Alzheimer's
Searching for a Cure
Joint FDA, NCI Program to Streamline Drug Development
The National Cancer Institute has joined with the FDA to benefit the more than 1 million Americans diagnosed with cancer each year.

FDA’s Response to Food, Dietary Supplement, and Cosmetic Adverse Events
The FDA is encouraging consumers to report problems with food and cosmetic products as part of an agency-wide initiative.

SARS: Protecting Against a Deadly Disease
Federal agencies are working to prevent the spread of an emerging infectious disease threat.

Cover Story
Alzheimer’s: Searching for a Cure
Researchers hold out hope for preventing and treating this devastating disease.

Hispanic Health: Renewed Collaboration
The FDA renews its commitment to help Hispanic consumers achieve good health.

FDA Works to Reduce Preventable Medical Device Injuries
More than 100,000 reports of preventable adverse health events involving medical devices come to the FDA each year. Reducing that number is a top priority for FDA Commissioner Mark B. McClellan.

FDA, Red Cross Reach Agreement to Improve Blood Safety
The American Red Cross signs a consent decree with the FDA to improve its blood storage practices and record keeping.

Speedy Approvals for New Cancer Treatments
The FDA approves drugs for lung cancer and bone marrow cancer.

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A boy wears a surgical mask as a precaution against severe acute respiratory syndrome in Hong Kong. For more on this deadly flu-like illness, see page 14.
In 1907, Alois Alzheimer, a German neurologist known for his efforts to unravel the mysteries of mental illness, described the case of a 55-year-old woman with severe memory loss, language problems, paranoia, agitation and difficulty moving.

Alzheimer examined the woman's brain tissue after her death. He found accumulations of protein that have since become the markers of a cruel disease that starts with simple forgetfulness and progresses to severe mental decline and death.

Alzheimer, known for his ability to teach and to express complex material simply through words and drawings, stressed the need to study the physiology of the brain in order to grasp the psychiatric implications.

A century later, scientists are making use of the latest imaging technologies to unlock the secrets of Alzheimer's disease and are looking into its potential prevention. For example, high levels of intellectual and physical activity seem to reduce the risk of Alzheimer's. Research continues on a number of fronts, including causes, treatments, risk factors, and identifying the disease in its early stage with an eye toward improving outcomes.

An estimated 4 million Americans have Alzheimer's, with about 360,000 new cases reported each year. More women than men are affected. In upcoming decades, the number of people with Alzheimer's and the cost of caring for Alzheimer's patients are likely to skyrocket with the aging of the baby boomer generation. For more on this devastating disease that poses a huge emotional and financial burden on those who have the disease and their families, see our cover story titled "Alzheimer's: Searching for a Cure," beginning on page 18.

According to the Institute of Medicine, over 1 million Americans are injured each year in adverse events involving medical products. In 2002, the FDA received reports of 111,000 adverse events, including deaths and serious injuries, related to medical devices.

The FDA regulates nearly 2,000 categories of medical devices, ranging from latex gloves to heart pumps. The FDA is working to design its regulatory requirements so that manufacturers keep the needs of patients and other users in mind during the design process. For more on the agency's efforts to protect consumers who use medical devices, see our feature article, "FDA Works to Reduce Preventable Medical Device Injuries," beginning on page 28.

More than 1 million Americans are diagnosed with cancer each year. Two federal agencies—the National Cancer Institute and the FDA—recently announced a collaboration of researchers and regulators aimed at speeding the delivery of new cancer drugs to patients who need them. For more on the joint effort, see our article beginning on page 11.

We also take a look at the renewal of an effort to improve the health of Hispanics and an agreement by the American Red Cross to improve the way it stores and keeps track of blood.

Ray Formanek Jr.
Editor

'To the Editor'

'Poison' versus 'English' Ivy

I have a question about your very informative article, “Outsmarting Poison Ivy and Its Cousins” in the September 1996 FDA Consumer (www.fda.gov/fdac/features/96_ivy.html).

I am sensitive to poison ivy. I understand that English ivy does not contain urushiol, but when I touch English ivy I get the same miserable reaction as with poison ivy. This happens even when there is no poison ivy in the area, or on anything that I have knowingly come in contact with.

I do wear plastic gloves when around English ivy. What else can I do to stop or reduce this sensitivity to English ivy? Since it is not the urushiol causing the reaction with English ivy, would the cleaning routine you recommend for poison ivy (washing with rubbing alcohol, water alone, then soap and water) also help with my reaction to English ivy?

Wade Shuford
Conover, N.C.

Jill Lindstrom, M.D., a medical officer in the FDA's Division of Dermatologic and Dental Drug Products, replies:

It is possible for English ivy to cause a contact dermatitis similar to a poison ivy rash. The same preventive measures would be recommended when a sensitive person comes in contact with English ivy as with poison ivy. However, according to current recommendations, washing the skin with regular soap and water and removing and laundering clothing should be sufficient. Rubbing alcohol isn't likely to add any benefit, and may be irritating to the skin. Note that, because the reaction starts so soon after contact, these measures need to be taken within 10 minutes of contact to be completely effective.
Breath Test Monitors Asthma

Doctors now have another tool to evaluate the response of their asthma patients to treatment with anti-inflammatory drugs. In May, the FDA cleared the NIOX Nitric Oxide Test System, a first-of-a-kind non-invasive system that measures the concentration of nitric oxide in exhaled human breath. A decrease in exhaled nitric oxide concentration suggests that anti-inflammatory treatment may be decreasing asthma-related lung inflammation. The lungs of people with asthma become inflamed and constrict, limiting airflow and making it hard to breathe. The disease affects about 15 million Americans.

With the NIOX system, patients use a mouthpiece that is connected to a computer by a breathing tube. The patient inhales nitric oxide-free air to total lung capacity and then exhales slowly into the mouthpiece. The nitric oxide concentration is displayed immediately on the computer screen.

The FDA cleared the NIOX system based on clinical studies of 65 patients—adults and children ages 4 and older with confirmed diagnoses of asthma. The patients were tested with the NIOX system before they began drug treatment and again two weeks later. Results showed that most patients had a 30 percent to 70 percent decrease of nitric oxide levels after two weeks of treatment with inhaled steroids.

The NIOX system is made by Aerocrine AB of Stockholm, Sweden.

Recall of Counterfeit Lipitor

The FDA is urging health care providers and people who take the cholesterol-lowering drug Lipitor (atorvastatin) to examine labels on the drug carefully following reports of counterfeit versions of the drug.

In May, Albers Medical Distributors Inc. recalled three lots of 90-count bottles of Lipitor. The company warned that these lots represent a potentially significant risk to consumers. The product was repackaged by Med-Pro Inc. of Lexington, Neb.

The lots in that recall were:
- 20722V—90-tablet bottles, 10 mg, Expiration 09-2004
- 04132V—90-tablet bottles, 10 mg, Expiration 01-2004
- 16942V—90-tablet bottles, 10 mg, Expiration 09-2004

The labels say "Repackaged by: MED-PRO, INC., Lexington, NE 68850."

Anyone who has Lipitor with these lot numbers should not take it and should return the product to the pharmacy where it was purchased. Many people who take Lipitor do not receive it in the 90-tablet bottles being recalled, but in smaller quantities from their pharmacists.

People taking Lipitor who have questions about their product should check with their pharmacists.

The FDA is working closely with Pfizer Inc., the manufacturer of Lipitor, as well as with health professionals on this counterfeit problem.

In carrying out its public health mission, the FDA regularly conducts investigations and testing to identify and remove products from the market that are counterfeit, have been tampered with, or are otherwise unsuitable. The FDA's Office of Criminal Investigations (OCI) continues to investigate the matter.

In April, the Pharmaceutical Research and Manufacturers of America, a trade association representing pharmaceutical and biotechnology companies, announced that its members would notify the FDA of suspected counterfeit cases within five working days as part of a voluntary program to combat the practice.

New Drug Helps Relieve Chemotherapy-Related Symptoms

Chemotherapy is often distressing for cancer patients due to the debilitating nausea and vomiting associated with the treatment. The symptoms can even cause patients to refuse further chemotherapy treatments. A new drug, recently approved by the FDA, can help prevent these symptoms when used in combination with other anti-nausea and anti-vomiting drugs.

Emend (aprepitant) is the first approved therapy that prevents the nausea and vomiting that many patients experience more than 24 hours after receiving chemotherapy.

Emend is given along with two other drugs for three days, starting just before a chemotherapy treatment is administered. It reduces nausea and vomiting in a new way—by blocking brain receptors called NK1 receptors. Emend can reduce nausea associated with chemotherapy treatments for cancers such as lung cancer, head and neck cancer, and some female cancers.

Over 1,000 people with cancer were studied while taking Emend, manufactured by Merck & Co. Inc., of Whitehorse Station, N.J. Fewer patients had symptoms of nausea and vomiting when the new drug was part of their treatment, compared with patients receiving standard medicines.
First Treatment for Fabry's Disease

The FDA has approved Fabrazyme (agalsidase beta), the first treatment for people with Fabry's disease. This serious genetic metabolic disorder affects about 1 in 40,000 men. Though it is believed that fewer women suffer the most serious consequences of the disease, they can also be seriously affected.

Because of a deficiency in the enzyme alpha-galactosidase A, Fabry's disease causes certain fats to accumulate in the blood vessels over many years, damaging various tissues and organs such as the kidneys and heart. As a result, people with Fabry's disease often must cope with significant pain and disability, and they typically have a shortened life span.

Fabrazyme is a version of the human form of the natural enzyme produced by recombinant DNA technology. When given intravenously, this replacement of the missing enzyme reduces a particular type of fat accumulation in many types of cells, including blood vessels in the kidneys and other organs. It's believed that this reduction of fat deposition will prevent the development of life-threatening organ damage.

The FDA approved Fabrazyme in April under an early approval mechanism. This policy accelerates approval for therapies that treat serious or life-threatening illnesses when studies indicate that early favorable outcomes are likely to predict clinical benefit. In this case, the manufacturer of Fabrazyme, Genzyme Corp. of Cambridge, Mass., performed biopsies looking at the cells lining the blood vessels within the kidneys and other organs in people with Fabry's disease. Many of the cells examined have shown significant clearance of fat deposits. Genzyme has committed to continue its clinical trial to verify Fabrazyme's benefit, and has set up a voluntary patient registry to follow the long-term progress of people treated with Fabrazyme.

New Regimen for Kidney Transplants

More than half of all new kidney transplant patients could potentially benefit from a newly approved drug regimen. The FDA has revised the labeling for Rapamune (sirolimus)—an anti-rejection medication—to allow new kidney transplant patients at low to moderate risk of organ rejection to stop taking cyclosporine two to four months after transplantation. By substituting higher levels of Rapamune for cyclosporine, it is hoped that kidney function will improve.

Currently, all kidney transplant patients are treated with a combination of medications that "turn off," or suppress, the body's immune response so that it will not reject the new organ. Three or more drugs, such as cyclosporine and steroids, are typically used. The revised labeling for Rapamune is the first approval of a cyclosporine-sparing regimen for new kidney transplant patients.

The combined use of Rapamune and cyclosporine may carry long-term risks to the transplanted kidney's function, but the newly approved regimen using higher levels of Rapamune may help kidney transplant patients get off cyclosporine sooner without increased risk of organ rejection. Stopping the use of cyclosporine earlier is likely to be associated with improved kidney function.

In 2000, the year the most recent statistics are available, there were more than 14,000 kidney transplants in the United States, according to the National Institute of Diabetes and Digestive and Kidney Diseases. Wyeth-Ayerst Pharmaceuticals Inc. of Philadelphia is the sponsor of the approved new drug application for Rapamune.

Treatment for Growth Hormone Disorder

Acromegaly, a potentially life-threatening disease triggered by an excess of growth hormone, causes headaches, profuse sweating, swelling, joint disorders, changes in facial features, and enlarged hands, feet, and jaw. If untreated, people with acromegaly often have a shortened life span because of heart and respiratory diseases, diabetes, and cancer.

The FDA recently approved Somavert (pegvisomant) to treat the condition. The drug is the first in a new class of drugs called growth hormone receptor antagonists. Somavert is approved for people who have not responded adequately to existing therapies. The most commonly reported side effects with Somavert in clinical trials were injection site reactions, sweating, headache, and fatigue. People should have tests to monitor liver function during the first six months of therapy.

Somavert will be marketed by Pfizer Inc. of New York City.
Improving Product Safety Through Data Mining

A recently established partnership will bolster the FDA’s ability to use the best science and the latest technology available to improve risk management of marketed products. The FDA has established a cooperative research and development agreement (CRADA) with Lincoln Technologies Inc. of Wellesley Hills, Mass. The purpose of this partnership is to use “data mining” to enhance the FDA’s ability to monitor the safety of drugs, biologics and vaccines after they have been approved for use.

Data mining is a technique using modern computing and statistical algorithms to extract meaningful, organized information from large, complex databases. Under the CRADA, the technique will be applied to data that the FDA already collects about adverse events involving approved drugs, biologics and vaccines. The specific data set used for data mining purposes does not include patient names, addresses, Social Security numbers or similar information.

