Practical Health

Insight (9)

PRUDENT USE OF ANTIBIOTICS

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When I started to work for the pharmaceutical industry back in 1985, the first real issue that came my way was the restriction that governmental institutes wanted to impose on the admission of certain medicines to the veterinary market. Hormones to improve meat quality and to increase bodyweight of cattle, and the admission of certain antibiotic preparations are just some examples. The famous Swan report on the use of antibiotics is still the main symbol of this era that was filled with lots of discussions but did not lead to any action except for the EU ban on antibiotics used for growth promotion. Also the growth promoting hormones, used in cattle, were banned by the EU but without much discussion and for pure economic reasons. In 1986 we already had large agricultural intervention schemes in place and we simply did not need more meat.

How different is the world today? Those of you that receive electronic newsletters and other types of communication will have noticed that prudent, or responsible, use of antibiotics is one of the main topics nowadays in our industry.

The word resistance development is seen everywhere and we 'the veterinarians' are getting the blame for everything in this matter. Basically they put the blame on us and the root of the problems relates to us overusing antibiotics in livestock. In the human field the doctors are very worried that they cannot cure their patients anymore because of this resistance development.

Now we see that real action is taken that leads to a reduction in veterinary use of antibiotics in certain countries. In 2014 several main international conferences were dedicated to this subject only. Scientists did report on the current status and the progress that is made. Why did we see no or little action in the 1980s and why do we see so much action now?

Reasons for change

Well there are several reasons for that change. Of course the resistance pattern in important (pathogenic for humans) bacteria has deteriorated dramatically. Secondly in the 1980s the governmental bodies did not really have the systems in place to find out what was happening in the veterinary field and had no system in place to impose sanctions, when needed.

Since then the information gathering and the legal environment has changed dramatically in several countries leading to the fact that now they can say: "We do not like what you do, for this and this reason and if you do not change your way of working we will make sure that you feel it in your wallet!" A powerful argument in an industry driven by economics.

This is the current situation in countries like the Netherlands. It is not only affecting the use of antibiotics in swine but across all species.

Importance of swine

Swine, however, in the field of antibiotic usage are very important. In the Third ESVAC report published in 2013 34% of all antibiotic products used in livestock in 2011 were used in pigs. For the period 2012-2013, the Netherlands reports a reduction of 30% in the swine segment only and a total reduction was 57.7% for all species for the period 2009 until 2013!

Was this only due to the governmental interventions? Yes and no. What it did for sure was create the right environment for the swine veterinarians, farm managers and producers, researchers etc to look for alternative to antibiotic usage intervention strategies.

If you now open industry related magazines, websites, newsletters etc you will see more and more information on, for example, probiotic and immune enhancers to fill the gap when the reduction in use of antibiotics is an issue. But there is more to it.

We all know that the way we keep our pigs is often far from optimal with regards to the development and expression of diseases. Stocking density, biosecurity and other management factors also play an important role when it comes to reducing the use of antibiotics. In short, we group all these efforts under the heading: alternative intervention strategies.

Vaccines are also seen more and more as tools to reduce the number of daily treatments with antibiotics. The industry, again so far in a small number of leading countries, is actively exploring the use of these alternative intervention strategies. And it takes courage to do so.

Antibiotics are relatively cheap, work under the most difficult conditions, are easy to use and require little additional knowledge when the decision is taken to use them. The positive effect of the alternative intervention strategies on the reduction of use of antibiotics is only visible when the antibiotic treatment is ceased when the alternative intervention strategy is implemented. And to abandon a comfortable umbrella type of protection takes courage to do so.

The massive uptake of PCV2 vaccination was the first real and tangible experience that antibiotics were not always required on a large variety of different farms. The same is true for those farms that implemented real batch farrowing and batch wise growing and finishing with a good physical separation between the age groups, as an example of a management factor that helped reduce antibiotic consumption.

Alternative strategies

There are more examples of different alternative intervention strategies that are useful in helping to reach the goal of reduction in the use of antibiotics. Responsible use of antibiotics is also a term that implies that you should motivate why to use an antibiotic in a certain case and not one of the other options that might exist.

After analysing the situation, it often comes back to the answer that there was no other option; the animal is sick and requires treatment. This is and will stay a good reason. The animal also has the right to receive – and we have the obligation to provide – treatment, even if it is an antibiotic.

But the question will be more often asked if there really was no alternative to prevent the disease from occurring, or to develop? As an incentive it is also important to realise that efforts made to prevent a disease often gives a better return on investment than efforts to cure a disease.

What will be our benefit of this whole exercise?

Well we all know that it is very difficult to develop new antibiotics. If we manage to develop new ones, they will be very expensive and their use will be restricted.

So for the future it is uncertain if we have access to new developed antibiotics when the currently available antibiotics stop working.

On the other hand, the limited information we have so far indicates that when we are reducing the use of the new antibiotics bacteria become sensitive to the old antibiotics again. And this is our benefit in the veterinary field.

When we apply the concept of responsible use of antibiotics and take the alternative intervention strategies really seriously, we will be able to use the current portfolio of antibiotics for a much longer period than when we do our best to speed up resistance development.

We only have to work very hard to assure that the lessons learned on how to reduce the number of antibiotic treatments in some leading countries are implemented by other countries.

This is also the reason for all these conferences and other communications to spread the news and hope they will follow the leaders.

The responsible use of antibiotics is definitely of interest to our industry and that is why we should actively work to implement the concept.

Multimillion dollar question

For the multimillion dollar question of whether responsible use of antibiotics in the veterinary field will solve the resistance problem in human medicine, I am less optimistic.

Nobody has an answer to this question.

The problems they are facing on a global level are enormous. In many countries the general public needs no prescription for purchasing any kind of antibiotic and the general public has a lack of knowledge on resistance development.

This, coupled with the increased level of international travelling and the many different ways of contact, makes the situation in the human health care situation very complicated and extremely difficult to control, irrespective of the realisations that we 'the veterinarians' might achieve! ■

Practical Health

Insight (10)

THE VALUE OF DIAGNOSTICS

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The use of diagnostic tools has increased dramatically in our industry over the past 25 years. For sure there were good reasons for this to happen, but what were the main drivers behind this rapid increase in usage? Is it only because there are more diseases now than 25 years ago? Or are there other reasons? To make a proper analysis we not only have to look back into the past but we also have to look to our colleagues in the animal protein production industry.

