



# Harvard Men's Health Watch

VOLUME 13 • NUMBER 9 | APRIL 2009

## Deep-vein thrombosis: Blood clots in your veins

Let's play a quick game of free association. We say "blood vessel disorder," and you say the first thing that comes to your mind. Whether you are a healthy man or a patient, a primary care physician or a specialist, an epidemiologist or a lab researcher, your answer is likely to focus on the body's arteries. It's no surprise, since arterial diseases account for heart attacks (the coronary arteries), most strokes (the carotid arteries and smaller arteries in the brain), and many amputations (the leg arteries). And there's more: arterial disorders are also the culprits in many cases

of kidney failure, dementia, intestinal bleeding, and even erectile dysfunction.

Healthy arteries are essential for good health. But the circulatory system has another set of blood vessels, the veins. Arteries carry oxygen-rich blood from the heart to all the body's tissues. Then veins swing into action, collecting the blood from the tissues and returning it to the heart and lungs so it can be circulated again and again.

Arteries get all the press, but veins deserve respect, too. More than that, they deserve the care that can help prevent venous disorders. Many venous disorders are mild, but some are serious. And one, *deep-vein thrombosis* (DVT)—the formation of a blood clot (thrombus) inside a blood vessel—can be life-threatening.

### Causes of:

#### Deep-vein thrombosis in men

##### Conditions that slow blood flow

- Immobility, including after surgery (particularly orthopedic surgery)
- Prolonged travel
- Trauma
- Bed rest, especially in a hospital
- Leg paralysis, strokes
- Heart failure



##### Conditions that increase blood clotting

- Various blood-clotting abnormalities
- Increased levels of homocysteine
- Various bone marrow malignancies

##### Conditions that injure veins

- Infections, inflammation
- Trauma, including intravenous catheters
- Previous deep-vein thromboses

##### Other conditions

- Advancing age
- Widespread cancer
- Certain medications (including estrogens and antipsychotics)
- Obesity
- Cigarette smoking

### Normal veins

One reason veins don't get the respect they deserve is that they are much simpler than arteries. Arteries are lined by *endothelial cells*, which produce chemicals that regulate the flow of blood by telling the muscle cells in the arteries' middle layer to contract or relax. In contrast, veins are thin-walled blood vessels that depend on the skeletal muscles around them to regulate blood flow.

Veins may be simple, but they have an elegant design of their own. In fact, this anatomy is particularly important for your leg veins, which have the challenge of carrying blood to your heart whether you are reclining in bed or standing upright. These veins have a series of one-way valves that allow blood to flow toward the heart while preventing backflow, and they depend on contractions of the leg muscles to overcome the force of gravity and propel blood to the heart. Even with vigorous calf muscle contractions, the pressure in veins is significantly lower than arterial blood pressure. ▶▶

### Inside

#### The 10 commandments of cancer prevention

Simple measures can help protect you from America's second leading cause of death. . . . . 5

#### Medical memo

##### Hearty humor

Many people claim laughter is good medicine. Now, a scientific study agrees. . . . 7

#### On call

##### Proscar and osteoporosis

Will medications that shrink your prostate also thin your bones? . . . . . 8

#### In future issues

Hernias  
Statins and prostate cancer  
Allergic rhinitis  
Age and performance  
Exercise and your joints

#### New Special Health Report from Harvard Medical School

**Workout Workbook:**  
9 complete workouts to help you get fit and healthy

To order, call 877-649-9457 (toll-free) or visit us online at [www.health.harvard.edu](http://www.health.harvard.edu).



Visit our new Web site, [www.health.harvard.edu](http://www.health.harvard.edu), for news from Harvard Health, information on diagnostic tools, access to back issues, and more.

## Knowledge Is Power

### EDITORIAL STAFF

**Editor** Harvey B. Simon, M.D.  
**Editorial Assistant** Kathleen Sweeney Laing  
**Copy Editor** Pat Cleary  
**Art Director** Heather Derocher  
**Illustrator** Harriet Greenfield, M.A.  
**Production Coordinator** Charmian Lessis

### EDITORIAL BOARD

Board members are associated with Harvard Medical School and affiliated institutions.

