Lumpy skin disease

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Introduction

First reported in Zambia (1929); Botswana (1943); South Africa (1944)

Periodic epidemics in African countries

Israel 1989

Since 2012: Spreading from Middle East to South-east Europe affecting in 2015 Greece, Bulgaria, Serbia, Kosovo, Albania and Montenegro

Economic importance

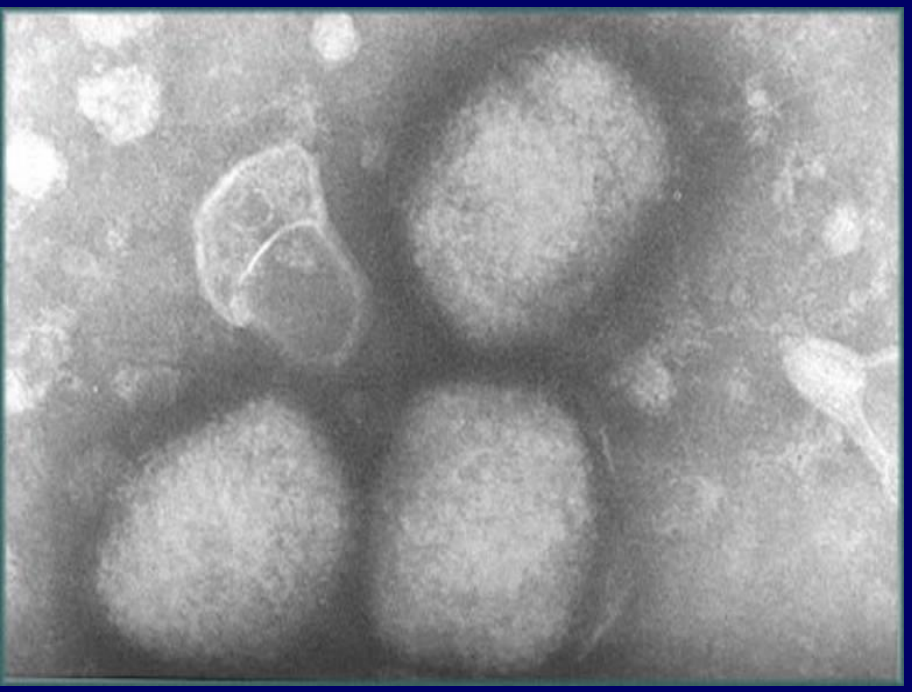
- low mortality
- prolonged debility
- damage to hides
- mastitis and orchitis
- abortion

Important poxviruses of vertebrates (Chordopoxvirinae)

GENUS	PROTOTYPE VIRUS	OTHER MEMBERS
Capripoxvirus	Sheeppox virus	Goatpox virus Lumpy skin disease virus
Parapoxvirus	Orf virus	Bovine papular stomatitis virus Pseudocowpox virus (paravaccinia) Sealpox virus
Suipoxvirus	Swinepox virus	
Orthopoxvirus	Vaccinia virus	Cowpox virus Camelpox virus Buffalopox virus Monkeypox virus Mousepox (ectromelia) virus Raccoonpox virus Uasin Gishu disease virus Taterapox virus
Leporipoxvirus	Myxoma virus	Rabbit fibroma virus Squirrel fibroma virus
Avipoxvirus	Fowlpox virus	Canarypox virus Pigeonpox virus Turkeypox virus Parrotpox virus and others
*Yatapoxvirus**	Yaba monkey tumour virus	Tanapox virus
*Molluscipoxvirus**	*Molluscum contagiosum* virus	

*Genus name proposed to and under consideration by the International Committee for the Taxonomy of Viruses

Aetiology



- Highly resistant
- Large virus: 230-300 nm
- One serotype
- Cross-reaction with other capripox viruses

Pathogenesis

Mechanical transmission (biting insects ?)

Poxviruses epitheliotropic

- multiplication at site of entry
- regional lymph node

Primary viraemia

- liver, spleen, lungs (systemic disease)

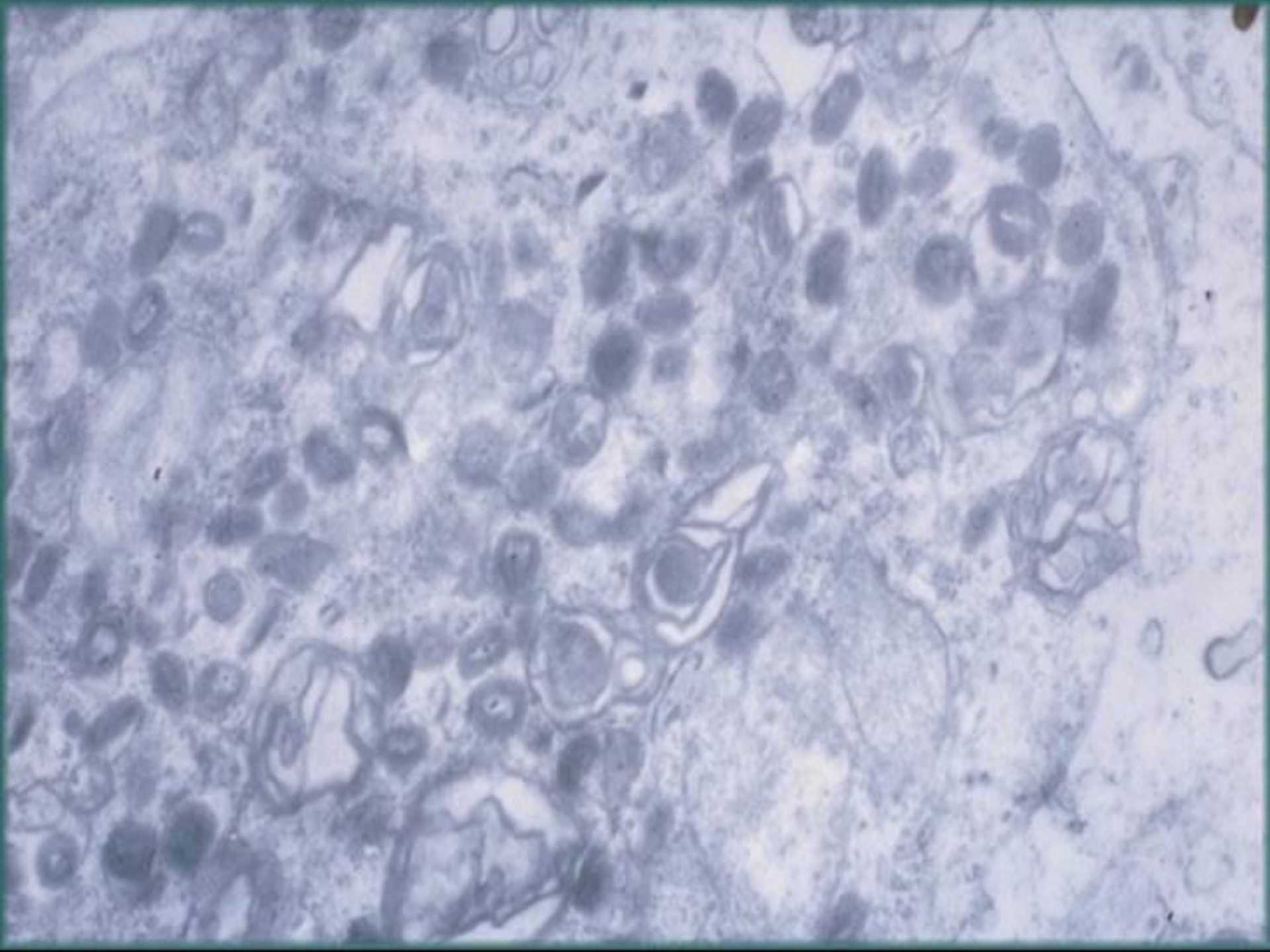
Secondary viraemia

- skin

Vasculitis and lymphangitis

- necrosis/infarction

Subclinical infections



Epidemiology: Distribution

- Limited to Africa for a long time: Large epidemics are sporadic

South East Europe

Caucasus

Epidemiology: Hosts

Cattle

- All breed and age susceptibility
- Incubation period: 8-15 days
- Viraemia: usually less than 2 weeks
- Carrier state?: stable virus:
  - virus in skin nodules (33 days or longer)
  - semen (how long?)

Transmission

- Mechanical transmission: blood-feeding insects and some African tick species – no data available on vector potential European insects and ticks
- Fomites: water and feed troughs and contaminated environment
- Iatrogenic transmission: injectable veterinary treatments and vaccinations
- Seminal transmission??
- Direct contact: mutual grooming??