In earlier days we basically had two different schemes. For suspected notifiable diseases like classical swine fever and foot and mouth disease it was obligatory to submit samples to a state owned veterinary laboratory for the definitive diagnosis. For all other diseases the visiting consultant veterinarian made the diagnosis within 20 minutes on the farm. In those days there was little debate to question this.

The general level of knowledge among the farming community on the different diseases was simply at a low level and the status of the veterinarian at a high level. To be more complete, at that time there was already a small group of veterinarians that submitted samples to get their suspicion confirmed by a diagnostic laboratory. However, logistics in general and the long lead time between submitting the samples and obtaining the final results were definitely major obstacles.

Since then the world has changed dramatically in all its aspects. Logistics, including transport under temperature controlled conditions, has improved and the turnaround time between sample submission/processing/result obtained, has shortened to a period that the whole effort makes sense.

Furthermore, valuable information was gathered with the help of diagnostics. We should never forget that we, in a business environment, are only willing to pay for something when it has proven to be of value for us. And that is exactly what diagnostics have proven to be when used correctly, for example, in our control/eradication programs.

Irrespective, in recent history, if we were targeting CSF virus, or FMD virus or Aujeszky's disease virus, without the different diagnostic tools these eradication programs would have taken much longer.

It is not even certain if they would have been successful and, if so, at a much higher cost.

Now diagnostics are used for a variety of reasons. Herd monitoring, is very different from the old custom of disease diagnostics and also different when detecting response to vaccination is demanded.

It should always be kept in mind that different tests give different answers and there are also specific facts related to specific pathogens. It is clear is that an ELISA for antibody detection gives different information compared to PCR or qPCRs for DNA or RNA detection. But we can also distinguish differences between the currently available ELISA for antibodies against PCV2 virus for example.

Still, as a general statement, we can conclude that all these diagnostic tools have proven their value when used in the proper way. The massive adoption of routine monitoring for diseases in the poultry industry is a clear example of its value. It has to do with our current attitude towards risk management.

To manage risks information is a key element and information is what diagnostic tests provide.

Using diagnostic testing

How to use a diagnostic test in a proper way relates very much to the question to which we want to have an answer.

Such a question determines not only the number of samples that need to be tested but also the type or age of the animals and the history of the animals.

For example, testing six week old pigs for PRRS field virus circulation does not make much sense when they are vaccinated with a modified live PRRS virus vaccine at 2-3 weeks of age.

When tested positive it can very well be the vaccine virus that is found in the sample so no reliable information on field virus circulation is obtained.

While taking samples at the moment of, or just before, vaccination that type of requested information can be generated and can provide very valuable information.

Of course here a PCR test, for PRRS virus RNA detection, should be used and not an ELISA because when antibodies are found they are most likely of maternally derived origin.

From the above, it is clear that there are many aspects to take into account in order to get back the information and value to your relatively easy question as you had hoped.

The number of samples that need to be tested to detect the presence of an antigen depends on the pathogen and the disease situation.

Statistics play an important role here and as a rule of thumb 30 samples per farm, taken at random, gives a 95% certainty that the presence of a pathogen is detected. This is not always true for PRRS virus.

As you might remember from a previous column, PRRS virus can hide in pockets. In such a case you have to test all animals.

When using diagnostic tools epidemiological and biological features of the pathogen should always be taken into account.

The use in disease diagnostics is another useful application. This is relatively straightforward. Samples are taken at the first signs of a disease and 4-6 weeks later a second sample-set is taken, preferably from the same pigs.

When the samples are tested on the same day in the same laboratory with the same test kit and the second sample shows a significant increase in titer (sero-conversion), we assume that the agent we tested for was the cause of the disease.

With herd monitoring we get the same information but plotted over a time scale. In herd monitoring we have two systems; we can take all the required samples on the same day (longitudinal sampling) or we can follow the same group of pigs over time (sequential sampling).

The longitudinal sampling method is more often practiced. Most take 10 samples from 6, 10, 14 and 18 weeks old and from 10 slaughter age pigs and 10 samples from replacement gilts, P1s and older sows.

The advantage here is that you can take and process all samples at the same time. This is, for more than one reason, a very efficient method.

The disadvantage is that possible variation in seasonal differences and differences in the farm can be missed.

The disadvantage of the sequential sampling is that it takes the full life span of a group of finishers before all tests are done (to avoid the variation between laboratory testing days) but it has as an advantage that a certain flow of pigs moving into the different parts of a farm can be closely followed. But of course here seasonal differences can still occur. So proper planning is still required!

Detecting response

Last but not least, we mentioned detecting response to vaccination. Here we also see major differences between pathogens, vaccines and tests. In the case of M. hyo vaccines we often see no measurable serological response at all after vaccination, although there are differences between vaccines.

The outcome, however, has no relation to protection. With ELISA we only measure serum-antibodies and these antibodies play no role in M. hyo protection. For measuring vaccination response to a PRRS vaccination, the same discussion applies.

The PRRS antibodies we measure tell us nothing about protection against a PRRS field virus infection. Protection against PRRS virus is mainly based on cellular immunity and next to that most PRRS field strains are only weak immunogenic.

So a positive ELISA result tells us only that the pig has been in contact with PRRS virus. This only applies for the older pig as young pigs can show a positive result based on antibodies that they got for free from the sow.

The last example is PCV2. Here we still have different opinions. Perfect protection against PCV2 field virus infection was demonstrated through passive immunity based on maternally derived antibodies only. This shows that antibodies do play a very important role in the protection against PCV2 infections.

