CONTROL OF BACTERIAL RESPIRATORY DISEASES

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INTRODUCTION

Bacterial diseases that are specifically associated with respiratory lesions and clinical signs are not numerous in swine. The main ones are porcine pleuropneumonia, enzootic pneumonia and progressive atrophic rhinitis. Other conditions can have a respiratory component, but since they are usually more septicemic in nature, they will not be discussed in this paper.

Porcine Pleuropneumonia (PPP)

Different approaches have been used to prevent losses associated with this condition. Herds to be established should naturally start with sows and boars that are free of *Actinobacillus pleuropneumoniae* (APP). Several techniques have been used to assess the status of swine herds toward this organism. Serology remains one of the most important, although tests conducted in many laboratories show an obvious lack of specificity. Communication between veterinarians of the purchasing and selling herds should take place. The selling herd's veterinarian can not only report on the supervisory program (serological monitoring, slaughter checks for PPP lesions or abnormal levels of pleuritis, bacteriological isolates from nasal and tonsillar swabs or biopsies, autopsies of dead pigs and observation of suspicious clinical signs) followed in the herd, but also of the APP status of other herds that have purchased animals from that source. In herds where unexpected positive results are found serologically, a technique used in Canada has proven of value to help determine whether or not these herds are infected. Biopsies of tonsils from seropositive animals are obtained, and magnetic beads coated with anti-IgG of APP are used to improve the sensitivity of the bacterial isolation procedure (1). Also using tonsils, Danish researchers have recently shown that a PCR combined with culture on selective medium was a highly sensitive method for detection of APP (2).

In most cases infection occurs following the introduction of asymptomatic carrier pigs, but instances where herds got infected by means other than contaminated pigs have now been documented (3). Albeit uncommon, indirect transmission is thus possible and must be kept in mind when prevention is considered.

Vaccination for APP has been studied extensively. Although some of the conventional vaccines available do reduce mortality and other losses associated with the condition, the protection is incomplete and their cost effectiveness has to be evaluated on a herd-by-herd basis. Most vaccines do not contain toxoids of the APP toxins (Apx), although these have been shown to be important in the pathogenesis of the disease. At least one, however, that contains a toxoid of the three toxins (Apx I, Apx II and Apx III) as well as a capsular antigen is now available in some countries. The preliminary results obtained with it appear encouraging (4).

The relation between serological titers obtained after vaccination and protection has been evaluated. Researchers from Japan found that protection from challenge was obtained when, using the complement fixation test, serological titers of vaccinated pigs reached 1/32 (5). Similar results were obtained with guinea pigs. US scientists also found a correlation between protection and serological titers obtained after vaccination (6,7). Utrera *et al.* showed that protection was directly correlated with levels of antibodies against the haemolytic activity and

not with antibodies against the capsule of APP (8). Similarly, Cruijsen *et al.* showed that neutralizing antibodies to Apx toxins in three or twenty week-old pigs was related to protection (9). Finally, the results of several groups indicated that passive transfer of serum IgG from APP convalescent pigs protects acceptor pigs against the disease (8,10,11). These observations suggest that the dosage of antibodies, particularly against the Apx toxins, might serve as an indirect and convenient way to possibly compare the efficacy of available or experimental vaccines.

One of the weaknesses of most APP vaccines is the lack of crossprotection. In other words, a vaccine only containing bacterins of serotypes 1 and 5 is not likely to protect against infections caused by other serotypes. Subunit vaccines containing cellular components that are common to all serotypes of APP as well as toxoids of the Apx toxins should, theoretically, offer at least a partial protection against the various serotypes.

It has been proposed that to obtain full benefit, vaccination should take place when piglets have lost as much as possible of their passively acquired antibodies (6,12). It thus seems that not only the product chosen, but also the timing of vaccination has to be evaluated if this preventive method is considered. Interesting results have been obtained by vaccinating pigs through an aerosol (13). This opens the door to possibilities to vaccinate pigs without having to individually manipulate them. In Australia, a program based on whole herd vaccination with an autogenous vaccine appeared to provide an excellent control on PPP in a 350-sow, farrow-to-finish operation (14).

The use of medicated or segregated early weaning techniques can help to prevent or reduce losses associated with PPP post weaning (15). The work of Fenwick *et al.* in this respect is worth mentioning (16). Using infected breeding herds, they tried to determine at what age piglets needed to be weaned to prevent contamination from the infected dams. Weaning at 11 days or less reliably prevented transmission, but not at 14 to 16 days of age or older. Field observations tend to go along with these data: segregated early weaning at 16-18 days offers a good, but incomplete protection against PPP outbreaks.

