PSA: eziologia, caratteri della malattia, sintomi e lesioni

Andrea Lombardo

DVM

IZSLT UOT TC – Sezione di Arezzo

Definizione

Malattia virale altamente (???) contagiosa e ad esito per lo più infausto, caratterizzata da lesioni emorragiche della cute e di tutti i parenchimi.

(Farina e Scatozza, 2001)

- ✓**Caldi, malati, rossi** (*hot, sick, red pigs*)

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african swine fever

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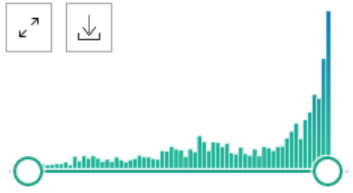

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Abstract

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Review

African swine fever – A review of current knowledge

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ARTICLE INFO

Keywords:
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ABSTRACT

African swine fever (ASF) is a viral hemorrhagic disease with exceptionally high lethality in domestic pigs and Eurasian wild boar. Over the last decade, ASF has emerged in several European and Asian countries and has now an unprecedented distribution. Against this background, the presented review focuses on current knowledge and advances in ASF virology, clinical disease upon infection with recent strains, epidemiology, diagnosis, and control. This review highlights knowledge gaps and controversial opinions related to ASF.

Eziologia: tassonomia e ultrastruttura

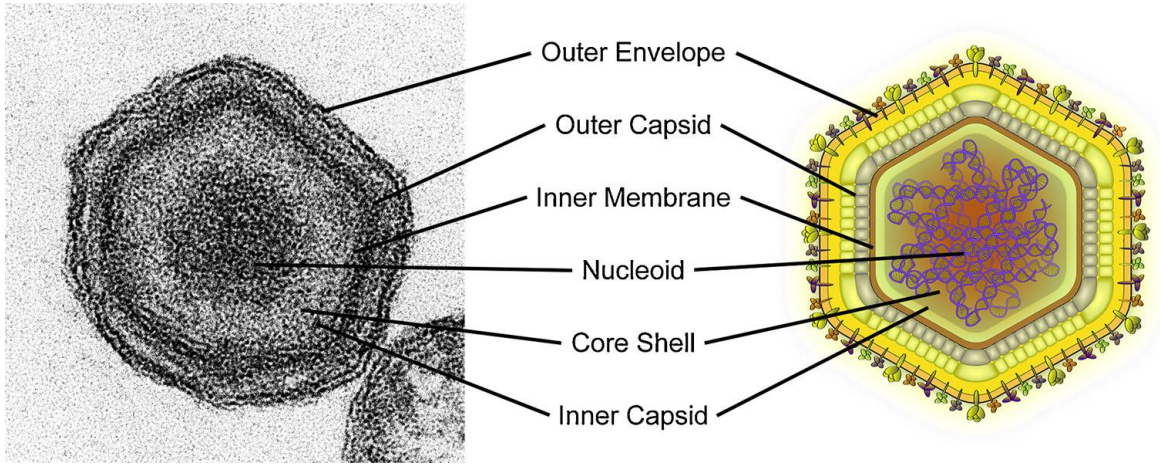
✓Unico membro del genere **Asfivirus**

- Fam. Asfarviridae (**"ASFAR"= African Swine Fever And Related viruses)**
- Ord. Asfuvirales
- Class. Pokkesviricetes *International Committee on Taxonomy of Viruses (EC 51, Berlin, Germany, July 2019)*

✓Unico virus a dsDNA trasmesso da artropodi

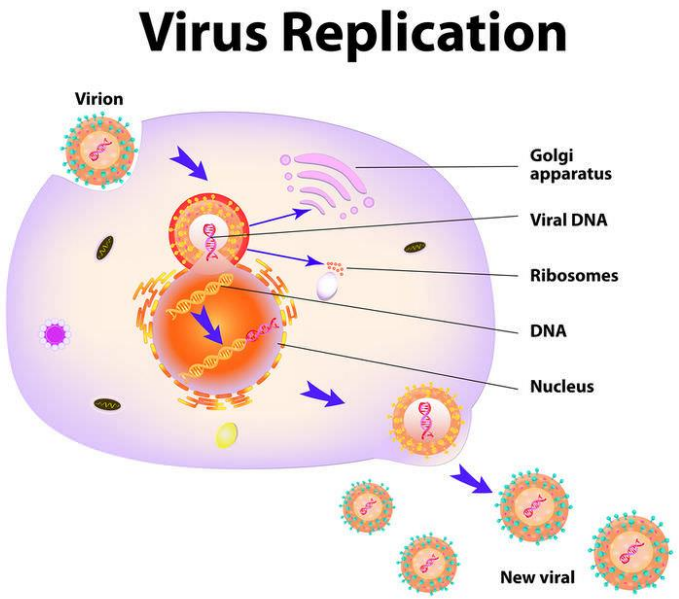
✓Virione strutturalmente molto complicato

- Dimensioni variabili (175 – 215 nm)



- Nucleoide coniugato con Coreshell (nucleoproteine)
- Inner layer o membrana interna (lipoproteine)
- Inner Capsid (icosaedrico)
- Inner membrane (adesa al inner capsid, icosaedrica)
- Outer capsid icosaedrico (1892–2172 capsomeri!!!)
- Envelope (acquisito durante il budding dalla membrana cellulare)

Eziologia: replicazione



- ✓Replicazione in cellule…
  - della linea monocito-macrofagica e APC
  - linfociti
  - Vari precursori midollari
  - endoteli,
  - epitelio renale,
  - epatociti (…)
- ✓Penetrazione nella cellula mediante adesione al recettore (forse CD45?)e induzione endocitosi claritrina dipendente/macropinocitosi
- ✓All'interno dell'endosoma: uncoating di envelopes e capsidi
- ✓Replicazione:
  - ✓ nel nucleo (nuclear phase) ???? Dubbia
  - ✓ in aggregati citoplasmatici perinucleari (virus factories)
- ✓Espulsione dei virioni tramite budding «seriali»
  - ✓ reticolo endoplasmatico/Golgi (acquisizione dell'inner envelope)
  - ✓ membrana cellulare (outer envelope)

Eziologia: genoma

✓Ds DNA

✓170 – 190 kb

✓151 – 167 ORFs

- Proteine di replicazione: DNApol, RNApol, fattori di riparazione e modificazione degli mRNA
- Fattori di adesione alle cellule: recettore per CD45 (LCA)
- Proteine strutturali: oltre 50. Quali gli epitopi da usare in diagnostica e vaccini?
- Interferenti immunologici (inibizione Interferoni di tipo I, interferenza nei pathways di apoptosi, inibizione della presentazione dell'antigene con MHC, induzione citochine proinfiammatorie)
- Più della metà delle ORFs non ha una funzione nota

✓Manca ancora la piena comprensione dei fattori di virulenza, struttura, adesione e replicazione

Eziologia: genotipi vs sierotipi

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Review

Genetic and antigenic diversity of African swine fever virus

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ARTICLE INFO

Keywords:
African swine fever
Genotypes
Serogroups
Hemadsorption
Cross-protection

ABSTRACT

African swine fever virus (ASFV) is the only known DNA arbovirus, and the ability to replicate efficiently in both insect and mammalian cells is encoded in its viral genome. Despite having a relatively low overall genomic mutation rate, ASFV demonstrates genetic diversity in certain genes and complexity in gene content in other genomic regions, indicating that ASFV may exploit multiple mechanisms for diversification and acquire new phenotype characteristics. ASFV antigenic diversity is reflected in the ability to type cross-protective viruses together into serogroups, largely based on antibody-mediated inhibition of hemadsorption. Here we review ASFV genetic signatures of ASFV type specificity, genome variability, and the hemadsorption as a means of defining virus antigenic type, and how these may be used toward defining antigenic and phenotypic diversity that is problematic for development of vaccine solutions to ASF.

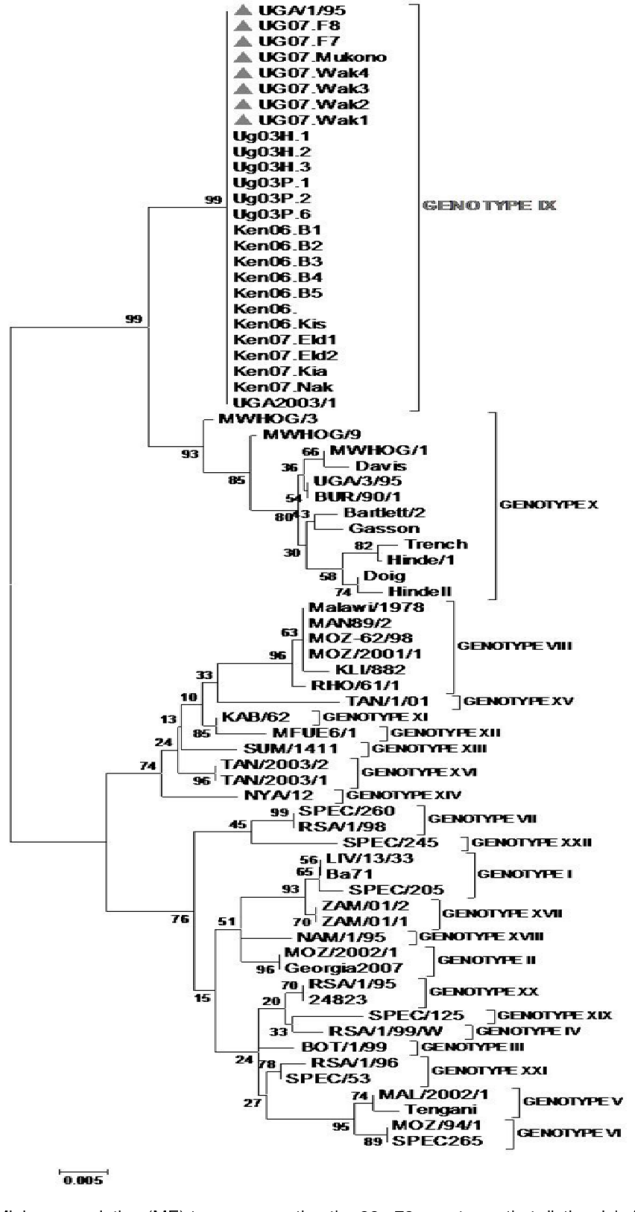
Eziologia: genotipi

✓Sistema a 24 (?) genotipi (Boshoff et al., 2007; Gallardo et al., 2011)

- Basato sul polimorfismo:
  - dei geni p54, p72, e pB602L
  - della lunghezza del genoma 170 e 193kbp
  - Della codifica proteica (proteomica) 150 -167 proteine
- Sistema complicato che rappresenta gli isolati africani

✓2 genotipi in Europa (Gen. I e Gen. II) (Wade et al., 2019)

- Isolati europei generalmente meno variabili di quelli africani
  - Genotipo I → Sardegna
  - Genotipi II → Recenti focolai europei ed asiatici



Eziologia: struttura antigenica e sierotipi

- ✓ **Il virus non stimola la produzione di anticorpi neutralizzanti….**
  - ✓Neutralizzazione virale inutilizzabile per la classificazione sierologica degli stipiti

- ✓**Non possiede emoagglutinina**
  - ✓Provoca emoadsorbimento sulla superficie di macrofagi sperimentalmente infettati
  - ✓Inibizione dell'emoabsorbimento utilizzato per diagnosi sierologica e sierotipizzazione (Malmquist, 1963)
  - ✓Sistema utilizzato fino agli anni '90 per tentativi di classificazione sierologica degli stipiti isolati
  - ✓Anticorpi anti CD2v/C-type lectin protein: recente candidato per lo studio della cross protezione tra stipiti

Eziologia: struttura antigenica e sierotipi

✓Emoassorbimento e inibizione dell'emoassorbimento

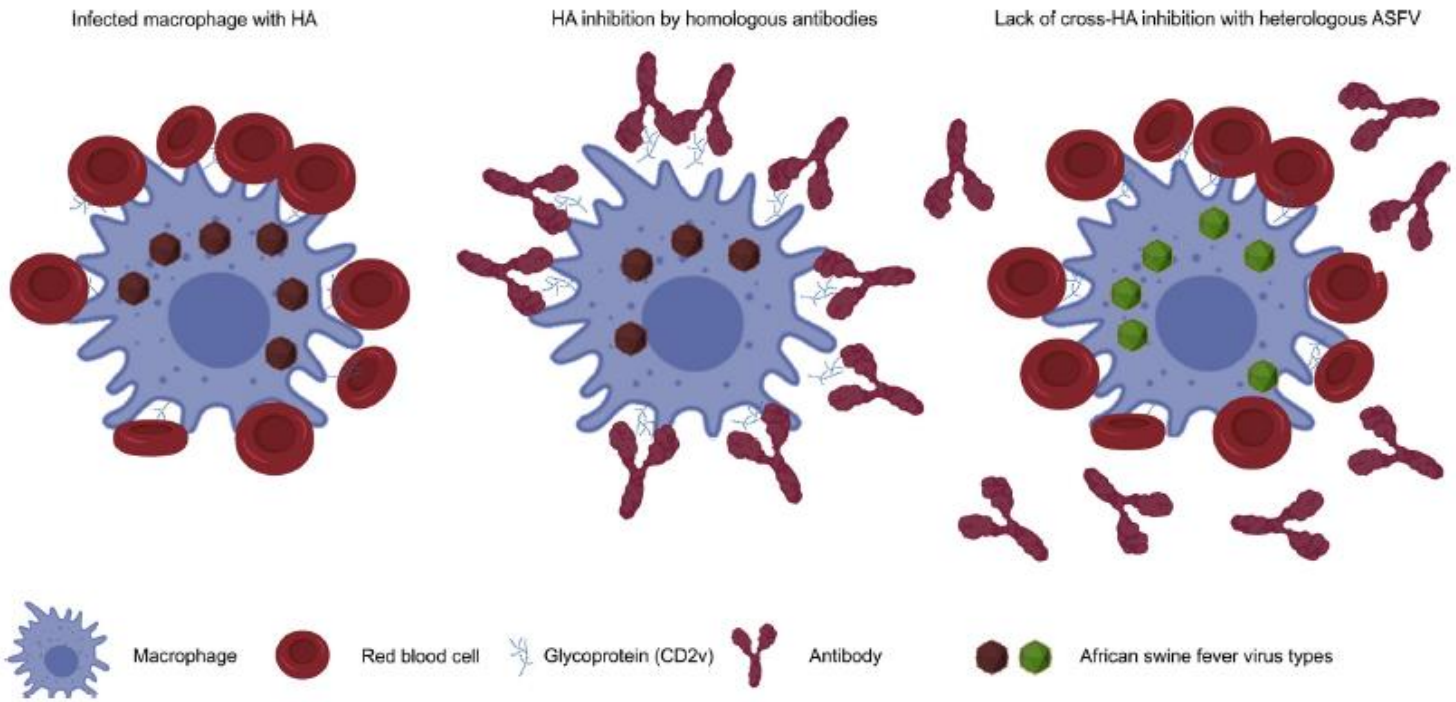


Fig. 2. The principle of ASFV hemadsorption (HA) and hemadsorption inhibition (HAI). The macrophage infected with ASFV is surrounded by red blood cells (hemadsorption). The serum from recovered pigs contains antibodies which may inhibit hemadsorption (HAI) caused by homologous ASFV strains (same serogroup). The macrophage infected by heterologous ASFV strain (different serogroups) will demonstrate "classical" HA picture regardless the presence of antibodies against heterologous ASFV serogroup.

Eziologia: struttura antigenica e immunogenicità

- ✓ Il virus non stimola la produzione di anticorpi neutralizzanti….o invece si??

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Review

Antibody-mediated neutralization of African swine fever virus: Myths and facts

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ARTICLE INFO

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Neutralization
Vaccine

ABSTRACT

Almost all viruses can be neutralized by antibodies. However, there is some controversy about antibody-mediated neutralization of African swine fever virus (ASFV) with sera from convalescent pigs and about the protective relevance of antibodies in experimentally vaccinated pigs. At present, there is no vaccine available for this highly lethal and economically relevant virus and all classical attempts to generate a vaccine have been unsuccessful. This failure has been attributed, in part, to what many authors describe as the absence of neutralizing antibodies. The findings of some studies clearly contradict the paradigm of the impossibility to neutralize ASFV by means of monoclonal or polyclonal antibodies. This review discusses scientific evidence of these types of antibodies in convalescent and experimentally immunized animals, the nature of their specificity, the neutralization-mediated mechanisms demonstrated, and the potential relevance of antibodies in protection.

