

# FDA Consumer

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

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**New Drug Label Spells It Out Simply**







**Donna E. Shalala, Ph.D.**

Secretary of Health and  
Human Services

**Jane E. Henney, M.D.**

Commissioner of Food and Drugs

**Lawrence Bachorik, Ph.D.**

Interim Associate Commissioner for Public Affairs

**Isadora Stehlin** /Editor

**Patricia N. Edwards** / Art Director

**Michael L. Herndon** / Production Manager

**Carol L. Ballentine** / Copy Editor

**Cover Design:** Richard Thompson Jr.

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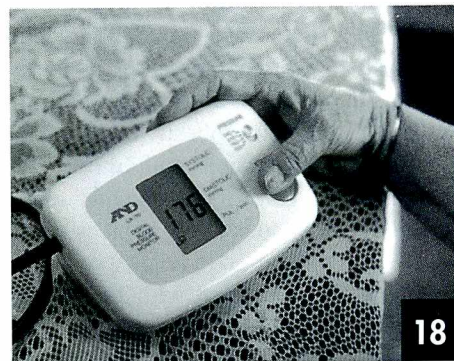
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These pills make up a typical daily regimen for an AIDS patient. Since 1996, this therapy has helped the AIDS death rate drop by nearly half. For the latest on AIDS treatments, see page 12.





## Infections, Deaths Prompt Arthritis Drug Label Change

In response to six deaths and other serious, nonfatal infections in patients taking the rheumatoid arthritis drug Enbrel (etanercept), the drug's marketers are expanding the product's warning about use in patients with infections.

Enbrel was approved last November to treat moderate-to-severe, active rheumatoid arthritis in patients who did not respond well to other treatments. When it was approved, the drug's labeling said it should not be given to patients with a blood infection called sepsis and should be discontinued if a patient develops a serious infection.

Since the drug's approval, 30 of the estimated 25,000 patients treated with Enbrel reportedly developed sepsis or other serious infections.

Based on adverse reaction reports to FDA and one of the drug's marketers,

Immunex Corp., the new labeling expands the sepsis warning to include patients with any active infection, including those that are chronic or localized. The new labeling also recommends that:

- patients who develop a new infection while taking Enbrel be monitored closely
- doctors carefully consider whether to prescribe Enbrel to patients with a history of recurring infections or underlying medical conditions, such as advanced or poorly controlled diabetes, that may predispose them to infections.

Immunex has informed physicians of the new safety concerns and the labeling revisions.

So far, controlled clinical studies have not shown an increase in serious infections in patients treated with Enbrel. It is unclear without further scientific studies

whether Enbrel is the actual cause of the serious infections in rheumatoid arthritis patients, but significant concerns remain, and FDA has asked Immunex to do additional studies to assess the risk.

As a condition of the drug's more recent May approval to treat some cases of *juvenile* rheumatoid arthritis, FDA is also requiring Immunex to follow all pediatric users and report how they do on the drug.

FDA asks people to report all cases of sepsis or other serious infection to the agency's MedWatch program, by calling 1-800-FDA-1088 (1-800-332-1088) or through the Internet at [www.fda.gov/medwatch/](http://www.fda.gov/medwatch/). Also, health professionals may call Immunex Professional Services, Seattle, at 1-800-IMMUNEX (1-800-466-8639) or co-marketer Wyeth-Ayerst Laboratories, Philadelphia, at 1-800-934-5556.

## Fat-Blocking Drug Can Help Fight Obesity

A newly approved anti-obesity drug works by blocking the body's absorption of fat, not by suppressing the appetite like other diet drugs.

Xenical (orlistat), approved by FDA in April, decreases a person's fat absorption by about 30 percent by preventing the body from breaking down dietary fats into smaller, absorbable molecules. It is the first anti-obesity drug in a drug class known as lipase inhibitors.

Xenical is for obese patients with a body mass index (BMI, a measure of weight in relation to height) of 30 or more, or for patients with a BMI of at least 27 who also have high blood pressure, high cholesterol, or diabetes. (A person 5 feet 5 inches tall who weighs 180 pounds, for example, would have a BMI of 30.)

In seven long-term clinical trials of



more than 4,000 patients, 57 percent of those who completed one year of treatment with Xenical lost at least 5 percent of their baseline body weight, compared with 31 percent of patients treated with a placebo for the same length of time.

The recommended dose of Xenical is one capsule with each main meal that includes fat. During treatment, the patient should be on a nutritionally balanced, reduced-calorie diet that contains no more than 30 percent of calories from fat. Also, because Xenical reduces the absorption of some fat-soluble vitamins and beta carotene, patients should take a supplement containing fat-soluble vitamins (A, D, E and K) and beta carotene.

The drug's most common side effects are oily spotting, gas with discharge, fecal urgency, fatty/oily stools, and frequent bowel movements.

Xenical is made by Roche Laboratories Inc., Nutley, N.J.



## Nearsighted Can Look to Implants to Improve Sight

Some mildly nearsighted people may now opt for acrylic eye implants to improve their vision rather than glasses, contacts, or eye surgery.

In April, FDA approved tiny, crescent-shaped devices called KeraVision Intacs that, when surgically implanted into the cornea (the membrane that covers the eye), can flatten the cornea and reduce or eliminate mild nearsightedness.

The Intacs implants are considered permanent, although they can be removed if necessary.

FDA approved the implants only for use in patients 21 or older. The safety and effectiveness of the implants have not been established for moderate or severe nearsightedness.

Approval was based on the manufacturer's safety and effectiveness data and the recommendation of the Ophthalmic Devices Panel, a group of outside experts. In clinical studies of 450 eyes, 97 percent of eyes were corrected to 24/40 or better and 74 percent were corrected to 20/20 or better.

Thirty-nine patients chose to have their Intacs removed because of side effects (such as glare or halos) or because they were unhappy with the corrected vision.

When the implants are removed, vision usually returns to its presurgery level, but some patients may experience vision problems such as glare or halos around lights.

At FDA's request, the implants' maker, KeraVision Inc., Fremont, Calif., is continuing to collect data on patients to determine the long-term effect of the implants on the cornea.

## Computerized Scanner Double-Checks Suspicious Mammograms

A new device will help radiologists determine whether a woman should be evaluated further when the results of her mammogram are unclear.

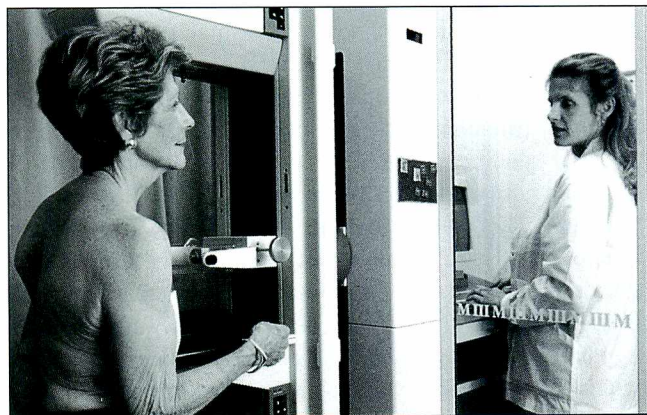
Approved by FDA in April, the T-Scan 2000 can potentially help identify women who should be referred for early biopsy and reduce the number of negative biopsies.

The T-Scan uses a hand-held scanner placed on the breast to evaluate certain suspicious areas detected on the mammogram. A computer connected to the scanner displays an image of the breast areas in question. The image is based on differences in the flow of electricity in malignant tumor tissue and surrounding normal tissue.

The T-Scan is intended as a follow-up to mammography, and does not replace mammography or other conventional methods of detecting or diagnosing breast cancer (such as clinical breast examination, ultrasound, or biopsy evaluation.)

Approval of the device was based on the results of three clinical studies of safety and effectiveness performed by the device's manufacturer, TransScan Medical Inc., Ramsey, N.J., and on the recommendation of an advisory panel of outside experts.

As a condition of approval, TransScan Medical is required to conduct a postmarketing study on the effects of hormonal changes during the menstrual cycle on the device's ability to detect and distinguish among breast abnormalities.



**Cancer's many faces ...** At one time cancer was thought to be a single disease that attacked different tissues. Then, over the years, it was recognized to be a hundred different diseases as determined by the particular tissue involved and the kind of cells within that tissue that were growing out of control. Now scientists at Memorial Sloan-Kettering Cancer Center in New York believe that cancer comes in countless variations, each with a genetically determined molecular "fingerprint" that indicates how deadly it is likely to be and how aggressively it should be treated. With this understanding, doctors can identify tumors insensitive to a particular form of treatment and prescribe the most effective therapy.



## FDA Warns About a Potentially Deadly 'Party Drug'

Prompted by reports of at least three deaths and several severe adverse reactions, FDA in May warned the public about a new group of products sold on the Internet, in health food stores, and through ads in muscle-building magazines. The agency declared one of the new products—1,4 butanediol (BD)—a Class I health hazard, meaning its use could pose a potentially life-threatening risk.

FDA considers BD products unapproved new drugs, and the products have been seized to prevent their sale and further illnesses and deaths.

Marketed alternatively as sleep aids, "party drugs," and dietary supplements, these BD-related products chemically resemble two other hazardous substances that FDA considers unapproved new drugs—gamma hydroxybutyric acid (GHB) and gamma butyrolactone (GBL). FDA has issued several warnings about GHB and GBL. Health officials believe that manufacturers of these products are renaming them and substituting BD for GBL.

Considered as dangerous as GHB and GBL, BD can cause dangerously low respiratory (breathing) rates, unconsciousness, vomiting, seizures, and death. Also, BD may increase the effects of alcohol and is even more dangerous when consumed with other depressant drugs.

Products that contain BD include Revitalize Plus, Serenity, Enliven, GHRE, SomatoPro, NRG3, Thunder Nectar, and Weight Belt Cleaner. The labels of suspect products may list 1,4 butanediol, tetramethylene glycol, gamma butyrolactone, or 2(3H)-furanone di-hydro as ingredients.

In issuing its warning on BD products, FDA said it could not ensure the effectiveness or safety of any sleep-aid product other than FDA-approved drugs. "People who use unapproved sleep inducement products, especially without proper medical supervision, may be unnecessarily exposing themselves to serious harm," the agency said.

## A mandatory hepatitis vaccine? ...

The national Centers for Disease Control and Prevention wants children in 11 western states with a high incidence of hepatitis A to be vaccinated against the disease. CDC recommends that states with at least 20 cases out of every 100,000 people—including Arizona, Alaska, California, Idaho, Nevada, New

Mexico, Oklahoma, Oregon, South Dakota, Utah, and Washington—get the vaccine. Hepatitis A is a highly contagious virus that can damage the liver. It is spread by personal contact when hands aren't washed after bathroom use or by contaminated food or water. An effective vaccine has been available since February 1995.



## Home Test Detects Hepatitis C

FDA has approved the first at-home test kit for detecting the hepatitis C virus, the nation's most common blood-borne infection and a major cause of liver damage.

The Hepatitis C Check, approved April 29, allows consumers to collect a blood sample on a piece of filter paper and mail it to a laboratory that tests for antibodies to the hepatitis C virus (HCV). The laboratory screens the sample with an FDA-licensed test for antibodies and confirms any positive samples with a different FDA-licensed test.

Consumers can obtain the results of their home tests anonymously by phone from an automated system or a health-care counselor. The kit's manufacturer, Home Access Health Co., Hoffman Estates, Ill., also offers education and counseling about HCV and referrals to doctors.

Hepatitis C, which can affect about 4 million Americans in its chronic form, can cause cirrhosis (irreversible and potentially fatal liver scarring), liver cancer, or liver failure. It is responsible for 8,000 to 10,000 deaths a year in the United States.

The Hepatitis C Check may not detect the virus if it was contracted in the previous six months. Also, the test does not show if the infection is presently active. This must be determined by a doctor's evaluation and additional testing.

(For more information about hepatitis C, see "Hepatitis C: New Treatment Helps Some, but Cure Remains Elusive" in the March-April 1999 *FDA Consumer*.)



## Device Ok'd as Alternative to Clot-Busting Drug

A device that uses jets of salty water to remove blood clots from blocked heart arteries or blood vessels grafted in bypass operations has received approval from FDA.

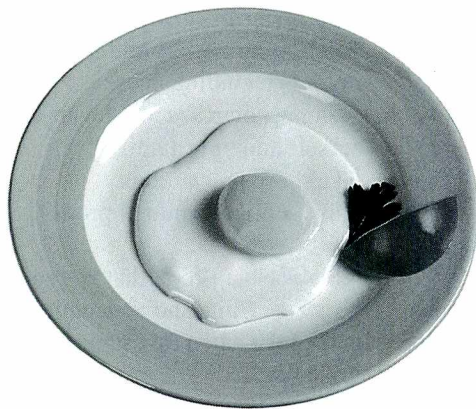
The AngioJet System offers an alternative treatment to "clot-busting" drugs such as tissue plasminogen activator (t-PA).

Because blockages in heart arteries are sometimes complicated by blood clots—which can cause a heart attack or death—doctors often use clot-busting drugs to clear the clots before performing angioplasty. But many patients cannot

take such drugs, so the AngioJet System gives them another option.

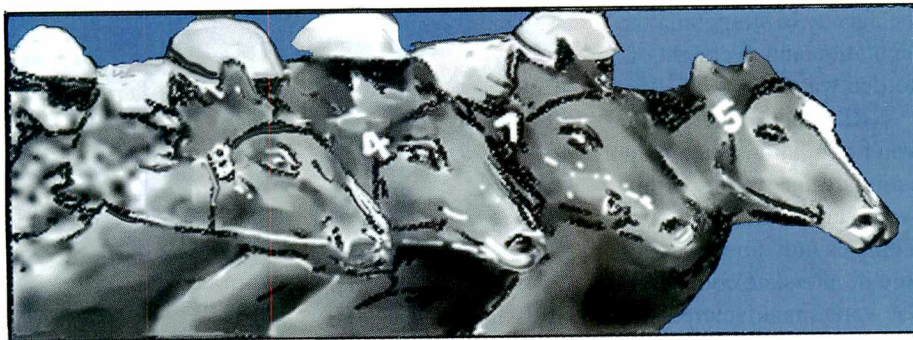
Several clinical studies showed the device's effectiveness. For example, in one trial where 180 patients were treated with the AngioJet System and 169 with urokinase, a clot-busting drug, results were similar. Another study showed that the AngioJet System could be used effectively with other treatments to remove blood clots during a heart attack.

FDA approved the AngioJet System less than six months after the manufacturer, Possis Medical, Minneapolis, submitted the marketing application.



**An egg a day ...** Eating one egg a day does not increase the risk for heart attacks or strokes, says a Brigham and Women's Hospital study of over 80,000 women and a separate study of nearly 38,000 men. Among healthy men and women, no significant differences in risk for heart disease or stroke were reported between those eating an average of up to one egg daily and those averaging less than one weekly. Diabetics, however, did face greater risks of heart attacks or strokes with a higher level of egg consumption.

**"Today" to return "tomorrow" ...** Once hailed as the most popular contraceptive available, the Today Sponge is coming back after the manufacturer removed it from the market in 1995 because it would be too expensive to correct the factory flaws FDA found. A small pharmaceutical company recently resurrected the nonprescription birth-control device after buying the rights to the product. Many women favored the sponge because of its simplicity, convenience, and the low risk of side effects. It is expected to be available again in drugstores, following FDA's final inspection of production operations, sometime in the fall.



## First Drug for Horse Ulcers Approved

The first drug for treating and preventing recurring stomach ulcers in horses and foals older than 4 weeks was recently approved by FDA.

The agency approved GastroGard (omeprazole) in March for these types of ulcers in horses, which are a common problem in stressful environments and can lead to death, especially among foals. Omeprazole was previously approved under the trade name Prilosec for intestinal and stomach ulcers and certain other stomach conditions in humans.

GastroGard is sold by Merial Limited, Iselin, N.J., and is available only through a licensed veterinarian. The safety of the drug in pregnant or lactating mares is not known.

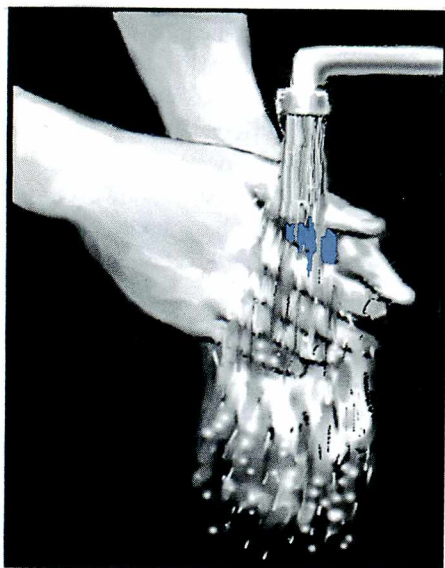
**Double dose ...** The recommended daily allowance for vitamin C should be doubled or even tripled, say government researchers, because of increasing evidence over the last two decades of the vitamin's cancer-fighting ability when consumed in fruits and vegetables. The National Institutes of Health says the allowance should be 100 to 200 milligrams instead of the current 60 milligrams established by the National Academy of Sciences in 1980. But researchers are not sure if benefits come from the vitamins themselves or from the vitamins plus other components of the food containing the vitamins. And they add that there is such a thing as too much vitamin C: 200 milligrams is the maximum the body can absorb. Larger amounts can increase the risk of kidney stones.



**Steps to stop *Listeria* ...** *Listeria* is a common food-borne bacterium that can cause symptoms including nausea, vomiting, cramps, diarrhea and fever. To protect yourself and your family from *Listeria*, take these precautions:

- Thoroughly cook raw animal products.
- Thoroughly wash all food that is to be eaten raw, such as fruits and vegetables.
- Keep foods to be eaten raw separate from uncooked meats.
- Wash hands, knives and cutting boards with hot soapy water.

In addition, those most vulnerable to *Listeria* infections, such as pregnant women, the elderly, and those with weakened immune systems, also should:



- Avoid all soft cheeses, including feta, Camembert, brie, and blue-veined cheeses (such as Roquefort).
- Cook hot dogs until the internal temperature reaches 165 degrees Fahrenheit, by either steaming or frying. Cooking in a microwave is not recommended.
- Avoid deli meats like salami, corned beef, bologna, and liverwurst, unless they get additional cooking (as in a hot corned beef sandwich).

**What you don't know can hurt you ...** How likely are consumers to respond to foods being recalled by a manufacturer? Not very, say researchers at the Centers for Disease Control and Prevention. In a study that tracked how consumers reacted to a recall of food contamination with *Salmonella* bacteria that had sickened an estimated 224,000 people, consumers weren't any more likely to have thrown away the product. More than 25 percent thought the product was still "okay." And 31 percent who had heard the warning and still had the product simply ignored the warning and ate the food anyway. Federal officials urge consumers who learn about a potentially tainted product to check their cabinets and refrigerators and throw out any found. Most food stores will offer a full refund for recalled food.

