

## MUSCLE ACHES AND PAINS

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

There are a number of muscle problems that can occur in HIV+ people, including muscle aches and pains (myalgia), muscle damage that can result in weakness and pain (myopathy), and muscle cramping. Each of these occurs in many HIV+ people, and in some cases may be so severe as to cause serious pain and disability. Diagnosis is mostly a matter of self-reporting the symptoms to your physician. In research studies, biopsies are sometimes done to assess myopathy but this is not the case for individuals. However, in order to distinguish between relatively minor muscle problems and what might be a severe and even potentially life-threatening problem like the rapidly ascending muscular weakness that may be caused (although rarely) by d4T, or the problems with controlling muscles that could indicate a serious neurological problem, it is extremely important to always call your physician immediately if any muscle problems develop. This is not a place to play physician if you're not one. Let an HIV-knowledgeable doc determine if your muscle problems relate to something serious. [For additional discussion on much more serious conditions that may cause certain muscle problems, see *Myelopathy, Memory Loss and Other Brain Problems*, and *Mitochondrial Support and Protection Against Oxidative Stress*.]

### What are the Causes?

There are several possible causes of HIV-associated muscle problems, and in many HIV+ people, it will not be unlikely for more than one of these to be present.

**Mitochondrial damage and other drug side effects.** It is believed that myopathy may result from damage to the mitochondria (the cells' energy factories) that occurs as a result of drug side effects, HIV infection, or some combination of these. Research has shown that the function of mitochondria is affected by nucleoside analogues (nukes or NRTIs), and that HIV+ people taking antiretrovirals have depletion of mitochondrial DNA (mtDNA, the genetic building block of the mitochondria). Dutch researcher Kees Brinkman, MD, and his colleagues have proposed that nuke-induced damage to the mitochondria (your cells' energy factories) may cause or contribute to myopathy, as well as lipodystrophy, neuropathy, and lactic acidosis (a potentially fatal buildup of lactic acid in the body). [For a much more in-depth discussion of mitochondrial toxicity, see *Mitochondrial Support and Protection Against Oxidative Stress*, and the *Mitochondrial Toxicity* section of NYBC's *Comprehensive Goals/Self-Care Guide*.]

Antiretroviral drugs that may cause mitochondrial damage-induced myopathy include all the drugs in the class of nucleoside analogues. However, the nukes that are more likely to affect mitochondrial function would be the most likely causes. In general, it is thought that d4T (Zerit®), ddC (Hivid®), AZT (alone in Retrovir® and also in the combination drugs Combivir® and Trizivir®), and ddI (Videx®) have the greatest potential for mitochondrial toxicity, while 3TC (Epivir®), abacavir (Ziagen®), and tenofovir (Viread®) are less likely to cause the problem. However, it is important to note that most of the evidence in support of this ranking has been derived from *in vitro* (test tube) testing so whether this will actually be the case in HIV+ people is not perfectly known.

Other drugs may also cause muscle problems, including the lipid-lowering drugs called statins that HIV+ people with elevated blood fats may be taking.

**Inflammation.** HIV causes body-wide inflammation, mostly through the increased production of inflammatory cytokines, cell-produced chemicals that are released as part of the body's immune response. It appears likely that this inflammation may contribute to some muscle aches and pains.

**Nutrient deficiencies.** Deficiencies of many nutrients may contribute to mitochondrial damage. Included would be deficiencies of any of the nutrients that work in countering oxidative processes (the whole list of antioxidant nutrients) or of the nutrients about which deficiencies are known to predispose people to mitochondrial damage (B vitamins and carnitine). In addition, magnesium deficiency may greatly increase the likelihood of muscle cramping.

### What are the possible treatments?

Depending on the particular type of muscle problem, there are a number of promising therapies. In addition to the things discussed here, note that because neuropathy (nerve damage) may actually be causing some muscle problems, using the therapies suggested for neuropathy may also help. (For information on this, see *Neuropathy*.)

**Acupuncture, massage, and chiropractic.** Both acupuncture and massage therapy can help with some muscle problems. Acupuncture is particularly helpful for pain relief. Chiropractic adjustments may also be useful since misaligned vertebrae in the spine could be contributing to muscle spasms and pain.

