

# EFFORTS



*Emphysema Foundation For Our Right To Survive*

Emphysema Takes Your Breath Away

October 2008

## **OSIRIS COMPLETES ENROLLMENT OF STEM CELL TRIAL TO TREAT PULMONARY DISEASE**

Osiris Therapeutics, Inc. announced today that it has completed enrollment in a human clinical trial designed to evaluate Prochymal, the Company's proprietary formulation of adult mesenchymal stem cells, for the treatment of moderate to severe Chronic Obstructive Pulmonary Disease (COPD). A total of 62 patients were enrolled in the Phase II trial at six sites throughout the United States.

"These stem cells have qualities that make them naturally well suited for the repair of lung tissue, and early clinical data are so far very encouraging," said Michelle LeRoux Williams, Ph.D., Vice President of Development at Osiris Therapeutics. "We are excited to learn more about the therapeutic utility of these cells in the lungs, not only for the treatment of COPD, but for other pulmonary conditions as well. This study will provide for us the necessary base for further rapid development of this remarkable stem cell technology in what could Mesenchymal stem cells have been shown to be effective in treating numerous lung diseases in pre-clinical animal models. The ability of the stem cells to reduce inflammation, block fibrosis or scarring and repair tissue damage suggests that they may be effective in reversing or preventing the progression of COPD. In an earlier human trial for heart disease, infusions of Prochymal were shown to improve lung function by a statistically significant margin compared to patients receiving placebo.

"We would like to thank our participating physicians and their teams for the remarkable job they did enrolling this study so quickly," said Robin Flannery, who coordinated the trial at Osiris. "But most of all, we would like to recognize and offer our sincere thanks to the patients who are participating in this historic trial. It is only with their cooperation that we seek to usher in a new era in the treatment of lung disease."

Osiris is investigating Prochymal in patients with COPD, the fourth leading cause of death in the United States. Over 12 million Americans have been diagnosed with the disease, and it is estimated that an additional 14 million Americans have the disease and have not yet been diagnosed.

### **About the Phase II Chronic Obstructive Pulmonary Disease Trial**

The Phase II trial is evaluating the safety and efficacy of Prochymal in conjunction with standard of care for improving

pulmonary function in patients with moderate to severe COPD. The clinical trial is a double-blind, placebo-controlled study. Patients were randomized to either Prochymal or placebo at a 1:1 ratio. Measurements used in the trial to detect potential improvements in subjects treated with Prochymal include pulmonary function tests, exercise capability, and quality of life assessments. In addition, exacerbations and hospitalizations due to COPD will be monitored for both safety and efficacy. Patients will be evaluated over the course of two years following initial Prochymal or placebo infusion.

### **About Prochymal**

Prochymal is a preparation of mesenchymal stem cells specially formulated for intravenous infusion. The stem cells are obtained from the bone marrow of healthy adult donors, avoiding the controversy surrounding embryonic and fetal cell sources. Prochymal is currently being evaluated in three, double-blind, placebo controlled Phase III studies, including steroid refractory GvHD, acute GvHD, and Crohn's disease. Prochymal has been granted Fast Track status by FDA for all three of these indications. Prochymal also obtained Orphan Drug status by FDA and the European Medicines Agency for GvHD. Prochymal is also being studied in Phase II trials for the treatment of acute myocardial infarction and type 1 diabetes. Additionally, the Department of Defense recently awarded Osiris a \$224.7 million contract to develop Prochymal as a treatment for acute radiation syndrome.

### **About Osiris Therapeutics**

Osiris Therapeutics, Inc. is a leading stem cell therapeutic company focused on developing products to treat medical conditions in the inflammatory, orthopedic and cardiovascular areas. Prochymal is being evaluated in Phase III clinical trials for three indications, including acute and steroid refractory Graft versus Host Disease and also Crohn's disease, and is the only stem cell therapeutic currently designated by FDA as both an Orphan Drug and Fast Track product. Osiris also has partnered with Genzyme Corporation to develop Prochymal as a medical countermeasure to nuclear terrorism and other radiological emergencies. Furthermore, Prochymal is being developed for the repair of heart tissue following a heart attack, the protection of pancreatic islet cells in patients with type 1 diabetes, and the repair of lung tissue in patients with chronic obstructive pulmonary disease. The Company's pipeline of internally developed biologic drug candidates

under evaluation also includes Chondrogen for arthritis in the knee. Osiris is a fully integrated company, having developed capabilities in research, development, manufacturing, and distribution of stem cell products. Osiris has developed an extensive intellectual property portfolio to protect the company's technology including 47 U.S. patents each having one or more foreign counterparts. Osiris, Prochymal and Chondrogen are registered trademarks of Osiris Therapeutics, Inc. More information can be found on the company's website, [www.Osiris.com](http://www.Osiris.com). <http://tinyurl.com/>



## **AUTOIMMUNITY A FACTOR IN COPD**

Pulmonary specialists at the University of Pittsburgh School of Medicine report that chronic obstructive pulmonary disease (COPD) is an autoimmune disease in many patients. Previous speculation that COPD may have an autoimmune component had remained previously unproven.

The finding, reported recently in the American Journal of Respiratory and Critical Care Medicine, holds particular relevance regarding possible future treatments, including a clinical trial of inhaled cyclosporine now enrolling patients at the University of Pittsburgh.

