# Acute Viral Infections of the Spinal Cord

James Bowen, MD
Director, Neurology Services
Multiple Sclerosis Center
University of Washington Medical Center

Viral infections of the spinal cord are important causes of transverse myelitis (TM). [1, 2] The presentation and clinical symptoms of TM have been described elsewhere and will not be repeated here. There are several points suggesting that infectious agents may be important in the pathogenesis of TM. As many as 40% of TM cases are preceded by an upper respiratory infection. In one report, 81% of TM cases were preceded by a febrile illness. [3] There is clear evidence that inflammation is present in TM, including elevation of CSF lymphocytes and neutrophils, and often the presence of elevated IgG levels or oligoclonal bands. Since TM involves a rather limited area of the nervous system, there must be some local factors provoking the inflammation at the affected site. One local factor that may be responsible is an infectious agent. There are many cases where the infectious agent has actually been cultured. These are described in more detail below.

Diagnosing infectious causes of TM can be difficult. There are a large number of infectious agents that can cause TM, and they generally do not have differentiating characteristics. Though there are a few tests that can identify several agents at once, e.g. cultures for herpes viruses, many tests require knowledge of the individual organism. In particular, serology tests and PCR testing search for only a single agent. The timing of the testing is also problematic. When patients present with an acute spinal cord syndrome, the initial diagnostic emphasis is on anatomical/surgical lesions. This leads to extensive clinical evaluations and imaging before blood work and lumbar punctures are performed. The search for infections can be delayed as a result. By the time an infection is sought, the infectious agent may be eliminated by the hosts immune system. Complicating the search further, when the patient presents it may already be too late to identify an infection. In some cases, it is likely that the symptoms of TM result from collateral damage from the immune attack rather than on the infection itself. Thus, when the patient develops symptoms the infectious agent is already being removed by the host's inflammatory response.

Infections causes TM can result from viral, bacterial, fungal, parasitic, or postvaccinal inflammation. Viral infections can include members of the herpes virus, enterovirus, influenza, lymphocytic choriomeningitis (LCM), or retrovirus families. [2] Viral causes are more common that others in developed countries. Parasitic causes predominate in less developed areas.

The herpes virus family includes a number of neurotrophic viruses. The PCR of spinal fluid is more often positive in herpes virus infections than culture. [4] **Epstein-Barr virus (EBV)** is the causative agent for mononucleosis. Though neurological illness may be seen in patients with mononucleosis, many cases occur in patients without other

systemic symptoms. The prognosis for EBV myelopathy is relatively good. [5-9] The heterophil antibody test may be normal, so it is better to diagnose EBV TM using PCR and culture. [10] Many cases are seen in the setting of immunocompromised hosts. [11] **Varicella zoster virus (VZV)** is most commonly associated with reactivation of prior infection (shingles). [12, 13] However, it may occur in patients preceding the rash, or in patients that never develop a rash. [14] The PCR can be negative in cases where the VZV antibodies are positive. [4] It is usually segmental and may include peripheral sensory changes. It may be recurrent. [15] It may be treated with antiviral agents such as acyclovir or famcyclovir. [16] Corticosteroids may also be helpful. **Cytomegalovirus (CMV)** has frequently been described in immune compromised hosts such as those with AIDS. [17] However, it may be seen in patients without immune compromise. [18, 19] It is often associated with lower motor neuron findings, though it can occur as an isolated myelopathy. **Herpes Simplex Virus (HSV)** myelitis may be due to either type 1 or type 2 HSV. [20] The course of the disease if often fairly aggressive with necrosis of the spinal cord. It is often associated with an encephalopathy as well. Like CMV, it may be associated with lower motor neuron findings. It can be treated with acyclovir. **Human Herpes Virus 6 (HHV6)** only rarely causes TM. [21, 22] It is of particular interest because its possible relation to multiple sclerosis. **Herpes B** may cause a myelopathy. [23] However, it is usually overshadowed by its overwhelming fatal outcome. It is transmitted through monkeys to humans.

