PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS (PRRSV): THE DISEASE THAT KEEPS BUGGING US

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ABSTRACT

This is a brief overview of the current situation regarding PRRSV, with an emphasis on information that has appeared in the literature within the last 5 years. This period has been marked by 1) A growing recognition of the high cost of PRRS to swine producers; 2) Continued producer frustration with the (poor) control of PRRS; 3) Heightened interest in regional elimination of PRRSV, but reluctance to proceed without more reliable methods of achieving the objective; 4) Reports (and "counter reports") of newly emerging, highly virulent, PRRSV isolates; and 5) Innovation in the application of diagnostics to surveillance.

PRRSV CHANGES IN GLOBAL DISTRIBUTION

PRRSV was diagnosed in Africa for the first time in June 2004 following outbreaks in Western Cape Province, South Africa (OIE, 2005a). Steps were taken to eliminate the disease, i.e., quarantine, stamping out, premise disinfection. Serologic tests did not identify additional infected sites at that time, but new outbreaks were identified in October 2005 (OIE, 2005b) and again in August 2007 (Beltran-Alcrudo et al., 2007). A source of the virus has not been determined and remains a point of strong interest.

Chile is on the verge of becoming the first country to eradicate PRRSV. Begun in 2001, by Chilean swine producers organization (ASPROCER) in coordination with animal health government agencies, the national PRRSV eradication program is close to achieving its objective. According to the Chilean swine producers organization (ASPROCER), the last PRRSV-positive pigs were sent to the abattoir on April 2, 2007. Chilean producers are currently in the process of culling all sows that were present at the time of infection (Anon, 2007).

ECONOMICS

The cost of PRRS due to reproductive outbreaks was recognized early in the PRRSV pandemic, e.g., in 1990 Polson et al. (1990) estimated losses at $236 USD per sow during an acute outbreak of reproductive PRRS due to infertility, abortions, stillbirths, and neonatal mortality. More recently, there is a developing recognition of the cost of PRRSV infection in

growing pigs. Of the $560 million USD PRRS was estimated to cost U.S. pork producers (Neumann et al., 2005):

- $250 million USD (45%) was due to declines in average daily gain and feed efficiency in growing pigs;
- $243 million (43%) resulted from mortality in growing pigs;
- $63 million (12%) was attributed to reproductive losses.

Estimates in the study were based on feed costs of $0.286 USD per kg. Since the study was conducted, feed costs in much of the western hemisphere have increased by 50% to 65% as a result of market demand for corn by ethanol manufacturers (Funderburke et al., 2007). Higher feed costs further exacerbate the negative effect of PRRSV on productivity and heighten the urgency to find effective interventions.

TRADE ISSUES

The possible introduction of the virus into PRRSV-free countries via the import of pig meat became a trade issue early in the pandemic. Bloemraad et al. (1994) first reported that virus was present in muscle tissue collected from viremic pigs, albeit at low virus titers, and that the virus was only slightly affected by storage for up to 48 hour at 4ºC (39ºF). Under experimental conditions, van der Linded et al. (2003) reported that PRRSV "could be infectious through the oral route via the feeding of meat obtained from recently infected pigs." In the field, Margar and Larochelle (2004) reported low levels of PRRSV in a small percentage of pig meat collected at an abattoir. When fed raw PRRSV-contaminated pig meat under experimental conditions, some pigs became infected. Several risk analyses were conducted to evaluate the probability of introducing PRRSV through the import of pig meat from PRRSV-infected countries (Banks et al., 2004; EFSA, 2005; Pharo, 2006). Ultimately, the conclusions of such analyses balance on the judgement that extremely rare events may (or may not) occur; events for which probability estimates are often unavailable.

PREVENTION

The objective of prevention programs is either to stop the introduction of PRRSV into negative herds or the introduction of new strains into PRRSV-infected herds (Dee et al. 2001). Animals and semen are the primary sources of PRRSV, but other sources of infection may also be important (Desrosiers 2004). Torremorell et al. (2004) reported that over 80% of new infections in commercial systems in the US were not due to pigs or semen, but to area spread from neighboring units, the movement of pigs in PRRSV infected transports, the lack of compliance of the biosecurity protocols, or perhaps introduction via arthropods.