**Cardiology** Patrick T. O'Gara, M.D.  
**Endocrinology** Gilbert H. Daniels, M.D.  
**Gastroenterology** Stanley J. Rosenberg, M.D.  
**Internal Medicine** Christopher M. Coley, M.D.  
 Stephen E. Goldfinger, M.D.  
 Russell S. Phillips, M.D.  
**Neurology** Colin McDonald, M.D.  
**Oncology** Marc B. Garnick, M.D.  
**Orthopedics** John M. Sillski, M.D.  
**Otolaryngology** Gregory W. Randolph, M.D.  
**Preventive Medicine** Edward L. Giovannucci, M.D.  
**Psychiatry** Greg L. Fricchione, M.D.  
**Radiation Oncology** William U. Shipley, M.D.  
**Surgery** David W. Rattner, M.D.  
**Urology** William C. DeWolf, M.D.  
 Niall M. Heney, M.D.

### CUSTOMER SERVICE

**Call:** 877-649-9457 (toll-free)  
**E-mail:** HarvardML@strategicfulfillment.com  
**Online:** www.health.harvard.edu/subinfo  
**Letters:** Harvard Health Publications  
 P.O. Box 9308  
 Big Sandy, TX 75755-9308

**Subscriptions:** \$32 per year (U.S.)  
**Back issues:** Harvard Health Publications  
 (\$5 each) P.O. Box 9309  
 Big Sandy, TX 75755-9309

**Bulk subscriptions:** StayWell Consumer Health Publishing  
 One Atlantic Street, Suite 604  
 Stamford, CT 06901  
 203-653-6266  
 888-456-1222 x31106 (toll-free)  
 ddewitt@staywell.com

**Corporate sales and licensing:** StayWell Consumer Health Publishing  
 One Atlantic Street, Suite 604  
 Stamford, CT 06901  
 jmitchell@staywell.com

### EDITORIAL CORRESPONDENCE

**E-mail:** mens\_health@hms.harvard.edu  
**Letters:** Harvard Men's Health Watch  
 10 Shattuck St., 2nd Floor  
 Boston, MA 02115

### PERMISSIONS

Copyright Clearance Center, Inc.  
**Phone:** 978-646-2600  
**Online:** www.copyright.com

Published monthly by Harvard Health Publications,  
 a division of Harvard Medical School

**Editor in Chief** Anthony L. Komaroff, M.D.  
**Publishing Director** Edward Coburn

## Deep-vein thrombosis (continued)

Leg veins are by far the most vulnerable to DVTs and other venous disorders. There are three types of leg veins. The *superficial veins* lie close to the skin; the *deep veins* are located deep in the muscles; and the *perforator veins* connect the other two systems, with blood normally flowing from the superficial to the deep veins, which carry more than 80% of the blood that flows from the legs to the heart.

### Deep-vein thrombosis

The blood clots that form in veins are different from the blood clots that form in arteries. Arterial clots are usually triggered by platelets, while venous clots are generally formed from the blood-clotting protein *fibrin* and red blood cells. The difference is important and explains why aspirin and other antiplatelet drugs are much better at preventing clots in arteries than veins.

Although venous clots can sometimes form without an obvious cause, the majority of DVTs are triggered by one of three conditions: slowed flow of blood, a boost in the activity of the blood's clotting system, or an injury to the vein wall.

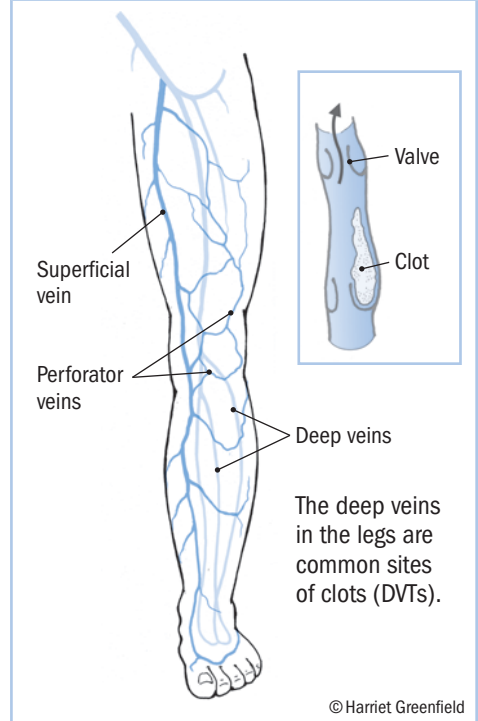
The table on page 1 lists some things that increase the risk of DVTs. It's a long list, which is why DVTs are so common; one of every 10 men will have a clinically evident DVT at some time in his life. And even though pregnancy, oral contraceptives, and estrogen therapy are additional risk factors, recurrent DVTs are more common in men than women.