### Water Sold State-to-State Safe to Drink, Agency Says

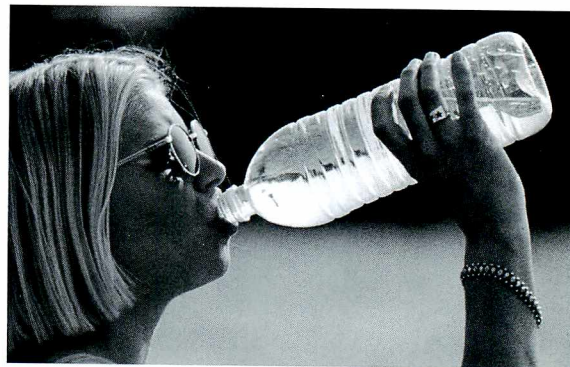
Bottled water sold in interstate commerce is safe to drink, FDA said following the release in March of a privately funded report that questioned the safety of such water. However, the agency said it would review the report, which was based on a four-year study by the environmental health group National Resources Defense Council, and would welcome other suggestions on how to improve the quality of bottled water.

NRDC's study found that of 1,000 bottles of 103 brands of bottled water tested, about one-third contained such contaminants as synthetic organic chemicals, bacteria, and arsenic. The organization said it undertook the study as part of a petition it submitted to FDA calling on the agency to strengthen its regulation and oversight of bottled water.

NRDC said FDA's bottled water regulations should apply nationally, as well as within every state. Currently, FDA regulates only bottled water sold in interstate commerce—not water manufactured and sold solely within a state. State authorities regulate the latter, although state laws governing bottled water are often based on FDA's standards.

FDA said in a published statement in March that its regulations cover all aspects of plant and manufacturing operations, equipment and procedures, as well as administrative matters, such as record-keeping and employee training.

These regulations "help protect the public against any health problem that could conceivably occur with bottled water products," the agency said.





# Breast Cancer

## Better Treatments Save More Lives

by Carol Lewis

Two different women. The same deadly disease. One thought she couldn't get it. The other was told she didn't have it. Both opinions were wrong.

In 1994, one week before turning 35, Cathy Young received the devastating news. "I thought people had to be in their 50s to get cancer," the Oak Grove, Mo., resident says. "And then it happened to me."

Linda Hunter, 42, recalls that in January 1995, her mammogram results came back normal. But skin changes on one of her breasts compelled her to seek a second, third and fourth opinion—all of which supported the initial mammogram findings. Her tenacity finally paid off when a fifth doctor she visited detected a rare form of the disease.

Every three minutes a woman in the United States learns she has breast cancer. It is the most common cancer among women, next to skin cancers, and is second only to lung cancer in cancer deaths in women. Only 5 to 10 percent of breast cancers occur in women with a clearly defined genetic predisposition for the disease. The overall risk for developing breast cancer increases as a woman gets older.

Although treatment is initially successful for many women, the American Cancer Society (ACS) says that breast cancer will return in about 50 percent of these cases.

"It's hard to say that things are back to normal when one survives breast cancer," says Young, "because a survivor always has a fear that one day the cancer may return."

New drugs, treatment regimens, and better diagnostic techniques have improved the outlook for many, and are responsible, according to ACS, for breast cancer death rates going down.

"Women have greater options in breast cancer treatment compared to a decade ago," says Harman Eyre, M.D., chief medical officer for ACS. "New drugs and procedures open up a whole new era of effective treatment."

### Breast Cancer Treatments

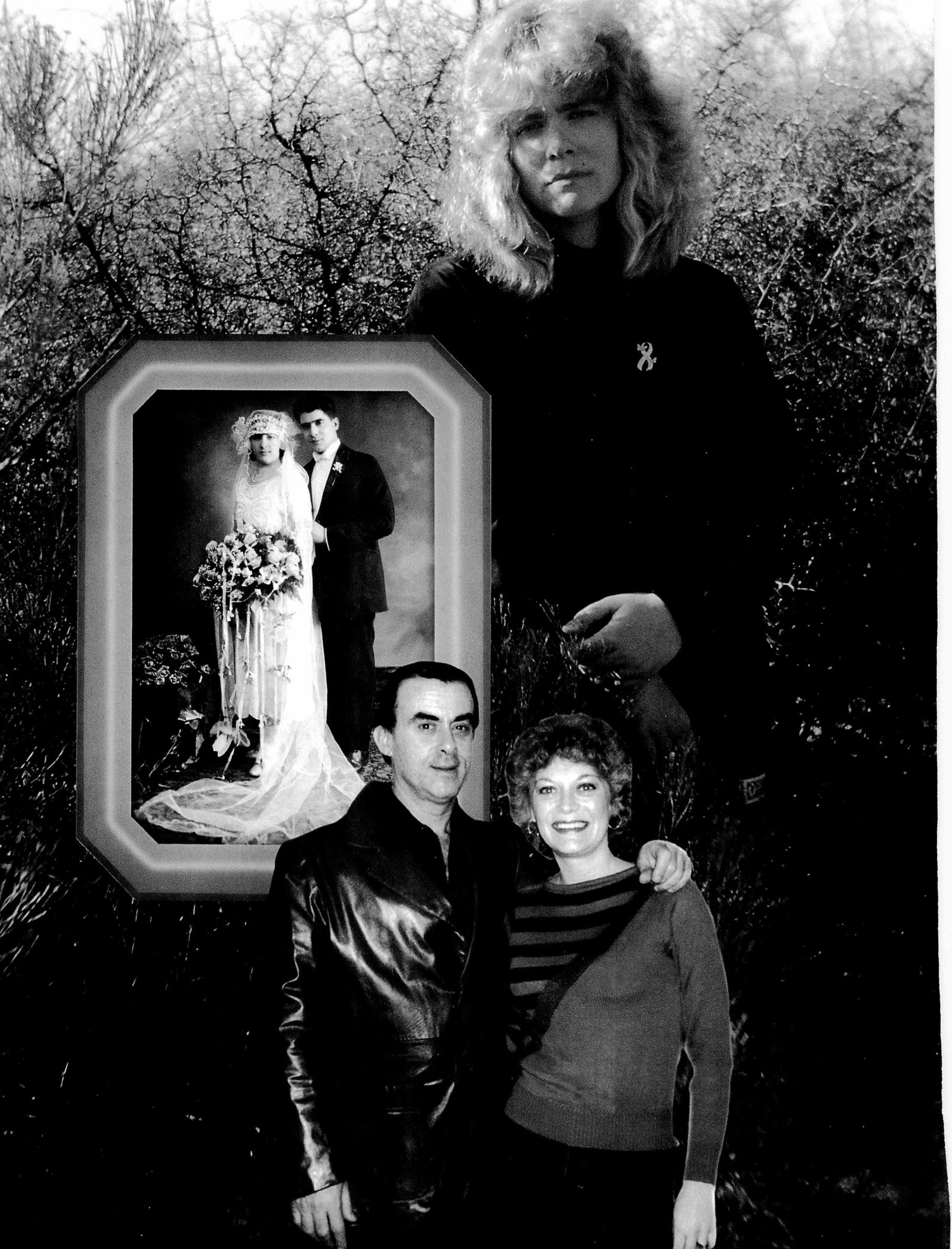
Breast cancer can be treated with surgery, radiation and drugs (chemotherapy and hormonal therapy). Doctors may use one of these or a combination, depending on factors such as the type and location of the cancer, whether the disease has spread, and the patient's overall health.

Most women with breast cancer will have some type of surgery, depending on the stage of the breast cancer. (See "Stages of Breast Cancer.") The least invasive, *lumpectomy* (breast-conserving surgery), removes only the cancerous tissue and a surrounding margin of normal tissue. Removal of the entire breast is a *mastectomy*. A *modified radical mastectomy* includes the entire breast and some of the underarm lymph nodes. The very disfiguring *radical mastectomy*, in which the breast, lymph nodes, and chest wall muscles under the breast are removed, is rarely performed today because doctors believe that a modified radical mastectomy is just as effective.

While removing underarm lymph nodes after surgery is important in order to determine if the cancer has spread, this procedure may add chronic arm swelling and restricted shoulder motion to the discomforts of the overall treatment. But a new method, *sentinel node biopsy*, still under investigation, allows physicians to pinpoint the first lymph node into which a tumor drains (the sentinel node), and remove only the nodes most likely to contain cancer cells.

To locate the sentinel node, the physi-  
(Continued on page 9)







## **"Women have greater options in breast cancer treatment compared to a decade ago."**

**—Harman Eyre, M.D., chief medical officer for the American Cancer Society**

*(Continued from page 7)*

cian injects a radioactive tracer in the area around the tumor before the mastectomy. The tracer travels the same path to the lymph nodes that cancer cells would take, making it possible for the surgeon to determine the one or two nodes most likely to test positive. The surgeon will then remove the nodes most likely to be cancerous.

**Radiation therapy** is treatment with high-energy rays or particles given to destroy cancer. In almost all cases, lumpectomy is followed by six to seven weeks of radiation, an integral part of breast-conserving treatment. Although radiation therapy damages both normal cells and cancerous cells, most of the normal cells are able to repair themselves and function properly.

Radiation therapy can cause side effects such as swelling and heaviness in the breast, sunburn-like skin changes in the treated area, and lymphedema (swelling of the arm due to fluid buildup) if the underarm lymph nodes were treated after a node dissection.

### **Drug Options Expand**

Drugs are used to reach cancer cells that may have spread beyond the breast—in many cases even if no cancer is detected in the lymph nodes after surgery. While doctors once believed that the spread of breast cancer could be controlled with extensive surgery, they now believe that cancer cells may break away from the primary tumor and spread through the bloodstream, even in the

earliest stages of the disease. These cells cannot be felt by examination or seen on x-rays or other imaging methods, and they cause no symptoms. But they can establish new tumors in other organs or the bones. The goal of drug treatment even if there's no detectable cancer after surgery, known as adjuvant therapy, is to kill these hidden cells. Not every patient, however, needs adjuvant therapy. Doctors will make recommendations regarding specific types of therapy based on the stage of the breast cancer. (See "Stages of Breast Cancer.")

FDA has approved several new drugs and new uses for older drugs in the past year that improve the chances of successfully treating breast cancer. These drugs include:

#### ***Herceptin***

About 30 percent of women with breast cancer have an excess of a protein called HER2, which makes tumors grow quickly. A genetically engineered drug, Herceptin (trastuzumab), binds to HER2 and kills the excess cancer cells, theoretically leaving healthy cells alone.

Herceptin, made by Genentech Inc., San Francisco, Calif., and approved by FDA in September 1998, is an intravenous treatment that is used alone in patients who have had little success with other drugs, or as a first-line treatment in combination with the drug Taxol (paclitaxel).

Recent follow-up research shows that Herceptin also may modestly extend the lives of terminal breast cancer patients. Updated survival figures reported from a two-year study by one of the drug's key developers from the University of California at Los Angeles showed the risk of death to be 16 percent lower in those getting Herceptin. Scientists say that while the improvement is small—it is especially noteworthy in a disease that until now has eluded many efforts to slow its progression to death.

Selection of patients who are most likely to benefit from Herceptin is im-

## Mammography: *A Lifesaving Step*



The American Cancer Society says that the best strategy for successfully beating breast cancer is to follow guidelines for early detection. Currently, the most effective technique for early detection is screening mammography, an x-ray procedure that can detect small tumors and breast abnormalities up to two years before they can be felt and when they are most treatable. (See "FDA Sets Higher Standards for Mammography" in the January-February 1999 *FDA Consumer*.)

Studies show that regular screening mammograms can help decrease the chance of dying from breast cancer. Finding a breast tumor early may mean that a woman can choose breast-saving surgery. Furthermore, she may not have to undergo chemotherapy.

To find a certified mammography facility near you, go to [www.fda.gov/cdrh/faclist.html](http://www.fda.gov/cdrh/faclist.html) on FDA's Website, or call the National Cancer Institute at 1-800-4-CANCER. ■

—C.L.

Kelly Munsell (top) has been in remission from breast cancer for two years. The FDA-approved drugs used in Kelly's treatments were not available years ago to her mother (bottom) and grandmother, who both died of breast cancer. (Yet family history is not a prerequisite for getting breast cancer. Only 5 to 10 percent of cases occur in women genetically predisposed to the disease.)



## New drugs, treatment regimens, and better diagnostic techniques are responsible for breast cancer death rates going down.

### Cancer Liaison Program

FDA's Cancer Liaison Program answers questions from patients, their friends and family members, and patient advocates about therapies for life-threatening diseases. The staff works closely with cancer patients, other federal agencies (including the National Cancer Institute), and cancer patient advocacy programs, listening to their concerns and educating them about the FDA drug approval process, cancer clinical trials, and access to investigational therapies.

For more information on the Cancer Liaison Program, call 301-443-4555 or 301-827-4460 or visit [www.fda.gov/oashi/cancer/cancer.html](http://www.fda.gov/oashi/cancer/cancer.html) on FDA's Website. ■

—C.L.

portant because of the possible serious risks from the drug, including weakening of the heart muscle that can lead to congestive heart failure.

FDA also approved in September a test called DAKO HercepTest to measure HER2 protein in tumors.

#### **Nolvadex**

A drug that has been used as a breast cancer treatment for more than 20 years, Nolvadex (tamoxifen citrate) was approved by FDA in October 1998 for breast cancer risk reduction in high-risk women.

Doctors know that estrogen promotes the growth of breast cancer cells. Tamoxifen interferes with the activity of estrogen by slowing or stopping the growth of cancer cells already present in the body. As adjuvant therapy, tamoxifen has been shown to help prevent the original breast cancer from returning, and also the development of new cancers in the other breast.

An NCI study showed that the drug reduced the chance of getting breast cancer by 44 percent in women who were judged to be at increased risk for the disease. FDA emphasizes, however, that tamoxifen, manufactured by Zeneca

Pharmaceutical Inc., Wilmington, Del., will not eliminate breast cancer risk completely, and should be used only following a medical evaluation of individual risk factors.

Due to potentially serious side effects, including endometrial (lining of the uterus) cancer and blood clots in major veins and the lungs, the American Society of Clinical Oncology recommends that patients talk with their regular health-care providers to determine whether individual medical circumstances and histories are appropriate for considering use of tamoxifen.

#### **Xeloda**

Xeloda (capecitabine), made by Hoffmann-La Roche, was approved by FDA in April 1998 for the treatment of breast cancer that has spread to other parts of the body (metastasized) and is resistant to both paclitaxel and an anthracycline-containing regimen. Xeloda does not kill the cancer cells directly. Instead, once the drug enters the cancer cells, it is metabolized to 5-fluorouracil (5-FU), a drug routinely used for breast cancer. The advantage of Xeloda, in addition to the convenience of its pill form, is that cancer cells ac-

tively convert it to 5-FU, but normal cells convert very little to 5-FU.

#### **Taxotere**

In May 1996, FDA gave accelerated approval to Taxotere (docetaxel) to treat patients whose locally advanced or metastasized breast cancer has progressed despite treatment with other drugs. The approval was conditional on the manufacturer, Rhône-Poulenc Rorer Pharmaceuticals, Inc., Collegeville, Pa., conducting additional studies. In June 1998, after additional studies confirmed its safety and effectiveness, FDA granted full approval.

Before these newer drugs, a doctor's first line of defense against breast cancer was to use combinations of the anticancer drugs Cytosan (cyclophosphamide) and Adriamycin (doxorubicin), with or without Aduvex (fluorouracil).

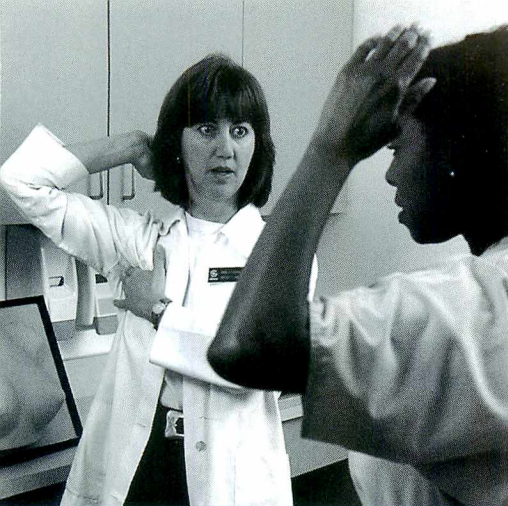
Chemotherapy (drug treatment) is given in cycles, with each period of treatment followed by a recovery period. The total course of chemotherapy can last three to six months, depending on the drugs and how far the cancer has spread.

Kelly Munsell of Tucson, Ariz., took the combination Adriamycin and Cytosan in six cycles, spaced three weeks apart, after doctors diagnosed her breast cancer in 1996 at age 27.

"Chemo for me was torture," Munsell recalls, describing profuse vomiting and severe weight gain as two of the serious side effects. But despite the discomfort, Munsell, whose mother and grandmother both died of breast cancer, is glad she underwent the grueling treatment two years ago. "My recent battery of tests came back negative for cancer," she says.

In addition to the drugs actually battling the disease, there also is help for patients in severe pain from cancer. FDA approved Actiq (oral transmucosal





## For More Information

Contact any of these organizations for more on breast cancer and support groups.

National Cancer Institute  
31 Center Drive, MSC 2580  
Bethesda, MD 20892-2580  
1-800-4-CANCER  
[www.nci.nih.gov](http://www.nci.nih.gov)  
<http://cancertrials.nci.nih.gov>

American Cancer Society  
1599 Clifton Road, N.E.  
Atlanta, GA 30329-4251  
1-800-ACS-2345  
[www.cancer.org](http://www.cancer.org)

National Alliance of Breast Cancer  
Organizations (NABCO)  
9 E. 37th St., 10th Floor  
New York, NY 10016  
1-800-719-9154 or (212) 719-0154  
[www.nabco.org](http://www.nabco.org)

Y-Me National Breast Cancer Hotline  
212 West Van Buren  
Chicago, IL 60607  
1-800-221-2141  
[www.y-me.org](http://www.y-me.org)

Susan G. Komen Breast Cancer  
Foundation  
5005 LBJ Freeway  
Suite 370  
Dallas, TX 75240  
1-800-IM-AWARE or 1-800-462-9273  
[www.pathology.washington.edu/komen/index.html](http://www.pathology.washington.edu/komen/index.html)

## Stages of Breast Cancer

Stages of breast cancer, according to the American Cancer Society, indicate the size of a tumor and how far the cancer has spread within the breast, to nearby tissues, and to other organs. Specific treatment is most often determined by the following stages of the disease:

**Carcinoma In Situ:** Cancer is confined to the lobules (milk-producing glands) or ducts (passages connecting milk-producing glands to the nipple) and has not invaded nearby breast tissue.

**Stage I:** Tumor is smaller than or equal to 2 centimeters in diameter and underarm (axillary) lymph nodes test negative for cancer.

