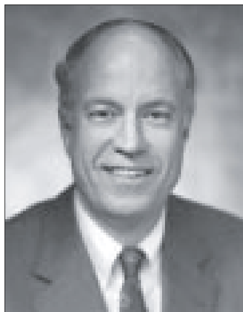
Facts and ideas from anywhere



William C. Roberts, MD

SCIENTIFIC HUMILITY

Belief in the protective powers of hormonal therapy was just overturned (1–6). The massive study of hormone replacement therapy in postmenopausal women had to be halted 3 years early because the estrogen-progestin combination appeared to cause an alarming increase in the frequency of invasive breast cancer, thrombosis, stroke, and heart attack. The pure-estrogen arm will continue. When the announcement was made, Wyeth Pharmaceuticals lost 24% of its value in 1 day. Thus, hormone replacement therapy in postmenopausal women joins tonsillectomy, antibiotics for ear infections, leeching, bleeding, lobotomies, and shock therapy for psychiatric disorders as common therapies eventually shown to be unnecessary or harmful. The belief that peptic ulcer disease was secondary to excessive acid in the stomach and/or stress has also vanished. Fetal tissue transplants for degenerative diseases and angiogenesis inhibitors as anticancer drugs have yet to pan out. Whether regenerative medicine via stem cells and cloning will turn out favorably is as yet unclear. There is no need for arrogance in medicine.

DRINKING WATER AND POLLUTION

The recently published *Global Environment Outlook 3*, a 450-page United Nations document (www.unep.org/geo/), indicates that about half of the world's rivers now are seriously depleted and polluted and that one third of the world's population is dependent on ground water, with the levels of ground water falling (7). By 2032, more than half the global population will face water shortages, 10% higher than the proportion predicted in 1995. Worst affected will be the people living in the Middle East—where oil resources, of course, are largest in the world but where 95% of the population is forecasted to face water shortages. By 2032, over 70% of the earth's land surface could be affected by the impact of roads, mining, cities, and other infrastructure developments made to satisfy the global population set to increase by 2 billion over the next 30 years. Although the number of people being served by better water facilities has increased from 4.1 billion in 1990 to 4.9 billion in 2000, 1.1 billion people in the developing world still have no access to safe drinking water, and 2.4 billion people currently lack adequate sanitation facilities. As a consequence, 4 billion cases of diarrhea and 2.2 million deaths occur each year. Intestinal worms affect 10% of the people in the developing world, 6 million people are blind from trachoma, and some 200 million people are affected by *Schistosoma (Bilharzia)*.

TRASH

It's almost trite to say that public health activities such as garbage collecting have done more good for humankind than physicians have ever been able to do. Our government leaders encourage economic growth, but as the economy grows so does the quantity of trash. New York City collects 11,000 tons of trash daily from its residences alone, and the city has no more space to dispose of it (8). It is now carrying trash to Pennsylvania and Virginia, and there is even talk of sending it to a Caribbean island. And what about nuclear waste? No state wants it stored in its acreage, and other states don't even want nuclear waste to travel through their borders. The waste management industry has talked of a cleaner and safer incinerator that will produce energy without creating tons of toxic residue, but that technology has not yet arrived and whether it actually will is unclear. Expanding the recycling programs, decreasing the amount of packaging, and encouraging composting have all been suggested as useful endeavors, but these are only small solutions to a much bigger problem. More buying means more trash, which means more pollution.

MORE ON STATINS

Statins have been available in the USA since 1987, and yet 15 years later most patients who have had atherosclerotic events and/or diabetes mellitus or who are at high risk for atherosclerotic events are not on statin therapy despite its proven benefit in decreasing first and repeat atherosclerotic events. The following are my recommendations for increasing the numbers of patients on statin therapy.

1. Shift the emphasis from secondary prevention and diabetes mellitus to primary prevention. Do not wait to start statin therapy until after an atherosclerotic event has occurred or diabetes mellitus has appeared. By the time either has appeared, one or more major epicardial coronary arteries are narrowed >75% in cross-sectional area by atherosclerotic plaque. Guidelines for lipid-lowering therapy, formulated by the adult-treatment panel of the National Cholesterol Education Committee in 1988 and revised in 1993 and in 2001, are based on *decreasing the risk* of developing first and repeat atherosclerotic events. Because it is rarely genetic in origin (the familial variety is present in only about 1 in 500 people), atherosclerosis in my view needs to be approached not primarily from the standpoint of decreasing risk but from the standpoint of actually preventing and/or arresting plaque formation. Pediatricians do not talk in terms of decreas-

ing the risk of measles, mumps, pertussis, and polio. They focus on total prevention of these conditions. The same approach can be applied to atherosclerosis.

But what serum cholesterol numbers are necessary to prevent atherosclerotic plaques from forming? The evidence is substantial that if over decades the serum total cholesterol is <150 mg/dL, the low-density lipoprotein (LDL) cholesterol is <100 mg/dL, and the high-density lipoprotein (HDL) cholesterol is >20 mg/dL, the chances of forming atherosclerotic plaques are slim. (I realize that many readers will be shocked by the mention of an HDL cholesterol of only >20 mg/dL. But this number applies only when the total cholesterol is <150 mg/dL and the LDL cholesterol is <100 mg/dL. If the total cholesterol is 200 mg/dL and the HDL cholesterol is only 21 mg/dL, an atherosclerotic event is likely.) Because nearly 45% of adults in the western world die from cardiovascular disease, these numbers need to be the goals of *all adults*, not just adults with atherosclerotic events and/or diabetes mellitus. Now lipid-lowering agents, which can achieve these goals in most patients, are available. Thus, lower the bar for those eligible for statin therapy!

