We are delighted that the International Pig Veterinary Society Congress 2004, decided to select South Africa as the host country for the 20th IPVS Congress. The Pig Veterinarians of South Africa will ensure that this congress lives up to the best traditions of previous congresses; incorporating an interesting and topical scientific programme, fascinating accompanying persons tours and an excellent social programme, allowing delegates the opportunity to network with their overseas colleagues.

This, the first IPVS congress on the African continent, will undoubtedly be of enormous benefit in generating solutions to the emerging pig veterinary challenges, especially those related to exotic and changing viral diseases, decreased use of antimicrobials and nutritional advances. The congress is important to further pig veterinary science in South Africa, to encourage younger veterinarians to join the pig industry, as a vehicle to generate funds for research and to improve the pig industry in Southern Africa.

South Africa is a magnificent and beautiful country, and offers tourists value for money. Thus, pre and post congress tours will be a major attraction for delegates to come to South Africa. Durban, in KwaZulu Natal, is a vibrant multi-cultured city with magnificent beaches, easily accessible game parks, theme villages and a moderate winter climate making it an ideal tourist destination. We urge our colleagues throughout the world to use this opportunity to get a glimpse of the continent’s rich and fascinating wonders and to enjoy the hospitality of their African friends.

Dr Peter Evans
Chairman: Local Organising Committee: IPVS 2008
AN UPDATE ON PRRSV PREVENTION, CONTROL, AND DIAGNOSIS

Jeff Zimmerman

College of Veterinary Medicine, Iowa State University
Ames, Iowa USA

Introduction
The purpose of this review is to highlight recent information and developments in the area of PRRSV prevention, control, and diagnosis. In particular, the information presented here is based on publications (2003-2006) in the refereed literature. This piece is not intended to provide a complete overview of PRRSV - extensive monographs are available elsewhere (4, 5).

Fifteen years after PRRSV was identified (1, 2), swine producers continue to experience severe PRRS losses. This fact has energized organizations responsible for swine health to act in concert to find solutions. In North America, these organizations include the National Pork Board, the American Association of Swine Veterinarians (AASV), and the USDA North Central 229 (NC-229) Committee (Methods for the integrated control, prevention, and elimination of PRRS). The AASV, in a position statement in line with the overall philosophy adopted by these organizations, has unambiguously stated that “… eradication of the disease (i.e., PRRS) from the North American swine industry is the long term goal” (3).

For future reference, many of the activities of these organizations are reported at http://www.PRRS.org/. In addition, the NC-229 Committee organizes the annual PRRS International Symposium. The Symposium is an opportunity to hear the latest research findings and exchange ideas with researchers and veterinarians involved with PRRS. This year the Symposium will be held in Chicago 1-2 December 2006 in conjunction with the Conference of Research Workers in Animal Diseases (http://www.cvmbs.colostate.edu/microbiology/crwad/satellit.htm).

Economics of PRRS
As previously summarized (6), a number of studies have evaluated the cost of PRRS in breeding animals and/or growing pigs. In the largest study to date, Neumann et al. (2005) described the effect of PRRS in breeding and growing pig populations in Midwestern (U.S.) swine farms. Health and productivity parameters of PRRS-affected and PRRS-unaffected swine farms were analyzed to estimate the impact of PRRS on individual farms. Thereafter, national estimates of PRRS incidence were used to determine the annual economic impact of PRRS on the U.S. swine herd. Importantly, the analysis only targeted the costs of farm level production losses due to PRRS, i.e., direct losses due to the impact of the virus on pig health. The study did not include indirect costs, e.g. costs associated with preventing the introduction of PRRSV into herds, costs associated with monitoring endemically infected herds, or costs associated with subclinical PRRSV infection.

In the U.S. national herd, Neumann et al. (2005) estimated that direct losses resulting from the effect of PRRSV on reproductive health, mortality, and rate and efficiency of growth resulted in $66.75 million in losses in breeding herds and $493.57 million in growing pig populations. By comparison, adjusted to Year 2004 dollars, annual losses in the U.S. due to classical swine fever (CSF) and Aujeszky’s disease (AD) viruses were estimated at $364.09 million (8) and $36.27 million (9), respectively, prior to their eradication. Unlike the PRRS study (7), a significant proportion of the CSF and AD estimates was the result of indirect costs, e.g., vaccination, serological testing/monitoring, etc.

Thus, PRRS imposes an unacceptably high cost on pig producers. For that reason, many pig producers and swine veterinarians have concluded that elimination of PRRSV is the best response to the disease. At present, although elimination of the virus is achievable, re-introduction of the virus through animals, fomites, and/or unknown routes (area spread) is common in swine-dense areas.