**Stage II:** Tumor is larger than 2 centimeters in diameter with negative lymph nodes, or tumor is less than or equal to 5 centimeters with positive lymph nodes.

**Stage III:** This stage is divided into substages known as IIIA and IIIB:

- **IIIA:** Tumor is larger than 5 centimeters with positive lymph nodes, or tumor is any size with lymph nodes that adhere to one another or surrounding tissue.
- **IIIB:** Tumor of any size has spread to the skin, chest wall, or internal mammary lymph nodes (located beneath the breast and inside the chest).

**Stage IV:** Tumor, regardless of size, has metastasized (spread) to distant sites such as bones, lungs, or lymph nodes not near the breast.

**Recurrent breast cancer:** The disease has returned in spite of initial treatment. ■

—C.L.

fentanyl citrate) Nov. 5, 1998, as a treatment specifically for cancer patients with severe pain that breaks through their regular narcotic therapy. A narcotic more potent than morphine, Actiq is in the form of a flavored sugar lozenge that dissolves slowly in the mouth. Actiq is approved for patients already taking at least 60 milligrams of morphine per day for their underlying persistent cancer pain.

### Looking Ahead

It is important for every woman to consider herself at risk for breast cancer, ACS says, simply because she's female. At the same time, however, studies continue to uncover lifestyle factors and habits that can alter that risk, and many new chemotherapy drugs and drug

combinations that are being tested in clinical trials. Drugs and procedures currently under investigation include bisphosphonates (a group of drugs routinely used to treat osteoporosis), monoclonal antibodies (similar to Herceptin), and angiogenesis inhibitors (drugs that keep blood vessels that nourish cancer cells from developing).

"While death rates from breast cancer are falling, and while there are a number of exciting new strategies being developed," says Michael A. Friedman, M.D., FDA's deputy commissioner for operations and former cancer research specialist, "we recognize that a great deal more needs to be done." ■

*Carol Lewis is a staff writer for FDA Consumer.*



# Attacking AIDS

## With a 'Cocktail' Therapy

by John Henkel

### Drug Combo Sends Deaths Plummeting

It was spring of 1996 when Beth Bye says she returned from the dead. The Wisconsin woman hadn't actually died, but with her body ravaged in the late stages of AIDS infection, she had run out of options, and death was, indeed, near. AIDS-related dementia and blindness had crept in—signs that her doctor told her meant time was short. She made funeral arrangements and considered moving to a hospice for her remaining days.

Then, as if to say “not so fast,” medical science handed her another option. New drugs called protease inhibitors, first approved in 1995, were about to revolutionize the treatment of patients infected with the AIDS virus. These drugs usually are taken with two other drugs called reverse transcriptase inhibitors. The combined drug “cocktail” has helped change AIDS in the last three years from an automatic death sentence to what is now often a chronic, but manageable, disease.

Within two months of beginning the triple cocktail treatment, also known as highly active antiretroviral therapy (HAART), Bye's viral load—a measure of new AIDS virus produced in the body—dropped to undetectable levels. Her red and white blood cell counts normalized, an important sign that the immune system was starting to work again. Suddenly she could do simple things she had long given up, such as walk the dog for 2 miles. Bye, now 40, was even able

to return to her teaching job and currently works 30 hours a week.

“My recovery was like being on death row and getting that last minute pardon from the governor,” she says.

This so-called “Lazarus Effect,” named for the biblical figure who was raised from the dead, has occurred with many AIDS patients who take the triple therapy. “It returns many who were debilitated and dying to relatively healthy and productive life,” says Richard Klein, HIV/AIDS coordinator for the Food and Drug Administration's Office of Special Health Issues.

Many health experts, in fact, credit the powerful HAART therapy with helping the domestic AIDS death rate to drop by 47 percent in 1997, the last year for which figures are available. Other factors have contributed as well, says Anthony Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases. “It is also likely that increased access to care, our growing expertise

and experience in caring for HIV-infected people, and the decrease in new HIV infections in the late 1980s due to prevention efforts are partly responsible for the reduction in HIV-related deaths we are seeing today.”

In 1997, for the first time since 1990, AIDS fell out of the top 10 causes of death in the United States, dropping from 8th to 14th place, according to the national Centers for Disease Control and Prevention. By 1998, about 16,000 people were still alive who would have died the previous year if AIDS mortality had continued at its former rate. Still, about 40,000 new infections occur yearly.

### A 'One-Two Punch'

So far, the combination HAART treatment is the closest thing medical science has to an effective therapy. The key to its success in some patients lies in the drug combination's ability to disrupt HIV at different stages in its replication. Re-  
*(Continued on page 14)*



**“My recovery was like being on death row and getting that last minute pardon from the governor.”**

**—Beth Bye, AIDS patient**

## **Speeding AIDS Drug Approvals**


With the emergence of AIDS, FDA put into place a program in the late 1980s that allows promising therapies for life-threatening illnesses to be approved conditionally before all necessary studies are completed. A key goal is to make treatments available to desperately ill patients who might have to wait years under the formal clinical trial and drug approval system for the same drug to be marketed.

Under the agency's accelerated approval regulations, a drug can be marketed without studies that show direct effects on clinical disease progression or death. Instead, FDA relies on “surrogate markers,” such as viral load, which are laboratory measurements intended to reliably predict a drug's ultimate clinical benefits.

FDA has three requirements for accelerated approval:

- The surrogate must have a “reasonable certainty” of predicting actual future clinical benefit.
- The drug's sponsor must complete postmarketing studies, providing the required data to verify the drug's clinical benefit.
- The sponsor must prove clinical benefit in a timely manner or FDA will revoke the accelerated approval. ■

—J.H.



AIDS patient Beth Bye displays a day's worth of prescription pills that make up the “triple cocktail” therapy she's been on since 1996. She credits the drug regimen with bringing her back from the brink of death and allowing her to return to a fairly normal lifestyle.



# What Is AIDS?

AIDS is a chronic disease that damages, and ultimately destroys, the immune system. Though HIV causes AIDS, many patients who test positive for the virus have not progressed to AIDS. According to the national Centers for Disease Control and Prevention, an AIDS diagnosis requires a positive confirmed blood test for HIV antibodies and at least one of the following:

- an opportunistic infection such as pneumocystis pneumonia
- an AIDS-related cancer, severe wasting, or dementia
- a reduction in the amount of the helper T cells—also called CD4 cells—that play a critical role in proper functioning of the immune system to below a count of 200 (healthy people usually have a helper T cell count between 600 and 1,000).

HIV depends on the cells it infects to make new copies of itself. The copies then infect other cells, spreading the virus. HIV destroys CD4 cells, and when the level of these white blood cells drops, the immune system weakens, allowing microorganisms that don't harm people with normal immune responses to cause serious infections in those with HIV.

HIV is transmitted primarily by sex (anal, vaginal or oral sex with an infected partner), by injections (sharing contaminated needles for drug use or accidental piercing with a contaminated needle), or from infected mother to child through pregnancy or breast-feeding.

Some HIV-infected patients progress to AIDS quickly while others can remain healthy for 10 years or more. Between initial infection and full-blown disease, a

middle phase called symptomatic HIV infection, or AIDS-related complex (ARC), occurs, prompting symptoms such as weight loss, diarrhea, and swollen lymph glands.

Scientists have recently discovered clues to why some patients develop AIDS quickly. In a study published last March in the journal *Science*, National Cancer Institute researchers found that inherited genes may set the clock for AIDS progression. Certain gene patterns tend to stave off AIDS, while others promote it. The researchers say the study may help lead to an AIDS-preventive vaccine or improved therapies against the virus. ■

—J.H.

(Continued from page 12)  
verse transcriptase inhibitors, which usually make up two drugs in the HAART regimen, restrain an enzyme crucial to an early stage of HIV duplication. Protease inhibitors hold back another enzyme that functions near the end of the HIV replication process. The combination can be prescribed to those newly infected with the virus, as well as AIDS patients.

FDA approved the first drug specifically to combat HIV and AIDS in 1987. Commonly known as AZT (zidovudine), it is in the family of reverse transcriptase inhibitors called nucleoside analogs. Others in this class include ddi (didanosine), ddC (zalcitabine), D4T (stavudine), 3TC (lamivudine), and most recently Ziagen (abacavir). In 1997, FDA approved Combivir, a mixture of AZT and 3TC that allows patients to reduce the number of pills needed, which can be upwards of 20 a day for certain drug combinations.

Viramune (nevirapine), the first reverse transcriptase inhibitor in a class called non-nucleoside analogs, was approved in 1996. The following year,

FDA approved a related drug, Rescriptor (delavirdine). In 1998, a third drug in this class, Sustiva (efavirenz) was approved.

Protease inhibitors, the last part of the triple cocktail, have only been on the market about three years. FDA approved the first one, Invirase (saquinavir), in late 1995.

Others approved since include Norvir (ritonavir), Crixivan (indinavir), Viracept (nelfinavir), and Agenerase (amprenavir). Viracept was the first of its class to be labeled for use in children and adults. Norvir and Agenerase are now approved for children as well. FDA also has approved Fortovase, a new formulation of saquinavir that comes in a soft gelatin capsule that allows more drug to be absorbed into the body than the earlier version.

## Regimen Has Drawbacks

Though the use of protease inhibitors with other AIDS drugs has had a drastic impact on the health of HIV and AIDS patients, there are drawbacks. For example, the HAART treatment is not an AIDS cure, says FDA's Klein. Though HIV, the virus that causes AIDS, may not be detectable in the blood following

successful HAART treatment, experts generally feel that the virus is still present, lurking in hiding spots such as the lymph nodes, the brain, testes, and the retina.

"The improved sense of well-being, and the belief that lower viral load means they will not transmit the virus, has translated, in some communities, to a lapse in certain prevention practices," Klein says. He adds that this is dangerous because infected people, even with diminished viral counts, can spread the virus.

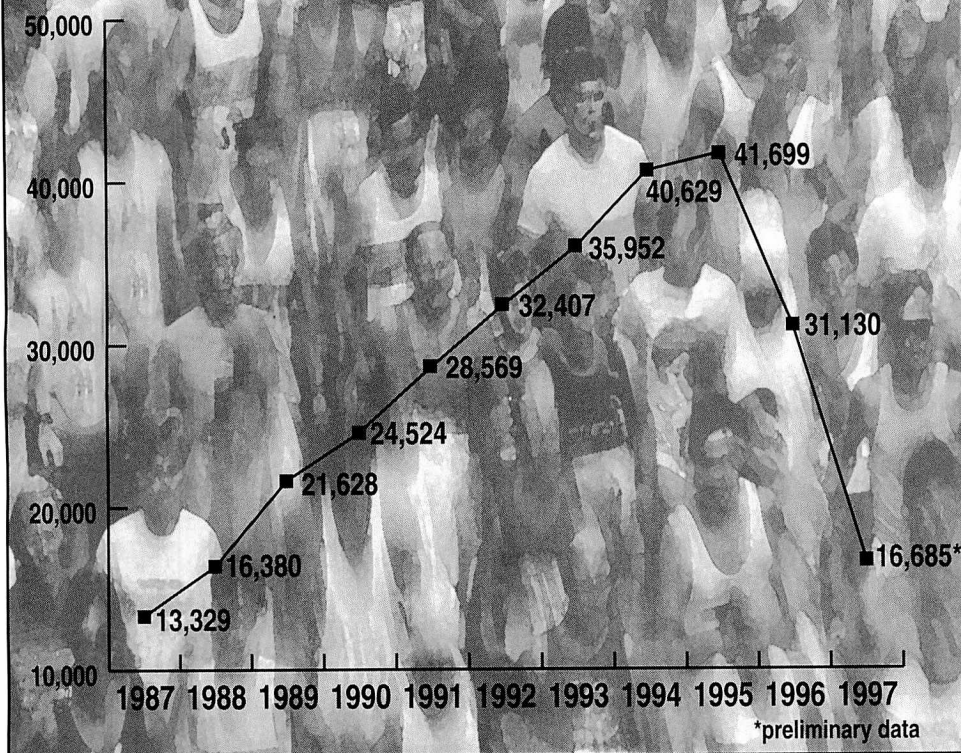
Another concern is that the combination therapy, besides being very expensive, requires a much more complicated treatment regimen. "Patients need to stay aware of and adhere to their dosing schedule," says Klein. "If not taken on a strict regimen, protease inhibitors can result in the emergence of HIV strains that are resistant to treatment." Numerous studies also have shown that viral load can rapidly "rebound" to high levels if patients discontinue part or all of the triple therapy regimen.

AIDS treatments may interact with many commonly prescribed drugs. For example, Pfizer Inc. plans to label its



## AIDS Deaths Since 1987

This chart includes deaths for all ages, races, and both genders. Though the AIDS epidemic began around 1979, data on deaths were unreliable until 1987. Figures from 1997 are preliminary.



Source: National Center for Health Statistics

impotence drug Viagra to warn of possible interactions with certain protease inhibitors, which appear to raise levels of Viagra in the blood.

AIDS drugs also may prompt onset of diabetes or a worsening of existing diabetes and hyperglycemia (high blood sugar), along with increased bleeding in people with hemophilia types A or B.

Some patients on triple therapy have experienced a type of weight redistribution where face and limbs become thin while breasts, stomach or neck enlarges. Some have nicknamed the appearance of fat deposits at the back of the shoulders "buffalo hump." Fat deposits in the mid-section are sometimes called "Crix belly," after the drug Crixivan, "although it has been seen in people taking all approved protease inhibitors," says Klein.

Research is currently under way to determine if protease inhibitors cause a permanent change in fat metabolism. "There is considerable concern over the

long-term effects for patients," says Klein, including the possibility that the cholesterol increases in some patients who experience fat redistribution could increase the risk for cardiovascular complications such as strokes or heart attacks. FDA has asked each of the makers of protease inhibitors to study these abnormalities.

### AIDS-Related Illnesses

Because AIDS patients have suppressed immune systems, they can fall prey to certain illnesses that people with healthy immune responses don't get, or get only very rarely. One common such illness is *Pneumocystis carinii* pneumonia (PCP), which can be life-threatening. Treatments to prevent PCP are NebuPent (aerosolized pentamidine), a fine mist inhaler, and drugs such as Bactrim and Septra that contain both trimethoprim and sulfa. Mepron (atovaquone) is approved for treating mild-to-moderate

PCP in pregnant women and patients who cannot tolerate standard treatment. Neutrexin (trimextrate glucuronate) also is approved for pregnant women and for moderate-to-severe PCP when given with Leucovorin (folinic acid).

Cytomegalovirus retinitis is a potentially severe AIDS-related eye infection that can lead to blindness. Approved treatments include ganciclovir, marketed as Cytovene in oral dosage and as Vitroset as an implant, Foscavir (foscarnet), and Vistide (cidofovir).

For mycobacterium avium, an infection that before AIDS was almost always confined to patients with severe chronic lung diseases such as emphysema, FDA has approved Biaxin (clarithromycin), Mycobutin (rifabutin), and Zithromax (azithromycin).

Kaposi's sarcoma (KS) is a type of AIDS-related cancer that causes characteristic purple or pink skin tumors that are flat or slightly raised. Intron A (human interferon-alpha), doxorubicin liposome injection, or daunorubicin citrate liposome injection can be used to treat KS. Panretin, a topical gel, also is approved for treating certain types of KS lesions.

AIDS wasting syndrome involves major weight loss, chronic diarrhea or weakness, and constant or intermittent fever for at least 30 days. Approved treatments include Marinol (dronabinol), Megace (megestrol), and Serostim (somatropin rDNA for injection).

### Pregnant Women and Children

In 1998 recommendations, the Public Health Service Task Force stated that the decision to take anti-HIV drugs during pregnancy should be made by the pregnant woman after her health-care provider has explained benefits and risks. There are some compelling reasons to take the drugs. For example, an HIV-positive pregnant woman who takes AZT after the first trimester decreases the chance of the baby being born with HIV. Studies show that AZT taken according to a strict regimen decreases by nearly 66 percent the odds of infecting the newborn.

The task force says women should consider delaying therapy until after the 10th to 12th week of pregnancy, after the



# For More Information

These organizations have more information on AIDS, clinical trials of treatments, and support groups:

FDA Office of Special Health Issues  
[www.fda.gov/oashi/aids/hiv.html](http://www.fda.gov/oashi/aids/hiv.html)

AIDS Clinical Trials Information Service (ACTIS)  
1-800-874-2572  
[www.actis.org](http://www.actis.org)

AIDS Education Global Information System (AEGIS)  
(949) 248-5843  
[www.aegis.com](http://www.aegis.com)

CDC National AIDS Clearinghouse  
P.O. Box 6003  
Rockville, MD 20849-6003  
1-800-458-5231

CDC National AIDS Hotline  
1-800-342-2437 (English)  
1-800-344-7432 (Spanish)  
1-800-243-7889 (TTY)

CDC Division of HIV/AIDS  
Prevention Homepage  
[www.cdc.gov/nchstp/hiv\\_aids/dhap.htm](http://www.cdc.gov/nchstp/hiv_aids/dhap.htm)

HIV/AIDS Treatment Information Service  
P.O. Box 6303  
Rockville, MD 20849-6303  
1-800-448-0440  
[www.hivatis.org](http://www.hivatis.org)

HIV InfoWeb  
[www.infoweb.org](http://www.infoweb.org)

Johns Hopkins AIDS Service  
[www.hopkins-aids.edu](http://www.hopkins-aids.edu)

## AIDS on Its Own Terms

Understanding AIDS and its treatment requires knowledge of a specialized vocabulary. Here are some commonly used AIDS terms:

**AIDS**—late stages of infection with the human immunodeficiency virus (HIV).

**AIDS-related complex (ARC)**—a disorder in which patients have some symptoms of HIV infection, such as weight loss and diarrhea. Also called HIV disease.

**Antibodies**—proteins produced in the blood that in a healthy immune system can prevent infection from foreign substances such as viruses.

**Antiretrovirals**—drugs such as AZT, ddC or ddI that can suppress the activity of HIV.

**CD4 cells (also called T4 cells or T-helper cells)**—a type of white blood cell that helps the body fight infection. When HIV enters CD4 cells, it inactivates or destroys them.

**CD4 cell count**—a critical indicator of AIDS progression that gauges the number of CD4 cells in one cubic millimeter of blood. Healthy adults usually have CD4 counts between 600 and 1,000. A count below 200 indicates severe suppression of the immune system.

**Cytomegalovirus (CMV) retinitis**—an eye infection common in AIDS patients that can lead to blindness.

**Dementia**—memory loss or other lessening of intellectual capabilities caused by HIV.

**Human immunodeficiency virus (HIV)**—a retrovirus that destroys CD4 cells and causes AIDS.

**Mycobacterium avium complex (MAC)**—an AIDS-related disorder caused by an organism that can infect the body at multiple sites by spreading through the blood.