### **Key Therapies for Myopathy**

**Mitochondrial Support.** Doing everything possible to help prevent mitochondrial damage may help to prevent, prevent worsening of, or reverse myopathy. Based on the research done to date, the most important nutrients for preventing this muscle damage and the pain and weakness that it can cause would be a broad spectrum of antioxidants, the B complex, and the amino acid L-carnitine. 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 protocol.

**Drug switches.** In most cases, myopathy is not severe enough to necessitate changing antiretroviral drugs, but for those in whom the muscle pain and weakness is serious, a drug switch may be worth considering. The most obvious possibility is to try to avoid the nucleoside analogues since they are the likely cause of the mitochondrial damage that leads to myopathy. Where possible, a nuke-sparing regimen could be used. In other words, use a combination such as the protease inhibitors ritonavir plus saquinavir along with a non-nucleoside reverse transcriptase inhibitor (NNRTI) such as nevirapine or efavirenz. Such combos are not known to adversely affect mitochondrial function and, thus, should not contribute to myopathy.

There is one important caveat, however. Although it would seem appropriate to look for possible substitutions for any drug that appears likely to be contributing to myopathy, there may not always be available substitutes. This may be a particular problem for people who are very treatment experienced with HAART meds. They may have become resistant to many previously used drugs, and might well be on the only combo currently available to them. Some people may also be intolerant of protease inhibitors or NNRTIs because of the symptoms that they cause. If the current HAART combo is otherwise working well and providing the anti-HIV benefits needed, it may be necessary to stay with those meds, while attempting to address the myopathy with the nutrients that provide mitochondrial support.

When nukes must be continued to maintain viral control, it would be advisable to try to use the drugs that may be the least likely to cause mitochondrial dysfunction. In general, it is thought that d4T (Zerit®), ddC (Hivid®), AZT (alone in Retrovir® and also in the combination drugs Combivir® and Trizivir®), and ddI (Videx®) have the greatest potential for mitochondrial toxicity, while 3TC (Epivir®), abacavir (Ziagen®), and tenofovir (Viread®) are less likely to cause the problem. However, it is important to note that most of the evidence in support of this ranking has been derived from *in vitro* (test tube) research so whether this will actually be the case in HIV+ people is not perfectly known.

Other drugs may also cause muscle problems, including the lipid-lowering drugs called statins that HIV+ people with elevated blood fats may be taking. Discussing with your physician possible substitutes for such drugs, where possible, is appropriate.

### **Key Therapies for Myalgia (Muscle Aches and Pains)**

**Glucosamine and Chondroitin** play an integral part of all connective tissue in the body. Glucosamine is especially important in the formation of the intestinal mucosa and the production of hyaluronic acid for joint (synovial) fluids. As such, it has been used to offset the ravages of arthritis or osteoarthritis. Chondroitin is commonly used quite successfully in conjunction with glucosamine to offset the pains and inflammatory damage of arthritis and joint-related pain.

**MSM (methyl sulfonyl methane).** MSM is a sulfur donor which naturopathic physicians report is very effective for relieving muscle aches and pains, as well as joint aches. Researchers have reported that HIV+ people lose much more sulfur daily than is normal (possibly losing up to 10,000 mg daily, when 850 mg is thought to be normal). Sulfur is an important component of protein and, thus, of muscle tissue. The high sulfur loss might mean that there are inadequate amounts for proper maintenance and repair of muscle tissue. The low level might also contribute to joint aches since sulfur is crucial for maintaining connective tissue integrity. Supplementation with MSM seems to give the body what it needs to build and maintain these tissues. Some naturopathic physicians report very good results using 3 to 6 grams per day (3,000 to 6,000 mg) of MSM, taken in divided doses though higher doses may be needed for HIV+ people. Patients using MSM have significant improvement in morning stiffness and pain, greatly decreased joint and muscle pain throughout the day, and generally improved ease of movement.

**Magnesium combined with Malic Acid:** For those with severe muscle fatigue and aches a dose of magnesium malate three times per day may be useful. Each tablet, 1,000 mg of magnesium malate, yielding 152 mg magnesium and 825 mg of malic acid. Muscle cramps, weakness and fatigue are all anecdotally said to improve using this. Muscle cramps, weakness and fatigue are all anecdotally said to improve using this.