Several members of the enterovirus family may cause TM. Several members of the **Coxsackievirus** family may cause TM. [2, 24-30] The **Echovirus** family is also well represented. [31-33] Both **hepatitis B** [34] and **hepatitis A** [35-37] have caused TM. The childhood diseases **rubella**, [38, 39] **measles,** [40] and **mumps** [41, 42] can cause TM. These cases are not limited to children, but may occur in adults. [43] **Poliomyelitis** has predominantly lower motor neuron changes. However, central nervous system damage also occurs with the disease. [26] Spinal cord damage, determined by MRI, may occur in cases of poliomyelitis that do not have paralysis. [44] Occasional cases of TM may precede the lower motor neuron phase of the disease. [45] Most cases in the developed world are due to live vaccine sources.

Retroviruses are a recently recognized cause of TM. There are two members of this family that are of particular concern in TM, HIV and HTLV-1. **HTLV-I and II** is endemic to South America, the Caribbean and Japan. It is also endemic in some Pacific Northwest costal groups including those in British Columbia. It usually presents with slowly progressing myelopathy rather than TM. It often has early sphincter involvement and radicular pain. **HIV** can cause TM, though it is usually subacute or chronic. [46, 47] It must be differentiated from other infectious causes of TM in those with immunodeficiency including members of the herpesvirus family, toxoplasmosis, cryptococcosis, tuberculosis and aspergillosis.

Rarely, other viruses are reported to cause TM. **Influenza** can cause TM, but is usually identified by the presence of the well-recognized upper respiratory infection. [48] **Lymphocytic Choriomeningitis (LCM)** predominantly causes TM in children. [49, 50] A single case of TM due to About 20% of **rabies** cases have myelitis, but the

presentation is primarily that of an encephalitis. **West Nile Virus** has been reported. [51] This may be of particular importance considering the spread of this organism to the North American continent.

There are several bacterial infections that can cause TM. **Lyme Disease (neuroborreliosis)** is the most commonly recognized. [52-55] It is seasonal, occurring in the spring and summer when ticks are most active, and geographically restricted. It typically has a myelopathy accompanied by radiculopathy, cranial neuropathy, or encephalitis. However, rare cases present with TM alone. It may be seen without preceding erythema chronicum migrans. [56] **Mycoplasma pneumoniae** is also relatively common among the bacterial causes of TM. [57-61] It usually occurs in children. About ¼ of neurological presentations of the infection are TM. [62] It can be treated with doxycycline with a good prognosis. [63] However, occasional cases have poor outcomes. [64] Cases have been reported of TM due to **Yersinia enterocolitica**[65]**, Chlamydia psittaci (Psittacosis)** [66, 67]**, Rochalimaea henselae (cat scratch fever)** [68, 69] Syphilis and tuberculosis are rare causes of TM now. [70]

The only fungal organism that causes TM with much frequency is cryptocossus. [71] It is more common in immunocompromised hosts.

A number of parasitic diseases can cause TM. In general, these may be identified in patients that have appropriate exposure histories. Eosinophils may be seen in the CSF. Mass effects in the spinal cord may be seen due to the organism or to eggs. Other cases have no mass effect. **Schistosomiasis** is the most common of these. [72-76] Both S. mansonii and haematobium may be responsible. The conus medullaris is a common site of involvement, though other levels of spinal cord involvement may be seen. **Toxoplasmosis** is usually seen in immunocompromised hosts, especially those with AIDS. [77, 78] Toxoplasmosis may be seen occasionally in immune competent hosts. **Cysticercosis, Toxocaraisis, Gnathostoma, and Angiostrongyllus** may all cause TM. [79-82]

