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Pseudorabies and the Move Toward Eradication

Scott L. Hinders*
Mark Schoenbaum D.V.M.**

Introduction

Pseudorabies (PR) is receiving more attention today than ever before. Why is this? Historically, PR can be traced back to the mid 1800’s in the United States. Although sporadic outbreaks were reported prior to 1975, it was not until the late 70’s and 80’s that the importance of PR was appreciated. This can possibly be explained by an increasing incidence of clinical disease outbreaks, and economic losses associated with those outbreaks. Three reasons have been suggested for the increase in recent outbreaks:

1. there has been a change in swine management towards intensification of production and confinement
2. there has been a successful eradication of Hog Cholera, and since it and PR can have similar clinical signs, more PR is being recognized
3. there has been an increase in awareness of PR as a disease entity

Transmission

Several epidemiologic factors are important in understanding any discussion of PR and its possible eradication. Pseudorabies virus (PVR) belongs to the Family Herpesviridae and has a fairly wide range of host susceptibilities.

Transfer of virus from animal to animal occurs most importantly through nose to nose contact. Aerosolization and oronasal contact provide a mode for infection where inhalation occurs. The primary site of replication is the tonsillar and pharyngeal area with dissemination from there. Fomites, contaminated feed, water, and bedding can play a role in harboring and transmitting the virus.

The environmental survivability of PRV is another important factor to consider when considering transmission. Papers published at Iowa State University illustrate conditions in which the virus can survive:

1. PRV is very labile at pH levels below 4 and above 9.
2. Long term PRV survival is temperature dependent.
   - up to 40 days at 37°C
   - up to 120 days at 4°C
3. PRV cannot survive beyond a few hours on clean concrete.
4. PRV can survive in
   - soil for up to 6 days
   - lagoon water for up to 2 days
   - manure for up to 2 days
5. Carcasses, infected placenta, and dead wild life may be potential sources of the virus.

A wide range of hosts are susceptible to PRV, but swine are the natural host and reservoir. PR is usually fatal in all other susceptible species. Cattle, sheep, goats, dogs, cats, and several feral animals such as mice, raccoons, and rats are examples of hosts susceptible to PR. Horses are reported to be susceptible experimentally, but are only rarely infected by natural means. There are mixed reports dealing with semen and preputial secretions as potential routes of pig to pig transmission. Larson reported that no virus was detected from preputial swabs of experimentally infected boars and considered it unlikely that virus will be found in preputial secretions or semen since neither urine nor genital tissue commonly harbor virus. Hsu et al did isolate the virus from preputial secretions of experimentally infected boars but not from the semen.

Bolin et al provided experimental evidence that embryos may be a potential source of infection for...
seronegative females if either the donor has been recently infected early in pregnancy or at ovulation, or if the embryos are contaminated with PRV in vitro. Neutralizing antibodies were detected in the recipient(s) 21 to 35 days after transfer. Reduced litter size or reproductive failure may also result.

Clinical Disease

The clinical picture produced by PR depends on several factors. An infection may vary from subclinical to clinical to possible death. Variation in severity of disease is primarily due to factors such as different virulence levels of the viral strains, the dose of viral exposure, the age of the pig exposed and infected, and the immunity level present. PR usually affects younger pigs more severely than older pigs. Suckling pigs may show dyspnea, fever, vomiting, diarrhea, and anorexia as well as CNS signs such as depression, trembling, ataxia, nystagmus, convulsions, and coma. Any combination may occur and death is often the result in animals showing CNS symptoms.

Nursery and growing pigs can show similar signs depending on their susceptibility as well as the virulence and dose of the virus. Sneezing, coughing, and anorexia with weakness or incoordination may be all that is seen. Secondary bacterial pneumonia and pleuritis may occur.

In pregnant gilts and sows the clinical picture changes altogether. The reproductive tract is the primary system affected. Table 1 shows a brief overview of how the reproductive system is affected.