### **Botanicals**

Herbalists recommend the following **analgesics:** Substances used for the symptomatic relief of minor aches and pains. Some of these may reduce inflammatory processes that can cause pain. Specifically used for the treatment of inflammatory pain (arthritis, tendinitis, myalgia, chondritis), spasmodic and vascular pain (migraines, muscular pain, uterine cramping), and neuralgic pain (herpes, sciatica, shingles).

**California Poppy (*Eschscholzia californica*):** Contains small amounts of alkaloids similar to those contained in the common poppy (*Papaver somniferum*). It is used as a nervine, sedative, and pain killer by American herbalists. It is especially useful for those who have trouble falling asleep. Like the common poppy, it interacts with opiate receptors and also affects neurotransmitter activity. It has also been shown to inhibit the degradation of catecholamines and the synthesis of adrenaline, dopamine, beta-hydroxylase, and monoamine oxidase (MAO-B) thereby having a positive affect on depression, stress and mental well-being.

**Dosage:** 1-3 mL of tincture twice daily.

**Caution:** It is not known whether subjects using this herb will show positive in drug testing screening. There have been anecdotal, but no confirmed, reports of this occurring with use of California poppy tincture and consumption of poppy seed muffins.

**Corydalis (*Corydalis yanhusuo*):** One of the most widely used botanicals in Chinese medicine for the treatment of pain. It contains a group of alkaloids that are approximately 40% of the strength of morphine. It is a strong antispasmodic and inhibits GABA-activated signals and appears to block the release of noradrenaline. It may also act through serotonin receptors.

**Dosage:** Equivalent of 1-3 g daily.

**Caution:** Contraindicated in pregnancy and in those on blood thinning medications. May potentiate the effects of conventional medications that work via serotonin receptors. Also used in Chinese medicine to improve blood circulation. Discontinue use or use with caution if subject to bleeding disorders or if taking anticoagulant medications.

**Willow bark (*Salix spp.*):** Rich in salicylates which were the precursors for aspirin. These act as cyclooxygenase (COX) inhibitors in a manner similar to aspirin but without affecting platelet aggregation or causing gastrointestinal disturbance. Willow bark preparations are typically used for pains due to inflammation and headache.

**Dosage:** The equivalent of 240 mg of salicin daily.

### **External Therapies**

**Acupuncture, massage, and chiropractic.** Both acupuncture and massage therapy can help with some muscle problems. Acupuncture is particularly helpful for pain relief. Chiropractic adjustments may also be useful since misaligned vertebrae in the spine could be contributing to muscle spasms and pain.

**Baths:** Herbal baths can be used to relieve general overall body aches. For this purpose, the essential oils of strongly aromatic herbs such as ginger, lavender, chamomile, lemon balm, or rosemary can be used. Approximately 10 drops of essential oil are dropped into the bath water. Alternatively, strong teas of the same botanicals can be added to bath water.

**Arnica:** Used for muscular aches. Can be applied as an oil, lotion or homeopathic salve.

**Caution:** Long-term use (except the homeopathic form) can cause contact dermatitis. Not for use on open wounds.

**Cayenne Pepper:** An external ointment of capsaisan derived from cayenne pepper is used for the relief of minor aches and pains.

**Rescue Remedy cream:** Though mainly used for cuts, burns, and skin irritation, the Bach Flower salve Rescue Remedy cream also can do wonders for aches and pains, especially from injuries such as dropping something on yourself or crushing a finger in a door.

**Rosemary Oil:** Massage into the temples for alleviation of minor headaches.

**St. John's Wort Oil:** Used for sharp, stabbing neuralgic pains and pains involving nerve endings (herpes, shingles).

**Caution:** Do not use St. John's wort externally in conjunction with ultraviolet therapies.

**Homeopathic remedies.** Homeopathic remedies can be self-administered for acute (short-term, self-limiting) forms of pain; for chronic pain, constitutional treatment by an experienced homeopathic practitioner is advisable. For muscle aches and pains from over-exertion (including jet-lag), or injuries and bruising from a blow or fall, the key remedy is *Arnica montana*. Other remedies for various types of injuries include *Hypericum*, for nerve injuries and puncture wounds that are worse from cold and touch; *Ledum*, for bruises, punctures, splinters, or a black eye that are worse from warmth, and *Bryonia*, for any pains worse from movement. For headaches and body aches due to a hangover, try *Nux vomica*. With homeopathic remedies the dosing is flexible: if the first dose brings some relief, repeat every few hours or when the pain begins to return; if severe, every 30 minutes to an hour. Decrease frequency as symptoms improve; discontinue when improvement is well established. If one dose brings no relief at all, it probably is not the correct remedy; try a different one. The standard potency for acute ailments is 30c; 6c or 15c will also work but may need to be repeated more frequently.

