Epidemiology, diagnosis and control of swine diseases

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Introduction

Admittedly, the title of this lecture is not particularly original or thought provoking. For many years the Howard Dunne Memorial Lecture has touched topics that were not necessarily related directly or totally to what veterinarians were academically formed to do, or have to deal with on a day to day basis. The idea I believe was to make sure that we would keep our eyes open on what might come in the future, and how it would affect our work and positioning within the swine industry. In this respect this year's lecture will be a bit different since it is completely centered on a more traditional or basic area of our work. I was told that the 2004 AASV annual meeting would focus on 'bugs and diseases', and this is what this lecture will be all about. It is naturally impossible to adequately cover the epidemiology, diagnosis and control of all swine diseases in a short document. However, it is possible to illustrate some of the points that I would like to make in this paper by using specific diseases and situations as examples. It is my hope that a few of the ideas, data and facts that will be discussed in the following lines may, in a very modest way, stimulate constructive discussions within our membership.

Epidemiology of swine diseases

To avoid losses associated with significant pathogens, we need to know by what means they find their way into swine barns.

The overrated importance of direct pig contacts in the transmission of swine pathogens

While at the veterinary college, 25 years ago, I was taught that direct pig contacts, or introduction of infected animals, was by far the most important means by which swine herds were getting infected with pathogens. Since then, most presentations, books, documents on the epidemiology of swine diseases that I have attended or read have suggested the same thing. But is this really so, or always so? My opinion is that under contemporary conditions, introduction of infected pigs is evidently important in the transmission of swine pathogens, but by no means as much as it may have been in the past, or as we seem to be told everywhere. This may be due at least partly to efforts that have been made to address the risk associated with the introduction of animals in swine farms. Note that I'm not referring here to endemic organisms already present in a given herd, that are vertically transmitted from the dams to their offspring and then introduced with piglets in the nursery, and eventually in the finishing unit, but to new infections coming from outside the existing herd. Following are the findings of some studies that evaluated the causes of herd infection for various conditions of importance in swine veterinary medicine.

Pseudorabies

In 1990, 120,598 US herds were tested for pseudorabies infection, and of these 2,156 were identified as newly infected.[1] Through epidemiological investigation, the most probable source of infection was identified in only 976 (45%) of these newly infected herds, and the movement of infected domestic swine was involved in half (49.8%) the cases. Area spread transmission between neighboring herds, usually within 1 km, was indicated in 46.3% of cases. This means that in this epidemiological study, the introduction of infected animals was documented to have been responsible for only about 23% of the total cases of new infection. Although one can admit that this percentage might actually have been higher, considering the number of herds with no determined source of infection, it appears to leave a majority of cases associated with transmission modes other than introduction of infected pigs.

Foot and mouth disease

The epidemic of foot and mouth disease (FMD) that struck UK in 2001 has cost over 4 billion dollars. It mainly occurred in an area where there were few pigs,

and pigs were involved in a minority of cases, but it is still of interest to see how this important pathogen appeared to spread between farms. Gibbens et al[2] have reported the most likely method of spread for the first 1847 cases of FMD during this epidemic. The authors were cautious in stating that the mechanisms of spread identified presented the best estimate of how infection arrived, but that these could later be corrected in the light of additional information. Less than 5 % of the cases were categorized as caused by introduction of infected animals. Seventy nine percent (79%) of the cases were thought to have been caused by local spread, defined in the document as infected premises that were located within 3 km of another infected premises and with more than one possible conveyor identified.

Hog cholera

In 1997 hog cholera was reported from the Netherlands and caused the local industry over two billion dollars in losses. Table 1 shows the distribution of the most likely routes of transmission before and after implementation of the first measures to stop the progression of the disease.[3] Of the 429 herds included in an epidemiological study of this epizootic, the introduction of infected animals was, overall, after putting together cases before and after implementation of measures, responsible for only about 3 % of the farms that became infected, while neighborhood infection was responsible for 12 times more. In this case the following requirements had to be met to define the so-called neighboring infection: infection of herds in close proximity (≤ 1 km) of a previously infected (source) herd in the absence of other possible contacts; the infectious period of the source herd started earlier than that of the neighborhood-infected herd; the infectious period of the infected source herd overlapped with the infectious period of the neighborhood-infected herd

Porcine reproductive and respiratory syndrome

Porcine reproductive and respiratory syndrome (PRRS) is also among the most important swine diseases worldwide, and is likely the most important at this time in North America. From 1999 to 2002, 44 cases of PRRS were diagnosed in sow herds of a Quebec integration company (Ménard J, personal communication, 2003). Most of these herds are located in pig dense areas. Since the multipliers of this company have remained PRRS negative over these four years, this means that none of the cases is thought to have been caused by the introduction of infected animals. The boar studs of the company also have remained negative during this period, so introduction of infected semen was not involved either. Although the trucks transporting replacement animals to commercial farms were washed and disinfected in what is believed to be an appropriate way, they were also used to transport culled animals from commercial farms to slaughter. So one cannot be sure that these trucks may not have been responsible for some of the cases. However, the same trucks were used to transport replacement animals to all commercial farms, and those not located in pig dense areas have remained, largely, unaffected. Furthermore, if these trucks had been responsible for introduction of certain viral strains into commercial farms, the same strains would likely have been found in multiple farms, which is not what was usually observed. In fact in most cases the strains identified in farms of the company were not strains that had been identified in the system before. Still, trucks were considered as one of the possible indirect transmission means for herds of that company, along

Table 1: Distribution of the most likely routes of transmission before and after implementation of the first measures during the hog cholera epidemic in The Netherlands in 1997-1998.

Transmission route	Before first measures (n = 39)	After first measures (n = 390)
Animal	17%	2%
Transport lorry	52%	11%
Person	6%	15%
Pick-up service rendering plant	-	13%
Artificial insemination with contaminated semen	-	8%
Slurry	-	1%
Neighborhood	22%	39%
Unknown	3%	11%

with contaminated material or equipment, and the so called 'area spread', which was thought to be among the most important factors (Ménard J, personal communication, 2003). In the same vein, Baekbo et al[4] reported that of 2500 PRRS negative herds that are monitored in Denmark, 6 to 7 % were becoming infected each year. Of these, the authors stated that only 15 to 20% were caused by the introduction of subclinically infected animals, the rest being mainly due to area spread.

Enzootic pneumonia

Enzootic pneumonia caused by *Mycoplasma hyopneumoniae* (MH) is again one of the most common and important swine diseases worldwide. Quebec investigators recently evaluated 37 farms that were all populated from the same MH-negative supplier herds.[5] Of these, 18 became infected over the years, and 19 are believed to have remained negative. Of the 18 herds that became infected, none was determined to have been infected by the introduction of infected animals. As will be detailed below, it is believed that all these farms likely got contaminated because of area spread, or neighborhood infection.

These data suggest that as veterinarians, we may have to change our tune. Although introduction of infected pigs should evidently be considered as a significant means by which herds can become infected, it is presently, for many diseases and situations, largely overestimated. At the same time and to the same extent, indirect means by which herds become infected with pathogens have been underestimated. This should be recognized so that resources can be allocated to determine what really are the causes of herd infection with every significant pathogen, and what relative weight or importance each of these causes actually has. Only then will it be possible to know if investments made to address this or that particular transmission means are worth it or not. We seem to have a long way to go in that respect. In fact, at this time, not only are we far from solutions to cope with transmission means that would have been both identified and at least partly quantified, we are not even agreeing on what these transmission means are. The ultimate example of this disagreement concerns the possibility for pathogens to be transmitted from farm to farm by aerosol, and this is the next topic that we will discuss.

The aerosol debate

For many years we have heard of or read dramatically opposed opinions over the possible aerosol transmission of swine pathogens. Some believe it plays little or no role in the transmission of swine pathogens in field situations, and that even if it were, there is not much that can be done about it anyway. Others think that aerosol transmission of swine pathogens does occur in field situations, that this element should be kept in mind when designing prevention or eradication programs of several diseases and that, although options are presently not numerous or perfect, some are worth considering, or at the very least evaluating. The following lines will try to shed some light on this controversial issue.

Some relevant swine pathogens that can potentially be transmitted by aerosol

This section of the document will evaluate the potential for seven different swine pathogens to be transmitted by aerosol. It does not summarize all studies on aerosol transmission of swine pathogens, but rather only some about these seven that were judged particularly relevant. I acknowledge right away that the studies referred to are favoring the aerosol hypothesis, and that I have disregarded those that were not necessarily in accord with it. Although I do accept this as a founded criticism, it should be said that studies, and particularly field studies concluding that aerosol transmission of the selected swine pathogens is impossible, or rare, or unlikely, are, themselves, not many. Furthermore, I felt that those who do not believe in the aerosol transmission of swine pathogens have had in the past significantly more opportunities to make their point at this and other US meetings, and that now was the time to give a chance to the opposite position.

Actinobacillus pleuropneumoniae

To a certain extent *Actinobacillus pleuropneumoniae* (APP) is a newcomer on the list of organisms potentially transmitted by aerosol. In fact evidence suggesting this possibility is more recent and not as well documented as for some of the other pathogens on the list. Three experimental studies have shown that APP could be transmitted by aerosol, over short distances, between pigs.[6–8] Nielsen et al[9] also showed that the organism could be identified in the air of infected farms. Desrosiers et al[10] described five different field cases of indirect transmission of APP where in at least one herd transmission through aerosol was considered the most probable source of infection. This mode of transmission was also considered a possibility in three more cases. Using a ribotyping technique, Fussing et al[11] concluded that airborne transmission was indicated in 5 of 12

Danish SPF herds where this transmission means was investigated. Finally, in a recent epidemiological study conducted between 1996 and 2001 in 3055 Danish herds, Zhuang et al[12] reported that aerosol was probably the major factor responsible for infection of herds with APP in the Danish SPF system.

Pseudorabies virus

In the early 80s different reports from UK suggested the possible aerosol transmission of pseudorabies virus (PRV) between farms. In one of them Gloster et al[13] investigated a series of 11 outbreaks that occurred in 1981 and 1982. Their results suggested that 7 out of 11 cases investigated could have resulted from airborne virus. The meteorological conditions were such that airborne virus could have blown from a source farm for many tens of hours to animals which were subsequently infected, and on the majority of farms the authors felt that disease spread by other means could be eliminated. In 1990 a paper by Christensen et al[14] reported long distance airborne transmission of PRV from Germany to Denmark. An epizootic during the winter of 1987-1988 was shown to correlate with an unusual prevalence of southerly winds, and the strains found in this epizootic had never been identified in Denmark before. Both conventional and SPF herds became infected, and there was a positive correlation between the risk of infection and size of the herd. These observations were said to support the hypothesis of airborne transmission of the organism. Three years later the same group reported another epizootic that occurred during the winter and spring of 1989-1990 in nearly the same areas as in 1987-1988.[15] It was associated with PRV strains different than those of the preceding epizootic and was again found to coincide with periods with southerly winds. The authors reported that given the comprehensive measures taken against spread of the disease, no other possibility than airborne transmission of virus could explain the recurrent epizootics. On a different continent, Scheidt et al[16] described an epizootic of pseudorabies in 10 Indiana swine herds. The pattern of spread, which occurred during the winter, was from west to east and north, and this coincided with the direction of prevailing winds. Other means of transmission were considered, but none was thought to be implicated in the epizootic. The authors concluded that aerosol transmission of PRV between herds was probable. In a case control study involving 80 herds of France, 40 that became infected and 40 that remained negative, the most important risk factor was found to be the presence of an infected herd within 1 km from the herd.[17] A higher level of biosecurity did not reduce the risk of infection, and the authors concluded that aerosol transmission of this virus is an important means of contamination. Finally, transmission of PRV through aerosol over short distance (15 meters) has been demonstrated experimentally.[18]

Porcine respiratory coronavirus

In 1989 Pensaert et al[19] reported that porcine respiratory coronavirus (PRCV) transmission occurred by the aerogenic route and that the virus may remain infectious over long distances (miles). The authors mentioned that sequential infections have been experienced in farms applying strict sanitary measures and situated several kilometers apart, and this in different European countries such as Belgium, The Netherlands, France, Denmark and England. In one case reported by Wesley et al[20], the virus was thought to have travelled 33 kilometers by air currents, infecting susceptible swine in a closed, well-managed herd. A serological screening of swine herds in Denmark in 1984 showed that PRCV had been introduced in the country. A cross sectional study of 408 Danish herds was carried out in 1985-1986 and the results indicated that closeness of a seropositive herd and herd size were associated with an increased risk of a herd being serologically positive.[21] There was no difference in the prevalence of PRCV between SPF and conventional herds, so that rigorous biosecurity measures did not seem to protect against PRCV. The authors concluded that the study supported the hypothesis of airborne transmission of PRCV. Bourgueil et al[22] showed that the virus can be recovered in the air of units containing infected pigs, between days 1 and 6 after experimental infection.