Table 1 - Reproductive Effects on Female Swine Due to PRV

<table>
<thead>
<tr>
<th>Infection</th>
<th>Possible causes of early embryonic death and reproductive failure.</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days-termination of pregnancy and embryonic resorption; repeat breeders</td>
<td>(1) Uterine inflammation is detrimental to implantation of the embryo.</td>
</tr>
<tr>
<td>day 40-partial or complete fetal death</td>
<td>(2) Luteal necrosis occurs and pregnancy terminates.</td>
</tr>
<tr>
<td>day 60-abortion in this time period is possible</td>
<td>(3) Infection of pre-implanted embryo and death.</td>
</tr>
<tr>
<td>late in gestation-macerated or mummified fetuses; stillborn or weak pigs born</td>
<td></td>
</tr>
</tbody>
</table>

Pathogenesis

Possible causes of early embryonic death and reproductive failure.

(1) Uterine inflammation is detrimental to implantation of the embryo.

(2) Luteal necrosis occurs and pregnancy terminates.

(3) Infection of pre-implanted embryo and death.

The most important sequela resulting from infection during gestation is impaired fertility. As many as 20% of sows in a recently recovered herd may not conceive at the next breeding. Delayed farrowing is also possible with sows' gestation periods being prolonged up to 17 days beyond the expected farrowing dates.

Infected boars typically will become febrile and may be reluctant breeders during the disease episode. They can also become weak, depressed, anorectic, and have some respiratory distress. Testicular effects may or may not be apparent. Some reports show that there is a mild degeneration of the seminiferous tubules(thinner walled). Mixed observations on semen quality have been reported. There may be no change in semen volume, sperm morphology, and concentration; or an increase in abnormal morphology such as proximal cytoplasmic droplets. The presence of more severe systemic disease and fever may account for the variation seen by different researchers.

Eradication-Background

PR has been on the increase worldwide in the 70's and 80's both in clinical and subclinical forms. The economic impact of the infection is due to factors such as loss in potential rates of gain and feed efficiency, death loss, vaccine expenditure, and reproductive failure. Restrictive sales, movement of swine, and additional disease control measures need to be considered.

Several conclusions have been drawn by regulatory officials and swine industry personnel concerning PR and its potential for eradication. Thawley summarized these conclusions as follows:

1. PR poses an increasing threat to efficient swine production in the U.S.

2. Complete control cannot be achieved by means of vaccines and restriction of livestock movement.

3. PR has a high potential for areawide eradication.

4. Potential future costs due to PR could far outweigh the cost of eradication.

In view of the above considerations, several areas of PR epidemiology and control needed to be carefully thought out, explored, and researched before possible PR eradication on an areawide basis could become a practical and effective reality. Two areas were cited as needing consideration: the latency of PRV, and the diagnostic ability to detect PRV antibodies.
Viral persistence (latency) is a characteristic of the herpesviruses and PRV is no exception. The ability to detect persistent infection in swine herds is an important consideration in a PR eradication program. Persistence of PRV in clinically normal pigs has been reported and shown that up to 85% of seropositive pigs, when stressed artificially with dexamethasone, will shed the virus intermittently in nasopharyngeal fluid. Papers as early as 1961 showed that farrowing sows could transmit PRV to their baby pigs, and that convalescent growing pigs could transmit PRV to healthy penmates. Lately, Beran et al. provided evidence that PRV could be detected from recovered pigs from 6 weeks to 13 months later utilizing tissue co-culture techniques. Persistent virus was most commonly found in the trigeminal ganglia and tonsils. In this study, virus was never detected in kidney, urine, spleen, rectum, or jejunum. Because of the potential shedding it is recommended that previously infected and recovered animals not be commingled with clean uninfected pigs.

It is important to consider the diagnostic tests available when looking at a potential eradication plan because accurate detection of infected herds and pigs is needed. Several immuno-diffusion assays have been developed and include the micro-immunodiffusion test (MIDT), the radial immunodiffusion enzyme assay (RIDEA), and others. These tests are reported to have good specificity, although their sensitivity may not be as high as other tests.

