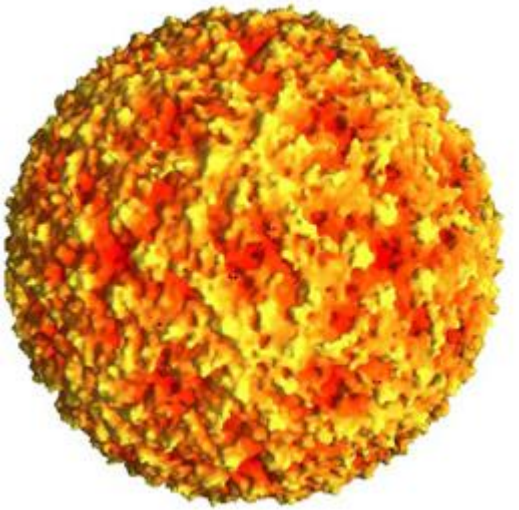
FEBRE AFTOSA



Prof. Dr. Paulo Eduardo Brandão
Departamento de Medicina Veterinária Preventiva e Saúde Animal
Faculdade de Medicina Veterinária e Zootecnia
Universidade de São Paulo

11/06/2017

Doença havia sido erradicada em 2009

Total animals affected

Species	Susceptible	Cases	Deaths	Killed and disposed of
Cattle	136	7	0	136

Measures applied

Movement control inside the country
Surveillance outside containment and/or protection zone
Surveillance within containment and/or protection zone
Traceability
Quarantine
Official destruction of animal products
Official disposal of carcasses, by-products and waste
Stamping out
Disinfection
Vaccination permitted (if a vaccine exists)
No treatment of affected animals

FEBRE AFTOSA

√ Por que é uma doença tão importante em termos $

√ Como se transmite

√ Inespecificidade dos sintomas

√ Por que a tecnologia de vacinas é um ponto crítico atualmente no controle

FEBRE AFTOSA

1. DEFINIÇÃO

DOENÇA VESICULAR INFECTO-CONTAGIOSA DE *ARTIODACTYLA* CAUSADA POR UM PICORNAVÍRUS (*FOOT AND MOUTH DISEASE VIRUS,* FMDV)

√ DEBILITANTE AO HOSPEDEIRO

√ ALTA TAXA DE ATAQUE, BAIXA MORTALIDADE

√ ELEVADO INTERESSE POLÍTICO-ECONÔMICO

√ NOTIFICAÇÃO OBRIGATÓRIA

√ SEM TRANSMISSÃO SUSTENTADA EM *H. sapiens sapiens*

1. DEFINIÇÃO

OIE-Listed diseases, infections and infestations in force in 2017

Resolutions passed by the International Committee and recommendations issued by the Regional Commissions instructed the OIE Headquarters to establish a single OIE list of notifiable terrestrial and aquatic animal diseases to replace the former Lists A and B.

The aim in drawing up a single list was to be in line with the terminology of the Sanitary and Phytosanitary Agreement of the World Trade Organization, by classifying diseases as specific hazards and giving all listed diseases the same degree of importance in international trade.

In order to create a single list of notifiable diseases, the OIE defined criteria to examine the inclusion or not of a given disease in the OIE single list that were approved in May 2004.

In 2005, the first single list composed of former lists A and B was used, and in the same year, an Ad Hoc Group on disease and pathogenic agents notification was organized to examine diseases according to the adopted criteria for listing diseases, and proposed a new list of diseases meeting the criteria that entered into force in 2006.

The list is reviewed on a regular basis and in case of modifications adopted by the World Assembly of Delegates at its annual General Session, the new list comes into force on 1 January of the following year.

For year **2017**, the list includes **116** animal diseases, infections and infestations.

Multiple species diseases, infections and infestations

- Anthrax
- Bluetongue
- Crimean Congo haemorrhagic fever
- Epizootic haemorrhagic disease
- Equine encephalomyelitis (Eastern)
- Heartwater
- Infection with Aujeszky's disease virus
- Infection with *Brucella abortus, Brucella melitensis and Brucella suis*
- Infection with *Echinococcus granulosus*
- Infection with *Echinococcus multilocularis*
- Infection with foot and mouth disease virus
- Infection with rabies virus

Cattle diseases and infections

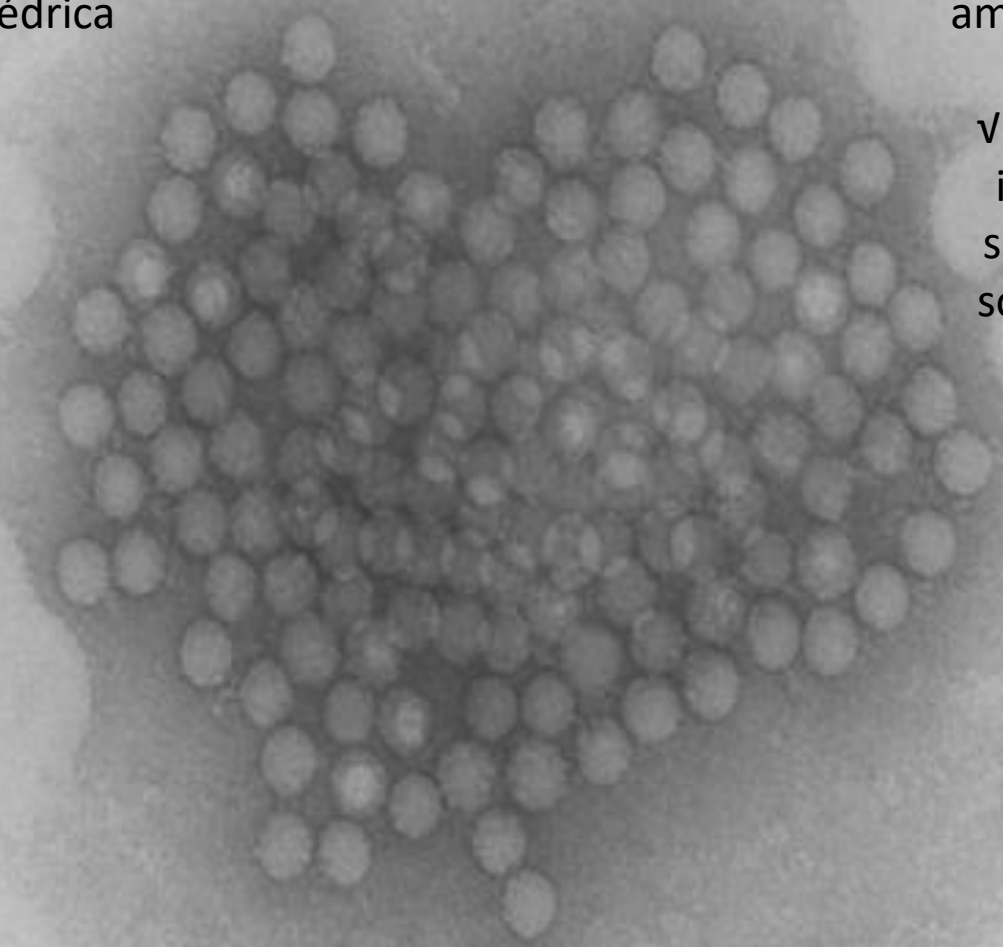
- Bovine anaplasmosis
- Bovine babesiosis
- Bovine genital campylobacteriosis
- Bovine spongiform encephalopathy
- Bovine tuberculosis
- Bovine viral diarrhoea
- Enzootic bovine leukosis
- Haemorrhagic septicaemia
- Infectious bovine rhinotracheitis/infectious pustular vulvovaginitis
- Infection with *Mycoplasma mycoides* subsp. *mycoides* SC (Contagious bovine pleuropneumonia)
- Lumpy skin disease
- Theileriosis

http://www.oie.int/

FEBRE AFTOSA

2. VÍRUS DA FEBRE AFTOSA

Não-envelopado
ss+RNA
Simetria icosaédrica
25-30nm



√ Resistência: éter, álcool, clorofórmio, iodóforos, amônio quaternário e fenol

√ Sensibilidade: radiação ionizante, hidróxido de sódio 2%, hipoclorito de sódio a 3%, formaldeído, pH<6 e >9

Order	Family	Subfamily	Genus	Type Species
PICORNAVIRALES				
	Dicistroviridae		*Cripavirus*	*Cricket paralysis virus*
			Aparavirus	*Acute bee paralysis virus*
	Iflaviridae		*Iflavirus*	*Infectious flacherie virus*
	Marnaviridae		*Marnavirus*	*Heterosigma akashiwo RNA virus*
	Picornaviridae		*Enterovirus*	*Human enterovirus C*
			Cardiovirus	*Encephalomyocarditis virus*
			Aphthovirus	*Foot-and-mouth disease virus*
			Hepatovirus	*Hepatitis A virus*
			Parechovirus	*Human parechovirus*
			Erbovirus	*Equine rhinitis B virus*
			Kobuvirus	*Aichi virus*
			Teschovirus	*Porcine teschovirus*
			Sapelovirus	*Porcine sapelovirus*
			Senecavirus	*Seneca Valley virus*
			Tremovirus	*Avian encephalomyelitis virus*
			Avihepatovirus	*Duck hepatitis A virus*
	Secoviridae	*Comovirinae*	*Comovirus*	*Cowpea mosaic virus*
			Fabavirus	*Broad bean wilt virus 1*
			Nepovirus	*Tobacco ringspot virus*
		Unassigned	*Cheravirus*	*Cherry rasp leaf virus*
			Sadwavirus	*Satsuma dwarf virus*
			Torradovirus	*Tomato torrado virus*
			Sequivirus	*Parsnip yellow fleck virus*
			Waikavirus	*Rice tungro spherical virus*

Virus Taxonomy
Classification and Nomenclature of Viruses
Ninth Report of the International Committee on Taxonomy of Viruses
Editors
Andrew M.Q. King, Michael J. Adams, Eric B. Carstens, and Elliot J. Lefkowitz

FOOT AND MOUTH DISEASE (FMD) ≠ HAND, FOOT AND MOUTH DISEASE (HFMD)

Arch Virol
DOI 10.1007/s00705-014-2067-6

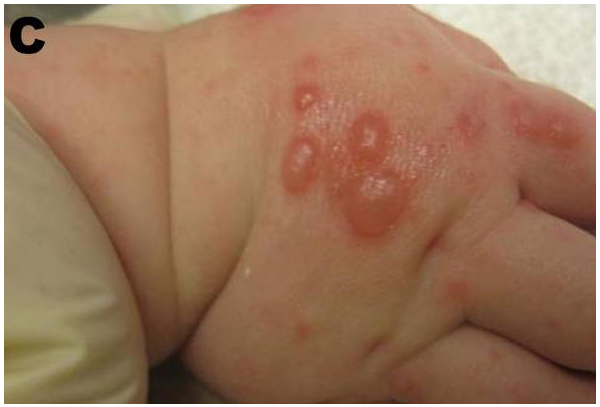
BRIEF REPORT

Genetic characterization of emerging coxsackievirus A12 associated with hand, foot and mouth disease in Qingdao, China

Xiaolin Liu · Naiying Mao · Weisen Yu · Qing Chai · Hui Wang · Weidong Wang · Lijuan Wang · Zhaoguo Wang · Wenbo Xu

Received: 27 December 2013 / Accepted: 22 March 2014

Abstract To characterize the genetic properties of coxsackievirus A12 (CVA12) strains isolated from hand, foot and mouth disease (HFMD) patients in Qingdao during 2008-2011, the complete genome and VP1 coding region were sequenced and analyzed. Phylogenetic analysis showed that all strains from China clustered into three different branches, suggesting multiple lineages of CVA12 co-circulating in Asia. Sequence analysis indicated a monophyletic group only when the P1 region was examined, indicating possible recombination between CVA12 *Picornaviridae* and is most commonly associated with enterovirus 71 (EV71) and coxsackievirus A16 (CVA16) [5]. Although EV71 and CVA16 are the major causative agents of HFMD and are distributed widely, other HEVs, including CVA2, 4, 5, 6, 9 and 10, have been associated with HFMD outbreaks [6–9]. However, the pathogen spectrum of HFMD and the circulation of HEVs have not been fully investigated because of the lack of molecular diagnostic methods in most clinical virology laboratories in China.



Flett K, Youngster I, Huang J, McAdam A, Sandora TJ, Rennick M, et al. Hand, foot, and mouth disease caused by coxsackievirus A6 [letter]. Emerg Infect Dis [Internet]. 2012 Oct http://dx.doi.org/10.3201/eid1810.120813

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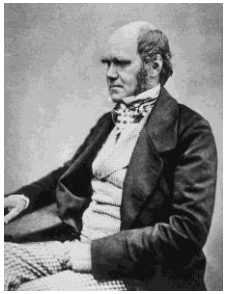


Vírus semelhantes, lesões semelhantes, hospedeiros diferentes:
Ancestralidade?
Paralelismo?