Swine influenza virus

Easterday et al[23] reported that in densely swine-populated regions, airborne spread may contribute to explosive epidemics over large geographic areas. Tofts[24] described an outbreak of SI where one of the herds involved became infected and had no known contacts with other infected herds, but was 4 km down wind of over 13,000 affected pigs on other farms. He concluded that transmission of the virus appeared to be by direct contact and local aerial transmission. Madec et al[25] described the extremely fast progression of swine influenza in an epizootic affecting herds of Brittany (France), that started in December 1981, so during the cold season. In 9 months it was estimated that approximately 70% of the herds had been infected, or about 4 million pigs, phenomenon never observed in that area before.

Evaluation of wind direction and disease progression was compatible with the involvement of aerosol as one of the causes for this rapid progression. Christensen et al[26] reported that the typical pattern of simultaneous influenza outbreaks in many herds of Denmark is highly suggestive of airborne transmission of this infection. They mentioned that in Danish epidemics, even though special precautions are taken against introduction of infectious diseases, SPF herds are attacked by influenza just as frequently as neighboring herds of conventional health status.

Mycoplasma hyopneumoniae

Goodwin[27] was among the first to suggest that aerosol transmission of MH between farms could occur. Two groups of herds in the UK were compared. One group included 55 herds that were previously free of MH, but got contaminated without a simple explanation as to how it occurred, and a second one of 57 herds that were, and remained, free of this organism. The risk of becoming infected with MH was found to be inversely related to the proximity of other pigs, and the crucial distance for maximum survival of a negative herd was about 3.2 km. Aerosol was considered to be the most likely reason for contamination, and there was a tendency for breakdowns to start in the autumn and winter, particularly in highly secure units. In Denmark, Thomsen et al[28] used a regression model to try explaining how Danish SPF herds were getting infected with MH. Their analysis, involving 204 herds, showed that the pattern of infections was in agreement with the hypothesis that both airborne transmission and spread through trade in subclinically infected animals are major causes of MH infections. The data also indicated that being close to a large infected herd was increasing the risk over a small infected herd. Swiss researchers also conducted a study to try understanding why MH-free herds in the Swiss SPF system were getting infected with the organism.[29] Forty-two case farms and 50 control farms were included in the investigation. Factors considered to be possibly associated with infection were: distance to the nearest non-SPF herd, the size of that herd, the density of pig population in the area, the distance to the next road regularly carrying pig transporters and differences in topography. The authors concluded that their results tended to support the hypothesis of airborne transmission of MH. Jorsal et al[30] reported that in the Danish SPF system, reinfections with MH were most frequent in the autumn and winter, and that the risk of reinfection was affected significantly by distance to the nearest non-SPF herd and distance to the nearest non-SPF herd with more than 500 pigs. The direction of the wind seemed to have an impact as well and the authors concluded that their results were in accordance with the hypothesis of windborne transmission. Stärk et al[31] also reported that in Switzerland more farms became infected during the colder months of the year, and that this was likely due to the more favorable conditions for survival of the organism. The analysis, that included a relation between the number of outbreaks vs temperature and relative humidity data, led the authors to state that aerosol transmission was likely to occur during certain periods of the year. In a recent study conducted in Denmark, Zhuang et al[12] reported that the risk of infection was strongly associated with pig density and distance to neighboring farms. The risk of infection also increased for larger herds, and average daily temperature, as well as rainfall, were negatively associated with MH infections. The authors concluded that airborne transmission of MH was probably the major factor in infection of Danish SPF herds with MH. An eradication program for MH is presently taking place in Switzerland, on a country basis. One study looked at reasons why herds located in an area where the infection had been eradicated during the years 1996 to 1999, became infected in 2000.[32] Both purchase of infected animals and aerosol transmission were considered the main reasons explaining re-infections. In a Quebec investigation 37 farms were all populated with animals coming from the same MH-free sources.[5] Over the years 18 of these farms became infected with MH and 19 are believed to have remained negative. All farms that became infected were within 1.5 km or less from infected premises. None of the 16 farms that were 2 km or more from infected premises is thought to have become infected. Twelve of the 18 infected farms began to show clinical signs between November and April. The investigation's conclusion is that aerosol was likely the main cause for these cases of area spread. Overall, seven epidemiological studies looked at transmission means of this pathogen, and all of them (7/7) supported the hypothesis of aerosol transmission.[5,27–32] It was also shown by Stärk et al[33] that it is possible to identify MH by Polymerase Chain Reaction (PCR) in the air of contaminated barns, and recently Fano et al[34] reported the infection of negative pigs that had been placed in a trailer 6 meters away from a small barn where pigs had been experimentally infected. The authors concluded that their results confirmed the hypothesis of aerosol transmission of MH. Finally, using a PVC tube to determine if MH RNA could be detected in the air at 1, 75 and 150

meters away from a point where the organism was aerosolized, it was found by Cardona et al[35] that all air samples were Nested PCR positive at all distances. Isolation attempts of the organism however were unsuccessful, which according to the authors could have resulted from the lower sensitivity of this detection method and from the heavy contamination level, by other bacteria, of the samples.

Porcine reproductive and respiratory syndrome virus

In 1991 a meeting on PRRS was organized in Brussels to which participated scientists and researchers from around the world. One of the conclusions of this meeting was the following: "The main means of spread of PRRS are the farm to farm movement of pigs and spread via airborne dispersion. The first outbreaks in a population have been frequently due to the movement of infected pigs but airborne transmission of the virus appears to be responsible for much of the subsequent neighborhood spread."[36] Robertson[37] reported the means by which the virus was thought to have spread in the first 100 reported cases in Great Britain. Aerosol was the most important with 63% of the cases. He also reported the tentative conclusions for 81 cases that occurred in Belgium in 1991 and for which airborne spread (Belgians talk more about neighborhood infection) was considered to have been involved in 69% of the cases. Vannier[38] described the progression of the virus in the French Côtes d'Armors from October 1991 to May 1992. He concluded that only aerosol transmission over short distance could explain the diffusion observed, which occurred during the cold season of the year. In The Netherlands, Komijn et al[39] stated that one of the reasons why the disease initially spread so fast in that country was that direction of the wind and weather conditions during the winter months favored the spread of airborne virus. The number of outbreaks thought to have been caused by PRRS went from 10 between December 17 of 1990 and January 13 of 1991, to 1019 between January 14 and March 10 of 1991. The presence of the virus in Denmark was identified for the first time in March 1992, and was suspected to have been introduced from Germany by the airborne route.[40] An epidemiological study was conducted in Denmark in 1996-1997.[41] Seventy three case herds and 146 control herds were included in the study. One of the conclusions was that biosecurity measures did not prevent infection of the herds, and the authors suggested that virus spread from neighbor herds by aerosol was a frequent mode of transmission. They used a formula to quantify the risk of neighborhood exposure. In their model, a herd located 300 meters away from an infected farm was 45 times more likely to become infected compared to the same size farm that would have no contaminated neighbor within 3 km. In another epidemiological study conducted in Denmark, this time for the period 1994-1998, a total of 344 genetic herds were evaluated.[42] The average annual incidence of infection was found to be about 8 %. The analysis indicated that the risk of infection was increasing with the pig density of PRRS positive neighbors, but decreasing with distance to them. The authors concluded that there was a predominant feature of local spread of PRRS virus in Danish pig herds, probably mainly via airborne transmission. In North America six different studies or field investigations reported transmission of the virus by the so called 'area spread'.[43–48] In each of these studies sequencing of strains suggested that what appeared to be the same strains were found, within a relatively short period of time, in neighboring farms without a simple explanation as to how they were introduced in these farms. In five of six studies the authors referred to the possibility for aerosol to be involved in this area spread, but it is understood that there are other possible transmission means, like insects, for example.[43,44,46–48] It should be noted however that in the epidemiological study conducted in Quebec by Larochelle et al[47], about 75% of the total PRRS strains identified (226) were from cases submitted in autumn and winter, and particularly from November through April, at a time of the year where for most of these cases insects involvement is unlikely. The same is true for 2 of the field investigations referred to above, where cases of area spread occurred in the cold season.[46,48] In one of these, six Quebec farms broke with PRRS within a month, in November-December.[48] All were within 100 meters to about 2 km from each other. Three were independent producers and three farms were owned by the same company. Four of the farms used negative replacement animals, as well as semen from a PRRS-negative boar stud. Strains from these 4 farms were sequenced and all found to be 99.5% homologous or more, using ORF 5. This is not to say that aerosol is the only possible cause of area spread for this virus. In another one of these field investigations 12 backyard pigs were thought to be responsible for the contamination of a negative sow herd located half a mile away.[45] One would think that even though it has been shown that as few as 20 virions were enough to infect a pig by intranasal inoculation, 12 pigs may not generate an aerosol capable of infecting pigs on such a distance. Without disregarding aerosol in that particular case,

which occurred during summer, transmission by other means, like insects for example, should remain on the list of possibilities. It should be mentioned as well that if only 12 pigs located half a mile away were really responsible for this indirect transmission, one can wonder if trucks or vans containing hundreds of pigs that could be viremic and shedding virus may not also constitute sources of contamination. Going back to aerosol per se, there seems to be ample field evidence suggesting the possibility for PRRS virus to be transmitted by aerosol. Nevertheless, PRRS virus is probably the organism over which the aerosol debate has been the hottest. The confrontation mainly came from the fact that reproducing aerosol transmission of this pathogen over short distances has been, at least in some of the experiments, either relatively difficult or impossible to demonstrate. These experiments were largely described at this and other meetings in the past, so I will not go over them. In Denmark though Kristensen et al[8] were able to readily infect negative pigs when 70, 10 or even as low as 1 % of the air getting in the closed unit where they were came from a unit, distanced by one meter, containing infected pigs. Finally, a recent study by Dee[49] looked at the possibility for the virus to be isolated in the air of a tube at different distances from its production point. Done during the winter, the study showed that the virus could be isolated at all distances tested, including the longest one which was 150 meters, and one of two pigs exposed to infected aerosol over this distance became infected.