Recent advances in the area of prevention primarily involve refinements in the area of biosecurity related to the transmission of virus. Otake et al. (2002a) showed that PRRSV was present on workers' coveralls, boots, and hands following 60 minutes of contact with acutely infected pigs. Thereafter, Dee et al. (2004a) demonstrated that elementary sanitation

procedures, e.g., changing coveralls, changing boots, and washing hands, were sufficient to inactivate virus and stop transmission. Likewise, Dee and co-workers have described, tested, and compared protocols involving cleaning, washing, disinfection, and drying that were effective at inactivating PRRSV on transport vehicles [Dee et al. (2004b,c; 2005a,b; 2007) and Dee and Deen (2006a,b)]. In addition, this research group has evaluated air filtration systems intended to reduce the likelihood of aerosol transmission (Dee et al., 2005c). Despite advances in this area, introduction of virus into "biosecure" herds is a problem, particularly in swine-dense areas. Acquiring the knowledge and techniques to reliably protect herds from the inadvertent introduction of PRRSV is vital to future progress.

CONTROL

PRRS control is intended to limit the clinical effects of the infection at various stages of production. As a general rule, control efforts begin by increasing breeding herd immunity, then work progressively toward control in growing pigs through partial depopulation, all-in/all-out pig flow, vaccination, intentional exposure to field virus, or a combination of approaches (Dee, 2003; McCaw, 2003; FitzSimmons and Daniels, 2003; Gillespie, 2003; Thacker et al., 2003). Current methods of PRRSV control were developed early in the course of the pandemic and have been extensively reviewed in the literature (Zimmerman and Yoon, 2003; Zimmerman et al., 2006). New approaches, methods, or protocols have not been described recently.

The major research investment in this area has been on vaccine research and development. Although some producers and veterinarians have reported good results with currently available PRRSV vaccine, it is doubtful that PRRSV control and eventual elimination could be achieved without broadly protective vaccines that reduce shedding and transmission.

EPIDEMIOLOGY AND ECOLOGY

Incremental improvements in understanding PRRSV epidemiology and ecology have been made in recent years, particularly related to transmission.

Pigs are susceptible to PRRSV by several routes of exposure, but the probability of infection by dose differs by route of exposure. Hermann et al. (2005) estimated the infectious $dose_{50}$ (ID_{50}), i.e., the dose required to infect one-half of the exposed animals, for oral and intranasal routes of exposure at $10^{5.3}$ $TCID_{50}$ and $10^{4.0}$ $TCID_{50}$, respectively. Based on data from Benfield et al. (2000), the ID_{50} for exposure via artificial insemination was estimated at $\sim 10^{4.5}$ $TCID_{50}$.

Thus, pigs are extremely susceptible to infection via parenteral exposure and much less susceptible by other routes investigated to date. In the field, potential parenteral exposures include standard husbandry practices, i.e., ear notching, tail docking, teeth clipping, tattooing, and inoculations with medications and biologics. Likewise, because PRRSV is present in oral fluids for several weeks following infection (Prickett et al., 2008a, 2008b), normal pig

behavior commonly results in parenteral exposures, i.e., bites, cuts, scrapes, and/or abrasions that occur during aggressive interactions among pigs (Kritas and Morrison, 2004).

Indirect transmission involves transmission by inanimate objects (e.g., equipment, instruments, clothing) or substances (e.g., water, food), living carriers (vectors), or aerosols. Otake et al. (2002b) corroborated needle-borne transmission of PRRSV under experimental conditions. Dee et al. (2002, 2003) showed that PRRSV could be moved extensively in the field on fomites in the field under winter conditions, i.e., below 0°C, but to a much lesser degree during warm weather, i.e., 10-16°C, again illustrating the importance of temperature in virus survival.

