



Harvard Men's Health Watch

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The crucial, controversial carotid artery Part II: Treatment

The carotid arteries carry oxygen-rich blood from the heart to the front half of the brain. But these crucial arteries can become narrowed by the cholesterol-laden plaques of *atherosclerosis*. Blood clots, or *thrombi*, can form on the plaques, then break off and travel as *emboli* to the brain, where they lodge in small arteries, interrupting the vital flow of blood to brain cells. If the interruption is partial or brief, the brain cells recover; the patient experiences a *transient ischemic attack* (TIA) with no permanent damage. But if the blockage is complete, brain cells die, producing a stroke.

In many cases, a TIA warns of a future stroke, giving doctors time to perform a *carotid ultrasound* test to see if the artery is mildly (less than 50%), moderately (50% to 69%), or severely (70% to 99%) narrowed. Last month, in Part I of “The Crucial,

Controversial Carotid Artery,” *Harvard Men's Health Watch* reviewed the diagnosis of *carotid stenosis* (narrowing), but once the diagnosis is established, several treatment options must be considered.

Treatment options

Carotid stenosis can be treated with medication or with a procedure to open the narrowed artery. In both cases, the goal is to prevent strokes. Medical therapy does this by administering drugs that prevent clot formation and improve vascular health. Artery-opening options involve either surgery to remove the atherosclerotic plaques clogging the artery or angioplasty with stenting, which uses a tiny balloon in a catheter to open the artery and a wire mesh stent to hold it open. Patients who undergo either procedure take anticlotting medication afterward, and all patients should work to correct the risk factors responsible for their basic disease, atherosclerosis.

Reporting warning symptoms

Patients hold the key to preventing strokes caused by carotid artery stenosis; their task is to recognize warning symptoms (see “The first decision,” at right) and to report them promptly to their doctors. How well do patients perform as reporters? To find out, investigators surveyed 1,662 patients enrolled in the Asymptomatic Carotid Atherosclerosis Study. At the start of the study, each patient received extensive instruction about warning symptoms and the need for speedy reporting. Despite these educational efforts, fewer than 40% of patients who experienced symptoms reported them within three days, and fewer than 25% reported them within 24 hours. It's a dangerous delay that can have shocking consequences.

The first decision: Medical therapy or an artery-opening procedure

Decisions like this are always hard, but in the case of carotid stenosis, two key factors can help make the right choice: first, the presence or absence of symptoms; and second, the degree of arterial narrowing.

The symptoms of carotid artery narrowing that warn of a high risk of stroke take the form of TIAs. They begin abruptly and resolve in less than 24 hours, often clearing up within an hour or two. The most common warning symptom is temporary visual loss in one eye; it may be complete blindness (*amaurosis fugax*) or partial loss “like a shade before my eye.” Other typical symptoms of carotid TIAs include slurred speech or an inability to use or understand words ▶▶

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Carotid artery (continued)

(*aphasia*), and weakness, clumsiness, and numbness or tingling of the face, hand, or leg on one side of the body. Visual symptoms point to a blockage in the carotid artery on the same side of the body as the affected eye. Aphasia suggests the blockage is in the artery that carries blood to the dominant half of the brain, usually the left side. Symptoms elsewhere in the body point to the narrowing of the carotid on the opposite side of the body.

Every patient with a TIA should have an urgent medical evaluation; at a minimum, this should include an electrocardiogram (ECG) to check for an abnormal heart rhythm that could send blood clots (emboli) to the brain and a Doppler ultrasound test to check the carotid artery. The ultrasound will answer the second key question: is the artery narrowed, and if so, how much? If a significant blockage is present, most medical centers recommend a more detailed imaging study (*magnetic resonance angiography* or *computed tomographic angiography*) before moving on to an invasive, artery-opening procedure.

As a result of careful clinical trials dating back to the early 1990s, doctors can now provide clear guidelines for symptomatic patients with narrowed carotids, but the treatment of patients who do not have carotid TIA symptoms remains controversial.

