

## Peripheral Artery Disease

Many medical conditions affect the network of arteries and veins that carry blood to and from the body's tissue. Such damage is generally referred to as peripheral artery disease (PAD).

Compromised peripheral blood supply leads to tissue **ischemia** (lack of circulation) and tissue **hypoxia** (lack of oxygen). As the result of those effects, there is a change in microcirculation and occurrence of edema (swelling). Edema further compresses capillaries and aggravates ischemia and loss of sensitivity (neuropathy).

Warning signs of PAD are pain, swelling, skin discoloration, itching and decreased hair. Frequent cold hands and feet, as well as dry flaky skin are usual signs of poor circulation. In such cases little cuts or wounds may not be able to heal in a "normal" period and may turn into "chronic", frequently complicated with infections and finally to the gangrene of the limb. If left untreated, gangrene progresses and the amputation of extremity (partial or complete) are unavoidable.

*Hyperbaric oxygen therapy is effective in correcting ischemia and hypoxia caused by PAD, promoting microcirculation, reducing swelling and inflammation and directly fighting infection to speed up wound healing.*

### Benefit of hyperbaric oxygen therapy

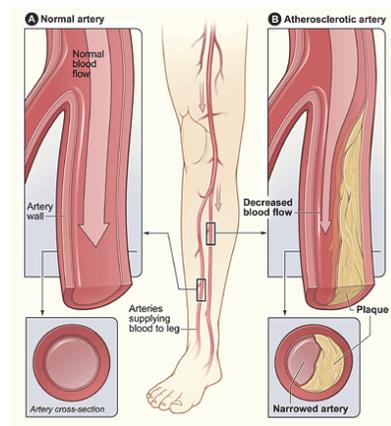
- improves tissue oxygenation and elimination of toxic substances, that were accumulated due to poor circulation and hypoxia
- relieves pain
- reduces swelling and inflammation
- improves sensitivity and reduces numbness
- triggers new capillary formation for improved local circulation and blood supply
- improves quality of blood and prevents blood clotting and chances of thrombosis
- enhances immune system response and increases the effect of antibiotics
- prevents/reduces infection rate
- reduces incidence of ulcer development

### HBO is beneficial

- stop further tissue damage
- provide optimal oxygen environment for all phases of wound closure
- promote new tissue growth and fast wound closure
- prevent excessive scar formation (caused by slow healing)
- prepare a host for skin grafting and increase chances of graft survival
- prevent/stop infection

### Treatment protocol for hyperbaric oxygen therapy

Medical hyperbaric oxygen sessions are two hours long at depth of 2.4 to 2.8 ATA with 60-90 minutes of pure oxygen while under pressure. HBO sessions are given in chambers. Number of HBO sessions needed depend on the seriousness of the condition and can be determined upon evaluation of the microcirculation.



# Sidestepping Peripheral Artery Disease

**Julian Whitaker, MD**

Do you have pain and cramping in your calf or thigh muscles after walking or climbing stairs? Does one leg or foot feel numb, weak, or colder than the other? Have you experienced hair loss or slow-healing sores in your lower extremities? These are the signs and symptoms of peripheral artery disease (PAD), a common and potentially serious condition that affects one in 20 middle-aged Americans and one in five people over age 70. PAD is to the legs what coronary artery disease is to the heart. Diseased, narrowed arteries (atherosclerosis) compromise blood supply to the lower extremities, and the pain that comes with exercise, called intermittent claudication, is essentially angina of the legs.

Conventional physicians treat PAD like they treat coronary artery disease—with drugs, angioplasty, stents, and bypass of blockages in the arteries of the legs. But as with heart disease, this approach is foolhardy and shortsighted. It may relieve symptoms, but it does not tackle the underlying problem. It's simply an invasive, expensive, temporary fix. Atherosclerosis is a systemic disorder, and it needs to be treated as such by addressing underlying risk factors, making lifestyle changes, improving nutritional status, and, if necessary, using noninvasive treatments to improve circulation and arterial health.

