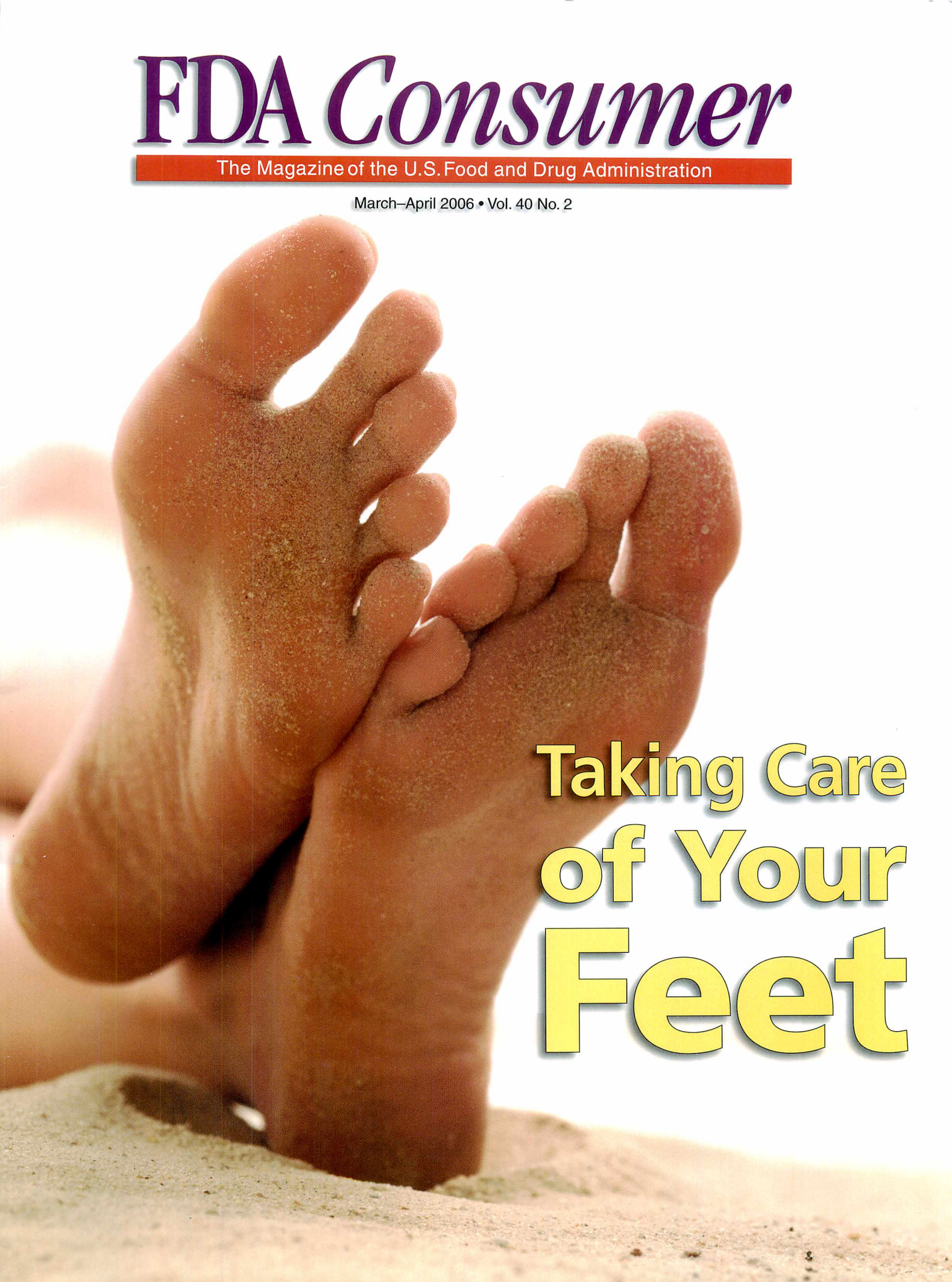


FDA *Consumer*

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

March–April 2006 • Vol. 40 No. 2



Taking Care
of Your
Feet

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FDA Consumer

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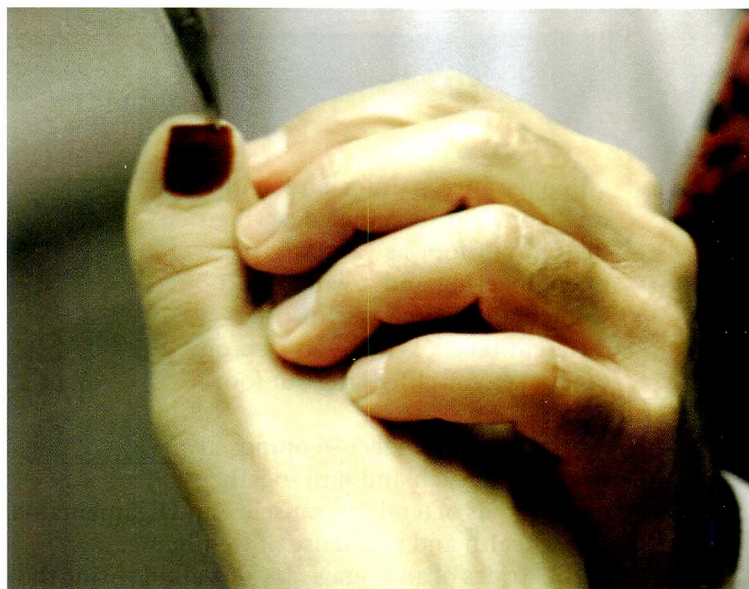
More treatment options include drugs to prevent a migraine attack as well as options to stop migraine pain.

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OBSERVATIONS

Renaissance painter and sculptor Leonardo da Vinci described the human foot as "a masterpiece of engineering and a work of art." Comedian George Carlin offers a different take: "When you step on the brakes your life is in your foot's hands."

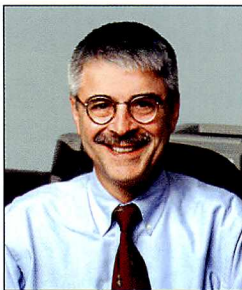
In any case, the feet—composed of 26 bones each and knit together by hundreds of tendons, muscles, and ligaments—are critical to health and to a sense of well-being.

The strides of an average day of walking bring the equivalent of several tons of pressure to the feet, according to the American Podiatric Medical Association (APMA). Little wonder, then, that foot ailments are among the most common health problems.

Studies indicate that 3 out of 4 Americans have some type of foot problem during their lives. And a number of diseases, such as diabetes, kidney problems, anemia, and cardiovascular disorders, often are first detected by symptoms in the feet, the APMA says. For more on foot health, including an illustrated chart showing some common foot ailments, see this issue's cover story titled "Taking Care of Your Feet," beginning on page 16.

Many researchers now believe that migraine results from genetic mutations at work in the brain. The National Institute of Neurological Disorders and Stroke (NINDS) says that studies of the more rare, familial subtypes of migraine are yielding information about specific genes and what they do, or don't do, to cause the pain of migraine headache.

According to the NINDS, there are two approaches people can use to treat migraine with drugs: preventing the



debilitating headaches and relieving the symptoms during a migraine. For more on migraine, its causes, and treatments, see our feature story titled "Managing Migraines," beginning on page 30.

The Food and Drug Administration has developed three distinct approaches intended to make important treatments for serious diseases available more rapidly to those who desperately need them: "fast track" designation of drugs, "accelerated approval," and "priority review."

Independent researchers affiliated with Tufts University in Boston reported in December 2003 that the clinical development time for fast track drugs was, on average, about two and a half years shorter than that for non-fast track drugs approved between 1998 and 2003.

Accelerated approval allows the FDA to approve drugs for serious or life-threatening illnesses based on clinical trials that indicate possible beneficial results. And the FDA has set a six-month goal for review of priority drugs—those offering a significant improvement over existing treatments or providing a treatment where no adequate therapy exists. For more on the FDA's efforts to make promising treatments available more rapidly, see our feature article titled "The FDA Speeds Medical Treatments for Serious Diseases," beginning on page 9.

We also take a look at the first inhaled alternative for the 5 million Americans who inject insulin or take pills to control their diabetes, the proper use of a potent skin patch used to control severe pain, and an FDA safety alert on blood glucose meters.

Enjoy!

Raymond Formanek Jr.
Editor

UPDATES

New Immune Globulin Product

The FDA has approved the first immune globulin product, called Vivaglobin, for under-the-skin (subcutaneous) injection to prevent serious infections in people with Primary Immune Deficiency Diseases (PIDD).

Vivaglobin, made from human plasma collected at U.S. licensed plasma centers, provides new delivery options for people who have PIDD. It is given on a weekly basis using an infusion pump, which means people can self-administer the product at home.

PIDD are inherited disorders that

affect an estimated 50,000 people in the United States. People who have PIDD require regular treatment with immune globulin in order to fight off or prevent potentially serious or life-threatening infections.

Other immune globulin products are administered either into a vein (intravenously) or into muscle (intramuscularly). Some people develop problems that make it difficult to administer needed medicines intravenously, and Vivaglobin may be helpful in providing them with an alternative route.

In clinical studies, the most common

side effects of Vivaglobin were mild or moderate injection site reactions such as swelling, redness, and itching.

As for all immune globulin preparations, plasma used for Vivaglobin is tested and found to be nonreactive for HIV and hepatitis viruses prior to its use, and the manufacturing process includes steps that further reduce the risk of transmission of viruses.

Vivaglobin is manufactured by ZLB Behring GmbH of Marburg, Germany.

FDA: So-Called 'Canadian' Products Really From Other Countries

An FDA operation found that nearly half of the imported drugs that the agency intercepted from four selected countries were shipped to fill orders that consumers believed they were placing with "Canadian" pharmacies. Of the drugs being promoted as "Canadian," based on accompanying documentation, 85 percent actually came from 27 countries. A number of these products also were found to be counterfeit.

"These results make clear there are Internet sites that claim to be 'Canadian' that, in fact, are peddling drugs of dubious origin, safety, and efficacy," says Acting FDA Commissioner Andrew von Eschenbach, M.D. "We believe that these 'bait and switch' tactics—offering patients one thing and then giving them something else—are misleading to patients and potentially harmful to the public health."

The FDA conducted its "Operation Bait and Switch" over a few days in August 2005 at the John F. Kennedy International Airport in New York, Miami International Airport, and Los Angeles International Airport. The FDA examined all mail parcels suspected of containing pharmaceuticals sent from four countries—India, Israel, Costa Rica, and Vanuatu—that the agency had previously noticed were sources of drugs apparently ordered from pharmacies alleged to be Canadian.

Out of nearly 4,000 parcels examined, almost 1,700, or about 43 percent, had been ordered from "Canadian" Internet pharmacies and were represented as being of Canadian origin. However, only 15 percent of these "Canadian" drugs actually originated in Canada. The remaining 85 percent were manufactured in 27 different countries. In addition to having been falsely promoted as being of Canadian origin, many of these drugs were not adequately labeled in English to help assure safe and effective use.

Thirty-two of the pharmaceuticals sampled, representing three distinct drug products, were determined to be counterfeit. The FDA is working closely with the Canadian drug regulatory and law enforcement authorities on this matter. Visit www.fda.gov/importeddrugs for more on imported drugs and www.fda.gov/counterfeit for additional information on counterfeits.

Treatment for Advanced Kidney Cancer

The FDA has approved Nexavar (sorafenib tosylate), a new anti-cancer medicine used to treat adults with advanced renal cell carcinoma, the most common type of kidney cancer.

The approval of Nexavar in December 2005 brings a much-needed option for this group of cancer patients, says Steven Galson, M.D., director of the FDA's Center for Drug Evaluation and Research. "The FDA is working hard to support the development of new and effective treatments for patients with cancer and other serious illnesses who have limited alternatives," Galson says.

In the United States, kidney cancer accounts for about 3 percent of all adult cancers. According to the Ameri-

can Cancer Society, about 32,000 new cases are diagnosed, and about 12,000 people die from the disease annually. Kidney cancer occurs most often in people between the ages of 50 and 70, affects men almost twice as often as women and, if detected early enough, may be curable surgically. But tumors that are advanced are difficult to treat. These are tumors that cannot be surgically removed or have spread to other parts of the body.

Two studies in people with advanced kidney cancer have shown that those treated with Nexavar had more time before tumor progression or death. In the larger study, most patients had previously received treatment with interleukin-2 or interferon. The median time to tumor progression or death in the Nexavar treated arm was 167 days compared to 84 days in people not treated with the drug.

Some common, temporary side effects reported with Nexavar are rash, diarrhea, increases in blood pressure, redness, pain, swelling, or blisters on the palms of the hands or on the soles of the feet.

Nexavar will be marketed by Bayer Pharmaceuticals Corp. of Westhaven, Conn.

We're eager to hear what you like and what you don't like. We also want to know the subjects you'd like to see covered.

To contact *FDA Consumer*:

Letters to the Editor should be 200 words or less. If you would like your comments to be considered for publication, please include your name, address, and telephone number during business hours. The editor reserves the right to edit letters for space and appropriateness. E-mail your letters to FDAC-letters@oc.fda.gov or send to the address below.

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General FDA questions: E-mail webmail@oc.fda.gov

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5600 Fishers Lane, Rockville, MD 20857

New Treatment for Myelodysplastic Syndrome

The FDA has approved the drug Revlimid (lenalidomide) for the treatment of a subtype of Myelodysplastic Syndrome (MDS) called deletion 5q cytogenetic abnormality.

MDS is a collection of disorders in which the bone marrow does not function normally and the body does not make enough normal blood cells. About 7,000 to 12,000 new cases of MDS are diagnosed yearly in the United States. Although MDS occurs in all ages, the highest prevalence is in people older than 60. Typical symptoms of MDS include weakness, fatigue, infections, easy bruising, bleeding, and fever.

People with MDS may need blood and platelet transfusions and antibiotic therapy for infections. In clinical trials, those treated with Revlimid no longer needed transfusions, with most patients becoming independent of transfusion by three months. The transfusion-free period lasted an average of 44 weeks.

"This new product will offer a much needed treatment option for patients suffering from this rare illness that, in some cases, has been found to progress to fatal forms of leukemia," says Steven Galson, M.D., director of the FDA's Center for Drug Evaluation and Research.

MDS can develop after treatment with drugs or radiation therapy for other diseases, or it can develop without any known cause. Some forms of MDS can progress to acute

myeloid leukemia (AML), a type of cancer in which too many white blood cells are made.

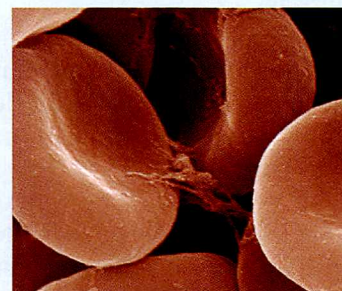
Revlimid is structurally similar to thalidomide, a drug known to cause severe birth defects. Additional studies are ongoing in animals to

address whether there is a risk that Revlimid will also cause birth defects when taken during pregnancy. While these studies are under way, the company is marketing Revlimid under a risk management plan called RevAssist, designed to prevent fetal exposure.

The FDA and the manufacturer will re-evaluate the risk management plan when results of further animal testing for birth defects are completed.

The labeling for Revlimid will include a "black box" warning and a Medication Guide regarding the prevention of fetal exposure. Additional black box warnings include the potential need to lower the dose because of suppressed blood counts and increased risk of blood clots.

Revlimid is distributed by Celgene Corp. of Summit, N.J.



cdc

Paxil and the Risk of Birth Defects

Early results of new studies for Paxil (paroxetine) suggest that the drug increases the risk of birth defects, particularly heart defects, when women take it during the first three months of pregnancy. Paxil is approved to treat depression and several other psychiatric disorders. The FDA is gathering additional data and waiting for final results of the studies to better understand the higher risk of birth defects.

The FDA advises health care professionals to discuss this potential risk with women who plan to become pregnant or are in the first three months of pregnancy. Health care professionals should consider discontinuing Paxil and switching to another antidepressant in these patients. But for some women who have already been taking Paxil, the benefits of continuing the

drug may be greater than the potential risk to the fetus.

"Stopping these medicines on your own can sometimes create more problems than it solves," says Sandra Kweder, M.D., deputy director of the FDA's Office of New Drugs. "A lot of these medicines are associated with withdrawal syndromes, which can be very problematic for many patients, so stopping is something that needs to be monitored carefully by your doctor."

The FDA advises health care professionals not to prescribe Paxil in women who are in the first three months of pregnancy or are planning pregnancy, unless other treatment options are not appropriate.

Early results of two studies indicate that women who took Paxil during the first three months of pregnancy were about one and a half to two times as

likely to have a baby with a heart defect as women who received other antidepressants or women in the general population. Most of the heart defects reported in these studies were holes in the walls of the chambers of the heart (atrial and ventricular septal defects).