FEBRE AFTOSA

2. VÍRUS DA FEBRE AFTOSA

Diversidade antigênica

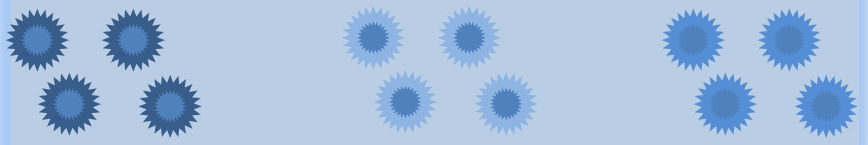
SOROTIPOS (n=7)
A (*Allemagne*)
O (*Oise*, França)
C
SAT (South African Territories) 1
SAT2
SAT 3
Asia1

Identidade de nucleotídeos no genoma total ≤86%

Identidade de nucleotídeos em VP1: 50-70%

Sem imunidade heteróloga entre sorotipos

SUBTIPOS
Populacões de FMDV antigenicamente polimórficas mas pertencentes ao mesmo sorotipo



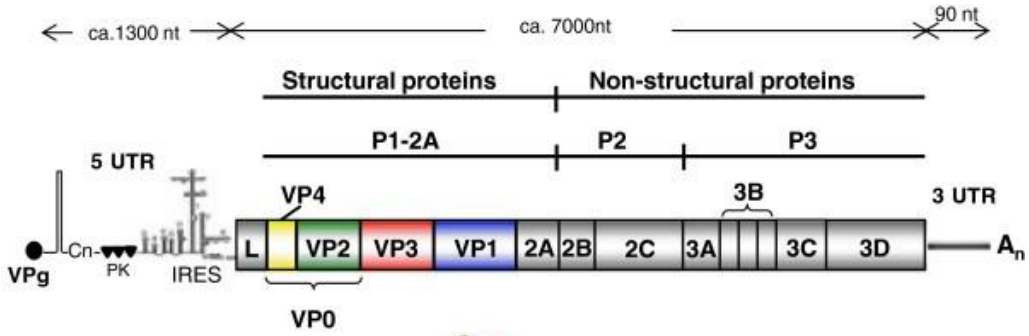
Imunidade heteróloga variável entre subtipos

FEBRE AFTOSA

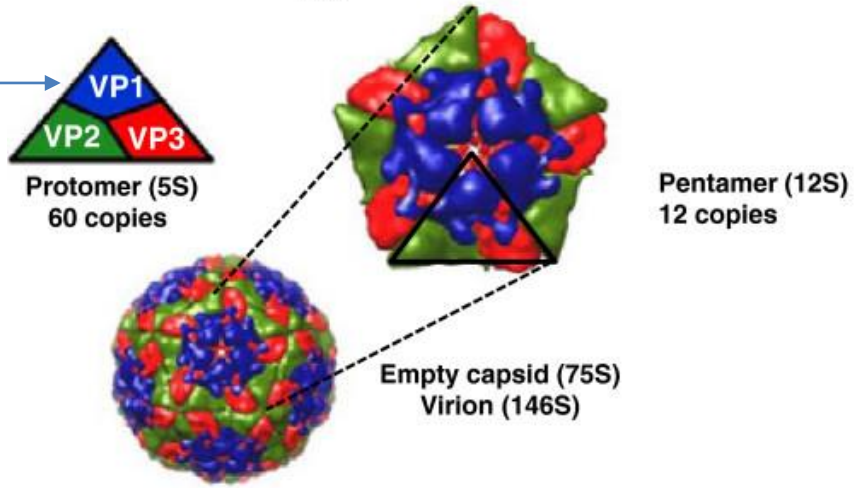
2. VÍRUS DA FEBRE AFTOSA

Genoma

RNA de sentido positivo, fita única, não segmentado
8.450 bases (2.332códons)
Estruturalmente monocistônico: poliproteína autoclivada co-traducionalmente



Variação antigênicia

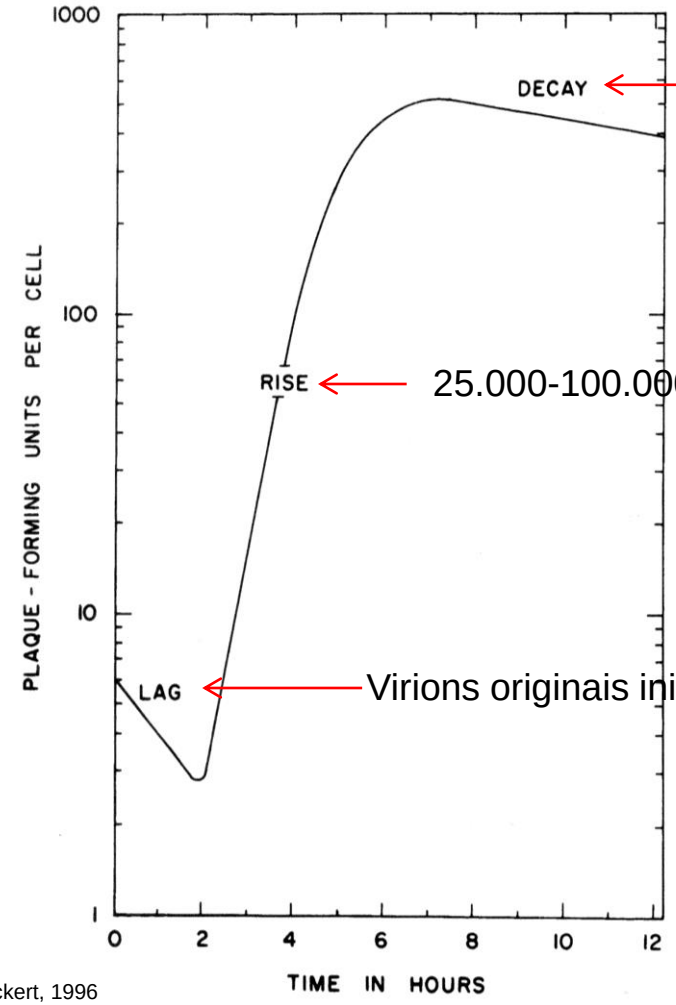


FEBRE AFTOSA

2. VÍRUS DA FEBRE AFTOSA

REPLICAÇÃO

- √ **Citoplasma**
- √ **5-10 horas (depende do status da célula)**
- √ **Tradução em polissomos (≥ribossomos)**



Fragmentação de gRNA dentro do virion por 3D encapsidada

25.000-100.000 novos virions/célula

Virions originais iniciando o ciclo viral

Rueckert, 1996

FEBRE AFTOSA

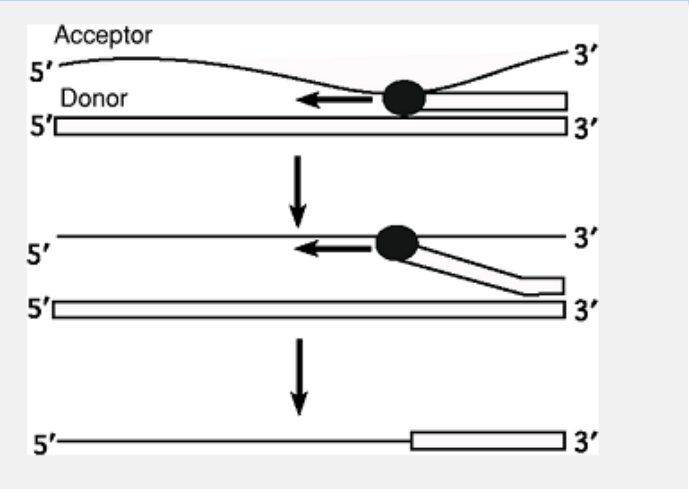
2. VÍRUS DA FEBRE AFTOSA

EVOLUÇÃO

Ausência de 3'-5' exonuclease: taxa de erro da RdRp=10^{-4}**

FONTES DE DIVERSIDADE NUCLEOTÍDICA

Recombinação por *Copy-choice/Template switching*: 10% a 20% dos genomas virais recombinam a cada ciclo viral!.



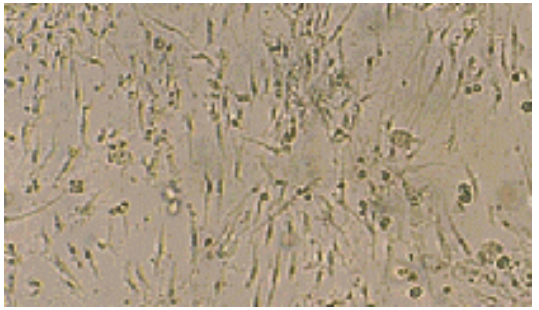
FEBRE AFTOSA

3. PATOGENIA MOLECULAR E CELULAR

Consumo de energia e precursores de proteínas e ácidos nucleicos da célula

Marginação da cromatina (1H PI)

Redistribuição da fosfolipase lisossomal: Alterações de permeabilidade da membrana plasmática (2.5-3 H PI)



FAO

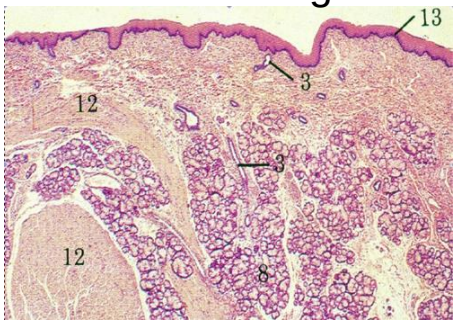
Proteína 3C: Clivagem da proteína de ligação a TATA do fator de transcrição IID: Inibição de DNA polimerase I, II e III

Proteína L: clivagem do complexo de ligação ao cap5': inibição da tradução de proteínas celulares

