

The quagmire of Enzootic Pneumonia: A view from the trenches

James F. Lowe, DVM, MS
Carthage Veterinary Service, Ltd
Department of Veterinary Clinical Medicine, University of Illinois

Enzootic pneumonia (EP) in swine is a significant cause of economic losses for the commercial swine industry. The primary agent in EP is *Mycoplasma hyopneumoniae* (*Mhp*), which is often accompanied by secondary infection such as *Pasteurella multocida*.¹ In addition, EP is a key component in the multifactorial Porcine Respiratory Disease Complex involving various combinations of bacterial and viral pathogens. *Mhp* colonizes the mucosal surfaces of the swine respiratory tract inducing a complex virulence process that includes attachment, cytotoxicity, and evasion and modulation of the host immune response¹. While improved diagnostic tests have been developed and new immunoprophylaxis tools have been devised, the fundamental challenge of an “external” pathogen still exists. All this has occurred while rearing systems have changed and shifted transmission patterns of *Mhp*. These changes created new challenges in the control of EP that have not been managed with optimum efficacy. These “advancements” in diagnostics, therapeutics and immunoprophylaxis for *Mhp* have done little to improve the control of EP. When these “advancements” are coupled with changes in rearing systems the march towards controlling EP has been stymied by promoting false hope and creating confusion around the root cause for EP in growing pigs.

Immunity to *Mhp* is dependent on the local (airway) immune response. Systemic measures of immune response, including circulating antibodies, correlate poorly with protection²⁻³. In addition, animals exposed to *Mhp* have circulating antibodies against *Mhp* for up to 200 days post exposure. Their systemic antibody status is not predictive of their infection status.⁴⁻⁵ These facts have led to challenges with developing sensitive and specific diagnostic tests that will allow us to accurately understand the transmission patterns of *Mhp* in swine herds and the factors that determine why EP outbreaks occur⁵⁻⁶. Even with new diagnostic tests there are many of the same challenges: the tests tend to be lab specific, an “external” pathogen exists in a place that is hard for the immune system to effectively attack, and the systemic immune response that we can measure is not related to protection. Worse has been practitioners’ confusion with the performance characteristics of new diagnostic tests. The relatively poor sensitivity and specificity of all of these tests has created a situation where it is difficult to understand what test results mean regarding the true *Mhp* status of the population. While there is more data than at any time in history on the “*Mhp* test status” of individuals and populations, there is less knowledge, through misclassification and extrapolation of facts regarding the true infection status of populations.

Somewhere along the line the focus changed from controlling the disease to eliminating the pathogen in many veterinarians’ minds⁷⁻⁸. This was expressed by the desire to have *Mhp* negative gilts and pigs⁹. It seemed that because the pathogen can be detected in samples, the assumption was made that elimination was possible and should be pursued with vigor. Much of this change in attitude happened as more data from new diagnostic tests were

available. Unfortunately, this data did not reliably predict the true infection status of pigs and populations. With this change in view, the quagmire was created, decisions were made about health strategies –sources, vaccines, preventative therapeutics – with information that was flawed. The base question is if this quagmire could have been avoided?

A veterinarian's job description in food supply medicine might be - *Promoting the well being of animals and making clients profitable over the long run by keeping clinical disease at bay.* With that "job description", multiple paths are possible to meet one's obligations. Often it is helpful to think about a series of key questions before one heads down a new path for fulfilling the job requirement. Those questions might include: Did I really think about what the client needs? Did I think about what is possible? Did I think about all the alternatives? Do I understand the probability of a "good" outcome, the magnitude and distribution of the potential outcomes and understand their impact on the financial success of the business? If one understands the answers to all these questions about EP control, then elimination of *Mhp* is not the obvious answer.

The basic nature of the veterinarian has also contributed to the confusion surrounding EP control. Veterinarians, when they see something that is not working, have a strong urge to think "I must need to do something new." This has been demonstrated by the numerous challenges with control of EP over last 10 years. There are many theories for these challenges including poor duration of immunity for vaccines, problems with vaccines, bad pig flow, other concurrent diseases and "changes" in *Mhp* that make it more virulent or not protected by current bacterins. The reasons are cloudy at best as to why there has been an increase in EP in some systems. The complete lack of well controlled data that accounts for all the influences that happen in the "real world" is the primary reason for this lack of clarity. All of this has confused and frustrated producers leading them to "want to do something." Vets are natural "doers", so the first response is to meet the client's expressed desire and "do something" right away. Often vets are better at "doing" than objectively measuring. They tend to "solve" the clients problem but are not always good at the follow up necessary to understand what happened and why. This leads to misinterpretation of what happened or why it failed. The best example of this is that the peer reviewed literature is devoid of case studies or large field studies to describe why control plans were successful or failed.