After vaccination we do not always see a sero-conversion, depending on the vaccine used. Some claim that antibodies against PCV2 virus are not important for protection in vaccinated pigs. Why can they say so? Sometimes it seems that in the case of PCV2 associated diseases, biological variation has no limit. ■

Practical Health

Insight (11)

IMMUNOLOGY

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Immunology, the science of the ultimate confusion! When scientists are giving a presentation on how immunology works we see beautiful and artistic flow charts appearing on screen at the same pace as action shots in a modern James Bond movie. For the audience, however, the take-home message is very different. We all know that in the James Bond movie everything is orchestrated and fake. In immunology it is also orchestrated but real. We still do not know all the mechanisms of immunology yet but we learn fast. The fact that the field of immune therapy is making strong progress in the battle against cancer, proves the point.

We as veterinarians believe that what we have done is good when for us, or for the owner, the benefit of our advice or intervention is visible or measurable. We do not need to know the underlying mechanism.

Sometimes, however, it is very useful to understand a bit of the underlying mechanism to explain why certain actions have not delivered the desired effect or allowed us to go for an even better result.

Here some basic understanding of certain aspects of immunology has its place. This column will not cover all details but will highlight one aspect that has intrigued me very much over the years and has become more clear recently.

New insights

New insights were discovered between a pathogen (in this case High Pathogenic (HP) PRRS virus) and the immune apparatus of the pig. These new insights make it easier to understand what we actually see happening in the field. It finds its rationale based on what has been discovered in the laboratory on how the immune apparatus works and secondly how this HP PRRS virus alters the normal immune response.

The basis is that the immune apparatus reacts when it is confronted with an agent that is both foreign to the body and dangerous for the individual. The pathogen invades the body and certain cells start to send out information to alert immune competent cells. The information distribution is carried out by messenger molecules (so called cytokines).

The reaction these messenger molecules initiate can be of the humoral (antibody) or cellular (immune competent cells) type, depending on the type of information that is sent out. This is called up-regulation, by pro-inflammatory cytokines, of the immune system.

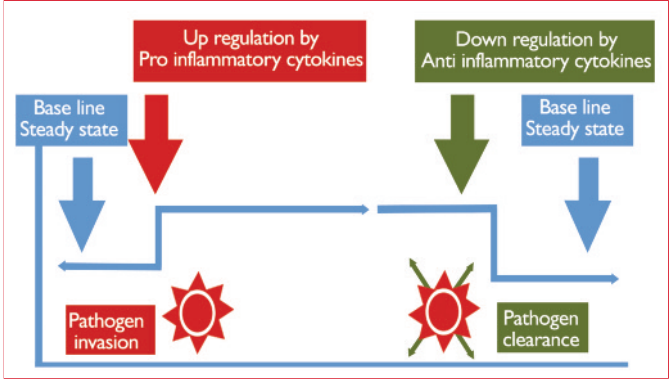
The immune system is always at work. There is always a certain baseline level of activities but when required it can step up the activities.

After a certain time period the pathogen is eliminated and the immune apparatus has to go back to normal base line levels. This is regulated by anti-inflammatory cytokines that down-regulate the immune system.

This down regulation of the immune reaction is a normal process because the activity level was increased and has to go back to normal base line levels (see Fig. 1).

If this down regulation does not take place, the immune system will exhaust the patient as we do see with auto-immune disorders where the down regulation process does not function normally.

Fig. 1. Normal immunological reaction.



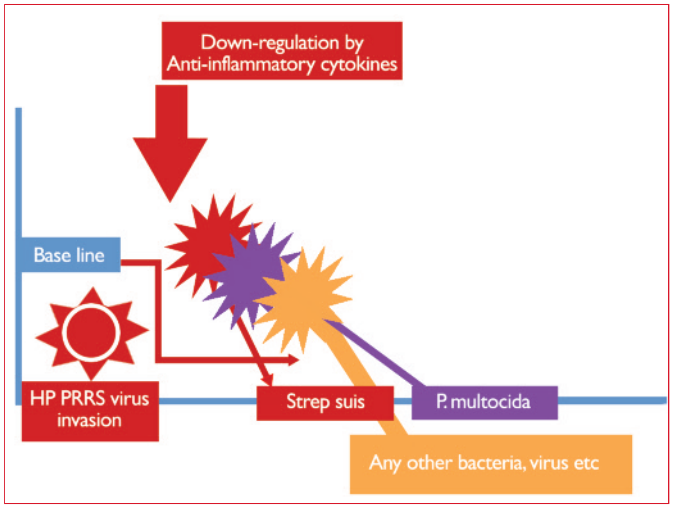


Fig. 2. Immunological reaction after a HP PRRS virus infection.

In the case of a HP PRRS infection the desired process as described above does not function correctly.

The messenger molecules that should up-regulate the immune system to start fighting against the invading HP PRRS virus do not appear and instead of these activators other messenger molecules that normally down regulate the immune system show up (see Fig. 2).

So the PRRS virus creates an environment in which it has no (immunological-)resistance and can freely harm the pig! But there is even more to this.

Because the immune system has left the base line level of activity and has moved to a lower level activity, the normal control of (resident and environmental-) bacteria is also compromised. And this is exactly what we see in the field when the HP PRRS takes its toll.

Pigs suddenly die of all kind of opportunistic bacteria that are present in our pigs or barns but are normally controlled by a functioning immune system. In the beginning of the HP PRRS episode in 2006, when all kind of different viruses and bacteria were discovered in the affected pigs, it was a puzzle to detect the real cause of the disease. It took some time to find out that it was the severe immune modulation of that specific PRRS virus strain that was the origin of the problems.

The fundamental work of Guo, Lager and others published in 2012 showed us how this worked. But the research carried out at CReSA by Diaz and others published earlier in 2006 also clearly showed how important the role of messenger molecules can be.

The immune system

From this example we can learn different things. Firstly, of course, how critical it is that the immune apparatus functions correctly.

Pathogens like PRRS, influenza and PCV2 virus who are all having in their own way an impact on the immune system, need to be controlled. M. hyo control is not different in relation to its negative impact on the immune system.

Secondly, within the PRRS virus family we have many different faces. This HP PRRS virus is very pathogenic and other field strains are less pathogenic. However, when bacterial infections are noted with a concurrent PRRS virus infection, attention for PRRS virus control will pay off. Simply because of the positive impact on the immune system and through this it will lead to a reduction in the use of antibiotics.