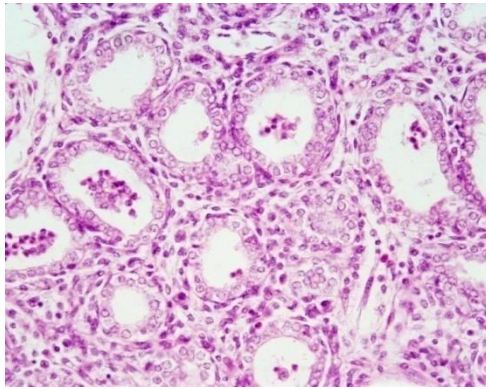
FEBRE AFTOSA

4. PATOGENIA SISTÊMICA

Replicação em mucosa de orofaringe

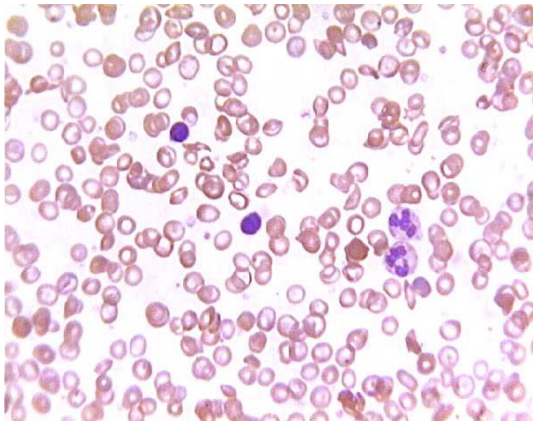


Trato respiratório superior

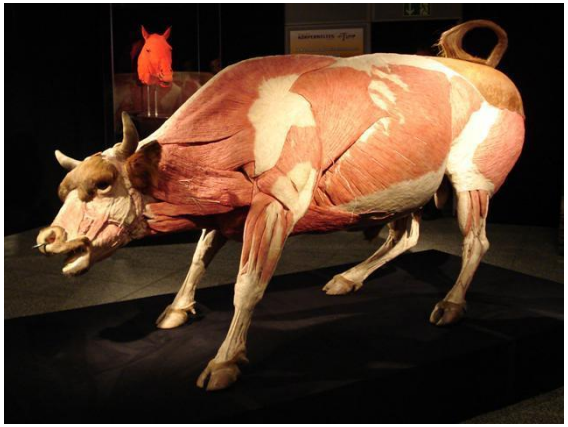


24-48h

Viremia



Disseminação sistêmica



PERÍODO DE INCUBAÇÃO: 2 A 20 DIAS

FEBRE AFTOSA

5. SINAIS E SINTOMAS

DIA 1: Febre, clareamento de epitélio, vesícula com conteúdo líquido

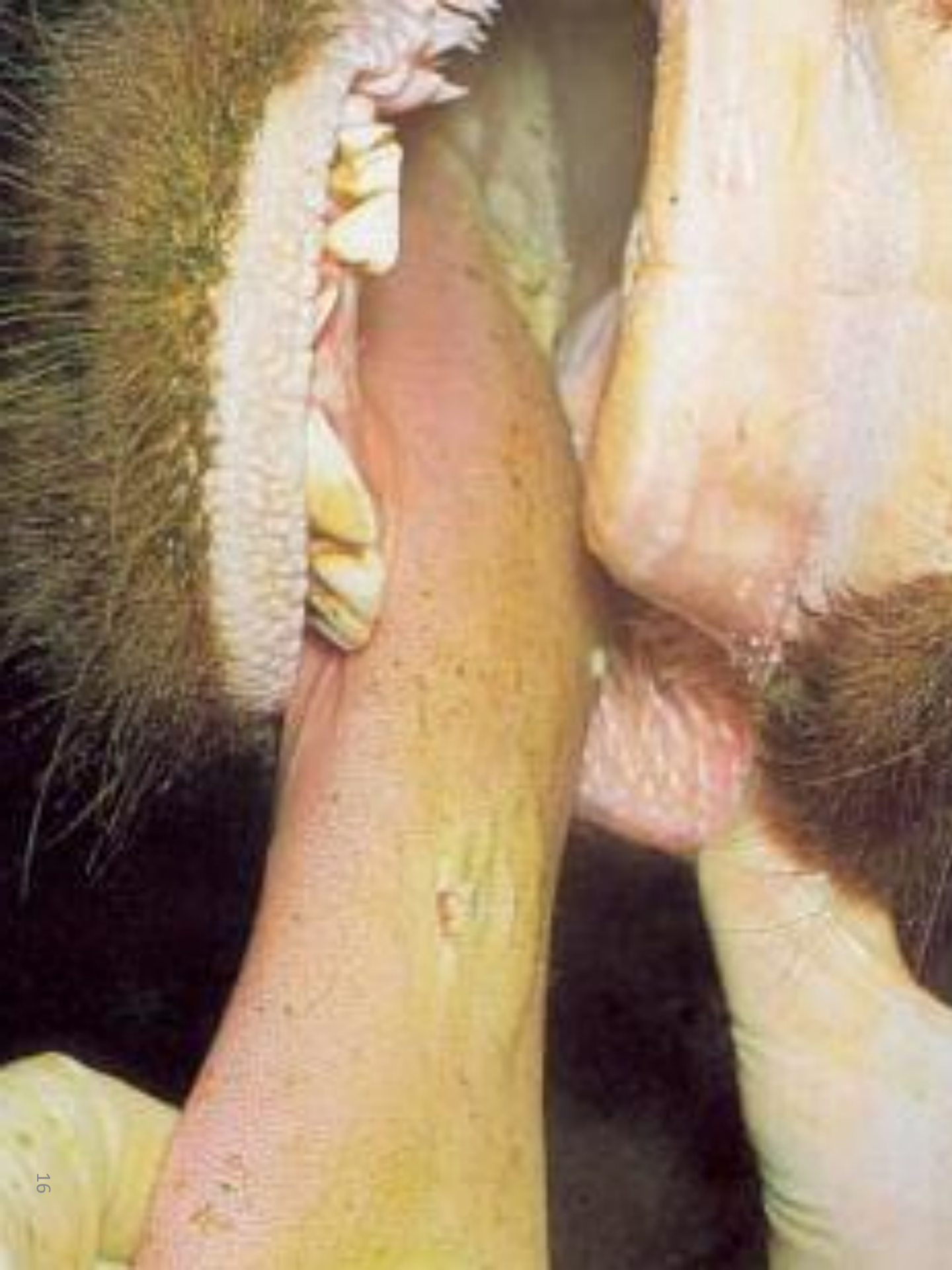
DIA 2: Ruptura de vesículas

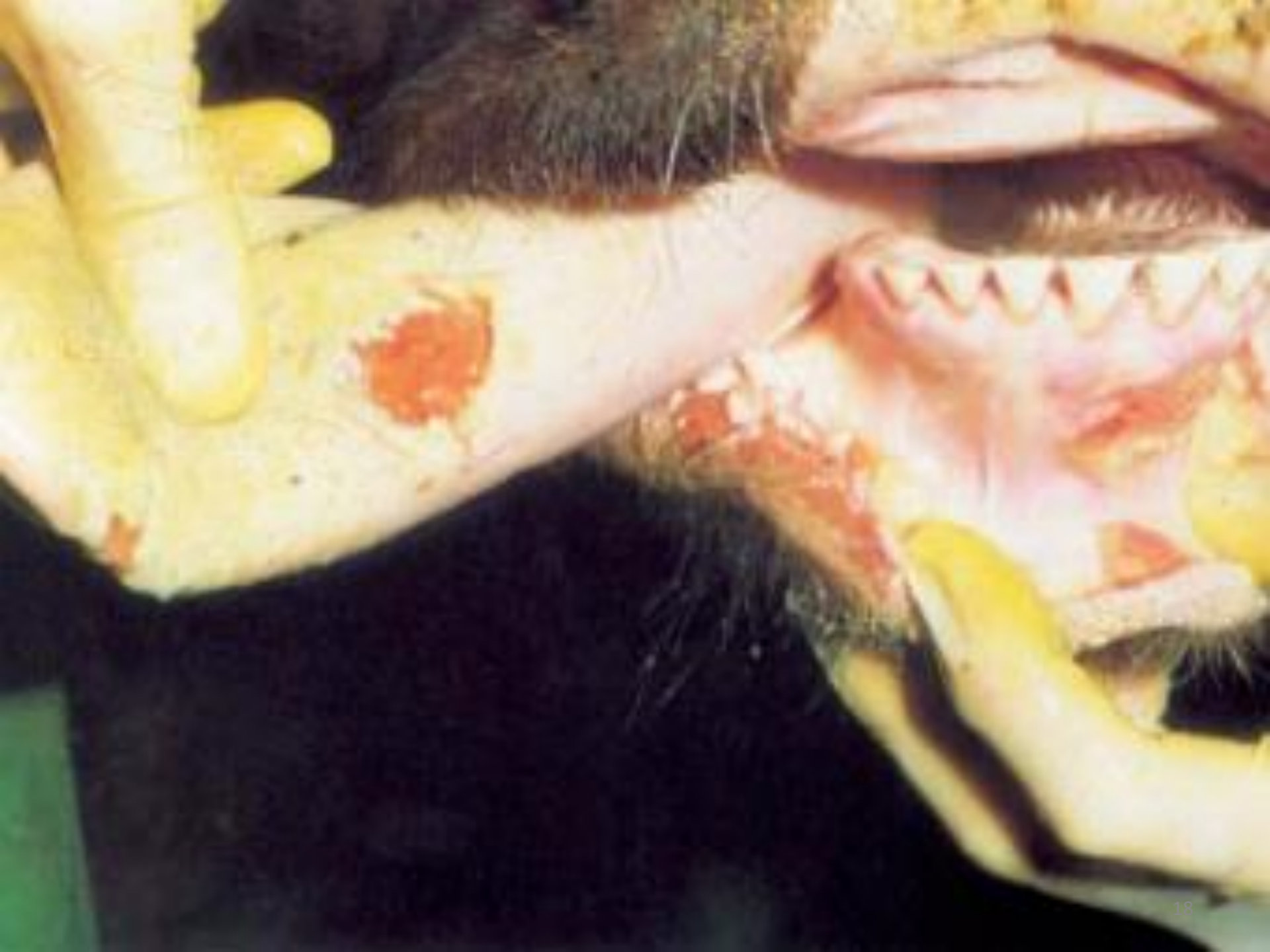
DIA 3: Deposição de fibrina

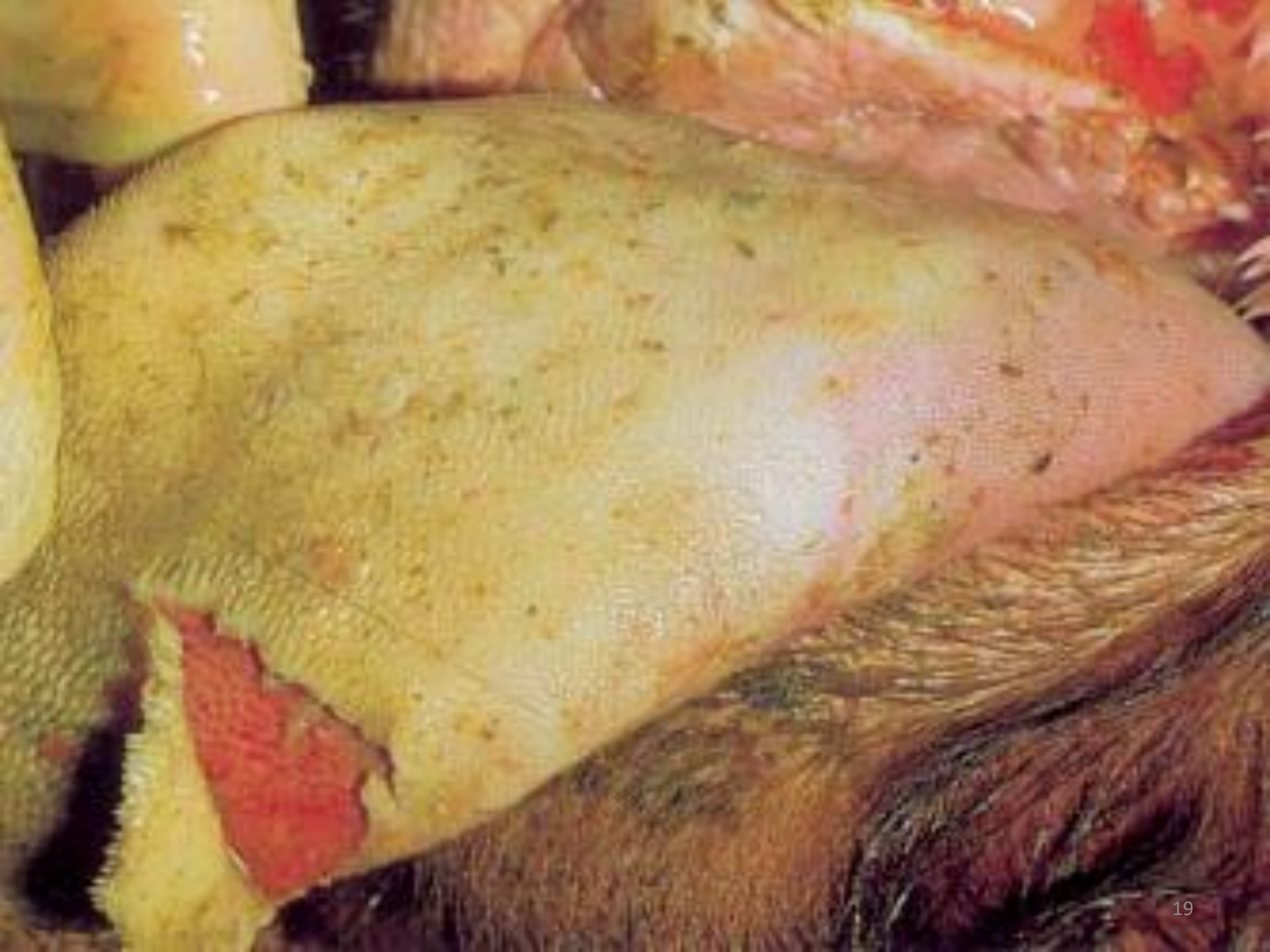
DIA 4: Recuperação do epitélio ao redor das lesões