| Organism | PCR | Serology | Culture | Treatment | Comments |
|---|---|---|---|---|---|
| **Herpes** | | | | | |
| EBV | + | + | + | + | |
| VZV | + | + | + | + | ± shingles |
| CMV | + | + | + | + | |
| HSV | + | + | + | + | |
| HSV6 | + | + | + | + | |
| Herpes B | | + | + | + | Exposure to monkeys |
| **Enterovirus** | | | | | |
| Coxsackie | | + | + | | |
| Echovirus | | + | + | | |
| Hepatitis | | + | | | Usually with systemic illness |
| Rubella | | + | + | | |
| Measles | | + | + | | |
| Mumps | | + | + | | Usually with systemic illness |
| Polio | | | + | | Usually lower motor neuron |
| **Retrovirus** | | | | | |
| HTLV-I, and II | | + | | | Exposure, chronic |
| HIV | | + | + | + | Exposure, chronic or subacute |
| **Other** | | | | | |
| Influenza | + | + | + | + | |
| LCM | | + | + | | |
| Rabies | + | + | | | Exposure, encephalitis |
| West Nile | | + | | | Exposure, seasonal |
| **Bacteria** | | | | | |
| Lyme | | + | | + | Exposure, rash, seasonal, usually radiculomyelitis |
| Mycoplasma | | + | | + | Often systemic illness |
| Yersinia | | + | | + | |
| Psittacosis | | + | | + | Bird exposure |
| Cat Scratch | | + | + | + | Cat exposure |
| Syphilis | | + | | + | |
| Tuberculosis | | | + | + | |
| **Fungal** | | | | | |
| Cryptococcal | | | + | | Immunosuppressed, Crypto Ag |
| **Parasitic** | | | | | |
| Schistosomiasis | | + | | + | Exposure |
| Toxoplasmosis | | + | | + | Immunosuppressed |
| Cysticercosis | | + | | + | Exposure, biopsy may be needed |
| Toxocariasis | | + | | + | |
| Gnathostoma | | + | | + | Exposure |
| Angiostrongyllus | | + | | + | Exposure |

## References:


1. Knebusch, M., H. Strassburg, and K. Reiners, *Acute transverse myelitis in childhood: nine cases and review of the literature.* Develop Med Child Neurol, 1998. **40**: p. 631-639.
2. Andersen, O., *Myelitis.* Curr Opin Neurol, 2000. **13**: p. 311-316.
3. Al Deeb, S., et al., *Acute transverse myelitis: A localized form of postinfectious encephalomyelitis.* Brain, 1997. **120**: p. 1115-1122.
4. Gilden, D., et al., *The value of cerebrospinal fluid antiviral antibody in the diagnosis of neurologic disease produced by varicella zoster virus.* J Neurol Sci, 1998. **14**: p. 140-144.
5. Breteau, G., et al., *Adenovirus myelitis and Epstein-Barr myelitis: Two unusual viral causes with similar presentations.* Rev Neurol (Paris), 2000. **156**: p. 789-799.
6. Corssaint, E., et al., *Severe meurological complicaitons in association with Epstein-Barr virus infection.* J Neurovirol, 1997. **3**: p. 460-464.
7. Shian, W. and C. Chi, *Acute Transverse myelitis in children: Clinical analysis of seven cases.* Chung Hua I Hsueh Tsa Chih (Taipei), 1994. **54**: p. 57-61.
8. Landgren, M. and e. al, *Diagnosis of Epstein-Barr virus-induced central nervous system infections by DNA amplification from cerebrospinal fluid.* Ann Neurol, 1994. **35**: p. 631-635.
9. Caldas, C., et al., *Case report: Transverse myelitis associated with Epstein-Barr virus infection.* Am J Med Sci, 1994. **307**: p. 45-48.
