

### Speakers

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### Sarah

Hello, this is Dr. Sarah Probst Miller with Carthage Veterinary Service. Welcome to our first edition of P's in a Pod. P's in a Pod covers practical tips on pigs, production and profitability. P's in a Pod is a monthly podcast brought to you by Fort Dodge Animal Health and Carthage Veterinary Service.

As a swine veterinarian, I've sat in conference halls and heard veterinarians discuss the possibility of an Agent X or co-factors in relation to PCV2. These discussions seemed to quiet down for awhile when we got our hands on PCV2 vaccine and saw how well it worked in the field. But, now we are hearing more than whispers of an additional agent as we realize there are a few herds here and there that struggle for control of PCVAD in spite of vaccination. As a swine vet, I'm very curious if TTV virus is the culprit behind that herd specific lowered vaccine effectiveness or if it is another factor. So, Dr. Connor, I'm eager to hear the results of your literature search and experience with TTV virus and how you think this information will impact my world as a swine vet.

### Joe

Thanks for the introduction, Sarah. Yes, TTV is a hot topic these days and for this first podcast, we thought it would be good to review the literature on TTV virus and discuss the interaction with PCV2 virus.

Torque Teno Virus, or more commonly known as TTV virus, has been in the limelight recently because of its interaction with PCV2 as a co-factor in producing post weaning multisystemic syndrome.

Let's start with a little history, Torque Teno Virus was first mentioned in scientific literature in 1997 when TTV virus was isolated from a human patient with hepatitis following a transfusion in 1997. Subsequently, viruses related to TTV virus were found in a number of other species. In fact, TTV is found in plasma in greater than 80 percent of the human population worldwide. TTV is sister to chicken anemia virus and porcine circoviruses in the circoviridae family. If we back out to genus, TTV's belong to the genus Anellovirus, single stranded DNA viruses that infect many vertebrate species. When assigned to this genus in 2008, the virus was thought to be ubiquitous but non-pathogenic. But now we are beginning to make some associations with disease and that is the root of this virus' current importance.<sup>1</sup>

### Sarah

Great Joe, another virus to think about. What makes this virus one to worry about?

### Joe

Well Sarah. It's everywhere. Oftentimes when we see something everywhere, we choose to ignore it. But this may be one to question. The ubiquitousness of the virus has been confirmed many times by research in domestic pigs, cats, and dogs. Japanese researchers found these species to be naturally infected with species specific TTV.<sup>2</sup> Researchers identified different TTV genomes from humans and pigs. They actually found two different nucleotide sequences from the pig (conveniently called 1 and 2), which confirm the TTVs are species specific.<sup>3</sup>

### Sarah

Ok so they found species specific TTV in pigs. How prevalent was it?

**Joe**

2008 Canadian research reports TTV virus found in 91 percent of plasma samples and 60 percent of fecal samples from a single pig herd in Quebec. Other researchers have identified TTV virus with varying prevalence ranging from 33 percent in the United States to 100 percent in Quebec and Saskatchewan. Researchers in Barcelona found 84 percent prevalence in TTV virus in wild boars. More recently, Segelas et al. 2008 published results of a retrospective study on TTV infections in Spain and found evidence of infection back to 1985, which is 14 years before it was reported in any species. In 2007, researchers in Barcelona identified TTV virus in pig semen in 72 percent of the samples. They found association between TTV infection and semen characteristics, but no clear evidence of virus affecting fertility. 2008 research confirms transmission in feces as a possibility.<sup>4</sup>

**Sarah**

So its prevalence in herds worldwide ranges from 33% to 100% depending on the herd. It's around. What does this mean for swine vets?

**Joe**

So yes, TTV is in a lot of species at high rates. This we know. The new information is that it may be linked to disease . . . maybe not as a cause, but as a co-factor. In pigs, research is showing TTV may contribute to PCVAD.

**Sarah**

So TTV and PCVAD?

**Joe**

Yes, the big one is the research showing a link between TTV and PCVAD.

This can be a bit confusing because early reports of TTV virus made no mention of related disease and described the virus as nonpathogenic. But, in 2006, possible links between TTV and other diseases began to be reported.<sup>5</sup> Some research observed a higher prevalence of TTV in the serum of sows affected by PMWS versus those sows not affected by PMWS. The difference was 97 percent versus 78 percent. Interestingly, they found this link only with TTV genotype 2 and not genotype 1. The link between TTV virus and other diseases was further confirmed in a paper by Gagnon et al. 2007 from Quebec, Canada.<sup>6</sup> Their work focused on the emergence of PCVAD in pigs in Canada. In samples examined from 13 cases, they found TTV virus in 69 percent of them.

