DISEASES OF THE RESPIRATORY SYSTEM

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General Discussion

In modern swine systems respiratory disease has evolved to more of a Porcine Respiratory Disease Complex (PRDC). This term is frequently used in lay and scientific text today. This complex of disease expression has likely developed because of industry management strategies that have focused on economies of scale and values created by food chain integration.

Although these strategies have eliminated many problems associated with continuous flow systems and associated diseases it has produced very large populations of mixed immune status pigs often on the same site. This has favored new syndromes by changing the ecology and evolution of a new set of economically important agents. This is a dynamic situation that is both complex and evolving.

• Although each of the various specific disease agents will be discussed many will be found together or in rapid succession in modern pig rearing facilities. Some of these agents when alone cause little disease or productivity impact but if present with PRRS virus serious consequences often occur. This is a challenge to the modern swine veterinarian who is limited by a decreasing number of antimicrobials and often ineffectual vaccines.
• Clinical signs of swine respiratory disease are little different from respiratory disease in other species. There can be a wide range of symptoms even in the same barn or production system. Multi-site production has led to a more age dependent onset of many agents and associated signs.
• Porcine respiratory disease is best compared to human respiratory outbreaks. Population size and contact rates affect both species. For example, whooping cough in daycare centers or seasonal influenza outbreaks spreading globally best mimic the respiratory issues faced in modern pig production.
• Coughing is common in pigs of all ages but varies with conditions, level of immunity, and specific agents.
• Dyspnea or “thumps” as it is described in pigs is a common sign with more chronic cases.
• Morbidity and Mortality is highly variable depending on the age, agents involved, and population size.
• Some respiratory disease has systemic origins.
• Parasitic (verminous) pneumonia is no longer common but may occur in back yard operations, pet, or zoo housed pigs.
• Respiratory disease complex is the most costly disease syndrome in US pig production.
Specific Agents in order of importance:

Porcine Reproductive and Respiratory Syndrome (PRRS) Virus

Introduction

- PRRS is a viral disease of pigs that causes two distinct clinical syndromes. Clinical signs are usually overlapping in breeding units where pregnant females display both reproductive failure and respiratory disease during outbreaks. The reproductive component of this virus has been discussed by Dr. McCaw and his notes should be used for reference. The virus affects pigs of all ages but older pigs and adults typically have shorter and reduced clinical severity when not pregnant.

- The virus causes persistent infections lasting three to four months or longer. A subset of alveolar macrophages is the only known tissue infected by the virus. Even so, this has a paramount effect on the immune system increasing the severity of many once passive agents present in pig operations.

- This viral agent has become the most economically significant US swine disease since Classical Swine Fever (Hog Cholera). There is a wide range of severity that is believed to be influenced by virus genetics, management, biosecurity, other pathogens, previous exposure, vaccine use, possibly pig genetics, and other factors.

History

- Clinical disease associated with this virus was first described in 1987 although some case reports go back to the winter of 1986. North Carolina, Iowa, and Minnesota all reported cases. It quickly spread throughout the US industry over the next few years. Interestingly a significantly different genetic strain spread through Western Europe almost simultaneously. PRRS has now spread around the world to every country where pigs are imported.

- To date no other species has been detected that can be infected with this virus although an early experiment with mallard duck shedding was reported. Rodents including mice and prairie dogs, cattle, horses, dogs, cats, goats, sheep, and repeated duck and other bird studies have been examined. The virus was originally called Swine Mystery Disease and where it originated is still a mystery.

- Some scientists believe the virus has been present in the pig for millennia and evolved into a pathogen as pig industries changed from isolated rural farms into large production centers. The virus has tremendous evolutionary potential but to date no other mammal species or biological vector has been detected.

Etiology

- PRRS is caused by an enveloped, single stranded, positive sense RNA virus in the genus *Arterivirus*. Other representatives are Simian Hemorrhagic Fever Virus (SHFV), Equine Arteritis Virus (EAV), and Lactate Dehydrogenase-elevating Virus (LDV). The original European isolate is known as the *Lelystad* virus from where it was
identified in the Netherlands. There are significant genetic and antigenic differences between these early isolates and now there is great variation within and between strains.

- The virus survives best in cold wet conditions partially explaining observed seasonal outbreaks. It is easily destroyed by drying, most disinfectants, and temperatures above 130˚ F. It is not viable in the environment. It can survive for 2 weeks in cool water and 8 days in lagoon slurry.

- The virus appears to disable or modulate significant macrophage signaling pathways blocking effective cell and humoral immune responses. This appears to also disable important pathways that would normally control other viral and bacterial pathogens as well.

**Epidemiology**

- Aerosol transmission appears to be non-significant beyond nose to nose contact but there are numerous reports suggesting airborne transmission is the only connection between farms during area spread events. This is difficult to document but suggest an aerial mechanical vector.

- The virus evades the immune system for extended periods leading to many persistently infected pigs. These pigs remain infectious for 150 days or longer but it appears that all eventually clear the virus.

- Virus is shed in the semen and is the only known infectious agent present in the US semen supply.

- The virus is highly infectious by less than 10 virions, and in field conditions highly contagious in an airspace (building). It is often very slow to spread from barn to barn or pen to pen without direct contact. Previous recovery from a different strain of PRRS virus appears to slow the spread of subsequent strains probably by reduced shedding.