Foot and mouth disease virus

An interesting paper published a long time ago described some of the findings concerning spread of FMD virus in a few outbreaks that occurred in UK.[50] It states: "As a recent paper shows, the airborne spread of foot-and-mouth disease is at least a possibility. The nucleus of the epidemic which began in this country in October, 1967, was a fan-shaped area north-east of Oswestry, Salop. Few outbreaks arose upwind of this area (the prevailing wind was south-west) which could not be explained by physical spread. This was suggestive, and the suggestion has been confirmed by the analysis of four earlier epidemics and the meteorological conditions at those times. All these epidemics were small but well documented: they were in Hampshire (1967), Northumberland (1966), Cheshire (1957), and Salop (1961). In none of them was there appreciable spread upwind from the initial centre." Criticizing the overly cautious approach of this paper concerning the involvement of aerosol in one of these outbreaks, Henderson[51] stated: "In my view the fan-shaped downwind distribution of outbreaks from Oswestry in 1967, together with the meteorological analysis of the earlier outbreaks, renders this conclusion inescapable." Since then the studies on aerosol transmission of FMD virus have become a lot more sophisticated and it is now possible to determine with much more precision if hypothesized aerosol trasnmission of the virus in various conditions makes sense or not. For example, Gloster et al[52] investigated a series of 23 outbreaks where the original outbreaks were separated from later ones by a sea passage. Their findings supported the hypothesis that under certain conditions, the airborne transmission of FMD over a long sea passage is possible. In one of these cases the virus was considered to have traveled from Denmark to Sweden over a distance of 100 km. Mathematical models have been developed that enable to forecast, to a certain extent, where the disease might hit next. Certainly one of the most revealing papers on aerosol transmission of any swine pathogen is the one by Donaldson et al[53]. On March 4, 1981, FMD was diagnosed in Brittany, France. English authorities asked specialists if meteorological conditions were favorable for the spread of the virus from France, to the UK. Advice was given that there were periods during which, if the virus emission was high, the atmospheric conditions were favorable for long-distance transportation of virus in sufficient concentrations to cause infection in an area extending from the Isle of Wight to Exeter. The risk was considered high for the Channel Islands but low for southern England, since at that time the furthest distance which had hitherto been reported for airborne spread of FMD was 100 km (from Denmark to Sweden, as seen above). However, outbreaks did, in fact, subsequently take place in both areas predicted, ie, in Jersey (March 19) and in the Isle of Wight (March 22), which for the latter is approximately 300 km away.[53,54] Strains of cases in Brittany, Jersey and Isle of Wight were all found to be type O FMD virus and detailed biochemical analysis failed to show any differences between them. Extensive investigations were carried out to see if other possible causes of infection like movement of animals, feedstuffs, vehicles and people might have been involved, but failed to identify any. While these studies and observations are more than 20 years old, Gloster et al[54] have reported that in the FMD outbreak that occurred in UK in 2001, the results were consistent with the hypothesis that the disease was spread to 7 of the 12 farms in the immediate vicinity of an infected farm by airborne virus, and airborne infection could not be ruled out for 3 other premises. The distances involved ranged from less than 1 km, up to 9 km. This

being said, it should be mentioned that although pigs are recognized as the most powerful emitters of aerosolized FMD virus, and as such are the greatest danger for aerosol spread of the organism, they are, according to recent research, relatively resistant themselves to infection by aerosol.[55,56]

Is aerosol transmission of swine pathogens possible or not?

At the end of the day, this is an important question since our decision to do something about it or not depends on the answer that we give to it. My perception is that the evidence presented in the preceding lines is, albeit often circumstantial, very strong. Nevertheless, following are some more comments that also militate in favor of the aerosol hypothesis:

- Several of the epidemiological studies or investigations that looked at airborne transmission of swine pathogens reported spread compatible with the direction of the winds, and in some cases clearly in the direction of the prevailing winds, during periods of cold weather when insects should not, realistically and for most cases, be involved.[14–16,25,38,39,50–53] The diseases and pathogens discussed in these references are PRRS, FMD, PRV and SIV. It is quite difficult to imagine something (pigs, other animals or birds, insects, trucks, fomites, people) other than air that would be responsible for diffusion of a pathogen in such a definite direction, under such environmental conditions. It is sometimes argued that if a PRRS outbreak, for example, starts in January, it does not necessarily mean that the organism was introduced in the preceding weeks. In other words the time period between introduction of the organism and apparition of clinical signs could be longer, and maybe months. If it were the case, potential sources of infection like insects could be introduced in the herd in August or September, but the problems could appear only during the winter. This, I also hear, may be particularly true if the dose of virus initially introduced is low, as could be the case with insects. Although this is certainly possible, and we do know of cases where the period between infection and apparition of clinical signs appeared to be months (in fact some herds become infected and don't seem to ever show clinical signs), the time period between introduction of infected animals and detection of clinical signs was reported to be between 2 and 5 weeks in two different investigations, where such a period was determined for several herds.[37,57] In a third one sow herds supplied by an AI center began to show clinical signs 3 to 5 weeks post confirmation of infection in the boar stud.[58] Furthermore, Yoon et al[59] have shown that when pigs are infected with only 20 FFU (fluorescent foci units) by intranasal or intramuscular inoculation, compared to 200,000, the difference in the time of apparition of clinical signs was calculated in days, not months. Taken together, these data suggest that although there probably can be large variations, sow herds that begin to show clinical signs on a given date have often been infected sometimes in the preceding 5 weeks.
- Numerous studies considered the impact of biosecurity measures on the probability of becoming infected or not with a given pathogen. It is believed that in herds following strict biosecurity rules (e.g. SPF, Minimal Disease), the likelihood of becoming infected because of people, trucks, fomites, rodents, birds or other types of indirect transmission means is reduced. In situations where there seems to be little difference between herds following strict biosecurity rules and others, the logical explanation should be that factors not affected by these rules are responsible for the infection. Air could certainly be one such factor, and several studies on some of the potential airborne pathogens discussed above found that a high level of biosecurity did not allow herds to avoid infection.[12,14,17,19,21,26–31,41] The diseases and pathogens discussed in these references are PRRS, PRV, SIV, MH, APP and PRCV. Although this can suffer exceptions (see below the prevention of problems associated with *Lawsonia intracellularis*), one could also ask why the same biosecurity rules that seem to be so efficacious in preventing infection of herds with organisms not believed to be transmitted by aerosol (e.g. *Brachyspira hyodysenteriae* and the mange mite), have been so disappointing for organisms like PRRS virus and MH? Factors like survival of the organism outside the host, dose needed to infect an animal and the relative prevalence of the disease in the area may vary and are among those that have to be considered, but the fact remains that some organisms are easily kept out of buildings where basic biosecurity protocols are observed, others not.
- It would seem to make sense that if a pathogen can be transmitted through the air, it should be

excreted in the air in one way or another. In this respect it is interesting to note that all pathogens that have been discussed above as potentially transmissible through air are, among others, excreted through the respiratory system of infected animals, so in the air.

- The French are now installing very expensive air filtration systems for their herds of high strategic importance, in an attempt to prevent infection of these herds by airborne pathogens. One would think that they must have serious arguments in favor of aerosol transmission to make this type of investment. It should be added that, as will be seen below, these units with filtered air do seem to remain negative to important pathogens suspected to be transmitted through the air.
- Can we continue to disregard the possibility for airborne transmission of any pathogen to occur when, by using mathematical models that consider elements such as environmental conditions, dose and survival of virus emitted in the air and direction of the winds, it is now possible to predict, for a pathogen like FMD virus, where it may hit next?[53]
- Dust has been found to travel thousands of kilometers in the air. For example, dust from the Sahara desert is said to reach the eastern United States about three times a year.[60] Dust from the Gobi desert can travel in the air and be detected on the coast of North America from British Columbia to Southern California. Why then should we be so refractory to the idea that some pathogens, which according to Zhuang et al[12] have to be associated to dust particles to form infective aerosols, might travel through the air between two hog barns?
- The present document is by no means a complete review of all papers suggesting that aerosol transmission of certain swine pathogens is possible. In this limited review, the number of researchers, scientists and practitioners stating that aerosol transmission of a given pathogen occurs, suggesting that it could occur or mentioning that this possibility cannot be ruled out, is over a hundred.[2,8,10–21,23–34,36–44,46–56,58,61–67] Those who believe in the possibility for pathogens to be transmitted through aerosol are not, thus, isolated or illuminated individuals.

So, finally, is aerosol transmission of certain swine pathogens possible or not? At the light of what is discussed above, my personal opinion is that there is ample evidence to suggest that it is. A more pertinent question however is which of the swine pathogens can clearly and definitely be transmitted that way and, perhaps even more importantly, how often does it occur, under what conditions and over what distances. This is where we are not as advanced as we should. It is not crucial to know if PRCV can be transmitted by aerosol or not, how often it does, and on what distance, because it is a pathogen of limited economic significance. But what about pathogens such as PRRS virus? It is the most important swine pathogen in North America, has been extremely costly to our industry for 17 years and yet, we are still arguing over questions as fundamental as how it gets transmitted. We would all agree on the fact that the best way to deal with a disease is not to have it. We would also all agree that to prevent introduction of a given pathogen in a swine barn, we need to know the different ways by which it can actually be introduced in that swine barn. In this respect, very simply, we have not done a good job, need to realize it, and do something about it. Although I am not an epidemiologist, it seems to me that as far as the aerosol debate is concerned, the following options are among those that should be considered:

- Determine, as has been done for FMD virus, the quantity of the suspected pathogen that is excreted in the air by infected animals, the quantity that is needed to infect an animal by aerosol and the survival time of this pathogen in various air conditions. Care should be taken, before reaching any definitive conclusions on a given pathogen, to consider the important differences that can exist between strains. For example adult pigs were found to release in the atmosphere 300 times less of the FMD virus strain responsible for the 2001 UK epizootic than what was observed for another FMD virus strain.[54]
- Compare the aerosol transmissibility of various pathogens in models that allow a certain quantification. For example, in their model, Kristensen et al[8] were able to infect pigs with PRRS virus with only 1% of the air coming from a group of infected pigs. They needed 70 % of the air from infected pigs to obtain the same results with APP. Similarly, the tube model developed by Dee et al[49] could also be used to compare the length over which various pathogens may be transmitted. If it were possible to transmit PRRS virus over a distance of 500 or 1000 meters, under a certain set of conditions and doses, but APP only

over 100 meters, then again it could give an idea of the relative potential for aerosol transmissibility of these pathogens in field conditions. It would be important to include in these studies, as controls, pathogens that are not suspected of being transmitted easily by aerosol.

– Epidemiological studies such as those conducted in Europe should also be undertaken in the US. If we take the example of MH, six studies have been published so far on this subject.[27–32] All of them are from Europe. A seventh, which should be submitted for publication soon, has been conducted in Canada.[5] Although all these studies have so far reached the same conclusion, one conducted under US climatic and environmental conditions could possibly help to reduce the apparent existing inhibition over this topic. The greatest need though would clearly be for PRRS, for which the state of uncertainty that presently prevails is, given the importance of yearly losses associated with it, hardly acceptable.
– Collect, compare and interpret the data presently available around the world in so called 'SPF', or 'High Health', or 'Minimal Disease' herds or systems, or in herds that were previously negative to a given pathogen and have become positive. These can be very instructive. In their attempt to eliminate MH and APP from Switzerland, Hege et al[32] found that of 3983 farms, 107 were reinfected in the year 2000. The incidence was 2.6% for MH and only 0.1 % for APP. A similar trend was observed in Denmark, where the data from Zhuang et al[12] showed that the level of infection of SPF herds for these pathogens was, between 1996 and 2001, 11.9% and 2.6% respectively. From these, one would think that if APP and MH can be transmitted by aerosol, MH may be more likely than APP to be transmitted that way, and/or to be transmitted on longer distances. In a different study on 344 genetic herds from the same country, the average annual incidence for PRRS infection was estimated to be about 8%.[42] Apart from the fact that all these studies concluded that aerosol transmission of these pathogens appears to be an important transmission means, and that this serves my point, the fact remains that putting together this type of data from 5 or 10 countries on selected pathogens would be a worthwhile exercise. If it were observed, and it clearly is in some countries, that biosecurity rules are easily stopping certain pathogens, but that others that appear to be the same everywhere are difficult to stop, it should mean that different modes of infection are involved. For sure many factors would have to be considered in the interpretation of these data before jumping to conclusions, but it would be unfortunate not to use such an interesting and valuable bank of information.
– It would be worthwhile to see if small herds that are poorly located, repeatedly got infected with different PRRS strains over the years in spite of following a rigorous biosecurity program, would remain negative if they were repopulated with negative animals and the buildings equipped with air filtration. If they become positive again, and no evident source of contamination can be found, the usefulness of this strategy in North American conditions could be questioned as far as PRRS is concerned. But what if they all remained negative?