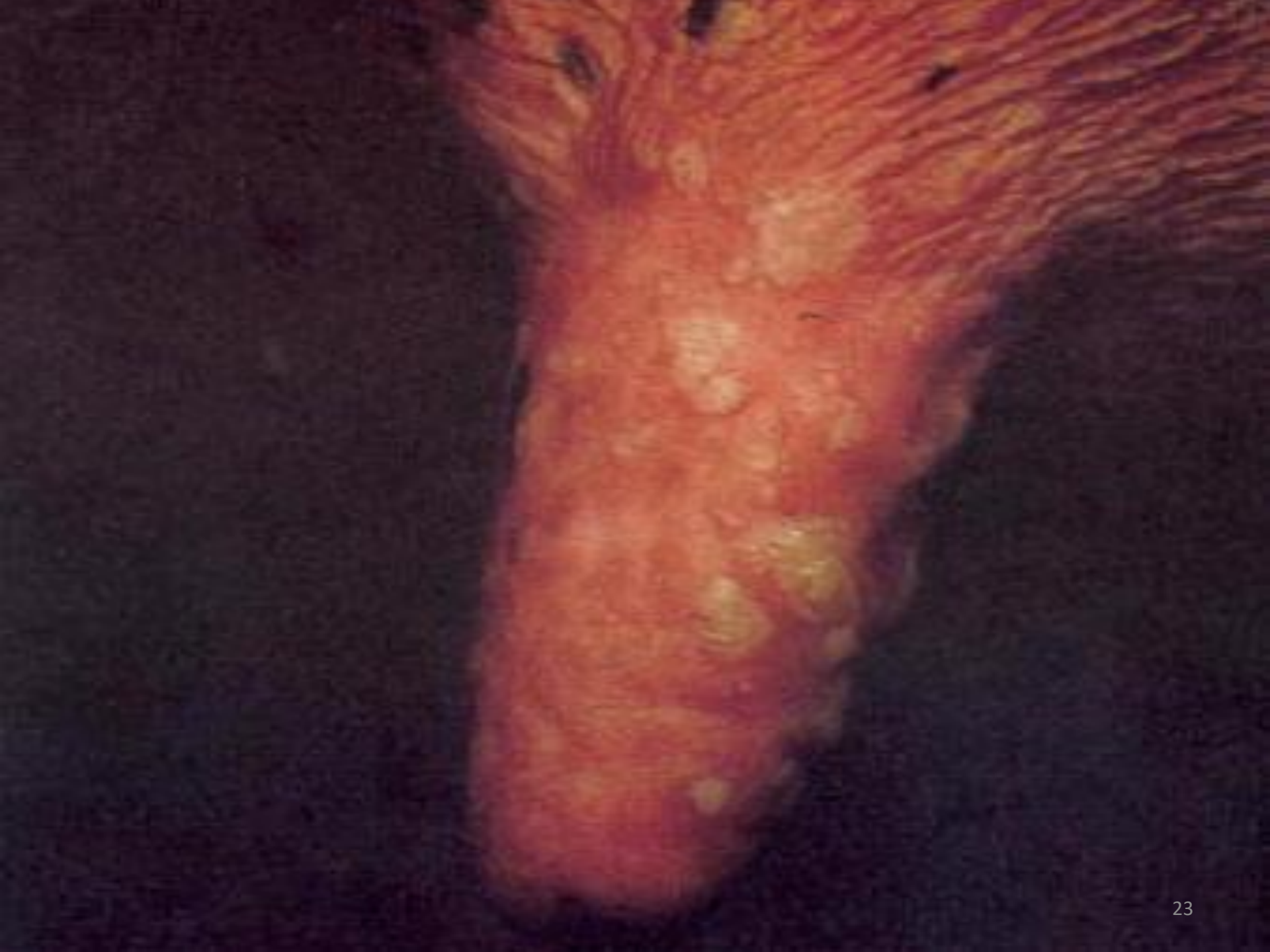
DIA 7: Tecido de Granulação

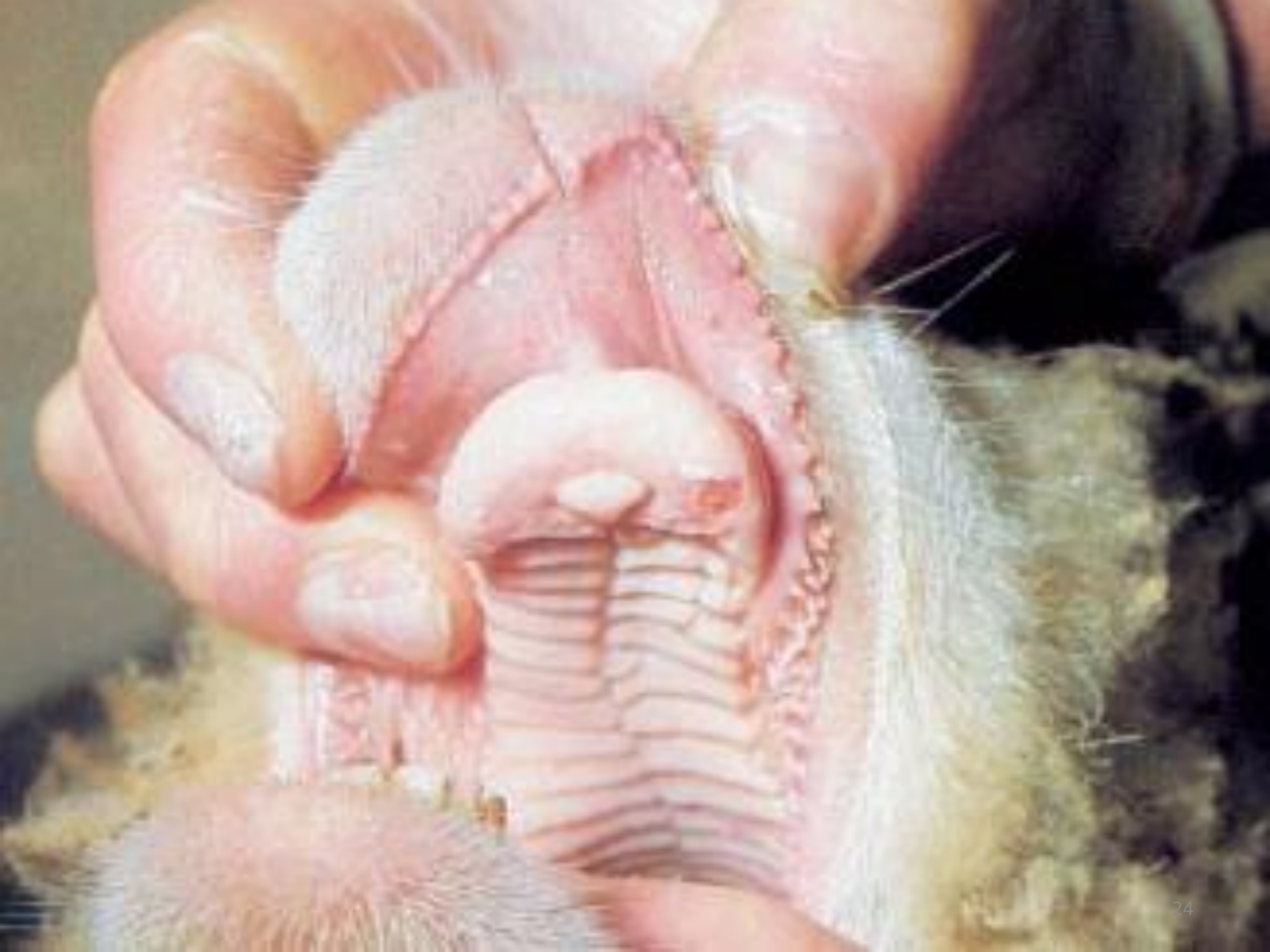
Depressão, anorexia, febre, miocardite, laminite, abortamentos