In the same time frame, a different report concluded that concurrent infection of TTV and PCV2 may result in PMWS. These studies did not clearly associate a link among TTV and PCV2 and PCVAD, but the next study did.<sup>7</sup>

This research focused on gnotobiotic pigs. In this research, pigs infected with either TTV or PCV2 virus alone did not develop into PMWS. However---now, Sarah, this is the important part---when pigs were first infected with TTV and then PCV2 one week later, they developed acute onset of PMWS with typical wasting.<sup>8</sup>

And then, the next sister experiment results are strikingly different. They did the opposite: infected pigs first with PCV2 and then TTV. PMWS did not occur suggesting the order of infection with these viruses is important.

This is the information that gives us reason to include TTV as a cofactor in PCVAD. At present, researchers and labs are unable to culture TTV virus and the development of any vaccine is likely to be slow.

**Sarah**

Very interesting. TTV before PCV2 resulted in acute PMWS but not the other way around. Hmm. Just curious Joe, did any other research show that TTV contributed to other disease as well?

**Joe**

Yes, more research in 2008 reported on disease models where sterile pigs were infected with PCV2, TTV virus, TTV, or both. They found that TTV could modify how PCV2 acted during PRRS virus infection of pigs.

**Sarah**

Interesting. Definitely some food for thought. Thanks Dr. Connor. Now from the field veterinarian perspective, I immediately have a lot of questions. We have identified another virus that helps cause disease but we apparently have no means of controlling it. So bear with me, Joe, I'm going to barrage you with questions. The first being . . . this is really neat but what do I do with this information?

**Joe**

Well, Sarah, there are more questions than answers at this point, but let me give it a shot. Let me start by reviewing what we know about infection and transmission. Genomic diversity amongst TTVs is remarkable. There are currently five genogroups in humans and two in pigs. Frequently, pigs are infected with more than one genogroup or several TTVs of the same genogroup. We do know transmission of porcine TTVs is very likely fecal/oral and aerosol-mediated. Recent study found TTV DNAs in boar semen.

In utero, TTV infection using gnotobiotic pigs results in histological changes of interstitial pneumonia and membranous local glomerulopathy. In utero infection appears to be a common mode of TTV transmission in swine. However, the incidence of infection varies by litter. The incidence cannot be predicted by TTV status of the sows. It looks like TTV virus may be responsible for reproductive disorders and fetal diseases in piglets. And right now, diagnostically, the only way to identify TTV is by PCR or viral DNAs as TTVs are unculturable in vitro. We are still learning what a PCR positive and TTV DNA viremia means to a pig. Pigs remain DNA positive for a long time, perhaps for a lifetime. How long viremia occurs is unclear. We know pigs can be DNA positive and not be viremic. So is viremia concentrated post infection? Post reinfection? In utero? Studies have shown TTV DNA viremia from 33% to 100% in all ages of swine and boar semen. At this time, I think any field testing should be done with interpretive caution. I worry about those few in a sow population that for whatever reason did not get exposed young and have their first viremic experience when they enter the sow herd. This leads to the main question.

**Sarah**

Yes, so what does this mean to the practitioner?

**Joe**

Absolutely. That's the question everyone should be asking. What does this information on TTV virus mean to practitioners and what do we do? There is a widely distributed virus within pig populations that typically does not cause any pathogenesis. However, it may be involved in insinuating PCV2 viruses and possible other viruses depending on the sequence of infection and age. Because the virus is not culturable, it is impossible to ascertain the influence in the pig populations to date except in research populations.

This leads us to our take home message. It is likely that exposure to TTV occurs in most piglets when they are young, but maybe not all piglets. And the common practice of feedback to developing gilts is the most practical strategy of managing this virus at this time. Hopefully feedback would help ensure a gilt's first infection would not occur close to her first pregnancy. And perhaps, ensuring that all sows have some form of maternal immunity can help pigs deal with infection. So for TTV control, we may need to look back to our sow farms and investigate the possibility of feedback programs. Of course other diseases, namely PRRS, will impact our choices here.