That is the last lesson that we learned: pigs suffering from an infection with an immune modulating pathogen need treatment with an antibiotic, whatever is sad about antimicrobial usage in veterinary medicine! ■

References available from the author on request

Practical Health

Insight (12)

Importance of subpopulations

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PCV2 virus infections were causing high morbidity and mortality throughout North America and Asia from 2004/2005 onwards and disappeared just as quickly starting from 2006 when PCV2 vaccines became available. In Europe the PMWS (Post-weaning Multi-systemic Wasting Syndrome) situation was quite different.

On individual farms throughout Europe, morbidity and mortality would go up and disappear in a wave-like pattern and PCV2 virus would always be detected. A direct relation between PCV2 virus and PMWS could not be made in those days. PCV2 virus was also detected in apparently healthy pigs, so it was regarded by many as a non-pathogenic finding. PMWS is also the name of a syndrome not a disease!

Implementing the 20 steps of Madec (a must for everyone working in the pork producing industry) was an attempt to reduce the impact of PMWS. It was however not always effective and it involved no action that was specifically directed against PCV2 virus.

In Australia they said in those days: we have PCV2 virus but no PMWS (to keep their border closed for imports from countries that suffered from PMWS) because the 20 steps of Madec did not give the desired effect!

'Circus' virus in USA

In the USA 'letters to the editor' appeared in spring of 2006 in which PCV2 virus was called Circus virus instead of the genus name Circovirus because of the huge variety in clinical symptoms in which PCV2 virus was detected. The disease was there, the pathogen was there but our diagnostic tools were not sufficient to explain the relation.

With the appearance of the PCV2 vaccines for piglets we, for the first time, had a specific tool in hand to fight against PCV2 virus and the results were dramatically positive. But does this mean that PCV2 is no longer causing economic damage? No, biology has too many variables to take such an easy-going position.

Here we will deal with one of the aspects that is of crucial importance when optimal control of PCV2 virus and possible economic damage is the goal. PCV2 virus is the smallest virus that we know to infect our pigs. Its genomic structure is also very small. It consists of only three different parts. Two of them are larger and have a well described function. Part one has all the genetic information and takes care of multiplication and number two takes care of the capsid around the genetic information. That is all there is and still it is so pathogenic.

Pathogenicity

Which part of the genome is responsible for the pathogenicity is still under study but we know the mechanism on how PCV2 virus exercises its pathogenicity. Immunemodulation is the correct wording and this basically implies that our complex immune system does not function properly. Important immune competent cells are loaded with PCV2 virus. The messenger molecules that they should send out after infection to activate the next level of immune cells are not released (or not produced) and the (PCV2 infected) pig does not react in a correct way to the PCV2 infection. Also the immunological reaction against other invading pathogens is impaired.

When PCV2 virus is the only pathogen that infects the pig, you will very often see no or very minor clinical symptoms. This also explains to a large extent why you can have PCV2 virus in apparently healthy pigs. In the laboratory we can still not induce PCV2 Associated Disease (PCVAD) or PCV2 Systemic Disease (PCVSD) with PCV2 virus alone. We can induce disease if we co-infect with another pathogen. Or is there a difference in pathogenicity between different PCV2 viruses and do we simply have the wrong PCV2 virus in our laboratory? Nobody knows for sure.

What we know is that intensification of the disease situation takes place by secondary pathogens. This characteristic will always influence any clinical study with PCV2 virus.

How much PCV2 virus do we need to cause how much intensification by the secondary infection and of which PCV2 virus? A question that we simply cannot answer. The easiest approach to this dilemma has always been to try to limit the amount of circulating PCV2 virus as much as possible. The hypothesis is that the presence of PCV2 virus is a risk factor. If we want to minimise risk factors then PCV2 control is one of them. In the case of PCVAD that means reducing the amount of PCV2 virus in the pigs to the lowest level possible.

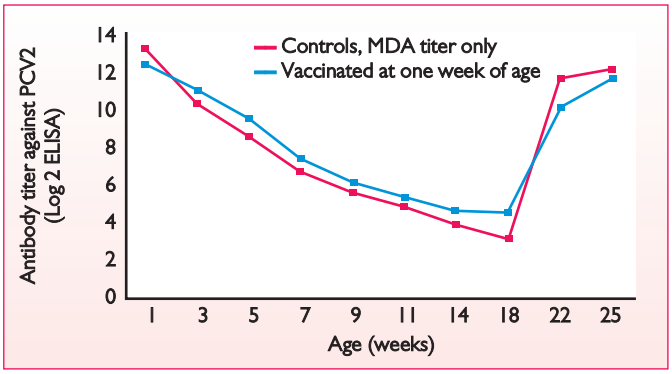

Fig. 1. Influence of MDA on vaccination response. Infection after 14 weeks, causing same symptoms in both groups (Palzer 2009).

The 20 steps of Madec provide the basis of good stockmanship and every pig farm manager should oblige his employees to follow these rules. PCV2 vaccination on top of the 20 steps provides ammunition to fight PCV2 virus specifically.

A good immune response following PCV2 vaccination is basically influenced by three different and independent factors: the piglets, the vaccine used and the vaccination procedure. For the piglets it is clear that they should be healthy at moment of vaccination. A PRRS virus infection at the moment of PCV2 vaccination can have a negative impact on the immune response depending on the infecting PRRS virus. The same is true when the young piglets are exposed to mycotoxins but these toxins use a completely different pathway, so it can even be in addition to each other!

The level of maternally derived (PCV2-)antibodies (MDA) is, for many of us, also important. When MDA levels are low the response to vaccination is good but the (MDA-) protection against field infection is absent. When MDA levels are high there is good initial protection but also interference with the response to vaccination (see Fig. 1).

When both high and low levels of MDA are present in a batch of piglets, you basically have sub-populations of protected and not protected piglets.

After vaccination of such a batch you end up again with subpopulations later in life. Using a potent vaccine may overcome such a situation just as creating uniform antibody titers in the breeders and plan the piglet vaccination based on MDA titers.

Vaccination procedure

The vaccination procedure and technique used is an undervalued process on many pig farms. On a 5,000 sow unit, producing 24 piglets (weaned) per year, 10,000 piglets have to be vaccinated every month! Because it is routine work, the farm manager is often not present, or only for a short period. The vaccination is done by the same staff that quickly hates the noise, the smell and the physical labour.