8. Concluding remarks

Despite original reports indicating the lack of neutralizing activity of sera from animals infected with ASFV, overwhelming evidence of neutralizing antibodies against this virus has been provided by numerous laboratories in the last 15 years. Moreover, several elegant experiments have revealed the relevance of antibodies in protection against this fatal disease. However, in terms of antibody-mediated neutralization, ASFV has uncommon particularities that are shared by other viruses. Several of these singularities may explain why some authors have concluded that ASFV does not induce neutralizing antibodies in pigs that have recovered from infection. The peculiarities of ASFV include loss of susceptibility to neutralization by cell culture passage as a result of changes in the phospholipid composition of viral membranes and/or the presence of sera blocking antibodies that inhibit complete neutralization. However, a number of ASFV proteins have been undoubtedly implicated in the induction of neutralizing antibodies during infection and assigned to one of the two neutralization mechanisms described for this virus. In addition, some critical epitopes in neutralization have also been characterized in proteins p72 and p54. Antibody-mediated neutralization is a key defense mechanism against viral infections. Although cell-mediated immune mechanisms may make a significant contribution to protection against ASFV, as in other viruses that infect macrophages, current data encourage us to explore vaccine formulations with the aim to maximize the induction of critical and potent neutralizing antibodies. Strategies to stimulate neutralizing antibodies should be considered feasible in the design of ASF vaccine programs.

Resistenza nell'ambiente/prodotti

- Rimane infettante entro un ampio range di pH (4-10) se ha a disposizione proteine (Geering et al., 2001)
- Resistente nei prodotti a base di carne (Efsa, 2009)
  - 15 settimane nelle carni refrigerate
  - 6 mesi nei prodotti trasformati tipo prosciutto (anche oltre se pH non scende sotto 4)
  - 399 giorni nel prosciutto di Parma
- Resistente nell'ambiente (Efsa, 2009)
  - 100 giorni nel letame umido
  - 18 mesi nel sangue a temperatura ambiente e sei anni nel sangue refrigerato
- Nelle carcasse:
  - recente studio in Lituania con sotterramento di carcasse infette e riesumazione a differenti timepoints (Zani et al., 2020):
    - Genoma virale con rtPCR presente dopo svariati mesi
    - Perdita della capacità replicativa in vitro quasi immediata

Resistenza nell'ambiente/prodotti

- **Influenza della composizione del suolo sulla vitalità del virus** (Carlson et al., 2020)
  - Considerati terreni con differenti pH, origine e struttura, contaminati con sangue di cinghiale infetto
    - Terreni sabbiosi o terriccio da giardini (+++vegetazione) → resistenza del virus per settimane
    - Terreni paludosi/umidi → resistenza del virus per alcuni giorni
    - Terreni acidi tipici delle foreste → inattivazione immediata
    - Aggiunta di acido citrico o idrossido di calcio → inattivazione immediata

- **Resistenza in liquami e letami**
  - Resistenza di 4 giorni nelle urine a 37°C (Davies et al, 2017)
  - Resistenza di 3 giorni nelle feci a 37°C (Davies et al, 2017)
  - Inattivato in 4 ore a 40°C nel letame in maturazione (Davies et al, 2017)
  - 100 giorni nel letame umido in inverno (EFSA, 2009)

Spettro d'ospite

- ✓ Suidi selvatici africani (carriers asintomatici)
  - ✓ Facocero
  - ✓ Potamocero
  - ✓ Ilocero
  - ✓ ….
- ✓ Cinghiale (sintomatico)
  - ✓ Sus scrofa
- ✓ Suino domestico (sintomatico)
  - ✓ Sus scrofa
- ✓ Ospiti infettati solo sperimentalmente
  - ✓ Coniglio
  - ✓ Capra
- ✓ Vettore
  - ✓ *Ornithodorus spp.*





Trasmissione

- ✓Attraverso la puntura del vettore (ove presente)
- ✓Contatto diretto tra malato e sano
- ✓Attraverso rifiuti, carcasse o residui di cucina infetti
- ✓Contatto indiretto (persone, veicoli, attrezzi, alimento ecc.)

Patogenesi

frontiers in Veterinary Science

REVIEW
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Comparative Pathology and Pathogenesis of African Swine Fever Infection in Swine

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African Swine Fever (ASF) is a viral disease that affects animals of the *Suidae* family, and soft ticks from the genus *Ornithodoros* can also be infected by the ASF virus (ASFV). The disease was first described in Africa at the beginning of the twentieth century as an acute disease characterized by high mortality and fatal hemorrhages. ASF has caused outbreaks in numerous countries and it continues to be devastating nowadays for the porcine sector in those countries affected, and a massive threat for those free of the disease. ASF can follow clinical courses from peracute to chronic in domestic pigs (*Sus scrofa*) depending on a variety of factors, including the immune status of the animals and the virulence of the ASFV strain. The key features of the pathogenesis of the disease in domestic swine are a) a severe lymphoid depletion including lymphopenia and a state of immunodeficiency, and b) hemorrhages. However, African wild swine like bushpigs (*Potamochoerus larvatus*), red river hogs (*Potamochoerus porcus*), and warthogs (*Phacochoerus africanus*) can be infected by ASFV showing no clinical signs of disease and acting as natural reservoir hosts. In this article we review the key features of the gross and microscopic pathology together with a description of the pathogenesis of ASFV infection in domestic pigs following the different clinical courses. The pathogenesis of ASF in wild and domestic swine is also described, what can provide important information for the design of control strategies, such as vaccines.

Keywords: African swine fever, pathology, pathogenesis, virus, swine

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Patogenesi

- ✓ **Penetrazione per via oronasale** (o intradermica se tramite vettore)
- ✓ **Prima replicazione in tonsille** (amigdale e anello del Waldeyer) o linfonodi satellite entro 24h
- ✓ **Prima viremia cellulo associata** (principalmente monociti, ma anche neutrofili ed eritrociti) entro 48h
- ✓ **Localizzazione** a livello di cellule monocito macrofagiche, APC, endoteli, precursori midollari della linea mieloide/eritroide, epatociti, guaine mieliniche ed epitelio tubulare del rene
- ✓ **Organi bersaglio**
  - **Linfonodi**
  - **Tonsille e altro MALT**
  - **Milza**
  - **Midollo emopoietico**
  - Fegato
  - Rene
  - Polmone

Patogenesi

- **La viremia attiva la cascata coagulativa tramite rilascio di PGE2 dai macrofagi infetti**:
  - conseguente DIC: trombosi e ischemie

- **Progressivo esaurimento delle piastrine e replicazione nei precursori megacariociti**:
  - Piastrinopenia: emorragie

- **Replicazione negli epatociti con inibizione sintesi proteica:**
  - ipoalbuminemia e calo dei fattori coagulativi: edemi ed emorragie

- **Replicazione negli endoteli e deposizione immunocomplessi:**
  - vasculiti, necrosi endoteli → aumento permeabilità vasale: edemi ed emorragie

- **Replicazione in macrofagi, leucociti e precursori midollari**:
  - I macrofagi infetti rilasciano citochine proinfiammatorie (IL-1, TNF-a, IL-6)→ "cytokine storm"→ apoptosi dei linfociti
  - leucopenia e immunosoppressione: sovrainfezioni nelle forme croniche

- **Replicazione nelle cellule della glia:**
  - demielinizzazione e richiamo di linfociti: encefalite linfocitica (tremori)

- **Negli animali che sieroconvertono:**
  - fenomeni di ipersensibilità da immunocomplessi (artriti, dermatiti, glomerulonefrite)

Segni clinici

✓Altamente variabili, dipendono dallo strain virale e dall'età e stato immunitario

- Popolazioni naive→ Forme iperacute ed acute
- Zone endemiche → Forme croniche o asintomatiche

✓Genotipo II (Sardegna a parte) il più coinvolto in Europa, patogeno sia per suino domestico che cinghiale con segni clinici sovrapponibili

✓Incubazione di 4 giorni - 2 settimane

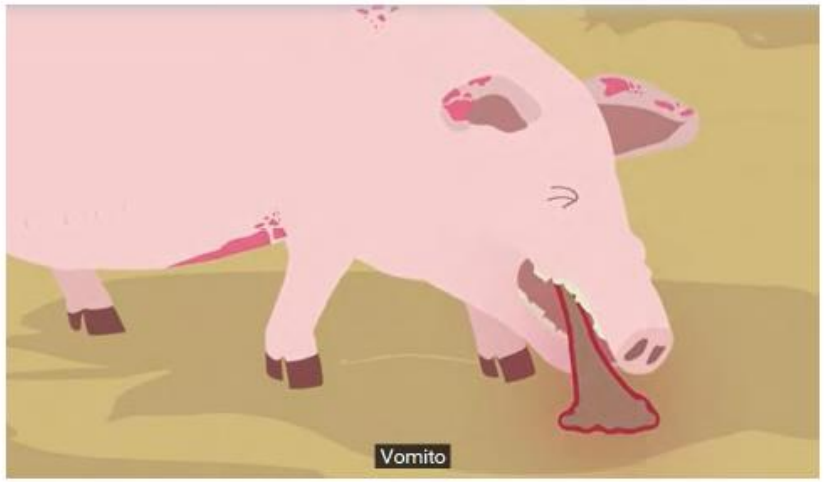
Segni clinici

- Stipiti altamente virulenti: forma iperacuta
  - mortalità fino al 100% entro 7-10 giorni dall'esordio dei segni
  - Segni:
    - cianosi
    - prostrazione
    - atassia
    - febbre (41°C)
    - Dispnea secondaria ad edema polmonare
    - Scolo nasale con o senza epistassi
    - Vomito/diarrea con o senza sangue
    - Emorragie cutanee
    - Aborto
  - Decorso fulminante con mortalità vicina al 100% in massimo 7 giorni

Segni clinici

- Stipiti moderatamente virulenti: forma acuta
  - Mortalità del 30-70% entro 7-20 giorni dall'esordio dei segni
  - Segni simili alla forma iperacuta altri +
    - congiuntivite mucopurulenta,
    - Lesioni emorragiche più marcate
    - Tremori (esito della compromissione encefalica)
  - Morte in 2 fasi distinte:
    - Durante la prima fase trombocitopenica e leucopenica
    - Durante la fase tardiva di apparente miglioramento a causa del danno vasale con eritrodiapedesi
- Stipiti a bassa virulenza: forma subacuta o cronica
  - Mortalità molto bassa o assente
  - forme paucisintomatiche con dimagrimento, sovrainfezioni respiratorie, ulcere cutanee, tumefazioni articolari, picchi febbrili altalenanti.
  - Sviluppo di anticorpi (non neutralizzanti…) dopo 7-10 giorni

Segni clinici



https://www.efsa.europa.eu/en/topics/topic/african-swine-fever

Segni clinici

Segni clinici

FIGURE 12
Clinical signs of acute African swine fever

A. *Pigs are visibly weak with fever and huddle to stay warm.*
B-E. *Bloody diarrhoea and distinct hyperaemic (red) areas on skin of neck, chest and extremities.*
F. *Cyanosis (bluing) at the tips of ears.*
G-I. *Necrotic lesions on skin of the abdomen, neck and ears.*

Fonte: FAO Manual –African Swine Fever detection and diagnosis

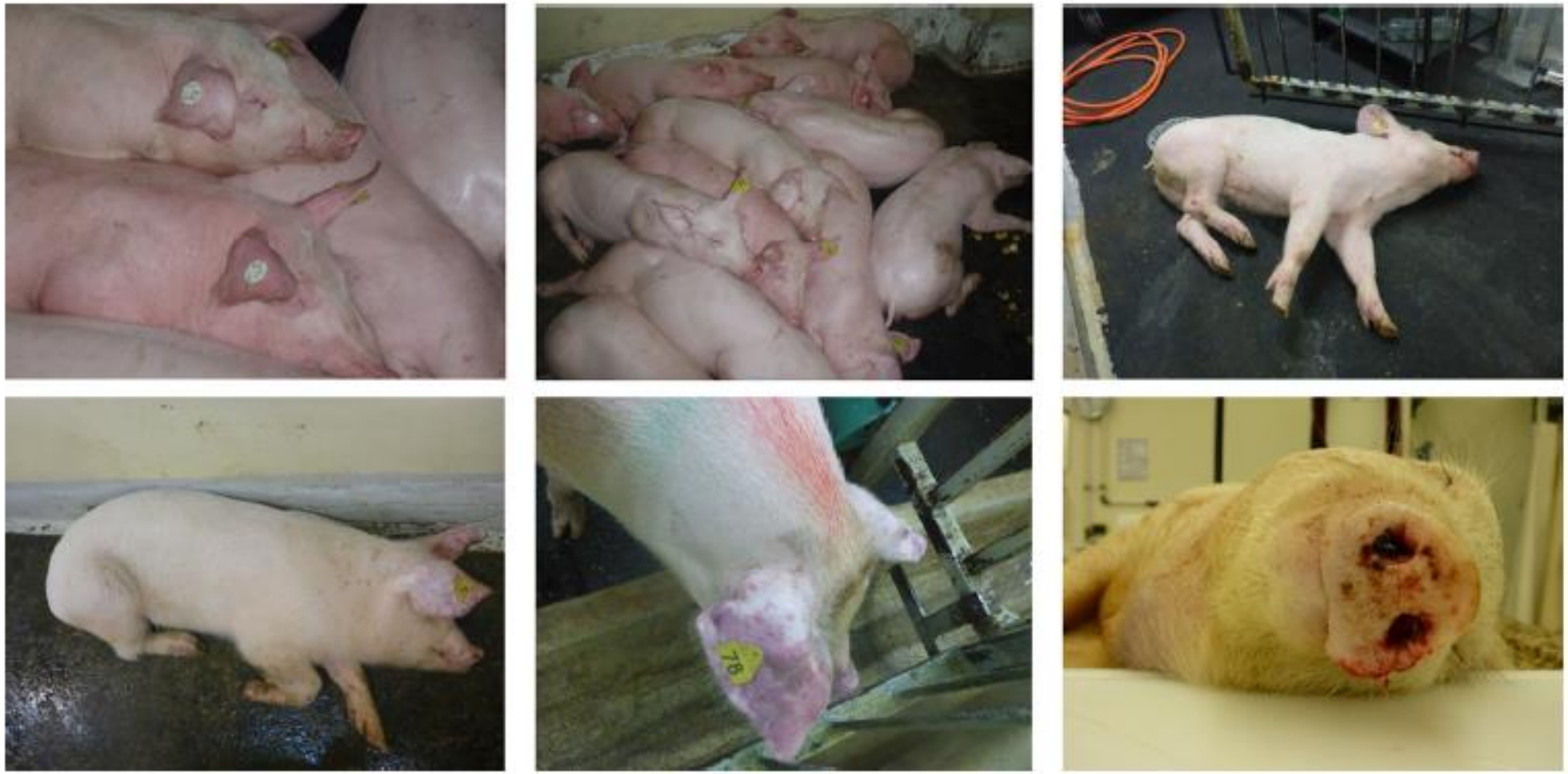


Fig. 2. Clinical signs of domestic pigs upon infection with highly virulent ASFV strains. First signs are observed app. four days post infection. They include high fever, reluctance to move, inappetence, and huddling (upper row left and center). Some animals develop conjunctivitis and gastro-intestinal signs (vomiting, diarrhea). With progression of the disease, animals become somnolent (lower row left), appear desorientated, and show dyspnea. In the final phase, affected animals may show seizures (upper row right) and haemorrhages (skin haemorrhages in the lower row center, epistaxis lower row right).

Fig. 3. Clinical signs in wild boar. The signs resemble the courses in domestic pigs. Depression and reduced liveliness are seen in most animal (see upper row left and center, lower row right). The same is true for dyspnea (the animal in the upper row right showed severe respiratory distress). Hind leg paresis (lower row left) and seizures (lower row center) can be observed in the final stage.

