Emerging viral infectious diseases of pigs: what’s next?

Joaquim Segalés
“From 1985 to 2010, novel pathogen species were identified at an average annual rate of 3”
Viruses on the spot…

Diseases of humans and their domestic mammals: pathogen characteristics, host range and the risk of emergence

S. Cleaveland*, M. K. Laurensen and L. H. Taylor
Centre for Tropical Veterinary Medicine, University of Edinburgh, Easter Bush, Roslin, Midlothian EH25 9RG, UK

Taxonomic classification of livestock emerging pathogens
New infectious diseases are being identified

Not only clinical diseases, but nowadays much higher capability to detect novel (or not so novel!) infections with unknown outcome

International trading is a well-known way to widespread pathogens (inadvertently) and eventually diseases
Such numbers have been expanded since 2001.

Besides novel or re-emerging clinical problems, technical improvements of diagnostic methods have accounted for this growing number of novel pathogens.

“Metagenomics is the study of genetic material recovered directly from environmental samples by means of a culture-independent approach and sequence-independent amplification.”

Review

New viruses in veterinary medicine, detected by metagenomic approaches

Sándor Belák a,b,c, Oskar E. Karlsson a,c, Anne-Lie Blomström a,c, Mikael Berg a,c, Fredrik Granberg a,c,*
Emerging and re-emerging infectious diseases

**DEFINITION:** An emerging disease is one that has appeared in a population for the first time, or that may have existed previously but is rapidly increasing in incidence or geographic range.
Emerging/re-emerging infectious viral diseases in pigs

Some examples:

- PRRS (emergence by late 80s)
- PCV2-SD (emergence by late 90s)
- CSF (Europe during late 90s, early 00s)
- ASF (Eastern Europe during last 10 years)
- SI pandemic H1N1 viruses (worldwide, since 2009) – ZOONOSIS
- PED (North-America, since 2013; Europe, since 2014)
- Nipah virus (South-east Asia during last 15 years) – ZOONOSIS
- Bungowannah virus (Australia since 2003) – ZOONOSIS?
- Menangle virus (Australia late 90s, early 2000s) – ZOONOSIS?
- Senecavirus A (USA mid 2000s, USA and Brazil since 2014)
- Porcine deltacoronavirus (North-America, since 2014)
- Atypical porcine pestivirus (North-America and Europe, since 2015)
Emerging/re-emerging viral infections in pigs

Some examples:

- Hepatitis E virus – ZOONOSIS
- Porcine endogenous retrovirus
- Porcine torovirus
- Porcine sapovirus
- Porcine lymphotropic herpesvirus
- Porcine kobuvirus
- Porcine parvoviruses (several)
- Porcine bocavirus
- Porcine astroviruses
- Torque teno sus viruses
- Swine orthopneumovirus
- Swine orthoreovirus
- Reston ebolavirus – ZOONOSIS
Emerging diseases: The past and the future

Robert Desrosiers, DVM, Dipl ABVP

Part 2: The past

a. How did we get infected?
b. What could have been done to avoid infection and/or reduce its spread?
c. Can we get rid of it?
Conclusions from the “past” * (Desrosiers, 2015)

- Clarifying the cause for some diseases is sometimes a long process (it took several years for some of them)
- The exact way of introduction of the pathogen is usually unknown
- Preventing their introduction would be very difficult taking into account that some of them were present long time before the disease became significant
- In spite of significant elimination efforts, all pathogens are still in North-America

* Referred to App, PRRSV, PCV2a, PCV2b, PEDV
Clarifying the cause for some diseases is sometimes a long process…

15 different etiologies were considered for PRRS!!!

ETIOLOGY. Epidemiologic and other observations prompted speculation that PRRS/SIRS was a transmissible disease caused by an infectious agent. Porcine parvovirus (PPV), encephalomyocarditis virus (EMCV), porcine enteroviruses (PEV), pseudorabies virus (PRV), porcine cytomegalovirus, hemagglutinating encephalomyelitis virus (HEV), classical swine influenza virus (SIV), transmissible gastroenteritis virus (TGEV), bovine viral diarrhea virus, border disease virus, Japanese B encephalitis virus, hog cholera virus (HCV), *Leptospira interrogans* serovar *bratislava*, *Chlamydia psittaci*, and mycotoxins were at one time considered potential etiologic agents (Bane and Hall 1990; Bolin and Cassels 1990; Mengeling and Lager 1990; Van Alstine 1990; Woollen et al. 1990). These infectious agents are not likely...
Clarifying the cause for some diseases is sometimes a long process…

- Most of them are **MULTIFACTORIAL DISEASES**
- The simple presence of the agent does not imply presence of disease
- Difficulties in culturing/detecting an associated agent… everyday less difficult!! (metagenomics)… or not (many agents have not yet been cultured)…
- Koch’s postulates difficult to fulfil; fulfilment of Evans Postulates?
Clarifying the cause for some diseases is sometimes a long process…

“The identity of the congenital tremors agent is not known”
Clarifying the cause for some diseases is sometimes a long process...