Getting it done as quickly as possible is the goal. To reach the required quality standard of the operation is often secondary. The result is that not all piglets receive the vaccine in a correct way.

So we have three different independent factors and all are capable of creating subpopulations by themselves. Just imagine the possible additive effect of these three.

PCV2 infection is costly. PCV2 vaccination is also costly. To have the optimal return on investment all aspects of PCV2 virus control should be considered. The ultimate aim is to avoid PCV2 virus susceptible subpopulations in your herd – at any moment! ■

Practical Health

Insight (13)

Anything new on App?

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To answer the question right away: not really. Infections with Actinobacillus pleuropneumoniae (App) bacteria have been with us for ages and they are still the cause of significant economic damage. Why we have not been able to make more progress in counteracting this financial burden in recent years is debatable. Marcello Gottschalk from Canada gave a very nice overview lecture at the ESPHM 2015 symposium in Nantes, France, with Arnaud Lebret following this presentation with practical App cases from France. These two presentations taught us that it is good to refresh our memory and to realise that App is still there, causing significant problems and that it is not easy to control. So what is the problem?

As we all know we have 15 serotypes of App spread all over the world. Australia has a different serotype 15 and because Australian pigs have a tendency to stay or end their life in Australia, we see very few cases, if any, of this specific serotype outside of Australia.

This serotype classification is next to the biotype classification (Biotype I and II) which is based on the need for an in-vitro (in the laboratory) growth factor that certain serotypes require to grow on the plate and others not. But also here within some serotypes you can have both biotypes. The importance of this observation is that you might fail in culturing the suspected App serotype if you assume it is a Biotype II, so you do not add the growth factor, but in fact it is a Biotype I and requires the growth factor.

Next to this, the geographical spread of disease causing serotypes is very much region dependent and different serotypes in different regions might show a different level of pathogenicity. To make it even more complex, the same serotype in the same area may be pathogenic on one farm and only cause minor problems on another farm in the same region. In short, there is an enormous amount of variation in presence, pathogenicity and isolation requirement between the different serotypes. This could very well be the reason for the lack of interest by the scientific community. When the enemy is so flexible that we cannot beat them, then we just have to live with it!

Diagnostics

Due to all the above mentioned characteristics of the App serotypes, efforts have been made to improve on the diagnosis, but it has proved not to be so simple as we had hoped for. Culturing to identify carriers is still done but has to reckon with from which tissue we will take which sample and of course with the requirements for growth.

Culturing is essential when autogenously based vaccines are considered. Serology is an option but has to take the serotype characteristics into account. ELISAs based on ApxIV avoid this serotype specific aspect but are not very sensitive and can therefore only be used on a herd basis and not on an individual animal basis.

Measuring antibodies after vaccination is only successful when the coating of the ELISA plates matches with the antibodies that are induced by the vaccine.

For example, coating the wells of the plates with a serotype 2 and then trying to measure antibodies induced by an Apx toxin vaccine, will not be good enough.

Absolutely nothing new?

Of course there are still some new things to mention. We have seen the introduction of some new vaccines.

We now have the ApxIV test kit at our disposal. There is general agreement that maternally derived antibodies do play a major role in reduced vaccine efficacy.

When breeding stock vaccination is indicated and executed you have to postpone the timing of the piglet vaccination. And, last but not least, we have seen the introduction of a slaughter line inspection protocol to assess the severity of an infection on a farm that is causing pleurisy and which might be related to an App infection.

This Slaughterhouse Pleuritis Evaluation System (SPES) was developed in Italy by the group of G. Merialdi, M. Dottori and P. Bonilauri.

During routine slaughterhouse inspections to check for lung lesions caused by Mycoplasma hyopneumoniae they realised that they could use their time even better by checking the whole lung for lesion and not for the typical M. hyo lesions only.

So they developed a system that looked at the whole lung and for a certain location the lesions were considered to be of M. hyo origin and for other locations and classification, an App infection belonged to the possibilities and should be investigated further. Fig. 1 shows an example and this split in location.

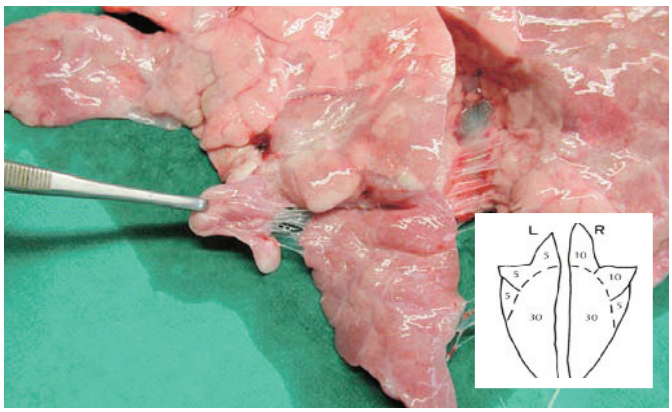
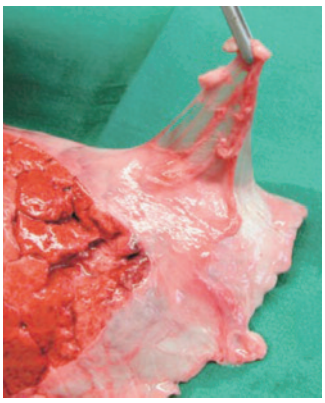


Fig. 1. M. hyo type of pleuritic lesion and schematic border with pleurisy originating from other pathogens. Typical location for a M. hyo induced lesion. A score of 1 in the SPES scoring system. Inset, the dotted borderline between lesions induced by M. hyo and other pleurisy inducing pathogens.

Fig. 2. Pleurisy induced by other pathogens. Dorsal/caudal location of pleurisy. Indicative for an App infection but other pathogens cannot be excluded. Further investigation is required. In the SPES scoring system this will be a 2 or a 3 depending on the total affected surface and if both lobes are affected.