- House flies, stable flies, and mosquitoes carry the virus for short periods and may contribute to geographic area spread and within sites.

- Pig transport vehicles are effective fomites and are major contributors to virus spread.

**Pathogenesis**

- Most infections occur when the virus reaches the tonsil or respiratory tract where it comes into contact with macrophages. Most virus replication appears to occur in lymphoid tissues where infected macrophages migrate (tonsil, spleen, thymus, Peyer’s patches, and lymph nodes). Pulmonary and intravascular macrophages are infected but only a very small percent of total macrophages.

- The resultant immune response is significant with detectable antibodies at fewer than 10 days to two weeks. ELISA tests readily pick up infected animals two weeks post infection. It appears that an effective neutralizing response takes many weeks longer.

- PRRS virus easily crosses the placental barrier. Early experiments indicated this only occurred after the 72 day of gestation but recent field experience indicates this can occur much earlier in gestation with certain stains and situations. The virus may kill all, some, or none of the fetuses during outbreaks. It has been speculated that fetal death may be caused by arteritis leading to hemorrhage in the umbilical vessels. In outbreaks many pigs are born alive but are viremic and suffer from interstitial pneumonia. These pigs often don’t survive the rigors of early neonatal life.
Recovered pigs appear to be fully resistant to re-exposure to homologous challenge but highly susceptible to heterologous strains.

**Clinical Signs**

- Uncomplicated interstitial pneumonia caused by PRRS virus is generally mild. This is usually only observed in research settings with high health piglets. Pigs are off feed for less than a week and appear to recover fully after one to two weeks. Even though there is apparent recovery pigs remain viremic for weeks with considerable variation in individual pigs.
- In the field morbidity always approaches 100% in individual rooms or barns. Nursery mortalities often approach 25% during virus movement through a system. These health breaks are complicated by a variety of viral and bacterial opportunists.
- *Haemophilus parasuis* greatly complicates PRRS and is the major cause of death in nursery situations.
- *Streptococcus suis* and other α Streptococcal bacteria are enhanced by PRRS virus leading to bacterial septicemia, pneumonia and meningitis.
- Pneumonic *Pasteurella multocida* (Type A) is normally a secondary invader but with PRRS can cause significant.
- Primary signs are lethargy, fever, depression, and subsequent stunting due to secondary diseases. Pre-weaned pigs born during outbreaks and nursery pigs often have a characteristic soft cough and “thump”.
- Herd or system stability will only develop if the virus is prevented from evolving. This is difficult to do in large populations where antigenic change is essential for virus survival. Herds that naturally control the evolutionary ability of the virus (small herds) typically eliminate it completely. Multi-site production where all growing pigs move away from the breeding herds at weaning can easily eliminate the virus through a rollover procedure described in the population health section.
- Repeated heterologous challenges will often lead to chronic respiratory disease in finishing pigs. This is usually complicated with influenza virus.

**Lesions**

- Infection results in mild to severe lymph node and lung involvement. Large tan colored lymph nodes can be found associated with every organ system. The interstitial pneumonia can vary from multifocal to lobular to diffuse. In the field this is often complicated by bacterial infiltration – nonsuppurative cases are rare but portions of the lung will have distinct microscopic lesions typical of PRRS. Mild Myocarditis, encephalitis, and rhinitis are often secondary lesions.
- Other infections that are commonly found in conjunction with PRRS are as follows: *Mycoplasma hyopneumoniae, Haemophilus parasuis, Streptococcus suis, Actinobacillus suis, Pasteurella multocida, Salmonella choleraesuis, Influenza virus, porcine circovirus, and porcine respiratory corona virus*. Typically three or more of these will be present leading to PRDC.

**Diagnosis**
Clinical signs and history usually point to a certain diagnosis especially in reproductive outbreaks. In large growing pig populations this is usually not as clear. In many stable systems the virus will be present but may not be the leading candidate for intervention. There are characteristic microscopic lesions but they are not pathognomonic and are often complicated by the presence of circovirus.

Today we rely on a number of testing procedures to support clinical observation. There is no replacement for doing representative postmortem examinations and laboratory analysis. My rule of thumb is post all the dead pigs in a barn that are reasonably fresh and euthanize and post at least 5 more with typical signs. This holds for all respiratory diseases. Use veterinary discretion but postmortem examinations should be viewed as a statistical process and representative numbers of samples must be collected to obtain an accurate diagnosis.

Virus isolation (VI), Immunohistochemistry (IHC), fluorescent antibody test (FAT), or detection of virus by polymerase chain reaction (PCR) may all be needed to make an accurate diagnosis. PCR has become the industry standard for diagnosis especially in naïve populations. In recent years sequencing of virus isolates has become popular but often leads to little information about the virulence of the virus. Serology (ELISA) is a great population tool but only indicates exposure. Paired sampling over time may increase the knowledge of when PRRS is active in a group of growing pigs but clinical signs are just as accurate when postmortems are also done.

**Control**

Most control strategies that attempt to live with the virus have been unsuccessful. Vaccines provide little cross protection against heterologous challenge and have met with limited success.

Area spread of new virus strains typically keep high risk systems in a constant state of outbreaks and viral pneumonia in growing pigs.

Recent attempts to replace field virus with vaccine virus by massive sustained vaccination of all adults and pigs in a system hold some promise but still do not protect from lateral introductions.