Data collected from millions of suspected drug-related adverse event reports and other electronic medical information could aid the FDA in identifying “signals” of adverse events and the patterns in which they occur. With more effective tools to detect such patterns, the FDA can act faster to evaluate and respond to these reports. For example, effective data mining would allow the agency to identify a pattern of adverse drug events in a specific population, and the agency could then communicate this knowledge sooner to medical professionals and patients.

Expanded Use of Brain Implant

People who experience the sustained, simultaneous muscle contractions of the rare movement disorder called dystonia now have another treatment for the condition, which forces affected body parts into abnormal and sometimes painful postures and movements. The Activa Dystonia Therapy System, a brain implant already used to treat Parkinson’s disease and essential tremor, was approved by the FDA in April to treat dystonia. The deep brain stimulator is manufactured by Medtronic Inc. of Minneapolis.

The system consists of electrodes and a neurostimulator. The electrodes are implanted into the brain and connected by wires under the skin to a neurostimulator implanted in the chest. The neurostimulator sends a constant stream of tiny electrical pulses to the brain, which suppresses symptoms. When the device is implanted in both sides of the brain, two separate systems are used. Patients touch a hand-held magnet over the neurostimulator to switch the device on and off.

The most recent approval broadens the use of the device to people with primary dystonia who get little or no relief with medication. Primary dystonia has no known cause, unlike secondary dystonia, which is caused by an underlying disease such as Parkinson’s, a brain tumor, or a stroke. Results in patients using the device varied, and the specific benefit for an individual cannot be predicted. But because of the debilitating nature of dystonia and the lack of other effective treatments, the FDA has determined that the probable health benefit for people with primary dystonia who get no relief with medication outweighs the risk of illness or injury from the device.

The FDA approved the device through a special regulatory process known as a humanitarian device exemption, which is designed to encourage the development and marketing of medical devices for people with rare conditions.
First Treatment for Rare Enzyme Disorder

The first treatment for people with certain forms of a rare genetic disease called MPS I has been approved by the FDA. MPS I occurs when a particular enzyme is absent or malfunctioning in the body. The enzyme normally breaks down molecules called glycosaminoglycans (GAG) in the cells. People with MPS I have a buildup of GAG in the cells, resulting in progressive cellular damage that affects appearance, physical abilities, organ functions and, in some cases, mental development.

The new biotechnology product, Aldurazyme (laronidase), is a version of the deficient enzyme. Aldurazyme helps prevent the buildup of GAG in the cells and has been shown to improve lung function and exercise ability.

Aldurazyme is approved for people with the Hurler and Hurler-Scheie forms of MPS I as well as those with the Scheie form with moderate to severe symptoms. Hurler syndrome is the most severe of the MPS I forms. Children with Hurler syndrome often die early from respiratory diseases and cardiac complications. Hurler-Scheie syndrome is less severe, but people who have it usually do not survive beyond their early 20s. Scheie syndrome is the mildest form, with many patients living well into adulthood.

Studies in Canada indicate that 1 in 100,000 babies born has Hurler syndrome, 1 in 115,000 has Hurler-Scheie syndrome, and 1 in 500,000 has Scheie syndrome. Similar studies have not been done in the United States.

Aldurazyme is manufactured by BioMarin Pharmaceutical Inc. of Novato, Calif.

New Drug-Device Combination Helps Keep Arteries Open

The first stent containing a drug that prevents coronary arteries from becoming clogged again after angioplasty has been approved by the FDA. So-called drug-eluting stents that combine drugs with medical devices may have a substantial impact on the occurrence of reblockages in patients who have heart disease.

The Cypher Sirolimus-Eluting Coronary Stent, a tiny metal mesh tube covered with the drug sirolimus, provides a mechanical scaffold to keep an artery open, while the drug is slowly released from the stent to prevent the build-up of new tissue that can reclog arteries.

Each year, 800,000 angioplasty procedures are performed in the United States to open clogged coronary arteries. In about 15 percent to 30 percent of patients, the artery becomes clogged again (restenosis) within a year, and it must be treated again with a procedure such as angioplasty or bypass surgery. In studies conducted by the manufacturer, Cordis Corp. of Miami Lakes, Fla., the stent reduced the rate of restenosis by about two-thirds.

Patients who are allergic to sirolimus or to stainless steel should not receive a Cypher stent. The FDA also cautions those who have had recent cardiac surgery and women who may be pregnant or are nursing. Patients who receive the drug-eluting stent likely will be required to take certain kinds of anti-platelet drugs for at least several months.

The FDA is requiring Cordis to conduct a 2,000-patient post-approval study to assess the long-term safety and effectiveness of the Cypher stent and to look for rare adverse events that may result from using the product.

FDA Approves Gleevec for Pediatric Leukemia

Gleevec (imatinib mesylate) tablets were approved in May to treat children with Philadelphia chromosome positive chronic myeloid leukemia (CML)—a rare, life-threatening form of cancer that accounts for 2 percent of all leukemia in children. This marks the first approval of a new pediatric cancer drug in more than a decade.

Gleevec is indicated for children whose disease is in the chronic phase and has recurred after stem cell transplant or for those who are resistant to interferon alpha therapy.

The FDA originally approved Gleevec in 2001 for CML in adults. It was approved to treat gastrointestinal stromal tumors in February 2002.

“We hope to see more products developed that improve pediatric cancer care, and we are working to facilitate their development and timely approval,” FDA Commissioner Mark B. McClellan, M.D., Ph.D., said in announcing the pediatric approval.

The new treatment was evaluated under the FDA's accelerated approval program. Gleevec was cleared for use in children based on data from its use in adults with CML, combined with study results showing good responses in a small number of children. More studies will be done to confirm that the drug has improved survival or resulted in other clinical benefit for children.

The most frequently reported problems with the use of Gleevec are nausea, vomiting, diarrhea, swelling that can be severe (edema), and muscle cramps. A considerable reduction in white blood cells and platelets also was reported with Gleevec treatment. Gleevec can be given to children once a day, or the daily dose may be split in two—one in the morning and once in the evening.

Gleevec is manufactured by Novartis Pharma AG for Novartis Pharmaceuticals Corp. of East Hanover, N.J.
Rapid Test for Aspergillus Infection

A new test will allow doctors to diagnose a potentially life-threatening fungal infection sooner. Invasive aspergillosis infections occur in people with leukemia, people who have received organ and bone marrow transplants, and in people whose immune systems are compromised by illness or chemotherapy. Although the number of invasive aspergillosis cases is estimated to be only a few thousand per year, the disease is very serious and has a mortality rate of between 50 percent and 100 percent.

The FDA cleared the test, Platelia Aspergillus EIA, in May. The test detects Aspergillus galactomannan antigen in blood, and results are available in about three hours. By comparison, it takes at least four weeks before results are available with the standard culture method of testing for Aspergillus.

Clinical studies at three cancer centers showed the test could accurately identify the presence or absence of the Aspergillus antigen. The centers tested 1,890 blood samples collected from 170 people. Thirty-one patients had proven or probable cases of invasive aspergillosis. The new test correctly identified 25 of the 31 people who had aspergillosis. The Platelia test correctly identified 132 of the 148 as not having the antigen.

The Platelia Aspergillus EIA test is manufactured by Bio-Rad Laboratories of Hercules, Calif.

GERD Implant Approved

A permanently implanted device called Enteryx has been approved by the FDA to help people with the symptoms of gastroesophageal reflux disease (GERD). GERD is a condition in which some of the stomach’s contents—including acid—backs up (refluxes) into the esophagus, causing heartburn or burning pain in the chest or back of the throat. More than 60 million American adults experience GERD, and about 25 million of them have daily symptoms.

Inserted through a thin tube called an endoscope, the device prevents the reflux of stomach acid into the throat, potentially allowing people with chronic GERD to avoid taking medications daily.

Mild heartburn can be treated by adopting dietary changes such as avoiding foods that cause heartburn and eating smaller portions. Treatment of chronic GERD, however, may also require prescription drugs to help keep the acid secretion in the stomach at a reduced level.

Enteryx, a product of Enteric Medical Technologies of Foster City, Calif., a wholly-owned subsidiary of Boston Scientific Inc., is approved for use in people who have GERD symptoms and who require and respond to certain medications. The device, a solution made up of a polymer and a solvent, is injected during an X-ray guided procedure into the wall of the lower esophagus.

After the injection, the solvent separates away and the polymer solidifies into a spongy material that is intended to help prevent the reflux. The device has been found to eliminate or reduce the need for medications and to improve the symptoms of GERD. In a year-long study of 85 patients, about two-thirds were able to discontinue all of their medications, while a few (9 percent) could reduce their dosage by at least half. Most (72 percent) noted an improvement in their symptoms when compared with taking no medications prior to the implant.

Although most of those in the study had improvements in their symptoms and medication requirements, evaluations of the esophagus done during the clinical trial showed evidence of persistent acid reflux in 61 percent of participants and low-grade inflammation in 37 percent of participants at 12 months.

The most common side effect seen with the Enteryx treatment was pain beneath the breastbone that usually lessened within two weeks. Other common side effects included temporary difficulty with swallowing, fever, sore throat, and gas, bloating, and belching.

The device should not be used in people who are unable to undergo endoscopy, or who have dilated veins in the esophagus due to liver disease.

FDA Statement on Ensuring ‘Safe Food’

Efforts to ensure that the food Americans eat is safe are working, according to a report titled “Scientific Criteria to Ensure Safe Food,” released in April by the National Academy of Sciences. The report, sponsored by the FDA and the U.S. Department of Agriculture, reinforces that significant progress has been made in reducing and preventing foodborne illness.

The report specifically cited the adoption of the Hazard Analysis and Critical Control Point (HACCP) approach to food safety, which the FDA requires for seafood and fresh juice. The HACCP approach is voluntary in the dairy industry, which has shown some progress in improving the safety of its products.

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Labeling Changes for Cholesterol Drug

The FDA has announced labeling changes for Zocor (simvastatin), which the agency approved in 1991 to lower cholesterol. The new labeling reflects results of the Heart Protection Study (HPS), a clinical trial involving more than 20,500 people. This research showed that Zocor is effective in reducing risks of fatal and non-fatal heart attacks and strokes, and in reducing the need for bypass surgery and angioplasty.

In the study, men and women who have heart disease or are at high risk because of diabetes, peripheral arterial disease, or a history of stroke or other cerebrovascular disease, were treated with either Zocor or a placebo for an average of five years. The average age of patients entering the HPS was 64 and the average LDL-C (low density lipoprotein C or “bad” cholesterol) level at baseline was 131 milligrams per deciliter. The trial population included a large number of people with diabetes and older people.

The risk of death from coronary heart disease was reduced by 18 percent in those treated with Zocor. The risk of having a non-fatal heart attack was reduced by 38 percent in this group. Zocor also reduced the risk of stroke by 25 percent and reduced the need for undergoing procedures to unblock clogged arteries.

The effect of Zocor in reducing the rate of cardiovascular events was seen in a number of subpopulations of people enrolled in the trial, including those with and without heart disease or diabetes, and regardless of gender, age, or baseline cholesterol levels. An important observation was that people who had diabetes, peripheral vessel disease, and cerebrovascular disease, but who had no evidence of heart disease, benefited from taking Zocor. The drug has been shown to be effective in reducing total cholesterol and LDL cholesterol.

Zocor is one of a class of cholesterol-lowering drugs called statins. As with other statins, Zocor should be used with a standard cholesterol-lowering diet. The dose of Zocor should be determined according to the goals of therapy and the response to the drug. People taking this type of medication should also be aware of any muscle pain, which may indicate rhabdomyolysis, a muscle breakdown disorder. Symptoms can include fatigue, weakness, fever, nausea and vomiting, and severe muscle pain. The disorder can cause electrolyte imbalances that could result in heart rhythm problems, cardiac arrest, or heart attack.

Zocor is manufactured by Merck and Co. Inc. of Whitehouse Station, N.J.

New Guidelines Set Lower Mark for High Blood Pressure

The National Heart, Lung, and Blood Institute (NHLBI) has set a new “prehypertension” level of any reading above 120 over 80 mm Hg as part of its new guidelines for the prevention, detection, and treatment of high blood pressure. The new category affects about 22 percent of Americans, or 45 million people.

The guidelines, approved by the Coordinating Committee of the NHLBI’s National High Blood Pressure Education Program (NHBPEP), also streamlined the steps by which doctors diagnose and treat patients and recommend diuretics as part of the treatment plan for high blood pressure in most patients.

“We also now know that damage to arteries begins at fairly low blood pressure levels—those formerly considered normal and optimal,” NHLBI Director Claude Lenfant, M.D., said in announcing the guidelines. “In fact, studies show that the risk of death from heart disease and stroke begins to rise at blood pressures as low as 115 over 75, and that it doubles for each 20 over 10 millimeters of mercury (mm Hg) increase.”

The guidelines were prepared by a special NHBPEP committee representing 46 professional, voluntary, and federal organizations and were reviewed by 33 national hypertension experts and policy leaders. The NHBPEP issues new guidelines when warranted by scientific advances. The last guidelines were issued in November 1997.

Results of more than 30 clinical studies worldwide, many of which were funded by the NHLBI, were considered in revising the guidelines.

