

# MENANGLE VIRUS



*The mission of the Swine Health Information Center is to protect and enhance the health of the United States swine herd through coordinated global disease monitoring, targeted research investments that minimize the impact of future disease threats, and analysis of swine health data.*

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## SUMMARY

### IMPORTANCE

- Menangle virus is a paramyxovirus carried by fruit bats in the genus *Pteropus*. It caused a large outbreak of reproductive disease and congenital defects at a swine farm in New South Wales, Australia, in 1997.
- To date, Menangle virus has not caused any further outbreaks. However, it remains a concern to the swine industry because of profound production losses it can cause. Menangle virus is also a concern for people working in close contact with pigs, since zoonotic transmission occurs.

### PUBLIC HEALTH

- Following the 1997 swine outbreak in New South Wales, Australia, two people working at the affected farm developed flu-like symptoms and a non-pruritic rash. Both fully recovered. Thirteen percent of exposed people developed neutralizing antibodies to Menangle virus.

### INFECTION IN SWINE

- Menangle virus causes reproductive failure (stillbirth, mummification) and congenital defects of the musculoskeletal system and central nervous system in affected piglets. Delayed return to estrus and pseudopregnancy can also occur.
- Piglets born alive are unaffected, and no clinical signs are seen in grower pigs.

### TREATMENT

- There is no specific treatment for Menangle virus infection.

### CLEANING AND DISINFECTION

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

### 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, and flowering or fruit-bearing trees should not be grown near swine buildings.
- During an outbreak, affected pigs (usually 10–16 weeks-of-age) should be moved to another site, and affected facilities should be thoroughly cleaned and disinfected. Following downtime, barns can be repopulated with unexposed or immune pigs (e.g., new breeding stock that are acclimatized prior to herd introduction).
- Standard biosecurity practices should also be in place.

## **TRANSMISSION**

- Pigs are infected with Menangle virus through ingestion of bat feces, urine, or tissues.
- Infected pigs also shed virus in feces and urine, and Menangle virus spreads from pig-to-pig via the fecal-oral or urinary-oral routes.

## **PATHOGENESIS**

- Menangle virus proliferates in secondary lymphoid tissue and intestinal epithelium. High viral load can be found in the tonsils, mandibular lymph nodes, jejunum, and ileum.

## **DIAGNOSIS**

- Tissues from fetal specimens (brain, lung, and myocardium) are used for virus isolation.
- Electron microscopy or virus neutralization (using specific anti-serum) are required to identify viral isolates, since Menangle virus is non-hemagglutinating and non-hemadsorbing.
- A quantitative real-time polymerase chain reaction (qRT-PCR) assay detecting the nucleocapsid gene has been described.
- Virus neutralization using serum or body cavity fluids from stillborns is most useful for routine testing.

## **EPIDEMIOLOGY**

- Fruit bats, particularly *Pteropus* spp., are the reservoir host. They are found throughout Australia, Southeast Asia, India, and Eastern Africa.
- Menangle virus was discovered during a single outbreak on a swine farm in New South Wales, Australia, in 1997.
- In 1997, nearly all pigs on the affected farm became seropositive. Approximately 60–70% of litters were affected during the outbreak, and farrowing rates dropped about 25%.

## **ETIOLOGY**

- Menangle virus is an enveloped RNA virus in the genus *Rubulavirus*, family *Paramyxoviridae*.
- There are two Menangle virus strains – a bat strain and a porcine strain.

## **HISTORY IN SWINE**

- The 1997 swine outbreak in New South Wales, Australia, occurred on a 2600 sow farrow-to-finish operation. Reproductive disease and congenital defects were seen in affected pigs.
- Following the initial spread, susceptible young pigs became infected in the post-weaning period, and this enabled persistence of Menangle virus in the herd.
- Menangle virus was detected on two associated farms; however, no breeding animals were present on these farms and no clinical disease was noted.

## **IMMUNITY**

- Seroconversion results in strong immunity to Menangle virus.
- There is no Menangle virus vaccine.
- Menangle virus is not antigenically related to other paramyxoviruses. There may be some cross-protection between bat and porcine Menangle strains.

## **GAPS IN PREPAREDNESS**

- No Menangle virus outbreaks have occurred since 1997.
- Menangle virus epidemiology is poorly understood, and there are no vaccines for infected pigs. More research is needed to prepare for and prevent further Menangle virus outbreaks in pigs.

# LITERATURE REVIEW: MENANGLE VIRUS

## IMPORTANCE

Menangle virus is a paramyxovirus carried by fruit bats in the genus *Pteropus*. It caused a large outbreak of reproductive disease and congenital defects at a swine farm in New South Wales, Australia, in 1997. To date, Menangle virus has not caused any further outbreaks. However, it remains a concern to the swine industry because of profound production losses it can cause. Menangle virus is also a concern for people working in close contact with pigs, since zoonotic transmission can occur.

