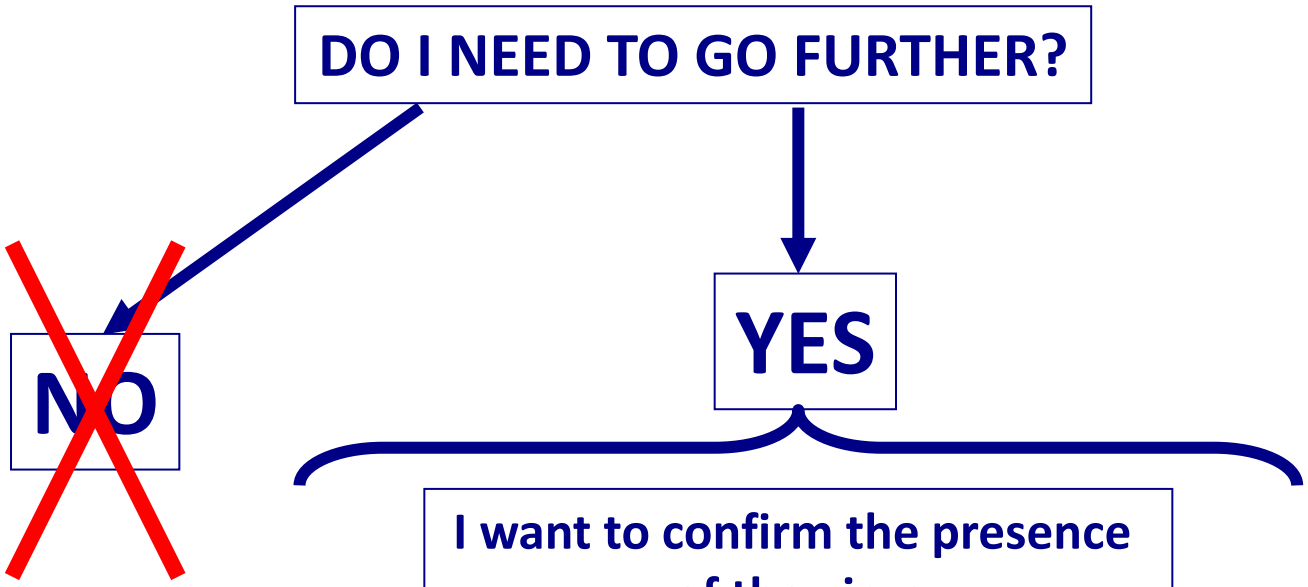
The real world… some examples

- PRRS virus:



The real world… some examples



- RT-PCR, IF, IHC, VI,…
- Antibody profile - seroconversion

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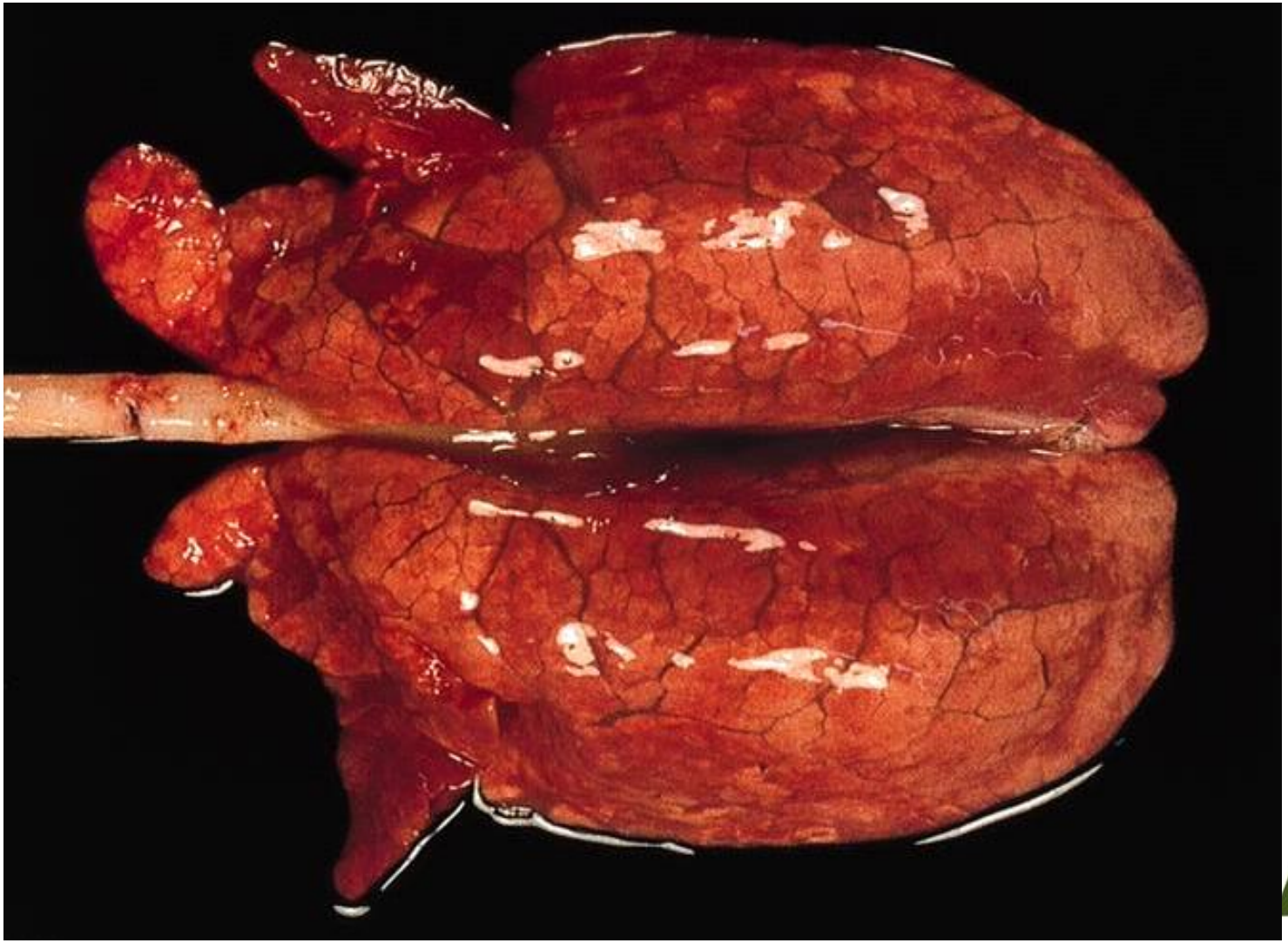
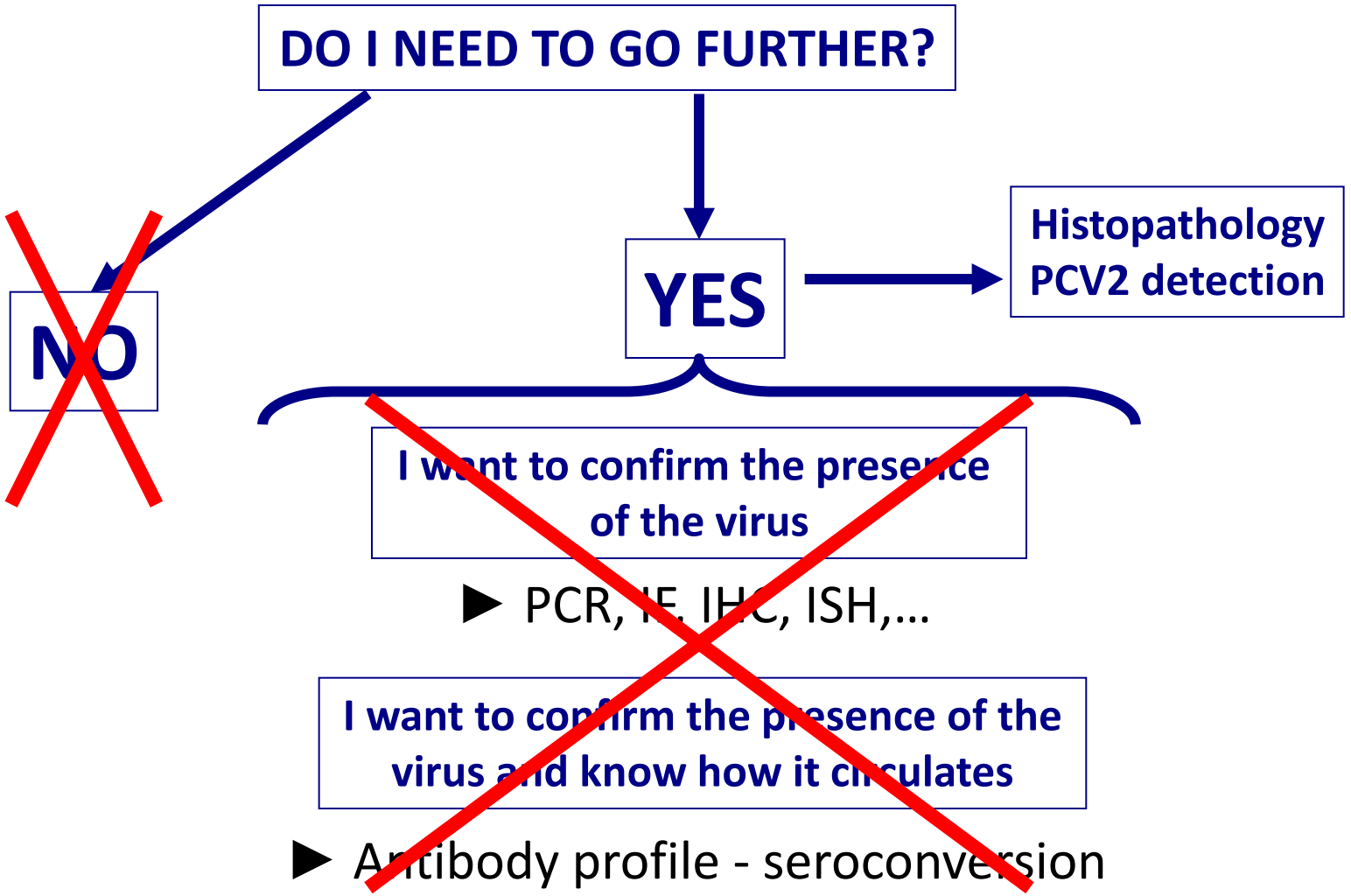
The real world… some examples

- PCV2-SD – porcine circovirus type 2



The real world… some examples



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Reliability of the laboratorial result

Own features of the analytical test:

- Sensitivity, Specificity, Repeatibility, Accuracy, etc.