The most successful control strategies have been elimination and exclusion through intensive functional biosecurity implementation. (Review the population health section)

*Mycoplasma hyopneumoniae* (Enzootic Pneumonia)

**Introduction**

Mycoplasmal pneumonia of Swine (MPS) is endemic in most commercial production systems around the world and the most common cause of respiratory disease in growing slaughter pigs. Affected pigs typically display a non-productive “hacking” cough that persists for weeks. Reduced growth rates and lowered feed conversion are common especially in chronic pigs with secondary infections.
Mycoplasma pneumonia occurs year round but clinically is at its worst during winter months when poor ventilation and ammonia levels contribute to the pathology.

Mycoplasma pneumonia appears to make PRRS more pathogenic. This may be due to the increased numbers of macrophages attracted to the lung during Mycoplasma infection.

History

Chronic pneumonia in swine has been recognized for more than a century. Clinical separation of Mycoplasma from Influenza occurred in 1948 and the chronic respiratory component was incorrectly believed to be caused by another undetermined virus. It became known as Virus Pig Pneumonia and remained so until 1965 when the disease was first experimentally reproduced in the US and England. The name hung on for many years and only recently appears to have died away.

Etiology

Mycoplasma hyopneumoniae is extremely fastidious and difficult to isolate and grow. Two other non-pathogens that are normal inhabitants of the respiratory tract, M. hyorhinis and M. flocculare are easier to grow and often complicate the isolation of M. hyopneumoniae. These non-pathogens also complicate the creation of Mycoplasma autogenous vaccines. This should be avoided since commercial vaccines are cross protective and effective.

This Mycoplasma does not survive once outside the pig even in moderate environments. It is easily and quickly killed by most disinfectants. Transmission is through direct contact with carrier pigs. There have been reports of aerosol transmission up to a half mile but these were made before molecular identity was possible and are doubtful. In recent years breeding stock companies have maintained large populations of M. hyopneumoniae free pigs.

There is plenty of evidence that M. hyopneumoniae is a primary pathogen and also exacerbates other pathogens specifically PRRS and Influenza viruses. This bacterium is a significant component of PRDC.

Epidemiology

It has long been thought that life carriers of M. hyopneumoniae exist but recent evidence disproves this notion. It appears that in multi-site production systems where no growing pigs are housed near the adult herds, only the gilt replacements have detectable Mycoplasma. Herd rollover elimination strategies have been very effective and it may be possible to eradicate this agent from modern production systems.

The Mycoplasma organism does exist in the lungs of infected pigs for months after recovery but contagiousness to naïve pigs ends at approximately 10 months post infection. Transmission from the P-1 females to offspring is the major contributing factor maintaining this endemic pathogen.
Pathogenesis/Lesions

- The organism is non-evasive and pathogenesis is believed to be the result of the immune response and disruption of the mucociliary apparatus. Outer membrane proteins appear to be the primary virulence factors and this may vary between isolates but as mentioned above is not a legitimate argument for autogenous vaccine use.
- Poor air quality has long been known to increase the severity of the disease. Winter ventilation conditions typically increase the severity of Mycoplasma respiratory disease and PRDC.
- Gross lung lesions are typically cranioventral consolidation but this is not pathognomonic. These lesions are usually found in the apical, intermediate and cardiac lobes but may extend into the diaphragmatic lobe in severe cases.
- Microscopic lesions may include lymphohistiocytic peribronchiolar cuffing, mucocellular exudates, and atelectasis. These findings are not specific and can be present with any bacterial pneumonia.
- Filling of the alveoli with mucus or mucopurulent material is typical and this material can be easily squeezed out of bronchi at cut surfaces.
- Secondary bacterial infections typically follow primary Mycoplasma pneumonia and are the major cause of Mycoplasma related mortality.

Clinical Signs

- A dry hacking non-productive cough is the primary clinical sign. This cough may persist for weeks in individuals and months in barns. Pigs typically do not have elevated temperatures unless secondary or other primary agents are involved.
- The incubation period for *M. hyopneumoniae* is approximately 6 weeks or longer in modern production systems. Since only a few carrier pigs are present, pigs usually don’t exhibit clinical signs until 8-10 weeks on the finisher. Influenza activity often follows this same pattern complicating both diagnosis and interventions. This natural delay allows significant time for strategic vaccinations plans.

Diagnosis

- Accuracy in diagnosis of Mycoplasmal pneumonia requires submission of quality samples and laboratory assistance. Isolation of the bacterium is slow and although confirmatory is insensitive. Immunohistochemical and fluorescent antibody techniques are the standards for diagnosis today. Enzyme-linked immunosorbent assay (ELISA) and complement fixation tests are available for herd basis tests but false positives cloud interpretation in naïve groups. Routine vaccination may also produce many false positives.
- Nested polymerase chain reaction (PCR) tests are available but are very sensitive, subject to lab cross contamination, and only indicate the presence of the microorganism not disease.
- Slaughter checks have been used to diagnose and determine the prevalence of Mycoplasmal pneumonia in pigs but many lesions heal and results are misleading. Lung examination at slaughter time only depicts the past six weeks of the pigs life.
Gross lesions are not pathognomonic for Mycoplasma and only indicate bacterial pneumonia.