**Sarah**

So should this impact my PCV2 vaccination strategy on farm?

**Joe**

Yes, great question, Sarah. What does the info mean for PCV2 vaccination timing? It appears that TTV before PCV2 infection leads to PCVAD in pigs. We are not likely to get PCV vaccination in front of TTV virus exposure. Pigs are very likely going to get infected with TTV in utero or in early lactation. Logic may lead us to think it would be ideal to get PCV2 vaccination in before TTV infection. A TTV/PCV2 disease worry may be if a sow farm is having high sow pig transmission of PCV2 and TTV and you are having a lot of PCV2 positive pigs in lactation. Then sow farm PCV2 vaccination protocols and pig PCV2 vaccination protocols may need to be addressed to reduce this in utero or early lactation shedding of PCV2. This would be another reason to vaccinate our gilts for PCV2 during acclimation or to consider PCV2 sow vaccination on herds with significant numbers of PCV2 positive pigs in lactation. But for the most part, at this time, if we are seeing problems with PCV2 vaccine, we need to check compliance of vaccine administration. We should not automatically point our fingers at TTV if we are seeing PCVAD peek through. We've had vaccine go in the pit before. We need to make sure all employees understand the importance of what they do each day in the barn so this very important work gets done correctly.

At this time, TTV does not impact PCV2 vaccination timing strategies drastically. I believe our next podcast will talk more about another factor of concern that may impact our PCV2 vaccination timing strategies more than TTV virus. Next month, Dr. Laura Greiner will be discussing Carthage Veterinary Service recent research on PCV2 maternal antibody.

**Sarah**

What further research do you anticipate helping us answer these questions?

**Joe**

Clearly more research on TTV is necessary and I would look toward this research giving us more guidelines on length of viremia post exposure, diagnostics, true disease impact, and control opportunities.

**Sarah**

Thanks Dr. Connor. This helps me with my thought process and gives me a strategy for approaching this disease or at least answering client questions about this disease. It looks like I need to review some feedback strategies with clients having some potential issues and recheck vaccination compliance. I've been monitoring some sow herds for PCV2 PCR positives when I do routine piglet PRRS PCR testing. If they are PCV2 negative for long periods of time, I've removed this test as routine, but I need to think about this a bit more. Maybe I need to leave it in to keep a closer eye on this. Dr. Lowe, after hearing this information and talks on this topic at a variety of conferences, how will TTV impact your world in a large system farm? Will you be undertaking additional diagnostics? How will you answer questions about TTV and what will you be doing?

**Jim**

Dr. Sarah thanks and Dr. Connor, it was some really valuable information. Let's stop and think about what all of this means. It really impresses me how little we understand about the biological diversity that occurs in nature today. We love to lump things into thoughts, pathogens, and non-pathogens, but really, the organisms that we identified are only the tip of the iceberg with respect to all the potential things that could cause disease in animals and people. So, with that said, where does it leave us? Well, I don't know. I think it reinforces to me several key health optimization strategies that we need to think about within production systems. First, diseases or agents like Torque Teno Virus, and there are many agents such as this, have the opportunity to really cause both endemic and epidemic disease in basic infection control measures. It would be highly beneficial to help limit the spread and emergence of these diseases within populations.

**Sarah**

Ok, that sounds great Jim. But what do you mean by infection control measures for a virus like TTV?

**Jim**

What do I mean by infection control measures? It really leads back to the basics that we sometimes forget. Those basics certainly include isolation of new animals arriving at the farm. I think more importantly than isolation is acclimation of new stock to existing stock on the farm. Even if we are using the same source every time the rearing of replacement gilts and all in/all out batches can certainly create divergent health statuses between batches that need to be acclimated to the endemic diseases present in the breeding herd. I had a couple of cases recently where they were not allowing enough acclimation time for the introduction of select weight gilts into the herd and we were seeing some reproduction consequences, particularly mummies, because of that. I am going back and rethinking what is the optimum weight and acclimation strategy in our gilts in the farms. Certainly, it continues to make you think that entering gilts as weaner pigs or feeder pigs would be advantageous with respect to acclimating those animals long prior to their breeding process.

