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Review Article

Prevention and Control of Respiratory Diseases Excluding *Mycoplasma Hyopneumoniae*

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Introduction

Significant changes in respiratory disease have occurred over the last 20 years. There are two primary reasons for this. In the first instance, there has been the occurrence of two major worldwide plagues-PRRS and PCV2-associated diseases. The second reason has been the considerable advances in vaccination, which have become available for some of the respiratory diseases, in particular *Mycoplasma hyopneumoniae*. Vaccines have also become available for porcine reproductive and respiratory syndrome virus (PRRS), influenza viruses (outside UK) and probably in the near future against porcine circovirus type 2 (PCV2).

Over the last 20 years the major infectious players in respiratory disease have had a reduced individual importance but their overall significance has been subsumed collectively into the Porcine Respiratory Disease Complex. This rapidly developed in the early nineties following the introduction of PRRS virus into the country and has subsequently been further compounded by the appearance of PCV2 infections. The major players in respiratory disease are shown in Table 1. The major clinical signs are shown in Table 2 and the ages at which the diseases occur is shown in Table 3.

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Table 1: Respiratory tract pathogens of the pig.

Primary	Viruses
	(Exotics; CSF, ASF, SVD, FMD, AD)
	PRRS Swine Influenza. (H1N1, H3N2 195852, H1N2)
	PRCV PCMV
	Porcine circovirus type 2
	Mycoplasma
	M. hyopneumoniae
	M.hyorhinis
	M.hyosynoviae
	Chlamydiae
	Fungi *Aspergillus*
	Bacteria
	Actinobacillus (Haemophilus) pleuropneumoniae
	Haemophilus parasuis
	***Pasteurella multocida* type D and type A**
	Actinobacillus suis
	Bordetella bronchiseptica
	Streptococcus suis
	Salmonella cholera-suis
Secondary	All the above plus many others, particularly *A. pyogenes*
Unknown status	Pneumocystis
	Encephalomyocarditis virus (EMCV)
	Paramyxovirus
	Blue-eye
	Fusarium moniliforme

*The serious primary pathogens are outlined in bold

Table 2: Major respiratory tract signs of the pig.

Primary clinical signs	Type	Site in respiratory tract	Agent (s) involved
Pyrexia Nasal discomfort	Ulcerative (Vesicular)	Nostril nasal cavity	FMD SVD
Pyrexia Haemorrhage	Haemorrhagic	All levels but particularly larynx-tonsil lymph nodes	Hog cholera African swine fever (BVD in pigs)
Sneezing	Rhinitis	Severe nasal cavity/lungs Mild nasal cavity/lungs Mild-severe nasal cavity progressive	Aujeszky's PCMV *B. bronchiseptica* *P. multocida* Toxigenic strains
Coughing Pyrexia	Tracheitis Bronchitis	Trachea Bronchi and below	Swine influenza 195852 *B. bronchiseptica* bronchitis
Dyspnoea Coughing?	Bronchiolitis (Enzootic pneumonia)	Small bronchi. Bronchioles Alveoli	*M. hyopneumoniae* *M. hyorhinis* Secondary bacteria PCV
Dyspnoea	Alveolitis Suppurative Necrotising Haemorrhagic	Alveoli	*P. haemolytica* *P. multocida* *S. suis* *H. parasuis* *A. suis* *A. pleuropneumoniae* *H. parasuis*
Dyspnoea	Interstitial pneumonitis	Alveoli	Swine influenza H1N1 Classical H3N2 PRRS PRCV

Table 3: Age specificity of respiratory disease in the pig.

Age	Common?	Disease severe / rare	Unimportant	Rare
First week	PCMV (inclusion body rhinitis) *B. bronchiseptica* PRRS	 (SF,ASF,SVD,FMD)	 *H. parasuis* *P. multocida*	Barking piglets ? Reovirus Adenovirus
Second week to weaning	*B. bronchiseptica* Streptococcal infections PRRS Swine influenza 195852	→ → (SF, ASF, SVD, FMD, Aujeszky's)	PCMV Enzootic pneumonia	Reovirus Adenovirus *H. parasuis*
Weaned pigs	 Enzootic pneumonia Atrophic rhinitis Salmonellosis Swine influenza 195852	Aujeszky's → → → →	*M. hyorhinis* Swine influenza HINI Swine influenza H3N2	Gas poisoning Pneumocystis
	Actinobacillus pleuropneumoniae PRRS	 → (SF,ASF,SVD,FMD)	Metastrongylus Ascarids	Fusarium Toxicity
Adults	PRRS Swine influenza 195852 Enzootic pneumonia breakdowns	→ → →	 Metastrongylus Ascarids Pulmonary oedema	