The fourth-leading cause of death and second-leading cause of disability in the United States, COPD is a lung disease commonly related to smoking that diminishes breathing capacity over time and includes conditions such as chronic bronchitis and emphysema. The National Institutes of Health estimates that 12 million adults have a current diagnosis of COPD, with an additional 12 million unaware that they have the disorder. <http://tinyurl.com/3s2qg6>



## **COMBINATION THERAPY FOR EXERCISE INTOLERANCE IN COPD**

### ***New combined approaches to reduce dynamic hyperinflation improve exercise intolerance in patients with COPD***

Chronic obstructive pulmonary disease (COPD) is a miserable disease; exercise intolerance is one of its most troubling symptoms. Moreover, it has recently been discovered that poor exercise tolerance is highly predictive of poor survival. Those who care for these patients are therefore highly motivated to seek ways to ameliorate exercise intolerance.

In recent years progress has come from what, at first glance, would seem to be an unlikely quarter. Although research expenditures for this disease are heavily weighted towards cell and molecular biology pursuits, physiological research (considered "old fashioned" in some quarters) has provided solid insights into rational treatment for exercise intolerance.

A key insight is that dynamic hyperinflation is a major mechanism limiting exercise tolerance in patients with COPD. This occurs when the increased metabolic requirements of exercise demand higher levels of pulmonary ventilation. This, in turn, requires that both tidal volume and respiratory rate increase. The patient with COPD is asked to exhale a larger volume in a shorter time, which becomes an impossible task

given flow limitation imposed by the increased expiratory airflow resistance. At some point the exhalation cannot be completed in the allotted expiratory time, full exhalation cannot be accomplished, and end expiratory volume increases. Eventually, dynamic hyperinflation leads to end inspiratory lung volumes that approach a limiting value (total lung capacity). As the inspiratory reserve volume shrinks, additional inspiratory volume cannot be achieved without greatly increased elastic work of breathing, since the lung is increasingly on a shallow portion of its pressure-volume curve. Severe dyspnoea results and exercise terminates when this sensation becomes unbearable.

## **THERAPEUTIC APPROACHES**

Pulmonary physiologists have been working to develop strategies to lessen dynamic hyperinflation at a given amount of exercise. Logically, approaches that either allow faster exhalation (reduced expiratory airflow resistance) or prolong the time allowed for exhalation (decreased respiratory rate) will allow fuller exhalation, thereby reducing dynamic hyperinflation and improving exercise tolerance.

To date, four distinct approaches have been defined that either lower expiratory airflow resistance or slow respiratory rate:

- N Oxygen supplementation.
- N Treatment with bronchodilators.
- N Heliox (79% helium, 21% oxygen).
- N High intensity rehabilitative exercise training.

### **Oxygen supplementation**

Oxygen supplementation reduces carotid body drive and slows respiration at a given level of exercise. Dynamic hyperinflation is reduced and exercise tolerance is substantially prolonged. Increasing inspired oxygen fraction up to roughly 50% confers progressively greater benefits. This occurs even in patients with COPD whose level of exercise desaturation does not meet the usual criteria for oxygen supplementation.

### **Treatment with bronchodilators**

COPD is now recognised as distinctly not a disease of irreversible airflow obstruction. In a substantial majority of patients with COPD treatment with bronchodilators yields clinically useful improvements in expiratory airflow, allows fuller exhalation in a given period of time, reduces dynamic hyperinflation, and prolongs exercise tolerance. Reduced dynamic hyperinflation accompanied by exercise tolerance improvements has been best demonstrated with long acting anticholinergic agents.

### **Heliox**

Heliox (79% helium, 21% oxygen) has a lower density than air and decreases airflow resistance. Breathing heliox lowers expiratory airflow resistance, decreases dynamic hyperinflation, and prolongs exercise tolerance.

### **Rehabilitative exercise training**

High intensity rehabilitative exercise training has been widely acknowledged to substantially increase exercise tolerance in patients with COPD. An important mechanism of the benefits of exercise training has recently been defined. As the exercising muscles become more fit, they release less lactic

acid at a given level of exercise. Since lactic acid stimulates respiration, after rehabilitative training exercise ventilation is lower, respiration is slowed, and dynamic hyperinflation is reduced.

### COMBINATION THERAPY

If any one of these interventions improves exercise tolerance, it seems logical that a combination of any two ('combination therapy') would yield even better results. There seems to be a minor competition among physiologically orientated laboratories to see which can demonstrate the effectiveness of these four treatments taken pairwise.

Our laboratory has shown that providing supplemental oxygen (3 l/min by nasal cannula) during a 7 week high intensity rehabilitation programme increased the tolerated work rates of patients during training and enhanced the improvements in exercise tolerance in comparison with COPD patients who trained while breathing room air. Patients who before training tolerated an average of 6 minutes of exercise at a given work rate breathing air tolerated an average of 26 minutes at the same work rate while breathing 30% oxygen after an oxygen supplemented training programme. For several participants it was apparent that, after training, their physiological capacity for exercise had improved to such a degree that the assigned work rate was now below the critical power; they were able to tolerate the work rate essentially indefinitely.

Peter Calverley's laboratory investigated the combination of helium and oxygen breathing. In a crossover design, patients with COPD performed an endurance shuttle walk test while breathing air, 28% oxygen in nitrogen, 21% oxygen in helium, or 28% oxygen in helium.<sup>8</sup> The latter mixture (high helium, high oxygen) yielded the highest shuttle walk distance. Whether 28% oxygen and 72% helium represents the optimal high oxygen/low density mixture for improving exercise tolerance remains to be determined.

A multicentre study showed that the benefits of a rehabilitative treadmill training programme were enhanced in a group of COPD patients receiving an effective long acting anticholinergic bronchodilator compared with a group receiving placebo. By the end of the training programme, the duration of a constant work rate treadmill task was increased by 79% in patients receiving bronchodilator treatment compared with those receiving placebo. Finally, in this issue of Thorax, Peters et al report that 50% oxygen breathing acts synergistically with bronchodilator therapy (ipratropium bromide) to reduce hyperinflation and improve exercise tolerance in patients with COPD.

