FMD NETWORK

CONTINGENCY PLANNING

Pigs and Foot and Mouth Disease

eufmd | FMD CONTINGENCY NETWORK | Food and Agriculture Organization of the United Nations

29 March 2018

Part 1: Clinical comparisons of FMD and Senecavirus-A (SVA) infection in pigs

Part 2: Do pigs become carriers of FMDV? Results of studies on this important issue

Welcome! We will begin at 15.30 CEST

Before the webinar begins, you can check that your sound is working by selecting ‘Meeting’ and ‘Audio Setup Wizard’.

If you have any problems, please use the chat box to ask for our help. You can also say hello to your fellow participants using this box.

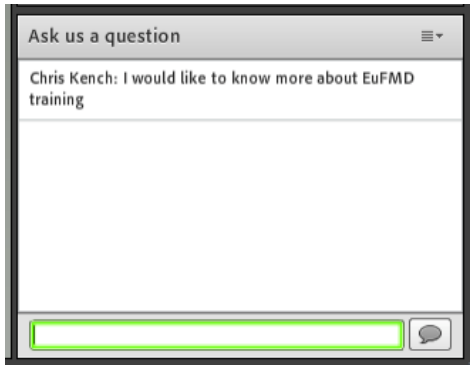
Agenda for today

- Introductions;
- First presentation
  Clinical comparisons of FMD and Senecavirus-A (SVA) infection in pigs;
- Questions and answers session;
- Second presentation
  Do pigs become carriers of FMDV? Results of studies on this important issue;
- Questions and answers session;

****We will be recording the webinar****

Introduction to the webinar screen

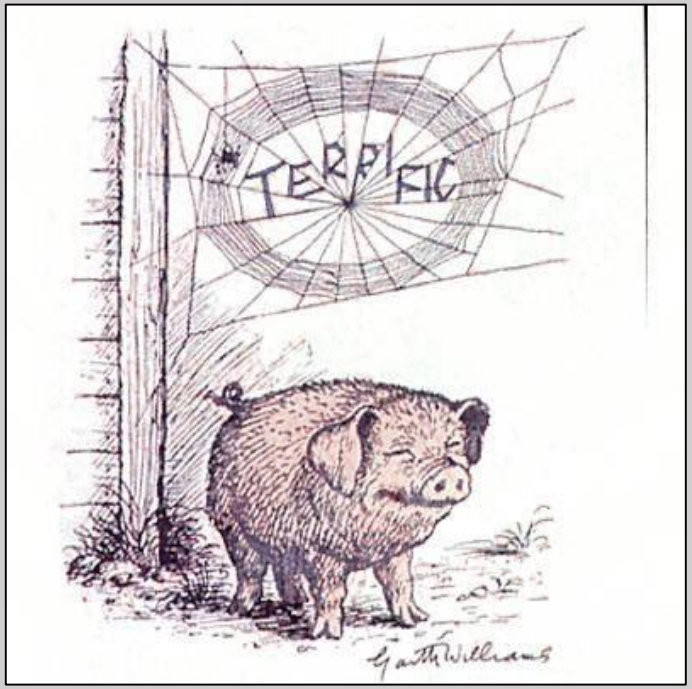
The chat box will be here for your questions



In your opinion, do pigs become carriers of FMD virus?

Clinical comparisons of foot-and-mouth disease (FMD) and Senecavirus-A (SVA) infection in pigs

Jonathan Arzt & Carolina Stenfeldt



Jonathan Arzt, DVM, MPVM, PhD, DACVP
Veterinary Medical Officer (Pathologist)
Plum Island Animal Disease Center
Agricultural Research Service, USDA

Vesicular Diseases of Pigs (Differentials)

Classical

- Foot-and-mouth disease
- Swine vesicular disease
- Vesicular stomatitis
- Vesicular exanthema of swine

Non-Classical

- Other Enteroviruses
- Thermal/caustic burns
- Parvovirus
- IVD = Idiopathic Vesicular Disease
- Senecavirus A

Vesicular Diseases of Pigs (Differentials)

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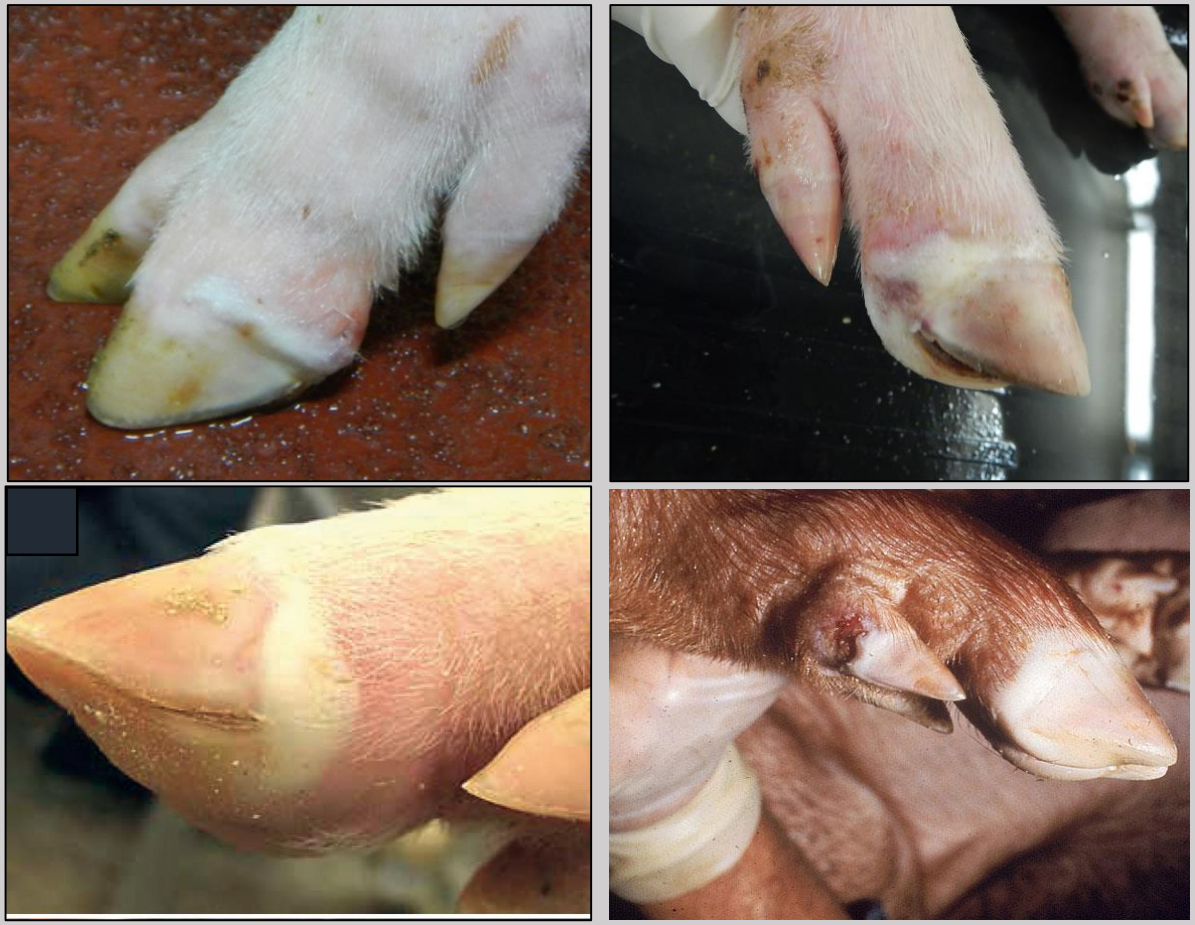
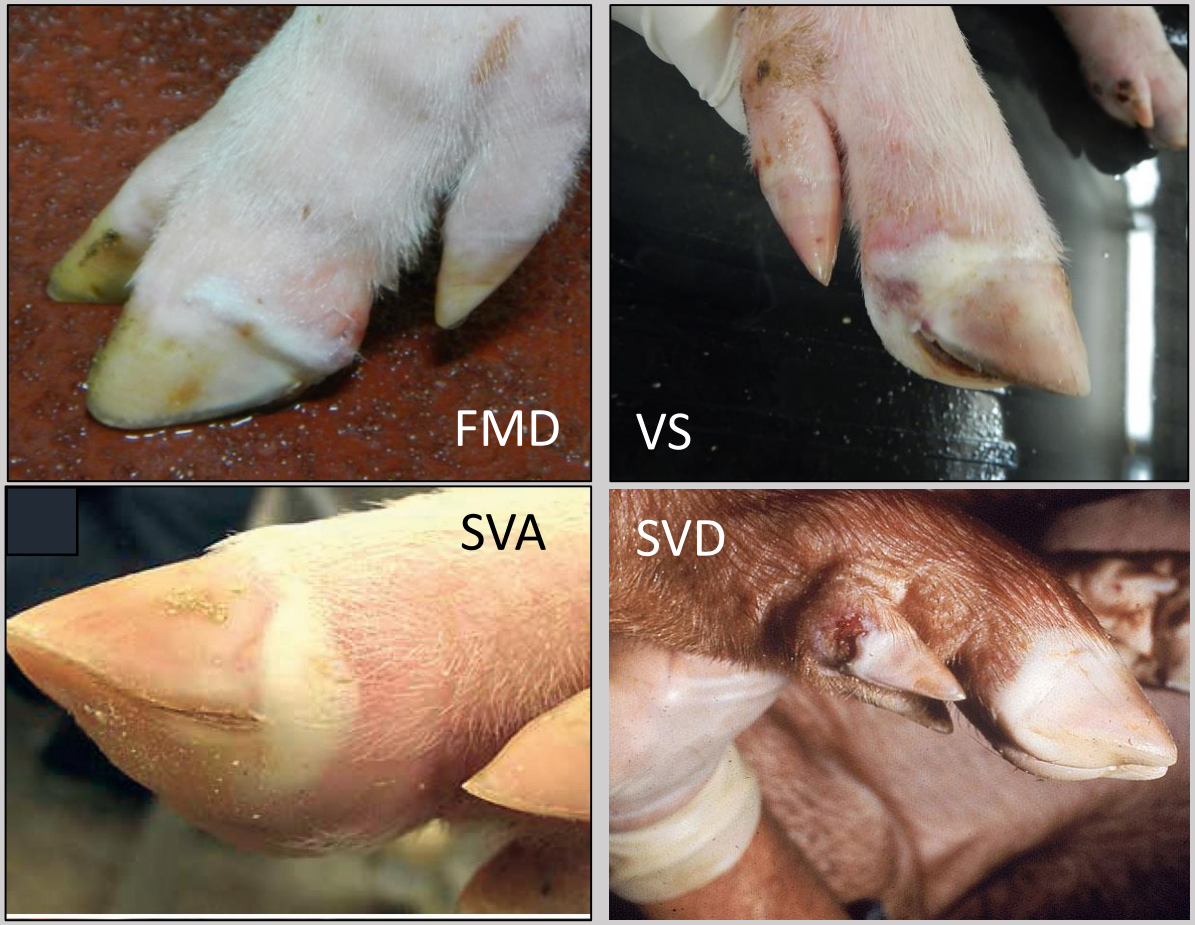
Clinical images: 4 pig vesicular diseases

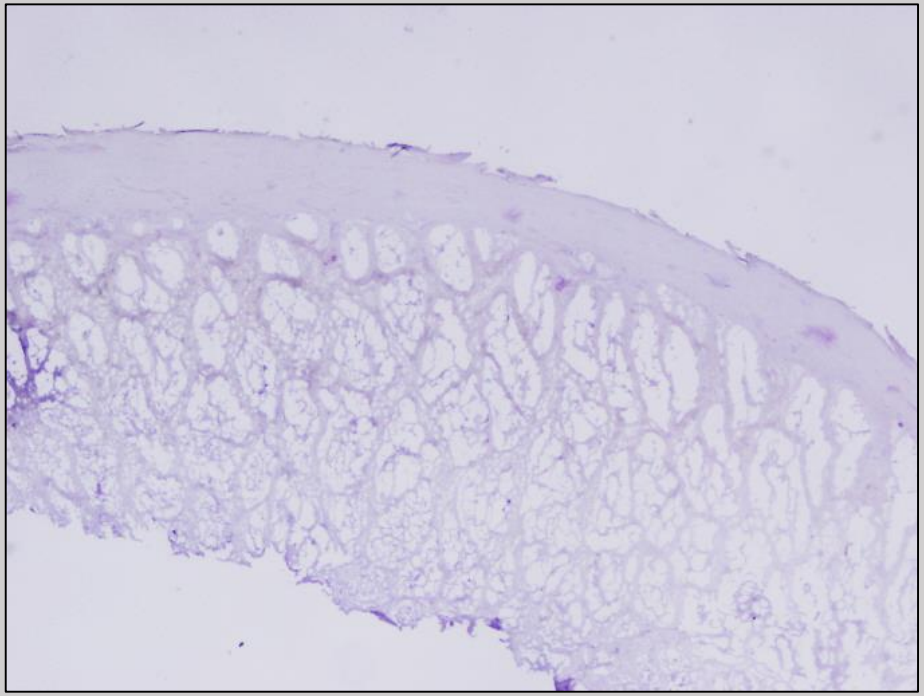


Clinical images: 4 pig vesicular diseases



Vesicle Morphology (indiscernible)