Control
- Numerous Mycoplasma vaccines have been on the market since 1980 and have traditionally been the primary control method in the global industry.
- The appearance of PRRS virus and the evolutionary changes in swine influenza have significantly changed the efficacy of vaccination programs.
- Today there is an ample supply of replacement breeding stock available in the US, Canada, Europe and other parts of the world. Stocking with negative females, repopulation, rollovers, and medicated early weaning (MEW) have been highly successful methods of elimination.
- Functional biosecurity and especially functional isolation monitoring techniques are essential in maintaining negative status.
- Multi-site systems tend to control Mycoplasma better than traditional systems because of greater opportunity to vaccinate during early incubation after maternal antibodies disappear.
- Antimicrobials have and continue to be important for control of secondary infections and Mycoplasma. Since the microorganism is not invasive it is difficult to achieve high levels of most antimicrobials where it is needed in the mucus with feed and water medications. Tetracyclines, tylosin, lincomycin, tiamulin, and enrofloxacin have claims on efficacy.

Haemophilus parasuis (Glasser’s Disease)(HPS)

Introduction
- This is a highly contagious and infectious disease primarily of nursery age pigs in modern production systems. Both acute and chronic infections are common. Pigs exhibit combinations of meningoencephalitis, polyserositis, polyarthritis, and severe pneumonia. The introduction of PRRS virus has significantly raised the importance of this agent.

History
- Glasser first reported this disease associated with a small Gram-negative rod in 1910. In 1931 it was isolated in association with swine influenza and named Haemophilus influenzae suis. Its name was changed again in 1943 and 1960 becoming Haemophilus parasuis in 1976 which still remains until today.

Etiology
- H. parasuis is a small Gram-negative rod which is difficult to isolate in many field cases. It will grow on blood agar next to a Staphylococcus streak or on agar fortified with nicotinamide adenine dinucleotide (NAD). It is a normal inhabitant of the nasal cavity and tonsils of normal pigs. Isolates from systemic sites are considered pathogens while other isolates appear to be benign genotypes.
• The bacterium often grows on serosal surfaces of the peritoneum, pleura, pericardium, joints and meninges. It is frequently called carpet heart by production personnel because of the fibrin accumulation and tags.
• There are at least 21 serotypes but more recently labs have started to genotype the bacteria. Genotyping is useful but not often predictive of virulence.
• Multiple serotypes may be present in the same pig or herd. There are often multiple pathogenic strains and several non-pathogenic strains present in the same system or farm.

Epidemiology
• H. parasuis is found everywhere there are pigs. Most genotypes appear to be non-pathogenic but dynamics of modern swine production appear to produce both early neonatal inoculation which is protective and pigs that are not colonized and susceptible. When these pigs are mixed outbreaks occur. This can be in the nursery of different sources of replacement stock mixed during acclimatization. A complex combination of colonization and immunity, timing of exposure and PRRS virus activity appear to play significant rolls in outbreaks.

Pathogenesis/lesions
• Factors that trigger onset of disease are poorly understood. The lesions associated with pathogenesis are associated with vasculitis and leakage of serum and accumulations of fibrinous exudates over serosal surfaces.
• As mentioned PRRS virus and also Influenza may lead to increased incidence and severity of disease.
• Affected pigs often become chronic and fail to respond to antimicrobial therapy when these other viral agents are present.
• Commingling growing pigs can lead to severe outbreaks without these viruses.
• In modern production systems bronchopneumonia and pleuritis are common findings with this bacterium.
• Cyanosis of the skin is often present in pigs that die especially on the “down” side. More chronic cases will have large amounts of serofibrinous or fibrinopurulent exudates in the peritoneal or pleural cavities.
• Lung lesions often appear to be embolic in peracute cases suggesting a hematogenous route.

Clinical Signs
• In mixed source pigs onset is generally acute. “Dog sitting” with posterior paresis is characteristic. Pigs that can rise and are forced to move often show severe signs of pain. Occasionally unilateral swelling and pitting edema of the ear are apparent. In acute onset cases typical polyserositis will be absent in most pigs that die during the first few day of the outbreak.
• This disease is commonly observed in nurseries on the second week of placement. This is especially apparent if PRRS virus is circulating in the same age group. This may be delayed if PRRS seroconversion is later.
It is usually easy to find the classic polyserositis lesions in this age pig especially in hospital pens. Choose non-treated pigs for postmortem examinations.

CNS signs will also be present in some pigs in all affected groups when PRRS virus is active.

In nursery or wean-to-finish barn situations morbidity may approach 50-75% and mortality can be as high as 25%. In these cases pigs do not appear to respond to antimicrobial therapy.

**Diagnosis**

- History and typical lesions are often all that is needed in nursery situations. Production personnel may call just to inform that they are treating again.
- Culture from systemic sites such as the meninges, cerebrospinal fluid, joints, peribronchial lymph nodes, serosal surfaces, and lung lesions are important because of the presence of non-pathogenic strains in most production systems.