### Symptoms

Many DVTs are clinically silent. In addition, a number of unrelated conditions can mimic the classic symptoms of DVTs. That makes diagnosis tricky; a high level of suspicion is the first requirement, so that doctors will order tests to evaluate a possible DVT.

Characteristic symptoms include calf pain, calf tenderness, and leg swelling. In most cases, only one leg is affected. The calf can feel tense and swollen, and the foot and ankle may be puffy as edema (fluid) accumulates. In severe cases, the leg may

## Leg veins and DVTs



feel warm or appear bluish; a swollen vein may also be visible. DVTs can cause fever.

Other problems that can mimic DVTs in the leg veins include muscle injuries, fractures, rupture of a Baker's cyst (a fluid collection behind the knee), accumulation of lymph fluid, and infections of the skin, muscles, or bones.

DVTs in the arm veins are relatively uncommon. Most develop in hospitalized patients as a complication of an intravenous catheter (IV), but some are caused by unusual physical effort or by abnormal pressure from a rib as the arm vein crosses into the chest. Asymmetric arm pain and swelling are typical symptoms. A DVT in an arm vein is less serious than one in a leg vein. DVTs in the veins of the pelvis and lower abdomen are very dangerous and are difficult to diagnose.

Superficial veins in the arm or leg can also harbor clots. The vein will be swollen, warm, and tender to the touch. Because complications are rare, therapy is much simpler than for DVTs (see page 4); in most cases, warm packs and nonsteroidal anti-inflammatory drugs such as aspirin or ibuprofen will do the trick.

## Complications

Most DVTs originate in the calf veins. Complications are uncommon if the clot remains in the calf; in fact, the body can often dissolve calf DVTs even without medication. Unfortunately, though, calf-vein DVTs are likely to extend upward to the veins of the thigh and pelvis, setting the stage for major complications.

The most serious complication is *pulmonary embolism*, which occurs when part of the clot breaks off and is carried by the blood to the lungs, where it can block the circulation and interfere with the flow of blood. Pulmonary embolism is a medical emergency. It's the most common preventable cause of death in hospitalized patients, and it takes up to 300,000 lives in the United States each year. Patients may develop chest pain, shortness of breath, a cough, blood-tinged sputum, low blood oxygen levels, low blood pressure, abnormal heart rhythms, or they may collapse. Most patients who succumb to pulmonary emboli die within two hours of the event, making prevention a top priority (see page 4).

Another important complication of DVT results from permanent damage

to the vein. The clot puts pressure on the vein and its valves. If the damage is severe enough, the valves are no longer able to prevent the backflow of blood. Patients with the *post-phlebotic syndrome* accumulate fluid in the affected leg, putting them at risk for infection, skin ulcers, and discoloration, as well as chronic pain.

The third important complication is recurrent DVTs, which are particularly common in men. That's why DVT patients require prolonged therapy and lifelong prevention.

## Diagnosis

Until recently, doctors thought they could diagnose a DVT by carefully examining a patient's legs. Unfortunately, though, this traditional tactic is not at all accurate.

Although old diagnostic criteria based on the physical exam have been discredited, new diagnostic tests are extremely useful. The standard method is ultrasound. Several techniques are available; all rely on the basic observation that a healthy vein will flutter when compressed by an ultrasound probe, but a clot-filled vein will not. Ultrasound is highly accurate (about

95%) for detecting symptomatic DVTs in the large veins of the thigh, but is less accurate (about 70%) for diagnosing clots in the calf veins. That's less of a problem than it might seem. Calf-vein DVTs are less dangerous because they are much less likely to break off and travel to the lungs.

If a patient has a low clinical probability of a DVT, a normal ultrasound may be all a doctor needs to rule out the diagnosis of DVT—but if doubt persists, he can repeat the ultrasound after a few days or order a *d-dimer* blood test (see below). And other imaging techniques can help. The old standby is venography, but it requires an injection of dye so the clot will show on an x-ray. New tests that use CT or MRI can avoid the need for injecting into an injured vein.