SVA Vesicle



FMD Vesicle

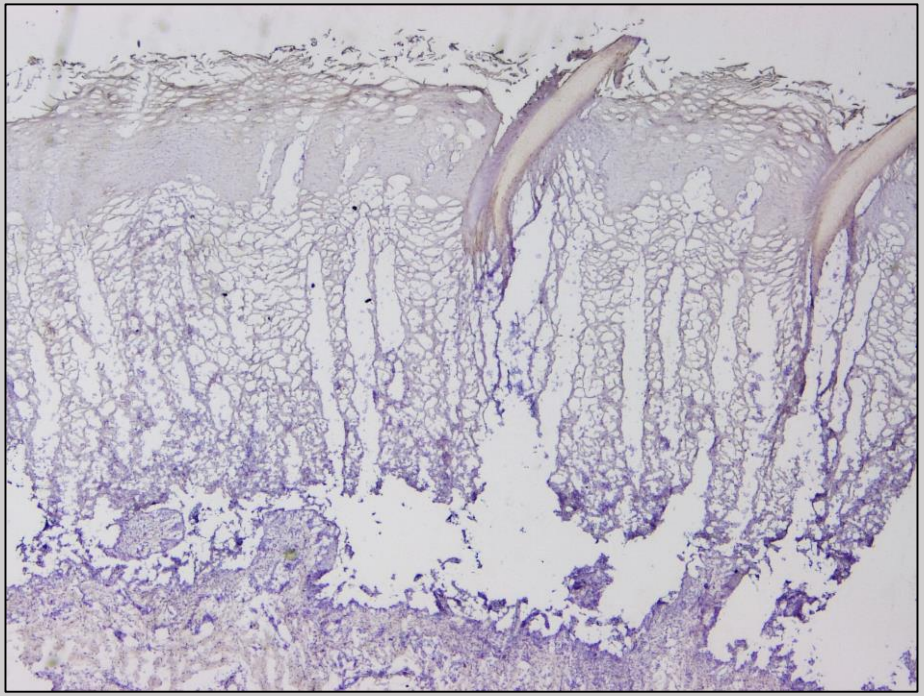


Image: E. Silva

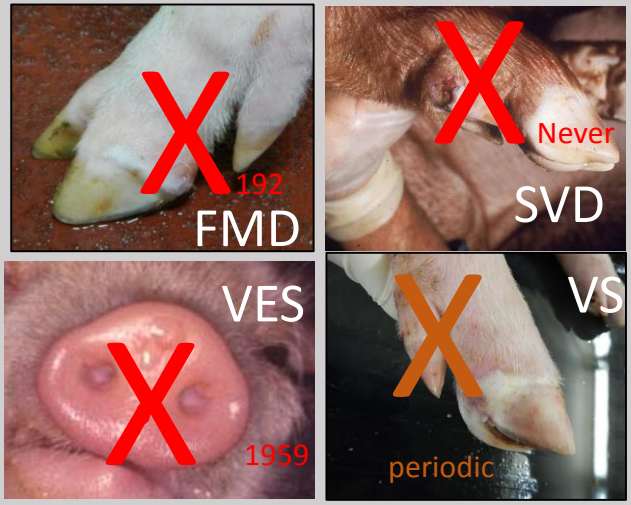
In a Diagnostic Scenario:
Must Differentiate by
Laboratory Diagnostics
(rRT-PCR)

Vesicular Disease Panda

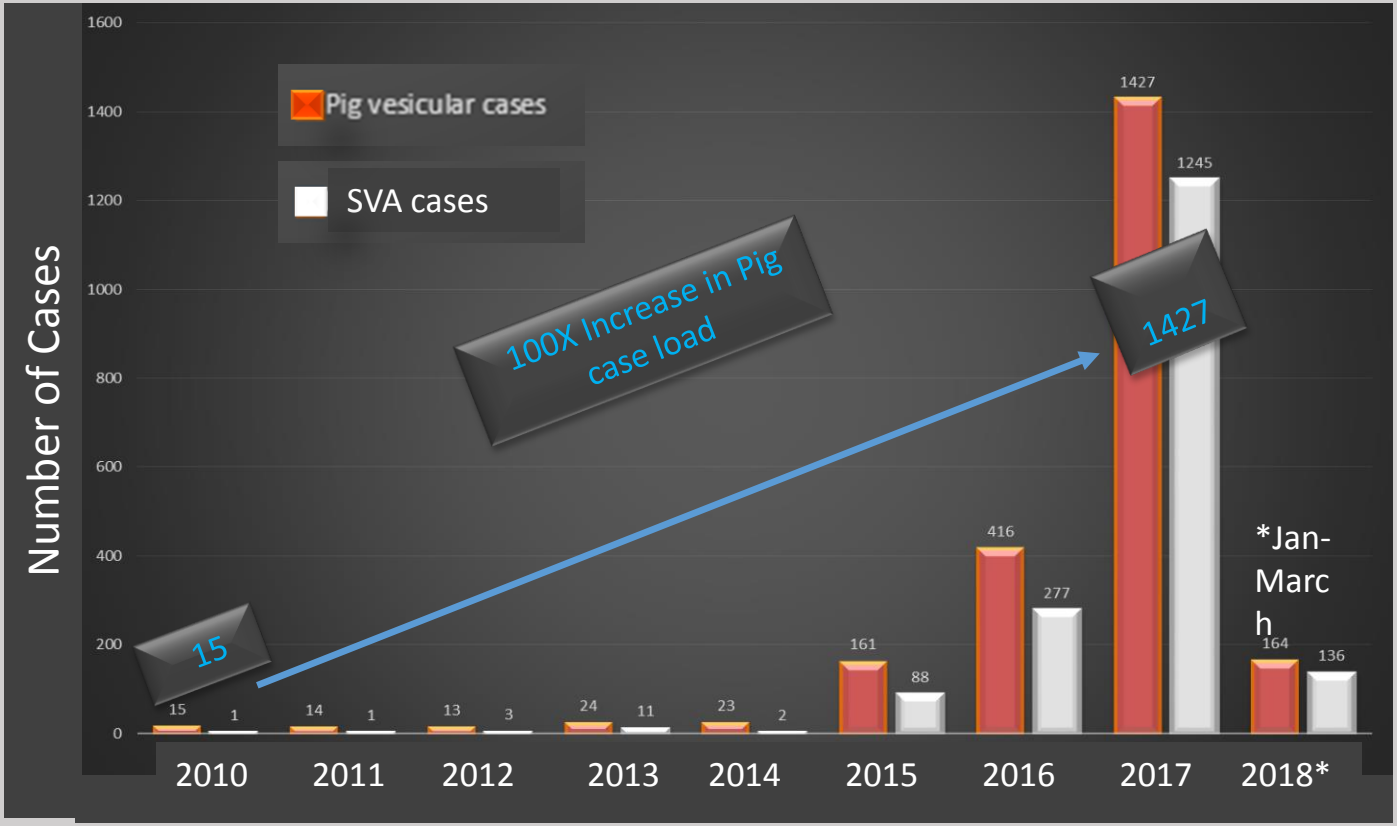
Why does SVA matter?

<u>Vesicular disease landscape (USA)</u>

- FMD free since 1929
- SVD-free (never occurred)
- VES-free since 1959
- VS periodic, limited, rare in pigs, previously “limited endemic” ?
- SVA……”endemic”… over the last 10 years?



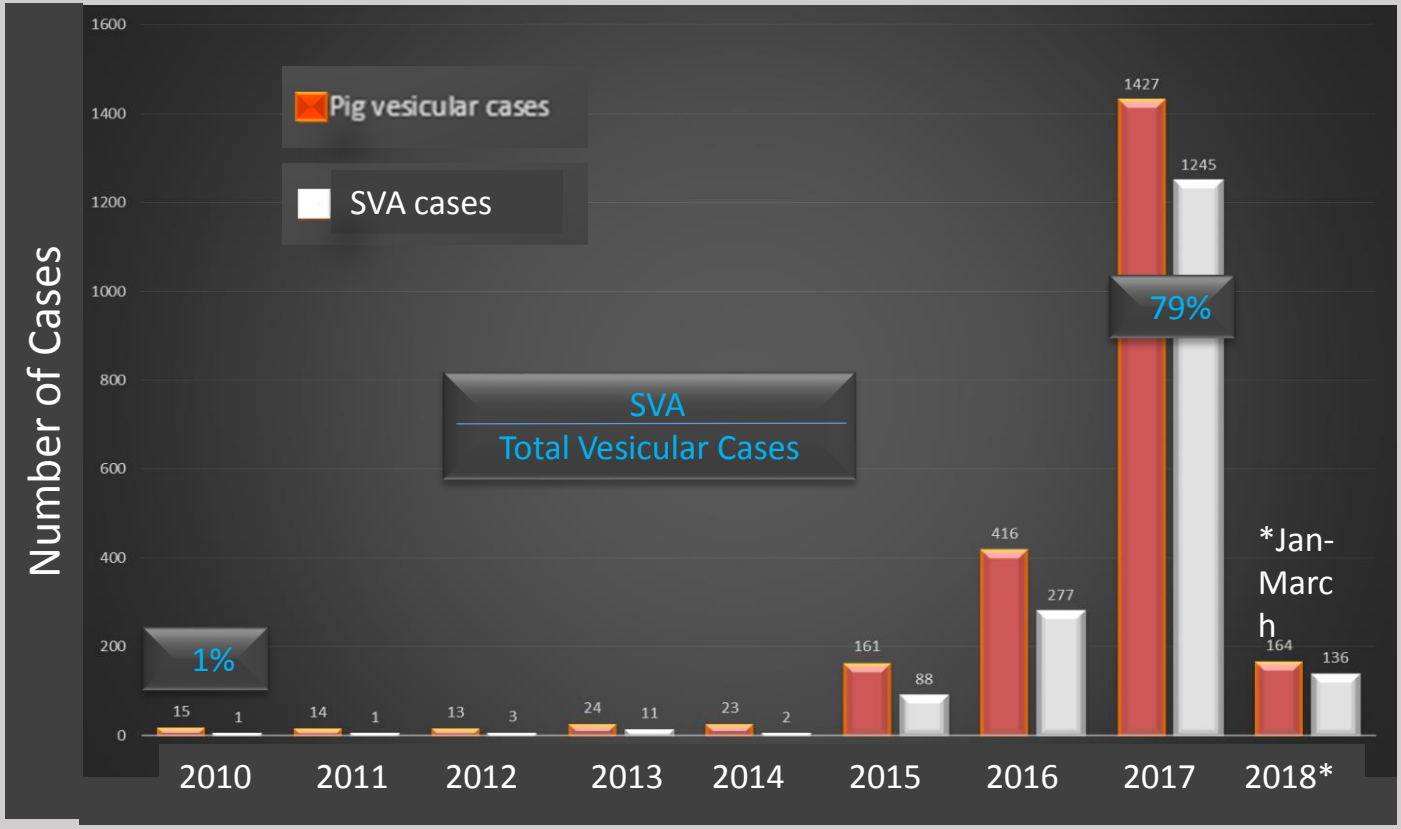
Pig Vesicular Case Submissions to Foreign Animal Disease Diagnostic Laboratory (FADDL) 2010-2018



How much SVA matters?!

From: Mayr & Sturgill, FADDL, APHIS, USDA

Pig Vesicular case submissions to FADDL 2010-2018

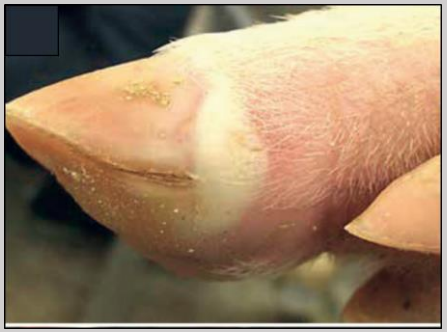


How much SVA matters?!