The FDA has asked Paxil's manufacturer, GlaxoSmithKline (GSK) of Research Triangle Park, N.C., to change the drug's pregnancy category from C to D, which is a stronger warning. Category D means that studies in pregnant women have demonstrated a risk to the fetus.

GSK updated the drug's labeling in September 2005 to add data from one study. As additional data have become available, the label has been changed to reflect the latest data. Visit www.fda.gov/cder/drug/advisory/paroxetine200512.htm for more information.

New Warnings for Two Eczema Drugs

Two topical eczema drugs now carry a "black box" warning about a possible risk of cancer. The FDA approved the updated labeling with the warning for Elidel Cream (pimecrolimus) and Protopic Ointment (tacrolimus). The agency also approved a consumer-friendly medication guide that pharmacists are required to give to patients when dispensing these prescription drugs to make them aware of this concern.

The new labeling also clarifies that these drugs are recommended for use as second-line treatments, meaning that other prescription topical medicines should be tried first. Use of these drugs in children younger than 2 is not recommended.

People who have eczema, or atopic dermatitis, have chronic itching and dry skin. Both drugs are applied to the skin to help control eczema.

Although a causal link has not been established, rare reports of cancer have been reported in people who had been

using these products.

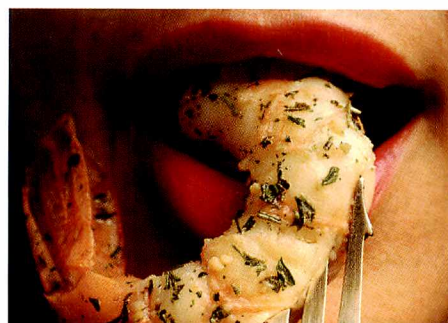
Studies are being conducted by the manufacturers of both drugs to try to answer questions about cancer risk, but it could be many years before the research is concluded. In the meantime, there is a benefit associated with these drugs when used appropriately.

Novartis Pharmaceuticals Corp. manufactures Elidel Cream and Astellas Pharma Inc., formerly Fujisawa Healthcare, manufactures Protopic Ointment.

Positive Seafood Report

Hundreds of samples of fish and shellfish from the waters affected by Hurricanes Katrina and Rita have come back contaminant-free, according to local, state, and federal officials, and there is no reason for people to be concerned about consuming seafood from the Gulf region because of the hurricanes.

The samples were analyzed for chemical and microbiological contaminants that could have been introduced by the hurricanes. The extensive seafood



Photodisc

tissue sampling occurred in an area from the estuaries of New Orleans to Gulf Shores, Ala. The sampled areas included Lake Pontchartrain, Mississippi Sound, and Mobile Bay, as well as the offshore areas of the northern Gulf of Mexico. Officials from Alabama, Mississippi, Louisiana, the FDA, the federal Environmental Protection Agency, and the National Oceanic and Atmospheric Administration were involved in the tests and analyses.

Additional monitoring is being done, and results will be announced as they become available.

The FDA Advances Scientific Research

To gain a better understanding of the health outcomes associated with marketed drugs, the FDA and the Agency for Healthcare Research and Quality (AHRQ) are launching an effort that will advance scientific research and will foster future research partnerships.

"Through this collaboration, we will gain an improved understanding of the health outcomes associated with marketed drugs that we will leverage to improve the quality of information we provide to the public," says Gerald Dal Pan, M.D., director of the FDA's Office of Drug Safety.

This endeavor also will include promoting collaborative drug safety and effectiveness research by the Centers for Medicare and Medicaid Services and by academic and professional organizations.

"The Effective Health Care Program compares treatment alternatives, including drugs, and communicates its findings broadly to help patients and health care providers make the best choices in their health care," says Jean R. Slutsky, director of the AHRQ's Center for Outcomes and Evidence. "A closer association between the AHRQ



CDC

and the FDA will help both agencies serve consumers and health care professionals better." ■

Safety Alert on Blood Glucose Meters

By Carol Rados

Glucose meters help people with diabetes check their blood sugar. And because diabetes that is not well-controlled can lead to complications such as blindness, these medical devices must be reliable, accurate, and easy to use and understand.



Photo Researchers Inc.

Blood glucose monitoring meter in patient's hand. The meter allows people with diabetes to measure their blood sugar level at home.

Recent problems reported to the Food and Drug Administration indicate that some people who use certain blood glucose meters may have problems properly setting the units of measurement on their meters or may inadvertently switch them. Also, in some cases, jarring or dropping the meter can cause the units to switch without the user being aware. These actions can lead to misinterpretation of glucose test results and to dosage errors in insulin or in oral diabetes medication.

Diabetes is a disease in which the body does not produce or properly use insulin. Insulin is a hormone that is needed to convert sugar, starches,

“Someone who is familiar with their meter is going to realize if it is displaying the wrong unit of measure,” says Tama Antonia Donaldson, director of public affairs at Abbott Diabetes Care in Alameda, Calif. Reports, however, indicate that in some cases, even those who are familiar with their meters have not realized the wrong measurement unit that is being displayed. Donaldson advises, “Users should verify that their meter displays the correct unit of measure each time they test.”

The Importance of Proper Testing

Checking blood glucose is a critical step in managing diabetes, says Joanna

als and users, when known, about the problem. In addition to verifying the correct unit of measure and code number each time, Zawadzki adds, “Patients should take the time to review their glucose meters with their diabetes health care providers and read the information that accompanies the device.”

As an added safety measure, Donaldson says that new models of meters have the correct unit of measure locked in place.

For information on how to change a unit of measurement for meter readings, users should refer to their owner’s manual or should contact the manufac-

‘As with any tool, a glucose meter has to be used correctly for it to be most effective.’

and other food into energy needed for daily life. According to the American Diabetes Association, about 20 million people in the United States, or 7 percent of the population, have the condition.

The problem meters are designed to report blood glucose levels in two different measurements—the U.S. standard—milligrams per deciliter (mg/dL)—and the standard used in Europe and elsewhere—millimoles per liter (mmol/L). The normal fasting blood sugar (glucose) for people who don’t have diabetes is usually less than 100 mg/dL or less than 5.5 mmol/L. The conversion factor between the two units of measure is 18, meaning a value in mg/dL equals 18 times the comparable value in mmol/L.

According to reports, users have accidentally changed one unit of measure to the other while setting their meter’s date and time, or while changing the battery. There also have been reports of the unit of measure changing after a meter was jarred or dropped.

K. Zawadzki, M.D., in the FDA’s Division of Metabolism and Endocrinology Products. Frequent testing and good recordkeeping give people the most accurate picture of diabetes control.

However, she says, “As with any tool, a glucose meter has to be used correctly for it to be most effective.” Blood glucose meters measure the amount of glucose in the blood and serve as an aid in monitoring the effectiveness of diabetes management at home or in a clinical setting. Glucose control can help prevent serious complications of diabetes, such as kidney failure, blindness, and amputations.

To date, at least three companies have reported this problem. It appears that companies making meters with the ability to report in both units of measure need to consider this problem in the design and labeling of their product.

Manufacturers are not instructing users to return their meters. Instead, the firms have issued worldwide notifications to all health care profession-

turer directly. People who think they may have been using the wrong readout on their meters for a long period of time, and who are now worried about their health, should contact their doctors immediately. ■

To report a problem with affected blood glucose meters

The FDA’s MedWatch Program
www.fda.gov/medwatch/
(800) 332-1088

Fraudulent, Unapproved Influenza-Related Products

The Food and Drug Administration considers the sale of unlicensed or unapproved influenza-related products as a potentially significant threat to public health and is taking action to protect consumers from fraudulent products that claim to prevent or treat seasonal or bird (avian) influenza in people.

Currently, there are no approved vaccines for preventing avian influenza in people, nor are there any drugs approved for treating the specific symptoms of avian influenza. Several vaccines and drugs have been approved to prevent and treat seasonal influenza, but it is often impossible for unsuspecting consumers to differentiate between

ers who take them, without providing any therapeutic benefits or protection against any type of influenza.

For example, the FDA, in cooperation with the U.S. Customs and Border Protection, recently intercepted products at the border that purported to be "generic" Tamiflu, but which, in fact, contained vitamin C and other

tenced in January 2006 to nine months in prison for operating a series of unauthorized influenza vaccine clinics at a college in Minneapolis, after pleading guilty to dispensing drugs without a doctor's prescription. The nurse admitted to diluting some of the vaccine with saline to increase the quantity of her supply, thereby reducing the quality and effectiveness of the vaccine.

In another action in December 2005, the FDA issued Warning Letters to nine companies marketing bogus flu products and making unproven claims that their products could treat or prevent avian flu or other forms of influenza. Eight of the nine products cited in the Warning Letters purported to be dietary supplements.

Examples of the unproven claims

Generally, the ingredients used and the conditions under which the products were manufactured are unknown ...

these approved products and those that are not genuine.

For the most part, the seasonal and avian influenza-related products marketed to consumers without a prescription or a specific endorsement by a registered pharmacy or health care professional are not approved by the FDA.

Generally, the ingredients used and the conditions under which the products were manufactured are unknown and, therefore, are potentially unsafe and ineffective. Additionally, advertised products may be counterfeit versions of genuine products, or impure, contaminated, subpotent, or superpotent products. In short, they may endanger the well-being and safety of consum-

substances not shown to be effective in treating flu. Although the drugs were similar in appearance to genuine Tamiflu, they offered no therapeutic benefit. In another recent case, special agents from the FDA Office of Criminal Investigations (OCI) worked with the FBI to arrest an individual in Texas who administered counterfeit influenza vaccine to employees attending a corporate-sponsored health fair. And in July 2005, another OCI investigation resulted in the indictment of an individual by a federal grand jury for his role in smuggling foreign, unlicensed influenza vaccines into the United States and attempting to sell the illegal vaccines to hospitals.

A licensed practical nurse was sen-

are: "prevents avian flu," "a natural virus shield," "kills the virus," and "treats the avian flu." The Warning Letters noted that the claims regarding avian flu are false and misleading because there is no scientific basis for concluding that the products are effective to treat or prevent avian flu.

The FDA is committed to investigating these matters and to seeking federal prosecution of those who are involved in the manufacture, promotion, or distribution of illegal, influenza-related products. Consumers who believe that they have seen a fraudulent product can visit www.fda.gov/oc/buyonline/buyonlineform.htm to report it. ■

The FDA Speeds Medical Treatments for Serious Diseases



Photo Researchers Inc.

A doctor discusses treatment options with a patient who has chronic myeloid leukemia, a condition that results from uncontrolled growth of a type of white blood cell called polymorphonuclear leukocytes.

By Carol Rados

The rapid development of better drugs to treat life-threatening illnesses is in everyone's interest. To address this important health care issue, the Food and Drug Administration has developed three distinct approaches that are intended to make important treatments available more rapidly to those who desperately need them: "fast track" designation of drugs, "accelerated approval," and "priority review."



Abbott Laboratories, Millennium Pharmaceuticals Inc., Novartis Pharmaceuticals Corp.

Shortened approval times and the maintenance of the FDA's high standards and safety have resulted in patients receiving life-saving treatments for serious diseases sooner. Examples include Kaletra (lopinavir/ritonavir), a treatment for HIV and AIDS; Velcade (bortezomib) to treat multiple myeloma, a prevalent blood cancer; and Gleevec (imatinib mesylate), a treatment for chronic myeloid leukemia.

These three approaches expedite the development and review of innovative agents for the most serious or life-threatening conditions, but represent very different kinds of effort. Because they all imply speed—and in order to avoid confusion—it is important that people understand the specific meaning of each and the distinction among them.

Fast Track

Fast track designation was part of the FDA Modernization Act (FDAMA) of 1997, important legislation that made significant changes in the regulation of food, medical products, and cosmetics. This approach is a process designed to facilitate the development and expedite the review of drugs that treat a broad range of serious diseases and fill an unmet medical need. Filling an unmet need means providing therapy where none exists or demonstrating superiority of a drug to existing therapies.

"Determining whether a disease is serious," says Patty Delaney, a public health specialist in the FDA's Office of Special Health Issues, "generally is based on whether the drug will have an impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one." AIDS, Alzheimer's disease, heart failure, and cancer are examples of the more obvious serious diseases. Epilepsy, depression, and diabetes, however, are also considered serious.

Any drug being developed to treat or prevent a disease that has no current therapy is directed at an unmet need. If there are existing therapies, a fast track drug must show some advantage over them, such as:

- superior effectiveness
- less serious side effects compared to an existing therapy
- improved diagnosis of a serious dis-

ease in which early diagnosis results in an improved outcome.

Drug manufacturers may request fast track designation at any time during the drug development process. The FDA will review the request and make a decision within 60 days, based on whether the drug fills an unmet medical need in a serious disease. Once a drug receives fast track designation, early and frequent communication between the agency and the drug company is encouraged throughout the entire drug development and review processes. The frequency of communication ensures that questions and issues are addressed quickly.

"With the fast track designation, FDA agrees to meet frequently with sponsors throughout the drug development process to agree on study designs and appropriate outcome measures," says Robert Temple, M.D., director of the FDA's Office of Medical Policy. "This allows companies to plan and carry

Drug manufacturers may request fast track designation at any time during the drug development process.

All treatments approved under the accelerated approval process must undergo further studies for clarifying a drug's clinical benefits.

out the most rapid possible responsible development," he says, "and it is perhaps the most important, yet underappreciated, aspect of fast track."

In addition to the opportunity for frequent communications with the FDA, a drug that receives fast track designation is eligible for two other important programs:

- Accelerated approval—based on an effect or "surrogate endpoint," such as a change in a laboratory measure, rather than a demonstrated effect on health, such as relief of symptoms or living longer. The surrogate endpoint has to be "reasonably likely" to predict the expected health benefit. Accelerated approval became possible by FDA regulation in 1992.

- Rolling review—completed sections of a new drug application (NDA) can be submitted individually, before all sections of the application are completed. Ordinarily, NDA review usually does not begin until the drug company has submitted the entire application to the FDA. Rolling review can allow problems to be resolved much earlier.

The Tufts Center for the Study of Drug Development, an independent, academic research group affiliated with Tufts University in Boston, reported in December 2003 that more than 50 disease indications had received fast track designation, and that clinical development time for fast track drugs was, on average, about two and a half years shorter than that for non-fast track drugs approved between 1998 and 2003.

Accelerated Approval

When a new drug is being studied, it can take many years and very large studies to learn whether patients experience such clinical benefits as having fewer strokes or living longer. In some cases, however, there is an effect on a

measurement like blood pressure or cholesterol that can serve as a surrogate for a showing of the hoped-for clinical benefit. The accelerated approval process was developed to make new drug products available for life-threatening diseases without adequate treatment before those clinical benefits were shown, but on the basis of a well-thought-out surrogate endpoint.

Temple says that some surrogate endpoints, such as lowered blood pressure, are so well-established that drugs for high blood pressure are granted regular—not accelerated—approval. Accelerated approval is for less well-established surrogates—those that are reasonably likely to predict clinical benefit based on epidemiologic data, results with other drugs that affect the same endpoint, or understanding of disease mechanisms.

For example, instead of having to wait to learn whether a drug actually can extend cancer patients' lives, the FDA might approve a drug based on evidence that the drug shrinks tumors at a reasonable rate, because that would be considered reasonably likely to predict a real clinical benefit—longer life. The use of such a surrogate endpoint can considerably shorten the time required to receive FDA approval.

Velcade (bortezomib), an injection to treat multiple myeloma, the second

most prevalent blood cancer in the United States, was approved in less than four months under the FDA's accelerated approval program in May 2003. The results of two studies showed partial or, in some cases, complete disappearance of tumors. The main study involved 202 people whose cancer had progressed even though they had received at least two previous types of chemotherapy. Velcade, which is marketed by Millennium Pharmaceuticals Inc., of Cambridge, Mass., is indicated only after two previous treatments have failed, since other treatments exist for earlier stages of multiple myeloma.

Most important, the drug showed a significant effect on people with multiple myeloma who have not responded to other treatments, which means it is likely to result in significant clinical benefit.

The agency bases its decision on whether to accept a proposed surrogate endpoint, such as tumor shrinkage, on its scientific support as a predictor of clinical benefit. The studies that demonstrate the effect of the drug on the surrogate endpoint must be adequate and well-controlled, the only basis, by law, for finding that a drug is effective. All treatments approved under the accelerated approval process must undergo further studies for clarifying a drug's clinical benefits. Therefore,

Maintaining High Standards and Safety While Shortening Approval Times

Since 1990, the average or median time for approving a priority drug—one that offers a significant improvement over a marketed drug or provides a treatment where none exists—decreased from about 25 months to six months. The average or median time for approving a standard drug—which offers at most only minor improvement over existing approved therapies—was cut in half, from 26 months to 13 months.