The d-dimer blood test can also help. As the blood-clotting protein fibrin breaks down, it releases smaller fragments into the bloodstream. D-dimer is a fibrin breakdown product that's easy to measure. A low level argues strongly against an active DVT, but a high level isn't nearly as helpful since a variety of conditions can boost d-dimer levels. The d-dimer test can also be

## Other disorders of veins

Although veins are relatively simple structures, a lot can go wrong with them. DVTs are the most serious problem, but the others are more common. In one study of 1,566 adults ages 18 to 65, 40% of men had varicose veins, 7% had excess fluid in their ankles due to venous insufficiency, and 1% had active or healed venous leg ulcers. In all, about 7 million Americans have chronic venous insufficiency. Here is a quick rundown on some disorders of veins:

**Varicose veins** are swollen, widened veins that are visible beneath the skin of the legs. Prolonged standing and increased abdominal pressure contribute to the problem. Most varicose veins are harmless, but some produce aching discomfort. If a varicose vein becomes wide enough to prevent its one-way valves from working properly, pressure builds up in the vein, leading to the other problems listed below.

To reduce the pressure in your veins, avoid prolonged standing, do lots of walking, don't cross your legs while you're sitting, and elevate your legs on a footstool when you can. Avoid constipation, since straining increases pressure

on veins. Reduce your dietary salt to fight fluid accumulation. Try compression stockings. And if your problems are severe, ask your doctor about treatments ranging from injections to removing the damaged veins with the newer laser and radio-frequency therapies.

**Chronic venous insufficiency** results from widening of the vein, damage to the elastic tissues on the vein's walls, and incomplete closure of the one-way valves. Blood pools in the vein, increasing pressure. Over time, the skin of the lower leg develops a brownish discoloration called *stasis dermatitis*. In addition, fluid builds up in the ankle, a problem called *edema*. Treatment may include compression stockings, leg elevation, salt restriction, and diuretics ("water pills").

**Venous ulcers** are caused by chronic venous insufficiency. Skin ulceration in the lower leg is always unsightly, often painful, and may become infected. Elevation, compression, and intensive wound care are required, and some patients need antibiotics or surgery. Lifetime care of a single patient with venous ulcers can cost more than \$40,000.

used to help determine the duration of anticoagulant therapy.

Some patients also benefit from blood tests to detect overactivity of the blood clotting system. Patients with a family history of DVTs, with unusual or recurrent DVTs, or with DVTs that develop before age 45 or without evident cause are appropriate candidates for testing.

Special tests are needed to diagnose the life-threatening complications of DVTs: pulmonary emboli. In many centers, the helical CT has become the standard test; however, an older, more invasive test, the *pulmonary angiogram*, remains the gold standard. A non-invasive test, the *ventilation-perfusion lung scan*, is much less accurate.

## Treatment

Anticoagulants are crucial. Although these medications are commonly referred to as “blood thinners,” they do not actually affect the viscosity (“thickness”) of blood. Instead, they inhibit the clotting process. That stops a DVT from extending up a vein and gives the body time to use its natural processes to dissolve the clot without allowing it to break apart and embolize to the lungs.

Therapy is divided into two phases. The first requires an injectable drug that produces immediate anticoagula-

tion. Next comes an oral medication that takes three to five days to kick in but allows convenient, prolonged therapy at home.

For decades, *heparin* has been the mainstay of rapid anticoagulation therapy. Although the drug is still useful, it has been largely replaced by newer derivatives, the *low-molecular-weight heparins*. Both types of heparin are effective, but low-molecular-weight heparin can be injected under the skin once or twice a day, while heparin requires an intravenous injection every four hours. In addition, the low-molecular-weight versions do not require blood tests to monitor therapy, making them suitable for home use. Another effective new drug is *fondaparinux*, which is injected under the skin once a day and also does not require routine blood tests to monitor therapy.

*Warfarin* (Coumadin, generic) is the only drug suitable for long-term oral treatment. It requires a blood test every few weeks to monitor therapy and facilitate adjustment of the dosage. Patients must also avoid medications and foods that might interact with warfarin. In general, patients with a first DVT and no risk factors for recurrence should continue therapy for three to six months. Patients with recurrent DVTs, certain clotting abnormalities or other risk factors, or major pulmonary emboli should continue warfarin for a year or longer; some patients require lifelong therapy.

The major complication of anticoagulant therapy is bleeding. In most cases, the risk can be minimized by careful therapy, but DVT patients who cannot take anticoagulants because of bleeding may need to have a filter placed in their major abdominal vein (the *inferior vena cava*) to protect them from pulmonary emboli.

Compression stockings can reduce the risk of permanent vein damage. Most patients should start wearing over-the-counter or custom-fitted elastic stockings within a month of the diagnosis of DVT, and they should

continue to wear them for at least a year. By gently squeezing the leg veins, they make it easier for the body to keep blood flowing up to the heart.

