TICK-BORNE ILLNESS ISN'T JUST LYME DISEASE
A Guide to the Powassan Virus

Coppe Laboratories, 2016.
# REFERENCES


(9) Centers for Disease Control and Prevention, February 2015.


Transmitted by the tick known to carry Lyme disease bacteria, the Powassan virus (POWV) is a member of the family of viruses that include such familiar names as Zika, West Nile, Yellow Fever, and Dengue Fever.

POWV is not a new virus. It was discovered in 1958 in Powassan, Ontario, following the death of a five-year-old boy with encephalitis. It is the only tick-borne member of the Flaviviridae family known to cause human disease in North America.

Like Lyme disease, Powassan virus is emerging in the same geographic areas throughout the Northeast and Midwest United States. It’s found in wooded and bushy areas as well as fields where Lyme-bearing ticks live.

Experts have suggested that the virus could be a bigger health hazard than Lyme disease.

“Wildlife studies have shown that Powassan virus is increasing in the New England area and human case reports are increasing in the upper Midwest. As more ticks become infected with Powassan virus and more people become exposed to them, Powassan could become epidemic like Lyme disease. Because it can be a serious disease causing fatalities and there is no treatment for it, Powassan has the potential to become a greater public health threat than Lyme disease.”

(Durland Fish, PhD)
EPIDEMIOLOGY

Powassan Virus is Similar to Tick-borne Encephalitis Virus (TBEV), a Health Issue in Europe

Because little research has been reported on POWV, much of the information we understand about this class of tick-borne viruses and their potential to cause illness comes from its European relative, the Tick-borne Encephalitis Virus (TBEV). POWV and TBEV are members of the Tick-borne encephalitis complex of viruses. In Europe and Asia, TBE is a serious health issue, with cases each year being referred to hospitals. With the ease of travel and the number of people pursuing leisure activities in endemic areas, there is evidence infections are on the rise.

Several European countries report that tick-borne encephalitis is one of the most serious infections of the central nervous system with thousands of cases each year being referred to hospitals. With the ease of travel and the number of people pursuing leisure activities in endemic areas, there is evidence infections are on the rise.

Experts have suggested that the U.S. POWV may be on the same growth curve as TBEV was in the 1990s when some countries initiated national vaccination programs resulting in the decline seen here.

TREATMENT

Treatment of Powassan Virus

Currently there are no medications or vaccines for Powassan virus and antibiotics are not effective. Many physicians recommend immune system boosters to provide the patient with natural defenses to manage and alleviate symptoms. When the conditions are severe and warrant hospitalization, treatment may include respiratory support, intravenous fluids, and medications to reduce swelling in the brain.

Co-infections Might Necessitate Extended Antibiotic Therapy When Powassan is Involved.

- Viruses belonging to the same family and genus as Powassan are known to inhibit immune function and interfere with a person’s ability to defend against other invading pathogens.
- Patients with co-infections may benefit from extended antibiotic therapy following acute infection.
- Immune modulatory drugs such as the interferons may be a future treatment option.

"You can get seizures, high fevers, and stiff neck. It comes on so suddenly that it's the kind of thing people go to the emergency room for."

– Daniel Cameron, MD; CBS NY, April 2015
Case Study 3:

A woman in her late fifties was bitten by a tick sometime during an 8-day camping trip in northern Wisconsin. After a few days of dizziness, non-productive cough and fear of noise, she went to the local emergency room. An acute fever (102.2°F) accompanied by severe headache and muscle pain prompted her admission to the hospital. Muscle weakness, nausea and vertigo were also present. On clinical examination no neurological abnormalities were detected. On the right buttock there was a red induration of 1 cm in diameter at the location of the tick bite. During the ten days of admission, headache and muscle pain were the main complaints. Serology for borreliosis was negative. Potential infection with POWV was suspected in an early phase based on the clinical picture (fever and headache) in combination with the registration of a tick bite and the recent leisure activities in a POWV endemic area. PCR on a plasma sample taken four days upon onset of disease showed POWV RNA and low titered POWV IgM antibodies, confirming an active POWV infection. The patient recovered gradually. One month later she had only mild headaches and hypersensitivity to noise.