From: Mayr & Sturgill, FADDL, APHIS, USDA

Senecavirus A (SVA)
(previously Seneca Valley Virus (SVV))

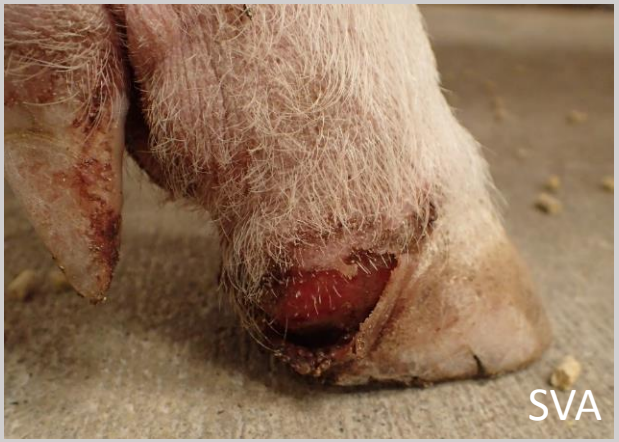
- Highly contagious and economically relevant viral disease of pigs and ……..?
- Etiology: Novel Picornavirus in novel genus (Senecavirus)
- Origin: First Identified in 2002 as a contaminant
- Experimentally Confirmed as cause of vesicular disease 2016
- Distribution:
  - Has been retrospectively associated with IVD cases as early as 1988 in USA and Canada
  - 2015 Reported as cause of IVD in Brazil, China, Thailand

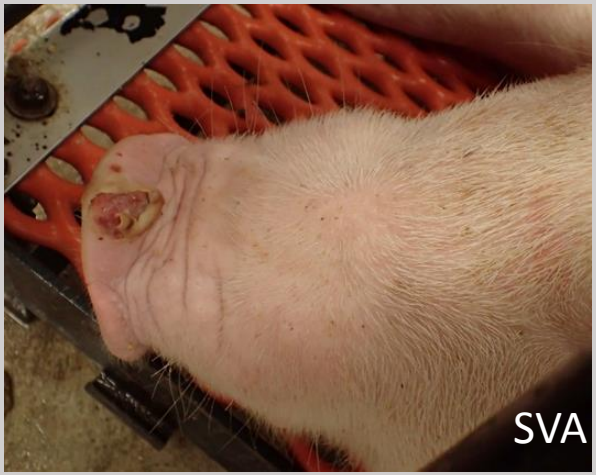


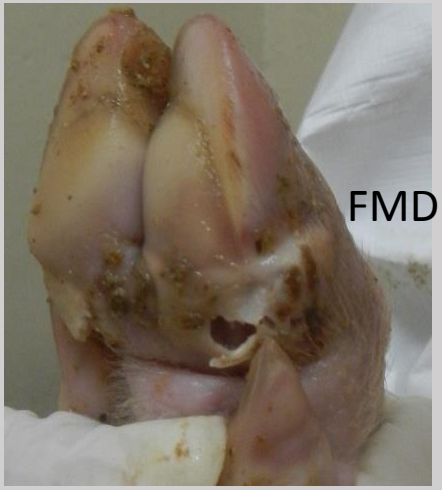
Montiel et al ‘16

Clinical Differences?

FMD & SVA vesicles; usually clinically indiscernible







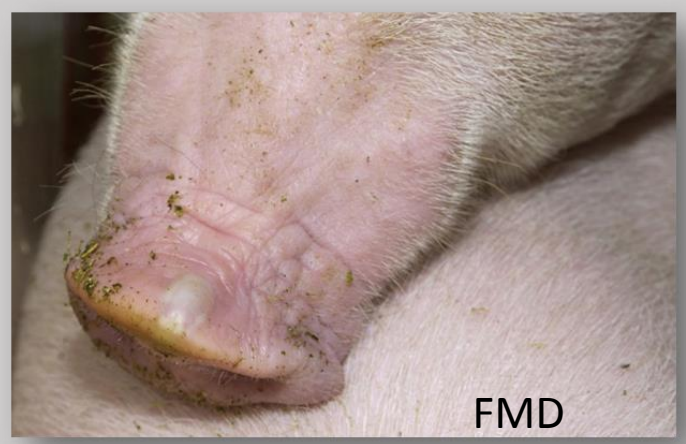
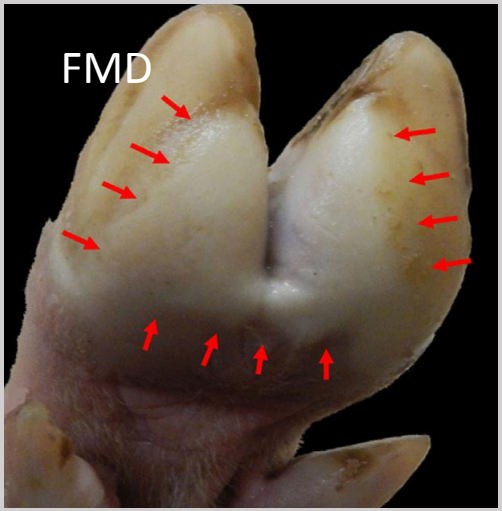
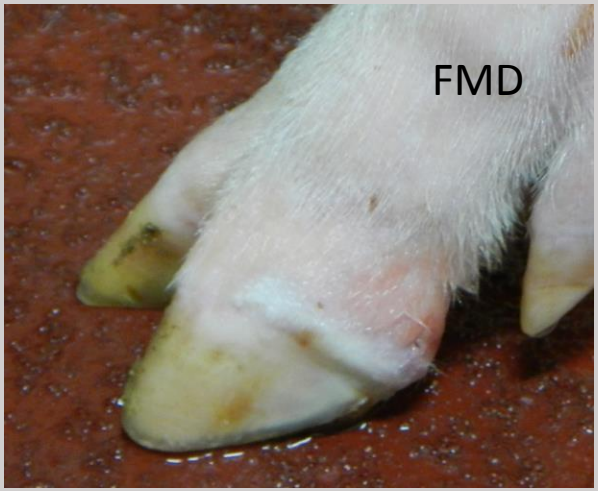


Photo Credits:
Buckley & Lager
Montiel et al ’16
Arzt & Stenfeldt

Early FMD Vesicles have characteristic swelling and whiteness





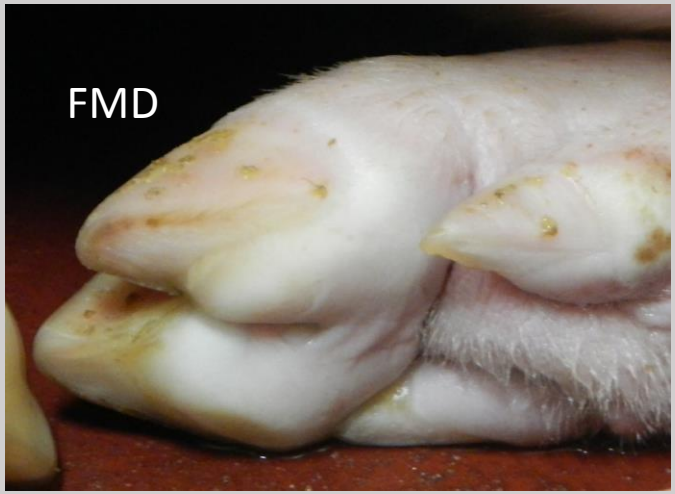
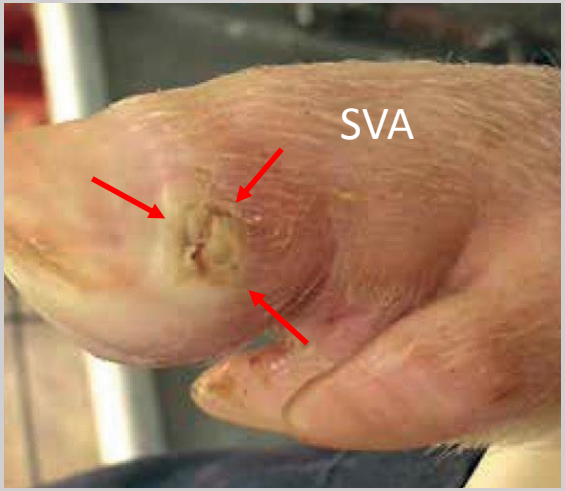
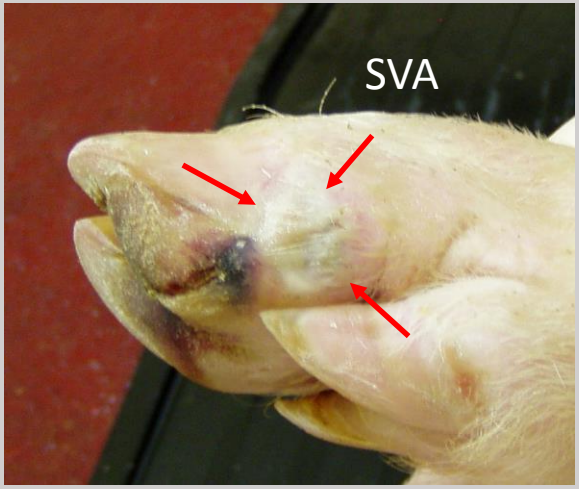
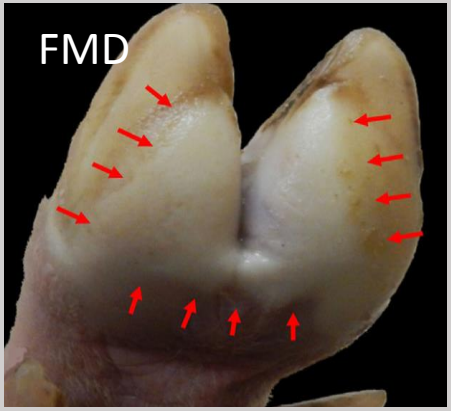


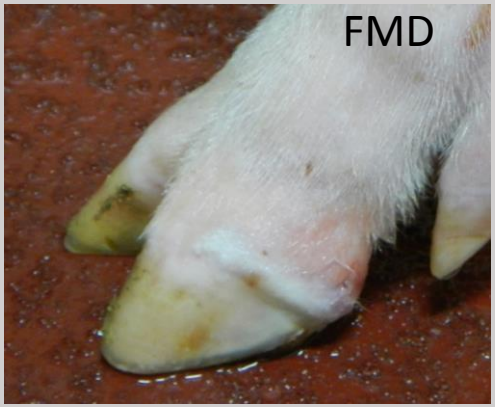
Photo Credits: Buckley & Lager, Montiel et al ’16, Arzt & Stenfeldt

By comparison, SVA Vesicles may have yellow-tinged hint of inflammation









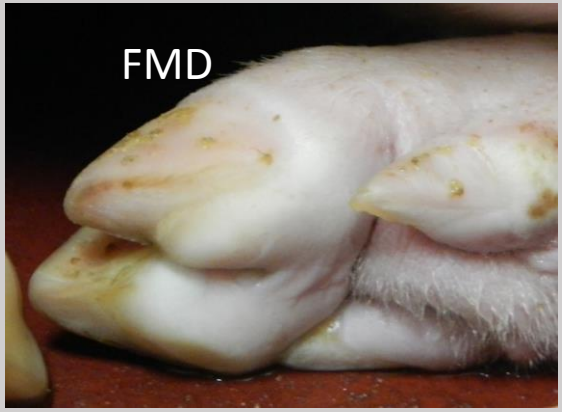
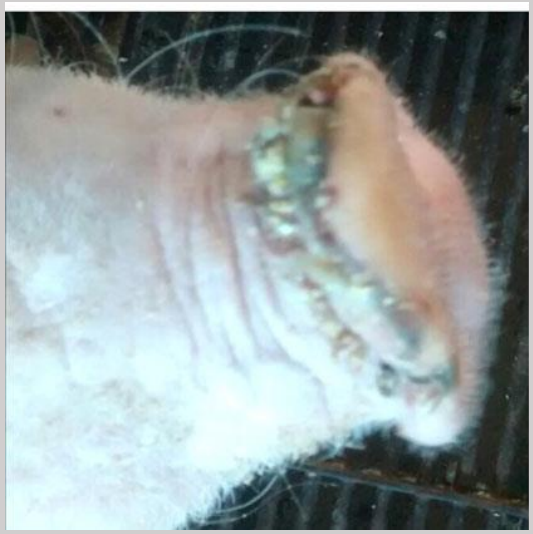


Photo Credits: Buckley & Lager, Montiel et al '16, Arzt & Stenfeldt

SVA Field cases
(distinct appearance from FMD)