Secondly, I think with respect to infection control, external and internal biosecurity continues to be important. We certainly spend a lot of time thinking about external biosecurity in production systems today with things such as truck washes, showers and fumigation chambers to bring equipment in. As herds have gotten larger, we need to spend as much time thinking about internal biosecurity and potential to promote endemic disease. What I mean by internal biosecurity, is things like changing needles between litters, adequate washing and control of tubs used to process pigs or split-suckle pigs, changing needles in sow gestation groups and other things like this which can promote disease transmission within the herd. These things with small herds were not as big a deal, because the herds were homogenous. Scott Dee has certainly shown with PRRS that we can get nice subpopulations

existing in relatively modest size herds. If we think about endemic diseases with very large herds the potential for multiple disease states are certainly high.

**Jim**

Finally, I think Torque Teno Virus is just another great example of the continuing evolution of disease that we see on a routine basis. As we think about designing systems or remodeling systems, we need to continue to have evolutionary principles in the back of our heads or the control of emergent diseases like TTV.

**Sarah**

Evolutionary principles? Ok Jim, expound practically on what you mean by this.

**Jim**

What evolutionary principles am I thinking about? Well, certainly we live in a soup of microorganisms both on and in all of the domestic animals and ourselves we work with. As stated earlier, we understand very little about the ecology of that microbial soup. What we know is that as we alter the environment, we change the soup. With the number of livestock in an area, we certainly create the potential for the ecology to be disruptive from what evolution has been routinely based on. Our livestock practices impact the ecological evolution of the microbial soup. These disruptions can create short-term imbalances in the ecology leading to over growth of some organisms that can produce disease. Rarely, and only rarely new significant pathogens emerge because they are more fit in the newly created environment which leads to new epidemic diseases.

What things might be advantageous to slow the pace of evolution? Things such as limiting internal contact and good biosecurity to lower the rate of transmission of organisms and minimizing contact between new and different hoof population, i.e. introduction of multiple novel sources in breeding herds. While in some cases, strict batch rearing can be advantageous for the reduction of some new disease emergence, batch rearing can promote the emergence of other epidemic diseases because of large, naïve populations.

**Sarah**

I get where you're coming from now. Ok so bring this home for me Jim. What should this mean to me the swine vet?

**Jim**

What is the take home in my mind? Well, Torque Teno Virus is probably one of many new potential pathogens that we will see emerge, but none of them will likely be epidemic disease outbreaks or will be significant challenges in the long run. Whether Torque Teno Virus is or is not a major pathogen, I think the jury is still out. But, it is certainly a great reminder that the microbial soup that we live in has the potential to adapt and evolve much more rapidly than we as hosts do and we will see, as we have seen for ions, the emergence of new clinical disease as a result of the changing ecology.

**Sarah**

Thanks Dr. Connor and Dr. Lowe for your valuable insights. From what I've heard, I've pulled together 3 short term and 3 long term action points for myself as a swine vet. In the short term, I am going to 1) review the acclimation programs on all sow farms and make sure they are occurring and that we are timing the acclimation correctly. I may move some acclimation programs up in time. 2) I am going to put a reminder on my calendar to check acclimation practices on every sow farm visit that occurs. This is to

make sure it is getting done consistently on all farms that are PRRS stable. 3) I am going to monitor PCV2 vaccine effectiveness and look to the obvious causes such as injection compliance first and look to TTV or other factors second. I will also do some piglet PCV2 PCR testing on herds where vaccine compliance is not a problem. For the long term approach 1) I am going to think hard about routine practices that occur daily, weekly in the sow farm and think about whether these practices are working to slow or speed up the ecological evolution. What can I do to help slow down the ecological evolution on a farm? 2) Also, I am going to continue to advise clients designing new facilities to look hard at having control of their incoming gilts from weaning to finish. There continues to be health reasons on many levels to have this control opportunity. 3) And thirdly, I'm going to think about re-implementing periodically the PCV2 PCR testing of piglets when the routine PRRS PCR testing is done.

You've given me some good tips to work on to best serve my clients. As always, it is so good to hear the concerns and knowledge of other swine vets and I appreciate the information. It will make me a better swine vet.

To get more action points from the field, tune into our next P's in a Pod where we will review recent research about PCV2 and maternal immunity. Dr. Laura Greiner will be presenting. Drs Connor and Lowe will talk to us about the information's application to us as swine vets and I'll come back to you with another list of action points. Drive safely and have a great day!

## References

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