But how can these therapies be afforded, the argument goes? These numbers can be achieved by following a vegetarian-fruit diet, which is the least expensive route. If that route is unsatisfactory, simply decreasing the quantity of flesh (muscle) consumed by one half would free up enough money to purchase the lipid-lowering agent(s). We seem to afford arterial angioplasty and stents, bypass, endarterectomy and resection, expensive diagnostic tests, and pacemakers and defibrillators without excessive thought, and yet there is no evidence that either arterial angioplasty or bypass prolongs life in most patients. In contrast, lipid-lowering therapy prolongs life by decreasing atherosclerotic events, including stroke. Thus, I say serum LDL cholesterol <100, total cholesterol <150, and HDL cholesterol >20 mg/dL for everybody. By doing that, the guidelines would be immediately simplified, and there would be no separation of so-called primary and secondary prevention or distinction between diabetics and nondiabetics.

The average LDL cholesterol in persons in coronary care units with acute coronary syndromes is about 145 mg/dL, and yet according to the most recent guidelines, an LDL cholesterol of 159 mg/dL in a patient with only 1 or no other atherosclerotic risk factor is considered “borderline” and not worthy of lipid-lowering drug therapy. This recommendation makes little sense to me. The Heart Protection Study demonstrated a significant reduction in first and repeat atherosclerotic events by simvastatin therapy in patients with pretreatment serum LDL cholesterol levels <115 mg/dL. In contrast to lipid-lowering agents, aspirin is recognized to decrease atherosclerotic events irrespective of the platelet count or the “stickiness” of platelets. Likewise, the prophylactic value of lowering an elevated systemic arterial pressure is well recognized irrespective of the magnitude of blood pressure elevation.

2. Eliminate the need for titration of statin drugs. This is done by starting the patient initially on the proper dose, i.e., the one that lowers the LDL cholesterol to <100 mg/dL. A major reason patients do not achieve this LDL cholesterol goal is that the dose of statin is too low and the dose is never raised. If the initial LDL cholesterol level is 185 mg/dL, for example, a drop of slightly more than 45% will be necessary to achieve an LDL cholesterol of <100 mg/dL. That would require 40 mg of atorvastatin or 80 mg of simvastatin.

In contrast to statins, niacin therapy needs to be titrated, starting with a low dose (such as 500 mg) and gradually increasing it to 1500 mg if necessary. Likewise, fibrates might best be titrated—at least when added to a statin drug.

3. Eliminate the requirement for liver function tests. Concern about hepatic dysfunction frightens patients, and yet acute liver failure produced by a statin drug is incredibly rare (<1 per 1 million patient-treatment years), a rate approximately equal to the rate of idiopathic acute liver failure. The evidence that liver failure is ever the result of statin therapy is at best tenuous! Minor elevations in hepatic enzymes, i.e., serum alanine aminotransferase enzyme (ALT), occur in 2.6% and 5.0% of patients on lovastatin 20 and 80 mg/day, respectively. These elevations are reversible with continuing therapy, are dose related, and are probably related to the cholesterol lowering per se! (Elevation of the serum aminotransferase [AST] levels can occur with either muscle or liver injury and is thus less specific than elevation of the ALT level.) In all of the 5-year, double-blind, placebo-controlled statin trials, no patient was permitted in the trial if his or her baseline ALT or AST was >3 times the upper limit of normal. When these trials were initiated, it was not appreciated that hepatitis C was common, and there are an estimated 3 million hepatitis C patients in the USA; that fatty liver, a cause of ALT elevation, was present in probably 50% of patients with diabetes mellitus, and there are an estimated 17 million diabetics in the USA; and that alcoholism can also alter hepatic enzymes, and there are probably 10 to 12 million habitual alcoholics in the USA. In other words, there are several causes for elevation of serum ALT. The danger for a patient with an elevated serum LDL cholesterol is arterial, not hepatic! Additionally, there is no evidence that statins further elevate ALT when the level of this enzyme is raised by another condition.

The requirement to do liver function tests in patients on statins needs to be removed from the package insert! If this were done, the money now used for tests for hepatic dysfunction could be applied to purchasing the drug, a malpractice worry would be removed, and both physicians and patients could quit worrying about potential liver damage. There is no logic in requiring liver function tests periodically for patients on statins but not for patients on fibrates or niacin. Television ads that call attention to the potential danger of statins to the liver frighten patients unnecessarily, and many patients appear to worry more about their liver than their arteries. This worry may be one reason why about 50% of patients on statins discontinue them in 1 year.

The only major concern of statin therapy is *myopathy,* and that occurs in about 1 in 10,000 person-years, a risk multifold less than the consequences of accumulating atherosclerotic plaques in arteries. In contrast, the risk of myopathy for patients on a fibrate is nearly 7 per 10,000 person-years. For the general population not on either a statin or a fibrate, the risk is 0.2 per 10,000 person-years. Elevation (<3 times the upper limit of normal) of the serum creatine phosphokinase occurs in as many as 30% of dyslipidemic patients not taking lipid-lowering agents. The risk of myopathy is less than that of a major bleed in patients taking aspirin or a nonsteroidal antiinflammatory drug.

In summary, atherosclerosis needs to be viewed as a potentially preventable disease. Atherosclerosis needs to be discussed in terms of plaque prevention, not in terms of decreasing risk. That means that LDL cholesterol in all adults needs to be <100 mg/dL with HDL cholesterol as high as possible but at least >20 mg/dL when the total cholesterol is <150 mg/dL. If patients are started on the dose of statin that lowers the LDL cholesterol to <100 mg/dL *from the beginning*, this action will usually eliminate the need for statin titration. Eliminate baseline and periodic liver function tests because the evidence that statin therapy alters them is tenuous and the fright produced in patients from worry about their liver may play a role in their discontinuing statin therapy. Monitoring for hepatotoxicity is ineffectual in preventing serious liver disease and may increase the risk of atherosclerotic events because of needless discontinuation of cholesterol-lowering therapy for false-positive results in patients who are benefiting from statin treatment. And, finally, statin drugs decrease the frequency of not only coronary events but also stroke (by 30%).

