

MYELOPATHY (SPINAL CORD DISEASE)

What's the Problem, and How Do You Diagnose It?

Myelopathy—or more precisely vacuolar myelopathy, the kind seen in some people with AIDS—is a degeneration of the spinal cord. Specifically, it involves degeneration of the nerves in the middle and lower thoracic spinal cord. Small holes (for which the medical term is vacuoles, hence the name of the disease) develop in the middle part of the spinal cord which controls the lower body. These holes gradually become larger over a period of months or years. Myelin, the protective coating around nerve fibers, is slowly destroyed, and the nerve fibers die. As more and more fibers are lost, the brain's signaling process is disrupted, blocking communication with the lower body.

Based on autopsy studies, it appears that these spinal cord changes may develop in from 22 to 55 percent of HIV+ people, although not always to a point that would cause serious symptoms. It is estimated that perhaps only 5 to 10 percent of HIV+ people may ultimately develop symptoms associated with the spinal cord changes. It often occurs in those with AIDS-associated dementia (the most extreme form of AIDS-associated Cognitive and Motor Complex). In fact, it is estimated that in one-third to two-thirds of dementia cases, this spinal cord problem will also be present. Initial symptoms are most often limb weakness which can cause difficulty in walking. When more advanced, the changes in the spinal cord can be quite devastating, causing not only partial paralysis or inability to control leg movement with resulting severe problems in walking, but also erection problems, increased frequency of urination, and inability to control the bowels and bladder. Much less frequently, this myelopathy may occur without the presence of dementia.

The disease's progress is variable, but most often slowly progresses through various stages of disability. For example, an initial difficulty with walking because of leg weakness or stiffness may progress to a need to use a cane. Eventually, as symptoms worsen, there may be a need for first a walker, then crutches, and finally a wheelchair. In rare cases, these problems may eventually develop into paralysis below the waist. Trouble with urinary and bowel control that initially just requires that someone rush to the bathroom, can later become full-fledged incontinence.

Misdiagnosis of myelopathy happens too often. The most common confusion is mistaking myelopathy for neuropathy. In some cases, the two conditions may both be present, making a correct diagnosis more difficult. David Simpson, MD, Director of the Neuro-AIDS Program at Mount Sinai Hospital in New York City, notes that with myelopathy, leg weakness will occur, while with neuropathy, there will not be weakness but rather pain or numbness. There are other conditions that may also cause some of the same symptoms as myelopathy so part of effective diagnosis requires ruling out other problems.

In some cases, certain symptoms may be attributed to other better known causes. For example, difficulty in getting an erection may be blamed on medication side effects, low testosterone, or HIV itself when it's actually myelopathy causing the problem. Frequent nighttime urination may be blamed on nightly water intake when, again, myelopathy is the true cause of the problem. In too many cases, it appears that HIV+ people may be uncomfortable even bringing such symptoms to their physicians' attention which could mean that considerable worsening may occur before the physician is even told of such problems. Because myelopathy is the neurologic condition about which the least is known in HIV medicine, some physicians (particularly those who are less HIV knowledgeable) may not even consider it as a possible diagnosis.

Neurologists recommend beginning a diagnosis of anyone who has neurologic symptoms by attempting to determine the location of the spinal problem. David Simpson, M.D., explains that if the neurologic exam reveals predominantly lower-extremity weakness, increased muscle tone, and increased reflexes, particularly in association with urinary symptoms, then a lesion of the spinal cord is likely, and the most common form of this in HIV+ people is vacuolar myelopathy. Since there is no specific test for myelopathy, looking for this typical symptom pattern is the key to increasing the likelihood of an accurate diagnosis.

Specialists believe that the most useful and objective diagnostic tool is the somatosensory evoked potential (SSEP) which is often prolonged in those with myelopathy. This test measures how quickly electrical signals travel from the brain through the spinal cord and which section of the spinal cord, if any, is damaged. Abnormally slow results often show up well before symptoms begin.

In HIV+ people who have some of these symptoms but not the typical combination, or who experience rapid worsening of symptoms, back pain, or “constitutional symptoms” (those that indicate a disorder of the whole body, including many infections) it is important to rule out other possible diagnoses. Included are the myelopathies that can be caused by various infections (including CMV, herpes virus, HTLV-1, and tuberculosis), lymphoma, or epidural abscess. Coinfection with human T-lymphotropic virus type 1 (HTLV-1) is common in injection-drug users and in those from regions where HTLV-1 infection is common, such as equatorial South America. Because HTLV-1 myelopathy cannot easily be differentiated from the vacuolar myelopathy most often seen in HIV+ people, it is important to consider this possibility. Other infections that might cause some of the same symptoms (although not usually the typical combination)

include toxoplasmosis, progressive multifocal leukoencephalopathy (PML), and syphilis. A spinal MRI (magnetic resonance imaging) may be recommended to check for tumors or spinal compression.