Biosecurity:

This is the cornerstone of eradicating disease and has been completely discussed in paper 1. Biosecurity is the main prevention for the control of swine respiratory disease and the rest is based on an effective control policy, vaccination policy and efficient management and environmental control.

It is still true that the only way that you can continue to succeed with a sustainable health programme is to have high herd health introduction through a true health pyramid with the absence of specific infectious agents. In this pyramid there should be particular attention to the critical points of vertical disease transmission i.e. those places that lead to disease transmission to more than one site.

Management and environmental control :

The arguments have been discussed for years and have not changed over 50 years. We need to keep pigs warm for economic growth, but we need to ventilate for respiratory health. This has been described in detail in paper 1 but a summary is provided here with the major recommendations shown in Table 4. The most important criteria for providing a "pneumonia-free" or reduced pneumonia environment were outlined by Sainsbury and Sainsbury(1979):- Note how similar these are to the comfort plans put forward to reduce PCV2 infections proposed by Madec et al. (1999), yet they were proposed years beforehand. In fact the lecture notes on pigs given by Professor Jet Jones to the final year students at the Royal Veterinary College in 1967 already contained these same points.

Table 4: Respiratory health recommendations

(1) Small pen groups are essential (10-20)
(2) Pigs should be clear of their excreta, and the lying area should be a clearly demarcated one
(3) Ventilation is usually under mechanical control and requires care to ensure constant draught-free air movement over and around the pigs
(4) Air should not travel to the pigs after it has been over dung, urine or a slatted area over a slurry channel
(5) Some bedding in the lying area will usually improve comfort and hygiene;
(6) It is preferable for the dunging area to be outside the lying section of the building
(7) The number of pigs in one air space should be limited (100 - 200);
(8) For the lying area to be dry, the slope on the floor must be adequate and the troughs and water bowls sited so that the floor does not become wet
(9) Since the air space must be relatively large, (in excess of $3m^3$ per pig) thermal insulation must be good
(10) Ventilation and ventilator controls must be simple and effective
(11) Pigs within a building should preferably be of similar age and weight so that the environmental requirements for each group are similar.

There are essentially four ways to use management techniques to prevent respiratory disease. Early weaning is not allowed in the EU and therefore cannot be used to control mycoplasmosis and other infections. In many cases there is also not enough land to allow for separate site production as in the USA. The disadvantage of these techniques of early weaning and separate sites of production is that there is no complete control of the agents which are picked up from the sow (the "suis-cides" -*A. suis*, *S. suis* and *H. parasuis*).

Firstly, use all-in/all-out to control pathogen build-up. This is the single most important weapon in health control. This facilitates cleaning, disinfection and pathogen removal. Most importantly it ensures that the group is mixed and moved together as a group, which considerably reduces the stress of production and that there is no cross infection with different ages of animals. At the very most three weeks production should be contained in the group and two weeks only is better. Animals that fall behind in growth rate should be removed to the hospital area for eventual finishing rather than put into the next group.

Secondly, keep the herd closed if possible with only the import of semen that is of high health status being used. If you have to import gilts, then do so from the same supplier of similar health status to yourself and preferably in large groups infrequently, with full quarantine and isolation before integration in to the herd. What this means in fact is keeping the herd stable.

Thirdly, keep the stocking density at a reasonable level, as this is the key to the background levels of gas, dust and both non-pathogenic and pathogenic organisms that the pig will have to deal with. Usually a finishing pig requires a minimum of $0.7m^2$ space and $3m^3$ of airspace.

Fourthly, keep a close eye on the other inter-current diseases or disorders e.g. parasitism or nutritional inadequacies such as vitamin E/selenium that will predispose to secondary disease.

