

Polymyalgia Rheumatica

Polymyalgia rheumatica is an inflammatory disease that usually affects women. It causes muscular pain and stiffness in the shoulders, neck, and hips (Salvarani C et al 2004; Hellmich B et al 2005).

In people with polymyalgia rheumatica, the synovial membranes and bursae, which line and lubricate the joints, become inflamed, causing pain and discomfort (Salvarani C et al 1997; Meliconi R et al 1996; McGonagle D et al 2001; Pavlica P et al 2000). Unlike the case with some other inflammatory diseases, such as rheumatoid arthritis, no permanent damage to either the joints or the muscles is associated with polymyalgia rheumatica. The disease typically resolves in a few years.

Nevertheless, during the disease course, polymyalgia is a painful condition that significantly affects quality of life. The standard conventional treatment for polymyalgia rheumatica involves nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids to reduce inflammation and pain. Unfortunately, this arsenal of treatment options is far from ideal. NSAIDs are rarely effective, so corticosteroids are generally used as first-line therapy. However, corticosteroid drugs are associated with significant side effects, including osteoporosis. The longer the treatment lasts, and the higher the doses used the more likely that a patient will suffer serious side effects. One major goal of conventional therapy is to use the smallest dose of corticosteroids possible and taper off these drugs as soon as symptoms resolve.

Nutritional therapy offers an important adjunct approach to polymyalgia rheumatica. Even though there is a lack of serious nutritional research into polymyalgia rheumatica, the inflammatory cascade that underlies the disease is well understood. By using proven anti-inflammatory supplements, it may be possible to reduce dosages of strong prescription drugs and reduce symptoms. In addition, the inflammation associated with the disease causes impairment of the adrenal hormone system, causing a deficiency in vital hormones that need to be replaced.

It is important to note that a significant number of people with polymyalgia rheumatica also suffer from a condition known as giant cell arteritis (Hellmich B et al 2005; Gonzalez-Gay MA 2004). Giant cell arteritis involves inflammation of the temporal artery (a major craniofacial artery), and other arteries can also be inflamed (Weyand CM et al 2003). Aneurysms can form in these weakened vessels (Honing ML et al 2005). Because the temporal artery supplies blood to the eye, blindness is a possible consequence of giant cell arteritis (Weyand CM et al 2004). Up to 75 percent of patients with giant cell arteritis may have aortitis (inflammation of the aorta), although the condition is not always diagnosed (Honing ML et al 2005). Recently, noninvasive imaging techniques, especially magnetic resonance imaging, have been used to determine the true degree of aortitis in patients with giant cell arteritis (Narvaez J et al 2005). Because of its significant consequences, patients with polymyalgia rheumatica should be carefully monitored for signs or symptoms of giant cell arteritis.

INFLAMMATION AND THE HPA AXIS

The hallmark of polymyalgia rheumatica is inflammation, probably caused by an autoimmune reaction in which the body's immune system is activated against itself (Brito J 1994; Cimmino MA 1997; Gitlits VM et al 2000; Meyer O et al 1996; Schmits R et al 2002). In people with polymyalgia rheumatica, inflammatory chemicals including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha) are released into the bloodstream. Besides causing the inflammation that leads to symptoms, these chemicals have a profound effect on the hypothalamic-pituitary-adrenal (HPA) axis, which is intimately involved in maintaining levels of vital hormones such as dehydroepiandrosterone (DHEA) and cortisol. Among people with polymyalgia rheumatica, it appears the HPA axis is depressed due to elevated levels of IL-6 (Cutolo M et al 2002a). As a result, DHEA levels are low (de la Torre B et al 1995; Nilsson E et al 1994; Cutolo M et al 2002b; Straub RH et al 2000a).

DHEA is a vital adrenal hormone that is converted into other hormones, including estrogen and testosterone. Low levels of DHEA have been associated with a wide variety of diseases, including inflammatory, autoimmune diseases such as rheumatoid arthritis and polymyalgia rheumatica.