The eradication of APP from infected herds has been reported from several countries (17). It usually involves a test and removal procedure where breeding animals found seropositive are culled, while the herd is kept under medication to prevent lateral transmission of the organism. Although it can and has been done successfully, failures are not uncommon and one should be cautious before investing time and money in this.

Pigs affected with PPP usually respond very well to parenteral treatment, when given early in the disease (18). It is also of interest to note that effective treatment of PPP through injection does not necessarily require the use of sophisticated, expensive products. Many isolates, for example, are still sensitive to simple penicillin and when so, this antibiotic affords very satisfactory results at a low cost. Different researchers have showed that pigs affected with PPP not only eat less, but also drink less (19,20). Oral routes of medication could thus be considered to prevent the disease in animals that are not already affected, but their use to effectively treat pigs that are acutely affected is, at the very least, questionable (18,21).

Antibiotic sensitivity results are a useful tool when comes time to select a product to treat APP infections. Unfortunately the limits of these results are frequently ignored, which can lead to treatment failures. Let us consider, for example, the case of oxytetracycline. According to the NCCLS (National Committee for Clinical Laboratory Standards) standards, a strain of APP is considered sensitive to tetracycline if its MIC (Minimum Inhibitory Concentration) is lower or equal to 4 mcg/ml. A strain with a MIC of 4 mcg/ml would thus be considered "sensitive", but to obtain 4 mcg/g of oxytetracycline in the lung tissue, through

feed or water medication, is both unrealistic and uneconomical. In fact, Pijpers and Verheijden showed that with 1600 g/ton of oxytetracycline, the level obtained in the lungs was only 0.71 to 1.09 mcg/g (21). With this level they were able, after medicating experimental pigs for six days, to completely protect them against a challenge with an APP strain that had a MIC of 1 mcg/ml. But not at 800 g/ton. When interpreting sensitivity results it is thus important to know, among other things, the MIC limits at which the causative strains are considered sensitive to a product, and the levels of this product obtained at the site of infection with the dosage and route of administration used.

Enzootic Pneumonia (EP)

Mycoplasma hyopneumoniae (MH) is the primary agent associated with EP (referred by some as Mycoplasmal or *Mycoplasma* pneumonia). In most cases other organisms, particularly *Pasteurella multocida* (PM), complicate the condition. Experimentally, pigs infected solely with MH will usually only show some coughing and the pulmonary lesions rarely involve more than 10-15 % of the lungs (R. Ross personal communication). When both MH and PM are used to infect pigs, clinical signs and lesions are usually more severe (22,23).

In the case of EP, prevention of the condition starts with the location of the farm. Herds populated with MH-free stock usually do not maintain that status for long, if contaminated herds are located nearby. According to Muirhead and Alexander, wind-borne transmission can occur at distances of up to three-km (24). This should thus be the minimum distance of separation from infected herds. MH-free gilts and boars are available in most countries. The status of herds supplying breeding stock can be monitored using the same principles as for APP.

In contaminated herds strategic and/or pulse medication programs have been used with success to limit losses (24-26). The combination of tiamulin with a tetracycline offers interest in these programs because it has good activity against both MH and PM.

Bacterins of MH are now available in more and more countries. Their cost-effectiveness is usually related to the severity of the problem. In herds where clinical signs and losses are obvious or significant, it is frequently worthwhile to use them (24). In other cases, the improvement in performance is generally not sufficient to pay for the vaccination program (27). Of particular interest is the use of MH vaccines in systems using SEW programs. In such herds, where MH is present in the sows but where infection of piglets appears to be minimal, problems often appear 6-12 weeks after introduction in the finishing units. In such instances vaccination has been used and in many cases found to be justified economically.

The optimal timing of vaccination remains debatable. Manufacturers commonly recommend vaccination of piglets at one and three weeks of age. However, many practitioners prefer to delay vaccination until the pigs are weaned, believing that a greater clinical efficacy is obtained. Theoretically, one could argue that if piglets have lost more of their maternal immunity, they might react better to an active stimulation. The scientific literature, however, is not clear as to whether or not one strategy is better than the other (28-30). In one study, conducted in Denmark, vaccination at one and three weeks or four and six weeks of age was compared in five herds. In all five herds the improvement in daily gain was greater in piglets vaccinated later (29). There was no evidence though that the level of maternally derived antibodies was responsible for the significant difference between the two groups. A second Danish study produced greater daily gain improvements in piglets vaccinated earlier (28). In Croatia, vaccination of pigs at 12 and 14 weeks of age resulted in major improvements when compared to unvaccinated controls (30). It can thus be concluded that vaccinating pigs later than is usually recommended can still result in benefits and, in some cases, might even be

preferable. It also has the advantage that it can reduce the time between implementation of the vaccination program and, observance of the results obtained.