Patients with carotid TIA symptoms or minor strokes should be considered for invasive therapy if they have a carotid artery that is narrowed by more than 50%. Patients with severe narrowing (70% to 99%) stand to benefit the most, but patients with moderate narrowing (50% to 69%) may also gain some protection against future strokes. Because men are at higher risk for stroke than women with a similar degree of stenosis, they are more likely to benefit from invasive therapy. But artery-opening procedures carry their own risks; patients will only benefit when the risk of severe complications (stroke, death) is 6% or less. Invasive therapy is most effective

when performed soon after the onset of symptoms, ideally within two weeks.

Patients who haven't had carotid TIA symptoms face a more difficult set of decisions, which often arise because of "routine" ultrasound screening tests (see Part I, last month). Those who have narrowing of less than 60% should be treated medically (see page 3). Asymptomatic patients with more severe narrowing can be treated with medication or with an artery-opening procedure; the latter provides a small advantage, reducing the risk of stroke from about 2% a year to about 1% a year, but the benefit is lost if the risk of severe complications is above 3%. Patients over age 75 and those with serious underlying illnesses are better off with medical therapy. But if a patient on medical therapy develops carotid TIA symptoms, he should be evaluated for an artery-opening procedure.

The second decision: Surgery or stenting?

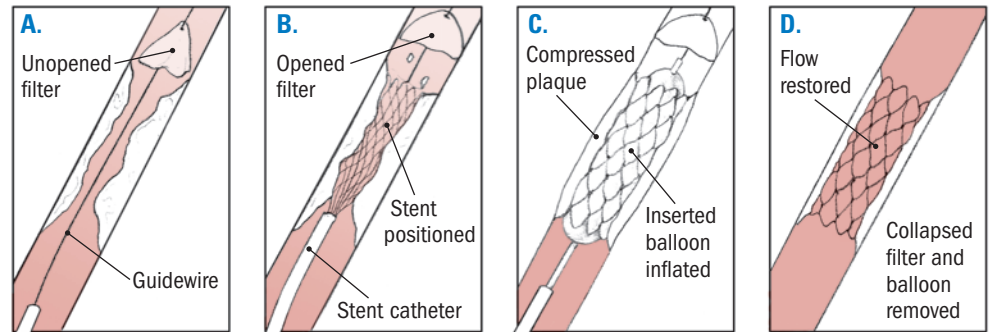
It took years of research to establish the relative merits of medical and surgical therapy, and even with all this study, uncertainties and controversies persist. Since angioplasty with stenting is a much newer way to open blocked carotids, the controversy about this option is even more intense.

Surgery for carotid stenosis is called *carotid endarterectomy*, which is performed under general anesthesia. The surgeon makes a small incision in the patient's neck to expose the diseased carotid. He opens the artery, "scoops out" the plaque, and sews the artery back together, sometimes introducing a patch taken from one of the patient's veins to make the channel wider. Carotid endarterectomy is a delicate operation that should be performed by highly experienced surgical teams. Stroke and death are among the risks of carotid endarterectomy; in the hands of a highly skilled surgeon and an experienced team, the risk of major complications is below 3%, but it can be much higher.

Carotid artery angioplasty with stent-

ing is a relatively new technique that uses the same technology that's been so successful in opening blocked coronary arteries. Under local anesthesia, the doctor inserts a thin tube, or catheter, into the patient's femoral artery in his groin. Using x-rays to show the way, he then threads the catheter up to the carotid blockage in the patient's neck (see figure). Next, he passes a wire through the catheter; when the tip of the wire is beyond the blockage, the doctor opens a tiny filter at the end of the wire to catch debris and clot fragments that might otherwise travel to the brain during the angioplasty itself. The next step