**Non-nucleoside reverse transcriptase inhibitors**—drugs that interfere with HIV duplication by binding to the reverse transcriptase enzyme and thereby inhibiting its activity.

**Nucleoside analogs**—drugs such as AZT that suppress HIV duplication by interfering with the reverse transcriptase enzyme.

**Pneumocystis carinii pneumonia (PCP)**—a type of pneumonia, rare in people with normal immune systems, that is common in AIDS patients.

**Protease inhibitors**—drugs such as Invirase and Crixivan that interrupt a key step in the action of the enzyme protease, thus interfering with the chemical sequence of HIV duplication.

**Reverse transcriptase**—an enzyme required for HIV to duplicate itself.

**Triple “cocktail” therapy**—use of a three-drug regimen to combat HIV infection. One of the three is usually a protease inhibitor. ■



**In 1997, for the first time since 1990, AIDS fell out of the top 10 causes of death in the United States.**

*(Continued from page 15)*

fetus's organs have gone through their most rapid development. This delay may minimize any adverse effects of AZT on fetal development, but it needs to be balanced with the health of the mother and possible transmission of HIV to the fetus.

Most children with HIV became infected from their mothers near the time of birth. This means that for many babies, treatment can be started soon after birth. Federal guidelines recommend that all HIV-infected children younger than 1 year and all HIV-infected children of any age with symptoms of HIV infection or evidence of immune suppression be treated with anti-HIV drugs. For HIV-infected children with no symptoms, therapy can be deferred if risk of disease is considered low based on viral load and immune status.

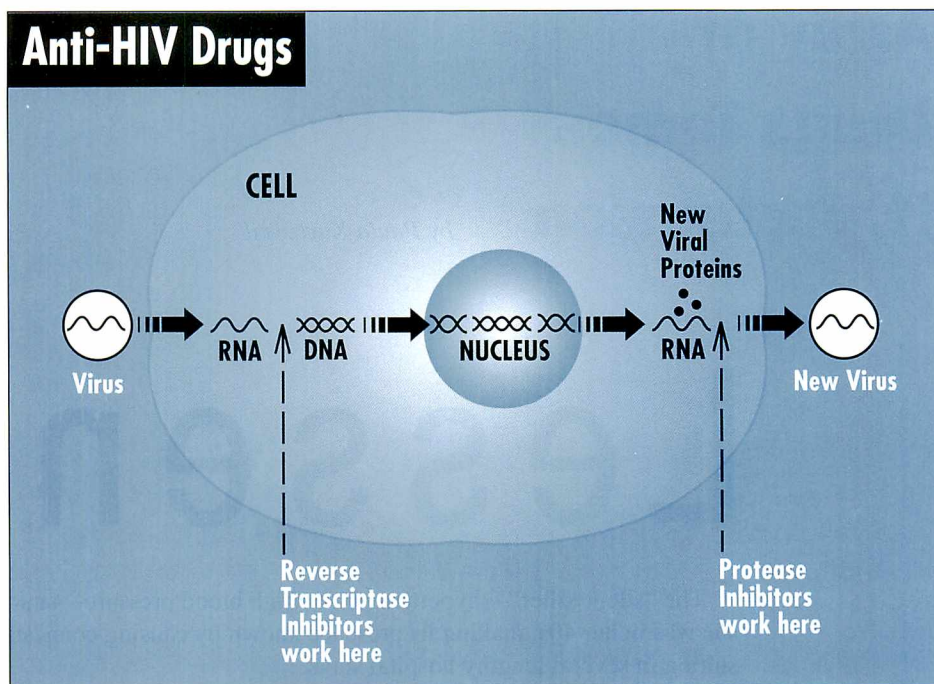
Triple combination therapy can be used for all HIV-infected infants, children and adolescents treated with HIV drugs. Infants during the first six weeks of life who have been exposed to HIV but whose HIV status is unknown can be treated with AZT as sole therapy. Infants diagnosed with HIV while receiving AZT alone should be switched to combination therapy.

#### **In the Future**

Though the AIDS death rate has dropped drastically, and educational efforts aimed at curbing the number of new HIV infections have had a small impact, experts say the next hurdles are to develop an AIDS-preventive vaccine and to create new therapies, such as ones that would effectively treat AIDS patients when drug-resistant strains of HIV develop. On both fronts, promising efforts are in progress.

For example, NIAID is conducting trials of three novel HIV vaccine ap-

## **Anti-HIV Drugs**



Source: National Institutes of Health

Reverse transcriptase inhibitors and protease inhibitors, the drugs in the highly active antiretroviral therapy (HAART) regimen, provide a "one-two punch," interrupting HIV's replication cycle at different points and reducing the virus in many cases to undetectable levels.

proaches. One trial is testing a vaccine applied to spots such as the moist tissues lining the urinary and reproductive tracts. This is because most HIV infections, such as those acquired through sexual exposure, are transmitted across these "mucosal" sites. Researchers theorize that a vaccine that prompts the body to produce antibodies at these sites may have a protective effect against the AIDS virus.

Another vaccine approach is using common *Salmonella* bacteria to deliver HIV proteins in a way that may trigger the body to produce a better immune response. A third study is examining a cancer drug, GM-CSF, to determine its effect on stimulating immunity. NIAID also is experimenting with a vaccine approach that "neutralizes" antibodies to HIV, which then bind to the virus in a way that may prevent it from infecting cells.

A new class of drugs called fusion inhibitors has been shown in early trials to block HIV's entry into cells, which may keep the virus from reproducing. These drugs hold particular promise for patients whose HIV viral loads have re-

bounded to elevated levels because the virus strains they carry have become resistant to triple combination therapy. Researchers reported at the 6th Conference on Retroviruses and Opportunistic Infections in February 1999 that one fusion inhibitor, T-20, significantly lowered virus amounts in a group of patients with drug-resistant viral strains.

Other therapies aimed at eradicating the virus that remains after successful combination treatment include drugs targeted at bolstering the immune system such as IL-2 (Interleukin-2) and G-CSF (Neupogen).

Though these and other potential treatments may individually or in combination help wipe out AIDS sometime in the future, what's really needed, says NIAID's Fauci, are types of drugs that don't yet exist. "These agents would ideally be potent, inexpensive, relatively nontoxic even after prolonged periods, active against viral strains resistant to currently available agents, and easy to administer." ■

*John Henkel is a staff writer for FDA Consumer.*



## **Array of Drugs Tames Hypertension**

*by Paula Kurtzweil*

# Lessening

The “silent killer”—hypertension, or high blood pressure—snuck up on my mother when she was in her 40s, making its presence known by causing congestive heart failure and resulting in several lengthy hospital stays.

Though her blood pressure measured as high as 250/150 during those initial touch-and-go days, she’s maintained a much-closer-to-normal blood pressure for the past 30 years, thanks to daily doses of antihypertensive drugs.

# The

Today’s range of drugs for treating high blood pressure makes it possible for people like my mother and the nearly 50 million other Americans who suffer from high blood pressure to lead normal, healthy lives well into their senior years. Exercise, regular blood pressure checks, healthy eating, maintenance of a healthy body weight, and other lifestyle changes can make a big difference, too.

Without these treatments, people with consistently high blood pressure face increased risks for heart attack, stroke and kidney disease. High blood pressure also can cause blood vessels on the eye’s retina to clog, eventually bursting and possibly damaging parts of the retina and impairing vision.

# Pressure

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**Regular Checkups  
Essential to Catch  
Symptomless Condition**





### What Is Blood Pressure?

Blood pressure is the force of blood against the blood vessel wall. High blood pressure occurs when there is increased tension or pressure in the arteries. The greater the pressure, the harder the heart has to work.

Blood pressure is measured with a device called a sphygmomanometer, which can be either manual or electronic. The blood pressure reading is written as a fraction: for example, 120/80.

The first number is the systolic pressure, which is the point at which the heart contracts to push the blood out to the rest of the body. When blood pressure is taken manually, this is the number at which a person taking the blood pressure first hears a pulse through the stethoscope. When an electronic device is used, the number appears on the display.

The second number is called the diastolic pressure, which represents the lowest point in the pressure of blood—right before another squirt of blood enters the arteries. When the blood pressure is

measured manually, this number is the point at which the person listening through the stethoscope stops hearing a pulse. On an electronic device, this number also automatically appears on the display.

Many people think that 120/80 is the perfect or normal blood pressure. But, says Robert Fenichel, M.D., deputy director of FDA's division of cardiovascular and renal drug products, "If your pressure is lower than that, good for you."

### Deciding What's High

Elevated blood pressure rarely makes itself known; it usually has no symptoms. That's why it's often referred to as the silent killer. Feeling nervous or tense, for example, doesn't necessarily translate into elevated blood pressure. Getting periodic blood pressure checks is the only way to catch high blood pressure early.

According to the National Heart, Lung, and Blood Institute of the National Institutes of Health, a blood pressure reading consistently higher than

Elizabeth Kurtzweil, 73, of Whitewater, Wis., checks her blood pressure at home with an electronic device. Daily readings enable her—and her doctor—to see how well the medicines she takes control her high blood pressure.

140/90 is a sign that the blood pressure needs to be brought under control.

Most doctors don't diagnose a person with high blood pressure on the basis of only one reading. People who find a visit to the doctor's office unnerving can have "white-coat hypertension," blood pressure that is only high when taken in the doctor's office. ("White coat" refers to the ubiquitous white lab coats many health professionals wear.) Others may have "labile hypertension," blood pressure that gets slightly elevated in certain situations but which is normal most of the time.

To rule these out, doctors may take a



patient's blood pressure later during the office visit and ask the patient to come back for two more visits, taking two readings during each of those visits. Many doctors also ask patients with elevated blood pressure to have their blood pressure checked in a setting other than a medical one. With one of the many electronic blood pressure measuring devices that consumers can buy without a doctor's prescription, patients often can check and record their blood pressure at home. To get as accurate a reading as possible, the doctor may ask the patient to bring the device in to the office to make sure it is calibrated properly. This can usually be done by comparing the device's readings with readings taken at the same time with the doctor's blood pressure equipment.

If a patient has consistently high readings in and out of the medical setting, the doctor will decide what type of treatment is appropriate: diet modification, increased exercise, medicine, or a combination of these.

## Treating Hypertension

Treatment can vary with the level of elevation of the blood pressure, as well as the patient's age and health. According to FDA's Fenichel, sometimes lifestyle changes can reduce blood pressure by 5 points or so. They include stopping smoking, reducing alcohol intake, losing excess weight, and making certain dietary changes, such as reducing sodium intake and possibly increasing potassium, calcium and magnesium intake. (See "Diet and Blood Pressure.") Some experts also recommend exercise and relaxation techniques, such as meditation.

"But," Fenichel says, "treatment with drugs is the only effective approach for attaining larger reductions in blood pressure."

FDA has approved numerous drugs for treating hypertension. These drugs work in different ways but the end result—reducing blood pressure—is the same.

Some of the most commonly used drugs to treat high blood pressure are:

## Who's at Risk?

Those at greater risk for high blood pressure, according to the National Heart, Lung, and Blood Institute, include:

- African Americans
- people with a family history of high blood pressure
- people who drink alcoholic beverages excessively
- people who are physically inactive

In addition, as many as 65 percent of people with diabetes have high blood pressure. ■

—P.K.

• **Diuretics.** Sometimes called "water pills," these drugs flush excess water and sodium from the body by increasing urination. This reduces the amount of fluid in the blood and flushes sodium from the blood vessels so that they can open wider, increasing blood flow and thus reducing the blood's pressure against the vessels. Often diuretics are used in combination with other high blood pressure drugs. Types of diuretics include thiazides, such as Diuril (chlorothiazide) and Esidrex (hydrochlorothiazide); potassium-sparing diuretics, such as Aldactone (spironolactone); and loop diuretics, such as Lasix (furosemide).

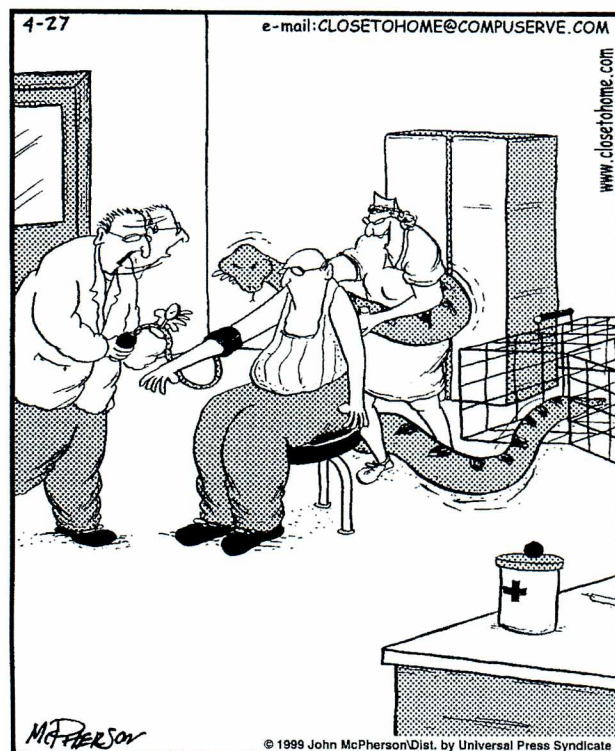
• **Beta blockers.** These drugs slow the heartbeat by blocking the effect of nerve impulses to the heart and blood vessels, thereby lessening the burden on the heart. Beta blockers include Inderal (propranolol), Lopressor (metoprolol), and Tenormin (atenolol).

• **ACE (angiotensin-converting enzyme) inhibitors.** These inhibit formation of the hormone angiotensin II, which causes blood vessels to narrow, thus increasing blood pressure. ACE inhibitors include Altace (ramipril), Capoten (captopril), and Zestril (lisinopril).

• **Calcium channel blockers.** These prevent calcium from entering the muscle cells of the heart and blood vessels, thus relaxing blood vessels and decreasing blood pressure. Some calcium channel blockers are Procardia (nifedipine), Isonipin (verapamil) and Cardiazem (diltiazem).

(Continued on page 23)

## CLOSE TO HOME JOHN MCPHERSON



"OK, last time your blood pressure was a bit on the high side. Let's see how it is ...  
KNOCK IT OFF, Mrs. Halstead!"

CLOSE TO HOME Copyright 1999 John McPherson. Reprinted with permission of UNIVERSAL PRESS SYNDICATE. All rights reserved.



# Diet And Blood Pressure

If you are overweight and have high blood pressure, a first step is to lose weight, usually through a combination of calorie reduction and increased physical activity. Eating certain kinds of food and avoiding others also may help you reduce your blood pressure or keep it from getting high in the first place.

Some dietary factors to consider in preventing and treating hypertension are:

## Salt and Sodium

Many studies in diverse populations have shown that a high-sodium intake is associated with higher blood pressure. The National Academy of Sciences, the American Heart Association, and the federal government's "Dietary Guidelines for Americans" recommend limiting sodium intake to 2,400 milligrams a day.

For cooking at home, low-salt and low-sodium cookbooks abound. Or simply spare the salt and, if you like, substitute other spices and flavorings, such as pepper, garlic, ginger, onion, or lemon juice. Watch out for some flavorings and ingredients, such as monosodium glutamate (Accent, for example), soy sauce, and some spice mixtures that contain large quantities of sodium.

Also, many processed foods are high in salt and other sodium-containing ingredients.

You can tell how much sodium is in packaged foods by reading the Nutrition Facts panel on food labels. There, manufacturers must list the amount of sodium (in milligrams) in a serving of the food and show (as a percentage) how that amount contributes to the daily reference

value for sodium, which is 2,400 milligrams.

To quickly identify foods with lower sodium contents, look for products with label claims like "no salt added," "low sodium," or "two-thirds less salt." These claims must meet government-enforced definitions, so that they mean the same for any product on which they appear.

If you eat out a lot, you may want to ask restaurants to hold the salt in your orders. Some may already offer lower sodium foods on their menus, so look for menu items with claims like "low sodium." Nutrition claims on menus must mean the same as they do on packaged food. (See "Today's Special: Nutrition Information" in the May-June 1997 *FDA Consumer*.)

Before using salt substitutes, which contain potassium chloride, check with your doctor just to make sure they're all right for you. In general, an increase in potassium can help attain a normal blood pressure, but there may be other factors, such as medicines you are taking and other health factors, that need to be considered.

(For more on salt in the diet, see "A Pinch of Controversy Shakes Up Dietary Salt" in the November-December 1997 *FDA Consumer*.)

## Alcohol

Some studies show that low to moderate consumption of alcohol, especially wine, may help reduce heart disease risks. But excessive amounts of alcohol are known to raise blood pressure. Also, if you're trying to lose weight, you need

to remember that alcoholic beverages are calorie dense, providing about 100 to 145 calories a drink but little nutritional benefit. Ask your doctor what is best for you when it comes to alcohol consumption.

## Calcium and Magnesium

Some studies have shown that people whose intakes of calcium are low are more likely to have high blood pressure, but a link has not been proven. The same is true of magnesium. Though the science is uncertain at this time, it can't hurt to eat a diet with sufficient calcium and magnesium. Good sources of calcium are dairy products, such as milk, yogurt and cheese. Choose low-fat or nonfat versions of these foods. Other sources of calcium are canned salmon, collard greens, broccoli, soy milk, tofu, and calcium-fortified orange juice and grain products. Good sources of magnesium are whole grains, green leafy vegetables, nuts, and legumes.

Check the Nutrition Facts panel on food labels to learn how much calcium is in a food. The amount of calcium in a serving and how that amount contributes to the daily reference value for calcium must be listed for all foods. Information about a food's magnesium content may be offered voluntarily.

## DASH Diet

In 1997, the National Heart, Lung, and Blood Institute of the National Institutes of Health released an eating plan that was found in clinical studies to lower systolic blood pressure by 5.5 points and diastolic pressure by 3. According to researchers, blood pressure reductions were seen within two weeks of starting the meal plan and maintained for the rest of the eight weeks of study by men, women, whites, and minorities alike. This meal plan, called Dietary Approaches to Stop Hypertension, or DASH for short, calls for a food intake similar to that recommended in the federal government's "Dietary Guidelines for Americans."

More information on the DASH diet is available on the Internet:

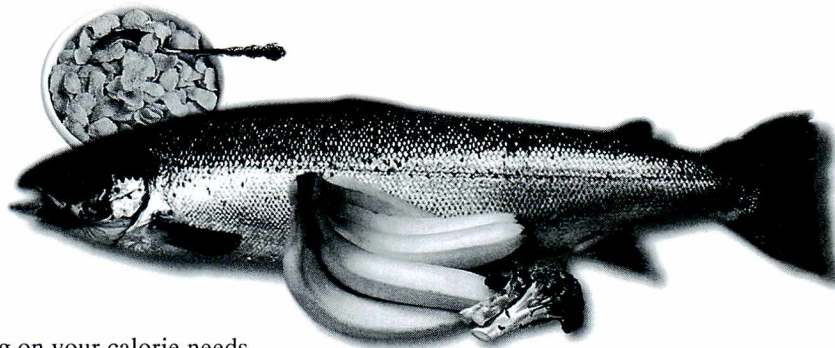
- <http://dash.bwh.harvard.edu/dashdietservings.html>
- [www.nhlbi.nih.gov/nhlbi/cardio/hbp/gp/dashdiet.htm](http://www.nhlbi.nih.gov/nhlbi/cardio/hbp/gp/dashdiet.htm). ■



It's easy to compare the sodium content of similar foods by checking the Nutrition Facts panels of food labels. The labels here show the difference in sodium content between regular (left) and reduced-sodium canned chicken noodle soup.



