Epidemiology and control of hazards in pork production chain – SAFEPORK
One health approach under a concept of farm to fork

support and help with the experimental work.

References
This paper is based on a master thesis, and all references can be found in this:
Available online: http://curis.ku.dk/portal/files/119192823/Final_edition_speciale.pdf

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Epidemiology of infection / control and mitigation option of foodborne pathogens and zoonotic diseases in the pork production chain.

Keynote lecture

Emerging swine diseases and infections: an increasing zoonotic threat
Joaquim Segalez – University Barcelona

Introduction

Emerging infectious diseases (EID) can be defined as those which incidence is increasing following its first introduction into a new host population or in an existing one as a result of long-term changes in its underlying epidemiology [1]. This concept can also include those diseases linked to pathogens expanding into an area in which it was not previously reported, or due to infectious agents that changed significantly its clinico-pathological presentation [2].

During last 10 years, much emphasis has been focused on human EID caused by pathogens of animal origin. All these zoonotic threats and events have emphasized the need for a “One Health” approach, which was summarized in the so called 12 Manhattan principles [3]. The “One Health” approach integrates communication, collaboration and coordination between public health, animal health and other communities at multiple levels to prevent, detect and control emerging or re-emerging infectious diseases at the animal–human–environment interface [4].

The number of novel conditions in swine included under the concept of emerging and re-emerging diseases has increased importantly during last 20-30 years [5]. Most of them are infectious diseases; their transmissibility and maintenance into a population is favoured by a number of phenomena, including intensive rearing practices and globalized/ international trading. The objective of the present review is to discuss about new swine diseases or novel presentations of already known diseases, as well as newly recognized infections with a not well-defined pathogenic effect in pigs, with specific emphasis on zoonotic diseases.

Monofactorial and multifactorial pig diseases

Traditionally, veterinarians have dealt with overt diseases, with the main task of counteracting them and getting profitability of the production system represented by a farm or a group of farms. Moreover, several decades ago, the most important diseases affecting pigs were considered mostly “monofactorial”, in which the sole presence of the infectious agent was sufficient to trigger significant disease or production losses [6]. In swine, most of these infectious diseases, such as classical swine fever (CSF), Aujeszky's disease (pseudorabies), foot-and-mouth disease or African swine fever (ASF), among others, have been controlled or are under control in many parts of the world by means of eradication programs (World Organization for Animal Health, OIE, www.oie.int). However, these diseases may appear sporadically in free-countries as a result of trading of life animals or animal products, or citizen travelling. This scenario of disease re-introduction is not unusual, and recent examples of emerging and re-emerging diseases would be ASF in Russia and Eastern Europe, and porcine epidemic diarrhoea (PED) in Europe and North-America.

There are a number of not so devastating infections compared to those considered as “monofactorial”,...
but with significant impact on the economy of the swine industry. Among them we can consider those caused by *Mycoplasma hyopneumoniae*, *Brachyspira hyodysenteriae*, *Actinobacillus pleuropneumoniae*, porcine reproductive and respiratory syndrome virus (PRRSV), swine influenza virus (SIV) and porcine circovirus type 2 (PCV2). Common to all of them is that they are considered “multifactorial” diseases, since the mere presence of the agent is not sufficient to trigger the disease [6]. In most of the cases, those diseases behave as endemic diseases in most parts of the world, but some exceptions can be perfectly classified as emerging or re-emerging pig diseases. Good examples would be the infection by certain serotypes of *A. pleuropneumoniae* in naive herds or the reproductive form of PRRS in sero-negative farms, which may behave as the previously mentioned “monofactorial” diseases. Moreover, other diseases have probably been there for a long time, but their relevance increased mainly in the last two decades, such as colibacillosis, Glässer’s disease, proliferative enteropathies, and swine influenza. Although the term “emerging” is probably old-fashioned nowadays for these conditions, we still consider PRRS and PCV2-associated diseases (PCVDs) as such. A good example of a truly emerging disease among these multifactorial threats would be the new pandemic human influenza virus A/H1N1 [7], although it should be considered also within the zoonotic disease group, and *Brachyspira hampsonii* [8].

**Zoonotic pigs’ infections**

The list of zoonotic agents that produce disease or infection in pigs is rather long (Table 1); in practical terms, a number of them are of significant importance, especially from the food safety point of view. Moreover, the list of zoonotic threats coming from pigs that should be considered as emerging is rather limited, but the awareness about them has increased during the last decade: hepatitis E virus (HEV), influenza viruses, livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA), Extended-spectrum beta-lactamases (ESBL) producing bacteria, *Streptococcus suis*, *Clostridium difficile*, and *Cysticercus cellulosae* [9,10]. There are also some pathogens that exert their action in limited geographical locations, such as Nipah, Bungowannah, and Menangle viruses, that have been described as the cause of swine disease in certain regions of the world (south-east Asia and Oceania, mainly) [11].