The serum virus neutralization test (SN) currently is the standard test for PRV antibodies. It has excellent specificity and sensitivity. A minimum of three days is necessary to get results because of the use of tissue cultures.

The enzyme-linked immunosorbent assay (ELISA) technique has been receiving more attention lately for use in detecting PRV antibodies. The ELISA technique is just as specific and more sensitive than the SN test. Advantages it may have over the SN test include a time factor (can be completed in a matter of hours), a standardized antigen can be prepared, and a lower quality serum can be used.

Vaccination

Vaccination of swine with either a modified live virus (MLV) or inactivated vaccine cannot prevent infection or reinfection, nor can it prevent latency or recrudescence. Vaccination may prevent clinical disease, thus decreasing economic losses. After pre-exposure vaccination, pigs may be sick a shorter length of time, and it has been shown that there is a decreased period of shedding. Prompt vaccination of nonimmune pigs upon clinical signs of PR will significantly decrease losses.

Eradication-Introduction

In early 1983 the National Pork Producers Council (NPPC), in association with the combination of the United States Department of Agriculture (USDA) and the Animal Plant Health Inspection Services (APHIS) laid the foundations for the development of the PR Pilot Projects to assess several questions concerning the eradicability of PR. Several guidelines were established as goals of these projects and are outlined in Table 2.

Table 2-Guidelines for PR Pilot Projects

Questions the Pilot Projects were to answer by design:

(1) Designed to determine the practicality of eradicating the disease from an area
(2) Designed to provide a definite answer to the question whether the disease can be eradicated from an area
(3) The government and producers must be prepared to accept the results and modify their approach accordingly
(4) That there be a scientific or technical committee assembled to decide the technical questions in the design of the project plans

In 1983 pilot projects were developed in Iowa and Illinois, and by late 1983 and 1984, federally funded projects also were initiated in Wisconsin, Pennsylvania, and North Carolina. The last three state’s projects became part of current state eradication programs.

Approved routes of herd cleanup include:
(1) test and removal, (2) offspring segregation, and (3) depopulation and repopulation as determined by the Livestock Conservation Institute (LCI). Each state set up its own objectives and project guidelines—see Tables 3 and 4 as an adapted version from Beran.

Other subobjectives considered for pilot projects included such things as determining PR spread from herd to herd and its control, evaluating different surveillance techniques, and control/cleanup strategies.

For the pilot projects, the first step needed was...
to locate infected herds. Testing from farm to farm was performed in Iowa and Illinois. The revised random sampling test schedule for Iowa was as follows:

- Herds < 100 adult breeding animals - test 25
- 100-200 adult breeding animals - test 27
- > 200 adult breeding animals - test 28

Once infection was diagnosed on a farm, a herd plan had to be developed to eliminate PR.

### Table 3 - State by State Pilot Projects 1983-1984

<table>
<thead>
<tr>
<th>State</th>
<th>Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iowa</td>
<td>Test feasibility of control and/or eradication of PR present in herds within an endemic area—Marshall County. Voluntary participation (99 + %)</td>
</tr>
<tr>
<td>Illinois</td>
<td>To eradicate PR from Pike and Macoupin Counties</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>State eradication</td>
</tr>
<tr>
<td>North Carolina</td>
<td>To control/eradicate PR from the state</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>To control/eradicate PR from the state</td>
</tr>
</tbody>
</table>

In the Iowa project, the majority of farms found infected choose the offspring segregation method of elimination. Killed vaccine was used in the Iowa project. Some overall conclusions cited by Spencer²⁶,²⁷ were that more infected herds were identified than anticipated both in Iowa and Illinois. The majority of the positive herds had no clinical signs of PR. Single SN titers in otherwise negative herds will occur and must be evaluated. The initial projects show that test and removal, and offspring segregation can be used successfully in eliminating PR from herds with no down time for producers. Any plan developed needs to consider economics along with the individual herd situation.