Tested sample/s:

- Selection criteria of the pig/s sampled
  - Single pig (at necropsy)
  - Pig population (serum, faeces, nasal swabs,…)
- Representativity of the farm problem
- Disease evolution vs. Sampling timing
- Quality of the sample (autolysis, haemolysis,…)
- Proper submission of samples to the laboratory

DEPENDS ON THE SUBMITTING VETERINARIAN

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But real life is much more complicate that just few examples on non-contextualised necropsy findings…

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Diagnostic approaches are as variable as problems in farms and as variable as veterinarians… let's see an example

CLINICAL CASE

LONG ONE

SHORT ONE

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General characteristics of the farm

- 320-sow, farrow-to-finish operation located in North-eastern Spain (Farm A)
- All in-all out management
- Weaning at 22-24 days of age
- Facilities constructed in 1975, subsequent re-modelations
- 2 workers (no work division)
- Feeding produced in the farm

Sanitary status

- Aujeszky's disease virus (ADV)
  - 3 times/year in sows and boar
  - once in fattening pigs at 10 weeks of age
- Porcine parvovirus (PPV) and erysipelas: combined vaccine used at 10-15 days post-partum
- Seropositive sows against Mhyo, porcine reproductive and respiratory syndrome virus (PRRSV) and ADV gE
- No current knowledge on the serological status of nursery/fattening pigs

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Fattening units

- Capacity to grow around 50% of the produced pigs
- Rest of the pigs are sold to another farm (Farm B) – one single source, fattening unit, in continuous flow

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First notice of the problem

- Farm A owner phones the vet
- 6 to 8 week-old pigs with severe respiratory problems – dyspnea, thumping, but no cough or associated mortality
- Morbidity: 20-25%
- Severe complains from the owner of farm B: severe respiratory problems (Mb 30-35%) with associated mortality (sudden)
- Both cases: several antibiotics were used (amoxicilin, self-made antibiotic mixture) – no proper work

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Vet's mind in front of the phone call…

1. It is a viral problem
2. It is a viral problem mixed with bacterial infections
3. It is a management and bad medication problem
4. Where did I leave the "Diseases of swine" book?

First visit at farm A (day 0)

- Late nursery pigs with fever, dyspnea, thumping, and stacking
- Few pigs with nervous clinical signs and arthritis
- High density of pigs per pen (<0.15 m^2/pig)
- One pig is necropsied by the veterinary practitioner: fibrinous polyserositis and arthritis
- No problems in breeding stock, farrowing or fattening pigs

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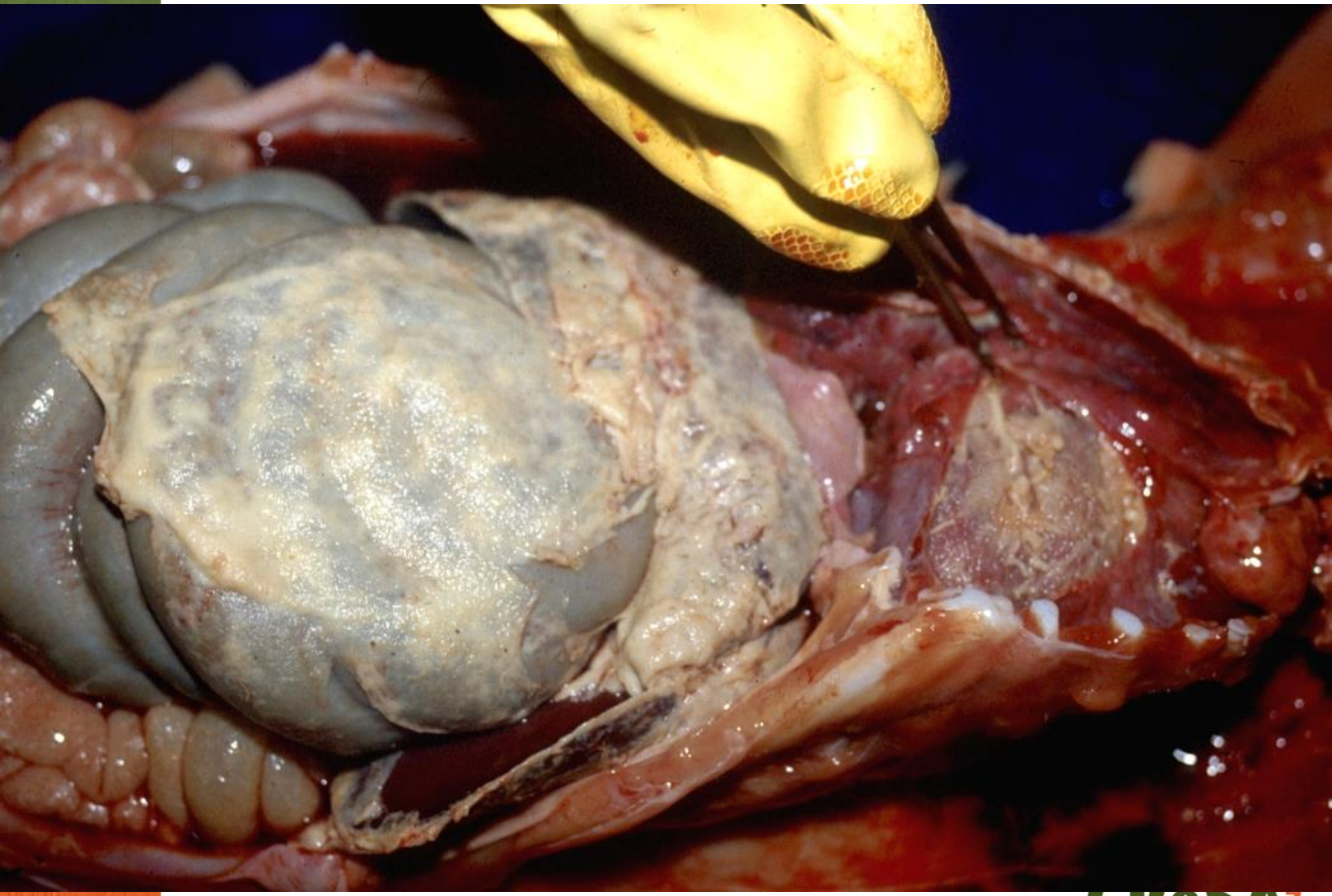

What's your etiological pressumptive diagnosis?

1. *Haemophilus parasuis* infection
2. *Streptococcus suis* infection
3. Bacterial septicaemia
4. All previous answers are correct

First approach

- Pressumptive clinical diagnosis: ***Haemophilus parasuis*** infection
- Measures:
  - 300-400 ppm of amoxicilin in feed
  - Injected amoxicilin in clinically affected pigs
  - Aspirin in water

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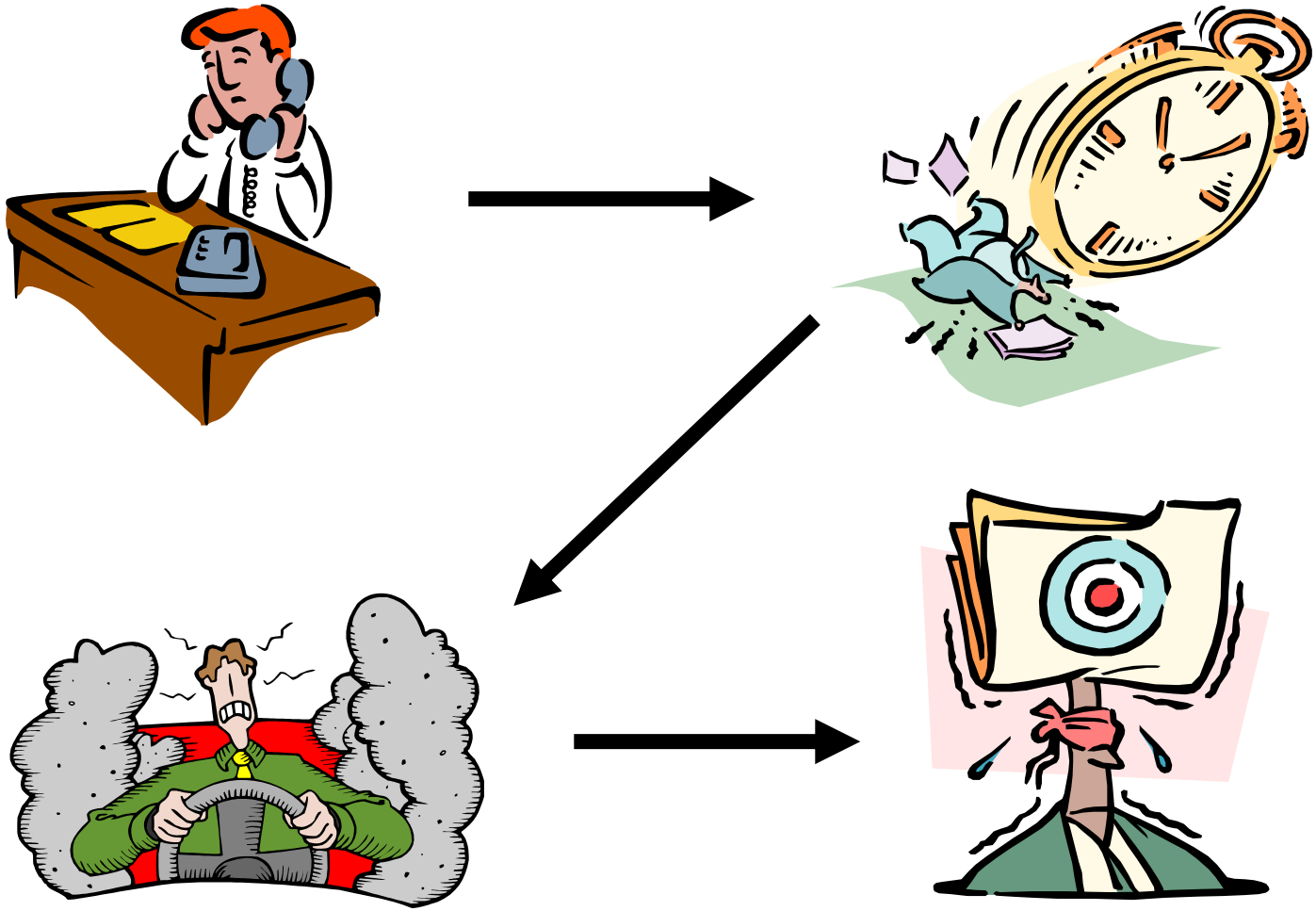
All that glitters is not gold!!