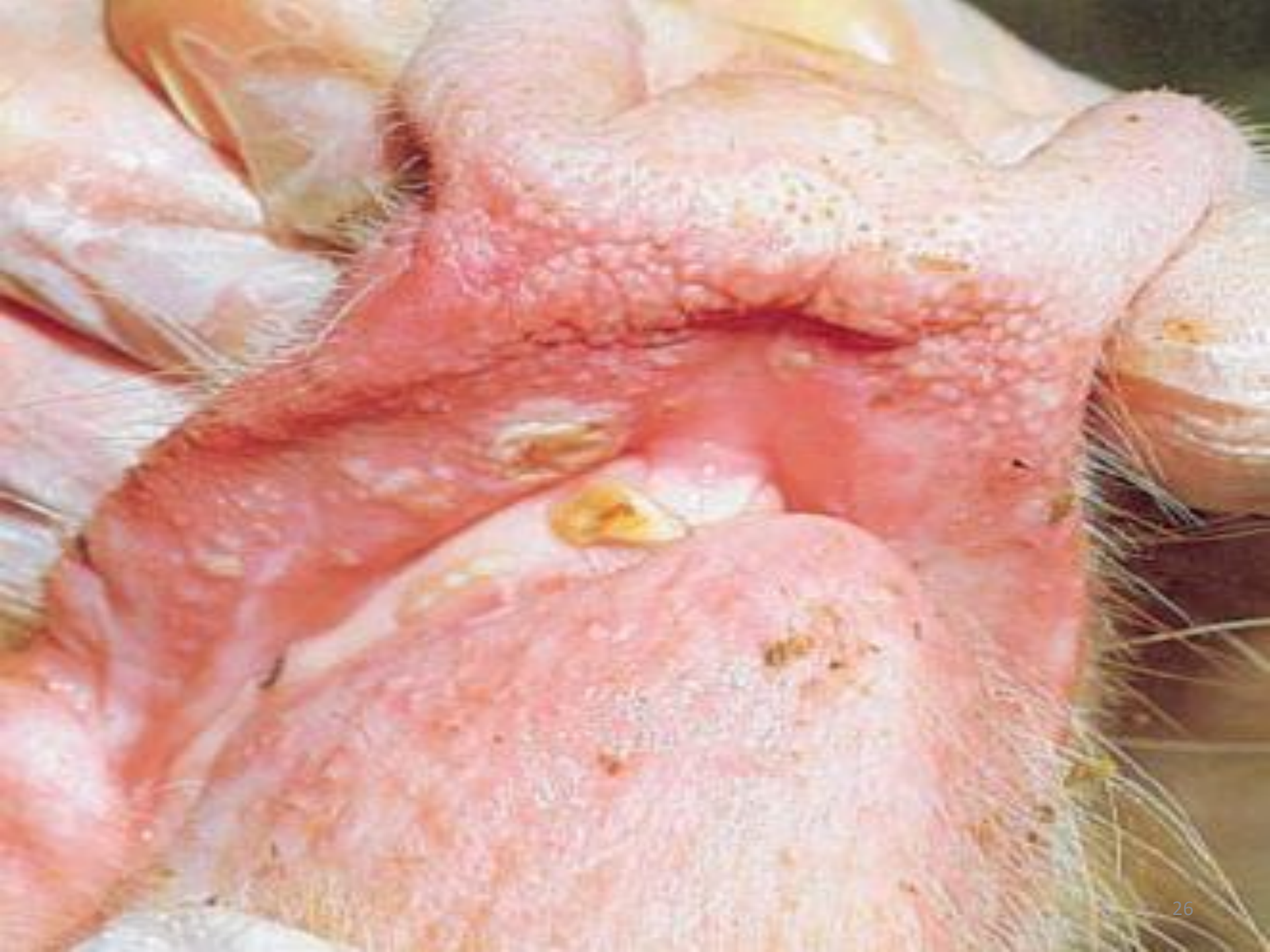


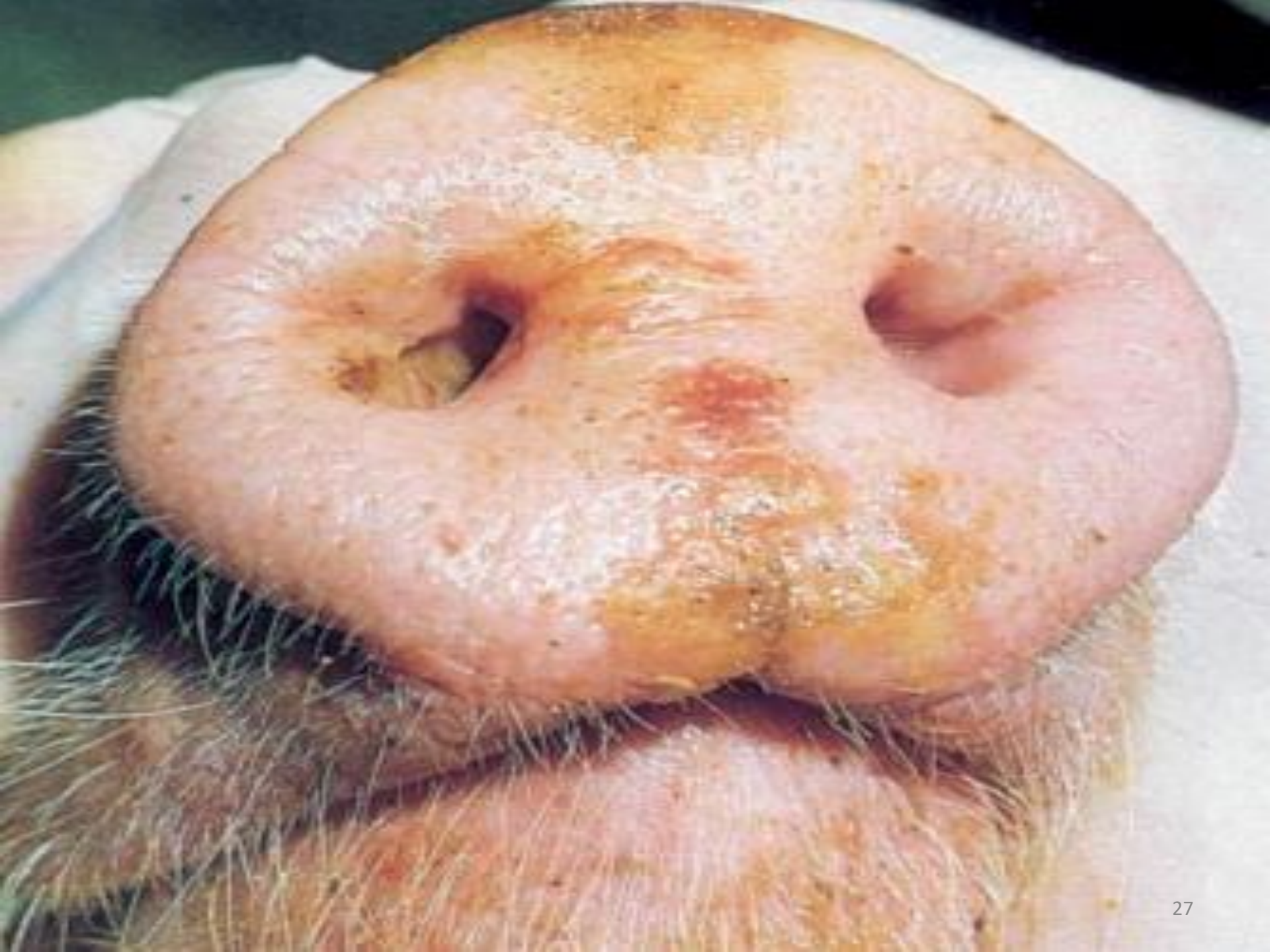


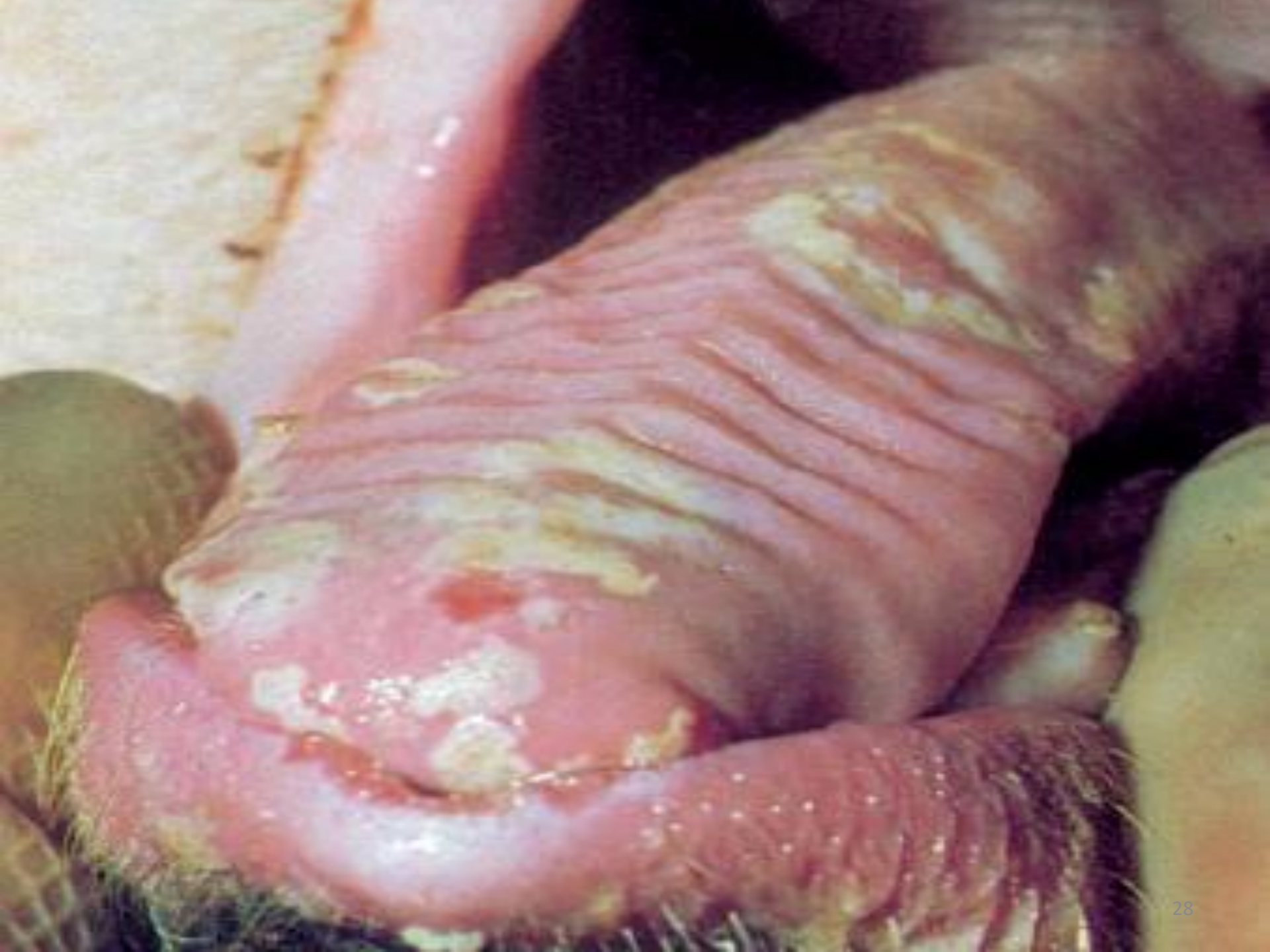


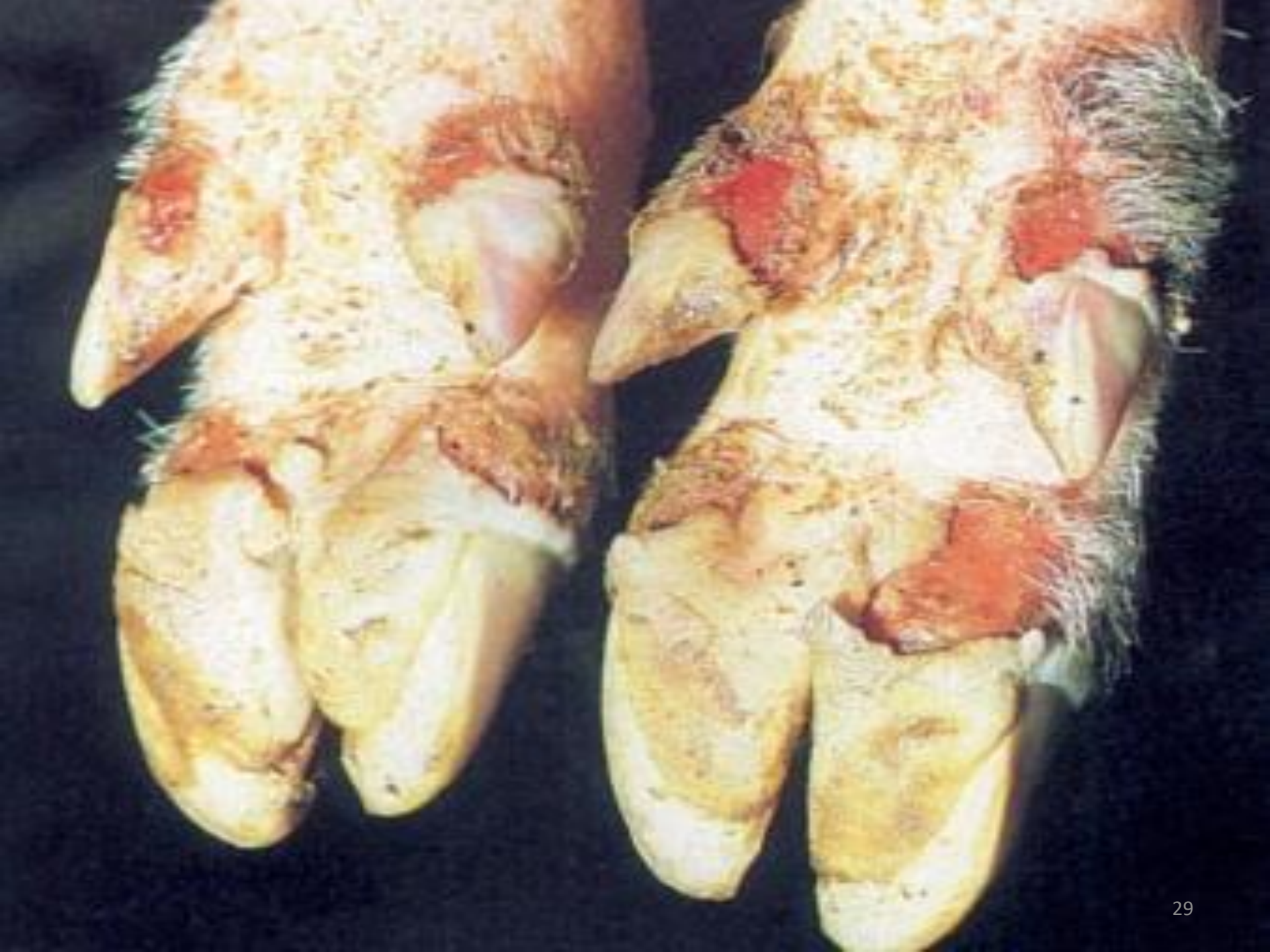












FEBRE AFTOSA

6. CADEIA EPIDEMIOLÓGICA

Fontes de Infecção

10^{14} partículas/dia
Durante 7 dias após início das lesões

Eliminadores assintomáticos

Longos períodos como portadores

Vias de eliminação

Sangue, leite, sêmen, urina, secreções respiratórias

Portas de entrada

√Vias respiratórias superiores
√ Lesões de pele e mucosas

SUSCETÍVEIS

ARTIODACTYLA

FEBRE AFTOSA

7. DIAGNÓSTICO

7.1 DIAGNÓSTICO EPIDEMIOLÓGICO

√ **PRESENÇA DE DOENÇA VESICULAR**

√ **INTRODUÇÃO DE ANIMAIS DE ÁREAS DE RISCO**

√ **AUSÊNCIA DE VACINAÇÃO EM ÁREA ENDÊMICA**

NOTIFICAÇÃO

FEBRE AFTOSA

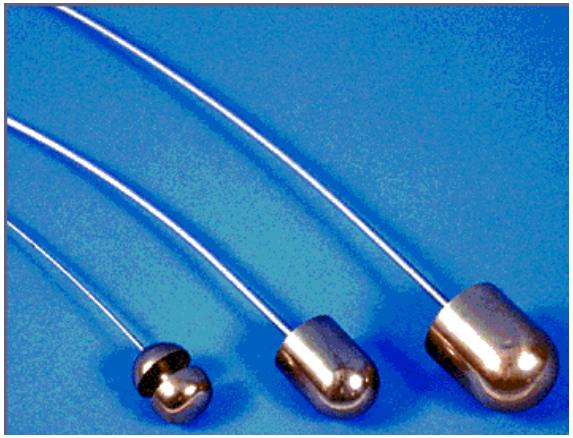
7. DIAGNÓSTICO

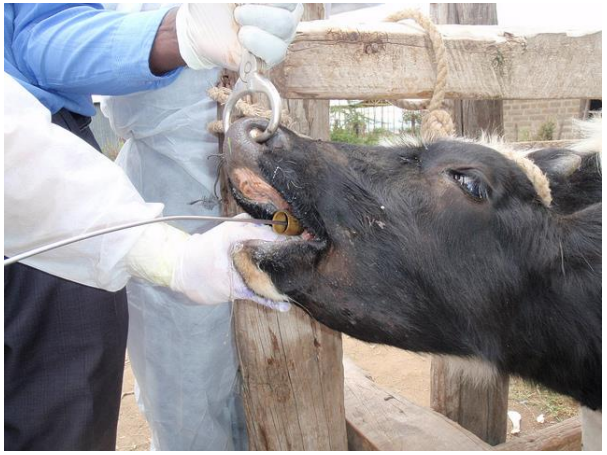
7.2 DIAGNÓSTICO DIRETO

AMOSTRAS

1 g DE TECIDO DE VESÍCULA NÃO-ROMPIDA EM MEIO DE TRANSPORTE pH 7,2-7,4 SOB REFRIGERAÇÃO

FLUIDO ORO-FARÍNGEO COLETOR PROBANG; CONGELAMENTO





FEBRE AFTOSA

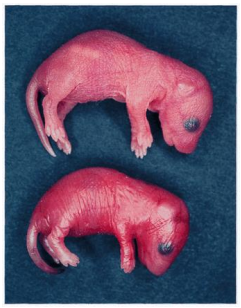
7. DIAGNÓSTICO

7.2 DIAGNÓSTICO DIRETO

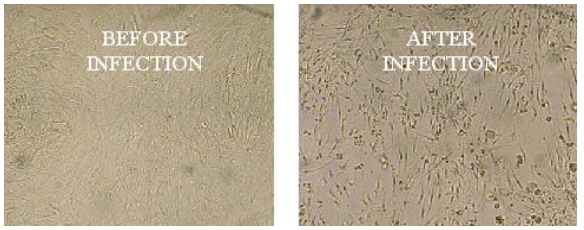
VÍRUS VIVO: BIOSSEGURANÇA NB4 LANAGRO/ MG