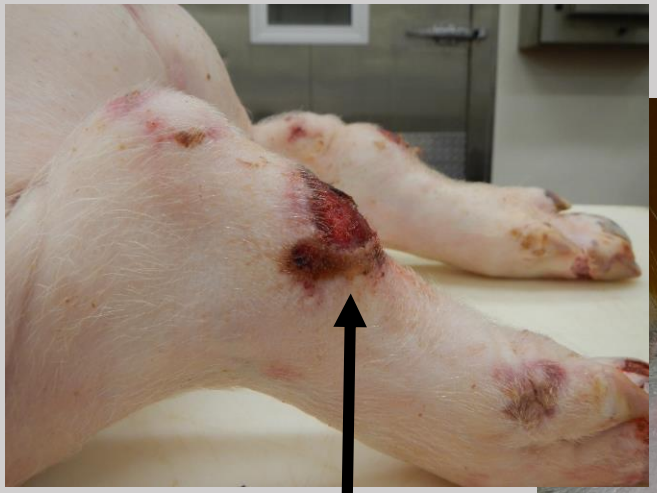


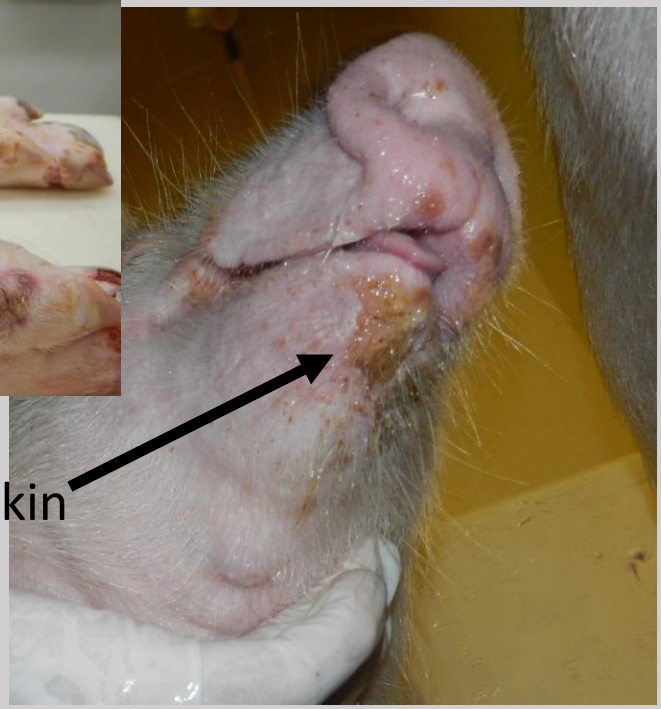
Leme et al ‘15

Brazil

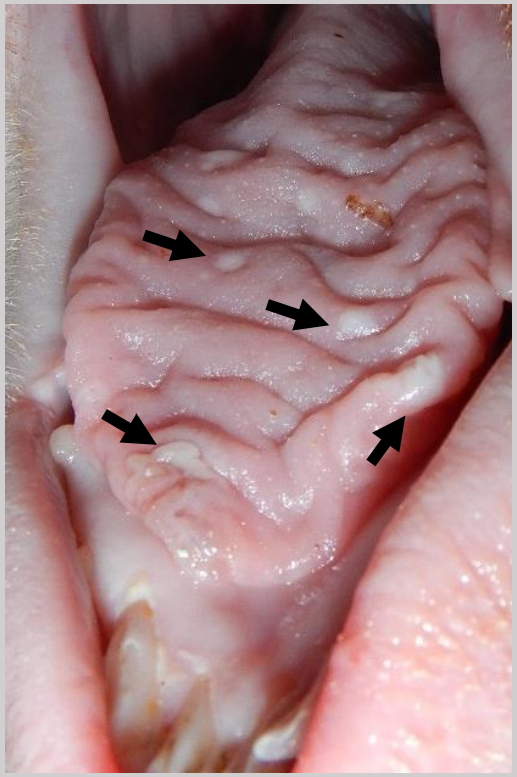
Leme et al ‘17

FMD lesions not described for SVA





Vesicles of Haired skin

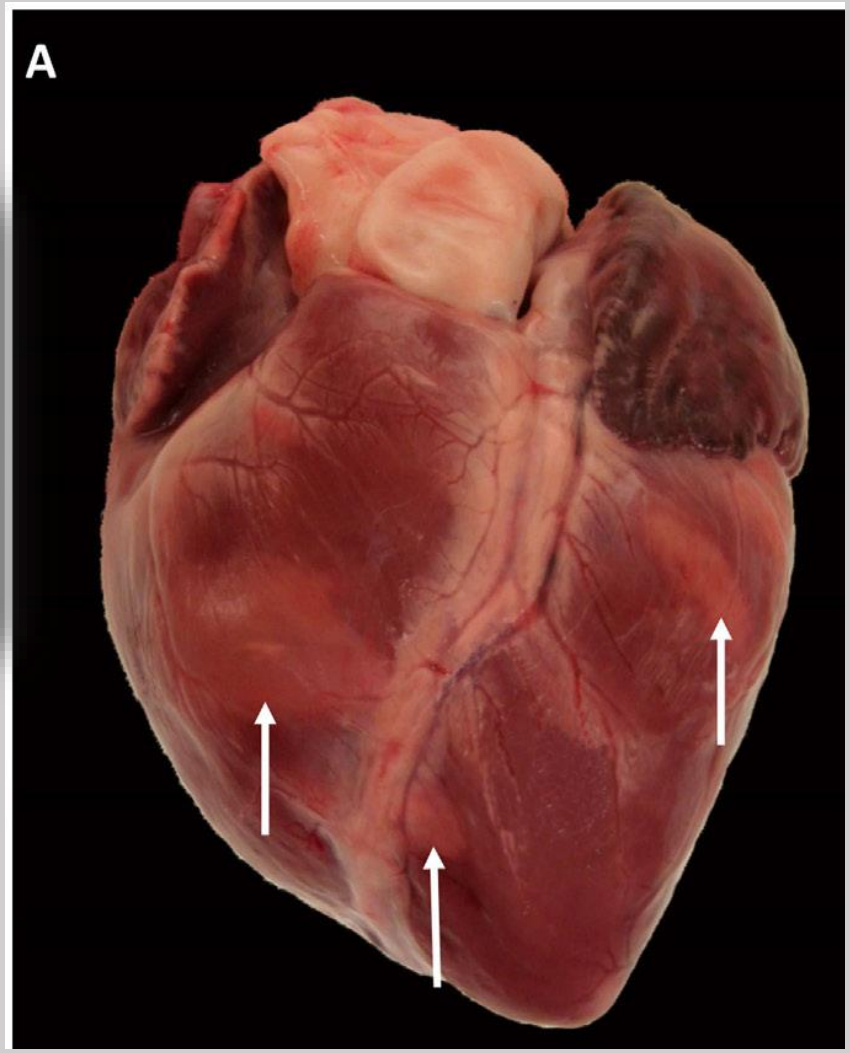


Vesicles of Tongue

Clinically Unambiguous Scenario

Vesicles
+Mortality
+Myocarditis
=FMD

Caveat: SVA neonatal mortality



Clinical differentiation by basic epidemiology

- FMD prevalence in naïve pigs generally quite high (70-90%)
- SVA prevalence lower and more variable (4-70%; 70-90% in sows)
- However, limited data available.

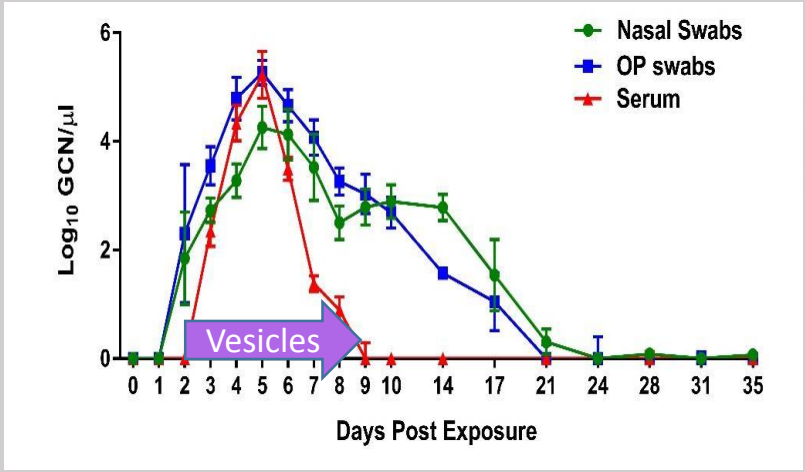
The morbidity and mortality rates of senecavirus-induced disease vary according to the affected pig category. In a herd that is affected for the first time, the morbidity rates range from 4 to 70% depending on the clinical signs and the pig age groups [20,23,33,34,37]. Senecavirus outbreaks presented morbidity rates of 0.5 to 5% in weaned pigs and 5 to 30% in finishing pigs and breeders [2,20,34], which varied according to the geographical region and the herd origin. Remarkably higher morbidity rates in sows were reported, reaching 70 to 90% [37]. However, the mortality in these categories is very low (≈0.2%), with pigs recovering soon after the remission of clinical signs that last for 10 to 15 days.

In newborn pigs, morbidity and mortality rates are considerably higher, especially in one- to four-day-old piglets, with morbidity rates that can reach 70%, but the mortality rates vary from 15 to 30% [2,23,24,33,34,37]. However, the clinical manifestations and the high mortality rates in piglets last for approximately 2 to 3 weeks in the affected herd.

Baker et al ‘17

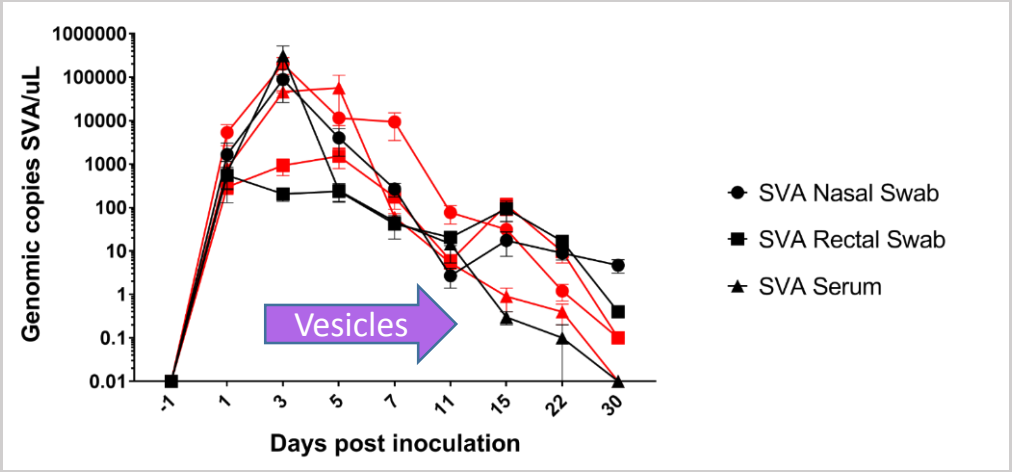
Infection Dynamics: Shedding & Viremia

FMDV



Stenfeldt et al, 2014

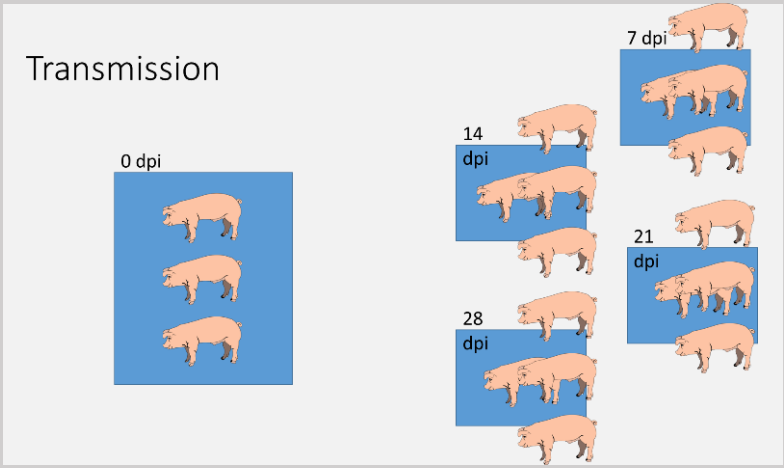
SVA



Courtesy: Buckley & Lager, ARS/USDA

SVA Transmission Studies

- Buckley, Lager, et al. Forthcoming



- Short Version: SVA is highly transmissible

Conclusions

- FMD and SVA infection are both dangerous transboundary diseases with many similarities (virological, clinical, epidmiological).
- Novel SVA incursion to SVA-free region is likely to have substantial economic consequences…..but, not as severe and absolute as FMDV (speculative).
- As with all vesicular diseases, definitive diagnosis must come from molecular diagnostics (usually rRT-PCR).
- Some clinical differences, particularly myocarditis, maybe inflammation and epi (speculative).
- SVA-free nations should consider potential impact of incursion for field investigation and laboratory diagnostics impact

Acknowledgements

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Tracy Sturgill

VPRU/ARS/USDA
Kelly M. Lager
Alexandra Buckley

Funding sources:

DHS IAA project "Improved Challenge Systems for FMD Vaccine and Biotherapeutics Testing In Cattle and Pigs"
National Pork Board: "Investigating potential existence of chronic, persistent foot-and-mouth disease virus infection in domestic pigs; implications for disease control strategies"

Bibliography: Recent FMD Pig Papers

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Stenfeldt C, Pacheco JM, Rodriguez LL, Arzt J. Early events in the pathogenesis of foot-and-mouth disease in pigs; identification of oropharyngeal tonsils as sites of primary and sustained viral replication. PLoS One. 2014 Sep 3;9(9):e106859. doi: 10.1371/journal.pone.0106859.