Transmission by vectors

- Outbreaks of LSD are more common during hot and humid seasons associated with an abundance of vectors
- The most important arthropod vector is likely to vary between affected regions, depending on the climate, season, environmental temperature, humidity and vegetation, favourable for the biology of different insect and tick species
- Experimental vector transmission: challenging



Mechanical transmission by blood-feeding insects

- *Aedes aegypti* mosquito
- Stable fly (*Stomoxys calcitrans*) and tabanids and others
- The role of other local insect species needs to be investigated
- The **big** question is: Does the virus multiply in insects? Biological transmissions



Transmission of LSDV by hard (ixodid) ticks

- Mechanical transmission has been demonstrated in common sub-Saharan ticks: *Rhipicephalus (Boophilus) decoloratus*, *Rhipicephalus appendiculatus* and *Amblyomma hebraeum.* Evidence of transovarial transmissions (more work to be done: virogenesis, role of ticks in epidemiology of LSD?).
- Closely related species in the Middle East region: *R. (Boophilus) annulatus*, *R. praetextatus* and *Hyalomma extravatum*
- No research carried out on European tick species



Role of birds and air currents in long–distance spread

- Contaminated flying insects may be carried short distances by air currents
- Role of birds as carriers of insects and ticks?

Wildlife disease?

What is evidence?

Arabian oryx (*Oryx leucoryx*) and Namibian oryx (*Oryx gazella*)

- Suspected clinical disease in one oryx in Saudi Arabia
- Suspected clinical disease in several oryx in the Kimberley area in South Africa

Springbok (*Antidorcas marsupialis*)

Suspected clinical disease in springbok in Namibia

Asian water buffalo (*Bubalus bubalis*)

- Suspected clinical disease in 5 Asian water buffalo in Egypt
- Serbia: Domestic buffalo?

African buffalo (*Syncerus caffer*)

- **Report of serological positive buffalo in Kenya. Incriminated as reservoir? (Davies, 1991)**

- **Experimental infection of two young African buffalo: no clinical disease (Young *et al*, 1970)**

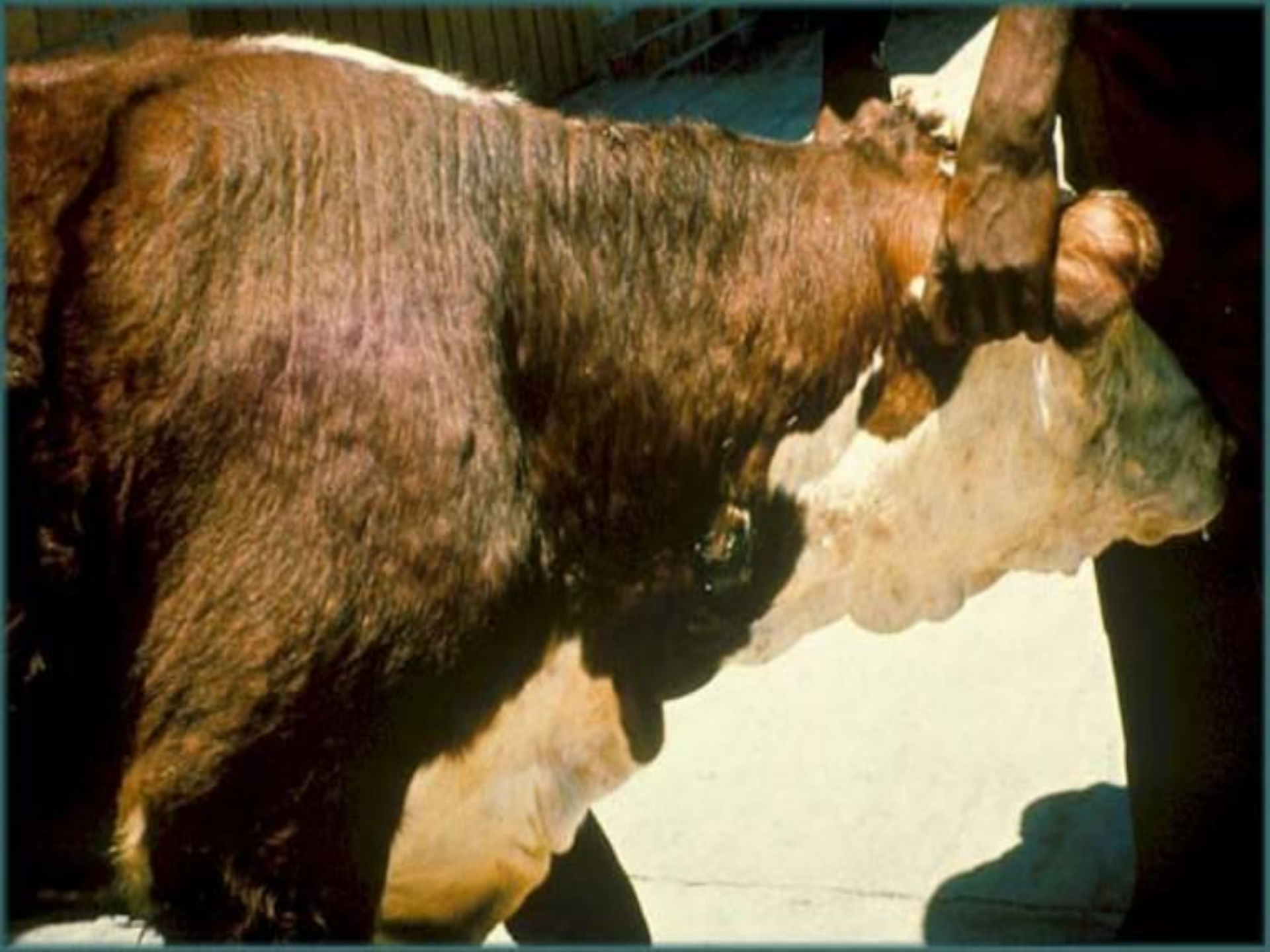
- **Nine seronegative buffalo (5 adults and 4 calves) and 2 cattle infected experimentally in boma in Kuger National Park (Howell and Coetzer, 1998)**
  - No clinical disease or serconversion in sera of the buffalo 42 days after infection
  - Two cattle: clinical disease 12 days after infections and seroconverted

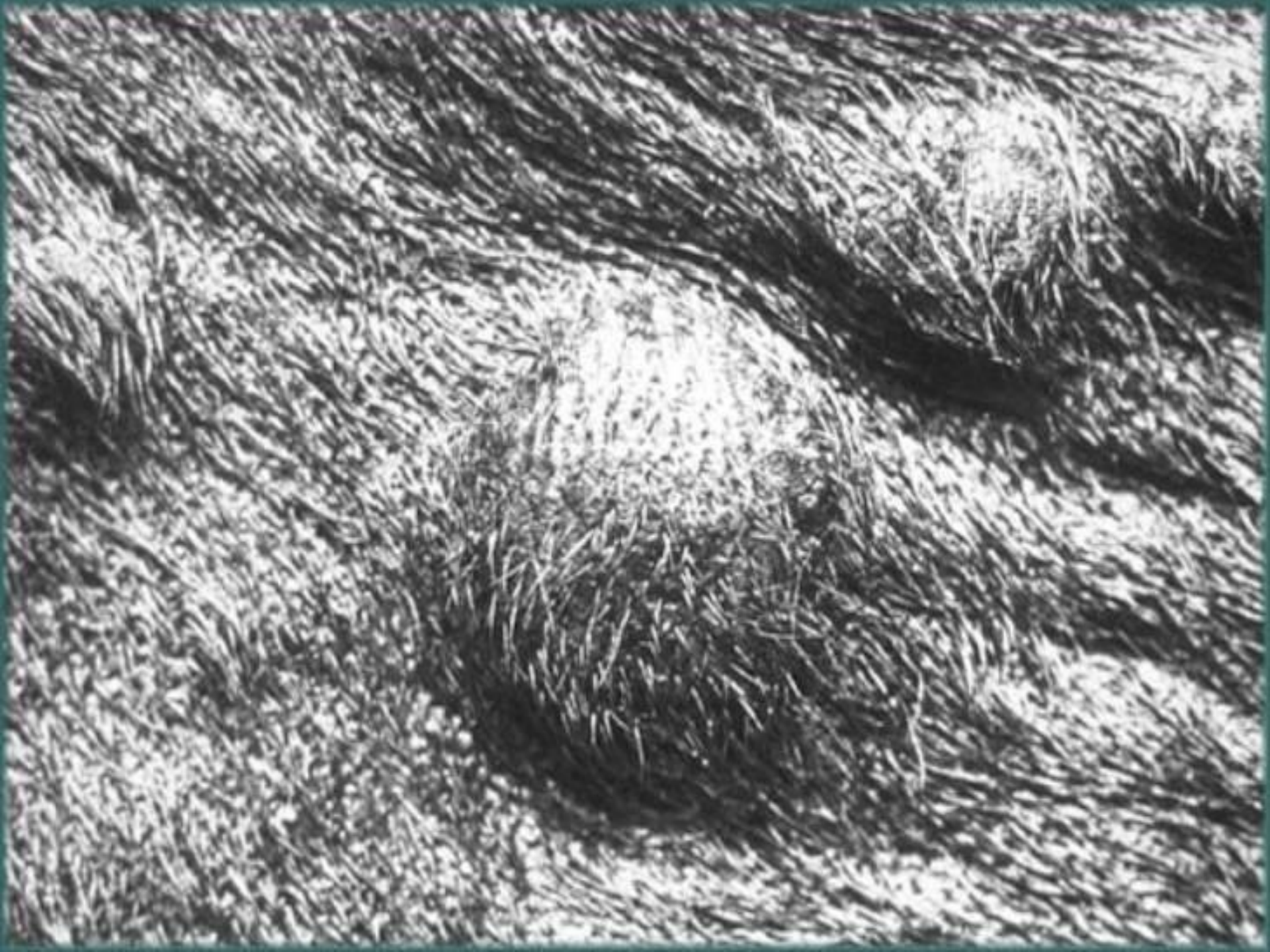
- **440 sera of culled African buffalo (1 – 20 year old) in Kruger National Park: negative serum neutralizing antibody titres (Howell and Coetzer, 1998)**