Compounding these challenges is the ancillary nature of veterinary services to the production process making it difficult to have the hard conversation to check and see if the program that is in place is being done correctly. This leads to changes being made without understanding what is happening in the system. Because of the chronic nature of EP and the delay between changes and outcomes it is hard for vets and producers to match the timing of expected results and interventions. This is compounded by placing WAY too much faith in "the bottle." There are expectations that an intervention (vaccine, anti-infective) can be made and that alone is enough to solve the problem. Unfortunately, this is almost never the case as vaccines and anti-infectives are great tools but are not the foundation that solid disease control is built upon. It can be likened to trying to build a house with boards that are the wrong length and thinking that a bigger hammer will make it right. All this leads to the use of the three most dangerous words in medicine: "In my experience." The

use of “experiential” medicine instead of science based approaches leads to frustration and failure of programs.

Looking at the challenges from the front lines, the barriers to successful control of EP are numerous and large missteps in control programs have created doubt in producers minds. First, while enzootic pneumonia is economically important, outbreaks of *Mhp* in negative herds are economically devastating. These outbreaks often happen when eradication plans did not account for exposure to new infections or the implications of new infections on these naïve animals in high risk endemic herds or areas. This has resulted in outbreaks of acute pneumonic mycoplasmosis that could have been prevented. Secondly, “vaccine failures” have resulted from over confidence in the powers of immunity. The killed bacterins available today work to control the economic losses from EP provided the pigs being immunized are not sick with some virus when it is given¹⁰⁻¹¹. There has been much discussion about timing and the interference of maternally derived immunity on bacterin efficacy. While the data is conflicting, the preponderance of the evidence suggests that protection is obtained regardless of the maternal immunity status and vaccine timing¹²⁻¹³. What is important about timing is that bacterin is administered before significant transmission of *Mhp* begins in the population. It is important to note that while immunization reduces clinical losses, it does not slow the spread of infection within a herd.¹⁴ In some cases it has been suggested that *Mhp* can be repeatedly eliminated from a population with the use of anti-infectives. This not only flies in the face of biological plausibility for a chronic infection that is slow to transmit and grow in the host (high number of carrier animals), there is no documented evidence in the peer reviewed literature to support the claim.

Sow herds are the problem¹ and that is the biggest problem as it is very challenging to understand what the transmission pattern is in breeding herds. This is compounded when gilts of a different *Mhp* infection status are introduced into the sow herd. In general, infected sow farms with a naive gilt source will experience down-stream pig flow challenges at some point in the future as transmission increases over time with more susceptible animals enter the breeding herds. There is data to suggest that once animals clear *Mhp* infection they are not likely to shed it to their offspring even with reexposure¹. This would suggest that acclimation of gilts is the key but acclimation of gilts is not easy to do on a repeatable basis without active transmission in the grow-out period. Predicting sow herd stability is the Holy Grail for this disease but right now there are major technical barriers to getting it done.

In conclusion there are several “big bucket” take home messages from both the literature and clinical experiences. First, matching the gilt and sow *Mhp* status with proper acclimation to the sow herd at an early age is critical. Secondly, all pigs should be immunized – yes, all the pigs, regardless of what you think the status of the sow farm is and that includes all of the gilts. There is no prize for being “test negative” in commercial production so with low cost bacterins there little cost to raising herd immunity and lowering the risk of losses over the long term. Third, antibiotics have to be at the ready if there are challenges and use of them in the sow herd should be a high priority to lower the number of infected pigs at weaning. In the future this may not be an option if anti-infective

use is limited by government action suggesting that current strategies need to be critically re-evaluated. Understanding what is happening at the level of the sow herd and how to build systems that are more resistant to the effects of small changes in agent transmission rates in the sow herd will be critical. This understanding will only be gained through large, blinded clinical trials that are expensive and hard to do. All of these facts suggest that a new model for understanding and managing EP is needed for the long term profitability of the North American pork business.

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