What are the Causes?

The cause of HIV-associated myelopathy remains unclear, although it has been shown that it has no correlation with levels of HIV in either the blood or spinal fluid, and that even antiretrovirals that cross into the central nervous system fail to yield improvement. Many studies have shown that a large percentage of HIV+ people have B-12 deficiency, a known cause of myelopathy, in general, as well as of neuropathy, dementia, and chronic fatigue. One study found a particularly high level of B₁₂ deficiency in people suffering from both myelopathy and neuropathy. Although an apparently conflicting study found that blood levels of B-12 in PWAs with myelopathy are usually “normal,” it’s important to know that leading nutrition researchers have found that the standard blood test for B-12 deficiency (the one used in this study) may give inaccurate information in HIV disease—“normal” blood levels do not preclude the possibility of tissue deficiencies, possibly due to HIV-associated problems with B-12 metabolism.

Alessandro Di Rocco, MD, Chief of the Division of Neuro-AIDS at Beth Israel Medical Center in New York City, and other researchers have theorized that myelopathy could be due to a chain of events in which HIV-induced dysregulation of cytokines—the chemical messengers between cells—results in the breakdown of a complex metabolic process that involves B-12, the essential amino acid methionine, and its derivative S-adenosylmethionine (SAME). Normally, after methionine is converted into SAME, it helps form and repair myelin. Since not only B-12 but also methionine have been found to often be too low in HIV+ people, this process may not be working properly, ultimately causing myelin degeneration and myelopathy.

What are the possible treatments?

There are no standard medical treatments for myelopathy itself, although there are drugs that are recommended to counter symptoms. However, the promising results seen in the research so far done with nutrient therapy, as well as the positive anecdotal reports from HIV+ people who have used nutrients to counter myelopathy, make this a must for anyone developing such problems.

Key Therapies

Crucial nutrients.

B-12, folic acid, and B-6. As discussed above, leading researchers theorize that myelopathy may result from a complex process that involves B-12. Alessandro Di Rocco, MD, Chief of the Division of Neuro-AIDS at Beth Israel Medical Center in New York City, believes that anyone with myelopathy should just be given B-12 supplementation. And earlier is better since research in geriatric medicine has shown that there may be a time window within which B-12 supplementation is able to help rebuild nerves, but that waiting too long may mean permanent damage. Since B-12 deficiency, a known cause of myelopathy, has been shown in many studies to be widespread in HIV disease—and researchers have noted that test results frequently do *not* accurately reflect deficiencies—supplementation with B-12 and folic acid would seem to be appropriate in anyone who seems to be developing the early symptoms that might indicate myelopathy, or anyone whose results from the somatosensory evoked potential (SSEP) indicate the slowing of signals from the brain to the spinal cord that may precede the development of symptoms. B-12 should always be given along with folic acid since they work together in the body, and taking folic acid alone could prevent the blood cell changes that might otherwise indicate B-12 deficiency. Due to the high homocysteine levels an dose of 5000mcg to 1,0000mcg of folic acid should be used along with 5000mcg of methylcobalamin (B-12). The methyl form of B-12 bypass absorption problems that may be present in many HIV+ people due to problems with the parietal cells that produce the intrinsic factor that is needed for absorption of B-12 consumed orally. Vitamin B-6, reported by researchers to be commonly deficient in HIV+ people, is vital for the formation of the sphingolipids which are involved in the development of the myelin sheath surrounding nerve cells. Supplementation with B-6 (50 mg, three times daily; this amount will be found in many B complex formulas and potent multivitamins) could help ensure adequate levels to support this process.

Methionine and SAME. A significant constituent of the myelin that sheathes nerves is the amino acid methionine, and it is thought that increasing methionine intake via supplementation may help rebuild this nerve covering. Quite some time ago, researchers at Mt. Sinai Hospital in New York City observed remarkable results in one HIVer suffering from the symptoms of myelopathy who recovered dramatically with the use of methionine. The results were so impressive that a pilot study was done to assess the potential usefulness of methionine in the treatment of myelopathy. In this study, seven out of nine HIV+ people with myelopathy who took three grams of methionine twice a day for six months showed various degrees of improvement in strength, sexual function, and bladder control. There was also measurable electrophysiologic

improvement in the majority of those treated with methionine. This dose of methionine (3,000 mg, twice daily) would certainly seem worth trying for anyone with myelopathy. A larger, placebo-controlled study of methionine treatment for myelopathy is now ongoing.