Controlled exposure:

This has been used to prevent HPS infections by using a low dose of live organisms to five day old pigs (Oliveira et al., 2001) and reduces mortality from 4.54% to 1.66%. It should not be used when you suspect that there is an active PRRS infection in the herd.

Prevention and treatment:

Despite all these general attempts, it is likely that prevention through vaccination may have to be used. Possibly with endemic infections, medication may have to be used as a preventative, particularly at those times when infections are acquired i.e. after mixing, moving or weaning. Mostly however, medication will be for therapeutic reasons. It is likely that at times there will be the need to treat with antimicrobials particularly to deal with bacterial infections such as *P. multocida*, *Actinobacillus pleuropneumoniae* and *Haemophilus parasuis.*

Firstly, the ideal respiratory treatment has to be fast acting, as most animals are severely affected. Animals can very quickly transmit the infection to other pigs in the pen and may even die. So speed of action is the most important feature of treatment.

Secondly, antimicrobial sensitivity is also important so always collect samples from untreated animals for sensitivity testing. This is in case the antibiotic used has no action against the organism subsequently found to be causing the outbreak or because the agent in that specific case is resistant.

Thirdly, the antibiotic must be in contact for sufficient time with the microorganism to inhibit it or preferably to cause its death. If the disease is serious with inappetance then farmers will inject the pigs especially if they are moribund but stockmen like it less if they struggle and will quickly resort to the often less effective water and feed formulations to treat or prevent the infection in the rest of the pigs. If there is a palatability problem then it is possible that affected pigs may not take in sufficient quantities of the drug to achieve therapeutic levels, but these cases are rare and more often than not are associated with water medication.

Many farmers elect not to give second parenteral injections so the development of single injection antibiotics with broad spectra of activity and a prolonged release over several days are welcome additions to the therapeutic armoury.

Intervention :

In the USA nowadays there are systems introduced for identifying when the level of morbidity exceeds 2% and the mortality exceeds 0.5%. At this point, which is known as the "flag" level, the service staff do a site inspection. This may or may not involve post-mortem examinations. Samples should be taken before the treatment is commenced particularly for diagnostic bacteriology and bacterial sensitivity testing. If the diagnosis is still unclear, they may or may not autopsy some untreated clinically affected pigs. Digital cameras are used to record clinical and pathological findings, and these can if necessary be forwarded to consultants. An initial diagnosis is made and the appropriate treatment is commenced.

It is especially important to realise that clinically ill animals will not eat and the initial treatment in serious outbreaks will have to be by parenteral methods i.e. intramuscular injections. With the onset of a successful initial response a longer term solution or prevention can be considered as necessary.

Vaccination :

Mycoplasma hyopneumoniae (M. hyo): Probably the biggest single plus in the treatment and control of respiratory disease in the last twenty years has been the development of vaccines for *M. hyopneumoniae.*

Atrophic rhinitis is caused by a mixed infection of *B. bronchiseptica* and *P. multocida* and usually starts in young pigs from 7-10 days of age. Clinically there is sneezing and the bacteria colonise the nasal mucosa and the toxins, usually from Type D *P. multocida*, which causes the destruction of the turbinate bones. The main nasal bones may grow unevenly causing twisting and foreshortening as the pig grows. Vaccines contain the toxoid of PM type D dermonecrotic toxin and inactivated BB cells and are given to sows and gilts to increase protection of the piglet. They can also be given to piglets if immune.

Actinobacillus pleuropneumoniae can cause a primary acute necrotising pneumonia on its own or in combination with *M. hyopneumoniae*. Some serotypes given in artificial infection studies can cause death within 24 hours, due to the toxic shock produced by its toxins. Fortunately, it is not as widely spread as enzootic pneumonia, but usually is a more severe infection. A number of vaccines have been produced, but none commercially at the moment, and do not offer complete protection against all serotypes. New vaccines bases on the toxins have been promised but are not yet forthcoming. If there is an on-going problem then autogenous are the most promising for control, as long as the strain used is the one that is causing the problem.

Streptococcus suis is quite well spread in many herds but did not always cause clinical problems. Commonly, *S. suis* type 2 was associated with meningitis in weaner and grower pigs, which were overcrowded. Following active PRRSV infection, it can cause coughing in young piglets from 16 days of age, but occasionally outbreaks of meningitis in finishers. Commercial *S. suis* vaccines offer generally poor protection and no effective vaccine for all strains is as yet available, but experimental ones now seem more promising. If there is a problem then autogenous vaccines may offer a solution.