“Our hypothesis is that some patients with ongoing symptoms who have not responded to antibiotics known to be effective against Borrelia may be infected with viruses or other antibiotic resistant bacteria.”

- Ian Lipkin, MD; Columbia University Press Release, February 16, 2016
Lyme Disease

Virus and Powassan Virus Look Like

One-third of these patients have incomplete form of the disease, meningoencephalitis. 30% of symptomatic adults will contract a severe form of TBEV/POWV infections are sub-clinical. About two-thirds of patients will experience all of the symptoms. About two-thirds of patients will experience all of the symptoms. About two-thirds of patients will experience all of the symptoms. About two-thirds of patients will experience all of the symptoms. About two-thirds of patients will experience all of the symptoms.

Sometimes high fevers can occur. The initial viremic stage is followed by 2-3 weeks of a symptom-free period. A significant increase in temperature after the quiescence indicates the beginning of the second stage where there is often central nervous involvement. Encephalitis can develop during the second phase.7

Not everyone infected with TBEV/POWV experiences all of the symptoms. About two-thirds of TBEV/POWV infections are sub-clinical. About 30% of symptomatic adults will contract a severe form of the disease, meningoencephalitis. One-third of these patients have incomplete recovery with neuropsychiatric symptoms becoming chronic. The overall fatality rate is about 1% and the severity of illness increases with the age of the patient.8

Because symptoms associated with TBEV/POWV closely resemble those of Lyme disease, the virus may be overlooked - yet directly contribute to disease long term.

Flu-like symptoms with TBEV
• Fever >38.0°C (101°F)
• Fatigue
• Headache
• Aching back and limbs
• Gastrointestinal symptoms
• Anorexia
• Nausea

For POWV, known cases have shown similar symptoms and timelines.

LYME BORRELIA Compare to POWV

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CASE STUDIES

Case Study 1:
A 60-year old male with a recent history of tick bites went to his doctor after complaining of weakness, headaches and fever. Initially he was treated with doxycycline for Lyme disease. After 14 days of therapy, he continued to have fevers, was weak and had difficulty walking.

At the insistence of his wife, he went to the emergency room when his temperature rose to 101.8°F. He was empirically treated with IV doxycycline and was admitted to the hospital.

Initial tick-borne disease testing included Lyme serology, which was non-reactive. Anaplasma, Babesia, and West Nile virus testing was also negative. His fever persisted and he continued to complain of generalized weakness. A POWV PCR and antibody panel was collected. RT-PCR showed 4.5 log copies/mL (whole blood) and the IgM antibody was positive (3 weeks after presentation).

Case Study 2:
A 69-year old male with a history of tick bites was evaluated at a local emergency room for progressive weakness, headache and fever. He was diagnosed with a urinary tract infection and was treated with ciprofloxacin. He continued to have fevers and progressive weakness with difficulty walking. He described difficulty in controlling the movement of his limbs. He returned to the emergency room when his temperature rose to 100.4°F and his weakness was pronounced. His neurological examination was suggestive of non-focal generalized weakness but without any loss of muscle power.

An initial infectious work up included:
• Anaplasma/Ehrlichia serology for IgG: negative
• Ehrlichia/Anaplasma PCR: negative
• West Nile IgM: negative
• Babesia IgM: negative
• Babesia PCR: negative
• Lyme serology: negative

He was empirically treated with IV doxycycline. He continued to have fevers during his admission. The POWV antibody panel was ordered. IgM for POWV by EIA was positive. The patient remained in the hospital for several days. His condition gradually improved and strength returned. He was discharged to a skilled nursing facility for further rehabilitation.