In a crossover study in 16 patients, the mean tolerance of a constant work rate increased by 57% and 31% when inhaling oxygen or receiving bronchodilator, respectively. The combination of oxygen and ipratropium increased exercise tolerance by an average of 87% over the control condition, demonstrating an approximately additive response. The mathematically inclined among us will note that only four of six possible permutations of these four interventions have so far been reported.

The successful combinations of heliox with exercise

training and of bronchodilators with heliox are waiting to be achieved.

Further, can studies of the simultaneous application of three interventions be far behind? Four studies of this kind could be planned, the requirement being the necessity to prove the superiority of the exercise tolerance improvements in response to three interventions over that of three groups in which combinations of two of the three interventions are applied. Will we see the day when a study appears in which simultaneous application of all four of these physiological manoeuvres are combined to ameliorate exercise intolerance and are proved to be superior to three groups in which three of the four interventions are given? One can only dream.

<http://tinyurl.com/4ddxqp>



### DRUG HOPE FOR CYSTIC FIBROSIS

An experimental drug is proving effective for treating the genetic disease cystic fibrosis (CF).

CF produces thick, sticky mucus that clogs the lungs and the pancreas, leading to life-threatening chest infections and problems with digestion. Existing treatments only ease symptoms, but the new drug, VX-770 restores function to defective proteins which cause the disease. The early trial results were presented at the BA Festival of Science.

One in 25 people in the UK is a carrier for a defective CF gene which disables or destroys a protein known as CFTR. Although carriers do not develop CF, they run the risk of passing the gene on to their children. Around 8,000 people in the UK have CF.

Defects in the CFTR protein affect the transport of chloride and other ions across cells. VX-770 is designed to increase the probability that the CFTR channel is open, thereby increasing chloride transport across the cell surface.

So far it has been tested in CF patients with a genetic defect known as G551D. Further clinical trials are necessary to learn more about the total number of patients who might benefit from the drug.

#### Trial results

One of the most recognisable symptoms of CF is salty sweat, caused by the failure of the sweat ducts to reabsorb sweat.

Patients who received 150mg twice a day saw the concentration of salt in their sweat decrease by almost 50% and lung function improve by 10%.

Lead researcher Dr David Sheppard from the University of Bristol said: "The early results with VX-770 suggest that drug therapies which target defects at the root of the disease have the potential to improve greatly the quality of life of CF patients." Researchers are testing other compounds that work in a similar way.

Rosie Barnes, chief executive of the Cystic Fibrosis Trust said: "The development of VX-770 is very encouraging for people with CF with a specific mutation of the CF gene - about 6% of those with CF in the UK.

"The CF Trust warmly welcomes any advances in the understanding and treatment of this terrible disease."

<http://tinyurl.com/3vhczw>

of all cystic fibrosis cases in that country and for about 10 percent of cases in the United States, where other genetic flaws in channel production predominate.

In the study, 23 Israelis with cystic fibrosis received the drug, designated PCT124, in two cycles -- three doses a day for 14 days, then three higher daily doses after a 14-day pause.

Salt flow reached the normal range in 13 of the 23 cases during the first treatment cycle and in nine of 21 cases in the second cycle. Kerem said the results were "encouraging," but added, "This was a short-term study without placebo, so it shows that a longer-term trial should be done." A longer trial probably will be started "early next year," Kerem said.

"We are planning a larger long-term study that will be international, in the United States and Canada and also in Europe," said Dr. Langdon Miller, chief medical officer of PTC Therapeutics, which sponsored the study.

PTC124 was developed through a screening program in which hundreds of thousands of compounds, with a light-emitting molecule called luciferase, were aimed at the genetically altered "stop" signal, Miller said. Several compounds hit the target and lit up. "We selected the best ones, did chemistry to modify them and came up with PTC124," he said.

Several initial studies, including the one in Israel, have shown that PCT124 can help produce salt-conducting channels that are "full length and fully functioning," Miller said.

The drug may be useful for a number of other genetic disorders caused by the same sort of mutation, he added. It already is being tried for another genetic condition, Duchenne muscular dystrophy.

<http://tinyurl.com/3h5jef>



## **MONEY WORRIES 'MAY HARM HEALTH'**

*The economic downturn could be bad news for our bodies, as well as our pockets, suggest specialists.*

Britons are cutting back on expensive fruit and vegetables, and gym membership, claims a report by the Blood Pressure Association. Some say they are drinking more alcohol than before the recent credit crunch.

The association is urging people to have their blood pressure checked for free this week at one of 3,000 locations across the UK.

Sustained high blood pressure, which can be caused by poor diet and lack of exercise, can raise the risk of heart attacks and strokes.

The survey, carried out jointly with Friends Provident, suggest that the costs of a healthy lifestyle will be the first to be jettisoned during a financial squeeze.

One in three of the 2,700 adults surveyed never or rarely eats the recommended amount of fruit and vegetables.

However, 16% of those questioned said they would have to cut back spending on these in the next six months - and 15% said they had already done this.

A fifth said they were having to cut back on gym use this year because of financial pressures.

However, our love for expensive, unhealthy takeaways has yet to be affected, with more than three-quarters of adults regularly buying takeaways or ready meals.

## **Pavement pounding**

Professor Graham Macgregor, the Blood Pressure Association's chairman, said: "It is clear that Britons are under pressure and this could have serious consequences.

"The dual effect on lifestyles of the credit crunch and lack of concern over long term health is putting the nation at risk of a blood pressure ticking time bomb."

A spokesman for the British Heart Foundation said that it was perfectly possible to have a healthy lifestyle - and save money.