Yamada M, Fukai K, Morioka K, Nishi T, Yamazoe R, Kitano R, Shimada N, Yoshida K, Kanno T, Sakamoto K, Yamakawa M. Early pathogenesis of the foot-and-mouth disease virus O/JPN/2010 in experimentally infected pigs. J Vet Med Sci. 2018 Mar 6. doi: 10.1292/jvms.17-0683.

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C. Murphy, J. B. Bashiruddin, M. Quan, Z. Zhang, S. Alexandersen. Foot-and-mouth disease viral loads in pigs in the early, acute stage of disease. Vet Record 2010.

Fukai K, Yamada M, Morioka K, Ohashi S, Yoshida K, Kitano R, Yamazoe R, Kanno T. Dose-dependent responses of pigs infected with foot-and-mouth disease virus O/JPN/2010 by the intranasal and intraoral routes. Arch Virol. 2015 Jan;160(1):129-39. doi: 10.1007/s00705-014-2239-4. Epub 2014 Oct 4.

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Baker KL, Mowrer C, Canon A, Linhares DC, Rademacher C, Karriker LA, Holtkamp DJ. Systematic Epidemiological Investigations of Cases of Senecavirus A in US Swine Breeding Herds. Transbound Emerg Dis. 2017 Feb;64(1):11-18. doi: 10.1111/tbed.12598. Epub 2016 Nov 25.

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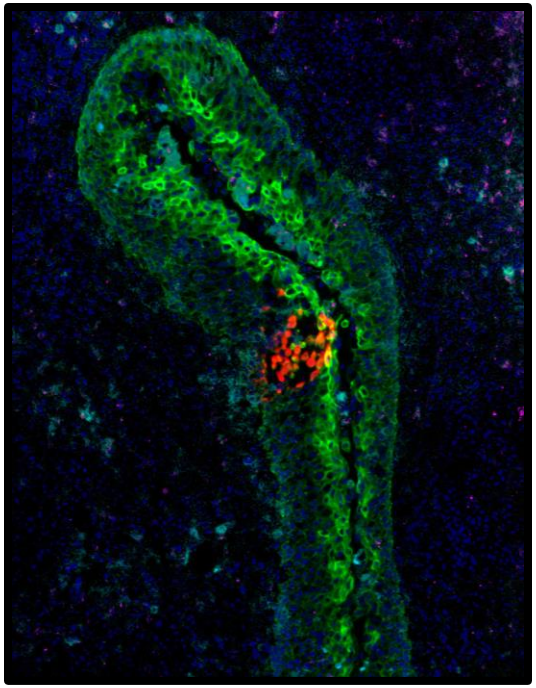
Questions and Answers

Do pigs become carriers of foot-and-mouth disease virus (FMDV)?

Carolina Stenfeldt & Jonathan Arzt

Foreign Animal Disease Research Unit, USDA-ARS, Plum Island, USA



USDA ARS

The FMDV Carrier state:

- **A large proportion of FMDV-infected ruminants develop persistent infection following virus exposure**
- **Defined by detection of infectious virus beyond 28 days after infection**
- **Problematic for disease control and deployment of ”Vaccinate-to-Live” strategies**
- **The epidemiological significance of FMDV carriers is debatable**
- **Extends the time required to return to ”FMD-free” status**
- **”Conventional wisdom”: Pigs do not become FMDV carriers**

FMDV persistence in pigs; Contradictory evidence?

A limited number of studies have demonstrated detection of FMDV RNA in porcine serum or tissues beyond the "threshold" of 28 dpi

The Veterinary Journal 1999, **157**, 213–217
Article No. tvjl.1999.0357, available online at http://www.idealibrary.com on IDEAL®

Fast Track

Evidence for the Persistence of Foot-and-mouth Disease Virus in Pigs

J.M.S. MEZENCIO, G.D. BABCOCK, E. KRAMER and F. BROWN.

Plum Island Animal Disease Center, P.O. Box 848, Greenport, NY 11944, USA

Rodríguez-Calvo *et al. Veterinary Research* 2011, **42**:22
http://www.veterinaryresearch.org/content/42/1/22

VETERINARY RESEARCH

RESEARCH Open Access

A replication analysis of foot-and-mouth disease virus in swine lymphoid tissue might indicate a putative carrier stage in pigs

Teresa Rodríguez-Calvo[1†], Fayna Díaz-San Segundo[1,2†], Marta Sanz-Ramos[3], Noemí Sevilla[1*]

SHORT COMMUNICATIONS

Veterinary Record (2008) **162**, 753-754

K. Orsel, DVM, PhD, Faculty of Veterinary Medicine, Department of Farm Animal Health, Utrecht University, Yalelaan 7, 3584 CL Utrecht, The Netherlands
H. I. J. Roest, DVM, **E. M. Elzinga-Bril**, DVM, PhD, **F. van Hemert-Kluitenberg**,

Detection of foot-and-mouth disease virus in infected pigs by RT-PCR four weeks after challenge

K. Orsel, H. I. J. Roest, E. M. Elzinga-Bril, F. van Hemert-Kluitenberg, A. Dekker

FOOT-and-mouth disease (FMD) is a contagious viral disease of cloven-hoofed animals including ruminants and pigs. The occurrence of disease in livestock has a great economic impact, especially for exporting countries. Export limitations are based partly on the existence of FMD carrier animals. Recently, Dekker and others (2003) showed that pigs cleared the virus within three to four weeks. This short communication describes a real-time reverse transcriptase (RT)-PCR study to identify FMDV RNA in the tonsils of pigs 31 to 32 days after initial inoculation with FMDV. The study focused on the tonsil because in ruminants the oropharynx is considered to be an important site of viral persistence.

TABLE 1: Results of a reverse transcriptase-PCR (RT-PCR) assay for foot-and-mouth disease (FMD) in 25 pigs vaccinated against FMD virus and then infected with a strain of FMD, and 31 unvaccinated and infected pigs

	Vaccination		
RT-PCR result	Yes	No	Total
Positive	2	11	13
Negative	23	20	43
Total	25	31	56

Transboundary and Emerging Diseases

Transboundary and Emerging Diseases

ORIGINAL ARTICLE

Foot-and-Mouth Disease in Feral Swine: Susceptibility and Transmission

F. Mohamed[1], S. Swafford[2], H. Petrowski[1], A. Bracht[1], B. Schmit[2], A. Fabian[1], J. M.Pacheco[3], E. Hartwig[3], M. Berninger[1], C. Carrillo[1], G. Mayr[1], K. Moran[1], D. Kavanaugh[4], H. Leibrecht[1], W. White[1] and S. Metwally[1]

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[3] Plum Island Animal Disease Center, USDA, ARS, Greenport, NY, USA
[4] USDA, APHIS, Wildlife Services, Athens, GA, USA

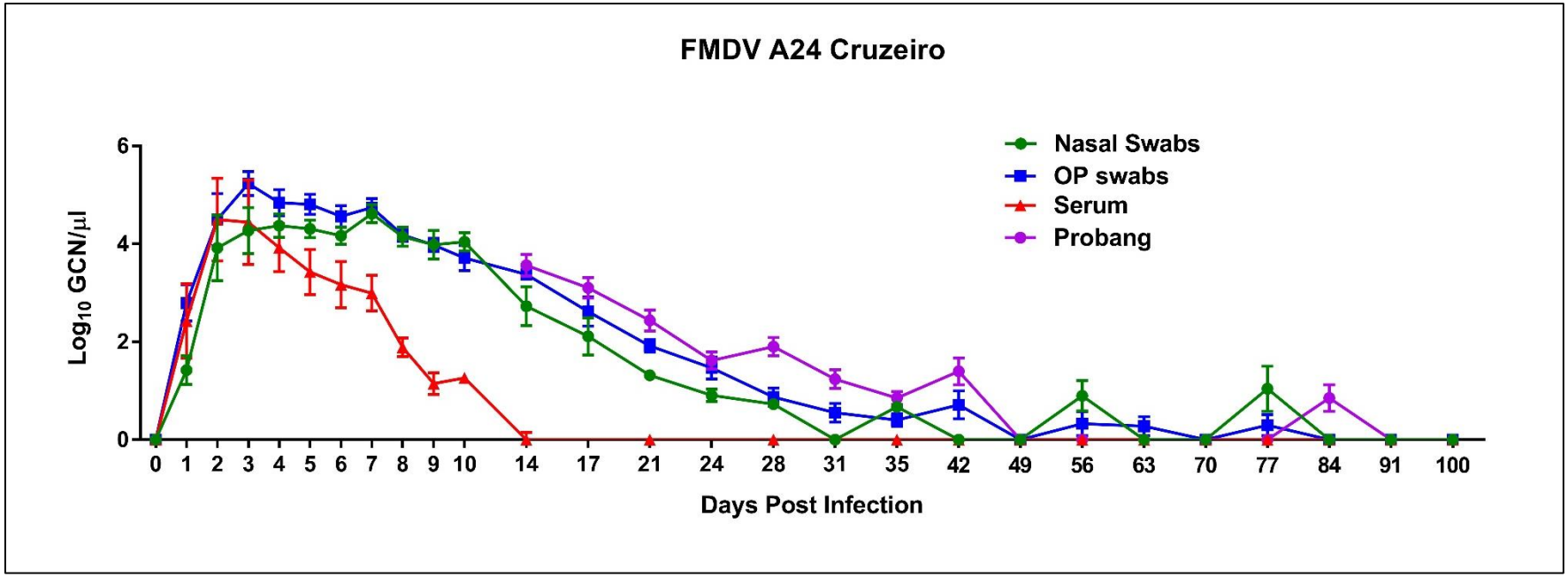
Are pigs true FMDV carriers?

Series of experimental investigations of the pathogenesis of different FMDV strains in pigs

- Detection of FMDV genome and infectious virus in blood, secretions, and tissues through acute to persistent phases of infection

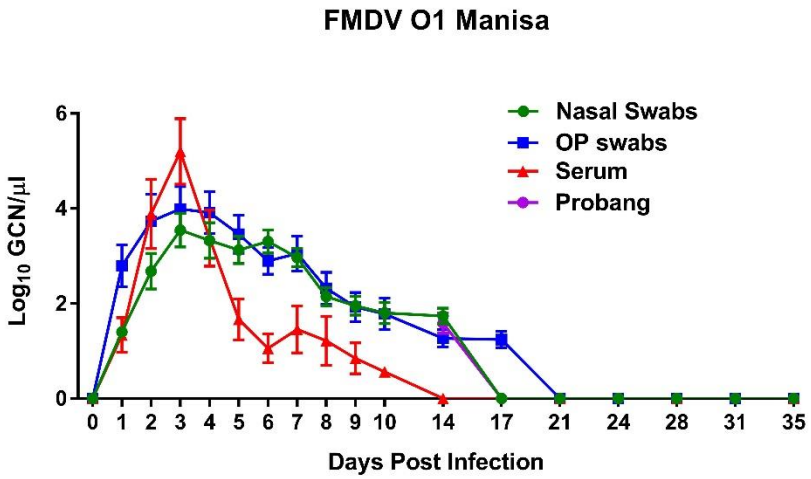
FMDV strain	Number of pigs	Duration of study
FMDV O1 Manisa	12	35 dpi
FMDV O/SKR/2010	6	35 dpi
FMDV A/SKR/2010	4	35 dpi
FMDV Asia-1 Shamir	4	35 dpi
FMDV A24 Cruzeiro	8	35 dpi
“	2	61 dpi
“	4	100 dpi