## **Change Your Lifestyle, Change Your Life**

The most significant risk factors for PAD are the same as for other cardiovascular diseases: diabetes, smoking, hypertension, and obesity, as well as nutritional deficiencies and elevations in blood lipids, C-reactive protein, and homocysteine. Therefore, the first thing you need to do is to get a handle on these conditions. Begin by cleaning up your diet and adopting an all-around healthy lifestyle.

You should also try to exercise. One of the most troubling aspects of PAD is its toll on physical activity. Intermittent claudication can make walking across the street a major ordeal and climbing stairs a nightmare. But according to a 2009 study published in *JAMA*, increasing your activity level is exactly what you should be doing.

Researchers from Northwestern University enrolled 156 patients who had PAD, with or without leg pain, in a six-month, three-times-a-week program of supervised treadmill or resistance exercise. When participants were retested at the study's conclusion, both groups—but particularly the treadmill exercisers—were able to walk longer distances. They also reported better quality of life.

## **Drugs Versus Supplements**

If you have symptomatic PAD, your greatest concern is likely the pain and debility caused by intermittent claudication. For this condition, doctors often prescribe Pletal (cilostazol), a drug that increases blood flow to the limbs. Pletal is not a very effective medication. Plus, it has a number of frightening side effects, including a black-box label warning that it "decreases survival" in patients with congestive heart failure. Another option is Trental (pentoxifylline), but this drug has no long-lasting effects.

Medications aimed at symptom control are not the best therapies for PAD. Like heart disease and diabetes, successful treatment of this condition requires an ongoing lifestyle program of diet, exercise, and nutritional supplements. One supplement with proven benefits is *Ginkgo biloba*, an herb with mild blood-thinning effects that is a popular PAD therapy in Europe. In a recent German study, researchers gave patients with moderate PAD and intermittent claudication 40 mg ginkgo supplements three times a day for 24 weeks, and their walking performance significantly increased.

Another is propionyl-L-carnitine. In a year-long clinical trial, this supplement improved walking distance in patients with relatively severe PAD by 44 percent compared to placebo. Inositol hexaniacinate, a form of vitamin B3 and no-flush cousin of niacin, has also been shown to extend the distance PAD sufferers can walk prior to the onset of debilitating pain.

### **More Supplements That Make a Difference**

PAD involves much more than pain in the legs. Poor blood flow to the extremities increases the risk of blood clots, which can lodge in narrowed arteries and cause serious complications. To minimize this danger, we give our patients Circulate, a product that contains Seanol, a seaweed extract, and nattokinase, an enzyme present in natto, a Japanese fermented food. Both of these unique compounds help normalize fibrinogen and other clotting factors in the blood. This not only reduces risk of potentially deadly blood clots but also improves overall circulation.

Patients benefit from vitamin K2 as well. K2 is active in the bones and soft tissues, escorting calcium into the bones where it belongs and out of the arteries and other soft tissues. When you have deficiencies in vitamin K2, calcium can build up in and contribute to hardening of the arteries. Dutch researchers have discovered very strong links between vitamin K intake, arterial calcification, and cardiovascular death.

We also recommend fish oil for its anti-inflammatory, anti-platelet, and cardioprotective effects, as well as an antioxidant-rich multivitamin and mineral supplement. Deficiencies of vitamins A, C, and E increase risk of PAD, and a low blood level of vitamin D was shown to raise risk by 80 percent.

### **The Dynamic Duo**

At Whitaker Wellness, we treat patients who have severe PAD with two additional noninvasive therapies that not only relieve the pain of intermittent claudication but also provide enduring improvements in blood flow throughout the body.

Enhanced external counterpulsation (EECP) is a mechanical therapy that rhythmically squeezes the lower extremities, forcing blood up through the legs and dramatically enhancing circulation. EECP works on multiple levels to heal diseased blood vessels. It reduces stiffness of the arteries and makes them more flexible and responsive, boosts the release of nitric oxide (a potent vasodilator), and stimulates the growth of new vessels around blocked arteries. Consequently, this therapy produces improvements in chest and leg pain, increases in exercise capacity, and often results in reduction of medications.