**Natural anti-inflammatories.** Since HIV-caused inflammation may play a role in causing myalgia, the idea of suppressing that inflammation is appealing. As mentioned earlier, it would appear advisable to use foods and nutraceuticals that have natural anti-inflammatory qualities. Because such foods have been used for thousands of years with no apparent adverse effects on immune responses, it seems likely that long-term consumption of them would be considerably safer than long-term use of drugs. Their anti-inflammatory effects are more subtle but might still provide substantial benefit. Naturally anti-inflammatory substances are found in the following foods and seasonings:

- garlic, ginger, turmeric
- bioflavonoid- and antioxidant-rich fruits and vegetables
- omega-3 fatty acid-rich foods such as fatty fish (e.g. salmon, mackerel, sardines, tuna, cod and halibut), flaxseed, and walnuts.
- chlorophyll-containing foods such as wheat grass juice and blue-green algae.

There are also specific nutritional supplements and herbs that counteract excess inflammation and may help to lower levels of tumor necrosis factor. These include N-acetyl-cysteine (NAC), carnitine, nettle leaf extract, grape seed extract and bilberry extract, as well as a broad spectrum of all the other important antioxidants (vitamin E, vitamin C, bioflavonoid complex, carotenoid complex, selenium, coenzyme Q-10, and alpha-lipoic acid). For more detailed information on the above foods and supplements, please see *NYBC's Core Nutrient Protocols* and *Counteracting Inflammation and Tumor Necrosis Factor* in the **Introduction**, as well as the description of *Health-Enhancing Nutrients* in *NYBC's Self-Care Guide*.

**Drug remedies.** Although aspirin and other over-the-counter pain medicines such as Tylenol (acetaminophen) may help counter muscle aches and pains, they won't eliminate the underlying cause. Therefore, always consider the other therapies listed here that may actually get at the source of the problem before or while you take pain meds. The choice of which pain meds you use should take into consideration a number of factors. First, discuss with your physician any possible interactions with other drugs you are taking before beginning any pain med.

Second, consider any other medical conditions you have and the effect that certain pain meds may have on them. For those with liver problems, acetaminophen (Tylenol) would be inadvisable. For those with ulcers, gastrointestinal bleeding problems, intestinal Kaposi's sarcoma, low platelets, kidney dysfunction or low serum albumin levels (common in those with wasting), aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) would be inadvisable.

In general, unless any such issues make it problematic, aspirin or buffered aspirin is probably the best choice for muscle pain treatment. Tylenol (acetaminophen) significantly lowers the body's level of the antioxidant glutathione. Since glutathione levels are already too low in HIV+ people, worsening this is not a good idea. In addition, the lowered levels of glutathione already present may significantly increase the chance for acetaminophen toxicity. Even in doses considered to

be in the routine therapeutic range, it is known that acetaminophen can cause liver injury in people with a tendency for glutathione deficiency. Aspirin also lowers glutathione, but to a much lesser extent.

If you are taking either aspirin or Tylenol long-term, the use of the nutrients that help normalize glutathione levels is very important. Included are alpha-lipoic acid, N-acetyl-cysteine (NAC), glutamine, and vitamins E and C. Appropriate doses would be NAC (500 mg, three times daily; always take with food to prevent gastrointestinal irritation); glutamine (5,000 to 10,000 mg daily, spread across four doses; a powdered form is best; mix in water or juice and take on an empty stomach); vitamin E (800 to 1,200 IU daily); vitamin C (because individual needs vary widely, recommended dosages range from 1,000 to 6,000 mg or more daily, with doses spread across the day and taken with meals; note that amounts in excess of individual tolerance can result in gas and diarrhea; if you develop sudden watery diarrhea when you begin or increase a vitamin C dose, know that this may be the cause.); selenium (200 to 400 mcg daily); S-adenosyl-L-methionine; (800 to 1,600 mg daily); and alpha-lipoic acid (200 to 400 mg, taken three times daily, preferably on an empty stomach; note that a time-released form is very important because alpha-lipoic acid has a very short half-life in the bloodstream. By using products that release the alpha-lipoic acid gradually over time, you increase the total time that the nutrient will be available and working in the body.) For much more information on these nutrients and their usefulness in restoring glutathione in HIV+ people, see this guide's *Introduction, Mitochondrial Support and Protection Against Oxidative Stress*.