“These findings have been remarkably consistent in demonstrating the critical importance of lowering blood pressure, irrespective of age, gender, race, or socioeconomic status,” says Aram V. Chobanian, M.D., dean of the Boston University School of Medicine and chair of the committee that produced the guidelines. “The data allow us to create a set of recommendations that are easier to use than past guidelines, which should in turn make it easier for clinicians to treat their patients’ hypertension.”

High blood pressure is a major risk factor for heart disease and the chief risk factor for stroke and heart failure, and also can lead to kidney damage. It affects about 50 million Americans—1 in 4 adults.

Treatment seeks to lower blood pressure to less than 140 mm Hg systolic and less than 90 mm Hg diastolic for most people. Treatment for those with diabetes and chronic kidney disease aims to lower blood pressure to less than 130 systolic and less than 80 diastolic.

The guidelines include new data on U.S. control, awareness, and treatment rates for high blood pressure. According to a national survey, 70 percent of Americans with high blood pressure are aware of it, 59 percent are being treated for it, and 34 percent have it under control. Those percentages represent a slight improvement over the rates a decade earlier, when 68 percent of Americans were aware of their high blood pressure, 54 percent were being treated for it, and 27 percent had it under control.

"Though improved, the treatment and control rates are still too low," says Chobanian. "The guidelines stress that most patients will need more than one drug to control their hypertension and that lifestyle measures are a crucial part of treatment."

Another key factor is the need for health care providers to pay more attention to systolic blood pressure in people age 50 and older. "From midlife on, systolic hypertension is a more important cardiovascular risk factor than diastolic," Chobanian says.

Key aspects of the new guidelines include:

- A new "prehypertension" level and merging of other categories.

The new guidelines change the former blood pressure definitions to: normal, less than 120 mm Hg systolic and less than 80 mm Hg diastolic; prehypertension, 120-139 mm Hg systolic and 80-89 mm Hg diastolic; stage 1 hypertension, 140-159 mm Hg systolic and 90-99 mm Hg diastolic; stage 2 hypertension, at or greater than 160 mm Hg systolic and at or greater than 100 mm Hg diastolic.

The guidelines do not recommend drug therapy for those with prehypertension unless it is required by another condition, such as diabetes or chronic kidney disease. But the report advises them—and encourages those with normal blood pressures—to make any needed lifestyle changes. These include losing excess weight, becoming physically active, limiting alcoholic beverages, and following a heart-healthy eating plan, including cutting back on salt and other forms of sodium. The report also recommends that people quit smoking.

As in the 1997 guidelines, the new report recommends that Americans follow the DASH (Dietary Approaches to Stop Hypertension) eating plan, which is rich in vegetables, fruit, and non-fat dairy products. Clinical studies have shown that DASH significantly lowers blood pressure. The decreases are often comparable to those achieved with blood pressure-lowering medication.

The guidelines recommend use of a diuretic, either alone or in combination with another drug class, as part of the treatment plan in most patients. The report notes that even though many studies have found diuretics to be effective in preventing hypertension's cardiovascular complications, they currently are not being used sufficiently.

The guidelines also list other drug classes that have been shown to be effective in reducing hypertension's cardiovascular complications: angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, beta blockers, and calcium channel blockers. The report also gives the "compelling indications"—or high-risk conditions—for which such drugs are recommended as initial therapy.

- Use of additional drugs for severe hypertension or to lower blood pressure to the desired level.

Most people will need two, and at times three or more, medications to lower blood pressure to the desired level.

- The guidelines also recommend that clinicians work with patients on blood pressure goals and a treatment plan.

To raise awareness about the dangers of high blood pressure, the NHLBI is developing special Web pages and educational materials for health care professionals, patients, and the public. These include an updated "Your Guide To Lowering High Blood Pressure" Web page, which can be found at www.nhbpi.nih.gov/hbp.

"The bottom line is that Americans must change how they think about blood pressure," says Ed Roccella, M.D., NHBPEP coordinator. "The sooner they take action, the better. It's vital that they adopt a heart-healthy lifestyle early, even if their blood pressure is normal."
Strict glucose control in type 1 diabetes reduces the risk of atherosclerosis, a benefit that persists for years, according to a study published in the June 5, 2003, issue of The New England Journal of Medicine.

Since 1993, when the Diabetes Control and Complications Trial (DCCT) ended, researchers have known that intensive glucose control greatly reduces the eye, nerve, and kidney damage of type 1 diabetes. Now, researchers conclude, the benefits of tight control also extend to the heart.

"Intensive control is difficult to achieve and maintain, but its benefits are even greater than we realized," says study chair Saul Genueth, M.D., of Case Western University in Cleveland. "The earlier intensive therapy begins and the longer it can be maintained, the better the chances of reducing the debilitating complications of diabetes."

The DCCT was a multicenter study that compared intensive treatment with conventional management of blood glucose in 1,441 people with type 1 diabetes. Intensive treatment involves at least three insulin injections a day or an insulin pump and frequent self-monitoring of blood glucose. The goal of intensive treatment is to keep hemoglobin A1c (HbA1c), which reflects average blood sugar levels over 60 to 90 days, as close to normal (6 percent) as possible. Conventional treatment at the time of the DCCT consisted of one or two insulin injections a day with daily urine or blood glucose testing.

After six and one-half years of the DCCT, HbA1c levels averaged 7 percent in the intensively treated group and 9 percent in the conventionally treated group. When the DCCT ended, those who had been assigned to conventional treatment were encouraged to adopt intensive control and were shown how to do it. Researchers then began a long-term follow-up study of the participants, called the Epidemiology of Diabetes Interventions and Complications (EDIC) study.

The DCCT could not study atherosclerosis because the participants were relatively young, and heart disease takes years to develop. In 1994-1995 and again in 1998-2000, EDIC researchers used ultrasound to measure the thickness of participants' carotid arteries, the two blood vessels in the neck that carry blood from the heart to the brain. Carotid wall thickness reflects the amount of atherosclerosis, or plaque build-up, in the artery. The thicker the arterial wall the greater the risk of later heart attack and stroke.

At the time of their first ultrasound, the diabetic participants' carotid wall thickness was similar to that of non-diabetic controls matched for age and gender. Five years later, however, the participants had thicker arterial walls than those of the non-diabetic group. In addition, the thickness of the carotid walls had increased less in the intensively treated group during the five years than in the conventionally treated group. "This finding strongly suggests that atherosclerosis progressed more slowly in the intensively treated group," noted Genueth.

Carotid thickening was also linked to known cardiovascular risk factors, including age, higher systolic blood pressure, smoking, LDL to HDL cholesterol ratio, and urinary albumin (a measure of kidney function). After adjusting for these factors, the researchers found that the differences in carotid wall thickness between the two groups were due to the differences in blood glucose levels during the DCCT.

"Now we know that intensively controlled glucose significantly reduces the atherosclerosis underlying heart disease just as it reduces damage to the eyes, nerves, and kidneys in people with type 1 diabetes," says David Nathan, M.D., of Massachusetts General Hospital, who co-chaired the DCCT-EDIC research group. "What's striking is that the benefits of intensive control persisted, despite a gradual rise in the HbA1c levels of the intensively treated group during the five years after DCCT ended."

Diabetes prevention is a major initiative of the Department of Health and Human Services.

About 17 million people in the United States have diabetes. About 1 million have type 1 diabetes. Formerly known as juvenile onset or insulin-dependent diabetes, type 1 diabetes usually begins in children and adults under age 30.

Type 2 diabetes accounts for up to 95 percent of all diabetes cases. Most common in adults over age 40, type 2 diabetes affects 6 percent of the U.S. population. It is strongly associated with obesity (more than 80 percent of people with type 2 diabetes are overweight), inactivity, and family history of diabetes, and is higher in some racial or ethnic groups. The prevalence of type 2 diabetes has tripled in the last 30 years, due in large part to the upsurge in obesity.
The more than 1 million Americans who are diagnosed with cancer each year may soon benefit from a collaboration between the Food and Drug Administration and the National Cancer Institute (NCI).

"This new collaboration between two key HHS agencies means that federal researchers and regulators will be working together more effectively than ever before," says HHS Secretary Tommy G. Thompson. "The result will be a more unified, integrated, and efficient approach to the technology development and approval process at a critical time for a disease that affects too many lives."

Under an agreement announced in June, the FDA and the NCI, part of the National Institutes of Health, will share knowledge and resources to help develop new cancer drugs and speed their delivery to the people who need them. The agreement will enhance existing programs and add new joint programs to the current cooperative efforts of the two agencies, both part of the Department of Health and Human Services.

"The FDA is committed to finding better ways to get safe and effective treatments to patients with life-threatening diseases as quickly as possible," says FDA Commissioner Mark B. McClellan, M.D., Ph.D. "At a time when the opportunities to reduce the burden of cancer are greater than ever, sharing tools and resources with our colleagues at the National Cancer Institute will help us fulfill that mission," he says.

Areas in which the two agencies will collaborate include:
- Identifying biological responses (biomarkers) in the body that can be used to measure the effects of treatment to help evaluate new cancer medicines
- Addressing joint technology development issues, such as diagnostic imaging and molecular targeting
- Advancing the development and evaluation process for using natural or laboratory-made substances to prevent cancer (chemoprevention agents)
- Reviewing current policies to identify other ways in which FDA and NCI collaborations can enhance the development and regulatory process for cancer technologies
- Improving consumer awareness of choices about diet and nutrition and the consequences for cancer prevention
- Enhancing staff capabilities through collaborative training, joint rotations, and joint appointments.

The new partnership is an important step toward the NCI's goal to eliminate suffering and death due to cancer by 2015, as well as toward the FDA's goals of improving the availability and use of safe and effective treatments for cancer. "The bottom line is that this collaboration holds great promise for getting better cancer drugs to patients sooner," says NCI Director Andrew von Eschenbach, M.D. "Our job is to translate the promise of this unique collaboration into real benefit for patients as soon as possible."

For more information:
Food and Drug Administration
www.fda.gov
National Cancer Institute
www.cancer.gov

Cancer Incidence Among Americans

- The leading cancer in men, regardless of race, is prostate cancer, followed by lung/bronchus and colon/rectal. Prostate cancer rates are 1.5 times higher in black men than white men.
- The leading cancer in women, regardless of race, is breast cancer, followed by lung/bronchus and colon/rectal in white women, and colon/rectal and lung/bronchus in black women. Breast cancer rates are about 20 percent higher in white women than in black women.
- Melanomas of the skin and cancer of the testis are among the top 15 cancers for white men, but not black men.
- Melanomas of the skin and cancer of the brain/other nervous systems are among the top 15 cancers for white women, but not black women.
- Multiple myeloma (cancer that arises in plasma cells) and cancer of the stomach are among the top 15 cancers for black women, but not white women.
- Multiple myeloma and cancer of the liver are among the top 15 cancers for black men, but not white men.

Source: DHHS, U.S. Cancer Statistics: 1999 Incidence
FDA's Response to Food, Dietary Supplement, and Cosmetic Adverse Events

By Linda Bren

A child's throat swells up after she eats a piece of fruit. A man gets short of breath after he takes a dietary supplement. A woman gets an eye infection after she uses mascara. Are these allergic reactions? Effects of chemical properties or contaminants? Or just coincidences?

Determining the cause of incidents like these and helping to prevent their recurrence is the focus of a new system within the Food and Drug Administration's Center for Food Safety and Applied Nutrition (CFSAN).

This summer, the center is launching its CFSAN Adverse Event Reporting System (CAERS) to help track and monitor adverse events related to foods, dietary supplements, cosmetics, food additives, and color additives—the five types of products regulated by CFSAN.

CAERS is part of an agency-wide effort to improve the reporting of adverse events to the FDA. Information-gathering tools, data management, and collaborations with health care institutions are being used to improve the systems for reporting and tracking adverse events related to drugs, medical devices, blood products, vaccines, radiation-emitting products, and drugs for animals, as well as the products included in CAERS.

An adverse event is any illness or injury that may be associated with a product or ingredient. Adverse event reporting systems typically detect only a small proportion of the events that actually occur, according to an April 2001 report from the Health and Human Services Office of Inspector General. For example, according to one estimate, the FDA receives reports of less than 1 percent of all adverse events associated with dietary supplements.

CFSAN receives about 7,000 complaints each year concerning the products it regulates—only about half of these are actual adverse events involving illness or injury. "But 7,000 complaints volunteered by consumers is only the tip of the iceberg," says Kenneth Falci, Ph.D., director of CFSAN's Office of Scientific Analysis and Support.

For the most part, reporting adverse
events associated with foods, cosmetics, dietary supplements, and food and color additives is voluntary. “When consumers, health professionals and manufacturers are diligent in reporting, it helps the agency to better understand what events are occurring and what can be done to keep them from happening again,” says Falci.

Most of the adverse events and other product complaints currently being reported to the FDA come in through two routes: to complaint coordinators in the FDA’s district offices around the country, and through MedWatch, the FDA’s adverse event reporting program for medical products. “That’s the way it has always worked and these options of reporting events will continue,” says Falci. But CAERS will make a difference by quickly getting this information about reported events to the right people to analyze it. Complaint data received by telephone, mail, e-mail or fax will be entered into CAERS and electronically transmitted to safety reviewers at CFSAN. Medical records and other hard copy data will be scanned into CAERS and also transmitted electronically. Then the detective work can begin.