Haemophilus parasuis also caused clinical signs in weaners and growers, especially arthritis (Glässers disease), when MDAs faded. All the three suis infections are thought to be transmitted from sows to piglets in the first week of life. *H. parasuis* vaccines are generally based on serotype 5 (Glassers serovar), but cross protection may cover approximately 60% of serotypes, although autogenous vaccines have claimed better success. Stabilisation of PRRS infection in the sow herd, by vaccination or even eradication, is important to prevent the early pre-weaning infections.

The wide range of serovars (15) has slowed the rate at which the use of a single vaccine for the control of HPP has been developed. The strains differ in their antigenicity, and it is likely that the virulence and

immunoprotection are closely related. Homologous protection seems good but there are considerable differences in the effectiveness of heterologous strain protection. For example the Porcilis Glassers vaccine from Intervet gives protection against serotypes 1, 12, 13, and 14 as well as serotype from which it is produced. This protection probably also lasts until the end of finishing at 21 weeks.

The selection of commercial or autogenous vaccines is an important decision. The other important decision is the timing of the vaccination in relation to maternal immunity and peak of piglet mortality.

It would appear that the progeny of unvaccinated sows have maternal antibody for only 2-3 weeks. They do not prevent colonisation but they do prevent clinical disease. If animals of 2-3 weeks of age are affected, then vaccinate the sows. If piglets have the infection 4-6 weeks after weaning, then vaccinate at weaning and again two weeks later. It is not a good policy to do both as the maternal antibodies induced may interfere with the subsequent piglet vaccination.

An HPS-*Erysipelothrix rhusiopathiae* (ER) bacterin available in the USA has been shown to give protection for at least 162 days against the ER component and 19 weeks against the HPS component following a single 2 ml injection given at 3-4 weeks of age.

A recent report has suggested that neither the commercial nor the autogenous vaccines tested reduced nursery mortality, whereas controlled exposure of piglets to the virulent *H. parasuis* strains present in the herd reduced mortality by 55%.

PCV2: At the 18th IPVS meeting in Hamburg two groups of authors suggested that both live (Charreyre et al, 2004) and dead PCV2 (Halbur et al, 2004) vaccines may work to control PCV2 associated diseases. Vaccination for the other endemic diseases on the farm should continue, as there is still no definitive evidence that vaccination predisposes to PMWS. For PRRS and EP, the continuance of vaccination is essential as both of these diseases are capable of triggering PMWS. In some instances they do resemble chronic Lawsonia sufferers. They also rarely find PDNS, but they do find PRRS and PCV2 occurring together (52%), *M. hyopneumoniae* in 36% and bacterial pneumonia in 22%, but SIV/PCV2 as a combination in only 5.4% and PCV2 alone in just 2%. Experimentally, the combination of *M. hyopneumoniae* and PCV2 produces a more severe infection. There are more DNA copies in serum, a longer PCV2 viraemia, more severe lung lesions and a higher level of PCV2 by IHC in the lymphoid areas (germinal centres) and lung.

Of great topicality is the question of whether the role of vaccination for other diseases makes PCV2 associated diseases worse or better or has no effect. Again a recent experiment of Pat Halbur's has shown that vaccination for APP and *M. hyopneumoniae* with bacterins at 3 weeks and one day prior to experimental infection with PCV2 produced a longer viraemia, a wider range of tissues with PCV2, an increased area of lymphoid depletion, and an increased incidence of lympho-plasmacytic hepatitis. The same authors also believe that the use of common adjuvant commercial vaccines may also enhance the severity of PCV2-associated diseases. A further series of experiments has shown that the use of some of the adjuvants may be the cause of such worries. Up to 21 days post-infection, all adjuvants increased PCV2 lymphoid depletion.

In the later stages of infection, only the oil in water adjuvants increased the length of the PCV2 viraemia, the amount of the PCV2 in the serum and tissue and the severity of the lymphoid depletion. The question is therefore quite a simple choice - either the PCV2 could possibly be worse or the concurrent disease for which you are vaccinating is not being protected against. The best time of vaccinating is also in doubt but appears to be 2-4 weeks prior to the expected challenge. At the recent 19th IPVS in Copenhagen (July16-19,2006) there were papers reporting on the efficacy of new vaccines in use in Europe and the recently released vaccines for PCV2 in the USA also appear to be working successfully in the start of their clinical trials.