Carotid artery angioplasty with stenting



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A. Using x-rays to show the way, the doctor threads a guidewire and filter up to the carotid blockage. **B.** The filter is opened and a catheter is passed to the blockage. **C.** A tiny balloon in the catheter is inflated to “squash” the blockage and open the stent. **D.** Finally, the catheter, balloon, and filter are removed, leaving the stent in place to hold the artery open.

is to insert a second tube that carries a tiny, collapsible wire mesh, or stent, over an inflatable balloon. When the apparatus is in place, the doctor inflates the balloon, which both expands the stent and “squashes” the plaque to open the artery. When the procedure is finished, the catheter, balloon, and filter are removed through the groin and pressure is applied to the femoral artery to prevent bleeding as the puncture closes. The stent remains in place to help keep the carotid artery open. Like endarterectomy, carotid stenting is a delicate procedure that requires a skilled and experienced medical team. In good hands, the risk of major complications, including bleeding, stroke, and death, is below 3%.

When researchers evaluate the relative merits of the two ways to open a blocked carotid artery, they must remember that rapidly developing technical improvements make comparison a moving target. Carotid endarterectomy has been in use since the 1950s and is still the gold standard. But stenting has improved substantially since it was first employed in the 1990s, and its much shorter recovery time has obvious appeal.

As things now stand, which procedure is best? It's a simple and impor-

tant question, but the answer is long and complex, in part because both techniques are effective and both are improving. A 2011 meta-analysis of 13 randomized clinical trials involving 7,477 patients may offer the best current summary of the available evidence. In the days and weeks following the procedure, surgery has the edge. Carotid endarterectomy produces fewer serious complications, including stroke and death, than stenting, though stenting is followed by fewer mild complications such as nonfatal heart attacks and damage to certain nerves. In the long run, over months and years, the differences narrow, but surgery still appears more successful.

Does this mean endarterectomy is the best choice for every patient? Not necessarily. In fact, individualized decisions are best, and four factors come into play:

- The first is the age and general health of the patient. In general, surgery is preferable for people 70 and above, while patients with medical problems that boost the risks of surgery may do better with stenting.

- The second factor is the nature of the carotid blockage. Carotid plaques that extend far up the artery toward the brain may be more suitable for stenting, while plaques that are ulcer-

ated on the surface or laden with clots might be best treated with surgery.

- A third factor is the skill and experience of the team that will be performing the procedure; national statistics from clinical trials may not apply to the real-world results in your hospital.

- Finally, each patient's preference should be considered; some will favor the faster recovery associated with stenting, while others may opt for the greater safety of surgery.

Before a doctor recommends surgery or stenting, he should remember that medical therapy is another effective treatment that has also improved substantially. Medical treatment is preferred for symptomatic patients with mild narrowing and also for many asymptomatic patients with moderate or even severe narrowing. And even patients who undergo artery-opening procedures need long-term medical therapy.

Medical therapy

Medical therapy is necessary to help prevent dangerous clots from forming in the carotid artery and to fight atherosclerosis, the process that blocks arteries in the first place.

The key drug for preventing clots is aspirin; it inhibits platelets, the tiny

blood cells that trigger the clotting process. Because platelets are so sensitive to aspirin, small doses will do this big job (see *Harvard Men's Health Watch*, December 2010). Most doctors recommend 81 to 325 milligrams (mg) of aspirin a day, starting as soon as the carotid blockage is diagnosed. *Clopidogrel* (Plavix) and *prasugrel* (Effient) are newer antiplatelet drugs that may be prescribed for patients who cannot take aspirin. A less powerful antiplatelet drug, *dipyridamole*, can also be administered with aspirin in a single tablet (Aggrenox) for enhanced protection.

Another essential aspect of medical therapy is blood pressure control—while aspirin should be started as soon as possible, elevated blood pressures should be lowered gently and gradually. *Angiotensin-converting-enzyme* (ACE) *inhibitors*, *angiotensin-receptor blockers* (ARBs), and *thiazide diuretics* are particularly desirable antihyper-

tensive medications in these circumstances. A long-term goal of maintaining blood pressure below 130/80 millimeters of mercury is probably best.