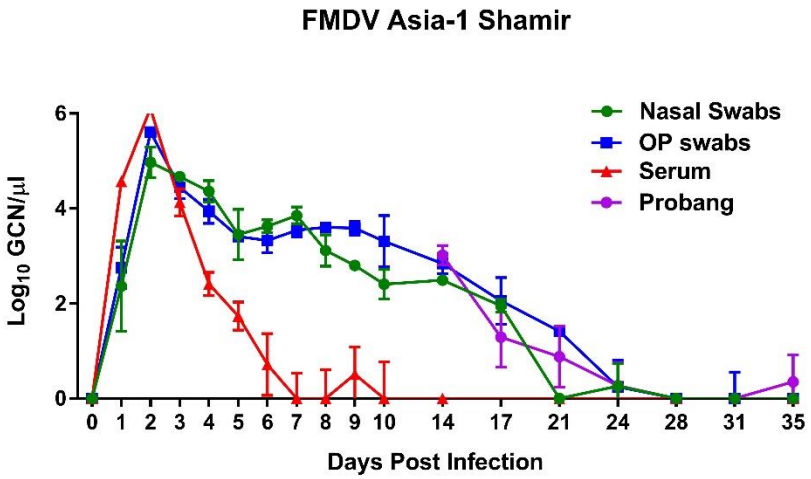
FMDV infection dynamics in pigs

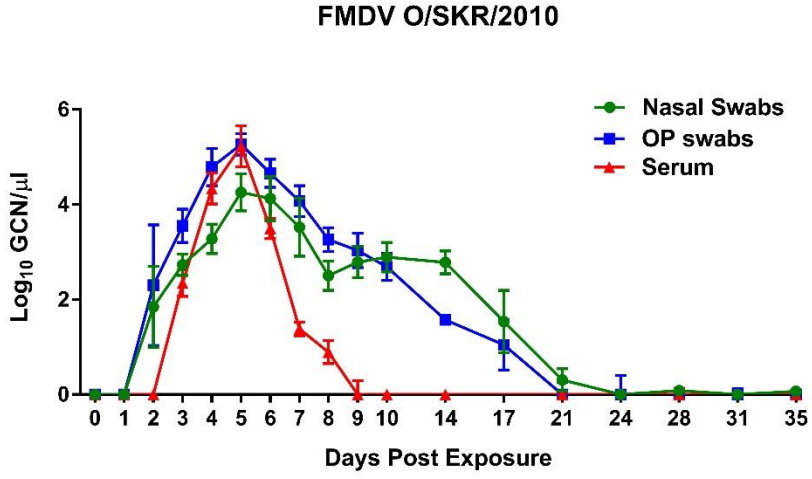


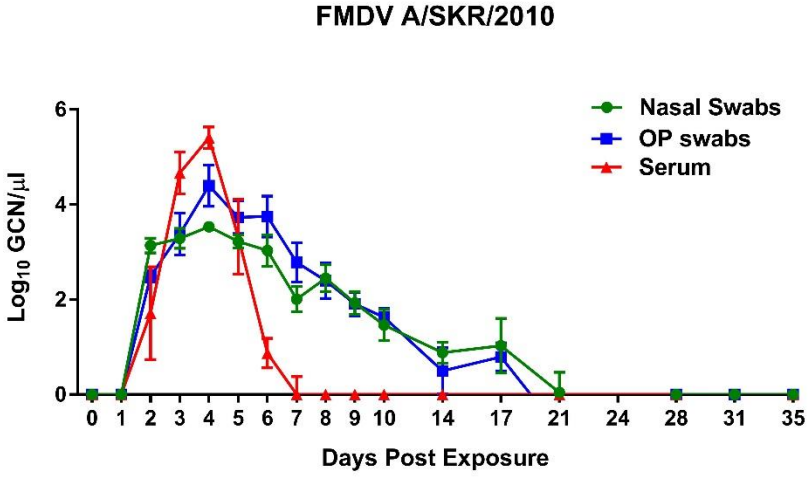
No infectious virus in serum or secretions ≥ 28 dpi !!!!