Swine Influenza (SIV): The difficulty of controlling swine influenza by vaccination comes from the fact that the viruses are always changing by either antigenic drift (perhaps 1% or 5-6 nucleotides change each year) or antigenic shift (when a re-assortment of genes takes place with a different species of the virus). Typical acute outbreaks are associated with finishing units, and were formerly in the winter months, but now may occur all the year round. In addition, the disease may be seen as a rolling inappetance or lethargy with a fall in reproductive performance in sows. Recent reports from the USA have suggested that the use of bivalent autogenous vaccines for both H1N1 and H3N2 have resulted in alleviation of the problem of sow infertility. Another recent US study has shown that they can also be used

with a multivalent leptospirosis and erysipelas vaccine, and that at least a 4-fold increase in titres was produced to all the vaccine ingredients. In most studies the younger the piglet challenged with virus, the higher the number of lung lesions, but in the vaccinated pigs, as the HI titres increased so the level of pneumonia (as judged by lesion scores) decreased. These studies have also shown that high maternal antibody titres also give good protection in the piglet to challenge and that the higher titres give greater protection. Ideally, in the USA producers will vaccinate the sows post-breeding with a bivalent SIV vaccine and then the piglets again prior to the disappearance of maternal antibody that occurs around week 13.

Vaccines for SIV are not used in the UK at present. Where SIV is a big problem the vaccination is used because it is the only way to guarantee an effective immunity. The incubation period is so short, the primary response does not prevent the appearance of clinical signs. Recent studies in the USA have shown that bivalent vaccines for H1N1/H3N2 have produced an effective local and serological response, did reduce the level of virus in the respiratory tract, and did stimulate memory lymphocytes. A vaccination strategy for the control of SIV infection should be instituted whenever there is a problem in the grow-finish units. It usually occurs here as the maternal antibody wanes in the later stages of the nursery unit. The real practical difficulty is in maintaining the vaccine when new strains emerge all the time.

PRRS: The current USA thinking is that eradication is the better bet than control because of the permanent ability of the agent to alter its genome with several variants appearing in the same herd and even the same pig. The major ability of the PRRS virus is to impair the reaction of the host to the virus, as it triggers neither a type or a type II response. This really means it avoids either a humoral or cellular response. Vaccination may therefore not produce a proper level of protection. Natural infection may persist with viraemia for several months and consequent shedding. Repeated natural or live virus vaccination may reduce the immune response. A killed vaccine such as Progressis (Merial) has safety advantages, in that there is no viraemia, and therefore no shedding or recombination with other PRRS viruses. Negative gilts now usually go into PRRS-positive herds and are quarantined and vaccinated. This avoids bringing in new strains of virus. The virus can however point mutate freely, and also recombine and can change also by deletion and insertion. A high degree of genetic divergence can be seen, even amongst the strains from the same farm. Despite all the work on bio-security, it seems that the major spread is via the pig.

Pig to pig contact, probably through the nosing of each other, is likely to be the major cause of the spread. As a result, it is the movement of pigs within a unit that is most important. Strictly all-in/all-out, with hospitalisation and isolation facilities and no moving of pigs backwards in the flow is absolutely essential. It may be necessary to depopulate and start again, but not without the necessary management changes. The real key is by stabilisation of the sow herd, which can only really be achieved by the use of one source of gilts, adequate quarantine (up to 8 weeks), if necessary positive gilts in to a positive herd and vice versa, and if not, making sure that all the animals are of similar status by vaccinating them. The results of vaccination vary but in any, care must be given after the maternal antibody has disappeared and as long as possible before the anticipated challenge as the neutralising antibodies take a long time to appear. In many cases the presence of viraemic pigs even from day one of birth makes it impossible to find a window in which to vaccinate them.