Always remember that long-term use of aspirin or other NSAIDs can cause damage to the intestines and gastrointestinal bleeding. In general, it is always best to only use such meds when you absolutely need them to reduce aches and pains, and avoid long-term use, if possible.

### **Key Therapies for Muscle Cramps**

**Acupuncture, massage, and chiropractic.** Both acupuncture and massage therapy can help with some muscle problems. Acupuncture is particularly helpful for pain relief. Chiropractic adjustments may also be useful since misaligned vertebrae in the spine could be contributing to muscle spasms and pain.

**Nutrient supplements.** Daily supplementation with magnesium (500–600 mg) can sometimes help to relieve muscle cramping. (Note that magnesium in excess of your needs can cause watery diarrhea so watch for this.) Vitamin E (800 to 1,200 IU daily) may also be helpful, especially for night-time leg cramping. Epsom salts, which contain magnesium, may also help ease muscle pain and cramping when dissolved in a hot bath (mix about 3 cups of the Epsom salts with the water before climbing in).

**Electrolyte replenishment.** In some HIV+ people, especially those experiencing vomiting and/or diarrhea, electrolyte imbalances could contribute to causing muscle cramps. In such cases, using the therapies designed to rebalance the body's electrolytes could help eliminate the cramping. For information on this, see the discussion on this in *Diarrhea*.]

**Homeopathic remedies.** For muscle or menstrual cramps relieved by warmth, the homeopathic remedy *Magnesia Phosphorica*, abbreviated *Mag Phos*, can be helpful. One pellet dissolved under the tongue or for ongoing, severe cramps, dissolve ten tablets in a cup of hot water and sip every few minutes. Other remedies for menstrual cramps include *Colocynthis* (for cramps relieved by hard pressure), *Belladonna* (for bearing-down pain that feels as though the uterus is trying to come out, with bright red bleeding), and *Chamomila*, for cramps in someone who is irritable, impatient and angry from the discomfort. With homeopathic remedies the dosing is flexible: if the first dose brings some relief, repeat every few hours or when the pain begins to return. Decrease frequency as symptoms improve; discontinue when improvement is well established. If one dose brings no relief at all, it probably is not the correct remedy; try a different one. The standard potency for acute ailments is 30c; 6c or 15c will also work but may need to be repeated more frequently.

**Herbalists recommend the following antispasmodics:** Used to relieve spasmodic pains, sleeplessness, and tension headaches. These botanicals are commonly used for anxiety, irritability and restlessness, sleeplessness due to anxiety and irritability; nervous dyspepsias, irritable bowels, and menstrual cramping.

**Black cohosh (*Actaea racemosa*):** Used since the 1800s in the US as an antispasmodic for various forms of neuralgic and muscular pain. It has also specifically been known for its affect in gynecology, most notably its use as a uterine antispasmodic and for menstrual disorders. Studies suggest that black cohosh may elicit an effect on dopamine and serotonin receptors as well as inhibit MAO.

**Dosage:** 0.5-1 mL of tincture twice daily.

**Caution:** Generally not to be used in pregnancy except under the care of a qualified health care professional. Excessive doses can cause headaches. May interact with medications that modulate serotonin, dopamine, and MAO.

**Chamomile (*Matricaria chamomilla*):** A gentle but effective antispasmodic, anti-inflammatory, and sedative. Constituents of chamomile have been shown to inhibit the formation of inflammatory mediators cyclooxygenase and 5-lipoxygenase. The sedative effect has been reported to be due to a binding to benzodiazepine receptors. Chamomile can be drunk as a beverage tea as needed. Can also be used in the bath.

