Update on porcine reproductive and respiratory syndrome (PRRS)

Thomas Blaha, Prof. Dr. med. sc.; Robert B. Morrison, DVM, PhD, MBA; Thomas Molitor, PhD; and Gert Wensvoort, DVM, PhD

In 1985, the first report of reproductive failure in sows was published in the United States. The syndrome manifested as abortions beyond the 100th day of gestation, with many stillbirths and mummies. At that time, we didn’t know either the identity of the causative agent nor whether the syndrome was contagious; thus, the syndrome was named “mystery swine disease.” In the next few years, occurrences of the disease were reported from all over the United States and Canada, although the disease didn’t appear to be spreading very quickly.

In Europe, the syndrome was first identified in 1990 in North Rhine-Westphalia, Germany, and it subsequently spread quickly throughout West Germany, to the Netherlands, Belgium, France, Spain, Austria, and East Germany. The first reports of the syndrome in Denmark occurred in 1992. During its “travels” through Europe, the disease became less and less clinically distinct in breeding herds; however, there were more and more reports of the disease influencing the respiratory health of finisher pigs. The European epidemic removed any doubt that the disease was infectious, and, in late 1991, the virus was first isolated in Lelystad, the Netherlands. Shortly thereafter, the virus was isolated in St. Joseph, Missouri in the United States.

In the spring of 1992, a First International Symposium on Porcine Reproductive and Respiratory Syndrome (PRRS) was held in St. Paul, Minnesota to discuss this disease. This Symposium was organized by the Swine Group of the College of Veterinary Medicine, University of Minnesota, and chaired by Dr. Robert B. Morrison. At that time, there were more questions than there were answers. However, a great deal more is now understood about the virus:

- the virus has been isolated worldwide;
- new diagnostic tools have been developed for detecting both antibodies and the antigen;
- vaccines have been developed; and
- control measures (management methods and vaccination) have been applied in the field.

However, because a host of questions remains, a Second International Symposium on PRRS was convened in Copenhagen, Denmark on August 5–8, 1995. The purpose of this symposium was to update our knowledge of PRRS, to exchange international experiences with PRRS, and to intensify scientific cooperation throughout the world. This Second International Symposium was organized by Dr. Sten Mortensen from the Danish Association of Pig Producers and Slaughterhouses and Dr. Thomas Blaha from the School of Veterinary Medicine, Hannover, Germany. Dr. Blaha chaired the meeting. Two-hundred twenty-five participants from 28 countries attended the second PRRS symposium, at which 40 papers and 17 posters were presented. In the following discussion, the presentations & posters are summarized.

**General overview**

The symposium was opened by the invited speakers Dr. Gert Wensvoort and Dr. Jeff Zimmerman, who each gave a summary of our current knowledge and a perspective on the syndrome in Europe and in North America, respectively. Both speakers agreed that while the reproductive disease of PRRS has a rather typical and distinct clinical presentation, the respiratory complex is ill-defined. Dr. Wensvoort proposed that we deal with this ambiguity by speaking of the PRRS reproductive disease and of the PRRS respiratory syndrome.

Drs. Wensvoort and Zimmerman discussed the many questions still unanswered, including:

- what role does PRRS virus (PRRSV) play in the respiratory syndrome?
- is our belief in airborne transmission justified?
- what are the pathogenic mechanisms for two such different clinical complexes, both caused by the same virus? and
- what are the protection mechanisms?

**Virology**

An excellent overview on our knowledge of PRRSV was presented by Dr. Janneke Meulenberg. Dr. Meulenberg reported that the entire genome of Lelystad virus has been sequenced. It contains eight open reading frames (ORFs) that encode the viral replicative polymerase (ORFs 1a and 1b) and six unidentified or structural proteins (ORFs 2, 3, 4, envelope glycoprotein, matrix protein, and nucleocapsid). One immediate outcome of the symposium was that an ad-hoc committee met and agreed on a nomenclature of the six identified proteins so that confusion due
to different names can be prevented in future research and publications. The nomenclature, based on available information on the structure and function of these viral polypeptides, is gp2, 3, 4, 5, and M and N.