Since 1996, 68 drugs for cancer therapies have received priority review and approval.

the drug company would still need to conduct studies to confirm that tumor shrinkage, for example, actually does predict that patients will live longer or show improvement in their symptoms.

If these follow-up studies show that the drug actually provides a clinical benefit, then the FDA would grant traditional approval of the drug. If not, the agency has regulatory procedures in place that could lead to removal of the drug from the market.

Priority Review

Prior to approval, each drug marketed in the United States must undergo a detailed FDA review process. The FDA has been classifying the likely benefit of a drug since the 1970s, initially in three categories: (A) a major advance over available treatments, (B) a modest advance, or (C) no real advance. More recently, the classification has been in two categories: a real advance (priority or P), or about the same effectiveness as available therapies (standard or S). The kinds of advances a priority drug might represent include:

- evidence of increased effectiveness in treatment, prevention, or diagnosis of disease
- elimination or substantial reduction of a treatment-limiting drug reaction
- simplification of a dosage regimen that is shown to enhance adherence to treatment schedule
- evidence of safety and effectiveness in a new subpopulation, such as children.

In 1992, under the Prescription Drug User Fee Act (PDUFA), a law that requires fees be paid by drug manufacturers when they submit an application to market a drug, the FDA agreed to specific goals for completing its review and taking action on drugs. These goals were different for priority and standard drugs.

For standard drugs, which offer at most only minor improvement over



FDA

Robert Temple, M.D., director of the FDA's Office of Medical Policy in the Center for Drug Evaluation and Research.

existing approved therapies, review and action were to be completed in 12 months. The 2002 amendments to PDUFA changed that goal to 10 months.

Priority drugs, or those that offered a significant improvement over marketed treatments or provided a treatment where no adequate therapy existed, were given a six-month review and action goal.

Priority review status can apply both to drugs that are used to treat serious diseases and to drugs for less serious illnesses. Most drugs that are eligible for fast track designation are likely to be considered appropriate to receive a priority review. Designation of a drug as priority does not alter the scientific or medical standard for approval, or the quality of evidence needed. Priority review also does not affect the length of the clinical trial period.

Success Stories

Since 1996, 68 drugs for cancer therapies have received priority review and approval. In some cases, reviews and

actions have been considerably faster than six months. The agency reviewed Gleevec (imatinib mesylate), a treatment for chronic myeloid leukemia, a rare, life-threatening form of cancer, in less than three months. The approval of Gleevec, manufactured by Novartis Pharmaceuticals Corp. of East Hanover, N.J., was based on evidence that the drug could substantially reduce the level of cancerous cells in the bone marrow and blood.

Shortened review times also have brought promising treatments to patients with AIDS more quickly, such as Kaletra (lopinavir/ritonavir), manufactured by Abbott Laboratories of Abbott Park, Ill., which was reviewed and approved in three and one-half months. Pegasys (peginterferon alpha-2A), a combination product for the treatment of hepatitis C, manufactured by Hoffman-LaRoche of Nutley, N.J., was approved for marketing in four months.

"Fast track, accelerated approval, and priority review have evolved over time," says Delaney. "The FDA has been vigilant in assuring that reducing the time necessary for drug development, associated with these approaches, has not compromised the safety and effectiveness of drugs for patients with serious diseases." ■

For More Information

Office of Special Health Issues
www.fda.gov/oashi/home.html
(301) 827-4460

Guidance for Industry: Designation, Development, and Application Review for Products in Fast Track Drug Development Program
www.fda.gov/OHRMS/DOCKETS/98fr/2004d-0014-gd10001.doc

Proper Use of Fentanyl Pain Patches



Photo Researchers Inc.

The fentanyl patch contains a powerful opiate painkiller. The patch should be used only by people who experience moderate-to-severe chronic pain that is expected to last for weeks or longer.

By Michelle Meadows

Fentanyl skin patches provide convenient and effective relief for many people who experience chronic pain, and who have been taking pain medications for long periods of time. But health care providers and patients should be aware that deaths and other serious problems have resulted from accidental overdoses related to inappropriate use of the fentanyl patch, the Food and Drug Administration says.

The patch is applied to the skin and delivers fentanyl, a potent, strong opiate analgesic. The drug is slowly absorbed through the skin into the bloodstream and can relieve pain for up to three days from a single patch application.

"After applying the first patch, it can take 12 to 18 hours to reach the peak of pain relief, with some early pain relief occurring at four to six hours after the first administration," says Donald R. Stanski, M.D., a professor of anesthesia at Stanford University who was involved with the clinical drug development of the first fentanyl patch in the 1980s.

The most frequent use of the fentanyl patch has been to treat pain in people with cancer, and it is only appropriate for patients who have developed a

overdoses that have occurred with both brand-name and generic fentanyl patches. The brand Duragesic (fentanyl transdermal system), manufactured by Janssen L.P. of Titusville, N.J., was approved by the FDA in 1990. A generic version, manufactured by Mylan Laboratories Inc. of Canonsburg, Pa., was approved in 2005.

In July 2005, the FDA issued a public health advisory on the fentanyl patch. Meyer says the advisory focuses on improving education about the signs of an overdose, proper patch application, drug interactions, proper storage and disposal of the patch, and safeguards for children.

The powerful pain-relieving properties of all opiates are countered by significant risks of depressed breathing that can cause unexpected death. Signs

dosing with short-acting opioids.

The patch also shouldn't be the first narcotic pain medicine that is prescribed. It should be used only in people who have been taking opiate analgesics for a period of time. It could be used if people have been taking at least 60 milligrams (mg) of oral morphine daily, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily, or an equally strong dose of another opioid for a week or longer. Stanski says, "This prior opiate dosing results in a degree of tolerance, or resistance to the opiate that is relevant when the patch is subsequently used." Children who are younger than 2 years should not use the fentanyl patch. It also shouldn't be used in children 2 years of age or older who are not already using other opioid narcotic

'With the patch, patients don't have to take multiple doses of oral medications to control the underlying chronic pain.'

degree of tolerance to the opiate analgesic effects because they have been previously using this type of drug, says Robert J. Meyer, M.D., director of the Office of Drug Evaluation II in the FDA's Center for Drug Evaluation and Research.

"Because the patch provides slow, continuous drug delivery, people with constant pain are less likely to experience waxing and waning of pain control," as occurs when the traditional oral medication or injections of the opiate wear off, Meyer says. Some people can experience breakthrough pain, which may require additional analgesic medication. "With the patch, patients don't have to take multiple doses of oral medications to control the underlying chronic pain," Meyer says. "But in some reports of overdose, we have seen misunderstandings about the recommended use of the product." Proper use of the patch that follows the drug's label is crucial.

The FDA is investigating deaths and

of an overdose include trouble breathing or shallow breathing, extreme sleepiness or sedation, an inability to walk or talk normally, and feeling faint, dizzy, and confused. People who experience these symptoms should seek emergency medical attention. Removing the patch won't reverse the problem; the drug is still absorbed into the body for more than 17 hours after the patch is removed.

Appropriate Use

The fentanyl patch should not be used for short-term, acute pain, pain that is not constant, or pain after an operation. "The patch is not for pain that occurs after surgery such as tonsillectomies or dental procedures," Meyer says.

The patch is only for people who experience moderate-to-severe chronic pain that is expected to last for weeks or longer and that cannot be managed by acetaminophen-opioid combinations, nonsteroidal analgesics, or as-needed

pain medicines. Patches should always be prescribed at the lowest dose needed for pain relief.

"Understanding and following directions is so important because of the potential for respiratory depression associated with all opiate analgesic medications, and especially with the fentanyl patch," says Stanski.

Some deaths have occurred because more than one patch was applied at the same time. Other problems associated with the patch include not removing one patch before applying another, and the failure of multiple caregivers to notice that someone else has applied a patch. The patches are clear, relatively transparent, and easily blend into the skin background.

The Institute for Safe Medication Practices (ISMP) received a report of a 77-year-old woman who died in March 2005 after using the fentanyl patch. Her primary care physician called in a prescription for the patch without examining her or educating her about

the drug. She did not receive education from the pharmacy either, according to the ISMP's report.

The woman's friend helped her place the patch on her buttock, and the woman later used a heating pad in that area. Heating pads, electric blankets, heat lamps, saunas, hot tubs, or heated water beds should not be used with the patch. "The heat will speed up the movement of fentanyl from the patch into the body much more rapidly than normal," Stanski says. "This creates a risk for an overdose situation."

Two days later, friends discovered that the woman had died. She had apparently used two of the five patches prescribed. According to the ISMP, in addition to using a heating pad with

herbal supplements.

Death and other serious problems have occurred because people were accidentally exposed to the fentanyl patch. According to Janssen, a patch was transferred from an adult to a child while hugging. In another case of unintended exposure, someone accidentally sat on a patch.

The ISMP says that a mother reported that her 4-year-old son died after applying the patch to his body. He either used a discarded fentanyl patch or a new one. She found him on the floor near an overturned trash can that contained discarded patches and wrappers.

Fentanyl patches should be stored in a secure place and kept out of reach

In June 2005, researchers from the University of Florida at Gainesville presented results of a study that found that the number of sudden deaths from fentanyl overdoses has been climbing nationwide. The study cited Florida Department of Law Enforcement records showing that abuse of the fentanyl patch resulted in the deaths of 115 people in Florida in 2004. Researchers said that many people who overdosed removed the full three-day dose from the patch and took it through injection, ingestion, or smoking.

As with other opiate drugs, there is a risk of becoming either addicted to the substance in the fentanyl patch or tolerant to the drug. The risk goes up for people who have a history of

As with other opiate drugs, there is a risk of becoming either addicted to the substance in the fentanyl patch or tolerant to the drug.

the patch, it is suspected that a second patch was applied without removing the first one.

Too much medication from a fentanyl patch also could be absorbed if a patch is damaged or broken. The effects may also be exaggerated if a person wearing a patch drinks alcohol, or takes other medicines that depress brain function. "As part of its pain-relieving effect, fentanyl also causes brain depression as seen by some sleepiness and sedation," Stanski says. "This can add to the effects of other drugs like sedatives and tranquilizers."

Fentanyl also should not be used with certain HIV drugs and antifungal medicines. "The HIV drugs slow the metabolism or breakdown of fentanyl in the body and can create an overdose situation," Stanski says. Patients should make sure their doctors know about all the medicines they are taking, including prescription and non-prescription medicines, vitamins, and

of children. According to Duragesic's labeling, patches should be disposed of by folding the adhesive side of the patch together so that it sticks to itself. The patch should then be flushed down the toilet immediately upon removal.

Addiction and Abuse

Fentanyl is a Schedule II controlled substance, the highest level of control for drugs with a recognized medical use. It comes under the jurisdiction of the Drug Enforcement Administration.

There have been reports of people extracting fentanyl from the patches and abusing the drug. Uncontrolled delivery of this potent drug is very dangerous and raises the risk of overdose. The New York State Department of Health has investigated incidents in which fentanyl patches have been stolen from hospital ward stocks or have been removed from the skin of patients. Stanski says, "This risk of abuse, fraud, and crime is a fact for all opiates."

mental problems, or who have been addicted to other medicines, street drugs, or alcohol. According to Janssen, concerns about addiction and abuse shouldn't interfere with the management of chronic, long-term pain. The manufacturer encourages physicians to screen and monitor patients to reduce the risk of problems.

To report adverse events related to fentanyl patch products, contact the FDA's MedWatch program at <https://www.accessdata.fda.gov/scripts/medwatch/> or call (800) FDA-1088. Fax reports to (800) FDA-0178. ■

For More Information

www.fda.gov/cder/drug/InfoSheets/patient/fentanylIPIS.htm

Taking Care of Your Feet

By Michelle Meadows

The human foot has 26 bones, 33 joints, and more than 100 tendons, muscles, and ligaments. With such a complex structure, a lot can go wrong. While some foot problems are inherited, many occur because of years of wear and tear.

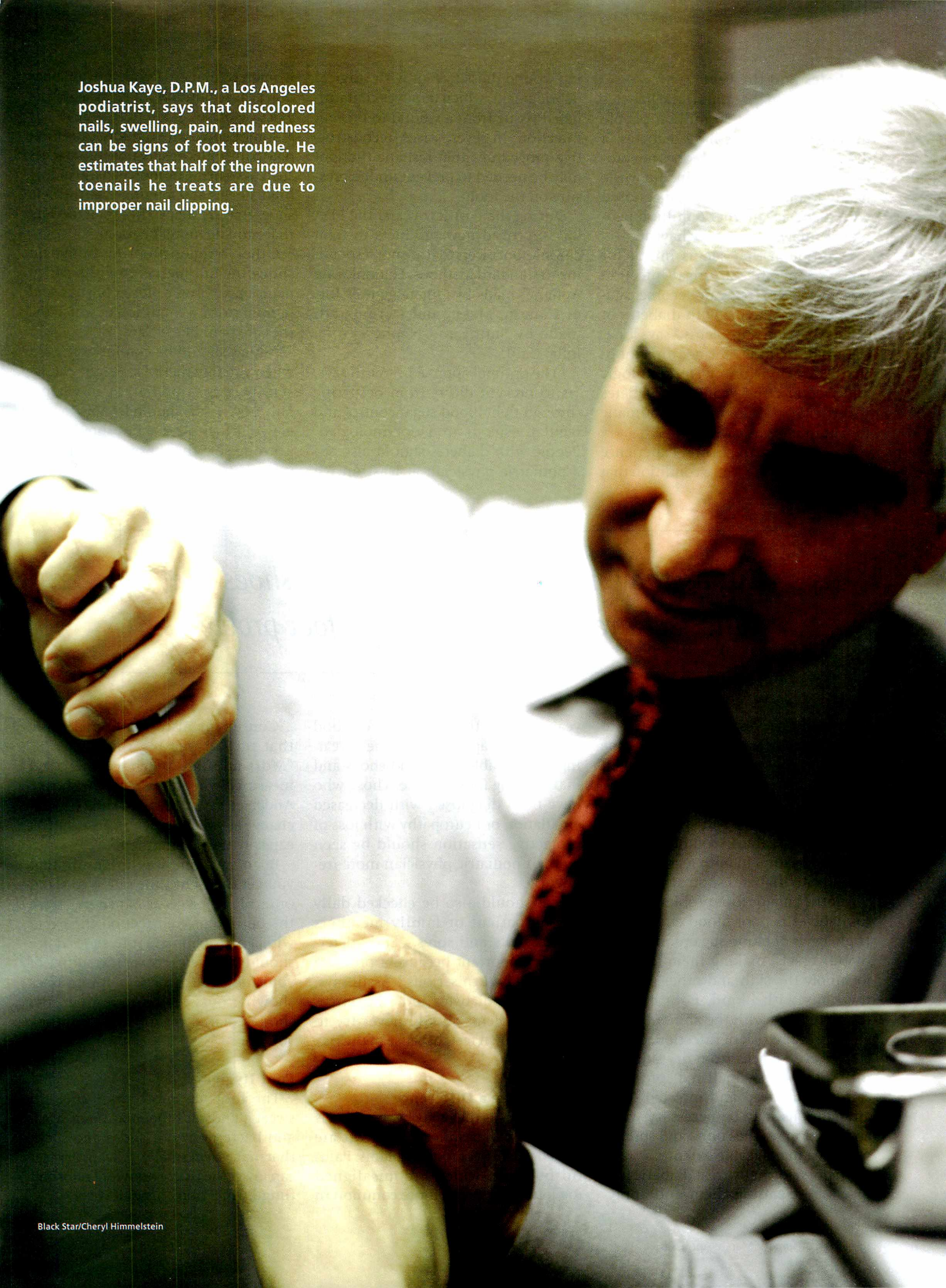
Signs of foot trouble include pain, excessively dry skin, thickened or discolored nails, swelling, redness, and unusual sensations. "Consumers should know that these symptoms are not normal," says Joshua Kaye, D.P.M., a podiatrist in Los Angeles. "Whatever the problem is, don't bury it in your shoe and hope it will go away."

Pain in the feet can trigger pain in the legs, hips, and back. Some foot problems can even signal a larger disease, which is why the American Podiatric Medical Association (APMA) suggests that people take their socks off when they go to their primary care physician for a regular checkup. In a recent APMA survey of more than 600 people, 73 percent said their feet were not routinely inspected at doctor visits.

Toenails that are rounded inward instead of outward could signal iron deficiency anemia. Kidney disease, heart disease, high blood pressure, and circulatory problems can cause the feet to swell. Tingling or numbness in the feet and slow-healing wounds could be signs of diabetes or other serious diseases, according to the APMA. Chronic stiffness in the toes could be a sign of arthritis.