She said: "If you are finding the credit crunch means you can no longer afford the gym, take to the pavements. "Integrating brisk walking into your everyday routine is good for your heart and free - it will also help relieve the extra stress that you may be feeling at this time.

"When out shopping remember that frozen and tinned fruit and vegetables provide the same benefits to your heart health as fresh.

"Giving up smoking and sticking to the recommended levels of alcohol will also help your heart and your pocket."

The Blood Pressure Association has come up with "Know Your Numbers!", a week-long effort to persuade people to have their blood pressure monitored.

Locations where checks will be available can be found on its website. <http://tinyurl.com/4sq959>



## **TREATING OBESITY AS AN ADDICTION?**

*Using a drug designed to fight drug addiction may be helpful in combating obesity.*

Vigabatrin, a drug designed as a potential treatment for people struggling with drug addiction, may also cause rapid weight loss in people suffering from obesity. In a current study, rats that were genetically bred to be obese lost 19 percent of their total weight during a 40-day period on Vigabatrin. Rats that were not obese lost 12 to 20 percent following the short-term drug treatment.

Researchers hypothesize that Vigabatrin is able to quench food cravings the same way to blocks drug cravings. "The fact that these results occurred in genetically obese animals offers hope that this drug could potentially treat sever obesity," Stephen Dewey, senior scientist at Brookhaven National Laboratory in Upton, N.Y., was quoted as saying.

Vigabatrin is also currently undergoing an FDA approved phase II clinical trail to combat cocaine and methamphetamine addiction. In previous trials it has been shown to block dopamine increases triggered by drug use and block the process in the brain that causes a high.

SOURCE: Synapse, published online 8/20/08



## **RECOGNIZING A STROKE**

*Blood Clots/Stroke - They Now Have a Fourth Indicator, the Tongue.*

Sometimes symptoms of a stroke are difficult to identify. Unfortunately, the lack of awareness spells disaster. The stroke victim may suffer severe brain damage when people nearby fail to recognize the symptoms of a stroke

## RECOGNIZING A STROKE - Remember The 1st Three Letters.... S.T.R.

Sometimes symptoms of a stroke are difficult to identify. Unfortunately, the lack of awareness spells disaster. The stroke victim may suffer severe brain damage when people nearby fail to recognize the symptoms of a stroke.

Doctors say a bystander can recognize a stroke by asking three simple questions:

- S \* Ask the individual to SMILE.
- T \* Ask the person to TALK and SPEAK A SIMPLE SENTENCE (Coherently) (i.e. It is sunny out today)
- R \* Ask him or her to RAISE BOTH ARMS.  
If he or she has trouble with ANY ONE of these tasks, call 999/911 immediately and describe the symptoms to the dispatcher.

## New Sign of a Stroke ----- Stick out Your Tongue

Another 'sign' of a stroke is this:

Ask the person to 'stick' out his tongue.. If the tongue is 'crooked', if it goes to one side or the other, that is also an indication of a stroke.

It is believed that if he help gets to a stroke victim within 3 hours the effects of a stroke can be totally reversed. The trick is getting a stroke recognized, diagnosed, and then getting the patient medically cared for within 3 hours, which is tough.



## MUSCLE CRAMPS

### Causes

A mineral deficiency of calcium and/or magnesium is probably the most frequent cause of night leg cramping.

Cramps are often caused by a lack of potassium, resulting in an electrolytic imbalance. Strenuous exercise with sweating and diarrhea or other bowel disease may cause loss of potassium and other important minerals. It is very important to replace them with supplements. Some people get leg cramps at night for no apparent reason. This is called restless legs syndrome.

Another cause may be a deficiency in hesperidin, one of the bioflavonoids (sometimes called vitamin P), naturally occurring nutrients usually found in association with vitamin C. These bioflavonoids, including Hesperidin, Citrin, Rutin, Flavones, Flavonols, Catechin and Quercetin, were found to be essential in correcting the night leg cramps.

Wine induces stomach cramps in some people. To ease the cramps or perhaps eliminate them altogether, take some olive oil before imbibing. Try some oil on bread, or on a salad.

Milk and other dairy products can cause abdominal cramping, bloating, gas and discomfort in some women. If you are eating dairy products to get calcium, try switching to yogurt, lentils, broccoli, cabbage, tofu, collard and other greens, turnips, rhubarb and almonds.

Gastroenteritis, caused by a virus that has entered the digestive tract or contaminated food or water, causes inflammation, cramping, nausea, vomiting and diarrhea. Severe cases can lead to dehydration, so be sure to drink fluids and balance your electrolytes (take Pedialyte for young children and the elderly, and sports drinks for everybody else.)

Diarrhea caused by intestinal parasites is the third leading cause of illness. If you have a number of the following symptoms: gas, diarrhea, chronic constipation, bloating, fatigue, skin rashes, nail biting, mood swings, insomnia, dry skin, brittle hair, hair loss, weight gain, bad breath, and muscle cramping, you should be tested for parasites.

### Tips

To stop leg/foot cramping, firmly press in on the upper lip. This is the meridian which is connected to the legs and feet.

Take a hot shower before going to bed, letting the water run down the part of your leg that gets cramps. Or, if you get cramps in the night, take a shower then. Get the water as hot as you can stand it, as this will help relax the muscles.

If you are in bed when you get a leg cramp, stretch your leg straight out and bend the toes back toward your head. Hold in this position for 30 seconds, relax, and repeat until the cramp is gone. This will stretch out your calf muscle. You may also do this standing up - push your heel onto the floor and bend your toes upward. This forces the calf muscle to lengthen.

If you get leg cramps frequently at night, start a stretching regimen before bed. Try pressing your toes against a wall to stretch out the calf muscles; hold for 30 seconds, relax, repeat several times.