PRRSV Diversity
Recent information regarding virus genetic and antigenic diversity is relevant to this discussion because of its implications for cross protection, vaccine efficacy, and diagnosis.

Two PRRSV genotypes are currently recognized - Type 1 (European) and Type 2 (North American). “Historically,” Type 2 isolates were considered more diverse than Type 1 isolates, but a series of recent publications have demonstrated greater diversity among Type 1 isolates than previously perceived. Pesch et al. (2005) in a study of 66 European viruses isolated between 1991 and 2002 reported evidence of on-going genetic drift, with recent isolates demonstrating increased genetic distance both to older isolates and among themselves. Similar conclusions were drawn by Mateu et al. (2006) in a recent study of Spanish PRRSV isolates. Expanding on this theme, Stadejek et al. (2006)
Recent studies have added to the body of knowledge on persistence. In particular, more recent studies tend to involve unquestionably the single most significant epidemiological feature of PRRSV infection. Perpetuating itself within herds and also plays an important role in moving virus between herds. Persistence is decreasing percentage of convalescent animals over time. Persistent infection is the key to the virus’ success in PRRSV persistence as a “smoldering” infection in which the virus is present at lower levels in a continuously through transmission experiments and by detection of virus in animals (4, 5). Allende et al. (2000) aptly described months post inoculation. As reviewed elsewhere, persistent PRRSV infection has been extensively documented PRRSV produces a chronic, persistent infection in pigs and infectious virus may be recovered from animal for several post inoculation. As reviewed elsewhere, persistent PRRSV infection has been extensively documented through transmission experiments and by detection of virus in animals (4, 5). Allende et al. (2000) aptly described PRRSV persistence as a “smoldering” infection in which the virus is present at lower levels in a continuously decreasing percentage of convalescing animals over time. Persistent infection is the key to the virus’ success in perpetuating itself within herds and also plays an important role in moving virus between herds. Persistence is unquestionably the single most significant epidemiological feature of PRRSV infection.

Recent studies have added to the body of knowledge on persistence. In particular, more recent studies tend to involve larger populations and follow animals for a longer period of time. For example, Batista et al. (2004b) studied persistent infection in 80 4-month old gilts inoculated with PRRSV isolate MN-30-100. Consistent with previous reports, tissue pools (tonsil, superficial inguinal and sternal lymph nodes) from 49 of 50 (98%) animals euthanized 30 - 100 days post inoculation (DPI) were PCR positive. Thereafter, 8 of 10 (80%), 3 of 10 (30%), and 2 of 10 (20%) were PCR positive at 110, 120, and 135 DPI, respectively. In an experiment based a similar experimental design, Molina et al. (2005) inoculated 109 2-week-old pigs with ATCC VR-2332, but expanded the monitoring period to 189 DPI. Between 147 – 189 DPI, approximately 10 – 30% of tissue samples (tonsil, superficial inguinal and submandibular lymph nodes) were PCR positive.

These studies continue to reinforce the perception of PRRSV as a highly persistent infection and expand the estimates of the period of persistence. However, significant questions remain. One of the key questions is, “What is that probability that a persistently infected animal will transmit virus to a susceptible herd mate?” It is not possible to answer this question at present because we have only a rudimentary understanding of the process of PRRSV transmission and the animal behaviors involved. Certainly, the probability of transmission is not fixed and, in a persistently infected animal, will decline over time until it eventually approaches zero. On the other hand, one of the functions of the population size and density of contemporary large production systems is to transform events with a negligible probability of occurrence into the commonplace.

Likewise, questions remain regarding the immune mechanism(s) by which the virus is ultimately eliminated from the pig. Thus, Batista et al. (2004b) concluded that neither neutralizing antibody nor INF-gamma, alone or together, was responsible for eliminating the virus. The absence of this information severely limits our ability to intentionally manipulate the immune system in order to facilitate the elimination of the virus – a limiting fact in vaccine development.

Transmission
Recent work in the area of transmission has become more quantitative and less descriptive in approach. Following the example originally set in work published by Nodelijk et al. (2000), the objective of work in this area is to understand the processes by which PRRSV maintains its cycle of infection.
Quantitative estimates of infection: Yoon et al. (1999) reported that exposure to 20 or fewer PRRSV particles by intramuscular exposure resulted in infection. Recent studies have shown that the probability that a given dose will result in infection differs significantly by route of exposure. Hermann et al. (2005) estimated the infectious dose $\text{ID}_{50}$ (ID$_{50}$), i.e., the dose required to infect one-half of the exposed animals, for oral and intranasal routes of exposure to be $10^{7.3} \text{TCID}_{50}$ and $10^{5.0} \text{TCID}_{50}$, respectively. Based on data from Benfield et al. (2000a), the ID$_{50}$ for exposure via artificial insemination was calculated at approximately $10^{4.5} \text{TCID}_{50}$.