Lesioni anatomopatologiche macroscopiche

- Variano in gravità come i segni clinici tra forme iperacute, acute e croniche/asintomatiche
- Emorragie cutanee con contorno iperemico/cianotico bluastro, esito prima della DIC/trombosi e vasculite dei vasi del derma, poi della sindrome emorragica
  - Orecchie
  - Arti
  - Grugno
  - Fianco
- Linfoadenomegalia emorragica multifocale (+++linfonodi ipogastrici, epatici, meseraici ed iliaci)
- Vario grado di splenomegalia (fino a 4 volte) con emorragie ed infarti. *Consistenza friabile*
- Edema polmonare e polmonite interstiziale (eliminazione del virus con l'espettorato/tosse)
  - Polmonite lobulare multifocale da sovrainfezioni nelle forme subacute e croniche
- Edema della colecisti con fango biliare e calcolosi (eliminazione del virus con le feci)
- Versamenti cavità sierose (pleuriche, peritoneali pericardiche) soprattutto nelle forme subacute
- Petecchie/ulcere:
  - Tonsille
  - Vescica
  - Rene (rene a uovo di tacchino)
  - Stomaco e Intestino
  - Epicardio
  - Pleure

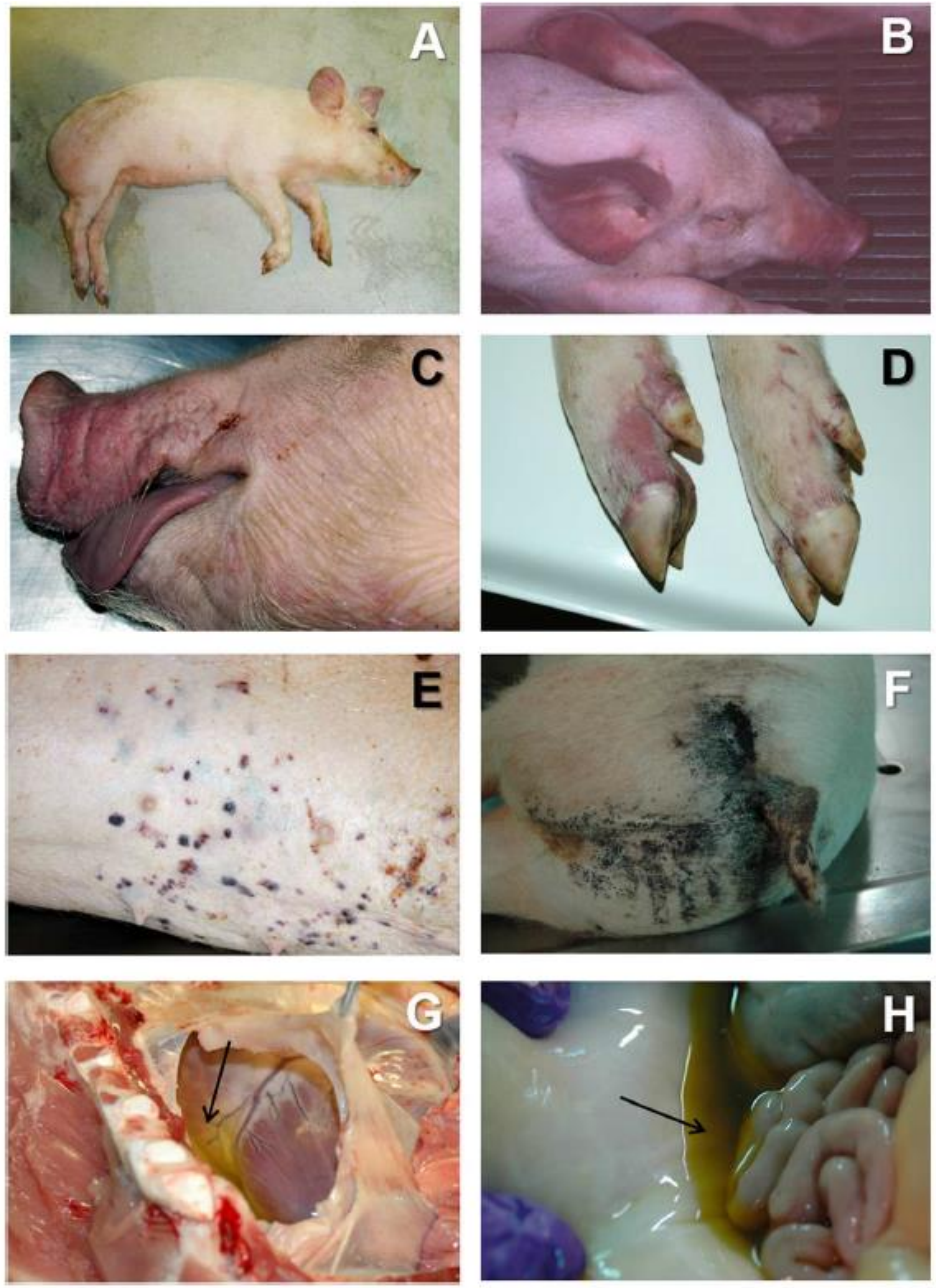


FIGURE 1 | (A) Lethargic animal in acute ASF. The animal show cyanosis ion the ears abdomen and limbs. **(B)** Severe cyanosis in an animal suffering from acute ASF, associated to very high hyperthermia (41–42°C). **(C)** Cyanosis in the snout and lips in acute ASF. **(D)** Cyanosis in the limbs in acute ASF. **(E)** Multifocal petechiae and ecchymosis in the skin in acute ASF. **(F)** Blood-stained perianal area in a pig affected by subacute ASF. **(G)** Severe hydropericardium (arrow) in subacute ASF. **(H)** Moderate to severe ascites (arrow) in subacute ASF.

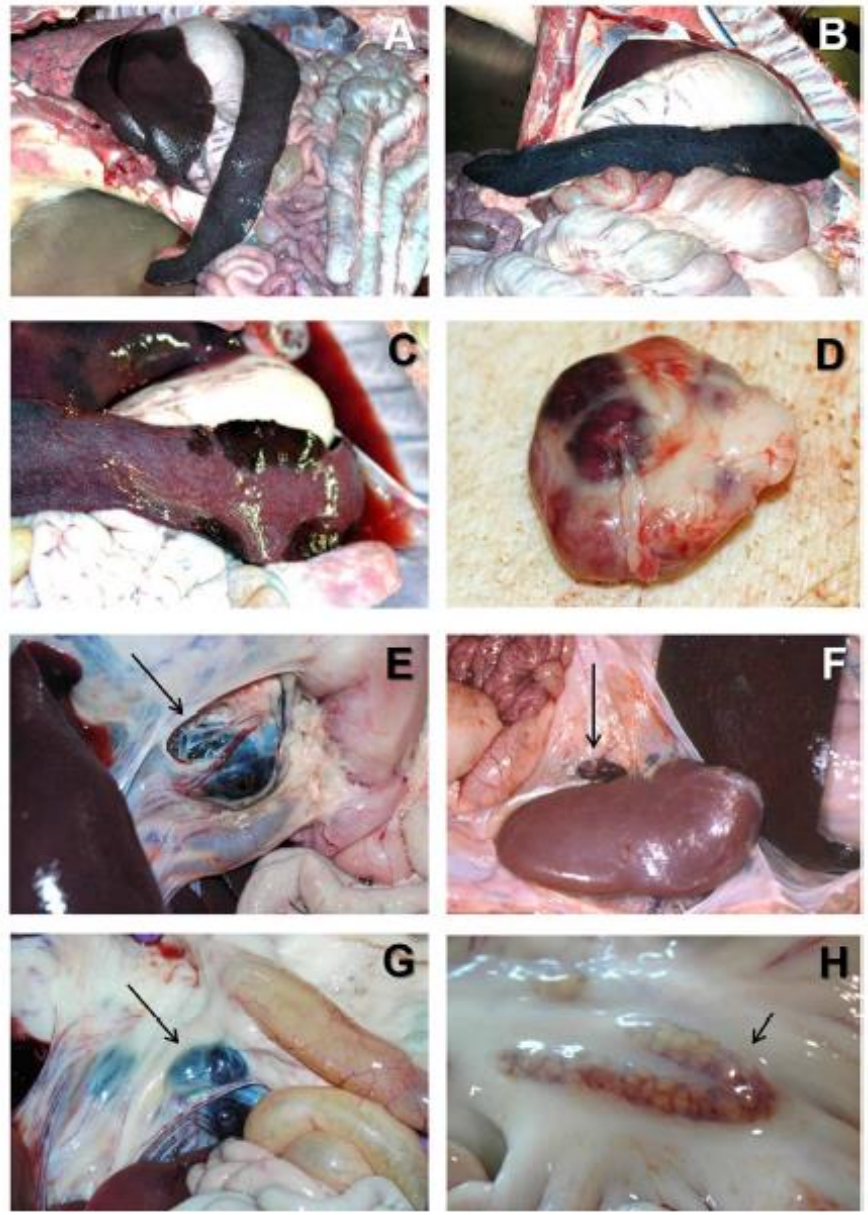


FIGURE 2 | (A) Severe hemorrhagic splenomegaly observed at the opening of the abdominal cavity of an animal with acute ASF. The liver is severely congested. **(B)** Very large, dark colored spleen with rounded edges (hemorrhagic splenomegaly), and occupying a large volume of the abdominal cavity in acute ASF. **(C)** Multiple areas of partial hemorrhagic splenomegaly in the spleen from an animal with subacute ASF. **(D)** Multifocal hemorrhages in a lymph node with a marbled appearance in acute ASF. **(E)** Severe hemorrhagic lymphadenopathy in the gastrohepatic lymph node (arrow) in acute ASF. **(F)** Severe hemorrhagic lymphadenopathy in the renal lymph node (arrow) in acute ASF. **(G)** Severe hemorrhagic lymphadenopathy in the ileocaecal lymph node (arrow) in acute ASF. **(H)** Moderate hemorrhagic lymphadenopathy in the mesenteric lymph node (arrow) in acute ASF.

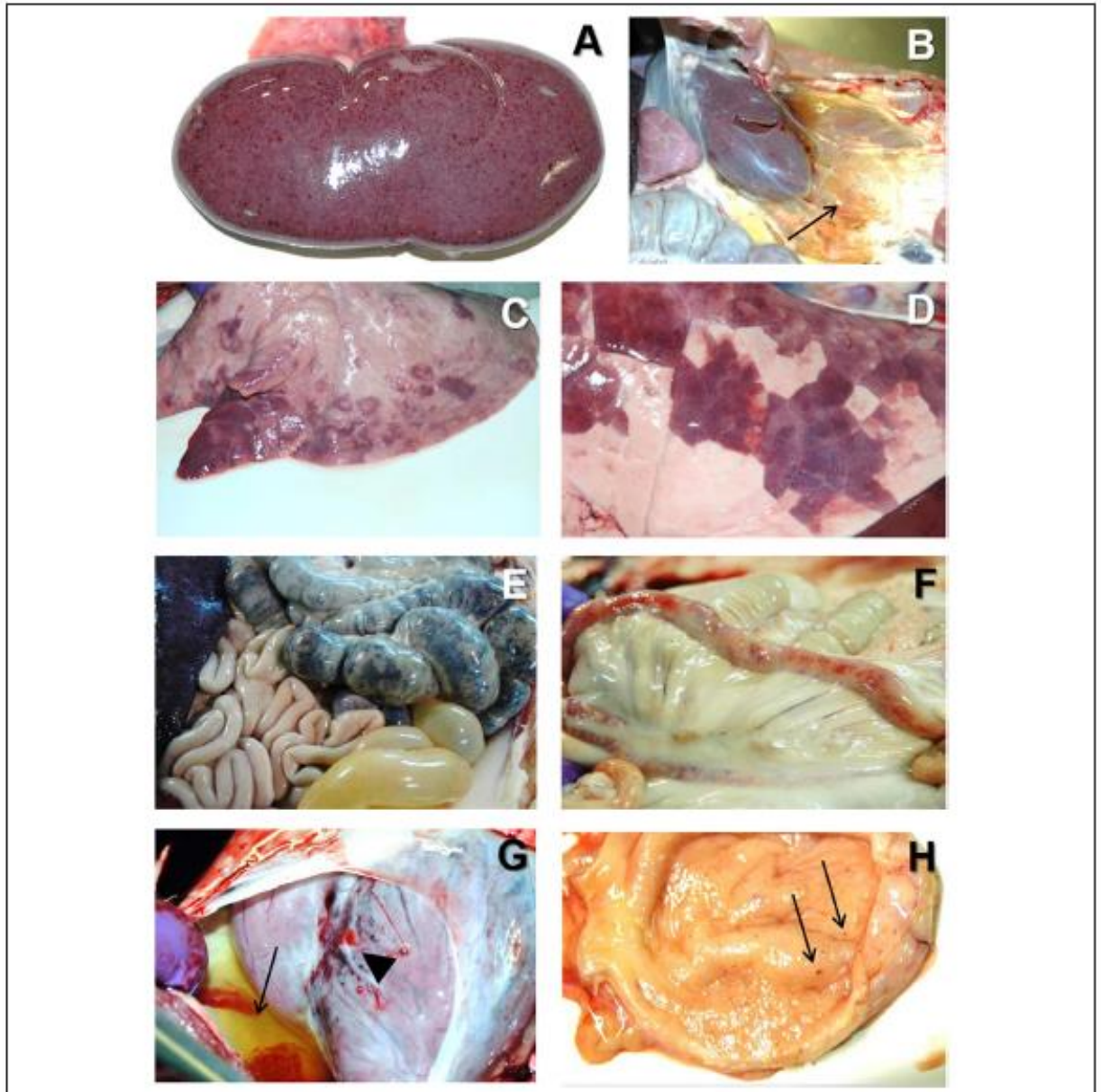
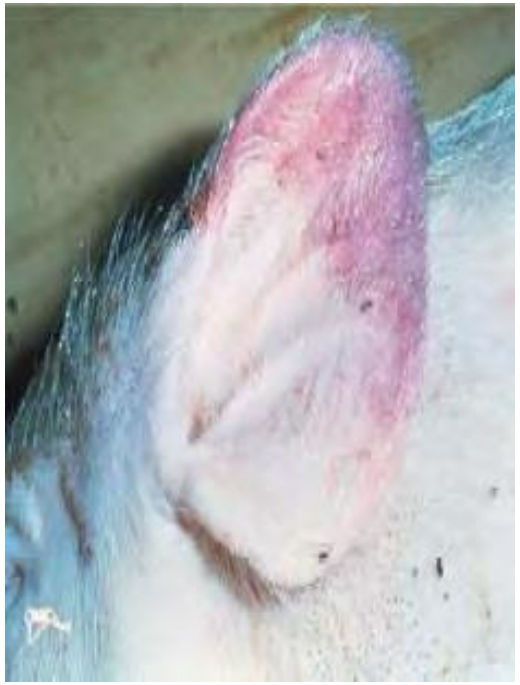
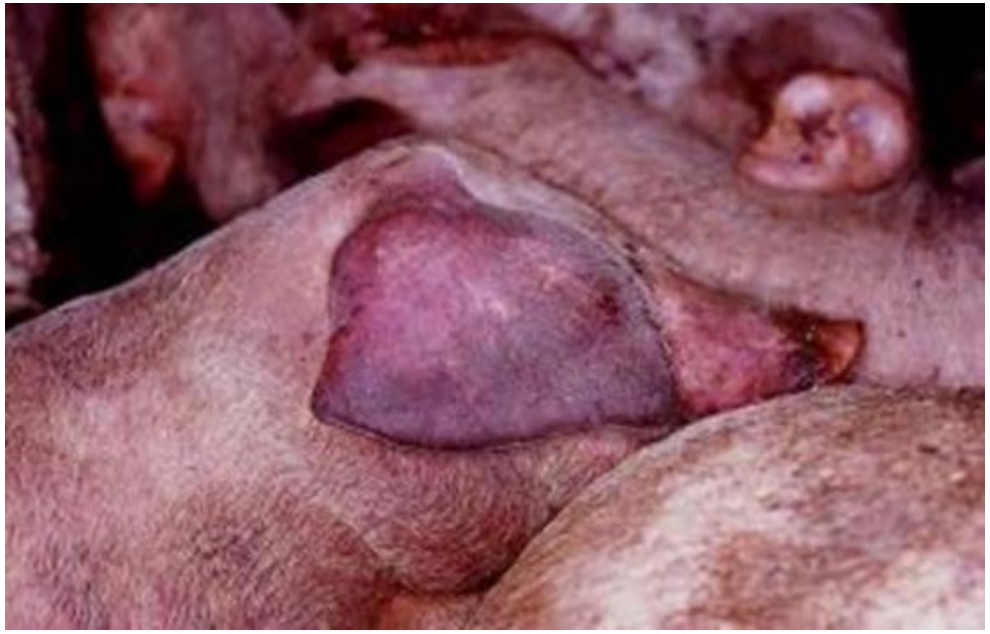


FIGURE 3 | (A) Multiple petechial hemorrhages in the cortical surface of the kidney in acute ASF. **(B)** Severe perirenal oedema (arrow) in a pig with subacute ASF. **(C)** Multifocal areas of lung consolidation and pulmonary oedema in subacute ASF. **(D)** Multifocal pneumonia with dark color areas in the diaphragmatic lobe of the lung in subacute ASF. **(E)** Severe extensive hemorrhagic colitis in subacute ASF. **(F)** Multiple petechial hemorrhages in the serosa of the small intestine in acute ASF. **(G)** Multiple petechial ad ecchymotic hemorrhages in the epicardium (arrowhead) together with severe hydropericardium (arrow) in subacute ASF. **(H)** Multiple petechial hemorrhages in the mucosa of the urinary bladder in acute ASF.