The average patient can return to exercise after about a month of treatment. Patients with massive DVTs that pose a risk for major leg problems may benefit from “clot-busting” (*thrombolytic*) medications.

## Prevention

Modern therapy for DVTs produces excellent results, but it’s complex and may cause bleeding or other side effects. That makes prevention the best treatment of all.

Since many DVTs and pulmonary emboli develop in hospitalized patients, doctors can prevent many of these major complications by prescribing anticoagulants. In most cases, low-molecular-weight heparin is best; the doses required for prevention are lower than those used to treat DVTs. High-risk patients, such as those who have had hip replacements, benefit from oral warfarin therapy after hospital discharge. Special pneumatic intermittent leg compression or graduated compression stockings can protect neurosurgical patients and others who cannot take anticoagulants. Although low-dose aspirin is very effective against arterial clots in patients with coronary artery disease, it is much less protective against venous clots and should generally be reserved for patients at low risk for DVTs.

Your doctors are responsible for protecting you from DVTs if you are hospitalized, but prevention is your job at home. Keep moving, walk nearly every day, and avoid prolonged bed rest. Stay as lean as possible, don’t smoke, and stay well hydrated.

Travel poses particular challenges. In the old days, it was called the Greyhound Bus Syndrome, but it’s now known as the Economy Class Syndrome. Any form of prolonged sitting can trigger DVTs, but air travel compounds the risk because of its cramped

### Warfarin and prostate cancer

Warfarin is used for the long-term oral treatment of DVTs and other disorders that increase the risk for the blood clots that cause strokes, pulmonary emboli, and other problems. A 2007 study of Canadian men age 50 and older raises the possibility that warfarin may also reduce the risk of prostate cancer. Men who took warfarin for four years enjoyed a 20% lower risk of prostate cancer than men who did not take the drug. There was no protection against other urogenital cancers. More research is needed on warfarin and cancer.

quarters and dry air, which makes the blood “thicker” and “stickier.”

Mobility is the key. Whenever possible, get an exit row, bulkhead, or aisle seat to give you more leg room. Don't cross your legs. Stretch, massage your lower legs, and pump your feet up and down for about 30 seconds every 30 minutes. Take a walk in the aisle at least once every hour or so. Drink plenty of fluids; water and juice are better than alcoholic or caffeinated beverages, which will fill your bladder nearly as much as your stomach.

DVTs are uncommon on flights of less than four hours, but the risk increases with longer trips, particularly those of eight hours or more. The risk is also higher in people who have had recent surgery, especially hip or leg operations, and in people with certain types of cancer, chronic leg swelling, or heart failure. Other risk factors include obesity, smoking, and any condition that's led to prolonged immobility or bed rest within two weeks of the trip. People with overactive blood clotting systems and those who have had previous episodes of deep-vein thrombosis face the highest risk of all. And the risk persists even after you've landed; patients who

undergo major surgery within a month after a long flight have an increased risk of postoperative blood clots.

Passengers at extra risk should consider breaking up very long flights into shorter segments. Below-the-knee elastic compression stockings can also help. Look for a pair that applies pressure of 20 to 30 millimeters of mercury (mm Hg); they are available at hospitals and large drugstores. Passengers who have significant problems with arteries or nerves in their legs should check with their doctors.

Aspirin is readily available, but although it's a very effective way to prevent clots in arteries, its value for deep-vein thrombosis is far less certain. People who need the fullest protection should ask their doctors about an injection of low-molecular-weight heparin before they take off.

### Moving on

The great actress Helen Hayes once said that resting is rusting. She may not have known any more about deep-vein thrombosis than the average guy, but she was clearly onto something. Mental stimulation will help keep your body (and brain) from “rusting.” And when

### Diet and DVTs

A 2007 report from the Atherosclerosis Risk in Communities Study suggests that your diet may influence your risk of developing a DVT. Scientists evaluated 14,962 middle-aged Americans over a 12-year period. They found that eating fish one or more times a week was linked to a 30% to 45% reduction in the risk of DVTs. A high intake of fruits and vegetables also appeared protective, but large amounts of red meat and processed meats were associated with increased risk.

it comes to your veins, keep the blood flowing to prevent DVTs, pulmonary emboli, and the post-phlebotic syndrome. At home or in an airplane, do what it takes to promote blood flow in your veins. Be sure your doctor considers DVT prevention if you are hospitalized, and cooperate fully with anticoagulant therapy to prevent or treat DVTs.