The following section of the document will briefly look at different strategies or means, including air filtration, that could possibly be evaluated to prevent the potential aerosol spread of various pathogens.

Options to consider to prevent introduction of airborne pathogens

Stärk[61] reported that long-distance transport and survival of airborne pathogens are favored by cool, damp, calm conditions in the absence of sunlight over flat, vegetation-free areas or water. Following are some examples of options that could be considered to prevent introduction of airborne pathogens.

Wind barriers

Natural obstacles such as woods surrounding pig barns would seem to be logical wind barriers. Henderson[51] reported that in one FMD outbreak, one barn surrounded by trees avoided infection while others in the same area that were not became infected. This naturally does not constitute a proof of efficacy, and more information is clearly needed before one can have an idea on how protective natural obstacles like trees can be. Although the concept appears weird, it would be interesting to see if non-natural, man-made barriers could allow a greater reduction of the risk. A main advantage here would be time, since trees would make many years before being high enough to constitute a decent wind barrier, while man made barriers could possibly be installed in a day or a week. More data are needed to evaluate how efficacious, if at all, natural or artificial wind barriers might be in preventing introduction of wind-borne pathogens.

Type of ventilation system and orientation of the barns

Looking at the transmission of infectious laryngotracheitis virus in poultry, a study by Johnson et al[64] showed that there was a 4-fold increase in risk of developing this disease for farms that were located within the high risk wind vector area, when compared to farms not located within a high risk wind vector area. Poultry houses with both east-west orientation and tunnel ventilation systems were at significantly reduced risk for clinical infectious laryngotracheitis (OR = 0.05; $P< 0.01$). It thus seems that the type of ventilation system and orientation of pig barns should be further evaluated as potential means to reduce risks associated with wind-borne pathogens.

Location of the farm

As for many other relevant parameters, the safe distance from infected herds to avoid area or aerosol contamination is a topic that has not been adequately covered. Goodwin[27] reported that a safe distance from MH infected farms appeared to be 3.2 km. Robertson[37] reported that of the first 100 PRRS cases evaluated in UK, 63 % were thought to have been caused by aerosol transmission. In this study, the distances over which aerosol transmission was thought to have occurred were the following: 57 % within 1 km, 31 % between 1 and 2 km, and 11 % between 2 and 3 km. Results were quite similar in Belgium where for 56 farms suspected to have been contaminated by aerosol spread, the percentages were: 50 % within 0.5 km, 40% between 0.5 and 2 km and 10 % over 2 km.[37] The Danes still believe that their country became infected in 1992 through airborne viral particles that had to travel at least 15 km between Northern Germany and Southern Denmark (Mortensen S, personal communication, 2003; Baekbo P, personal communication, 2003). Most of this however was over water, which is known to increase the distance over which airborne pathogens can survive and travel. Tofts[24] suspected the infection of a farm by SIV over a distance of 4 km, and Wesley[20] referred to another anecdotal report of a farm suspected of becoming infected with PRCV by aerosol over a distance of 33 km. In a Danish study on the transmission of PRV, Christensen et al[14] suggested that airborne transmission of the virus over distances of 15 to 40 km, and in one case 80 km, constituted the most likely mode of introduction. There are very few data concerning the distance over which APP could possibly travel through aerosol. In one case reported by Desrosiers et al[10], the most likely explanation for infection was considered to be aerosol over a distance of 400 meters. Larsen[65] reported that APP could infect farms by aerosol on distances of 500 meters. Finally the distance record, so far, belongs to FMD virus which, as mentioned above, is thought to have travelled over a distance of about 300 km between France and the Isle of Wight, in UK.[53,54] Again though this was over water. It is important here to mention that since many of these reports on distances traveled by airborne pathogens are anecdotal and often cannot be convincingly proven, they should not all be considered as scientifically accepted or definitive. It should also be said that because a non-infected farm is located relatively close to infected premises, it does not mean that it will automatically or rapidly become infected. A multitude of factors, along with distance, have to be considered. One of them is the size of the infected and recipient farms. The larger the farms, the more likely they are to serve as a source of infected airborne particles, or as a potential target. Given the size of pig units in the US, this is a factor that should, at least theoretically, increase the risk of this mode of transmission occurring.

Regional control program

If some pathogens of importance are difficult to keep outside swine barns when herds in the neighborhood are infected, one possibility is to implement a regional control program where all farms in an area have to follow the same rules and be of the same health status for one or a few given diseases. A practical example of such a situation are certain eradication programs for MH. Because it is possible to eradicate MH from infected herds, and because it has been found so difficult to keep herds MH-free if neighboring herds remain infected, there are now efforts in some countries to eliminate the organism in a determined area, on a company basis or even on a whole country basis, such as in Switzerland.[32,62] A similar program was implemented for PRRS in the Pays de la Loire region of France.[63] The virus was first identified in that region in November 1992. An epidemiological survey was carried out in February 1993, and only 11 out of 2310 herds were found infected. An agreement between groups of producers was made with the aim of preventing spread of the virus. The program, that involved among others depopulation and repopulation of some herds, was considered a success. Two years after the first outbreak 98% of the population had remained PRRS-free. A set of rules has been established that seems to allow this region, located next to the heavily PRRS-positive Brittany, to remain virtually uninfected.

Air filtration

In 1995, a paper by Dutertre et al[66] stated this (translation of the French text): "The multiplication of cases where disease transmission occurs by aerosol has triggered the interest of genetic breeders and artificial insemination centres in techniques of air filtration, to reinforce the sanitary protection of their herds." The objective when using these air filtration systems is to limit the risk of introducing bacteria or viruses that may possibly be transmitted through the air. At the Station de Pathologie Porcine de Ploufragan, which is a place where many of the researches on swine infectious diseases are conducted in France, such an air filtration system has been installed in 1979 for a SPF herd. Although a lot of experiments have been done only 20 meters away from the herd protected by air filtration since its installment, with many swine pathogens such as hog cholera, pseudorabies, swine influenza and PRRS viruses, this herd has maintained its SPF status for all these years (Cariolet R, personal communication, 2002). This station is located in Brittany, where 50% of the swine production is done in France, on a small fraction of the country's territory. Unfortunately, the systems of air filtration are very expensive, and are restricted at this time to herds for which it is vital to maintain a high health status. Apart from the Ploufragan station, I know of at least 17 farms in France that are equipped with such a system. Because of the cost these are normally limited to high health boar studs and nucleus herds of different companies. The efficacy of these systems appears to have been excellent. It is interesting to note, for example, that none of the farms that have installed a system of air filtration seems to have been infected with PRRS virus yet. I have visited one of these farms that was located only about 200-250 meters from a PRRS positive farm, and it has remained negative now for a few years. These results do not constitute a final proof in themselves, but given the difficulty to maintain herds free of this pathogen in North America, they are, at the very least, worthy of a more thorough evaluation.

Other strategies

If, one day, it were accepted that some important swine pathogens can be transmitted by aerosol, and that systems like those of air filtration significantly reduce the risk of herds becoming infected, it is likely that bright minds around the world would eventually find ways to make it more affordable, or develop other strategies that may, at a cheaper cost, prevent pathogens from being introduced into swine barns through the air.

Duration of the carrier state and shedding of important pathogens

At this time it is probably appropriate to say a few words about the direct role that pigs themselves can play in the epidemiology of swine diseases. If not, I could be perceived as desperately biased or blind. In fact I don't disagree that, ultimately, infected pig farms are the main source of infection for uninfected farms. Where I disagree is on how pathogens get from these infected farms to uninfected farms, and on the overrated importance that has been and is still placed on direct introduction of bugs through sub-clinically infected animals. Nevertheless, one elementary piece of information that we should obviously have for each significant swine disease is how long pigs can remain asymptomatic carriers of the causative organism, and how long they can actually infect other pigs after their initial contact with the pathogen in question. The following lines will look at duration of the carrier state and shedding period for six of our important swine pathogens. It should be realized that these periods are based on data available at the time of writing, and future studies may prove that they have to be changed or updated.

Porcine reproductive and respiratory syndrome virus

The longest time that the live PRRS virus has been identified in a pig after infection is 157 days.[68] The longest time that genetic material from the virus has been identified by PCR in a pig after infection is 251 days.[69] Only a year after the virus was identified, Terpstra et al[70] showed that pigs infected experimentally were able to infect a sentinel animal placed in contact 8 weeks post infection, but not at 20 and 26 weeks, even if for the latter the infected animals had been subjected to immunosuppression (with prednisolone). Other studies that looked at how long pigs infected after birth could shed the virus and infect in contact sentinel pigs gave the following results: no transmission at 77 and 91 days;[71] no transmission at 90 days;[72] transmission at 42 days, but not at 56, 70 and 84 days;[73] 56 days, but not at 70 and 83 days;[74] 60 and 62 days, but not at 67 and 69 days;[75] 86 days;[76] 99 days.[77] The longest identified period of shedding, for pigs infected after birth, is thus at this time 99 days. However pigs infected *in utero* (infection of pregnant sows at day 90 of gestation) were able to infect sentinel pigs at 64, 84, 98 and 112 days of age, but not at 260 days.[78] In another study where again sows were infected at day 90 of gestation, the pigs

of these infected sows were able to infect sentinel pigs at 154 days of age, after being subjected to movement stress and given exogeneous corticosteroids.[79]

Swine influenza virus

It is generally believed that following infection with SIV, pigs remain carriers and shed the virus for only short periods of time. For example, Vannier et al[80] were able to isolate SI virus from the nasal cavities of one of 13 pigs 29 days after experimental infection, but pigs that had been infected 30, 45 and 60 days previously and put in contact with negative sentinel pigs did not infect them. Janke[81] reported that most pigs will shed the SIV virus only for 5-7 days after infection, and that peak virus load in the airways was present 24 hours after infection, with very little left in many pigs by 72 hours post infection. Similarly, Clavijo et al[82] showed that the virus could be isolated from nasal swabs in all pigs (30/30) 3 and 5 days post infection, but in none (0/15) 11 days post infection. Furthermore, the virus could not be isolated from any of the 73 tissue samples (tracheobronchial lymph nodes, lung, tonsils) tested from pigs euthanized 14 days after infection. Brown[67] reported that 7 to 10 days appeared to be the typical period of shedding, but that one pig in a study conducted many years ago was apparently found to excrete the virus for over 4 months.[83] Easterday et al[23] stated that there are no clear data to support or reject the existence of a long-term true carrier state of influenza viruses in swine.

Mycoplasma hyopneumoniae

Desrosiers[84] reviewed some of the data available on this topic. The end result is that we just don't know at this time how long pigs can remain carriers of this organism, or how long they can shed. Some authors believe that it could be as long as the life of the animal, while others suggest that it should be rather short, since eradication programs based on removal of animals that are 10 months of age or younger appear to be quite successful. However, we do know that pigs can remain carriers for at least 81 days since Sørensen et al[85] were able to isolate the organism from the lungs, but not from the nasal cavities, for that time period after experimental infection.

Actinobacillus pleuropneumoniae

Nielsen[86] was able to isolate the organism 4 months after experimental infection, from the nasal cavity and lung, and Desrosiers[87] showed that 6 months after cessation of clinical signs, naturally infected pigs were able to infect at least one of several negative pigs placed in adjacent pens. Finally, of 4 pigs that had been inoculated experimentally with APP serotype 5 on days 0, 7, 42, 79 and 114, the organism could be isolated from the tonsils of two pigs on day 359, so 8 months after the last inoculation.[88]

Lawsonia intracellularis

Guedes et al[89] have recently showed that *Lawsonia intracellularis* (LI) could be identified, by PCR, in feces of experimentally infected pigs for up to 12 weeks, in an experiment that was stopped 13 weeks post infection. Shedding was found to be intermittent.