### Table 4 - Conditions of Project Plans

<table>
<thead>
<tr>
<th>area</th>
<th>Iowa</th>
<th>Illinois</th>
<th>N. Carolina</th>
<th>Wisconsin</th>
<th>Penn.</th>
</tr>
</thead>
<tbody>
<tr>
<td>enrollment</td>
<td>Marshall</td>
<td>Pike and Macoupin</td>
<td>statewide</td>
<td>statewide</td>
<td>statewide</td>
</tr>
<tr>
<td>disease detection</td>
<td>herd sampling</td>
<td>herd sampling</td>
<td>mandatory</td>
<td>mandatory</td>
<td>mandatory</td>
</tr>
<tr>
<td>vaccine</td>
<td>yes</td>
<td>yes</td>
<td>yes by permit only</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>vaccination</td>
<td>yes encouraged in infected and high risk herds</td>
<td>yes by permit only</td>
<td>yes</td>
<td>yes permit only</td>
<td>yes permit only</td>
</tr>
<tr>
<td>quarantine</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>slaughter</td>
<td>at approved plans</td>
<td>most by depopulation</td>
<td>most by test and removal</td>
<td>clean up required by 2 years</td>
<td>clean up required by 6 mo.</td>
</tr>
</tbody>
</table>

### Eradication-Plans Used Toward The Goal

The pamphlet entitled *Swine Pseudorabies Eradication Guidelines (2nd Ed.), Plans for Elimination of PRV From a Swine Herd* is an excellent source of information and should be referred to by anyone involved in eradication of PR from a herd. This handout discusses the accepted plans of PR eradication from a herd, providing broad outlines and specific recommendations. One must remember and consider every herd as unique. Different plans or combinations of plans are used in order to successfully eliminate disease from the herd. An individualized plan is needed for each herd.

Considerations for each farm in developing a plan should include:

1. The type of management—the housing, breeding herd size, vehicle traffic, herd addition practices, dead animal disposal, and proximity of PR in the neighborhood.

2. Role of fomites and viral latency.

3. Viral survivability depends on what conditions are present. See Table 5 for additional virus survivability information.

4. Serological tests like the SN and Elisa, even as accurate and valid as they are, can provide false positives and negatives. Also remember that an infection can be ongoing in the early stages (incubation period) and not have a seroresponse present yet (prior to 10-14 days).

5. Frequent sampling of a representative sample in a herd may be more valuable than 100% testing at infrequent intervals.

6. Strict isolation is necessary for offspring segregating procedures.

7. Vaccination does not prevent viral infection or spread within a herd, nor latency, but does reduce or eliminate clinical signs.
### Table 5-Conditions under which PRY Can Survive (LCI)

<table>
<thead>
<tr>
<th>Survival Length</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>140 days</td>
<td>@ 39°F with ideal conditions (ie. damp bedding)</td>
</tr>
<tr>
<td>30 days</td>
<td>@ 65°F</td>
</tr>
<tr>
<td>10 days</td>
<td>@ 75°F</td>
</tr>
<tr>
<td>24 hours</td>
<td>@ 99°F</td>
</tr>
<tr>
<td>up to 7 weeks</td>
<td>on wood boards</td>
</tr>
<tr>
<td>6 months</td>
<td>@ refrigerator temperatures</td>
</tr>
<tr>
<td>very short</td>
<td>on clean concrete, green plants, or well cured hay, direct sunlight, and dry conditions quickly inactivate the virus.</td>
</tr>
</tbody>
</table>

Before a plan is decided on, the following factors should be evaluated: the prevalence of PR infection in the herd, management ability of the personnel, value of genetics, area PR status, disease profile of herd (other diseases present?), and especially financial considerations.

Table 6 shows where and under what conditions the various plans for eradication might be applied. The information presented is revised from the LCI guide for PRV eradication previously mentioned.