"Changes in the structural appearance of the foot can also be signs of abnormalities such as tendon rupture, rheumatoid or osteoarthritis, or neuropathic disease," says Barbara Buch, M.D., acting clinical deputy director of the Food and Drug Administration's Division of General, Neurological and Restorative Devices.

Joshua Kaye, D.P.M., a Los Angeles podiatrist, says that discolored nails, swelling, pain, and redness can be signs of foot trouble. He estimates that half of the ingrown toenails he treats are due to improper nail clipping.



Diabetes and the Feet

According to the American Diabetes Association, about 20 million people in the United States have diabetes, a disease in which the body does not produce or properly use insulin. But while nearly 15 million have been diagnosed with diabetes, another 6 million people are unaware that they have it.

"A problem that seems minor for many people, like a fungal infection or sores on the feet, can become catastrophic in someone with diabetes or other circulatory problems," says Jonathan Wilkin, M.D., former director of the FDA's Division of Dermatologic and Dental Drug Products. Diabetes is the leading cause of non-traumatic foot amputations each year.

People with diabetes may experience neuropathy in the feet, a condition that

ing wound dressings, or with surgical debridement, which removes contaminated tissue from a wound to prevent infection. In severe cases, reconstructive procedures that reshape the foot may be needed to prevent undue pressure on the foot.

During the past few years, the FDA has approved new products to treat chronic foot ulcers that are not responding to standard methods. Examples are Apligraf, made by Organogenesis Inc. of Canton, Mass., and Dermagraft, made by Smith and Nephew in La Jolla, Calif.

"The optimal approach," Assili says, "is to prevent ulcers from occurring through tight blood sugar control and regular visits to an endocrinologist." People with diabetes should also see a podiatric physician at least once a

women than men. Poorly fitting shoes don't cause bunions, but can aggravate existing ones.

Some people with bunions can eliminate pain with conservative approaches such as wearing bunion pads, avoiding high heels, and buying comfortable shoes that are shaped like their feet and that provide more toe room.

Other common problems from tight shoes include nerve growths called neuromas, corns, calluses, blisters, and hammertoes, a condition in which the toes are bent like a claw.

"Shoes should be comfortable right when you buy them," says Jane Andersen, D.P.M., a podiatrist in Chapel Hill, N.C. "You should be able to wiggle your toes. And shoes should have a strong sole that flexes at the ball of your foot."

As stylish as they may be, high heels and shoes that squeeze the feet are linked to a host of foot problems.

affects the nerves and the ability to feel pain and heat or cold. "Someone without sensation in the feet can literally step on a nail and not know it," says Amir Assili, D.P.M., a podiatrist in Gaithersburg, Md. Assili says a 28-year-old man who came in complaining of a loss of sensation in both feet was diagnosed with diabetes soon after.

Another major foot problem linked to diabetes is poor blood circulation. High levels of blood sugar damage the blood vessels, making them less able to supply the skin and other parts of the body with blood. Poor circulation interferes with the ability to heal and raises the risk of infection. Minor cuts or even cracks from dry skin can turn into ulcers, small red sores that can become deep and infected. Foot amputations may be necessary when an infection reaches bone and spreads beyond a manageable extent.

Doctors normally treat diabetic foot ulcers by cleaning them and apply-

ing year and practice the basics of good foot care that apply to everyone—wearing comfortable socks and shoes and maintaining foot hygiene. Those who have been diagnosed with decreased circulation or neuropathy with loss of protective sensation should be seen by their podiatric physician more frequently.

Feet should also be checked daily by the patient or family members for any cuts and sores. "Early detection is important because a problem can quickly turn serious," Assili says. People with diabetes and other circulatory problems should never try to treat their own feet, because of the risk of infection.

Shoes Make a Difference

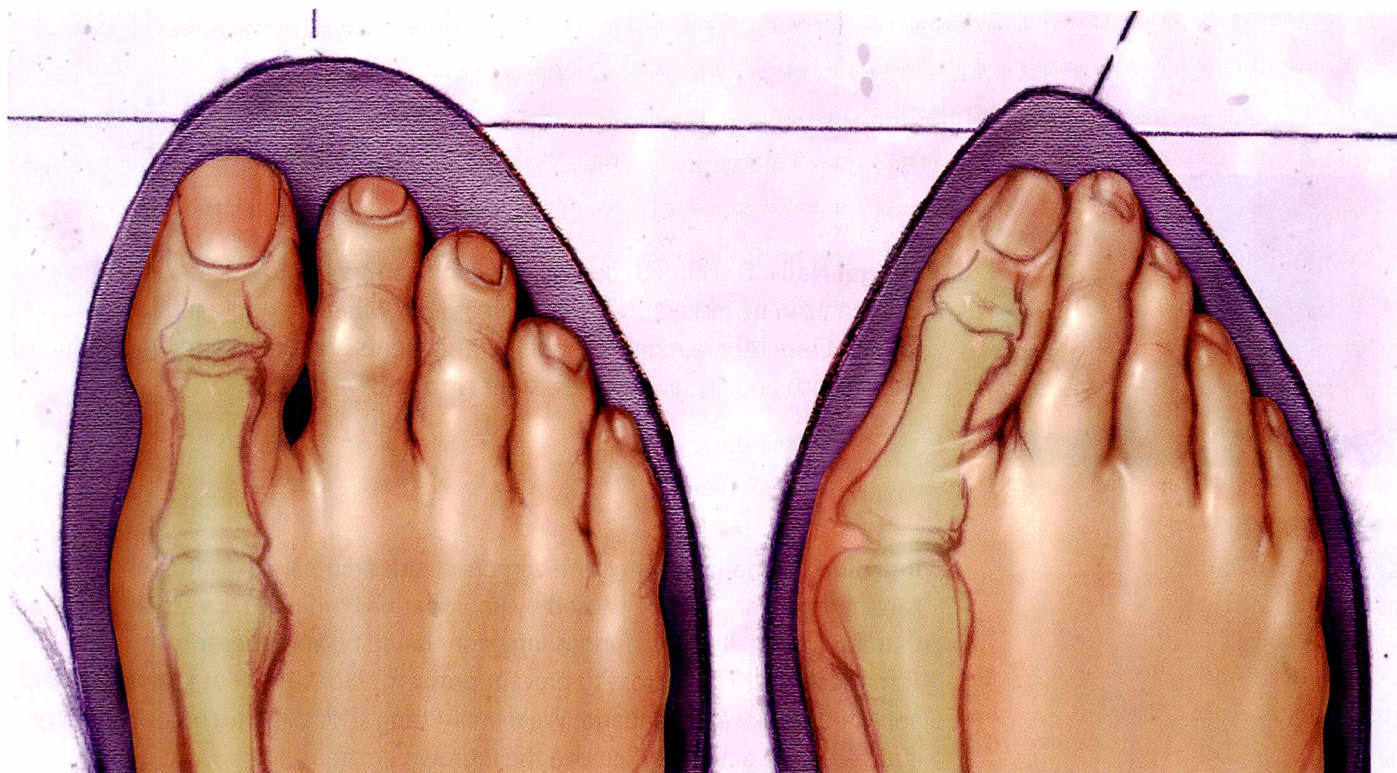
As stylish as they may be, high heels and shoes that squeeze the feet are linked to a host of foot problems. Painful bunions, which are misaligned toe joints, are much more common in

Consumers also should make sure that they're wearing the right size. "Most adults don't have their feet measured when they buy new shoes," Andersen says, "but your shoe size can change as you get older because the feet can spread and lengthen."

Buch says one way to ensure that you get the right shoe size is to stand on a blank piece of paper and trace the outline of your feet on the paper with a pen at home. "Your shoe choice should completely cover the outline of your foot," Buch says, "with no lines showing outside the shoe when the shoe is placed on top of the outline you traced."

Foot Hygiene

The foot has more than 250,000 sweat glands. It's the mixture of sweat and bacteria in our shoes and socks that makes feet smelly. "Clean, dry feet can lower the risk of both foot odor and fungus infections," says Kaye.



Phototake

An illustration showing a foot with the big toe joints properly aligned inside a shoe with flat heels (left) and a foot with the big toe joint deformed inside a high-heeled shoe.

Feet should be washed every day with soap and lukewarm water, especially between the toes, and then dried completely with a soft towel. Any mild soap or antibacterial hand soap works fine.

"People spend a lot of time shampooing and conditioning their hair and applying soaps and lotions to their body, but then probably don't spend 10 seconds washing their feet," Kaye says. "Washing the feet with a wash cloth or similarly abrasive product is important because it helps remove the dead skin, bacteria, and fungus." For patients who can't reach their feet during a shower because of obesity, arthritis, or instability, Kaye recommends using a long-handle brush like a shower back brush.

People who want to soak their feet should use warm, soapy water, Kaye says. "Soaking feet in Epsom salt can cause excessive drying of skin," he says. "This is an important consideration for diabetics or with those who have existing dry or fragile skin. Consider soaking feet in warm water with a small amount of liquid dishwashing

solution that has skin softeners. There is no benefit in soaking feet in Epsom salt compared to regular table salt."

Some people tell Kaye they soaked their feet in very hot water because they were trying to kill bacteria. He says, "Unfortunately, that type of home treatment often results in skin burns. If someone is diabetic or has poor circulation, hot water bottles or heating pads also shouldn't be used on the feet."

Applying moisturizing lotion on the feet after bathing can alleviate dry skin. "During dry winter months, apply a small amount of lotion a few times per day," Kaye says. "Inexpensive generic creams are usually equally effective as expensive brand-name products."

Kaye estimates that half of the ingrown toenails he treats are due to improper nail clipping. "Toenails should be trimmed straight across and not too short," he says. "Many people incorrectly cut the corners, leaving a small point of nail that then grows into the skin or they accidentally cut the skin."

People who pamper themselves with a salon pedicure also need to make sure

that proper cutting and safety measures are followed. In the last few years, there have been reports of infections linked to nail salon whirlpool footbaths that hadn't been properly cleaned or disinfected.

Andersen suggests that people check to see that salons and their employees are licensed. "You could ask how they clean their tubs and instruments and how often," she says. "Some people bring their own instruments." People with diabetes should exercise caution when having salon treatments, and may be advised by their physicians to avoid treatments by anyone other than a trained podiatric or medical specialist.

Exercise Right

Wearing inadequate and worn-out shoes is a common mistake for athletes, says James Losito, D.P.M., team podiatrist for the Miami Heat basketball team and professor of podiatric biomechanics at Barry University in Miami Shores, Fla.

"Running shoes should be discarded after 200 miles to 400 miles of use

Common Foot Ailments



Fungal Nails: Discolored toenails. Infection can spread to other nails. Fungal infection can be picked up in damp areas like swimming pools and locker rooms. Clean, dry feet help prevent it. Treatments are topical and oral antifungal medications and, in severe cases, surgery to remove the nail.



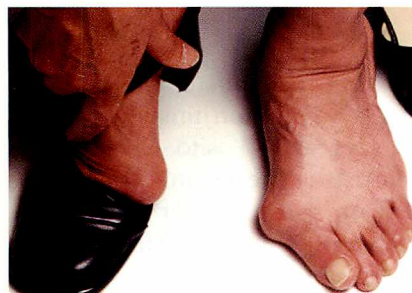
Ingrown Toenails: Nails whose corners or sides dig painfully into skin, often causing infection. Can be caused by improper nail trimming, pressure from shoes that are too small, injury, fungus infection, heredity, and poor foot structure. Trim toenails straight across to prevent problems. Soak the foot in soapy water, apply antiseptic, and bandage. Wear well-fitting shoes. If a toenail is painful or infected, the doctor may remove the ingrown portion.



Athlete's Foot: A skin disease that can spread from the feet to other parts of the body and is caused by fungus. This disease doesn't typically spread from person to person. Signs are dry, scaly skin; itching; inflammation; and blisters. Athlete's foot can be prevented by daily washing with soap and water, drying feet, changing sweaty shoes and hose and socks regularly, and wearing shoes or sandals in public environments like the locker room or pool.



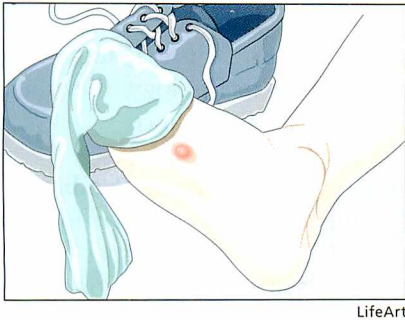
Warts: Caused by a virus that enters the skin through small cuts and infects the skin. Children tend to be more susceptible than adults. Most warts are harmless, though they can be unsightly and painful. They can be caused by walking barefoot on dirty ground. Treatments include over-the-counter and prescription topical acids, and laser or surgical removal.



Bunions: Misaligned big toe joints that can become swollen and tender. The first joint of the big toe slants outward, angling the big toe toward other toes. Bunions tend to run in families, but can be aggravated by tight shoes. Conservative treatment includes padding, choosing shoes with wide toe box, and orthotic devices. Pain medicines and surgery to relieve pain may be needed in severe cases, but should not be done for cosmetic purposes.



Hammertoes: The toes are bent like a claw. This condition occurs most frequently with the second toe because of bunion slanting. It can be caused by muscle imbalance or can be made worse by tight shoes or tight socks. Pain medicine or orthotic devices may help. Surgery may be needed to realign toes.



LifeArt

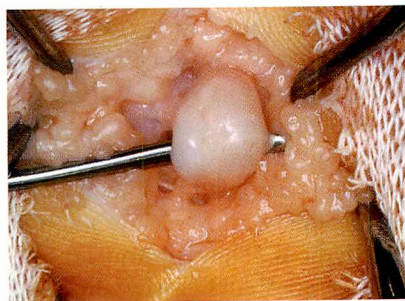
Blisters: Caused by skin friction, especially from poorly fitting shoes. A band-aid should be worn until the blister heals, and socks should be worn with shoes. If the blister breaks, it should be washed, and an antiseptic and sterile bandage applied. It shouldn't be popped. It should be drained only by a professional.



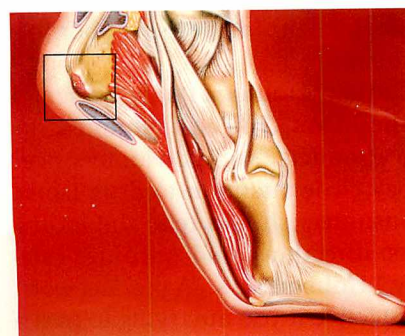
Corns and Calluses: Protective layers of dead skin cells. Calluses appear on the soles of the feet, and corns appear on top of toes. They are caused by friction from skin rubbing and shoes. Pain may be relieved by moleskin or padding. They should never be cut with an instrument.



Plantar Fasciitis: Stretching or tearing of the plantar fascia, which runs along the bottom of the foot and supports the arch of the foot. Heel pads, pain medicines, or cortisone injections may help. Other conservative care includes splinting, stretching, avoiding walking barefoot, and physical therapy. Shock wave treatments use shock wave energy to relieve inflammation and are an alternative to surgery.



Neuroma: Enlarged benign growths of nerves, most commonly between the third and fourth toes. This nerve condition is caused by bones rubbing against and irritating the nerves. It is also caused by abnormal bone structure or pressure from poorly fitting shoes. It may cause pain, burning, or numbness between toes and in the ball of the foot. Treatment includes padding, taping, orthotic devices, and cortisone injections. Sometimes, surgical removal is required.



Heel Spurs: Calcium growths on the underside of the foot bones often associated with plantar fasciitis. Pain may occur if there is inflammation. Treatments range from exercise and custom-made orthotics to anti-inflammatory medication. ■

and they should fit correctly," Losito says. "There should be a thumb-width of length between the longest toe and the end of a shoe. Failure to wear the correct shoe size can result in runner's toe, calluses, ingrown nails, fungal nail infections, and hammertoe deformities."

People also should purchase the right shoe for the sport. "Many injuries occur because someone is wearing a running shoe while playing basketball," Losito says.

Another common cause of athletic injuries is doing too much too soon. "Both overuse training habits and worn-out shoes could result in stress fractures, heel pain or heel spur (plantar fasciitis) or shin splints," he says.

warrants medical attention. Contrary to popular belief, it's possible to walk, even if a foot bone is broken.

Orthotic Devices

Orthotic devices are intended to make the feet more comfortable, minimize stress on the foot, or improve an abnormal or irregular walking pattern. An orthotic device could be a conservative approach to a foot problem, a preventive measure to avoid problems, or a useful support after foot surgery.

According to the American Academy of Orthopaedic Surgeons, orthotic devices commonly used include union shield pads, arch pads for people with a flat foot, and heel inserts for people with plantar fasciitis. These devices

be adequately packaged and properly labeled, and have establishment registration and device-listing forms on file with the FDA. Legally marketed Class I devices are subject to the least regulatory control because they present minimal potential for harm to the user. But when orthotic devices make a new health claim or a claim for certain treatments, or use a fundamentally different technology, they must go through FDA clearance.