CFSAN medical personnel will investigate incidents and look for trends across multiple adverse event reports to help the agency determine the cause and the action needed. If one product is found to cause multiple adverse events, agency actions could result in the product’s recall, a consumer advisory, or regulatory action such as improved product labeling.

CFSAN’s initial action is to send a letter to the firm whose product is allegedly associated with an adverse event. In the case of a consumer death, the letter is sent within 24 hours of receiving an adverse event report. “We want to be transparent, open, and honest,” says Falci, and “let the company know we have received this information.” Letters will refer to a report from either a consumer or health care professional but will not provide names or other information that could be used to link the individual to the reported event.

A real-time reporting feature of CAERS will allow the FDA to use the system as a counterterrorism tool. The system is designed to scan and report information for similar occurrences around the nation, and to provide information that can be used to develop an early warning capability for foodborne illness and other adverse events. Even when an adverse event doesn’t signal a national security threat, “CAERS can enhance the ability of the agency to respond to consumer injury, in an appropriate manner, with all due haste,” says Falci.

Although CAERS is expected to improve the speed of reviewing and analyzing adverse events, Falci sees the new system as the genesis of an even better adverse event reporting system. “CAERS is the beginning of the exercise to improve food adverse event reporting throughout the nation,” he says. “The quality of the data reported in a voluntary system ranges from excellent to poor, as there is currently no standard way of reporting,” adds Falci. An improvement to CAERS may be the use of a standard questionnaire or form to encourage consistent reporting of events.

Kenneth Falci, Ph.D., leads the FDA’s efforts to respond to consumer injuries related to food, dietary supplements and cosmetics.

Reporting Adverse Events
Consumers can play an important public health role by reporting to the Food and Drug Administration any adverse events or other problems with FDA-regulated products.

Timely reporting allows the agency to take prompt action. Report what happened as soon as possible. Have the following information ready:

- Description of the adverse event
- Name, address, and phone number of the doctor or hospital if emergency treatment was provided
- Name of product and manufacturer
- Any codes or identifying marks on the product label or container
- Name and address of the store where you purchased the product and the date of purchase.

To report an emergency that requires immediate action, such as a case of foodborne illness or a drug product that has been tampered with, call the FDA’s main emergency number, staffed 24 hours a day: 301-443-1240.

To report a non-emergency adverse event, contact the FDA district office nearest you. Look up the FDA’s phone number under the Department of Health and Human Services in the blue U.S. government section of the telephone directory. Or check the phone numbers listed by state at www.fda.gov/opacom/backgrounders/complain.html.

Adverse events regarding medical products may also be reported to the FDA’s MedWatch program at 1-800-FDA-1088 (1-800-332-1088) or www.fda.gov/medwatch.

Also report the problem to the manufacturer or distributor shown on the product label and to the store where you purchased the product.
SARS Protecting Against a Deadly Disease

Chinese security guards wear masks to protect against the SARS virus as they patrol central Beijing in early June.

By Carol Rados

From Texas to Taiwan, people are taking precautions to protect themselves from a virulent respiratory illness that is sweeping some areas of the globe as readily as the common cold. Severe acute respiratory syndrome (SARS)—which has killed hundreds of people and sickened thousands—is causing people to don face masks, avoid traveling, wash their hands constantly, and call their doctors at the first sign of a sniffle.
SARS was first recognized in February 2003 after a sudden outbreak of unexplained pneumonia that affected people in China and several other Asian countries. Symptoms included coughing, fever and shortness of breath. More than 700 SARS deaths in 29 countries had been reported to the World Health Organization (WHO) by the first week of June. In the United States, a handful of SARS cases and no deaths had been reported through early June, according to the Centers for Disease Control and Prevention (CDC). So far, all of the SARS cases in the United States have been among travelers returning to this country from other parts of the world. Department of Health and Human Services Secretary Tommy G. Thompson says, "Cases in the United States have had relatively less severe manifestations of people also experience mild respiratory symptoms. After two to seven days, people with SARS may develop a dry cough and have trouble breathing. In 10 percent to 20 percent of cases, patients require the use of a ventilator to help them breathe. According to the CDC, SARS appears to be spread by close person-to-person contact. Potential ways include touching the skin of other people or objects that are contaminated with infectious droplets and then touching the eyes, nose, or mouth. Or the virus can be transmitted when someone who is sick with SARS coughs or sneezes droplets into the air and someone else breathes them in. It's also possible that SARS can be spread more broadly through the air, or by other ways that are currently unknown.

Recent results from WHO's Communicable Disease Surveillance and Response studies have produced the first scientific data on how long the SARS virus can live in various places and conditions. The results demonstrate that the microbe can linger outside an infected person's body for at least 24 hours. However, CDC Director Julie L. Gerberding, M.D., M.P.H., says, "Finding a virus on a surface does not necessarily mean that surface has anything at all to do with transmitting the virus from one person to another." Thinking back to the early days of HIV infection, she says, "We had a lot of data coming out indicating that HIV could survive on tabletops for prolonged periods of time, but in fact, tabletops were not a mode of transmitting HIV from one person to another."

**Early signs of a SARS infection include a fever greater than 100.4 F, headache, an overall feeling of discomfort, and body aches.**

Coronaviruses are a group of viruses that have a halo or crown-like appearance (corona) when viewed under a microscope. Thus far, laboratory results have not provided conclusive evidence that a new coronavirus is the cause of SARS. Additional specimens are being tested to learn more about this coronavirus and its link with SARS.
SARS and the U.S. Blood Supply

At this time, it is not known whether severe acute respiratory syndrome (SARS) can be transmitted through blood. As a precaution, however, the Food and Drug Administration has issued guidance on prudent steps to safeguard the U.S. blood supply from SARS.

The FDA is taking this interim measure to protect the blood supply while more is learned about the disease. Highlights of the guidelines include:

- A donor must be in good health at the time of donation.
- Potential donors who may recently have been exposed to or have experienced SARS are temporarily prohibited (deferred) from donating blood.
- Blood establishments should encourage anyone who has already donated blood to report any SARS-related exposure that occurred up to 14 days before donation, SARS illness or treatment that occurred up to 28 days before their donation, or SARS illness or treatment occurring within 14 days after donation.
- Potential donors who recently have been to areas of the world in which a relatively large number of cases of SARS have been reported should be deferred from donating blood for 14 days after their return to the United States.
- Donors who have suffered from an acute case of SARS or suspected SARS, as evidenced by a combination of symptoms and travel history, should be deferred from donating until 28 days after their symptoms are resolved and any treatment is completed.

Gerberding adds that it’s difficult to draw conclusions from experiments such as those that look at the longevity of microorganisms on environmental surfaces because the methods used vary.

Viral Cause Suspected

Scientists at the CDC and elsewhere have unraveled the genetic code of a previously unrecognized coronavirus in patients with SARS. Coronaviruses have a halo or crown-like appearance under a microscope, and are a common cause of mild to moderate upper-respiratory illness in humans. In animals, coronaviruses are associated with respiratory, gastrointestinal, liver and neurologic disease. While the new coronavirus is the leading suspect for the microbe that causes SARS, other viruses are also under investigation as potential culprits.

Results of the first major epidemiological study of SARS, published in the
The CDC says the best defense against SARS is frequent, thorough hand washing with soap and water.

May 24, 2003, issue of The Lancet, indicate that the average incubation period (time between infection and onset of symptoms) of SARS is estimated to be six to 10 days. The authors of the study stressed that reducing the time from the onset of symptoms to hospital quarantine is one of the most important public health measures that can be taken to reduce SARS transmission, and to potentially eradicate the disease.

In the absence of effective drugs or a vaccine for SARS, scientists are moving rapidly on multiple fronts to control the disease. Because there isn’t yet a full understanding of the natural course of illness in someone infected with the SARS virus, the CDC says that it likely will take various government agencies and private organizations working together to halt its spread.

The FDA and SARS

The Food and Drug Administration is carefully tracking the progress being made in defining, treating and, ultimately, defeating the SARS virus, to ensure that all the agency’s resources are aggressively, safely, and smartly deployed. The FDA is committed to providing the prompt regulatory oversight needed to help defeat SARS as soon as possible.

The FDA is working closely with the CDC and the National Institutes of Health on the development of reliable diagnostic tools that will help identify the microbe responsible for SARS. One such experimental laboratory test already has been developed by the CDC. In addition, the FDA is ensuring that adequate supplies of various medical products will be available in the event of a broader spread of the disease in the United States.

The FDA’s Center for Devices and Radiological Health is charged with guaranteeing the reliability of diagnostic tools. And the agency’s Center for Drug Evaluation and Research is helping to identify drugs that may be effective in combating the agent that causes SARS. The Center for Biologics Evaluation and Research (CBER) is part of a team that is facilitating the development of several potential vaccines. CBER is working with other government agencies and the private sector to address many of the most difficult early issues in vaccine development.

The FDA has already approved dozens of tests for use in diagnosing different types of acute respiratory syndromes, and has put in place a postmarket surveillance program to measure how well those tests are working. The tests do not diagnose SARS; rather, they help to diagnose other conditions that may have symptoms similar to SARS. In this way, physicians can rule out SARS as a diagnosis.

Because so many organizations are working together on this important public health issue, the United States is now better ready to respond to any escalation of SARS cases.

The CDC says the best defense against SARS is frequent, thorough hand washing with soap and water. Contrary to what many people think about surgical masks for protection, the CDC does not recommend their routine use in public, stating that the masks are not 100 percent effective against the SARS virus. The CDC also advises against travel to certain areas worldwide. (See www.cdc.gov for up-to-date travel advisories.) Only when there are no additional cases of transmission within affected communities, says Gerberding, will there no longer be a need for travel advisories to those countries.

Anyone who experiences a fever greater than 100.4 F along with a cough or difficulty breathing should call a doctor. In addition, those coming in contact with others who have either the same symptoms or have traveled to SARS-affected areas are at increased risk of SARS. Many people infected with SARS, however, recover within a couple of weeks.

Who’s Doing What About SARS?

For updates on what’s being done to combat SARS:

Food and Drug Administration
www.fda.gov/opacom/hottopics/sars/

Centers for Disease Control and Prevention
www.cdc.gov/ncidod/sars/

National Institute of Allergy and Infectious Diseases
www.niaid.nih.gov/factsheets/sars.htm

World Health Organization
www.who.int/csr/sars/en/

Bogus SARS Prevention Products

The Food and Drug Administration and the Federal Trade Commission are warning Web site operators making claims or suggesting that their products will protect against, treat, or even cure severe acute respiratory syndrome (SARS) that it is against the law to make such claims in the absence of scientific evidence. No products have been found effective in preventing, treating or curing SARS. Operators are being warned to remove any misleading or deceptive claims from the Internet. Consumers are being told to "hold on to your money."
Alzheimer's
Searching for a Cure

By Linda Bren

It was 1997 when an alarm went off in Vivian Freed's head. She knew something was wrong with her 85-year-old mother, who had always planned her trip to celebrate Thanksgiving with her children down to the last detail. But that year, she got the airline tickets for the wrong days. Freed also found out that her mother had been missing doctors' appointments and social engagements, so she flew from her home in Rockville, Md., to her mother's home in Florida to check on her.

"Everything that she had done perfectly before was a mess," says Freed. The bills weren't paid, and the medications that her mother had been giving to her ailing father weren't right. "We realized we needed to do something," says Freed, after a doctor diagnosed her mother with Alzheimer's disease.

Freed's sister, Annette Heller, later "adult-napped" her parents and moved them to Maryland under the pretense of just visiting. "They didn't really notice that she was packing up more things than they would need for just a visit," says Freed.

Her parents were fiercely independent and would have objected to moving. "It would have been much nicer to give them closure, but it wasn't possible," Freed says.

Not long after Freed moved her parents into an assisted living facility in Maryland, her father passed away. "The day after he died, Mom remembered what happened, but never did again," she says. "Mom kept asking, 'Where's Daddy?'"

As her mother's mental and physical health continued to deteriorate, Freed moved her into a small group home where she got 24-hour care. Alzheimer's disease, along with worsening vision, prevented her mother from recognizing Freed. "It was a very slow demise," she says. Her mother died at age 90 in 2002.
"Ultimately, Alzheimer’s is fatal,” says William Thies, Ph.D., vice president of medical and scientific affairs at the Alzheimer’s Association in Chicago. “Until research provides the answers, Alzheimer’s will continue to exact a terrible toll on those with the disease, as well as on their families, friends and caregivers.”

But an explosion of Alzheimer’s research in the last 10 years and its continuing momentum hold out hope for potential preventions and treatments for this devastating disease.

Rising Numbers

Health care costs for the roughly 4 million Americans with Alzheimer’s disease (AD) exceed $100 billion a year, according to the Alzheimer’s Association. As baby boomers age during the next few decades, the number of victims and the dollar costs of care are expected to almost quadruple.

As age increases, so does the risk of getting AD. For each five-year age group beyond 65, the percentage of people with AD doubles, according to the National Institute on Aging (NIA). Nearly half of those over age 85 have it. A small number are diagnosed with “early-onset Alzheimer’s,” which can strike people in their 30s, but most AD cases are among older people. A person with AD lives an average of eight years after the onset of symptoms, but some live as long as 20 years.