He continued to improve neurologically. At his last follow-up, 4 months after his hospitalization, he continued to have some muscle weakness particularly in his quadriceps. His range of motion in the knee joint was also restricted.
Testing for Powassan Virus by Coppe Laboratories

Until now, laboratory testing for Powassan virus has been limited to the Centers for Disease Control (CDC) and a few state laboratories. Coppe Laboratories, a CLIA-certified diagnostic laboratory, has developed both a direct and indirect test for Powassan virus. Coppe Laboratories is the only reference laboratory to offer this testing.

Reverse transcription PCR and serologic testing are the preferred diagnostic tests for the Powassan virus. Coppe Laboratories offers both testing methods to provide complete results for both acute and long-term infections.

Environmental and Clinical Studies

Powassan Virus in the Ticks

A 1999 study by Ebel, et al., showed that 4.6% of the ticks in the upper northeastern region of Wisconsin harbored the POWV. A study presented by Coppe Laboratories with ticks from the same endemic area showed:

- Borrelia was present at an overall rate of 39.2%
- Anaplasma was found in 1.3%
- Babesia was found at an overall rate of 6.8%
- POWV/Flavivirus was found at an overall rate of 5.3%

In the same study, tick pools (1-5 ticks/pool) from across Wisconsin were analyzed. Data presented showed:

- 11% of the tick pools harbored Borrelia
- POWV/Flavivirus was found in 6% of the tick pools
- 8% of the tests tested had co-infection with Borrelia, POWV/Flavivirus, or Babesia

The study was particularly important because the ticks gathered were not “questing” ticks but actual ectoparasites attached to a blood host. Ticks collected were both ixodes and Dermacentor ticks - males, females, nymphs and eggs. Ticks carried both Borrelia and POWV, and Dermacentor ticks also carried Borrelia. The authors concluded that further investigation is needed to determine if Dermacentor ticks transmit infection to humans. Currently the ixodes tick is considered the sole vector of the disease.

This analysis provided data that the POWV is increasing and the pattern of distribution is spreading to a larger area.

Interpretation of RT-PCR Results

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Incidence of Powassan Virus in Acute Tick-borne Illness Samples

In a study of 106 patients with suspected acute tick-borne disease, 10.4% were positive by immunofluorescent assay (IFA) for POWV. All patients had evidence of recent tick exposure. The authors concluded "Infection with POWV may be underdiagnosed and the virus may contribute to the acute and/or persistent symptoms often associated with Lyme disease diagnosis." [16]

Correlation Between Chronic Symptoms of “Lyme-like” Disease and POWV

Knox et al., studied 250 patients with a diagnosis of post-infectious fatigue. [17] These patients experienced intense fatigue not improved by rest and worsened by physical or mental exertion. Many had signs of weakness, muscle pain, insomnia and cognitive impairment that persisted for more than six months. Many reported patterns of remission and relapse. These patients had been previously tested for Lyme disease and found negative.

Blood samples were examined by Coppe Laboratories for presence of Borrelia and POWV. While 2.4% had evidence of a Borrelia infection, a full 13% had evidence of exposure to a POWV/Flavivirus. The study suggests there may be a link between POWV and the chronic symptoms experienced by this group of patients.

Who should be tested for POWV?

- Patients with a recent tick bite. Studies have shown 5–11% of ticks to be infected with POWV in Lyme endemic areas.
- Patients with Lyme disease (tick-borne illnesses) who have been treated with antibiotics and have persistent symptoms consistent with post-treatment (chronic) Lyme disease.
- Patients with tick exposure who have tested negative for Lyme disease or other tick-borne illnesses who continue to have symptoms.
- Patients with tick exposure and unexplained neurologic symptoms.
- Chronic fatigue syndrome (CFS) patients or Post-Infectious Fatigue (PIF) patients with tick exposure.

