THE UNTOLD STORY OF BUSH'S BAD INTEL



July 28, 200

Cholesterol -And Beyond

Statin Drugs Have Cut Heart Disease.

Now Researchers Hope They Can Beat Alzheimer's, Multiple Sclerosis & Osteoporosis



You Want STATINS With That?



You know you should exercise, but you also know that little pill will let you eat rich food and still keep your cholesterol down. Now scientists think it might even fight Alzheimer's.

BY DAVID NOONAN

Barninka just fine. In the mid1990s, the São Paulo insurance
broker was in his mid-50s, prospering and reasonably fit, carrying
80 judiciously arranged kilos on his 1.8meter frame. He exercised regularly, consulted a physician yearly and, except for a
stinky-cigar habit and a soft spot for *churrasco* (fatty barbecued meat so popular
in Brazil), managed to keep mostly to a
sensible diet. So in 1996, when he called
on his doctor for a checkup before a

planned trip to Israel, he had good reason to expect it would be a routine in-and-outer. It wasn't. Barninka didn't make the flight. In fact, "I never left the hospital," he says. "My doctor told me my arteries were all

Cao Hollong, 67 Beijing, China Cholesterol: 400 After statins: 260 Other factors: Sticks to a relatively low-fat diet and walks once a day

Health

clogged up. I said, 'Are you sure you have the right patient?' "Barninka underwent a quintuple-coronary-bypass operation and vowed he would never again take his health for granted.

Barninka was willing to change. He cut back on the churrasco, upped his workout on the treadmill and gave up the stogies. But that alone wasn't going to be enough to trim his cholesterol, which had soared to 270, and there wasn't much more he could do to make his lifestyle more healthful. His job still required him to work 11-hour days planted mostly in his chair. Is it stressful? "Are you kidding?" he says, "Stress plus!" His doctor, though, started prescribing 20

milligrams of Lipitor daily. After five years on the pills, Barninka, 60, has dropped five kilos and his cholesterol is down to 180.

Welcome to the age of statins. If you aren't taking a cholesterol-lowering drug yourself, chances are you know someone who is. And it's not necessarily an overweight, out-of-shape sports fan in his 50s who ventures off the couch only in search of chips and beer. Millions of high-cholesterol sufferers of every age and description-from Gen-Xers to their octogenarian grandparents—depend on prescription drugs to scour their bloodstreams of LDL cholesterol, the waxy goo that can block arteries and cause heart attacks and strokes. And,

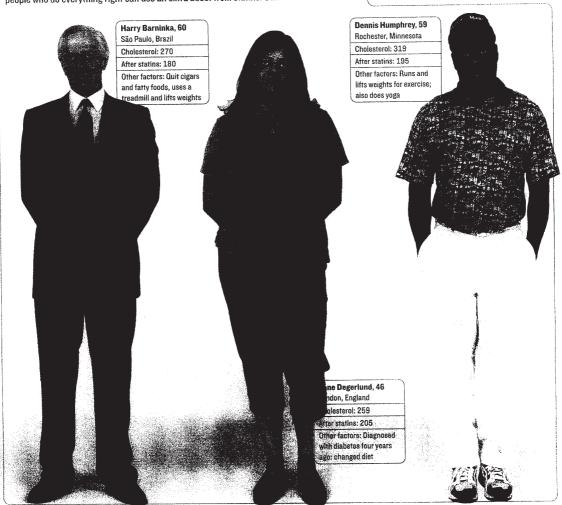
according to health experts, millions more should be taking statins to help ward off cardiovascular disease. Statins have become so critical in the war against cholesterol that a leading statin researcher compares them to the ultimate miracle med. Says Dr. Rory Collins of Oxford University: "Statins are the new aspirin."

His bold words could be an understatement. Promising new research is underway to investigate statins as a treatment for a number of other disorders, including Alzheimer's disease, multiple sclerosis, osteoporosis and even cancer. "I'm very, very hopeful," says Alzheimer's researcher Dt. Larry Sparks of Sun Health Research Institute in Sun City, Arizona, who is nearing the end of a yearlong clinical trial of statins.