Most men spend much more time thinking about SUVs than DVTs. That's okay if you're at low risk, but before you fly across the country or check into a hospital, you should show your veins the respect they deserve. ♥

## The 10 commandments of cancer prevention

**A**bout one of every three Americans will develop some form of malignancy during his or her lifetime. This year alone, about 1,437,000 new cases will be diagnosed, and more than 565,000 people will die of the disease. Cancer is the second leading cause of death in America, and as deaths from heart disease decline, it's poised to assume the dubious distinction of becoming our leading killer.

Despite these grim statistics, doctors have made great progress in understanding the biology of cancer cells, and they have already been able to improve the diagnosis and treatment of cancer. But instead of just waiting for

new breakthroughs, you can do a lot to protect yourself right now.

Get regular check-ups, including the screening tests that can help detect cancer before it causes any symptoms. For men between 15 and 35, that means a periodic doctor's testicular exam along with regular self-exams. All men older than 50 should have regular screening for colon cancer, and they should make an informed decision about testing for prostate cancer (see *Harvard Men's Health Watch*, May 2008). Men with risk factors should begin both processes even earlier, and every man should routinely inspect himself for signs of melanomas and other skin cancers.

Screening tests can help detect malignancies in their earliest stages, but you should always be alert for symptoms of the disease. The American Cancer Society developed this simple reminder years ago:

- C** Change in bowel or bladder habits
- A** A sore that does not heal
- U** Unusual bleeding or discharge
- T** Thickening or lump in the breast or elsewhere
- I** Indigestion or difficulty in swallowing
- O** Obvious change in a wart or mole
- N** Nagging cough or hoarseness ▶▶

It's a rough guide at best. The vast majority of such symptoms are caused by nonmalignant disorders, and cancers can produce symptoms that don't show up on the list, such as unexplained weight loss or fatigue. But it is a useful reminder to listen to your body and report sounds of distress to your doctor.

Early diagnosis is important, but can you go one better? Can you reduce your risk of getting cancer in the first place? It sounds too good to be true, but it's not. Scientists at the Harvard School of Public Health estimate that up to 75% of American cancer deaths can be prevented; the table below summarizes their research on the causes of cancer in the United States. The American Cancer Society is only slightly less optimistic about prevention, estimating that about 60% of America's cancer deaths can be avoided. And a 2005 study argues that over 2.4 million of the world's 7 million annual cancer deaths can be blamed on nine potentially correctable risk factors.

You don't have to be an international scientist to understand how you can

try to protect yourself and your family. The 10 commandments of cancer prevention are:

- 1 Avoid tobacco** in all its forms, including exposure to secondhand smoke.
- 2 Eat properly.** Reduce your consumption of saturated fat and red meat, which appears to increase the risk of colon and prostate cancers (see *HMHW*, January 2008). Limit your intake of charbroiled foods (especially meat), and avoid deep-fried foods. Increase your consumption of fruits, vegetables, and whole grains. Although other reports are mixed, two large 2003 studies found that high-fiber diets may reduce the risk of colon cancer. And don't forget to eat fish two to three times a week; you'll get protection from heart disease, and you may reduce your risk of prostate cancer.
- 3 Exercise regularly.** Physical activity has been linked to a reduced risk of colon cancer, and it may even help prevent prostate cancer. Exercise also appears to reduce a woman's risk

of breast and possibly reproductive cancers. Exercise will help protect you even if you don't lose weight.

- 4 Stay lean.** Obesity increases the risk of many forms of cancer. Calories count; if you need to slim down, take in fewer calories and burn more with exercise (see *HMHW*, January 2006).
- 5 If you choose to drink, limit yourself to one to two drinks a day.** Excess alcohol increases the risk of cancers of the mouth, *larynx* (voice box), *esophagus* (food pipe), liver, and colon; it also increases a woman's risk of breast cancer. Smoking further increases the risk of many alcohol-induced malignancies.
- 6 Avoid unnecessary exposure to radiation.** Get medical imaging studies only when you need them. Check your home for residential radon, which increases the risk of lung cancer. Protect yourself from *ultraviolet radiation* in sunlight, which increases the risk of melanomas and other skin cancers. But don't worry about *electromagnetic radiation* from high-voltage power lines or *radiofrequency radiation* from microwaves and cell phones. They do not cause cancer.
- 7 Avoid exposure to industrial and environmental toxins** such as *asbestos fibers*, *benzene*, *aromatic amines*, and *polychlorinated biphenyls (PCBs)*.
- 8 Avoid infections that contribute to cancer**, including hepatitis viruses, HIV, and the *human papillomavirus*. Many are transmitted sexually or through contaminated needles.
- 9 Consider taking low-dose aspirin.** Men who take aspirin or other nonsteroidal anti-inflammatory drugs appear to have a lower risk of colon cancer and possibly prostate cancer. It's an unproven benefit, and aspirin can produce gastric bleeding and other side effects, even in low doses. On the plus side, though, low-dose aspirin does protect