Just one pig was necropsied !!!

Day 7



Second visit at farm A and first visit at farm B (day 7)

Farm A (6-10 wk-old pigs):

- Same problems of the previous week, but 30-40% morbidity
- Now with mortality (>5% in two days)

Farm B (10-13 wk-old pigs):

- 50% morbidity
- 25% mortality in the oldest pigs
- Necropsy of one pig: fibrino-necrotizing pleuropneumonia

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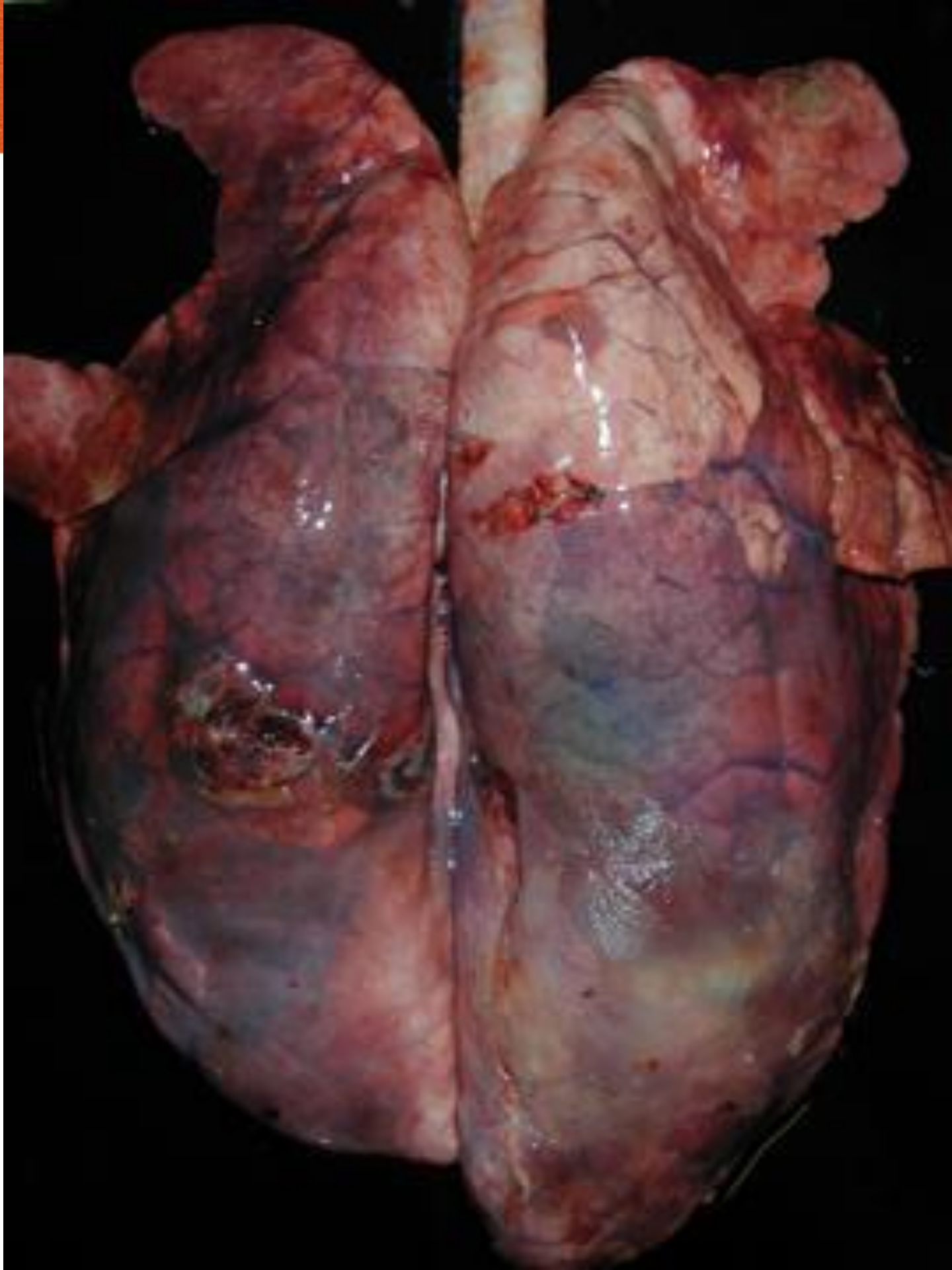
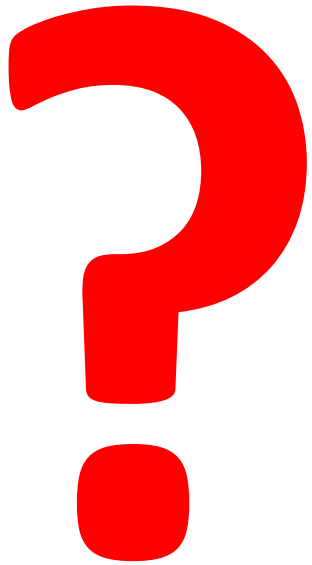


Second approach

- Pressumptive clinical diagnosis: ***Actinobacillus pleuropneumoniae*** infection
- Measures (added):
  - Tilmicosin in feed (farms A and B)

What should you do to establish the global diagnosis?



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What they did…

To send 7 affected 2-month-old pigs from farm A to a diagnostic laboratory:

- Necropsy
- Histopathology
- Bacteriology
- Virology

Gross lesions

	PIG No.						
LESION	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Tip ear necrosis	+	-	-	-	-	+	-
Palpebral edema	-	+	-	+	-/+	+	-/+
Lymphadenopathy	-	+	-	+	-	-	+
Non-collapsed lungs	+	-	+	+	-	+	+
Pulmonary consolidation	+	+	+	+	-	-	-
Myocardial hemorrhages	-	-	-	-	+	-	-
Hidrotorax	-	-	-	-	+	-	-
Fibrinous polyserositis	-	-	+	-	-	-	-
Gastric wall edema	+	+	-	-	-	+	-
Fibrinous ileitis	+	-	-	-	-	-	-

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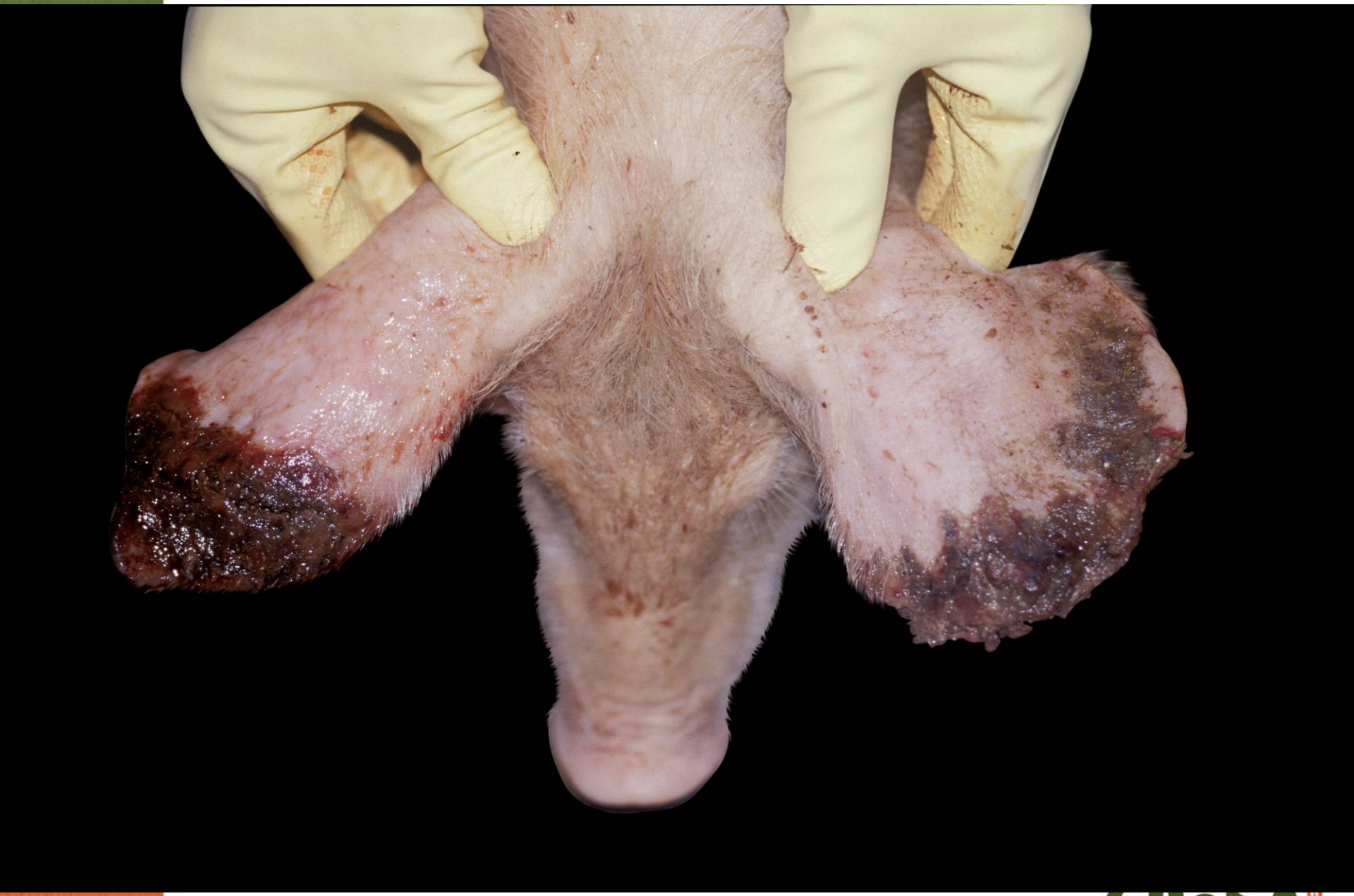