**Dosage:** As tea, 1-2 tablespoons of herb steeped for 10 minutes in boiled water. Drink 2-3 cups daily.

**Caution:** May potentiate the effects of conventional medications which interact with benzodiazepine receptors, such as Valium.

**Cramp bark (*Viburnum opulus*):** One of the primary North American botanicals used for its antispasmodic activity. While especially useful for the treatment of menstrual cramps, it is also used for smooth muscle relaxation in general. Also specific for lowering stress induced hypertension.

**Dosage:** 1-2 mL of tincture three times daily.

**Kava (*Piper methysticum*):** Used in the South Pacific for centuries as an anxiolytic and muscle relaxant. Numerous double-blind, placebo controlled studies have reported on its effectiveness for the treatment of anxiety. It is also extremely effective as a muscle relaxant and anticonvulsant. Specific indications of kava include: nervousness, restlessness, anger, sleep disturbances, and muscle tension. Part of its action is considered to be due to a binding of kavalactones to GABA receptors.

**Dosage:** Equivalent to 120 mg of kava lactones daily.

**Caution:** Recently there have been reports of hepatotoxicity associated with kava use. This appears to be a rare occurrence, probably due to a single bad batch. Discontinue use if symptoms such as nausea, malaise, and jaundice occur. Therapeutic doses can cause loss of muscular coordination. Do not drive or operate heavy equipment when using kava. May potentiate the effects of alcohol, barbiturates, or antidepressants.

**Passion Flower (*Passiflora incarnata*):** Primarily used for sleeplessness, passion flower is an effective antispasmodic used for muscular and neuralgic pain (see Nervines section).

**Dosage:** 2-4 mL of tincture twice daily.

**Skullcap (*Scutellaria lateriflora*):** Specific for nervous tension, muscular cramping, seizures, anxiety, irritability and restlessness, sleeplessness due to anxiety and irritability; nervous dyspepsias, irritable bowels, tension headache, and menstrual cramping.

**Dosage:** 2-4 mL of tincture twice daily.

**Caution:** The potentially hepatotoxic germander (*Germander chamaedrys*), is often confused with skullcap in commercial products. Therefore, proper identity of the plant used in the product must be determined prior to use.

#### **Nutraceuticals and Remedies for Muscle or Joint Aches and Cramps:**

Black cohosh x 2 oz	15-30 drops 2 x/day
Chamomile Flowers x 4 oz	30 - 60 drops 2 x/day
California Poppy x 8 oz	30-90 drops 2 x/day
Corydalis x 100 grams	1- 2 teaspoons per day in water
Vitamin E 400IU x 250	2-3/d (0-1B, 1L, 1D)
Ginger Oil x 1 oz	drop
Glucosamine & Chondroitin 500/400mg x 120	3-6/d (1-2B, 1-2L, 1-2D)
Kava 30% 250mg x 120	2/d (1B, 1D)
Lavender Oil x 1 oz	drop

MSM 1,000mg x 180	6-10/d (2-3B, 2-3L, 2-4D)
Magnesium Malate 1,000mg x 180	3/d (1B, 1L, 1D)
Passion Flower x 4 oz	60-120 drops 2 x/day
Rosemary Oil x 1 oz	drop
Skullcap x 4 oz	60-120 drops 2 x/day

**External specially compounded pain medications and nutrients:** Compounded ketoprofen 20% PLO gel should be rubbed about ½ gram of gel to the sites of inflammation and an additional ½ gram (100mgs) into inside of the wrist or behind the knees. If there are muscle spasms, use baclofen 2% ketoprofen 20% in a transdermal gel like PLO, or controlled release capsules of baclofen, which limits the side effects of the drug. Also, acetyl-d-glucosamine, which is the metabolite of both glucosamine and chondroitin. In a sublingual drop, combines with MSM. Ten to twenty drops under the tongue, 3 times a day for acute issues then twice a day as the symptoms subside. Acetyl-d also has the advantage of not being from shellfish as glucosamine is, and therefore less likely to raise allergy problems. **These are available from Life Science Pharmacy at 845-781-7613.**

**Quinine sulfate.** Quinine sulfate taken in the evening can help some people who get night-time muscle cramps.