Non-Prescription Drug Products

The types of OTC products for foot health include pain medicines such as nonsteroidal anti-inflammatory drugs and products that treat athlete's foot, corns, calluses, blisters, and warts.

Walking or jumping on hard surfaces and failing to stretch and do warm-ups may also cause shin splints, plantar fasciitis, and heel spurs.

"It is important to start out slowly and increase distance, duration, and pace gradually. For runners, I recommend no more than a 10 percent increase per week."

Walking or jumping on hard surfaces and failing to stretch and do warm-ups may also cause shin splints, plantar fasciitis, and heel spurs. Losito says, "There is no solid evidence to confirm that stretching actually decreases the likelihood of injuries, but it makes sense to maintain flexibility through gentle stretching, especially following exercise."

According to the American Academy of Podiatric Sports Medicine, the most common pain associated with jogging is runner's knee, which can be caused by rolling in or down on the foot. With aerobics, rising on the toes can cause an inflamed Achilles tendon. Stress fractures can be caused by running and other repetitive strain. Sharp pain, bruising, or swelling after a foot injury

are sold over-the-counter (OTC) at drugstores and sporting stores. They can be custom made and also sold by podiatrists, physical therapists, or orthotic companies.

Consumers might do well to try a less expensive OTC orthotic device first. "But if the problem doesn't go away after six weeks, you may need to seek a professional consultation and a custom orthotic may be indicated," says Eddy Gosschalk of Southern California Orthotics and Prosthetics. "People who are at risk for developing wounds or who have an unusual foot shape tend to need a custom orthotic." To create a custom orthotic, a plaster cast is taken of your foot and sent to a laboratory.

Most orthotic devices are considered "Class I exempt" by the FDA. This category means they are exempt from pre-market notification requirements. But they still must be manufactured under a quality assurance program, be suitable for intended use,

Depending on the intended use, some OTC foot products, such as lotions for moisturizing the skin, are considered cosmetics and not drugs. There are medicated powders and creams to treat athlete's foot. For corns and calluses, there are nonmedicated pads to improve comfort when walking, as well as medicated pads and patches that work to get rid of dead skin. Similar products are used to shrink warts. These products are typically made of salicylic acid. They should be used with care so that healthy skin isn't harmed, and they should never be used by people with diabetes or poor foot circulation.

Matthew Holman, Ph.D., a scientist in the FDA's Office of Nonprescription Products, says consumers need to pay close attention to drug labels. "Consumers should read the indications, directions, and warnings carefully," Holman says. "A product won't be effective if you are trying to treat a



Joshua Kaye, D.P.M.

Los Angeles podiatrist Joshua Kaye, D.P.M., performs bunion surgery.

condition that's not in the label. If it says to only use the product on intact skin with no open sores, that's important. If a product isn't working or the condition becomes worse, you need to seek a doctor's advice." People with heart disease, diabetes, and circulation problems should never self-treat because of the risk of infection.

Prescription Drugs

Prescription drugs for treating the feet include pain medicine, antibiotics for infections, and antifungal medicine. For instance, an ingrown toenail may require antibiotic or antifungal treatment if it becomes infected. For bunions and hammertoes, a cortisone injection may be given to relieve inflammation and pain.

Fungal nails make toenails thick, brittle, and discolored to white, yellow, or brown. The fungus grows deep in the nail bed, and it won't go away on its own. It also can spread to other toenails. "Discolored nails aren't always

from fungus," says Andersen. "They could also be from trauma due to exercise or psoriasis, so we take a fungal culture to make a diagnosis."

Penlac (ciclopirox), made by Dermik Laboratories of Berwyn, Pa., is an example of a topical antifungal. It is generally used daily for several months for mild to moderate nail fungus. Side effects include irritation and redness around the nails. Oral medications for fungal infections, including fungal nails and athlete's foot, are Lamisil (terbinafine) made by Novartis Pharmaceuticals of East Hanover, N.J., and Sporanox (itraconazole), made by Janssen Pharmaceuticals of Titusville, N.J. These medicines travel through the bloodstream to attack the fungus. The tablets are taken daily for about 12 weeks. It takes about nine months for a healthy nail to grow in.

The most commonly reported side effects of the oral antifungals are headaches and stomachaches. In 2001, the FDA put out a public health advi-

sory about both drugs and announced labeling changes. Both drugs have been associated with serious liver problems resulting in liver failure and death in rare cases. The FDA and the maker of Sporanox also warned against using Sporanox for those who have a heart condition, because of safety concerns.

Patients using these drugs should immediately report symptoms of persistent nausea, anorexia, fatigue, or vomiting, upper right abdominal pain or jaundice, dark urine, or pale stools. A simple blood test is used to check liver function during treatment.

Foot Surgery and Other Procedures

Common types of foot surgery include surgery to correct bunions, surgery for fungal nails when medications don't work, and surgery to reduce arthritis pain. For people who have chronic ingrown toenails, a procedure called matrixectomy may be used to prevent recurring problems. Andersen says, "We

Shock Wave Therapy

The most common cause of heel and arch pain is painful stretching or tearing of the plantar fascia, which runs along the bottom of the foot and supports the arch of the foot. Extracorporeal shock wave treatment is an outpatient procedure in which a medical device uses shock waves



SanuWave

to relieve chronic heel pain. A dome filled with water is placed against the heel so shock waves pass through. The shock waves increase blood flow to trigger the healing process so that inflammation and pain subside.

FDA-approved devices for this procedure are the Ossa-tron, made by SanuWave Inc. of Marietta, Ga.; The Epos

Ultra, made by Dornier MedTech, Kennesaw, Ga.; and the Orsabone Pain Relief System, made by Orthometrix Inc., White Plains, N.Y. People who have bleeding disorders, who are taking blood-thinning medication, or who are pregnant, should not undergo shock wave therapy. Complications can include mild neurological symptoms and tears in the tissue in the bottom of the foot. ■

the nonsurgical options with their doctor, and the benefits and risks of surgery. It is also important to consider the doctor's experience and results with the procedure.

The American Orthopaedic Foot & Ankle Society (AOFAS) has released statements warning about trends in cosmetic surgery to improve the appearance of the foot. "Some women are getting surgeries to shorten toes and narrow their feet so they can fit into fashionable shoes," says Sharon Dreeben, M.D., chairwoman of the AOFAS Public Education Committee and an orthopedic surgeon in La Jolla, Calif.

"A woman recently called asking if I would inject collagen into her heel, and she will probably go doctor shopping to find someone who will do it," Dreeben says. "Some people want more padding to have cushion for high heels. But cosmetic foot surgery can result in chronic pain, infection, and nerve injury."

Dreeben has had to fix problems from cosmetic foot surgery that went wrong. "One woman had bunion surgery even though she hadn't been experiencing pain," she says. "She ended up with more problems, including nerve pain and difficulty walking."

The AOFAS defines cosmetic foot surgery as surgery that is aimed at only improving appearance. Dreeben says, "Foot surgery should only be used if the goal is to provide pain relief, improve function, or enhance quality of life during normal activities of daily living."

"I tell people: One difference between cosmetic surgery on the face and cosmetic surgery on the feet is that you don't walk around on your face. When you readjust one piece in the foot, it can affect everything." ■

For More Information

American Podiatric Medical Association
www.apma.org
(800) FOOTCARE

American Orthopaedic Foot and Ankle Society
www.aofas.org
(206) 223-1120

numb the toe and remove the smallest amount of the nail on the side, usually about one-eighth of an inch, and then use a chemical to kill the root or remove the root of the nail surgically."

Sometimes, bunions can be treated without surgery, but when bunions limit or affect one's daily activities, bunion surgery may be appropriate. Pain is the big factor here. Kaye says, "Bunion surgery may also be warranted if there is chronic inflammation and the person gets no relief from nonsteroidal anti-inflammatory drugs and other conservative treatments."

Kaye says there are two main components to bunion problems. "One problem is the pain associated with shoe pressure against the bony enlargement," he says. "The second condition is a stiff toe joint that causes internal joint pain during movement of the big toe. Both or either of these problems can occur."

Advanced surgical techniques have improved outcomes for bunion surgery. The type of surgery needed depends on the patient's age, activity level, and degree of deformity. Kaye says he doesn't only remove the "bump of bone," which won't usually produce

lasting results. "We realign the bone and use a surgical screw for stable bone alignment," he says. Recovery time usually takes about four weeks.

"The precision in which the bone is cut, shaped, and realigned is critical," Kaye says. Though consumers may see lasers publicized to treat bunions, lasers can't cut bone or correct bunions, he says. Lasers are not cleared by the FDA for these indications.

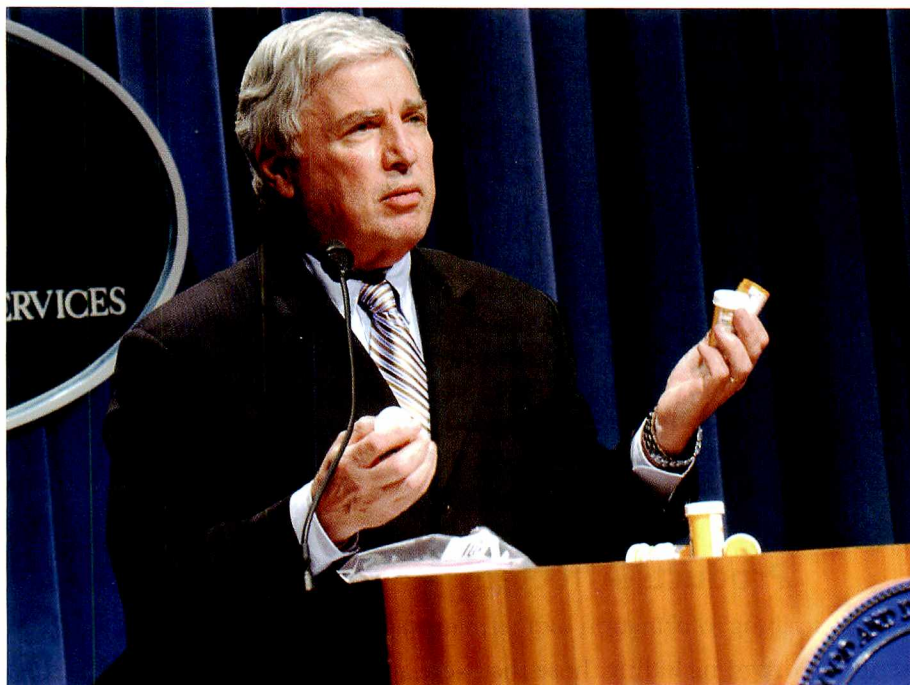
According to the American College of Foot and Ankle Surgeons, there have also been advances in less invasive foot and ankle surgery. Newer surgical plates and screws let surgeons repair fractures with less trauma. Smaller incisions mean less bleeding and tissue damage.

In ankle arthroscopy, surgeons look at the ankle joint with a fiber optic camera system. This technique has been applied to knee surgery for several years, but now it's being used for bones and joints in the foot and ankle. This type of surgery can relieve inflammation from arthritis and ligament damage, with reduced recovery time as compared to open surgical procedures.

Before considering any surgery, people should always explore and discuss

The FDA Announces New Prescription Drug Information Format

In January 2006, the Food and Drug Administration unveiled a major revision to the format of prescription drug information, commonly called the package insert. To manage the risks of medication use and to reduce medical errors, the newly designed package insert will provide the most up-to-date information in an easy-to-read format that draws physician and patient attention to the most important pieces of drug information before a product is prescribed. The new format also will make prescription information more accessible for use with electronic prescribing tools and other electronic information resources.



Acting Commissioner of Food and Drugs Andrew C. von Eschenbach, M.D., says the new prescription drug label provides important information in a format that is better understood and more accessible. The FDA implemented the change to make the labels more useful for doctors and their patients.

Electronic Drug Labels

In November 2005, the FDA began requiring drug manufacturers to submit prescription drug label information to the agency in a new electronic format. This format will allow health care professionals and the public to more easily access the product information found in the FDA-approved package inserts for all approved medicines in the United States.

Under the new regulations, drug manufacturers are required to submit prescribing and product information in a structured product labeling (SPL) format that gives accurate, up-to-date drug information using standardized medical terminology in a readable, accessible format.

With embedded computer tags, information in the SPL format can be electronically managed, allowing a user to

search for specific information. These tags can instruct computers to read specific sections of a drug label including product names, indications, dosage and administration, warnings, description of drug product, active and inactive ingredients, and how the drug is supplied.

Having the labels submitted to the FDA in SPL will improve the drug labeling review process, so that the agency can provide immediate access to the most recent information about medications to doctors and patients. Physicians will be able to quickly search and access the specific information they need before prescribing a treatment, resulting in fewer prescribing errors and better-informed decisions. ■

"Providing healthcare professionals and patients with clear and concise information about prescriptions will help ensure safe and optimal use of drugs, which translates into better health outcomes for patients and more efficient delivery of healthcare," says Health and Human Services Secretary Mike Leavitt. "By improving the package insert to make it more useful for healthcare providers in their day-to-day clinical practice, we are making it easier for them to explain the benefits and risks of medications for their patients."

Each year, about 300,000 preventable adverse events occur in hospitals in this country, many as a result of confusing medical information. Research shows that prioritizing the warning information has a greater impact on reducing such events. Therefore, the new prescription label provides the most important information about a prescription product in a format that is better-understood, more easily accessible, and more memorable for physicians. By making these changes, the FDA is seeking to simplify the information on prescription drug labels, making the labels more useful for physicians and their patients.

"Americans are over-

whelmed with the complexity of health information. We have hit a point of information overload and the public health message is being diluted," says Surgeon General Richard H. Carmona, M.D. "This is of great concern when it comes to making sure a patient knows how to use prescription drugs safely and effectively. This problem is compounded by prescription medication information that reads more like legal disclaimers than useful or actionable health information."

Revised for the first time in more than 25 years, the new format requires that the prescription information for new and recently approved products meet specific graphical requirements and includes the reorganization of critical information so physicians can find it quickly. Some of the most significant changes include:

- a new section called *Highlights* to provide immediate access to the most

important prescribing information about benefits and risks

- a *Table of Contents* for easy reference to detailed safety and efficacy information
- the date of initial product approval, making it easier to determine how long a product has been on the market
- a toll-free number and Internet reporting information for suspected adverse events, to encourage more widespread reporting of suspected side effects.

"The new label design makes it easier for doctors to get access to important information about drug safety and benefits, and this in turn will help them have more meaningful discussions with their patients," says Acting Commissioner of Food and Drugs Andrew von Eschenbach, M.D. "This redesigned label is a big step in our commitment to giving health professionals the tools and information they need to optimize their clinical practice and choose among a growing number of effective treatments to make more personalized prescribing decisions for their patients."

The most notable change is the addition of a summary outlining the most important information about a product, prominently displayed at the top of the page. Designed to help health

Products Affected

The new prescribing information requirements apply to:

- prescription drugs, including those that were approved on or after the effective date of the final rule
- drugs that had been approved in the five years before the effective date of the final rule
- older drugs for which there is a major change in the prescribing information, for example, approval of a new use. ■

care professionals find the information they need quickly, *Highlights* will typically be half a page in length and will provide a concise summary of information about specific areas including: *Boxed Warning*, *Indications and Usage*, and *Dosage and Administration*. This section also will refer the health care professional to the appropriate part of the *Full Prescribing Information*. In addition, drug makers will be required to include a list of all substantive recent changes made within the year, to ensure that health care professionals have immediate access to the most up-to-date information about the product before prescribing it.

Over the past 10 years, the prescrib-

ing information for newly approved products has become more complex, and specific information is often difficult to locate. Physicians will now be able to find critical information more quickly, through a new *Table of Contents* that refers readers to detailed information located in the label. The *Full Prescribing Information* is reorganized to give greater prominence to the most important and most commonly referenced information. As a result of feedback from two national physician surveys, the *Indications and Usage* and the *Dosage and Administration* sections are moved to the beginning of the *Full Prescribing Information*.

about the potential risks involved in taking a specific treatment and steps for managing those risks. If the FDA has approved patient information for a prescription drug, it will be printed at the end of the label immediately after the *Patient Counseling Information* section or will accompany the label so it can be easily shared.

"In the last month, we have announced important steps toward creating an electronic environment for drug safety and effectiveness information that can provide patients and healthcare professionals with critical information at the point of care," says von Eschenbach. This revised prescription information format, in combination with

nlm.nih.gov. In the future, this new information will also be provided through a Web site called facts@fda, a comprehensive Internet resource designed to give one-stop access to information about all FDA-regulated products.

In December 2000, before issuing the proposed rule, the agency evaluated extensive information it received on the usefulness of the present prescription drug labeling for health care professionals to determine how content and format could be improved. The agency used feedback from focus groups, national physician surveys, a public meeting, and written comments to design the new prescription infor-

Over the past 10 years, the prescribing information for newly approved products has become more complex, and specific information is often difficult to locate.