High cholesterol was first recognized as a major risk factor for heart disease more than 40 years ago, but no one really

THE PATIENTS: Lowering Risk

Sticking to a low-fat diet and exercising can often bring down cholesterol levels, but even people who do everything right can use an extra boost from statins. Some case histories:



ROM LEFT: PHOTOGRAPH BY CLAUDIO EDINGER FOR NEWSWEEK PHOTOGRAPH BY SASHA BEZZUROV FOR NEWSWEEK (2

started worrying about it until the 1980s, when tests for it became common. In the past few years the concern has taken on new urgency, as health experts have raised their estimates of the number of people who should take cholesterol-lowering drugs. In May 2001, the U.S. National Institutes of Health (NIH) issued aggressive new cholesterol guidelines that nearly tripled overnight the number of people in the United States who should be using statins, from 13 million to 36 million. According to an independent analysis of the NIH guidelines, the number of people under 45 who ought to be on cholesterollowering drugs jumped 201 percent, to 12

million, while the pool of drug candidates 65 and older increased 131 percent, to 10 million. In France, home of such heartstopping delicacies as sauce béarnaise and quiche lorraine, 12 million people have high cholesterol, but fewer than 3 million take statins. After studying 81,000 people, Brazilian Society of Cardiology concluded recently that 40 percent of Brazilian adults suffer from high cholesterol, up 10 percent from a decade ago. Even in Japan, where traditional sushi is easy on the arteries, 20 million people have high cholesterol, but only 4 million take statins. Statins got another boost in late 2001, when Collins and his team released the world's largest randomized study of statins (they followed 20,000 patients for up to eight years), which showed that cholesterol-lowering drugs reduced the risk of heart attack and stroke by at least one quarter for those at highest risk.

That was supersize news in the land of the double bacon-cheeseburger: in the United States, statin sales jumped a whopping 32.5 percent in the two years ending in March 2003. Of course, the billions of dollars the drugmakers spent marketing and advertising statins (\$1.4 billion in 2002) certainly helped. Last year alone, global sales reached \$21.7 billion as doctors wrote more than 118 million statin prescriptions, ac-

ALTERNATIVE MEDICINE

Surprise! Traditional Chinese remedies can lower cholesterol

Lame Cures That Work

BY SARAH SCHAFER

verv day, Fan Zhengjun drinksa bitter green brew, bert weter and part crushed "pseudoginseng." Practitioners of tradi-

glaseng." Practitioners of traditional Chinase medicine consider this plant, local to southern China an effect with the level chinase: terol, and Pan, the rim 1886 yearold vice director of the Cul Yue-Li Traditional Medicine Research Center in Beijing, had long prescribed it for his own patients. When this dectorated him he had high cholbstared in 1997, he decided terry it himself. "Now my blood pressure and cholesterol are normal," he says," Every day, il drink two cups, and I take a walk."

Many Chinese people mistrust Western medicine; and high-cholesterol sufferers like Fan are no exception. They believe the condition; is only a symptom of imbalances in the brity. When gi, or energy, is not flowing smoothly, only traditional medicine can cleanse the blood and get the qi running again. Western scientists have never been confartable with this explanation, but they confirm that some traditional medicines really do lower cholesterol.

The most recent study shows that green and black teas do the trick, David Maron, wheart doctor at Vanderbilt University in

Nashville, Tennosseg had 240 Chinese men and women -- already on low-fat diets to lewer their cho-lesterol -- reke enaggy lie of realex-tracts every day for \$2\$ weeks. The treatment reduced low-density lipoprotein (LDL) cholesterol (the "bad" kind) by an average of 16 percent: Although the study was sponsored by Nashville-based Nashai Biotech, which sells the capsules in China; Maron performed the tests on the condition. that he publish the results no mai ter what. The findings, published in Archives of Internal Medicine in 400 including rec June, surprised him: Heavy-team drinking populations have always had fewer cases of high choics + terol and other health problems, but Maron didn't expect to find such a strong cause and effect relationship. His study is the first to show that some combination of chemicals found naturally in green and blacktea significantly lowers cholesterol. (Green tea alone won't do it, past studies have shown.) "On top of [a low-fat] diet, it could be the equivalent of having a 16 to 24 percent lower risk of having a beart attack."