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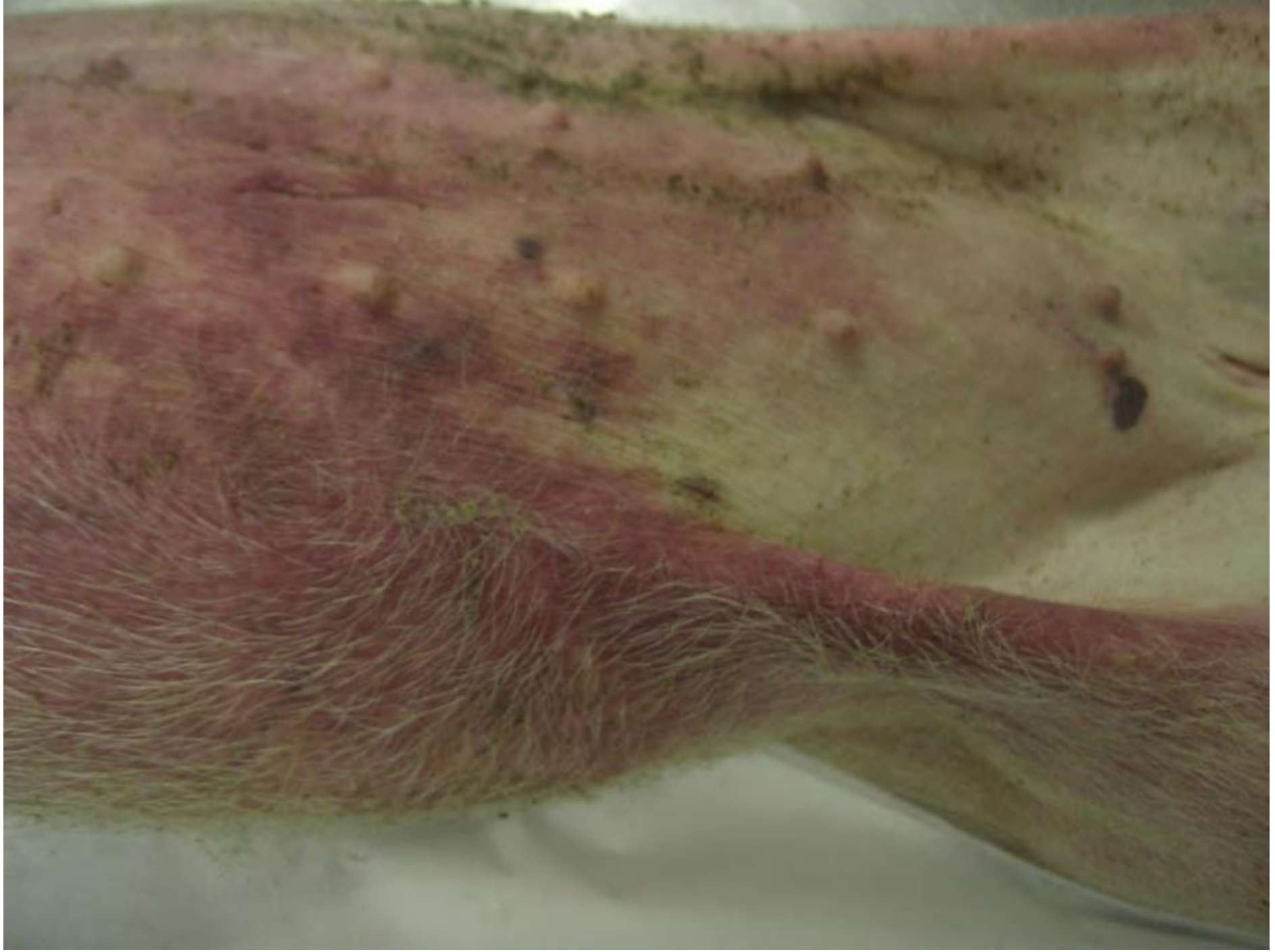

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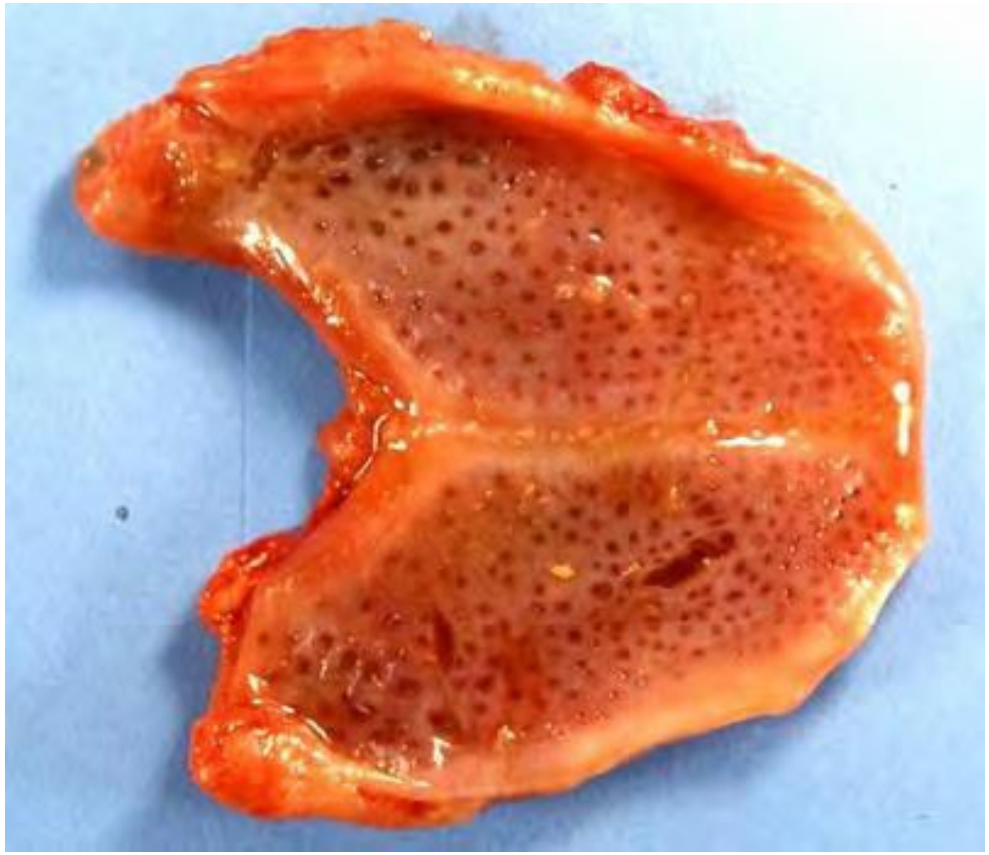

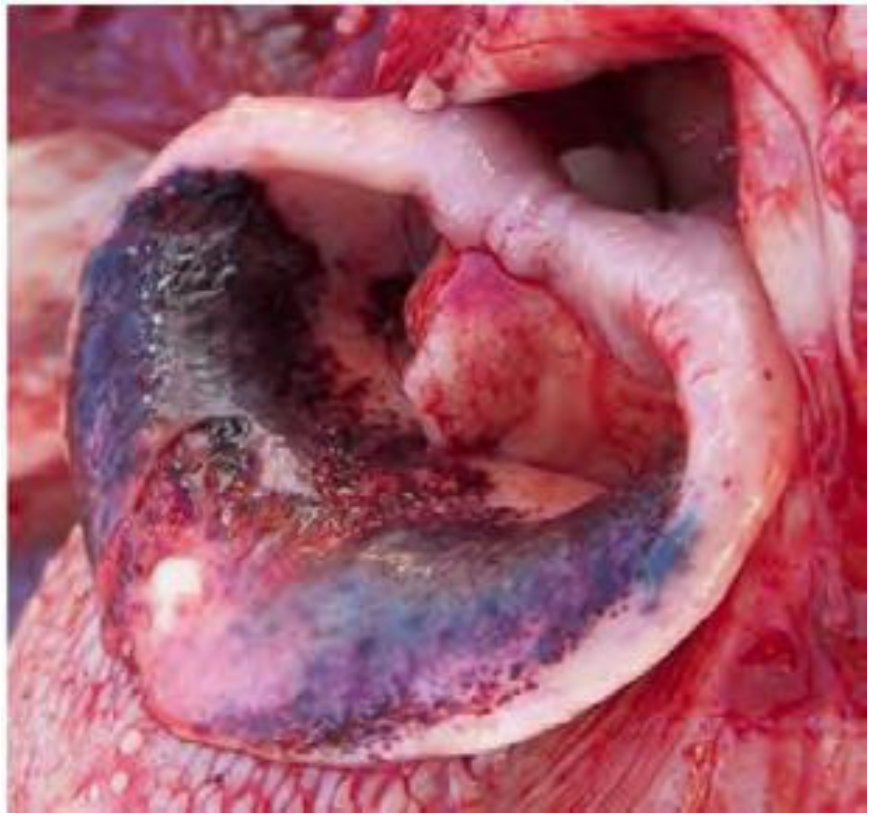

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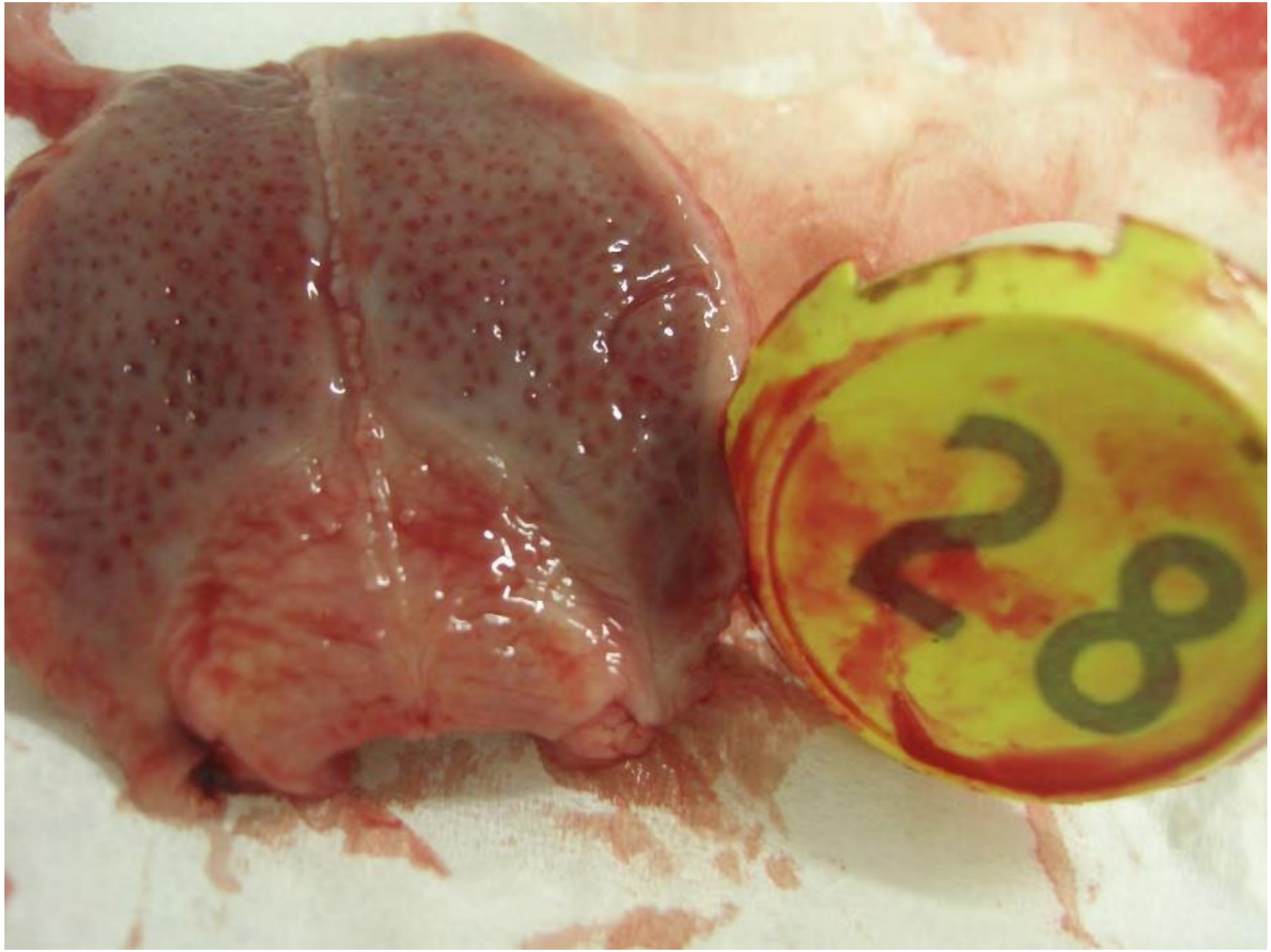

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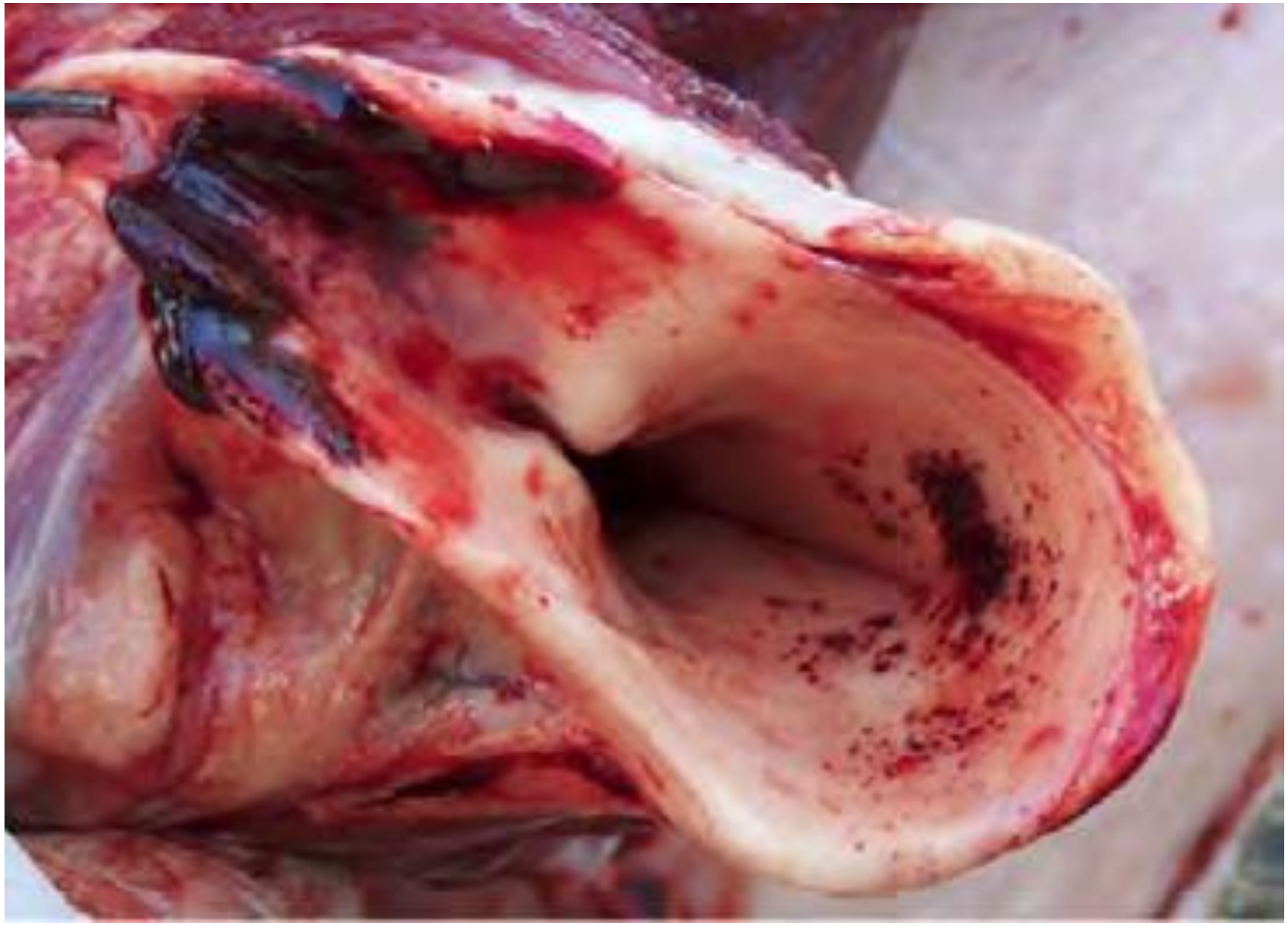