The virus has substantial variation in its genome, although observations to date have been with ORF 2-7, which represent only about 20% of the genome. We know that this part of the virus has approximately 34% variation between American and European strains and 2%-8% variation within American or European isolates. Compared to, for example, Herpesviruses, PRRSV is relatively unstable and is undergoing continual genetic changes. It was reported that even in one pig, clusters of genetically different isolates can be detected.

Monoclonal antibodies are available on both sides of the ocean. Multiple monoclonals should be used for diagnostics, because a single monoclonal may miss some isolates. Despite the advances in the PRRS virology, large gaps remain in our understanding of the function of the individual polypeptides.

**Immunology**

Dr. Tom Molitor gave an invited paper on the immune responses to PRRSV entitled “Double-Edged Sword”, referring to the fact that there is an unexplained paradox in the immunology of PRRS. On the one hand, there is the strong clinical impression of many practitioners and epidemiologists that PRRS infection leads to an increase of diseases in the field, and, on the other hand, there is no evidence of systemic, functional immunosuppression. The short-term reduction of macrophages is restricted mainly to the lung and does not explain the often-reported aggravation of respiratory distress. There is seemingly a variety of antigen-specific responses to the virus, both humoral and cell-mediated. However, we do not know which responses are protective in the case of the reproductive disease and the respiratory syndrome. Little is known about the host mechanism that prevents re-infection and about the cross-protection of American versus European strains despite their antigenic differences. Further investigations into the defense mechanisms of pigs against PRRSV are necessary.

**Diagnostics**

Dr. Anette Bøtner presented the progress in PRRS diagnosis that has been made since 1992. She gave an informative overview on the currently available diagnostic methods to detect both antibodies and antigens. In the following session, ELISA procedures (direct, indirect, and blocking tests as well as tests with PRRSV proteins expressed by baculovirus) were described. One paper reported that detecting specific IgM can detect the infection at an earlier stage. This range of diagnostic tools can, reasonably combined, differentiate between acute and chronic infections of herds, provided no single animals are investigated, but instead that serological profiles of the herds in question are conducted. The IPMA on macrophage monolayers is still the most sensitive test for detecting an early serological response. As for the diagnostic procedure for preventing the importation of PRRS-positive pigs into PRRS-negative countries (e.g., Sweden), the recommendation is not to rely on testing the individual animals that are to be moved, but instead to investigate the herd of origin (serological profile via a representative random sample) and then to repeat the test during the quarantine after the animals arrive.

**Pathogenesis**

The session was opened by a presentation by Dr. Kristien van Reeth. She summarized the scientific achievements that have been reported since 1992. Although PRRS-induced reproductive disease is still of great importance and interest, there has been relatively little new information on the pathogenesis of the abortions and stillbirths. In contrast, there have been many investigations on the pathogenesis of the respiratory syndrome in growing pigs. Many investigators have attempted to reproduce the respiratory syndrome with PRRSV and a myriad of bacteria; results have been variable, at best. To summarize, it was acknowledged that the respiratory syndrome ascribed to PRRSV is difficult to characterize and reproduce. This indicates that the syndrome in growing pigs, as described in the field, may be multifactorial in nature. This observation, coupled with the lack of evidence for generalized immunosuppression, led to the caution that we should not assign all health impairments in PRRS-positive herds to PRRSV.

Viral persistence has been detected as long as 157 days after initial challenge. The virus appears to persist mainly in alveolar macrophages and oropharyngeal lymphoid tissue. As for the molecular pathogenesis and cellular morphogenesis, no differences between the strains Lelystad, VR-2332, and JJ1882 (MLV vaccine strain) could be found, although there are marked differences in the speed of replication and, seemingly, in their virulence.

**Epidemiology**

Dr. Emmanuel Albina gave an overview on the current knowledge on the epidemiology of PRRSV and the latest data on the prevalence of PRRSV in France. The most striking feature of the occurrence of PRRSV is that the seroprevalence of herds is associated with the density of herds within regions. Apart from France, studies on PRRSV seroprevalence were presented for Canada, Poland, and Germany (Westphalia). Investigations into the transmission of PRRSV revealed that apart from the pig-to-pig infection (contact and droplet transmission), birds may be included in the infection chain. The importance of artificial insemination (AI) remains speculative because there are rather differing results on the infectiousness of semen from infected boars (the French experiences differ from the German and Danish). There was strong evidence that PRRSV could be shed in semen for extended periods of time after experimental infection (detected up to 92 days in semen).