Conclusion :

With regard to PRDC as a whole, vaccinate for the disease you want to control not because of any decisions related to PCV2. This is unless, on the individual unit, you can convince yourself that the vaccines and vaccination practices are involved in the re-emergence of respiratory or wasting diseases. Secondly, if PRRS is involved, then stabilise the breeding herd, alter the mechanics of pig flow, particularly go to all-in/all-out by building with thorough cleaning, disinfection and drying and use vaccination. Always keep at the back of your mind the possibility of pigs or semen bringing in new virus strains (particularly as the EU expands). Most of all, try and put into the system the individual pig care that is present in organic units where PCV2 associated diseases and PRDC appear to be less prevalent.

Treatment :

Atrophic rhinitis: Should vaccination fail or not be used then control is by vaccination of the sows, but antimicrobials such as trimethoprim/sulphonamide

combinations, tetracyclines, amoxycillin even fluoroquinolones have been used.

Porcine respiratory disease complex: The Porcine Respiratory Disease Complex is essentially enzootic pneumonia, i.e. *Mycoplasma hyopneumoniae* with the addition of secondary bacteria such as PM, SS or HPS. In addition, the predisposing viral factors may be PRRS, or PCV2 or SIV. The key organism is the *Mycoplasma*, which is sensitive to many antimicrobials including the tetracyclines, lincomycin, pleuromutilins (tiamulin and valnemulin), fluoroquinolones (by injection), and macrolides (tylosin, tilmicosin and acetylisovaleryltylosin). However, they may not be so effective clinically where there are secondary bacterial infections except for the tetracyclines, tilmicosin, and tiamulin, given in the drinking water and fluoroquinolones given by injection. Following on from the initial therapy, the antimicrobials should be added to the feed for 1-3 weeks when you expect the challenge. This is usually after weaning in the late nursery or grower phase and the treatment can be deemed strategic use.

Continuous low-level drug inclusion is to be discouraged, but pulse dosing, although sometimes considered to be erratic, has proven quite effective under some circumstances, especially when the timing interval has been suitably established. However, if the necessary diagnostic work has been done to show when infection occurs, then it is easier to apply the correct medication programmes to prevent clinical infection. In some cases rather than anticipating the infection, prompt treatment can be given during the early stages of the infection. This normally has to given via the drinking water rather than in the feed, as there may be several days delay for the feed to be delivered and consumed. A suitable medicated-water delivery system needs to be available.

Streptococcus suis and Haemophilus parasuis: Both diseases respond well, prophylactically to penicillins, trimethoprim/sulphonamides, and *H. parasuis* to tetracyclines, but in the pre-weaned piglets it requires injections.

Post-weaning multisystemic wasting syndrome: As yet, there is no panacea for control of PMWS, probably because the exact cause is still unknown although all pigs affected with classical PMWS are PCV2 positive. In management terms, the Madec 20 point plan is used. This is very similar to advice given to Royal Veterinary College students in the 1960's by Professor J.E.T. Jones and is not new. Rarely if ever in the UK are more than 4-5 points carried out and for effective control it is probably necessary to include about 20 of these. These are described in Table 2.

A variation on this system was produced by the late Mike Muirhead and outlined just four main points 1) limit pig to pig contact, 2) remove "stress" from the system- it is a killer, 3) good hygiene and 4) good nutrition (Muirhead, 2002). Batch farrowing has proved useful, mainly because it allows proper cleaning, disinfection and an all-in/all-out policy to be adopted (Dennis, 2002). Partial depopulation and treatment with Pulmotil have also been successful (Waddilove, 2003) in controlling the build up of infection, and are especially useful if there is control of other diseases such as PRRS and EP.

Others have commented on the use of vitamin E and selenium in the control of the problem, but it is likely that the effect of these is to help fight the secondary infections where there may be toxic oxygen radical damage. Serotherapy is not to be recommended for safety reasons. However, the words of Donadeu et al. (2003) are accurate in that "no general control strategy exists as yet". Recently Dr Pat Halbur and his co-workers at Iowa State University have analysed their case submissions and found that PCV2 associated disease is rarely found in conjunction with alimentary disease.

Antimicrobial use in the pig: The bulk of antimicrobials used in swine are via the feed, possibly 80%. Dose intake is directly linked to feed intake and inclusion level. One of the common problems veterinarians encounter regarding efficacy is under-dosing. If the animal is sick with a high temperature it will stop eating and many do not drink at the same level as when healthy.