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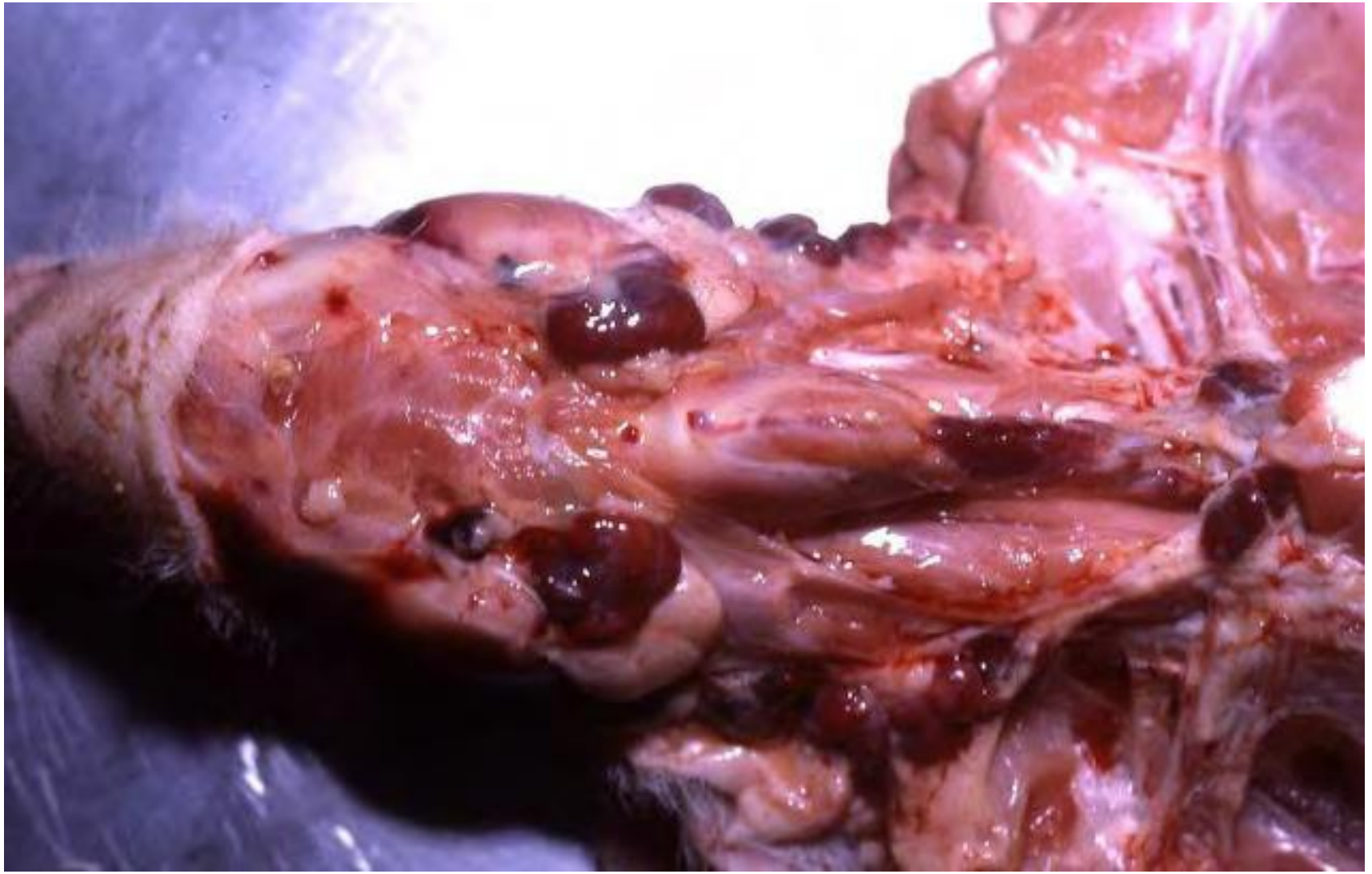

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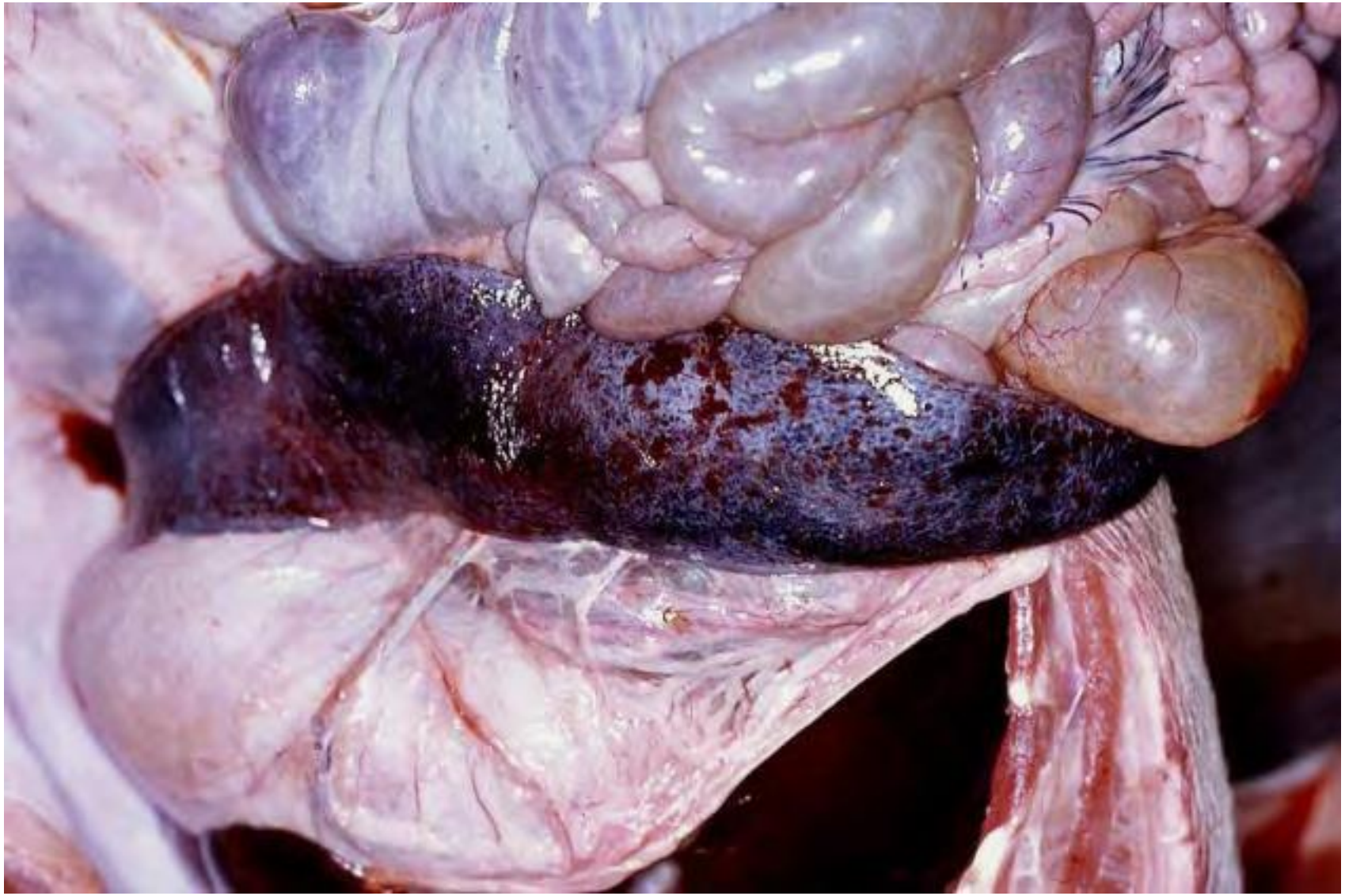

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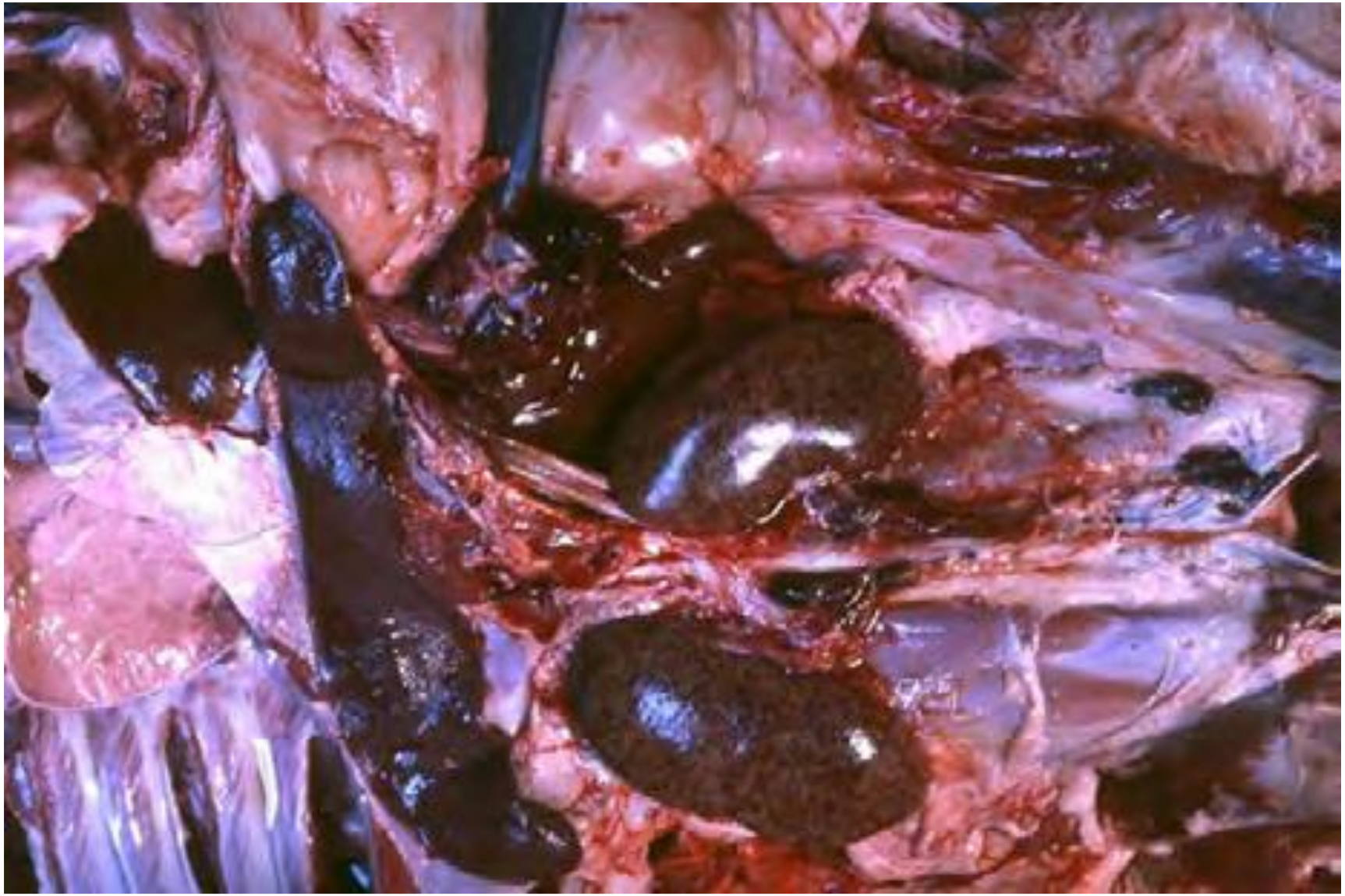

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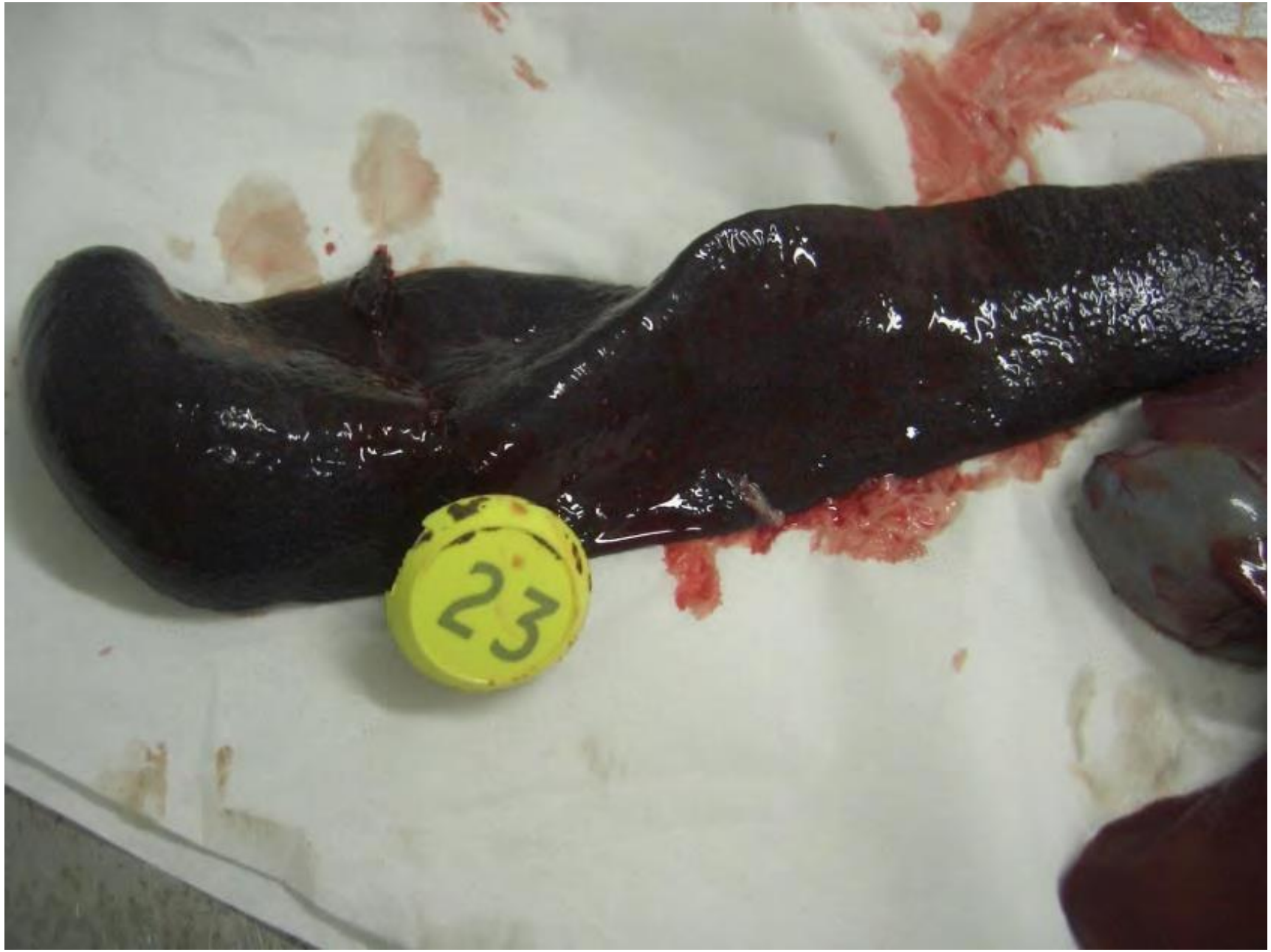