Scientists have just begun to study other traditional Chinese high-cholesterol remedies, but they have a long way to go. Most Chinese remedies actually contain a hodgepodge of plants and herbs.

that have yet to undergo rigorous scientific study, whether alone or incombination. One popular elixir, for exemple, mixes furmeric with cartall pollen, lorus leaf and other ingredients. If these treatments prove as effective as tea, even traditional Chinese dectors aren't in the province of the provi

yeast, contain natural forms of statin. More important, commercial statins have been well tested, and are proven defenses against heart-disease-related deaths. Tea has a long way to go before it can make that claim. For one thing, it's unclear how safe tea capsules are in the long run. It may be natural, but Maron gave his subjects the equivalent of seven cups of high-quality black tea and about seven cups of green tea a day, a pretty strong dose. And scientists don't know whether tea works for everyone. Eventually, extracts may prove to be a useful supplement to statins. For borderline patients like Fan, extracts combined with diet might be just the thing to avoid the waiting room altogether.



BON & SMITH-FOODPD

cording to IMS Health. All those pills mean big profits for Big Pharma, but there's no denying that statins prevent a lot of pain and suffering. Heart disease remains the leading cause of death in the developed world, taking more than 3.5 million lives each year. With people less inclined than ever to do the things-like eating less saturated fat and exercising-that are known to lower cholesterol and reduce the risk of heart attack, statins have emerged as perhaps our most reliable weapon against a relentless killer. While experts recommend lifestyle changes as the primary treatment for high cholesterol, not everyone can reach his target LDL level that way. "For those that can't, the drugs are crucially important because they will provide a degree of LDL lowering that lifestyle alone won't, in most cases, achieve,' says Dr. James Cleeman, head of the NIH's National Cholesterol Education Program.

RITICS OF DRUG THERAPY say the NIH guidelines and Collins's study are flawed by an implicit assumption that people can't or won't change their behavior. They say statins can reinforce bad habits and actually serve as a disincentive to get up and move. "Most people can accomplish comparable reductions in LDL [the bad cholesterol) by diet and lifestyle alone, if the changes are comprehensive enough, says Dr. Dean Ornish, head of the Preventive Medicine Research Institute in Sausalito, California. In a 1998 study, Ornish reported a 40 percent reduction in LDL after one year among a group of patients with heart disease who followed a rigorous program, including 30 minutes of moderate exercise daily, and a low-fat, vegetarian diet. (Statins have been shown to reduce LDL by 25 to 60 percent.) Ornish also notes that taking pills isn't necessarily easy, citing one study that found 65 percent of statin users stopped taking their medicines after a year. Dr. Donald Fedder of the University of Maryland-Baltimore, who wrote an analysis of the new NIH guidelines in which he expressed some concern about overprescribing statins, says physicians need to present their patients with all the options. "You've got to give the intelligent patient a [chance]," says Fedder. "I wouldn't want to be on the Ornish diet because I'm a carnivore. But if you follow his diet you will not have to take any pills."

While the doctors in the front lines of the war against heart disease agree that lifestyle changes should be the cornerstone of cholesterol-lowering therapy, they also say their

STATINS: What's After Cholesterol?

Revised NIH guidelines have made millions of new patients eligible for cholesterol-lowering drugs. But statin use could expand even more if cutting-edge research is borne out. Studies suggest that the drugs may also slow the progression of major diseases like Alzheimer's

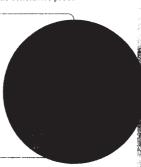
Old Treatments and New

Statins, long known to fight heart disease, have shown promise in combating a number of other ailments. More research is needed to provide conclusive proof.

CORONARY ARTERY DISEASE: The original

target of statin therapy. By reducing blood cholesterol, the drugs help keep arteries clear.

A study of 20,000 high-risk patients found that the drugs reduced heart attack and stroke by at least 25%.



BONE FRACTURES:

440, 20

Studies have shown that statins increase bone formation in rodents,

If these benefits role, up in humans; stating may prove a novel treatment for osteoporosis— one that actually builds abone rather than just preventing its loss.



MULTIPLE SCLEROSIS:

Statins may limit the progression of MS by blocking the immune response that damages nerve tissue.

■ One small study found that statins reduced new brain lesions by 40%. But it's too early to tell if this will prevent disability.

Should You Be on Statins? The Guidelines

Diet and exercise can reduce cholesterol, but your doctor may find that you need drugs, too. The decision is based on your family medical history, your own health history and your risk factors.

1 EVALUATE YOUR MEDICAL HISTORY:

Are you suffering from heart disease or diabetes, with LDL over 130? If so, you are a candidate for treatment. If not, read on.