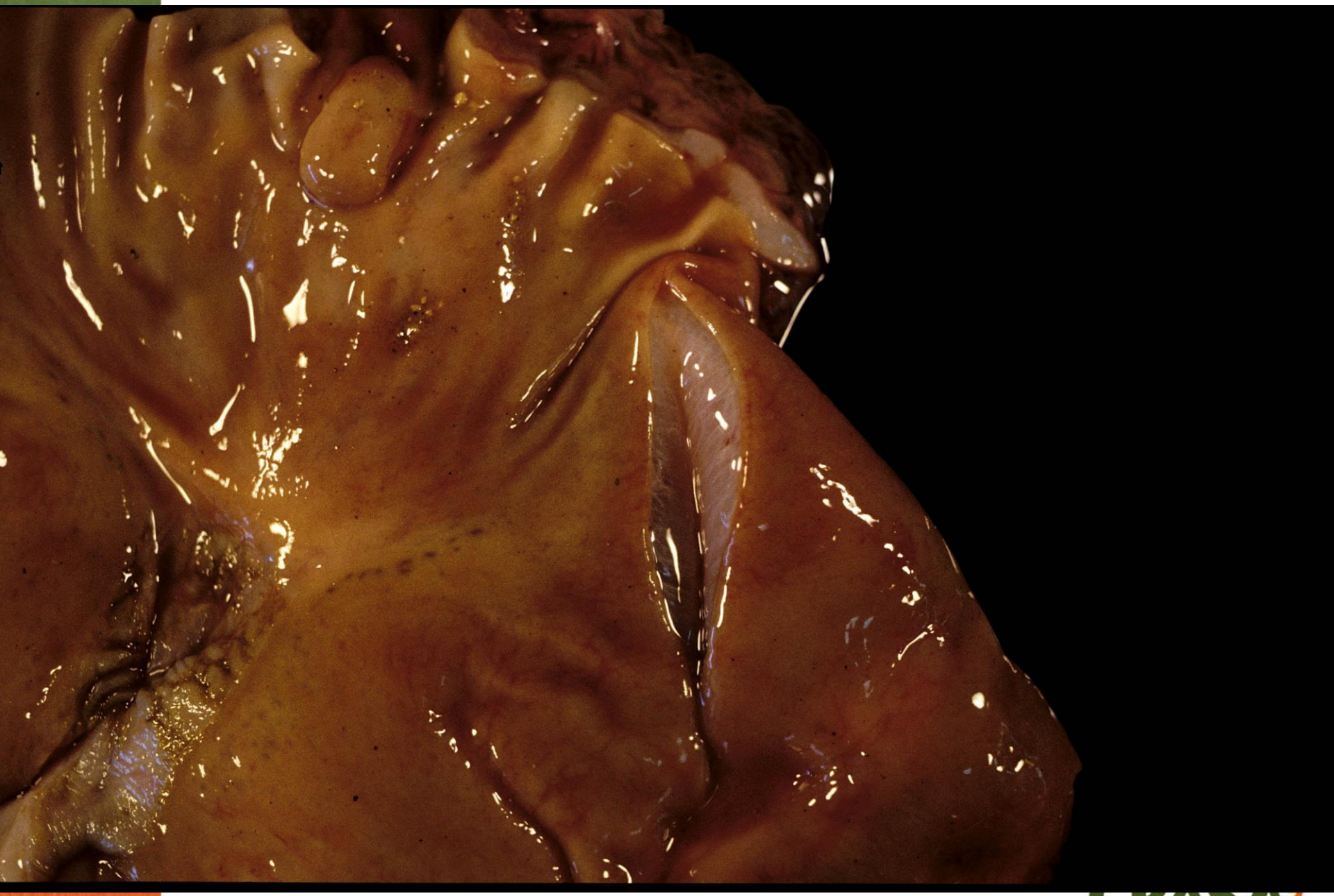

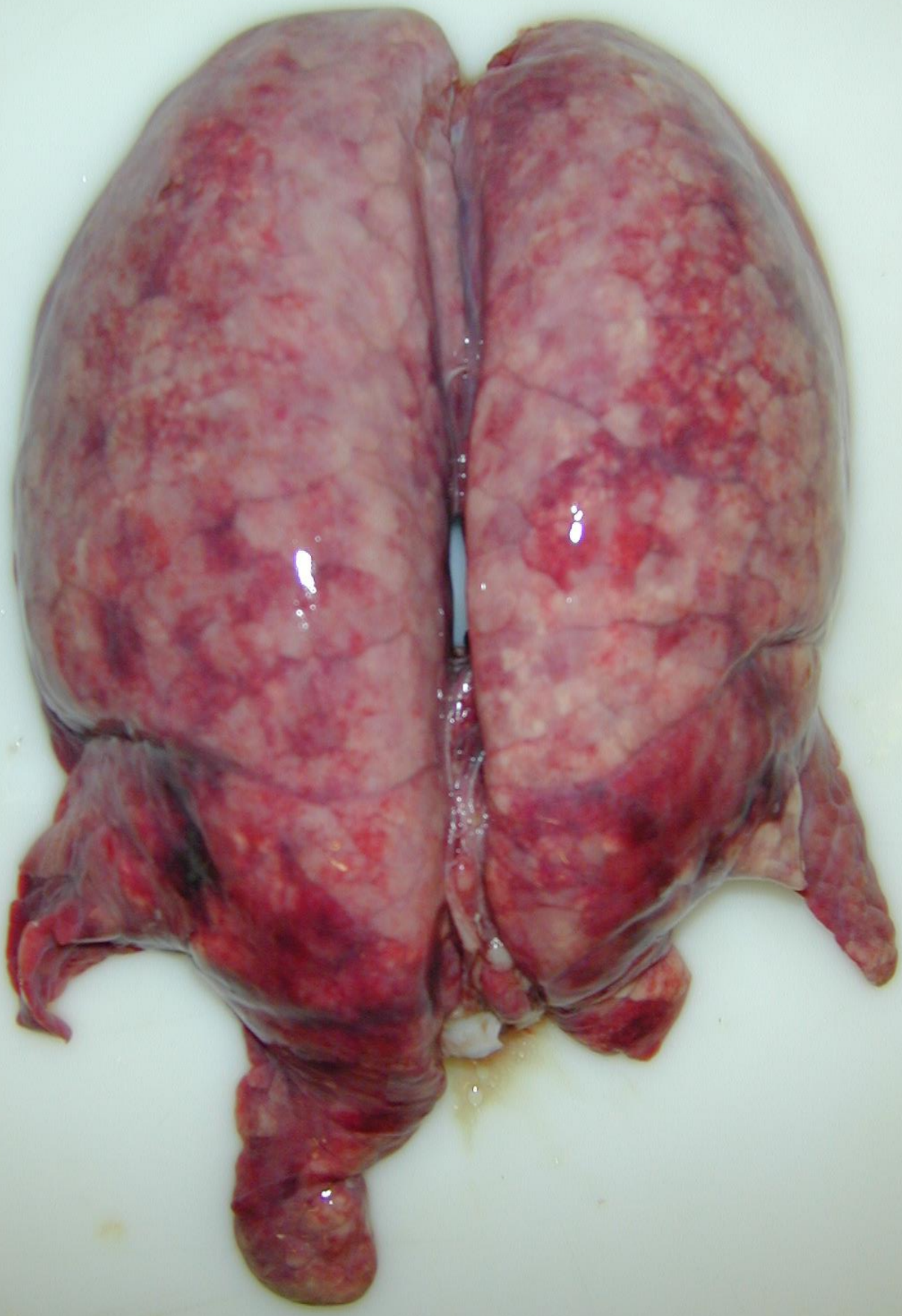

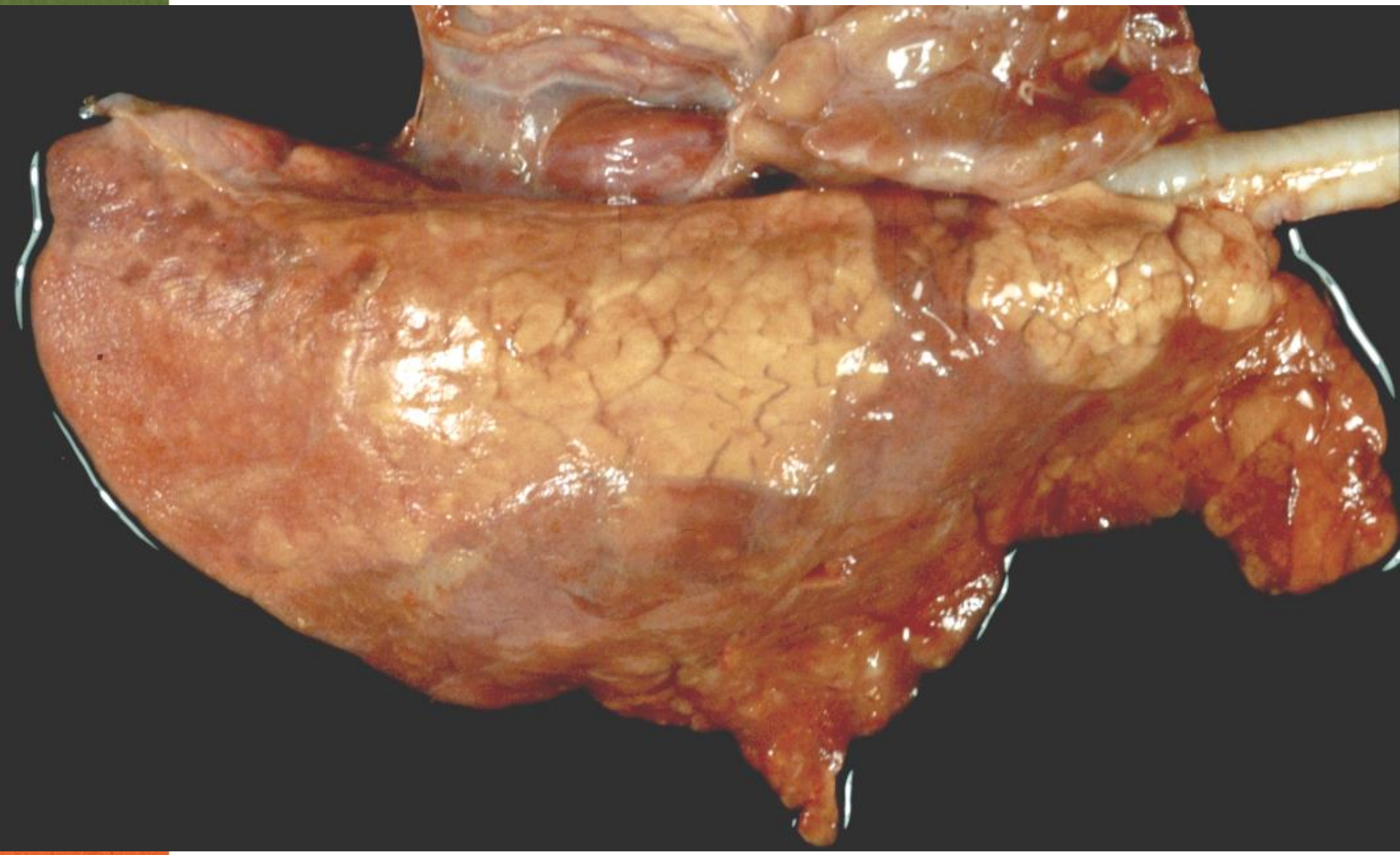