**Control**

- *Haemophilus parasuis* is typically sensitive to β-lactam antimicrobials. Preventative administration of oral (feed/water) antimicrobials is usually of little value. In situations where PRRS virus is circulating along with *H. parasuis*, treatments appear to do little other than reduce mortality.
- Rapid diagnosis and intervention is critical in all cases. Therapy should always be started prior to laboratory confirmation. Outbreaks in breeding age females require whole population injections for several days unless effective residual antimicrobials are available.
- Vaccines are somewhat effective if outbreaks occur in pigs after they reach 10 weeks age. Autogenous vaccines are very good in these cases. However, nursery breaks are not prevented by vaccine. This is most likely do to challenge timing and blocking by maternal immunity.
- Inoculating pigs with on farm virulent isolates while still suckling has been a successful approach. This makes sure all piglets are colonized by farm strains prior to loosing maternal antibodies. Management of the live inoculum is a challenge for most production systems. Quality control is essential in the lab as well as on farm.

**Swine Influenza (SI)**

**Introduction**

- Swine influenza is an acute infectious respiratory disease of pigs.
- The virus typically moves rapidly through modern pig sites. Pigs are generally off feed for 48 hours. A barking cough is typical with classic H1N1 virus types but not as apparent with some of the newer re-assortment strains.
- Pigs often demonstrate sudden temperature spikes, ocoulonasal discharges, prostration, and weakness. A typical barn will have paroxysmal coughing, thumping, and few if any pigs at the feeders. This may make a remarkable change in 48 hours but coughing
often remains for a week or more. Mycoplasmal pneumonia will complicate the severity and rate of recovery.

- The virus is widespread in the US and rest of the world. Numerous distinct genetic types exist along with antigenic drift variants.

**Historical perspective**

- The classic swine flu is a Type-A H₁N₁ Influenza virus that apparently entered pig populations around the world and especially the United States associated with the human Spanish Flu pandemic of 1918. The actual death toll from this outbreak is unknown but estimated to be between 20 – 30 million people. It is interesting that the virus quickly became species adapted and remained remarkably stable for nearly 75 years in pig populations. Recent isolates in the United States and elsewhere around the world demonstrate that antigenic drift and shift is in a new dynamic state. Many re-assortment strains (shift) are present in the industry along with some more classic viruses.

- Today the Center for Disease Control (CDC), World Health Organization (WHO) and many other organizations around the world have intense interest in influenza viruses. The recent outbreaks in Asia with high pathogenic avian strains that jumped species to humans has raised the concern that another world pandemic may soon occur. This is a very interesting virus and one of the classic zoonosis. Waterfowl and perhaps other reservoir avian species maintain all genetic types of influenza viruses without clinical repercussions.

**Etiology**

- Over the past 8 years three subtypes of H₃N₂ viruses, several subtypes of H₁N₂ viruses, and numerous H₁N₁ viruses both drift and shift varieties have widely circulated in the United States swine industry.

- The antigenic surface of the influenza virus is primarily composed of glycoprotein spikes. There are 13 hemagglutinins (H) and 9 neuraminidases (N). The hemagglutinins are believed to be the more important antigenic site conferring immune protection.

- Antigenic shift is thought to be a result of concurrent infections with different influenza’s in the same animal but there is also evidence that the virus occasionally recombines with its own RNA genetic segments. For example matrix coding RNA incorporated into hemagglutinin RNA. This is only reported in South American avian isolates.

- The virus survives outside the host for a short time but less than two weeks under normal production conditions. It is easily destroyed by a wide range of disinfectants, drying and heat.

- The virus is traditionally grown in 9-12 day chick embryos and this is still the source of virus for vaccine production. It will also grow on a variety of cell culture lines but consistent titer issues have prevented adoption by the animal health industry.

**Epidemiology**

- There is a growing body of evidence that indicates swine influenza viruses are moved by human caretakers and that many of the viruses present in the US swine population today have genetic components that arrived from widely circulating human strains. Although the pig has long been considered a potential mixing vessel for avian and
swine strains, there is little evidence that swine are the source of re-assortment strains that jump to humans. Humans and pigs share a common receptor site creating potential for exchange of circulating viruses.

- It is important to keep swine populations separate from birds especially waterfowl and the pig water supply must also be protected and purified if surface/reservoir water is used. “Mixing vessel” opportunity is especially concerning in Asia where there are many small farms with pigs, ducks, chickens, and humans living in close proximity with no existing biosecurity barriers to separate them.

- Cross protection between different strains of virus is generally negligible. Most of the commercial vaccines have struggled in the field because they are often obsolete by the time they clear the regulatory process. Likewise traditional HI tests fail to detect most circulating strains. Many labs now run a battery of HI tests based on circulating isolates but this will fail to identify future viruses. Isolation of virus and sequencing is the best method to evaluate and diagnose recurrent influenza like clinical signs.

- Well made and current autogenous vaccines may be necessary to control influenza in large production systems.

- An immunological phenomena known as “original antigenic sin” may be important in pigs just as it is in humans. When exposed to a virus after prior exposure or vaccination, the rapid immune response needed to protect is memory B-cell based. Thus the starting immune response and neutralizing antibodies produced are specific for the previous exposure and not the invading strain. In this scenario vaccine may do harm verses prevent illness.

**Pathogenesis/Lesions**

- The influenza virus has a tropism for bronchial epithelia cells. It enters the pig through nasopharyngeal route. Viremia is very unusual and transient when it does occur. The incubation period is often less than 24 hours which explains the rapid onset, high morbidity, and quick recovery.

- Lesions are typical of most viral pneumonias. Cranioventral involvement is normal but in severe cases more than 50% of the lung may be involved. Interlobular edema is usually present and bronchi contain blood stained fibrinous exudate. Affected lung tissue is typically purple and a clear demarcation zone adjacent to healthy tissue is apparent. Some of the newer circulating strains are more pathogenic than older isolates and are associated with large areas of lung consolidation.