DIRECT DIAGNOSTIC TESTING

**POWV/Flavivirus Present in Post-Infectious Fatigue Patients**

Out of 250 patients with post infectious fatigue

32 screened positive for POWV

**POWV Acute Test**

- Measurement of the actual virus RNA
- Used in determining acute infection in those individuals who have symptoms for less than six weeks

**POWV Serology Test**

- Measurement of patient’s antibody response to the virus
- IgG and IgM antibodies specific for Powassan detected
- Test is useful for determining stage of infection including chronic disease

**Who should be tested for POWV?**

The PCR or direct test measures viral RNA and will be positive in the first 4 weeks after symptoms occur. Neurological symptoms appear around 2 weeks after the tick bite and can include confusion, speech difficulties, stiff neck and memory loss. At about 4 weeks post tick bite, the serology tests, measured by an enzyme immunoassay (EIA), will become positive. [14]
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TICKS CAN TRANSMIT MORE THAN ONE PATHOGEN. POWASSAN VIRUS SHOULD BE CONSIDERED WHEN TESTING FOR LYME DISEASE.
Lyme Disease
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This case represents an acute POWV infection with long-term neurologic manifestations.

**Case Study 2:**
A 69-year old male with a history of tick bites was evaluated at a local emergency room for progressive weakness, headache and fever. He was diagnosed with a urinary tract infection and was treated with ciprofloxacin. He continued to have fevers and progressive weakness with difficulty walking. He described difficulty in controlling the movement of his limbs. He returned to the emergency room when his temperature rose to 100.4°F and his weakness was pronounced. His neurological examination was suggestive of non-focal generalized weakness but without any loss of muscle power.

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<tr>
<td>Late or long-term symptoms</td>
<td>Fatigue, confusion, paralysis, speech difficulties, memory loss, encephalitis, chronic headache</td>
<td>Fatigue, pain, joint and muscle aches, chronic headache, sleep disturbances</td>
</tr>
</tbody>
</table>

**For POWV, known cases have shown similar symptoms and timelines.**

**Flu-like symptoms with TBEV**
- Fever >38.0°C (101°F)
- Fatigue
- Headache
- Aching back and limbs
- Gastrointestinal symptoms
- Anorexia
- Nausea

**Immuno-fluorescent antibody (IFA) test demonstrating the presence of Powassan antibodies from blood.**
Case Study 3:
A woman in her late fifties was bitten by a tick sometime during an 8-day camping trip in northern Wisconsin. After a few days of dizziness, non-productive cough and fear of noise, she went to the local emergency room. An acute fever (102.2ºF) accompanied by severe headache and muscle pain prompted her admission to the hospital. Muscle weakness, nausea and vertigo were also present. On clinical examination no neurological abnormalities were detected. On the right buttock there was a red induration of 1 cm in diameter at the location of the tick bite. During the ten days of admission, headache and muscle pain were the main complaints. Serology for borreliosis was negative. Potential infection with POWV was suspected in an early phase based on the clinical picture (fever and headache) in combination with the registration of a tick bite and the recent leisure activities in a POWV endemic area. PCR on a plasma sample taken four days upon onset of disease showed POWV RNA and low titered POWV IgM antibodies, confirming an active POWV infection. The patient recovered gradually. One month later she had only mild headaches and hypersensitivity to noise.

“Our hypothesis is that some patients with ongoing symptoms who have not responded to antibiotics known to be effective against Borrelia may be infected with viruses or other antibiotic resistant bacteria.”
- Ian Lipkin, MD; Columbia University Press Release, February 16, 2016

The Incidence of POWV in the United States is Underreported

In the United States, only the severe encephalitis cases of POWV have been reported, thus diminishing the incidence. Even though only life-threatening cases of infection have been identified, there has still been a 375% increase in the cases of Powassan encephalitis reported in the last five years.ª

Ticks can harbor and transmit a number of pathogens - including Borrelia, POWV, Anaplasma/Ehrlichia and Babesia. Co-infection and co-transmission of pathogens is common.¹⁰

POVV is unique among these pathogens in that transmission time from the tick to the host has been documented to be 15 minutes or less, thereby making usual tick diligence ineffective.

