

# FDA *Consumer*

Magazine of the U.S. Food and Drug Administration

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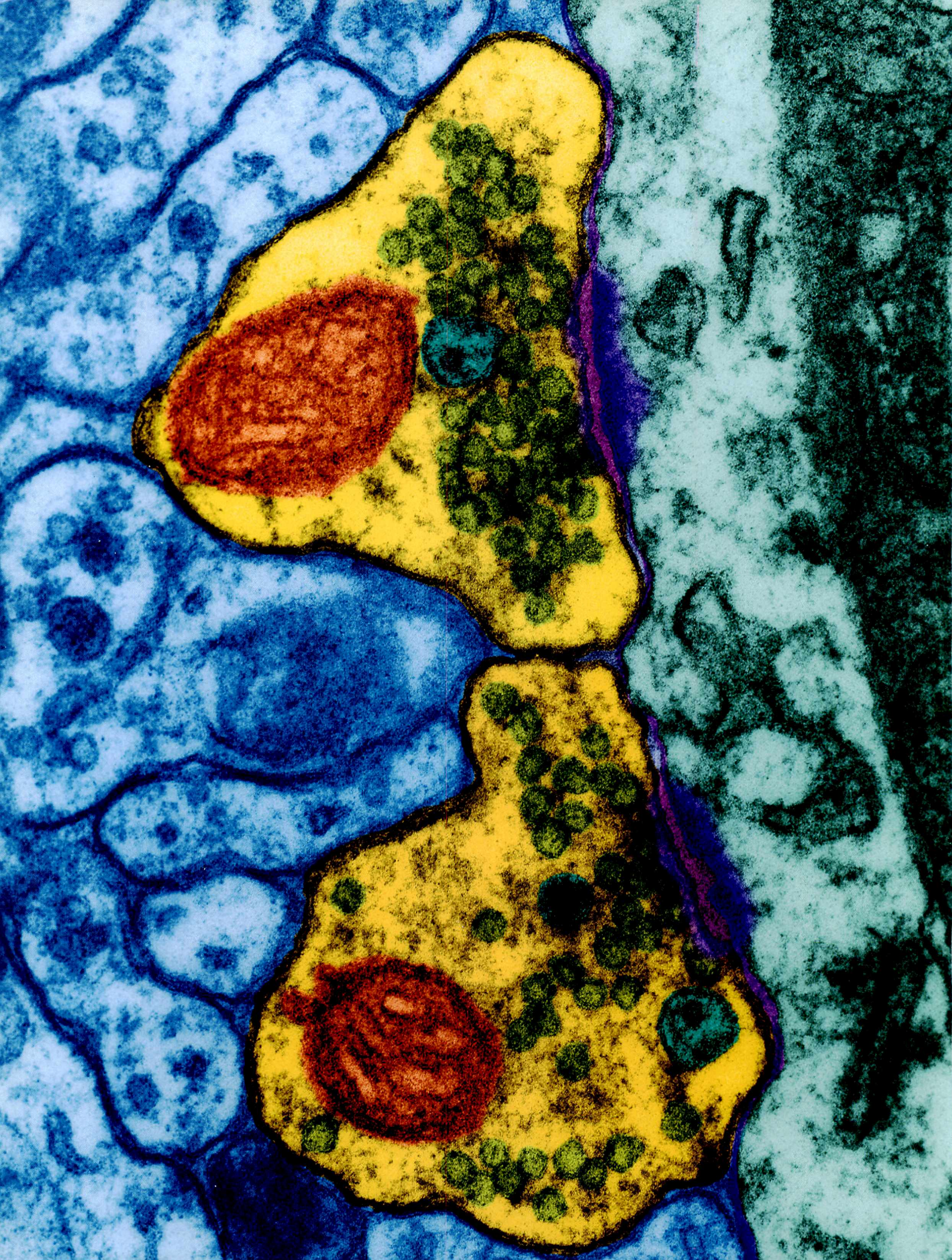


## **Joint Replacement:**

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## **An Inside Look**







U.S. Department Of Health And Human Services

# FDA Consumer

The Magazine of the U.S. Food and Drug Administration

March–April 2004 • Vol. 38 No. 2

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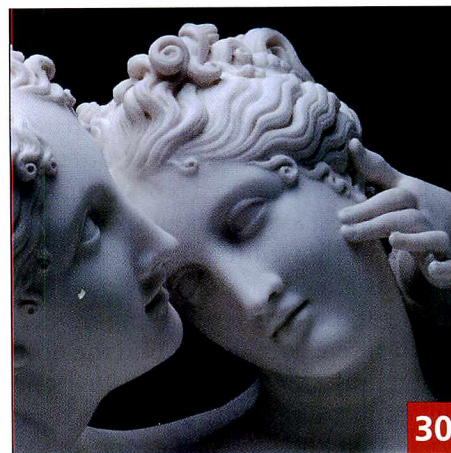
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Pain and other sensory impulses are transmitted to the brain by nerve cells called **neurons**. The impulses move from neuron to neuron through minute spaces called **synapses** (purple areas). To learn more about pain, see page 22.



## OBSERVATIONS

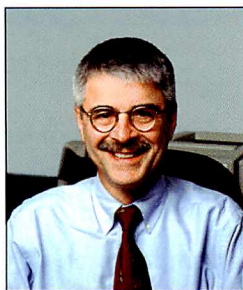
Our knees and hips are among the body's hardest working joints. They allow us to twist, turn, dance, jump, stand, walk, run, climb stairs, swing a golf club, kick a soccer ball, or even hit a home run. All that wear and tear can take a toll, and osteoarthritis can result, even among younger people.

About 500,000 hip and knee replacements are done annually in the United States, according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Successful replacements of knees and hips have helped keep people mobile, comfortable, and independent.

Researchers are studying the types of patients most likely to benefit from hip and knee replacement surgery. In addition, new technologies and materials involving prosthetic devices for hip and knee replacement and advances in surgical techniques are being developed.

Questions remain, however, concerning which prosthetic designs and materials and which surgical techniques and rehabilitation approaches yield the best long-term outcomes. The National Institute on Aging and NIAMS are among the federal agencies looking for answers. For more on hip and knee replacement and the FDA's role, see our cover story titled "Joint Replacement: An Inside Look," beginning on page 12.

Stub your toe or hit your thumb with a hammer and the resulting sensation that races through your nervous system



to your brain to alert you to possible injury is called acute pain. Chronic pain is different. The pain signals continue for days, weeks, months, and even years.

Headaches, low-back pain, arthritis-related pain, and pain related to damage to the nervous system itself are among the most common causes of chronic pain, according to the National Institute of Neurological Disorders and Stroke.

Clinical studies have found that people with chronic pain sometimes have lower-than-normal levels of the body's own pain relievers called endorphins in their spinal fluid. Researchers are working to develop new painkillers and also are studying the effects of stress on chronic pain. For more on chronic pain, see our feature story titled "Managing Chronic Pain," on page 22.

No doubt about it—Americans want to look good. Nearly 7 million of us had some type of cosmetic procedure—surgical or non-surgical—done in 2002, according to the American Society of Plastic Surgeons. The vast majority, 5 million, chose the non-surgical option, rather than going the nip-and-tuck route to smooth wrinkles or to lift age-related sags. Find the latest on so-called vanity drugs in our feature titled "Science Meets Beauty: Using Medicine to Improve Appearances," on page 30.

We also take a look at the 2003–2004 flu season, the FDA's ban of the dietary supplement ephedra, and the agency's crackdown on illegal products.

*Ray Formanek Jr.*  
*Editor*

## UPDATES

### **New Product for Treating Facial Wrinkles**

Restylane (hyaluronic acid), approved by the FDA in December 2003, is the third injectable product available to treat facial wrinkles. Restylane is different than the other approved products in that its effects last longer, about six months.

Studies showed that Restylane, classified as a medical device by the FDA, is safe and effective for filling moderate-to-severe wrinkles around the nose and mouth. Most people needed one injection to get optimal correction, while about one-third of people tested needed more than one injection to get a satisfactory result.

The two other injectable products approved by the FDA are collagen in-

jections for correcting soft tissue deficiencies such as wrinkles and acne scars, and botulinum toxin (Botox Cosmetic) for treating frown lines between the eyebrows. The effects of both treatments last as long as four months.

Restylane is manufactured by Q-Med AB of Uppsala, Sweden.

### **Counterfeit Surgical Mesh**

Health care professionals have been alerted by the FDA to watch out for a counterfeit product labeled as Prolene polypropylene mesh, which is used in hernia repair and other surgery. The authentic Prolene mesh is manufactured by Ethicon Inc. of Somerville, N.J.

Preliminary testing of the counterfeit Prolene indicates that some samples are

not sterile. Although the FDA has not received reports of excess infections with the counterfeit product, the agency is concerned about its sterility.

The FDA continues to test the material and is investigating whether the product is being marketed. In the meantime, the agency recommends that health care professionals carefully examine all polypropylene mesh products and not use any suspected of being counterfeit. The counterfeit mesh is labeled with lot numbers RBE609 (expiration date 1/07) and RJJ130 (expiration date 7/07). It can be further identified by one of the following:

- a packaging seal that does not open smoothly
- an additional small seal on the top



corner edges of the package

- a fabric end that is jagged or not cleanly cut on the 3-inch side
- an Ethicon logo in a thicker than usual typeface.

The "Public Health Notification on Counterfeit Polypropylene Mesh" can be viewed at [www.fda.gov/cdrh/safety/121903.html](http://www.fda.gov/cdrh/safety/121903.html).

### Tips to Prevent Hospital Bed Fires

Since 1993, the FDA has received 95 reports of fires that involved electrically powered hospital beds. The agency has prepared a list of safety tips for hospitals and other medical facilities to help prevent such fires.

The majority of the reports involved fires ignited by such causes as the overheating of the bed motor or capacitors, arcing at the plug and wall plate, and missing components in the wiring of the bed. The remaining reports identified smoke or flames that came from the bed, but no conclusion was reached as to the cause of the fire. Smoking in bed was the cause of one fire reported to the FDA.

The safety tips, released in December 2003, apply to both electrically powered and manual health care beds and to adjustable medical beds. One list of tips is for clinical staff and another list is for mechanical maintenance staff.

The FDA is seeking additional information on fires involving hospital beds. Some medical facilities are required to report problems with medical devices, including hospital beds, to the FDA. Health care providers employed by these facilities should use their established procedures for reporting hospital bed fires to the agency. All other health care providers may submit their reports to MedWatch, the FDA's voluntary reporting program.

The reports can be submitted by phone at (800) FDA-1088; by fax at (800) FDA-0178; by mail to MedWatch, FDA, HF-2, 5600 Fishers Lane, Rockville, MD 20857, or online at [www.fda.gov/medwatch/how.htm](http://www.fda.gov/medwatch/how.htm).

The safety tips are available at [www.fda.gov/cdrh/safety/bedfires.html](http://www.fda.gov/cdrh/safety/bedfires.html).

### DNA-Based Lab Tests

Two tests approved by the FDA in December 2003 will help identify people with an increased risk of developing blood clots in their legs and elsewhere. The tests—called Factor V Leiden kit and Factor II (prothrombin) G20210A—identify hereditary abnormalities in two proteins involved in blood clotting. Five to 10 percent of Americans have at least one of these genetic abnormalities. Left untreated, blood clots can cause death.

To do the tests, millions of identical copies of a person's Factor V or Factor II gene segment are made using a process called polymerase chain reaction (PCR). A fluorescent tag then binds to the DNA and is used to measure the presence or absence of the clotting mutation.



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The tests represent a significant advance in technology. The FDA has cleared other genetic tests in the past, but these are the first tests that are specific for these particular mutations.

The DNA-based tests are manufactured by Roche Diagnostics Corp. of Indianapolis.

### Improving Health Care for Children

The FDA can now require certain research that will improve the quality of health care for children. This authority was granted to the agency under a new law known as the Pediatric Research



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Equity Act. Signed by President Bush in December 2003, the law allows the FDA to require drug firms to conduct pediatric studies of drugs when needed to ensure that the drugs are safe and effective when used in children.

"The Pediatric Research Equity Act of 2003 will allow FDA to close the knowledge gap when it comes to treating children," says FDA Commissioner Mark B. McClellan, M.D., Ph.D. "FDA will now have clear authority to require pediatric studies of drugs when other approaches are not sufficient to ensure that drugs are safe and effective for children."

Prior to the act, studies of drug effects in children were done infrequently, and doctors had to rely on adult test results when prescribing drugs to children.

"Prescription drugs can do more than ever to cure diseases, including illnesses in children," says McClellan. "But it is not good medicine to assume that children can be treated like little adults. Parents and health professionals deserve confidence that medicines used to treat children are safe and effective. FDA will use this important new law to require pediatric studies, when necessary, to give parents and doctors the confidence they deserve."



## First Chewable Oral Contraceptive

A first-of-its-kind tablet is the latest addition to the selection of oral contraceptives available to women. Ovcon 35, approved by the FDA in November 2003, is a spearmint-flavored tablet that can be chewed or swallowed whole.

Ovcon 35 contains a progestin (norethindrone) and an estrogen (ethinyl estradiol), ingredients found in contraceptive products that are already marketed. Directions for use tell women that if the pill is chewed and then swallowed, they should drink an 8-ounce glass of liquid immediately afterwards so that the full dose of medication reaches the stomach and no residue is left in the mouth.

Risks associated with Ovcon 35, manufactured by Bristol-Myers Squibb Co. of Princeton, N.J., are similar to those of all birth control pills and include an increased risk of blood clots, heart attack, and stroke. The product labeling also warns that cigarette smoking by women, especially those older than 35, increases the risk of serious cardiovascular side effects from use of combination hormonal contraceptives.

## New Treatment for Advanced Prostate Cancer

Men with advanced cases of prostate cancer now have an additional treatment option. In November 2003, the FDA approved Plenaxis (abarelix), a drug given as an injection. Plenaxis lowers the male hormone testosterone, a key factor involved in most prostate cancer growth.

Because of an increased risk of serious and potentially life-threatening allergic reactions, use of Plenaxis is restricted to advanced prostate cancer patients who have no alternative therapy. The drug is distributed directly to physicians and hospital pharmacies enrolled in a risk management program. Plenaxis is not distributed through retail pharmacies.

The effectiveness of Plenaxis in lowering testosterone production was demonstrated in a study of 81 men with advanced prostate cancer. The study showed that the men could avoid surgical castration by undergoing at least 12 weeks of treatment. Some men also experienced other benefits, such as decreased pain. But three of the men ex-

perienced serious allergic reactions, one of which included loss of consciousness.

Because of the risk of low blood pressure and fainting as part of the allergic reaction, men being treated with Plenaxis should be monitored for at least 30 minutes after receiving a dose of the drug in their health provider's office. The most common side effects of Plenaxis are hot flashes, sleep disturbances, back pain, breast enlargement or pain, and constipation.

Plenaxis is marketed by Praecis Pharmaceuticals Inc. of Waltham, Mass.

## Revised Draft Guidance Document for Breast Implants

A draft FDA guidance document released in January 2004 should give those seeking marketing approval for breast implants—particularly those filled with silicone gel—a better understanding of the information that should be provided for the FDA to evaluate the safety and effectiveness of these medical devices. The guidance document includes modified recommendations for mechanical testing, determining modes and causes of rupture, clinical studies, post-approval requirements, and labeling.

"This revised guidance is our view on the information needed to provide a reasonable assurance of safety and to allow women and physicians to make informed decisions about silicone implants," says Mark B. McClellan, M.D., Ph.D., Commissioner of Food and Drugs.

The January guidance document updates a previous version published in February 2003, which has been useful to sponsors and the FDA in preparing and reviewing premarket approval applications. By updating the document, the FDA is more clearly identifying the type and amount of scientific data that will allow the FDA to evaluate whether these products are safe and effective.

The draft updated guidance document can be viewed at [www.fda.gov/cdrh/ode/guidance/1239.html](http://www.fda.gov/cdrh/ode/guidance/1239.html). ■

## Microbiologist Appointed to Direct FDA's Foods Center

Joseph A. Levitt, J.D., retired from the FDA on Dec. 31, 2003, after serving as director of the agency's Center for Food Safety and Applied Nutrition (CFSAN) for six years. Robert E. Brackett, Ph.D., was appointed director, effective Jan. 1, 2004.

"As a staff attorney, Commissioner's chief of staff, deputy center director, and center director, Joe has clearly had a unique and lasting impact on the health of Americans," FDA Commissioner Mark B. McClellan, M.D., Ph.D., said in announcing the change. "With a career-long commitment to improving America's health and strengthening FDA, Joe leaves our food and nutrition center as a world-class organization, ready to meet the challenges ahead."



Robert E. Brackett

Brackett was recruited to the FDA in 2000 and has been crucial to strengthening CFSAN's scientific expertise in food safety and counterterrorism. "As our food and nutrition center faces more challenges and responsibilities than ever—as well as better science to meet them—FDA is indeed fortunate to be able to call upon Dr. Bob Brackett," McClellan added.