Although EECp has been studied primarily as a treatment for coronary artery disease, it benefits the entire vascular system. Debra Braverman, MD, author of *Heal Your Heart With EECp*, reports that PAD patients who are treated with EECp have predictable improvements in circulation in the legs that allow them to walk longer before pain sets in. Although EECp may not be suitable for some patients with extremely severe disease, Dr. Braverman predicts that it will become a routine treatment for PAD in the future.

We often use EECp in conjunction with hyperbaric oxygen therapy (HBOT). Italian researchers found that when patients with various stages of PAD, ranging from mild pain on walking to severe pain at rest, breathed 100 percent oxygen in a pressurized environment, 70 percent had reductions in clinical symptoms. Ankle-brachial index, a popular test used to diagnose PAD, also improved in nearly half of these patients.

### **A Silent Stalker**

PAD can fester for years without symptoms—and when they do appear, they're all too often chalked up to aging or fatigue. Please understand that PAD does not exist in a vacuum. Atherosclerosis is not localized to the legs or the heart. It's a systemic disorder, and problems in one area are usually indicative of problems elsewhere.

If you are in your 50s, 60s, or 70s, my best advice to you is to take the recommendations offered in this article seriously, make the necessary lifestyle changes, and start using appropriate nutritional supplements—even if you haven't been diagnosed with PAD or cardiovascular disease. This comprehensive approach is the only way to ensure that “every day, in every way, you will get better and better.”

### **Recommendations**

- Therapeutic daily doses of the supplements recommended for intermittent claudication are ginkgo extract 120 mg, propionyl-L-carnitine (or regular L-carnitine) 2,000 mg, and inositol hexaniacinate 4,000 mg, taken in divided doses. I suggest trying these one at a time and giving each a two- or three-month trial until you find what works for you.
- Doses of the other recommendations are as follows: nattokinase 2,000 FU (fibrin units), vitamin K2 (the MK-7 form) 100–150 mg, vitamin A 20,000 IU (mostly as beta-carotene), vitamin C 1,000 mg, vitamin E 400 IU, fish oil 2,000 mg of EPA/DHA, and aspirin 81 mg. Do not take ginkgo, nattokinase, or vitamin K if you are on Coumadin (warfarin).
- To figure out how much vitamin D you need, test your blood level and take enough to increase it to 50–80 ng/mL. Most of my patients require 5,000 IU daily to achieve optimal blood levels. If your homocysteine is high, consider increasing your daily intake of folic acid to 2,000–5,000 mg and your B12 to 1,000–2,000 mg, retest your level, and adjust your dosages accordingly.

# The Role of Hyperbaric Oxygen Therapy in Patients with Peripheral Arterial Disease

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Hyperbaric oxygen therapy (HBO) has been successfully utilized for a variety of conditions including diabetic foot and lower extremity ulcers, problem healing in irradiated fields and osteomyelitis (as well as other less frequent indications). So what is the role of HBO in patients with peripheral arterial disease?

## What is Hyperbaric oxygen therapy and how does it work?

HBO is the breathing of pure oxygen at increased atmospheric pressure. We utilize chambers, in which the entire patient is sealed in a “chamber”. We pressurize the chamber with 100% oxygen and increase the pressure to 2.0 – 2.4 atmospheres. In comparison, this pressure would be about the same as a scuba dive to about 50 feet of water. In this environment, hemoglobin molecules are saturated with oxygen and even more oxygen is dissolved into the plasma of the blood. This allows the delivery of super-oxygenated blood (about 15 times the amount of oxygen delivered to the tissues if the patient were breathing room air at 1 atmosphere of pressure) to the capillary beds. This has many beneficial effects on wound healing. These include improved fibroblast function and collagen deposition, more efficient leukocyte function, an increase in the amounts of growth factors in the wound bed, and a synergistic bactericidal effect with some antibiotics. Oxygen in concentrations achieved in the HBO chamber actually diffuses into bone and also has a bactericidal effect in patients with osteomyelitis. The most important effect in our diabetic patients and in the patients with wounds in irradiated tissues is angiogenesis which is most likely mediated by stem cell recruitment from bone marrow. A new capillary bed can be achieved in diabetics with small vessel disease and in patients with localized tissue ischemia from radiation therapy.