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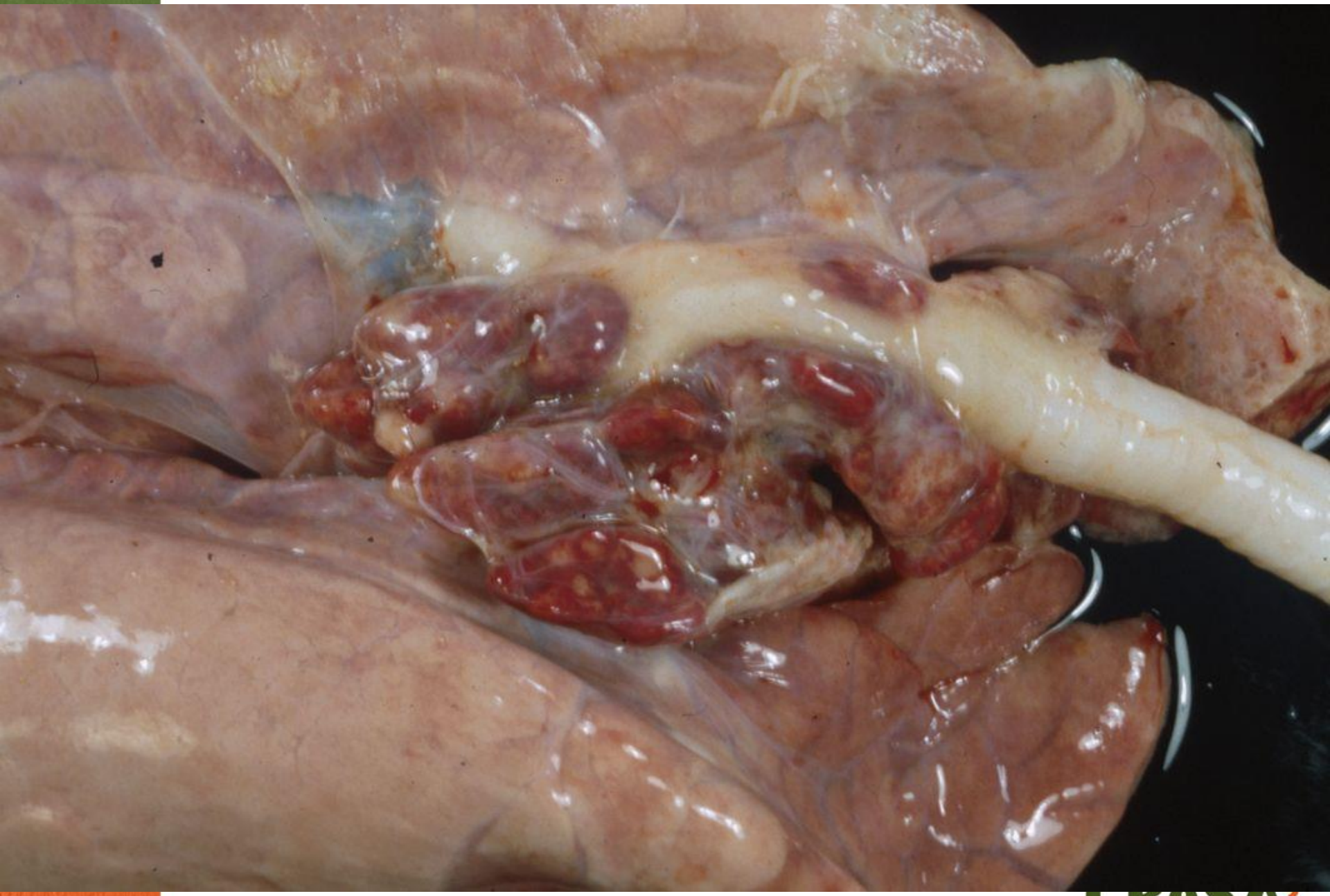