## Even Moderate Amounts of Exercise Can Prevent Weight Gain

Moderate amounts of exercise, such as walking 12 miles per week, may help prevent weight gain and can promote weight loss in non-dieting individuals, researchers say.

Results from the National Health and Nutrition Examination Survey 1999 indicate that an estimated 61 percent of U.S. adults are either overweight or obese, defined as having a body mass index (BMI) of 25 or more, according to the Centers for Disease Control and Prevention.

Obesity is associated with a higher risk for several health problems, including heart disease and diabetes. It is widely believed that diet combined with physical activity plays an important role in weight management, but the amount of activity needed to prevent weight gain is unknown, according to Cris A. Slentz, Ph.D., of the Duke University Medical Center, Durham, N.C., and colleagues.

The researchers investigated the effects of different amounts and intensities of exercise on weight. The results are published in the Jan. 12, 2004, issue of *Archives of Internal Medicine*.

The randomized, controlled trial in-

cluded 182 sedentary overweight men and women, ages 40-65 years, who were assigned to one of several groups: high amount/vigorous intensity exercise (equivalent to jogging about 20 miles per week at 65 percent to 80 per-



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cent peak oxygen consumption); low amount/vigorous intensity exercise (equivalent to 12 miles of jogging per week at 65 percent to 80 percent peak oxygen consumption); or low amount/moderate intensity exercise (equivalent to 12 miles of walking per week at 40 percent to 55 percent peak oxygen consumption). A fourth group in the study,

the control group, did not exercise.

The study lasted eight months and participants were asked not to change their diets during this time. Body weight and waist and hip circumference were measured. The researchers found that there was a clear relationship between the amount of physical activity and amount of weight loss, with the most weight loss seen in the high amount/vigorous intensity group, and the least in the low amount/moderate intensity group.

The control group gained weight over the study period. Compared with the control group, all exercise groups significantly decreased their waist and hip circumference measurements.

"These findings strongly suggest that, absent changes in diet, a higher amount of activity is necessary for weight maintenance and that the positive caloric imbalance observed in the overweight controls is small and can be reversed by a modest amount of exercise. Most individuals can accomplish this by walking 30 minutes every day," the authors wrote. ■

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**General FDA questions:** E-mail [webmail@oc.fda.gov](mailto:webmail@oc.fda.gov).

**Mailing address:** Food and Drug Administration (HFI-40), 5600 Fishers Lane, Rockville, MD 20857



# Ephedra Ban: No Shortage of Reasons

By Carol Rados

The Food and Drug Administration has banned the sale of dietary supplements containing ephedra (ephedrine alkaloids) due to concerns over their cardiovascular effects, including increased blood pressure and irregular heart rhythm. The final rule, published Feb. 6, 2004, becomes effective on April 12, 2004.

"This FDA rule reflects what the scientific evidence shows—that ephedra poses an unreasonable risk to those who use it," Health and Human Services Secretary Tommy G. Thompson said. "The regulations prohibit the sale of dietary supplements containing ephedra, and we intend to take swift action against anyone who puts consumers at risk by continuing to sell such products after the prohibition takes effect."

The action banning ephedra, often referred to as ma huang, marks the first time that the FDA is taking formal action to halt the sale of a dietary supplement ingredient since passage of the Dietary Supplement Health and Education Act (DSHEA) in 1994.

Ephedra is a naturally occurring substance found in plants. Its principal active ingredient is ephedrine, an amphetamine-like compound that potentially has powerful stimulant effects on the nervous system and heart. Like an amphetamine, ephedra increases both blood pressure and heart rate, decreases appetite, and makes the user feel energetic.

In synthetic form, ephedrine is regulated as a drug under the Federal Food, Drug and Cosmetic Act (FD&C Act), and is allowed as an ingredient in over-the-counter drugs to treat asthma, nasal congestion, and minor eye irritation. In recent years, however, dietary supplement products containing botanical ephedra, often in combination with caffeine, another type of stimulant, have been promoted to help people lose weight and enhance sports performance and energy. At the same time, ephedra has been sus-

pected of causing unreasonable health risks or injuries.

## Evidence of Harm

There is strong scientific evidence of harm associated with the use of ephedra products. The FDA has been reviewing information for many years about ephedra's effects in the body, its safety and effectiveness, and the adverse event reports associated with its use. The agency found that supplements containing ephedra show little evidence of effectiveness, except for short-term weight loss. The agency also found that the herbal substance raises blood pressure and stresses the circulatory system. These reactions have been linked to serious health problems, including heart ailments and strokes.

One review sponsored by the National Institutes of Health concluded that ephedra is associated with higher risks of mild-to-moderate heart palpitations, psychiatric and upper gastrointestinal effects, and symptoms of hyperactivity of the autonomic nervous

system, such as tremor and insomnia, especially when taken with caffeine and other stimulants. Another review showed that, for people taking more than 32 milligrams daily, the rate of hemorrhagic (bleeding) strokes among ephedra users was significantly higher than that recorded for non-users. Some ephedra-containing dietary supplement labels recommend daily doses of up to 100 milligrams.

Additionally, a study of calls to poison control centers revealed a disproportionate rate of reactions to ephedra relative to other herbal products. In short, the evidence shows that ephedra is associated with an increased risk of alarming side effects, possibly even deaths.

## The Dietary Supplement Law

A dietary supplement is a product taken by mouth that contains a dietary ingredient, such as a vitamin, mineral, herb, other botanical, or amino acid. Substances intended to supplement the diet, such as enzymes, organ tissues, glandulars, and metabolites, also fall in

## Products Affected by the Ban

All currently marketed dietary supplements are affected by the ban if they contain a source of ephedrine alkaloids, including:

- ephedra
- ma huang
- sida cordifolia
- pinellia.

The rule does not pertain to:

- traditional Chinese herbal remedies
- herbal teas regulated as conventional foods subject to FDA regulation under other sections of the law
- drugs that contain chemically synthesized ephedrine. ■





FDA/Michael Ermarth

**Ephedra can have dangerous effects on the nervous system and heart.**

this category. Dietary supplements can be extracts or concentrates, and may be found in many forms, such as tablets, capsules, softgels, gels, liquids, or powders. People take dietary supplements for many reasons, including weight loss, energy, disease prevention and management, and health maintenance.

Whatever their form, the FDA regulates dietary supplements under a different set of laws than those covering "conventional" foods and drug products. Under DSHEA, manufacturers are responsible for ensuring that a dietary supplement is safe before it is marketed. They are not required to obtain FDA approval before producing or selling dietary supplements, but they must make sure that product label information is truthful and not misleading. Once a dietary supplement reaches the market, the FDA can take formal action against any dietary supplement shown to be unsafe, such as ephedra. The burden of proof for showing a dietary

supplement is unsafe rests with the FDA.

### Interim Measures

Based on the FDA's recent comprehensive evaluation of the science, as well as a review of adverse event reports associated with products containing ephedra, the agency alerted consumers to stop buying and using these products immediately. In December 2003, the agency notified firms manufacturing and marketing these products of its intent to issue a final rule prohibiting their sale.

Why a rule? A rule is the most efficient and powerful way to be sure that ephedra-containing dietary supplements stay off the market, as the FDA intends. The rule describes the scientific basis for the

FDA's conclusion that dietary supplements containing ephedrine alkaloids present an unreasonable risk of illness or injury, and are therefore adulterated under the FD&C Act, when used either as suggested in the labeling, or as they are ordinarily used if the labeling doesn't specify use.

"This final rule will protect consumers by ensuring that these dangerous products are removed from the market and never sold," says FDA Commissioner Mark B. McClellan, M.D., Ph.D.

If a firm continues to market dietary supplements that contain ephedra after the April 2004 effective date of the rule, the FDA can forbid the manufacturer or distributor from continuing to distribute the products, or the agency can initiate action to remove them from the market.

The February 2004 announcement of the FDA's ephedra ban continues a process that started in June 1997, when the FDA first proposed limits on its use, including a required statement on ephedra-containing dietary supplements

warning that ephedra is hazardous and should not be used for more than seven days. In February 2003, the agency announced a series of measures that included strong enforcement actions against firms making unsubstantiated claims about their ephedra products. The agency has also taken action against dietary supplements containing synthetic ephedrine, since this material does not meet the definition of a dietary ingredient.

### Immediate Action

While working on the final rule, the FDA was actively protecting the public health through a series of high-profile enforcement actions aimed at addressing the public health danger or false or misleading product promotion. Such actions included inspections that resulted in voluntary compliance, voluntary recalls, warning letters, seizures and injunctions, criminal enforcement, and joint enforcement actions with the Federal Trade Commission (FTC) and the Department of Justice.

For example, in 2003 the FTC brought four enforcement actions challenging deceptive claims about safety and side effects for ephedra supplements marketed as bodybuilding aids and energy boosters, and as alternatives to street drugs like Ecstasy. In these cases, the marketers both overstated the benefits and understated the risks of using the products.

In light of the FDA's actions, some ephedra products already have been removed from the market, and the demand for ephedra products has declined significantly. Many companies have reformulated their products to remove ephedra, while others pulled products from the market altogether.

The FDA says there is now concern over some of the alternative ingredients to ephedra, such as bitter orange, which contains synephrine, another form of stimulant with properties similar to ephedrine. ■





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# FDA Launches Campaign on OTC Pain Relief Products

In January 2004, the FDA launched a national education campaign on the safe use of over-the-counter pain relief products.

"Pain relievers and fever reducers are safe drugs when used as directed, but they can cause serious problems when used by people with certain conditions or those who are taking specific medicines," says FDA Commissioner Mark B. McClellan, M.D., Ph.D. "We want to remind consumers who take these products that it's important to follow current dosing and label directions carefully."

The FDA's campaign focuses on OTC pain and fever reducers that contain acetaminophen and non-steroidal anti-

inflammatory drugs (NSAIDs), which include products such as aspirin, ibuprofen, naproxen sodium and ketoprofen.

Many OTC medicines sold for different uses have the same active ingredient. For example, a cold-and-cough remedy may have the same active ingredient as a headache remedy or a prescription pain reliever. To minimize the risks of an accidental overdose, consumers should avoid taking multiple medications with the same active ingredient at the same time.

Acetaminophen is an active ingredient found in more than 600 OTC and prescription medicines, such as pain relievers, cough suppressants and cold medications. It is safe and effective when used correctly, but taking too much can lead to liver damage and

even death. The risk for liver damage may be increased in people who drink three or more alcoholic beverages per day while using acetaminophen-containing medicines.

NSAIDs are common medications that are used to relieve fever and minor aches and pains. These products can cause stomach bleeding, with an increased risk in consumers who are over 60, are taking prescription blood thinners, are taking steroids, or have a history of stomach bleeding. NSAIDs may also increase the risk of kidney problems in people with pre-existing kidney disease, or who are taking a diuretic.

In September 2002, the FDA's Non-Prescription Drugs Advisory Committee recommended changes to labeling of certain OTC drug products, including acetaminophen and NSAIDs. They advised that these changes are needed to better inform consumers about the products' ingredients and the possible side effects caused by improper use. The FDA is reviewing various labeling changes that better reflect the latest scientific knowledge about oral OTC pain relievers.

The FDA recommends that consumers talk with health care providers or pharmacists if they have questions about using OTC medicines, and especially before using them in combination with dietary supplements or other OTC or prescription medicines. ■

The FDA's educational campaign will provide advice on how to avoid taking more than the recommended doses of pain medicines and will raise awareness of the underlying health conditions that increase risk. The campaign will include:

- an OTC pain reliever brochure to be distributed in pharmacies and by health care providers
- a newspaper article to be distributed to 10,000 community papers across the country
- a reprint of an *FDA Consumer* article called "Use Caution with Pain Relievers" that will be distributed at national health conferences and made available for reprinting in health publications
- two print public service ads that will be sent to about 100 major magazines.

All of these materials are available on the FDA's Web site at [www.fda.gov/cder/drug/analgesics/](http://www.fda.gov/cder/drug/analgesics/). ■





CDC

In the United States, the flu season can run from November through March, and even past March in some years.

# A Look at the 2003–2004 Flu Season

*By Michelle Meadows*

**O**verall, the flu hit people in the United States earlier than usual during the 2003–2004 flu season, and lab tests showed evidence of a strain of the virus that's typically associated with more severe seasons. Taking a cue from the flu season just ending, experts say it's not too early to make a note for this fall: Vaccination is the best protection against the flu and can prevent many illnesses and deaths. Even for people who come down with the flu after vaccination, the illness is generally less severe than in people who didn't get vaccinated.



## A Serious Illness

Media reports in November 2003 highlighted flu-related deaths in children in Colorado. But experts stress that flu, a contagious respiratory illness caused by the influenza virus, is serious every year. "Influenza is always the most important cause of acute respiratory illness that causes patients to seek medi-

cine about one month apart.

In addition to deaths, many more children have been hospitalized. Glezen says, "I think we need to take greater notice of the serious consequences of a vaccine-preventable disease like influenza."

Though it hasn't been in the news as much as the flu cases in children, older

care providers. The CDC purchased additional doses of flu vaccine from the two manufacturers of inactivated flu vaccine licensed in the United States: Aventis Pasteur of Swiftwater, Pa., and Evans Vaccines, a subsidiary of Chiron Corp. with manufacturing facilities located in Liverpool, England. Some people mistakenly thought that this

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*The main symptoms of the flu are headache, fatigue, body aches, cough, sore throat, and congestion.*

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cal care each year," says Paul Glezen, M.D., a professor of molecular virology and microbiology at Baylor College of Medicine in Houston. "Children are hit hard each year. This is a particularly bad epidemic, and we have had several deaths here in Texas, though not the same publicity as with Colorado."

Between October 2003 and early January 2004, the deaths of 93 children younger than 18 had been reported to the Centers for Disease Control and Prevention (CDC), according to preliminary data. Of the 45 children with a known vaccination status, one child had received adequate vaccination, 33 were not vaccinated, five were reported as vaccinated but the interval between vaccination and onset of illness had not been documented, and six children had received one dose of vaccine. It is recommended that children younger than 9 who haven't been previously vaccinated receive two doses of the flu vac-

people also face a disproportionate number of hospitalizations and deaths due to flu every year. Millions of the people who get the flu—about 10 percent to 20 percent of Americans each year—recover in a week or two without complications. But about 36,000 people die each year from the flu and 114,000 per year are hospitalized, according to the CDC.

The main symptoms of the flu are headache, fatigue, body aches, cough, sore throat, and congestion. The illness can result in complications such as pneumonia, bronchitis, dehydration, and sinus and ear infections. People at high risk for flu complications include children ages 6 to 23 months, adults 65 and older, pregnant women in the second or third trimester during flu season, and people of all ages with underlying chronic conditions, such as heart disease and asthma or other lung diseases.

## Supply and Production

Consumer demand for the flu vaccine increased considerably after reports in November 2003 of flu-related deaths in children. Manufacturers had produced about 87 million doses for the 2003–2004 flu season, including 4 million doses in the form of FluMist, a new nasal spray vaccine made by MedImmune Inc. of Gaithersburg, Md.

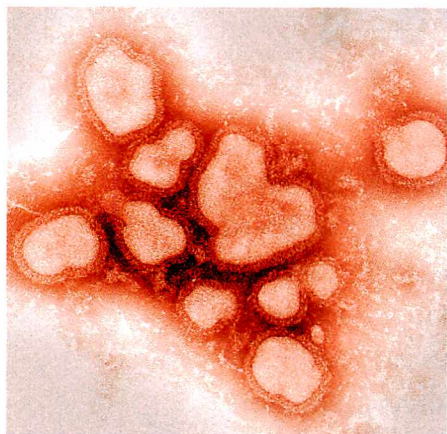
Because some states had excess supplies of flu vaccine, while other areas ran out, the CDC encouraged state health departments to coordinate with local health officials and other partners to redistribute vaccine among health

care providers. The CDC purchased additional doses of flu vaccine from the two manufacturers of inactivated flu vaccine licensed in the United States: Aventis Pasteur and Evans prepared additional doses that they had not previously intended to market because demand for the vaccine appeared to have peaked in early to mid-November. The CDC also negotiated a contract for another 3 million doses of FluMist that state and local health departments could purchase as needed.

A new flu vaccine is required most years because the circulating flu viruses mutate frequently, producing new strains from year to year. Besides selecting suitable viruses, producing the flu vaccine involves growing the viruses in eggs and conducting tests to ensure safety and purity.

"Most of the surveillance data about the emergence of new influenza viruses are collected in January and February, and in most years, we've finalized [the selection of] strains by March," says Roland Levandowski, M.D., a virologist in the FDA's Center for Biologics Evaluation and Research. "The vaccine has to be made by early summer to be ready for fall."