# DASH Diet



This meal plan is based on 2,000 calories a day. Depending on your calorie needs, your number of daily servings may vary from those listed. Consult your doctor or a dietitian to determine your calorie needs.

Food Group	Daily Servings	Serving Size
Grains and grain products	7 to 8	1 slice bread 2 to 1 <sup>1</sup> / <sub>4</sub> cup dry cereal 2 cup cooked rice, pasta, or cereal
Vegetables	4 to 5	1 cup raw leafy vegetables 2 cup cooked vegetable 6 oz vegetable juice
Fruits	4 to 5	6 oz fruit juice 1 medium fruit 1 <sup>1</sup> / <sub>4</sub> cup dried fruit 2 cup fresh, frozen or canned fruit
Low-fat or nonfat dairy foods	2 to 3	8 oz milk 1 cup yogurt 1.5 oz cheese
Meats, poultry, fish	2 or fewer	3 oz cooked lean meat, poultry (skinless white meat), or fish
Nuts, seeds and dry beans	4 to 5 per week	1 <sup>1</sup> / <sub>3</sub> cup nuts 2 Tbsp seeds 1 <sup>1</sup> / <sub>2</sub> cup legumes
Fats and oils	2 to 3	1 tsp soft margarine or butter 1 tsp regular mayonnaise <i>or</i> 1 Tbsp low-fat mayonnaise 1 Tbsp salad dressing <i>or</i> 2 Tbsp "light" salad dressing 1 tsp oil (olive, corn, canola, safflower, or other)
Sweets	5 per week	1 Tbsp maple syrup, sugar or jelly 1 <sup>1</sup> / <sub>2</sub> cup sherbet 3 pieces of hard candy

(Source: National Heart, Lung, and Blood Institute)



# Treating High Blood Pressure

Blood Pressure Stages (mm Hg)	No Risk	Medium Risk*	High Risk**
High-normal (130-139/85-89)	Lifestyle changes	Lifestyle changes	Lifestyle changes and drug therapy
Stage 1 (140-159/90-99)	Lifestyle changes (up to one year)	Lifestyle changes (up to six months)	Lifestyle changes and drug therapy
Stages 2 and 3 (160 or higher/ 100 or higher)	Lifestyle changes and drug therapy	Lifestyle changes and drug therapy	Lifestyle changes and drug therapy

\* have one or more of these risk factors: smoking, abnormal blood lipid levels, diabetes, over 60 in age, male or postmenopausal female, or family history of heart disease involving women under 65 or men under 55

\*\* have heart disease, history of stroke, kidney disease, diabetes, the eye disease retinopathy, or peripheral arterial disease with or without other risk factors

(Source: National Heart, Lung, and Blood Institute's *Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure*, 1997)

(Continued from page 20)

• **Alpha-beta blockers.** These combine the actions of alpha blockers, which relax blood vessels, and beta blockers, which slow the heartbeat. The dual effect reduces the amount—and thus pressure—of blood through blood vessels. Alpha-beta blockers include Normodyne and Trandate (both labetalol).

Often, combinations of two drugs from different classes are used to improve the drugs' effectiveness.

Many doctors begin newly diagnosed hypertensive patients with diuretics or beta blockers. The Sixth Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, released by NIH's National Heart, Lung, and Blood Institute in November 1997, recommends diuretics or beta blockers as the first line of treatment. However, based on a patient's situation—for example, use of other medicines—doctors may choose to start treatment with another antihypertensive drug.

Some specifics to JNC's first-line recommendation are noted in the report—for example, it recommends that in African Americans, one of the groups most at risk for hypertension, diuretics alone should be the first agent of choice—pro-

vided there are not other conditions that prohibit their use—because of this group's increased sensitivity to salt. For hypertensive people with diabetes or kidney disease, the guidelines recommend that initial drug treatments include ACE inhibitors.

## Finding What Works

Like most drugs, blood pressure medicines can have side effects, ranging from the unpleasant—such as skin rash, sleepiness and weight gain—to the severe, including depression, hallucinations, heart dysfunction, and liver disease. Patients who begin a drug treatment and develop symptoms that they did not have before should discuss them with their doctors. With the great variety of medicines, it is likely that another antihypertensive drug or dosage level can help control blood pressure with few or no side effects.

In my mother's 30-year history of high blood pressure, she's switched drugs only a few times or varied the dosages, mainly to gain better control of her blood pressure. But she's never had any qualms about taking the medicine.

"I had a lot of relatives who probably had the same problem I do, but they died early because they didn't have the medi-

cines that they do now," she says. "I'm thankful to have them. I wouldn't be around enjoying the good life that I do."

Paula Kurtzweil is a member of FDA's public affairs staff. Judith Willis, also a member of FDA's public affairs staff, contributed to this article.

## For More Information

National Heart, Lung, and Blood Institute  
Information Center  
P.O. Box 30105  
Bethesda, MD 20824-0105  
1-800-575-WELL (1-800-575-9355)  
[www.nhlbi.nih.gov/nhlbi/cardio/hbp/gp/hbinfo.htm](http://www.nhlbi.nih.gov/nhlbi/cardio/hbp/gp/hbinfo.htm)

American Heart Association  
7272 Greenville Ave.  
Dallas, TX 75231  
1-800-AHA-USA1 (1-800-242-8721)  
[www.amhrt.org](http://www.amhrt.org)

Hypertension Network  
[www.bloodpressure.com](http://www.bloodpressure.com)



# Chlamydia's

## Quick Cure

**Fight Against 'Silent' STD Includes  
New Screening Test, One-Dose Drug**

by Tamar Nordenberg

Anna Lange\* had no symptoms when she went to a Wake County, N.C., sexually transmitted diseases clinic earlier this year to pick up her birth control pills. But a routine test revealed that the 20-year-old Lange had chlamydia. "She came in and had no complaints," says Peter Leone, M.D., the clinic's medical director, "and then 'boom'—she was diagnosed with a sexually transmitted disease."

The sexually transmitted disease chlamydia usually comes with no tell-tale symptoms, so most people don't even know when they are infected. But left untreated, the so-called "silent epidemic" of chlamydia threatens to cause reproductive damage and infertility in many of the 3 million to 4 million Americans who get it each year. "Chlamydia's consequences can be devastating," says Diane Mitchell, M.D., an obstetrician-gynecologist and medical reviewer with the Food and Drug Administration.

Routine chlamydia screening and early, effective treatment are the keys to reducing chlamydia's toll, according to Penny Hitchcock, chief of the National Institutes of Health's sexually transmitted disease branch. Two recent medical advances, she says, constitute "very important breakthroughs" in controlling the rampant disease: a new drug treatment recently approved by FDA to cure chlamydia in a single oral dose, and a

\* not her real name





# Should You Get Tested?

The national Centers for Disease Control and Prevention recommends annual chlamydia screening for all sexually active adolescent girls and for other females who may be at high risk for chlamydial infection, such as those who:

- are less than 25 years old
- don't use barrier contraceptives consistently
- have new or multiple sex partners
- have signs of a possible cervical infection
- have previously had an STD.

"Females who are at risk because of their age and sexual activity need to get screened at least once a year," says researcher Gale Burstein, M.D. She and other chlamydia experts have recently questioned whether that is even enough.

Based on a study they conducted in 1998, Burstein and her colleagues at Johns Hopkins University recently recommended a twice-yearly screening of sexually active female adolescents. In tracking more than 3,000 sexually active Baltimore high school girls for three years, they found that more than a quarter of them tested positive for chlamydia at least once in that time frame.

Routine screening is recommended for pregnant women, also, because of the risk that their babies will become infected with chlamydia at birth.

There are no recommendations for routine screening among males, which Burstein says makes it especially likely that their chlamydial infection will be overlooked. "There is a lot of chlamydia in men that we're missing, and they are a major reservoir of infection. We're really only putting a band-aid on the problem because, even if we're screening the women, some are going back to their partners and getting reinfected." ■

—T.N.

urine-based screening test that, unlike other tests, does not require a swab sample of cells from the genital area.

## Price of Sex

Caused by the *Chlamydia trachomatis* bacteria and transmitted during vaginal, oral or anal sexual contact with an infected partner, chlamydia is the most reported bacterial infection in the United States and the most common bacterial (and thus curable) sexually transmitted disease by far, ahead of gonorrhea and syphilis.

A person can become infected at any age, but "it's adolescents that we're most worried about," Hitchcock says. "Far and away, the age group most affected are the 15- to 19-year-olds. If you're sexually active and you're in that age group, you're at risk." Studies show that young adults in Lange's age group, 20 to 24, are the second most affected group.

While wearing a condom may help reduce the risk of chlamydia, anyone who

is sexually active can get the disease. (See "Condoms and Chlamydia.")

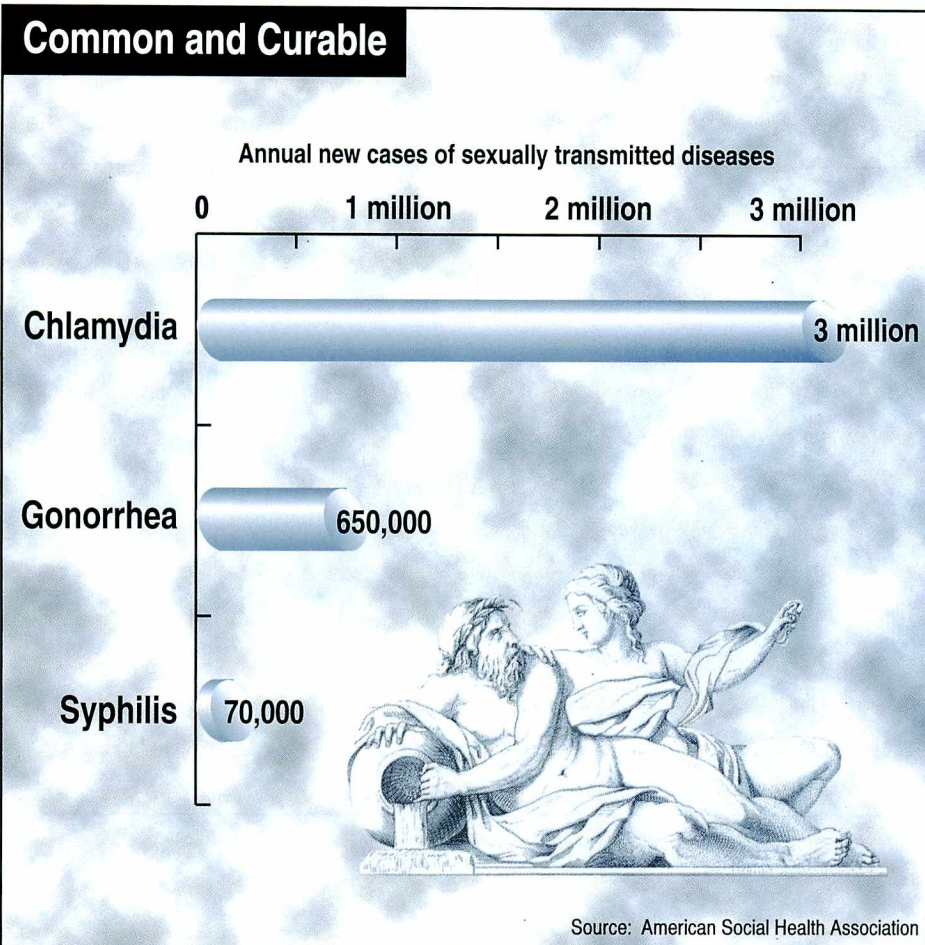
Symptoms of chlamydia, when they occur, usually appear within one to three weeks of exposure. In women, signs can include unusual vaginal discharge or bleeding, burning during urination, or lower abdominal pain. Men, like women, may have pain during urination, or they may notice a burning and itching around or discharge from the penis or pain and swelling in the testicles.

More often, though, chlamydia lives up to its reputation for silence. Experts estimate that up to 75 percent of women and 50 percent of men with chlamydia have no symptoms or symptoms so mild that they don't seek medical attention.

Chlamydia is "a very insidious disease," says Hitchcock. "Because it rarely causes symptoms, people don't know they're infected. So they don't get treated, and they infect their partners, who also don't get treated."

Without treatment, the national Cen-

## Common and Curable



Chlamydia, gonorrhea and syphilis. All are prevalent and treatable sexually transmitted diseases. But none is more common, or more easily cured, than chlamydia.



**Annual chlamydia screening is recommended for all sexually active adolescent girls and for other females who may be at high risk.**

## Condoms and Chlamydia

The only sure-fire way to avoid getting chlamydia and other sexually transmitted diseases is by abstaining from sex or being in a mutually monogamous relationship with an uninfected partner. Having multiple partners increases your risk of getting the disease, according to experts.

Anna Lange was especially surprised when she was diagnosed with chlamydia because, besides not having any symptoms, she had been in a monogamous relationship for six months. “We explained to her that the diagnosis didn’t mean that either she or her current boyfriend had been unfaithful,” says Peter Leone, M.D., medical director at Anna’s STD clinic. “We couldn’t tell her when or from whom she’d gotten infected. But she did have a history of unprotected sex for a couple of years previously, and she could have become infected at any time during this period.”

While even “protected” sex with a condom can’t *completely* prevent transmission of chlamydia or some other sexually transmitted diseases, experts recommend correct and consistent condom use to reduce the chances of getting chlamydia or other STDs. ■

—T.N.



ters for Disease Control and Prevention estimates, chlamydia can lead in up to 40 percent of cases to pelvic inflammatory disease, a serious infection of the woman’s fallopian tubes that can also damage the ovaries and uterus. (See “A Threat to Fertility.”) Also, women infected with chlamydia may have three to five times the risk of getting infected with HIV if exposed, according to CDC.

It’s not known whether chlamydia infection causes fertility problems or other long-term consequences in men. “We are worried—though we don’t have a lot of evidence—that chlamydia infection could cause chronic problems in men,” Hitchcock says. “But as far as we know, the biggest price is paid by young women.”

Babies sometimes pay a price, as well. Babies who are exposed to chlamydia in the birth canal during delivery can be born with pneumonia or an eye infection called conjunctivitis, both of which can be dangerous unless treated early with antibiotics.

### Simple Screening and Treatment

Because so many people are at risk for chlamydia and because the disease can ravage a woman’s reproductive system without so much as a symptom, experts recommend regular, widespread screening to detect the disease. (See “Should You Get Tested?”)

Traditional methods of screening require a health professional to collect a swab sample of genital secretions. For women this type of test “minutely prolongs” a pap smear, FDA’s Mitchell explains. “At worst, it can feel like a tiny menstrual cramp, but most women don’t experience any discomfort.” Male samples are obtained by inserting a swab into the end of the penis.

In the past, the sample had to be “cultured” in a laboratory to look for *C. trachomatis*, and it could take three days or more for results to become available. Also, accuracy of results could vary greatly based on the lab staff’s level of expertise and experience.



## The only sure-fire way to avoid getting chlamydia and other STDs is by abstaining from sex or being in a mutually monogamous relationship with an uninfected partner.

Today, a number of tests are available to supplement or sometimes replace the relatively expensive and slow traditional culture. The three major types of nonculture tests are:

- **Direct fluorescent antibody test.** This oldest alternative to culture uses a scientific method called staining to make chlamydia easier to spot under a microscope. DFA can give quicker results than culture and can be performed on specimens taken from the eye, cervix or penis.
- **Enzyme immunoassays.** This test to detect the presence of the cells of *C. trachomatis* comes in some forms that allow use in small, unsophisticated laboratories that don't have special lab equipment. Because testing can be done where the specimen is collected, results are more rapid than with culture, access to testing is increased, and costs can be lower.
- **Tests to detect the genes of *C. trachomatis* in urine, as well as genital samples.** Developed and approved in the last few years, these tests can accu-

rately identify even very small numbers of genes in a specimen. These tests can be expensive, but are becoming more popular among public and other labs because of their accuracy and the relative ease of collecting urine samples. "Now we can screen women and men who don't think they are ill without doing an invasive sampling, so people are much more likely to participate in screening programs," Hitchcock says.

No one screening method is best, Leone says. "It's a tradeoff. We're constantly balancing what is the cheapest test with what is the most sensitive, what is easiest to get from the patient versus what will pick up the most infections."

At Leone's clinic, Lange was tested using the enzyme immunoassay method. She doubted the results at first, Leone says. "We explained to her that yes, the test was accurate, and she really needed to be treated even though she had no symptoms."

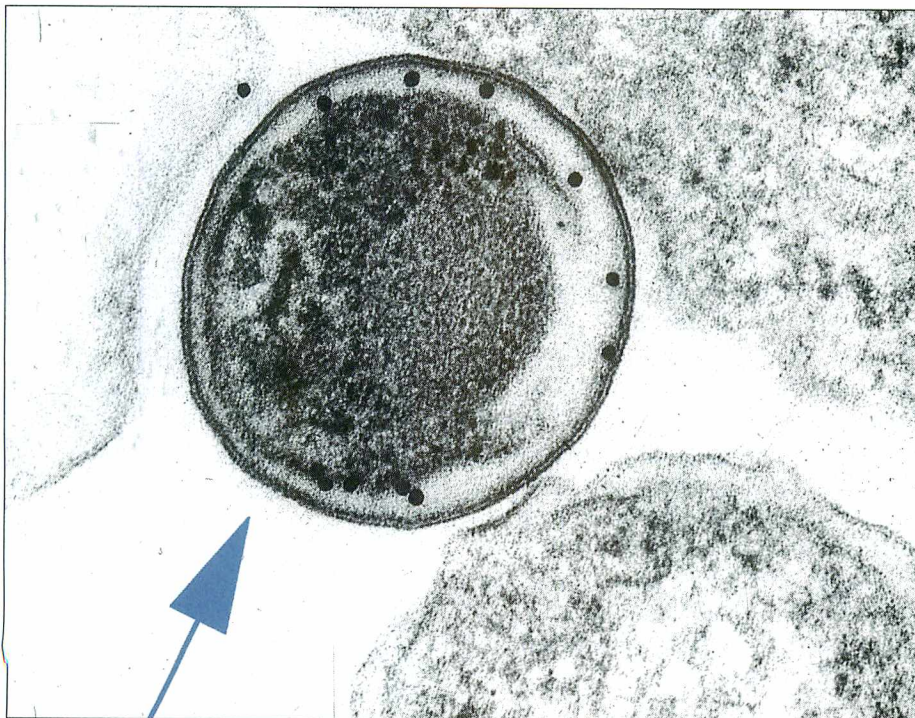
Lange and her boyfriend both took the antibiotic azithromycin (Zithromax), a

prescription drug approved by FDA in 1997 to cure chlamydia in one dose. "It's a breakthrough because we can observe therapy rather than depending on people to adhere to a more complicated regimen," Hitchcock says. Doxycycline (sold under several brand names), the other antibiotic approved and commonly used to treat chlamydia, is generally taken twice a day for seven days.

