MENANGLE VIRUS

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SUMMARY

Etiology
- Menangle virus (MenPV) is an enveloped RNA virus in the genus Rubulavirus, family Paramyxoviridae.
- There are two known strains: bat MenPV (bMenPV) and pig MenPV (pMenPV).

Cleaning and Disinfection
- MenPV does not survive well in the environment.
- Like other paramyxoviruses, MenPV is susceptible to acids, alcohols, aldehydes, alkalis, halogens, and oxidizing agents.

Epidemiology
- Fruit bats, particularly Pteropus spp. are the reservoir host. There has only been one observed outbreak of MenPV in swine, which occurred on a single farrow-to-finish farm in New South Wales (NSW), Australia in 1997.
- During the NSW outbreak, two swine workers became ill with flu-like symptoms and a non-pruritic rash. Thirty-three out of 251 people exposed to MenPV became seropositive.
- Although only one outbreak has occurred, bats of the genus Pteropus are distributed throughout Australia, Southeast Asia, India, and Eastern Africa.
- In 1997, 60–70% of litters were affected during the outbreak; farrowing rates also dropped approximately 25%.

Transmission
- Pigs acquire MenPV through ingestion of bat-contaminated feces, urine, or tissues. The virus spreads pig-to-pig via fecal/urinary-oral transmission.

Infection in Swine/Pathogenesis
- MenPV causes reproductive failure. Affected litters may contain piglets that are mummified, stillborn, or born with teratogenic defects (musculoskeletal or CNS). Delayed return to estrus and pseudopregnancy can also occur.
- In the 1997 outbreak, no clinical signs were observed in grower pig units.
Diagnosis

- Virus isolation has been successful from stillborn pigs with CNS degeneration. A quantitative real-time polymerase chain reaction (PCR) assay detecting the nucleocapsid gene has been described. Monoclonal antibodies have been generated to react to nucleocapsid protein epitopes, and can be used to detect viral particles through Western blot assays and enzyme linked immunosorbent assay (ELISA).
- Virus neutralization assays can detect neutralizing antibodies to MenPV in the serum, and possibly body cavity fluids, of affected swine.

Immunity

- Seroconversion to MenPV results in strong immunity.
- There is no MenPV vaccine.
- MenPV is not closely related to other paramyxoviruses; however, there is serum neutralizing antibody cross-reactivity between pMenPV and bMenPV, which may provide some cross-protection.

Prevention and Control

- Bats must be excluded from swine barns to prevent contamination with feces, urine, or tissues. Swine barns should not be located near potential bat roosting areas and feeding areas.
- Standard biosecurity practices should also be in place.

Gaps in Preparedness

- There is currently no vaccine for MenPV.
- Validated diagnostic tests are also lacking.
OVERVIEW

Menangle virus (MenPV) is an enveloped paramyxovirus belonging to the genus *Rubulavirus*. There are two known strains: bat MenPV (bMenPV) and pig MenPV (pMenPV).¹

Bats, pigs, and humans can all become infected by MenPV. There has only been one observed outbreak of MenPV which occurred on a single swine farm in New South Wales (NSW), Australia in 1997. MenPV was introduced to pigs from fruit bats roosting near the swine facilities. Clinical signs in swine include mummified fetuses, stillbirths, teratogenic defects, delayed return to estrus, and pseudopregnancy. Teratogenic deformities in piglets include musculoskeletal and CNS defects. Affected piglets can also have effusion and hemorrhage in the body cavity.

MenPV is zoonotic. In 1997, two of the workers on the affected swine farm came down with flu-like symptoms followed by a non-pruritic rash. Thirty-three out of the 251 people possibly exposed to MenPV developed neutralizing antibodies to MenPV.

The *Pteropus* genus of fruit bats are the primary reservoir hosts of MenPV. Neutralizing antibodies to MenPV are commonly found in three of the *Pteropus* species in Australia. MenPV infection of *Microchiroptera* species, the suborder of all bats in North America, has not been documented. Fecal/urinary-oral transmission is suspected in swine because of the slow spread of MenPV. The outbreak in NSW lasted 21 weeks. Experimentally infected pigs excreted virus from the urine and the nasal, oral, and rectal mucosa. Transmission from pigs to humans is suspected to be parenteral or permucosal.

Virus isolation from stillborn cases has only been successful when there is histological or gross CNS degeneration. New techniques, including improved procedures and *Pteropus alecto* kidney cell lines, have allowed MenPV isolation from *P. alecto* urine. Primer sequences for a quantitative, real-time polymerase chain reaction (PCR) to detect the nucleocapsid gene have been described. Monoclonal antibodies have been generated to react to nucleocapsid protein epitopes, and can be used to detect viral particles through Western blot assays and enzyme linked immunosorbent assay (ELISA). Virus neutralization assays can detect neutralizing antibodies to MenPV in the serum of affected swine. Antibodies may be detectable from the body cavity fluid of stillborn piglets.