## PUBLIC HEALTH

Menangle virus is zoonotic. Following the 1997 swine outbreak in New South Wales, Australia (see *History in Swine*), 13% (33/251) of exposed people developed neutralizing antibodies to Menangle virus.<sup>1</sup> Two workers from the affected swine facility developed flu-like symptoms for one week, followed by a red, non-pruritic rash.<sup>1</sup> Illness in these workers occurred two months before Menangle virus was isolated from the operation.<sup>1</sup> Notably, one affected worker had contact with pigs during farrowing; the other performed necropsies without wearing personal protective equipment.<sup>1</sup> Parenteral or permucosal transmission was suspected.<sup>2</sup>

## INFECTION IN SWINE

Menangle virus infection causes reproductive failure in sows and teratogenic defects in fetuses involving the musculoskeletal system and central nervous system.<sup>3,4</sup> Abnormalities noted during the 1997 New South Wales, Australia, outbreak included:

- Stillbirths, mummified and semi-mummified fetuses of varying sizes, and aborted fetuses
- Arthrogryposis, craniofacial deformities, scoliosis/kyphosis, and hydrodactyly<sup>5</sup>
- Degeneration of the cerebellum, cerebrum, brain stem, and spinal cord, as well as hydrocephaly<sup>5</sup>
- Body cavity effusion, epicardial hemorrhage, pulmonary hypoplasia,<sup>11</sup> and subcutaneous edema<sup>5</sup>

In affected units, farrowing rates declined by approximately 20%<sup>4</sup> (from 80.2 to 63.2%).<sup>10</sup> Abortions are not as common with Menangle virus as with other reproductive diseases.<sup>4</sup> However, delayed return to estrus and pseudopregnancy can occur at high rates.<sup>3</sup> In the 1997 New South Wales, Australia outbreak, decreased farrowing rates were more often seen in older sows, while younger sows experienced a higher proportion of affected litters.<sup>4</sup> Piglets born alive were unaffected, and grower pigs did not show any signs of clinical illness.<sup>3</sup>

Histological lesions associated with Menangle virus infection<sup>5</sup> included:

- Variable neuronal degeneration, from a single neuron to extensive necrosis and liquefaction
- Eosinophilic intranuclear and cytoplasmic inclusion bodies in neurons and neuroglial cells
- Foamy macrophages in extensive areas of malacia
- Multifocal to locally extensive gliosis, with microglial cell and astrocyte proliferation
- Macrophage and lymphocyte infiltration in perivascular regions of the CNS
- Multifocal myocarditis in fetuses, with regions of lymphocytic infiltrates

## TREATMENT

There is no specific treatment for Menangle virus infection.<sup>3</sup>

## CLEANING AND DISINFECTION

### SURVIVAL

Menangle virus survives poorly in the environment.<sup>3</sup>

### DISINFECTION

Generally, paramyxoviruses are susceptible to acids, alcohols, aldehydes, alkalis, halogens (sodium hypochlorite), and oxidizing agents. Menangle virus may have some resistance to biguanides, phenolic compounds, and quaternary ammonium compounds.<sup>6,7</sup>

## **PREVENTION AND CONTROL**

### **DISEASE REPORTING**

Menangle is not an OIE-listed disease. There are no restrictions for importation of animals from countries or zones affected by Menangle virus. Any suspicious clinical or necropsy findings should always be reported to the USDA and your State Animal Health Official.

### **DISEASE PREVENTION**

Fruit bats are the primary source of infection for pigs. *Pteropus* spp. and other bats should be excluded from swine barns to prevent contamination with their feces, urine, and tissues.<sup>3</sup> Outdoor walkways should also be covered. Swine barns should not be located near potential bat roosting areas and feeding areas.<sup>3</sup> Additionally, flowering or fruit-bearing trees should not be grown near swine buildings.<sup>3</sup>

Following an outbreak, Menangle virus could become endemic in large swine herds due to the continuous introduction of susceptible animals. To prevent this, new breeding stock should be acclimatized prior to herd introduction.<sup>3</sup>

### **DISEASE CONTROL**

Menangle virus can be eradicated from endemically-infected herds. Steps to take<sup>3</sup> include:

- Move affected age groups (usually pigs 10–16 weeks-of-age) to another site while infection is active
- Thoroughly clean and disinfect affected swine facilities
- Repopulate facilities with unexposed or immune pigs after a few weeks of downtime

Maintaining a closed herd and an all-in/all-out system is also recommended.<sup>3</sup>

### **TRANSMISSION**

Menangle virus is carried by fruit bats in the genus *Pteropus*.<sup>6</sup> Fruit bats shed virus in the urine, and probably in the feces and other secretions/excretions. Both fecal and urinary shedding have been documented in pigs.<sup>2</sup> Transmission is not well understood, but fecal-oral or urinary-oral transmission is suspected.<sup>3</sup> Piglets become infected via *in utero*.