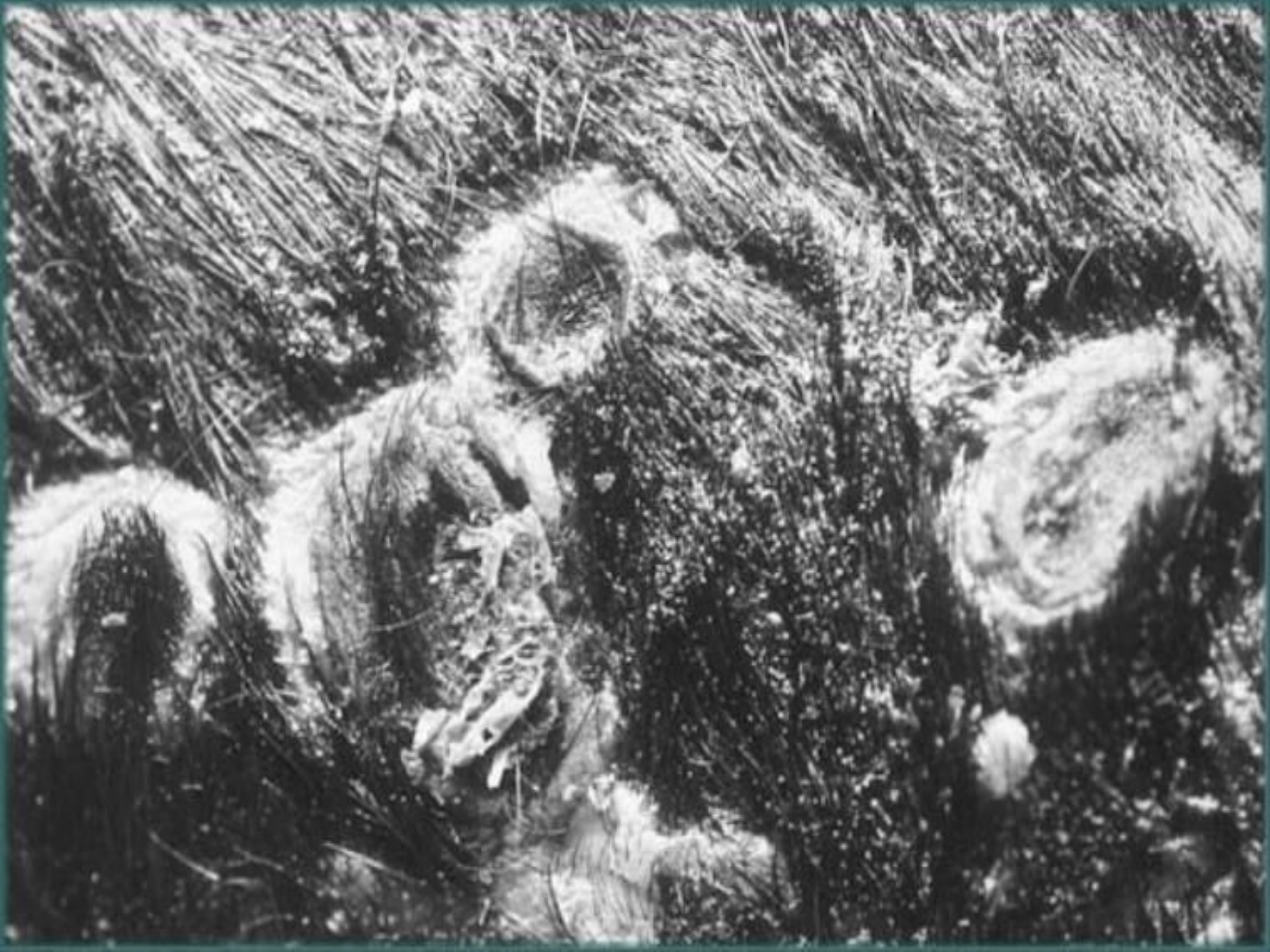
Impala (*Aepyceros melampus*) and giraffe (*Giraffa camelopardalis*)

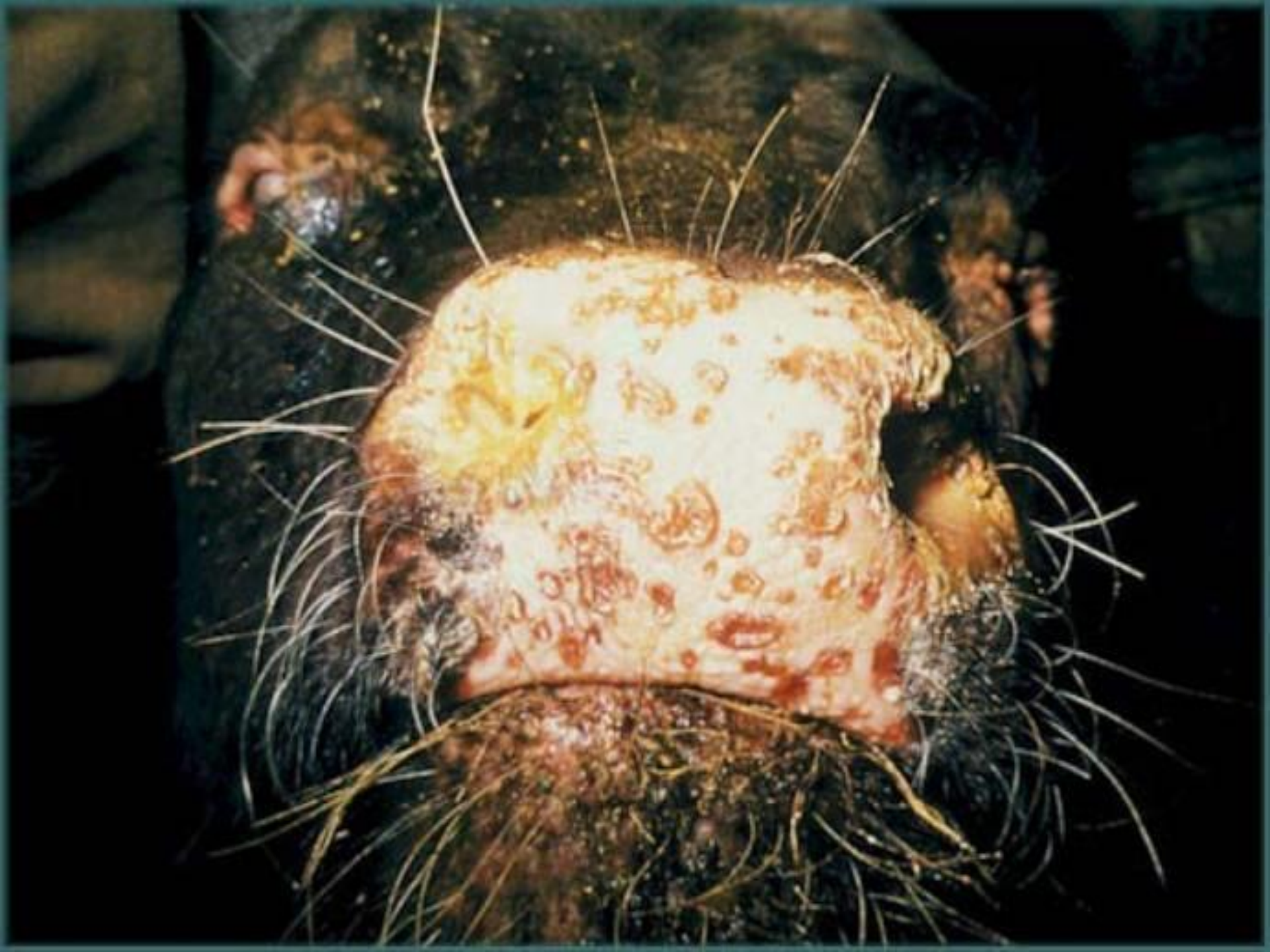
Both species highly susceptible to experimental infection (Young *et al*, 1970)