Thus, the infectivity data indicate that pigs are extremely susceptible to infection via exposures involving breaks in the skin, and much less susceptible by all other routes investigated. In the field, potential exposures of this type include standard husbandry practices, i.e., ear notching, tail docking, teeth clipping, tattooing, and inoculations with medications and biologics. Otake et al. (2002a) documented needle-borne transmission of PRRSV under experimental conditions. Likewise, because PRRSV is present in oral fluids for weeks following infection, normal pig behavior commonly results in exposure and transmission, i.e., bites, cuts, scrapes, and/or abrasions that occur during aggressive interactions among pigs. Kritas et al. (2004) reported that 16.3% pigs in finishing barns showed evidence of having received tail bites. Bierk et al. (2001) specifically associated PRRSV transmission with aggressive behavior between carrier sows and susceptible contacts.

Spread between herds: Spread between herds is the biggest obstacle to future elimination/eradication efforts. In swine-dense areas, successful elimination of PRRSV from herds or systems is routinely followed by the reintroduction of virus. In most cases, the source of the virus is never determined because the introduction occurred well before its presence in the herd was recognized. Possible mechanisms of spread between herds include the movement of infected animals or contaminated fomites (equipment, semen, biologics), or spread via arthropods, aerosols, water, or non-porcine hosts. Torremorell et al. (2004) reported that over 80% of new infections in a large U.S. commercial system were due to area spread from neighboring units, the movement of pigs in PRRSV-infected transports, lack of compliance with biosecurity protocols, or the possible introduction via insects. Pesente et al. (2006) found that the primary means of PRRSV spread in farms was the introduction of infected animals. Identifying methods to stop PRRSV spread between herds is a key element in achieving successful eradication programs.

Aerosols: Airborne transmission of PRRSV has been postulated to play an important role in area spread, but airborne transmission of PRRSV has not been easy to demonstrate under controlled conditions. In two recent field studies (34, 35), exhausted air from buildings housing acutely infected pigs to sentinels failed to transmit PRRSV. Under experimental conditions, transmission from infected to susceptible pigs over a distance of 1.0-2.5 meters has been successful in approximately 50% of the attempts (36 – 40). In contrast to the pattern of poor airborne transmissibility generally observed, Kristensen et al. (2004) reported that, in three trials of approximately 50 acutely infected pigs each, PRRSV was transmitted over a distance of one meter to approximately 50 susceptible pigs when 1%, 10%, or 70% of air was exchanged.

A clear definition of the role of PRRSV airborne transmission awaits quantitative information, e.g., the quantity of virus excreted by pigs, the rate of inactivation of aerosolized virus, and the infectious dose for pigs by aerosol exposure. Some of this information will be available in the near future, e.g., stability (half-life) estimates of infectious PRRSV in aerosols (42) and the dose-response for aerosol exposure (Joseph Hermann, personal communication) are forthcoming.

Arthropods: Preliminary reports suggested a possible role for arthropods in PRRSV transmission. For example, PRRSV was detected in, or on, wild-caught flies and mosquitoes (43, 44) and, under experimental conditions, mechanical transmission of PRRSV was demonstrated by mosquitoes and house flies (Musca domestica) (45 - 47). However, it is important to recognize that it is not unique to isolate non-arthropod borne infectious agents from wild-caught arthropods. For example, Stewart et al. (1975) confirmed the presence of infectious classical swine fever (CSF) virus in wild-trapped mosquitoes by bioassay and demonstrated mechanical transmission of CSF virus by Aedes aegypti under experimental conditions. Even so, CSF virus is not generally considered an arthropod-borne disease. At this juncture, additional data, particularly experiments evaluating vector competency, are needed in order to arrive at a cohesive understanding of the role of arthropods in the transmission of PRRSV.