Continued on page 8

## The causes of cancer

Risk factor	Percentage of cancer deaths
Smoking and tobacco use	30
Obesity and diet (red meat vs. fruits and vegetables)	30
Lack of exercise	5
Carcinogens in the workplace	5
Viruses (hepatitis, human papillomavirus)	5
Family history of cancer	5
Body size (taller, bigger people get more cancer)	5
Women's reproductive factors (late or no childbearing, late menopause, early periods)	3
Excessive alcohol consumption	3
Poverty (aside from bad diet)	3
Environmental pollution	2
Excessive exposure to sun	2
Medical procedures, drugs	1
Salt, food additives, contaminants	1

Source: "Harvard Report on Cancer Prevention, Vol. I: Causes of Human Cancer" (1996), Vol. 7, pp. 53-55.



### Hearty humor

The mind and body are inseparable aspects of the human organism, two sides of the precious coin called mankind. Physical health has a powerful influence on mental outlook. The reverse is also true, but scientists who study the mind-body connection typically focus on the link between negative emotions and cardiovascular illness. They have learned, for example, that stress raises blood pressure and increases

**During laughter, blood flow increased 22%, making the net difference between blood flow during stress and blood flow during laughter more than 50%.**

cardiac risk, that hostility and anger can be truly heartbreaking, and that depression and social isolation contribute to heart attacks and impair recovery and rehabilitation (see *Harvard Men's Health Watch*, February and September 2006).

It's easy to see why doctors study illness, but there is another piece of the puzzle that also deserves attention. No less an authority than Charlie Chaplin observed that "Laughter is the tonic, the relief, the surcease from pain." It's one thing for a comic genius to tout the benefits of a good laugh, but another for scientists to confirm that humor really is good medicine. Now, however, doctors at the University of Maryland have taken a step in that direction.

Studies of actual heart attacks or strokes require a large number of patients, take a long time, and cost a lot of money. Fortunately, there are useful ways to evaluate cardiovascular health in the laboratory. One of

the newest and most sophisticated methods is to monitor *endothelial function*.

The endothelium is the innermost of the three layers that form the walls of all arteries. Formerly dismissed as a passive lining, the filmy layer of endothelial cells is now known to have a crucial role in vascular health. Among other things, endothelial cells produce *nitric oxide*, which has two vital functions. It keeps the arterial lining smooth and slippery, preventing damaging inflammation and artery-blocking blood clots. Nitric oxide also relaxes the smooth muscle cells of the artery's middle layer, preventing spasms and allowing the artery to *dilate*, or widen, to increase blood flow to tissues that need extra oxygen.

Atherosclerosis, the disease that leads to heart attacks and strokes, takes a toll on endothelial cells, reducing nitric oxide production so that arteries become stickier, narrower, and stiffer. Tobacco use, even passive smoking, and age itself can produce similar problems. In contrast, exercise improves endothelial function, making arteries more supple and functionally younger (see *HMHWS*, June 2006). Statins and certain other medications can also help. And now, scientists have asked if humor might have similar benefits.

To find out, scientists measured endothelial function in 20 healthy men and women with an average age of 33. Each volunteer was studied after an overnight fast that included abstinence from alcohol, aerobic exercise, and vitamins and supplements. Endothelial function was measured at rest, after stress, and after humor. The stress was provided by watching the harrowing opening scene of the 1998 film *Saving Private Ryan*. The laughter was elicited by viewing scenes from the 1996 comedy *Kingpin*



or the 1998 film *There's Something about Mary*.

Mental stress produced a significant drop in endothelium-dependent blood flow in 14 of the 20 volunteers; the average drop was 35%, which was highly significant. In contrast, 19 of the 20 subjects demonstrated improved endothelial function during laughter. On average, blood flow increased 22%, so the net difference between blood flow during stress and laughter exceeded 50%.