Although a complete understanding of airborne transmission has not been achieved, progress has been made. Research in this area is challenging, in part because airborne transmission is not necessarily easily reproduced. For example, transmission from infected to susceptible pigs over a space of 1.0-2.5 meters has been successful in approximately 50% of the attempts (Lager and Mengeling, 2000; Otake et al., 2002c; Torremorell et al., 1997; Wills et al., 1997). In contrast, Kristensen et al. (2004) reported airborne transmission in three trials over a distance of one meter from ~50 acutely infected pigs to ~50 susceptible pigs when 1%, 10%, or 70% of air was exchanged. In a field setting, airborne transmission did not occur over distances of 15 meters (Trincado et al., 2004) and 30 meters (Otake et al., 2002c).

A more complete understanding of the process of aerosol transmission is required if we are to understand the reasons for the observed differences in transmission. Work to date suggests some possibilities. For example, the conditions under which experiments are conducted may affect transmissibility. Herman et al. (2007) evaluated the effect of temperature and relative humidity (RH) on the half-life (T1/2) of aerosolized virus. PRRSV was most stable at low temperature and low relative humidity, e.g., T1/2 at 5°C and 10% RH was 215 minutes vs. 6 minutes at 40°C and 90% RH. Cho et al., (2006, 2007) suggested that PRRSV isolates may vary in their transmissibility via aerosols, but also acknowledged that the hypothesis requires additional testing.

This is a critical area of research because of its possible role in area spread of PRRSV. The potential for airborne transmission of PRRSV will not be fully understood until additional information is available, including better estimates of the quantity of virus excreted by pigs, the probability of infection by aerosol exposure dose, and the influence of virus strain on aerosol transmissibility.

PRRSV DIAGNOSTICS

Technical developments and improvements in diagnostics are on-going. Innovations include the use of alternate blood collection devices (Broes et al., 2007), blood sampling approaches that do not require venipuncture (Reicks et al., 2006), testing based on oral fluids rather than serum (Prickett et al., 2008a, 2008b), and pen-side rapid assays (Lyoo et al., 2005).

Specific comments must be made regarding PCR-based assays. First, several recent publications document that PCR-based assays provide less than the perfect diagnostic performance we expect. That is, both false positive and false negative results occur with PRRSV PCR-based assays and results may vary between laboratories (Fetzer et al., 2006; Truyen et al., 2006; Wagstrom et al., 2000). Similar observations are not unique to PCRs for PRRSV. Similar observations have been made regarding PCR-based assays for the detection of HIV (Lelie et al., 2002) hepatitis B (Valentine-Thon et al., 2001), and hepatitis C (Shirm et al., 2002).

Perfect tests are not required for the control of PRRSV, but accurate and realistic estimates of assay performance are vital to the interpretation of test results. PCR-based diagnostics will continue to improve, but a critical and independent evaluation of the diagnostic performance of PCR-based assays and on-going improvements in laboratory quality control should be part of the process.

A further PCR-related observation is that PCR-detectable PRRSV RNA appears to be more stable in the environment than had been expected. Under conditions in which infectious virus was inactivated, Hermann et al. (2007) reported that the concentration of virus measured by quantitative RT-PCR remained stable. The implication is that environmental monitoring using PCR-based assays may result in the detection of non-infectious virus and trigger responses not appropriate for non-infectious virus. Further research in this area is needed.

CONCLUSIONS

Despite recent gains in basic and applied science, reliable solutions for the control of clinical losses on farms and the spread of PRRSV between farms have continued to elude us (Kahler, 2004). To date, we have not identified an ecologic weakness in the virus that could be used to control it in our contemporary production systems. Faced with on-going PRRS losses, the general consensus in North America is that PRRSV eradication is the best solution (Burns, 2006). Whether an eradication program could succeed without an "Aujeszky-like vaccine" is a point of discussion, but if we are to proceed, the availability of excellent diagnostics becomes paramount. That is, in the absence of an "Aujeszky-like vaccine", aggressive monitoring based on rapid, affordable, accurate, on-site tests will be the primary tool for the prevention, control, and eradication of PRRSV.

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