Nearly every patient with carotid stenosis should receive a statin drug, with a goal of reducing LDL (“bad”) cholesterol to 100 milligrams per deciliter (mg/dL) or less; 70 mg/dL or less may be even better. In addition to lowering LDL cholesterol, statins help by stabilizing carotid artery plaques (see *HMHW*, April and May 2011); they even improve the outcome of patients who have had carotid endarterectomy operations.

Lifestyle modification is also vital both to prevent further damage to the diseased carotid arteries and to protect against atherosclerosis in other arteries. Patients must eliminate all tobacco products, including exposure to secondhand smoke. Regular exercise reduces the risk of carotid stenosis

and slows the progression of atherosclerosis. Walking for 30 to 40 minutes a day is a fine place to start. Because patients with carotid stenosis are at risk for coronary artery disease, they should get their doctor's okay before attempting intense exercise. People with diabetes should aim for good blood sugar control. Last but not least, all overweight patients should work toward girth control; a recent study reported that weight loss can actually help reverse carotid artery narrowing over a two-year period.

A good diet can help. That means reducing saturated and trans fats by cutting down sharply on whole-fat dairy products, red meat, fried foods, and products made with trans fat. Because salt raises blood pressure, it is important to restrict sodium, ideally to less than 1,500 mg a day (see *HMHW*, October and November 2010). Eat lots of fish, fruits, vegetables, and whole grains. Cut back on portion size and

Stress and the carotid artery

A person's susceptibility to disease depends on many things, from genetics to health habits, environmental exposures, and even luck. Psychological factors, too, play a role in many illnesses, with heart disease topping the list. Although the link between stress and the heart is well established, the coronary arteries are not easily accessible for direct study. But ultrasound can accurately measure carotid artery thickness and plaques. Can the carotid artery provide information about stress and atherosclerosis?

A series of reports says it can. A Canadian study evaluated 351 adults for atherosclerosis risk factors such as smoking, hypertension, high cholesterol, diabetes, and obesity. Each person was also given the Stroop Color-Word Interference Test, a computerized system for producing frustration and stress during mental tasks. Subjects were monitored during the test to determine whether or not they responded to frustration with stress. Each person also underwent a carotid artery Doppler ultrasound test. Even after taking other risk factors into account, high-stress individuals were more likely to have carotid artery atherosclerosis than low-stress people. And when 136 of the subjects were restudied after two years, high stress was associated with the progression of carotid artery disease.

A joint European-American investigation looked at the question another way. It measured job stress, cardiovascular risk factors, and carotid artery thickness and plaques in 591 men ages 42 to 60. The carotid artery ultrasounds were repeated after four years to evaluate disease progression. When the findings were analyzed, stress was linked to progression of carotid artery disease, even after accounting for the impact of other risk factors.

Similar results were reported by a Finnish study of 901 men between the ages of 42 and 60. Each man underwent a battery of tests to evaluate his blood pressure's response to mental stress, and each had a carotid ultrasound. The results suggest that stress can take a toll on the carotid arteries: the men whose blood pressures shot up the highest in response to mental stress were the most likely to have abnormally thickened carotid arteries.

Psychological factors appear to affect the carotid arteries of women, too. A study of 209 healthy middle-aged women found that pessimists were more likely to have progressive thickening of their carotids than optimists. Finally, researchers from the Netherlands and Germany linked high levels of the stress hormone cortisol to carotid artery atherosclerosis.

calories if you need to lose weight, but don't swear off all liquid calories if you enjoy alcohol and can drink responsibly. In fact, low-dose alcohol has been linked to a reduced risk of carotid stenosis, but large amounts have an adverse effect on the crucial artery. That makes one to two drinks a day ideal for vascular health in men, counting 5 ounces of wine, 12 ounces of beer, or 1½ ounces of spirits as one drink.

Comprehensive medical and lifestyle therapy is effective; it slows the progression of carotid atherosclerosis, lowers the risk of stroke, and reduces the need for artery-opening procedures.