The addition of a new *Patient Counseling Information* section places greater emphasis on the importance of communication between health care professionals and patients. This new section is designed to help doctors advise their patients about important uses and limitations of medications. It also will serve as a guide for discussions

new requirements for electronic labels and requirements for bar codes on drugs, will dramatically improve the way health care professionals and consumers obtain information about prescription drugs, he says.

The new prescription information format will be integrated into the FDA's other e-Health initiatives and standards-setting efforts through a variety of ongoing initiatives at the agency. As prescription information is updated in this new format, it will be used to provide medication information for *DailyMed*, a new interagency online health information clearinghouse that will provide the most up-to-date medication information free to consumers, health care professionals, and health care information providers.

The *DailyMed* is now making up-to-date information about FDA-regulated products widely available on the Internet free of charge. This information can be accessed through the National Library of Medicine at <http://dailymed>.

mation format. The FDA determined the most common practices for using prescription drug labeling, as well as information considered to be the most important, and then developed the new format based on this information. The new drug labeling requirements will be phased in gradually and initially will apply to newly and recently approved prescription drugs and to drugs that receive approval for new uses. The agency is encouraging drug makers to consider complying with the new labeling requirements earlier on a voluntary basis. All drugs approved within the past five years are included, and they will gradually be converted to the new prescribing information format. ■

For More Information

The FDA's Center for Drug Evaluation and Research
www.fda.gov/cder/regulatory/physLabel/default.htm

First Inhaled Insulin Product Approved

There is a new, potential alternative for many of the more than 5 million Americans who take insulin injections, with the Food and Drug Administration's approval of the first-ever inhaled insulin. Exubera, an inhaled powder form of recombinant human insulin (rDNA) for the treatment of adult patients with type 1 and type 2 diabetes, is the first new insulin delivery option introduced since the discovery of insulin in the 1920s.

The safety and efficacy of Exubera have been studied in about 2,500 adult patients with type 1 and type 2 diabetes.

"Until today, patients with diabetes who need insulin to manage their disease had only one way to treat their condition," Steven Galson, M.D., director of the FDA's Center for Drug Evaluation and Research, said after the approval on Jan. 27, 2006. "It is our hope that the availability of inhaled insulin will offer patients more options to better control their blood sugars."

Diabetes is a disease that affects the amount of insulin and sugar in a person's body. Exubera is a human form of insulin and, as such, lowers blood sugar concentrations by allowing the blood sugar to be taken up by cells as a source of fuel. Exubera is a powdered form of insulin that is able to be inhaled into the lungs through the patient's mouth using a specially designed inhaler.

There are two major types of diabetes—type 1 and type 2. People with type 1 diabetes produce virtually no insulin. In type 2, the most common form of the disease, the body does not produce enough insulin or effectively use insulin. If people with diabetes do not properly control their blood sugar levels, serious complications including heart disease, kidney failure, blindness, and nerve damage may develop.

The safety and efficacy of Exubera have been studied in about 2,500 adult patients with type 1 and type 2 diabetes. In clinical studies, Exubera reached peak insulin concentration more quickly than some insulins, called regular insulin, administered by an injection. Peak insulin levels were

achieved in about 50 minutes (range 30 minutes to 90 minutes) with Exubera inhaled insulin compared with 105 minutes (range 60 to 240 minutes) with regular insulin.

In type 1 diabetes, inhaled insulin may be added to longer-acting insulins as a replacement for short-acting insulin taken with meals. In type 2 diabetes, inhaled insulin may be used alone, along with oral medications that control blood sugar, or with longer-acting insulins.

Exubera prescriptions will be accompanied by a Medication Guide containing FDA-approved information written especially for patients. Pharmacists are required to distribute Medication Guides with products that the FDA has determined are important to health, and patient adherence to directions for use is crucial to the product's effectiveness. Patients are advised to read the entire Medication Guide and to talk to their health care provider if they have questions.

Like any insulin product, low blood sugar is a side effect of Exubera, and patients should carefully monitor their blood sugars regularly. Other side effects associated with Exubera therapy seen in clinical trials included cough, shortness of breath, sore throat, and dry mouth.

Exubera is not to be used by those who smoke or by those who have quit smoking within the last six months. Exubera is not recommended for patients who have asthma, bronchitis, or emphysema. Baseline tests for lung function are recommended before beginning treatment and are recommended to be repeated every six months to 12 months thereafter.

While Exubera has been extensively studied for safety, the sponsor has committed to performing long-term studies to confirm the continued safety of Exubera after it is marketed and to examine more thoroughly the issue of the efficacy and safety of Exubera in patients with underlying lung disease.

Exubera is manufactured by New York City-based Pfizer Inc. ■

Exubera, an inhaled form of recombinant human insulin for the treatment of type 1 and type 2 diabetes, provides an alternative for the more than 5 million Americans who inject insulin to control their blood glucose levels.



Managing Migraines

Terri Burchfield, 41, of McLean, Va., says people who don't experience migraines don't understand the debilitating pain and disability caused by the headaches. Burchfield is one of about 30 million Americans who suffer from migraines.



Flying overseas to wine and dine clients may sound like a glamour job, but Terri Burchfield didn't feel very glamorous when her head was throbbing and she was running to the bathroom to throw up. "I was expected to go to dinner with associates and clients," says the 41-year-old McLean, Va., resident and former Wall Street investment banker. "I was in such pain and so nauseous. The last thing I wanted to do was eat and converse for hours with important clients. But I had no choice, I just had to get through it."

Burchfield is one of about 30 million Americans who suffer from migraines. According to the American Council for Headache Education (ACHE), 1 in 4 U.S. households has at least one person who has migraines. And 3 out of 4 people with migraines are female.

Although there is no cure, "today, there are great new medications and a better understanding of migraines," says Lisa Mannix, M.D., neurologist and medical director of Headache Associates in Cincinnati. "You don't have to suffer."

In the past 10 years, the Food and Drug Administration has approved more than 10 new drugs for migraine, and more are under development, says Eric Bastings, M.D., a neurologist in the FDA's Division of Neurology Products. Migraine medications, combined with lifestyle changes and avoiding migraine triggers, can make a tremendous difference to people who have migraines.

More Than a Headache

Migraine is a physical illness, and people who have it are called migraineurs by health care professionals. Although headache is the most recognized symptom of migraine, nausea, vomiting, distorted vision, and sensitivity to light and sound are other common symptoms that accompany the headache. The headache is typically pulsating or throbbing. The pain usually occurs on one side of the head, but it can be on both sides.

Burchfield describes one migraine that landed her in the emergency room: "I was doubled over in pain. The head

pain was so severe, it was emanating throughout my entire body. I've never had pain that even comes close."

A migraine attack, left untreated, can last from several hours to several days, or even longer. Attacks can strike as frequently as several times a week or as rarely as once a year.

According to the ACHE, about 1 in 5 migraineurs has warning symptoms, known as an aura, that occur 15 to 30 minutes before the head pain begins. The aura may consist of flashing or shimmering lights, a graying out of vision, tingling sensations in an arm or leg, or difficulty talking.

Migraineurs without aura may experience vague symptoms before the headache, such as mental fuzziness, mood changes, and fatigue.

Misunderstood Migraines

"Migraines are often unrecognized and are treated as ordinary headaches," says Robert Temple, M.D., director of the FDA's Office of Medical Policy in the Center for Drug Evaluation and Research. Without a proper diagnosis, people with migraine may be treated with simple pain medications instead of the migraine treatments now available, Temple says.

In addition, many health providers may not be aware of the benefits of the newer preventive treatments, says Richard Lipton, M.D., professor and vice chairman of neurology at the Albert Einstein College of Medicine in New York. "Consumer education and physician education are both needed."

There's a lot of misinformation about migraines, and blame is often placed on

the person instead of the disease, says Michael John Coleman, co-founder of Migraine Awareness Group: A National Understanding for Migraineurs (MAGNUM). "Some people are still inappropriately being told 'it's all in your head,' and that they're manifesting this behavior to get out of responsibility at work or to avoid personal or social situations. They're being sent to psychiatrists instead of neurologists or headache specialists."

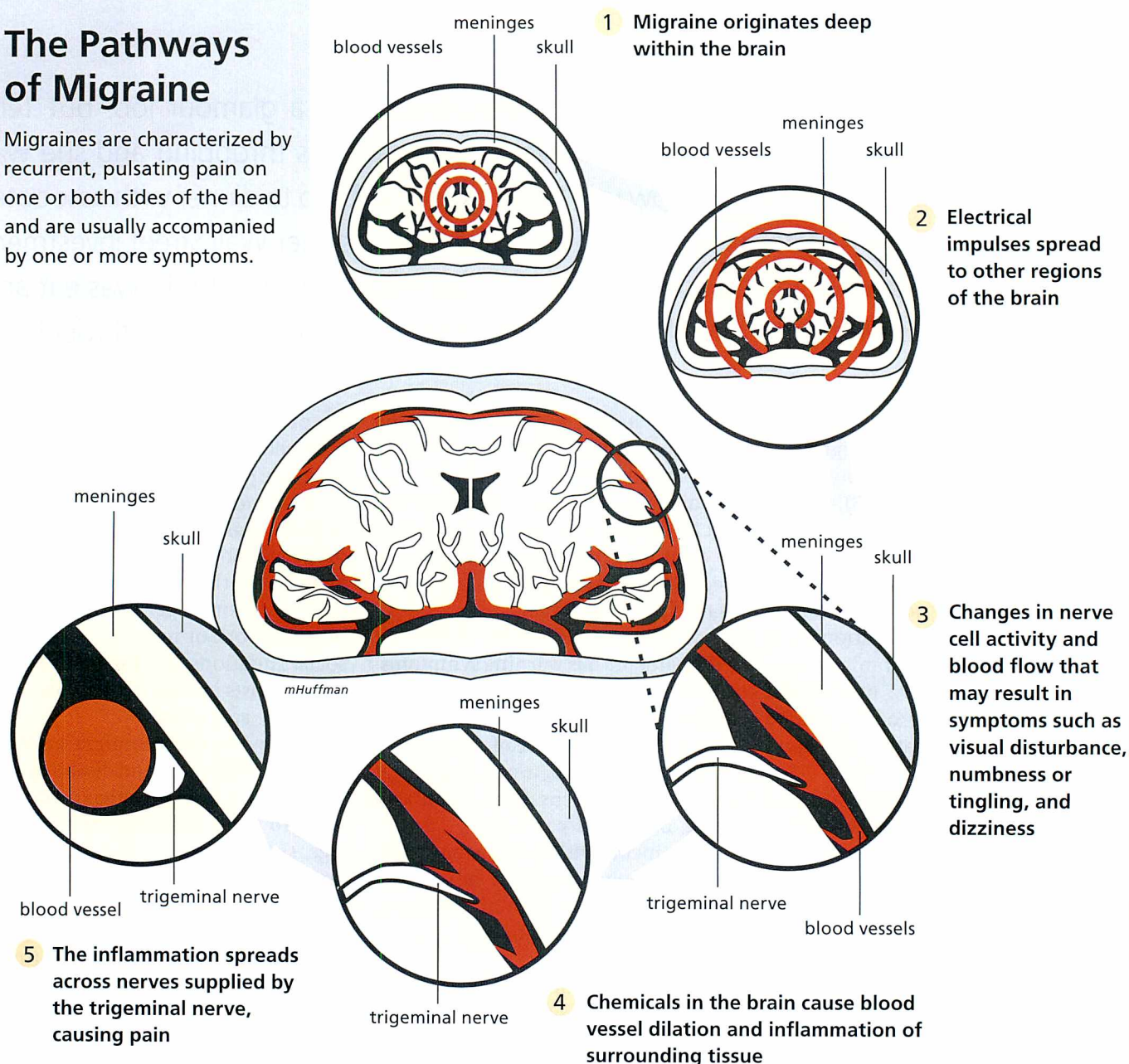
Those who don't get migraines don't understand the pain and disability, says Burchfield. Like many migraineurs, she tried to hide her migraines. In college, she used bathrooms on different floors of the dormitory when she was in pain and felt nauseous, she says. "I didn't want to be seen running out of the same bathroom all the time." Once she graduated and landed a job that required a lot of traveling, the migraines became more frequent and more disruptive. And sometimes, her symptoms were misinterpreted by others. "I'm sure I looked pale and sweaty and I couldn't talk much," she says. "I would run to the bathroom quite a bit to hide the pain and nausea. One of my associates pulled me aside one day and asked if I was bulimic."

Even Burchfield's family didn't understand at first. When visiting her sister and her children out of town, Burchfield's migraines often forced her to retreat to the quiet of a dark room. "My sister said, 'If my kids are too loud, you can stay in a hotel.'"

Today, Burchfield often tells people when she has a migraine, but sometimes reluctantly. The word "migraine"

The Pathways of Migraine

Migraines are characterized by recurrent, pulsating pain on one or both sides of the head and are usually accompanied by one or more symptoms.



© National Headache Foundation

is often misused for any bad headache, she says, "so I never know how someone is going to take it. If I had another condition, such as epilepsy, it would be different. People would believe that, but they don't always believe that you have a migraine that's incapacitating."

Causes and Triggers

Migraine used to be known as a vascular disorder, says Lipton, caused by abnormal blood vessels that affected the brain. It was thought that the blood vessels tightened (constricted), reduc-

ing blood flow to the brain, which produced the aura. Then the vessels opened (dilated), producing pain.

"The newer theory is that migraine is a neurovascular disorder," Lipton says. The perpetrator may be the brain itself—not the blood vessels, he says. Changes in the brain may cause changes in the blood flow. Also contributing to migraines are brain chemicals called neurotransmitters and channels in nerve cells that regulate the movement of minerals across them.

Migraines have a genetic link. The National Headache Foundation (NHF)

estimates that 70 percent to 80 percent of migraine sufferers have a family history of migraine.

While the precise mechanisms of migraine are unclear, experts do know that people with migraines react to a variety of stimuli, called triggers. "The person inherits a predisposition for attacks and in the setting of the appropriate triggers, has an attack," says Lipton.

There's a long list of triggers that can set off an attack, and not everyone has the same triggers. Some triggers, like weather patterns, are uncontrollable,

but others, such as diet and behavior, can be modified. "Not keeping the same eating or sleeping patterns can trigger a migraine," says Seymour Diamond, M.D., co-founder and director of the Diamond Headache Clinic in Chicago. "We see them often on weekends when people oversleep and don't have breakfast."

Certain foods or additives may be migraine triggers. Common triggers, according to the ACHE, are hot dogs and luncheon meats containing nitrates, monosodium glutamate (MSG), chocolate, artificial sweeteners such as aspartame, and a chemical called tyramine found in sour cream, yogurt, aged cheeses, and nuts. Alcohol, particularly red wine, is a trigger for many people. Other triggers are physical exertion, fatigue, bright lights,

front or glass of red wine will trigger a migraine." A combination of triggers is more likely to set off an attack.

Diagnosis and Treatment

There is no test to confirm a diagnosis of migraine. Obtaining a patient's full medical history and doing a physical exam including a thorough neurological evaluation can help a physician diagnose it, says Bastings. In some cases, the physician may recommend magnetic resonance imaging (MRI) of the head or other procedures and tests to rule out a blood clot or brain tumor.

A combination of taking migraine medications and avoiding triggers is the main treatment for managing migraines.

There are two approaches to treating

migraines: taking medication at the beginning of an attack to relieve the symptoms (acute treatment), or taking daily medication to reduce the frequency and severity of attacks (preventive treatment). The FDA has approved drugs for both of these approaches.

Drugs to Relieve Symptoms

Symptom-relieving drugs are most effective when taken at the start of a migraine attack. "If a medicine works, the idea is to take it as early in the attack as possible," says Diamond, "to prevent other symptoms from progressing."

Over-the-counter (OTC) drugs may help relieve mild or moderate symptoms of migraine. The FDA has approved three OTC products specifically for migraine: Excedrin Migraine, Advil Migraine, and Motrin Migraine Pain. Excedrin Migraine is a combination of aspirin, acetaminophen, and caffeine. Both Advil Migraine and

A combination of taking migraine medications and avoiding triggers is the main treatment for managing migraines.

second-hand smoke, some medications and, in women, hormonal irregularities. Anxiety, stress, or relaxation after stress can also be triggers, according to the National Institute of Neurological Disorders and Stroke (NINDS).

Coleman, who has suffered from migraines since he was 6, is concerned about the emphasis some doctors place on stress as a migraine trigger, particularly those who fault the patient for not handling stress well. "It's a myth that the inability to handle stress is the reason people get migraines," he says. "The most stressful thing about migraine is the disease itself and its impact on a person's quality of life."