2 COUNT YOUR RISKS: How many risk factors for heart disease do you have?

- **38** Smoking
- High blood pressure

- Low level of good cholesterol
- Family history of early heart disease
- **■** Age (men 45+, women 55+)

3 DETERMINE YOUR 10-YEAR RISK: If you have

two or more risk factors, calculate your chances of having a heart attack in the next 10 years. An online calculator test is available at

nhlbi.nih.gov/guidelines/ cholesterol/index.htm

4 TEST YOUR BAO CHO-LESTEROL: A doctor willuse both risk levels: and LDL to make the final call: For example, a patient with an LBL-level of 130 might get staffins if he has two risk factors and a 10% or greater chance of having a heart attack in 10 years.

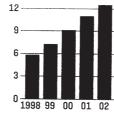


ALZHEIMER'S: Statins could reduce amyloid plaques in the brain, since cholesterol drives the production of amvloid. Plagues are a hallmark of Alzheimer's. One study found a 39% reduction in the risk of Alzheimer's among people on statins.

Statin Sales

Statins are the top-selling class of drugs in America. And demand could swell as the population ages and researchers uncover more potential uses for the drugs.

\$15 billion



AORTIC-VALVE DISEASE: Hardening of the aortic valve can eventually lead to congestive heart failure. Statins could help patients avoid surgery. One study showed that statins slowed ssion of valve disease by 50%.



Statins lower cholesterol in t wo ways. First, they block an enzyme that the body needs for cholesterol production. Second, they boost the liver's ability to remove LDL from blood.

bod



The liver has receptors on its surface that grab harmful cholesterol (LDL) and clear it from the **bloodstream**. This helps keep blood LDL at safe, healthy levels

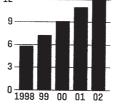


The receptors can malfunction, losing their ability to clear LDL from the blood. Cholesterol can then build up, damaging arteries and leading to heart disease

STATINS IN ACTION:

Statins work by increasing LDL-receptor production in the liver. The extra receptors help remove excess blood cholesterol, bringing it down to safer levels

-JOSH ULICK and ANNE UNDERWOOD



fast-food-loving patients simply aren't up to the task. "There is a great deal of truth in what Ornish is doing," says Dr. Sidney Smith, professor of medicine at the University of North Carolina-Chapel Hill and former president of the American Heart Association. "The problem is that the changes needed are frequently very difficult. For some it's an inability to break habits, but for many the reality is it's just not palatable."

That's certainly true for statin user Cao Huiliang. Twenty years ago, in his late 40s, he was having some health problems, including trouble sleeping. His doctor told him he had a total cholesterol count of 400 and prescribed some medicine, but he soon stopped taking it because it made him nauseous. "I didn't feel anything," he says, "so I didn't pay attention." For years afterward, Cao suffered from chest pains, for which he took traditional Chinese remedies—he still keeps a little red plastic bottle of pills in his pocket. Two months ago, though, the pains got so bad that he checked into Anzehn Hospital in Beijing. Cao, now a trim 67year-old with thick white hair, sits around in his pajamas while doctors try to gauge the extent of his illness. Meanwhile, his doctor has prescribed statins.

The rising popularity of statins, first introduced in 1987, has been accompanied by twin epidemics of obesity, which now includes 300 million adults worldwide, up from 200 million in 1995, and diabetes, which is expected to climb from 176 million at present to 370 million by 2030. Both conditions are preventable, and their rise is due in large part to what might be called couchpotato syndrome. Although experts recommend at least 30 minutes of exercise daily, fewer than half of U.S. adults (more than 60 percent of whom are overweight or obese) get any regular exercise at all, and other developing countries can't be far behind.

While statins help control high cholesterol, that's just one of the many risk factors

Kelly, 57

terol: 230

statins: 160

died at 63

factors: A family

v of heart desease;

for heart attack. Others-including high blood pressure, smoking and obesity-are not affected by statins. "So you have an enormously greater benefit if you fix the obesity, if you exercise, if you eat the low-saturated-fat and lowcholesterol diet" in addition

to using the drugs, Cleeman says. "It's a one-two punch: lifestyle and drugs.

Though it has developed a rather ugly reputation, cholesterol is essential for the formation of cell membranes and hormones. Our bodies make all the cholesterol we need; it's synthesized in the liver. The problem is, the food we eat, particularly the saturated fat in it, can elevate LDL. There is



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also a genetic condition in which the body makes too much LDL. An excess of LDL cholesterol can accumulate in arteries that feed the heart and brain and lead to a heart attack. HDL cholesterol, the "good" kind, takes away excess cholesterol.