Transmissible gastroenteritis virus

Morin et al[90] inoculated newborn pigs with jejunal or rectal contents of 4 to 6 month old pigs infected 4, 7, 15, 35 and 60 days previously. Jejunal contents of pigs was shown to still contain viable virus up to day 35 post infection, while it was only up to day 7 for rectal contents. These results suggested that pigs would shed the virus for only a short period of time in their feces. Most authors report on the subject that pigs remain carriers of transmissible gastroenteritis (TGE) virus for only a few weeks.[91] However Underdahl et al[92] reported more than a quarter of century ago that live virus was identified in the intestines and lungs of pigs up to 104 days post infection.

As can be seen, the information that we have on duration of the carrier state or shedding period for some of our important pathogens is often not as defined as would be needed. However as far as these six pathogens are concerned it would seem that TGE and SI viruses are the only pathogens for which the carrier state and shedding periods appear to be, in most but not necessarily all cases, a few weeks. For the other ones these periods have to be calculated in months and possibly, for some, in years. A more accurate idea of how long pigs can shed pathogens could be of interest, among others, in planning possible eradication programs. For example, it has been known for a while that it is possible to eradicate TGE from infected herds by deliberate and simultaneous exposure of all animals to the virus, closing the herd to new introductions for a few months, then resuming introduction of negative animals.[93] This strategy, to a much lesser extent, has also been used for PRRS. In two reported cases the program was a success.[94,95] In another not only did it not succeed, but the losses associated with this strategy were much greater than for other eradication strategies used, that were not however successful either in eliminating the virus.[96]

Diagnosis of swine diseases

Efficient control of health problems starts with knowing what we're dealing with.

PCR, Nested PCR, Real Time PCR, RFLP, PFGE, RAPD, Immunohistochemistry, *In situ* hybridization, sequencing, etc. The list of new and sophisticated techniques that have been developed to detect and identify pathogens of importance keeps getting longer and longer. These new techniques have improved significantly our ability to obtain a proper diagnosis when dealing with health problems or assessments in pigs. This section however will look at two more basic ways to determine the cause of these problems. The first one includes the simple observation of particular clinical signs and gross lesions, and the second one is serology.

Clinical signs and gross lesions

At a time when diagnostic laboratories are becoming increasingly technical and, one must admit, useful, we may have a tendency to rely too heavily, or even entirely on these laboratories and to minimize the value of observations that we, ourselves, can gather in the field. As practitioners our credibility is improved when producers and personnel realize that we are not only there to take specimens, send them to the lab and wait for results, but have an opinion on what's going on and on what the possibilities are before the lab results are received. This is particularly true when dealing with acute and severe conditions where losses are such that one cannot wait for lab results before implementing an initial therapy. Since this meeting's focus is on bugs and diseases, I thought it would be relevant to show during the presentation a few slides of clinical signs and lesions that are particularly suggestive or revealing of some of the main diseases we have to deal with. This is legitimate because the proper control of health problems starts with an accurate diagnosis, and the first step in the search of a diagnosis is a good clinical evaluation. For obvious space reasons, this part of the presentation is not included in the document.

Serology

Serological tests are clearly one of the most useful ways for practitioners to evaluate the health status of swine herds, and to help obtain a diagnosis on disease problems in field situations. As such, they are probably the diagnostic tools that are the most frequently used by practitioners. Interpretation of results obtained with these various tests is thus very important. In this respect, it is worthwhile to question ourselves as to whether or not our knowledge of what these tests are telling us is adequate. If one is to use serological tests, it seems logical that he or she knows for each important swine disease how soon after infection pigs become positive, how long they remain so and how many weeks or months maternal antibodies last in field situations. The same is true for the serological response associated with the various vaccines that are used in swine medicine. Without this knowledge of what theoretical or 'normal' results should be, the usefulness of results obtained in field situations becomes much more limited. This section looks at some of the serological results that, according to scientific literature, should be expected for four important swine diseases, as well as to results obtained in field cases where serology was performed.

Porcine reproductive and respiratory syndrome virus

Benfield et al[97] reported that PRRS virus antibody kinetics of the IPMA, IFA and ELISA tests are similar, and that antibodies are detected 7-14 days after infection, reach maximal titers by 30-50 days, and then gradually decline to low or undetectable levels by 4-6 months after infection. Dee et al[98] found that about 4 to 4.5 months following natural infection, only 35 of 120 animals were still seropositive. On the opposite, in an experimental infection by Lager et al[99] 11 females tested between 233 and 604 days after infection were still all seropositive. In this case though the IFA test used as antigen the strain that had been used as challenge, which might have affected positively the detection duration of antibodies. Maternal antibodies to PRRS are usually gone by the time pigs reach 5-10 weeks of age.[97] Animals vaccinated with the modified live vaccines presently available commercially in North America are thought to have antibody kinetics relatively similar to the one observed after infection with field strains (Lager K, personal communication, 2003). In an experiment where 12 PRRS negative gilts were vaccinated with such a vaccine on days 0 and 28, all seroconverted (IDEXX HerdChek PRRS ELISA) and the average S/P ratio for 6 of them, that were tested on day 250, was 0.37 with a range of 0.18 to 0.55.[100] Some animals do remain seropositive following vaccination for periods of time greater than one year (Desrosiers, unpublished data; Lager K, personal communication, 2003).

Clinical case: A PRRS negative herd became infected without knowing the origin of the infection.[94] It was

decided to try an eradication program that is based on introduction of as many gilts as possible, deliberate exposure of the whole herd and then closure for 23 weeks. The program was a success in that following introduction of negative gilts after the closure period, these gilts have remained negative and the herd has produced negative animals for a few years, before it was unfortunately destroyed by fire. It should here be mentioned, as seen above, that this technique is not without risk and has not been successful in all cases where it was implemented.[96] Since we knew the approximate time at which animals came in contact with the organism, and since this organism stopped circulating in the herd afterwards, it gave us a nice opportunity to see how long antibodies would last after natural infection. Four to 5 months after infection 28 of the 29 animals tested were positive, and the twenty-ninth had an S/P ratio of 0.32. Twenty months after infection more than a third of the animals (9/25) that were present at the time of infection were still seropositive. Table 2 shows S/P ratios (IDEXX HerdChek PRRS ELISA) obtained for some of the sows. These results show that there are field situations where PRRS antibodies following natural infection can last for much longer than 6 months. In this particular case, some sows lost their antibodies as would be expected over time, while for others these antibodies remained very constant. Two sows that were tested for a longer period of time were still clearly positive 28 months post exposure, using both the IDEXX HerdChek PRRS ELISA and an IFA test.

Swine influenza virus

Janke[81] reported that using the classic serological test for SIV, hemagglutination inhibition (HI), antibodies can be detected within 5-7 days of infection, with many pigs exhibiting titers reaching 1/80 by 1 week postinfection, peaking at 1/320-1/640 by 2-3 weeks postinfection and that antibody concentrations will remain high for several weeks before beginning to decline. Easterday et al[23] reported that maternal antibodies to SIV last 2 to 4 months, depending on the initial level, and that substantial amounts of antibody may be found for at least 6 months after infection. Finding references that specifically looked at long term duration of antibodies to SIV is a real challenge. Very few papers seem to have been published on the subject. In one of them, published in 1975, Renshaw[101] reported that pigs that were experimentally infected could still be seropositive, using a HI test, on day 441 after infection. Only four pigs however were infected and followed serologically. On the opposite, antibodies obtained following vaccination with a commercial product were of short duration in one recent report.[102] The vaccine was administered twice two weeks apart and, using an ELISA and a HI test, animals reached their peak titer 2 weeks and declined to negative levels by 10 weeks after revaccination.

Clinical case: A 150 sow herd, that at one point in time was positive to PRRS virus, APP, mange, atrophic rhinitis and MH, was now negative to all these pathogens following a successful program of segregated and medicated early weaning. The herd, which was closed to animal introductions from the outside and used an internal replacement system, was also negative to SIV, and in April 2001 all 20 blood samples obtained in

Table 2: S/P ratios (IDEXX HerdChek PRRS ELISA) in sows of a previously negative herd that were deliberately exposed to PRRS virus in January 1999, and where viral circulation stopped in the months following exposure.

Sow #	May 1999	Jan 2000	Sept 2000	Jan 2001	May 2001
1	0.32*		0.03		
2	0.53		0.04		
3	0.82		0.00		
4	0.97		0.09		
5	1.15		0.14		
6	0.80		0.76		
7	0.74		0.69		
8	1.25		0.91		
9	1.02	1.67	1.06	1.19	1.09**
10	1.55		2.01	1.87	1.64**

* Positive when ≥ 0.4

** Tested also using an IFA test, both sows were positive at 1/64

Table 3: Antibody titers (HI) in sows of a previously negative herd that was exposed to swine influenza virus in May 2001, and where the virus stopped circulating in the following months.

Sow #	Nov 2002	Sept 2003	Sow #	Nov 2002	Sept 2003
1*	≥ 1/640**	≥ 1/640	12	1/10	< 1/10
2	1/160		13	< 1/10	< 1/10
3	1/80	1/80	14	< 1/10	< 1/10
4	1/320		15	< 1/10	
5	1/20		16		< 1/10
6	≥ 1/640	1/320	17		< 1/10
7	1/160	1/160	18		< 1/10
8	≥ 1/640		19		< 1/10
9	1/320		20		< 1/10
10	1/160		21		< 1/10
11	< 1/10	< 1/10	22		< /10

* Sows 1 to 10 were in the herd in May 2001; sow 11 was born in the herd in July 2001, sow 12 in August 2001, sows 13-22 from Sept 2001 to November 2002.
** Positive when ≥ 1/10

finishing pigs were found negative.[103] In May 2001, significant coughing was suddenly noted in finishing pigs, less so in nursery piglets, and sows had virtually no clinical signs. The problem lasted about 2 weeks and only one finishing pig died. Blood samples obtained in June showed all finishing pigs tested to be positive to SIV H1N1, using a HI test. However, blood samples of finishing pigs obtained in January, April and July 2002, as well as in May and October 2003, were all negative, and it was concluded that the virus had stopped circulating in this farm in the months following the outbreak. Blood samples were obtained from 15 sows in November 2002, so 18 months after the outbreak of May 2001. Table 3 shows that all 10 sows (1 to 10) that were present in the herd in May 2001 were positive. The four sows found to be seronegative in November 2002 were sows that were born after May 2001, and so were not present in the herd at the time of the clinical outbreak. Fifteen sows were also tested in September 2003, including 8 that had been tested in November 2002. Four of 5 sows that were positive in November 2002 were still positive in September 2003, and the 3 that were negative at the first sampling were also negative at the second. The remaining sows tested were younger animals that were born in 2002 and were introduced in the sow herd, from the finishing unit, in 2003. They were all negative. In this particular case, 11 of 11 animals tested with the HI test were still seropositive 18 months post exposure, and 4 of 5 were seropositive 28 months post exposure. One sow (# 1) was still positive at the highest dilution tested 28 months post exposure. This shows that there are cases where antibodies to SIV can persist at high levels for a long time, and that high serological titers do not necessarily mean a recent infection.

Mycoplasma hyopneumoniae

In an excellent paper on the diagnosis of MH, Sørensen et al[85] reported that antibodies to MH were detected with an ELISA test as early as 8 days following experimental infection, with an average of 22 days. Four pigs that were followed serologically for 8 months were still positive at that time. Rautiainen et al[104] reported that in a herd where a successful eradication program was implemented, antibodies to MH were shown to persist more than three years in some sows. Interestingly, colostrum and not serum was used in that particular study. Studying a cohort of pigs born from seropositive sows, Morris et al,[105] reported that maternal antibodies waned at 30 days of age in pigs that initially had a low concentration of antibodies, and at 9 weeks in those that had a high initial concentration. In one study antibodies (Tween 20 ELISA) obtained following vaccination with 4 different commercial vaccines were found to be of short duration, as many animals were negative 45 days post vaccination, and the level of these antibodies differed significantly from one vaccine to the other.[106] The pigs came from a herd in which the sows had low serum antibody concentrations against MH. In another study where 3 commercially available vaccines were

tested for the presence of antibodies (DAKO ELISA) 16 weeks post vaccination, all pigs (12/12, 12/12, and 12/12) were still seropositive (Desrosiers, unpublished data). For one of the three vaccines the pigs were also tested using the IDEXX ELISA and the Tween 20 ELISA, and respectively 100% and 92% of the pigs were seropositive 16 weeks post vaccination. In this last study though the pigs vaccinated came from a herd totally negative to MH.