For the Powassan virus, successful tick feeding is facilitated by factors in the tick saliva. This saliva-activated transmission makes it easier for the virus to quickly enter the person and begin replicating.¹¹,¹²,¹³

POWV can be transmitted from a tick to a human in 15 minutes or less.
EPIDEMIOLOGY

Powassan Virus is Similar to Tick-borne Encephalitis Virus (TBEV), a Health Issue in Europe

Because little research has been reported on POWV, much of the information we understand about this class of tick-borne viruses and their potential to cause illness comes from its European relative, the Tick-borne Encephalitis Virus (TBEV). POWV and TBEV are members of the Tick-borne encephalitis complex of viruses. In Europe and Asia, TBE is a serious health issue, with 10,000-15,000 cases reported each year, and the number of reported cases increasing steadily in countries with no vaccination program. 

Several European countries report that tick-borne encephalitis is one of the most serious infections of the central nervous system with thousands of cases each year being referred to hospitals. With the ease of travel and the number of people pursuing leisure activities in endemic areas, there is evidence infections are on the rise.

Experts have suggested that the U.S. POWV may be on the same growth curve as TBEV was in the 1990s when some countries initiated national vaccination programs resulting in the decline seen here.

TREATMENT

Treatment of Powassan Virus

Currently there are no medications or vaccines for Powassan virus and antibiotics are not effective. Many physicians recommend immune system boosters to provide the patient with natural defenses to manage and alleviate symptoms.

When the conditions are severe and warrant hospitalization, treatment may include respiratory support, intravenous fluids, and medications to reduce swelling in the brain.

Co-infections Might Necessitate Extended Antibiotic Therapy When Powassan is Involved.

- Viruses belonging to the same family and genus as Powassan are known to inhibit immune function and interfere with a person’s ability to defend against other invading pathogens.
- Patients with co-infections may benefit from extended antibiotic therapy following acute infection.
- Immune modulatory drugs such as the interferons may be a future treatment option.

“...You can get seizures, high fevers, and stiff neck. It comes on so suddenly that it’s the kind of thing people go to the emergency room for.”

- Daniel Cameron, MD; CBS NY, April 2015
Transmitted by the tick known to carry Lyme disease bacteria, the Powassan virus (POWV) is a member of the family of viruses that include such familiar names as Zika, West Nile, Yellow Fever, and Dengue Fever.

**Some Facts About the Powassan Virus (POWV)**

- The Powassan virus incubation period (time from tick bite to onset of symptoms) ranges from one week to one month.
- Common symptoms include fever, headache, vomiting, weakness, confusion, stiff neck, and in more serious cases, seizures, speech difficulty and loss of coordination.
- POWV can infect the central nervous system, resulting in severe neuroinvasive disease: encephalitis and meningitis.
- About 50% of patients with encephalitis have permanent neurological symptoms, such as recurrent headaches, muscle weakness and memory problems.
- Approximately 10% of POWV encephalitis cases are fatal.
- Antibiotics are ineffective.
- POWV is transmitted by the same tick causing Lyme disease, Babesiosis, Anaplasmosis, and Ehrlichiosis.
- Co-infection of Powassan and Borrelia bacteria may warrant more aggressive therapy.

POWV is not a new virus. It was discovered in 1958 in Powassan, Ontario, following the death of a five-year-old boy with encephalitis. It is the only tick-borne member of the Flaviviridae family known to cause human disease in North America.

Like Lyme disease, Powassan virus is emerging in the same geographic areas throughout the Northeast and Midwest United States. It’s found in wooded and bushy areas as well as fields where Lyme-bearing ticks live. Experts have suggested that the virus could be a bigger health hazard than Lyme disease.3

"Wildlife studies have shown that Powassan virus is increasing in the New England area and human case reports are increasing in the upper Midwest. As more ticks become infected with Powassan virus and more people become exposed to them, Powassan could become epidemic like Lyme disease. Because it can be a serious disease causing fatalities and there is no treatment for it, Powassan has the potential to become a greater public health threat than Lyme disease."  

(Durland Fish, PhD)3