Past, present, and future

Carotid artery blockages pose a substantial risk of stroke. Decades ago, doctors discovered that low-dose aspirin can inhibit platelets, prevent clot formation, and reduce that risk. Surgeons have improved carotid endarterectomy, the operation that removes carotid blockages. The operation should be strongly considered for patients with carotid TIA symptoms and severe (70% to 99%) narrowing, and it may help selected symptomatic patients with 50% to 69% narrowing and some symptom-free individuals with 60% to 99% narrowing. More recently, carotid artery angioplasty with

stenting has emerged as another less invasive way to open blocked carotids, particularly for certain patients with serious medical conditions.

More progress is sure to follow. But the best outcome for all requires a return to the basics. Medications can control blood pressure, cholesterol, and diabetes, and a good diet, regular exercise, and eliminating tobacco exposure can control these risk factors and improve vascular health. A drink or two may also help. All in all, it's a time-honored package of prevention for protecting all arteries—and that's something we can all toast. ♥

ED pills and benign prostatic hyperplasia

No part of the human body is immune to the effects of aging. Many men face the double whammy of smaller erections and larger prostates as the clock ticks on. Although both erectile dysfunction (ED) and benign prostatic hyperplasia (BPH) become much more common as men age, they are very different problems with separate causes, unique symptoms, and unrelated consequences. Until now, treatments for the two conditions have also been different; in fact, medical and surgical therapies for BPH can sometimes even cause ED. But new research suggests that the most popular and effective drugs for ED may substantially reduce the symptoms of BPH.

BPH: A primer

The prostate is a walnut-shaped gland at the base of the bladder. As part of the reproductive system, its job is to produce fluid for semen. But when things go wrong, the gland causes problems with urination, not sex. That's because the *urethra*, the tube that carries urine out from the bladder, runs right through the prostate.

In young men, the prostate is about an inch and a half long and

weighs about two-thirds of an ounce. Starting in middle age, the gland begins to enlarge—and it doesn't take much enlargement to make urination difficult.

BPH causes three types of symptoms:

- Bladder storage symptoms include urinary urgency and frequency, excessive nighttime urination, and incontinence.
- Voiding symptoms include hesitancy, a weak urinary stream, straining to void, and incomplete bladder emptying.
- Post-voiding symptoms include dribbling after urination.

These lower urinary tract symptoms (LUTS in medical lingo) are common; they begin to mount as men enter their 60s, and they often increase as the prostate continues to enlarge over time. By the age of 80, about 25% of all men have BPH that is bothersome enough to require treatment, and countless others have mild symptoms they can "live with." Fortunately, though, serious complications are much less common; they include acute urinary retention, blood in the urine, bladder stones, urinary tract infections, and kidney dysfunc-

tion caused by the buildup of pressure in the urinary tract.

Because complications are relatively infrequent, many men can manage BPH themselves with simple lifestyle measures (see box, page 6). When more help is needed, doctors can prescribe medications or recommend surgery.

Two groups of medications are effective for BPH:

The **alpha blockers** relax smooth muscle cells in the prostate and bladder neck. The older drugs, *terazosin* (Hytrin, generic) and *doxazosin* (Cardura, generic) can cause dizziness by lowering the blood pressure too much in some men with BPH. The newer selective alpha blockers *tamsulosin* (Flomax, generic), *alfuzosin* (Uroxatral), and *silodosin* (Rapaflo) have much less effect on blood pressure. All these medications act within days to weeks, and about 70% of men with BPH improve. Side effects may include nasal stuffiness, headache, dry mouth, and decreased ejaculation (less likely with alfuzosin).

The **hormone blockers**, *finasteride* (Proscar, generic) and *dutasteride* (Avodart), shrink the gland by blocking the conversion of testosterone to dihy-

drotosterone, the male hormone that stimulates the prostate. These drugs work slowly, over six months or longer, and they are only helpful for men with rather large prostates. Side effects may include ED.

