DISCONTOOLS

Porcine circovirus 2 (PCV-2)
Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on *Porcine circovirus 2* (PCV-2). They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details are available on the web site at http://www.discontools.eu/.

Disease profile

2. *Porcine circovirus 1* is a non-pathogenic virus found as a contaminant of porcine cell lines and in pigs. *Porcine circovirus 2* (PCV2) is associated with several disease manifestations in pigs. More recently, two more porcine circoviruses (PCV-3 and PCV-4) have been described and associated with different pathological conditions; while PCV-3 disease association seems clear, no conclusive evidence for PCV-4 has been yet demonstrated. PCV-2 is by far the most important PCV, with several genotypes described (PCV-2a to PCV-2i, being PCV-2a, PCV-2b and PCV-2d the most frequent ones) with >90% homogeneity at the nucleotide level. PCV-2 is the necessary but not usually self-sufficient cause of a variety of manifestations of what have come known as Porcine circovirus diseases (PVCD). There is some evidence that the severe PCVD seen globally by the end of past century was linked to the emergence of specific genotypes, but the variability of disease may also be related to many other factors such as immune status to PCV-2, time of infection, pig genetics, standards of management in the widest sense, and to the health of the herd and other concurrent diseases.

3. All species within the *Suidae* family appear to be susceptible to PCV-2 infection, including wild boar and feral pigs. Many pigs are infected without displaying clinical signs of disease (PCV-2-subclinical infection) and some of these animals act as carriers. The first PCVD to be identified was the so-called Post Weaning Multi-Systemic Wasting Syndrome (PMWS, now as PCV-2-systemic disease, PCV-2-SD) in which disease was found in postweaning pigs. In the early cases in some countries there was also a severe systemic condition called Porcine Dermatitis and Nephropathy Syndrome (PDNS), an immuno-complex disease, which was extremely difficult to differentiate from ASF/CSF but which was later shown to be circumstantially associated with PCV-2. Another clinical manifestation is related to mid-late term abortions or farrowing with increased numbers of stillborn and mummies (PCV-2-reproductive disease). In addition, PCV-2 has been shown to contribute to a variety of disease complexes including enteric and respiratory disorders and gastric ulcers, probably because of the systemic infection (PCV-2-SD).

Risk

4. The virus transmits easily because of its ubiquitous nature in the environment and as not yet completely understood effects on the host make it very difficult to control. In experiments, PCV-2 in-contacts are not always infected, and infection does not always produce disease. There is no evidence of human infection, no evidence of vectors and probably most pigs become infected during their lifespan. The costs of the infections are difficult to quantify but were considerable before the availability of vaccines (calculated in 2009 as 5.7 billion € for the 27 countries of the EU). The loss of profitability was due to variation in growth rate, increased morbidity and mortality of postweaning pigs and reproductive failure together with increased veterinary charges and antibiotic use.

Diagnostics

5. Clinical signs, gross post-mortem, particularly enlarged inguinal lymph nodes, histopathology with demonstration of PCV2 material by IHC or ISH, which is available in many laboratories worldwide. Quantification of virus load in serum by real time qPCR has been used as a proxy for diagnosis in many countries, but the results are difficult to interpret, especially to predict clinical impact at individual level. Serological tests are not helpful for diagnosis as most pigs are seropositive (due to natural infection, vaccination, or colostrum intake) and there is a lack of any predictive test that could identify pigs that will progress to severe disease. Diagnosis is still complex and is best made at the

herd level with the necessary help of local laboratories. The existing tests are probably adequate although the development of pen-side test that assess need and/or impact of vaccination would be beneficial. Antibody detection tests and PCR/qPCR methods are excellent for monitoring the infection and eventually to predict the most efficient timing of vaccination.

Vaccines

6. Vaccines for control of PCV-2 infections in sows and piglets are available. They are recombinant, inactivated, and chimeric-inactivated products Also vaccines where PCV-2 is combined with *Mycoplama hyopneumoniae* are available. Very high (80-100%) of pig farms use PCV-2 vaccines, with some differences between different countries. All vaccines appear to be successful in reducing losses due to PCVD and are capable to produce protective levels of antibodies and cellular immunity to piglets or in colostrum to be transferred to the piglets. Possible improvements would be to reduce the number of injections or replace them with other easier routes and consider including more antigen combinations in vaccines against common pig pathogens. No vaccines sold as marker vaccines are available but the subunit vaccines could be regarded as marker vaccines if diagnostic tests were developed targeting virus subunits not present in the vaccines. There is also a need to maintain surveillance of the viral populations under vaccination pressure since emergence of new virus genotypes may happen. Although no evidence of immune escaping against vaccine strains has not been documented for PCV-2, it cannot be ruled out. Vaccines are not effective against other PCVs.

Pharmaceuticals

7. None are available at present. The effect of existing antiviral drugs against PCV2 is virtually unknown, since very little has been published in the literature and all at laboratory and/or experimental levels. It is unlikely to find a cost-effective antiviral product for a ubiquitous virus, especially in the light of timing needed to infect the whole group of animals versus moment of administration. Passive immunisation is not used to control PCV-2 at present.

Knowledge

8. There are still significant areas of uncertainty in the understanding and knowledge about PCV-2 especially in relation to pathogenesis, immunology, and epidemiology. The mechanisms of pathogenesis are largely unknown, but as molecular understanding of viral pathogenesis increases, new developments may take place.

9. Continuing research on the fundamental immunology of the pig and its relation to PCV-2 infection is needed. The role of cell-mediated immunity to PCV-2 is still poorly known, although neutralising antibodies and cellular immune response (measured as IFN-gamma producing cells) are considered the major immunological components to control the infection. PDNS is a hypersensitivity type 3 reaction in which the associated antigen is attributed to PCV-2; however, not clear demonstration has been yet obtained. Also, continuous monitoring of PCV-2 and its genotypes is fundamental to assess potential changes in immune protection related epitopes. New vaccine product development based on combination of genotypes is currently happening and is a novel area of interest since better immune coverage might be generated.

Conclusions

10. PCV-2 continues being a very significant pathogen for the swine industry, causing several clinical-pathological manifestations known as PCVD, and being PCV-2-SD the most important one. Changes in the epidemiology of the virus has prompted the appearance of disease in already vaccinated farms, so, the use of diagnostic tests is still a major need.

11. The availability of effective vaccines is preventing funding more research as the impact of the infection is limited in vaccinated herds. However, there is a need for continued population monitoring of the viral population, and to study of the pathogenesis and immunology. A repeatable, reproducible model of experimental disease is still missing. Reliable economic tools for costs/benefits assessments are also needed to assess the impact of such endemic diseases.