Clinical case: For about 10 years two MH infected herds had been producing MH-negative pigs by using a segregated and MEW program. One of the elements of the program involved vaccination of sows twice before farrowing. Piglets born from these sows were followed serologically (DAKO ELISA) and in one test, the number of seropositive pigs at weaning, 70 days, 133 days and 160 days of age were 5/5, 13/19, 3/20 and 0/20 respectively. (Bonneau M, personal communication, 2003). Maternal antibodies can thus last much longer than 9 weeks if sows in a naturally infected herd have been vaccinated before farrowing. These results are in agreement with those of Jayappa et al[107], who found that in an infected herd where sows were vaccinated once before farrowing, only at 15 weeks of age had all pigs become serologically negative.

Actinobacillus pleuropneumoniae

Few authors have looked at how long APP antibodies would last after infection. Nielsen[86] showed that experimentally infected pigs became seropositive within the first 2 weeks following exposure, reached peak values after 2 to 7 weeks and then titers remained constant up to termination of the experiment (week 16 post infection). These results were obtained with both a complement fixation test and an indirect hemagglutination test. In a study conducted in Quebec, of 4 pigs that were experimentally infected with APP serotype 5 on days 0 and 7, one always remained negative to an ELISA test, one seroconverted but was negative on day 94 and two seroconverted and were still positive on day 352.[88] Concerning maternal antibodies, they lasted in different studies until piglets reached between 3 and 10 weeks of age.[87,108] A peculiarity of APP serology is that pigs can be carriers of the organism without being seropositive, a fact that can have important implications in prevention programs.[109,110] This type of situation is normally observed immediately after infection with a pathogen but before the time period necessary for antibodies to be produced, but in the case of APP, pigs can be found carriers and seronegative long after infection. Dee et al[111] have recently reported that the same could be true, in some pigs, for PRRS virus. It is known that commercial APP vaccines vary in their ability to produce antibodies.[112,113] However, data on duration of antibodies following the use of APP vaccines available in North America appear to be scarce. In one small study that again dates almost 20 years and that involved very few animals (15), 5 pigs were vaccinated with one of three APP vaccines and followed serologically afterwards (Desrosiers, unpublished data). Two of 3 vaccines hardly produced any titers in vaccinated pigs, and all were negative 9 weeks post second vaccination. The third had average CFT (Complement Fixation Test) titers on weeks 2, 9, 13 and 16 weeks post second vaccination of 1/75, 1/14, 1/6 and 0 (all negative). To complicate the picture further, it should be mentioned that many if not most of the tests presently used have been developed to detect antibodies against APP infection, not against APP vaccination, and that this can have an impact on the results obtained. This is due to the fact that antibodies produced following vaccination (e.g. often directed against the capsule or toxins) may be different than antibodies that are mainly detected by serological tests (e.g. directed against the LPS). Thus, depending on the test used and on what specific antigens the vaccine contains, low or negative antibody titers following vaccination should be interpreted with caution. (Gottschalk M, personal communication, 2003)

Clinical case: In a small finishing unit, eleven pigs that were in a pen where one pig had died of pleuropneumonia (serotype 1) and where most others had shown clinical signs were followed serologically.[87] Two weeks after cessation of clinical signs, 6 of 10 pigs tested were positive, using the tube agglutination test with 2-mercaptoethanol. A month later 10 out of 10 were positive, and 7 months after clinical signs, 11 out of 11 were still positive. A few females from this experiment were kept for breeding in an isolated building. Two of 3 animals tested 15 and 27 months after natural infection were still seropositive when using a CFT and an ELISA test.[114]

A few comments here can be made. It is surprising to see that for a topic as important on a diagnostic point of view as serology, the data available are often surprisingly scarce, based on very small numbers, or even contradictory. It would thus seem logical, if proper interpretation of serological results is to be made, to conduct studies that would help validate what serological response should be expected when animals become

naturally infected with a pathogen, whether in the presence of maternal immunity or not, or are vaccinated with a given product. The same is true for antibodies obtained after consuming colostrum from sows of variable immune status. Another conclusion from these results is that high serological values do not necessarily mean that the animals tested had a recent contact with a given pathogen. In fact high serological values can be obtained in animals that have come in contact with certain pathogens more than two years before. This emphasizes the limits of taking only one set of samples at one point in time to find the etiology of a clinical problem. Ideally in such cases paired acute and convalescent sera should be tested. Clinically affected animals should be identified, sampled, the sera frozen and the same animals re-tested about 4 weeks later. Acute and convalescent samples should be submitted to the lab at the same time, and if possible a demand should be made to have both sera from the same animal tested on the same plate. So many factors can have an impact on the results obtained that what can be done to limit variations should be done. Following are a few other examples of problems that may have to be dealt with, or factors that may have to be considered when interpreting serological data:

- The problem of false positive results
  - Certainly one of the most frequent and frustrating problem to deal with. A boar stud becomes infected with PRRS virus, but has sold potentially contaminated semen before detection was made. In a nucleus herd where numerous sows had been inseminated with the potentially contaminated semen, 35 have their serum tested with the IDEXX HerdChek PRRS 2XR ELISA test. One female, inseminated 7 weeks previously is found positive (0.42). The positive serum is tested with a blocking ELISA and found positive, but is negative to both an IFA IgG and an IFA IgM test. The sequence of events shows that the positive female was likely a false positive.
  - In a recent study, 1639 and 2496 serum samples originating from naïve herds were respectively tested with the former IDEXX HerdChek PRRS ELISA and the new IDEXX HerdChek PRRS 2XR ELISA. The percent of animals found positive, so considered false positives, was 0.5 % for the former test, and 1.4 % for the new version. Although this may not seem as a big difference, the % of case submissions that had a single sample testing falsely positive went from 12 % with the former test, to 33 % with the new one.[115] In a different study that also compared these two tests from IDEXX, specificity was found to be the same, but the new IDEXX HerdChek PRRS 2XR ELISA produced S/P ratios that were higher than the former IDEXX HerdChek PRRS ELISA, while antibodies appeared to decline sooner.[116]
- The problem of false negative results
  - Thirty convalescent sera taken 4 weeks after the onset of an acute and confirmed influenza outbreak revealed only low or negative results to a standard H3N2 serological test.[117] Only 7 pigs were considered positive, all at the lowest titer considered specific (1/40). When the strain isolated from the herd was used to do the HI test, rather than the strain normally used in the standard test, high and convincing titers were obtained (2 pigs at 1/320, 7 at 1/160). These results demonstrated the value of testing convalescent sera with homologous virus when serology results are unexpectedly negative, and when this homologous virus is available.
  - The same can be said about a different pathogen and a different test. A Minnesota sow herd experienced a severe episode of abortion confirmed to be caused by PRRS in May 2002.[117] When tested by an IFA test, only one of 21 sows was found to be seropositive, but when the field strain of the outbreak was used in the IFA test, 18 of 21 sows were found positive. The same samples tested with the IDEXX HerdChek PRRS ELISA were all found positive.
  - Opposite results were obtained recently when a previously PRRS-negative boar stud became infected. Fifteen boars were looked at more closely using various tests. Fourteen of 15 boars rapidly became positive to a PCR test done on serum. All of them (14/14) became positive to both an IFA IgG and a blocking ELISA test in the following weeks. However, only 8 of the 14 boars became positive to the IDEXX HerdChek PRRS 2XR ELISA test, indicating that in this particular case, either the IDEXX test showed a reduced sensitivity, or antibodies would have been detected in the other 6 boars later than with the other two serological tests (Klopfenstein C, personal communication, 2003).
  - Five negative sentinel boars were tested serologically every two weeks as the PRRS monitoring

program in another negative boar stud. At one point in time, two of 5 boars were found positive using the IDEXX HerdChek PRRS 2XR ELISA test. Five different boars tested two weeks previously had been found negative. Since the sera from these boars had been preserved, it was decided to test them using an IFA IgM and a PCR test, to see if infection would have been detected earlier with these tests. Both gave positive results (Delorme M, personal communication, 2003). In this case it is not that the ELISA truly gave a false negative result, but simply that IFA IgM tests are reported to detect antibodies earlier than IFA IgG and ELISA tests, and could thus be of value in situations where earlier detection of antibodies is desired. Furthermore, because these IgM antibodies are only detectable for a few weeks after infection, their presence in the serum means that this infection was very recent, which can again be of value in trying to determine the time of infection of selected animals.[118]

- The possible impact of farrowing on serological results
  - Farrowing might have an impact on the serological response of sows.[119] Nine sows were tested for MH antibodies 4 weeks before parturition, and then every week until parturition. Every week antibodies decreased and were at 51% of their initial value at farrowing. Thereafter, the amount of antibodies to MH increased significantly and reached 75% of the initial value 2 weeks post farrowing. A second study on this topic also showed declining MH antibodies in the last weeks of pregnancy.[120] This could suggest that the reduction occurring at farrowing might be due to the influx of antibodies that are transferred to colostrum. It would be interesting to see if this decline, observed with MH in these studies, could also be obtained with other pathogens and other serological tests.
- The interference of maternal immunity on seroconversion following vaccination
  - Maternal antibodies can impact both efficacy and seroconverion following vaccination of piglets with SIV. Wasmoen et al[121] showed that the percentage of pigs that seroconverted following vaccination was 80 and 100 % for pigs with titers at the time of vaccination of 0 and 1/10, while it was 15, 20, 0 and 0% for those with initial titers of 1/20, 1/40, 1/160 and 1/320 respectively. Other studies suggest that the presence of maternal antibodies to other pathogens could have an impact on the response to vaccination. Thacker et al[106] reported that the response to APP vaccination was modified by passively acquired antibodies. Jayappa et al[107] reported that very high levels of MH antibodies did interfere with active immunization, while lower levels did not. Finally field data suggest that maternal immunity could also modify the serological response observed following vaccination with PRRS modified live vaccines.[122], (Desrosiers, unpublished data)
- The potential value of colostrum samples as an alternative to serum samples
  - Colostrum might be an interesting alternative to serum for detecting antibodies to various pathogens in some health monitoring programs. Colostrum samples can easily be taken by producers and frozen, and then sent to the laboratory for testing. This technique has been evaluated in some countries for pathogens like PRRS, MH, APP and toxigenic *Pasteurella multocida*.[123–125] In the case of PRRS, MH and APP, for which the comparison was made, the results suggested that sensitivity could be greater with colostrum than serum. Furthermore, Polson et al[126] have reported that testing less animals more often may be better than testing more animals less often, if the goal is to detect infection in a previously negative herd as early as possible. Since the collection of frequent samples is simplified when using colostrum, because they can be taken by the producer, it would make sense to evaluate the value of this strategy in monitoring programs of different diseases.

As can be seen, while serology is extremely useful in swine medicine, it is also very complex and can be, at times, frustrating. Practitioners that are faced with results that do not seem to make sense should, if not totally confident in what they know of the disease in question and of the test limitations, have the wisdom to consult an expert from the laboratory where the test was conducted, and possibly the humility to contact veterinary colleagues who might have more practical experience with this test and disease. Of the various options that can be considered in situations where the results obtained are not what was expected, let's mention: testing the same samples at the same lab with one or a few different serological tests (e.g. IFA and/or blocking ELISA test if positive to IDEXX HerdChek PRRS 2XR ELISA); testing the same samples with the same test but with a different strain of the organism used as antigen in the test or, when available and if applicable, with

the strain involved in the problem; testing the same samples at a different lab, with or without the same test; testing the same samples with a test detecting the antigen, not antibodies (e.g. PCR test on serum and/or tonsillar scrapings if positive to IDEXX HerdChek PRRS 2XR ELISA); testing the same animals, and other in contact animals 2-3 weeks later; if the animals are in quarantine, contacting the supplier to determine if anything abnormal has been noted clinically or serologically on the farm of origin, or if other recent purchasers of animals from the same source have reported anything abnormal (clinical signs or unexpected serological results); putting negative sentinel pigs in contact with animals with doubtful results and testing them in the following days (PCR) or weeks (serology), to see if the suspect animals are shedding the organism of concern; ultimately, autopsy of one or a few positive animals and submission of tissues to the laboratory if all other tests used are not conclusive. The relevance of these different options will naturally vary greatly from one situation to another.