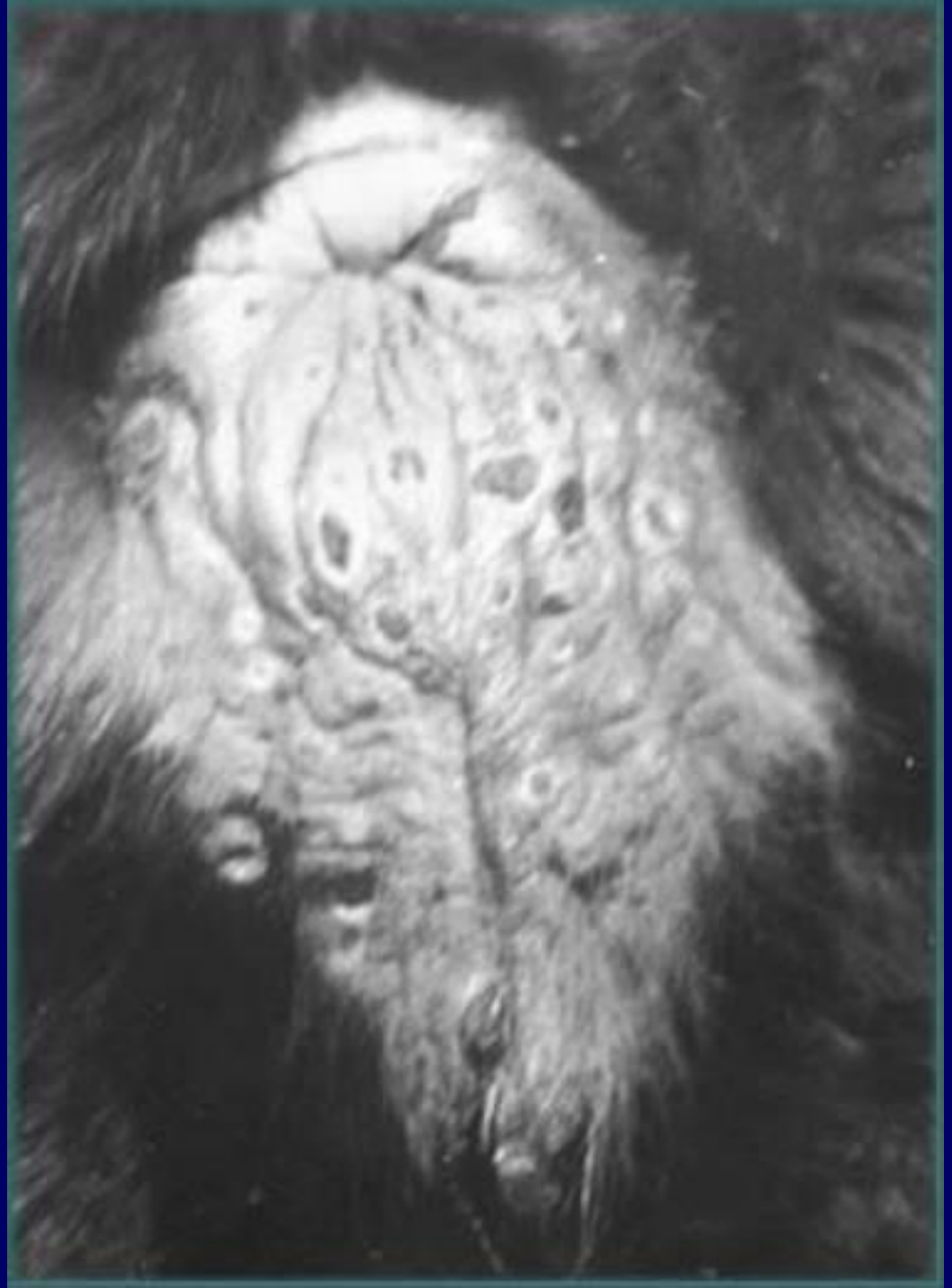
Clinical signs and Pathology

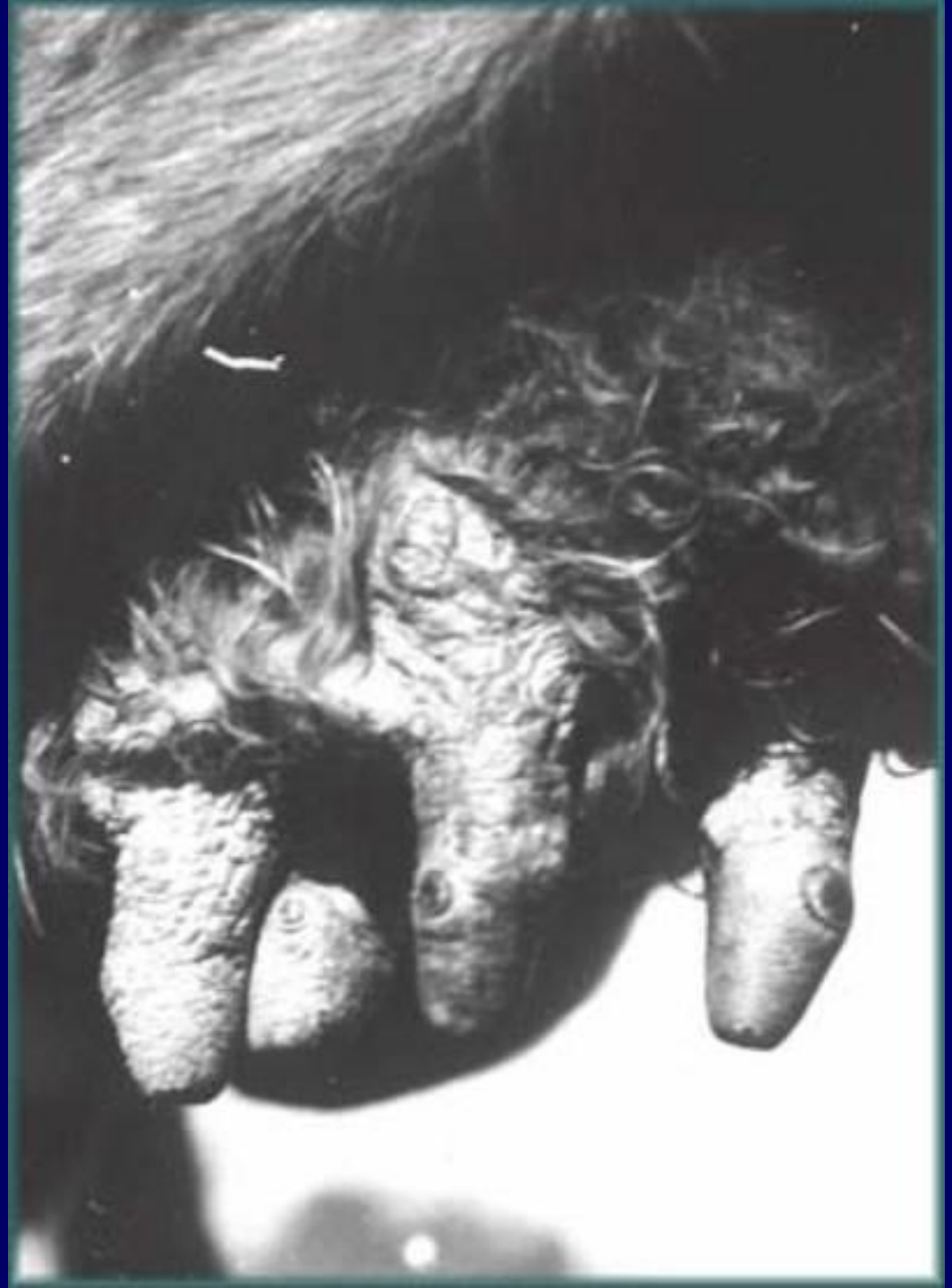