Burchfield says her migraines are not stress-related, adding that she's pulled all-nighters to do papers or projects, with no migraine. Red wine and MSG are triggers for her. So are weather and altitude changes, making it difficult to travel. "But it's not always predictable," she says. "Not every weather

migraine with drugs: taking medication at the beginning of an attack to relieve the symptoms (acute treatment), or taking daily medication to reduce the frequency and severity of attacks (preventive treatment). The FDA has approved drugs for both of these approaches.

"Treating migraines is not a 'one-size-fits-all' condition," says Lipton. "There is a broad spectrum of treatment based on the frequency, severity, and disability of migraines." Migraines range from mild to severe, and some people with mild migraines do fine with over-the-counter medications, Lipton says. People with more disabling migraine may need more powerful, acute medications. And some migraine sufferers need preventive treatment.

No matter what drug you use, "always carry your medication with you," advises Burchfield. "Just because your migraines are unpredictable and you haven't had one in a while doesn't

Motrin Migraine Pain contain ibuprofen and are in the class of medications called nonsteroidal anti-inflammatory drugs (NSAIDs).

It's easy to get confused when confronted with aisles of pain relievers at the drugstore. What makes OTC migraine treatments different from other OTC pain relievers?

"The sponsoring companies did studies and submitted to the FDA supporting data to show that their drug is effective for treating the symptoms of migraine," says Andrea Leonard-Segal, M.D., acting director of the FDA's Division of Nonprescription Clinical Evaluation.

OTC migraine drugs may contain the same ingredients as some other OTC pain relievers, says Leonard-Segal. For example, Excedrin Migraine and Excedrin Extra Strength both contain the same amounts of aspirin, acetaminophen, and caffeine. And Advil Migraine and Motrin Migraine Pain

contain 200 mg of ibuprofen, the same amount found in some other Advil and Motrin products. But the migraine products have different dosing instructions listed on the label.

Prescription migraine drugs come in various forms: oral tablets to be swallowed with water, orally disintegrating tablets that dissolve in the mouth, nasal sprays, and injectables. The choice of drug and route of administration should be based on a discussion between the patient and physician, says Bastings. "People with nausea or vomiting may find it harder to take a pill, and a nasal spray or injectable may be more appropriate for them."

A class of drugs called triptans is generally the physician's first-line treat-

ment to relieve migraine symptoms, says Diamond.

Imitrex (sumatriptan) was the first triptan developed to treat migraines. First introduced as a self-injection, it is also available in tablet and nasal spray form. Six other triptans have been approved by the FDA. Triptans are thought to work by increasing the level of the neurotransmitter serotonin in the brain. Side effects include nausea, dizziness, and muscle weakness. In very rare cases, triptans have caused heart attacks and death because they can produce severe narrowing (constriction) of the coronary arteries.

Burchfield uses a triptan in pill form, but if she waits too long after the migraine symptoms start, she takes an injectable. "It usually works quickly," she says, often relieving the symptoms within an hour. Before she took medication, the pain lasted "a minimum of four hours," she says. Although medication rids her of pain, she feels slug-

Drugs to Prevent Migraine

gish for several hours after taking it. "I still can't function normally. My body has no energy."

Another class of drugs, ergot derivatives, is approved to treat migraine symptoms. Ergot derivatives are associated with more severe side effects. They may be harmful to unborn children or nursing infants, and should not be taken by pregnant or nursing women.

The triptans and ergot derivatives should not be taken by people who have a history of heart disease or uncontrolled high blood pressure.

Drugs to Prevent Migraine

Preventive drugs "should be considered for patients who have more than two acute migraine attacks each

see benefits right away, Lipton says, but for most, "it takes at least a month before you can judge if it works."

In June 2005, an NHF-sponsored study indicated that 40 percent of migraine sufferers—nearly 12 million people—could benefit from preventive therapies, yet only 1 in 5 people with migraine were using these medications. "This doesn't mean you have to treat them with preventives," says Lipton, the lead study researcher, but that their attacks are frequent and severe enough that "it's worth thinking about preventive treatment."

Lipton understands that some people don't want to take daily medication. "It's a lifestyle choice. But if the patient is paralyzed by the fear of the

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month or whose daily activities are seriously compromised by headaches," says Diamond. You may also be a candidate for preventive therapy if you use pain-relieving drugs more than twice a week, or if pain-relievers aren't working for you.

Four medications approved by the FDA to help prevent migraine are currently on the market: the beta-blockers propranolol and timolol, and the anti-convulsant drugs topiramate and divalproex sodium. Side effects of beta-blockers include fatigue, dizziness, nausea, cold hands and feet, and a slowed heart beat. Side effects of anti-convulsants include skin tingling, fatigue, dizziness, insomnia, depression, weight loss, and difficulty concentrating. Unlike the acute prescription drugs for migraine, preventive drugs may be taken safely by people with high blood pressure.

All the preventive drugs must be taken daily to be fully effective. Some people

next attack, they may want to use a preventive."

It's important for physicians to discuss expectations with their patients when it comes to migraine medications, especially preventives, says Lipton. "Preventive medications can decrease migraine occurrence ... as well as reduce the severity and duration of migraines that do occur. But there is rarely 100 percent effectiveness."

Yet some people have high expectations. Lipton says he's seen patients go from having seven migraines a month to one migraine a month on a preventive drug. "When I ask them how it's working, they say 'It's terrible, I had a migraine last night.' "Physicians need to explain to patients that "if the frequency is cut by half or more, they're doing pretty well."

More Is Not Better

Taking symptom-relieving headache medicine more than a couple of days a

FDA-Approved Drugs for Migraine Headaches

Brand Name	Generic Name	Manufacturer/ Distributor	Indication for Adults*
Amerge tablets	naratriptan hydrochloride	GlaxoSmithKline	acute treatment of migraine attacks
Axert tablets	almotriptan malate	Ortho-McNeil Neurologics Inc.	acute treatment of migraine attacks
Frova tablets	frovatriptan succinate	Endo Pharmaceuticals	acute treatment of migraine attacks
Imitrex tablets, injection, nasal spray	sumatriptan succinate	GlaxoSmithKline	acute treatment of migraine attacks
Maxalt tablets and Maxalt-MLT orally disintegrating tablets	rizatriptan benzoate	Merck	acute treatment of migraine attacks
Zomig tablets, nasal spray; and Zomig-ZMT orally disintegrating tablets	zolmitriptan	AstraZeneca	acute treatment of migraine
Relpax tablets	eletriptan hydrobromide	Pfizer	acute treatment of migraine
Migranal nasal spray	dihydroergotamine mesylate	Valeant	acute treatment of migraine headache
Topamax tablets, sprinkle capsules	topiramate	Ortho-McNeil Neurologics Inc.	prevention of migraine headache
Depakote ER tablets	divalproex sodium	Abbott Laboratories	prevention of migraine headache
Blocadren tablets	timolol maleate	Merck	prevention of migraine headache
Inderal tablets, capsules	propranolol hydrochloride	AstraZeneca	prevention of migraine headache
Over-the-Counter Products			
Excedrin Migraine tablets, caplets	acetaminophen, aspirin, caffeine	Novartis Consumer Health	treatment of migraine
Advil Migraine capsules	ibuprofen	Wyeth Consumer Healthcare	treatment of migraine
Motrin Migraine Pain caplets	ibuprofen	McNeil Consumer & Specialty Pharmaceuticals	treatment of the pain of migraine headache

*No migraine products are currently approved by the FDA for use in children.

Source: FDA

week can set off a vicious cycle called rebound. As each dose of medicine wears off, the pain reappears, leading patients to take even more medicine. The overuse of medicine actually starts causing headaches.

"Rebound headaches can occur with any migraine drug," says Bastings, whether it's OTC or prescription. Talk to your doctor if you're caught in a rebound cycle.

Leonard-Segal cautions people taking OTC migraine drugs to "be aware that these drugs contain aspirin and acetaminophen or ibuprofen, active ingredients found in other pain-relieving and fever-reducing OTC products." People should not take additional drugs with these ingredients, or take drugs that contain other pain relievers or fever reducers, without asking a doctor or pharmacist first.

No matter what medication you choose, it's important not to take more than the maximum number of doses recommended on the label, adds Bastings.

Non-Drug Treatment

Whether or not you take medications for migraine, making lifestyle changes and avoiding triggers can help reduce migraine frequency and symptoms.

Experts advise establishing a daily routine: eat regularly, exercise regularly, and try to get up and go to bed the same time every day.

Learn your triggers and avoid them. "Triggers are idiosyncratic," says Lipton. "What triggers a migraine in you may not trigger a migraine in me. The challenge for patients is learning their own triggers."

Physicians recommend keeping a written record, or diary, of migraine attacks, including what you ate, drank, or did 24 hours before the attack. "We don't want to make people overly compulsive about it," says Diamond, "but by keeping a diary, they may spot a particular trigger."

Diamond also advises his patients to limit themselves to two caffeine-containing liquids—such as coffee, tea, or cola drinks—per day.

"Caffeine is a two-edged sword," says Lipton, who also advises limiting caffeinated beverages. If caffeine is taken with a painkiller, it makes the painkiller more effective, he says, which is why it's an active ingredient in some migraine drugs. "The down side is that caffeine withdrawal is a potent headache trigger." Many people who drink a lot of coffee early in the morning have weekend migraines, Lipton adds. "They sleep through their first three cups of coffee and have a horrible caffeine withdrawal headache."

Coleman urges people to read food labels to make sure they're not consuming an ingredient that's a migraine trigger for them. If aspartame appears to be a trigger for you, "avoiding diet drinks but eating diet cookies won't help if the cookies contain aspartame."

Biofeedback is another tool that may help control migraines. With this technique, clinicians use special equipment to teach patients how to monitor and control certain physical responses, such as muscle tension and heart rate. "Biofeedback is not a cure-all but is a good adjunctive," says Diamond. "It's very helpful for a great number of people."

Women and Migraine

Three times as many women as men get migraines, and experts believe that hormones play a big role. "In chil-

dren, the prevalence of boys and girls with migraine is equal," says Mannix. "The discrepancy doesn't begin until puberty when girls start menstruating and having hormonal fluctuations."

The NHF estimates that more than half the migraines in women are menstrually related, occurring right before, during, or after a woman has her period. Some women report that these menstrual migraines are more severe and last longer than migraines they may have at other times of the month.

"There is strong evidence linking migraine with estrogen," says Mannix. Estrogen levels drop right before a woman has her period, and this fall in estrogen may trigger a migraine attack in some women. During pregnancy, when estrogen levels are high, some women have fewer and less severe migraines.

After menopause, when estrogen levels are low, some have fewer attacks and milder symptoms, but others have worse migraines. "About two-thirds of female migraineurs improve with menopause, but one-third do not," says Bastings. "Changes in estrogen level can trigger different reactions among patients, and it is not clear why this happens."

"Women should not have to tolerate menstrual migraine pain," says Mannix. "It is treatable. The most important thing is that women get diagnosed and work with their health care provider to get the best treatment."

Some studies have associated migraine with an increased risk of stroke, particularly in women younger than 45 who get migraine with aura. "The evidence is very solid that these women are at increased risk for stroke," says Lipton. They have three times the risk than that of women younger than 45 who do not have migraines, he adds. "That may seem like a scary statistic, but even though the relative risk triples, the absolute risk is very, very low." This means that the risk for women younger than 45 without migraine is 10 per 100,000 versus 30 per 100,000 for women younger than 45 with migraine with aura.

A woman who has migraine with aura, takes oral contraceptives, and

smokes goes from a three-fold risk for stroke to a 12-fold risk, says Lipton. "I'm not saying that women with migraine should not take oral contraceptives," he adds, "but I am advising them not to smoke."

Children and Migraine

Migraines are most commonly experienced between the ages of 15 and 55, but children and adolescents are not immune. The American Academy of Neurology estimates that migraines occur in 3 percent of preschool children, 4 to 11 percent of elementary school children, and up to 23 percent of teen-agers.

Children with migraine tend to have pain on both sides of the head, usually without aura. They often have nausea and excessive vomiting. Some children get "abdominal migraine," vomiting with no headache. According to the NINDS, researchers have found that these children usually develop headaches as they get older.

No OTC or prescription migraine products currently are approved for use in children, but physicians may recommend that children take certain drugs approved for adults, with careful monitoring. ■

For More Information

National Institute of Neurological Disorders and Stroke
www.ninds.nih.gov/disorders/migraine

American Council for Headache Education
www.achenet.org
(856) 423-0258

National Headache Foundation
www.headaches.org
(888) 643-5552

MAGNUM, The National Migraine Association
www.migraines.org
(703) 739-9384

Food Labels Identify Allergens More Clearly

By Linda Bren

When you drink a glass of milk, are you consuming casein and lactoglobulin? How about potassium caseinate and lactalbumin?

According to food scientists, all of these substances are proteins found in milk. And until recently, food manufacturers could use technical terms such as these on food labels without further explanation, instead of listing the more common term "milk."

That changed at the beginning of 2006, when a new food labeling law, the Food Allergen Labeling and Consumer Protection Act (FALCPA), took effect.

Under FALCPA, food labels are required to state clearly whether the food contains a "major food allergen." The law identifies as a major food allergen any of eight allergenic foods: milk; eggs; fish such as bass, flounder, and cod; crustacean shellfish such as crab, lobster, and shrimp; tree nuts such as almonds, walnuts, and pecans; peanuts; wheat; and soybeans. The law also identifies as a major food allergen any ingredient that contains protein derived from any of these eight foods.

The plain language declaration requirement of FALCPA also applies to flavorings, colorings, and incidental additives that are or contain a major food allergen.

"FALCPA recognizes that eight major foods or food groups account for 90 percent of all food allergies in the United States, and some allergic reactions may be severe or life-threatening," says Robert E. Brackett, Ph.D., director of the Food and Drug Administration's Center for Food Safety and Applied Nutrition (CFSAN).

About 2 percent of adults and 5 percent of infants and young children in the United States suffer from food allergies. About 30,000 consumers require emergency room treatment, and 150 Americans die each year because of allergic reactions to food.

There is no cure for food allergies. Avoidance of the food that causes the allergy is the only way a person can prevent a reaction. The improved label will make it easier for food allergic people and their caregivers to identify and avoid foods that contain major food allergens, says Catherine Copp, policy advisor in the CFSAN. For example, if a product contains the milk-



EyeWire

Ingredients: Enriched flour (wheat flour, malted barley, niacin, reduced iron, thiamin mononitrate, riboflavin, folic acid), sugar, partially hydrogenated soybean oil, and/or cottonseed oil, high fructose corn syrup, whey (milk), eggs, vanilla, natural and artificial flavoring, salt, leavening (sodium acid pyrophosphate, monocalcium phosphate), lecithin (soy), mono- and diglycerides (emulsifier)

derived protein casein, the product's label will have to use the term "milk" in addition to the term "casein" so that those with milk allergies can clearly understand the presence of the allergen they need to avoid.

"We're very excited about this change," says Anne Muñoz-Furlong, founder and CEO of The Food Allergy & Anaphylaxis Network based in Fairfax, Va. "People with food allergies will be able to tell right away whether a food is safe for them to eat or not."

Food allergies are on the rise in children, says Muñoz-Furlong, and the improved food labeling information will be especially helpful to children who must learn to recognize the presence of substances they need to avoid. Parents often take children with them when they shop for groceries, she says. "They want to teach children early on to start reading food labels. They have the children read the label to them and figure out if the product contains an allergy-causing food and whether it should go in the grocery cart or go back on the shelf."

"When the child is too young to read, parents will read the label to the child," adds Muñoz-Furlong. "It's almost impossible to keep the attention of a 5-year-old when you say 'ammonium caseinate,' but when you say 'milk,' the child with a milk allergy will instantly say, 'That's not good for me.'"

Manufacturers must identify the presence of a major food allergen in one of two ways: in the list of ingredients, manufacturers must state the source of an allergenic ingredient in parentheses after the name of that ingredient; or after or next to the ingredient list, manufacturers must add "contains" followed by the name of the source of each allergenic ingredient in the food. For example:

Option 1:

Ingredients: *Enriched flour (wheat flour, malted barley, niacin, reduced iron, thiamin mononitrate, riboflavin, folic acid), sugar, partially hydrogenated soybean oil, and/or cottonseed oil, high fructose corn syrup, whey (milk), eggs, vanilla, natural and artificial flavoring, salt, leavening (sodium acid pyrophosphate, monocalcium phosphate), lecithin (soy), mono- and diglycerides (emulsifier)*

Option 2:

Contains Wheat, Milk, Eggs and Soy

"These statements are not required if the major food allergen's common name already identifies its food source," says Copp. For example, the ingredients whole wheat flour, butter-milk, and peanut butter already state that they contain wheat, milk, and peanuts, respectively, so no further explanatory terms are required.