- The sequelae to influenza outbreaks are secondary bacterial pneumonia and often gastric ulcer outbreaks with acute and chronic mortalities.

- Microscopic lesions usually include obstruction of airways with fibrinopurulent or fibrinous exudates with necrosis and degeneration of airway epithelium.

- Pathogenesis varies with the different circulating influenza variants and depending on prior exposure or maternal antibodies levels. Cross protection between variants will usually be minimal.

**Diagnosis**

- Diagnosis can be a challenge when new variants go through a system. HI and newer ELISA tests may not pick up new variants. Paired serology is always recommended but
it may mistakenly indicate negative results. Directigen Flu-A is a rapid test that can be run on tissues which picks up the A-antigen on all type A influenza’s.

- It is important to recognize that serological tests are unreliable in many systems and herds today. PCR is another reliable method but costly. Sequencing is typically done on the H gene only but some labs are looking at the whole viral genome. These tests are useful when relying on autogenous vaccines for control allowing logical virus switching when new isolates are discovered.
- Nasal swabs collected from febrile pigs are a good diagnostic tool. Swabs with viral transport media shipped on ice achieve good results. A drop of glycerol added to the saline media may improve viral survival in transit.

Control

- As mentioned, control is becoming more challenging in today’s evolving environment. A combination of extensive monitoring and autogenous vaccine has been used successfully in large systems. Issues still remain because of the lag time between discovery of a new variant and getting the vaccine into the field. This often takes 90 days for the new vaccine to clear USDA hurdles.
- Influenza has become a year round issue in large systems and clinical signs are often less pronounced muting the value of history and typical “flu” clinical observations as reliable observations for making a diagnosis.
- Biosecurity is not effective in preventing influenza. Even so replacements should be screened and never introduced when exhibiting clinical signs.
- Sow herd vaccination is widely used to protect piglets through the nursery phase. If nursery breaks occur in vaccinated systems new variants will be present and increasing the number of vaccinations per year is malpractice.
- Vaccination of growing pigs presents some timing issues. Pigs typically retain maternal antibodies until 10 weeks of age or longer. If sow vaccinations protect the nursery then it will be difficult to protect finishing pigs which suffer greatest mortality and have added fixed and variable cost attached to them.
- Vaccination programs take time to make substantial differences in large production systems. They require extensive monitoring, sequencing of isolates, strategic vaccines (autogenous), and good timing of administration.

Actinobacillus pleuropneumoniae (APP) & A. suis

Introduction

- These are two closely related bacteria that can be highly contagious, cause severe necrotizing pneumonia, high morbidity and high mortality. In naïve populations the onset and spread will be rapid with many acute deaths in the first 48 hours of the outbreak. A. suis is typically much milder and less contagious but in mixed source pigs can be clinically very similar although more responsive to treatment.
- These bacteria only appear in pigs. Both have world wide distributions. APP has long been an issue in Europe and Canada. In the US it has become less common in modern multi-site systems. This may be largely due to a few negative breeding stock companies
dominating the industry expansion during the 1980’s. *App* is still present in some North Carolina production systems.

**Historical perspective**
- APP was first diagnosed in the United States in 1957. It became widespread by the late 1970’s though spread by small purebred breeders and small breeding stock companies. Early serologic tests were notoriously unreliable but were the basis of many lawsuits. Some cross reacted with *A. suis* which in most cases could be managed with occasional antimicrobial therapy in affected groups. Because of the severe economic impact of APP many herds were depopulated to eliminate this agent. The pig is the only known reservoir.

**Etiology**
- *Actinobacillus pleuropneumoniae* is a hemolytic Gram-negative, capsulated, coccobacillary rod. There are 12 recognized serotypes in Biotype I and three in Biotype-II. It is not uncommon for isolates to also be designed as non-typical or cross reactive to two serotypes.
- APP secretes 4 cytotoxins (exotoxins) designated as ApxI, (serotypes 1, 5, 9, 10, & 11) ApxII, (all serotypes except 10), ApxIII, (2, 4, 6, & 8) and ApxIV. These toxins are the RTX group. Each serotype may secrete some or all of the toxins. Serotypes 1, 3, 5, and 7 are reported as the most common in the US but that has changed over the last several years and is system and geographic dependent.
- *Actinobacillus suis* is closely related to APP and may contain one or more of the RTX toxins. Hemolysin producing strains are typically most pathogenic. The bacterium requires NAD for growth similar to HPS. Outbreaks typically occur in finishing pigs but occasionally in individual adults, and nursery pigs.