How does humor help the endothelium? More studies will be required to find out. One likely possibility is a reduction in the level of stress hormones such as *adrenaline* and *cortisol*. Another is a direct boost in nitric oxide production. Exercise improves endothelial function through similar mechanisms; perhaps, then, the noted editor Norman Cousins was right when he said, "Laughter is a form of internal jogging." Or, since alcohol in moderate doses improves vascular health, playwright Sean O'Casey may have had the answer when he explained, "Laughter is wine for the soul."

More experiments are needed to confirm the observation from the University of Maryland, and long-term studies are required to find out if mirth can help stave off heart attacks and strokes. Till then, laugh at whatever tickles your fancy.

Mark Twain may have exaggerated a bit when he claimed that "Humor is mankind's greatest blessing." Still, a chuckle a day may help keep the doctor away. ♥

men from heart attacks and the most common type of stroke; men at the highest risk reap the greatest benefits.

**10 Get enough vitamin D.** Many experts now recommend 800 to 1,000 IU a day, a goal that's nearly impossible to attain without taking a supplement. Although protection is far from proven, current evidence suggests that vitamin D may help re-

duce the risk of prostate cancer, colon cancer, and other malignancies (see *HMHW*, February 2007). But don't count on other supplements. Careful studies show that selenium, vitamins C and E, beta carotene, folic acid, and multivitamins are not protective, and that some may do more harm than good (see *HMHW*, November 2007, March 2008, and February 2009).

These lifestyle changes will yield another cancer-preventing benefit: if you stay healthy, you won't need cancer treatments (chemotherapy, radiotherapy, drugs that suppress the immune system) that have the ironic side effect of increasing the risk of additional cancers.

As always, prevention is the best medicine. ♥



ON CALL

Proscar and osteoporosis

**Q** I am 76 years old, and I've had an enlarged prostate for at least 10 years. I've been taking Proscar for about a year, and it seems to be helping quite a bit. I have not noticed any side effects, but I'm worried that if the medicine reduces testosterone levels enough to shrink my prostate, it will also give me osteoporosis. Should I change medications, or take Fosamax like my wife?

**A** The prostate gland is stimulated by testosterone, the major male hormone; that's a bad thing for older gents at risk for *benign prostatic hyperplasia* (BPH; an enlarged gland), or prostate cancer. Testosterone also increases bone calcium content, a good thing. *Finasteride* (Proscar) and its newer rival, *dutasteride* (Avodart) block the action of testosterone in the prostate, but they will not interfere with bone mineralization. It sounds like a paradox, but it's not. Here's why.

Bones respond directly to testosterone, as do many other male tissues: testosterone produces the strong, large muscles, deep voice, facial and body hair, sex drive, and tendency toward aggressiveness that characterize the male gender by acting directly on a man's organs and tissues. But the prostate and the scalp's hair follicles are a bit different. To affect these organs, testosterone must first be converted to *dihydrotestosterone* (DHT). In turn, DHT stimulates the prostate and stuns the scalp hair, producing unwelcome changes in many men.

Testosterone is converted to DHT by an enzyme called *5-alpha reductase*. Finasteride and dutasteride inhibit the enzyme; they lower DHT levels in the prostate and blood by 70% to 90%, but they do not reduce testosterone levels. As a result, long-term use can shrink the prostate by about 25%, and it may stimulate some hair follicles that are not too far gone, but it will not melt muscles or turn baritones into sopranos. According to published reports, only 4% to 5% of men notice decreased sex drive or erectile dysfunction while on the medications.

Bones are also spared. A randomized clinical trial of 117 men proved the point: after four years of therapy, men taking 5 mg of finasteride a day had the same bone mineral density as men taking a placebo.

On the other hand, men who need androgen-deprivation therapy to control advanced prostate cancer are at risk for *osteoporosis* ("thin bones") because treatment drastically lowers testosterone levels (see *Harvard Men's Health Watch*, October 2008). Like your wife, they can benefit from *alendronate* (Fosamax), a drug that increases bone calcium (see *HMHW*, December 2008). But men taking 5-alpha reductase inhibitors for BPH don't have to worry about their bones. Your wife's Fosamax supply is safe.

HBS

Harvey B. Simon, M.D.

Editor, *Harvard Men's Health Watch*



Send us a question for On call

By mail | Dr. Harvey B. Simon  
*Harvard Men's Health Watch*  
10 Shattuck St., 2nd Floor  
Boston, MA 02115

By e-mail | mens\_health@hms.harvard.edu  
(Please write "On call" in the subject line.)

Because of the volume of correspondence we receive, we can't answer every letter or message, nor can we provide personal medical advice.