(This piece in slightly different form also appeared in the September 15, 2002, issue of *The American Journal of Cardiology.* A full reference list is available in that piece.)

USEFULNESS OF AN ANTIDEPRESSIVE DRUG (SERTRALINE) FOR MAJOR DEPRESSION IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION OR UNSTABLE ANGINA PECTORIS

Approximately 20% of patients with acute coronary syndromes develop a major depressive disorder, and its occurrence constitutes an independent risk factor for morbidity and mortality. No published evidence has existed that antidepressant drugs are safe or efficacious in patients with unstable ischemic heart disease. To fill this void, Glassman and colleagues (9) from 40 outpatient cardiology centers and psychiatry clinics studied 369 patients with a major depressive disorder after acute myocardial infarction (74%) or unstable angina pectoris (26%). Patients were randomly assigned to receive sertraline in doses of 50 to 200 mg/day (n = 186) or placebo (n = 183) for 24 weeks. The incidence of severe cardiovascular adverse events was 14.5% with sertraline and 22.4% with placebo. These results suggest that sertraline is a safe and effective treatment for recurrent depression in patients with recent acute myocardial infarction or unstable angina.

OBESITY AND HEART FAILURE

Several studies have shown a relation between body mass index (BMI) and left ventricular hypertrophy and dilatation, known precursors of heart failure. Whereas extreme obesity has been associated with heart failure, data are limited regarding the influence of overweight and lesser degrees of obesity on the risk of heart failure. To fill this void, Kenchaiah and colleagues (10), primarily from Framingham, Massachusetts, investigated the relation between BMI and the incidence of heart failure among 5881 participants in the Framingham Heart Study. During follow-up (mean, 14 years), heart failure developed in 496 subjects. After adjustment for established risk factors, there was an increase in the risk of heart failure of 5% for men and 7% for women for each 1-increment increase in BMI. Compared with patients with a normal BMI (<25 kg/m^2), obese subjects (BMI >30 kg/m^2) had a doubling of risk of heart failure. Thus, a way to reduce the frequency of heart failure is to lose weight. On the basis of these findings, overweight, particularly obesity, should be added to the list of risk factors for the development of heart failure. This excess risk cannot be fully explained by accompanying conditions such as systemic hypertension, coronary artery disease, and diabetes mellitus.

BIVENTRICULAR PACING IN CHRONIC HEART FAILURE

In approximately 30% of patients with chronic heart failure, left ventricular contractility is depressed and there is a conduction delay in the onset of right or left ventricular systole. Such dyssynchrony is manifest in the electrocardiogram by the QRS interval's lasting >120 msec. The finding of an intraventricular conduction delay has been associated with clinical instability and an increased risk of death in patients with heart failure.

Devices that make use of atrial-synchronized biventricular pacing to coordinate right and left ventricular contraction have been developed, and early studies have suggested that cardiac function and quality of life can be improved by these devices (*Figure 1*). Abraham and colleagues (11) for the MIRACLE Study Group studied 453 patients with moderate to severe symptoms of heart failure associated with a left ventricular ejection fraction <35% and a QRS interval of >130 msec. Compared with the 225 patients in the control group, the 228 patients assigned

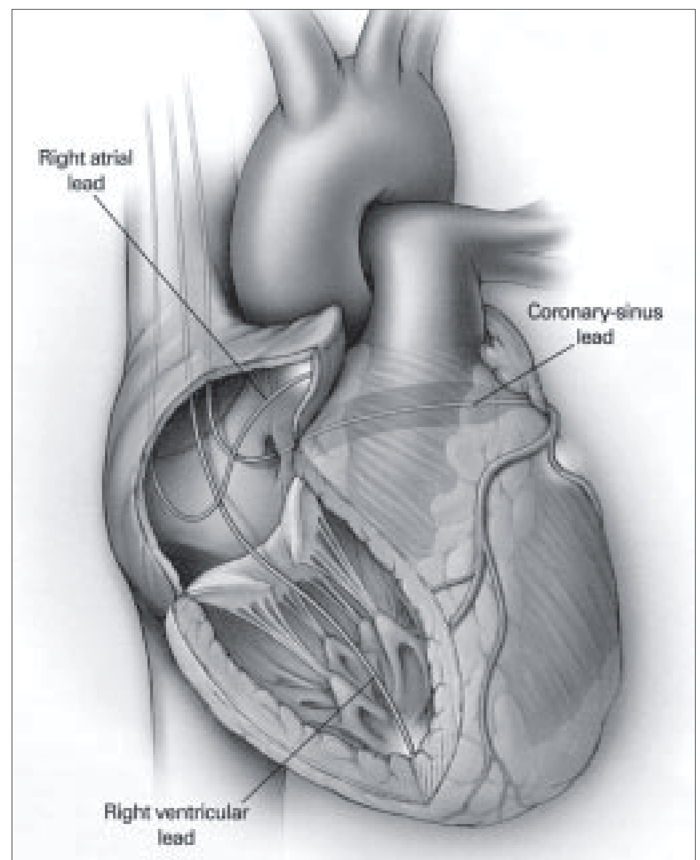


Figure 1. Placement of the 3 pacing leads for resynchronization therapy. Two leads allow pacing of the right atrium and right ventricle. The third lead is advanced through the coronary sinus into a venous branch that runs along the free wall of the left ventricle and allows early activation of the left ventricle, which would otherwise be activated late during the conduction. Reproduced with permission from Hare JM. Cardiac-resynchronization therapy for heart failure. *N Engl J Med* 2002; 346:1902–1905. Copyright © 2002 Massachusetts Medical Society. All rights reserved.

to cardiac resynchronization at 6 months had an improvement in the distance walked in 6 minutes (+39 meters vs +10 meters), functional class, quality of life, time on the treadmill during exercise testing (+81 seconds vs +19 seconds), ejection fraction (+4.6% vs –0.2%), hospitalizations (8% vs 15%), and intravenous medications for treatment of heart failure (7% vs 15%). Thus, resynchronization results in significant clinical improvement in patients who have moderate to severe heart failure and an intraventricular conduction delay.