FALCPA applies to both domestically produced and imported packaged foods that the FDA regulates. So even if you purchase a box of candy from overseas, it should be in compliance, says Copp. Raw agricultural commodities, such as fresh fruits and vegetables, are exempt from FALCPA. So are highly refined oils made from one of the eight allergenic foods identified by the law.

FALCPA establishes two separate processes that food manufacturers can use to request an exemption for their product from the FALCPA declaration requirement—the notification and petition processes. "The notification process may be used by manufacturers who can demonstrate that their ingredient does not contain an allergenic protein; the petition process may be used by a manufacturer who can demonstrate that, although the ingredient does contain protein derived from an allergenic food, the ingredient does not cause an adverse reaction that poses a risk to human health," says Felicia Billingslea, director of the FDA's Division of Food Labeling and Standards.

The law applies only to products labeled on or after Jan. 1, 2006, so until products labeled before that date are sold or otherwise removed from the market, consumers will continue to see some products without the plain language allergen labeling on grocery store shelves, says Copp, "particularly nonperishables such as canned goods."

Even if consumers have purchased a product in the past that does not aggravate their allergies, they should not take it for granted that it will always be nonallergenic, says Copp. "We encourage consumers to always read the ingredients list, because manufacturers may

change their product formulation."

The FDA will enforce the new law. "We intend to document violations of the law when inspecting manufacturing plants," says Betty Harden, an FDA consumer safety officer in the Office of Compliance. A food product that contains an undeclared allergen may be subject to recall. In addition, a food product not properly labeled may be misbranded and subject to seizure and removal from the marketplace.

FALCPA also requires the FDA to submit a report to Congress on food allergens, particularly with respect to identifying ways to reduce or eliminate cross-contact and stating the risk of cross-contact on food labels. Cross-contact occurs when a residue or other trace amount of an allergenic food is unintentionally incorporated into another food that is not intended to contain that allergenic food; cross-contact may occur during harvesting, transportation, manufacturing, processing, or storage.

In addition, the agency is required to propose a regulation by August 2006, and to issue a final regulation by August 2008, to define the term "gluten-free" for voluntary use in food labeling. Gluten is a term that describes a group of proteins that occur naturally in certain grains, including wheat, barley, and rye. When present in certain amounts, gluten can cause a serious reaction in people with celiac disease, a chronic digestive disease that damages the small intestine and interferes with absorption of nutrients from food. About 2 million people in the United States have this disease.

"Consumers susceptible to celiac disease need accurate, complete, and informative labels on food to protect themselves," says Billingslea, "and a standardized definition of 'gluten-free' and use of the term on labels will help."

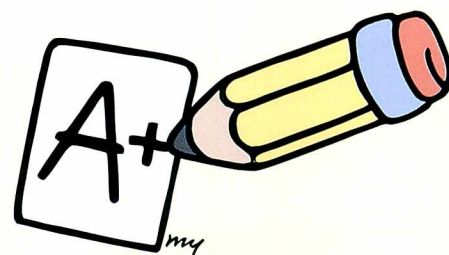
For More Information

The FDA's Food Allergens Page
www.cfsan.fda.gov/~dms/wh-alrgy.html

Take the FDA Consumer Quiz

Do discolored toenails always mean foot fungus? How many drugs has the FDA approved over the last decade to treat migraine headaches? What problem with blood glucose meters prompted the FDA to recently issue a safety alert? To find out how much you know about these and other health-related topics, take our quiz.

Hint: The answers to all of these questions can be found in the March–April 2006 issue of FDA Consumer (and at the bottom of this page).



1. How many bones are in the human foot?
 - a. 15
 - b. 26
 - c. 36
 - d. 42
2. Which of the following is among the common problems caused by ill-fitting shoes?
 - a. nerve growths called neuromas
 - b. hammertoes
 - c. blisters
 - d. calluses
 - e. all of the above
3. Which of the following statements is false?
 - a. Fungal nails usually clear up on their own.
 - b. Fungal nails can cause discoloration.
 - c. Discolored nails may indicate that fungus is present.
 - d. Antifungal medicine may cause headaches.
4. Which of the following can cause ingrown toenails?
 - a. improper nail trimming
 - b. pressure from shoes
 - c. blisters on the feet
 - d. washing feet with Epsom salt
 - e. a. and b.
5. The fentanyl skin patch should not be used to treat pain in which of the following people:
 - a. children younger than 2 years
 - b. people who have cancer
 - c. people who are experiencing short-term pain
 - d. a. and b.
 - e. a. and c.
6. Three out of four people who suffer from migraines are:
 - a. older than 55
 - b. younger than 25
 - c. asthmatic
 - d. men
 - e. women
7. How many drugs has the FDA approved in the last decade to treat migraine headaches?
 - a. 4
 - b. 8
 - c. 10
 - d. more than 10
8. In some women, migraine is linked strongly to:
 - a. increasing progesterone levels
 - b. falling estrogen levels
 - c. breast implants
 - d. osteoporosis
 - e. fibromyalgia
9. When present in foods in certain amounts, gluten can cause a serious reaction in people who have:
 - a. celiac disease
 - b. epilepsy
 - c. diabetes
 - d. ulcers
 - e. inflammatory bowel disease
10. What are the three FDA approaches to expedite the development and review of new drugs for serious or life-threatening conditions?
 - a. standard, priority, and accelerated approval
 - b. fast track, slow track, and accelerated track
 - c. fast track, accelerated approval, and priority review
 - d. rolling review, priority review, and standard review
11. Recent problems with blood glucose meters prompted the FDA to issue a safety alert because:
 - a. the units of measurement were being switched accidentally
 - b. the on/off switch malfunctioned
 - c. the unit failed to display a reading
 - d. all of the above

Answers:

1. b 2. e 3. a 4. e 5. e 6. e 7. d 8. b 9. a 10. c 11. a

Treating Migraine: Be Proactive

By Suzanne E. Simons



Nearly 30 million people in the United States have migraine headaches. The recent American Migraine Prevalence and Prevention Study, the largest-ever study of migraine sufferers, found that 18 percent of women and 6 percent of men have this disease. While these numbers are staggering, the sad truth is that most people who suffer from migraines are undiagnosed and undertreated.

The good news is that migraines are treatable, but you must take the first step and get diagnosed.

Migraine is usually characterized as a throbbing, one-sided headache that is accompanied by either sensitivity to light or nausea, or both. This type of headache often causes significant disability. The pain can be severe, causing the sufferer to require bed rest. Migraines, too, tend to run in families. In fact, if both parents have migraines, their child has a 75 percent chance of developing them.

If migraine is affecting your life, causing you to miss time from work, family, or social occasions, make an appointment with your health care provider to specifically talk about your headache problem. Before going for your visit, keep a headache diary. Record how frequently you get your headaches, how long the pain lasts and its severity, where the pain is located, which medications you took, and how they affected your headache. Also record other factors such as your emotional state and, if you are a woman, whether the headache was immediately before, during, or after your menstrual cycle. You should also keep a log of the foods you eat. Both of these tools can be helpful to your health care provider.

Most migraine diagnoses are made by taking a complete medical history. Since there is no test to determine migraine, your health care provider will use the information gathered during your visit to make the diagnosis. If tests such as a CT scan are ordered, they are usually used to rule out other diseases.

Be a partner in your health care. Make a list of questions before going to see your health care provider. Write down the answers during your visit so you can review them later. You may not have all of your questions answered on your first visit, so ask them in order of importance. It may be helpful to have a family member accompany you to the visit, as well.

Be sure you understand what medications have been prescribed and how to take them. Some medications are

meant to be taken at the beginning of a migraine attack. These are called acute medications. Others should be taken daily, whether or not you have a headache, and these are known as preventive medications. In some instances, you will take a medication daily to prevent attacks as well as an acute medication periodically to treat a migraine that does occur.

Many different medications are used to treat migraine; some of these are migraine-specific such as the class of drugs called triptans. It is interesting to note that many of the medications that successfully treat migraine are actually medications for other conditions. Several anti-epileptic medications are indicated to treat migraine. Other medications such as beta blockers, calcium channel blockers, and tricyclic antidepressants are often prescribed for migraine.

Tell your health care provider if you are taking supplements or over-the-counter products or both to treat your migraine, as these may interact with medications that may be prescribed.

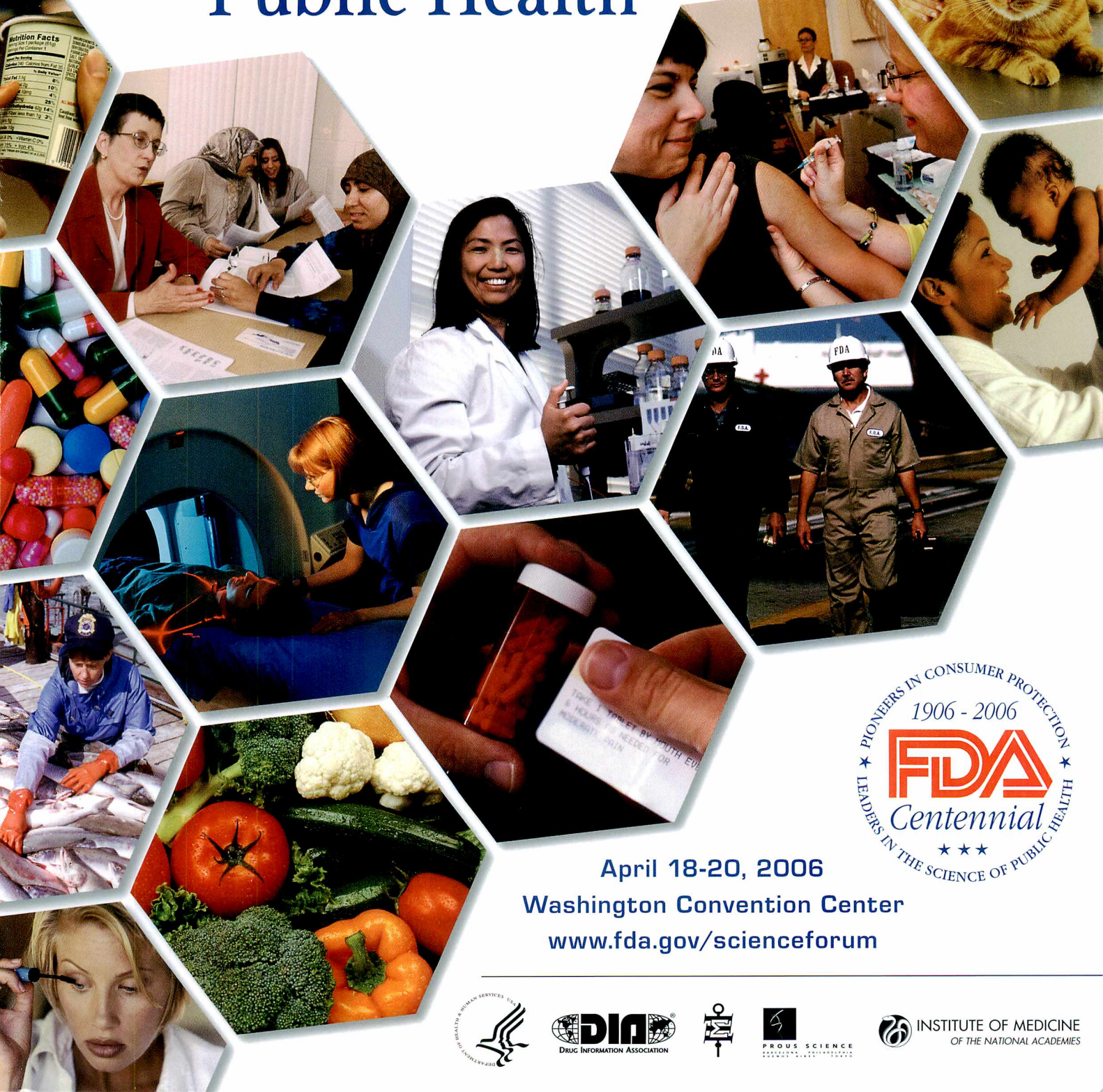
Finding the right medication for you may require some trial and error. Some medications may take several weeks or months before they become fully effective. Different doses of the same medication may need to be tried. Tell your health care provider about any side effects you may experience, and take your medication as directed.

Lifestyle modifications, too, can be helpful in lessening the frequency and duration of migraine attacks. It is important to maintain a regular sleep-wake cycle, getting up at the same time on weekends as on weekdays. Don't delay or skip meals. Watch your caffeine intake as caffeine can be a trigger in susceptible people. Get plenty of physical exercise, even if it is simply walking. Biofeedback, stress reduction exercises, guided imagery, and visualization are other nonmedicated ways to deal with migraine.

Life with migraine can, at times, be challenging, but by becoming educated about the disease and being proactive, you can empower yourself to live life fully. ■

Suzanne E. Simons is executive director of the National Headache Foundation in Chicago.

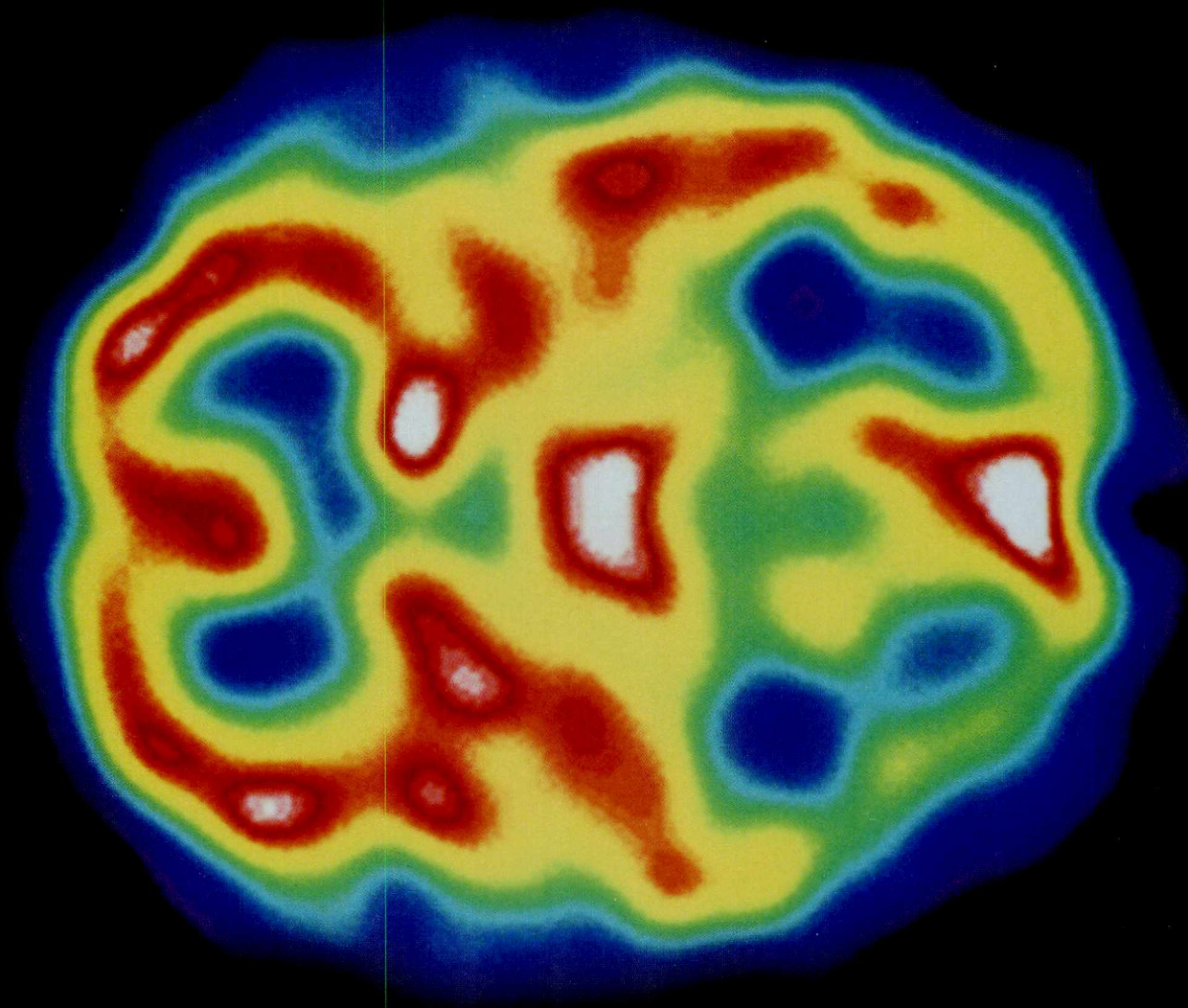
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Migraine

An image of a person's brain during a migraine attack. The red areas are metabolically active and the green areas indicate reduced blood flow and low brain activity.

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