In experimentally infected 6-week-old pigs, Menangle virus has been found on nasal, oral, and rectal mucosal surfaces, as well as in urine where it can be excreted for 20 days.<sup>2</sup> It is unknown whether vertical transmission through semen is possible.<sup>3</sup> Transmission via fomites seems unlikely since Menangle virus does not survive well in the environment. Additionally, sentinel pigs placed in a contaminated environment three days after infected pigs were removed did not seroconvert.<sup>2</sup>

Menangle virus is shed in low amounts for a short period of time, which may be due to its dissemination through infected lymphocytes.<sup>2</sup> During the 1997 outbreak, transmission of Menangle virus was slow and seemed to require direct contact between pigs.

### **PATHOGENESIS**

Menangle virus proliferates in secondary lymphoid tissue and intestinal epithelium.<sup>2</sup> In experimentally infected pigs, intranasal inoculation lead to high viral load in the tonsils, mandibular lymph nodes, jejunum, and ileum; moderate viral load in the caudal lung, colon, and rectum; and low viral load in the renal cortex and bladder.<sup>2</sup> In cell monolayers, Menangle virus induces cell rounding, lysis/detachment, and syncytia formation.<sup>5</sup>

### **DIAGNOSIS**

Many pathogens can cause signs similar to Menangle virus in pigs, but the most common is porcine parvovirus.<sup>3</sup>

## TESTS TO DETECT NUCLEIC ACIDS, VIRUS, OR ANTIGENS

Menangle virus can be isolated from tissues from stillborn piglets, and success is most likely when gross or histological abnormalities of the brain are present. The virus replicates in baby hamster kidney (BHK-21) cells<sup>3</sup> and others.<sup>8</sup> Cytopathic effect may not be observed until 3–5 passages are completed. Menangle virus has been isolated from the urine of *Pteropus alecto*, the black flying fox, using improved isolation procedures and *P. alecto* kidney cell lines.<sup>9</sup> Electron microscopy or virus neutralization (specific anti-serum required) can be used to identify viral isolates.<sup>3</sup> Menangle virus is non-hemagglutinating and non-hemadsorbing.

A quantitative reverse transcriptase polymerase chain reaction (q-RT-PCR) assay has been described for detection of Menangle virus. It is based on sequences of the nucleocapsid gene, and works with tissues, swabs of mucosal surfaces, and excretions like feces and urine.<sup>2</sup> IgG1 monoclonal antibodies (MAbs) have been generated to react to epitopes of the nucleocapsid protein.<sup>10</sup> MAbs can be of use to detect viral particles through Western blot and enzyme linked immunosorbent assays (ELISAs).<sup>10</sup>

## TESTS TO DETECT ANTIBODY

Virus neutralization is most useful for routine testing. Antibodies to Menangle virus can be detected in the serum of affected swine<sup>3</sup> and possibly in body cavity fluids of stillborn piglets.<sup>11</sup>

## SAMPLES

Tissues from fetal specimens (brain, lung, and myocardium) are used for virus isolation.<sup>3</sup> Secondary lymphoid organs and intestinal epithelium are preferred for qRT-PCR.<sup>2</sup> Serum and fetal body cavity fluids are useful for detection of antibodies with virus neutralization assays.<sup>11</sup>

## EPIDEMIOLOGY

### SPECIES AFFECTED

Bats, pigs, and humans can be infected with Menangle virus.<sup>3</sup> Fruit bats (suborder *Megachiroptera*, genus *Pteropus*) are the primary reservoir hosts.<sup>3</sup> They do not become ill, although the reasons for this are unclear.<sup>12</sup> Fruit bats are not found in the continental United States. It is not known whether Menangle virus infection occurs in bats native to North America (suborder *Microchiroptera*).<sup>3</sup>

### GEOGRAPHIC DISTRIBUTION

Menangle virus was discovered during a single outbreak on a swine farm in New South Wales, Australia, in 1997 (see *History in Swine*).<sup>3</sup> No further outbreaks are known to have occurred. Fruit bats of the genus *Pteropus* are distributed throughout Australia, Southeast Asia, India, and Eastern Africa.

### MORBIDITY AND MORTALITY

In the 1997 outbreak, farrowing rates dropped approximately 20% in 60–70% of swine litters on the farm.<sup>4</sup> Nearly all pigs on the affected farm become seropositive.