These results are intriguing but also a bit frightening. It takes time to insert these catheters, particularly into the coronary sinus, and these devices are terribly expensive. And there are about 3 million people in the USA with chronic heart failure. If these devices were inserted in a large percentage of these patients, the medical care bank would soon be bankrupt.

RELIGIOUS INVOLVEMENT AND CIGARETTE SMOKING IN YOUNG ADULTS

Whooley and colleagues (12) from several US medical centers studied 4569 adults aged 20 to 32 years, including approximately equal numbers of blacks and whites and men and women, from 4 US cities to determine whether frequent attendance at religious services was associated with less cigarette smoking. A total of 4544 participants completed the tobacco questionnaire. Of those who attended religious services less than once per month, 34% were current smokers; among those attending 1 to 3 times per month, 30% were smokers; and of those attending religious services once per week or more, only 17% were smokers. The prevalence of smoking ranged from 12% among Jewish participants to 36% among Baptists. Overall, Baptists and Pentecostals who attended religious services less than once a month or never had the greatest prevalence of smoking. Jewish and Presbyterian participants had the lowest prevalence of smoking regardless of how frequently they attended religious services. Whether less smoking may explain part of the association between religious involvement and decreased mortality is unknown.

EXTENDED-RELEASE NIACIN FOR DYSLIPIDEMIA IN DIABETES MELLITUS

Use of high doses of niacin has been discouraged in patients with diabetes mellitus because of reported increased fasting blood glucose levels during therapy. The benefits of niacin for cardiac risk reduction, however, may outweigh any adverse consequences of a rise in fasting blood glucose levels. Extended-release niacin (Niaspan) is a prescription formulation for once-daily administration. The extended-release niacin provides lipid-modifying efficacy equivalent to that of intermediate-release niacin but with less flushing while avoiding the hepatotoxicity of other long-acting niacins. Grundy and associates (13) from several medical centers randomized 148 patients with type 2 diabetes mellitus to placebo or to 1000 or 1500 mg/day of extended-release niacin. Both niacin groups had sharp increases in high-density lipoprotein cholesterol levels (+19% to +24% vs placebo) and reductions in triglyceride levels (–13% to –28% vs placebo). The values at baseline and at the end of the 16-week study for glycosylated hemoglobin levels were insignificantly different in the 2 treatment groups and in the placebo group. Thus, extended-release niacin in doses of 1000 and 1500 mg/day alter lipid levels beneficially in patients with type 2 diabetes with relatively small effects on glucose control.

MORE ON GOOD AND BAD DIETS

Dean Ornish had a piece recently in the *New York Times* entitled “A diet rich in partial truths” (14). Ornish, whose hometown is Dallas, makes some good points. The high-protein diet is almost always high in fat, and although pounds can be lost on this kind of diet, the weight loss is usually temporary, blood flow to the myocardium is actually worsened, and heart disease may become more severe. The high-protein diet is correct in discouraging the eating of too many simple carbohydrates like sugar, white flour, and white rice because these foods are absorbed quickly, causing the blood glucose to spike, which in turn provokes an insulin response that accelerates the conversion of calories to fat. The solution is not to go from simple carbohydrates to pork rinds and bacon, but to go from simple carbohydrates to whole foods with complex carbohydrates like whole wheat, brown rice, fruits, vegetables, grains, and legumes in their natural forms. These foods also are naturally high in fiber, which slows their absorption and prevents a rapid rise in blood glucose. Fiber also fills before too many calories are consumed, whereas large amounts of simple sugar can be eaten without feeling full. Additionally, the complex carbohydrates contain at least 1000 substances that have anticancer, anti–heart disease, and antiaging properties, and this diet has been proven to reverse the progression of coronary artery disease in most people.

Ornish has convinced Medicare to pay for this latter diet in a pilot study involving 1800 patients, and he and his colleagues have shown not only that this diet is useful in preventing or slowing the progression of atherosclerosis but that it may stop or reverse the progression of early prostate cancer as well. The more closely people followed the diet, the more their heart disease reversed and the lower their prostate-specific antigen level became.

It’s not that fats are bad. Most of us simply eat too much of them. Fish oil and flaxseed oil are good for us because they provide the kind of fatty acids that can substantially reduce the incidence of atherosclerosis and also prevent some forms of cancer, but we need only a few grams a day. Because fat has more calories per gram than either protein or carbohydrates, when we eat less fat we consume fewer calories without having to eat less food.

ANTIBIOTICS IN LIVESTOCK

Senators Edward Kennedy and Jack Reed recently introduced a bill addressing the overuse of antibiotics in livestock (15). It is estimated that at least 50% of antibiotics used in the USA go to farm animals, mostly to animals that are not sick. The antibiotics are used mainly to promote growth and prevent diseases. Banning the nontherapeutic use of certain antibiotics in livestock as well as the use of all fluoroquinolones in poultry would help preserve these drugs for the needs of humans. The US Food and Drug Administration (FDA) first sought to ban certain antibiotics in animal feed decades ago, but Congress postponed rulings pending further research. The research is in. The World Health Organization and the American Medical Association now oppose the nontherapeutic use of antibiotics in nonhuman animals. The FDA process for removing drugs from agriculture use, however, can take years. The proposed legislation would help

speed the process by switching the burden to industry to prove that nontherapeutic use of certain important classes of drugs in animals would not compromise human health interests. The House companion bill is in the Committee on Energy and Commerce on which 3 Texans serve. This is important legislation.