Combination therapy with an alpha blocker and a hormone blocker may reduce the risk of complications for men with large prostates and moderate to severe BPH.

Before modern medications were introduced, surgery was the only effective treatment for BPH. Although many men with BPH do well with drugs, others still need surgery. Several approaches are available:

- The *transurethral resection of the prostate* (TURP) has been the gold standard for BPH therapy. In recent years, though, its luster has tarnished—not

because of problems with the operation itself (it's actually gotten better), but because of new medical and surgical rivals. Although results vary, TURP reduces BPH symptoms in 80% to 90% of patients. But there can be complications. Early problems include infection or bleeding. Late complications include dry ejaculation (50% to 75%), ED (5% to 10%), and incontinence (1% to 3%). And since the prostate can enlarge again, up to 20% of TURP patients require more treatment within 10 years.

- Newer, less invasive therapies. It sounds like alphabet soup: men who are considering new ways to treat BPH are now confronted by a bewildering array of initials, such as TUMT, TUNA, TUIP, HIFU, CLAP, TUBD, and believe it or not, many others. That's because urologists have devised

many new therapies for BPH. Some use the energy from lasers, microwaves, ultrasound, or electricity to destroy unwanted prostate tissue, while others rely on tiny incisions in the gland. Because these therapies are new, they are not available in all hospitals. Long-term results are not known, but most appear more effective than medication, but less successful than TURP. Still, they may be worth considering since they generally have a lower risk of complications than TURP and allow a quicker return to normal activities.

Although BPH treatment has come a long way, it's far from perfect. Attempts to improve symptoms with herbs have been disappointing, but doctors continue to work on other approaches, ranging from improved laser surgery to Botox injections. And although ED pills would seem unlikely candidates to treat BPH, new studies suggest they may help.

Lifestyle management of BPH

In a few men, BPH is severe enough to require immediate treatment. But because BPH progresses slowly and serious complications are uncommon, most men can decide for themselves if and when they should be treated. And many men with mild to moderate symptoms find that simple lifestyle adjustments are able to take the BPH bother out of daily life. Here are a few tips:

- Reduce your intake of fluids, particularly after dinner.
- Limit your intake of alcohol and caffeine, and avoid them after mid-afternoon; both are diuretics that increase urine flow.
- Avoid medications that stimulate muscles in the bladder neck and prostate. *Pseudoephedrine* and other decongestants are the chief culprits.
- Avoid medications with *anticholinergic* properties that weaken bladder contractions. Antihistamines such as *diphenhydramine* are the most common offenders. Various antidepressants and antispasmodics have similar properties.
- If you are taking diuretics for high blood pressure or heart problems, ask your doctor to try to reduce the dose or substitute another medication that will work as well without increasing urine flow.
- Never pass up a chance to use the bathroom, even if your bladder does not feel full. Take your time so you empty your bladder as much as possible. Plan to stop at regular intervals during auto trips. Request an aisle seat for air travel or at theatrical and sports events.
- When you are in new surroundings, learn the location of the bathroom before you really need it.
- Make your nighttime trips to the bathroom easy and safe. Be sure there is enough light to see where you're going, but avoid bright light that jolts you awake, making it hard for you to get back to sleep. Be sure there are no electrical cords, telephone wires, loose rugs, or stray objects that might trip you up.

ED pills and sexual function

An erection is a hydraulic event that depends on a sixfold increase in penile blood flow. The crucial chemical for erections is *nitric oxide*, which transmits the impulses of arousal between nerves and also relaxes muscle cells in the penile arteries, causing them to widen and admit more blood.

Nitric oxide is essential for a normal erection, but it does not act alone. It signals the arterial cells to produce *cyclic guanosine monophosphate* (cGMP), the chemical that increases the flow of blood to the penis. But the tissues of the penis also produce *phosphodiesterase-5* (PDE-5), an enzyme that breaks down cGMP.