**Epidemiology**
- Pigs that survive APP typically become carriers for a considerable period or perhaps life. Recent eradication attempts in Europe have been successful in small herds with and without antimicrobial intervention. Rollover attempts in the United States in large herds have not been successful.
- APP is a direct contact disease although clothing, boots, buildings and transport trailers will remain contaminated and infectious for a period of a few days under most production conditions. Like all pathogenic agents cold, wet, and cloudy conditions favor microbial survival.
- APP has a world wide distribution but some serotypes are geographic specific. The bacterium is generally believed to be species specific and other reservoirs have not been discovered. Short downtimes between infected vs. non-infected pigs have always been successful in eradication clean-ups supporting this assumption.
- Over the years most APP outbreaks have been the result of purchased genetic additions. Tests have not been reliable and chronically infected herds often have few if any clinical indications of disease. Modern breeding stock companies generally have successfully eliminated APP although most are *A.suis* positive and a few still have low virulence strains of APP.
Pathogenesis/Lesions

- There is significant variation in virulence between serotypes but this is also geographic/country dependent. This may be because stereotyping is not directly linked to the number and types of RTX toxins present.
- The RTX toxin group is generally highly toxic to endothelial cells and alveolar macrophages. Vasculitis is followed by thrombosis, infarction, and toxic shock. This can occur in a matter of a few hours with high virulence strains. Pigs can appear normal, active, and feeding and within a few hours cyanotic, high fevers, gasping for air, and struggling for survival. In these cases treating some pigs is their final stressor.
- Fulminating APP is apparent in naïve pigs but colostral immunity with gradual exposure appears to be protective.
- Lesions are generally found in respiratory tract but hemorrhages will be present in other organs typical of fulminating septicemias especially with *A. suis*. Lungs will be full of blood tinged froth, feel solid similar to liver, with areas of hemorrhage, necrosis, fibrinous pleuritis. The diaphragmatic lobes will have dorsal areas of destruction which is not pathognomonic but classic for this disease. Fibrinous pericarditis and pleural adhesions are also common.

Clinical Signs

- The clinical appearance of this disease can be deceiving between acute outbreaks and endemic herds with the same agent.
- In outbreaks acute deaths are common often before the caretakers notice other clinical signs. These are always some of the best, fastest growing pigs. Cyanosis, mouth breathing, severe dyspnea, bloody foam from the mouth and nostrils, and a shallow dry cough. Generally coughing is not a notable clinical sign.
- Morbidity and mortality are very high when naïve pigs are exposed to highly virulent strains but may be negligible in chronically infected continuous flow herds. In these cases pleuritis is apparent on slaughter inspections or postmortem examination of finishing pigs. Growth rates will be depressed compared to non-infected herds.
- Lung abscesses are common postmortem finding in chronic herds but APP is only rarely present in these lesions.

Diagnosis

- Anytime a rapidly spreading high mortality respiratory disease is encountered APP should be suspected. Lung lesions as described above are classic for APP but *A. suis* must be part of the differential diagnosis.
- Culture identification is the gold standard for diagnosis.
- Serology can be misleading and has a history of leading veterinarians to mistaken conclusions. Serological tests developed by Marcello Gottschalk are the only reliable ones available today. All serology should be evaluated on a population basis only – never on a single or small group of pigs.
- Other pathogens that must be ruled out are *Salmonella choleraesuis*, pneumatic *Pasteurella multocida*, and PRDC.
Control

- Control of virulent strains of APP has proven challenging. Modern pig flows (multi-site) exacerbate outbreaks in growing pig populations. For this reason, APP has been eliminated from the breeding herds in most US systems.
- This is one disease that depopulation is easily justified because of the tremendous cost of remaining positive.
- Commercial vaccines in the US have not proven to be efficacious. They may reduce mortality but do little to recover the real disease costs which in endemic herds is rate gain, feed:gain, morbidity, and slaughter condemnations.
- Much improved vaccines are available in Europe where the disease is far more prevalent today.
- Medicated early weaning is a cost effective method of elimination while preserving valuable genetics.
- Elimination may be possible in small breeding herds.
- Resistance to antimicrobials is typically not an issue but rather timing of administration. In acute cases the treatment is nearly too late. Penicillin’s, ceftiofur, tilmicosin, tiamulin, and enrofloxacin are all effective in sub-acute and chronic cases.

Honorable Mention Swine Respiratory Disease

Pneumonic Pasteurellosis - *Pasteurella multocida* (PM)

- A bacterial pneumonia of swine that is considered secondary or opportunist to other viral and bacterial agents, verminous pneumonia, or poor ventilation and noxious gases/dust.
- PP has worldwide incidence and presence.
- It occasionally occurs as meningitis in suckling pigs.
- This bacteria is found in many species of domestic mammals and birds.
- The bacterium was originally studied by Louis Pasteur and later named for him.
- *P. multocida* is a Gram-negative coccobacillus which grows well on enriched media. It is a facultative anaerobe.
- The bacterium is a normal inhabitant in the nasal passages and respiratory tract of pigs.
- There are 5 capsular serotypes (A, B, D, E, F) and 16 somatic serotypes. Type A and D are found in swine and typically type A’s are pneumonic.
- PM is ubiquitous in swine and swine strains are fully species adapted.
- Pathogenesis only occurs when normal resistance has been lowered by other primary pathogens or extremely bad environmental and stressful conditions.
- When PM enters deeper portions of the lung abscesses form in areas of microthrombosis.
- In chronic pneumonia pigs (“thumpers”) PM is often isolated but it is doubtful that it acted as the lone infectious agent.
- Control is dependent on good husbandry, avoiding mix sourcing, control of other infectious pneumonic agents, and preventative antimicrobial therapies.
- Many feed and water antimicrobial medications have PM claims but it is doubtful that they are useful in the field as strictly PM interventions.
• Once PM causes damage in the lung it is not economically reasonable to treat. Long term parenteral antimicrobial treatments may be effective but impractical.