Control of swine diseases

Now that we know what we're dealing with and, hopefully, how it got into the barn, what can we do about it?

Prevention of swine diseases: The example of porcine proliferative enteropathy caused by *Lawsonia intracellularis*

I have chosen to use this particular pathogen as an example for three main reasons. First it causes another disease that has interesting features on an epidemiological basis. Second it is a common problem so likely something that every swine practitioner has to deal with and third, it can effectively be prevented, among others, by both medication and vaccination, which allows us to evaluate the pros and cons of each of these two basic strategies. The epidemiological interest comes from the fact that it is difficult to maintain high health herds negative to this pathogen and, quite often, we don't know how they get infected. Here are two examples. Herd A is populated with animals obtained by hysterectomy. It is well located, closed to new introductions and observes strict biosecurity rules. It has remained negative to most important pathogens, but not to LI. About 4 years after population, clinical signs of ileitis were observed and no source of contamination could be found (Fast H, personal communication, 2003). Herd B was also populated with animals obtained by hysterectomy, does not use any medication that could prevent LI problems and all serological results so far have been negative. Herd B was used to populate herds C and D, where again strict biosecurity rules are observed. Both herds have remained negative to most important pathogens over the years, but not to LI (Boucher B, personal communication, 2003). So this pathogen finds its way into our swine herds by means that, again, we have not yet identified. Aerosol spread should not theoretically be as likely to occur for this enteric pathogen as it could be for some of the respiratory organisms like MH or PRCV. In the case of LI, one wonders if other animal species, particularly rodents, could possibly play a role in the epidemiology. This should certainly not be put aside for the moment as the list of species other than pigs from which this pathogen has been identified keeps getting longer and longer: rats, mice, hamsters, Guinea pigs, rabbits, dogs, foxes, ferrets, deer, horses, emus, ostriches and even monkeys. In a recent paper by Tomanova et al[127] it was found that LI was detected by nested PCR in the feces of foxes (2/31), deer (1/194) and gray wolves (2/23) in the wilderness of Slovakia. So wolves now have to be added to the list as well. Whether other animal species, birds, insects or something else can be involved in the epidemiology of this condition in pigs, efforts should be made to better understand why previously negative herds with apparently excellent biosecurity rules become infected. I see 5 main ways by which one could prevent problems associated with LI. The first one is to populate the herd with LI-free animals and do what is necessary to maintain the herd negative. This is easier said than done since the availability of animals that are clearly LI-free would at this time be very limited. Furthermore, as we have just seen, maintaining a herd LI-negative would not necessarily be a simple task. So this alternative is not one that can presently be widely used. The second is to eradicate LI from herds that are already infected. There are a few reports of small herds where eradication programs have seemingly and at least temporarily succeeded, so it appears that it could be possible to achieve.[128,129] However, in a larger study where it was attempted in 9 herds, 7 of them were infected again by 15 to 22 months after the eradication program, so we may need more time and data before concluding on the potential benefit of this strategy.[130] The third option would be to use management, nutrition, hygiene and pig flow strategies to reduce the risk of having losses associated with this pathogen. Unfortunately, to my knowledge, none of these strategies has yet produced totally predictable or consistent results. Segregated and

early weaning would appear to be a logical possibility, but in one study piglets were found to shed the organism when only 10 days of age, and multiple site systems using early weaning have not, in many cases, solved LI-related problems.[131] Option 4 is to rely on the use of antimicrobials. Several antibiotics can be used to prevent ileitis and while they can be efficacious at preventing losses associated with it, they at the same time can serve to control other pathogens that are covered by their spectrum of activity, and can also, in some cases, return more than they cost simply because of improved growth performances. The use of these products also has some limitations. The first that comes to mind is the ever increasing pressure that is placed on the use of antibiotics in animals, particularly those that are also used in human medicine, that are in families of products used in human medicine or that could possibly induce cross resistance to human pathogens. Most of the products used to prevent ileitis, with the possible exception of one, would fall into one or all of these categories. A second limitation is that to obtain an efficacious prevention, these antibiotics need to be used at a high enough level, and when this is done, the immune system of the animal may not be stimulated. The consequence of this is that the animal may remain susceptible to the pathogen if it comes in contact with it after medication is stopped. For example, Collins et al[132] have shown that if infected with LI a first time and not treated, animals would become immune and protected against a second challenge. This second challenge was done after the pigs had ceased to shed LI following the first challenge. If oxytetracycline were used at 50 ppm in the feed, pigs experimentally infected with LI became infected but showed less severe clinical signs than pigs that were not medicated. However if the dose of oxytetracycline used were 300 ppm, the animals were completely protected, but their immune system was not stimulated and these animals, after removal of the antibiotic, were susceptible to a second challenge and developed clinical signs of the disease. The third limitation of antibiotics in the prevention of swine diseases thus depends on the second one, and it is that to allow effective long-term prevention, the products often have to be used for a long time. There are however some indications suggesting that pulse dosing programs could be a way to reduce the total time when medication is applied, and to possibly limit the development of resistance to pathogens.[133,134] The fifth option is vaccination. There is presently only one vaccine available to prevent ileitis. One of the comparative disadvantages that this vaccine may have, compared to antibotics, is that it will only cover LI, and is thus limited, in a certain way, in its spectrum of activity. A second disadvantage is the price which, in the absence of on-farm economic data, could be perceived as being relatively high when compared to other vaccines presently available and to some of the medication programs that can be used. A third limitation, particularly for smaller herds, is the fact that the minimum number of doses for now is 100, which is too much in cases where only 20 or 50 gilts are introduced and need to be vaccinated. The recent advent in the US of a lyophilized form of the product, available in a 50-dose format, should address this problem at least partly. Finally, although a few years of usage have shown that the product appears to be safe, some may still be concerned about the potential dangers that could be associated with the use of live vaccines. There are however advantages. First it is not an antibiotic, so will not induce resistance to either animal or human pathogens. Secondly, testimonials from practitioners are showing that the product is effective in field situations and third, it seems that immunity is long lasting and that, although still too early to conclude, animals might need to be vaccinated only once to be protected for a long time, and possibly for their whole productive life. Because it is not injected, this kind of product also offers advantages over traditional vaccines. Given in the water, administration is quick and easy. It removes the risk of injury to personnel, eliminates a chore that no one likes to do, the product is welfare friendly since the animal is not stressed or suffering following vaccination, and there are obviously no injection site reactions or risk of broken needles in the meat. Since I work for the company that does sell the only LI vaccine currently available, it would not be appropriate for me to make recommendations on what should or not be used, so practitioners should choose the alternative that best fits the various clinical situations they have to deal with in the field based on their past experience, testimonials from credible colleagues or data available in the literature.

The treatment of swine diseases: The example of porcine pleuropneumonia caused by *Actinobacillus pleuropneumoniae*

Medications are and will still be needed in the foreseen future for the treatment of pig diseases. APP is a pathogen on which I had to work a lot in a previous life, and it well serves the points that I would like to make on this issue of treatment. After graduation, I worked for a

company that was buying 15 kg piglets from producers and raising them under contract in finishing units. The piglets that were mixed in these finishing units usually came from between 25 and 60 different sources. As can be imagined, mixing pigs from that many sources was a good strategy to get into health problems, and porcine pleuropneumonia was the most important. The majority of the strains we had to deal with at that time were of serotype 1, which were usually the most virulent. Table 4 shows the results of two different strategies that were used to treat acute cases of pleuropneumonia in finishing units of that company.[135] The first strategy consisted in putting antibiotics in the feed and water and to only inject pigs that were the most severely affected. The results to this strategy were very poor (11.4 % mortality) even if in retrospect, both the choice of products and the dosages used were probably not optimal. Furthermore a fair or valuable comparison between the two strategies would have required more data. In any way, because the results were so poor, it was rapidly put aside. I then decided to go into some barns that had acute problems with pleuropneumonia and to do the injection chore myself. This was done to determine whether or not pigs injected properly, which means with the right product, the right dosage and at the right time, would survive or not. It quickly became obvious that APP was responding very well to such an approach, and that few pigs would die if treated that way. This was true even when dealing with very acute and severe cases of the disease. From then the producers under contract were advised that antibiotics would not be added to the feed and water anymore when dealing with that condition, and that they would have to rely entirely on injections to save their pigs. In very severe cases pigs showing dyspnea or polypnea were injected twice a day, until they stopped showing clinical signs. This was particularly true if the product used had a short half-life. Although the producers under contract were initially not happy with that approach, because it evidently increased their labor, they quickly realized that if done properly, it was a better strategy than to rely on antibiotics in the feed or water. Once an APP outbreak was diagnosed, it would usually last between 2 and 5 weeks in a given barn. After that the clinical signs stopped, as most animals would have come in contact with the organism and become immune. Some people have recommended to inject all pigs in a given barn for 2 or 3 days in a row, in serious cases of APP. I do see weaknesses in this strategy and have not favored it in the past. The main reason was that, as can be seen in Table 4, immediate and excellent results were obtained when we began using the injection strategy only for pigs showing dyspnea and polypnea, so we did not feel that a different approach would improve anything. A second reason was that those who had tried that strategy before were often reporting that clinical signs would abate, only to start again after one or a few weeks. This made sense to me because in most cases, only 5 to 20 % of the pigs would usually show dyspnea and/or polypnea on a given day. Treating pigs that have not yet been infected would leave these animals fully susceptible, once the protective effect of the antibacterial would be gone. Furthermore, even if they were coming in contact with the pathogen while protected by the antibiotic used, it is not sure that their immune system would be adequately stimulated and that they would become immune, as we have seen above for LI. These relapses were usually not observed when only sick pigs were treated. In that case the disease would gradually move within the barn until no more susceptible pigs were present. Then clinical signs would normally stop and not reappear. I did recommend however to inject all pigs in some pens, or even in a room, if I felt that we were losing control or that there were just too many sick pigs in these pens to start determining which ones required an injection and which ones did not. I must admit here that these positive results with the injection strategy were obtained at a time when most of the finishing units of that company were using a feeding system where pigs were fed on the floor twice a day or more. This made detection of sick pigs easier. I must also admit that in hot conditions, sometimes all pigs are breathing abnormally and it then becomes

Table 4: Results obtained with two different strategies to treat acute cases of pleuropneumonia in finishing units of a Quebec integration company.