In normal circumstances, the penis generates enough cGMP to produce a rigid erection and enough PDE-5 to end the erection when ejaculation is complete. But in many men with erectile dysfunction, this intricate system is out of balance, and *sildenafil* (Viagra), *ildenafil* (Levitra), or *tadalafil* (Cialis) often sets things right. The ED pills all

inhibit PDE-5, increasing the supply of cGMP; in about 70% of men with ED, the extra cGMP will allow firm and sustainable erections to develop in response to sexual stimulation.

In ED, pills are generally safe and well tolerated. In a few cases, they can produce painful prolonged erections (*priapism*). And they can occasionally lower blood pressure by widening arteries elsewhere in the body. That's why men who take any form of nitrate medication should never use ED pills, and it's why men with ED who take alpha blockers for BPH should choose a selective alpha blocker and must use ED pills with caution. Although these medications are generally safe for the heart, men with recent heart attacks or strokes, uncontrolled hypertension, or unstable angina should also abstain from ED pills.

The more common but less serious side effects of ED pills may also involve the arteries. Flushing, headaches, and nasal congestion head the list; other adverse reactions include backaches, muscle pain, indigestion, and rashes. These are all temporary symptoms, but sudden visual impairment or abrupt hearing loss, though rare, are serious indeed and can be permanent.

Beyond ED

Although the PDE-5 inhibitors have found huge success treating ED, they are beginning to show benefit for other conditions. Sildenafil and tadalafil have already been approved to treat *pulmonary hypertension*, an uncommon but very serious condition. And while ED pills have not yet been approved for other problems, research suggests they may help some patients with mountain sickness, Raynaud's phenomenon, heart failure, and possibly even stroke.

Because all these conditions involve blood vessels, scientists have had good reason to think ED pills may help. But BPH is different; it develops when *stromal* and *epithelial* cells in the prostate multiply and form microscopic

nodules. Since BPH is a benign tumor, not a vascular problem, logic tells us that ED pills should be ineffective. But logic has its own limits, and new research suggests that ED pills may indeed reduce symptoms of BPH.

Laboratory evidence

Most men think of BPH as a mechanical problem, with the enlarged prostate narrowing the urethra and obstructing the flow of urine, much as stepping on a garden hose blocks the flow of water. Indeed, mechanical obstruction *is* a major cause of lower urinary tract symptoms in BPH; that's why men with enlarged prostates respond to hormone-blocking medications that shrink the gland, while others need surgical procedures that eliminate excess tissue. Still, many men with BPH respond to alpha blockers that don't target mechanical obstruction; these medications work because they relax smooth muscle cells in the prostate and bladder neck, which facilitates the passage of urine.

Experiments with bladder and prostate tissue from men and mice show that nitric oxide and cGMP relax muscle cells in the bladder and prostate, much as these chemicals relax smooth muscle cells in the arteries of the penis and other organs. In addition, research shows that PDE-5 is present in the bladder and prostate, where it breaks down cGMP. That means drugs that target PDE-5 should be able to increase levels of cGMP in the bladder and prostate, thus helping muscle cells relax so urine can flow more easily. Since the ED pills inhibit PDE-5, they should be able to reduce symptoms of BPH.

Clinical evidence

The first ED pill, sildenafil, was approved in 1998. Almost instantaneously, it revolutionized the treatment of ED—but it took four years for researchers to report that the little blue pill also appeared to reduce symptoms of BPH, and even now, only a handful of stud-

ies have examined the possible role of ED pills in BPH.

Despite the lag, the studies are favorable. In randomized clinical trials, sildenafil, vardenafil, and tadalafil all appear to reduce lower urinary tract symptoms in men with BPH. The trials were brief, lasting 8 to 12 weeks, but several studies enrolled over 1,000 men. Men with both moderate and severe lower urinary tract symptoms improved. BPH symptoms improved to a similar degree in men with ED and in those with normal sexual function; obesity did not interfere with the benefits.