### Underused Tools

Widespread chlamydia screening among women can get results, as was demonstrated in a recent study supported by NIH. Researchers at Seattle's Group Health Cooperative of Puget Sound and the University of Washington found that symptomless women who were screened and treated for chlamydial infection were almost 60 percent less likely than unscreened women to develop pelvic inflammatory disease.

With such effective tools for screening and treatment, why has it proved so difficult to stop the spread of this microorganism? The answer, experts agree, is



The chlamydia organism (indicated by arrow) is positioned to infect a human cell.

## Another Chlamydia Making Headlines

The *Chlamydia trachomatis* bacteria that cause the sexually transmitted disease should not be confused with *Chlamydia pneumoniae*. These other bugs, which can cause colds and pneumonia, have been in the news because investigators are researching their possible link with atherosclerosis, a clogging of the arteries that causes most heart attacks and strokes. Add this type of chlamydia to smoking, a bad diet, and a sedentary lifestyle as possible contributors to heart disease. ■

—T.N.



# A Threat to Fertility

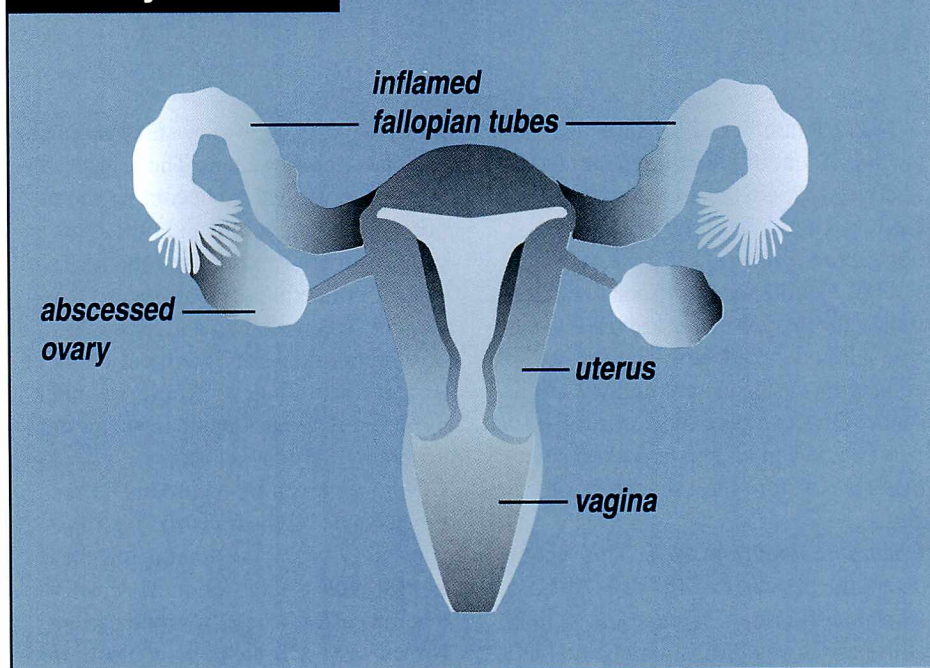
Pelvic inflammatory disease is caused when the *C. trachomatis* bacteria move from the cervix (where they enter during sexual intercourse) to the uterus and fallopian tubes, in some cases scarring the tubes enough to make fertilization impossible.

"These women may never be able to have children," says Penny Hitchcock, an expert in sexually transmitted diseases, "unless the problem can be surgically corrected, which is uncommon and expensive."

Even if the fallopian tubes are not completely blocked, scarring can interfere with the passage of the fertilized egg into the uterus. A blocked egg may instead implant in the fallopian tube, creating an ectopic or tubal pregnancy, which endangers the mother's life and results in loss of the fetus. ■

—T.N.

## Chlamydia's Toll



Often with no warning, chlamydia can cause pelvic inflammatory disease, which can damage a woman's fallopian tubes and other reproductive organs.

that not enough at-risk young people are getting tested.

"There are about a million reasons people don't get tested," Mitchell says. "They might feel uncomfortable, or not have insurance, or just not know they should be tested for chlamydia."

Also, doctors often fail to discuss the issue of sexually transmitted diseases with their young patients, according to Gale Burstein, M.D., a chlamydia researcher at Johns Hopkins University. "Physicians have to make a commitment to ask all of their adolescent patients if they are sexually active. But doctors are sometimes uncomfortable pursuing that line of questioning," Burstein says, adding that "a sexually active adolescent woman is more likely to test positive for chlamydia than for tuberculosis, yet TB tests are done much more routinely."

Beyond encouraging more young people to get routinely screened for chlamydia, experts are searching for

other avenues to control this sexually transmitted disease. Recently, researchers at Stanford University and the University of California at San Francisco uncovered new information about the chromosomes of *C. trachomatis*, providing promising leads for developing new antibiotics and even a vaccine. Hitchcock, whose agency supported the study, says she and other STD experts at NIH are "very excited about the new opportunities for vaccine development."

Until the hope of a vaccine is realized, those who choose to be sexually active should use condoms—for what they're worth. "Condom use clearly prevents HIV infection and gonorrhea, as well as pregnancy," Hitchcock says. "Use a condom, but not with blinders on, either. Don't kid yourself that condoms make sex risk-free." ■

Tamar Nordenberg is a staff writer for FDA Consumer.

## For More Information

about chlamydia and other sexually transmitted diseases:

- Call CDC's National STD Hotline at 1-800-227-8922
- Write to NIH's National Institute of Allergy and Infectious Diseases: NIAID Office of Communications 31 Center Drive (MSC-2520) Building 31 Room 7A50 Bethesda, MD 20892-2520 [www.niaid.nih.gov/publications/stds.htm](http://www.niaid.nih.gov/publications/stds.htm)



# New Drug Label Spells It Out SIMPLY

by Tamar Nordenberg

**There's a simpler substitute for the word "assistance": *help*.**

**For "discard": *throw away*.**

**And for "aggravate": *make worse*.**

Soon, consumers could see the plain-speaking terms in place of longer, harder-to-understand ones on everything from aspirin for aches and pains to zinc chloride for canker sores. A new Food and Drug Administration regulation allows these pairs of words and some others to be used interchangeably on the labels of nonprescription, or "over-the-counter," drugs.

In addition to permitting some word swaps, the new rule *requires* that all OTC drug labels contain certain information—such as ingredients, doses and warnings—in a standardized format.

The rule, published in the March 17, 1999, *Federal Register*, covers some 100,000 nonprescription products, including those like sunscreens that have both drug and cosmetic uses. The goal of the uniform label is to help consumers understand a nonprescription drug's benefits and risks and take the medicine correctly.

The new rule, said Vice President Al Gore when he announced it March 11, will "ensure that the labels on medicine we buy over the counter are no longer written in language that is over our heads. Starting here and now, when children wake up sick in the middle of the night, parents won't have to read a dictionary to read the directions. And people won't need a magnifying glass to find out what's in their medicine."

FDA hopes the new "Drug Facts" labels will improve the way consumers choose and use over-the-counter medicines just as the simplified "Nutrition Facts" labels have helped consumers eat less fat and otherwise improve their eating habits.

"People have told us, and studies have confirmed, that the food labels are working," says Peter Rheinstein, M.D., director of the medicine staff in FDA's Office of Health Affairs. "What's lacking in many OTC labels is readability, consistency—all the things the new food label has. It's not that the information isn't there already. Sometimes it's just hard to find."

Debra Bowen, M.D., who led the FDA team that wrote the regulation, sees the similarity with  
(Continued on page 30)



# Out With The Old... In With The New


To help consumers understand the information about OTC drugs, labels like the one below will be replaced with new, simply-written "Drug Facts" labels much like the example on the right.

(Continued from page 29)

the standardization of the food label, and adds that using a drug correctly requires even more elaborate information about risks and benefits. So it's all the more important, Bowen says, "to provide not only complete information about the drugs, but complete information in a readable, clear and simple format."

## Just the Facts

Americans buy about 5 billion over-the-counter drugs each year, according to government estimates, to treat their headaches, heartburn, coughs and colds, and other routine health problems. According to the Consumer Healthcare Products Association, a trade group that represents nonprescription drug makers, more than 600 OTC drugs contain ingredients and dosages that 20 years ago were available only by prescription.



**INDICATIONS:** Provides effective, temporary relief of sneezing, watery and itchy eyes, and runny nose due to hay fever and other upper respiratory allergies.  
**DIRECTIONS:** Adults and children 12 years and over—1 tablet every 4 to 6 hours, not to exceed 6 tablets in 24 hours or as directed by a physician. Children 6 to 11 years—one half the adult dose (break tablet in half) every 4 to 6 hours, not to exceed 3 whole tablets in 24 hours. For children under 6 years, consult a physician.  
**EACH TABLET CONTAINS:** Chlorpheniramine Maleate 4 mg. May also contain (may differ from brand): D&C Yellow No. 10, Lactose, Magnesium Stearate, Microcrystalline Cellulose, Pregelatinized Starch.  
**WARNINGS:** May cause excitability especially in children. Do not take this product unless directed by a physician, if you have a breathing problem such as emphysema or chronic bronchitis, or if you have glaucoma or difficulty in urination due to enlargement of the prostate gland. May cause drowsiness; alcohol, sedatives and tranquilizers may increase the drowsiness effect. Avoid alcoholic beverages, and do not take this product if you are taking sedatives or tranquilizers without first consulting your physician. Use caution when driving a motor vehicle or operating machinery. As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product. Keep this and all drugs out of the reach of children. In case of accidental overdose, seek professional assistance or contact a Poison Control Center immediately.  
Store at controlled room temperature 2°-30°C (36°-86°F).  
Use by expiration date printed on package.  
Protect from excessive moisture.  
For better identification keep tablets in carton until used.

Made in U.S.A.





Over-the-counter drugs are very safe as a rule, but not risk-free, Rheinstein says. "Just because something is sold over the counter," he says, "doesn't mean it's absolutely safe. Any medicine that's strong enough to help you also has the power to hurt you if you don't take it right."

Taking a medicine right can help avoid dangerous adverse reactions, it's true, but Rheinstein adds that a person who uses a medicine incorrectly can be harmed in another important, although perhaps less dangerous, way: "If you buy a drug without having all the information, you may not get all the benefit it can provide," he says. "The new rule will help people get all the benefit they're paying for."

The new label's simple language and easy-to-read format should help people compare drug products to choose the

best one to treat their illness, get the drug's full benefit, and avoid unnecessary adverse reactions.

Under the rule, OTC drug labels must comply with these requirements:

- Information must be presented in a standardized, easy-to-follow format, usually on the package's outside container or wrapper. Under the title "Drug Facts," the product's active ingredients will be listed first, along with the purpose for each, followed by uses, warnings, directions, and inactive ingredients. Listing inactive ingredients is a new requirement that should help consumers avoid products that may cause an allergic reaction. Also, FDA recommends, but doesn't require, that manufacturers include a phone number on the label for consumers to call for more information.
- Simple language must be used to communicate critical information, such as a

drug's ingredients, dose and warnings. For example, the term "uses" replaces "indications," and some other technical words like "precautions" and "contraindications" won't be used anymore, either. Studies have shown that consumers often have difficulty using the information as currently presented on OTC drugs. One study, for example, reported that 70 percent of caregivers could not measure the correct dose of medicine for their child, a problem that puts that child at risk of being overmedicated or undermedicated.

- The label must be printed in type large enough to be easily read and use other graphical methods to improve readability, such as bullets, a certain amount of spacing between lines, and thin lines separating label sections. Studies have shown that many older Americans in particular can't read the small type on

## Drug Facts

### Active ingredient (in each tablet)

Chlorpheniramine maleate 2 mg.....Antihistamine

### Purpose

**Uses** temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: ■ sneezing ■ runny nose ■ itchy, watery eyes ■ itchy throat

### Warnings

Ask a doctor before use if you have

- glaucoma ■ a breathing problem such as emphysema or chronic bronchitis
- trouble urinating due to an enlarged prostate gland

Ask a doctor or pharmacist before use if you are taking tranquilizers or sedatives

When using this product

- you may get drowsy ■ avoid alcoholic drinks
- alcohol, sedatives, and tranquilizers may increase drowsiness
- be careful when driving a motor vehicle or operating machinery
- excitability may occur, especially in children

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

### Directions

adults and children 12 years and over	take 2 tablets every 4 to 6 hours; not more than 12 tablets in 24 hours
children 6 years to under 12 years	take 1 tablet every 4 to 6 hours; not more than 6 tablets in 24 hours
children under 6 years	ask a doctor

### Drug Facts (continued)

**Other information** ■ store at 20-25°C (68-77°F) ■ protect from excessive moisture

**Inactive ingredients** D&C yellow no. 10, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch



## Simplified Label Earns 'No Gobbledygook' Award for FDA

"The New Label—It's Clearly Better" goes the slogan for FDA's over-the-counter drug label change. For leading the effort to develop the new, "clearly better" label, the agency's Debra Bowen got a Plain Language award from Vice President Al Gore.

Gore's "No Gobbledygook" awards recognize those in the federal government who write with their readers in mind. "People should be able to understand what we write the first time they read it" is the simple reminder to government employees from Gore's National Partnership for Reinventing Government. ■



## Supplement Facts

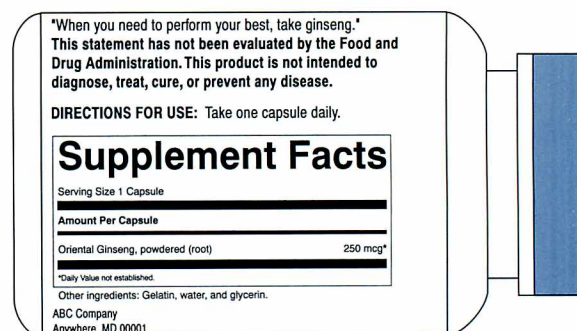
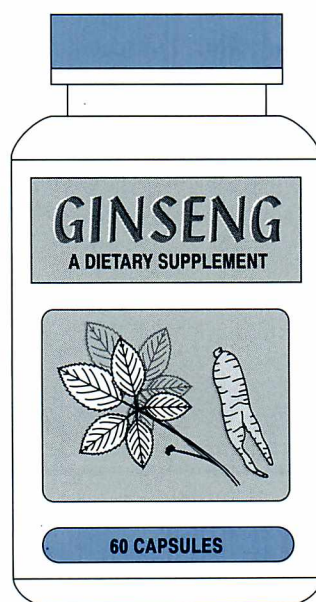
Like processed foods and now over-the-counter drugs, dietary supplements, too, must begin carrying standardized labels with information about their ingredients. The "Supplement Facts" panel will tell consumers the amounts of specific nutrients—vitamins A and C, calcium, iron, and sodium, for example—in vitamin and mineral products. For herbal products, the label will state the part

of the plant used in the product (such as the root, stem or leaf).

The new rule went into effect March 23, but supplement makers can sell their remaining stock of products labeled before that date. FDA plans to check marketed dietary supplements to make sure they are complying with the rule.

(For more on dietary supplements, see "An FDA Guide to Dietary Supplements" at [www.fda.gov/fdac/features/1998/598\\_guid.html](http://www.fda.gov/fdac/features/1998/598_guid.html).) ■

—T.N.



some current labels. This increases their risk of taking the wrong dose of a medicine or taking a medicine that could be harmful if combined with another drug they are using.

OTC medicines must begin carrying the new labels within two to six years, depending on the drug, but FDA expects many products to have the new labels sooner.

### Lightening the Load

FDA estimates that changing the labeling will cost drug companies about \$58 million. Will drugs cost you more because of this rule? FDA doesn't regulate drug prices, but the agency doesn't expect prices to increase as a result of the regulation because most OTC drug labels are routinely reprinted every few years.

"We're doing what we can to make the rule nonburdensome," Rheinstein says.

"Drug companies shouldn't have to throw out any labels, but in most cases can use up the old supplies first." For packages that are too small for the standardized labeling, the rule allows a modified format containing the most critical information.

Drug companies support the idea of making their labels more consumer-friendly, according to Joseph Doss of the Consumer Healthcare Products Association. "We have often said that, next to the medicine itself, the most important thing is the label," Doss says. "The label is what separates OTC medicines apart from other drugs. There, the consumer has all the information needed to take the products safely and effectively." ■

*Tamar Nordenberg is a staff writer for FDA Consumer.*





## Clinical Trials for Cancer

More than 60 resources related to cancer clinical trials can be found on a Website sponsored by FDA's Office of Special Health Issues. Most of those listed have toll-free numbers, and many have Websites. Included on [www.fda.gov/oashi/cancer/trials.html](http://www.fda.gov/oashi/cancer/trials.html) are the National Cancer Institute, which offers access to clinical trials for more than 100 types of cancer, and renowned treatment centers such as the Mayo Clinic and Memorial Sloan-Kettering Cancer Center.

## Home Testing for the AIDS Virus

During the 1990s, home-testing kits came into their own. Screening tests for hepatitis C, cholesterol, illegal drugs, and, of course, pregnancy, are now on the market. Consumers also can test at home for HIV-1, the virus that causes AIDS. But only one such kit is approved—the Home Access Express HIV-1 Test System. Other test systems promoted on the Internet and through print promotions are not approved, though they sometimes claim approval falsely. You can read all about these bogus tests on [www.fda.gov/cber/infosheets/hiv-home2.htm](http://www.fda.gov/cber/infosheets/hiv-home2.htm). Included is the “Lei-Home Access HIV Test,” which landed a businessman in jail for five years for selling the useless kits. (For the full story on these bogus kits, see page 34.)

The Website, sponsored by FDA's Center for Biologics Evaluation and Research, also answers frequently asked questions about home-test kit reliability, counseling, and confidentiality of results.

## Government Senior-ity

The federal government offers many programs designed to help senior citizens maintain good health. But these are spread across many agencies—such as FDA, the National Institute on Aging, the Health Care Financing Administration, even the Veterans Administration—so finding the information might be confusing. Now a Website called Access America for Seniors ([www.seniors.gov](http://www.seniors.gov)) brings federal health information for older Americans together in one spot. Information on senior health issues, insurance, food assistance, nursing homes, and hospitalization is available at a click. The Social Security Administration hosts the site, which also includes information for seniors on taxes, volunteer activities, travel, and educational opportunities.