The question of whether PRRSV can be transmitted via pork is of major concern in some countries. The only study on this revealed
that the virus can be detected in pork directly at slaughter at a very low prevalence. However, there are no data on the longevity of the virus in pork and its ability to survive the acidification of the meat after slaughter. There is also no experimental evidence of an oral infection via contaminated feed, nor any epidemiological evidence that the virus has been imported into PRRSV-free regions via pork. All infections of free regions that have been reported in the literature and during the Symposium were presumed due to either infected animals being imported or to airborne transmission.

Two epidemiological studies on the risk factors for the infection of free herds with PRRSV and for the severity of the clinical presentation of PRRS both in breeding and in finishing herds were presented. Both studies ranked the sources of the PRRS spread as follows:

- first and most frequent is pig movement,
- airborne spread is second, but only over short distances (only in rare exceptions more than 2000 m), and
- third, although still under discussion, is artificial insemination.

The two studies also concluded that the primary risk factors for the clinical expression of PRRSV infection of herds are the herd health status and the hygiene level, as well as the quality of the herd health management. These factors have a much greater influence on the clinical signs than factors such as herd size, production system, and origin of piglets. That is, the higher the pre-infection herd performance and herd health status, the lower the losses due to the infection with PRRSV. This was true in breeding and in finishing herds.

**Control**

The invited speaker of the last session was Dr. Scott Dee, who presented the result of field trials to control PRRS by partially depopulating the nurseries. Porcine reproductive and respiratory syndrome was eliminated from the growing pigs from 32 farms out of 34 by this method. Partially depopulating the nurseries led in all cases to a dramatically improved growing pig performance and increased profitability of the farms in question. Although 12 of the herds became reinfected, the improvement in productivity was maintained. This report emphasized again the importance of management practices to ameliorate the clinical presentation of PRRS and to stop the spread of PRRSV. A French study on the eradication of PRRS by depopulating infected herds in regions with a low prevalence showed the possibility of controlling PRRS if there is serological monitoring and if all owners are motivated to contribute to the eradication.

First experiences with vaccines were presented at the Symposium. A modified live vaccine, produced by Boehringer Ingelheim, has been licensed in the United States since 1994. Also, an inactivated viral vaccine has been licensed in Spain and tested in Greece ("Cy-Blue"). A recombinant (ORF 3) vaccine has been developed in Spain. Whereas the Boehringer Ingelheim vaccine is licensed for use in feeder pigs to ameliorate the respiratory syndrome due to PRRSV, the inactivated and the recombinant vaccines are reported to prevent the reproductive disease due to PRRSV. First positive field experiences with the Boehringer live vaccines were presented from the United States.

**General conclusions**

Although the clinical presentation of the reproductive disease of PRRS is at present not as severe as at the start of the European epidemic, it remains a concern to the pig industry, both in countries and regions that are currently not infected and for the many countries in which the national herds are serologically PRRS-positive. The importance of PRRSV for the respiratory disease complex of pigs demands intensified research, not only with experimental but also with epidemiological studies. The disease seems to be occurring all over the world, with only a very few countries that are PRRS-free (e.g., Sweden and Switzerland and some parts of East Germany). Legal restrictions to the trade with live pigs are only reasonable in the case of countries verified to be free of PRRS.

At present, the control of PRRS is based on:

- observing and monitoring the PRRS status regularly, particularly in the breeding herds,
- increasing the management and the herd-health status of herds at risk, both to decrease the spread of the virus and to decrease the clinical presentation of the syndrome, and
- controlling and eradicating the virus in low-prevalence areas and increasing the resistance to the virus via vaccination and/or reducing the infection pressure through managerial methods such as partial depopulation and multiple-site production.

Since many questions are still unanswered, research on PRRS should be continued. The participants of the symposium in Copenhagen appreciated the announcement from Dr. Philippe Vannier that he will organize a Third International Symposium on PRRS in Ploufragan, France.