In these clinical trials, ED pills were administered daily. The medications were well tolerated, but since the studies ended within 12 weeks, long-term efficacy and safety cannot be assured. Still, tadalafil is approved for daily use by men with ED, and both sildenafil and tadalafil are approved for daily use by patients with pulmonary hypertension.

Time to double down?

The ED pills are not currently approved to treat BPH. Indeed, more research is needed to evaluate long-term efficacy and safety. It will also be important to conduct head-to-head comparisons between ED pills and medications already approved for BPH. Scientists should also evaluate combination therapy, particularly since doctors worry that ED pills may excessively lower blood pressure in men taking alpha blockers for BPH. And because the ED pills are much more expensive than BPH medications, cost is a factor in long-term therapy, especially since insurance does not cover ED pills for BPH.

Older men may be impatient for new research results to flow in. But since many older gents have both ED and BPH, they may already be getting dual benefit from the ED pills. Our ancestors boasted of killing two birds with one stone, but modern men will be delighted to target two problems with one pill. ♥



Electronic cigarettes

Q After smoking for over 15 years, I finally quit eight months ago, but I still miss my cigarettes. I recently heard about electronic cigarettes. Are they safe?

A Whatever you do, don't give in to the lure of cigarettes, or all your hard work and health gains will go up in a puff of smoke.

Now to your question. The short answer is that nobody knows if electronic cigarettes, also marketed as e-cigarettes, are safe. That's because e-cigarette makers have not submitted their products for FDA approval, which would require proof of safety and efficacy. Still, preliminary studies from New Zealand, Greece, and the FDA itself raise concerns.

E-cigarettes come in a variety of shapes; some look like cigarettes, pipes, or cigars, while others are disguised as pens or other socially acceptable items. Whatever their shape, they all are built around a rechargeable battery-operated heating element, a replaceable cartridge that contains nicotine and other chemicals, and an atomizer that converts the chemicals into an inhalable vapor.

There are three reasons to worry about e-cigarettes. First, the dose of nicotine delivered with each puff may vary substantially. An FDA analysis recorded nicotine doses between 26.8 and 43.2 micrograms per puff—and it also detected nicotine in all the products labeled as nicotine free.

Second, the e-cigarettes all deliver an array of other chemicals, including *diethylene glycol* (a highly toxic substance), various *nitrosamines* (powerful carcinogens found in tobacco), and at least four other chemicals suspected of being harmful to humans.

Third, by simulating the cigarette experience, e-cigarettes might reactivate the habit in ex-smokers and could also be a gateway into tobacco abuse for young people who are not yet hooked.

We need scientific studies of e-cigarettes. Until then, it's *caveat emptor*, buyer beware. And for an ex-smoker on the brink of relapse, it's also important to remember that there are a variety of well-studied, FDA-approved nicotine replacement products. Each is vastly preferable to smoking—and to electronic cigarettes.

More dietary advice

Q I read last month's *On call* column about dietary guidelines and caloric percentages, but I'm not a math guy. Any chance you could put it in English for me?

A I feel your pain. The numbers are important, but they can be dull, even downright oppressive. And truth to tell, when I do the shopping, I bring my list but leave my calculator on my desk. But that doesn't mean choosing food at random. Instead, a few simple rules of the aisle will help you fill your pantry with healthful foods. Here is a list of the choices we make in our house:

HBS

Choose	Instead of
Baked, broiled foods	Fried foods
Fish	Meat
Whole-grain breads, cereal, pasta	White bread, refined grains
Unsalted nuts	Salted nuts
Beans, soybeans, lentils	Meat, cheese, eggs
Nonfat dairy products	Whole-fat dairy products
Olive oil or canola oil	Shortening
Spreads with plant stanols	Butter or stick margarine
Fresh, unprocessed foods	Processed foods
Fruits and vegetables	Snack foods and desserts
Various spices and seasonings	Salt and high-sodium sauces
Water or sugar-free beverages	Sugary beverages such as sodas

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