The three strains in the vaccine for 2003–2004 were called A/Panama, A/New Caledonia, and B/Hong Kong. A new strain called A/Fujian was identified, but too late to include the virus in vaccine production. This year's predominant flu strains circulating turned out to be similar to the Fujian strain that wasn't included in the vaccine. Questions have been raised, and studies are



CDC

Microscopic photo of influenza A virus.



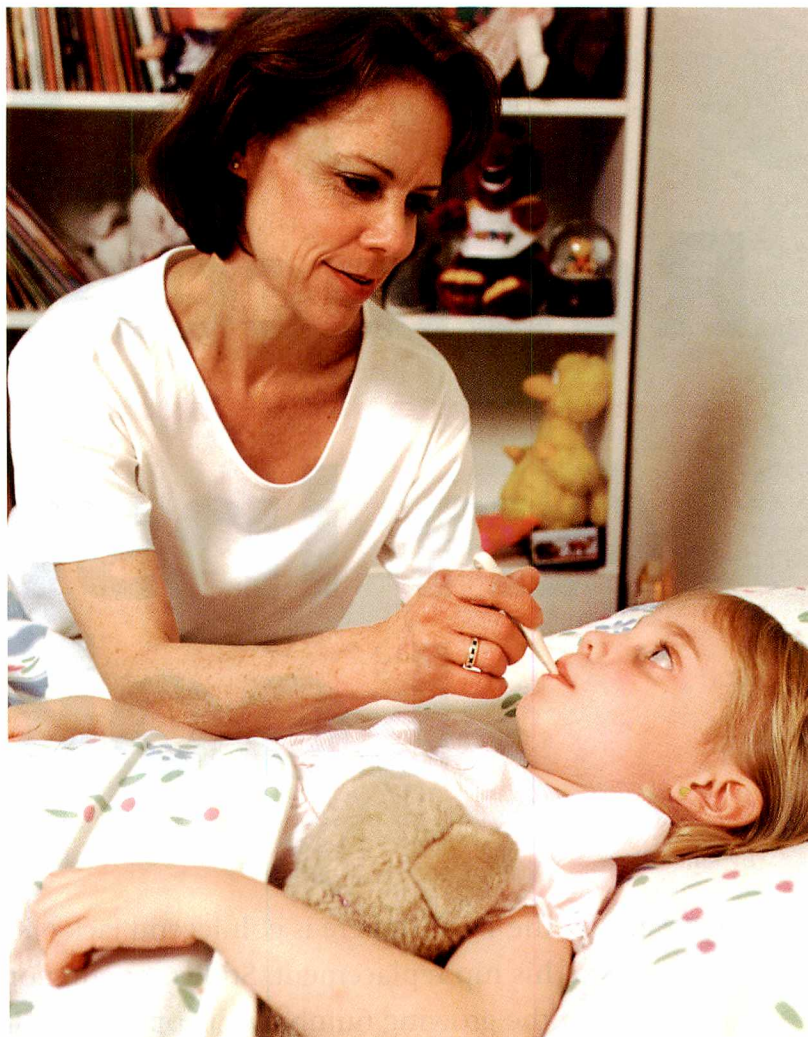
still being done, about whether this year's flu vaccine was a good enough match to protect against the Fujian strain. But experts say that, even in years when the vaccine is not a good match, it usually provides some protection.

Levandowski says the FDA is convinced that flu vaccine, if fully used by those at risk, can save many more lives annually. The agency is working with vaccine manufacturers to promote production. Jesse Goodman, M.D., director of the FDA's Center for Biologics Evaluation and Research, says, "We are working with the National Institutes of Health, CDC and manufacturers to encourage and support both increased vaccine production and innovation in vaccine development. The goals are to better meet the challenges posed by changing strains from year to year and to be better prepared for the possibility that new influenza A viruses will emerge from animal reservoirs. Such an event is currently occurring in Asia, where a multi-country outbreak of avian influenza poses a significant threat of the virus recombining with human influenza and causing a new global pandemic. New technologies and the entry of more manufacturers in the U.S. flu vaccine market can help better prepare us for such threats and also help to provide sufficient vaccine to accommodate expanding recommendations for use." A disease is considered pandemic when it occurs widely throughout a large region.

According to the CDC's Advisory Committee on Immunization Practices, about 185 million Americans should receive the flu vaccine each year. "Nearly 100 million more doses of vaccine would be needed to fully implement these recommendations, a fact that should make the market more appealing to current and future manufacturers," says Dennis O'Mara, associate director for adult immunization at the CDC.

### Prevention and Treatment

Along with preventing the spread of flu through vaccination, it's important to wash hands frequently, cover mouths and noses when sneezing or coughing, avoid close contact with people who are sick, and stay home when ill to lower the chance of infecting others.



Photodisc

**The flu can be especially dangerous for children and older people.**

If you get the flu, rest and drink plenty of fluids. Medications can help relieve symptoms such as pain and congestion. For some people, prescription antiviral drugs approved by the FDA may be appropriate. These drugs aren't meant to replace the flu vaccine, but they are approved to prevent and treat symptoms and can help shorten the time the flu lasts by about a day.

Medications containing aspirin should be avoided in children because of the potential for Reye syndrome, an illness associated with the use of aspirin during influenza infections. Reye syndrome is characterized by malfunction of the liver, often preceded by nausea and vomiting and followed by drowsiness. In severe cases, coma and death may result.

Flu usually can be treated without a trip to the doctor, but always contact your health care provider if you or your child experience any of the following

symptoms: difficulty breathing, a high temperature for more than four days, changes in skin color, lack of fluid intake, lethargy, irritability, seizures, chest pains, feeling faint, or feeling confused.

Flu vaccine is not recommended for people who are allergic to eggs or who have had a reaction to the flu vaccine in the past. But for most people, the benefits of vaccination outweigh the risks.

During a telebriefing in December 2003, CDC Director Julie Gerberding, M.D., said that deaths and hospitalizations from the flu occur year after year. "I think what's different about this year is people are really focusing on the flu, and it's getting the kind of attention that it probably should have had for a long time." ■



# Joint Replacement:

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# An Inside Look

*By Linda Bren*

**T**urn on the TV and there is golf legend Jack Nicklaus extolling the virtues of his hip replacement. Still competing on the links, Nicklaus is among the growing number of people in the United States each year who have a hip joint replaced. So is rock star Eddie Van Halen, who was 43 when he had his hip replaced in 1999, the same year as Nicklaus.

Cases like these are laying to rest the stereotype that only the aged and the inactive receive hip replacements. The same holds true for those who have knee joints replaced.

The American Academy of Orthopaedic Surgeons (AAOS) calls total hip replacement an orthopedic success story, "enabling hundreds of thousands of people to live fuller, more active lives." In 2001, about 165,000 hip joints were replaced in U.S. hospitals, according to the National Center for Health Statistics. The same year, 326,000 knees were replaced. Total knee replacement is "highly successful in relieving pain and restoring joint function," says the AAOS. And a hip or knee replacement lasts at least 20 years in about 80 percent of those who get them.

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**Marathon runner and cyclist James Puglisi trains hard 10 months after hip resurfacing surgery. This alternative to hip replacement currently is conducted only in FDA-approved clinical studies.**







But despite their success, hip and knee joint replacements still have drawbacks. There may be complications. They don't always last a lifetime and when they fail, surgery may be needed.

As artificial joints and surgical techniques to implant them continue to evolve, the medical community and patients hold out hope for joint replacements that cause fewer problems, last longer, and move more like a healthy natural joint.

geon removes the diseased or damaged parts and inserts artificial parts, called prostheses or implants. These prostheses are considered medical devices, which are regulated by the Food and Drug Administration.

### **Why Joint Replacement?**

The most common reason for having a hip or knee replaced is osteoarthritis, according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases

bone and cartilage. Rheumatoid arthritis generally starts in middle age, but can also affect children and young adults.

Loss of bone caused by poor blood supply (avascular necrosis), which led to Van Halen's hip replacement, and bone tumors may be other reasons for joint replacement.

### **Hip Replacement Surgery**

The hip joint is a ball and socket, allowing a wide range of motion. The ball

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## *The most common reason for having a hip or knee replaced is osteoarthritis.*

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### **What is Joint Replacement?**

Joints are formed by the ends of two or more bones connected by tissue called cartilage. Healthy cartilage serves as a protective cushion, allowing smooth, low-friction movement of the joint. If the cartilage becomes damaged by disease or injury, the tissues around the joint become inflamed, causing pain. With time, the cartilage wears away, allowing the rough edges of bone to rub against each other, causing more pain.

When only some of the joint is damaged, a surgeon may be able to repair or replace just the damaged parts. When the entire joint is damaged, a total joint replacement is done. To replace a total hip or knee joint, a sur-

(NIAMS). This degenerative joint disease, marked by the breakdown of the joint's cartilage, is not limited to older people. Although it most commonly affects people over age 45, younger men and women also can get this disease.

Some people are born with a deformed joint or defective cartilage, which leads to osteoarthritis. Excess weight, joint fracture, ligament tears, or other injury can damage cartilage and cause osteoarthritis.

Rheumatoid arthritis is another condition that may be alleviated by hip or knee joint replacement. This chronic inflammation of the joint lining causes pain, stiffness, and swelling. The inflamed lining can invade and damage

of the joint, the top of the thighbone (femoral head), moves within the hollow socket (acetabulum) of the pelvis. A layer of cartilage allows the ball to glide smoothly inside the socket.

In total hip replacement, the surgeon cuts away the ball part of the joint, replacing it with a ball attached to a stem that is wedged into a hollowed-out space in the thighbone. Damaged cartilage and bone are removed from the socket and a cup-like component is inserted into the socket (see page 15).

Hip replacements may be cemented or uncemented. If cemented, the hip parts are held in place with a fast-curing "bone cement" made from a type of polymer. If uncemented, the joint components are specially made to either press into the bone for a tight fit (press-fit) or to allow new bone to grow into the porous surface of the implant, holding it in place (biological fixation).

### **Hip Resurfacing**

An alternative to total hip replacement is an operation called hip resurfacing. Unlike the prostheses used in total hip replacement, which are made to replace the femoral head, resurfacing prosthesis designs allow the head to be preserved and reshaped. The resurfaced bone is then capped with a metal prosthesis. Like total hip replacement, the socket is fitted with a prosthesis.

In the United States, hip resurfacing

### **How Do You Know It's Time for Surgery?**

Jeffrey T. Nugent, M.D., orthopedic surgeon at Piedmont Hospital in Atlanta, says that if you are experiencing any of these signs, you should speak to your rheumatologist or orthopedic surgeon about the possibility of joint replacement:

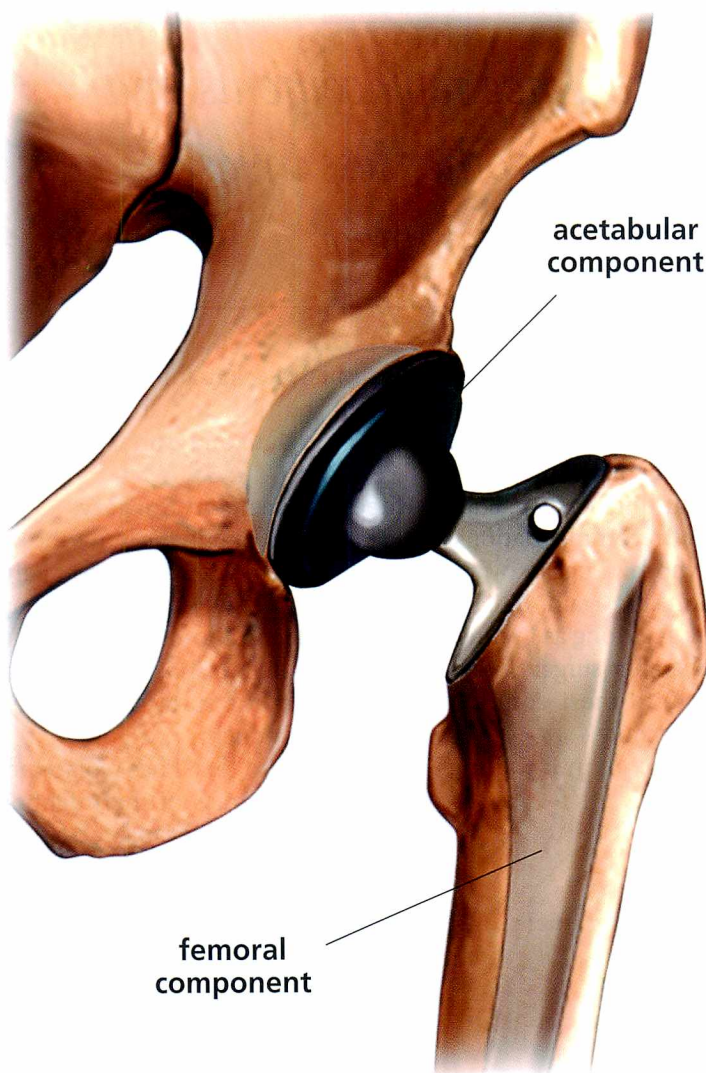
- you are unable to sleep at night because of the pain
- you've tried a series of different medications that don't help alleviate the pain, or the medication you have been on no longer works
- you feel that the pain from your arthritis is keeping you from regular outings, such as visiting friends, going shopping or taking a vacation
- your activity is restricted to the point where you have trouble getting out of a chair, going up stairs, getting off the toilet, or getting up from the floor. ■

*From "All You Need to Know About Joint Surgery," ©2002, Arthritis Foundation*

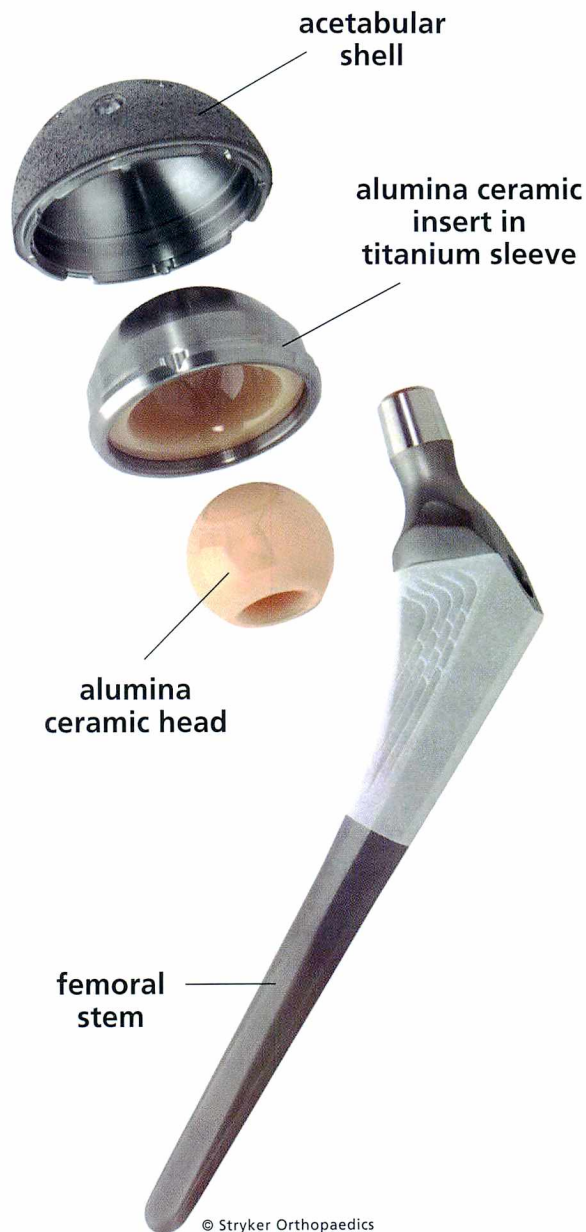


# Hip Replacement

In total hip replacement, artificial parts replace the damaged ball at the end of the thighbone (femur) and the socket within the pelvic bone.



© 2004 Nucleus Medical Art



© Stryker Orthopaedics

This alumina ceramic-on-ceramic bearing surface design is one of several hip replacement products approved by the FDA for use in the general population.

is being conducted only in FDA-approved clinical studies. It is necessary for each manufacturer of a hip resurfacing device to collect clinical data on its resurfacing design. The data collected in these studies will be used to demonstrate whether each hip resurfacing design is safe and effective for market approval in the United States. Pres-

ently, no manufacturer has obtained FDA approval to market its hip resurfacing design.

Not everyone is a candidate for resurfacing; the femoral head may be too damaged to hold the resurfacing component. "Good bone stock is required," says Michael Mont, M.D., director of the Center for Joint Preservation and

Reconstruction at Sinai Hospital in Baltimore.

James Puglisi considers himself fortunate to have good bone stock. Puglisi was 47 when he began limping because of a burning, aching pain in his hip that spread through his leg and into his knee and ankle. For this marathon runner and cyclist, just walking and standing became



painful, and sometimes the pain was so intense that it would wake him up during the night.