ISOLAMENTO

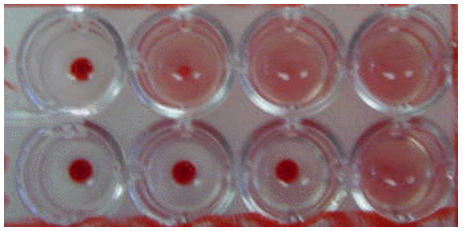
Camundongos 2-7 dias de idade



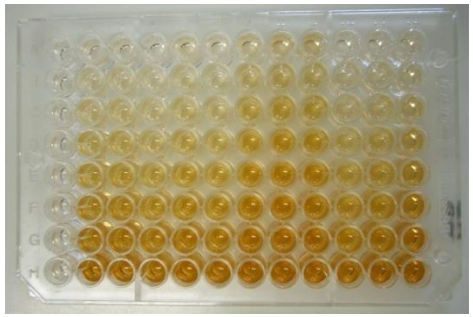
Células BHK-21



FIXAÇÃO DE COMPLEMENTO



ELISA



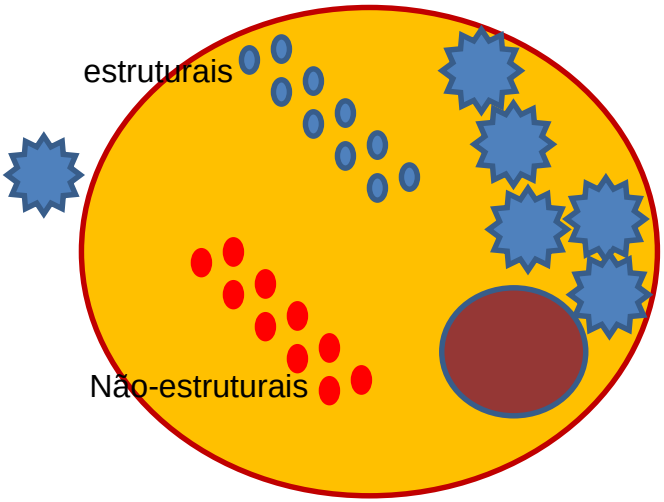
PCR

FEBRE AFTOSA

7. DIAGNÓSTICO

7.3 DIAGNÓSTICO INDIRETO

1. PROTEÍNAS ESTRUTURAIS VIRAIS
   PROTEÍNAS NÃO-ESTRUTURAIS VIRAIS



ANTICORPOS CONTRA PROTEÍNAS ESTRUTURAIS (VIRION; CITOPLASMA)

ANTICORPOS CONTRA PROTEÍNAS NÃO ESTRUTURAIS (CITOPLASMA)

APRESENTAÇÃO AO SISTEMA IMUNE

EM CASO DE VÍRUS INATIVADO

ANTICORPOS CONTRA PROTEÍNAS ESTRUTURAIS (VIRION; CITOPLASMA)

ANTICORPOS CONTRA PROTEÍNAS NÃO ESTRUTURAIS (CITOPLASMA)

2. POR QUE É IMPORTANTE DIFERENCIAR ANIMAIS VACINADOS DAQUELES NATURALMENTE IFECTADOS?

FEBRE AFTOSA

7. DIAGNÓSTICO

7.3 DIAGNÓSTICO INDIRETO

AMOSTRA: SORO SANGUÍNEO

ELISA 3D, 3ABC

√ VIAA (virus infection-associated antigen):3D

√ Detecção de anticorpos anti-proteínas não estuturais

√ Diferenciação entre vacinados e infectados: vacinados não têm anticorpos contra proteínas não-estruturais (dependendo no n. de vacinações e pureza da vacina)

ENZYME-LINKED IMMUNOELECTROTRANSFER BLOT ASSAY (EITB)

√ Para confirmação após triagem

FEBRE AFTOSA

7. DIAGNÓSTICO

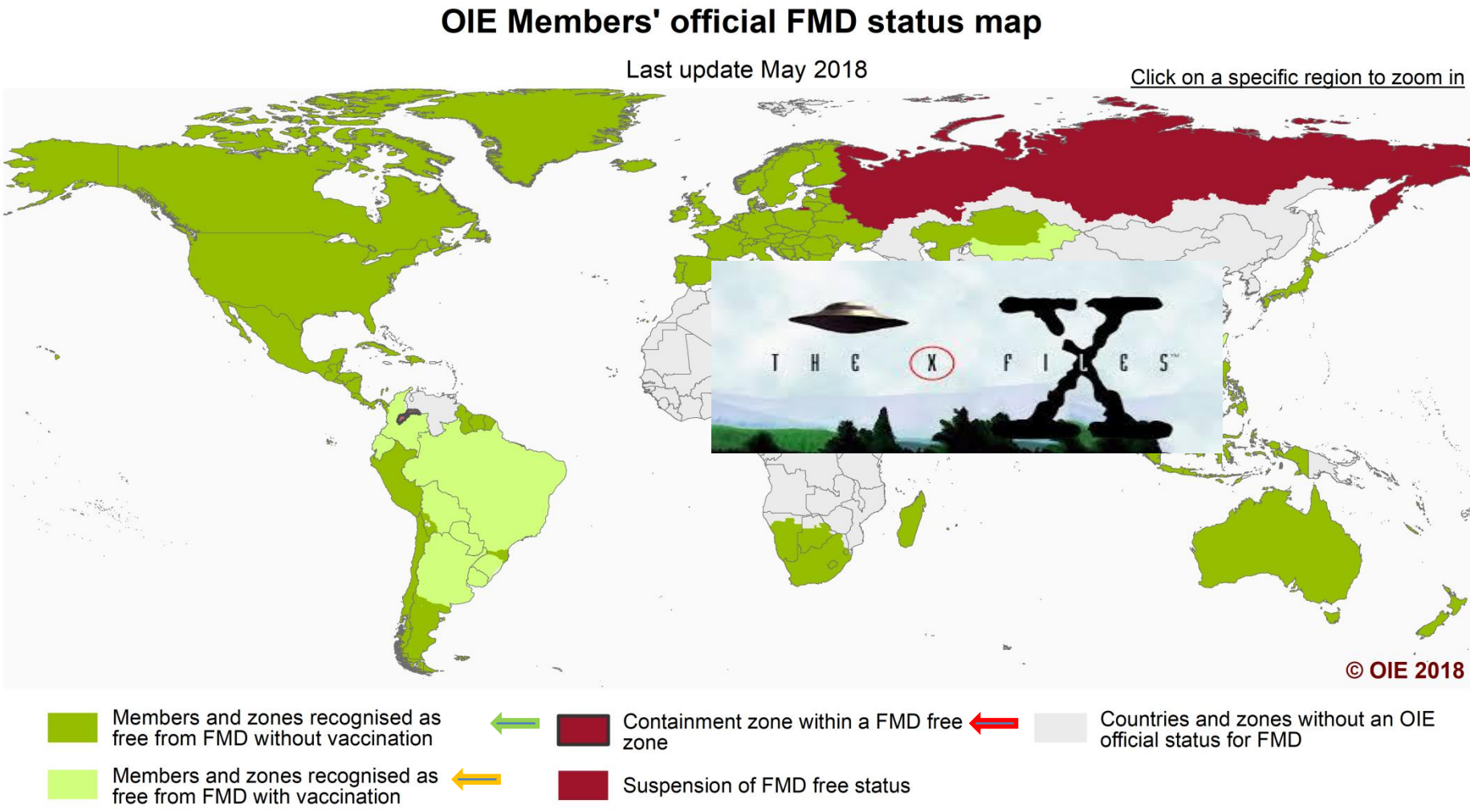
7.3 DIAGNÓSTICO DIFERENCIAL

DOENÇAS CLINICAMENTE INDISTINGUÍVEIS
ESTOMATITE VESICULAR
DOENÇA VESICULAR SUÍNA
DOENÇA EXANTEMÁTICA DOS SUÍNOS

OUTRAS DOENÇAS
BVD
IBR
BLUETONGUE
ESTOMATITE PAPULAR BOVINA

FEBRE AFTOSA

8. DISTRIBUIÇÃO MUNDIAL



FEBRE AFTOSA

9. CONSEQUÊNCIAS DE INTERESSE ECONÔMICO

Preventive Veterinary Medicine 112 (2013) 161–173

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

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

The economic impacts of foot and mouth disease – What are they, how big are they and where do they occur?

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ARTICLE INFO

Article history:
Received 29 January 2013
Received in revised form 15 July 2013
Accepted 17 July 2013

Keywords:
Economics
FMD
Review
Impact

ABSTRACT

Although a disease of low mortality, the global impact of foot and mouth disease (FMD) is colossal due to the huge numbers of animals affected. This impact can be separated into two components: (1) direct losses due to reduced production and changes in herd structure; and (2) indirect losses caused by costs of FMD control, poor access to markets and limited use of improved production technologies. This paper estimates that annual impact of FMD in terms of visible production losses and vaccination in endemic regions alone amount to between US$6.5 and 21 billion. In addition, outbreaks in FMD free countries and zones cause losses of >US$1.5 billion a year.

FMD impacts are not the same throughout the world:

1. FMD production losses have a big impact on the world's poorest where more people are directly dependent on livestock. FMD reduces herd fertility leading to less efficient herd structures and discourages the use of FMD susceptible, high productivity breeds. Overall the direct losses limit livestock productivity affecting food security.
2. In countries with ongoing control programmes, FMD control and management creates large costs. These control programmes are often difficult to discontinue due to risks of new FMD incursion.
3. The presence, or even threat, of FMD prevents access to lucrative international markets.
4. In FMD free countries outbreaks occur periodically and the costs involved in regaining free status have been enormous.

FMD is highly contagious and the actions of one farmer affect the risk of FMD occurring on other holdings; thus sizeable externalities are generated. Control therefore requires coordination within and between countries. These externalities imply that FMD control produces a significant amount of public goods, justifying the need for national and international public investment.

Equipping poor countries with the tools needed to control FMD will involve the long term development of state veterinary services that in turn will deliver wider benefits to a nation including the control of other livestock diseases.