## What role does HBO play in acute arterial ischemia?

A patient can develop acute arterial ischemia through trauma (crush injury or direct arterial trauma) or from emboli. After the acute arterial injury or blockage is corrected a compartment syndrome can develop. HBO can play a role in these patients post-revascularization by reducing edema and increasing the oxygenation of injured tissues. Often fasciotomy can be avoided and tissue salvaged before frank necrosis can occur. This usually involves a short course of hyperbaric therapy, sometimes on a twice daily schedule, until edema resolves and all tissue is viable.

## What role does HBO play in peripheral arterial disease and tissue loss (ulcer)?

Patients often present with lower extremity ulceration and non-palpable pulses. If the rest of the history and physical exam indicates significant peripheral arterial disease, then non-invasive testing is ordered. This may include a test called a trans-cutaneous oxygen measurement (or “TCOM”) as well as the standard lower extremity arterial Doppler study (LEAS). Consideration would also be given in performing a TCOM in a diabetic patient with palpable pulses to see if they have significant small vessel disease secondary to their diabetes. If the patient has very low tissue oxygenation at the distal leg or foot level or critical limb ischemia is determined on LEAS study then revascularization (either surgical bypass or endovascular revascularization) would be needed before there would be anticipation that these ulcers would heal. Hyperbaric oxygen therapy is NOT going to be beneficial in the patient with critical limb ischemia which cannot be corrected. **Once a patient with an arterial ulcer has been successfully revascularized, then HBO would be indicated to help speed healing when there is also deep tissue involvement, osteomyelitis or persistent small vessel disease after the inflow has been corrected.**

In summary, **Hyperbaric Oxygen Therapy is a useful adjunctive treatment in patients with acute arterial ischemia, patients with arterial ulcer and deep tissue involvement after successful revascularization and in diabetic patients with good inflow but significant small vessel distal disease.**

# Hyperbaric Oxygen Therapy in Grade IV Peripheral Arterial Disease with Severe Comorbidity

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**Aim:** A large number of patients with grade IV peripheral artery disease (PAD) cannot afford risk of revascularization surgery cause a severe comorbidity. Hyperbaric oxygen therapy (HBOT) has been reported as a valid a secure alternative treatment.

**Methods:** A 70 years old Caucasian male, suffering from a grade IV peripheral artery disease (according to Fontaine's clinical classification) with bilateral calcaneus infected ulcers, has reached our Center after he has non been eligible to revascularization due to comorbidity for ischemic chronic cardiopathy, mitral aortic valvulopathy, diabetes mellitus insulin dependent, chronic renal failure, multifactor anemia and obstructive sleep apnea syndrome in C-PAP treatment. The patient, in 13 months period, underwent three cycles of 22 hyperbaric oxygen therapies, breathing 100% oxygen for 75 minutes at 2,5 atmosphere (ATA), daily for five days a week. The initial peripheral transcutaneous oximetry (PtcO<sub>2</sub>) was 43 mmHg on the right foot and 34 mmHg on the left foot. PtcO<sub>2</sub> increased during HPOT, reaching 1133 mmHg on the right foot and 727 mmHg. During the same period patient underwent a three times a week advance wound care, a cycle of specific antibiotic therapy for Staphylococcus Aureus.

**Results:** Hyperbaric oxygen therapy, by increasing local oxygen supply, has encouraged ulcer healing preserving the low extremities.

**Conclusion:** Hyperbaric oxygen therapy has been a successful alternative treatment in an invaliding grade IV peripheral artery disease not eligible to revascularization surgery for severe comorbidity.

## Hyperbaric Oxygen Therapy Improves Peripheral Nerve Regeneration

Several studies have documented the effectiveness of hyperbaric oxygen in models of acute and delayed crush injury. Intermittent exposure to hyperbaric hyperoxia serves to interrupt the injury cycle of edema, ischemia and tissue necrosis' as well as hemorrhagic hypotension, which in turn leads to former edema and ischemia. Tissue ischemia is countered by the ability of hyperbaric oxygen to elevate tissue oxygen tensions. Furthermore, edema is reduced, secondary to hyperoxia-induced arteriolar vasoconstriction, leading to improved tissue viability, thereby reducing necrosis. Hyperbaric oxygen has also been studied in models of peripheral nerve injury. Researchers from the US Air Force School Aerospace Medicine and Louisiana State University recently sought to determine what, if any, morphologic changes are associated with hyperbaric oxygen treated peripheral nerve injury. Their model involved a crushed sciatic nerve in the rabbit.