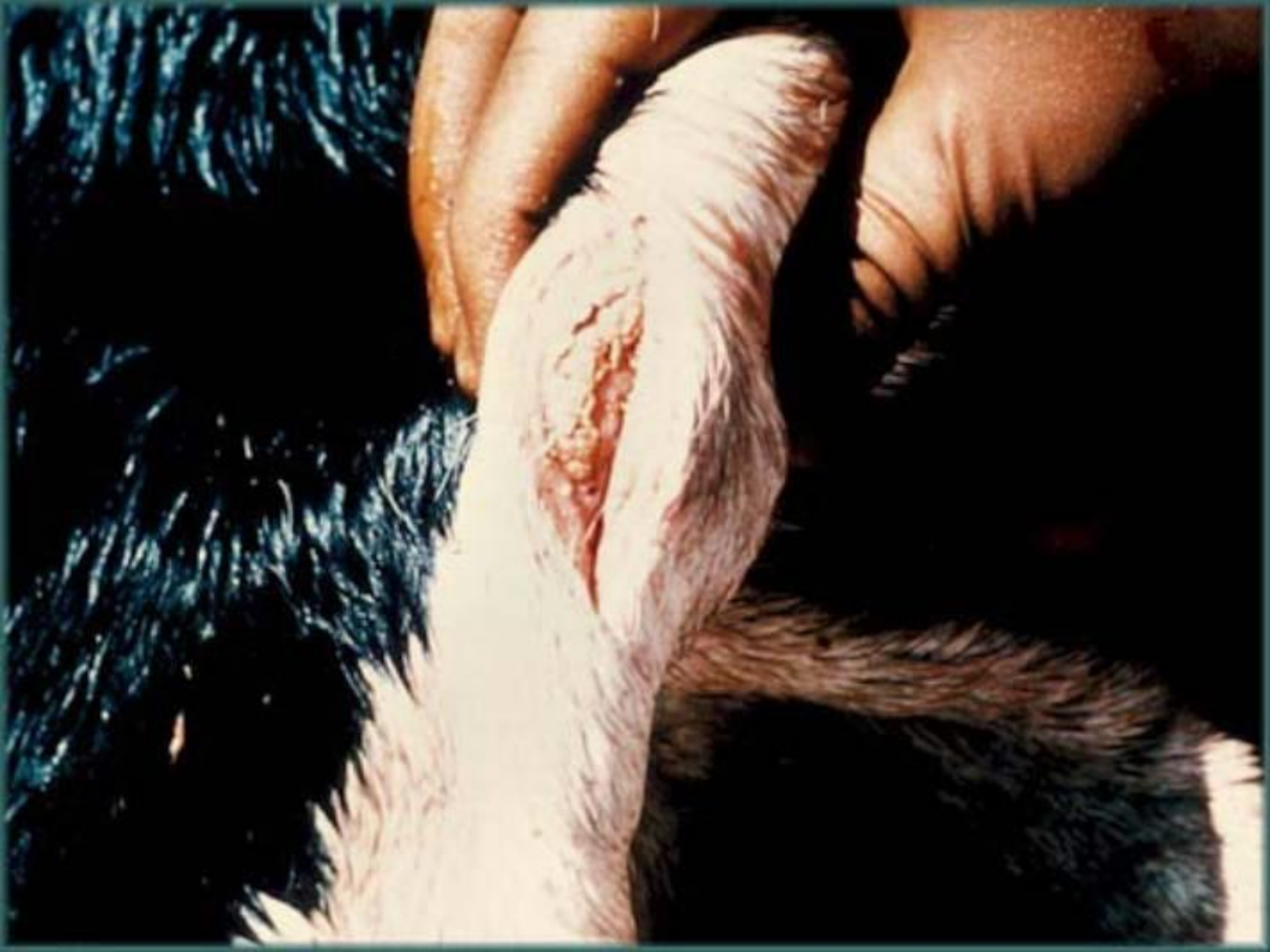


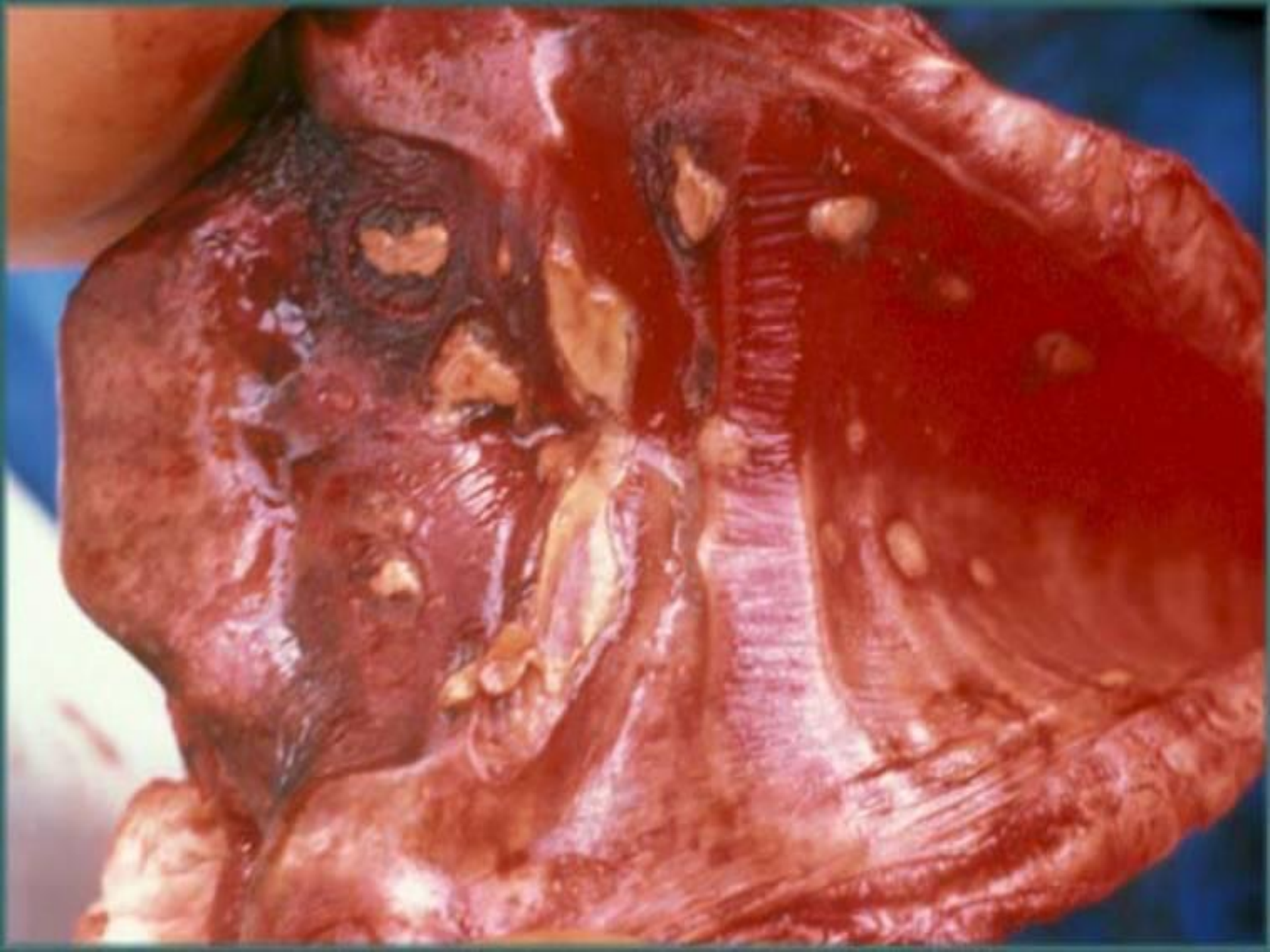


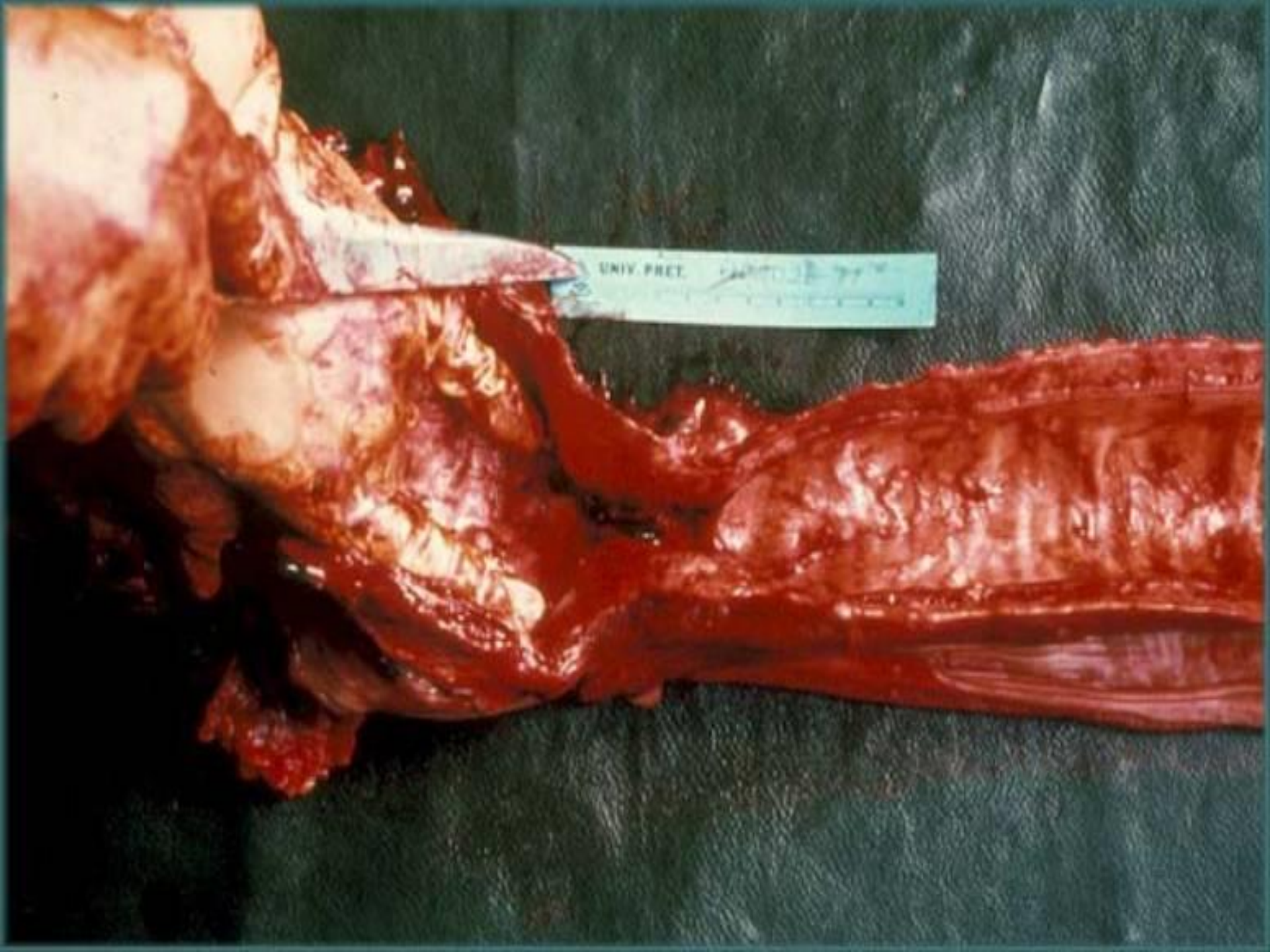