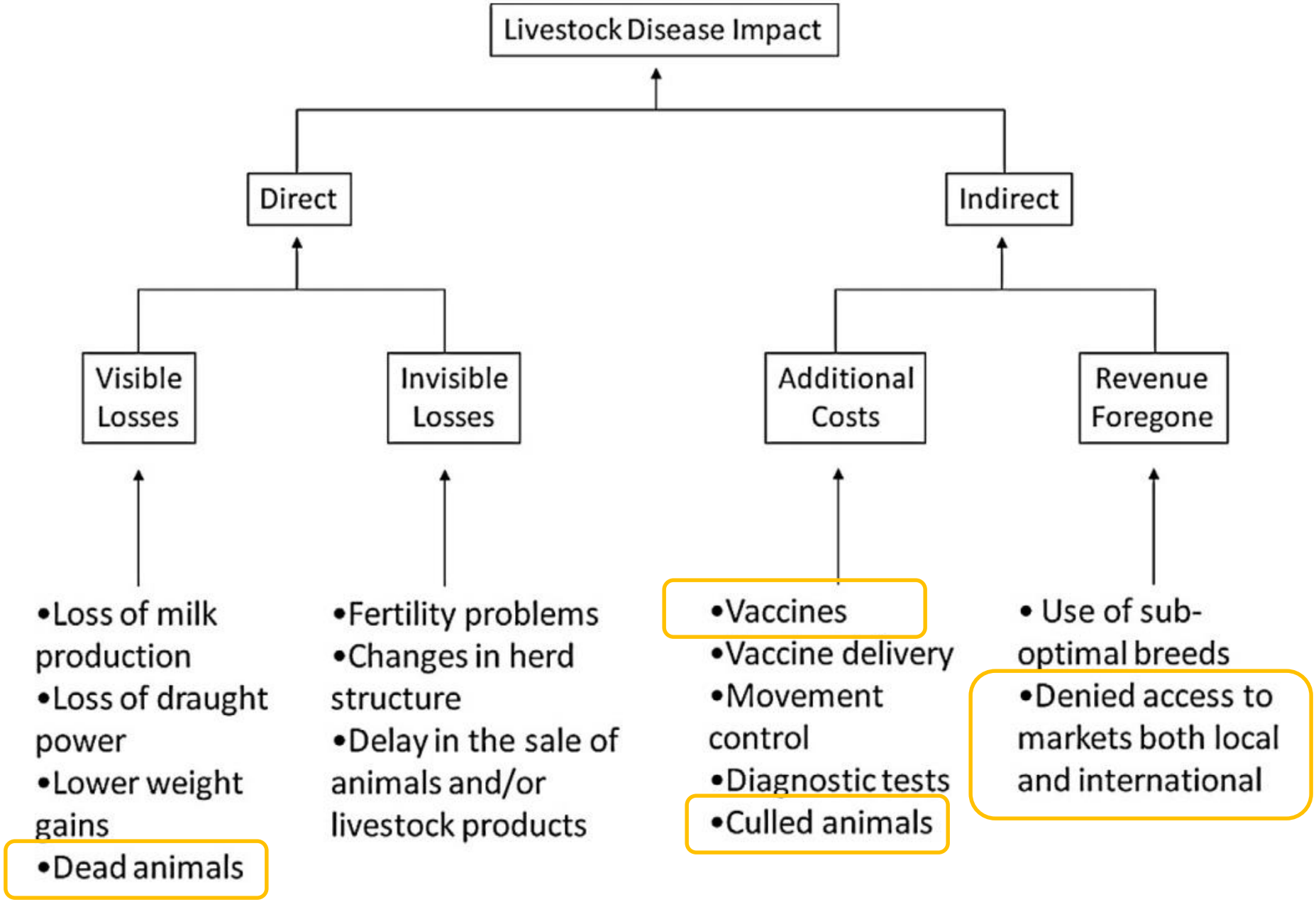
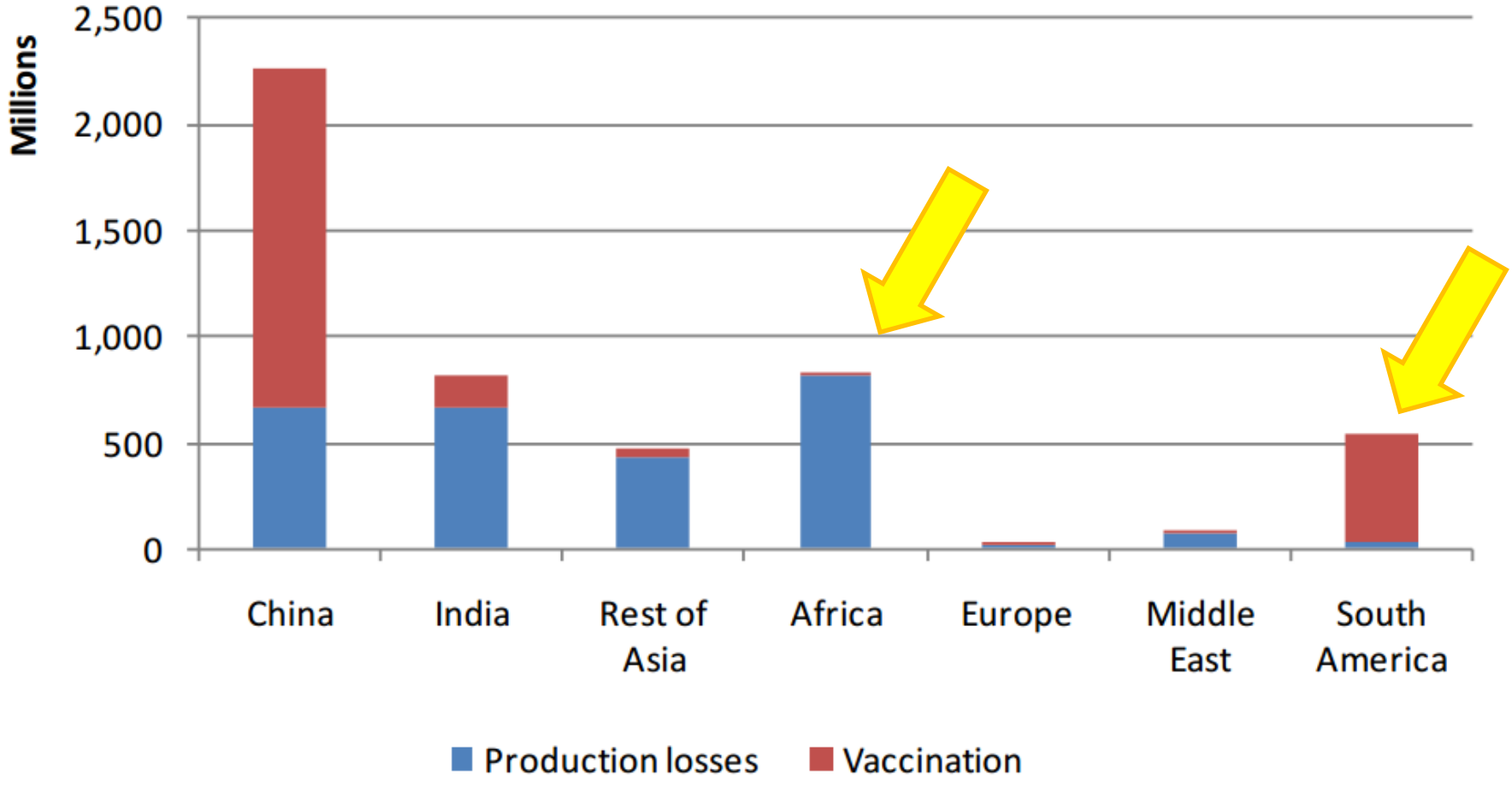
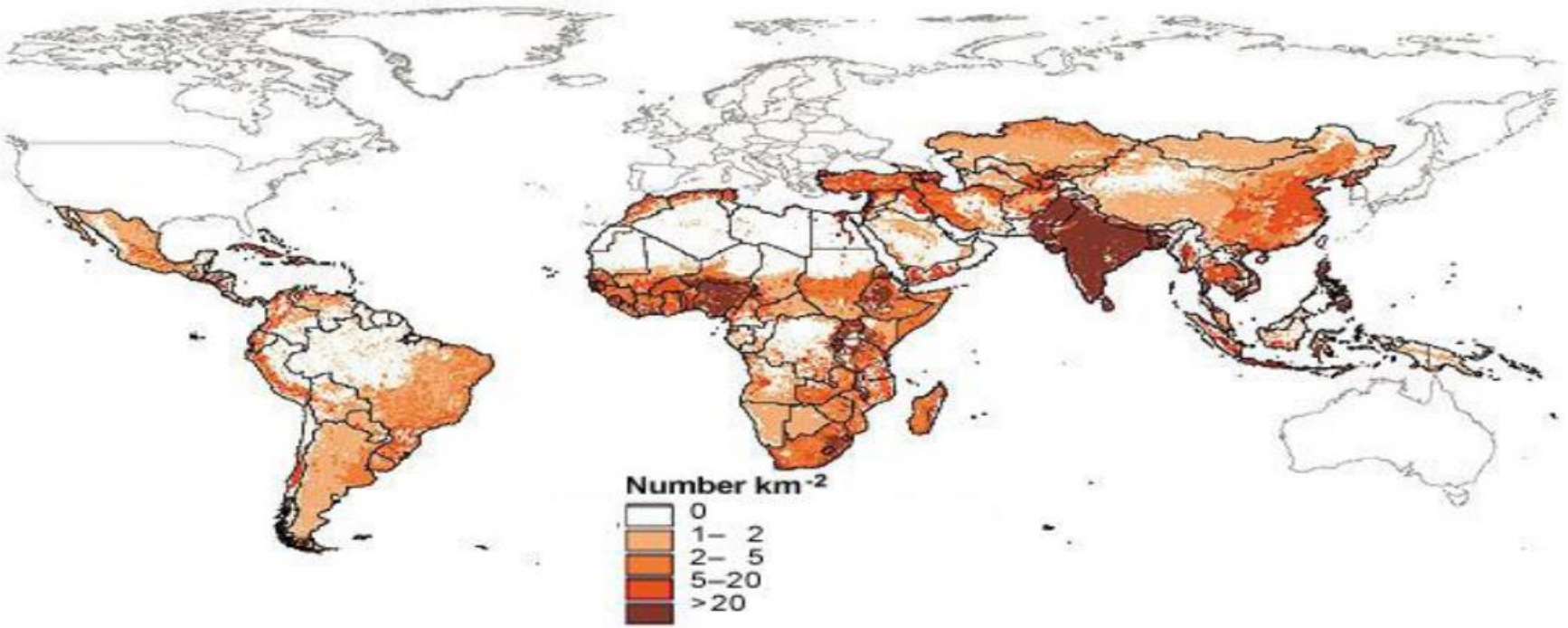


Fig. 2. The impacts of foot-mouth-disease (Rushton, 2009).

FMD production losses and vaccination costs by region (US$ million/year)



Density of poor people dependent on livestock



Royal Veterinary College

FEBRE AFTOSA

10. PROFILAXIA E CONTROLE

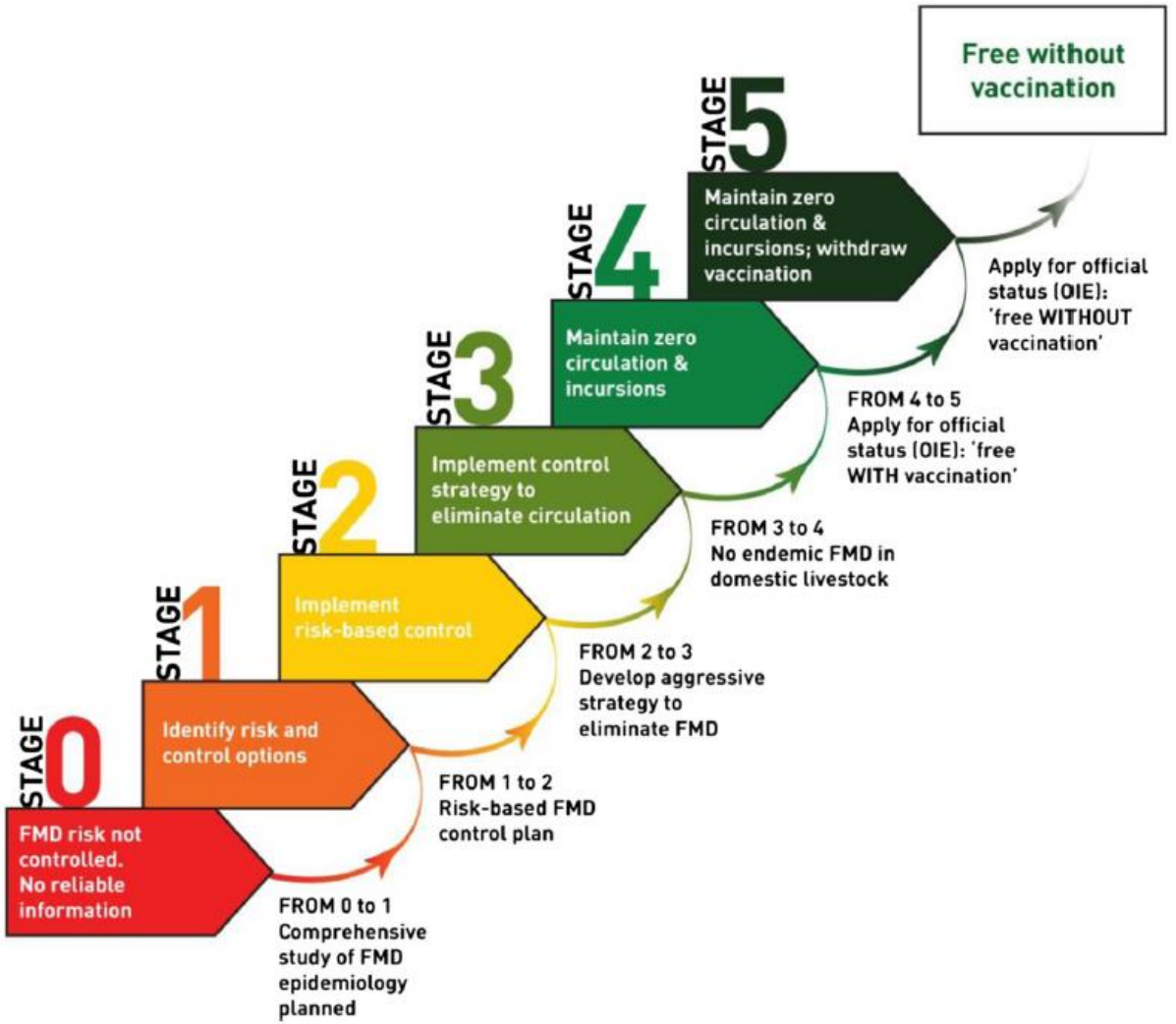


Figure 3 The FAO/EuFMD/OIE Progressive Control Pathway for FMD. The status of countries on the PCP-FMD is evaluated according to defined criteria. Countries with endemic disease are in stages 0 to 3 while countries with no endemic disease within livestock are at stage 4 or above. The image was kindly supplied by EuFMD.