They made a scoring system ranging from 0 to 4, with 0 of course for the lungs without any lesion. Score 1 is reserved for typical M. hyo lesions, and will thus not count for assessing the (other than M. hyo-) pleurisy incidence. Scores 2-4 are given in relation to the severity of the observed pleurisy (see Fig. 2).

A relatively simple exercise that can be done with the slaughter line running at its normal speed.

Normally the team consists of two persons, with one doing the scoring and informs the score to the second person that also notes down the animal identification number.

A worldwide tool

This SPES system is now used in a number of countries all over the world and has proven to be a useful tool to get more insight into the animal health status of the pig farm.

It gives direction to further diagnostic actions and information on the success of a treatment regime can be gathered. Next to this, it does not matter which pathogen is causing the observed pleurisy. However, pleurisy always costs money so this SPES type of information is important.

Pleurisy is a reason for a reduced ADWG and for an increase in antibiotic usage and it will lead to cleaning of carcases, at a cost, in the slaughterhouse. App infections have already been with us for a long time and are often frustrating, but we have to stay alert! ■

Practical Health

Insight (14)

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ATROPHIC RHINITIS

One of the best documented diseases that affects our pigs is Atrophic Rhinitis (AR). The groundbreaking work of Dr Marten de Jong, carried out at the end of the last century, revealed the disease causing mechanism and this is still recognised as the basis for AR related clinical symptoms. AR is present in different forms ranging from mild to very severe but in all its manifestations it is costing money. So what do we know about the way AR develops?

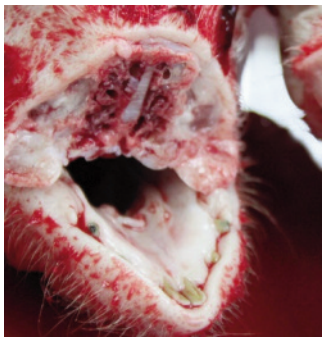
In the very young piglet we see damage to small parts of the nasal mucosa. This can be caused by many different factors but an infection with Bordetella bronchiseptica is the most likely one. Other infectious and non-infectious factors include acid fluid and when too high levels of CO2 or NH3 are present.

When Pasteurella multocida (Pm) bacteria are present it will colonise on these damaged mucosa. It is essential that this Pm produces the dermo-necrotic toxin (DNT, and Pm DNT) for atrophic rhinitis to develop. Again this all has to happen in the young piglet.

The Pm DNT has a very specific action. This toxin basically activates cells that resorb the bone structure (so called osteoclast cells) through the excretion of enzymes. Next to that they dissolve the bone calcium salts by excreting acids. This all happens in the young pig that should be very busy building up bones! The DNT works very locally and because the Pm DNT colonises the nasal mucosal, the damage is noted in the bony structure (conchae) that form the nasal cavity.

At IPVS in Barcelona a paper was presented in which the researchers reported on the effect of daily injection of Pm DNT in the hind leg of a dog. They were capable of inducing the same kind of bone resorption in this hind leg as we see in the case of AR in our pigs!

Infection with Bordetella bronchiseptica only causes reversible AR, while the involvement of PM DNT leads to non-reversible AR.



A case of atrophic rhinitis found during routine post-mortem.

The photo shows a practical case of deformation of the conchae in the nose of a pig. This was found during a routine post-mortem carried out in a diagnostic laboratory in Thailand.

The most often used location to cut this section of the nose is just behind the second premolar. Before cutting the nose it is, however, important to look for the other characteristics that can be observed in a case of AR.

Most typically is a shortening of the upper jaw with the result that the lower jaw becomes 'longer' than the upper jaw. This can easily be seen when the location of the front teeth of both upper and lower jaw are examined.

Normally the front teeth of the upper jaw are falling over the front teeth of the lower jaw. In a case of AR, however, the front teeth of the lower jaw fall over the front teeth of the upper jaw. By retracting the skin at the side of the mouth, this can be noted. This is easy to check even when the pigs are still in their pens. Even easier is to look for a dirty line on the skin between the corner of the eye and the nose.

Because of the deformation of the nose the canal (the so called ductus lacrimalis) that runs from the corner of the eye to the inside of the nose becomes blocked.

This means that the normally produced fluid that smears the eye cannot be disposed of by normal means and, as a consequence, it runs over the skin and dirt sticks to it, hence the dirty line. There can be more reasons for this line but when AR is suspected this dirty line (that can be seen from a distance) is a very good reason to inspect the animal more carefully. Last but not least, the text books will mention a blood tinged nose but this is a rare event. The position of the teeth and the dirty line are seen more frequently.

Snout score	0	1	2	3	4
Decrease ADG (%)	0	0	-3	-6	-12

Table 1. Relation between snout score and average daily weight gain.

An economic issue?

The nasal cavity with its mucosa is an important part of the very basic (innate) immune system of every animal, including humans. Its large surface due to all its curves and its high concentration of blood vessels makes it an excellent trap for all kind of pathogens that are then eliminated. This is impaired when AR strikes.

When the conchae are affected it leads to larger spaces and less contact between the incoming air (possibly with pathogens) and the mucosal lining. A second consequence is that colder air gets into the lungs, also with possible negative implications. This all results in a higher level of viral and bacterial infections in the lungs. The lungs of our pigs are renowned for their limited extra capacity. A lung infection, which is of course already of economic importance by itself, leads almost immediately to a reduced intake of oxygen and therefore to growth retardation.

AR can range from mild to severe so different scoring systems have been developed. Fig. 1 shows such a scoring system. This system is important because it gives an indication of the level of economic damage that can occur. Table 1 shows the relation between the scoring system and growth retardation.

How to check for AR?

There are different ways to check for AR related damage. In a lot of countries most farmers and veterinarians know where to look and will check the pigs for signs of AR during farm visits. There are also countries where additional checks are done.