Example on metagenomics use:

Astrovirus as a possible cause of congenital tremor type All in piglets?

Anne-Lie Blomström¹, Cecilia Ley¹ and Magdalena Jacobson²*

But PAstV was also in the brain of healthy pigs...
Clarifying the cause for some diseases is sometimes a long process…

Example on metagenomics use:


Discovery of a novel putative atypical porcine pestivirus in pigs in the USA

Article

Atypical Porcine Pestivirus: A Possible Cause of Congenital Tremor Type A-II in Newborn Piglets

Ad de Groof, Martin Deijs, Lars Guelen, Lotte van Grinsven, Laura van Os-Galdos, Wannes Vogels, Carmen Derks, Toine Cruijzen, Victor Geurts, Mieke Vrienhoek, Janneke Suijskens, Peter van Doorn, Leo van Leengoed, Carla Schrier, and Lia van der Hoek.
The exact way of introduction of the pathogen is usually unknown...

- Sequencing might help in establishing the potential origin of the pathogen, but not the specific way of introduction

PCV2, Vidigal et al., 2012

PEDV in USA, Huang et al., 2013
The exact way of introduction of the pathogen is usually unknown...

- **Phylogeography**

Study of the **historical processes** that may be responsible for the **contemporary geographic distributions of individuals**. This is accomplished by considering the geographic distribution of individuals in light of the **patterns** associated with a gene **genealogy**

Directly, genetically connected Cuban and other haplotypes are highlighted in gray.
Lecture at the AASV 2015 meeting

Emerging diseases: The past and the future

Robert Desrosiers, DVM, Dipl ABVP

- Known pathogens that we don’t have in the country
- Known pathogens that we already have in the country but that could get worse
- Harmless organisms that we don’t have in the country that will become significant pathogens
- Harmless organisms that we already have in the country that will become significant pathogens

Part 3: The future
Known pathogens that we don’t have in the country…

Not that easy to stop sometimes… preparedness is key, but in most of the cases we act when the “enemy is already inside”…

- PED in North-America
- ASF in Russia and Eastern European countries
Known pathogens that we don’t have in the country…

ASF in the world (2016) – www.oie.int
Known pathogens that we don’t have in the country…

ARE YOU SURE????

“A disease or infection may exist in a given country or region depending on the enthusiasm you are looking for it”

Carlos Pijoan, U of M, USA
Known pathogens that we don’t have in the country…

ARE YOU SURE????

The example of Senecavirus A: subclinical infection or the cause of a vesicular disease?

Leme et al., 2015
Known pathogens that we don’t have in the country…

ARE YOU SURE????

Atypical porcine pestivirus: already present in Spain since 1997

Canturri et al., 2017 ESPHM
Known pathogens that we already have in the country but that could get worst...

Specially applicable to pathogens with high capabilities to change:

- **FASTER EVOLUTION**
- **SLOWER EVOLUTION**

**Mutation rate (mutations/site/replication)**
- Retrovirus
- ssRNA
- ssDNA
- dsDNA

**Substitution rate (substitutions/site/year)**
- Retrovirus

Holmes ED. 2009.
Harmless organisms that we don’t have in the country that will become significant pathogens…

Harmless organisms that we already have in the country that will become significant pathogens…

If they are harmless, it is very likely that nobody is looking for them!! (who is paying it???)

Again, metagenomics and surveillance are sources of increasing numbers of newly discovered infectious agents
Harmless organisms… THE EXAMPLE OF PCV2…

Diagnostic criteria already fulfilled in 1986

PCV2 already in Europe in 1962

ISSN 0931-1793

Short Communication

Veterinary Microbiology

Retrospective study on the occurrence of porcine circovirus 2 infection and associated entities in Northern Germany

Bjoern Jacobsen a,1,*, Lars Krueger a,1, Frank Seeliger a, Michael Bruegmann a, Joaquim Segalés b, Wolfgang Baumgaertner a
Harmless organisms… THE EXAMPLE OF TTSuV…

Molecular characterization of porcine TT virus, an orphan virus, in pigs from six different countries

N.E. McKeown, M. Fenaux, P.G. Halbur, X.J. Meng

Prevalence of swine Torque teno virus in post-weaning multisystemic wasting syndrome

Torque teno sus virus 1 and 2 viral loads in postweaning multisystemic wasting syndrome (PMWS) and porcine dermatitis and nephropathy syndrome (PDNS)

Vaccination of pigs reduces Torque teno sus virus viremia during natural infection

Alexandra Jiménez-Melsió, Fernando Rodriguez, Ayub Darji, Joaquim Segalés, Vivian Cornelissen-Keijzers, Erwin van den Born, Tuija Kekarainen
Table 1
The formerly used nomenclature for porcine paroviruses and the current classification based on the International Committee on Taxonomy of Viruses (ICTV).