There is no specific vaccine or treatment for MenPV. Because *Pteropus* bats are the reservoir hosts, naïve pigs must be kept away from urine, feces, and tissues of affected bats. Outdoor walkways should be covered and swine facilities should not be proximal to roosting or feeding areas of bats. *Pteropus* bats are found in Eastern Africa, India, Southeast Asia, and Australia, making these regions the most plausible possible sites for a future MenPV outbreak.
LITERATURE REVIEW

1. Etiology

1.1 Key Characteristics
Menangle virus (MenPV) is an enveloped RNA virus in the genus Rubulavirus, which also contains porcine rubulavirus (Blue eye disease). MenPV has typical Paramyxoviridae morphology and does not possess hemadsorption or hemagglutination activity.

1.2 Strain Variability
Two strains of MenPV that share 94% of the genome have been isolated: bat MenPV (bMenPV) and pig MenPV (pMenPV). Between the two strains, 99% amino acid homology is found for the M protein; 98% homology for the N, F, and L proteins; and 96% homology for the V, P, and HN proteins. There are differences in the neutralizing effects of pMenPV antibodies against pMenPV and bMenPV. Sera from pigs and rabbits exposed to pMenPV were two to four-fold less reactive against bMenPV than pMenPV. The differences in neutralization are due to alterations in the HN gene between the strains, the primary target of antibody-mediated neutralization.

2. Cleaning and Disinfection

2.1 Survival
Survivability of MenPV in the environment is poor.

2.2 Disinfection
Paramyxoviruses are susceptible to acids, alcohols, aldehydes, alkalis, halogens, and oxidizing agents, and MenPV has limited susceptibility to biguanides, phenolic compounds, and quaternary ammonium compounds.

3. Epidemiology

3.1 Species Affected
Bats, pigs, and humans can all become infected by Menangle virus. There has only been one observed outbreak of MenPV which occurred on a single swine farm in New South Wales (NSW), Australia in 1997. Species around the affected swine unit, including rodents, birds, cattle, sheep, cats, and a dog, were all seronegative for MenPV. Fruit bat species of the genus Pteropus are the primary reservoir hosts for the diseases in Australia. Neutralizing antibodies to MenPV are commonly found in three Pteropus spp. in Australia. Infection in Microchiroptera species, the suborder of all bats in North America, has not been documented.

3.2 Zoonotic Potential
There have only been two cases of human illness associated with MenPV. After the outbreak in NSW, 33 out of the 251 people possibly exposed to MenPV developed neutralizing antibodies. Two of the workers from the operation of the original outbreak had flu-like symptoms for one week, followed by a red, non-pruritic rash which also lasted for a week. Illness in these two workers occurred two months before MenPV was isolated from the operation. Parenteral or permucosal transmission was suspected. Notably, one affected worker had contact with pigs during farrowing; the other performed necropsies without personal protective equipment.

3.3 Geographic Distribution
Menangle virus was discovered during a single outbreak on one swine farm, in New South Wales, Australia, in 1997. The farm was a farrow-to-finish operation with approximately 2,600 sows.
reservoir species, bats of the genus *Pteropus*, are distributed throughout Australia, Southeast Asia, India, and Eastern Africa.  

3.4 Morbidity and Mortality
Farrowing rates during an outbreak can drop approximately 25%, and percentage of affected litters can rise to 60–70%.  

4. Transmission
Fecal/urinary-oral transmission between pigs is suspected because of MenPV’s slow spread throughout the affected swine unit in 1997. The MenPV outbreak lasted for 21 weeks. In eight experimentally infected pigs, MenPV shedding was found from nasal (5–7 days post-infection, DPI), oral and rectal mucosal surfaces (5–9 DPI), and urine (7–10 DPI). One of the experimentally infected pigs was found to shed MenPV in the urine at days 16 and 20. It is unknown whether vertical transmission through semen is possible. MenPV viremia is of short duration and low titer, somewhat due in part to the dissemination of virus through infected lymphocytes.

5. Infection in Swine/Pathogenesis
The tissue tropism of MenPV is secondary lymphoid tissue and intestinal epithelium, both of which are preferred sites of virus proliferation. Experimentally infected pigs inoculated intranasally were found to have high MenPV RNA loads in tonsil, mandibular lymph node, jejunum, and ileum samples; medium RNA loads in caudal lung, colon, and rectum samples; and low RNA loads in renal cortex and bladder samples.

5.1 Clinical Signs
MenPV induces profound reproductive failure. Fetuses in litters affected by MenPV may be mummified, stillborn, aborted, or born with teratogenic defects (musculoskeletal or CNS). Delayed return to estrus and pseudopregnancy can be observed at high rates. In the NSW outbreak, older sows experienced decreased farrowing rates while younger sows experienced a higher proportion of affected litters. There were no clinical signs in grower pig units where the virus was detected in NSW.