DHEA replacement therapy has been shown to inhibit inflammatory cytokines and decrease IL-6 levels (Straub RH et al 1998; Straub RH et al 2000b). In one study, DHEA administered with glutamine and arginine allowed for lower dosages of prednisone (a corticosteroid) among women with polymyalgia rheumatica (Meno-Tetang GM et al 2001; Petri MA et al 2002). DHEA also protects against the risk of infection caused by reduced immunity in steroid-treated animals (Gennari R et al 1997) and increases bone density (Villareal DT et al 2000).

DIAGNOSIS OF POLYMYALGIA RHEUMATICA

Diagnosis of polymyalgia rheumatica requires ruling out other conditions, such as rheumatoid arthritis (RA), polymyositis, systemic lupus erythematosus, and thyroid problems (Beers MH et al 2005; Samanta A et al 2002).

Polymyalgia rheumatica is rare in people less than 50 years old, and patients are usually more than 60 years old (Beers MH et al 2005). It is twice as common in women as in men (Labbe P et al 1998; Beers MH et al 2005). Because polymyalgia rheumatica and giant cell arteritis frequently occur in the same patients, they may represent different aspects of a single condition. Most researchers, however, think that polymyalgia rheumatica and giant cell arteritis are different conditions with similar manifestations (Cimmino MA 1997; Gonzalez-Gay MA et al 2004; Cantini F et al 2004; Gonzalez-Gay MA et al 2003).

The first step in diagnosing polymyalgia rheumatica is obtaining a clinical history from the patient. The main diagnostic criteria for polymyalgia rheumatica are hip and shoulder pain, coupled with exclusion of other possible causes (Samanta A et al 2002). In addition, a number of blood tests may be used to measure inflammation. For example, patients with polymyalgia rheumatica usually have an elevated erythrocyte sedimentation rate (Beers MH et al 2005; Zlonis M 1993). C-reactive protein and IL-6 are also elevated in patients with polymyalgia rheumatica (Beers MH et al 2005; Samanta A et al 2002). These pro-inflammatory indicators, however, are elevated in response to inflammation anywhere in the body and cannot be used to definitely diagnose polymyalgia rheumatica.

If giant cell arteritis is suspected, a temporal artery biopsy is indicated, although corticosteroid treatment may start without waiting for the biopsy results (Weyand CM et al 2003). Other blood vessels (including the aorta) can be visualized with magnetic resonance imaging or ultrasound to determine the extent of inflammation.

Treatment with steroids usually begins promptly. Most patients respond very quickly to corticosteroids. In fact, if the symptoms don't resolve rapidly, your physician may want to conduct additional tests to determine whether the diagnosis was correct.

OSTEOPOROSIS PREVENTION

Osteoporosis prevention and bone preservation are important facets of treatment for polymyalgia rheumatica. Both the disease itself and the corticosteroids used to treat it are known to increase bone loss (Dolan AL et al 1997). All patients, especially postmenopausal women, need to take calcium and vitamin D to avoid problems associated with osteoporosis (Barilla-LaBarca ML et al 2002). In some cases prescription medications are needed to reverse osteoporosis (Gerster JC et al 1998; Richy F et al 2005; Turbin RE et al 1999).

Calcium and vitamin D. Calcium is important to maintain adequate serum calcium so that bone demineralization can be prevented. Vitamin D or a vitamin D analog is necessary for the body to absorb and utilize calcium. Studies have shown that vitamin D analogs (alfacalcidol or calcitriol) are readily converted to active form in the body (Reginster JY et al 2005; Richy F et al 2005).

Bisphosphonates. Bisphosphonates are prescription drugs that slow the rate at which calcium is removed from the bones; they have been shown to increase bone mass and strength (Adachi JD et al 2000a,b).

Vitamin K. Vitamin K consists of vitamins K1 and K2; vitamin K3 is a synthetic form (Bern M 2004). Maintaining adequate vitamin K levels is crucial for bone mineralization, blood clotting, cell growth, and blood vessel health (Bern M 2004). Vitamin K1 (phylloquinone) has anti-inflammatory effects, while synthetic vitamin K3 does not (Eichbaum FW et al 1979).