A Disease of the Brain

AD is a brain disorder that occurs gradually. It starts with mild memory loss, changes in personality and behavior, and a decline in thinking abilities (cognition). It progresses to loss of speech and movement, then total incapacitation and eventually death. It is normal for memory to decline and the ability to absorb complex information to slow as people get older, but AD is not a part of normal aging.

Researchers aren’t exactly sure what causes AD, but they do know that people with the disease have an abundance of two abnormal structures in the brain: plaques and tangles (see images, pages 22 and 23). Plaques are dense, sticky substances made up of accumulations of a protein called beta-amyloid. Tangles are twisted fibers caused by changes in a protein called tau. The beta-amyloid plaques reside in the spaces between the billions of nerve cells, or neurons, in the brain, and the neurofibrillary tangles clump together inside the neurons. Plaques and tangles block the normal transport of the electrical messages between the neurons that enable us to think, remember, talk and move. As AD progresses, nerve cells die, the brain shrinks, and the ability to function deteriorates.

Treating the Symptoms

There is no cure for AD, but there are drugs to treat some of the symptoms. The Food and Drug Administration has approved four prescription drugs for people with mild to moderate AD: Cognex (tacrine), Aricept (donepezil), Exelon (rivastigmine), and Reminyl (galantamine). "All of them work by the same mechanism,” says Russell Katz, M.D., director of the FDA’s Division of Neuropharmacological Drug Products. The drugs increase the level in the brain of acetylcholine—a chemical that nerves use to communicate with each other. "People with AD are deficient in this neurotransmitter, and the drugs work by inhibiting an enzyme called cholinesterase that breaks down the acetylcholine,” says Katz. “These cholinesterase inhibitors have an effect on the symptoms, but we have no evidence that they have any effect on the underlying progression of the disease. During treatment, as far as we know, the nerve cells are still dying and the various plaques and tangles are still forming.”

"There’s healthy debate about whether these drugs actually affect the course of the illness,” says Trey Sunderland, M.D., chief of the Geriatric Psychiatry Branch of the National Institute of Mental Health (NIMH). According to the data, says Sunderland, "If people are on the cholinesterase inhibitors, they tend to go to nursing homes later than people who are not on the inhibitors.” Some researchers have reported a delay of up to 22 months in going to nursing homes, he adds.

Treating the Disease

Scientists continue to search for treatments to slow the progress of AD and to hold the disease off as long as
possible. "If you could delay the onset of symptoms by five years, the total number of new cases projected into the future would be cut in half," says Steven Ferris, Ph.D., director of the Alzheimer's Disease Center at the New York University School of Medicine. "Within the next five to 10 years, we will at least one therapeutic strategy," says Sunderland. "Both prognostic and therapeutic options are needed. If you had a preventative dmg that potentially had toxicity associated with it, you wouldn't want to give it to everybody—only the subpopulation at greatest risk."

Today, AD can be diagnosed conclusively only by examining the brain after death. But physicians can make a probable diagnosis on living patients by taking a complete medical history, administering neurological and psychological tests, and doing a physical exam, blood and urine laboratory tests, and a brain-imaging scan. Once symptoms begin, the disease can be diagnosed with up to 90 percent accuracy by experienced physicians, according to the NIA.

But do people start getting AD before symptoms show themselves? "That's the big question in Alzheimer's disease: When does it really begin?" says Sunderland. No one knows for sure, he says, but research "suggests that the illness may predate clinical symptoms by years and maybe decades."

Advances in neuroimaging—taking pictures of the brain to measure its structure and activity—may allow researchers to see the accumulation of plaques and tangles at various points in time. Neuroimaging may one day

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**PET Scan of Normal Brain**  
**PET Scan of Alzheimer's Disease Brain**

Imaging techniques such as positron emission tomography (PET) can detect mild changes in the brain before symptoms such as memory loss appear. PET also makes it possible for scientists to measure deposits of various chemicals in the brain, and the rate at which different regions metabolize glucose, the brain's only fuel.

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be able to slow down the disease in people who already have symptoms and do a much better job at identifying people at high risk of getting Alzheimer's who do not yet have symptoms," Ferris predicts. And once new treatments come along to slow down the disease, those treatments may be given to people at high risk, he adds, so a growing number of people will live longer but not long enough to get AD.

**Diagnosing Alzheimer's**

Scientists are uncovering clues to better diagnose the disease and to determine who is at risk. "It is my hope that in time for the baby boomers, there will be both a prognostic test, as well as prove useful in monitoring the progression of the disease and assessing people's responses to drug treatment.

Another early indication of AD could be found in a person's spinal fluid, which, like the brain, carries beta-amyloid and tau proteins. In a study at the NIMH, Sunderland's team of researchers was able to diagnose AD in most cases by measuring the levels of these proteins in spinal fluid. These measurements, or biomarkers, may help scientists identify people at risk for AD, says Sunderland. "By establishing a person's baseline and tracking levels over time, we might be able to interpret gradual changes as a sign that he or she is developing the disorder."
Sunderland’s study, which included physical examination of more than 200 participants and an analysis of over 50 similar studies, is reported in the April 23, 2003, issue of the Journal of the American Medical Association (JAMA). While work in this area is inflammatory drugs, antioxidants, and estrogen are some of the substances that have been studied, but study results have been conflicting. These studies don’t prove causation, warns Thies of the Alzheimer’s Association. “All they really tell us is it’s a good place to start doing clinical trials.” And researchers are doing just that.

**The Heart and Head Connection**

Studies have shown a link between known risk factors for heart disease—high blood pressure, high cholesterol levels, and diets high in saturated fats and trans fats—and an increased risk for AD. There is also evidence that an elevated level of homocysteine, an amino acid in the blood, presents a risk for both heart disease and AD. Further, taking cholesterol-lowering drugs (statins) is associated with a lower occurrence of AD.

Currently investigational in nature, spinal fluid testing may become a valuable routine diagnostic tool in the future.

**Delaying the Disease**

Some studies hint that a variety of existing drugs and supplements may be useful in delaying AD or stopping its progression. These studies are preliminary, and their findings would need to be demonstrated in adequately designed and conducted studies before their conclusions can be considered proven, says Katz.

Cholesterol-lowering drugs, anti-inflammatory drugs, and antioxidants, among other substances, are commonly used to reduce inflammation and pain, have a reduced likelihood of developing AD, according to some studies. NSAIDs, currently investigational in nature, spinal fluid testing may become a valuable routine diagnostic tool in the future.

**Anti-inflammatory Drugs**

People who take large doses of nonsteroidal anti-inflammatory drugs (NSAIDs), commonly used to reduce joint inflammation and pain, have a reduced likelihood of developing AD, according to some studies. NSAIDs, currently investigational in nature, spinal fluid testing may become a valuable routine diagnostic tool in the future.

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“What is good for the heart may be good for the head,” says Thies, and healthy lifestyle behaviors such as exercising, eating healthily, and managing blood pressure and cholesterol may be of value in protecting people from AD.

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**What is good for the heart may be good for the head.**

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Healthy nerve cells in the brain (neurons) have support structures called microtubules, which guide nutrients and molecules from the cell’s body down to the ends and back. A special kind of protein, tau, makes the microtubules stable. Tau is changed chemically in people with Alzheimer’s disease. It begins to pair with other threads of tau and they become tangled up together. When this happens, the microtubules disintegrate, collapsing the neuron’s transport system. This may result first in communication malfunctions between neurons and later in cell death.

Large-scale clinical trials are being conducted to clarify the link between cardiovascular risk factors and AD. In addition to statins, substances being tested for slowing and preventing AD are folate (a form of B vitamin) and vitamins B6 and B12, which may lower homocysteine levels.

The Alzheimer’s Disease Education and Referral Center, NIA

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An amyloid plaque is made up of dense protein deposits that clump around nerve cells in the brain and block the transport of electrical messages between nerve cells.

which include over-the-counter aspirin and ibuprofen, as well as some prescription drugs, such as Celebrex (celecoxib), may reduce the inflammation in the brain associated with AD.

None of the studies performed with the anti-inflammatory drugs to date are definitive, cautions Katz, and these drugs would need to be studied in scientifically rigorous trials before the effects of these drugs on AD could be accepted. One of these trials, the Alzheimer’s Disease Anti-Inflammatory Prevention Trial (ADAPT), was launched in 2001 to test the effectiveness of some NSAIDs in preventing AD. The study of more than 2,500 healthy participants age 70 and over is sponsored by the NIA and is scheduled to run between five and seven years.

Antioxidants

Researchers are also looking at antioxidants to possibly prevent cognitive decline. Antioxidants, such as vitamin E, vitamin C and carotene, may help break down “free radicals”—cell-damaging compounds that are byproducts of normally functioning cells. The natural defenses of cells protect against these compounds, but these protective mechanisms decline as a person ages.

Some study results have suggested that antioxidants may protect against cell damage and lessen the likelihood of getting AD. But a four-year study of nearly 1,000 older people conducted at Columbia University found that consuming carotenes or vitamins C and E either through the diet or by supplements did not decrease the risk of developing AD. “This large-scale study is at variance with earlier indications that these supplements are effective as a treatment for Alzheimer’s,” says Thies. “This tells us that more work needs to be done before we completely understand the value of these agents.”

The results of this study are published in the February 2003 issue of Archives of Neurology.

“There are virtually shelf-fuls of compounds capable of acting in an antioxidant fashion,” says Thies. One of these, Ginkgo biloba, used for thousands of years in Chinese herbal medicine, has been shown in a small study to result in a modest improvement in cognition, social behavior and performing activities of daily living, such as dressing and eating. A larger study (about 3,000 participants) funded by the National Institutes of Health (NIH) is currently investigating the effectiveness of Ginkgo in preventing or delaying cognitive decline in older adults.

The FDA cautions consumers that some supplements may interact with prescription and over-the-counter medicines and cause serious harm. Check with your doctor or health care provider before taking any dietary supplement, including herbs.

Estrogen

Several epidemiological studies have linked the female hormone estrogen to improved memory and possible delay or prevention of AD in women. But a large, long-term clinical trial sponsored by the NIH has provided evidence to the contrary. In the trial, part of the Women’s Health Initiative Memory Study (WHIMS), women 65 and over taking estrogen combined with another hormone, progestin, had twice the rate of dementia, including AD, than those women not taking the hormones. The study, published in the May 28, 2003, issue of JAMA, also found that the hormone combination did not protect against the development of

Eluding Alzheimer’s

No cure or prevention for Alzheimer’s disease exists yet, but experts offer some advice to help prolong mental health:

“The best thing people can do is to try to plan for their later years and try to remain as functional as possible,” says William Thies, Ph.D., vice president of medical and scientific affairs at the Alzheimer’s Association in Chicago. “And stay connected to the world, because the literature suggests that social isolation is a contributor to unhealthy aging.”

Steven Ferris, Ph.D., director of the Alzheimer’s Disease Center at the New York University School of Medicine, makes three recommendations:

• Stay mentally active. “The more you challenge the brain, the more you’ll be able to maintain it,” says Ferris. “When you’re stimulating the brain, you’re growing more interconnections and maybe even growing new neurons. The more brain cells and connections you have, the longer you’ll be able to function well, even if you get Alzheimer’s.”

• Stay physically active. Physical exercise improves brain function as well as benefiting the rest of your body.

• Have a healthy diet and stay in good physical health. These are essential for maintaining good brain function.

Trey Sunderland, M.D., chief of the Geriatric Psychiatry Branch of the National Institute of Mental Health, encourages people to participate in Alzheimer’s research studies so that they learn about the illness and are followed carefully for any incremental change that might occur in their health. “Our volunteers have found that they actually get reassured by being in a study,” says Sunderland. “For the most part, we’re telling them—in our long-term follow-up studies—that they continue to be normal.”

The Alzheimer’s Disease Education and Referral Center, NIA
mild cognitive impairment, a form of mental decline less severe than dementia.

New Drug Development

New drugs are emerging from the basic science laboratories and moving toward testing in human trials. “The ones furthest along are based on the amyloid hypothesis,” says Thies. The hypothesis is that AD starts with the accumulation of amyloid plaques, and that limiting this accumulation will change the progress of AD.

Scientists have isolated enzymes called secretases, which are thought to lead to the formation of beta-amyloid. Secretases are categorized as proteases, the same type of enzymes that are targeted by protease inhibitors to treat AIDS. Drugs called secretase inhibitors are being developed to block beta-amyloid formation, and some of these drugs are now being tested.

Another approach to plaque attack is to stimulate the body’s immune system to destroy the beta-amyloid. Scientists developed a vaccine that put amyloid into the blood in the hopes of making antibodies to destroy the plaques. The vaccine was successful in transgenic mice—special mice that were injected with human genes that caused them to develop AD-like plaques. But when tested in a human trial, some people showed inflammation of the brain (encephalitis). Further vaccination was stopped, but study participants continue to be followed. Although this particular vaccine may be disappointing, many scientists believe that the strategy of fighting AD by stimulating the immune system still remains an important potential avenue to slow or prevent the disease.