## ETIOLOGY

### CHARACTERISTICS OF PARAMYXOVIRUSES

Menangle virus is an RNA virus belonging to the family *Paramyxoviridae*. Paramyxoviruses are large (100–350nm), enveloped, single-stranded RNA viruses.<sup>3</sup> Virions are pleomorphic, and can take on a spherical or elongated form. They have a layer of surface spikes and a herringbone-shaped nucleocapsid.<sup>3</sup> Paramyxoviruses have six open reading frames (ORFs) encoding the structural genes N (nucleocapsid), L (polymerase), P (phosphoprotein), M (matrix), F (fusion), and G/H/HN (attachment glycoproteins).<sup>13</sup>

There are seven genera in the family, four of which affect mammals: *Rubulavirus*, *Henipavirus*, *Respirovirus*, and *Morbilivirus*. Paramyxoviruses of swine<sup>3</sup> include:

- Menangle virus and porcine rubulavirus (blue eye), genus *Rubulavirus*
- Nipah virus and Hendra virus, genus *Henipavirus*
- Porcine respirovirus 1 (porcine parainfluenza virus 1), genus *Respirovirus*

## CHARACTERISTICS OF MENANGLE VIRUS

The Menangle virus genome contains 15,516 nucleotides.<sup>14</sup> There are two Menangle virus strains that share 94% homology overall – a bat strain and a porcine strain.<sup>1</sup> The M proteins are most similar, followed by the N, F, and L proteins. The V, P, and HN proteins are least similar.<sup>1</sup>

There are differences in the neutralizing effect of porcine strain antibodies against bat and porcine Menangle viruses.<sup>1</sup> Sera from pigs and rabbits exposed to porcine Menangle virus were two to four-fold less reactive against bat strains compared to porcine strains.<sup>1</sup> This is likely due to differences in the HN gene between strains, the primary target of antibody-mediated neutralization.<sup>1</sup> Menangle virus does not possess hemadsorption or hemagglutination activity.<sup>11</sup>

## HISTORY IN SWINE

The only known Menangle virus outbreak occurred on a single swine farm in New South Wales, Australia in 1997. The farm was a farrow-to-finish operation with approximately 2600 sows.<sup>15</sup> Reproductive disease and congenital defects were seen in affected sows and fetuses. No clinical disease occurred in growers.

About six months after the outbreak began, Menangle virus was widespread on the farm. More than 90% of pigs (of all ages) on the farm became seropositive. Following the initial spread, susceptible young pigs became infected in the post-weaning period, and this enabled persistence of Menangle virus in the herd. Since replacement animals were exposed to the virus prior to mating, further reproductive losses were prevented. Two people that worked on the swine farm became ill.<sup>1</sup> Menangle virus was detected on two associated farms; however, no breeding animals were present on these farms and no clinical disease was noted.<sup>3</sup> Testing of other animals near the affected farm, including rodents, birds, cattle, sheep, cats, and a dog, showed that all were seronegative.<sup>11</sup> In 1999 another paramyxovirus, Nipah virus, emerged in Malaysia and spread from fruit bats to domestic pigs.<sup>16, 17</sup>

## IMMUNITY

### POST-EXPOSURE

Pigs exposed to Menangle virus develop high neutralizing antibody titers. Persistent infection is thought to be very unlikely.<sup>3</sup> Neutralizing antibodies to Menangle virus are commonly found in *Pteropus* spp. in Australia.<sup>18</sup>

## VACCINES

There are currently no vaccines for Menangle virus.

## CROSS-PROTECTION

Menangle virus is not closely related to other paramyxoviruses. Its main antigenic gene sequence (HN protein) shares <20% sequence homology with other subfamily members,<sup>19</sup> and primers corresponding to conserved regions of representative paramyxoviruses do not amplify Menangle virus.<sup>14</sup> However, there is antigenic cross-reactivity between Menangle virus and Tioman virus, a rubulavirus isolated from fruit bats in Malaysia.<sup>20</sup> In addition, a monoclonal antibody has been generated with cross-reactivity to the N protein of Tioman virus.<sup>10</sup> Cross-reactivity has been documented between bat and porcine Menangle virus strains, indicating that cross-protection may occur in individuals.<sup>1</sup>

## GAPS IN PREPAREDNESS

Although no Menangle virus outbreaks have occurred since 1997, the virus remains a concern to the swine industry because of profound production losses it can cause and risk to human health. Menangle virus epidemiology is poorly understood, and there are no vaccines for infected pigs. More research is needed to prepare for and prevent further Menangle virus outbreaks in pigs.

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