Since methionine is normally converted into SAME, and it is then the SAME that helps form and repair myelin, another trial using SAME has been considered by federal researchers but is not yet ongoing. There have been anecdotal reports of very good results from those who have used SAME. Some have experienced significant improvement of symptoms, including increases in strength and ability to walk unassisted, and an apparent slowing or perhaps even halting of disease progression. Based on anecdotal reports, the effective dose of SAME was 400 milligrams twice daily. It is important to choose SAME products that are enterically coated and stabilized.

Lecithin and fatty acids. Lecithin (phosphatidylcholine) is a phospholipid, a type of fat important in the structure of all membranes. They are beneficial to myelin sheath production and, thus, nerve protection. Cell membranes are largely composed of phosphatidylcholine, as are the protective sheaths surrounding the brain. Food-grade lecithin is a substance commonly used as a food additive and nutritional supplement that contains phosphatidylcholine, as well as other phospholipids, including phosphatidylinositol and phosphatidylethanolamine. [To avoid confusion, note that to a chemist lecithin *is* phosphatidylcholine; we are using the term here to refer to the food-grade lecithin granules available in health food stores as a supplement. It consists mostly of the B-vitamins choline and inositol along with linoleic acid and other fatty acids, glycerin, and phosphorus.

Although lecithin is a lipid, it is partly water-soluble and thus acts as an emulsifying agent. Most lecithin is derived from soybeans, but egg lecithin (from egg yolks) is also available; some studies show that this form is more beneficial for HIV+ people. Other sources of lecithin include brewer's yeast, grains, legumes, fish, and wheat germ. For anyone concerned about preventing myelopathy, some naturopathic physicians recommend 1 tablespoon of lecithin granules twice daily. It can be blended into protein or fruit shakes (which it will make creamier), or sprinkled on cereal or oatmeal or on salads. For those with already present myelopathy, try 1 tablespoon, four times daily, along with a plentiful intake of omega 3 fatty acids, essential because of their anti-inflammatory effects and their incorporation into cell membranes. Eating fatty fish (such as salmon, mackerel, sardines, tuna, cod and halibut) is a particularly good source of anti-inflammatory omega-3 fatty acids. Eating several meals weekly that contain such fish would be a good idea. Ground flaxseed, which can be eaten with cereal or added to casseroles or soups or other foods, are also a rich source of omega-3's. Eating a handful of walnuts several times per week will also contribute to your total intake of these important fatty acids.

Antioxidants. With the high level of oxidative stress that is present in HIV disease, it is possible that oxidative damage to nerves could be contributing to myelopathy. Daily supplementation with antioxidants might contribute to preventing or preventing worsening of the problem. The best approach is definitely to combine all these nutrients, rather than just choosing one. Please refer to *the Mitochondrial Support and Protection Against Oxidative Stress* section of the *Introduction*, on p. xx, for NYBC's recommended protocols.

NYBC Nutraceuticals for Myelopathy:

Folic Acid 800mcg x 250	6-10+/d (2-3B, 2-3L, 2-4D)
Lecithin 35% 1200mg x 200	4/d (2L, 2D)
Methylcobalamin 5000mcg x 100	1 day
Omega-3 1,000mg x 200	4-6/d (1-2B, 1-2L, 2D)
P-5-P (B6) 50mg x 60	1-3/d (0-1B, 0-1L, 1D)
SAMe 200mg x 60	4/d (2L, 2D)

Intravenous immunoglobulin (IVIg). Another treatment being studied at Mount Sinai is intravenous immunoglobulin (IVIg), a solution of bacteria-fighting antibodies that may also act as an anti-inflammatory agent, slowing injury to spinal cord cells. A small pilot study of IVIg showed promising results, although they were temporary, thus indicating the likelihood that any long-term benefit might require long-term use of IVIg.

Treatment of myelopathy-caused symptoms. When myelopathy can't be reversed, medications can help lessen or eliminate some symptoms. Methanetheline may help control urinary frequency. For anyone with myelopathy, it will be important to watch for urinary tract infections, and treat any that develop immediately. Baclofen or dantrolene may diminish stiffness, spasms and cramps in the legs. Physical therapy may also help with such symptoms. Viagra might help

resolve sexual dysfunction, although its use must be carefully considered in light of the possibility of serious interactions with many drugs, including protease inhibitors, poppers and others. It is recommended that lower doses be used in anyone currently on an antiretroviral regimen that includes either a protease inhibitor or an NNRTI. The usual recommendation for such people is to limit Viagra use to one 25 mg pill in any 48-hour period. [For additional information on approaches to reversing sexual problems, see *Sexual Difficulties*.]