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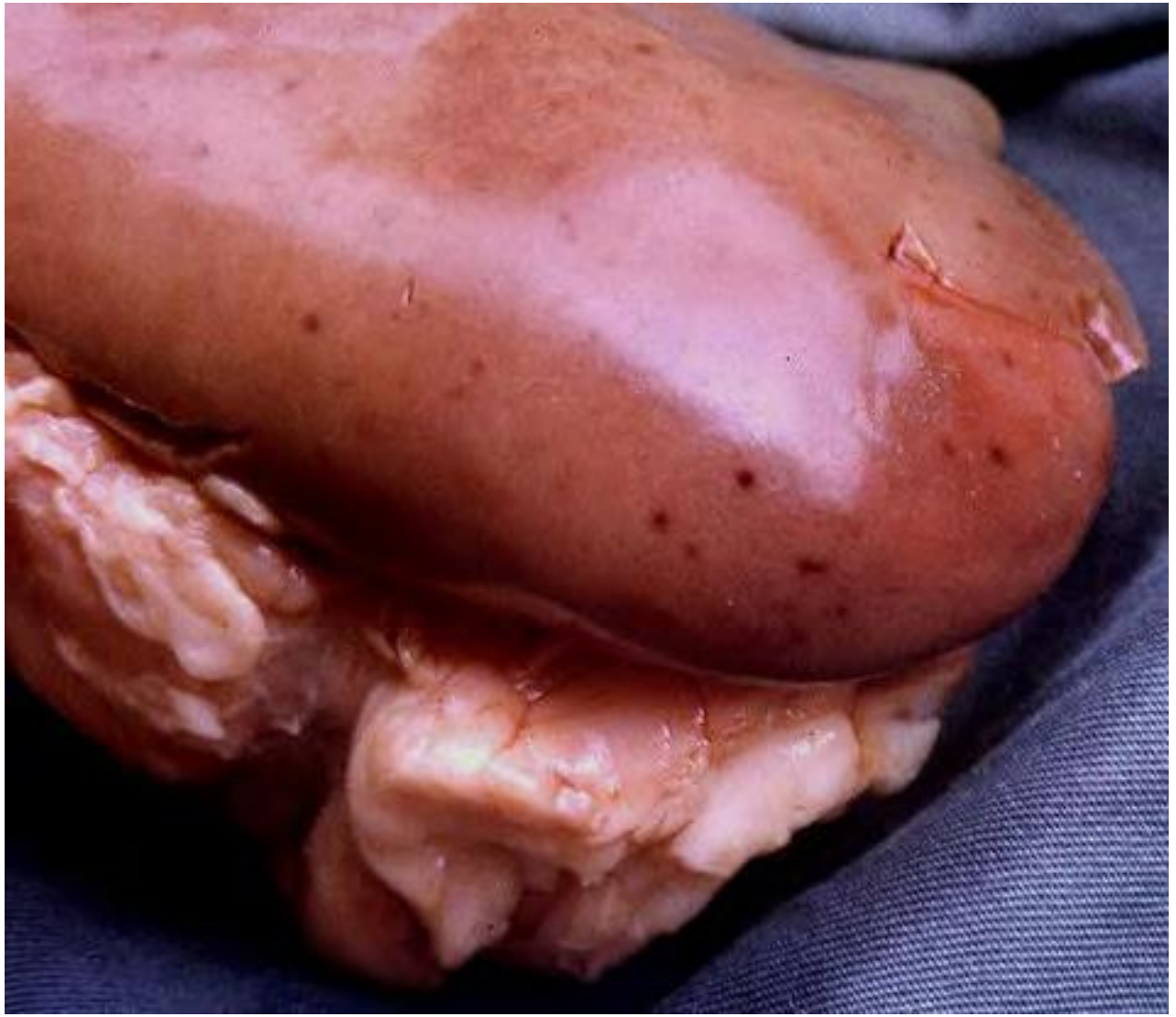

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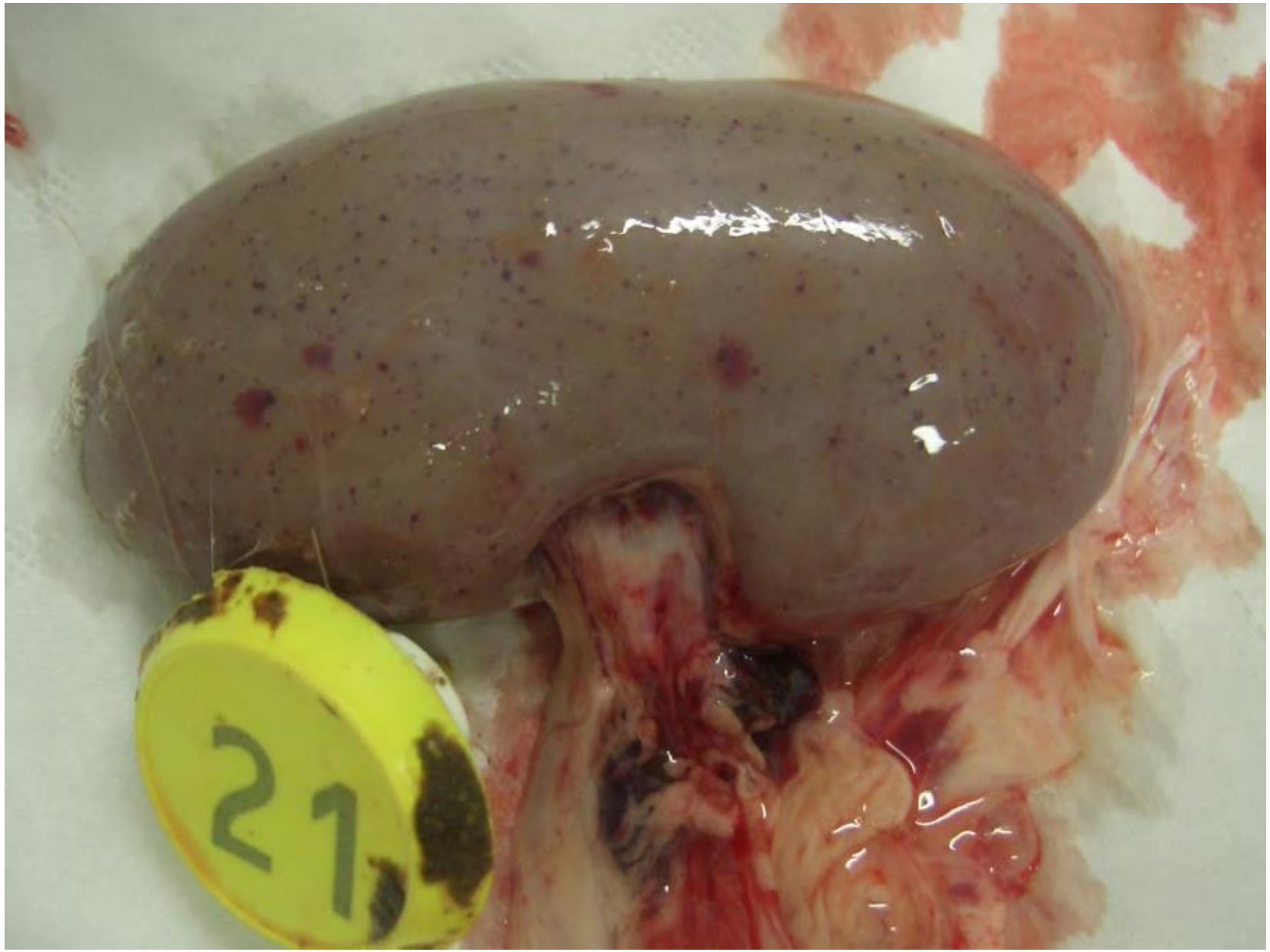

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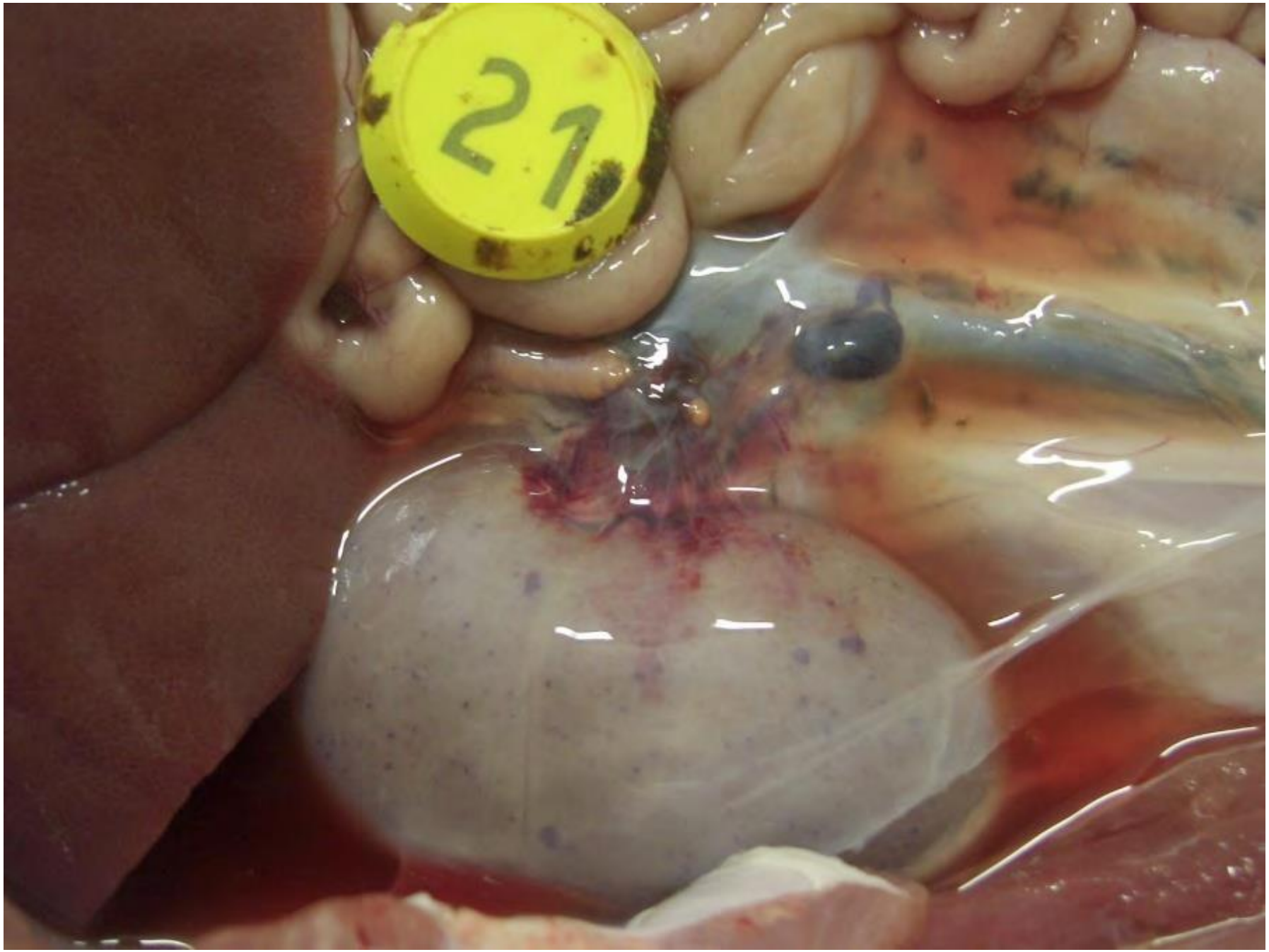

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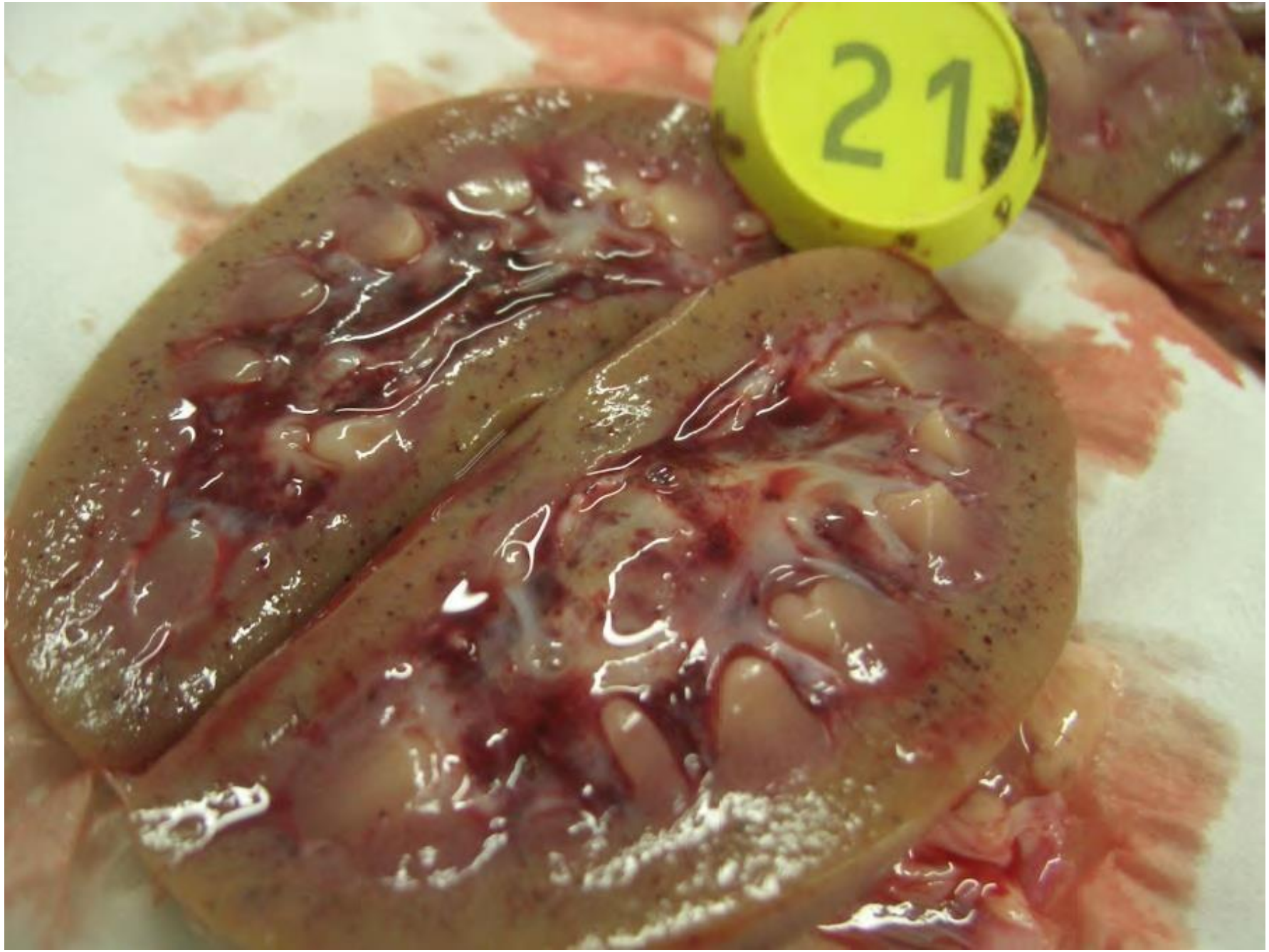

