Porcine reproductive and respiratory syndrome - PRRS
Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on PRRS. 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. This disease is the most important endemic pig disease causing continuously negative impact on health and welfare of piglets and sows and production losses. Until 2018 PRRSV was divided into two genotypes, PRRSV-1 (former European type) and PRRSV-2 (former American type), sharing only 55-70% of similarity at the genome level. According to the newest classification of International Committee on Taxonomy of Viruses, previous genotypes are now considered to form two distinct species with proposed names Betaarterivirus suid 1 and Betaarterivirus suid 2, classified within two separate subgenuses in the Genus *Betaarterivirus* of the *Arteriviridae* Family.
Historically, the occurrence of PRRSV-1 (Betaarterivirus suid 1, prototype strain Lelystad) was limited to Europe and PRRSV-2 (Betaarterivirus suid 2, prototype strain VR2332) to North America and Asia. Due to the use and spread of PRRSV-2-based vaccine in Europe and movement of infected pigs, mixtures of both species are present on all the continents nowadays. Still, PRRSV-1 is the most prevalent in Europe, and PRRSV-2 in America and Asia. A large variation existing within each species leads to their division into subtypes/clades/lineages. PRRSV-1 is further divided into at least four subtypes: 1, 2, 3 and 4. While subtypes 2, 3 and 4 have only been detected in the Eastern Europe, all PRRSV-1 strains found in Central and Western Europe up to date have belonged to subtype 1.
3. The clinical outcome of PRRS virus infections is very different in between strains. In general, strains of PRRSV-1 tend to be less aggressive than the ones of PRRSV-2. However, in both species highly virulent strains may emerge, including PRRSV-2 strains causing high mortality in sows in North America and High Fever Disease in Asia, as well as PRRSV-1 strains of subtypes 2 and 3 (Lena and Bor) and several subtype 1 strains of elevated pathogenicity identified throughout Europe.
4. A variety of clinical syndromes have been described from subclinical to high morbidity/mortality (up to 30-50% with highly virulent strains). They may last 3 months or longer, especially when naïve animals are introduced, until they settle down. Once infected, herds tend to remain so, especially large herds or closed herds, as there is a continuous presence of susceptible pigs such as piglets and naïve replacement gilts.

Risk

5. The rapid mutation of the virus may result in a high virulent strains that may cause extremely high mortality and destroy large part of the population in a very short time, as occurred in Asia with the emergence of the High Fever Disease PRRS virus. This led to a mortality of 30-50% in pigs and caused problems with the security of food supply. In other countries with less pathogenic strains, the loss of production increases preproduction costs of finishing pigs and reduces the income of farmers. Import restrictions only concern countries free from PRRSV infections (Sweden, Finland, Norway, Switzerland, Brazil, Australia, New Zealand) or countries with implemented eradication program (Chile, Hungary). In most of the other countries PRRS remains endemic.
6. The virus is transmitted horizontally (direct contact, contaminated fomites, airborne, via semen) and vertically (mainly after 70 days of gestation). Indications exist that the replication and transmission power of PRRS in the respiratory tract is linked with the potential to spread airborne. PRRS virus is stable in an aerosol at low temperatures. Because co-infections of PRRS virus with bacteria result in an aggravation of the clinical outcome, antibiotics are used in large amounts. The extensive use of antibiotics during PRRS virus-bacterial co-infections may induce resistance, which forms a danger to a public health.

Diagnostics

7. A number of serological methods are available for diagnosis. In general, they have good specificity and sensitivity. For initial monitoring/diagnosis, a wide variety of ELISAs has been developed, capable of identifying antibodies induced by strains of both PRRSV species. In order to confirm the initial positive results, and to differentiate genotypes/strains, ORF5 ELISA and the indirect immunoperoxidase monolayer assay (IPMA) or indirect immunofluorescence (IIF) using alveolar macrophages and MARC-145 cells can be applied. Diagnostic kits (PCRs, ELISAs) are available worldwide and are very effective to determine the presence of PRRS virus in a population. Nevertheless, it is questionable if they can pick up all circulating isolates considering the ability of the PRRS virus to mutate rapidly. PCRs/ELISAs should be continuously validated with the appearance of new PRRS virus isolates. It is important to monitor the genetic sequences of new viruses to ensure that they are detected in the existing PCR/ELISAs. To achieve this, a pan-European PRRS database should be created that would allow simultaneous comparison of PRRS isolates representing most countries in Europe. This requires regular pathological studies for new virus strains, isolation of the virus, whole genome sequencing and antisera production. This approach is also essential to study the evolution of the virus and its genetic changes.

Vaccines

8. Both live attenuated and inactivated vaccines are available containing either PRRSV-1 or PRRSV-2. Inactivated vaccines are safe but not efficacious, as it has been demonstrated that they cannot control viremia post-challenge by themselves. They can only boost the existing immune response in sows. Inactivated vaccines do not protect naïve animals and give only boost reactions when the animals have been previously exposed to the field virus or Modified Live Vaccines (MLVs). MLVs have been proven to reduce clinical signs, viremia and shedding post-challenge, as well as to reduce virus transmission in vaccinated populations. In regards to safety, some limited horizontal and vertical spread can be found, as well as vaccine strain shedding. These characteristics differ between vaccine strains. Although it was initially assumed that the efficacy of attenuated vaccines depends on the homology to the field virus, it has been proven lately that vaccine efficacy also depends on the capacity of the vaccine to induce cellular immunity and, probably, virus-neutralizing antibodies. Nevertheless, vaccine efficacy is always partial. Therefore, proper vaccination regimes should be applied together with strict biosecurity measures. Otherwise field virus evolution will accelerate due to vaccine induced selection pressure.

9. As vaccine protection is partial, there is an urgent need for new generation vaccines that provide universal protection. Additionally, it would be highly appreciated to differentiate vaccinated animals from infected ones (DIVA vaccines). To achieve this, new approaches of vaccine production should be considered, such as multivalent vaccines or subunit vaccines.

Pharmaceuticals

10. No antivirals are available against PRRS virus, but, as coinfections with bacterial diseases are very common, high levels of antibiotics are used to control them.

Knowledge

11. There are significant areas of uncertainty in the understanding and knowledge about PRRS, especially in relation to pathogenesis, immunology, and epidemiology. Although PRRS virus research has already solved several aspects of the virus-target cell interaction, huge gaps are remaining in the understanding of the replication in relation to receptors, disassembly, transcription and translation, assembly and release. More fundamental knowledge on virus-host interactions (active immune responses, immune evasion, virulence factors) is essential to develop new generation adaptable vaccines that would be effective. The basis of pathogenicity and virulence are largely unknown, together with the mechanisms of virus persistence. Further understanding is needed on the way in which PRRS virus negatively impacts the immune response, in particular with regard to other pathogens, i.e. PCV2 and bacterial infections.

12. Whole genome analysis should be carried out in order to obtain correct genetic trees. These trees will be very important in epidemiological studies (evolution), pathogenesis research (pathogenicity,

virulence, immune evasion) and immunological analysis (identification of B- and T-cell epitopes, vaccine development). In this context it is important to understand which parts of the genome are linked with ability to spread, pathogenicity, virulence, immune evasion and immunogenicity.

Conclusions

13. PRRS virus is currently one of the most important infectious pathogens of pigs. The virus is genetically on the move and the high mutation rate is problematic for diagnosis and future control of PRRS. There is major concern over the possibility that high virulent strains may emerge and that these PRRS virus mutants may be difficult to control by using the currently registered vaccines, as by now, none of the available vaccines induces universal and total protection. Many knowledge gaps exist.