Cramping often comes while you are exercising. follow these tips:

Keep hydrated. As you sweat, you lose important electrolytes, which are needed to prevent cramps.

Warm up for 10-15 minutes before exercising. This will stretch out the muscles you will be using.

If you exercise and get cramps after eating, you have probably begun your exercise too soon after eating. As you digest, your body diverts blood from your muscles and cramping can result.

Take magnesium, potassium and calcium supplements daily, especially before exercising.

## REMEDIES

### Folk

Apple cider vinegar: Drink a mixture of two teaspoons of vinegar and one teaspoon of honey in a glass of warm water. Apple cider vinegar is high in potassium.

Aspirin: (or ibuprofen) taken at the earliest signs of menstrual cramps will help relieve them. Aspirin helps stop the production of prostaglandins, part of the process that causes cramps.

Calcium: A calcium deficiency causes muscle cramps or involuntary movement of muscles. If you are prone to leg cramps at night, take a calcium supplement (calcium lactate is preferred), a warm cup of milk, or chew on some Tums an hour before going to bed. However, we do not recommend taking Tums on a regular basis due to its interference with your normal digestive process. We suggest that if you get frequent leg cramps you take a calcium supplement daily. Taking magnesium with the calcium will aid in the absorption of the calcium and prevent calcification of various organs and soft tissues. 200-300 mg of calcium before bedtime is recommended.

Chamomile tea: A study showed that drinking five cups of this tea each day for two weeks reduced the pain of menstrual cramps. The tea increased the level of glycine in the urine. Glycine is an amino acid that helps relieve muscle spasms and relax the uterus.

CoQ10 may aid in relieving muscle cramps.

Magnesium will help the smooth muscles that surround your arteries to relax, and your body uses it to process calcium. Try taking 400 mg of magnesium before bed. A calcium/magnesium supplement, taken one hour before bedtime, is recommended.

Mustard: For years coaches have given mustard to their athletes with leg cramps. Cramps are sometimes caused by a deficiency in acetylcholine, the neurotransmitter that stimulates your muscles to work. Mustard has acetic acid, which helps the body make more acetylcholine. Take a spoonful or two of mustard.

Pickle juice: As with mustard coaches have given pickle juice to their athletes with leg cramps. Cramps are sometimes caused by a deficiency in acetylcholine, the neurotransmitter that stimulates your muscles to work. Pickle juice has acetic acid, which helps the body make more acetylcholine. Take a few ounces of pickle juice.

Quinine/tonic water: Drinking four to eight ounces of tonic water (make sure it has quinine in it!) an hour before going to bed is a very effective remedy for most people. If it is too tart for you, add some lemon for flavoring. You should notice a difference within a few days, otherwise discontinue. OTC quinine was banned by the FDA because of health risks, but there is enough quinine in tonic water to help most people. <http://tinyurl.com/5zvu48>



## ARTERY PLAQUE RUPTURE CAN OCCUR WITHOUT SYMPTOMS

*But this makes build-up more vulnerable to future bursts, researchers find*

Plaque ruptures in arteries can occur without causing any symptoms, say researchers at Boston University School of Medicine.

Atherosclerotic plaque often develops at branch points or curving portions of arteries, where blood flow is slowed and more turbulent. Plaque development is common in the carotid arteries, which supply the head and neck with oxygenated blood. The sudden rupture of artery plaque can lead to complete artery blockage that causes a heart attack or stroke.

The researchers reported about a patient with severe blockages in both the left and right carotid arteries. The patient was examined prior to operations to remove the plaque in both arteries.

Two months after removal of the left carotid artery plaque, the patient experienced plaque rupture in the right carotid artery. But the patient didn't suffer a stroke or any other symptoms. This is likely because the blood clot didn't grow large enough to block the flow of blood the brain, the researchers said.

"This illustrates the healing of silent atherosclerotic ulceration, which is a specific type of rupture detected by

MRIs over a period of two months," project leader James Hamilton, a professor of biophysics and physiology, said in a school news release. "This has not been reported previously. In the past, there had been evidence of plaques removed from the carotid and human coronary artery through postmortem specimens that s Hamilton and colleague Alik Farber, chief of vascular and endovascular surgery at Boston Medical Center, said these hemorrhages "disappear" into the plaques but make the plaque more vulnerable to future rupture.

<http://tinyurl.com/4mh9o5>



## BEST WAY TO A CLOGGED HEART? THROUGH THE WRIST

*Study: Angioplasty approach lowers risk of bleeding, eases discomfort*

The best path to a clogged heart may be through the wrist. About a million artery-clearing angioplasties are performed in the United States each year, and the usual route is to thread a tube to the heart through an artery in the groin.

Now a major study shows going through the wrist instead can significantly lower the risk of bleeding — without the discomfort of lying flat for hours while the incision site seals up. Just one in 100 angioplasties is done via the wrist, and the approach isn't for everyone. But Monday's study promises to spur more specialists to use the method.

"In experienced hands, it can be done more," said Dr. Sidney Smith, heart disease chief at the University of North Carolina at Chapel Hill and a past president of the American Heart Association, who wasn't part of the study. "This approach, when done by experienced operators, has advantages."

Angioplasty is prized as a quick, minimally invasive way to restore blood flow in a clogged artery. A tiny balloon is inflated at the site of the blockage, pushing back the clog. Doctors often also insert a mesh tube called a stent to keep the artery propped open. It can be done during a heart attack, to alleviate worsening symptoms that signal a heart attack is imminent, or for nonemergency relief of recurring chest pain.

Who's the best candidate for an angioplasty versus other treatments is hugely controversial. But once that decision has been made, the new study addressed whether the through-the-wrist route works as well.