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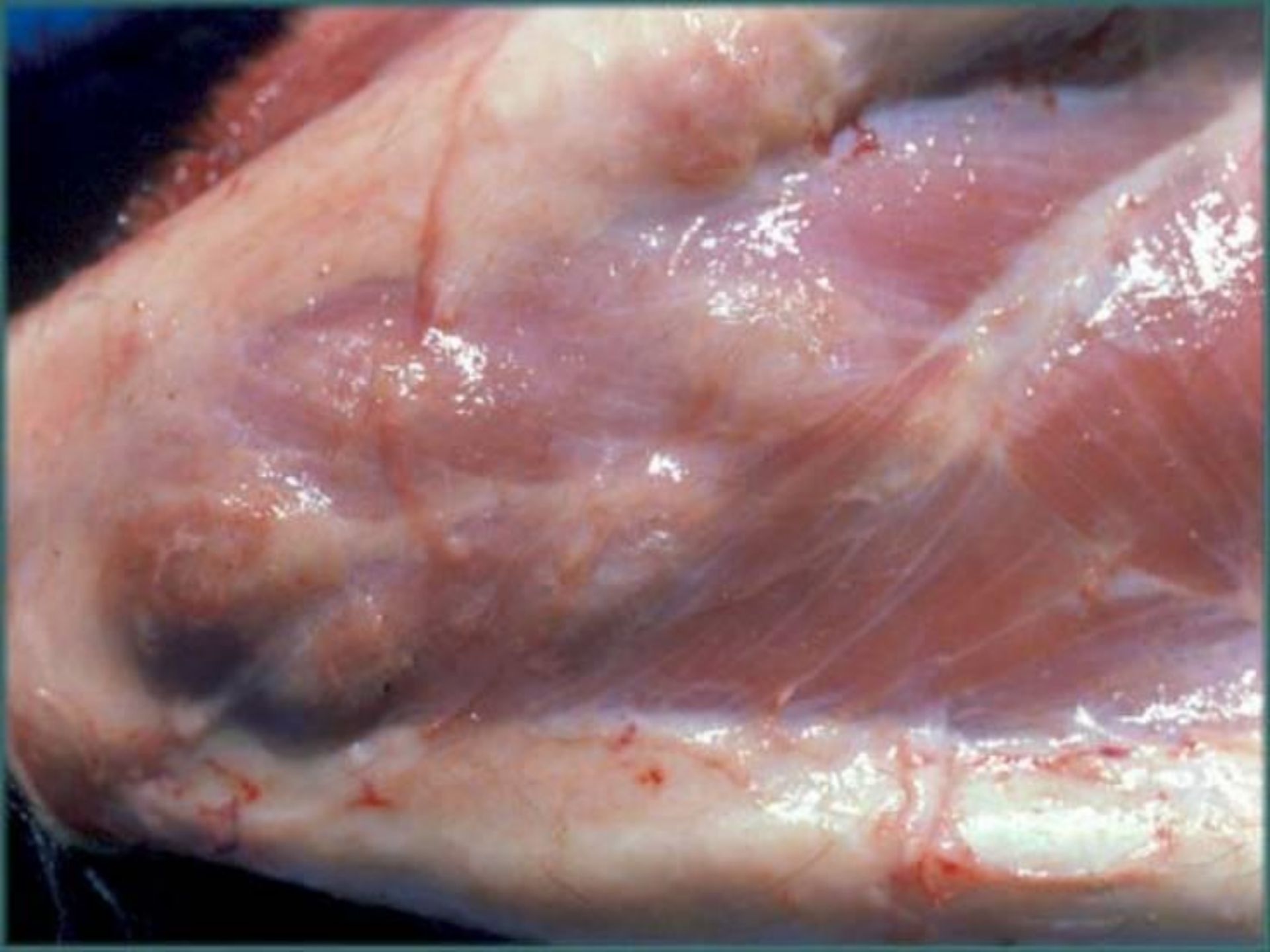