10. Grose, C., W. Henle, and G. Henle, Feorino, PM, *Primary Epstein-Barr virus infections in acute neurologic diseases.* N Engl J Med, 1975. **292**: p. 392-395.
11. Gruhn, B. and e. al, *Successful treatment of Epstein-Barr virus-induced transverse myelitis with gancyclovir and cytomegalovirus hyperimmune globulin following unrelated bone marrow transplant.* Bone Marrow Transplant, 1999. **24**: p. 1355-1358.
12. Echevarria, J., I. Casas, and P. Martinez-Martin, *Infections of the nervous system caused by varicella-zoster virus: a review.* Intervirology, 1997. **40**: p. 72-84.
13. Flamholc, L., *Neurological complications in herpes zoster.* Scand J Infect Dis, 1996. **Suppl ;100**: p. 35-40.
14. Caminero, A., et al., *Myelitis associated with varicella-zoster virus in the absence of cutaneous zoster.* Rev Neurol (Paris), 1996. **24**: p. 1532-1535.
15. Baik, J., et al., *Recurrent herpes zoster myelitis.* J Korean Med Sci, 1997. **12**: p. 360-363.
16. de Silva, S., et al., *Zoster myelitis: improvement with antiviral therapy in two cases.* Neurology, 1996. **47**: p. 929-931.
17. Burke, D., et al., *The utility of clinical and radiographic features in the diagnosis of cytomegalovirus central nervous system disease i AIDS patients.* Mol Diag, 1999. **4**: p. 37-43.
18. Baig, S. and M. Khan, *Cytomegalovirus-associated transverse myelitis in a non-immunocompromised patient.* J Neurol Sci, 1995. **134**: p. 210-211.
19. Giobbia, M., et al., *Cytomegalovirus-associated transverse myelitis in a non-immunocompromised patient.* Infection, 1999. **27**: p. 228-230.
20. Nakajima, H., et al., *Herpes simplex virus myelitis: Clinical manifestations and diagnosis by the polymerase chain reaction method.* Eur Neurol, 1998. **38**: p. 163-167.
21. Hill, A., E. Hicks, and P. Colye, *Human herpes virus 6 and central nervous system complications.* Develop Med Child Neurol, 1994. **36**: p. 651-652.
22. KacKinzie, I., D. Carrigan, and C. Wiley, *Chronic myelopathy associated with human herpesvirus-6.* Neurology, 1995. **45**: p. 2015.
23. Holmes, G., et al., *B-virus (herpes virus simiae) infection in humans: Epidemiologic ivestigation of a cluster.* Ann Intern Med, 1990. **112**: p. 833-839.
24. Yoshimura, K. and T. Kurashige, *A case of poliomyelitis-like syndrome. 1998 Oct;20(7):540-2.* Brain Dev, 1998. **20**: p. 540-542.
25. Ku, B. and K. Lee, *Acute transverse myelitis caused by Coxsackie virus B4 infection: a case report.* J Korean Med Sci, 1998. **13**: p. 449-453.
26. Tuteja, U., et al., *Enterovirus specific IgM responses in children with acute and chronic paralytic syndrome.* J Trop Med Hyg, 1995. **98**: p. 367-372.
27. Graber, D., et al., *Acute transverse myelitis and coxsackie A9 virus infection.* Pediatr Infect Dis J, 1994. **13**: p. 77.
28. Grist, N. and E. Bell, *Paralytic poliomyelitis and nonpolio enteroviruses: studies in Scotland.* Rev Infect Dis, 1984. **6, Suppl 2**: p. S385-S386.