### Table 6-LCI Suggested Eradication Plans

- **Plan Test and Removal**
  - Conditions
  - (C) Phased Test and Removal with Vaccination
    - (i) used where there is an increased risk of failure to clear PRV
    - (ii) there is a minimal interruption of pig flow and a reduced cost to the procedure
    - (iii) test all sows and boars, vaccinate with killed vaccine to boost immunity and decrease possible shedding until all of the original positive sows are removed from the herd at their next weaning and replaced with unvaccinated gilts
    - (iv) remove all positive boars immediately
    - (v) 4 months after vaccination, retest sows and immediately remove positives remaining; retest herd in 30 days as in A

#### Offspring Segregation
- Effective because of colostral protection received from an immune sow. Antibodies usually not detectable after 12 weeks but may persist up to 16 weeks of age in some pigs.
- **(A) Immediate Offspring Segregation**
  - (i) wean selected gilts at 3-4 weeks of age and move them to new clean facilities
  - (ii) isolate new pens to prevent nose to nose contact among pigs and between pigs and wildlife
  - (iii) use separate equipment and vehicles for each herd
  - (iv) test isolated gilts at 16 weeks of age; if some are seropositive, remove them and retest remaining gilts in another 30 days—if positive at the second testing, whole pen(s) should be considered as positive and removed from the segregated herd.
  - (v) depopulate original herd and clean up as described in next plan
  - (vi) retest new gilt herd prior to entry into original facility

- **(B) Delayed Offspring Segregation**
  - (i) pigs are weaned and kept on original premises but separated from sow contact
  - (ii) test replacement gilts @ 12 weeks and move negatives to a separate, segregated growing facility at this time
  - (iii) retest remaining gilts @ 14 and 16 weeks and move negatives in with (ii)
  - (iv) market/depopulate positive gilts with the rest of the herd
  - (v) retest gilts 30 days after last addition to the segregated herd
  - (vi) depopulate and clean as described in the next plan
Depopulation/Repopulation

Plan that is most likely to succeed, especially with a high level of infection, or an actively progressing disease with an increasing rate of infection, and where separation of livestock is difficult to maintain.

(i) warm, dry months are the best time as these conditions inactivate the virus quickly
(ii) plan requires a lot of planning to market pigs, blood testing, finding a repopulation source, cleaning and disinfection
(iii) most economical route is to sell pigs off over a period of months as they reach market weight, or to sell feeders to quarantined facilities
(iv) cleanup-
   a) thoroughly clean all manure and debris from pens, lots, and equipment and then disinfect
   b) repeat (a) after one week
   c) allow facilities to remain empty for a minimum of 30 days
   d) dirt lots need to be scraped to clean soil, tilled to expose soil to sunlight, and left idle for 30 days
   e) pump pits, and clean and disinfect as part of cleanup; do so a second time once buildings are totally cleaned up
   f) with a lagoon waste handling system, do not use a recycling flush system during a PR outbreak or the cleanup period (virus is inactivated in lagoons by the first 2-3 days)
   g) if building has plastic ventilation bags, clean or replace them
   (v) if phased depopulation is used, clean and disinfect areas as animals leave and repeat this for the whole building once it is emptied.

Disinfectants that are recommended for use in PRV cleanup areas are orthophenolphenate compounds, phenolic compounds, 2% Na hydroxide, Na3PO4, and chlorhexidine. Good rodent control is recommended when eliminating PR.

Eradication-European Efforts

European efforts to eradicate and control PR can provide an important lesson for the U.S. in its own efforts to eradicate. The program in Great Britain met with great resistance early in 1980 when not enough producer support was found for an eradication scheme. In 1982 however, with a sharp increase in the number of identified newly infected herds, the final decision was to move toward eradication through an indemnity funded slaughter with compensation program. Support from over 75% of the producers led to the effort which began in March of 1983. Initially in Great Britain, it was felt that vaccination was too expensive an approach toward eradication, and that it was inadequate in controlling the spread of infection. Also, there was the problem associated with future interpretation of serology.

All herds with confirmed disease or evidence of infection were slaughtered. Compensation for pigs marketed, and to owners for the cost of disruption while their units sat empty has been provided. Veterinary and associated costs are paid by government funds.