Increasing resistance against antimicrobial substances in bacteria is one of the major problems in human as well as in veterinary medicine. Such scenario prompted the raise of the so-called multiresistant bacteria (MRB), which display reduced susceptibility against different antibiotic drugs, and they are considered of exceptional clinical importance, since the therapeutic options are becoming very limited or no longer exist [10]. The most common MRB in human and veterinary medicine is the MRSA, but other MRB colonizing the human digestive tract as well as the intestine of livestock have come into focus. ESBL-producing bacteria induce nosocomial infections in humans, with a rising incidence, and livestock has frequently been found to carry these bacteria. In fact, carriage of ESBL-producing bacteria in pig farmers has been found associated with occurrence in pigs [12]. Other potential pathogens in the animal (including pig) digestive tract are vancomycin-resistant enterococci strains (VRE). As an interesting example, recently, vancomycin resistant *Enterococcus faecium* related to humans and pigs was found in dust from pig breeding facilities, suggesting that dust could represent a vehicle of transmission of strains and antibiotic resistance genes between food-producing animals and man [13]. Among zoonotic emerging bacteria, *Clostridium difficile* should be highlighted, since although it is not an MRB, its therapeutic options for humans are very limited, posing a potential extra-threat coming from animals [10].

*Taenia solium* taeniasis/cysticercosis (*Cysticercus cellulosae*) is a zoonotic disease complex in which humans are the final host and pig the normal intermediate host. When people consume undercooked infected pork, they can develop a tapeworm. Humans can act as accidental intermediate hosts of *T. solium*, and develop cysticercosis. In humans, the cysticerci often lodge in the central nervous system causing neurocysticercosis (NCC) [14]. Although considered eradicated in Europe, an increase of NCC probably due to imported cases via travellers or immigrants has occurred in recent years. Therefore, at least in terms of frequency of cases, this human disease is considered a re-emerging threat [14]. Conversely, the role of pigs in Europe to transmit this disease is probably negligible.

Among emerging viruses, HEV is probably the only that have recently drawn more attention. Although the evidence as a zoonotic pathogen is nowadays clear [10,11], the true impact of the swine HEV infection on human health is probably negligible in most parts of Europe. Moreover, it is known that this virus can cause asymptomatic infections in humans. Among other emerging viruses, it is very likely that Nipah virus is the most concerning one for human health. Spillover from *Pteropus* bats triggered an outbreak in the pig population in Malaysia in 1998 [10]. A high proportion of pigs experienced clinical affection to Nipah virus infection, but most cases recover after several days of illness. In order to minimize economic losses, farmers attempted to take sick pigs to market, and trading sick pigs accelerated Nipah virus spread across the country. Overall human mortality due to Nipah viral infection was 40% [10]. Finally, influenza viruses have always been on the spot in swine production, since pig has been considered for long as “mixed vessels” for the transmission from birds to pig and pig to human. Although this role is under debate, it is true that the H1N1 influenza virus pandemic of 2009 heightened the awareness of influenza viruses as zoonotic pathogens. However, the same virus was a good example of reverse zoonosis in Norway, where the pig population was completely naïve against influenza viruses before the income of the pandemic strain coming from humans [15].

**Discussion**

Infectious emerging diseases appearance has been usually characterized by sudden, unpredictable outbreaks, sometimes of epidemic proportion [16]. Despite improvements in global health, both at human and animal sides, outbreaks of infectious diseases still occur, and new infections have emerged and will probably continue emerging in the future. The control of a given disease/Infection might be very difficult per se, and sometimes to live with an endemic scenario could be worse than to eradicate it and being threatened by the risk of re-infection. Such situation is especially important when dealing with livestock diseases/infections, since the loss of production or competitiveness may cause significant economic disadvantages, not only for the producers but also for a country or region as a whole. In contrast, a significant number of emerging swine zoonosis does not behave as usual outbreaks of disease in this species; in fact, in a number of cases, the causal agent may remain subclinical or pigs are just carriers.

It is hard to predict what will come next in the swine industry in terms of diseases and infections, but the advent of PRRSV by late 80s and beginning of 90s, PCVDs by late 90s, the pandemic A/H1N1 by 2009 and PED in North America and Europe in 2013/14 implies to have new clinical disease emergences every 7-8 years. Moreover, the frequency of swine pathogen discovery is much higher; 98 new pathogen species have been described in pigs between 1985 and 2010, with 48 (49%) being bacteria, and 44 (45%) being viruses. Importantly, 48 out of these 98 species (43%) are zoonotic [17].

Therefore, the risk of emerging and re-emerging diseases with significant economic losses, infections with unknown impact on production and diseases/infections with zoonotic potential is high and deserves preparedness and proper basic and applied research. Pig production is a good example of a globalised industry, and swine veterinarians and researchers in conjunction with producers, consumers, and stakeholders should join efforts for more global, collaborative, and action-oriented approaches towards logical and practical solutions [5].
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References


Table 1. List of zoonotic agents that produce disease or infection in pigs (adapted from Khan et al., 2013). Pathogens with asterisk indicate those with potential foodborne transmission.