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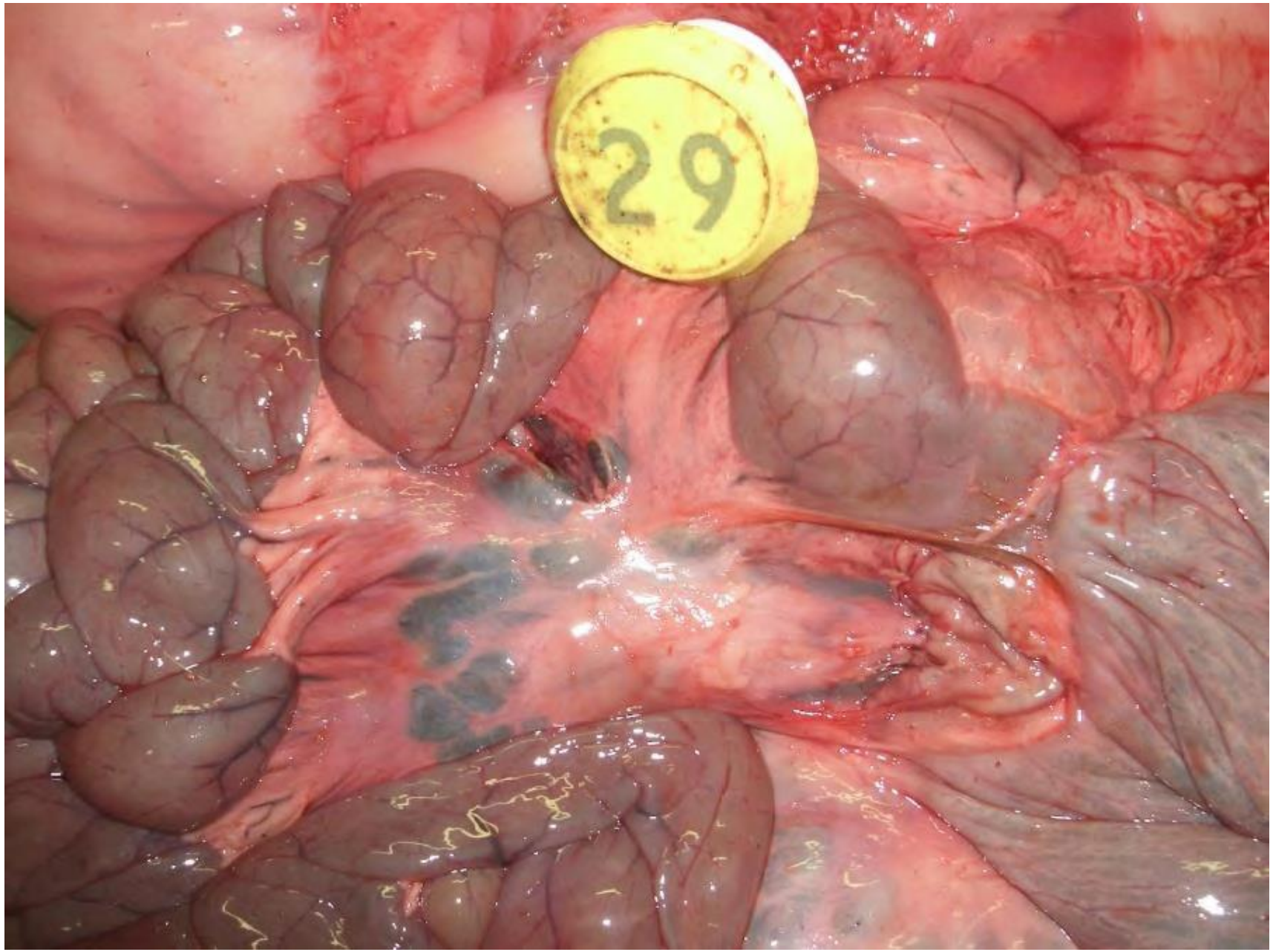

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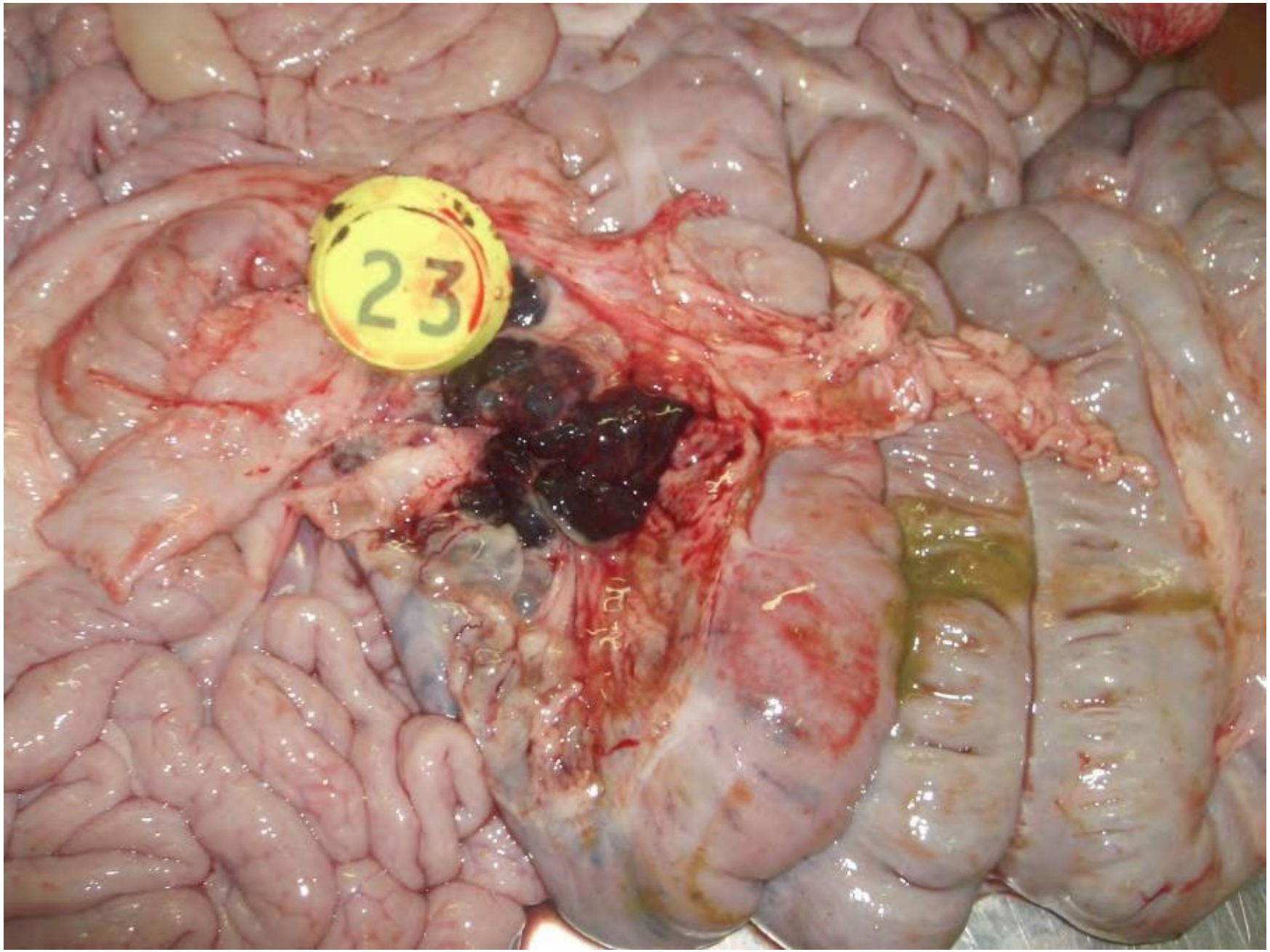
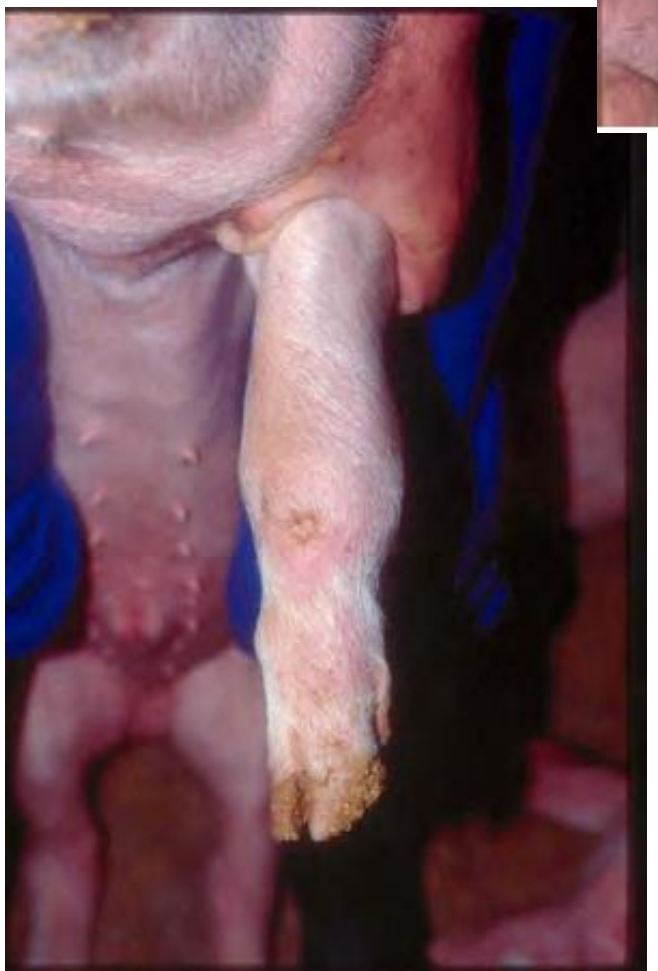


Foto: IZS UM

Forme croniche

- Febbri transitorie e ricorrenti
- Crescita stentata
- Polmonite e sovrainfezioni respiratorie
  - lesioni necrotiche caseose che mineralizzano
- Ulcere cutanee
- Problemi articolari



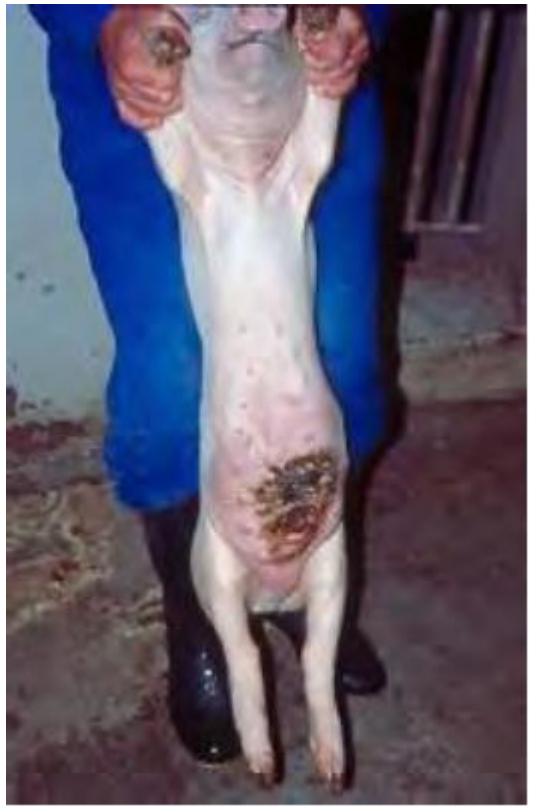


FIGURE 17

Typical lesions observed in chronic forms of African swine fever

A-F. *Moderate to severe joint swelling, often combined with reddened areas of skin that become raised and necrotic.*

G. *Additional necropsy findings include edematous lymph nodes.*

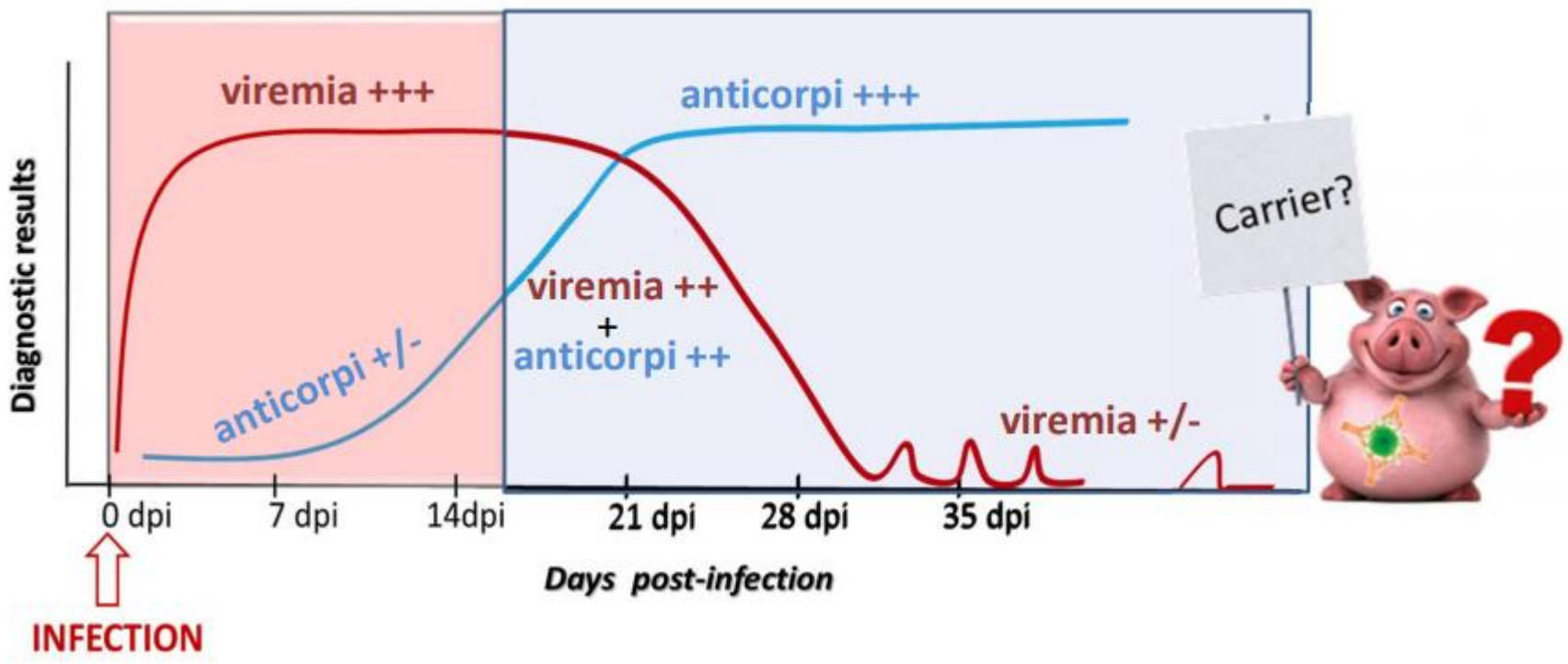
H. *Pneumonia with caseous necrosis and mineralization of the lungs.*