It is essential to treat inappetent pigs by injection to get them to start eating the medicated feed. Age of pig is also important. Most dose rates are based upon a 20 kg pig eating 1 kg of feed/day or 5% of bodyweight. Finishing pigs are often given restricted feed to control fat deposition, in male castrates especially, and there can be a halving of relative feed intake to 2.5% from 80 kgs and above. Lactating sows are usually fed to about 2.5% and dry sows can be fed at a rate of 1% of bodyweight. To achieve a target dose of chlortetracycline to treat a uterine infection, five times the normal inclusion is required. This is also important in eradication programmes,

to ensure the correct dose is administered to the various age groups. Most in-feed administration gives relatively lower plasma levels, especially products that are metabolised in the liver due to the slower passage down the gut. Products excreted via the kidney are not normally affected. It must also be remembered that some products given orally are not absorbed from the gut, such as the aminoglycosides and aminocyclitols so it is of little use to give them orally for systemic or respiratory infections. Soluble products given via the drinking water or in liquid feed, pass through the stomach more quickly and are therefore more quickly absorbed and therapeutic levels can be achieved in the lung e.g. tiamulin to treat respiratory infections such as *A. pleuropneumoniae*, but these levels are not reached when it is given in the feed.

The major antimicrobial families and actives used in pig production are described in Table 5.

Newer antimicrobials: Tulathromycin (Draxxin) is one of a new class of antibiotics called triamilides, which are part of the macrolide group. The drug accumulates in the lung tissue and preferentially in the neutrophils and macrophages, and is for use in the treatment of *P. multocida, A. pleuropneumoniae* and *M. hyopneumoniae*. The pre-slaughter time withdrawal time is 33 days and therefore it can be used in the finishing unit until the pigs are 70-80 kg

Florfenicol (Nuflor®) is a fluorinated analogue of thiamphenicol, is a broad-spectrum antibiotic developed specifically for veterinary use. It is useful for a wide range of bacterial respiratory disease. Both two injections of 15 mg/kg administered at 48 hour intervals and the same dosage rate daily for 3 days were effective at controlling swine respiratory disease caused by the bacterial agents shown in Table 1.

Ceftiofur is an extended spectrum cephalosporin licensed for the treatment of swine bacterial respiratory disease. In a recent study to assess the MIC values now compared to four years ago it was shown that the values had not changed and that the antibiotic was very active for APP, PM, and *Streptococcus suis.*

Fundamentally, the pharmacokinetic/pharmacodynamic principles apply in the pig as in any other species especially for injectable products. However, these principles and relationships for non-septicaemic infections are only just being determined, especially for bacteriostatic drugs, such as in the gut or respiratory tract and variations between the different mode of action of the antimicrobials and the sites of infection are only just being established. For example the plasma levels of tulathromycin are well in excess of the MIC 90 for *M. hyopneumoniae*, but it is only the lung concentration which exceeds the MIC 90 for *A. pleuropneumoniae* and *P. multocida* for which it is also indicated.

Finally, other questions to be asked include:- What is the most effective medication? By what route to get a rapid response? Does it need prophylactic follow-up treatment to keep the disease away until the pigs go for slaughter? And finally can a metaphylactic approach be used for future batches? Can the disease be eradicated in the long term is also a major consideration for breeder finishers, or different sourcing for finishers only?

Another conundrum is that most of the antimicrobials in pig medicine are bacteriostatic, such as the tetracyclines, macrolides, lincosamides and pleuromutilins and require an intact immune system to help remove the organism. It is sometimes very difficult to achieve high enough levels at the site of infection to either have a bactericidal effect or a complete eliminatory effect. Immunosuppressive viruses (PRRSV, PSV2) and *Mycoplasma* do not help this situation. The major bactericidal compounds such as the fluoroquinolones, aminoglycosides and cephalosporins raise strong concerns about their use; because of potential resistance transfer to man of antimicrobial resistant strains of bacteria.

Conclusion:

A good diagnosis is the core of the problem and to ensure that the correct organism is recovered from the sample or dead animal, which ideally should not have received prior treatment. Reliable antimicrobial sensitivity testing is also invaluable to guide the clinician to an effective therapy.