Prevention

The objective of PRRSV prevention programs is to stop the introduction of PRRSV into negative herds or to stop the introduction of new strains into PRRSV-infected herds. Effective prevention programs are based on an understanding of the routes of PRRSV transmission and the methods (biosecurity) that will most effectively achieve the objective. By necessity, biosecurity protocols must be designed and implemented for everything entering or leaving the farm, e.g., pigs, semen, feed, water, personnel, supplies and materials, vehicles and transport, etc. Extensive descriptions and discussions of recommended protocols are available elsewhere (1, 2).
A series of recent publications have evaluated and validated methods for disinfecting transport vehicles (49-53). The investigators found that cleaning, power washing, and drying (≥8 hours) was highly effective in inactivating infectious PRRSV (49, 50, 51). Disinfectants or heat (51) were shown to be useful in reducing the time necessary to disinfect vehicles, but disinfectants were not equally effective against the virus (52, 53). PRRSV is highly stable at temperatures below freezing, but even under such conditions Dee et al., (2005b) found that an efficacious disinfectant used in combination with 40% methanol or 10% propylene glycol was highly effective. Thus, PRRSV was inactivated by drying and/or disinfectants, but the disinfectant should be selected based on its demonstrated efficacy against PRRSV. Although tested for transport vehicles, these observations should be equally for other applications in the field.

Building on the work of Amass et al. (2000) that showed contamination of personnel by contact with PRRSV-infected pigs, Dee et al. (2004c) tested the efficacy of four treatments to prevent the introduction of PRRSV into farms on personnel and fomites. Standard methods, i.e., the use of disposable plastic boots, the use of boot baths to disinfect PRRSV-contaminated plastic boots, and the “bag-in-a-box” system were shown to be effective.

Overall, recent work has reinforced the perception that PRRSV is relatively labile in the environment and that standard cleaning and disinfecting protocols should be effective in the control of the environmental contamination of PRRSV. Of course, this perception clashes with our inability to effectively control spread between herds.

**Diagnostics**

In a general sense, it is valid to state that adequate diagnostics for PRRSV are generally available. That is, both PCR-based assays for detecting virus and antibody screening tests are accessible to producers and veterinary practitioners in most parts of the world. PCR-based assays were adapted to the detection of PRRSV not long after the initial discovery of the virus - 3 refereed publications described diagnostic applications of PCR to PRRSV in 1994 (56, 57, 58). Initially assumed to provide perfect test performance, perhaps the earliest indication of potential performance problems with PCR-based assays was a report by Wagstrom et al. (2000). Based on results of randomly ordered serum samples from 102 experimentally infected animals, the diagnostic sensitivity of an RT-nPCR assay was 26% and diagnostic specificity was 96%. Upon re-test, diagnostic sensitivity improved to 69% and diagnostic specificity to 99%. Recent publications suggest that PCR performance will require on-going attention. Tryuen et al. (2006), in a “check test” of 16 laboratories performing PCR-based assays for PRRSV, found accuracy to be highly variable among laboratories, with the majority of errors being false negative results. On the other hand, Fetzer et al. (2006) have reported problems with false positive results. Research on PCR-based assays continues to be an active area of research (62-67) and continued evolution should be anticipated.

Thus, although antibody screening and PCR-based assays are generally available, it is also probably true that current assays are not adequate to the task of regional or national PRRSV elimination/eradication because of: (1) lack of performance standardization among laboratories running PCR-based assays; (2) lack of a rapid confirmatory assays for samples with suspected false positive results on antibody screening assays; and (3) lack of a rapid on-site (pig-side) screening assay.

**Eradication**

Eradication protocols have been developed for eliminating PRRSV from infected farms, including total depopulation/repopulation, partial depopulation, segregated early weaning, test-and-removal, and herd closure (1, 2). Methods described in the recent literature include both the use of modified-live vaccine (Gillespie and Carroll 2003) and intentional exposure to field virus (Fano et al. 2005).

A growing consensus in North America is that elimination/eradication is the best (and perhaps only) solution for PRRS. This would follow the example of Chile, a country that has nearly eradicated PRRSV from within its borders (Ruiz et al. 2003). In North America, however, elimination of virus from herds in pig-dense areas is typically followed some time later by re-infection. For that reason, there is a growing consensus that elimination/eradication must be implemented on a regional basis.

One of the questions currently under debate is whether such an effort could be successful in the absence of vaccine(s) capable of significantly reducing the rate of transmission (71). The difficulty of achieving consistent control using current vaccines reflects to our incomplete understanding of PRRS immunology. That is, our knowledge is largely incomplete concerning the events initiating immunity, key immunologic targets for antibody and cytotoxic T cell-directed protection, molecular and cellular mechanisms regulating the immune response, the consequences of PRRSV genetic diversity, and the effect of host genetic variation on immune resistance to PRRSV (4).

Although vaccine research has received the majority of the capital investment in PRRSV research, the prospect for a “PRV-like vaccine,” i.e., highly efficacious, capable of stopping transmission, and differentiable, seems remote. The example from the human medical community is that even large investments in resources may not produce the
be wise to continue to develop and evaluate all possible solutions, including but not limited to vaccines.

References