Cardiologists have preferred working through the femoral artery in the groin because it is a larger blood vessel than the wrist's radial artery, easier to tug catheters through. When the procedure's over, heavy pressure — often a sandbag — is applied for several hours until the puncture site quits bleeding and essentially seals itself. But heavy bleeding and related complications are a risk, happening in anywhere from 2 percent to sometimes as many as 10 percent of patients.

Catheters have gradually gotten smaller and more flexible, and previous small studies had suggested the wrist approach could be safer because that puncture site can be bandaged. In one earlier study, the wrist method even trimmed hospital costs because patients were discharged sooner.

So Duke University researchers turned to a national registry — analyzing more than half a million angioplasties

performed at 600 U.S. hospitals between 2004 and 2007 — to see how often wrist angioplasties are done, and the results.

**One key caveat: These were first-time, non-emergency cases.**

But just 1.3 percent of the angioplasties were done through the wrist. Both methods were equally effective at clearing heart arteries, lead researcher Dr. Sunil Rao reported in the *Journal of the American College of Cardiology: Cardiovascular Interventions*.

The wrist method cut the bleeding risk by nearly 60 percent: Nearly 2 percent of patients treated the usual way bled, compared with slightly fewer than 1 percent of those treated via the wrist. The method may be gaining steam: In early 2007, the researchers measured a sudden jump, as the wrist method accounted for about 3.5 percent of angioplasties performed then.

Rao himself uses wrist angioplasty almost exclusively, but it takes extra training that many cardiologists haven't received. Still, the heart association's Smith said training isn't difficult, and the need may be growing: Obesity can limit traditional access, plus more patients today have disease-damaged leg arteries.

"The procedure is not one that would be recommended for everybody," Smith cautioned. But, "there are definitely groups of patients where this can be done with the same results and fewer complications."

<http://www.msnbc.msn.com/id/26273955/>



## NEW LINK BETWEEN GUM AND HEART DISEASE

Scientists have discovered a new link between gum disease and heart disease, which could ultimately save lives, an international meeting of scientists at Trinity College in Dublin has been told.

The autumn meeting of the Society for General Microbiology was told that heart disease is a leading cause of death worldwide. However many people have none of the common risk factors associated with it, such as smoking, obesity and high cholesterol.

In recent years, chronic infections have been linked to atherosclerosis, or hardening of the arteries, which is the main cause of heart attacks. Gum disease is one of the most common infections of humans and there are now over 50 studies linking gum disease with heart disease and stroke.

Speaking at the meeting, Prof Greg Seymour of the University of Otago Dunedin in New Zealand, explained that a number of theories have been put forward to explain the link between oral infection and heart disease.

"One of these is that certain proteins from bacteria initiate atherosclerosis and help it progress. We wanted to see if this is the case, so we looked at the role of heat shock proteins," he said.

Heat shock proteins are produced by bacteria as well as animals and plants. They are produced after cells are exposed to different kinds of stress conditions, such as inflammation, toxins, starvation and oxygen and water deprivation. Because of this, heat shock proteins are also referred to as stress proteins. They can work as chaperone molecules, stabilising

other proteins, helping to fold them and transport them across cell membranes.

Because heat shock proteins are produced by humans as well as bacteria, the immune system may not be able to differentiate between those from the body and those from invading pathogens. This can lead the immune system to launch an attack on its own proteins.

"When this happens, white blood cells can build up in the tissues of the arteries, causing atherosclerosis," Prof Seymour said.

He explained that the researchers had found white blood cells called T cells in the lesions of arteries in patients affected by atherosclerosis.

"These T cells were able to bind to host heat shock proteins as well as those from bacteria that cause gum disease. This suggests that the similarity between the proteins could be the link between oral infection and atherosclerosis," he said.

This molecular mimicry means that when the immune system reacts to oral infection, it also attacks host proteins, causing arterial disease. These findings could fundamentally change health policy, highlighting the importance of adult oral health to overall health and wellbeing. In other words, the control of gum disease should be essential in reducing the risk of heart disease.

"This is a significant step towards a more complete understanding of heart disease and improving treatment and preventive therapies. An understanding of all the possible risk factors could help lower the risk of developing heart disease and lead to a significant change in disease burden," Prof Seymour added.

<http://tinyurl.com/4zqoer>



## 8 NATURAL PAIN RELIEVERS

You're in pain, and ibuprofen just won't cut it. Nonsteroidal anti-inflammatory drugs, or NSAIDs, don't agree with your stomach, and you're wary of stronger meds.

Fortunately, you have alternatives — natural ones. From herbs that attack inflammation to techniques that leverage the brain's remarkable healing powers, nature offers many treatments for conditions such as arthritis, fibromyalgia, and even muscle strains.

Here are eight natural remedies that may enhance or replace conventional antidotes, and leave you happier, healthier, and pain free.

### **Capsaicin: For arthritis, shingles, or neuropathy**

What the science says: An active component of chile pepper, capsaicin temporarily desensitizes pain-prone skin nerve receptors called C-fibers; soreness is diminished for 3 to 5 weeks while they regain sensation. Nearly 40 percent of arthritis patients reduced their pain by half after using a topical capsaicin cream for a month, and 60 percent of neuropathy patients achieved the same after 2 months, according to a University of Oxford study. Patients at the New England Center for Headache decreased their migraine and cluster headache intensity after applying capsaicin cream inside their nostrils.