“We are still searching for the sequence of events where we can intervene and cure the disease without causing harm,” says Marcelle Morrison-Bogorad, Ph.D., associate director of the NIA’s Neuroscience and Neuropsychology of Aging Program. Morrison-Bogorad notes that scientists may someday be able to inject a substance into the blood to draw amyloid from cerebral spinal fluid and the brain. “This can happen in transgenic mice—we don’t know whether it happens in humans yet.”

Risk Factors

The two biggest risk factors for getting AD are age and genetics, neither of which is in our control, says Thies. Scientists have identified several genes that play a role in early-onset AD, a rare form of the disease that strikes people as young as in their 30s. For late-onset AD, defined as showing symptoms after age 65, a gene that produces a protein called apolipoprotein E (ApoE) appears to play a role. The gene comes in several forms, or alleles. Having the ApoE4 allele increases the risk for getting AD, according to the NIA.

About 40 percent of people with AD have the ApoE4 allele, but inheriting it doesn’t mean a person will definitely get AD. Some people with the gene never get the disease, and some without it do develop AD. Once researchers know more about how genetics affects AD, people could be genetically screened and then treated based on their genetic factors.

Some studies have shown that participating in mentally stimulating activities, such as reading books, doing crossword puzzles, or going to museums, may be associated with a reduced risk of AD. Researchers speculate that repetition might improve certain cognitive skills, making them less susceptible to brain damage.

This “use-it-or-lose-it” theory may have value, but further study is needed, says Morrison-Bogorad. AD may actually cause people to stop doing mentally challenging activities because the disease makes it harder to do them, she says. “It’s impossible to tease out the cause and effect in these studies. We can only say it’s correlative—not causal.” Morrison-Bogorad does encourage mental activity. “It keeps you nimble—whether it helps prevent Alzheimer’s, we don’t know.”

For More Information

Alzheimer’s Disease Education and Referral (ADEAR) Center
National Institute on Aging
1-800-438-4380
www.alzheimers.org

Alzheimer’s Association
1-800-272-3900
www.alz.org

The Brain’s Vital Statistics

- Adult weight: about 3 pounds
- Adult size: a medium cauliflower
- Number of neurons: 100,000,000,000 (100 billion)
- Number of synapses (the gap between neurons): 100,000,000,000,000 (100 trillion)

Source: NIA

Tracking Down Trials

To find clinical trials on Alzheimer’s disease and dementia at centers throughout the United States, see the ClinicalTrials.gov database at http://clinicaltrials.gov/. ClinicalTrials.gov provides easy access to information on clinical trials for a wide range of diseases and conditions, including Alzheimer’s disease. The National Institutes of Health (NIH), through its National Library of Medicine, has developed this site in collaboration with all NIH institutes and the FDA.
Alzheimer's is a disease of the brain, and the affected regions shrink as the disease progresses. One of the first areas affected is the hippocampus, important for forming memories. Next affected is the cerebral cortex, where thinking, learning, speaking, remembering, and making decisions take place. As the disease becomes more severe, changes occur in other areas of the brain.
Hispanic Health: Renewed Collaboration

By Linda Bren

Cinco de Mayo commemorates the May 5, 1862, Battle of Puebla, in which a band of Mexican patriots defeated a formidable French army force twice its size. Over the past 15 years, Cinco de Mayo has taken on a greater significance as a day to celebrate and honor the heritage, cultural pride, and unity of Hispanic-Americans.

This year, Cinco de Mayo marked a celebration of another kind: a renewed collaboration between the Food and Drug Administration and the National Alliance for Hispanic Health (NAHH), the oldest and largest network of U.S. health and human service providers for Hispanic consumers. FDA Commissioner Mark B. McClellan, M.D., Ph.D., and Jane L. Delgado, Ph.D., president and chief executive officer of the Alliance, chose the day to sign a letter of commitment to work together to help Hispanic communities across the nation achieve good health.

"The FDA is committed to making sure that consumers have the latest and best information to make decisions about their health," McClellan said. "We are going to redouble efforts to make sure that happens in the Hispanic community."

"For almost 100 years, the FDA has protected the public's health," added Delgado. "When we can use a food label to make decisions about nutrition, have access to safe and effective vaccines, when women can safely use mammography and Pap smears to obtain reliable information about cancer risks—that is because the FDA is doing its job to protect the public's health. Today, by renewing a focus on outreach to Hispanic health consumers, the FDA is again demonstrating its leadership and commitment to building a healthier future for all."

To help empower members of the growing Hispanic population to take charge of their health, the FDA is expanding consumer access to Spanish-language health information and initiating joint opportunities for community outreach with the Alliance.

The Spanish publications currently offered by the FDA cover a broad range of topics, including diabetes, arthritis treatments, using medicine safely, eating for a healthy heart, keeping food safe, and vaccinating children to protect them from serious diseases. Many
of these publications are distributed to Hispanic consumers by the FDA’s public affairs specialists, a team of more than 40 health educators around the country. These specialists speak at conferences, participate in health fairs, develop community education programs, work with the Hispanic media, and conduct other outreach activities to the Hispanic community.

Recent outreach activities have included presenting healthy cooking demonstrations to Hispanic childcare providers in New York City and sharing information on diabetes, breast cancer and nutrition at Hispanic Women’s Health Day in Dallas. In North Carolina, home of one of the fastest-growing Hispanic communities in the country, FDA educators shared literature on food and drug safety with consumers at La Fiesta del Pueblo, a two-day event in Chapel Hill celebrating Latino culture.

Another means of delivering information is through the newly launched Su Familia, a toll-free National Hispanic Family Health Helpline developed and operated by the Alliance. Unveiled in March by Health and Human Services Secretary Tommy G. Thompson, the helpline gives consumers free, reliable, and confidential health information. “People can get basic information in Spanish and English that will help them prevent and manage chronic conditions such as diabetes,” says Delgado. Hispanics are nearly two times more likely to have diabetes than non-Hispanic whites, according to the Centers for Disease Control and Prevention.

The Su Familia helpline is staffed by bilingual and culturally proficient information specialists. By providing a ZIP code, callers can be referred to local health providers who speak Spanish or who have Spanish-speaking staff, including community and migrant health centers. Su Familia staff work diligently to identify Spanish-speaking providers throughout the country, especially in new and emerging Hispanic communities, to add to the helpline’s database of over 20,000 health providers.

Callers to Su Familia can also request basic health information and receive consumer-friendly bilingual fact sheets. The several thousand calls coming in to the helpline each month pertain to a variety of issues, says Eliana Loveluck, director of the Alliance’s Center for Consumers. Callers request information ranging from diabetes and nutrition, to immunization schedules for children and flu vaccinations for adults, to breast cancer screening, breastfeeding, birth control, and HIV and AIDS.

Although the majority of callers are Spanish-speaking consumers, some are non-Spanish-speaking providers asking for specific information, says Loveluck. Recently, a number of providers have asked for the Spanish names for the types of fish (shark, swordfish, king mackerel, and tilefish) that pregnant women, nursing mothers and young children should avoid because they contain higher levels of methylmercury.

Hispanics are the nation’s largest racial or ethnic minority group, with a population of 40 million. By 2050, a quarter of the U.S. population is projected to be Hispanic, according to the U.S. Census Bureau.

The helpline is funded by the Office of Minority Health of the Health Resources and Services Administration, an agency of the Department of Health and Human Services.

The FDA and the Alliance are working closely to provide leadership and community outreach projects throughout the year and are currently planning key events for Hispanic Heritage Month, September 15 through October 15, 2003.

“By renewing our collaboration with the NAHH and the Hispanic commu-
FDA Works to Reduce Preventable Medical Device Injuries

By Carol Rados

Medical devices help to alleviate pain, overcome disability, and sustain life. They also, on occasion, fail to operate properly or are misused in ways that are associated with injuries and deaths.

Betty Davis’ wheelchair, for example, caught fire, badly burning over 25 percent of her body in January 1999. A quadriplegic confined to a wheelchair since 1976, the 65-year-old Tucson, Ariz., resident knows the importance of a well-maintained machine that works as intended. “I’m a very active quad,” she says, but when the fire started, “all I could do was sit there and watch my arms and legs burn.”

Faulty wiring short-circuited the battery charger in Davis’ wheelchair. Davis says she put the chair on charge after a blinking light indicated the battery was running low. But Davis detected a spark, and immediately disconnected the charger. The spark, however, turned into a flame. Though authorities don’t know why, Davis’ attempt to reach 911 through her emergency medical pendant failed. Fortunately, a neighbor was nearby at the time and threw water on her to extinguish the fire.

“My legs and arms were on fire and my hair was burning,” Davis recalls. “And from the burns, my skin is so thin you can rub it off.”

According to the Institute of Medicine (IOM), about 1.3 million Americans are seriously injured each year by adverse events involving medical products. More people die in any given year due to medical errors occurring in hospitals (between 44,000 and 98,000) than from motor vehicle accidents (43,458), breast cancer (42,297), or AIDS (16,516).

Inadequate device design, poor manufacturing quality, improper device maintenance, and user error all contribute to adverse events associated with medical devices. In 2002 alone, the FDA received reports of more than 111,000 adverse events, including serious injuries and deaths, related to medical devices.

Whether it’s failure of a device to operate properly or failure of the user to operate the device correctly, the Food and Drug Administration says that many of the adverse events associated with product problems are preventable. In Davis’ case, for example, a $5 fuse would have prevented the short that occurred between the charger and the wheelchair’s battery. Davis’ wheelchair should have been designed with one.

Nearly 1,800 categories of medical devices exist, and they vary in both complexity and risk potential. That means that the problems associated with medical devices are as diverse as the number of medical devices on the market. Moreover, as health care and the system that delivers it become more complex, opportunities for errors increase.

While it’s unlikely that product-related problems and patient injuries can be eliminated, the FDA believes that many adverse events can be prevented by designing systems that make it hard for people to do the wrong things and easy for them to do the right things. “In many cases,” says Mary Weick-Brady, deputy director of the FDA’s Division of Surveillance Systems, “a device may have been designed properly but the user may have used it wrong.” In short, manufacturers can design errors out of the system and build checking and monitoring functions into the system.

For example, because breathing tubes used in ventilators often pop out of place, manufacturers have alarms built into the ventilators to alert health care workers when a tube becomes disconnected. Future designs featuring networking systems could recognize that health care workers are not always present when an alarm goes off. Built-in networking systems would allow the appropriate health care providers to be notified of an alarm wherever they may be.

FDA guidelines now call for manufacturers to consider the needs of the users and patients when designing equipment. Well-designed devices are consistent with the user’s experience, and they are logical and not confusing. Also, they minimize the need for
depending on the user’s memory and making mental calculations; do not overtax the user’s strength, dexterity, visual ability, or auditory capacity; alert the user to device-related problems; prevent users from making fatal errors that could otherwise occur easily; and are supported by readable and understandable labeling.

And the FDA wants products to be tested under actual or simulated use conditions to demonstrate that the potential for user error has been minimized.

The agency currently guides the development of new devices, evaluates the results of clinical trials and new products before they are marketed, ensures quality systems are in place in manufacturing plants, and continues to identify and respond to adverse events that are reported in the United States. The FDA plans to expand its knowledge of medical device errors by linking with new sources of data, perhaps from other government and outside organizations. In addition, the agency will focus on educating patients and health care professionals on how to avoid potential threats posed by medical devices.

Improved patient safety through reducing preventable adverse health events is one of five agency priorities set by Commissioner of Food and Drugs Mark B. McClellan, M.D., Ph.D. Other priorities include science-based risk management, better information for consumers, counterterrorism, and a strong FDA at the forefront of biomedical science and technology.

What Is A Medical Device?

Simply defined, a medical device is an instrument, such as a stethoscope or an artificial hip joint, used for diagnosis, treatment or prevention of disease, injury or other condition that is not a drug, biologic or food. The FDA regulates more than 100,000 medical devices ranging from simple thermometers, tongue depressors and heating pads to heart pacemakers, intrauterine devices, and kidney dialysis machines. Some devices, such as bandages, have retained their same basic form and function, while others have become more complex.

Heart defibrillators, for example, designed to deliver electric shocks to restore normal heart rhythms, have progressed from large machines to devices small enough to be implanted inside the chest wall. Other developments include surgical tools that enable surgeons to operate on a fetus while still in the womb. Diagnostic devices also have evolved so that many tests, such as those used to determine whether a woman is pregnant or to detect blood clotting, can be used at home. And some surgical procedures, such as gallbladder removal, can now be done using laparoscopic instruments that require only small incisions, which can reduce hospital stays and help speed recovery. Patient care has improved dramatically as a result of these changes.

Product Problems

Once a medical device goes into widespread use, unforeseen problems can still arise. But through the use of regulatory controls and the device classification process, the FDA provides reasonable assurance that the product will be effective, while not posing unacceptable risks to patients once it is on the market. (See “Class Clarification,” page 33.)

Postmarket medical device problems—those seen after a device has been approved and is in general use—generally fall into one of three broad categories: device problems, use problems, and clinical problems.

Mechanical, electrical or software-related malfunctions, manufacturing defects in product design or development, or problems with materials are all considered to be device-related problems. Use problems may be associated with inadequate or misleading labeling, confusing instructions, inadequate packaging, design problems that make the device
difficult to use, or inadequate training in the use of the device. Clinical problems can occur with a patient who is sensitive or allergic to a device, or who has a pre-existing condition that makes the device difficult or risky to use.