## Campaigning Against Colon Cancer

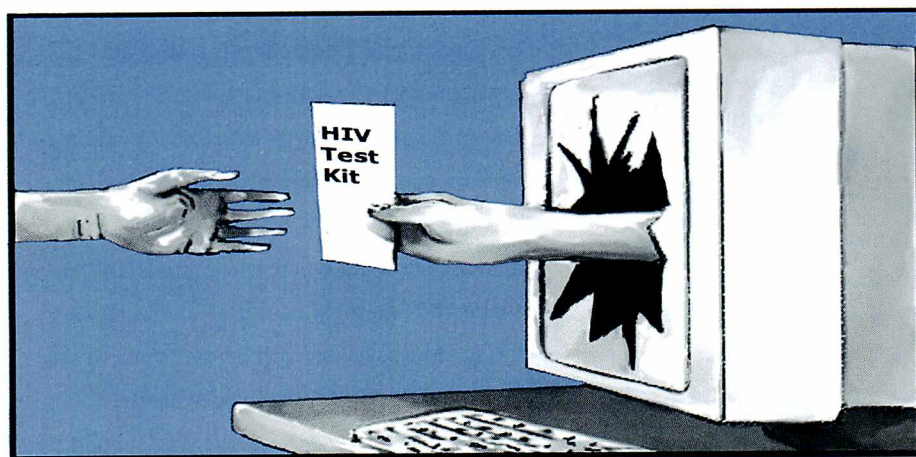
An estimated 129,400 Americans will be diagnosed with colon cancer this year, and 56,000 will die. But many of these deaths could be prevented if consumers aged 50 and older would get a simple screening test that can detect small growths in the colon before they become malignant and deadly. To help consumers understand colon cancer, a Website sponsored by the national Centers for Disease Control and Prevention explains how men and women can reduce their risk of dying from this disease by early detection. The site has artwork showing where the colon is and explains the two most common screening tests: blood stool tests and physician exams of the rectum and lower colon. The Website, [www.cdc.gov/cancer/screenforlife/](http://www.cdc.gov/cancer/screenforlife/), is part of a massive campaign by CDC, the Health Care Financing Administration, and the National Cancer Institute to educate consumers about preventing the disease.





# Internet Sales of Bogus HIV Test Kits Result in First-of-Kind Wire Fraud Conviction

by Paula Kurtzweil



For the first time in FDA history, an individual has been convicted on wire fraud charges stemming from Internet use to sell an illegal medical product. Previous wire fraud charges involving illegal medical products were based only on telephone and facsimile use.

Lawrence "Larry" Greene, of Los Banos, Calif., is serving a five-year, three-month prison term for selling unapproved HIV test kits for home use over the Internet, as well as through phone solicitations to pharmacies in California's Central Valley.

Greene, 52, sold more than 100 of the test kits in 1996 and 1997, before he was jailed by local authorities on unrelated charges. An informant provided information that enabled FDA's Office of Criminal Investigations (OCI) to collect evidence that led to Greene's November 1998 conviction in the U.S. District

Court for the Eastern District of California.

In fall 1997, FDA recalled the HIV test kits, as well as about 38 illegal hepatitis A test kits Greene marketed, from 35 to 40 California drugstores that had bought Greene's products. The recall was only the second in FDA history to be conducted by the agency itself. (The first was in 1977.) Generally, manufacturers recall their products voluntarily, but Greene could not recall the kits himself because he was in prison.

HIV (human immunodeficiency virus) is the virus that causes AIDS. The only approved HIV home-test kit currently marketed in the United States is the Home Access HIV-1 Test System, made by Home Access Health Corp., of Hoffman Estates, Ill.


Greene sold his unapproved HIV test

kit under the names Lei-Home Access HIV Test and Personal HIV Test Kit. Like the approved home-test kit, Greene's kits required a sample of blood. But unlike the legitimate kit, which requires a drop of blood to be placed on specially treated, pre-tested paper, Greene's version directed users to place a drop of blood on an opened Band-Aid attached to a card that was then returned to Greene. Even though he didn't send the blood samples to a laboratory for testing and had no scientific or factual basis for making a decision, Greene provided users with fabricated test results. He also did not provide counseling, as the manufacturer of the approved HIV test kit is required to do when it informs users of test results.

"It's unbelievable what he did," said Susan Corrales, a consumer safety officer in FDA's Center for Biologics Evaluation and Research. "There was no evidence that the blood samples were tested by a laboratory. His wife said he could tell whether a person was HIV negative or not by holding the sample up to a light. He was basically flipping a coin and saying yes or no."

FDA learned of Greene's illegal home-test kit in September 1997 through industry complaints to the agency's Center for Biologics Evaluation and Research, which regulates HIV home sample collection kits. The complaints alleged that an unapproved HIV home-test kit was being marketed on the Internet and in newspapers and magazines.





The center identified the kit's manufacturer as Lei-Home Access Care, a division of Jin-Greene Biotechnology Inc., of Sunnyvale, Calif. Greene was the owner of both.

Despite several visits, FDA investigators were not able to gain access to the building at the Sunnyvale address. Their knocks on the door went unanswered, even though the investigators could hear people talking inside.

About this time, an informant called FDA to express concerns about Greene's activities. The informant provided sufficient information, including sales records, to link Greene to the Internet marketing of the illegal test kits.

The district office forwarded the case to OCI, which tracked down Greene's home address in Los Banos. There, an OCI special agent interviewed Greene's wife, who mentioned that Greene had sold some of his kits to drugstores in California's Central Valley. OCI also learned that Greene was incarcerated at the local county jail.

FDA investigators visited the drugstores, many of which, according to Andrea Scott, a compliance officer in the agency's San Francisco district office, were "mom-and-pop" operations. When told about the phony HIV test kits, she said, "the pharmacists were totally snowed. They were flabbergasted and [a little bit] humiliated that they had been duped."

The pharmacists reported that they had sold several of the kits to their customers. "That's when we knew we had a recall on our hands," Scott said.

FDA investigators removed the kits from the pharmacies and posted notices in English and Spanish on the doors of the drugstores, warning consumers who may have bought kits to be retested for HIV infection. The notices also were given to representatives of high-risk

AIDS groups for their dissemination.

From sales records, OCI learned that Greene also had distributed kits to about 30 Internet customers as far away as New York and Florida. FDA notified the Internet customers that the test they had purchased was not reliable and that they should seek a health professional to be retested with an approved test.

On Sept. 26, 1997, FDA issued a press release, urging pharmacists to remove the unapproved HIV test kits from their shelves and advising consumers who had bought them to consult with a health professional about other available approved tests.

The press release also cautioned against use of Greene's hepatitis A kit, called the In-Home Hepatitis A Test Kit, which had been sold only to the drugstores—not over the Internet. FDA has not approved a home-test kit to detect hepatitis A, a virus that can cause a food-borne liver disease.

Greene's kits were packaged in plain white cardboard boxes with only a computer-generated label affixed to the outside. The box's contents included the opened Band-Aid for placing a drop of blood, as well as a stylus for pricking the finger and another little Band-Aid to place over the wound.

"[They were] nothing like you and I would buy," Scott said. "They were very amateurish in appearance."

Greene's HIV home-test kits sold for about \$40 each on the retail market, about the same as the legitimate kits.

A Dec. 11, 1997, OCI-obtained federal grand jury indicted Greene and his two companies on seven counts of mail fraud and 36 counts of wire fraud related to selling the unapproved kits. At the arraignment hearing on the indictment, Greene was denied bail and transferred from county jail to federal custody.

Greene waived his right to a jury and

served as his own lawyer before U.S. District Judge Robert Coyle during a two-day trial in November 1998. Among those who testified were representatives of the company that set up the Website for Greene and the company that took phone orders for kits.

Coyle convicted Greene on Nov. 18, 1998, of six counts of mail fraud and 11 counts of wire fraud. Finding that Greene's conduct was extreme in the emotional impact he inflicted on his victims, Judge Coyle sentenced Greene Feb. 24, 1999, to a punishment more severe than usual for a fraud case. Also, the judge agreed with the prosecution's conclusion that Greene was a prime candidate for recidivism. In fact, while in prison awaiting his conviction on the charges related to selling the bogus HIV test kits, Greene tried to extort \$500 from a fellow prisoner's mother for legal counsel he said he provided to her son. Greene is not licensed to practice law.

FDA continues to monitor the marketplace, including the Internet, for illegal HIV test kits. According to Susan Corrales, Internet marketing of such kits tends to be common. She cited the public's heightened awareness of HIV as the reason. "People are looking for an HIV test that is confidential and provides test results in the privacy of their homes," she said. "And Internet selling of these unapproved kits is one way to take advantage of this."

Scott agreed. "[Greene's HIV test kit] was a dangerous product we were able to get off the market," she said. "But there are a lot of other companies out there trying to take advantage of people's fears by scamming them out of their money. That's the scary part."

*Paula Kurtzweil is a member of FDA's public affairs staff.*



## Imported Fruit Blamed For Rare Typhoid Outbreak

A tropical fruit popular in Hispanic American homes was the source of a recent outbreak of a disease rarely seen in the United States: typhoid fever.

Health officials believe that frozen mamey fruit from Central America contaminated with potentially dangerous bacteria caused 14 cases of typhoid in the Miami area between December 1998 and February 1999. All of the sickened people, who required hospitalization, reportedly recovered.

Though the products also were sold elsewhere in the United States, no other related typhoid cases were reported. Federal and state officials removed the fruit from circulation in February and March, preventing any further sickness.

Typhoid, a primarily water-borne infection caused by the bacterium *Salmonella typhi*, produces persistent and high fever, abdominal cramps, loss of appetite, and fatigue. Though potentially life-threatening, the disease normally can be cured if treated promptly with antibiotics.

Hispanic households use frozen mamey (pronounced *mam-may*) to make a shake-like drink called *batidos de mamey*. The products have not caused any reported problems in the past.

In Florida, the clustered cases puzzled health officials because the disease is rare in the United States. When it shows up, it is usually in travelers returning from a visit abroad. But an investigation by state authorities and the national Centers for Disease Control and Prevention showed that those sickened had not traveled.

"There were just too many clustered cases to attribute to travelers," says Mike Chappell, investigations director in FDA's Florida district office. "Those numbers of clustered cases could be explained by a traveling group: for example, a group of firefighters who travel to Guatemala. After drinking contaminated water, some of them come back and then develop typhoid fever. But that wasn't the case with this outbreak."

So in early February, Florida Health Department and CDC officials focused their efforts on finding the common elements in the cluster of cases showing up

in the Miami area. They determined that in all the cases, the people had consumed frozen mamey either at home, where it had been bought from a food store, or in a restaurant. Florida officials immediately embargoed the fruit to keep it from being distributed.

Having pinpointed the outbreak cause, officials set out to trace the origin of the contaminated fruit. FDA joined the investigation on Feb. 18 and, by evaluating data provided by state health officials and CDC, identified El Sembrador brand frozen mamey produced in Guatemala and possibly Honduras as the most likely source. Epidemiological data from South Florida showed that this brand was in homes and in restaurants where those exposed ate the product.

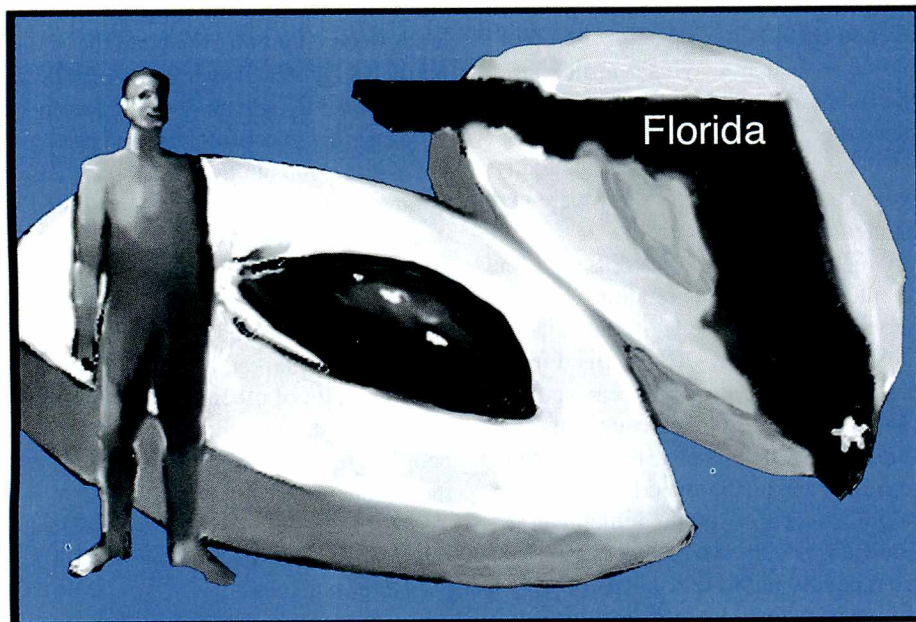
On Feb. 20, FDA publicly warned consumers not to eat the El Sembrador brand of frozen mamey.

FDA and Florida officials collected samples for laboratory analysis but were unable to isolate the *S. typhi* bacterium. FDA's southeast regional laboratory in Atlanta did, however, find high concentrations of both fecal coliform and *E. coli* bacteria in the samples, signs that the products had heavy bacterial contamination and possibly harbored the typhoid bacteria.

In late February, FDA officials inspected a frozen mamey production plant in Guatemala that health officials there had closed down weeks earlier because of the outbreak. "Even though we got there after the facility was closed," says Chappell, "it was obvious that the product was produced under [substandard] sanitation conditions."

Also, the contamination could have occurred as a result of Hurricane Mitch, which hit Guatemala hard in late 1998, possibly polluting the water supply used to make the fruit product.

On March 8, FDA announced the voluntary recall of El Sembrador frozen mamey, along with two other brands also suspected of being contaminated:





La Fe and a product with no brand name produced by Agrodex in Guatemala. At press time, these products were awaiting destruction. Other brands of frozen mamey not associated with the outbreak are still available.

—John Henkel

### Generic Drug Company Ordered to Upgrade

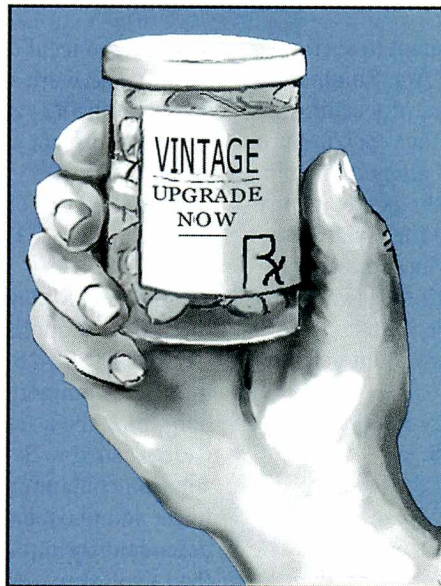
An Alabama manufacturer of more than 90 generic prescription drugs and several over-the-counter drugs was ordered to comply with federal manufacturing regulations after FDA inspectors repeatedly cited the company for violations.

Under a consent decree of permanent injunction entered in the U.S. District Court for the Northern District of Alabama Nov. 30, 1998, Vintage Pharmaceuticals Inc., headquartered in Huntsville, Ala., and company president William S. Propst agreed to upgrade current practices at its two manufacturing facilities and maintain mandatory controls.

Under the terms of the consent decree, Vintage agreed to hire an independent expert to help the company ensure that its production processes, facilities and controls comply with current good manufacturing practice (CGMP) regulations. CGMP regulations require drug products to meet safety, quality and purity controls, and drugs that do not meet these controls are considered by FDA to be adulterated and thus subject to regulatory action.

Although Vintage's violations were not life-threatening, Joseph Hayes, a compliance officer with FDA's Nashville district office says, "With the controls they were using and the procedures they were following, there was always the potential for having a real problem."

FDA became aware of deficient practices at the company's Huntsville plant



during a routine inspection in August 1997. Investigators found that Vintage Pharmaceuticals failed to:

- identify and validate manufacturing processes
- document and report shelf-life studies to support drug expiration dates
- follow written procedures required for various production and process controls.

FDA issued the company a warning letter in August 1997, and, in response, Vintage Pharmaceuticals promised to remedy the deficiencies.

Concerned that problems identified at the company's Huntsville facility could also be present at its sister facility in Charlotte, N.C., FDA's Nashville district office alerted the Atlanta district office to its findings. Investigators from that office and the Charlotte resident post inspected Vintage's Charlotte facility, which manufactures prescription and over-the-counter tablets and capsules. That inspection turned up similar, as well as new, violations.

"Some of the most significant violations found at the Charlotte facility involved the firm's failure to investigate and correct product stability problems," says Eric Weilage, an investigator with FDA's Atlanta district office. In addi-

tion, the facility's heating and ventilation system was not working properly. Weilage says the firm had not specified acceptable temperature and humidity ranges and was not monitoring these conditions.

FDA reinspected both facilities three times between October 1997 and August 1998, each time finding continuing CGMP deviations in laboratory controls, cleaning processes, quality control practices, and record keeping. Because the company failed to correct the deficiencies, FDA sought an injunction to halt the manufacture of any below-standard products.

In a court-ordered inspection Oct. 13 to 23, 1998, FDA found that the company had improved some of its operations—for example, conducting accelerated studies for drug expiration dates and improving its validation of certain production processes. But the company's overall drug manufacturing processes still did not comply with CGMPs. This led to the consent decree of permanent injunction.

The consent decree requires the expert hired to help Vintage Pharmaceuticals comply with CGMPs to inspect and provide FDA with written reports on the company's progress six months and 12 months from the date of the decree.

Vintage can seek to dissolve the decree after one and a half years if its controls are found to comply with federal law.

As part of the consent decree, U.S. District Judge Edwin Nelson authorized FDA at any time during the first three years of the consent decree agreement to randomly inspect the company's facilities to determine how well the company is complying with CGMPs. If violations are found, FDA can order the company to cease manufacturing or recall certain drugs.

—Carol Lewis



## SUMMARIES OF COURT ACTIONS



Summaries of Court Actions are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Summaries of Court Actions report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce or while held for sale after shipment in interstate commerce.

Summaries of Court Actions are prepared by Food and Drug Division, Office of the General Counsel, HHS.

### SEIZURE ACTIONS

#### *Food/Contamination, Spoilage, Insanitary Handling*

**PRODUCT: Shrimp, frozen, peeled**, at Tampa, Fla. (M.D. Fla.); Civil Action No. 95-1575-Civ-T-24(B).

**CHARGED** 9-25-95: While held for sale after shipment in interstate commerce at Americold, in Tampa, Fla., the articles of food were adulterated in that they consisted in whole or in part of decomposed shrimp—402(a)(3).