FMDV infection dynamics in pigs









Detection of infectious FMDV in porcine tissues

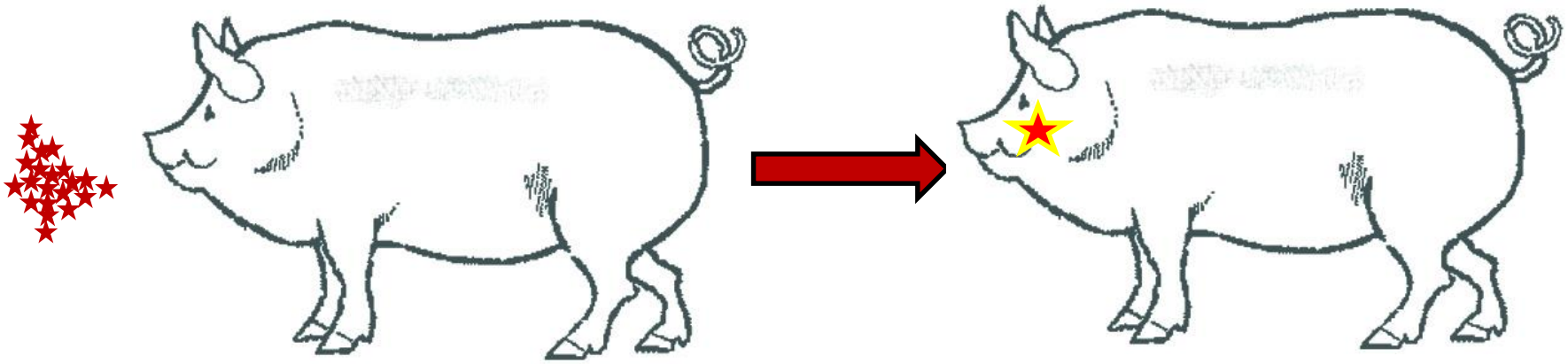
Exposure

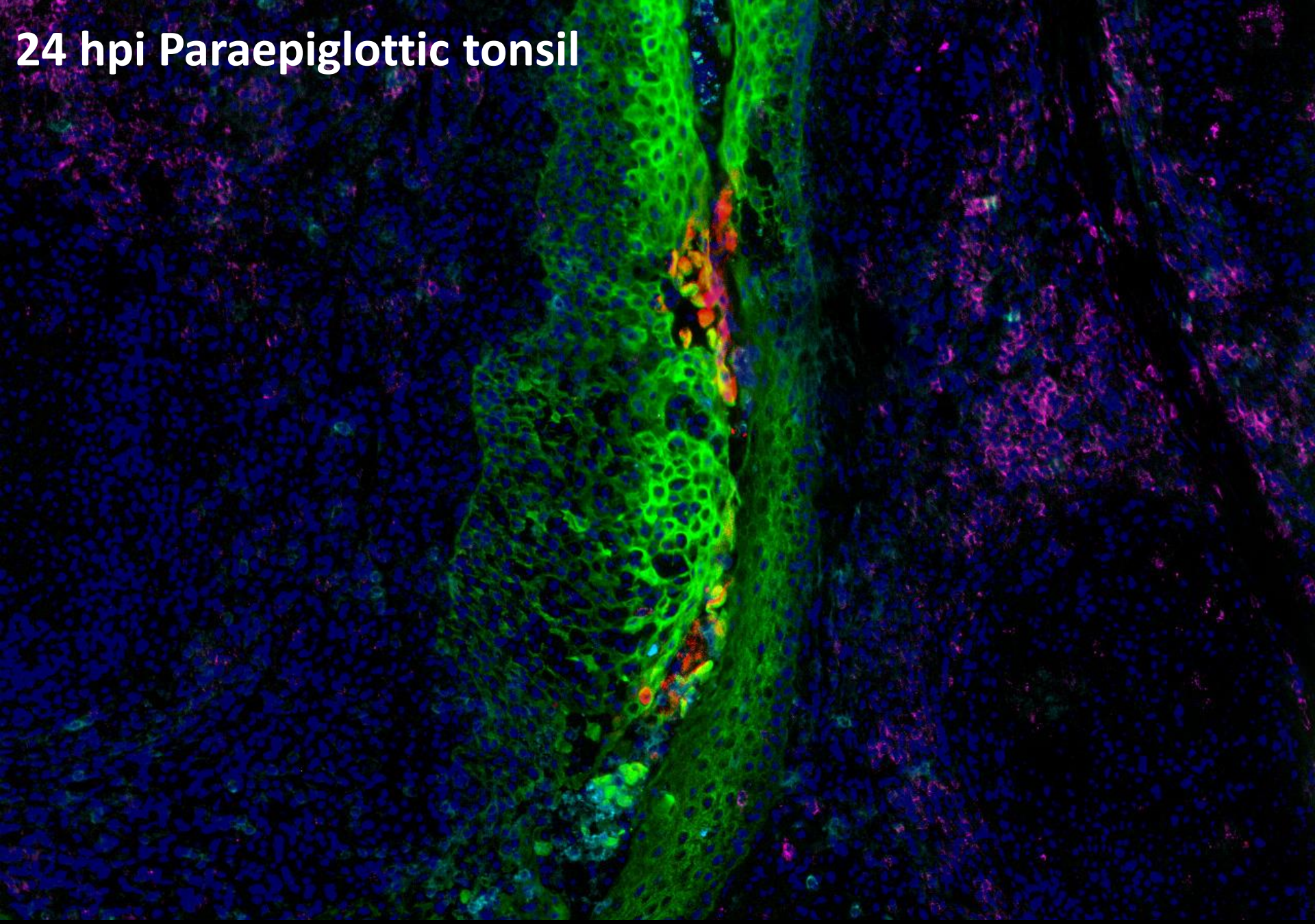
0 HPI

Primary infection

6-24 HPI

Primary infection in oropharyngeal tonsils




24 hpi Paraepiglottic tonsil
Cytokeratin (epithelium), FMDV VP1 CD172a CD8

Detection of infectious FMDV in porcine tissues

Subclinical Infection

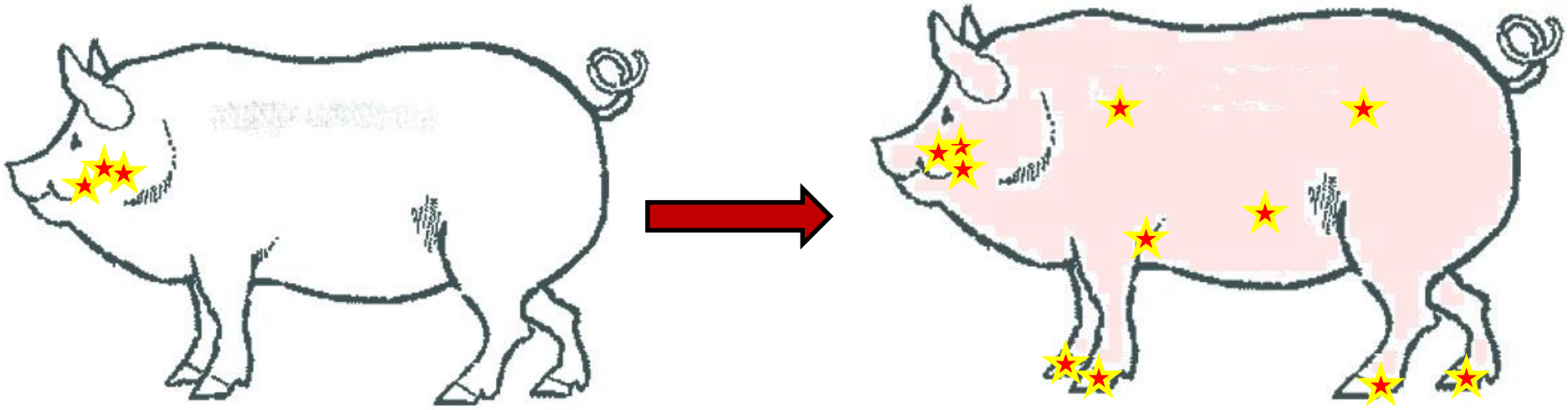
12-24 HPI

Viral replication in tonsil epithelium

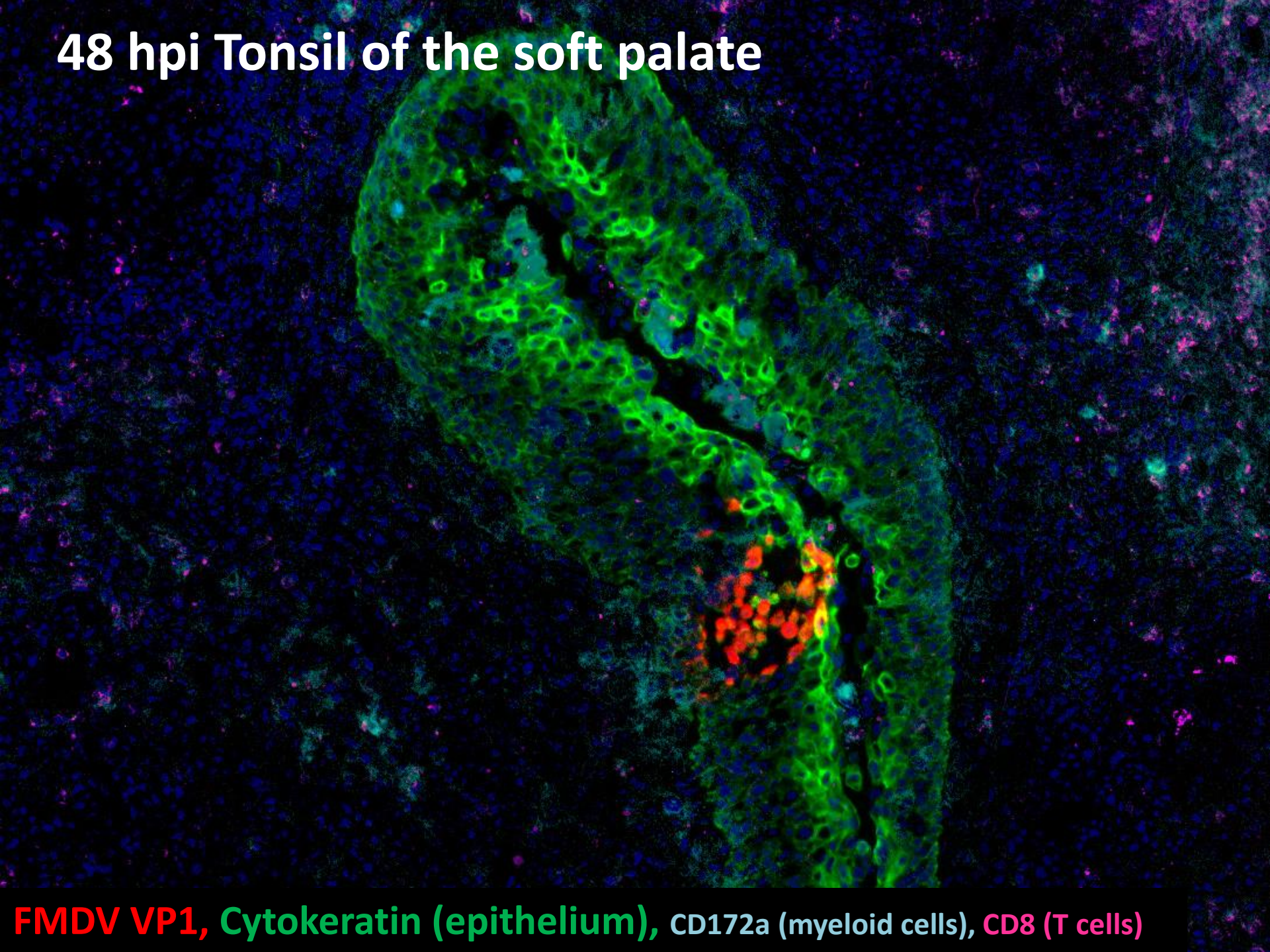
Clinical infection

48 HPI

Viremia, viral replication in tonsil epithelium and at lesion sites



48 hpi Tonsil of the soft palate

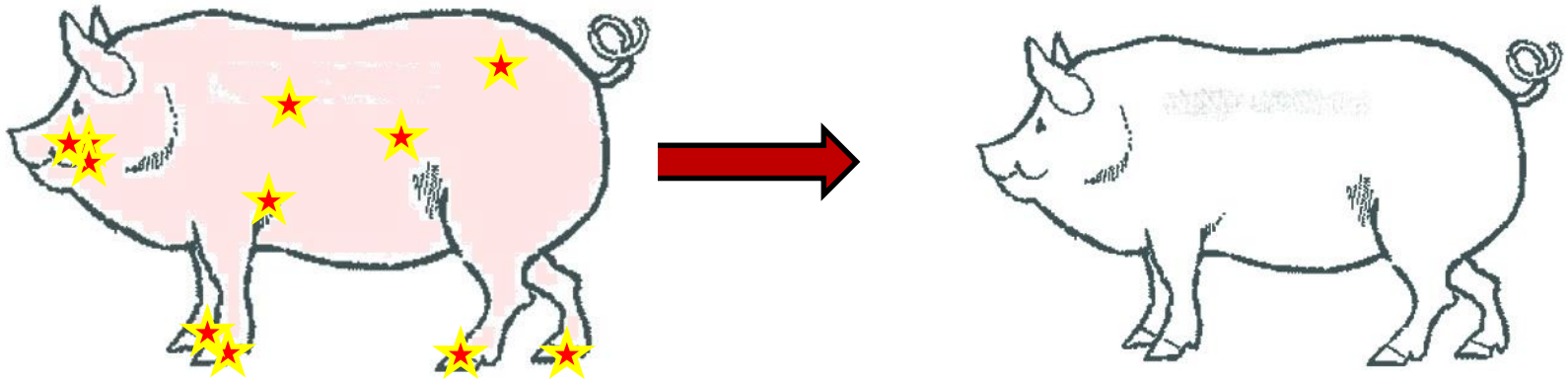


FMDV VP1, Cytokeratin (epithelium), CD172a (myeloid cells), CD8 (T cells)

Detection of infectious FMDV in porcine tissues

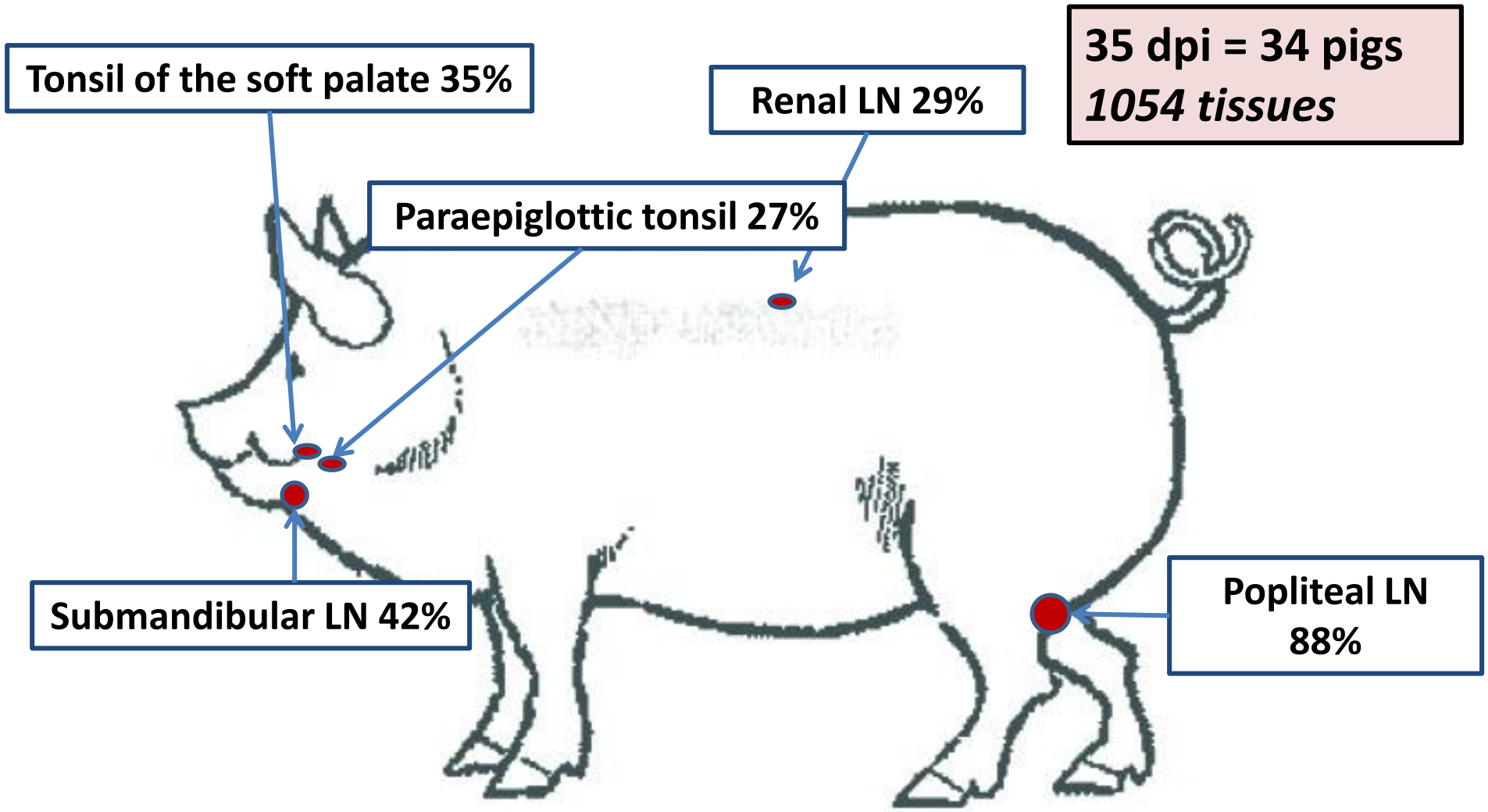
Clinical infection

FMDV clearance



≥28 dpi: NO persistence
of infectious FMDV in porcine tissues

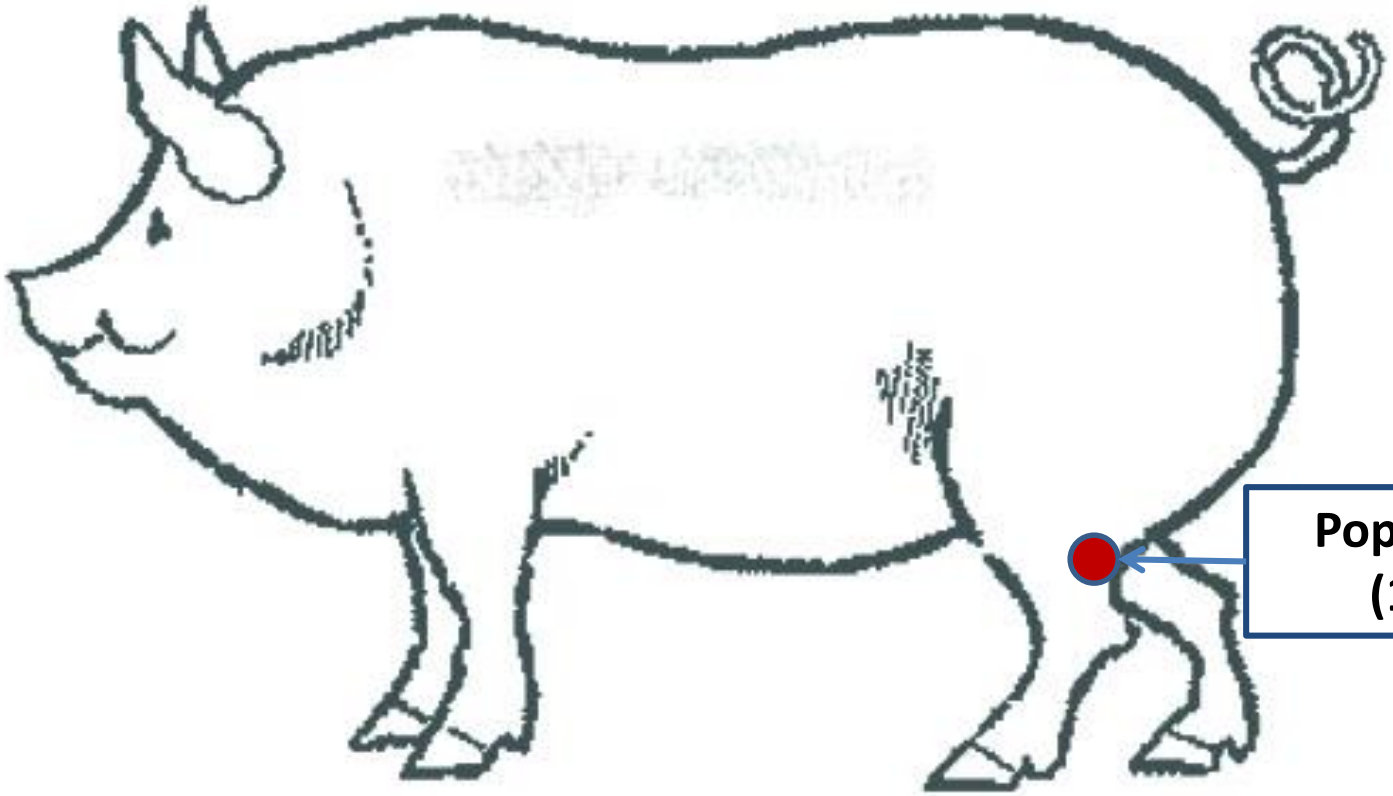
"Persistent phase": Detection of FMDV RNA in tissues