Puglisi was diagnosed with osteoarthritis, brought on by an abnormally formed hip joint. He was advised by his orthopedic surgeon to wait as long as possible before getting a total hip replacement because it might wear out with his active lifestyle and require one or more revisions.

in a study on hip resurfacing. Mont performed Puglisi's resurfacing operation in March 2003 and Puglisi returned home after a four-day stay at Sinai Hospital. Gradually putting more weight on his new hip, Puglisi was able to be full weight-bearing (walking without a cane or crutches) after three months. Now pain-free, the 50-year-old is back to cycling 200 miles a week and anticipates running again soon. "I'm so

period to give a patient time to build strong muscles. He also says he doesn't "totally condone heavy sporting activities" after resurfacing. "You do it at your own risk," he says, adding that if the resurfaced hip ever fails, it can be converted to a total hip replacement.

Current hip resurfacing technology is too new to know how long the resurfaced hip will last. Puglisi has volunteered to return to Sinai Hospital for

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*'We usually recommend total knee replacements and partial knee replacements after other less invasive treatments have been attempted.'*

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Revision surgery, which replaces both artificial parts and damaged bone, is more difficult than first-time surgery, says NIAMS. The outcome is generally not as good because bone is not as strong as when first operated on and the supporting ligaments may be damaged.

"But the pain was getting to the point where I needed to do something," says Puglisi.

Puglisi flew from his home in Amherst, N.Y., to Baltimore to take part

happy with the results," he says. "I had forgotten what it was like to have a pain-free life, and now I have it back. It feels as normal as my other hip."

Puglisi notes that different surgeons may have different recommendations. Another surgeon who saw Puglisi's X-rays told him he shouldn't run again. "But Dr. Mont was OK with it as long as I waited at least six months after surgery," says Puglisi. "He just told me I couldn't bungee jump or parachute!"

Mont advises the six-month waiting

an annual checkup for the next 10 years to help clinical investigators gather long-term data on resurfaced hips.

#### **Knee Replacement Surgery**

The largest joint in the body, the knee joint is formed where the lower part of the thighbone (femur) joins the upper part of the shinbone (tibia) and the kneecap (patella). Shock-absorbing cartilage covers the surfaces where these three bones touch.

In a standard total knee replacement, the damaged areas of the thighbone, shinbone and kneecap are removed and replaced with prostheses. The ends of the remaining bones are smoothed and reshaped to accommodate the prostheses (see page 17). Pieces of the artificial knee are typically held in place with bone cement.

A knee replacement usually involves three to four days in the hospital. The recovery period depends on a patient's general health, age, and other factors, but many people can resume their normal activities four to eight weeks after surgery.

"While a knee replacement can dramatically improve the quality of life for a person with debilitating knee pain, it is major surgery," says Gerard Engh, M.D., director of knee research at Anderson Orthopaedic Research Institute in Alexandria, Va. "We usually

### **What to Ask the Surgeon**

Here are some questions to ask your surgeon about joint replacement:

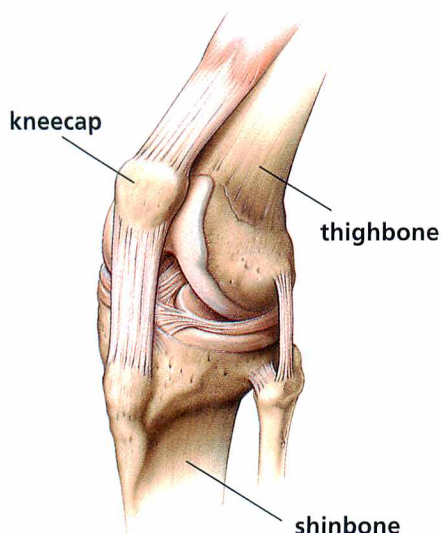
- What makes someone a good candidate for joint surgery?
- What are the risks involved in joint surgery?
- Would there be any other non-surgical treatments I haven't yet tried that would ease my pain and help me move more easily?
- How would surgery help my particular problem?
- What would not change after the operation?
- How long is the recovery process?
- What is involved in the recovery process?
- What type of procedure would you recommend for me?
- How often in the past year have you performed this operation?
- Can you tell me what the outcome (decreased pain, improved function) has been for most of these patients?
- Can you provide the names of several people I could contact to discuss their experiences with surgery? ■

*From "All You Need to Know About Joint Surgery," ©2002, Arthritis Foundation*

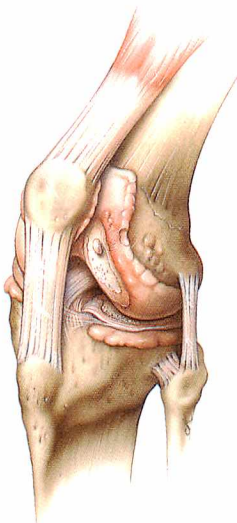


# Knee Replacement

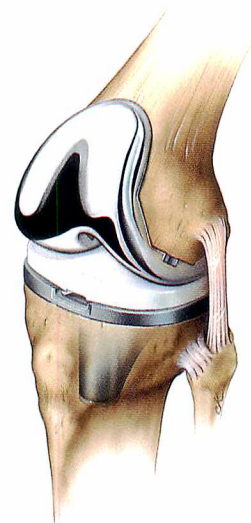
Healthy Knee



Damaged Knee



Total Knee Replacement



© 1997-2002 Zimmer Inc.

In a normal knee, the bone surfaces that come together at the joint—thighbone, shinbone and kneecap—are smooth and hard. A cushioning layer of tissue (cartilage) prevents direct contact between these bones. When the cartilage is damaged, these bones rub together, causing friction, pain and, eventually, deterioration of the bone surfaces. In total knee replacement surgery, the joint is replaced with metal and plastic implants.

recommend total knee replacements and partial knee replacements after other less invasive treatments have been attempted."

But most who opt for knee joint replacement are generally happy with the results. Ninety percent of those who have total knee replacement report fast pain relief, improved mobility, and better quality of life, according to a panel of independent experts. The panel was convened at a conference in December 2003 sponsored by the National Institutes of Health (NIH) and cosponsored by the FDA and other federal organizations.

The panel concluded that, overall, total knee replacement surgery is a safe, very successful, and relatively low-risk treatment for decreasing pain and increasing mobility in people who are not helped by nonsurgical treatments. Follow-up studies showed that revision surgery was needed in 10 percent of knee replacements after 10 years, and

in 20 percent after 20 years, according to the panel.

## Where the FDA Fits In

Artificial joints are medical devices, which must be cleared or approved by the FDA before they can be marketed in the United States. In addition, FDA permission is required before a company can test a new or redesigned prosthesis in human studies. The data gathered in these studies, which take place in specific hospitals, may then be used to support a company's application for marketing its prosthesis to surgeons and hospitals throughout the United States.

What does the agency look for before clearing a prosthesis for marketing? "It has to be proven safe and effective," says Barbara Zimmerman, chief of the FDA's orthopedic devices branch. "FDA assures safety and effectiveness using different means depending on the risks of a particular device and the technology that it presents."

For devices with a history of safe and effective use, frequently those using established technology, the FDA relies on a set of general controls to determine which devices can be marketed, says Zimmerman. "These general controls are augmented with special controls such as standards or standard test methods.

"For devices involving new uses or advanced technology, FDA often requires that a particular device be demonstrated to be safe and effective through clinical trials," she says.

## The Risks of Replacement

Like any surgery, hip and knee joint replacement carries certain life-threatening risks, such as infection, blood clots and complications from anesthesia. Other complications include nerve damage, dislocation or breakage after surgery, and wearing out or loosening of the joint over time. After hip replacement surgery, one leg may be shorter than the other.



Infection is an ongoing risk for people with joint replacements. Not only can it occur in the hospital, but it can happen years later if bacteria travel through the bloodstream to the replacement area.

In the rare case that an infection spreads to the new joint and does not clear up with antibiotic treatment, the joint must be replaced. This usually requires two surgeries—one to remove the infected joint and another surgery later to insert the new joint. Between surgeries, the infection is treated with antibiotics.

In 2001, the FDA approved a temporary artificial hip for people with hip joint infection. The temporary hip, called Prostalac, can be inserted and left in place for about three months after the infected hip is removed. It consists of a metal stem and ball that fits into the thighbone, a plastic cup that attaches to the hipbone, and a bone cement that contains antibiotics. The antibiotics in the cement, along with oral antibiotics taken by the patient, help to treat the infection. The temporary hip allows a person some movement while healing.

## The Wear Problem

The most commonly used FDA-approved joint prostheses for knees and hips are made of metal and plastic. The metal is usually titanium or a mixture of cobalt and chromium. The plastic is a high-density polyethylene.

Although the metal in a prosthesis is highly polished and the polyethylene is intended to be wear-resistant, the daily rubbing of these surfaces against each other during normal movements creates tiny particles of debris. After many years, these wear particles may damage the surrounding bone, loosen the prosthesis, and require another knee or hip joint replacement.

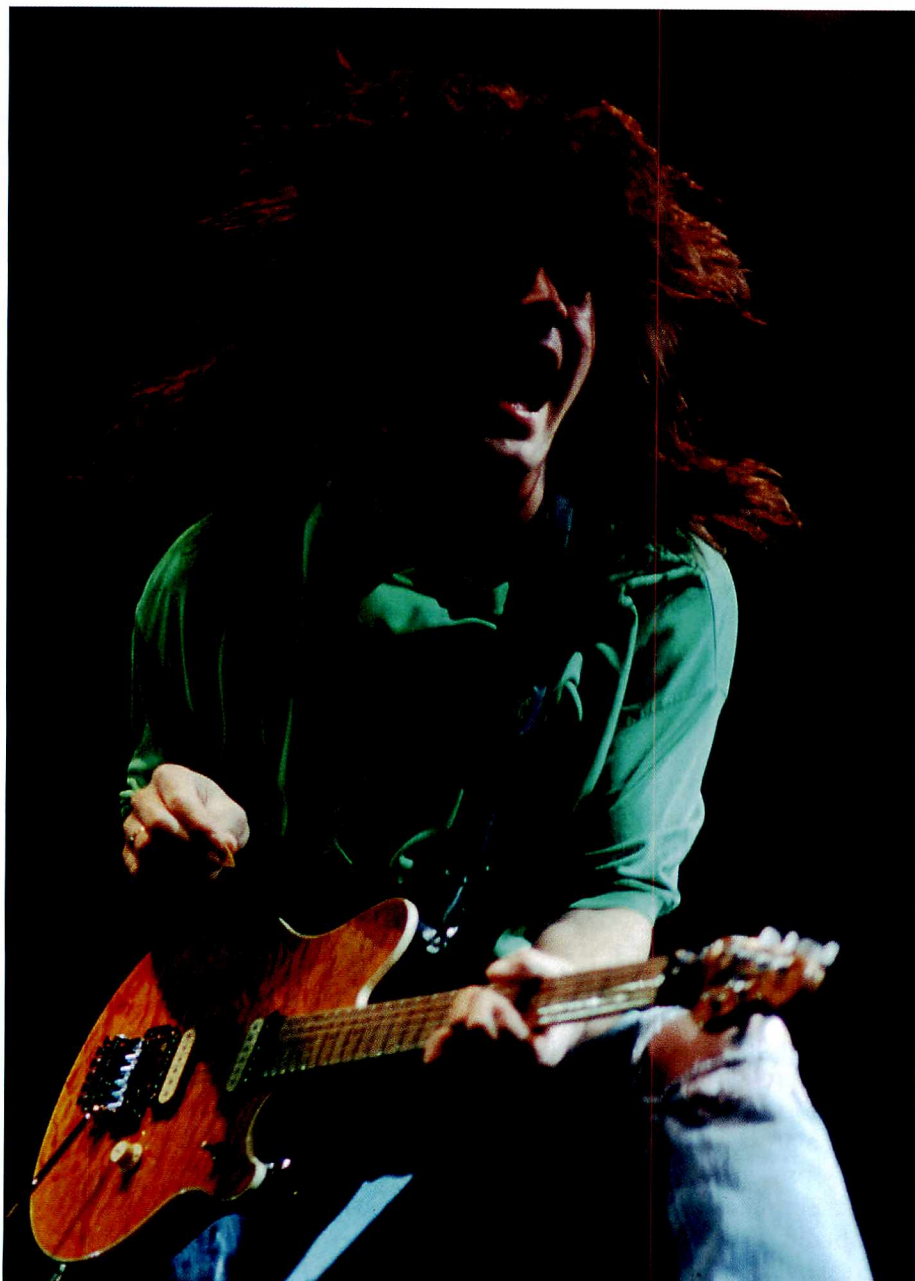
"The 'Achilles tendon' of any artificial joint over the long term is wear," says Anderson Orthopaedic's Engh. "Any time you have parts moving against each other, there has to be wear."

In an effort to solve the wear problem of metal-on-polyethylene in the hip joint, manufacturers have produced hip prostheses with three other kinds of surfaces: metal-on-metal, ceramic-on-polyethylene, and ceramic-on-ceramic. Unlike the clay ceramic used in pottery, the ceramic used in hip joint replacements is made from aluminum or zirconium chemically combined with oxygen for strength and durability.

Metal-on-metal and ceramic hip prostheses are decades old, but modern materials, designs, and manufacturing methods have improved upon earlier versions, says Engh. He cautions that, although modern investigational products have shown good wear in mechanical simulations in the laboratory, it's how well they work in people over the long term that is the real test. "Very often it's best to select an implant that's been on the market for a while rather than something that's brand new," says Engh.

A few metal-on-metal and ceramic-on-ceramic hip prostheses are FDA-approved for use in the general population; others are approved only for use in carefully controlled studies. However, a large number of ceramic-on-polyethylene prostheses are available for use in the general population.

When choosing a prosthesis, the surgeon will consider many factors, including the patient's age, weight, gender,



Getty Images

**Eddie Van Halen of the rock group Van Halen received a hip implant in 1999 at the age of 43. He continues to rock audiences with his dynamic energy on stage.**



anatomy, activity level, medical history and general health, says A. Seth Greenwald, D.Phil., director of orthopaedic research and education at the Lutheran Hospital in Cleveland, part of the Cleveland Clinic Health System. The device's performance record and the surgeon's own experience with the device also will be considered.

### **Surgical Skill**

Choosing the appropriate prosthesis is only one part of the equation for successful hip or knee joint replacement. "The most important factor in joint replacement success is the surgeon," says Greenwald. "The first question I'd ask the surgeon is, 'How many have you

designed, materials, and manufacturing methods to try to lengthen the life of artificial knees and hips, surgeons are refining techniques or developing new ones to try to improve the outcomes. Doing surgery through smaller incisions and performing less radical surgeries are among these efforts.

People are seeking minimal-incision knee and hip replacement surgery, says Engh. Instead of the traditional 6- to 12-inch-long incision used in a standard total knee replacement, some surgeons are performing the surgery through a 4- to 5-inch incision. And instead of the typical 10- to 12-inch incision in a total hip replacement, surgeons are operating through one 4-inch

invasive total knee replacement through an incision of 4 to 6 inches, bending the joint through the opening to expose different parts of it to work on. In a standard knee replacement, the entire joint is visible through a longer incision. Mont uses cutting procedures, leg positionings, and techniques that do not involve dislocating parts of the knee as in traditional replacement.

Even as researchers and surgeons continue to offer more options in prostheses and surgical procedures, Garino says the current technology is hard to beat. A hip or knee replacement is likely to last 20 years, he says. "The average patient takes a million steps a year. I challenge you to go home and find

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*"The most important factor in joint replacement success  
is the surgeon."*

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done and what are your complications?"

Jonathan Garino, M.D., agrees. "There are a number of good devices out there," says Garino, an orthopedic surgeon with the University of Pennsylvania Health System. "But even if you have the best technology in the world, it has to be implanted correctly." It falls to the surgeon to put the device in right, but it falls to the patient to take care of the new joint, says Garino. Regular exercise is important, but high-impact activities, such as running and jumping, generally are discouraged.

The independent panel convened by the NIH in December 2003 to study total knee replacements also concluded that proper surgical technique was one of the most important factors leading to successful knee replacement. Studies have found that the more knee replacements a surgeon performs, the lower the rates of complication, according to the panel. Similarly, complication rates fall in hospitals with increasing numbers of operations performed.

### **Surgical Techniques**

While prosthesis makers are changing

cut or two 2-inch cuts.

"The [minimal-incision surgery] technique minimizes trauma to muscles, tissue and tendons and has less bleeding during surgery," says Garino. Patients have less pain after surgery, enabling them to walk with full weight sooner. The hospital stay is usually reduced as well.

"There are many advantages as long as we don't compromise our ability to put the implants in correctly," says Engh, adding that minimal-incision surgery is a more difficult operation to perform. "If you assemble a model ship on a desktop, it's easier to do, but if you try to assemble it within a bottle it is technically more difficult," he says. The technical difficulty also adds to the operating time. "The longer a patient is in surgery, the higher the risk of infection," says Engh.