ANTICYTOKINE THERAPY

TNF-alpha levels are elevated in patients with polymyalgia rheumatica. This important inflammatory cytokine is at the start of the inflammatory cascade (Tortora GJ et al 2003). In mouse fibroblasts, TNF-alpha increases nuclear factor (NF)-kappa B in the cells, which in turn stimulates the production of IL-6 (Shibanuma M et al 1994). Thus, blocking TNF-alpha may help patients with polymyalgia rheumatica avoid or reduce corticosteroid use.

In one study, seven patients with polymyalgia rheumatica and diabetes mellitus or osteoporosis were treated with Infliximab (Remicade®), a prescription TNF-alpha blocker. After six months they experienced clinical improvement and had significantly decreased IL-6 and erythrocyte sedimentation rate levels (Migliore A et al 2005). The authors suggest that Infliximab may be used as a steroid-sparing agent, and it may also be useful as a first line of treatment in patients who should avoid corticosteroids.

In another study, four patients with polymyalgia rheumatica who had relapsed were treated with Infliximab (3mg/kg) at weeks 0, 2, and 6 (Salvarani et al 2003). Three of the four patients went into remission by two weeks, and the fourth was able to tolerate a lower prednisone dose. Together these small-scale studies suggest that blocking TNF-alpha may be a useful strategy for treating polymyalgia rheumatica.

N-acetylcysteine. N-acetylcysteine (NAC) is a well-known antioxidant that also helps regulate production of inflammatory

cytokines. In one study, NAC modulated IL-6 production through an NF-kappa B mechanism (Shibanuma M et al 1994).

Plant extracts. A number of plant extracts have also been shown to decrease NF-kappa B, including stinging nettle extract (Riehemann K et al 1999); helenalin from arnica flowers (Lyss G et al 1997); a spiroketal compound found in chamomile and *Plagius flosculosus* (Calzado MA et al 2005); oleandrin from oleander (Manna SK et al 2000b); resveratrol from grapes and other fruits (Manna SK et al 2000a); 1'-acetoxychavicol acetate (ACA) from *Languas galanga* (Ichikawa H et al 2005); curcumin (Jobin C et al 1999); ergolide from *Inula britannica* (Whan HJ et al 2001); rocaglamides extracted from *Aglaia* (Baumann B et al 2002); and tetrandrine from Han-Fang Chi, a Chinese herb used to treat rheumatic disorders (Ho LJ et al 2004).

STEROID-SPARING DRUGS

In treating polymyalgia rheumatica and giant cell arteritis, one major goal of therapy is to reduce the dosage of steroid to help reduce side effects (Hellmich B et al 2005). Because of the risk of blindness and other consequences of arterial inflammation (such as thrombosis and aneurysms), high doses of corticosteroids are used when giant cell arteritis is suspected. Although these high doses bring with them the additional risk of significant side effects, most clinicians feel that the risk associated with giant cell arteritis justifies this approach (Chang RW et al 1983; Weyand CM et al 2004).

Methotrexate. Methotrexate is a folate antagonist with anti-inflammatory, immunosuppressive, and antiproliferative actions (Majumdar S et al 2001). Studies of methotrexate in addition to prednisone have been contradictory. Some studies suggest that methotrexate decreases the total steroid dose needed by patients (Ferraccioli GF et al 2000; Caporali R et al 2004).

Methotrexate increases homocysteine levels (Aksu K et al 2001), so people taking methotrexate should consider supplements with vitamins B6, B12, and folate to lower homocysteine (Sunder-Plassmann G et al 2000; Guthikonda S et al 2006).

Pentoxifylline. Pentoxifylline (PTX) is an anti-inflammatory drug that has been used for more than 20 years (Pollice PF et al 2001; Abdel-Salam OM et al 2003) and is well tolerated (Lin SL et al 2005). PTX suppresses inflammation by decreasing synthesis and secretion of cytokines, including interleukin-1, IL-6, interleukin-8, and TNF-alpha (Mandell GL 1995; Graninger W et al 1995; Dorazil-Dudzic M et al 2004; Neuner P et al 1994; Pollice PF et al 2001). While no published studies of PTX in patients with polymyalgia rheumatica or giant cell arteritis exist, it is possible that PTX will be a treatment for polymyalgia rheumatica in the future. Research shows that a combination of fish oil (omega-3 fatty acids), alpha-linolenic acid, and PTX can reduce synthesis of IL-6 (McCarty MF 1999).