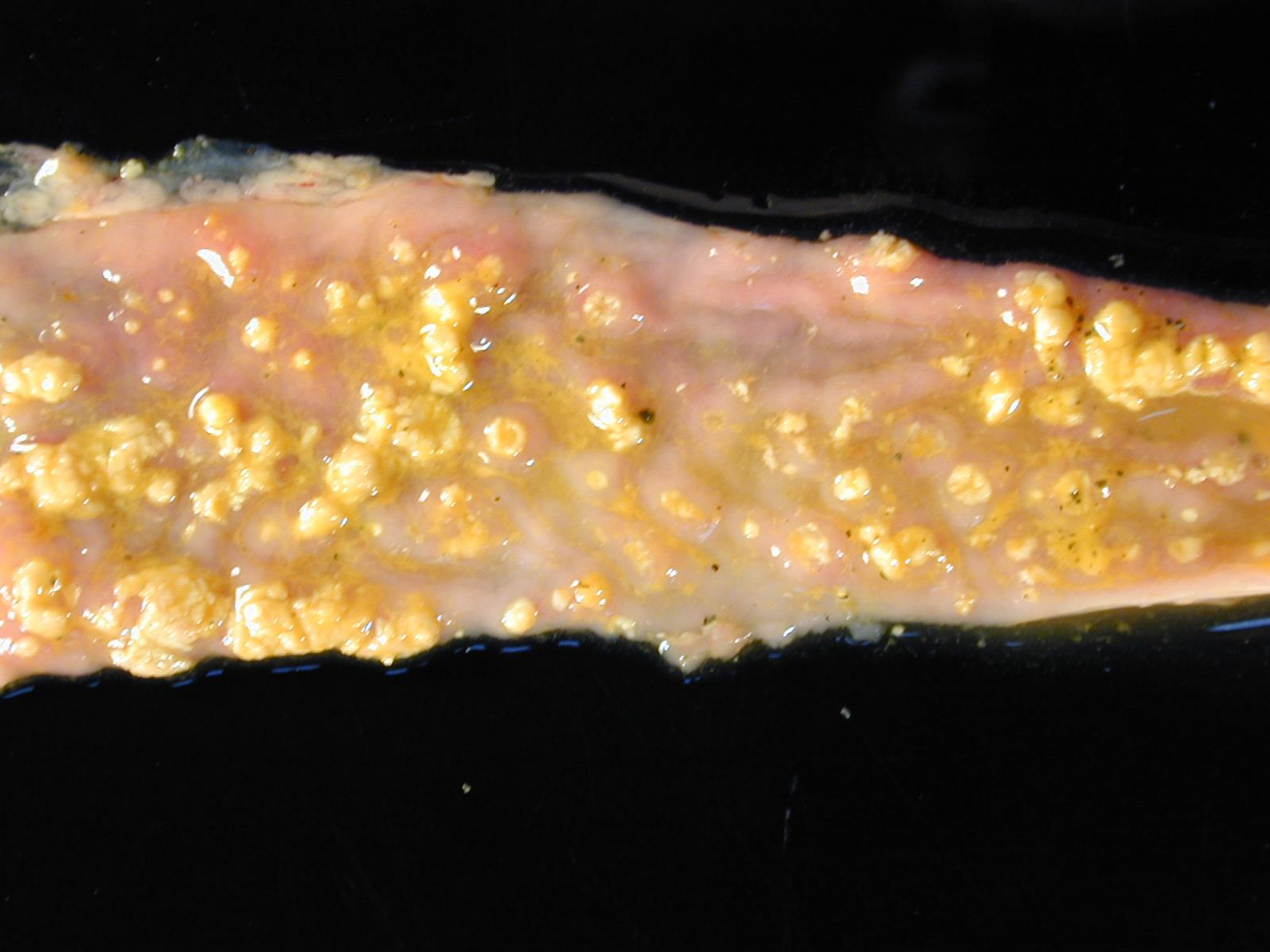

Gross lesions

1. Tip ear necrosis and polyserositis are compatible with bacterial septicaemia
2. Palpebral and stomach wall edema are compatible with oedema disease
3. Lymphadenopathy and non-collapsed lungs are indicative of viral infection
4. All answers are correct

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Gross lesions

Fibrinous ileitis in 1 pig; this is compatible with:

1. *Lawsonia intracellularis* infection
2. *Salmonella enterica* infection
3. *Brachyspira hyodysenteriae* infection
4. All answers are correct

Gross lesions (conclusions)

Oedema disease

Viral disease

Bacterial pulmonary disease

Septicemic bacterial disease (*H. parasuis*)

Myocardial lesions ?

Fibrinous ileitis ?

It was decided to maintain treatments

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Laboratory results – a week after

Histopathology

No pigs showed typical microscopic CNS lesions of oedema disease; which are they?

1. Non-suppurative meningoencephalitis
2. Simmetric, bilateral mielomalacia of medullary ventral horns
3. Suppurative encephalitis
4. Simmetric, bilateral encephalomalacia of the brain stem

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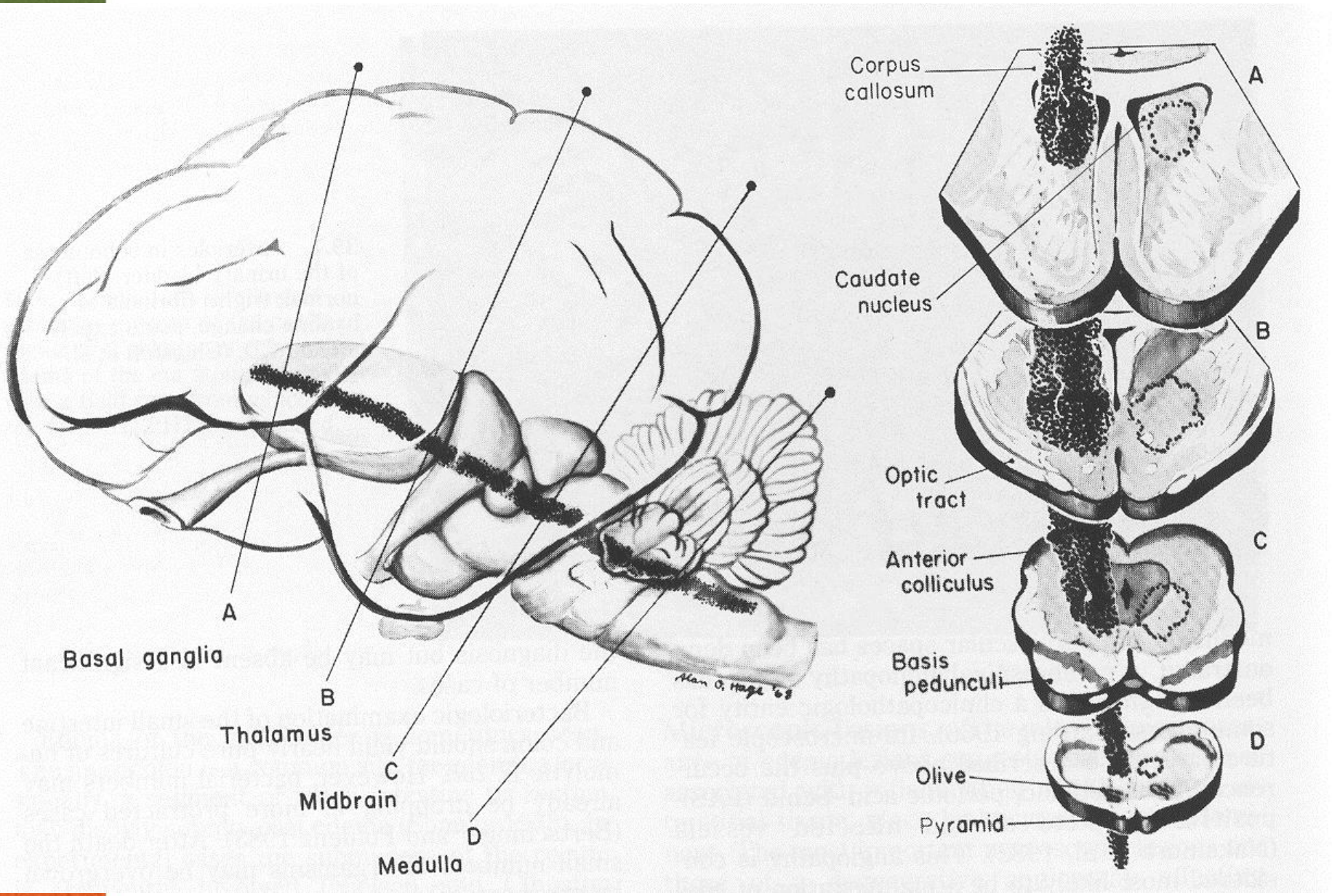
Oedema disease



Does the absence of microscopic findings discard oedema disease ?

1. Yes... They are pathognomonic and are always present
2. No... In a very few cases they are not present
3. No... They are rarely present in acute cases
4. No... Only pigs showing clear CNS clinical signs have these lesions

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Histopathology

Lymphocyte depletion together with histiocytic inflammatory infiltration of lymphoid tissues:

1. PRRSV infection
2. Porcine circovirus type 2 infection
3. *Salmonella cholerae-suis* septicaemia
4. Classical swine fever

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Histopathological results

- Subacute interstitial pneumonia in pigs No. 1, 3, 4, 5 and 6
- Myocardial degeneration with hemorrhages together with centrolobular hepatic necrosis (pig No. 5)
- Fibrino-purulent meningitis (pig No. 3)

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Viral pathogen detection

	PIG No.						
PATHOGEN	**1**	**2**	**3**	**4**	**5**	**6**	**7**
PRRSV	-	-	+	+	-	+	-
PCV2	+	-	+	+	-	+	+

Bacteriology

- Small intestine of pigs No. 1, 2, 5 and 6
- Toracic swab of pig No. 3
- Meningeal swab of pig No. 3
- Lung samples were not taken !!

Results:

- β-haemolytic *Escherichia coli* (pigs No. 1 and 6)
- Non-haemolytic *E. Coli* (pigs No. 2 and 5)
- *Haemophilus* spp. (pig No. 3)

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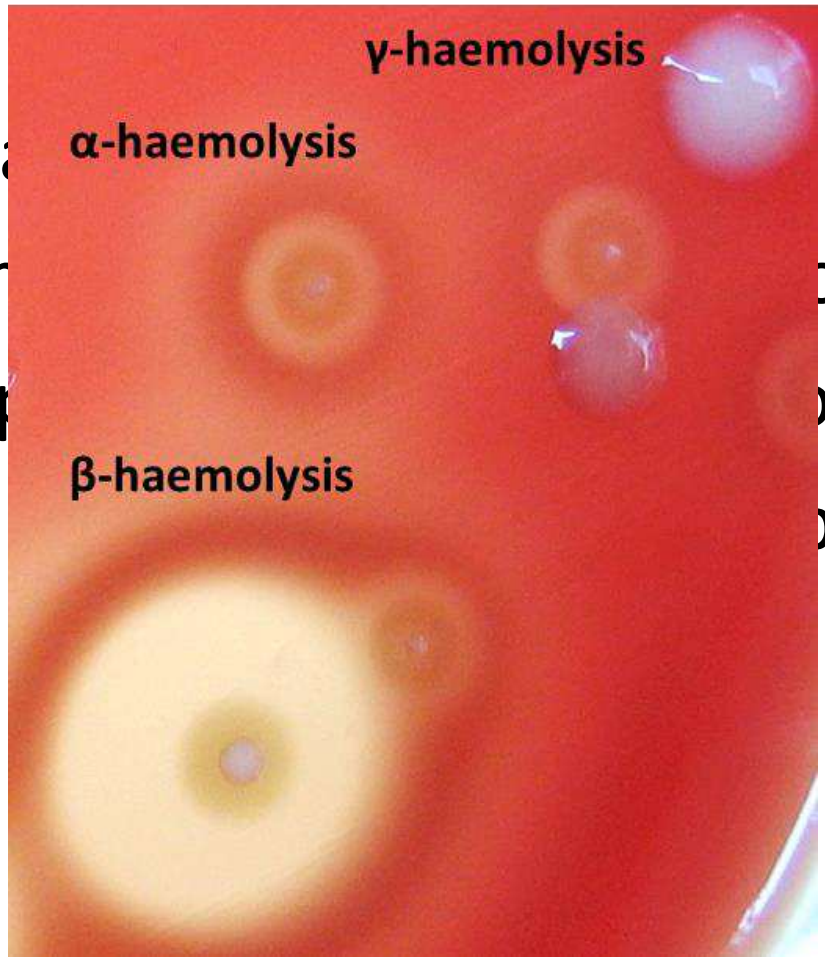
Bacteriology

Do you know what means β-haemolysis?