**Tuberculosis (TB)**
• Almost all cases of tuberculosis in US swine are caused by *Mycobacterium avian*. There are numerous serovars including *M. intracellulare* which are all considered part of the same complex.
• Swine TB is still a significantly costly problem in the US industry.
• Slaughter condemnations account for most of the cost but losses in route and prior to slaughter also occur. Caseous lymphadenitis is the main postmortem finding.
• Wild birds, weathered sawdust, and water are the main sources of exposure. In large systems that use surface water, condemnations will be greater than pigs from other sources. Humans are most often exposed to this agent by frequenting outdoor hot tubs.
• The disease is self-limiting in pigs and believed to be non-contagious.
• Few pigs in the US are exposed to birds or chickens today. In slaughter pigs that can be tracked back to their source farms (Integrators) drinking water is the most likely source of infection.

**Bordetella bronchiseptica (BB)**
• This bacteria is a normal inhabitant and colonizer of the upper respiratory track of pigs. It is associated with sneezing in nursery age piglets especially where air quality is questionable and when concurrent infections with Inclusion Body Rhinitis virus occur.
• It can occasionally be recovered in pure culture from bronchopneumonia cases of young pigs. Clinical signs are a “whooping” cough and dyspnea.
• BB may be important for normal colonization with *H. parasuis* preventing systemic infections.
• BB is a motile Gram-negative aerobic rod or coccobacillus.
• BB is ubiquitous in pig populations. It was once believed to be the causative agent associated with progressive atrophic rhinitis but this is not valid. Rhinitis caused by BB is regenerative.

**Salmonella choleraesuis**
• Although this bacteria is usually associated with the GI tract it can cause severe necrotizing pneumonia.
• S. choleraesuis is a highly host-adapted salmonella. There have been a few rare cases of human infections, which almost always end in mortality. There are no associated risk factors between pig exposure and human disease.
• *S. choleraesuis var. kuzendorf* is most frequently isolated in pneumonic cases. The bacterium appears to be filtered out in the diaphragmatic lobes and can be confused with APP or *A. suis* on gross examination.
• Several highly efficacious modified live vaccines are available in the US and provide excellent control in pigs from positive breeding farms.
• Pigs that become infected will have high temperatures, lethargy, remain off feed and thus quickly have an empty appearance (“slab sided”). Cyanosis and dyspnea may occur before death. Dead pigs will usually be purple on the down side.
• Case mortality rates are high but morbidity levels in affected groups will usually be less than 10%.

Pseudorabies virus (Aujeszky’s disease)
• This virus is covered in another section but when present in the United States was a major contributor to winter PRDC in growing pigs.
• The first published report of the disease was in 1813 in cattle. The virus was discovered in 1910. It became a major problem in US swine production during the 1970’s. Eradication at a national level began in 1989 and this was completed in 2002.
• The virus is in the herpes group and different isolates often had wide variation in pathogenicity. Carriers and latent infections/contagiousness are a common component of this virus.
• The virus is easily spread by direct contact, nasal secretions, transport vehicles/trailers, clothing, airborne and other routes.
• The virus is associated with bronchitis, bronchiolitis, alveolitis, inclusion bodies, and hemorrhagic foci of necrosis. Uncomplicated cases are mild.

Porcine Respiratory Corona Virus (PRCV)
• This is a highly contagious and infectious respiratory virus of pigs.
• It first appeared in Europe in the mid 1980’s.
• The virus is a TGE mutant with a large deletion of 621 to 681 nucleotides from the S glycoprotein gene which is thought to have changed the tissue tropism from gut to respiratory epithelial cells.
• Serum from PRCV infected pigs cross reacts with the TGE serum neutralization test which may be the most important concern.
• As the virus spread across Europe cases of TGE disappeared. That has not been the case in the US where it has complicated TGE diagnosis and increased the number of TGE endemic nurseries.
• As a respiratory agent it is not of any clinical significance. Early investigators incriminated the virus as part of the PRDC syndrome but that does not appear to be a reality in field situations.

Ascaris suum (porcine round worm)
• This is the large round worm of swine and their most common gastrointestinal parasite.
• The life cycle of this worm is direct. Eggs survive in the environment for many years contaminating buildings and surrounding grounds. These eggs are resistant to all disinfectants, environmental, and weather conditions.
• Once the eggs hatch in the gut the larvae go through a hepatotraceal migration. Liver and lung damage followed by death can occur with massive exposure. This was common in the days when new genetic stock usually boars were housed in dirt isolation lots. After repeated use a build up of infective embryonated eggs would lead to massive exposure.
• Pigs with heavy infestation have a productive asthmatic cough, dyspnea, become unthrifty,
• Modern all-in, all-out production has greatly reduced the significance of this parasite. Although the eggs are extremely resistant they can be washed out of buildings over time all but eliminating exposure. Adults mount an effective immune response and clear infestations over time. The egg only becomes infective after a 30 to 60 day period which is greater than the suckling period. These factors have created a natural unexpected control mechanism through modern production practices.

• It is extremely rare to find round worms or pathology in nursery pigs but they do survive in continuous flow finisher sites and farms. A number of effective anthelmintics are available for feed, water, or individual per os treatment. Cost effective use is doubtful in true all-in, all-out and multi-site production systems. Individual treatment is practiced in many breeding herds but is not cost effective or warranted.