NUTRITIONAL THERAPY

Unfortunately, data are scant regarding the effect of many dietary supplements in polymyalgia rheumatica, perhaps because few research dollars are being directed at natural remedies for this condition. Because of the significant side effects associated with drugs prescribed for polymyalgia rheumatica, however, Life Extension recommends that patients do everything possible to reduce their use of these drugs, including pursuing natural remedies that have been proven to reduce inflammatory cytokine levels.

Fish oils. The inclusion of omega-3 fish oils in the diet has been shown to help with autoimmune and inflammatory diseases (Kelley DS 2001; Simopoulos SP 1999, 2002) by suppressing synthesis of TNF-alpha (Endres S et al 1989). Vitamin E and fish oil work together to decrease pro-inflammatory cytokines, including IL-6 and TNF-alpha, in mice (Venkatraman JT et al 1999a,b). Omega-3 fish oils have been useful in patients with a variety of inflammatory diseases, including rheumatoid arthritis and atherosclerosis (Simopoulos SP 1999). Studies in humans with rheumatoid arthritis suggest that fish oil and vitamin E decrease inflammation in humans (Tidow-Kebritchi S et al 2001). Moreover, fish oil supplementation has shown anti-inflammatory effects, including decreased use of anti-inflammatory drugs, for patients with a variety of other chronic inflammatory diseases (Simopoulos SP 2002).

Vitamins C and E. Vitamin E is an antioxidant with anti-inflammatory actions. The alpha-tocopherol form of vitamin E can decrease inflammation that contributes to atherosclerosis (Singh U et al 2005). Alpha-tocopherol supplementation has been shown to decrease C-reactive protein levels (Singh U et al 2005). Vitamin C is an antioxidant (Das 1989) that also has anti-inflammatory properties and blocks NF-kappa B activation by TNF (Bowie AG et al 2000).

Methylsulfonylmethane. Sulfur is a mineral found in several amino acids, the building blocks of all the proteins in the body. Methylsulfonylmethane (MSM) is a natural metabolite of dimethyl sulfoxide (Richmond VL 1986). MSM is used as a dietary supplement by many people and is naturally found in fruits, vegetables, grains, and animals (cow's milk is a rich source) (Parcell S 2002; Richmond VL 1986). MSM has been studied in patients with a variety of conditions, including arthritis, allergies, and fibromyalgia, among others. MSM appears to have little or no toxicity (Horvath K et al 2002).

Studies have shown that MSM can decrease pain and increase mobility in patients with osteoarthritis (Kim LS et al 2006).

Curcumin and ginger. Curcumin has been shown to reduce NF-kappa B in a wide variety of settings, including autoimmune

diseases and cancer. It is a well-known antioxidant and anti-inflammatory (Yadav VS et al 2005). Ginger has also been documented to reduce multiple inflammatory chemicals, including NF-kappa B and many others, and to be effective against a variety of inflammatory diseases, including autoimmune diseases that are characterized by an elevation of NF-kappa B (Aggarwal BB et al 2004).

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Patients who are diagnosed with polymyalgia rheumatica will likely be prescribed corticosteroids. Life Extension advises patients to take the following supplements to help prevent steroid-induced osteoporosis:

- **Calcium**—at least 1200 milligrams (mg) daily, along with essential cofactors, such as boron, zinc, and magnesium
- **Vitamin D**—up to 2000 international units (IU) daily
- **Vitamin K**—10 mg daily

In addition, the following nutrients that help protect against inflammatory events in the body or reduce the dosage requirements of NSAIDs and corticosteroids may provide some relief:

- **Omega-3 fatty acids**—1000 mg docosahexaenoic acid and 1400 mg eicosapentaenoic acid daily
- **DHEA**—15 to 75 mg daily to start, followed by blood testing in three to six weeks to ensure adequate levels of this vital hormone
- **Arginine**—1800 mg daily
- **Glutamine**—1000 to 2500 mg daily
- **NAC**—500 to 1500 mg daily
- **Vitamin E**—400 IU daily (with 200 mg gamma tocopherol)
- **Vitamin C**—1 to 3 grams (g) daily with food
- **MSM**—1000 mg daily
- **Curcumin**—900 to 1800 mg daily
- **Ginger extract**—500 to 1000 mg daily
- **Topical analgesic cream**—Apply to sore muscles as needed

PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at www.LifeExtension.com.

