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.

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

29 March 2018
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)

**Classical**
- Foot-and-mouth disease
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- Vesicular stomatitis
- Senecavirus A

**Non-Classical**
- Other Enteroviruses
- Thermal/caustic burns
- Parvovirus
- IVD = Idiopathic Vesicular Disease
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)
Why does SVA matter?

Vesicular disease landscape (USA)

- 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.
SVA Field cases (distinct appearance from FMD)

Leme et al '17
Brazil

Canada → USA transboundary
Pasma et al '08

Leme et al ‘15

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.

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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**

- **Vesicles**

**SVA**

- **Vesicles**

---

*Stenfeldt et al, 2014*

*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, epidemiological).

• 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
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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


Bibliography: Select SVA Papers


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
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.
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

<table>
<thead>
<tr>
<th>FMDV strain</th>
<th>Number of pigs</th>
<th>Duration of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMDV O1 Manisa</td>
<td>12</td>
<td>35 dpi</td>
</tr>
<tr>
<td>FMDV O/SKR/2010</td>
<td>6</td>
<td>35 dpi</td>
</tr>
<tr>
<td>FMDV A/SKR/2010</td>
<td>4</td>
<td>35 dpi</td>
</tr>
<tr>
<td>FMDV Asia-1 Shamir</td>
<td>4</td>
<td>35 dpi</td>
</tr>
<tr>
<td>FMDV A24 Cruzeiro</td>
<td>8</td>
<td>35 dpi</td>
</tr>
<tr>
<td>&quot;</td>
<td>2</td>
<td>61 dpi</td>
</tr>
<tr>
<td>&quot;</td>
<td>4</td>
<td>100 dpi</td>
</tr>
</tbody>
</table>
FMDV infection dynamics in pigs

FMDV A24 Cruzeiro

No infectious virus in serum or secretions ≥ 28 dpi !!!!
FMDV infection dynamics in pigs

FMDV O1 Manisa

FMDV Asia-1 Shamir

FMDV O/SKR/2010

FMDV A/SKR/2010

Days Post Infection

Days Post Exposure
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  

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

FMDV clearance
“Persistent phase”: Detection of FMDV RNA in tissues

35 dpi = 34 pigs 1054 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

Popliteal LN (100%)
“Persistent phase”: Detection of FMDV RNA in tissues

100 dpi = 4 pigs
72 tissues

FMDV RNA-free!
Detection of FMDV capsid antigen in lymphoid tissue
35 dpi, Popliteal Lymph node

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

**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


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, PAIDC Research Participation Program, Oak Ridge, TN, USA

**OPEN ACCESS Freely available online**

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

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2. Oak Ridge Institute for Science and Education, PAIDC Research Participation Program, Oak Ridge, Tennessee, United States of America

**REVIEW**

The Pathogenesis of Foot-and-Mouth Disease in Pigs

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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

VISIT

EMAIL
eufmd@fao.org for details
Thank you for your attention!