Jamal SM, Belsham GJ.Vet Res. 2013 Dec 5;44:116

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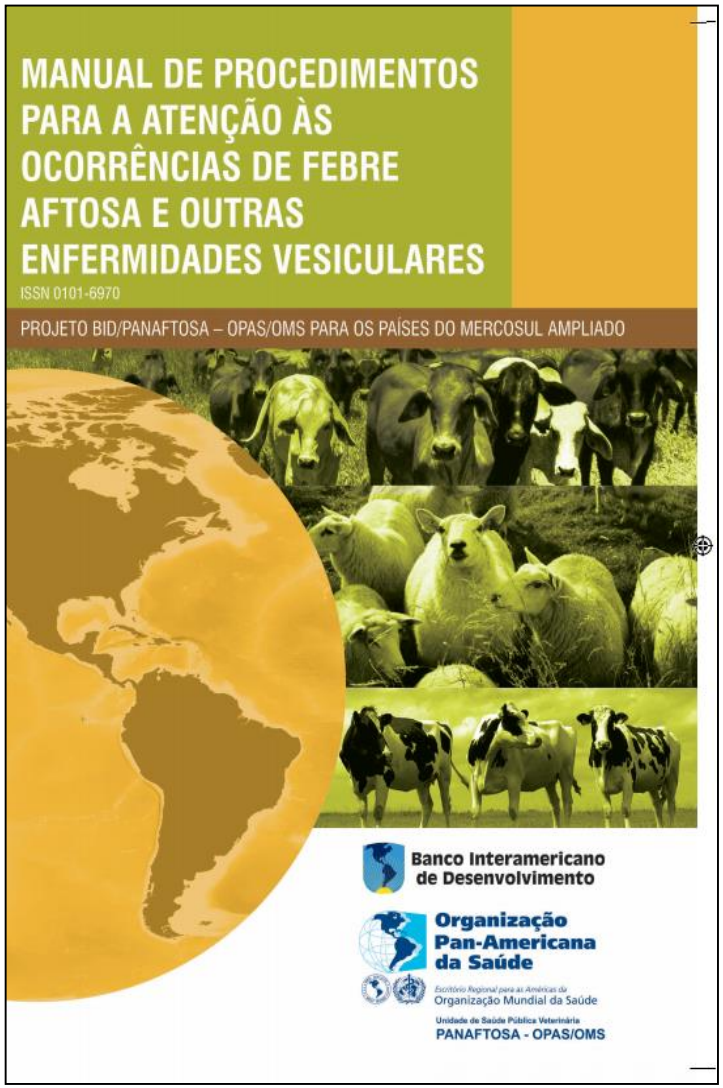

http://www.agricultura.gov.br/

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10. PROFILAXIA E CONTROLE

Figura 1 Representação das principais fases do sistema de vigilância para doenças vesiculares

Sintomas

Laboratório

Sintomas, Laboratório

FEBRE AFTOSA

10. PROFILAXIA E CONTROLE

MEDIDAS APLICÁVEIS AS FONTES DE INFECÇÃO

√CONTROLE DE MOVIMENTAÇÃO ANIMAL

√ EUTANÁSIA DE ANIMAIS INFECTADOS, RECUPERADOS E COMUNICANTES***

√ QUARENTENA

FEBRE AFTOSA

10. PROFILAXIA E CONTROLE

MEDIDAS APLICÁVEIS AS VIAS DE TRANSMISSÃO

ESTABELECIMENTO DE ÁREA DE PROTEÇÃO SANITÁRIA	Área perifocal : r=3km Área de vigilância: área perifocal + 7km Área tampão: área de vigilância + 15 km
DESINFETANTES	hidróxido de sódio a 2% carbonato de sódio a 4% ácido cítrico a 0,2%

FEBRE AFTOSA

10. PROFILAXIA E CONTROLE

MEDIDAS APLICÁVEIS AOS SUSCEPTÍVEIS

VACINAÇÃO:

√ Bovinos e bubalinos

√ O+A+C

√ Vacina inativada, oleosa, 5mL (2ml em 2019), “livre” de nsps

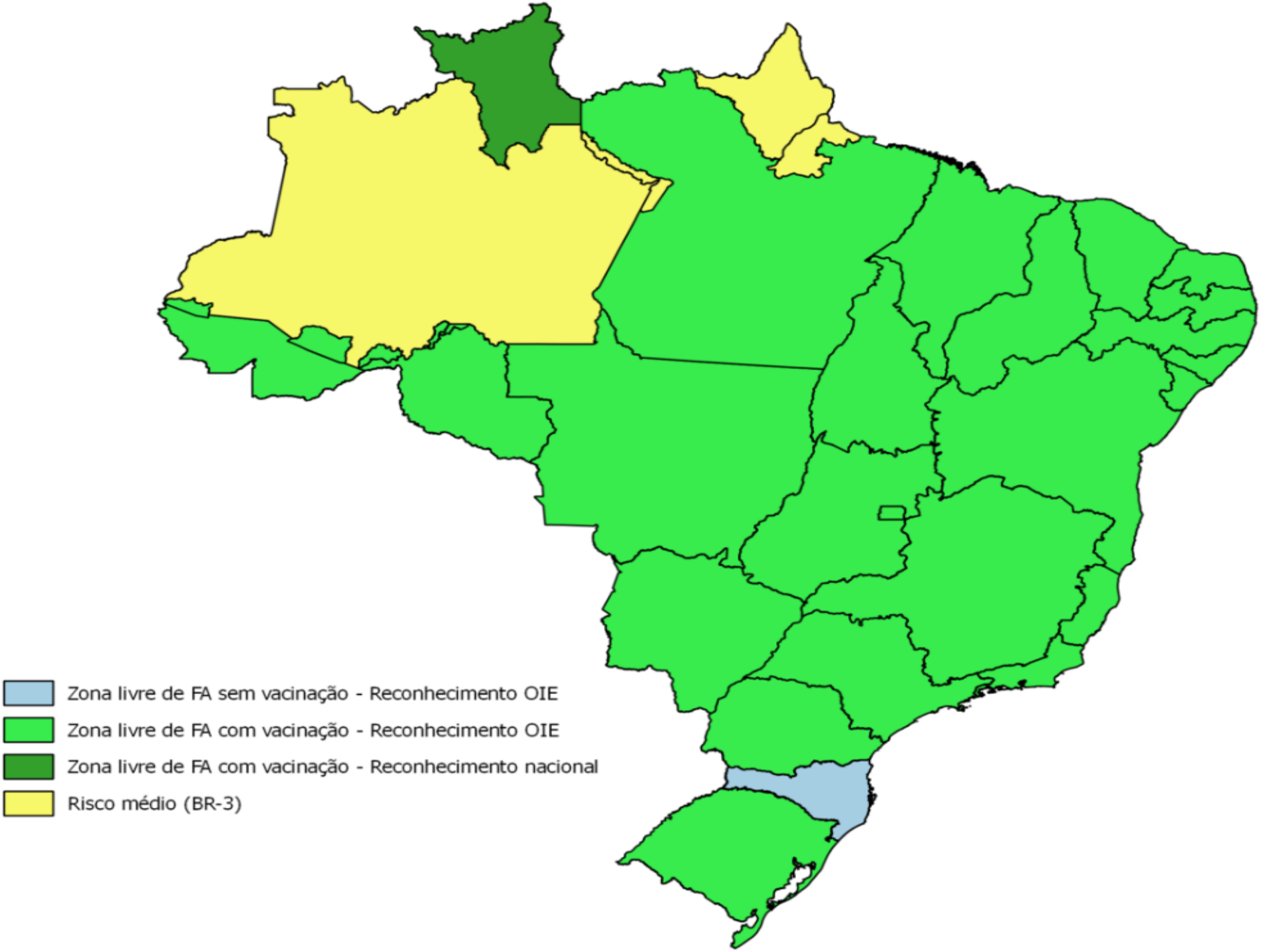
Calendário nacional de vacinação dos bovinos e bubalinos contra a febre aftosa 2018*

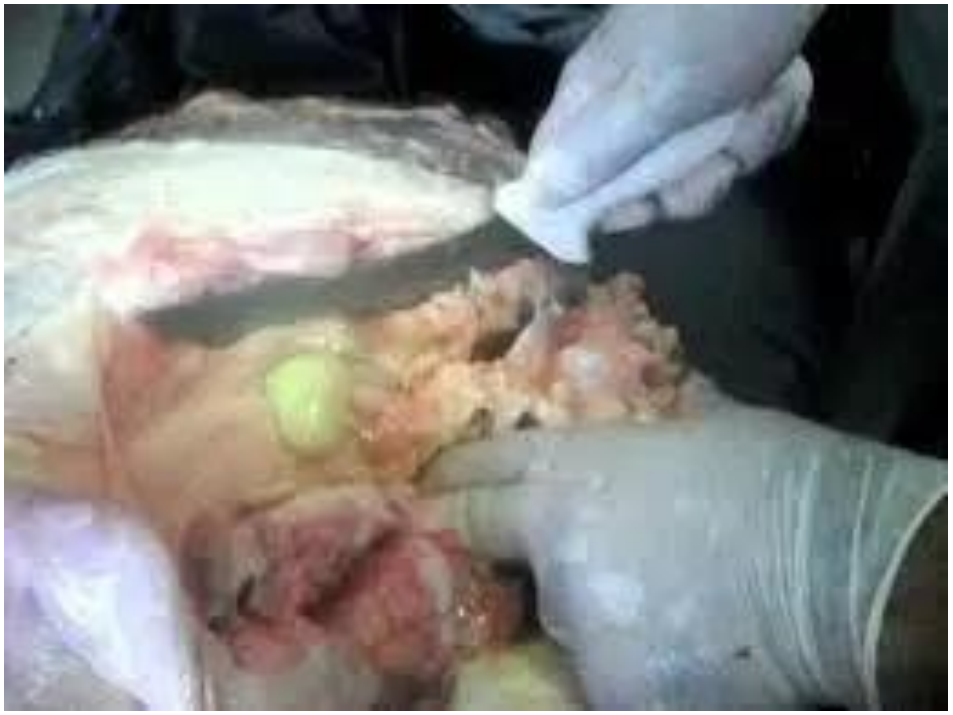
UF	JAN	FEV	MAR	ABR	MAI	JUN	JUL	AGO	SET	OUT	NOV	DEZ
ACRE					3						1	
ALAGOAS					1						3	
AMAPÁ [a]									4	4	4	
AMAZONAS [b]			1	1	1		1	1			1	
BAHIA					1						3	
CEARÁ					1						3	
DISTRITO FEDERAL					1						3	
ESPÍRITO SANTO					3						1	
GOIÁS					1						3	
MARANHÃO					1						3	
MATO GROSSO [c]					1						3	4
MATO GROSSO DO SUL [d]					1	4					3	4
MINAS GERAIS					1						3	
PARÁ [e]			1	1	1		1	1	4	4	3	
PARAÍBA					1						3	
PARANÁ					3						1	
PERNAMBUCO					1						3	
PIAUÍ					1						3	
RIO DE JANEIRO					1						3	
RIO GRANDE DO NORTE					1						3	
RIO GRANDE DO SUL					1						3	
RONDÔNIA [f]				1						3		
RORAIMA [g]				1 / 1	1					3 / 1	1	
SÃO PAULO					1						3	
SERGIPE					1						3	
TOCANTINS [h]					1			4	4		3	

Legenda:

Estratégias de vacinação autorizadas pelo MAPA (IN 44/2007)

- **1** = vacinação de todo o rebanho bovino e bubalino.
- **2** = vacinação de animais com menos de 12 meses (não aplicada).
- **3** = vacinação de animais com idade até 24 meses.
- **4** = vacinação anual de todo o rebanho bovino e bubalino.


Zona livre de FA sem vacinação - Reconhecimento OIE
Zona livre de FA com vacinação - Reconhecimento OIE
Zona livre de FA com vacinação - Reconhecimento nacional
Risco médio (BR-3)



Suspensão de importação de carne bovina pelos EUA: abscessos

Vacina ou vacinação?

FEBRE AFTOSA

11. REFERÊNCIAS

Berryman S, Brooks E, Burman A, Hawes P, Roberts R, Netherton C, Monaghan P, Whelband M, Cottam E, Elazar Z, Jackson T, Wileman T. Foot-and-mouth disease virus induces autophagosomes during cell entry via a class III phosphatidylinositol 3-kinase-independent pathway. J Virol. 2012 Dec;86(23):12940-53.

Fajardo T Jr, Rosas MF, Sobrino F, Martinez-Salas E. Exploring IRES region accessibility by interference of foot-and-mouth disease virus infectivity. PLoS One. 2012;7(7):e41382.

Jackson T, Mould AP, Sheppard D, King AM. Integrin alphavbeta1 is a receptor for foot-and-mouth disease virus. J Virol. 2002 Feb;76(3):935-41.

Jamal SM, Belsham GJ. Foot-and-mouth disease: past, present and future. Vet Res. 2013 Dec 5;44:116.

Knight-Jones TJ, Rushton J. The economic impacts of foot and mouth disease - what are they, how big are they and where do they occur?Prev Vet Med. 2013 Nov 1;112(3-4):161-73.

Martínez MA, Carrillo C, González-Candelas F, Moya A, Domingo E, Sobrino F. Fitness alteration of foot-and-mouth disease virus mutants: measurement of adaptability of viral quasispecies. J Virol. 1991 Jul;65(7):3954-7.

Morelli MJ, Wright CF, Knowles NJ, Juleff N, Paton DJ, King DP, Haydon DT. Evolution of foot-and-mouth disease virus intra-sample sequence diversity during serial transmission in bovine hosts. Vet Res. 2013 Mar 1;44:12.

Peng JM, Liang SM, Liang CM. VP1 of foot-and-mouth disease virus induces apoptosis via the Akt signaling pathway. J Biol Chem. 2004 Dec 10;279(50):52168-74.

Rieder, E.; Brum, M.C.S. Picornaviridae. IN; FLORES, E. F. Virologia Veterinária. 2ed. Editora UFSM: Santa Maria, 2012. 1007p.

Rueckert, R. R. Picornaviridae: Th eviruses and their replication. In: Fields, B. N.; Knipe, D. M.; Howley, P. M. Fields Virology. 3ed. Lippincott-Raven: Philadelphia. 1996. 2950p.

Weaver GV, Domenech J, Thiermann AR, Karesh WB. Foot and mouth disease: a look from the wild side. J Wildl Dis. 2013 Oct;49(4):759-85.