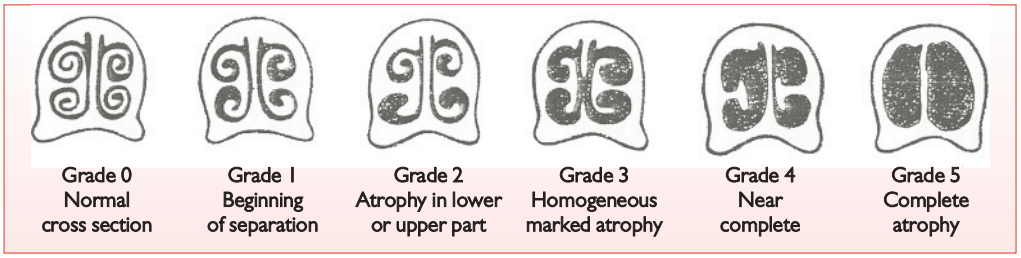
During routine post mortems a check on AR should be included.

There are countries where routine inspection for AR is done in the slaughterhouses by using special equipment. Power driven cutters cut the noses of pigs in a split second so that the nasal cavity can easily be examined.

How to prevent AR?

When it comes to prevention, we see major differences between the continents. Ranging from depopprepop to simple control by vaccination to eradication of Pm DNT from the farm by using certain vaccines and the introduction of PM DNT free gilts. These different schemes have all been successful. It is just a matter of choice and any choice is good, as long as it prevents the economic damage caused by atrophic rhinitis. ■

Fig. 1. Example of an atrophic rhinitis scoring system.



Practical Health

Insight (15)

ASF: THE HUMAN FACTOR

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It is no wonder African Swine Fever (ASF) attracts a lot of attention in our swine world nowadays. It is a devastating disease with no treatment and no vaccine available to fight or prevent infections with this virus. It is still expanding its presence and there is a lot of discussion between policy makers and their scientific advisors on how to control the spread of the disease. In addition, the general knowledge of swine farmers, in those countries that are currently under the threat of ASF, on aspects like biosecurity and ways of spreading this virus is highly variable. This is the key weak element in the control of ASF.

ASF was first described in Kenya in 1921 but the first case was most probably seen around 1907. In total, 22 different genotypes are described and they are based on differences in the major capsid protein. The disease was confined to the African continent until 1957 and all different genotypes are present in Africa.

The African wild hog population (warthogs etc) is the main reservoir of ASF virus beside the soft tick, and outbreaks in the domestic swine population are frequently reported.

From 1957 onwards ASF was introduced to South America, the Caribbean and Europe – starting with Spain and Portugal with material coming from Angola. ASF was successfully eradicated in those European countries by the mid 1990s by a slaughter policy only.

The start of the most important recent outbreak occurred in 2007 in Georgia. A genotype II ASF virus was introduced in the local swine population from Eastern Africa. This was most likely due to swill feeding with material originating from a ship travelling between ports in the respective countries. From here the virus spread to Armenia and all over Russia. Wild boars played no role in the long distance transport of infectious material, here it was purely the human factor.

Outbreaks of ASF were reported in Ukraine in August 2012. Belarus followed in June 2013 and in 2014, the presence of African swine fever was reported in Estonia, Latvia, Lithuania and Poland (see Fig. 1).

In regional (short distance cross-border) infections the infected wild boar population will have had its impact.

Reason for ASF spread

The main reason for the spread of ASF is lack of knowledge or simply ignorance. It is extremely difficult to have any control program for ASF in place when the pig farming community is not strictly adhering to the very basic rules of biosecurity. After the last outbreak of ASF in the Netherlands in 1986, swill feeding was completely forbidden. Allowing swill feeding under the condition that the swill is cooked before feeding to the pigs, is difficult to control and easy to breach.

The FMD outbreak in the UK in 2001 was also thought to be related to feeding uncooked swill with devastating consequences.

The 1997/1998 CSF virus outbreak in the Netherlands is also related to feeding contaminated material to pigs.

These three examples (ASF, FMD and CSF) make it absolutely clear that the human factor in spreading these diseases is of prime importance. It is no wonder that, when looking at biosecurity protocols, activities involving human behaviour get so much attention. It is also no wonder that many backyard farms, with often only a very small number of pigs, are present in the current regions where ASF is causing problems.

In the epidemiology of ASF virus infections, local conditions play a crucial role. Besides swill feeding contact with the local (ASF virus infected) wild boar population is also important.

Contact here should be seen in the widest possible context. Often in these rural areas the farming community is also involved in wild boar hunting, making transport of ASF virus infected material from the hunting field to the swine farm a realistic option.

Secondly, on these smallholder schemes, wild boar access to the domestic swine population is not well guarded.

Sometimes litters are born from a domestic sow with clear evidence that the male was a wild boar! Wild boar are present, in large numbers, in the border regions between the affected East European countries. Fig. 1 also shows that the outbreaks are concentrated in the different border regions. Besides the human factor, wild boar is an important source for regional spreading of ASF virus. Humans are the factor in long distance spreading of ASF virus.

Warthogs roaming around freely in the bush in Kenya.

Level of mortality

In the current East European situation it was observed that the ASF virus strain that is circulating is causing a near 100% mortality in affected (sick) pigs (both in wild boar and domestic pigs).

However, the morbidity (number of animals in a population that become sick) is low making the total mortality low. It is estimated at even less than 5% of the affected population. This is due to the fact that this ASF virus has a very low level of contagiousness. Direct contact with meat, blood, body fluids, etc or contaminated fomites or direct contact between sick and healthy animals is necessary.

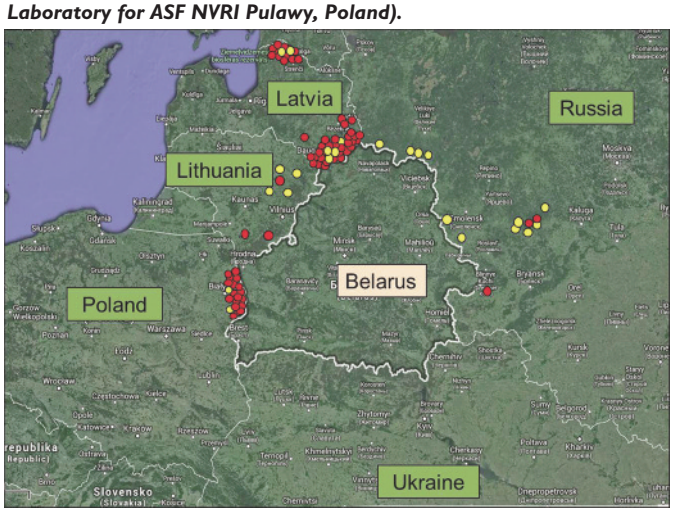
The situation so far has also revealed that the majority of the cases occur in the wild boar population. With the low level of mortality it will be very, very difficult to kill the whole wild boar population in order to get ASF virus out of the wild boar population and the region. Hunting is an option but has its limitations.