Exposure to hyperbaric oxygen across the range of current clinical dose schedules was compared to untreated, and pressure (hyperbaric air) controls. A pathologist blinded as to group documented the oxygen extent of nerve regeneration via morphologic analysis of electron micrographs. All of the animals exposed to hyperbaric were reported to demonstrate advanced stages of a healed nerve, in contrast to both control groups. As this research was limited to a determination of regeneration of morphology, the exact effects of hyperbaric oxygen were not known. The authors speculate, however, that there may be several suggesting increased myelination, decreased edema, reduced internal collagen and improvements in neurofilamentous material density. They conclude that this study provides additional evidence of a link between tissue oxygen levels from hyperbaric oxygen treatment and the health of peripheral nerves.

... all animals exposed to hyperbaric oxygen "demonstrated characteristics expected of in the advanced stages of a healed nerve"

# Effect of Hyperbaric Oxygen Therapy on Nerve Regeneration in Early Diabetes.

Aydin A, Ozden BC, Karamursel S, Solakoglu S, Aktas S, Erer M.

Nerve regeneration in diabetes is essential for reversal of neuropathy as well as the recovery of nerves from injury due to acute nerve compression and entrapment. Endoneural hypoxia due to hyperglycemia-induced blood flow reductions is observed early in the course of diabetes, and the resultant ischemia plays a role in the diminished neural regeneration. Hyperbaric oxygen therapy is capable of producing tissue hyperoxia by raising oxygen tensions in ischemic tissues, and was shown to be beneficial in the reversal of experimental ischemic neuropathy. In this study, an experimental diabetes model was used to evaluate the functional and histomorphological effects of hyperbaric oxygen therapy on early diabetic nerve regeneration. Our results indicate that there is significant histomorphological impairment of nerve regeneration, even in very early stages of diabetes. However, no beneficial effects of hyperbaric oxygen therapy could be demonstrated at this stage. Copyright 2004 Wiley-Liss, Inc.

## Hyperbaric Oxygen Therapy and Neuropathy

Viera C, Galvez C, Carrasco B, Santos C, Castellanos R.

**INTRODUCTION:** There are some occlusive disorders in the vasa nervorum and metabolic changes diminishing oxygen liberation by erythrocytes at the capillary blood vessels, and these disturbances lead to endoneural microhypoxia. Hyperbaric oxygen reverts hypoxia in the diabetic neuropathy. **OBJECTIVE:** We studied motor and sensitive peripheral neuroconduction in nine diabetic patients, with distal symmetrical polyneuropathy, during normoglycemia. Four of them were insulin dependent and five were non insulin dependent.

**PATIENTS AND METHODS:** The electrophysiological studies were done before treatment with hyperbaric oxygen, in a week, three and six months later. The abnormal electrophysiological parameters detected in diabetics were terminal latencies (enlarged), velocities of conduction (slowed) and distal amplitudes of compound action potentials (reduced). **RESULTS:** Neither distal latencies nor distal amplitudes and conduction velocities in peroneal nerve showed significant changes in the statistical analysis. We observed slower conduction velocities in the motor fibers of the median nerve in the examination performed six months after treatment. There was an increase of distal latency and retardation of the velocity of conduction six months later after treatment in the sensitive fibers of median nerve, whereas the amplitudes of sensitive action potentials decreased progressively. These changes suggest large diameter peripheral fibers didn't receive benefit with hyperbaric oxygen treatment.

**CONCLUSIONS:** In all patients disappeared all symptoms of dysesthesias, paresthesias, distal pains and cramps in the legs and arms, suggesting functional changes in small unmyelinated fibers which we can't test with conventional techniques to prove it.