The blood tests discussed in this section are available through Life Extension National Diagnostics, Inc. For ordering information, call anytime toll-free 1-800-208-3444, or visit us online at www.LifeExtension.com.

POLYMYALGIA RHEUMATICA SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Calcium

- Do not take calcium if you have hypercalcemia.
- Do not take calcium if you form calcium-containing kidney stones.
- Ingesting calcium without food can increase the risk of kidney stones in women and possibly men.
- Calcium can cause gastrointestinal symptoms such as constipation, bloating, gas, and flatulence.
- Large doses of calcium carbonate (12 grams or more daily or 5 grams or more of elemental calcium daily) can cause milk-alkali syndrome, nephrocalcinosis, or renal insufficiency.

Curcumin

- Do not take curcumin if you have a bile duct obstruction or a history of gallstones. Taking curcumin can stimulate bile production.
- Consult your doctor before taking curcumin if you have gastroesophageal reflux disease (GERD) or a history of peptic ulcer

disease.

- Consult your doctor before taking curcumin if you take warfarin or antiplatelet drugs. Curcumin can have antithrombotic activity.
- Always take curcumin with food. Curcumin may cause gastric irritation, ulceration, gastritis, and peptic ulcer disease if taken on an empty stomach.
- Curcumin can cause gastrointestinal symptoms such as nausea and diarrhea.

DHEA

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.
- DHEA can cause androgenic effects in woman such as acne, deepening of the voice, facial hair growth and hair loss.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

Ginger

- Do not take ginger if you have a bile duct obstruction or gallstones. Ginger may stimulate bile production.
- High doses of ginger (6 grams or more) can cause damage to the stomach lining and ulcers.
- Ginger can cause allergic skin reactions.
- Consult your doctor before taking ginger if you take blood thinners such as warfarin (Coumadin). Ginger can increase the risk of bleeding.

L-Arginine

- Do not take L-arginine if you have the rare genetic disorder argininemia.
- Consult your doctor before taking L-arginine if you have cancer. L-arginine can stimulate growth hormone.
- Consult your doctor before taking L-arginine if you have kidney failure or liver failure.
- Consult your doctor before taking L-arginine if you have herpes simplex. L-arginine may increase the possibility of recurrence.

L-Glutamine

- Consult your doctor before taking L-glutamine if you have kidney failure or liver failure.
- L-glutamine can cause gastrointestinal symptoms such as nausea and diarrhea.

MSM

- MSM can cause headache or gastrointestinal symptoms such as nausea and diarrhea.

NAC

- NAC clearance is reduced in people who have chronic liver disease.
- Do not take NAC if you have a history of kidney stones (particularly cystine stones).
- NAC can produce a false-positive result in the nitroprusside test for ketone bodies used to detect diabetes.
- Consult your doctor before taking NAC if you have a history of peptic ulcer disease. Mucolytic agents may disrupt the gastric mucosal barrier.
- NAC can cause headache (especially when used along with nitrates) and gastrointestinal symptoms such as nausea and diarrhea.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatinine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic

anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin D

- Do not take vitamin D if you have hypercalcemia.
- Consult your doctor before taking vitamin D if you are taking digoxin or any cardiac glycoside.
- Only take large doses of vitamin D (2000 international units or 50 micrograms or more daily) if prescribed by your doctor.
- See your doctor frequently if you take vitamin D and thiazides or if you take large doses of vitamin D. You may develop hypercalcemia.
- Chronic large doses (95 micrograms or 3800 international units or more daily) of vitamin D can cause hypercalcemia.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

Vitamin K

- Do not take vitamin K if you are taking warfarin sodium unless, the vitamin K is specifically prescribed by your physician.

For more information see the Safety Appendix

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