How to try it: Capsaicin ointments and creams are sold in pharmacies and health stores. For arthritis or neuropathy, try

0.025 percent or 0.075 percent capsaicin cream one to four times daily; best results can take up to 2 weeks, says Philip Gregory, PharmD, a professor at Creighton University and editor of the Natural Medicines Comprehensive Database. But research on capsaicin and headaches remains limited — and don't expect stronger versions anytime soon: "Current formulations are better suited for more acute problems, like a sore muscle or an arthritis flare-up, than everyday pain and stiffness," Gregory says.

#### **InflaThera or Zyflamend: For arthritis**

What the science says: Both supplement brands contain ginger, turmeric, and holy basil, all of which have anti-inflammatory properties. Turmeric (a curry ingredient) may be the best: A component, curcumin, eases inflammatory conditions like rheumatoid arthritis and psoriasis, according to the Methodist Research Institute in Indianapolis. Researchers are now testing Zyflamend in RA patients, but some experts are already sold: "Each herb has its own scientific database of evidence," says James Dillard, MD, author of "The Chronic Pain Solution."

How to try it: ProThera, InflaThera's maker, will only sell to health care professionals, so your doctor has to order it for you; that said, it's reportedly stronger (and slightly cheaper) than Zyflamend. InflaThera's suggested dosage is twice daily with food. For the more readily accessible Zyflamend, take one capsule two or three times daily, but avoid it near bedtime — each pill contains 10 mg of caffeine (another version, Zyflamend PM, is reportedly less stimulating). Buy Zyflamend at [swansonvitamins.com](http://swansonvitamins.com) or

[immunesupport.com/zyflamend.htm](http://immunesupport.com/zyflamend.htm). Or, save money and try curcumin to start: Taking 500 mg four times daily, along with fish oil and a diet low in animal fat, can ease arthritis, says Jane Guiltinan, ND, immediate past president of the American Association of Naturopathic Physicians.

#### **Arnica: For acute injury or post surgery swelling**

What the science says: This herb comes from a European flower; although its healing mechanism is still unknown, it does have natural anti-inflammatory properties. Taking oral homeopathic arnica after a tonsillectomy decreases pain, say British researchers, and German doctors found that it reduces surgery-related knee swelling.

How to try it: Use homeopathic arnica as an adjunct to ice, herbs, or conventional pain meds, suggests Guiltinan. Rub arnica ointment on bruises or strained muscles, or take it in the form of three lactose pellets under the tongue up to six times per day. Boiron is among the most reputable arnica manufacturers.

#### **Aquamin: For osteoarthritis**

What the science says: This red seaweed supplement is rich in calcium and magnesium. A preliminary clinical study showed that the ingredients may reduce joint inflammation or even help build bone, says David O'Leary of Marigot, Aquamin's Irish manufacturer. In a study of 70 volunteers published in *Nutrition Journal*, Aquamin users reduced arthritis pain by 20 percent in a month, and had less stiffness than patients taking a placebo.

How to try it: Marigot recommends 2,400 mg a day (two capsules) of Aquamin in tablet form, sold domestically in

products such as Aquamin Sea Minerals and Cal-Sea-Um. A 60-pill jar of Swanson Vegetarian Aquamin Sea Minerals costs about \$6 at [swansonvitamins.com](http://swansonvitamins.com).

#### **SAM-e (S adenosylmethionine): For osteoarthritis**

What the science says: SAM-e is made from a naturally occurring amino acid and sold as capsules. Doctors aren't entirely sure why it tamps down pain, but it reduces inflammation and may increase the feel-good brain chemicals serotonin and dopamine.

Studies by the University of Maryland School of Nursing and the University of California, Irvine, showed that SAM-e was as effective as some NSAIDs in easing osteoarthritis aches; the California researchers found that SAM-e quashed pain by 50 percent after 2 months, though it took a few weeks to kick in. SAM-e produced no cardiovascular risks and fewer stomach problems than the conventional meds.

How to try it: Costco and CVS both carry it; a month's supply costs \$30 to \$60. Guiltinan prescribes 400 to 1,600 mg daily, often with turmeric or fish oil. SAM-e can interact with other meds, especially MAO-inhibitor antidepressants, so it's vital to talk with your doctor before taking it (and avoid SAM-e entirely if you have bipolar disorder).

Also, inspect the packaging before buying, advises Gregory: Make sure the product carries a USP or GMP quality seal, contains a stabilizing salt, has a far-off expiration date, and comes in foil blister packs — SAM-e can degrade rapidly in direct light.

#### **Fish oil: For joint pain from arthritis or autoimmune disorders**

What the science says: Digested fish oil breaks down into hormonelike chemicals called prostaglandins, which reduce inflammation. In one study, about 40 percent of rheumatoid arthritis patients who took cod-liver oil every day were able to cut their NSAID use by more than a third, Scottish scientists recently reported. People with neck and back pain have fared even better: After about 10 weeks, nearly two-thirds were able to stop taking NSAIDs altogether in a University of Pittsburgh study.

How to try it: Taking 1,000 mg is proven to help your heart, but you should up the dose for pain. For osteoarthritis, try 2,000 to 4,000 mg daily; for rheumatoid arthritis and autoimmune diseases associated with joint pain (such as lupus), consider a much higher dose of upwards of 8,000 mg daily — but ask your doctor about such a large amount first, says Tanya Edwards, MD, medical director at the Cleveland Clinic's Center for Integrative Medicine. (The same rule applies if you take BP or heart meds, as omega-3s can thin the blood.) Read the nutrition label carefully: The dosage refers to the amount of omega-3s in a capsule, not other ingredients. Nordic Naturals ([nordicnaturals.com](http://nordicnaturals.com)) and Carlson ([carlsonlabs.com](http://carlsonlabs.com)) are both reputable brands; for something stronger, GNC's Triple-Strength Fish Oil ([gnc.com](http://gnc.com)) has 900 mg of omega-3s per capsule.