<table>
<thead>
<tr>
<th>Pathogen (Scientific Name)</th>
<th>Non-Pathogenic Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus anthracis*</td>
<td>Leptospira interrogans</td>
</tr>
<tr>
<td>Balantidium coli</td>
<td>Listeria monocytogenes*</td>
</tr>
<tr>
<td>Brucella spp.</td>
<td>Menangle virus</td>
</tr>
<tr>
<td>Bungowannah virus</td>
<td>Methicillin-resistant Staphylococcus aureus</td>
</tr>
<tr>
<td>Burkholderia pseudomallei*</td>
<td>Microsporum spp/Trichopyton spp.</td>
</tr>
<tr>
<td>Cryptosporidium suis</td>
<td>Nipah virus</td>
</tr>
<tr>
<td>Cysticercus cellulosae*</td>
<td>Norwalk virus*</td>
</tr>
<tr>
<td>Ebola reston virus</td>
<td>Pasteurella multocida</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>Salmonella spp.</td>
</tr>
<tr>
<td>Erysipelothrix rhusiopathiae</td>
<td>Sarcocystis suihominis*</td>
</tr>
<tr>
<td>Escherichia coli*</td>
<td>Streptococcus suis</td>
</tr>
<tr>
<td>Extended-spectrum beta-lactamases (ESBL) producing bacteria*</td>
<td>Swine influenza viruses</td>
</tr>
<tr>
<td>Francisella tularensis*</td>
<td>Toxoplasma gondii*</td>
</tr>
<tr>
<td>Giardia spp.</td>
<td>Trichinella spiralis*</td>
</tr>
<tr>
<td>Hepatitis E virus*</td>
<td>Vesicular stomatitis virus</td>
</tr>
<tr>
<td>Japanese encephalitis virus</td>
<td>Yersinia enterocolitica*</td>
</tr>
</tbody>
</table>

Pork meat is estimated to be responsible of 10 to 20% of human salmonellosis cases. Control strategies at the farm could reduce contamination at the slaughterhouse. One of the targeted sector of the production is the maternity, where sows could be Salmonella reservoirs. The aim of this study was to characterize the faecal microbiome of sows excreting or not Salmonella during gestation phases. A total of 76 sows were selected and fecal matters were analysed at the beginning or the end of gestation period. Salmonella detection was conducted using a method including two selective enrichment media (MSRV and TBG). Nine (9) isolates per positive samples were collected. Among the 76 sows tested, 31 were shedding Salmonella. The sows in the first third of their gestation shed significantly more frequently Salmonella (22/29) than those in the last third (7/47) ($\chi^2$ P < 0.05). The shedding status of 19 of the sows that were previously sampled in the first third of their gestation was followed, this time in the last third, confirming reduction of the shedding. Association between changes in the intestinal microbiome and this evolution of Salmonella shedding will be explored. MiSeq sequencing is currently being conducted on the feces to identify shifts in the composition or diversity in the microbial community that could be associated to these variations. A large number of Salmonella isolates that were collected were genotyped by a high resolution melt (HRM) technique. These results showed the presence of a major HRM profile (136 isolates / 169) and two minor profiles (24 and 9 /169).

Introduction

In Canada, Salmonella is estimated to cause 269.26 infection per 100 000 inhabitants each year making this pathogen a priority in public health [1]. Pork meat was estimated to be responsible of 10 to 20% of reported human salmonellosis cases in Europe and therefor is an important source of this pathogen [2]. Better control strategies at the farm could help to reduce the contamination of the carcass at the slaughterhouse. Indeed it has been shown that the influx of contaminated pigs at the slaughterhouse was a risk factor for the contamination of the carcasses of the pigs during slaughter and hence of the products that reaches the consumers [3]. In the porcine production, sows can be an important Salmonella reservoir with contamination levels usually higher than the pigs in the fattening phase [4]. These carrier sows could be an important contamination source for the piglets [2, 5]. The dynamic of the excretion of Salmonella by the sows during gestation is still not very well known. It seems important to better understand the different factors that could influence this excretion to better understand the transmission of this microorganism to piglets. The aim of this study was to characterize the variation of the excretion of Salmonella by the sows in the gestation phase in relation with the faecal microbiome.

Material and method

Sampling: A total of 76 sows at various gestation stages were selected randomly in a breeding farm known for its frequent Salmonella contamination. For each selected sows 100 gr of fresh fecal matter were collected and analysed. After the first sampling 19 of the 76 sows that were sampled at the beginning of their gestation (first 50 days) were sampled a second time at the end of this period (last 50 days). For each sampled sows 1.5 ml of feces was also collected and frozen in liquid nitrogen for 16s rRNA amplicon MiSeq sequencing.