Not all patients are candidates for minimal-incision surgery. People who are obese, have had previous hip or knee surgery, or those with unusual anatomy may be excluded, says Garino.

Minimally invasive surgery is another option for some patients. At Sinai Hospital, Mont performs a minimally

something in your house that you use a million times a year that has lasted for 20 years with no maintenance." ■

### **For More Information**

American Academy of Orthopaedic Surgeons

(800) 346-AAOS (346-2267)

<http://aaos.org/>

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Information Clearinghouse  
(877) 22-NIAMS (226-4267)

TTY: (301) 565-2966

[www.niams.nih.gov/hi/](http://www.niams.nih.gov/hi/)

Arthritis Foundation

(800) 283-7800

[www.arthritis.org](http://www.arthritis.org)



# GRAS:

## Time-Tested, and Trusted, Food Ingredients

By Carol Rados

If Marco Polo were to attempt to bring back spices from the Orient today, he would have more to worry about than pirates. The 13th century explorer now would be required to prove that his cargo is not toxic, does not cause birth defects, and will not interfere with nutrition or affect individuals with allergies—unless the flavorings already are “generally recognized as safe” (GRAS) by the Food and Drug Administration.



FDA/Michael Ermarth



GRAS is one of four legal categories set up by Congress under the 1958 Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act (FD&C Act). At the time, knowledge about food science and the potential long-term harmful effects of food chemicals on health were beginning to surface. Congress decided it was not necessary for the food industry to prove the safety of substances such as salt, sugar, and spices intentionally added to foods if they were already generally regarded as safe by qualified scientists.

### New Food Additives

The FDA approves new ingredients for use in the food supply based on reviews of extensive scientific research on safety. To market a new food additive, a manufacturer must first petition the FDA for its approval. The petition must provide convincing evidence that the proposed additive performs as it is intended. Animal studies using large doses of the additive for long periods often are needed to show that the substance would not cause harmful effects in people when eaten in expected amounts. Studies of

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*A GRAS substance ... is one that has a long, safe history of common use in foods, or that is determined to be safe based on proven science.*

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A GRAS substance, therefore, is one that has a long, safe history of common use in foods, or that is determined to be safe based on proven science. If, however, new evidence suggests that a GRAS substance may no longer be safe, the FDA can prohibit its use or require further studies to determine its safety.

Some substances may be GRAS for one use, but not for others. For example, some uses of a food substance are intended for a narrowly defined population, such as newborn infants who consume infant formula as the sole item of the diet. In this case, there may be special considerations associated with that population, but not with general use of the food substance.

Manufacturers add substances to foods to prevent spoilage or to enhance appearance, taste, texture, or nutritive value. Without them, cakes wouldn't rise, salt would lump, bread would mold more easily, ice cream would separate into ice crystals, and marshmallows would harden into bite-sized rocks. Food additives allow us to enjoy a variety of safe, wholesome, and tasty foods all year round. They also help make convenience foods readily available.

the additive in humans also may be submitted to the FDA.

If an additive is approved, the FDA issues a regulation that may include the types of foods in which it can be used, maximum amounts to be used, and how it should be identified on food labels. To further assure safety, the FDA may require the manufacturer to monitor its use. All additives are subject to ongoing safety reviews as scientific understanding and methods of testing continue to improve.

If ingredients such as new sweeteners are added to conventional foods without being approved by the FDA, the food may be considered adulterated or misbranded. The FD&C Act prohibits marketing conventional foods containing ingredients that are not either GRAS or newly approved by the FDA, as well as health claims made about their use on the product's labeling. ■

### For More Information

The FDA Center for Food Safety and Applied Nutrition  
[www.cfsan.fda.gov/~lrd/foodadd.html](http://www.cfsan.fda.gov/~lrd/foodadd.html)

"Everything Added to Food in the U.S."  
[www.cfsan.fda.gov/~dms/eafus.html](http://www.cfsan.fda.gov/~dms/eafus.html)

## Regulatory Categories for Substances Added to Foods

Other than pesticides and animal drugs, substances added to foods fall into four legal categories.

- **Food additives**—substances that have no proven track record of safety and must be approved by the FDA before they can be used.

- **Generally recognized as safe (GRAS)**—substances for which use in food has a proven track record of safety based either on a history of use before 1958 or on published scientific evidence, and that need not be approved by the FDA prior to being used.

- **Prior-sanctioned**—substances that were assumed to be safe by either the FDA or the U.S. Department of Agriculture before 1958, to be used in a specific food. (For example, while the preservative nitrate can be used in meat because it was sanctioned before 1958, it cannot be used on vegetables because they were not covered by the prior sanction.)

- **Color additives**—dyes that are used in foods, drugs, cosmetics and medical devices and must be approved by the FDA before they can be used.

GRAS or prior-sanctioned status does not guarantee a substance's safety. Sometimes new evidence shows that a substance may not be as safe as it was commonly thought to be. If new data suggests that a substance under either of these categories may be unsafe, the FDA may take action to remove the substance from food products or require the manufacturer to conduct studies to evaluate the newly raised concern. ■







# Managing Chronic Pain

*By Michelle Meadows*

**H**elen Dearman, 52, of Houston, had a broken back for more than a decade and didn't know it. After falling from a ski lift in Mt. Hood, Ore., when she was 23, Dearman was diagnosed with a broken left arm and thought that was her only injury.

Her arm healed. But she developed excruciating back pain that made it hard to sleep and move around. "I worked as a teacher, so some doctors suggested that the problem was from standing on my feet all day," Dearman says. "Others told me it was all in my head. For years, I left doctors' offices feeling desperate for help."

The pain grew worse during her 30s. One morning, Dearman woke up with stabbing pains in her back and could barely walk. This time, her husband took her to an orthopedic surgeon who specialized in back problems. He took X-rays that revealed three old fractures in Dearman's spine.

"When the doctor showed me the X-rays, I cried," Dearman says. "Someone had finally given me the words and understanding for all the pain I had been suffering from for so long."

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**Helen Dearman holds the battery-powered drug infusion pump that was implanted into her abdomen in 1995. She now uses a newer model of the device, which delivers pain medication continuously into the fluid surrounding her spine.**



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## *'Chronic pain goes on and on— for months or even years.'*

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### **Pain That Persists**

By definition, acute pain after surgery or trauma comes on suddenly and lasts for a limited time, whereas chronic pain persists. "Acute pain is a direct response to disease or injury to tissue, and presumably it will subside when you treat the disease or injury," says Sharon Hertz, M.D., deputy director in the Food and Drug Administration's Division of Anti-Inflammatory, Analgesic, and Ophthalmologic Drug Products. "Chronic pain goes on and on—for months or even years."

Common types of chronic pain include back pain, headaches, arthritis, cancer pain, and neuropathic pain, which results from injury to nerves. In

Dearman's case, her untreated back injury caused her spine to twist out of place, not only resulting in severe back pain, but also putting intense pressure on the nerves in her legs. "I often felt pain shooting down my legs," she says, "like a jolt of electricity."

Experts say the first step in treating chronic pain is to identify the source of the pain, if possible. Many people with chronic pain try to tough it out, according to research from the American Academy of Pain Medicine. But persistent pain should never be ignored because it could signal disease or injury that will worsen if left untreated. Sometimes, it turns out that the cause of pain is unknown. Fibromyalgia, for

example, is characterized by fatigue and widespread pain in muscles and joints. While scientists have theorized that the condition may be connected to injury, changes in muscle metabolism, or viruses, the exact cause is unclear.

Regardless of the type of chronic pain, the physical and emotional effects can be devastating. Dearman says, "My teaching career suffered, my children were confused about why I always felt bad, and our finances were ruined." Sometimes, she says, she even considered suicide.

### **Finding Relief**

Dearman believes the first two surgeries she had to repair the fractures in

## **Chronic Headaches**

More than 45 million Americans have chronic headaches, according to the National Headache Foundation. The most common types include tension headaches, which are associated with muscle tension. These are sometimes described as feeling like a tight band squeezing the head. Cluster headaches are marked by severe pain around one eye. Migraines are characterized by throbbing pain on one side of the head. Most people with migraines also experience nausea and sensitivities to light and sound.

Andrew Fano, 38, of Lincolnshire, Ill., who has had migraines since he was 12, says headaches used to wipe him out for days. But things improved in 1992 when the FDA approved Imitrex (sumatriptan), the first drug in a class known as triptans. This class of drugs marked a huge leap forward for headache sufferers. Unlike some previous drugs that dulled the perception of pain, triptans stop the pain by narrowing blood vessels in the brain and reducing inflammation.

Fano's migraine treatment now includes a newer triptan called Frova (frovatriptan). Side effects include nausea, dizziness, and dry mouth. He also takes the pain reliever Vicodin as needed, sticks to a regular sleep schedule, and avoids red wine and other migraine triggers.

Migraines, tension headaches, and cluster headaches are considered primary headaches because they are not caused by underlying illness. "But it's important to rule out disease, especially when headaches are resistant to treatment," says Seymour Diamond, M.D., founder and executive chairman of the National Headache Foundation.

Diamond performed an MRI (magnetic resonance imaging) on Fano a couple of years ago. "We assessed him for a possible brain aneurysm, but luckily, there wasn't a problem," he says.

Most headaches can be successfully treated with over-the-counter pain relievers. But you should seek professional help for headaches if they persist or get worse or if the headaches are keeping you from work and social activities. "You should also see a doctor if you've never had headaches before and you start having them, if you get headaches upon exertion, or if headaches are accompanied by a stiff neck, fever or neurological symptoms like dizziness or blurred vision," Diamond says.

For more information, contact the National Headache Foundation at (888) 643-5552, [www.headaches.org/consumer/](http://www.headaches.org/consumer/). ■



her back and realign her spine were necessary. But she questions the four surgeries that followed. "I talked myself into the operating room more than once because I was desperate to feel better," Dearman says. "Even when doctors told me there was only a small chance another surgery would help, I wanted to take the chance." But after several surgeries, Dearman's pain only seemed to be getting worse.

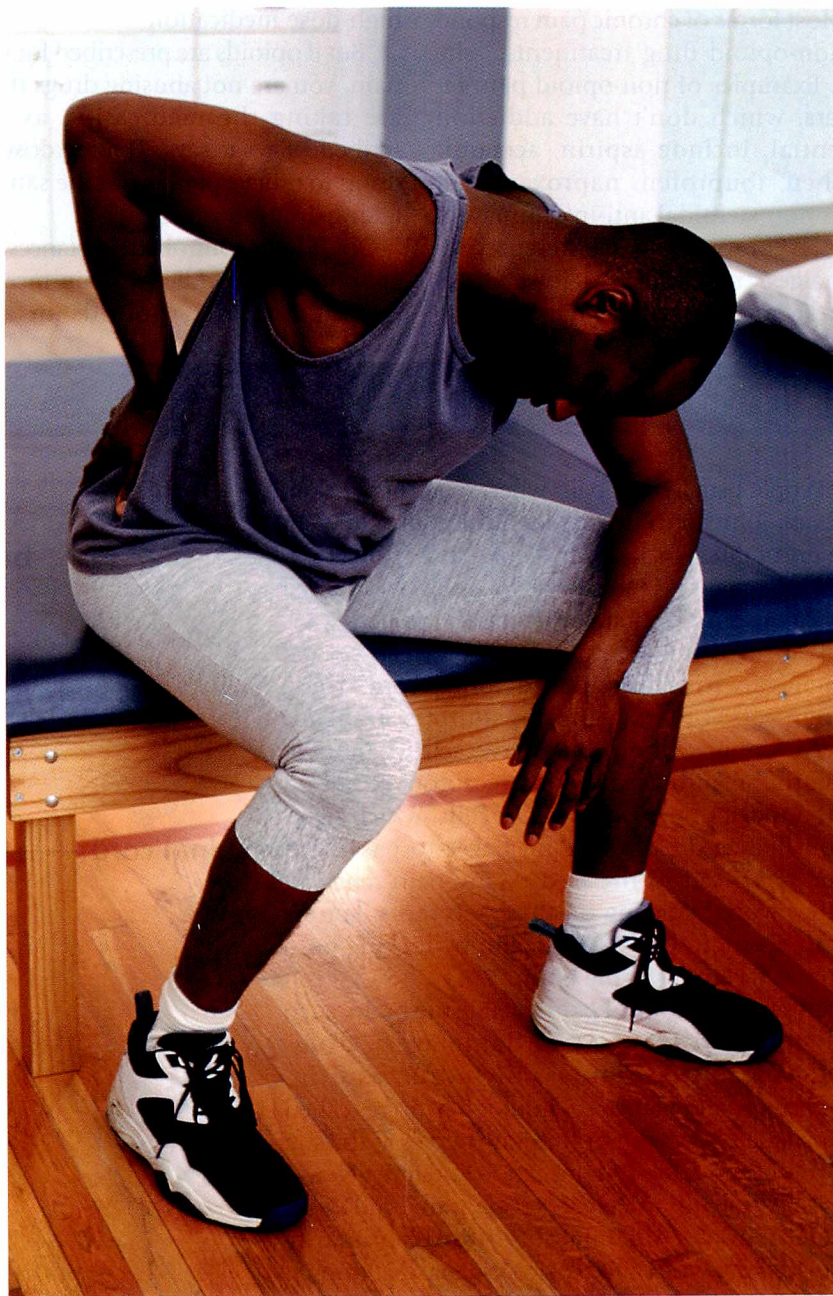
The turning point occurred in 1995 when a physical therapist referred Dearman to a pain management specialist, a professional who takes a multidisciplinary approach to managing pain. She was treated by a team of pain experts. Doctors and nurses worked with her to manage pain medications. Psychologists addressed her depression and anger, and physical therapists helped improve her strength and mobility.

Dearman finally found effective drug treatment with a pump implanted into her abdomen that delivers morphine through a catheter into the fluid surrounding her spine. The pump, called an intrathecal drug infusion pump, is used for severe pain only after other oral and intravenous drug therapies have failed. The pump is programmed to deliver a controlled amount of medication continuously. Risks include surgical complications, such as infection, and complications with the catheter or pump. "It doesn't take away all the pain, but it's a drastic improvement and allows me to be in control of the pain," says Dearman, who also takes other pain medication as needed.

Seddon Savage, M.D., a pain specialist on the faculty of Dartmouth Medical School in Hanover, N.H., says there are times when it's impossible to eliminate pain. "The goal of pain management is to provide as much pain relief as possible and improve functioning," Savage says.

Because pain varies from person to person, treatment is individualized. Someone with arthritis may do well with occasional use of an over-the-counter pain reliever, whereas someone else with arthritis may need a prescription pain reliever and regular aerobic exercise to feel good.

"Treatment for chronic pain is about



Photodisc

**Chronic pain disables, to some degree, about 86 million Americans, according to the American Chronic Pain Association.**

much more than medication," Savage says. It can also involve stress relief and relaxation, physical therapy, improved sleep and nutrition habits, and exercise. Dearman says that through a multidisciplinary approach to pain management, she also learned to pace her activities so that she is realistic about how much she can do in a certain time period.

Savage recommends that people seek professional help for chronic pain when they feel that pain is interfering with their quality of life. "Start with your primary care physician, who may

refer you to other specialists," she says. "Consider asking your doctor about a pain management specialist if you feel that your pain is just not getting better over time." Another reason to seek advice from a specialist is if you are experiencing intolerable side effects from medications.

#### **Concerns About Drug Abuse**

One of Dearman's biggest fears was of becoming addicted to pain medications. "It's a common concern for both patients and health providers," says Savage, who specializes in addiction.



"Most forms of chronic pain respond to non-opioid drug treatments," she says. Examples of non-opioid pain relievers, which don't have addiction potential, include aspirin, acetaminophen, ibuprofen, naproxen, and other non-steroidal anti-inflammatory drugs. A combination of different types of analgesic medications at lower doses is often more effective than a single

high-dose medication.

"But if opioids are prescribed for your pain, you are not abusing drugs if you are taking the medication as prescribed," Savage says. "Taking doses of drugs to relieve pain is not the same as taking drugs to get high."

Opioids are controlled substances that are potentially addictive. Pain medications containing opioids include

Vicodin (hydrocodone), OxyContin and Percocet (oxycodone), MS-Contin (morphine), Tylenol #2, #3 and #4 (codeine), and the Duragesic Patch and Actiq (fentanyl).