E. COLI ON THE TABLETOP

Adachi and colleagues (16) from Houston, Texas, found *E. coli* organisms in 47 of 71 tabletop Mexican sauces in Guadalajara, Mexico, and in 10 of 25 tabletop sauces from Mexican restaurants in Houston, Texas. The median number of *E. coli* colonies per gram of sauce was 1000 in the Guadalajara sauces vs 0 in the Houston sauces. Among sauces tested from Guadalajara, 4 of 43 contained enterotoxigenic *E. coli,* and 14 of 32 contained enteroaggregative *E. coli*. Thus, avoid the tabletop sauces in Mexican restaurants in Guadalajara and be careful of those elsewhere.

WEST NILE

West Nile is a mosquito-borne virus that was unknown in North America until it appeared in New York City late in 1999 (17–19). It has spread across the Mississippi River to 37 other states and is expected soon to reach the West Coast. It is unclear why Louisiana, which has reported 85 human cases this year, has been hit so hard. Only 1 in 5 people who are infected have symptoms, and most suffer a mild fever that goes away after 3 to 6 days. One in 150 develop a serious illness. Although young people have developed the severe form during the present outbreak, the risk is greatest for people over age 50. There is no human vaccine and no antiviral medicine to treat it. In 1999, severe West Nile infection occurred in 62 patients and 7 died; in 2000, there were 21 serious cases and 2 died; in 2001, there were 66 severe cases and 9 died; and by mid-August 2002, there were 160 severe cases and 9 died.

The West Nile virus is mostly spread between mosquitoes and birds and can be transmitted to humans only under specific circumstances. An infected mosquito may transfer the West Nile virus to a bird when the insect feeds on it. Once the bird is infected, it can transmit the disease to mosquitoes for only 4 to 5 days. In that time, many birds migrate hundreds of miles. Another mosquito may feed on the bird's blood hundreds of miles from the first location and become infected with the virus. The infected bird can develop symptoms from the virus and die. The newly infected mosquito can pass on the virus when it feeds on a human.

Female mosquitoes feed on blood to get enough energy to lay eggs. The infected mosquito lays its eggs in still pools of water. An adult male mosquito lives 7 to 10 days; females may live >30 days. The mosquito usually stays within 1 mile of where it is hatched. Mosquitoes, of course, are most active from spring until late October and between dusk and dark. Mosquitoes are a food source for several animals, including fish, birds, and bats.

The following are some tips to protect oneself from mosquito bites. Stay indoors when mosquitoes are active, mainly dawn and dusk. Wear long-sleeved shirts and long pants when possible. Apply insect repellent, preferably those that contain DEET, to exposed skin. This chemical doesn't kill mosquitoes; it only repels them. Remove mosquito-breeding sites by emptying containers where standing water collects, such as old tires, buckets, gutters, and ditches. Repair screens. Put mosquito netting over infant carriers when outside.

THE INTESTINAL PILLCAM

Recently, Dr. Daniel C. DeMarco gave a splendid talk on the Given capsule at medical grand rounds. Each year >11 million people in the USA are tested for gastrointestinal ailments including inflammatory bowel disease, gastric ulcer, and cancer (20). The usual examinations involve a 3- to 9-foot-long endoscopic tube inserted through the mouth, nose, or anus. It can be painful, and sedation is usually required. Given Imaging of Israel has produced a far friendlier option: a camera swallowed like a pill (*Figure 2*). The manufacturer based its invention on missile research done for the Israeli military. In August 2001, the FDA cleared the Given capsule for use in spotting abnormalities in the small intestine. The capsule is swallowed, and as it moves down the digestive tract, its tiny camera snaps 2 pictures per second, about 50,000 in all. The capsule transmits the images to an 8-gigabyte hard drive worn on the patient's belt. Within a day or two, the pillcam is passed painlessly. The disk drive is plugged into a computer outfitted with software that assembles the images into an hour-long color video. These images can be frozen, rewound, e-mailed, or printed. The workstation and data recorder cost $20,000, and the capsule, $450. In contrast, a flexible endoscope can cost up to $35,000 plus $60,000 for the video equipment. The pillcam has some drawbacks. Its view angle is limited; it can't stop at trouble spots, as an endoscope can; and it can get stopped by a bowel obstruction.

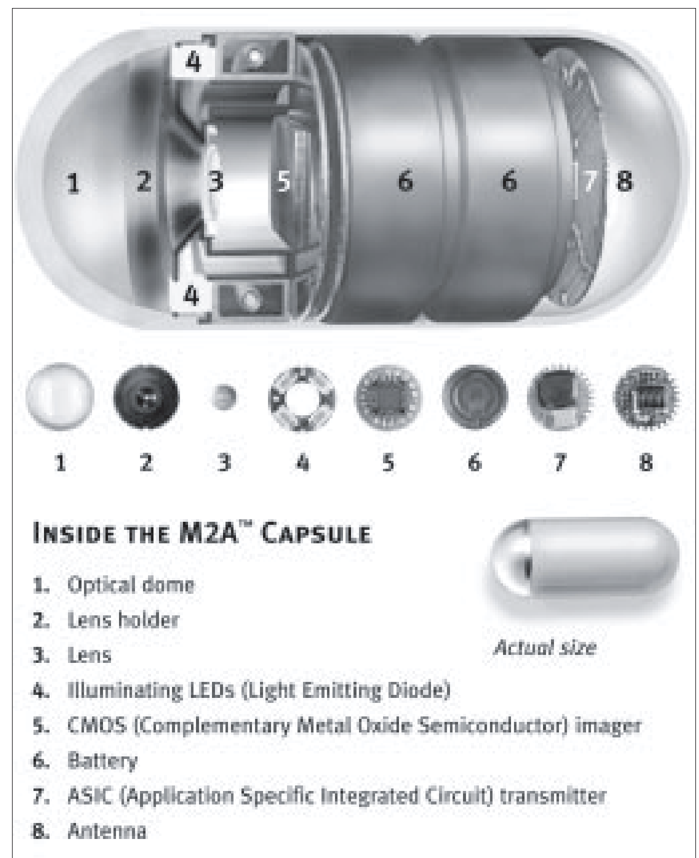


Figure 2. The Given capsule. Reproduced with permission from Given Imaging.