Fonte: FAO Manual –African Swine Fever detection and diagnosis

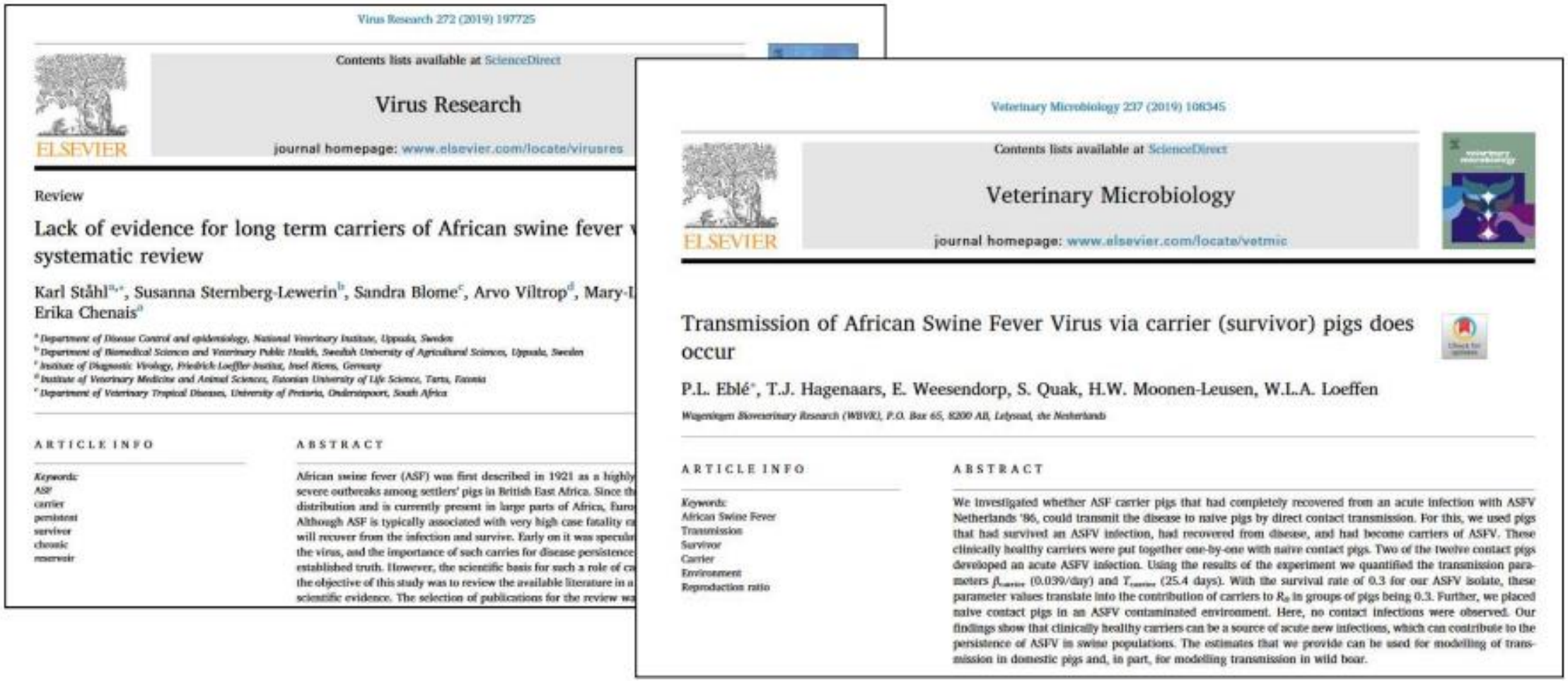
Se sopravvivono???
PSA Carrier Status (animali persistentemente infetti)

- ✓Animali convalescenti possono diventare carrier
- ✓Presenza contemporanea di Virus + Ab:
  - viremia segnalata per 4-5 settimane con evidenze fino a 11 mesi
  - Localizzazione virale in organi linfoidi
  - Contemporanea sieroconversione e presenza del virus
- ✓Possibili fenomeni di riacutizzazione ed eliminazione virale
- ✓Domande:
  - ✓Reale incidenza?
  - ✓Significato epidemiologico?

Carrier Status



Carrier Status



Virus Research 272 (2019) 197725

Contents lists available at ScienceDirect

Virus Research

journal homepage: www.elsevier.com/locate/virusres

Review

Lack of evidence for long term carriers of African swine fever v
systematic review

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ARTICLE INFO

Keywords:
ASF
carrier
persistent
survivor
chronic
reservoir

ABSTRACT

African swine fever (ASF) was first described in 1921 as a highly
severe outbreaks among settlers' pigs in British East Africa. Since th
distribution and is currently present in large parts of Africa, Euro
Although ASF is typically associated with very high case fatality r
will recover from the infection and survive. Early on it was specula
the virus, and the importance of such carries for disease persistence
established truth. However, the scientific basis for such a role of ca
the objective of this study was to review the available literature in a
scientific evidence. The selection of publications for the review wa

Veterinary Microbiology 237 (2019) 108345

Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

Transmission of African Swine Fever Virus via carrier (survivor) pigs does occur

P.L. Eblé*, T.J. Hagenaars, E. Weesendorp, S. Quak, H.W. Moonen-Leusen, W.L.A. Loeffen

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ARTICLE INFO

Keywords:
African Swine Fever
Transmission
Survivor
Carrier
Environment
Reproduction ratio

ABSTRACT

We investigated whether ASF carrier pigs that had completely recovered from an acute infection with ASFV Netherlands '86, could transmit the disease to naive pigs by direct contact transmission. For this, we used pigs that had survived an ASFV infection, had recovered from disease, and had become carriers of ASFV. These clinically healthy carriers were put together one-by-one with naive contact pigs. Two of the twelve contact pigs developed an acute ASFV infection. Using the results of the experiment we quantified the transmission parameters $\beta_{carrier}$ (0.039/day) and $T_{carrier}$ (25.4 days). With the survival rate of 0.3 for our ASFV isolate, these parameter values translate into the contribution of carriers to R_0 in groups of pigs being 0.3. Further, we placed naive contact pigs in an ASFV contaminated environment. Here, no contact infections were observed. Our findings show that clinically healthy carriers can be a source of acute new infections, which can contribute to the persistence of ASFV in swine populations. The estimates that we provide can be used for modelling of transmission in domestic pigs and, in part, for modelling transmission in wild boar.

The Veterinary Journal 233 (2018) 41–48

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Review

African swine fever: A re-emerging viral disease threatening the global pig industry

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ARTICLE INFO

Keywords:
African swine fever
Control
Epidemiology
Immune responses
Pathogenesis
Vaccination

ABSTRACT

African swine fever (ASF) recently has spread beyond sub-Saharan Africa to the Trans-Caucasus region, parts of the Russian Federation and Eastern Europe. In this new epidemiological scenario, the disease has similarities, but also important differences, compared to the situation in Africa, including the substantial involvement of wild boar. A better understanding of this new situation will enable better control and prevent further spread of disease. In this article, these different scenarios are compared, and recent information on the pathogenesis of ASF virus strains, the immune response to infection and prospects for developing vaccines is presented. Knowledge gaps and the prospects for future control are discussed.

The existence of sub-clinical or inapparent infections has also been suggested in survivor pigs, which are infected but do not display clinical signs or the lesions described in chronic disease. Virus can persist for prolonged periods in tissues or blood from recovered pigs or following infection with low virulence isolates, which might contribute to virus transmission, disease persistence, sporadic outbreaks and ASFV introduction into disease-free zones (Penrith and Vosloo, 2009; Costard et al., 2013; Gallardo et al., 2015). Recent studies in Africa have identified ASFV sequences in apparently healthy pigs in Uganda (Kalenzi Atuhaire et al., 2013) and Kenya (Thomas et al., 2016), suggesting that reduced virulence isolates may be circulating in these regions. There is limited experimental evidence for transmission from persistently infected to naïve animals. The relevance of carrier animals in the field is not clear.

A potential role of carrier domestic pigs as a source of infection has been suggested in Kenya and Uganda, in which healthy pigs can

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ORIGINAL ARTICLE

WILEY Transboundary and Emerging Diseases

No evidence for long-term carrier status of pigs after African swine fever virus infection

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Funding information
Friedrich-Loeffler-Institut, Intramural Funding

Summary

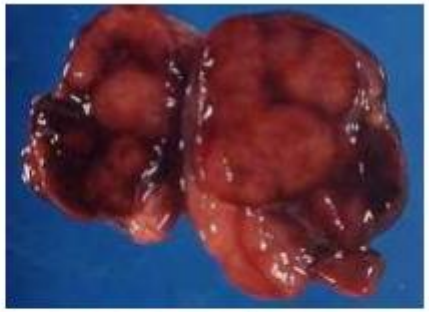
This study targeted the assessment of a potential African swine fever virus (ASFV) carrier state of 30 pigs in total which were allowed to recover from infection with ASFV "Netherlands'86" prior exposure to six healthy sentinel pigs for more than 2 months. Throughout the whole trial, blood and swab samples were subjected to routine virological and serological investigations. At the end of the trial, necropsy of all animals was performed and viral persistence and distribution were assessed. Upon infection, a wide range of clinical and pathomorphological signs were observed. After an initial acute phase in all experimentally inoculated pigs, 66.6% recovered completely and seroconverted. However, viral genome was detectable in blood samples for up to 91 days. Lethal outcomes were observed in 33.3% of the pigs with both acute and prolonged courses. No ASFV transmission occurred over the whole in-contact phase from survivors to sentinels. Similarly, infectious ASFV was not detected in any of the tissue samples from ASFV convalescent and in-contact pigs. These findings indicate that the suggested role of ASFV survivors is overestimated and has to be reconsidered thoroughly for future risk assessments.

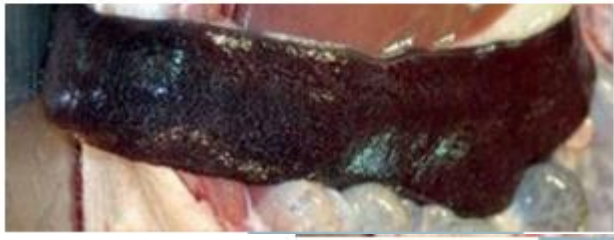
KEYWORDS
African swine fever, carrier state, long-term persistence, transmission, virus shedding

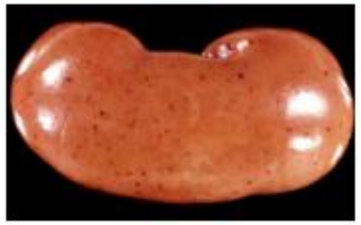
Diagnosi

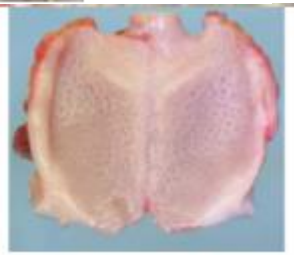
✓Raccolta campioni:

- Animali in vita: sangue con e senza edta
- Animali morti/necro:
  - milza
  - tonsille
  - midollo osseo
  - linfonodi
  - polmone
  - rene



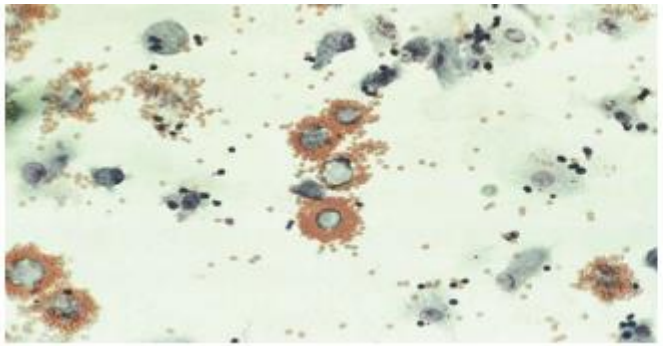






Diagnosi

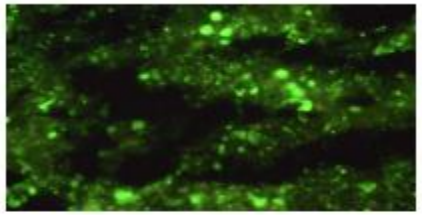
- Diagnosi diretta:
  - ✓Isolamento ed identificazione:
    - colture di monociti, precursori midollari di suino o macrofagi alveolari inoculate con sangue intero o omogenato di organo.
    - Emoadsorbimento di eritrociti di suino sulla superficie delle cellule infette



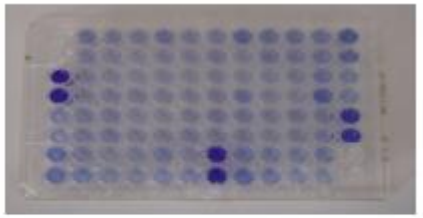
Malmquist, 1960

Diagnosi

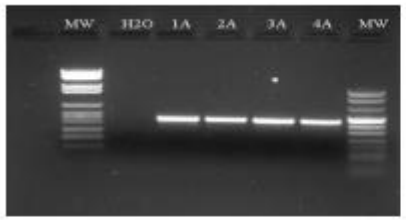
- Diagnosi diretta:
  - ✓Ricerca antigeni virali
    - ✓Immunoistochimica/immunofluorescenza diretta su sezioni istologiche
  - ✓ELISA Ag
    - ✓Proteine nucleocapsidiche
  - ✓PCR e Real Time PCR

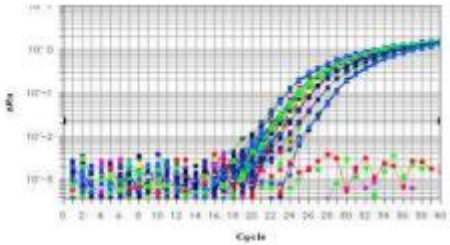


IFD



ELISA-Ag





PCR & Real Time PCR

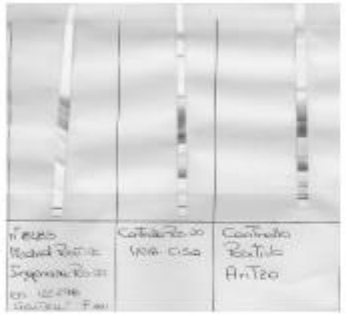
Diagnosi

- Diagnosi indiretta:
  - ✓ELISA Ab
  - ✓Pen side test
  - ✓Immunoblotting
  - ✓Immunoperossidasi

ELISA-Ab

Screening

Pen side test (Ag&Ab)



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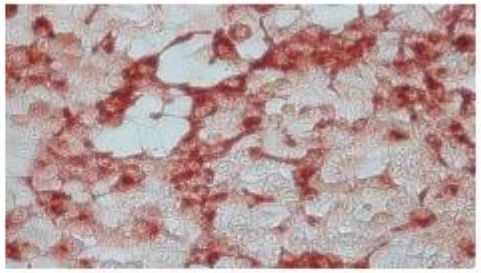

IPT

Conferma

Vaccini

- Virus inattivato non induce protezione
- Adjuvanti classici non efficaci
- Passaggi seriali di vaccini attenuati hanno causato dagli anni ‘60 reazioni post-vaccinali (efficace ma non sicuro)
- Virus molto complesso (> 80 proteine), ancora non conosciuti gli epitopi target
- Fase intracellulare difficilmente «attaccabile» dalla stimolazione vaccinale umorale
- Meccanismi patogenetici indiretti dovuti all’interferenza immunitaria
- Anticorpi neutralizzanti non effettivi
- Complicata la diagnostica DIVA

Vaccini

Vaccine 32 (2014) 3879–3882

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Brief report

Modern adjuvants do not enhance the efficacy of an inactivated African swine fever virus vaccine preparation

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ABSTRACT

African swine fever (ASF) is among the most devastating viral diseases of pigs. In recent years, the disease has spread alarmingly. Despite intensive research activities, promising vaccine candidates are still lacking. For this reason, a study was undertaken to re-assess inactivated ASFV preparations with state-of-the-art adjuvants. Inactivated preparations of ASF virus (ASFV) "Armenia08" were adjuvanted with either Polygen™ or Emulsigen®-D, respectively, and used to immunize six weaner pigs two times with a three-week interval. Six weeks after the first immunization, animals were challenged with the homologues highly virulent ASFV. Although ASFV-specific antibodies were detectable in all but one vaccinated animal prior to challenge, no protective effect of immunization was observed. All animals developed acute-lethal ASF and had to be euthanized within eleven days post challenge. A slightly accelerated clinical course in vaccinees could even indicate an antibody dependent enhancement, which could also influence efficacy of other vaccine approaches.

Vaccini

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Simultaneous Deletion of the *9GL* and *UK* Genes from the African Swine Fever Virus Georgia 2007 Isolate Offers Increased Safety and Protection against Homologous Challenge

Vivian O'Donnell, Guillermo R. Risatti, Lauren G. Holinka, Peter W. Krug, Jolene Carlson, Lauro Velazquez-Salinas, Paul A. Azzinaro, Douglas P. Gladue, Manuel V. Borca

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African swine fever: A review of cleaning and disinfection procedures in commercial pig holdings

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ABSTRACT

African swine fever (ASF) is one of the most important diseases in pigs. Since there are no effective vaccines against the virus, farm biosecurity and good farming practices are the only effective tools to prevent the spread of the ASF virus (ASFV) in pig holdings. Hence, an important component of farm biosecurity is the Cleaning and Disinfection (C&D) procedure.

Precise indications regarding the ideal disinfectant against ASFV are lacking, but every country has approved and/or authorized a list of biocides effective against ASFV. Lipidic solvents, which destroy the envelope of the virus and commercial disinfectants based on iodine and phenolic compounds are effective in inactivating the ASFV. This review describes the C&D protocol to apply in pig holdings with particular reference to ASFV.