29. Dery, P., M. Marks, and R. Shapera, *Clinical manifestations of coxsackievirus infections in children.* Am J Dis Child, 1974. **128**: p. 464-468.
30. Matthews, T. and S. Bailey, *Transverse myelitis - association with coxsackie B3 infection?* Arch Dis Child, 1977. **52**: p. 518-519.
31. Kibe, T., et al., *Serial MRI findings of benign poliomyelitis.* Brain Dev, 1996. **18**: p. 147-149.
32. Barak, Y. and J. Schwartz, *Acute transverse myelitis associated with ECHO type 5 infection.* Am J Dis Child, 1988. **142**: p. 128.
33. Takahashi, S., et al., *Acute transverse myelitis caused by ECHO virus type 18 infection.* Eur J Pediatr, 1995. **154**: p. 378-380.
34. Matsui, M., et al., *Recurrent demyelinating transverse myelitis in a high titer HBs-antigen carrier.* J Neurol Sci, 1996. **139**: p. 235-237.
35. Beeri, R., et al., *Transverse myelitis heralding hepatitis A.* J Clin Gastroenterol, 1995. **20**: p. 262-263.
36. Tyler, K., R. Gross, and G. Cascino, *Unusual viral causes of transverse myelitis: hepatitis A virus and cytomegalovirus.* Neurology, 1986. **36**: p. 855-858.
37. Breningstall, G. and K. Belani, *Acute transverse myelitis and brainstem encephalitis associated with hepatitis A infection.* Pediatr Neurol, 1995. **12**: p. 169-171.
38. Bitzan, M., *Rubella myelitis and encephalitis in childhood. A report of two cases with magnetic resonance imaging.* Ann Pediatr (Paris), 1989. **36**: p. 689-691.
39. Cecille, A., et al., *[A case report of post-rubella myelitis in an adult]*. Pathol Biol (Paris), 1999. **47**: p. 531-533.
40. Beauvais, P., T. Billette de Villemeur, and J. Richardet, *[Acute isolated myelitis due to measles]*. Neuropediatrics, 1987. **18**: p. 84-87.
41. Venketasubramanian, N., *Transverse myelitis following mumps in an adult -- a case report with MRI correlation.* Acta Neurol Scand, 1997. **96**: p. 328-331.
42. Bansal, R., et al., *Myelitis: a rare presentation of mumps.* Pediatr Neurosurg, 1998. **38**: p. 204-206.
43. Hess, J. and S. Bamborschke, *[Acute transverse myelitis after rubella infection in an adult]*. Nervenarzt, 1993. **64**: p. 278-281.
44. Bruno, R., *Paralytic vs. "nonparalytic" polio: distinction without a difference?* Am J Phys Med Rehabil, 2000. **79**: p. 4-12.
45. Foley, K. and H. Beresford, *Acute poliomyelitis beginning as transverse myelopathy.* Arch Neurol, 1974. **30**: p. 182-183.
46. Denning, D., et al., *Acute myelopathy associated with primary infection with human immunodeficiency virus.* Br Med J, 1987. **294**: p. 143-144.
47. Jerez, P., A. Palao, and C. Leiva, *HIV myelopathy as the presenting symptom of acquired immunodeficiency syndrome.* Rev Neurol (Paris), 1998. **26**: p. 1008-1010.
48. Salonen, O., et al., *Myelitis associated with influenza A virus infection.* J Neurovirol, 1997. **3**: p. 83-85.
49. Linssen, W., F. Gabreels, and R. Wevers, *Infective acute transverse myelopathy. Report of two cases.* Neuropediatrics, 1991. **22**: p. 107-109.
50. Humbertclaude, V., et al., *[Acute myelitis of an unusual cause in a child: the lymphocytic choriomeningitis virus]*. Arch Pediatr, 2001. **8**: p. 282-285.
51. Gadoth, N., S. Weitzman, and E. Lehmann, *Acute anterior myelitis complicating West Nile fever.* Arch Neurol, 1979. **36**: p. 172-173.
52. Huisman, T., et al., *Unusual presentations of neuroborreliosis (Lyme disease) in childhood.* J Comput Assist Tomogr, 1999. **23**: p. 39-42.
53. Rousseau, J., et al., *Acute transverse myelitis as presenting neurological feature of Lyme disease.* Lancet, 1986. **2(8517)**: p. 1222-1223.
54. Olivares, J., et al., *Lyme disease presenting as isolated acute urinary retention caused by transverse myelitis: an electrophysiological and urodynamical study.* Arch Phys Med Rehabil, 1995. **76**: p. 1171-1172.
55. Kohler, J., *Lyme borreliosis: a case of transverse myelitis with syrinx cavity.* Neurology, 1989. **39**: p. 1553-1554.
56. Reik, L., W. Burgdorfer, and J. Donaldson, *Neurologic abnormalities in Lyme disease without erythema chronicum migrans.* Am J Med Sci, 1986. **81**: p. 73-78.