No infectious virus isolated from any tissues harvested ≥ 28 dpi

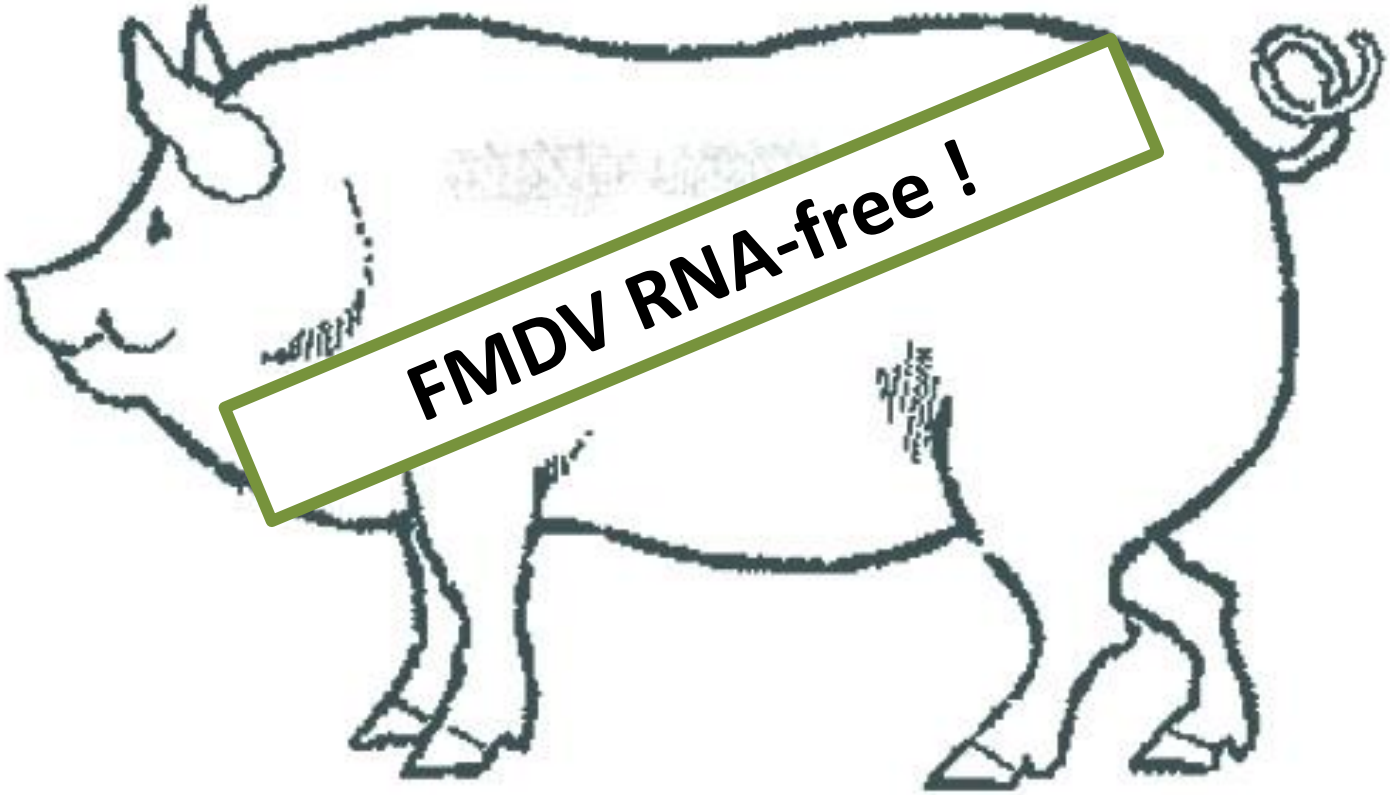
“Persistent phase”: Detection of FMDV RNA in tissues

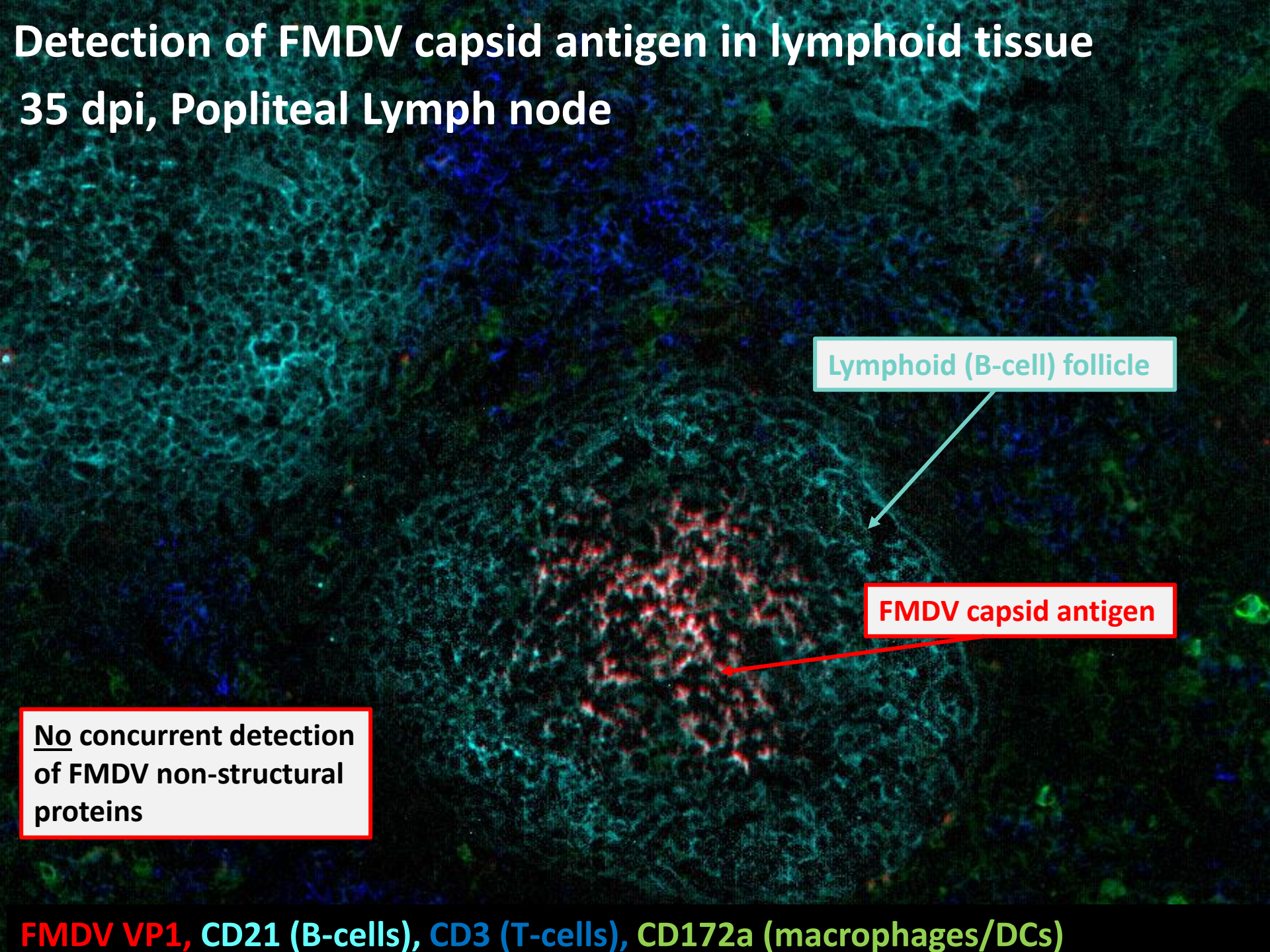
61 dpi = 2 pigs
36 tissues



“Persistent phase”: Detection of FMDV RNA in tissues

100 dpi = 4 pigs
72 tissues




Detection of FMDV capsid antigen in lymphoid tissue
35 dpi, Popliteal Lymph node
Lymphoid (B-cell) follicle
FMDV capsid antigen
No concurrent detection of FMDV non-structural proteins
FMDV VP1, CD21 (B-cells), CD3 (T-cells), CD172a (macrophages/DCs)

Key findings:

- ***No infectious virus in secretions beyond 21 dpi***
  - *Substantial decrease in FMDV RNA shedding by approx 21 dpi*
  - *Scattered RNA-positive samples through longer duration*

- ***No persistence of infectious virus in tissues***
  - *Detection of FMDV RNA in lymphoid tissues at 35 dpi*
  - *Low prevalence of FMDV RNA detection at 60 dpi*
  - *No detection of FMDV RNA at 100 dpi*

- ***No detection of FMDV non-structural proteins in lymphoid tissue***
  - *Detection of FMDV capsid protein in select lymph nodes at 35 dpi*
  - *No detection at later time points*

NO infectious virus beyond 28 dpi !!

Conclusions

Domestic pigs are unlikely to be competent long term carriers of infectious FMDV

- Transient persistence of viral degradation products in lymphoid tissue is common in convalescent pigs

Implications?

- Could differences in FMDV persistence justify implementation of species-specific FMDV response strategies?

- Specifically, if pigs do not become FMDV carriers, could that challenge current regulation of “Vaccinate to live” policies?

Bibliography

Transboundary and Emerging Diseases

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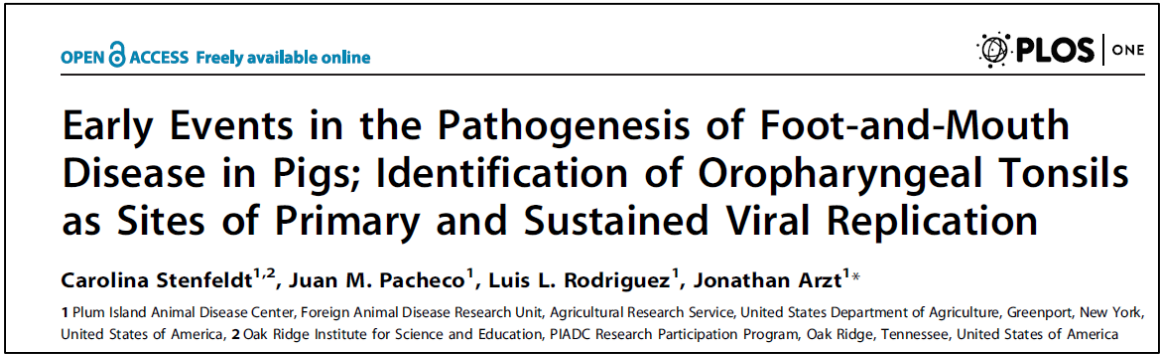
ORIGINAL ARTICLE

Detection of Foot-and-mouth Disease Virus RNA and Capsid Protein in Lymphoid Tissues of Convalescent Pigs Does Not Indicate Existence of a Carrier State

C. Stenfeldt[1,2], J. M. Pacheco[1], G. R. Smoliga[1], E. Bishop[1], S. J. Pauszek[1], E. J. Hartwig[1], L. L. Rodriguez[1] and J. Arzt[1]

[1] United States Department of Agriculture, Agricultural Research Service, Foreign Animal Disease Research Unit, Plum Island Animal Disease Center, Greenport, NY, USA
[2] Oak Ridge Institute for Science and Education, PIADC Research Participation Program, Oak Ridge, TN, USA



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PLOS ONE

Early Events in the Pathogenesis of Foot-and-Mouth Disease in Pigs; Identification of Oropharyngeal Tonsils as Sites of Primary and Sustained Viral Replication

Carolina Stenfeldt[1,2], Juan M. Pacheco[1], Luis L. Rodriguez[1], Jonathan Arzt[1]*

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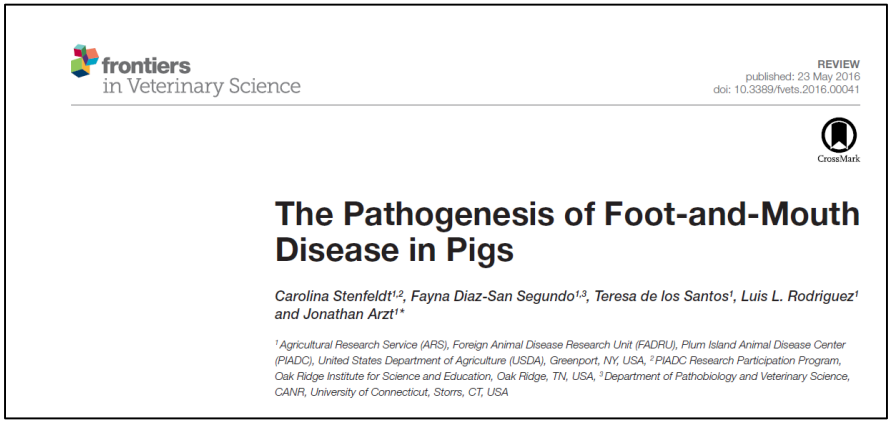

frontiers in Veterinary Science

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The Pathogenesis of Foot-and-Mouth Disease in Pigs

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[1] Agricultural Research Service (ARS), Foreign Animal Disease Research Unit (FADRU), Plum Island Animal Disease Center (PIADC), United States Department of Agriculture (USDA), Greenport, NY, USA, [2] PIADC Research Participation Program, Oak Ridge Institute for Science and Education, Oak Ridge, TN, USA, [3] Department of Pathobiology and Veterinary Science, CANR, University of Connecticut, Storrs, CT, USA

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US National Pork Board "Investigating potential existence of chronic, persistent foot-and-mouth disease virus infection in domestic pigs; implications for disease control strategies"

Questions and Answers

Short Term Placements needed!

The EuFMD Commission has an opening for individuals to join the team in Rome under the **Short Term Placement** (STP) program

APPLY

for 2019 by 28 June

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Thank you for your attention!