June Dahl, Ph.D., director of the American Alliance of Cancer Pain Initiatives and professor of pharmacology at the University of Wisconsin-Madison Medical School, says she recently

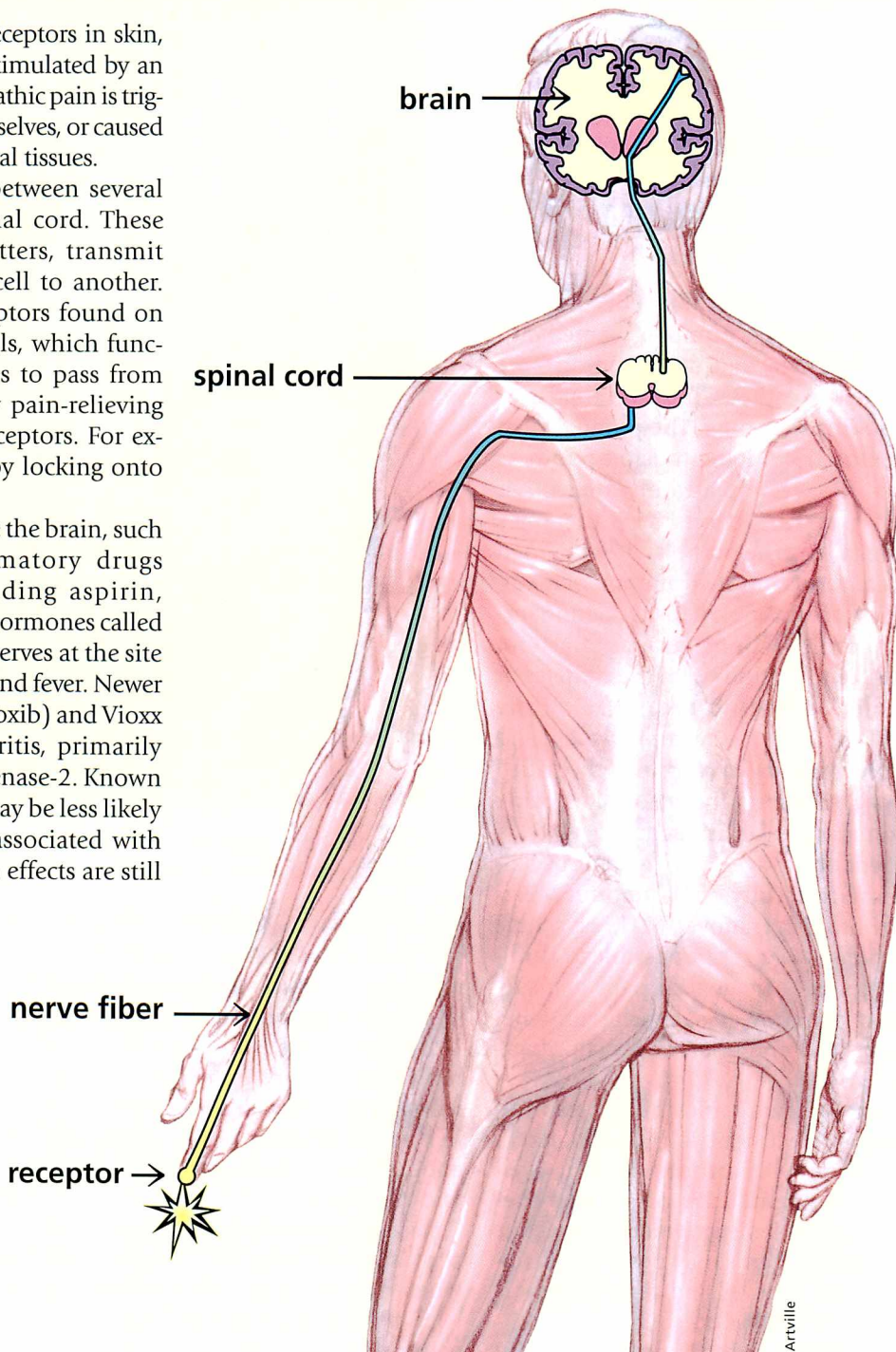
## Pain Basics

People usually feel pain when receptors in skin, bones, joints or other tissues are stimulated by an injury or threat to the body. Neuropathic pain is triggered by changes in the nerves themselves, or caused by changes in the brain or peripheral tissues.

Pain involves the interaction between several chemicals in the brain and spinal cord. These chemicals, called neurotransmitters, transmit nerve impulses from one nerve cell to another. Neurotransmitters stimulate receptors found on the surface of nerve and brain cells, which function like gates, allowing messages to pass from one nerve cell to the next. Many pain-relieving drugs work by acting on these receptors. For example, opioid drugs block pain by locking onto opioid receptors in the brain.

Other drugs control pain outside the brain, such as non-steroidal anti-inflammatory drugs (NSAIDs). These drugs, including aspirin, ibuprofen, and naproxen, inhibit hormones called prostaglandins, which stimulate nerves at the site of injury and cause inflammation and fever. Newer NSAIDs, including Celebrex (celecoxib) and Vioxx (rofecoxib) for rheumatoid arthritis, primarily block an enzyme called cyclooxygenase-2. Known as COX-2 inhibitors, these drugs may be less likely to cause the stomach problems associated with older NSAIDs, but their long-term effects are still being evaluated. ■

Source: National Institutes of Health





took a call from a man with cancer who said he stopped taking an opioid pain medication on his own for fear that he was becoming addicted. "But what he described were not signs of addiction, but signs of physical dependence," Dahl says.

Addiction is characterized by craving and compulsive use of drugs. Physical dependence occurs when a person's body adapts to the drug. If someone has become physically dependent on a drug and suddenly stops taking it, withdrawal may occur. These symptoms can include muscle aches, watery nose and

been considerable drug abuse involving OxyContin, which the FDA approved for moderate-to-severe pain in 1995. The FDA strengthened warnings for oxycodone in 2001, while continuing to recommend appropriate pain control for people living with severe pain.

But experts say that finding a balance between cracking down on drug abusers and protecting people in pain is an ongoing struggle. "Some doctors fear regulatory scrutiny for over-prescribing these drugs," Dahl says. "And concerns about the small segment of people who

are important because they give people with pain the coping skills needed to take an active role in their recovery. "Sometimes doctors tell people they'll have to learn to live with the pain," Cowan says. "But too often they stop short of telling them how to accomplish that."

Dearman says finding effective treatment and gaining the skills to live with her pain made all the difference. "It's about being a person first and not letting pain define who you are," she says. "Our motto is: Pain may be unavoidable, but suffering is optional." ■

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## *'Pain may be unavoidable, but suffering is optional.'*

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eyes, irritability, sweating, and diarrhea. Physical dependence is a normal response to repeated use of opioids and is distinct from psychological addiction.

Savage says that in prescribing potentially addictive medications, doctors should consider patients' personal and family histories of addiction, as well as psychological and social stressors that may affect medication use. Also, some people who begin taking opioid medications for pain as prescribed may later discover that they are using the medication for its psychic brain effects. Physicians need to be aware of this potential adverse effect, and should educate patients and their families about appropriate use of addictive drugs.

To better guide physicians, the Federation of State Medical Boards adopted guidelines for the use of controlled substances for pain treatment in 1998. The guidelines advise physicians on patient evaluations, treatment plans, and medical records.

The use of opioids in pain treatment remains controversial for several reasons. The rate of addiction in the properly treated pain population is unknown. The media has highlighted problems of addiction to pain medicine among celebrities. And there has

abuse drugs ends up interfering with effective pain management for others."

Sheryl Kaufman, 40, of Boston, who uses oxycodone and a fentanyl patch for severe pain associated with breast cancer, says she recently filed a grievance with a pharmacy over her struggles to get prescriptions filled.

"They made me feel like a criminal," she says. "Sometimes I've had to go without pain medication for two to three days because of delays in filling prescriptions."

### **The Value of Support**

Dearman's experiences with chronic pain led her to establish the National Chronic Pain Society in 2002. The organization provides peer support for people with chronic pain and their families.

"We give people support for dealing with all of the issues that can go along with chronic pain—not having your pain taken seriously, frustration over not finding relief, how to communicate your pain to your doctor, and how to maintain relations with your family," Dearman says.

Penney Cowan, executive director of the American Chronic Pain Association, another peer support organization in Rocklin, Calif., says support systems

### **For More Information**

American Academy of Pain Management  
13947 Mono Way #A  
Sonora, CA 95370  
(209) 533-9744  
[www.aapainmanage.org](http://www.aapainmanage.org)

American Pain Society  
4700 W. Lake Ave.  
Glenview, IL 60025  
(847) 375-4715  
[www.ampainsoc.org](http://www.ampainsoc.org)

American Pain Foundation  
201 N. Charles St., Suite 710  
Baltimore, MD 21201  
(888) 615-7246  
[www.painfoundation.org](http://www.painfoundation.org)

American Chronic Pain Association  
PO Box 850  
Rocklin, CA 95677  
(800) 533-3231  
[www.theacpa.org](http://www.theacpa.org)

National Chronic Pain Society  
PO Box 903  
Tomball, TX 77377  
(281) 357-4673  
[www.ncps-cpr.org](http://www.ncps-cpr.org)



# Agencies Team Up to Protect Food Supply



U.S. Customs and Border Protection

Customs inspectors pull the contents from a seaport container as more containers are removed from the ship.



The Food and Drug Administration and U.S. Customs and Border Protection (CBP) have launched a new joint effort to protect the nation's food supply. Under a Memorandum of Understanding (MOU) signed in December 2003, thousands of Customs agents are now authorized to inspect foods imported into the United States.

Signed by FDA Commissioner Mark B. McClellan, M.D., Ph.D., and CBP Deputy Commissioner Douglas Browning, the agreement allows the FDA to commission CBP officers in ports and other locations to conduct, on the agency's behalf, investigations and examinations of imported foods. This unprecedented FDA-CBP collaboration significantly strengthens the implementation of the Bioterrorism Act to ensure the security of imported foods.

"This MOU is an important milestone in our extensive efforts to protect the safety and security of the national

the movement of legitimate trade."

Building on a long history of close FDA-CBP cooperation, the agreement includes steps to enhance the two agencies' teamwork in training, day-to-day operations, and information sharing. Under the agreement, the FDA can commission all the CBP officers the two agencies consider necessary to enforce new food safety and security regulations. The FDA and CBP will provide specialized training for the commissioned CBP employees who will carry out this work, and both agencies will expand their existing

faith" effort at complying with the new rules. During the phase-in period, the FDA and CBP will primarily rely on educating firms and individuals. After the phase-in period of education, CBP will begin to impose civil monetary penalties, and ultimately the FDA and CBP will refuse shipments. Both agencies will continue to ensure that imported products are safe for human or animal consumption throughout the phase-in period.

"Our intention all along has been to implement the Bioterrorism Act in a way that would protect consumers

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*'We are committed to using the bioterrorism law to safeguard our food supply to the fullest extent possible ...'*

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food supply," McClellan said at the signing ceremony on Dec. 3, 2003. "It enables us to work more efficiently with CBP, combining their strong resources with our own expertise in keeping on the alert for potentially hazardous foods and responding to possible threats. We are committed to using the bioterrorism law to safeguard our food supply to the fullest extent possible, without imposing any unnecessary costs or restrictions on food imports."

"We are pleased to be an integral part of this new initiative to safeguard the country's food products," Browning added. "This agreement reflects close cooperation and countless hours of discussion not only with FDA, but with our trade partners here and around the world. It also supports our twin goals of securing the border from terrorists and terrorist weapons while ensuring

cooperative arrangements to directly share information affecting the safety and security of imported foods.

The FDA and CBP have issued a compliance policy guide that describes their strategy for maintaining an uninterrupted flow of food imports while improving their safety. The policy guide deals with the enforcement of two regulations based on provisions of the Bioterrorism Act. These regulations require:

- advance notice to the FDA of shipments of foods imported or offered for import into the United States, and
- registration with the FDA of domestic and foreign facilities that manufacture, process, pack, or hold food for consumption in the United States.

Both regulations took effect on Dec. 12, 2003. These new requirements have a phase-in period, ending on Aug. 12, 2004, for companies to make a "good

without obstructing the food imports on which we depend for 20 percent of all fresh produce and up to 60 percent of all the seafood consumed in the United States," said McClellan. "The goal of the transition policy is to provide complete clarity and education about the new import requirements, and achieve a higher level of U.S. food security without disrupting trade."

"We at the CBP for decades have worked closely with the FDA in ensuring the safety and security of imported foods, especially perishables, that reach our dinner tables every day," CBP Commissioner Robert C. Bonner said. "The Bioterrorism Act provides us with yet another highly effective tool to safeguard America's food supply from the terrorist threat." ■



# Science Meets Beauty:

## Using Medicine to Improve Appearances

*By Carol Rados*

**A** smaller nose. Bigger breasts. Slimmer thighs. Plumper lips. Less hair on the body. More hair on the head. Whether we're looking to tighten our tummies or lighten our laugh lines, America's fascination with youth and beauty has long fueled the development of medical products for cosmetic purposes. And if such "vanity drugs" can be shown to be safe and effective, the Food and Drug Administration just may approve.

The ongoing fight to delay or reverse the aging process has dermatologists and cosmetic plastic surgeons responding with products like Restylane (hyaluronic acid), one of a handful of soft tissue fillers recently approved by the FDA to treat facial wrinkles. Restylane is an injectable gel that acts as a filler to remove the wrinkle, producing instantaneous results. Such products are not as invasive as facelifts, eyelid surgery, and other reconstructive procedures. And they are more effective and last longer than creams, lotions and other topical products, whether over-the-counter or prescription. In addition, the fact that the treatments result in little or no downtime makes them more attractive to those seeking a quick fix. Without making a single incision, doctors can erase wrinkles, acne scars and sun damage in a matter of minutes.

"This is a huge industry," says Jonathan K. Wilkin, M.D., a medical officer in the FDA's Division of Dermatologic and Dental Drug Products. "The way people try to move the clock back is through the skin." Basically, he says, through various products and procedures, "they are addressing the effects of gravity on the skin over time."





Corbis

**People have been captivated by the ideas of youth and beauty since antiquity.**

### **Aging Skin 101**

An increased understanding of the structure and function of the skin is helping to drive the development of products that reduce the visible signs of facial aging, according to the American Academy of Dermatology (AAD).

With aging, all skin cells begin to produce excess amounts of free radicals—unstable oxygen molecules that, under ideal circumstances, are removed by

naturally occurring antioxidants within the skin's cells. In aging skin cells, antioxidants are in short supply. The free radicals generated are left unchecked and cause damage to cell membranes, proteins, and DNA. These free radicals eventually break down a protein substance in connective tissue (collagen) and release chemicals that cause inflammation in the skin. It is a combination of these cellular and molecular

events that leads to skin aging and the formation of wrinkles, the AAD says.

Considerable research has been done to understand the aging process, and studies now show that products containing bioactive ingredients (those that interact with living tissues or systems) can benefit sun-damaged, discolored, and aging skin, giving consumers new choices for restoring their overall appearance. But why is the FDA



reviewing products that simply make people look and feel good when typically the agency evaluates disease-fighting treatments?

"If something that is being implanted into the body could have health consequences, we're concerned about it," says Stephen P. Rhodes, M.S., chief of the FDA's Plastic and Reconstructive Surgery Devices Branch. "Wrinkle fillers affect the structure of the face and could have such health consequences."

### Facing Facts

Under the Federal Food, Drug and

almost identical to that in all living organisms. Hyaluronic acid is a structural component of skin that creates volume and shape. Concentrations of hyaluronic acid throughout the body decline with age, causing undesirable changes in the skin. Restylane binds to water and provides volume to easily fill in larger folds of skin left by tissue loss around the mouth and cheeks. "This makes it a structural action," says Rhodes, "much like a chin implant."

In contrast, cosmetics are defined as substances that cleanse, beautify, promote attractiveness, or alter the appear-

(which affects the follicles where the hair is formed) and clean hair.

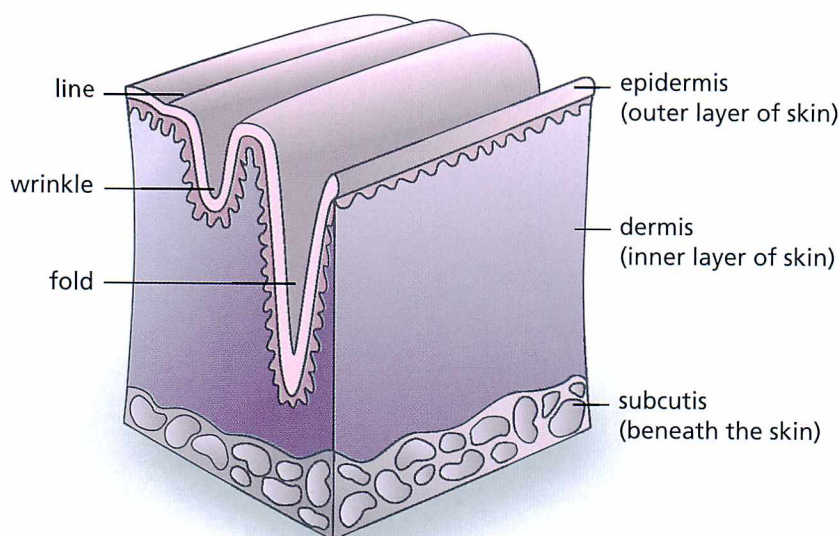
Warning letters issued by the FDA recently to firms that marketed hair care products with claims such as restoration of hair growth and hair loss prevention illustrate an important distinction between the legal definitions of cosmetics and drugs. Warning letters officially inform companies that they may be engaged in illegal activities, and instruct manufacturers on how to bring their products into compliance with the law. Hair growers and hair loss prevention products, because of their mechanism of action, are considered drugs, not cosmetics, and these firms were not meeting the legal requirements for marketing a drug.