BOTULINUM-BASED DRUGS

Botox, Myobloc, and Dysport (available only in Europe) are 3 botulinum-based drugs now on the market (21). Botox was approved by the FDA for strabismus (crossed eyes) and for blepharospasm (excessive blinking of the eyes) in 1989, and in 2000, it was approved for cervical dystonia, a neck disorder that causes the head to be bent in an awkward position. Botox was approved by the FDA in April 2002 for "temporary improvement of the glabellar facial lines," meaning to relax the wrinkles normally found between the eyes.

The cosmetic effects of Botox were discovered by accident by an ophthalmologist, Dr. Carruthers, in Vancouver, Canada, who noticed that facial injections of Botox relaxed a patient's wrinkles. Only in 1999 did the manufacturer, Allergan of Irvine, California, get interested in the cosmetic side of the drug. The new demand for the drug for cosmetic purposes pushed sales to $310 million in 2001, and sales are projected to reach $420 million in 2002. The drug is also used for a number of unapproved indications, including migraine headache, involuntary facial tics, temporomandibular joint pain, chronic neck pain, spasmodic dysphonia, upper limb spasticity, axillary hyperhidrosis, equinus deformity (frozen feet), urinary incontinence, and lower back pain. Physicians, mainly plastic surgeons, dermatologists, and anesthesiologists, offer Botox injections for $350 to $500 per 100-unit vial, which is usually adequate for most cosmetic treatments. Pain management treatments, however, require larger amounts of the drug (several vials), pushing the cost to usually >$1000. Most treatments must be repeated several times a year. At present, insurance companies do not pay for treatment with this drug.

RELATION OF DEMAND FOR COSMETIC FACIAL PLASTIC SURGERY AND ITS COSTS

Alsarraf and colleagues (22) from Boston evaluated the relation between cosmetic facial plastic surgery prices and demand. Data were derived from a survey sent to every active fellow, member, or associate of the American Academy of Facial Plastic and Reconstructive Surgery (n = 1727) assessing the cost and frequency of 4 common cosmetic facial plastic surgery procedures (face lift, brow lift, blepharoplasty, and rhinoplasty for 1989 and 1999). They found a significant association between increasing surgical fees and total charges for cosmetic facial plastic surgery procedures and increasing demand for these procedures. The association of increased price with increased demand held for each of the 4 procedures studied, across all US regions, and for both periods surveyed. Thus, cosmetic facial plastic surgery procedures function as luxury goods in the marketplace. This observation stands in contrast to other traditional goods for which demand typically declines as price increases.

EFFECT OF HAND-RUBBING WITH AN AQUEOUS ALCOHOLIC SOLUTION VS TRADITIONAL SURGICAL HAND-SCRUBBING ON SURGICAL SITE INFECTION RATES

Surgical site infections increase morbidity and medical care costs. Parienti and colleagues (23) from Caen, France, compared 2 hand-cleansing methods—a hand-rubbing protocol with 75% aqueous alcoholic solution containing propanol-1, propanol-2, and mecetronium etilsulfate and a hand-scrubbing protocol with antiseptic preparation containing 4% providone iodine or 4% chlorhexidine gluconate—in 4387 patients. Fifty-five of 2252 patients (2.44%) in the hand-rubbing protocol had surgical site infections compared with 53 of 2135 (2.48%) in the hand-scrubbing protocol. Compliance with the recommended duration of hand antisepsis was better in the hand-rubbing protocol compared with the hand-scrubbing protocol. Further, surgeons experienced less skin dryness and skin irritation after using the aqueous alcoholic solution. Thus, hand-rubbing with aqueous alcoholic solution, preceded by a 1-minute nonantiseptic hand wash, was as effective as traditional hand-scrubbing with antiseptic soap in preventing surgical site infections.

FDA ADVISORY ON XENOTRANSPLANTATION

The FDA recently issued an advisory to remind physicians and clinical investigators that its definition of xenotransplantation includes any procedure that involves the transplantation, implantation, or infusion into a human recipient of human body fluids, cells, tissues, or organs that have had ex vivo contact with live nonhuman animal cells, tissues, or organs (24). The definition includes human embryos cocultured with living nonhuman animal cellular material, such as bovine tubal cells or Vero cells, and includes feeder layer cells irradiated to render them nonproliferative.

The clinical use of xenotransplantation raises serious concern about potential transmission of infectious disease from nonhuman animals to humans. This potential exists when live animal cells, tissues, or organs are implanted directly into a human or when human cells are exposed to live animal cells by ex vivo contact. These concerns may extend beyond the recipient because of the potential for subsequent transmission of an infectious agent to the general population. Infections originating from animals that have been known to infect and be transmitted among humans include HIV and swine influenza. Since any virus can be latent, the lack of symptoms at the time of embryo transfer, or in the short term, does not alleviate all concern.