5.2 Postmortem Lesions
In the NSW outbreak, various deformities were seen. In 90 samples, there were 49 stillbirths, 20 mummified fetuses, 15 semi-mummified fetuses, and 6 aborted fetuses. Gross skeletal lesions included arthrogryposis (18%), craniofacial deformities (9%), scoliosis/kyphosis (4%), and hypodactyly (1%). Gross CNS lesions, which were observed in 52% of the fetuses, included cerebellar degeneration (48%), cerebral degeneration (33%), brain stem degeneration (17%), spinal cord degeneration (10%), and hydranencephaly (11%). Gross visceral lesions included body cavity effusion (24%), epicardial hemorrhage (13%), and pulmonary hypoplasia (9%). Subcutaneous edema (8%) was also observed.

6. Diagnosis

6.1 Clinical History
In affected farrowing units, farrowing rates can decline from the expected rate by approximately 20%. A farrowing rate decline from 80.2% to 63.2% was seen in the NSW outbreak. Abortions are not as common with MenPV as other reproductive diseases.

6.2 Histopathology
Histological lesions were observed in the CNS of affected fetuses and piglets and included a variable magnitude of neuronal degeneration from a single neuron to extensive necrosis and liquefaction. Eosinophilic intranuclear and cytoplasmic inclusion bodies can be found in neurons and neuroglial cells,
lesions consistent with other Paramyxoviridae.\textsuperscript{11} Foamy macrophages may be found in extensive areas of malacia.\textsuperscript{11} Multifocal to locally extensive gliosis may be seen in areas.\textsuperscript{11} In areas of less severe neuronal degeneration, microglial cell and astrocyte proliferation may be seen.\textsuperscript{11} Macrophages and lymphocytes may be found in the perivascular regions of the CNS.\textsuperscript{11} Multifocal myocarditis was also found in fetuses, with regions of lymphocytic infiltrate in the myocardium.\textsuperscript{11} When isolated in cell monolayers, cytopathic effects from MenPV include cell rounding, lysis/detachment, and syncytia formation.\textsuperscript{11}

6.3 Tests to Detect Nucleic Acids, Virus, or Antigens
Menangle can be cultured in baby hamster kidney (BHK-21) cells and others.\textsuperscript{2} Cytopathic effect may not be observed until 3–5 passages are completed. Virus isolation from swine samples has only been successful from stillborn fetuses with coinciding histological or gross CNS degeneration.\textsuperscript{11} MenPV isolation has recently been documented in urine of \textit{Pteropus alecto}, the black flying fox, using improved isolation procedures and \textit{P. alecto} kidney cell lines.\textsuperscript{12} Electron microscopy or virus neutralization (specific anti-serum required) can be used to identify the isolate.\textsuperscript{2} Primers for a qRT-PCR detecting sequences of the nucleocapsid gene of MenPV have been described.\textsuperscript{7} IgG1 monoclonal antibodies (MAbs) have been generated to react to epitopes of the nucleocapsid (N) protein.\textsuperscript{13} MAbs can be of use to detect viral particles through Western blot assays and ELISA.\textsuperscript{13}

6.4 Tests to Detect Antibody
Virus neutralization assays can detect antibodies to MenPV in the serum of affected swine.\textsuperscript{3} Antibodies may be detectable in body cavity fluids of stillborn piglets.\textsuperscript{3}

6.5 Samples
Tissues from fetal specimens (brain, lung, and myocardium) are useful for virus isolation.\textsuperscript{2} Secondary lymphoid organs and intestinal epithelium, due to high viral loads, are preferred sample sites for qRT-PCR.\textsuperscript{7} Serum and fetal body cavity fluids are useful for detection of antibodies with virus neutralization assays.\textsuperscript{3}

7. Immunity

7.1 Post-exposure
Seroconversion to MenPV results in strong immunity due to high neutralizing antibody titers, and persistent infection in both piglets and adults is thought to be very unlikely.\textsuperscript{2}

7.2 Vaccines
There are currently no vaccines for MenPV.

7.3 Cross-protection
MenPV has limited antigenic relatedness with other paramyxoviruses due to the main antigenic gene sequence (HN protein) of MenPV possessing limited homology (<20% sequence homology).\textsuperscript{14} However, a monoclonal antibody has been generated with cross-reactivity to the N protein of the Tioman virus, another \textit{Rubulavirus} in fruit bats.\textsuperscript{13} Additionally, there is serum neutralizing antibody cross-reactivity between pMenPV and bMenPV, which may provide cross-protection in individuals.\textsuperscript{1}

8. Prevention and Control
There is no specific treatment available for MenPV.\textsuperscript{2} Because \textit{Pteropus} spp., and possibly other bats, are a source of virus, bats must be excluded from swine barns to prevent contamination with their feces, urine, and tissues.\textsuperscript{2} Swine barns should not be located near potential bat roosting areas and feeding areas.\textsuperscript{2}
MenPV could become endemic on larger swine facilities where there would continuously be naïve pigs to infect. Closing the herd and using all-in, all-out management, with cleaning and disinfection between groups, are effective biosecurity measures that should be put into place.  

Menangle virus is not covered in the OIE Terrestrial Animal Health Code.

10. Gaps in Preparedness
There are currently no vaccines available for MenPV in the National Animal Health Laboratory Network (NAHLN) or at the National Veterinary Service Laboratories (NVSL).
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