57. Westenfelder, G., et al., *Acute transverse myelitis due to Mycoplasma pneumoniae infection.* Arch Neurol, 1981. **38**: p. 317-318.
58. Yoshizawa, T., et al., *Transverse myelitis associated with Mycoplasma pneumoniae infections.* Eur Neurol, 1982. **21**: p. 48-51.
59. MacFarlane, P. and V. Miller, *Transverse myelitis associated with Mycoplasma pneumoniae infection.* Arch Dis Child, 1984. **59**: p. 80-82.
60. Mills, R. and L. Schoolfield, *Acute transverse myelitis associated with Mycoplasma pneumoniae infection: a case report and review of the literature.* Pediatr Infect Dis J, 1992. **11**: p. 228-231.
61. Goebels, N., et al., *Extensive myelitis associated with Mycoplasma pneumoniae infection: magnetic resonance imaging and clinical long-term follow-up.* J Neurol Sci, 2001. **248**: p. 204-208.
62. Smith, R. and L. Eviatar, *Neurologic manifestations of Mycoplasma pneumoniae infections: diverse spectrum of diseases. A report of six cases and review of the literature.* Clin Pediatr (Phila), 2000. **39**: p. 195-201.
63. Abele-Horn, M., et al., *Transverse myelitis associated with Mycoplasma pneumoniae infection.* Clin Infect Dis, 1998. **26**: p. 909-912.
64. Heller, L., et al., *Transverse myelitis associated with mycoplasma pneumoniae: case report.* Paraplegia, 1990. **28**: p. 522-525.
65. Sotaniemi, K., *Neurologic complications associated with Yersiniosis.* Neurology, 1983. **33**: p. 95-97.
66. Williams, W. and R. Sunderland, *As sick as a pigeon--psittacosis myelitis.* Arch Dis Child, 1989. **64**: p. 1626-1628.
67. Crook, T. and B. Bannister, *Acute transverse myelitis associated with Chlamydia psittaci infection.* J Infect, 1996. **32**: p. 151-152.
68. Pickerill, R. and J. Milder, *Transverse myelitis associated with cat-scratch disease in an adult.* JAMA, 1981. **246**: p. 2840-2841.
69. Salgado, C. and M. Weisse, *Transverse myelitis associated with probable cat-scratch disease in a previously healthy pediatric patient.* Clin Infect Dis, 2000. **31**: p. 609-611.
70. Hernandez-Albujar, S., et al., *Tuberculous radiculomyelitis complicating tuberculous meningitis: case report and review.* Clin Infect Dis, 2000. **30**: p. 915-921.
71. Gumbo, T., et al., *Cryptococcus myelitis: Atypical Presentation of a Common Infection.* Clin Infect Dis, 2001. **32**: p. 1235-1236.
72. Suchet, I., et al., *Spinal cord schistosomiasis: a case report and review of the literature.* Paraplegia, 1987. **25**: p. 491-496.
73. Bennett, G. and J. Provenzale, *Schistosomal myelitis: findings at MR imaging.* Eur J Radiol, 1998. **27**: p. 268-270.
74. Haribhai, H., et al., *Spinal cord schistosomiasis. A clinical, laboratory and radiological study, with a note on therapeutic aspects.* Brain, 1991. **114**: p. 709-726.
75. Ueki, K., J. Parisi, and B. Onofrio, *Schistosoma mansoni infection involving the spinal cord. Case report.* J Neurosurg, 1995. **82**: p. 1065-1067.
76. Ferrari, T., *Spinal cord schistosomiasis: A report of 2 cases and review emphasizing clinical aspects.* Medicine, 1999. **78**: p. 176-190.
77. Mehren, M., et al., *Toxoplasmic myelitis mimicking intramedullary spinal cord tumor.* Neurology, 1988. **38**: p. 1648-1650.
78. Thurnher, M., M. Post, and J. Jinkins, *MRI of infections and neoplasms of the spine and spinal cord in 55 patients with AIDS.* Neuroradiology, 2000. **42**: p. 551-563.
79. Schmutzhard, E., P. Boongird, and A. Vejjajiva, *Eosinophilic meningitis and radiculomyelitis in Thailand, caused by CNS invasion of Gnathostoma spinigerum and Angiostrongylus cantonensis.* J Neurol Neurosurg Psychiatry, 1988. **51**: p. 80-87.
80. Goffette, S., et al., *Eosinophilic pleocytosis and myelitis related to Toxocara canis infection.* Eur J Neurol, 2000. **7**: p. 703-706.
81. Wang, C., et al., *Transverse myelitis associated with larva migrans: finding of larva in cerebrospinal fluid.* Lancet, 1983. **1(8321)**: p. 423.
82. Kishore, L., et al., *Intramedullary spial cord cysticercosis - a case report and literature review.* Indian J Pathol Microbiol, 1991. **23**: p. 219-221.