#### **Methylsulfonyl-methane (MSM): For osteoarthritis**

What the science says: MSM is derived from sulfur and may prevent joint and cartilage degeneration, say University of California, San Diego, scientists. People with osteoarthritis of the knee who took MSM had 25 percent less pain and 30

percent better physical function at the end of a 3-month trial at Southwest College of Naturopathic Medicine and Health Sciences. Indian researchers also found that MSM worked better when combined with glucosamine.

How to try it: Start with 1.5 to 3 g once daily and increase to 3 g twice daily for more severe pain, suggests Leslie Axelrod, ND, a professor of clinical sciences at Southwest. Patients in the Indian trial improved on dosages as low as 500 mg three times daily. Vendors of OptiMSM, the brand tested in Axelrod's trial, can be found at [optism.com](http://optism.com).

<http://www.msnbc.msn.com/id/26136767>



## ASPIRIN AND ATHEROSCLEROSIS

Aspirin has become one of the most widely used medications in the world, owing to its ability to reduce pain, fevers, inflammation, and blood clotting. In animal studies, aspirin has also been shown to prevent atherosclerosis, though none of its known mechanisms of action would seem to account for this. In a new study, though, researchers have uncovered the mechanism that may explain aspirin's ability to prevent arterial plaque buildup.

Using cell culture and mouse models, Sampath Parthasarathy and colleagues observed that aspirin—specifically its active byproduct salicylate—can greatly increase the expression of two proteins: paraoxonase 1 (PON1) and apolipoprotein A1 (ApoA1); in the mouse studies, low dose aspirin supplements could increase PON1 and ApoA1 levels by 7- and 12- fold, respectively.

Both of these proteins are beneficial components of the HDL complex, the "good cholesterol" that helps prevent atherosclerosis; ApoA1 removes bad cholesterol from the bloodstream while PON1 is an antioxidant that breaks down toxic lipid peroxides.

The researchers also noted that the heightened expression of PON1 was accompanied by an increase in a receptor called AHR (aryl hydrocarbon receptor); this was intriguing as a chemical known to attach to AHR is resveratrol, the "heart healthy" component of red wine. <http://tinyurl.com/4lglx1j>



## HORMONE DISCOVERY MAY HELP COMBAT DIABETES: STUDY

Scientists have identified a member of a new class of hormones produced by body fat that they think could lead to fresh approaches to combat diabetes and other conditions related to obesity.

The hormone prevents the liver from accumulating fat and enhances the body's ability to control glucose, scientists led by Gokhan Hotamisligil of the Harvard School of Public Health wrote on Thursday in the journal *Cell*. Their work involving the hormone, called palmitoleate, was in mice, but the hormone is also found in people.

While other known hormones are either protein-based or steroid-based, this one is the first example of a class made out of fatty acids, Hotamisligil said. The researchers are calling this new group of hormones lipokines.

Hormones act like the body's chemical messengers, traveling through the blood to influence cells and organs in

processes such as growth and development, metabolism, sex and mood. If the hormone's role in people is the same as in mice, it may become a valuable weapon against type 2 diabetes or fatty liver disease, Hotamisligil said.

"Scientists previously had known about palmitoleate but had not identified it as a hormone. All evidence is pointing that it's coming from fat cells," Hotamisligil said in a telephone interview. "One of its roles is to communicate with the liver and prevent it from accumulating fat, which can occur as people become obese," he said. "It also encourages muscle to take up glucose from blood and dispose of it. It works almost as well as the hormone insulin at pushing sugar out of the blood," he added.

Insulin regulates the absorption of sugar into the cells. People with diabetes have blood sugar levels that are too high. Those with type 2 diabetes, the form closely related to obesity, are resistant to the effects of insulin or produce too little of it.

The researchers said that as body fat increases, less palmitoleate is produced. So in obese people, the beneficial functions of this hormone in controlling blood sugar levels and preventing fat accumulating in the liver would be diminished. "When you need it the most, you produce the least," Hotamisligil said.

Doctors potentially could give palmitoleate to people or come up with ways to stimulate the body to produce more to prevent or improve illnesses like diabetes, and a simple test looking at blood levels of palmitoleate potentially could be used to signal risk for conditions like diabetes.

The scientists identified palmitoleate as a hormone with the help of scientists from Lipomics Technologies of West Sacramento, California. The company was acquired on Wednesday by Tethys Bioscience Inc of Emeryville, California. <http://tinyurl.com/4uy3nc>



Chapped Lips ? Avoid This . . .

If the cooler fall air has you reaching for your lip balm, flip it over and look at the label. You might want to ditch it if you see this in the ingredient list: phenols. Why? These compounds actually strip the top layer off your lips, according to RealAge skin expert Dr. Amy Wechsler.

### Peel Appeal?

Phenols are included in some lip balms (Blistex, for one) to help remove very dry, chapped skin off the surface of lips. But if you're just trying to keep lips moist, the phenols can backfire by removing your lips' natural protective layer. That may also explain why some people get addicted to them, Wechsler writes in her new book, *The Mind-Beauty Connection* -- the stripping effect can leave lips feeling raw, so you reach for more balm.

### Careful Lip Care

To break this vicious lip-balm cycle, Wechsler recommends opting for a good moisturizing lip balm instead. One of her personal favorites is pure, simple Vaseline petroleum jelly. (Use it at night, since it offers no sun protection.) If you need to slough a bit of dry skin from your lips, just brush them very gently with a soft, wet toothbrush.

<http://www.realage.com/ct/tips/6964>

don't forget!

Information in this newsletter is for educational purposes only. Always consult with your doctor first about your specific condition, treatment options and other health concerns you may have.



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