The following simple steps can help consumers and health care providers avoid common problems associated with medical devices:
- Read and understand the instructions and labeling, and know for whom the device is appropriate.
- Inspect and test equipment prior to use.
- Make sure that devices are properly maintained and serviced.
- Avoid using a device that has malfunctioned.
- Avoid using a device past its suggested expiration date for sterility or shelf life (length of time before the product deteriorates).

### Reporting Product Problems
Reporting medical device problems is an important part of patient safety. Concerns about the quality, performance, or safety of any medical device should be reported. Consumers and health care providers using medical devices are in the best position to provide the information that manufacturers and the FDA need to determine whether an adverse event presents a public health risk.

"By reporting adverse events to the FDA," says Suzanne Rich, a registered nurse who works in the FDA’s Division of Postmarket Surveillance, "health care providers help to rapidly identify significant health hazards associated with these products, and the FDA can provide timely feedback to the health care community about safety issues involving medical products.” This reporting, she adds, translates into patient safety.

The FDA is improving several systems for reporting adverse events that are associated with the use of agency-approved products. These systems advance the public’s health by giving the agency quicker and more detailed information on potential problems with health care products.

The key to effective reporting is to understand the difference between the FDA’s two complementary systems for national medical device adverse event reporting. Through the Medical Device Reporting (MDR) system, manufacturers and distributors of devices, as well as user facilities (hospitals, outpatient and nursing home personnel to accurately identify and

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The vast amount of information about adverse medical outcomes that reaches the FDA through these systems is analyzed and, if necessary, requests are made for additional information and studies to determine the need for further action. Such reporting ultimately forms the basis for several actions the FDA may take once an adverse event or product problem has been identified:

- **Publication in the media and clinical peer-reviewed journals** alerts health care practitioners to hazards associated with medical device use.
- **Labeling changes** may be required of the manufacturer to add new information to the product’s packaging that alerts users to precautions during device use.
- **Boxed warnings** may be required of the manufacturer to be placed in a
prominent place on the product’s labeling to ensure that patients and doctors won’t miss them. The agency reserves these warnings for the most serious adverse events, including life-threatening problems occurring that were not observed in clinical trials.

- **Medical and safety alerts** in the form of letters and Web Notifications are used to provide important safety information about a product to health professionals, hospital administrators, risk managers, pharmacists, news media, and others. They are also sent (by e-mail or fax) to the MedWatch Partners—more than 170 health professional specialty and consumer organizations that work with the FDA to help keep their members informed about medical product safety information and reporting.

- **Product recalls and withdrawals** involve the firm’s correction or removal of a product from the market and may require taking the product off the market permanently. Recalls usually are conducted voluntarily by the manufacturer, and are completed within six to 12 months. In rare instances, where the manufacturer or importer fails to initiate a recall voluntarily, the FDA has the regulatory authority to order the firm to recall the defective device.

A company-initiated recall took place in early 2000 when Invacare Corporation, the manufacturer of Davis’ wheelchair, voluntarily sent letters to its dealers stating that battery wiring harnesses were configured improperly and had the potential to cause a fire. The widespread recall has been expanded to include additional wheelchairs, and is still ongoing.

Once it is determined that a product will be recalled, an evaluation of the health hazard it presents is conducted by the FDA. The agency then assigns a numerical value (I, II, III) to the recall to indicate the relative degree of health hazard (see “Class Clarification,” page 33). The recalling firm develops a strategy for recalling the device, based on FDA-mandated criteria, such as the health hazard evaluation results, ease in identifying the product, degree to which the product’s deficiency is obvious to the consumer, and more. Ordinarily, the recalling firm is responsible for conducting recall effectiveness checks—a means of verifying that their customers have received the notice and have taken appropriate action, as requested by the recalling firm. Only after the FDA reviews the firm’s efforts and determines its success will the agency issue a “close-out” letter terminating the recall.

Cooperation between the FDA and its regulated industries has proven to be the quickest and most reliable method to remove potentially dangerous products from the market, says Christy Foreman, chief of the FDA’s Orthopedic, Physical Medicine and Anesthesiology Devices Branch. “We do rely heavily on the firms to be honest, truthful and forthcoming in their reporting,” she adds. “A warning sign of an ineffective recall is hearing about additional accidents.”

And from where Davis sits, that translates into yet another grave concern. “My friends in wheelchairs didn’t hear about this problem until it...”

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**Summary of FDA’s Medical Device Reporting Requirements**

<table>
<thead>
<tr>
<th>User Facility</th>
<th>Report of deaths and serious injuries (January 1 and July 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths (also report to Manufacturer)</td>
<td>Serious injuries (report to Manufacturer or FDA if Manufacturer unknown)</td>
</tr>
<tr>
<td>5-day report on events requiring immediate remedial action and other designated events</td>
<td>30-day report of deaths, serious injuries and malfunctions</td>
</tr>
<tr>
<td>Certification of compliance with regulation</td>
<td></td>
</tr>
</tbody>
</table>

Source: FDA/CDRH
Knowing Where to Look

How and whether people find out about device recalls depends largely on manufacturers' and retailers' diligence, consumer vigilance, and media assistance. Recalls are officially announced in two ways: the FDA publishes a press release and a weekly Enforcement Report that contains all enforcement actions including recalls, field corrections, seizures, and injunctions. This report is published on the Internet at www.fda.gov/opacom/Enforce.html. Secondly, manufacturers distribute recall notifications to communicate the potential medical device hazard.

For various reasons, however, medical device recalls can go unnoticed—some say because reporting systems are voluntary, recall information doesn't get into the right hands, registered letters are sent to old addresses, hospitals don't see notices because they are swamped with so many other responsibilities, or perhaps there are mixed signals on the urgency of the problem.

Consumers and health care professionals who don't want to rely on their own vigilance can regularly access the most serious alerts and get additional safety information from the FDA home page: www.fda.gov. For device-related information, click "Medical Devices," and then the "Safety Alerts" link under "Health Topics." MedWatch is another source of safety information about devices and other FDA-regulated medical products. MedWatch posts safety alerts for all Class I recalls of devices, drugs, and biologics. E-mail notification of the recalls reaches MedWatch partners and about 30,000 subscribers at the time of the Web posting. This information can be accessed on the MedWatch Web site at www.fda.gov/medwatch/safety.htm. These two Web sites give instructions for how to sign up to receive e-mail notification of new safety alerts.

The FDA now has another means to communicate device safety information to health care personnel: FDA Patient Safety News, a news show that is broadcast on medical satellite networks to over 4,000 hospitals and nursing homes across the country. Designed for physicians, nurses, pharmacists and risk managers, the show features information on new medical products, FDA safety notifications and product recalls, ways to protect patients when using medical products, and more.

Looking Ahead

"The future holds still more promise," says McClellan. The current systems "and other great strides are part of a vision of what can be accomplished if all of us in government, the health professions, academia and industry continue to work toward better health information systems—and more generally," he says, "toward a health care system that helps patients and health professionals make better decisions supported by safer and more effective medical treatments."

Class Clarification

The terms Class I, Class II and Class III are used by the Food and Drug Administration in two different ways, both for categorizing medical devices by their complexity and potential risk, and for indicating the seriousness of a product recall. This double use can be confusing: for example, Class I medical devices are those that are the least complex and carry the least risk, but a Class I product recall is the most serious kind, indicating that the problem could cause serious injury or death.

Device Classifications

The FDA has established classifications for the approximately 1,800 different generic types of devices and grouped them into 16 medical specialties. Each of these types is assigned to one of three regulatory classes based on the level of control necessary to assure safety and effectiveness. The three classes and the requirements that apply to them are:

- Class I, General Controls—subject to the least regulatory control. They present minimal potential for harm to the user and are often simpler in design than the other classes of devices.
- Class II, General Controls and Special Controls—those for which general controls alone are insufficient to assure safety and effectiveness, and existing methods, such as special labeling requirements or mandatory performance standards, are available to provide such assurances.
- Class III, General Controls and Premarket Approval—the most stringent regulatory category for devices for which insufficient information exists to assure safety and effectiveness solely through general or special controls. These devices usually support or sustain human life, are of substantial importance in preventing impairment of human health, or present a potential, unreasonable risk of illness or injury.

Recall Classifications

The Food and Drug Administration assigns a numerical designation of I, II, or III to a particular product recall to indicate the relative degree of health hazard presented by the product being recalled.

- Class I recalls represent the highest level of risk and are reserved for products that could likely cause serious health problems or death.
- Class II recalls represent a moderate likelihood of death or serious injury.
- Class III recalls represent those in which exposure to the defective product isn't likely to cause any health consequences.
A team of Food and Drug Administration investigators inspected the American National Red Cross and found numerous deviations from FDA law.

Consent Decree of Permanent corrective action necessary.
The American Red Cross has agreed to tighten its procedures and processes for the manufacture of blood products as part of an amended consent decree with the Food and Drug Administration. If the Red Cross fails to comply with blood safety rules and other requirements, heavy fines can be imposed.

The amended decree, signed by the organization and the FDA in April, follows 17 years of serious and persistent violations of blood safety rules. In a prepared statement, the Red Cross said that previously debated issues between it and the FDA have been resolved and that the amended consent decree marks "a new era of cooperation."

"I am hopeful that the acceptance of this agreement by the American Red Cross' new leadership reflects a new willingness to implement a management culture that expects and achieves good blood safety practices," says FDA Commissioner Mark B. McClellan, M.D., Ph.D.

As part of the amended decree, the Red Cross agreed to upgrade its blood collection program to comply with government standards aimed at ensuring blood safety. The agreement was struck after years of negotiations failed and the FDA filed a motion to hold the Red Cross in civil contempt.

The Red Cross is responsible for 45 percent of the nation's blood supply. Independent and community blood facilities contribute another 45 percent to the pool, and hospitals contribute 10 percent.

In the original 1993 consent decree, the Red Cross had agreed to establish clear lines of managerial control over a newly established quality assurance system in all regions, to enhance training programs, and to improve computer systems, records management, and policies for investigating and reporting problems.

Since 1993, a number of safety problems were identified by FDA inspections. In an inspection at Red Cross biomedical headquarters in Arlington, Va., in 2000, the FDA found that the Red Cross was unable to track blood products well enough to enable expedient recalls, was not maintaining an accurate record of deferred donors, and was not labeling blood components correctly. An inspection in 2002 found continuing issues with quality assurance, donor deferral, product labeling, traceability of blood components, and investigation of donors implicated in post-transfusion infections.

The amended decree includes many of the provisions contained in the 1993 consent decree. However, in addition to heavy financial penalties, the updated document provides a series of deadlines for completing requirements of the decree, and it addresses additional violations observed since 1993.

"The new financial penalties in the consent decree create an important new incentive for the American Red Cross to improve the processes and controls necessary for making safer blood products," says McClellan.

Over the years, the FDA has strengthened the safeguards that protect patients from unsuitable blood and blood products. Blood donors, for example, are now asked specific and direct questions about risk factors that could indicate possible infection with a transmissible disease. This "up-front" screening eliminates about 90 percent of unsuitable (deferred) donors. The FDA also requires blood centers to maintain lists of unsuitable donors to prevent the use of their blood. In addition, blood donations now are tested for six infectious agents.

Concurrently with the strengthening of safeguards, the FDA has significantly stepped up its oversight of the entire blood industry. On-site inspections are conducted at least every two years. If problems are found at any blood establishment, appropriate regulatory or legal actions are taken, and inspections of that facility are done more often to ensure compliance with regulations.

The Red Cross has agreed to retain outside consultants to evaluate aspects of its quality assurance program and to reimburse the FDA for costs associated with inspections the agency considers necessary to evaluate the organization's compliance with the amended decree.

When the agreement was announced in April, McClellan said he would like to see "management changes that create an environment where the kinds of specific problems seen over the last 17 years are less likely to happen." Marsha Johnson Evans, Red Cross president and chief executive officer since August 2002, has promised to restore the public's trust in the organization.
Speedy Approvals for New Cancer Treatments

Two cancer treatments have been approved by the FDA under an accelerated approval program that gives people suffering from serious or life-threatening diseases earlier access to promising new drugs. Approval of such drugs is based on an encouraging effect of a drug, such as tumor shrinkage, before there is actual evidence of improved survival or other clinical benefit. As required by the accelerated approval regulations, drug sponsors perform additional studies to verify the projected clinical benefit.

Velcade (bortezomib) is a new treatment for multiple myeloma, a cancer of the bone marrow. Multiple myeloma is the second most prevalent blood cancer after non-Hodgkin’s lymphoma. Velcade, the first in a new class of anticancer agents known as proteasome inhibitors, is marketed by Millennium Pharmaceuticals Inc. of Cambridge, Mass.

Iressa (gefitinib) was approved as a single agent treatment for people with advanced non-small cell lung cancer, the most common form of lung cancer in the United States. Cancer of the lung and bronchus is the leading cause of cancer death in both sexes in the United States. Iressa is marketed by AstraZeneca LP of Wilmington, Del.

Velcade is indicated for people with multiple myeloma whose disease has relapsed after two prior treatments and who have demonstrated resistance to their last treatment. Out of 188 patients evaluated for response to Velcade, 28 percent showed a response, which lasted a median time of one year. Another trial in 54 people with relapsed multiple myeloma showed similar responses.