Statins work by inhibiting an enzyme (HMG-CoA reductase, a name only a scientist could love) in the liver, thereby blocking production of cholesterol. This triggers a vacuuming effect in which the liver sucks up the LDL cholesterol in the bloodstream. Recent studies have found that statins also reduce the level of C-reactive protein (CRP), a marker for inflammation of blood vessels. Elevated levels of CRP have been associated with increased risk of heart attack. In addition, a new drug, Zetia, from Merck/Schering-Plough, inhibits the absorption of choesterol in the intestine; it's used alone and in combination with statins to lower choles-

terol. Statins do carry risks. The two main complications are liver problems, which occur in about 1 percent of patients, and myopathy, a painful muscle condition, which affects about one patient in a thousand. (Quitting the drugs stops both side effects.)

Popular as statins are, it could be that we ain't seen nothin' yet if they turn out to be effective against Alzheimer's disease, multiple sclerosis and other disorders. Researchers are cautious, to say the least. "We tell people not to take drugs for things that aren't proven," says Dr. Robert Green, associate professor of neurology at Boston University School of Medicine. But some of the early results are intriguing. Green authored a study that showed a 39 percent reduction in Alzheimer's risk in people who had been taking statins at least six months.

Though not everyone agrees on the underlying causes of Alzheimer's, many believe that a protein called beta amyloid, or A-beta, plays an important role. A-beta can form a plaque that is always found in the brains of Alzheimer's patients. Sparks thinks that elevated cholesterol may "augment the production" of A-beta plaque in the brain. "It may not be the only thing that induces it," he says, "but it certainly helps it along. And if I can get rid of this agent that's helping production of this toxin, maybe I can slow down the disease." Sparks is about to complete a clinical trial involving 65 mild- to moderate-Alzheimer's patients, The patients on statins received 80mg of Lipitor daily. (The research was funded in part by Pfizer, Lipitor's maker.)

The possibility that high cholesterol contributes to Alzheimer's disease is particularly frightening, "We've heard a lot about obesity and the coming epidemic in diabetes," says Harvard neurologist Rudy Tanzi, who

DIAGNOSTICS

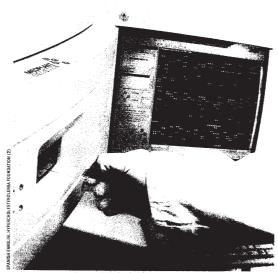
A quick test can flag a gene that confers high cholesterol

An Ounce of Prevention

BY ERIC PAPE

ow do you explain those rail-thin people who eat nothing but fish and vegetables, and who yet somehow manage to rack up dangerously high cholesterol levels? They suffer from an inherited disorder, called familial hypercholesterol. According to the World Health Organization, more than 10 million people, or one in 500, have the condition, which makes it one of the most common hereditary ailments in the West and probably worldwide. Diagnosis has been difficult because the condition can be triggered by at least 900 or so different genetic mutations, and those are only the ones scientists know about. "In some European countries there are two or three hundred mutations," says biologist Miguel Pocovi at the University of Zaragoza. Because Spain is less ethnically diverse than some other European countries, it has relatively few mutations-about 150 have been found-Pocovi and his colleagues were able to catalog them all in a national registry.

In October, the work will yield a



practical benefit. The Spanish national pharmaceutical firm Laboratorio Lazer, based in Barcelona, is introducing a "biochip" that can detect Spain's mutations (those in Pocovi's registry). Rather than having to sequence the gene that causes familial hypercholesterol for each patient, which takes months and

costs about €2,000, doctors will only have to draw a few drops of blood. The chip flags the presence of DNA in the patient's blood that matches one of the known mutations. Doctors can render a diagnosis within 48 hours, at a cost of €350. Pocovi expects other pharmaceutical firms to follow soon with biochips that detect muta-



QUICK TEST: A new 'biochip' diagnoses 'familial hyper-cholesterol' within 48 hours

tions common to other countries. That's good news to the 200,000 people around the world who die from the condition each year, most never even knowing they had it. "It's a slow-ticking bomb, says Pedro Mata, a doctor at Fundación Hipercolesterolemia Familiar, in Madrid, "If these people are not treated in advance, they have a life expectancy that is 20 to 30 years lower." The chip is also expected to make it more convenient for doctors to diagnose the condition early-which might help them persuade patients to pre-empt high cholesterol by adopting a healthier lifestyle.

thinks other experimental cholesterol drugs may fight Alzheimer's better than statins. "I worry about the coming epidemic of Alzheimer's, based on the clear molecular link of cholesterol and A-beta production."