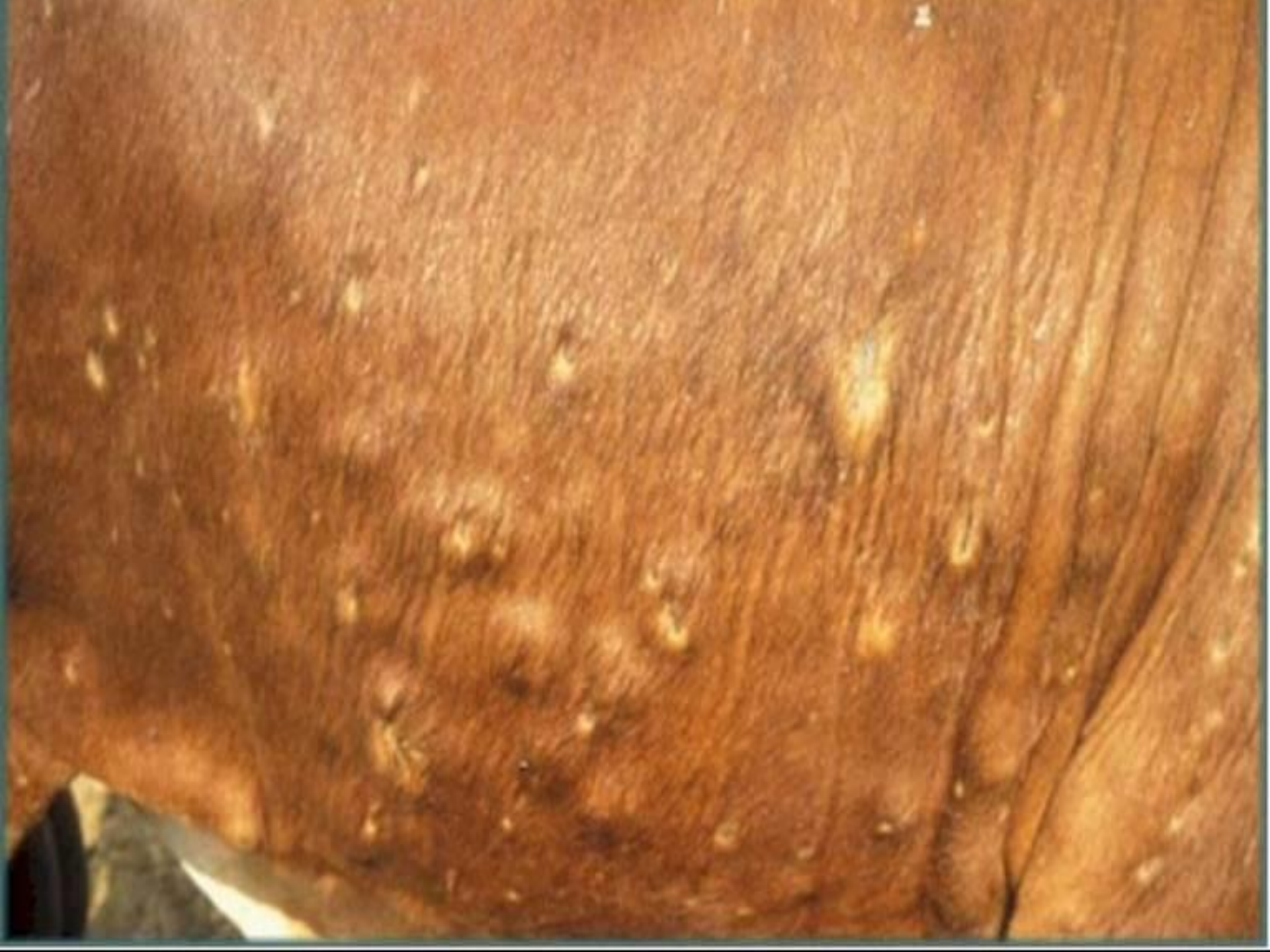

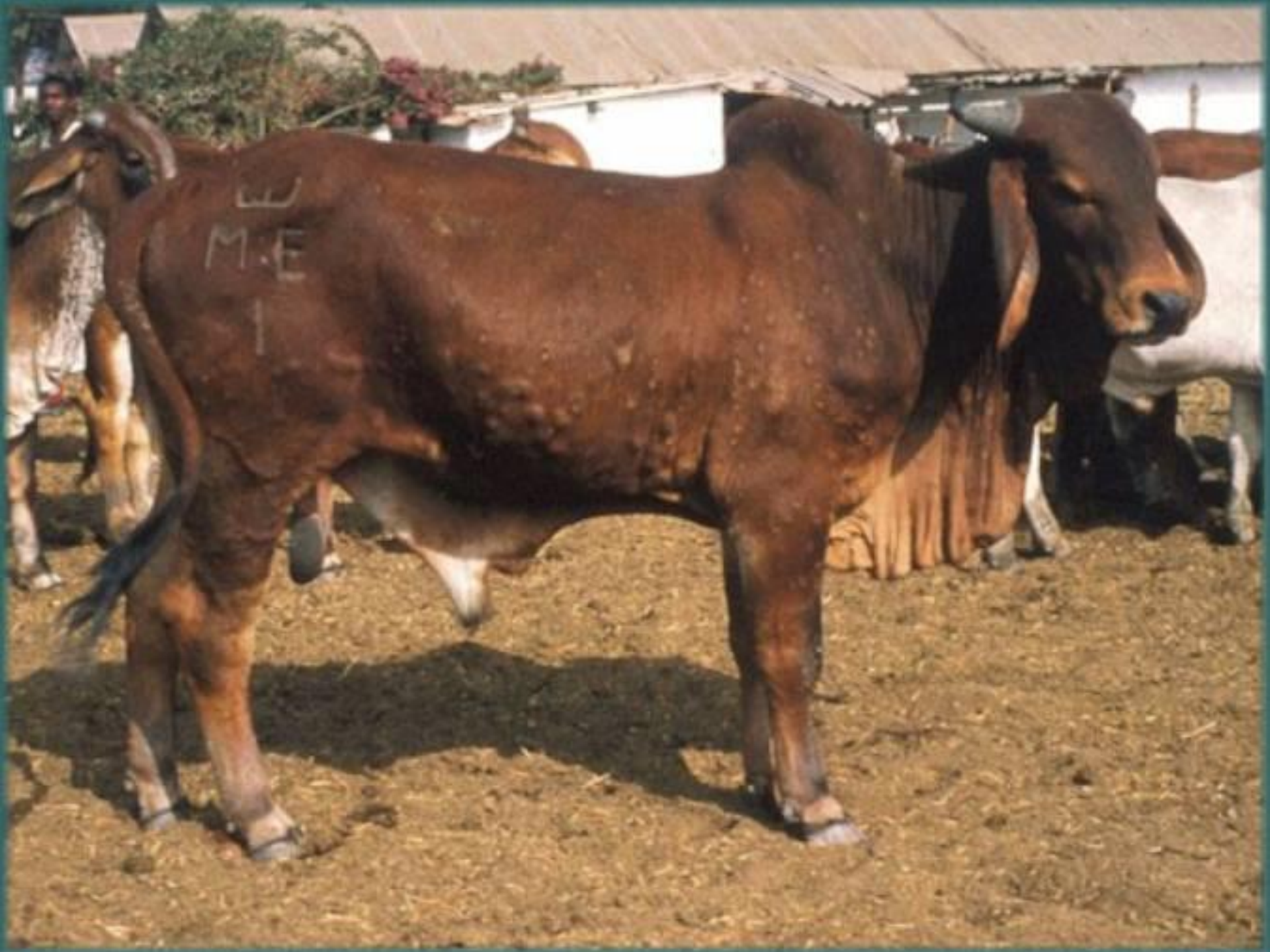
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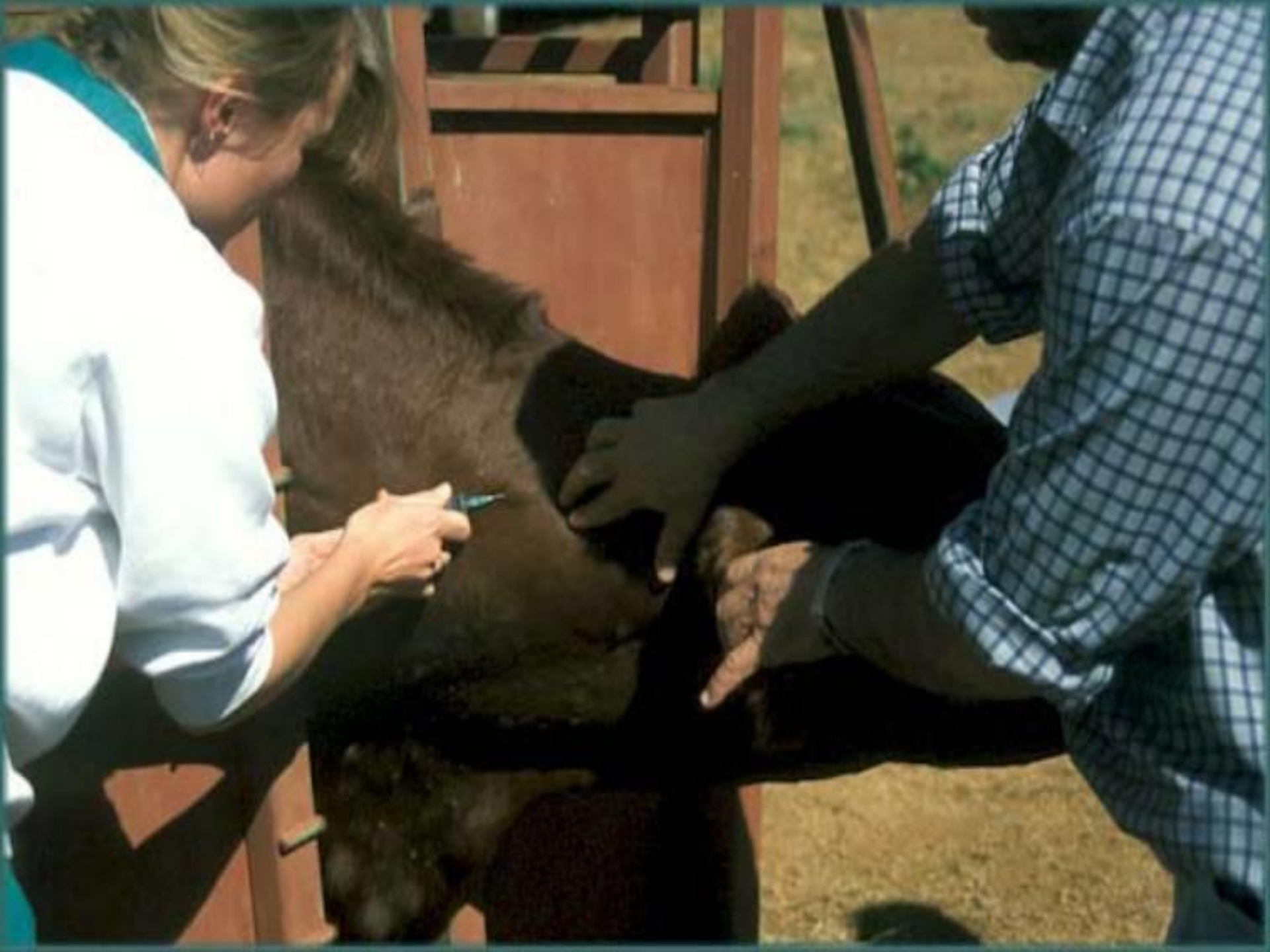