EFFECT OF MANDATORY PARENTAL NOTIFICATION ON ADOLESCENT GIRLS' USE OF SEXUAL HEALTH CARE SERVICES

Mandatory parental notification for adolescents to obtain prescribed contraceptives is a controversial issue. Recently, legislation that would prohibit prescribed contraceptives for adolescents without parental involvement was introduced in 10 states and in the US Congress. Reddy and associates (25) studied girls <18 years old who sought services at all 33 Planned Parenthood family planning clinics in Wisconsin (n = 118) in 1999, and 85% responded. Nearly 60% indicated they would stop using all sexual health care services, delay testing or treatment for HIV or other sexually transmitted diseases, or discontinue use of specific sexual health care services if their parents were informed that they were seeking prescribed contraceptives. Thus, mandatory parental notification for prescribed contraceptives would impede girls' use of sexual health care services, potentially increasing teen pregnancies and the spread of sexually transmitted diseases.

HAROLD SHIPMAN, MD

Until 1998, Dr. Harold Shipman was a solo general practitioner in Hyde, United Kingdom, a working-class town of 22,000 people located just outside of Manchester. Dr. Shipman had

>3000 patients. An official inquiry into his actions has revealed that Dr. Shipman was responsible for the deaths of at least 215 people, most of them elderly patients, and possibly an additional 45 more (26, 27). The investigators believe that Dr. Shipman began killing patients, most often using injections, for unexplained reasons in 1975 shortly after he began to practice medicine. His murderous ways were undetected for years, and he was able to practice medicine despite being fined for becoming addicted to painkillers and illegally using patients' prescriptions to obtain drugs for himself. Despite the unusually high number of deaths occurring among his patients and the fact that a number of them died while in his office, law enforcement officials and medical authorities did not become suspicious of his activities until 1998. Publicity surrounding his arrest for murdering an elderly patient prompted a number of bereaved relatives of other patients to tell authorities that their loved ones might have been murdered as well. Investigators quickly found a pattern of elderly patients dying from unexplained causes. Some died after they were injected with large doses of heroin; others were killed with high doses of painkillers that the doctor obtained in unusually large quantities. His youngest victim was 41 and the oldest, 93. Why Dr. Shipman killed was not determined during his trial. He will be in jail the rest of his life.

PARAPLEGIC SWIMS THE ENGLISH CHANNEL

In 1982 at the age of 11, Jason Pipoly of San Antonio, Texas, tried to become the youngest person ever to swim the English Channel. At that time, cold weather and the threat of hypothermia forced him out of the water 5 miles short of his goal. In 1998, a back injury from an automobile accident left him paralyzed from the chest down. That did not prevent him, however, from swimming the channel from Dover, England, to Cap de Gris Nez, France, on August 18, 2002 (28). During the swim he got terribly sleepy; he hadn't slept well the previous night because of a noisy wedding party in his hotel. During the 21-mile, 13-hour, 48-minute swim, he encountered schools of jellyfish, slicks of diesel fuel, and islands of floating trash across the choppy waters.

"PET OWNERS" TO "PET GUARDIANS"

Owners of pets in Rhode Island and in 7 other cities including Los Angeles have recently changed the phrase "pet owners" to "pet guardians" as a way to raise consciousness and prosecute people inclined to view their animal companions as disposable goods (30). This change also raises the legal status of pets such that courts might view animals as something more akin to humans rather than property. If a pet can have a guardian then the guardian can be removed for not doing his or her job and another guardian can be appointed to speak for the pet. In 2001, Tennessee became the first state to permit owners of pets who are killed to sue for emotional damages. At least 13 law schools offer courses in animal law.

TEN COMMANDMENTS FOR RESPONSIBLE PET GUARDIANS

These commandments are as follows (30):

1. My life is likely to last 10 to 15 years. Any separation from you will be painful.
2. Give me time to understand what you want of me.
3. Place your trust in me; it is crucial for my well-being.
4. Don't be angry with me for long, and don't lock me up as punishment. You have your work, your friends, your entertainment. I have only you.
5. Talk to me. Even if I don't understand your words, I understand your voice when it's speaking to me.
6. Be aware that however you treat me, I'll never forget it.
7. Before you hit me, remember that I have teeth that could easily crush the bones in your hand, but I choose not to bite you.
8. Before you scold me for being lazy or uncooperative, ask yourself if something might be bothering me. Perhaps I'm not getting the right food, I've been out in the sun too long, or my heart may be getting old and weak.
9. Take care of me when I get old. You, too, will grow old.
10. Go with me on difficult journeys. Never say, "I can't bear to watch it" or "Let it happen in my absence." Everything is easier for me if you are there. Remember, I love you.

THE KING OF CLUBS

Robert H. Dedman, Sr., died on August 20, 2002, at the age of 76 (31). He founded ClubCorp Inc. and built it into a $1.7 billion enterprise after acquiring the land for Brookhaven Country Club in 1957. By collecting golf courses and clubs into one company, he broadened the golf and country club market for more than just the wealthy elite. He became a very wealthy man who was generous with his money, giving it mainly for education (at Southern Methodist University, the University of North Texas, and the University of Texas at Austin), and health (University of Texas Southwestern Medical Center at Dallas, Zale Lipshy University Hospital, RHD Memorial Medical Center). In his 1999 autobiography, *King of Clubs: Grow Rich in More Than Money*, Dedman provided "10 rules of order":

1. A sense of balance must apply to all areas of your life, not just your livelihood.
2. It's so important in life to have a life plan. Planning is a prelude to balance.
3. The more you learn, the more you earn. Even more importantly, the more you learn, the more you live.
4. A positive mental attitude is a key ingredient to a balanced, long, and happy life.
5. Humor is one of the best ways to get and keep a positive mental attitude. When times get tough, humor helps . . . even sick humor.
6. It's nice to be important but even more important to be nice.
7. Setting up "win-win" relationships is the ultimate measure of success in life . . . and in business.
8. Be a giver, not a taker. They don't put luggage racks on hearses for a good reason.
9. Integrity, good health, family, and friends are worth more than anything money can buy.
10. Don't forget to have fun. The more fun you have, the more money you make. It works both ways. The more money you make, the more fun you have.