TATINS ARE ALSO GETTING a serious look as a possible treatment for multiple sclerosis, which afflicts about 2.5 million people worldwide. MS is an autoimmune disorder that destroys myclin, the fatty sheath around nerve cells. This fall, Dr. Scott Zamvil, a neurologist at the University of California, San Francisco, will launch the first placebocontrolled clinical study of MS patients taking statins. Because the object of the study is to test the effectiveness of statins in suppressing the development of the disease, the 152 subjects will be people who have had

only their very first attack of MS. The research is an extension of work Zamvil and colleagues did on mice. That study, published last fall in Nature, showed that statins reversed paralysis in mice with MS and prevented relapse of the disease. While it's not known exactly how statins work against MS, Zamvil, who has received a competitive research grant from Pfizer, says the drugs prompt the cells that attack the nervous system in MS to instead secrete molecules that protect it.

Statins also show potential for protecting against aortic-valve disease, a hardening of the valve between the heart and the aorta, and osteoporosis, the age-related deterioration of bone that leads to fractures. And a Dutch study released

last month found that people who had been using statins for four years or more had a 20 percent reduction in their cancer risk, especially prostate and liver cancer. There are a few caveats, however. It was only an association study based on analysis of existing data, not a placebocontrolled clinical study, the gold standard of medical research. And there have been other statin-cancer studies with neutral or negative findings.

It will be years before we know whether statins will work against these other conditions. But there's little mystery about their effectiveness in preventing heart disease. We may be lazy and we may be fat and we may feel guilty about taking the darn things. But we're better off with them than without them.

With ANNE UNDERWOOD, MAC MARGOLIS, SARAH SCHAFER, MARIE VALLA, DALIA MARTINEZ, DAN MOREAU, JOAN RAYMOND, ARTHUR KIMBALL STANLEY and PETER BAILEY

TEST YOURSELF

What do you know about cholesterol?

The Right Stuff

TRUE or FALSE?

- 1. The body needs cholesterol
- The best way to reduce cholesterol is to limit cholesterol-rich foods, such as eggs.
- 3. To lower your cholesterol, you should stop eating all meat.
- 4. Any total cholesterol level below 240 is fine.
- 5. All vegetable oils are good for the heart.
- Lowering cholesterol can help people who have already had a heart attack.
- 7. Exercise can raise good cholesterol.
- 8. Women don't need to worry about high levels of cholesterol and heart disease.

THE ANSWERS

Question 1: TRUE. Cholesterol is a soft, way substance that the body uses to build cell membranes and makinterfold hormones, such as estrogen restriction and cortisone. The problem len't cholesterol par set but excess cholesterol—particularly the "bad" LDL cholesterol, which contributes to plaque buildup in the arteries.

Question 2: FALSE. Although so -called dietary cholesterol does raise blood cholesterol in most people, the chief oulprit is safurated fat. The most effective way to egitrol blood chalesterol is to reduce roods highth sacurated fat, such ge tulls fat chasee cream burteratument

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Upwartign Science: Transteres - the pain fell which Cogenate of vegetable of a right path herd mangath seron filman which of productive seron seron path holds regrat (The thop as of the pain). high in saturated fat and can also raise cholesterol. Focus instead on the other vegetable oils, including oilive and canola, which contain mostly monounsaturated and polyunsaturated fats.

Question 6: TRUE. People who have had one heart attack are at higher risk for a second, but lowering cholesterol can greatly reduce that risk. If you have heart disease, your LDL level should be less than 100.

Question 7: TRUE. "Exercise should he part of any program for feart health," says Dr. Ronald frauss, founder of the American Heart Association's Council on Authorition, Physical Activity and Metabolism, "At least half an hour eddy is recommended."

Office measures that can help graise HDL include losing weight and stopping smoking.

Question 8: FMSE. Before menopause, women tend to have lower cholesterol lavels than men. But afterward, their levels go up, along with their risk for heart' disease. For both men and women, heart disease is the leading cause of death.

Adapted from the National Cholesterol Education Program. For more information, see hhibt nih.gov/chd.