<table>
<thead>
<tr>
<th>Virus</th>
<th>ICTV current classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porcine parvovirus (1)</td>
<td>Ungulate protoparvovirus 1</td>
</tr>
<tr>
<td>Porcine parvovirus 2</td>
<td>Not yet classified</td>
</tr>
<tr>
<td>Porcine parvovirus 3, porcine hokovirus, PARV4-like</td>
<td>Ungulate tetraparvovirus 2</td>
</tr>
<tr>
<td>Porcine Cnivirus</td>
<td>Ungulate tetraparvovirus 3</td>
</tr>
<tr>
<td>Porcine parvovirus 4</td>
<td>Ungulate copiparvovirus 2</td>
</tr>
<tr>
<td>Porcine parvovirus 5</td>
<td>Not yet classified</td>
</tr>
<tr>
<td>Porcine parvovirus 6</td>
<td>Not yet classified</td>
</tr>
<tr>
<td>Porcine bocavirus</td>
<td>Porcine bocaparvovirus 2, 3, 4 and 5</td>
</tr>
</tbody>
</table>

Streck et al., 2015
Harmless organisms (or not?)…
MORE TO COME… AND SOON…

RAPID COMMUNICATION

Senecavirus A: An Emerging Vesicular Infection in Brazilian Pig Herds

R. A. Leme¹, E. Zotti², B. K. Alcântara³, M. V. Oliveira¹, L. A. Freitas¹, A. F. Alfieri¹ and A. A. Alfieri¹

¹ Laboratory of Animal Virology, Department of Veterinary Preventive Medicine, Universidade Estadual de Londrina, Londrina, Paraná, Brazil
² Department of Veterinary Medicine, Pontifícia Universidade Católica, Toleda, Paraná, Brazil
³ Multi-Use Animal Health Laboratory, Molecular Biology Unit, Department of Veterinary Preventive Medicine, Universidade Estadual de Londrina, Londrina, Paraná, Brazil

Detection and Genetic Characterization of Deltacoronavirus in Pigs, Ohio, USA, 2014

Leyi Wang¹, Beverly Byrum, and Yan Zhang¹

A Novel Pathogenic Mammalian Orthoreovirus from Diarrheic Pigs and Swine Blood Meal in the United States

Athanam Thimmasandra Narayanappa,a Harini Sooryanarain,a Jagadeeswaran Deventhiran,a Dianjun Cao,a Backlyalakshmi Ammayappan Venkatachalam,a Devalah Kamiranda,b Tanya LeRoith,a Connie Lynn Heffron,a Nicole Lindstrom,a Karen Hall,a Peter Jobst,a Cary Sexton,c Xiang-Jin Meng,a Subbiah Elankumaran,a
Harmless organisms (or not?)…
MORE TO COME… AND SOON…

**Short Communication**

Feral swine virome is dominated by single-stranded DNA viruses and contains a novel *Orthopneumovirus* which circulates both in feral and domestic swine

Ben M. Hause, Aiswaria Padmanabhan, Kerri Pedersen and Thomas Gidewski

**Rapid Communication**

Detection of a novel sapelovirus in central nervous tissue of pigs with polioencephalomyelitis in the USA

P. H. E. Arruda, B. L. Arruda, K. J. Schwartz, F. Vannucci, T. Resende, A. Rovira, P. Sundberg, J. Nietfeld, B. M. Hause
Let’s expand our view on viruses: THE VIROME

“The collection of organisms inhabiting the human body, the **microbiome**, is an integral component of our physiology”

Cho and Blaser, 2012

The mammalian **virome** includes viruses that infect cells of the animal host, endogenous viral elements, and viruses that infect members of the microbiome, most notably phages that replicate in bacteria

Virgin, 2014
Let’s expand our view on viruses: the VIROME

- The general concept that viruses are present ONLY when disease is present is wrong

- When a virus encounters a mucosal surface, the interplay between viral invasion and host antiviral defense strategies ultimately determines the severity and outcome of the infection (from subclinical infection to severe disease and, eventually, death)

- **RESIDENT VIRUS** versus **PERSISTENT VIRAL INFECTION**
- The host anti-viral response is dictated in part by genetics and can vary with genetic polymorphisms across the population
Conclusions

• The overall picture on viral infections of swine has evolved significantly

1992: 20 chapters
175 pages

2010: 24 chapters
266 pages

New Diseases of Swine book planned to be published in 2017-18
Conclusions

- Current research has prompted to evolve at different dimensions (veterinarians and researchers)

My pigs are sick

\[ \text{LET’S FIND THE CAUSE...} \]
\[ \text{Is it viral?} \]

I have a virus

\[ \text{LET’S FIND THE disease...} \]
\[ \text{Is there any?} \]
Conclusions
Let’s think beyond…

- Are we really prepared against emerging diseases?
- Can be the newly discovered viruses, presumably harmless today, the deadly pathogens of tomorrow?
- Are we discovering the “resident” viruses of the pig virome?
- Are those new viruses partly explaining the clinical outcomes we see nowadays in our farms?
- Do we need to increase cross-talking between veterinarians and researchers?
Thank you very much for your attention