The most commonly reported adverse events reported in Velcade treatments. The response rate, defined as at least 50 percent tumor shrinkage lasting at least one month, was about 10 percent. There were more dramatic responses in some people, and the median duration of response was seven months. On Sept. 24, 2002, the FDA’s Oncologic Drugs Advisory Committee recommended that in third-line treatment of NSCLC, where there are no viable treatment options, a 10 percent response rate was reasonably likely to predict clinical benefit, and recommended that Iressa be approved.

There appeared to be substantial differences in response rates in subsets of patients. For example, there were higher response rates for women (about 17 percent) than for men (about 5 percent). Common side effects reported with Iressa in clinical trials were nausea, vomiting, diarrhea, rash, acne, and dry skin. Iressa may also cause fetal harm when given to pregnant women.

A significant safety concern emerged just after the advisory committee meeting. Reports from Japan described the occurrence of serious and sometimes fatal interstitial lung disease (ILD) in people treated with Iressa. The FDA extended its review of Iressa by three months to review these reports.

After careful review of information from all sources, including a comprehensive analysis of information from clinical trials and an expanded access program for Iressa involving 23,000 people, the FDA determined that the incidence of ILD was about 2 percent in the Japanese experience and about 0.3 percent in the U.S. expanded access program, with about one-third of affected patients dying from this toxicity. The FDA believes that this rare but serious toxicity of Iressa does not outweigh the benefits demonstrated in people with advanced NSCLC.
Need to Talk About Health? Try a Hot Line

When you have questions about health topics, you may seek answers online or in a library. But sometimes a human voice is just what you need. For those times, the National Library of Medicine (NLM) has a Web site with lists of toll-free hot lines that will put you in touch with someone who can talk about any of more than 200 disorders and other health subjects. Need information about Parkinson’s disease, hepatitis, diabetes, or hearing aids? There’s a hot line for it. How about some answers to questions about Medicare, family problems, environmental health, or even fire prevention? Just pick up the phone.

The site also links to hot lines for information on aging, substance abuse, maternal and child health, disabilities, AIDS, and cancer. Hot line sources range from federal, state and local agencies to professional societies, support groups and voluntary organizations. Many of the hot lines also are available in Spanish.

For NLM’s Health Hotlines, go to http://sis.nlm.nih.gov/hotlines.

FDA Bioterrorism Web Site Widens Its Scope

The FDA’s bioterrorism Web site is now called “counterterrorism” to reflect its recently broadened range of information sources on other aspects of terrorism. Originally launched in 2001 as a response to the anthrax attacks of that year, the site initially focused on bioweapons. Now it offers information on nuclear terrorism, including two fact sheets explaining the use of potassium iodide and Prussian blue, products that can be used in response to radiation contamination. The site also contains a summary of the FDA’s role in various counterterrorism programs, such as cosmetics, veterinary products, and toxicological research.

At www.fda.gov/oc/opacom/hottopics/bioterrorism.html, the site also functions as a gateway to counterterrorism information from other government sources, such as the Department of Homeland Security, the Centers for Disease Control and Prevention, and the Federal Trade Commission. For example, one link takes you to tips on how to avoid online marketers of bogus counterterrorism products. Another gets you to advice on what to do if you find a suspicious piece of mail.

The FDA manages another Web site that explains the many counterterrorism actions the agency is taking under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. It is at www.fda.gov/oc/bioterrorism/bioact.html.

How to Lower Your Cholesterol Levels

The statistics are sobering: One out of every 2 men and 1 out of every 3 women will develop heart disease during their lifetimes, according to the National Heart, Lung, and Blood Institute (NHLBI). Whether you are young, middle-aged, or an older adult, you can reduce your risk of having a heart attack by keeping your cholesterol at recommended levels.

On a site called Live Healthier, Live Longer, the NHLBI advises that “Cholesterol Counts for Everyone” and explains the latest federal guidelines for cholesterol levels, which were finalized in 2002. Along the way, the site (www.nhlbi.nih.gov/cholesterol) tells all about coronary heart disease and its connection to cholesterol levels.

A ‘Scrapbook’ for Teen Consumers—By Teen Consumers

Teen-agers, who spend billions of dollars in the marketplace, should strive to be savvy consumers. But to do so, they need to learn to properly evaluate goods and services when their moms and dads aren’t there to help.

So how can teens acquire this edge that will help set them up in the “real world”? A group of high school students from Washington state has created a Web site that can help. It’s called Teen Consumer Scrapbook, and it has many helpful tips on personal health, cars, buying things, finances, and dozens of other subjects.

In the finances section, for example, teens can learn about scholarship scams, budgets, investing, credit cards, and paying for college. On the site’s health and safety page, teens can get information on fast food, smoking, tanning, piercing, eating disorders, and tattoos.

To open the Teen Consumer Scrapbook, go to www.wa.gov/ago/teenconsumer.

John Henkel is a member of the FDA’s Website Management Staff.
Colorado Couple Caught Defrauding Drug Companies

By Michelle Meadows

A Colorado couple falsified forms, opened phony pharmacies to buy drugs at a discount, and then illegally resold them on the wholesale market in a scheme that swindled pharmaceutical companies out of millions of dollars. According to the FDA’s Office of Criminal Investigations (OCI), Darin D. Asay and his wife, Wendy E. Almanza, of Evergreen, Colo., recruited several friends and relatives to help them in the scam.

Pharmacies that provide medications exclusively to people in institutional settings such as nursing homes and hospitals are commonly called “closed-door pharmacies.” Pharmaceutical companies typically sell drugs to this type of pharmacy at lower prices than those charged to retail pharmacies and drug wholesalers. Because of the varying prices, manufacturers typically require closed-door pharmacies to sign an “own-use” clause that allows them to dispense the drugs only to patients in institutional settings.

According to court papers filed in the U.S. District Court for the District of Colorado, Asay, Almanza, and their accomplices opened at least eight “shell” closed-door pharmacies in several states, including Colorado, Texas, Arizona, and Idaho. They made it look like they ran legitimate pharmacies and signed various own-use certifications even though they intended to sell the drugs to wholesalers.

The criminal activities started in 1993, when Asay and Almanza opened a wholesale distribution company called Intermountain Distributors in Golden, Colo. They also arranged to do business as Principal Pharmacy Consultants and Empire Distributors. Their associates, Nigel Jones and Anita Renee Wier Jones of Plano, Texas, operated a pharmacy called Colorado Institutional Services.

The defendants joined drug buying groups that obtained drugs at a lower price for institutional pharmacies. On their membership applications, those operating the scam made false statements concerning the number of nursing home patients they served. Asay, Almanza and others in the scheme directed their shell pharmacies to order large quantities of discounted drugs, and then arranged for the pharmacies to deliver the drugs to wholesale distribution companies to be sold for profit.

In 1994, the Arizona Board of Pharmacy inspected a closed-door pharmacy in Mesa, Ariz., and discovered several state code violations, including a non-pharmacist working without a registered pharmacist present. The inspection also revealed that the pharmacy had purchased drugs from wholesalers at reduced prices and shipped them to Intermountain Distributors. The Arizona Board of Pharmacy referred the matter to the FDA, and the OCI office in Kansas City, Kan., handled the case.

Additionally, the Colorado Board of Pharmacy inspected Principal and Intermountain in 1994 and noted that both businesses had a small drug inventory and that Principal had a small number of prescriptions on file—characteristics of closed-door pharmacies involved in drug diversion, according to court papers. A federal search warrant executed at one of the defendants’ pharmacies revealed that the only prescriptions on file were for family members of the defendants. Searches of the offices of Intermountain Distributors Inc., Principal Pharmacy Consultants, Colorado Institutional Services, and other pharmacies turned up business records that documented the fraudulent activities, investigators say.

Some of the defendants’ false statements were transmitted by interstate wire transmission, and wholesalers sent payments to the defendants by mail, commercial interstate carrier, and wire transfers. Asay and Almanza deposited more than $23 million in proceeds from the mail and wire fraud scheme into several bank accounts under different business names.

The federal government seized the couple’s Colorado mansion and other belongings. The Rocky Mountain News in Denver reported that the $6 million home had 11 bathrooms, a home theater, and a 2,700 square-foot heated deck. Asay and Almanza pleaded guilty to mail fraud in connection with their scheme to defraud manufacturers. In 2001, Asay and Almanza received prison sentences of six and a half and three years, respectively. The court also ordered the couple to pay restitution to the defrauded drug companies. Nigel and Anita Jones also were ordered to pay restitution and received probation. Seventeen drug companies received total restitution of nearly $5 million. ■
Imagine living with a parent who goes to the grocery store, only to return hours later with no knowledge of where they have been or where they left the car. Or kissing your husband of 50 years and having him ask, "Who are you?"

For the 19 million Americans who care for persons with Alzheimer's disease (AD), these experiences are commonplace. Most of us appreciate how AD victimizes those it afflicts. What we may not realize, is that this tragic disease has more than one victim. There are other, "hidden" victims: the family, friends and caregivers of the person with Alzheimer's.

When families first receive a diagnosis of Alzheimer's disease, they vacillate between trying to get information and trying to find some other, less terrifying explanation for the symptoms they see. In the earliest stages of the disease, it is easy to dismiss the forgetfulness, confusion and subtle personality changes as depression or stress. Most of the time, the person with Alzheimer's seems fine. Many are still driving, working and living alone. One of my clients played golf and did volunteer work for two years after his diagnosis.

However, AD is progressive. As the disease destroys more brain cells, the initial symptoms worsen and new ones appear. The person with Alzheimer's has difficulty remembering who they are or what they did five minutes ago. They need direction to complete routine tasks like making coffee. They have trouble putting sentences together or understanding what is being communicated to them. Easily overwhelmed by a world that has become confusing and nonsensical to them, they react with extreme anger and distress over seemingly minor events.

This is the point when the hidden victims seek help. The terrible truth can no longer be denied: The person they love has Alzheimer's disease. Each and every day, AD will steal another piece of them, turning them into a stranger who, cruelly, still looks like the person they once loved. The worst part for the caregiver is the overwhelming feeling of helplessness. For no matter what they do, they can't stop AD from taking their loved one away. There is no treatment to restore lost capabilities and there is no cure.

Grief is an inevitable reaction. But this is a grief unlike any other. The person is still here. They look healthy. Sometimes, because of the fluctuating nature of the disease, they even seem like their old selves. Then they ask you, while they stand in their home of 35 years, where they are, and you know you have lost them. It is hard to grieve under these circumstances and hard to get other people to understand and acknowledge your loss. With a course that can last up to 20 years, families call it "the funeral that never ends."

AD also victimizes caregivers physically. As the person with Alzheimer's becomes increasingly incapacitated, they require constant supervision, 24 hours a day. Families must assume all of the responsibilities of a person who has Alzheimer's. Assistance is needed for all of their activities, such as bathing, grooming and toileting. Most of these efforts are met with anger and resistance, since the person with the disease often doesn't recognize their need for help. The demands are so great that many caregivers give up their jobs, their social lives and their recreational activities, at a time when they need them most. It takes a toll; 50 percent of caregivers become depressed and 80 percent report high stress and stress-related symptoms.

When caregivers try to seek help they discover another problem. Help is available but it is very expensive. In-home care costs up to $18 an hour. Residential care costs between $2,500 and $6,000 a month. Furthermore, there are virtually no insurance benefits for these services. Another problem is that we have no way of predicting, at the time of diagnosis, how long the person with Alzheimer's will live. In the face of a lengthy, chronic illness with limited resources for long-term care, caregivers often postpone seeking the help they need.

Until a cure is found, Alzheimer's disease will continue to take a toll on the emotional, physical and financial resources of the hidden victims. They deserve recognition and support. They need to know they are not alone.

For support groups and other information for the hidden victims of Alzheimer's disease, contact the Alzheimer's Association. You can find your local chapter by calling 1-800-272-3900 or checking www.alz.org/findchapter.asp.

Terry Ullman is a psychotherapist and geriatric care manager in private practice in Bethesda, Md., where she specializes in Alzheimer's disease and caregiving.
To make the public aware of the risks of consuming untreated juice, the FDA advises children, older people, and those with weakened immune systems to ...

**Read the Label**

Make sure your juice or cider is pasteurized or otherwise treated.

Look for pasteurized or otherwise treated products in your grocers’ refrigerated sections, frozen food cases, or in nonrefrigerated shelf-stable containers, such as juice boxes, bottles, or cans.

Juice or cider that’s pasteurized or treated in another way to kill harmful bacteria may not say so on the label, so look for a warning label to avoid purchasing untreated juice or cider.

**When in doubt ...**

Don’t hesitate to ask if a juice or cider product is treated, especially for products sold in refrigerated cases of grocery or health food stores or at cider mills or farm markets.

**Warning:** This product has not been pasteurized and therefore may contain harmful bacteria that can cause serious illness in children, the elderly, and persons with weakened immune systems.

For more information on handling food safely, contact: The U.S. Food and Drug Administration Center for Food Safety and Applied Nutrition Food Information Line at 1-888-SAFEFOOD (toll-free), 24 hours a day. Or visit FDA’s Food Safety Web site at: www.cfsan.fda.gov