Following the diagnosis, is a suitable effective vaccine available for a long-term approach, either to solve the whole or part of the problem? Antimicrobials are and will be essential to maintain the health, welfare and productivity of pigs. It is critical to maintain the availability of the antimicrobials that are currently available to combat current and future disease problems as they arise. There is therefore a responsibility on behalf of the users of these medicines to maintain their efficacy, by not allowing resistance to develop, on behalf of animals humans. If the products are withdrawn from

Table 5: Major antimicrobial families, actives, formulations and their use in pigs.

Family / antimicrobial	Formulations	Use / indication
Tetracyclines:		
Oxytetracycline	Inj, WS, FP	*M. hyopneumoniae*
Chlortetracycline	WS, FP	*P. multocida*
Tetracycline	WS	*A. pleuropneumoniae*
Doxycycline	Inj, WS, FP	*H. parasuis*
Trimethoprim / sulphonamide:	Inj, OD, WS, FP,	*P. multocida*
		B. bronchiseptica
		A. pleuropneumoniae
		S. suis
		H. parasuis
Penicillins:		
Pen G	Inj, FP	*S. suis*
Pen V	WS, FP	*P. multocida*
		H. parasuis
		A. pleuropneumoniae
Synthetic penicillins:		
Amoxycillin	Inj, WS, FP	*S. suis*
Ampicillin	Inj, WS	*P. multocida*
Plus clavulanic acid	Inj, WS (few countries)	*H. parasuis*
		A. pleuropneumoniae
Cephalosporins:		
Cephalexin	Inj	*S. suis*
Ceftiofur	Inj	*P. multocida*
Cefquinome	Inj	*H. parasuis*
		A. pleuropneumoniae
Fluoroquinolones:		
Enrofloxacin	Inj, OD	*M. hyopneumoniae*
Danofloxacin	Inj	*P. multocida*
Marbofloxacin	Inj	*A. pleuropneumoniae*
		H. parasuis
		E. coli
Thiamphenicols:		
Thiamphenicol	Inj	*P. multocida*
Florfenicol	Inj, WS, FP	*A. pleuropneumoniae*
		H. parasuis
		S. suis
		B. bronchiseptica
Macrolides:		
Tylosin	Inj, WS, FP	*M. hyopneumoniae*
Acetylisovaleryltylosin	WS, FP	*Plus A. pleuropneumoniae*
Spiramycin	FP	*H. parasuis*
		P. multocida
Tilmicosin	WS, FP	*S. suis (resistance)*
Triamilide:		
Tulathromycin	Inj	
Lincosamides:		
Lincomycin	Inj, WS, FP	*M. hyopneumoniae*
Pleuromutilins:		
Valnemulin	FP	*M. hyopneumoniae*
Tiamulin	Inj, WS, FP	*Plus A. pleuropneumoniae*

*Inj: injection, OD: oral dosing, WS: water soluble / solution, FP: feed premix

use, as has been seen in the US with fluoroquinolones for poultry, they will never be restored and that vital product will be lost for future use.

As a result of some of the above issues, a list of preferred antimicrobials for certain infections was requested to be drawn up as first, second and last choice antimicrobials on the basis of relative clinical importance of the antimicrobial in human medicine(last choice), PK/PD and likely clinical response and susceptibility of the pathogen (see Table 6).

Table 6: First, second and last resort choice of various antimicrobials to treat common porcine infections

Infection (disease)	First choice	Second choice	Last resort
M. hyopneumoniae (Enzootic pneumonia)	Tetracyclines (Pig vaccination)	Pleuromutilin	Macrolide, Lincosamide
P. multocida/ (Pneumonia)	Tetracyclines	Trimethoprim/Sulfa	Amoxycillin
A. pleuropneumoniae (Pleuropneumonia)	Tetracyclines (Pig vaccination)	Trimethoprim/Sulfa	Amoxycillin, Florfenicol, Cephalosporin, Fluoroquinolone
H. parasuis (Glässers disease)	Penicillin Tetracycline (Pig vaccination)	Amoxycillin Trimethoprim/Sulfa	Amoxicillin & clavulanate, Florfenicol, Cephalosporin
S. suis (Meningitis)	Penicillin	Amoxycillin, Trimethoprim/Sulfa	Cephalosporin