In a small French experiment, piglets born from MH-vaccinated sows were protected against a challenge with both MH and PM (31). This indicates that maternal immunity seems to offer protection to piglets against MH, but also that PM is mainly a secondary agent that needs a triggering factor to get established in the lungs.

In an experiment comparing four vaccines, there appeared to be minimal correlation among an *in vitro* lymphocyte proliferation assay, antibody titers, and severity of lung lesion (32). Of these assays, though, serum antibody levels appeared to be the best indicator of protection against MH. Recently, Djordjevic *et al* also found that IgG and IgA antibody concentration in serum and respiratory tract washings, after vaccination, did not provide a useful prognostic indicator of protection from EP (33).

It is the author's opinion that the "18 week wall" described in the United States is primarily associated with *Mycoplasma hyopneumoniae*. Since it is virtually impossible to reproduce the severe clinical signs and losses that can be associated with this syndrome by using only MH, one has to admit though that other organisms are probably present as well. Nevertheless, the role of *Mycoplasma* seems to be predominant for several reasons. First the condition is generally not present in MH-free herds. Secondly, it is usually preceded by a gradual increase in coughing that fits well with what we know of this organism. Third, gross and microscopic lesions compatible with those seen in enzootic pneumonia are normally present. Fourth, MH can in most cases be identified through isolation or other techniques and last, the use of MH vaccines is often useful to help prevent the losses associated with the "syndrome".

It is possible to eradicate MH from infected herds without completely depopulating them (34,35). It is also possible for contaminated sow herds, in field situations, to produce MH-free piglets (36).

Although the MICs of MH strains to compounds like tiamulin and lincomycin are very low and can usually be attained at the lung or even at the bronchial mucus level, response to treatment, even by injection, is not as successful as for PPP. In the case of enzootic pneumonia it is clearly preferable to prevent than to treat the disease.

Progressive atrophic rhinitis (PAR)

This condition is not usually a significant problem in herds using a strict all in-all-out system in the different phases of production, and where good environmental conditions are maintained. This is particularly true for those who have adopted modern technologies like SEW.

Prevention of PAR starts, as is always the case, by making sure that the etiological agent is not introduced into the herd. To maintain herds free of *Bordetella bronchiseptica* may not be justified since the organism does not, by itself, normally produce a severe condition. Furthermore, it is a fairly common organism that is present in most herds, including those of breeding stock producers.

A more logical approach is to avoid introducing toxigenic *Pasteurella multocida* (TPM), the main cause of concern in this condition. Different techniques are now available that help to identify herds that are infected with TPM. One of the most interesting is used in Finnish herds under the national supervisory program (37). Within this system herds are monitored on a regular basis using an ELISA test to detect antibodies to the dermonecrotic toxin of the

bacterium. Because colostral samples contain higher levels of antibodies than serum and are easy to get, they are preferred to run the test.

ELISA and PCR techniques to detect carriers of TPM have been evaluated in several countries. In Canada a comparison of these two sensitive methods has recently been undertaken and the latter was found to be more sensitive (A. Broes, personal communication). This is in accordance with results obtained in The Netherlands (38). Using these techniques, different researchers have succeeded in eradicating the condition from contaminated herds, through a test and removal procedure (38-40).

To be efficacious, vaccines should contain components that will prevent the attachment of *Bordetella bronchiseptica* to the nasal mucosa, but more importantly a toxoid of the PM toxin. Such vaccines are available in most countries and can be useful in control programs.

In herds where the disease is a concern, the first step should be to improve environmental conditions and to make sure that a strict all in-all-out system is observed. If this is not sufficient, it can be recommended to vaccinate all adult stock twice four to six weeks apart and then vaccinate sows prior to each subsequent farrowing (24). Depending on the time when clinical signs are observed, vaccination of the pigs may also have to be recommended. A laborious but often successful procedure consists of multiple injections of piglets between birth and weaning (for example days 1, 7, 14 and 21). Products like long acting oxytetracycline, amoxycillin or ceftiofur are among those that have produced good results in these circumstances. Finally, in particularly severe or acute cases a combination of these strategies may need to be used at the same time, plus the medication of nursery and sow (5-7 days pre-farrowing and lactation) diets with products like tetracyclines.

CONCLUSION

In most cases it is possible, with the tools available, to efficiently control bacterial diseases that are specifically affecting the respiratory system of swine. It is important though to keep in mind that in field situations, mixed bacterial and viral infections are frequent and that these pose a greater challenge to the veterinary practitioner.

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