1. No ha
2. Incor ood-agar
3. Comp d-agar
4. Lack lood-agar

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Antibiogram

Antibiotic	*E. coli* (1)	*E. Coli (*6)	*Haemophilus (*3)
Colistine	S	S	ND
Ceftiofur	S	I	ND
Apramicine	S	S	ND
Enrofloxacin	S	S	S
Sulf+Trim	S	S	ND
Neomicine	S	S	ND
Flumequine	S	S	ND
Lincoespectin	S	S	ND
Amoxicilin	R	R	S
Doxiciclin	R	R	ND
Ampicilin	ND	ND	S
Cefalexin	ND	ND	S
Gentamicin	ND	ND	I

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Laboratory results (conclusions)

WHAT DO YOU THINK YOU HAVE?

PRRS and PCV2-SD

Oedema disease – postweaning colibacilosis

Bacterial pneumonia

Glässer's disease

Possible Salmonellosis ?

Possible Se/vit E deficiency ?

Third visit at farm A (day 16)

- No sudden death and CNS clinical signs are observed now
- Mean clinical picture includes growth retardation and respiratory distress
- Morbidity of 30-35%
- Rest of pigs apparently healthy
- Information on farm B: one batch with 50% morbidity and 35% mortality

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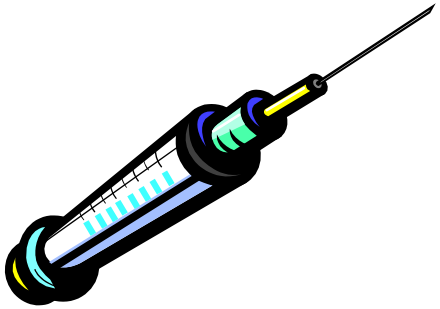
Implemented changes



- Maintenance of amoxicilin (for Glässer's disease)
- Inclusion of colistin in feed (for oedema disease)
- To control vitamin E and Se levels in feed
- Management changes

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Management changes

- To assess the correct pig density per pen (at least 0.7 m^2/pig in fattening units and 0.2 m^2/pig in nurseries)
- Habilitation of “hospital facilities” for diseased animals (3 day medication; euthanasia if they not respond in 5 days)
- Use of boots and overall exclusive for the “hospital facilities”
- Foot-bath with disinfectant for each building entrance
- Since then, to clean pits and 7-10 days of empty period (instead of 3-4 days)
- Vaccination and revaccination against ADV

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New visit to farm A (day 50)

- No problems in nurseries (mortality of 2% in the last batches)
- Last batch of fattening pigs had 4% of pigs in “hospital facilities”
- Farmer’s opinion: the improvement is very clear... But... He thought that “the enemy was still inside”

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Some thoughts...

- Outcome of disease = Mixed pathogens and its interaction with management systems and facilities
- Difficulties to implement an effective therapy if strict management restructuration and appropiate follow up is not established
- Importance of laboratory analysis in mixed diseases (unique diseases in a farm are quite rare!!)

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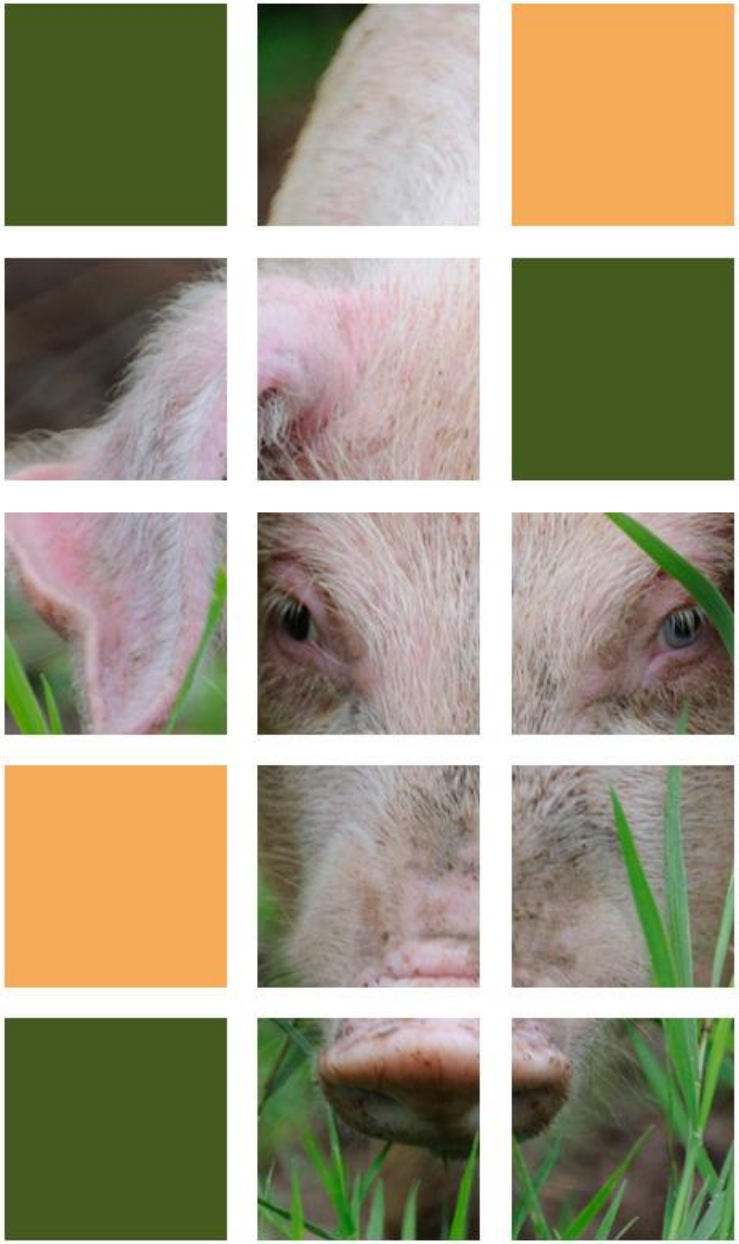

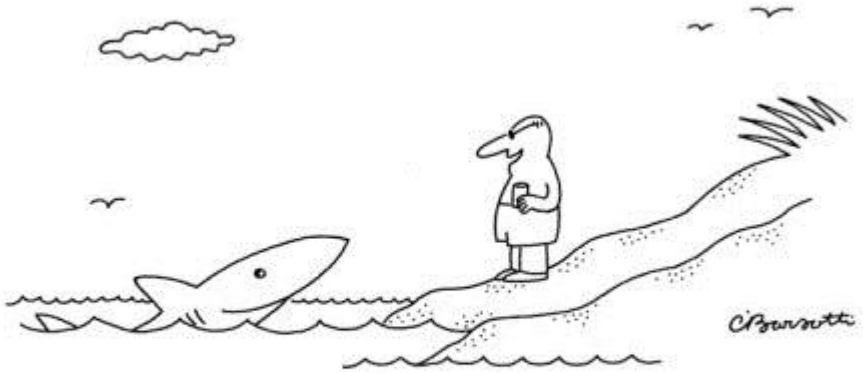

"Impressed? Well, wait until I tell you about this next case."

General characteristics of the farm

- 3-site farm of 7,000 sows, located in Aragon (Spain)
- Seronegative against ADV
- Seropositive against PRRSV – “stable”
- Seropositive against Mhyo
- Good productivity, with mortalities considered acceptable for all phases (14% in farrowing crates, 2% in nursery and 4% in fatteners)

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PRRSV farm stability

What do they mean by the farm is “PRRSV-stable”?

1. PRRSV is circulating freely at all stages
2. PRRSV is circulating at the sow level but not at nursery
3. PRRSV is not circulating but sows are sero-positive
4. PRRSV is not circulating and all age-groups are sero-positive

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PRRSV farm stability

Figure 1: Breeding-herd classification for porcine reproductive and respiratory syndrome virus (PRRSV) according to shedding and exposure status.

Herd category	Shedding status	Exposure status
Positive Unstable (I)	Positive	Positive
Positive Stable (II-A)	Uncertain	Positive
Positive Stable (II-B) (Undergoing Elimination)	Uncertain – undergoing elimination	Positive
Provisional Negative (III)	Negative	Positive
Negative (IV)	Negative	Negative

Holtkamp et al., 2011

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Characteristics of the problem

- Respiratory problem in pigs at the end of the lactation period and during nursery (first half, mainly)
- Progressive loss of weight, dyspnea and coughing
- Mortality associated to loss weight; mortalities evolved rom 14 to 18% during lactation and from 2 to 4% in the nurseries

Coughing and dyspnea in lactating and nursery pigs… differential diagnoses?