MEDICARE AND PAYMENTS TO PHYSICIANS

The Centers for Medicare and Medicaid Services (CMS) reduced Medicare fees for physicians by an average of 4.9%, and that edict took effect on January 1, 2002 (32). Congress and the

Table. Logistic regression results for "very satisfied," ranked from high to low odds ratio*

Specialty	Odds ratio	Lower 95% confidence limit	Upper 95% confidence limit
Geriatric internal medicine	2.04	1.19	3.49
Neonatal and perinatal medicine	1.89	1.04	3.42
Infectious diseases	1.49	0.79	2.81
Dermatology	1.48	1.01	2.15
Pediatrics	1.36	1.21	1.53
Other specialty (n < 40)	1.27	1.05	1.53
Allergy and immunology	1.21	0.69	2.10
Medical oncology	1.14	0.73	1.80
Endocrinology and metabolism	1.11	0.65	1.90
Cardiothoracic and thoracic surgery	1.08	0.67	1.73
Nephrology	1.06	0.64	1.74
Pediatric psychiatry	1.03	0.66	1.61
Occupational medicine	1.02	0.62	1.67
Urology	1.01	0.71	1.43
Family practice†	1.00	. . .	. . .
Rheumatology	1.00	0.62	1.60
Emergency medicine	0.91	0.73	1.13
Orthopaedic surgery	0.89	0.69	1.16
Psychiatry	0.88	0.72	1.09
Neurological surgery	0.87	0.49	1.53
Neurology	0.87	0.60	1.25
Cardiovascular disease—cardiology	0.86	0.65	1.13
General surgery	0.85	0.67	1.08
Plastic surgery	0.85	0.54	1.34
General practice	0.84	0.64	1.10
Physical medicine and rehabilitation	0.80	0.49	1.30
Internal medicine	0.80	0.69	0.92
Ophthalmology	0.75	0.60	0.94
Gastroenterology	0.73	0.54	0.98
Otolaryngology and rhinolaryngology	0.70	0.50	0.98
Obstetrics-gynecology	0.63	0.52	0.76
Pulmonary diseases	0.61	0.43	0.86
Gynecology	0.42	0.20	0.88

*Reproduced with permission from reference 34. Additional covariates in the model include age, board certified, foreign medical school graduate, female sex, percentage of revenue from managed care, region of practice, rural/town (population <200,000), income, increased work hours in previous week, full owner, and part owner.

†Comparison group.

Bush administration have been unwilling to fix this pay reduction for the 550,000 physicians who provide care to the program's 39 million disabled or elderly beneficiaries. In contrast, the president's budget includes major spending increases for the military, homeland security, and the National Institutes of Health but suggests only that Congress "smooth out adjustments in the [Medicare] physician update system in a budget-neutral manner." Come on, Mr. President.

MEDICARE DRUG BENEFIT

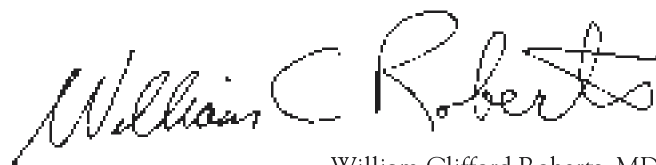
In June 2002, the Republican-controlled House of Representatives passed the Medicare drug benefit bill by a vote of 221 to 208 (33). Beginning in 2005, the plan would have subsidized drug purchases for those >65 years at an estimated cost of $320 billion for the first 8 years. The Democrat-controlled Senate wanted a more expensive plan whose projected cost would have exceeded $400 billion in fewer years.

When Congress created Medicare—federal health insurance for those >65 years—in 1965, coverage was modeled after private insurance plans. Typically, drugs were not paid for. Since then, a pharmacological revolution has increased the importance of drugs, and private insurance has expanded. As a result, Medicare is outdated. In 1999, about 38% of people over age 65 had no insurance coverage for drugs, and the remaining 62% had some coverage through company-sponsored retiree insurance and a hodgepodge of government programs. For retirees, drug costs averaged $584 in 1999 for those without insurance. One estimate puts out-of-pocket costs for drugs as high as $1052 in 2002. Even by these figures, 68% of recipients have costs of <$1000 and only 9% have costs >$3000.

At present, the government-sponsored retirement benefits—mainly Social Security, Medicare, and Medicaid—constitute almost 8% of the gross domestic product. By 2030 this figure will reach 14%. A drug benefit would bloat costs further. Social Security and Medicare are pay-as-you-go programs supported by current taxes. Federal spending now is nearly 20% of the gross domestic product. Paying for future retirement costs, even without a drug benefit, will require steep tax increases, deep cuts in other spending from defense to schools, larger budget deficits, or combinations of these. The simple truth is that the country cannot afford Medicare drug benefits.

PHYSICIAN CAREER SATISFACTION AMONG VARIOUS SPECIALTIES

Leigh and colleagues (34) from California analyzed data from 12,474 physicians in the late 1990s asking them whether they were either "very satisfied" or "dissatisfied" with the specialty that they had chosen. The mean age of the physicians surveyed was 48 years. Nearly 80% were board certified, 20% were graduates of foreign medical schools, and 20% were women. The physicians spent an average of 55 hours a week working. The *Table* shows the results. After controlling for work hours, income was among the most important predictors of being "very satisfied." Those with the highest satisfaction were the physicians in geriatric internal medicine, neonatal-perinatal medicine, dermatology, and pediatrics. The most dissatisfied physicians included those in otolaryngology and rhinolaryngology, obstetrics-gynecology, ophthalmology, orthopaedic surgery, and internal medicine.



—William Clifford Roberts, MD

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