Strategy	# units	# pigs	% mortality	Drug cost (Can $)
Feed and water	3	3,613	11.4	4.79
Injections	35	46,059	2.34	3.03
Controls*	62	84,599	1.92	1.97

* Finishing units where no clinical signs of pleuropneumonia were observed

difficult to determine which pigs are not breathing normally because of APP, or because of the heat. The fact remains that to be successful in treating acute cases of pleuropneumonia, a few points must in my opinion be kept in mind. The first one is that pigs affected with the acute form of this condition don't eat much. This would be widely accepted, and has been proven experimentally.[136] The second point, which is not widely recognized, is that they don't drink much either. Pijpers et al[136] showed that pigs infected experimentally could see their water consumption temporarily drop to as low as 10% of what it was before infection. A third one is that if the pigs have the right concentration of the right antibiotics in the lungs at the time they become infected, they should not get sick. This was demonstrated again by Pijpers et al[137] in a nice experiment. An APP strain with a MIC for oxytetracycline of 1 (g/mL was used in a challenge experiment. Pigs were fed for 6 days a ration containing either no antibiotics, or 400, 800 or 1600 ppm of oxytetracycline, then challenged with the APP strain. The pigs were then euthanized 2 days after infection and their lungs examined. The average concentration of oxytetracycline obtained in homogenized lung tissue was 0.25, 0.57 and 0.83 μg/g of lung tissue for the three levels of medication. All pigs treated with 1600 ppm were totally protected (0% lung lesions) while for those receiving 800 and 400 ppm, 8 of 11 and 2 of 6 were protected. The authors stated that complete protection was obtained at 1600 ppm because it produced concentrations of the drug in the lung tissue that were equal to the MIC of the strain. Determining what is the 'right' concentration of an antimicrobial product can however be an issue, since both the concentration obtained in relation to the MIC and the time period during which it is obtained can have an impact on efficacy, and can vary from one antimicrobial product and one pathogen to another. For example time above the MIC is regarded as the most important parameter of pharmacodynamic effect of δ-lactam drugs against Gram-negative bacilli.[138] What is also important to keep in mind is that if pigs are already sick at the time they receive medication in the feed or water, efficacy is likely to be compromised because of the reduction in consumption, and thus in dosage that will occur. My personal belief is that for various diseases, treating only sick pigs by injection is often the most cost-effective method and should be the first one considered. Furthermore, this is in accord with one of the guidelines that AASV has established (Basic Guidelines of Judicious Therapeutic Use of Antimicrobials in Pork Production) that recommends to 'limit therapeutic antimicrobial treatment to ill or at risk animals, treating the fewest animals indicated.'[139] When it is not possible to treat only individual pigs because there are too many sick animals, the disease is too acute to detect and treat sick ones before they die, labor is a problem, etc., then the idea should be to reach, in target tissues, the right concentration of a drug to which the involved organism is sensitive before this organism gets there. In very acute cases of certain diseases (e.g. high mortality in peracute conditions associated with *Haemophilus parasuis* in a previously naïve herd), feed and water medications might not do the job and it may be necessary to initially inject the whole group of exposed animals to avoid death losses. The choice of the product to use is also worth briefly discussing. Daniels et al[140] reported on the sensitivity of about 1800 APP isolates tested at Iowa State University between 1991 and 1997. The percentage of APP strains found susceptible to 14 antimicrobial agents tested were the following: ampicillin (71 %), apramycin (63%), ceftiofur (98%), clindamycin (9%), erythromycin (12%), gentamycin (97%), neomycin (79%), penicillin (23%), spectinomycin (17%), sulfadimethoxine (6%), tetracycline (26%), tiamulin (71%), trimethoprim/sulfadiazine (88%) and tylosin (2%). Both tilmicosin and florfenicol were not evaluated, as these products were not available at the time. If water or feed medication is used, absorption through the gastrointestinal tract will evidently have to be taken into account. For example, in the Daniels et al[140] study a fairly high percentage of strains were susceptible to aminoglycosides, but given the poor intestinal absorption of these drugs, they are not a logical alternative if an oral treatment for pleuropneumonia is chosen. A rational approach would be to use the product that is the cheapest on the list of those to which the organism involved is sensitive. Other criteria however may also have to be considered. Another one of the AASV guidelines on judicious use of antimicrobials states: 'Antimicrobials considered important in treating refractory infections in human or veterinary medicine should be used in animals only after careful review and reasonable justification. Consider using other antimicrobials for initial therapy.'[139] This makes even more sense when one considers that we are not likely to see many newer antimicrobial agents become available to swine veterinarians in the near future. AASV also supports and is committed to objectives developed by AVMA's Steering Committee on Judicious Therapeutic Antimicrobial Use, one of them being to 'preserve therapeutic efficacy of antimicrobials'.[139] It seems likely, from what can be observed in field

situations, that these guidelines and objectives, albeit valuable, may not be specific enough. Certain products, that are our last resort drugs for some important pathogens, are sometimes used indiscriminately for various bacterial diseases for which they are not really needed. Furthermore these products are also occasionally used and promoted for situations where the goal is mainly to improve performance. Such usages seem contrary to AASV guidelines, will inevitably increase the speed at which swine pathogens will acquire resistance to these crucial drugs and could eventually precipitate decisions on what we can or cannot use in veterinary medicine. In an editorial of the reputed New England Journal of Medicine, Dr. Gorbach of Tuft University stated that the use of certain drugs that have important uses in humans should be prohibited in animals.[141] Although establishing guidelines on the judicious use of antimicrobials was excellent, it would now appear appropriate for AASV to go a step further and complement these guidelines with more specific directions and practical examples. A firmer position from our association, particularly concerning the usage of last resort drugs, could help reduce the speed at which swine pathogens will become resistant to them, and could also insure that they remain available to veterinarians for years to come.

Production of negative pigs from infected herds

Different technologies have been developed over the years that allow to either eradicate various pathogens from infected herds, or to produce negative pigs from these positive herds. Another presentation at this meeting will deal more specifically with this topic, but I would like to use an example to demonstrate that this can be done even for various pathogens at the same time. I was only involved in preliminary discussions on planning this program and the real 'maître d'oeuvre' was Dr. Réal Boutin, a colleague veterinarian from Quebec. The program was described elsewhere and I will not go into details, but here is the summarized story.[142] A small purebred herd of 100 sows was selling replacement gilts and boars. The herd was infected with atrophic rhinitis, mange and enzootic pneumonia, for which there were clinical signs, and with pleuropneumonia, for which there were no clinical signs, but positive serological reactions. Two successive PRRS outbreaks decided the owner that it was time to do something about the health status of his herd. The strategy was to use vaccination and medication programs in sows to increase maternal immunity and reduce as much as possible the possibility for sows to shed organisms to their piglets, and medication of piglets, to help them either remain free, or eliminate these organisms if they became infected. Young piglets were to be early weaned (oldest pigs were 10 days old) in a different building located 75 meters from the other one, and become the sows and boars of the new « clean » herd. The two buildings became two different farms. Different people were working in them and different equipment was used in each of them as long as the old barn, where pigs were under medication to reduce as much as possible shedding of some of the pathogens concerned, was not totally emptied, washed and disinfected. More than 4 years after the last infected animals have left the site, all laboratory tests conducted so far on the five targeted pathogens have been negative. The herd is closed to all introductions of live animals, located more than 4 km from any other swine barns in an area of low pig density, and follows strict biosecurity rules. This program was used in another small herd with similar results. At least on a small scale basis, it is thus possible to eliminate multiple pathogens from swine herds.

Fine tuning of multiple site systems

Another point that I feel merits further evaluation in the control of swine disease is the now very popular multiple site system. Although the early descriptions of this system made many of us dream of a better world, the results in at least a few aspects have not been what was hoped for. It has not for example been the ultimate solution as far as mortality rates and drug costs are concerned. Yet multiple site systems have been exploited very successfully in some organizations, and it is worthwhile to question ourselves on factors that could explain why it works so well in some cases, and is not up to expectations in others. I would like here to briefly describe a situation that has kept fascinating me over the years, and that has a relation with multiple site systems. The Deschambault station is operated by the CDPQ (Centre de Développement du Porc du Québec) and is used to evaluate breeds and breeding programs in relation to different carcass and meat quality traits, growth rate, feed efficiency, and so on. The station, that includes a nursery and a finishing room within the same building, each with a capacity of about 400 pigs, began to operate in 1994. It is operated on an all in - all out basis by site in an area of very low swine density. The closest pig barn is two kilometers from the station. Piglets from 20 to 30 different herds are introduced at an average age of 12 days (range 10 to 16) in one or two days. The health status of the different herds supplying piglets is variable,

some being free from most important pathogens, others being positive to organisms like PRRS virus, MH, APP, the mange mite, etc. The program, that was designed by another friend veterinarian from Quebec, Dr. André Broes, is described elsewhere.[143] Fifteen batches of about 400 pigs have been produced in that station so far. The average mortality rates have been 1.66 % (min 0.86 % – max 3.32 %) and 2.32 % (min 0.30 % - max 4.58 %) in the nursery and finishing phases respectively (Broes A, personal communication, 2003). One of the most impressive results obtained in that station is the total drug cost in finishing, which is lower than 10 cents per pig. No drugs have ever been put in the finishing feeds (25 kg to slaughter) for growth promotion, prevention or treatment. In only one batch was it judged necessary to add medication in the water, to address a *Streptococcus suis* meningitis problem. The medication cost in finishing is thus limited for the most part to the few individual pigs that are injected in each batch. The program has not allowed to consistently produce pigs that are negative to various pathogens, as serological results from samples taken at the end of the finishing period have proven that many batches were positive to PRRS, MH, APP and so on. But the pigs have been doing great clinically with, when considering that they came from 20 to 30 different sources, an extraordinary low cost for medication in finishing. It is clear that the overall program used at the Deschambault station cannot be integrally applied in all commercial systems. But given the remarkable results that have been obtained there, one would think that some elements of this program are worth considering by those who are not satisfied with the results they obtain in their own multiple site systems.

Concluding remarks

These concluding remarks should be viewed as simple opinions coming from a single veterinarian, and not as truths that the overall scientific community would endorse.

- On an epidemiological point of view
  - I would contend that we, as a profession, have over-emphasized the role of direct pig contacts in the transmission of swine pathogens, and underestimated the importance of farm location, pig density and indirect transmission means.
  - As far as the 'aerosol debate' is concerned, it is my hope that the present document may contribute to clarify the situation at least partly, and my belief that we will hear more in years to come about techniques such as air filtration. This being said, we should keep in mind that aerosol is only one of the various indirect transmission means by which swine pathogens can get transmitted, and make sure that we're not guilty of seeing it everywhere.
- On a diagnosis point of view
  - Let's not forget that a thorough clinical evaluation can still go a long way in identifying the causes of health problems.
  - Serology is and will remain an important diagnostic tool, but correct interpretation of serological results precludes that the practitioner knows what the antibody response is following natural infection, vaccination and absorption of colostrum, with the tests used and for the various pathogens of importance, as well as the limitations of these different tests. Given the discrepancies that can be observed between published serological data and some field results, efforts to understand the reasons for these discrepancies would be welcome.
- On a control point of view
  - The AASV guidelines on judicious use of antimicrobials are well founded, but it would be worthwhile to verify to what extent they are understood and applied in the field.
  - It is possible to eradicate certain diseases from infected herds, but in some situations and for some diseases, it may be easier and/or more successful to produce negative pigs out of positive herds.
  - Recent technologies like early weaning and multiple site systems have produced great and consistent results in some specific situations. The key elements of success in these situations should be studied further so that once identified, they can be applied in the many others where results are not satisfactory.
- What about tomorrow?
  - If I were asked today on what our main efforts in swine veterinary research should be put in the next 5 or 10 years, I would be tempted to answer on epidemiology. This may come as a surprise, but there are reasons. We know that healthy pigs perform much better than sick ones, are cheaper to produce, require less labor, are less likely to need antibiotics treatments, to have drug residues or injection site reactions, and so on. We know how to produce pigs that are negative to many different pathogens. What we have not found is

how to maintain herds negative to these various pathogens, on a large-scale basis. This should only be possible once epidemiological studies will have shown how these herds become infected to start with, and what is the relative importance of the different infection sources.

– Over the years, swine veterinarians have become increasingly involved in fields like nutrition, genetics, building design, economics, statistics, management and so on. This can conceivably be a differential advantage, but have we gone too far, when there is so much to know and so much unknown on purely health issues? Admittedly all these connected fields have their interest and can to a certain extent be intermingled with health problems. However, it is both revealing and possibly worrying to note that the Howard Dunne Memorial Lecture, which over the years has been one of the main events of the annual AASV meeting, is for the first time this year focusing on diseases and pathogens since 1988. Realistically, other professionals can replace us in many of the fields that we are presently touching, and often do a better job in these than we do. But none of them can do so with 'bugs and diseases'. We are, in this respect, both unique and necessary. Meeting and possibly exceeding expectations in this very important field where we cannot be replaced should thus, in my opinion, remain high on our priority list.

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