Those with experience in wild boar hunting will agree that killing all wild boars, in an open region, by hunting only is extremely difficult.

The only option we have is to create a physical barrier between the farm-kept domestic pig population and the wild boar population, including their meat and other leftovers from slaughtering.

That barrier depends on us, humans, which is essentially the weakest factor! ■

Fig. 1. The geographical spread of recent outbreaks of ASF in East European countries, including 2015 data. The yellow dots show the locations where ASF was detected in the domestic pig population. The red dots indicate detection of ASF in the wild boar population. The outbreaks occur mainly in the border regions (National Reference Laboratory for ASF NVRI Pulawy, Poland).



Practical Health

Insight (16)

HAEMOPHILUS PARASUIS

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Haemophilus parasuis (H. parasuis) is one of the smaller bacteria that is affecting our pigs and this little bug is a continuing source of problems on pig farms across the world, both on low and high health status farms. It used to be a disease popping up after stress encountered by, for example, transportation. Typically problems occur when clean, unprotected replacement gilts or boars enter a H. parasuis infected farm. Nowadays, it is a much more commonly encountered disease, which makes a correct diagnosis also more important.

The disease is characterised by an acute spreading of the bacteria to the major membranes that are covering vital organs.

The medical terminology describing the infections of these vital parts is covered with 'fibrino-purulent poly-serositis' like around the lungs (pleuritis), around the heart (pericarditis) and around the intestinal organs (peritonitis), including joints (arthritis) and the brains (meningitis). The photograph, right, shows lesions that can be seen when H. parasuis is causing problems.

Strain differences

There are 15 different serovars known of H. parasuis and they behave quite differently (see Table 1). This is next to the experience that of all cultured isolates roughly 35% of them are classified as 'non-typable' simply because they do not fit with the current method of classification.

It requires a special laboratory technique to grow H. parasuis and when a pig is treated with antibiotics before a sample is taken, the chance to isolate the H. parasuis bacteria is very small.

Last but not least, H. parasuis can also be found in healthy pigs. Samples taken from the upper respiratory tract and analysed for example by routine bacteriology or a PCR method, can be positive (up to 100%), while no clinical cases of H. parasuis are seen on the farm.

H. parasuis is a normal inhabitant of the upper respiratory tract of the pigs. Only when the situation changes or when the combination of a stress factor combined with a new introduction takes place, will clinical disease become evident. It is clear that in this confusing situation we need additional diagnostic tools.

New developments

Researchers have discovered that when an infection takes place with H. parasuis or when pigs are vaccinated against H. parasuis, a certain type of antibody is detectable in the blood of these pigs.

These specific antibodies are not seen when H. parasuis is normally present in the upper respiratory tract.

This makes it possible to differentiate between a 'normal' detection of the bacteria by, for example, PCR on nasal swabs and getting more evidence for the 'suspicion' that H. parasuis is involved in the clinical picture that is observed.

These specific antibodies are directed against a certain protein that is specific for H. parasuis and is called OppA (oligopeptide permease A).

This OppA is located inside the H. parasuis bacteria and is presented by the macrophages to the immune system of the pig during a clinical infection with H. parasuis.

This discovery made a whole new era of investigational work possible.

Table 1. Differences between different H. parasuis serovars.

H. parasuis Serovar	No of strains evaluated	Virulence
1, 5, 10, 12, 13, 14	10	Death within 96 hours
2, 4, 15	10	Severe polyserositis and arthritis at necropsy
8	1	Mild clinical signs and gross lesions
3, 6, 7, 9, 11	8	No clinical signs and gross lesions

Typical polyserositis, as is often seen when pigs are suffering from H. parasuis infection.

The same antibodies against OppA are present after a vaccination with H. parasuis vaccines, irrespective if this is an avirulent live or an inactivated (whole-) bacterial vaccine.

Next to this all researchers have shown that this OppA is specific for H. parasuis and is not present in a series of other bacteria like those belonging to the Actinobacillus group, or Bordetella, Streptococcus, Pasteurella etc.

Response to vaccination

It was shown that vaccines containing a highly purified OppA subunit induce a serological response in vaccinated pigs (IgG was detected after vaccination), but this response did not provide any protection in a vaccination-challenge model.

It is generally accepted that protection against clinical symptoms induced by H. parasuis is based on circulating antibodies.

By using normal H. parasuis vaccines and this highly specific OppA ELISA for checking post vaccination serology, the researchers could follow vaccination responses and create different profiles in breeding stock and their piglets.

After vaccination of the breeders the induced antibodies (measured by the OppA ELISA) were transferred to the piglets (so called MDA or Maternally Derived Antibodies).

By using a PCR test on nasal swabs the presence of H. parasuis in the upper respiratory tract can be detected. When using the correct bacteriological procedures the involvement of H. parasuis in the infection can be shown.

These three different tests provide different information and are fully complementary.

Vaccination induces protective immunity but when no follow up vaccination is given this immunity weans off in the breeders and they will no longer transfer any MDA to the piglets. These breeders will become susceptible to H. parasuis infection again.

MDA will protect the piglets against an early infection with H. parasuis but this passive protection will last for a couple of weeks only, normally until the beginning of the nursery phase.

When these piglets are raised on H. parasuis infected farms, vaccination of the piglets is indicated. H. parasuis is transferred from the breeding stock to the young piglets in the farrowing unit.

The H. parasuis OppA ELISA provides us with a new specific tool to monitor our pigs for vaccination and infection control.

The H. parasuis PCR will show the presence of the pathogen, irrespective of any H. parasuis related problem but provides us with a clear warning! Finally bacteriological examination, together with the clinical picture and the post-mortem findings, will close the case.

Indeed exceptional diagnostics! ■