Unlike drugs and medical devices, neither cosmetic products nor cosmetic ingredients are reviewed or approved by the FDA before they are sold to the public. The agency only acts against cosmetic products found to cause harm after they are on the market.

### Cosmetics or Drugs?

Much confusion exists about the status of cosmetic products having medicinal or drug-like benefits, says Linda Katz, M.D., M.P.H., director of the FDA's Office of Cosmetics and Colors. Although the FDA does not consider the term "cosmeceutical" to be a valid product class, Katz says it is used throughout the cosmetic industry to describe products that are marketed as cosmetics but that have drug-like effects. Tretinoin (retinoic acid), the biologically active form of vitamin A, for example, is not prohibited from use in cosmetics. However, when it is used topically for treating mild to moderate acne, sun-damaged skin, and other skin conditions, it is recognized by the FDA as a drug. This is because it acts deep at the skin's cellular level by increasing collagen.

According to the AAD, the answer to whether or not cosmeceuticals really work lies in the ingredients and how they interact with the biological mechanisms that occur in aging skin. The regulatory question the FDA faces when considering such products, Katz says, "is whether or not a manufacturer is making a structure or function claim."



**As we get older, two components of our skin—collagen and elastin—degenerate, setting the stage for the appearance of wrinkles, creases, folds, and furrows. The breakdown of these components, accelerated by sun exposure and gravity, results in the sagging skin of old age.**

FDA/Renée Gordon

Source: National Institute on Aging

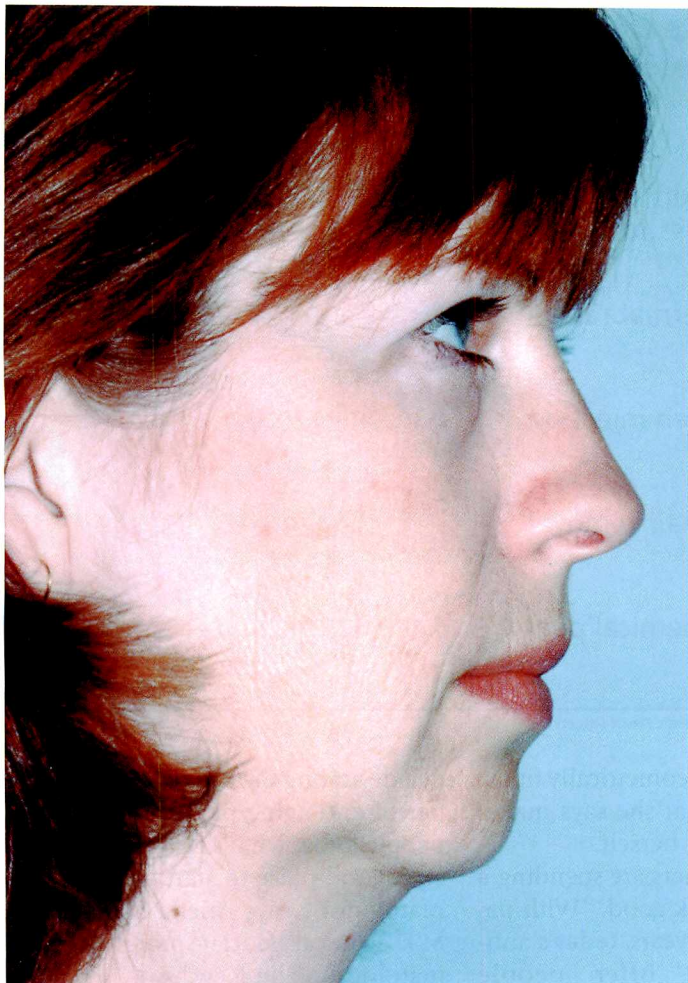
Cosmetic Act, the FDA legally defines products by their intended uses. Drugs are defined as products intended for treating or preventing disease and affecting the structure or any function of the body. A medical device is a product that also is intended to affect the structure or function of the body, but which does not achieve its primary intended purposes through the chemical action of a drug—nor is it dependent on being metabolized.

The hyaluronic acid in Restylane, although biosynthetically produced (formed of chemical compounds by the enzyme action of living organisms), is

ance, without affecting the body's structure or function. This definition includes skin-care products such as creams, lotions, powders and sprays; perfume; lipstick; fingernail polish; and more.

Different laws and regulations apply to each type of product. Some products must comply with the requirements for both cosmetics and drugs. This happens when a product has two intended uses, such as an antidandruff shampoo. A shampoo is a cosmetic because it is intended to clean hair. An antidandruff shampoo is a cosmetic and a drug because it is intended to treat dandruff





Craig R. Dufresne, M.D.

Laura Bradbard of Gaithersburg, Md., shown before and after reconstructive facelift surgery that corrected a receding chin, restored facial balance, and erased an overall look of fatigue.

The FDA uses different standards when evaluating the risks and benefits of products used for cosmetic treatments than for therapeutic uses of products. Steven K. Galson, M.D., M.P.H., acting director for the FDA's Center for Drug Evaluation and Research, adds that products like tretinoin and Restylane that are not indicated for serious or life-threatening conditions are subject to close examination by the agency because of the benefit-to-risk ratio.

"Because these products are for cosmetic purposes, they must be extraordinarily safe," Galson says. This means that the FDA may allow someone to incur a greater risk from products that treat medical conditions, rather than from those that are intended for cosmetic purposes. "We generally won't tolerate much risk for a drug whose primary use is cosmetic," he says.

### Welcome Side Effects

Many cosmetic treatments are the result of common disease therapies whose unexpected side effects were pleasant surprises. Vaniqa (eflornithine hydrochloride), the first prescription drug for removing unwanted hair, is a topically applied version of a drug that was originally developed to treat African sleeping sickness. Similarly, minoxidil originally had been prescribed as an oral tablet to treat high blood pressure. As a result of side effects that included hair growth and reversal of male baldness, Rogaine (2 percent minoxidil) was the first drug approved by the FDA for the treatment of hair loss (androgenetic alopecia).

"There's a lot of serendipity in drug development," says the FDA's Wilkin. A pill to help smokers quit, for example, evolved out of the unexpected observation that a drug intended to treat depres-

### Before electing to have a cosmetic procedure

- Discuss it with a physician who can refer you to a specialist in the fields of dermatology and aesthetic plastic surgery.
- Begin with a consultation to find the right doctor, and select one who is qualified to do the procedure you want.
- Make sure the doctor you choose is certified by an appropriate medical board.
- Have realistic expectations about the benefits you want to achieve.
- Compare fees—insurance does not usually cover elective procedures. ■



sion also seemed to take away the desire to smoke. Bupropion was first marketed in 1989 by GlaxoSmithKline as an antidepressant under the name Wellbutrin. After doctors noticed that patients being treated with Wellbutrin gave up smoking spontaneously, studies were done to show that the product could help smokers quit, as well. As a result, the slow-release form of bupropion, marketed as Zyban, was approved by the FDA in 1997 as an aid to smoking cessation treatment.

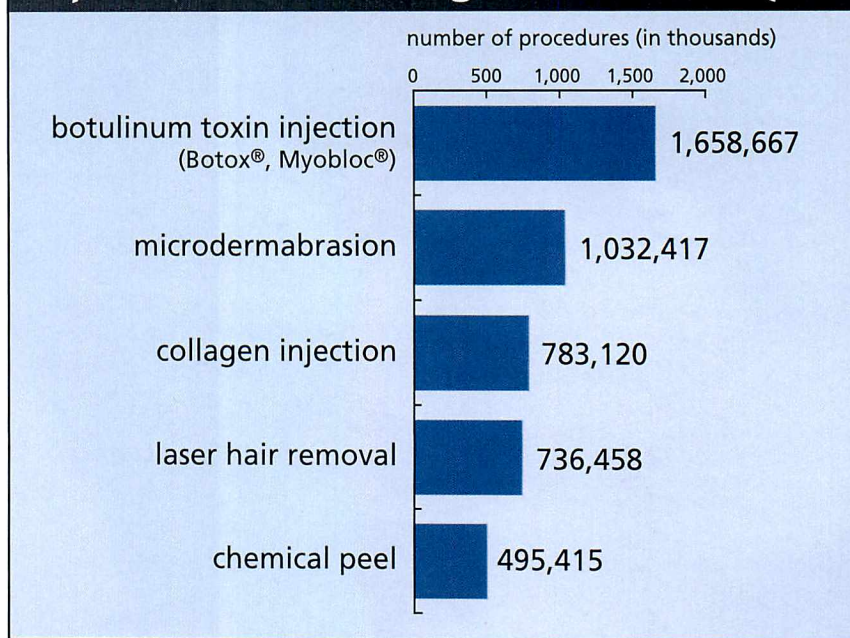
Some pharmaceutical companies, however, apparently aren't ready to enter the vanity drugs arena. Patrick Davish, the global product communications spokesman for Merck & Co. Inc., says that the drug company has no "cosmetic" drugs in its product pipeline at this time.

"The fact that we don't participate in that market right now—I'm not sure that's reflective of any particular deliberation or decision," he says. "That's just not where the science has taken us."

### **Saving Face**

According to the American Society for Aesthetic Plastic Surgery (ASAPS), nearly 7 million Americans underwent surgical and nonsurgical cosmetic pro-

## **Top 5 Cosmetic Nonsurgical Procedures (2002)**



Source: American Society for Aesthetic Plastic Surgery

cedure gave me a chin that geometrically fit my face," and a look that she says makes her feel better about herself.

Like Bradbard, others are spending a lot of money to look good. "With patients living 90-plus years, today's anti-aging modalities offer people noninvasive procedures that mimic true facelifts," says Craig R. Dufresne, M.D.,

decide among the overwhelming number of anti-aging procedures, how do people know what's right for them?

"A good place to start is with a dermatologist," says Arielle N.B. Kauvar, M.D., clinical associate professor of dermatology at the New York University School of Medicine. "Dermatologists are trained in the health, function and

## *'A good place to start is with a dermatologist.'*

cedures in 2002. Laura Bradbard was one of them.

Despite the sudden explosion of such "lunchtime" techniques as Restylane for erasing wrinkles, and Botox (botulinum toxin type A) for smoothing out frown lines, Bradbard, of Gaithersburg, Md., opted for a longer-lasting reconstructive facelift that included a chin implant, eyelid surgery, and surprisingly, only a few days of pain-free recovery.

"None of this was medically necessary," admits Bradbard, a 48-year-old FDA press officer, "but I had been feeling worn out and tired. What I saw in the mirror was sad." Bradbard says she didn't get a facelift to look younger; she only wanted her face to look more balanced. In the end, she says, "My doctor

a plastic and reconstructive surgeon in Chevy Chase, Md., who performed Bradbard's surgery. However, Dufresne says he suggested reconstructive surgery for Bradbard because "she wanted to deal with structural changes to restore facial balance," which was more than the chemical action of a drug could produce. "And skin product application (such as wrinkle fillers) following a facelift," adds Dufresne, "will actually allow the facelift or any other reconstructive procedure to last longer and make a great result even better."

### **Seeking Professional Advice**

Since it is often difficult for people to determine the validity of claims made about topical products and to

disease state of the skin, and people could save time, money and confusion by seeking the advice of a dermatologist rather than guessing what might work for them."

Kauvar says a dermatologist's recommendations can help consumers make informed decisions. "People shouldn't hunt and peck for products," she adds. "Not knowing what type of skin you have is why so many people try unnecessary products that can often do more harm than good."

An expert in laser procedures, Kauvar says that, in the past, techniques for improving aging skin required invasive laser or surgical procedures, which produced open wounds and required long recovery times. Today, she says, people



can choose from a variety of non-ablative (non-wounding) laser treatments that are designed to reverse, improve or erase the early signs of aging, take very little time to perform, and have a minimal, if any, recovery time.

While Bradbard wasn't interested in removing wrinkles at the time of her

products that have proven, over time, to be most effective at reversing the aging process. Most doctors agree that the leading product to prevent premature wrinkles and sun damage is sunscreen. A broad-spectrum sunscreen that protects the skin from both UVA and UVB rays, with a sun protection factor (SPF)

a man's body differs from a woman's, products or procedures can have different effects. The facial area in men contains hair, for example, and their skin is thicker. This means the blood supply is greater—and so is the risk of bleeding—but it also could mean better healing.

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*If a procedure is performed poorly,  
the physical and emotional scars could be carried for life.*

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facelift, given what she knows about new technologies and drug delivery systems today, she says, "I would consider both non-invasive procedures and another facelift down the road, depending on how much my skin changes. I would ask my doctor what would give me the best results with the longest-lasting effects."

#### Buyer Beware

Anti-aging products that promise to diminish wrinkles and fine lines are found on many store shelves. However, dermatologists recommend that people consider only those procedures and

of 15 or higher, can prevent the skin from looking older than it is.

According to the ASAPS, it's important to realize that although certain products and procedures are effective, they are also limited by the skin's normal aging process. A product that has been deemed effective for erasing wrinkles doesn't necessarily erase wrinkles—there are lots of variables that determine its effectiveness.

For example, the active ingredient in a drug must be delivered to the skin at a therapeutic concentration and remain in the skin long enough to have an effect. Also, because the composition of

And cosmetic procedures come with risks. If a procedure is performed poorly, the physical and emotional scars could be carried for life. Understand the risks and side effects that may be involved.

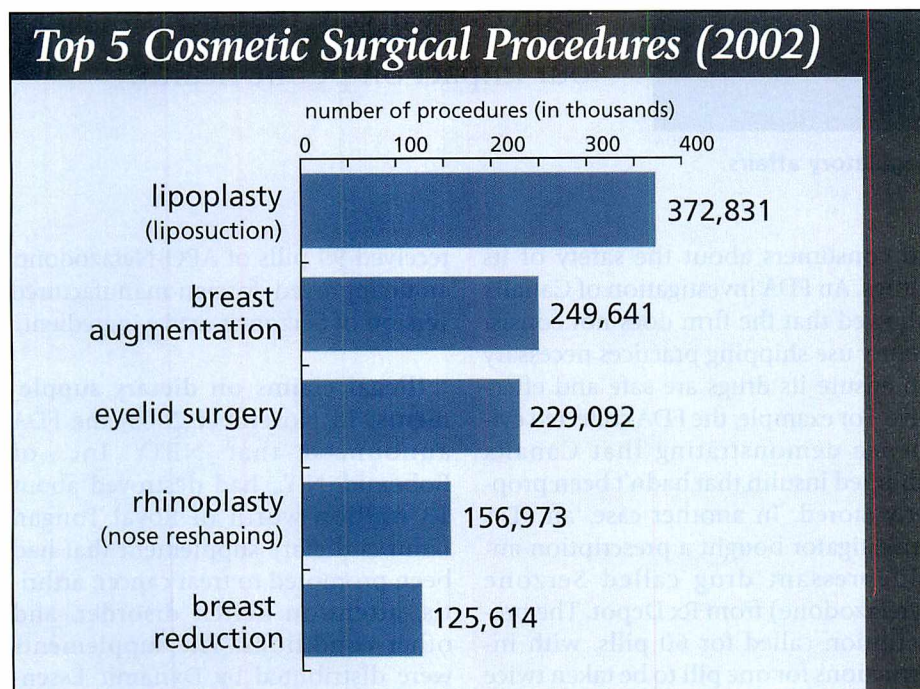
"My wanting to improve my appearance is like my husband's desire to restore a vintage automobile," says Bradbard. "We both want something to look good for as long as it can." ■

#### For More Information

American Academy of Dermatology  
PO Box 4014  
Schaumburg, IL 60168-4014  
(888) 462-3376  
[www.aad.org](http://www.aad.org)

American Society for Dermatologic Surgery  
5550 Meadowbrook Drive, Suite 120  
Rolling Meadows, IL 60008  
(800) 441-2737  
[www.aboutskinsurgery.com](http://www.aboutskinsurgery.com)

American Society for Aesthetic Plastic Surgery  
11081 Winners Circle  
Los Alamitos, CA 90720  
(888) 272-7711  
[www.surgery.org/public](http://www.surgery.org/public)



Source: American Society for Aesthetic Plastic Surgery



# FDA Crackdown on Illegal Products



John M. Taylor, FDA associate commissioner for regulatory affairs.