1. Swine influenza virus infection
2. *Mycoplasma hyopneumoniae* infection
3. Management and environmental problems
4. All are correct

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Characteristics of the problem

- Until that moment, only nursery pigs were necropsied; pulmonary craneo-ventral consolidation was observed
- 7 pigs were submitted for pathological and microbiological analyses
  - Four 3-week-old piglets
  - Three 4-week-old piglets

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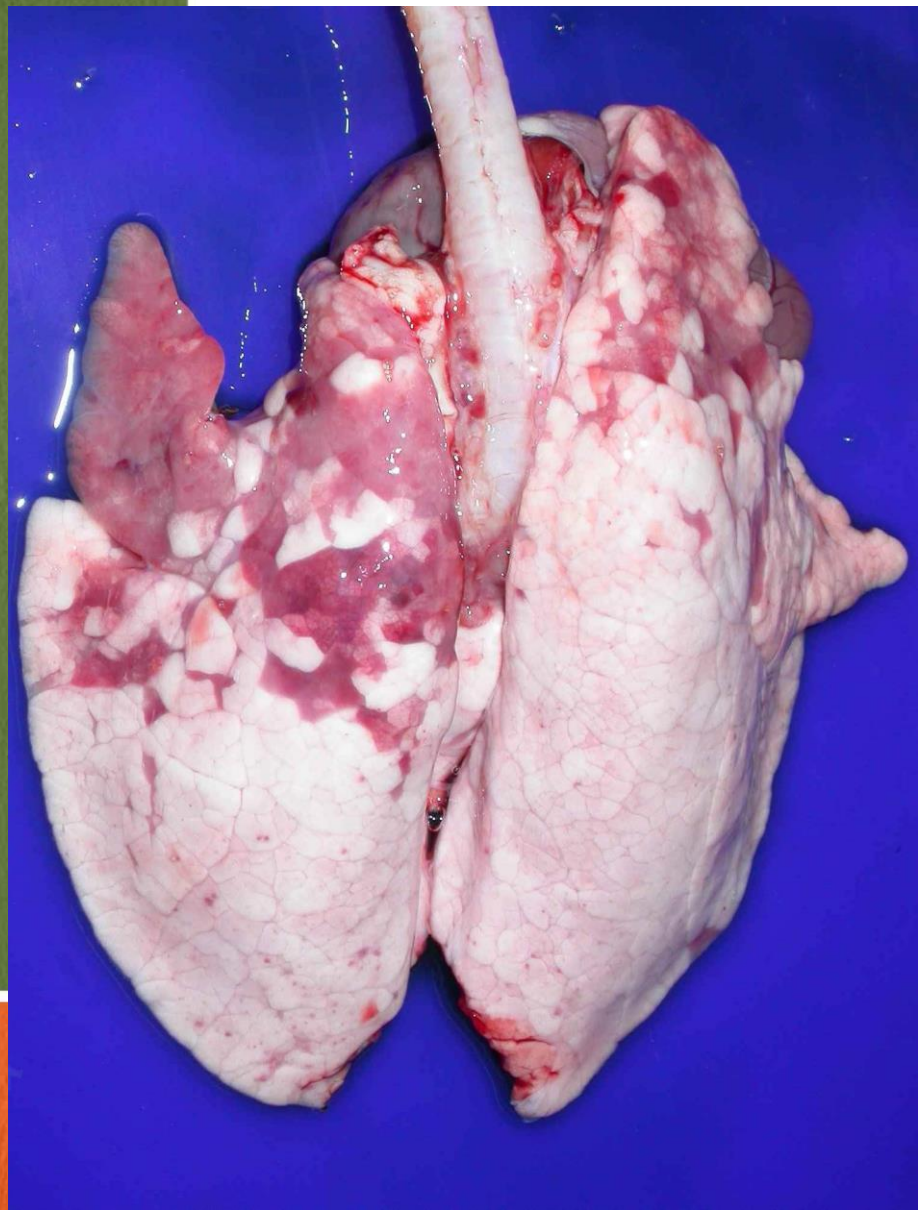
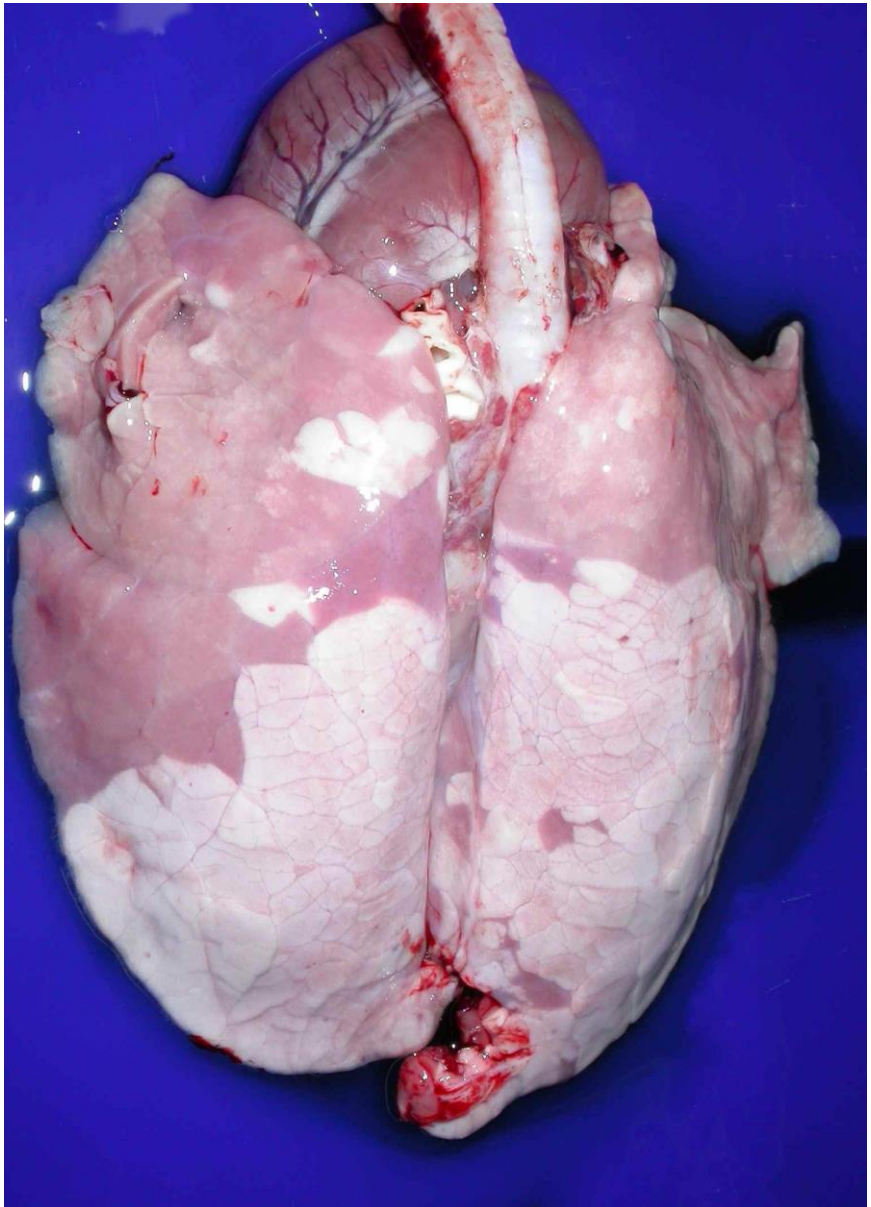
Lesion observed in all studied pigs





Which is your presumptive diagnosis?

1. *Mycoplasma hyopneumoniae* infection
2. Swine influenza virus infection
3. *Pasteurella multocida* infection
4. *Bordetella bronchiseptica* infection

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Clinical case evolution

- Injectable antibiotic treatment is maintained (in those more severely affected pigs; amoxicilin) as well as doxiciclin in water
- Coughing and dyspnea is persisting, although to a lesser degree

Laboratory results

Pathological report:

- All pigs showed:
  - Catarrhal-purulent bronchopneumonia
  - Broncho-interstitial pneumonia

Bacteriology:

- Lack of significant pathogens in 5 lungs
- *Bordetella bronchiseptica* in one lung
- *Bordetella bronchiseptica* and *Pasteurella multocida* in another lung

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What can cause a broncho-interstitial pneumonia?

1. *Mycoplasma hyopneumoniae* and swine influenza infection
2. PRRS and swine influenza viruses
3. PCV2, PRRS and swine influenza viruses
4. *Bordetella bronchiseptica, Pasteurella multocida* and *Mycoplasma hyopneumoniae* infections

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Laboratory results

PCR:

- PRRSV: Negative
- *Mycoplasma hyopneumoniae*: Negative

Immunohistochemistry:

- PRRSV: Negative
- SIV: 2/7 positives

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Global interpretation of results and evolution of the problem

- Final diagnosis established as SIV infection together with bacterial co-infections
- Difficulties to control the viral infection:
  - Very big farm (7,000 sows) – subpopulations?
  - Immunization? Vaccine schedule?
- The case evolved towards lesser problems, but during a quite long period (6-8 months), when it dissapeared – herd immunity?

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Take home messages

Diagnostic procedures are key elements in pig health and management

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Field of constant evolution and, even the basis relies on a good and sound clinical investigation, laboratory testing has represented a technical revolution during last 10 years

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New technological platforms (quantitative real-time PCR, sequencing with phylogenetic analysis, microarrays,…) are on the horizon if not here

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Take home messages

Diagnostic procedures are key elements in pig health and management

Field of constant evolution and, even the basis relies on a good and sound clinical investigation, laboratorial testing has represented a technical revolution during last 10 years

New technological platforms (quantitative real-time PCR, sequencing with phylogenetic analysis, microarrays,…) are on the horizon if not here

Pig veterinarians must have the sufficient knowledge on the laboratory tests to be used. Their understanding will provide a more critical and reasonable interpretation of results

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Take home messages

BE SELF-CRITICAL WITH ALL YOUR FINDINGS:

Did you really answer the “key question”?

Was it properly formulated?

Did you do everything you need to answer it?

THE PROPER ASSESSMENT OF YOUR CASES WILL ALLOW YOU SWITCHING FROM:

WHAT I THINK I HAVE
TO
WHAT I HAVE AND WHAT I DO NOT HAVE

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THANK YOU VERY MUCH FOR YOUR ATTENTION

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