Diagnosis

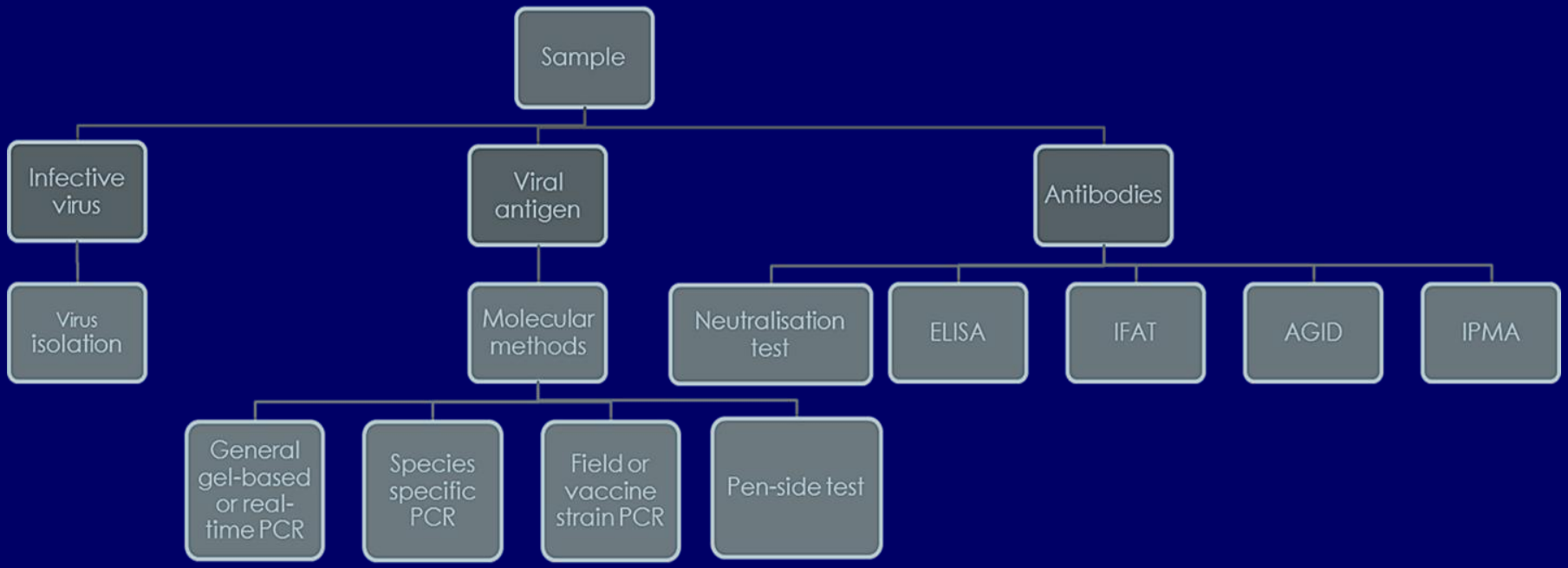
Presumptive diagnosis

- clinical and pathological features

Confirmation of diagnosis

- negative staining : TEM
- virus isolation
- PCR
- Serology: -virus neutralization test
  -ELISA
- Pathology: immunoperoxidase staining

Detection of the antigen/infectious virus and antibodies against LSDV



Diagnostic tools and reference laboratories

- Tests:
  - For primary detection of the LSD virus - validated, specific and highly sensitive group-specific PCR methods
  - If clinical signs are detected in cattle vaccinated with a LSDV containing vaccine - PCR method to differentiate the attenuated vaccine from the virulent field strain
  - If clinical signs are detected in cattle vaccinated with a SPPV containing vaccine or in wild ruminants - Species-specific genotyping PCR methods
- National ref labs:
  - Competent staff, facilities, funding, equipment, kits, materials, reagents
  - Testing performed according to good laboratory practice
  - Appropriate QA system in place
- International reference laboratories provide diagnostic service, training, research and biobank of different strains/isolates (OIE ref lab in Pirbright Institute and EU ref lab is Coda Cerva in Begium)

Limitations of Serology

- Neutralization test is gold-standard but time- and labour-consuming and requires working with live virus and cell cultures, limited to biosecurity level 3 labs
- Naturally infected cattle can not be serologically differentiated from vaccinated animals (no DIVA vaccine available)
  - Antibodies can be usually detected for three to six months after natural infection
  - After vaccination, antibodies appear within 15 days and reach the highest level in 30 days, dropping then below detectable levels, some vaccinated animals do not seroconvert although fully protected
  - Some individuals showing mild disease may develop only a low levels of neutralizing antibodies that cannot be detected using currently available neutralization test - Interpretation negative test result is challenging.
- Urgent need for a DIVA vaccine against LSD as well as ELISA

Differential diagnosis

Pseudo-lumpy skin disease

Dermatophilosis

Insect bites

Control

Endemic countries

Quarantine and movement control

- Ineffective

Immunoprophylaxis

- Attenuated Neethling strain
  - Live attenuated LSDV vaccines provide good protection in cattle and is superior to sheeppox virus (SPPV) vaccines (Ben-Gera *et al* 2015)
- Where distribution of SPP and GTP overlaps with LSD
  - SPPV vaccines may be used for cattle against LSDV
  - GTPV containing vaccines are not yet used against LSD but has been demonstrated to provide good protection against LSDV

Supportive therapy

Control

Non-endemic countries

- Ban on animal movement
- Vaccination
- Culling of infected animals

Vaccines on the market

- LSDV containing vaccines:
  - LSDV Neethling strain by Onderstepoort Biological Products (OBP)
  - Attenuated LSDV field strain by MSD Animal Health
- SPPV containing vaccines against LSDV:
  - Yugoslavian RM65 SPPV vaccine (at a 10 times stronger dose than used for sheep) is commonly used for cattle in the Middle East
  - Romanian SPPV vaccine for cattle in Egypt
  - Bakirköy SPPV (3 times sheep dose) used in cattle in Turkey
  - Russian SPPV
- No DIVA (Differentiation of Infected from Vaccinated Animals) vaccine available
- Inactivated vaccines are expected to appear on the market shortly
- Huge increase in demand of vaccines has led to longer waiting times to obtain vaccines from manufacturers

Vaccination regime and adverse reactions

- Annual vaccinations
- Opened and reconstituted vaccine should be used during the same day
- Regional vaccinations should be preferred to ring vaccinations
- All animals should be vaccinated (100% coverage) including pregnant females and young calves
- Calves from vaccinated/naturally infected mothers are vaccinated between 3 to 4 months of age
- Local reaction at the vaccination site
- Some animals show general reaction and drop in milk production
- Diagnostic PCR assay available to differentiate between field and vaccine viruses

Photo courtesy Dr Shlomi Levi