FDA

During 2003, the Food and Drug Administration took significant strides to address the growing threat of illegal drugs and false health claims related to dietary supplements. "Our major priority is to continue fostering the legitimate manufacture, sale and use of FDA-regulated products while maintaining a zero-tolerance approach to illegal practices," says John Taylor, the FDA's associate commissioner for regulatory affairs. "We're working to allocate resources in a way that maximizes our impact on public health."

Here are some examples of recent actions by the agency:

**Warnings on imported drugs:** The FDA has long been concerned about the dangers faced by consumers who buy medications outside of the United States. During the fall of 2003, the FDA issued warnings and filed complaints against Rx Depot of Lowell, Ark., and CanaRx Services of Detroit to stop them from importing drugs from Canada. The FDA considers these operations illegal and dangerous.

CanaRx made misleading assurances

to consumers about the safety of its drugs. An FDA investigation of CanaRx showed that the firm does not consistently use shipping practices necessary to ensure its drugs are safe and effective. For example, the FDA collected evidence demonstrating that CanaRx shipped insulin that hadn't been properly stored. In another case, an FDA investigator bought a prescription antidepressant drug called Serzone (nefazodone) from Rx Depot. The prescription called for 60 pills, with instructions for one pill to be taken twice a day for 30 days. But the investigator

received 99 pills of APO-Nefazodone, an unapproved, foreign-manufactured version of Serzone's active ingredient.

**Illegal claims on dietary supplements:** In November 2003, the FDA announced that NBTY Inc. of Bohemia, N.Y., had destroyed about \$3 million worth of Royal Tongan Limu, a dietary supplement that had been promoted to treat cancer, arthritis, attention deficit disorder, and other conditions. The supplements were distributed by Dynamic Essentials, an NBTY subsidiary in Lake Mary,



## Import Blitz Reveals Safety Concerns

Mail shipments of foreign drugs to U.S. consumers often contain dangerous, unapproved or counterfeit drugs, according to two "blitz exams" conducted by the Food and Drug Administration and U.S. Customs and Border Protection (CBP).

Import blitz exams are targeted examinations of parcels at a select number of mail facilities over a specific time. The exams help the FDA understand trends in the illegal importation of unsafe drugs, target future shipments and sources of such drugs, and seek partnerships with other federal, state and international partners to combat the problem.

Generally, due to the huge volume of parcels entering the United States, the FDA and CBP don't have sufficient resources to perform comprehensive examinations of all mailed packages. Through review of historical data and experience, FDA and CBP personnel are able to identify parcels likely to contain imported drug products.

One round of blitz exams was conducted last summer in mail facilities in Miami, New York City, San Francisco, and Carson, Calif. Of the 1,153 imported drug parcels examined, 88 percent contained unapproved drugs from many countries.

Here are some examples:

- **Drugs different from those approved by the FDA:** Roaccutane, an unapproved version of the acne drug Accutane (isotretinoin), was imported into the United States from Thailand. Taro-warfarin, an unapproved version of warfarin, was imported from Canada. Warfarin is used to prevent blood clots.
- **Drugs requiring careful dosing:** Inspectors discovered unapproved versions of Dilantin (phenytoin) from the Philippines, unapproved versions of Synthroid (levothyroxine) from Canada, and unapproved versions of Glucophage (metformin) from Canada and the Philippines.
- **Drugs with inadequate labeling:** Most of the drugs came without adequate labeling or instructions for proper and safe use. Some of the drug labeling was not in English.

- **Drugs inappropriately packaged:** In some cases, the drugs were in baggies, tissue paper or envelopes. Some drugs arrived crushed or broken.

- **Drugs withdrawn from the market:** Buscapina, an unapproved drug that came from Mexico, appeared to be the pain and fever drug dipyrrone. The FDA removed dipyrrone from the market in 1977 because of potentially fatal side effects.

- **Animal drugs not approved for human use:** One drug called clenbuterol is banned by the International Olympic Committee as a performance-enhancing drug. Clenbuterol is approved to treat airway diseases in horses, but is not approved for humans.

- **Drugs with potential for dangerous interactions:** Unapproved versions of Viagra (sildenafil) were shipped from the United Kingdom, India, the Philippines and Japan. Unapproved versions of Zocor (simvastatin) came from Canada. These drugs can cause significant interactions with other drugs.

- **Drugs requiring screening and monitoring:** Unapproved versions of the cholesterol drug Lipitor (atorvastatin) came from Ireland, Thailand, Japan, the Philippines, Canada, Argentina, New Zealand, England, and Brazil. Unapproved versions of Pravachol (pravastatin), another cholesterol drug, came from Canada. For both drugs, screening and monitoring of patients' liver function are needed.

- **Controlled substances:** More than 25 different imported controlled substances were referred to the Drug Enforcement Administration.

A second import blitz exam, done in November 2003 at the Buffalo, Chicago, Dallas, and Seattle postal facilities and at the Memphis and Cincinnati courier hubs, found 1,728 unapproved drugs, including so-called "foreign versions" of FDA-approved drugs. The blitz also found recalled drugs, drugs requiring close physician monitoring, and drugs containing addictive controlled substances. ■

Fla. After an FDA investigation of the firm's New York and Florida locations, Dynamic Essentials decided to cease operations and destroy the product.

In October 2003, the FDA announced it had entered a consent decree of permanent injunction against several corporations, including Hi-Tech Pharmaceuticals, National Urological Group, National Institute for Clinical Weight Loss, American Weight Loss Clinic, and United Metabolic Research Center to prevent the sale of unapproved and misbranded products. The defendants repeatedly sold dietary supplements that

made false claims about treating obesity and erectile dysfunction.

"Getting rid of these products underscores the message from FDA to those who would mislead consumers about their health," says FDA Commissioner Mark B. McClellan, M.D., Ph.D. "We will not tolerate companies that raise false hopes for preventing and treating illnesses, when there are more scientifically proven steps than ever before that consumers can take to improve their health."

**Drugs seized from repackager:** In September 2003, the FDA seized all

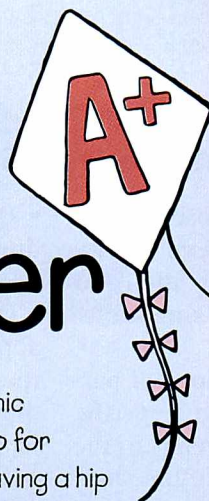
drug products labeled in a foreign language and/or repacked by Alliance Wholesale Distributors and Local Repack in Richton, Ill. The FDA's inspections of Local Repack revealed that the company failed to report customer complaints to the FDA and failed to maintain complete records, along with numerous other deficiencies. The FDA determined that many of the products at Local Repack were of unknown origin, and their storage and handling conditions were unverifiable. ■



# Take the FDA Consumer QUIZ

Do you know how many Americans deal with the pain of chronic headaches? How does the FDA classify antidandruff shampoo for regulatory purposes? What's the most common reason for having a hip or knee replaced? To find out how much you know about these and other health-related topics, take our quiz.

Hint: The answers to all these questions can be found in the March-April 2004 issue of *FDA Consumer* (and at the bottom of this page). Good Luck!



**1. How many hip joints were replaced in U.S. hospitals in 2001?**

- a. about 50,000
- b. about 75,000
- c. about 165,000
- d. about 300,000

**2. The most common reason for having a hip or knee replaced is:**

- a. osteoarthritis
- b. rheumatoid arthritis
- c. bone tumors
- d. avascular necrosis

**3. Ninety percent of those who have total knee replacement report the following:**

- a. fast pain relief
- b. improved movement
- c. better sex
- d. better quality of life
- e. a, b, and d

**4. How many Americans underwent surgical and nonsurgical cosmetic procedures during 2002?**

- a. nearly 7 million
- b. 16 million
- c. 30 million
- d. 100,000

**5. Under a December 2003 agreement, how many U.S. Customs and Border Protection officers can be commissioned by the FDA to inspect and investigate imported foods?**

- a. 2,000
- b. 5,000
- c. 10,000
- d. as many as the two agencies consider necessary

**6. How many Americans have chronic headaches?**

- a. 10 million
- b. 25 million
- c. 35 million
- d. more than 45 million

**7. Which of the following groups are at high risk for flu complications?**

- a. children ages 6 months to 23 months
- b. adults ages 65 and older
- c. pregnant women in the second or third trimester during flu season
- d. people of all ages with underlying chronic conditions such as heart disease or lung disease
- e. all of the above

**8. Of the 1,153 imported drug parcels examined during a "blitz" at mail facilities in the summer of 2003, what percentage contained drugs not approved by the FDA?**

- a. 8 percent
- b. 25 percent
- c. 50 percent
- d. 88 percent

**9. An antidandruff shampoo is regulated by the FDA as:**

- a. a drug
- b. a cosmetic
- c. both a drug and a cosmetic
- d. a medical device

**10. Another name for ephedra is:**

- a. energy booster
- b. ma huang
- c. dietary muscle supplement
- d. speed

## Answers

1. c, 2. a, 3. e, 4. a, 5. d, 6. d, 7. e, 8. d, 9. c, 10. b



By John Henkel

## The Facts About *Trans* Fats in Foods

In 2003, the FDA published a rule requiring food manufacturers to list on labels the amount of *trans* fats contained in their foods. *Trans* fats are created when liquid oils are solidified for products such as margarine. Though they are found in many commonly eaten foods, *trans* fats have been shown to raise levels of LDL ("bad" cholesterol) and to increase the risk of coronary heart disease.

What does the FDA's *trans* fats rule mean for consumers? To help sort it out, the agency has created a Web site with helpful background on *trans* fats and how to use the new labeling to plan a healthful diet.

Included is information on:

- the difference between various types of fats
- sample labels showing where the *trans* fat numbers are found
- practical tips on how to reduce consumption of *trans* fats (and other unhealthy fats as well).

Also on the site is a fun "pop quiz" in which you pick the most heart-healthy spread to put on your toast.

Get up to speed on *trans* fats by going to [www.cfsan.fda.gov/~dms/transfat.html](http://www.cfsan.fda.gov/~dms/transfat.html).

## One-Stop Shop for Recalls Info

The federal government plays a major role in ensuring that unsafe products are taken off the market through its various recall programs. In the past, however, it could be difficult to find information not only about recalls, but also about which agency handles what recall. But now, a newly launched Web site makes it possible to locate current government recall information quickly.

With [www.recalls.gov](http://www.recalls.gov), the Consumer Product Safety Commission has created a gateway to seven recall categories: consumer products, motor vehicles, boats, food, medicine, cosmetics, and environmental products. Say you want to know what food products have been recalled in the last month. On the [recalls.gov](http://www.recalls.gov) home page, just click on "foods," which will take you to a screen where you can pick either the U.S. Department of Agriculture (for meat, poultry and eggs) or the FDA (for all other food products). Both agencies have lists of current recalls.

Through [recalls.gov](http://www.recalls.gov), you also can report a dangerous product, learn important safety tips, and sign up for e-mail lists to be notified of recalls.

## How to Prevent Permanent Hearing Loss

The numbers are staggering: Thirty million Americans are exposed daily to levels of noise high enough to put them at risk of permanent hearing loss. Ten million in this country have already suffered irreversible hearing damage from noise at work, in recreation settings, or at home.

Is it possible to head off this damage before it occurs? Yes, and the National Institute on Deafness and Other Communication Disorders, through its "Wise Ears" campaign, can show you how.

At [www.nidcd.nih.gov/health/wise/](http://www.nidcd.nih.gov/health/wise/), you'll find:

- a gauge for determining how loud is too loud
- resources for educators (videos, classroom activities)
- 10 ways to recognize hearing loss
- how to protect your hearing when shooting a gun.

The site also links to free brochures and other information on hearing loss, which can be viewed online or ordered in printed form.

## Keeping Track of Your Fruits and Veggies

You hear the advice all the time: Eat at least five vegetables and fruits daily. That advice is backed up with compelling evidence that doing so can improve your health and cut the risk of cancer, heart disease, diabetes, and other serious diseases.

But how do you get started? The National Cancer Institute says it can be as easy as having juice at breakfast or adding some extra veggies to your next sandwich. On its *Eat 5 to 9 a Day* Web site (<http://5aday.nci.nih.gov>) NCI offers a wealth of tips designed to make eating fruits and veggies fun and tasty. The site is loaded with recipes for any meal or snack during the day. It demystifies what a serving size is, and it explains how to boost fruit and veggie consumption in school lunches.

Also on the site is "Rate Your Health Habits," an interactive page that allows you to rate your daily intake of fruits and vegetables and your physical activity to help reach goals for optimum health. ■

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*John Henkel is a member of the FDA's Website Management Staff.*



# The State of Pain Management

By B. Eliot Cole, M.D., M.P.A.



Over the last 25 years, there has been a growing sense in health care that pain has been under-managed and that many people have needlessly endured awful levels of pain for no purpose. I think that we got to this place because health practitioners lacked the skills needed to recognize and control pain or they refused to give adequate amounts of medications because they feared the scrutiny of regulatory bodies.

It was not that long ago that health care students were actually taught that the “first dose of morphine should be the last one” and that “no one ever died from pain, they just wished that they could.” At least three generations of physicians, nurses and pharmacists were taught to fear pain-relieving medications that were derived from opium poppies (opioids).

By the late 1980s and early 1990s, Americans began to demand that more be done to relieve their unnecessary pain. Better pain management techniques were developed. These included preemptive strategies to isolate the surgical area from the central nervous system by giving epidural, spinal or regional anesthesia along with general anesthesia; more consistent use of patient-controlled analgesia (PCA) equipment; and protocols for administering pain relievers around the clock rather than “as needed” for predetermined periods. Fellowship programs were initiated to train anesthesiologists, neurologists and psychiatrists to provide real solutions for pain, regardless of its cause. Nurses and pharmacists, along with many other health care professionals, worked closely with pain management specialists.

Because of these improvements, we now hear about our friends and family members having nearly painless surgery. We know people who walk, talk and visit with loved ones only hours after major heart surgery. We have come to expect that pain of short duration (acute pain) is easily controlled. But, sadly, we know of people who suffer from pain lasting weeks, months and years after some illness or surgery. For these people, we have not yet entirely solved the puzzle that causes them to suffer. Much progress has been made in pain treatment, but there is still a failure to entirely account for the complexity of chronic pain.

Pain management programs exist in virtually every state, but many people with chronic pain never satisfactorily regain control over their pain. Some continue to be managed as though they only had acute pain, some have not been

accurately diagnosed, and others never have all of their issues addressed or properly treated. Some turn in desperation and frustration to unproven treatments or submit to risky procedures hoping that something—anything—might make them feel better.

We must continue to improve education about pain treatments that have clear benefits, while also acknowledging that there are risks. For example, we don’t fully understand the implications of starting people in pain on long-term therapy with opioid analgesics. There is also a need to consider the degree of pain relief relative to the cost and risk of some surgeries.

Due to issues of drug abuse and diversion of many of our medications, I am increasingly concerned that manufacturers will be reluctant to develop new release formulations or that regulatory agencies may take action against those prescribing the most potent pain-relieving medications. This will sadly lead to a chilling effect and limit access to treatment for patients in need of relief.

Additionally, there is still a lack of access to pain management services for too many of our citizens. People of color, people living in poverty, and those living in rural locations still lack the full range of pain management services. We have much work left to do and must view modern pain management as a job not yet completed.

There have been great advances in technology and pharmacology over the past 25 years. We have improved our ability to control pain and have developed well-crafted protocols for medication administration that allow people with terminal illness to die with comfort and dignity. Yet, the field of pain management is still young and evolving. It will take more time to know the best strategies for managing pain for all patients under all circumstances.

The great hope is that, in the next few years, the basic mechanisms of pain will be more completely understood, and treatments will continue to improve. In the meantime, health care practitioners of many disciplines have more opportunities than ever to learn about caring for people who experience pain. We remain committed to educating consumers that pain is often treatable and nearly always manageable. ■

*B. Eliot Cole, M.D., M.P.A., is the director of education for the American Academy of Pain Management, located in Sonoma, Calif.*



# Buying Medicine from Outside the U.S. is Risky Business



**It's a gamble  
you can't afford  
to take.**

If you buy foreign medicine from an Internet site, from a storefront business that offers to order foreign medicine for you, or during visits outside the United States, you are taking chances with your health. Foreign dealers—who are not always pharmacists—can give you the wrong medicine, wrong strength, or wrong directions. The medicine can be old, fake, or contain dangerous ingredients. The FDA cannot guarantee the safety of medicine bought from outside the United States.

**Don't play games with  
your health.**

Check with the National Association of Boards of Pharmacy (<http://www.nabp.net/vipps/consumer/listall.asp>), or your local state board of pharmacy, to determine whether a Web site or online pharmacy is licensed and in good standing within the United States. You should report to the National Association of Boards of Pharmacy ([www.nabp.net/vipps/consumer/report.asp](http://www.nabp.net/vipps/consumer/report.asp)) any adverse reactions you have had to a medicine purchased from outside the United States.



**FDA**

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