The first herds tested were those with a prior history of confirmed disease, next a move toward finding infected herds without a prior diagnosis of PR, and finally to survey pigs at slaughter. General comments can be made in regard to their program. They found a higher incidence of positive herds than anticipated (as did pilot projects in U.S.). Two views are held by producers depending on prevalence of disease in their area:

(1) few complaints about eradication in low prevalence areas
(2) general opposition to eradication in areas of high prevalence

In Ireland, PR Control is through a vaccination program. Their view on control is to eliminate the disease, although the virus will still be present. They claim that the decline in clinical outbreaks being seen is due to the vaccination program. Vaccination of negative sow herds is suggested under the following conditions:

(1) negative herd in a high density pig population area
(2) breeding and feeder production units where security risks existed in association with movement of feeder pigs to a positive finishing unit
(3) those conscious of serious financial losses if outbreaks should occur

One must realize that a depopulation/repopulation policy is not the only way or necessarily the right way to begin an eradication program, as Britain is doing. It is more applicable in a situation where there is low disease prevalence and funds are available for compensation. It would be necessary at the end of an eradication program when incidence is low.

Eradication-United States Efforts

In the U.S., preliminary data presented at the 1985 Proceedings of the U.S. Animal Health Association meeting by Hallum showed some important trends and producer practices that will have to be considered in the move towards eradication. It is apparent now that PR tends to be more prev
lent in larger herds than in smaller herds, with the average size of infected herds being about 50% larger than that of uninfected herds. They tend to purchase higher numbers of breeding animals which increases their risk of acquiring the infection.

It is interesting to note that close to 70% of the producers questioned in the Marshall County project in Iowa never tested their purchased breeding stock at the time of purchase, while only 17% said they always did. Only 56% of these same producers said they always placed purchased animals into any kind of isolation and observation period at the time of purchase, while 20% said they never did. In terms of vaccination, most positive herds did vaccinate in an attempt to prevent clinical outbreaks, and 50% of the negative herds vaccinate as a precaution for fear of contracting PR.

It was also shown in Marshall County that those sample herds testing positive to PRV clearly had more clinical cases of TGE, Mycoplasma pneumonia, and Hemophilus pleuropneumonia. However, it was not known whether this difference was due to subclinical effects of PR, or associated with management practices.

Of the positive herds detected in Marshall County, only 41% claimed to have experienced a clinical PR outbreak at some time. Losses during these outbreaks were primarily deaths of suckling pigs and stillborn/mummies were a distant second. As stated before, the problems most commonly seen are respiratory disease and setbacks in gain. These are most important in terms of losses to the producer.

While North Carolina, Wisconsin, and Pennsylvania have already been working toward state eradication, Iowa has been going through the planning stages in proposing a state eradication plan. Illinois now requires sow PR testing annually for feeder pig producers, and Minnesota is considering such a plan at this moment.

Across the board backing by the swine industry, veterinarians state disease control and extension personnel is necessary if any attempt is to be successful in reaching this goal of eradication. The following components are necessary in any eradication plan considered: legislative and regulatory authority to be able to test all herds for evidence of infection and to regulate movement, requiring herd cleanup plans to be formulated and carried out, and determining amounts needed and sources of funds. In Iowa it is proposed that program funds shall support such items as blood collection and serological testing. A goal of two years from the time of diagnosed infection to complete cleanup and certification as negative is desired by one of the approved methods of control listed in Table 6. Of the presently licensed vaccines, the killed vaccines will be allowed for general use, with the MLV vaccines recommended only for use during clinical PR outbreaks. The extent of funds available is unknown, so that much of the cleanup cost may have to be borne by herd owners. The projected time table in Iowa is to expand the PR eradication program to all counties over a six year period with eight years as a target for statewide PR eradication.

**Conclusion**

PR is largely a subclinical disease under management conditions now used. It has the ability to produce latent infection, and shedding is possible even from immune pigs. Even vaccinated immune pigs are susceptible (although less so) to disease. Eradication has been proposed because it is believed that there is an economic benefit in doing so, that the knowledge and control methods available are effective, and that PR has a high potential for area-wide eradication.

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