**DISPOSITION:** Claimants appealed the district court's order that required them to pay costs incurred by the State of Florida, but the U.S. Court of Appeals of the Eleventh Circuit affirmed the district court's order. The articles were reconditioned into "chum", or fish bait. (F.D.C. No. 67101; S. No. 95-681-946; S.J. No. 1)

**PRODUCT: Shrimp, frozen**, at St. Petersburg, Fla. (M.D. Fla.); Civil Action No. 95-1947-Civ-T-24(C).

**CHARGED** 11-24-95: While held for sale after shipment in interstate commerce at Sigma International, Inc., in St. Petersburg, Fla., the articles of food were adulterated in that they consisted in part of decomposed shrimp—402(a)(3).

**DISPOSITION:** Claimants appealed the district court's order that required them to pay costs incurred by the State of Florida but the U.S. Court of Appeals of the Eleventh Circuit affirmed the district court's order. The articles were reconditioned into "chum" (fish bait). (F.D.C. 67114; S. No. 95-712-273; S.J. No. 2)

**PRODUCT: Shrimp, frozen**, at Tampa, Fla. (M.D. Fla.); Civil Action No. 96-2602-Civ-T-24(E).

**CHARGED** 12-18-96: While held for sale after shipment in interstate commerce at Americold Corporation, in Tampa, Fla., the articles of food were adulterated in that they were washed in Sea Fresh, a commercially available aqueous solution containing copper sulfates, and in chlorine, lemon juice, and phosphates to conceal damage or inferiority of the defendant

shrimp, and were made to appear of greater value than they were—402(b)(3) and 402(b)(4). The articles were further adulterated in that they consisted in part of decomposed shrimp—402(a)(3).

**DISPOSITION:** The articles were destroyed. (F.D.C. No. 67163; S.J. No. 3)

**PRODUCT: Shrimp, frozen**, at St. Petersburg, Fla. (M.D. Fla.); Civil Action No. 96-2603-Civ-T-24(C).

**CHARGED** 12-18-96: While held for sale after shipment in interstate commerce at Sigma International, Inc., in St. Petersburg, Fla., the articles of food were adulterated in that they were washed in Sea Fresh, a commercially available aqueous solution containing copper sulfate, and in chlorine, lemon juice, and phosphates to conceal damage or inferiority of the defendant shrimp, and were made to appear of greater value than they were—402(b)(3) and 402(b)(4). The articles were further adulterated in that they consisted in part of decomposed shrimp—402(a)(3).

**DISPOSITION:** Claimants appealed the district court's order that required them to pay costs incurred by the State of Florida but the U.S. Court of Appeals of the Eleventh Circuit affirmed the district court's order. The articles were reconditioned into "chum", or fish bait. (F.D.C. No. 67164; S.J. No. 4)

**PRODUCT: Shrimp, frozen**, at Plant City, Fla. (M.D. Fla.); Civil Action No. 96-2601-Civ-T-25(B).

**CHARGED** 12-19-96: While held for sale after shipment in interstate commerce at Tampa/Lakeland Refrigerated Services, in Plant City, Fla., the articles of food were adulterated in that they were washed in Sea Fresh, a commercially available aqueous solution containing copper sulfate, and in chlorine, lemon juice, and phosphates to conceal damage or inferiority of the defendant shrimp, and were made to appear of greater value than they were—402(b)(3) and 402(b)(4). The articles of food were further adulterated in that they consisted in part of decomposed shrimp—402(a)(3).

**DISPOSITION:** The articles were destroyed. (F.D.C. No. 67165; S.J. No. 5)

**PRODUCT: Shrimp, frozen**, at St. Petersburg, Fla. (M.D. Fla.); Civil Action No. 97-197-Civ-T-24(A).

**CHARGED** 2-5-97: While held for sale after shipment in interstate commerce at Sigma International, Inc., in St. Petersburg, Fla., the articles of food were adulterated in that they consisted in whole or in part of decomposed shrimp—402(a)(3).

**DISPOSITION:** Claimants appealed the district court's order that required them to pay costs incurred by the State of Florida, but the U.S. Court of Appeals of the Eleventh Circuit



affirmed the district court's order. Furthermore, the articles were reconditioned into "chum", or fish bait. (F.D.C. No. 67167; S.J. No. 6)

PRODUCT: **Shrimp, frozen**, at Plant City, Fla. (M.D. Fla.); Civil Action No. 97-198-Civ-T-23(A).

CHARGED 2-5-97: While held for sale after shipment in interstate commerce at Tampa/Lakeland Refrigerated Services, in Plant City, Fla., the articles of food were adulterated in that they consisted in part of decomposed shrimp—402(a)(3).

DISPOSITION: The articles were destroyed. (F.D.C. No. 67168; S.J. No. 7)

PRODUCT: **Wheat, Light-Brown, Oblong-Shaped**, at Naples, Ill. (C.D. Ill.); Civil Action No. 94-3007.

CHARGED 1-13-94: While held for sale after shipment in interstate commerce at Consolidated Grain and Barge Co., in Naples, Ill., the article of food was adulterated in that it consisted in whole or in part of a filthy substance by reason of the presence therein of insects—402(a)(3).

DISPOSITION: Pursuant to a consent decree of condemnation, the article was reconditioned. (F.D.C. No. 66913; S. No. 94-611-032; S.J. No. 8)

#### *Drugs/Human Use*

PRODUCT: **Acne cream**, at Bronx, N.Y. (E.D. N.Y.); Civil Action No. 98-CIV-3962.

CHARGED 6-4-98: While held for sale after shipment in interstate commerce at Nels Laboratories, Inc., in Bronx, N.Y., the articles of drug for the treatment of acne were misbranded in that their labeling failed to bear adequate directions for use and failed to bear adequate warnings—502(f)(1) and 502(f)(2).

DISPOSITION: Pursuant to a default judgment, the articles were destroyed. (F.D.C. 67231; S. No. 98-751-265; S.J. No. 9)

PRODUCT: **Oxygen**, at New Iberia, La. (W.D. La.); Civil Action No. 98-1363.

CHARGED 7-24-98: While held for sale after shipment in interstate commerce at Welder's Equipment Center of New Iberia, Inc., in New Iberia, La., the articles of drug were adulterated in that the methods used in and the facilities and controls used for their manufacture, processing, packing, and holding did not conform to and were not operated and administered in conformity with current Good Manufacturing Practice (GMP) regulations—501(a)(2)(B). The articles were misbranded in that the labels of the high-pressure cylinders failed to bear an accurate statement of the quantity of contents—502(b)(2).

DISPOSITION: Pursuant to a consent decree of condemnation, the articles were reconditioned. (F.D.C. No. 67234; S. No. 98-763-239; S.J. No. 10)

PRODUCT: **Oxygen**, at Hendersonville, Tenn. (M.D. Tenn.); Civil Action No. 3-98-0170.

CHARGED 2-25-98: While held for sale after shipment of one or more of their components in interstate commerce at Ed Medical, Inc., in Hendersonville, Tenn., the articles of drug were adulterated in that the methods used in and the facilities and controls used for their manufacture, processing, packing, and holding did not conform to and were not operated and administered in conformity with current good manufacturing practice (GMP) regulations—501(a)(2)(B). The articles were misbranded in that the labels of the cryogenic home units failed to bear adequate directions for use—502(f)(1).

DISPOSITION: Pursuant to a consent decree of condemnation, the articles were reconditioned. (F.D.C. No. 67208; S. No. 97-777-010; S.J. No. 11)

PRODUCT: **Oxygen**, at Mankato, Minn. (D. Minn.); Civil Action No. 97-2310.

CHARGED 10-16-97: While held for sale after shipment of one or more of their components in interstate commerce at Praxair Distribution, Inc., in Mankato, Minn., the articles of drug were adulterated in that the methods used in and the facilities and controls used for their manufacture, processing, packing, and holding did not conform to and were not operated and administered in conformity with current good manufacturing practice—501(a)(2)(B). The articles were misbranded in that the labels of the cryogenic home units failed to bear adequate directions for use—502(f)(1). The articles were further misbranded in that the labeling of the cryogenic vessels failed to bear the statement "Caution: Federal law prohibits dispensing without prescription"—503(b)(4).

DISPOSITION: The articles were reconditioned. (F.D.C. No. 67207; S. No. 97-557-804; S.J. No. 12)

#### *Drugs/Veterinary Use*

PRODUCT: **Veterinary Drugs**, at Des Moines, Iowa (S.D. Iowa); Civil Action No. 4-98-CV-90941.

CHARGED 9-11-98: While held for sale after shipment in interstate commerce at Mortar & Pestle Veterinary Pharmacy, Inc., in Des Moines, Iowa, the articles of drug were adulterated in that the methods used in and the facilities and controls used for their manufacture, processing, packing, and holding did not conform to and were not operated and administered in conformity with current good manufacturing practices ("GMP")—501(a)(2)(B). The articles were further adulterated in that they were unapproved new animal drugs within the meaning of 21 U.S.C. Section 321(v)(1)—501(a)(5). The articles were misbranded in that they failed to bear adequate directions for use—502(f)(1).

DISPOSITION: The FDA district office is working with the



claimant and the U.S. Marshal's Service to get the claimed articles reconditioned and the unclaimed articles destroyed. (F.D.C. No. 67240; S. No. 98-688-688 et al.; S.J. No. 13)

### *Medical Devices*

**PRODUCT: Baoding Iron Balls, 65 cases, more or less, and accompanying booklet**, at Hanover, Pa. (M.D. Pa.); Civil Action No. 1:CV-93-1842.

**CHARGED** 11-29-93: While held for sale after shipment in interstate commerce at Hanover Direct, Inc., in Hanover, Pa., the article of device was adulterated in that it was a Class III device under 21 U.S.C. Section 360c(f), and there was no approved premarket approval application in effect pursuant to 21 U.S.C. Section 360e—501(f)(1)(B). The article was misbranded in that its labeling was false and misleading and otherwise contrary to fact and failed to bear adequate directions for use for the purpose for which the article was intended—502(a) and 502(f)(1). The article was further misbranded in that it was manufactured, prepared and processed in an establishment not duly registered under 21 U.S.C. Section 360, it was not included in the list required by 21 U.S.C. Section 360(j), and a notice or other information respecting the device was not provided as required by 21 U.S.C. Section 360(k)—502(o).

**DISPOSITION:** A default decree was entered on March 29, 1994, but on the day that destruction was scheduled to take place, the U.S. marshals discovered that the product had been removed by Hanover Direct, Inc., the distributor. The government considered criminal and injunctive relief against Hanover and ultimately negotiated a consent decree of condemnation and injunction. A consent motion to vacate the default judgment together with a claim and the consent decree were filed on Feb. 27, 1996. (F.D.C. No. 66797; S. No. 93-634-611; S.J. No. 14)

**PRODUCT: Latex Examination Gloves**, at Sacramento, Calif. (E.D. Calif.); Civil Action No. S-98-1422 LKK JFM.

**CHARGED** 7-24-98: Defendant property was seized pursuant to a federal search warrant executed at Alliance Medical Supplies, Inc., in North Highlands, Calif. and put into the possession of the U.S. Postal Service in Sacramento, Calif. The defendant article was adulterated in that it was a device which was classified under 21 U.S.C. Section 360c(f)(1) into Class III and there was no approved application for premarket approval in effect pursuant to 21 U.S.C. Section 360(e) and no investigational device exemption in effect pursuant to 21 U.S.C. Section 360j(g)—501(f)(1)(B). The article was misbranded in that a notice or other information respecting the device was not provided to the Food and Drug Administration at least 90 days prior to introduction into interstate commerce as required by 21 U.S.C. Section 360(k)—502(o).

**DISPOSITION:** The seized products were destroyed. (F.D.C. No. 67243; S. No. 94-704-901/906; S.J. No. 15)

**PRODUCT: Ultrasound Scanner System**, at Gainesville, Ga. (N.D. Ga.); Civil Action No. 2:96-CV-0085-WCO.

**CHARGED** 6-17-96: While held for sale after shipment in interstate commerce, the article of device was misbranded in that its labeling failed to bear adequate directions for use for the purposes for which it was intended, and the article was not exempt from the requirements of 21 U.S.C. Section 352(f)(1) under 21 C.F.R. Section 801.109, because it was not being used on the prescription or other order of a licensed practitioner in the course of his or her professional practice—502(f)(1). Furthermore, the article was adulterated in that when used for unapproved indications, it was a Class III device under 21 U.S.C. Section 360c(f) and it did not have an approved application for premarket approval in effect pursuant to 21 U.S.C. Section 360e or an approved application for an investigational device exemption under 21 U.S.C. Section 360j(g)—501(f)(1)(B).

**DISPOSITION:** The seized device was released to the claimant upon payment of costs. The claimant entered into a consent decree enjoining her from using the device without a written prescription from a licensed practitioner, and from distributing promotional literature without the statement that a written prescription was required. (F.D.C. No. 67134; S. No. 96-720-397; S.J. No. 16)

### **INJUNCTION ACTIONS**

**DEFENDANT: Veterinary Pharmaceuticals, Inc., and Sierra Pharmaceutical, Inc., and Harold M. Des Jardins and James K. Mann**, at Hanford, Calif. (E.D. Calif.); Civil Action No. CIV F-99-5222.

**CHARGED** 3-3-99: At their Sierra plant in Mexicali, B.C., Mexico, the defendants produced various veterinary pharmaceuticals to be imported into and distributed within the United States. These pharmaceuticals were parenteral, or injectable, products intended for use in the cure, mitigation, treatment, or prevention of disease in animals, and were therefore drugs within the meaning of the Food, Drug, and Cosmetic Act, 21 U.S.C. 321 (g)(1)(B).

The products were misbranded in that they were dangerous to health when used in the dosage or manner or with the frequency or duration prescribed, recommended or suggested in the labeling thereof—502(j). The products were further misbranded in that their labeling was false and misleading—502(a). The products were adulterated because their purity or quality fell below that which they purported or were represented to possess—501(c). The products were further adulterated in that the methods used in and the facilities and controls used for their manufacture, processing, packing, or holding did not conform to or were operated or administered in conformity with current good manufacturing practice—502(a)(2)(B).

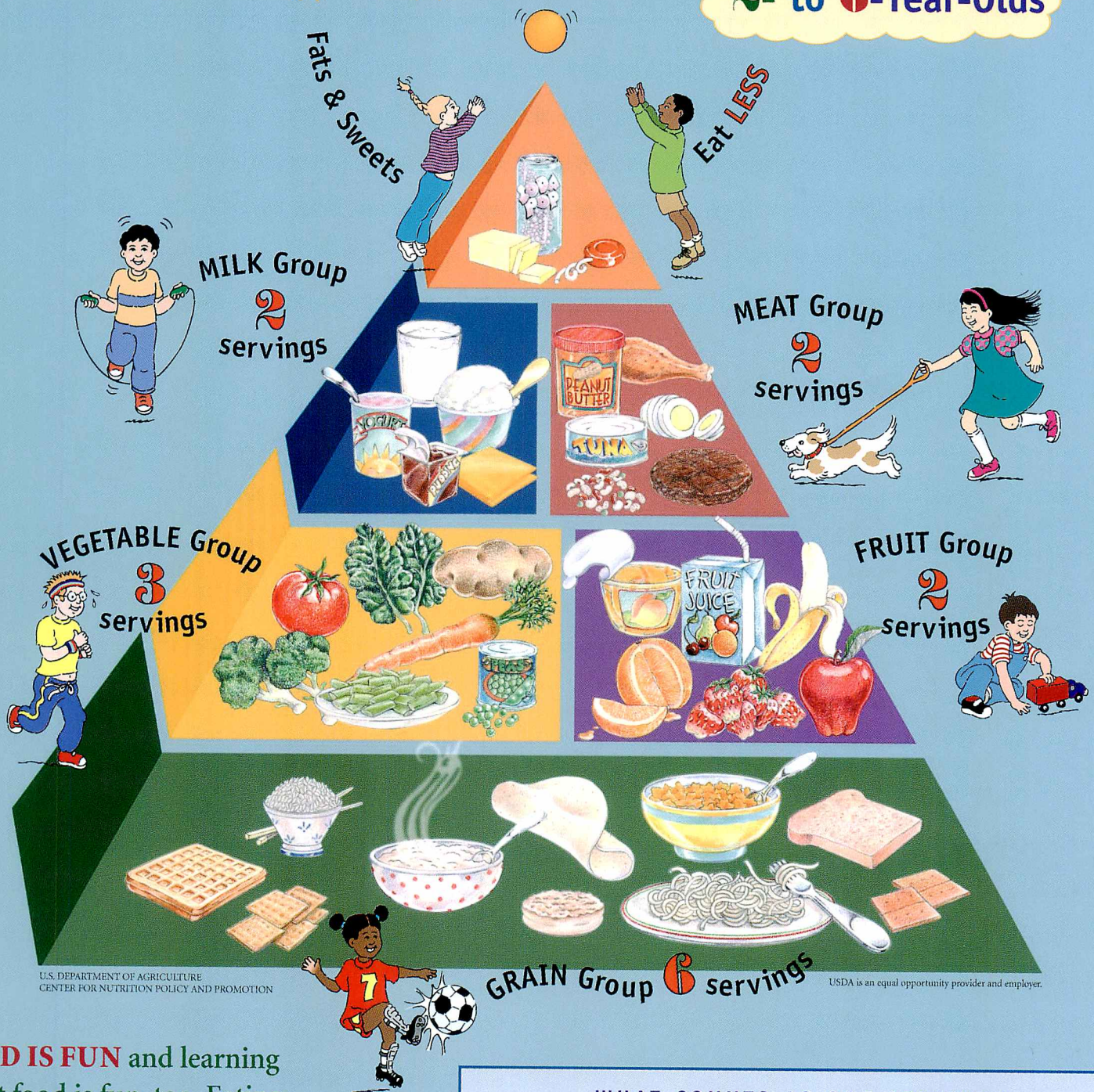
**DISPOSITION:** A consent decree of permanent injunction was filed, and the parenteral products were destroyed. (Inj. No. 1431; S. No. 98-733-228; S.J. No. 17)



# FOOD Guide PYRAMID

## for Young Children

A Daily Guide for  
2- to 6-Year-Olds



**FOOD IS FUN** and learning about food is fun, too. Eating foods from the Food Guide Pyramid and being physically active will help you grow healthy and strong.

U.S. Department of Agriculture  
Center for Nutrition Policy and Promotion  
March 1999  
Program Aid 1648

### WHAT COUNTS AS ONE SERVING?

#### GRAIN GROUP

1 slice of bread  
1/2 cup of cooked rice or pasta  
1/2 cup of cooked cereal  
1 ounce of ready-to-eat cereal

#### VEGETABLE GROUP

1/2 cup of chopped raw or cooked vegetables  
1 cup of raw leafy vegetables

#### FRUIT GROUP

1 piece of fruit or melon wedge  
3/4 cup of juice  
1/2 cup of canned fruit  
1/4 cup of dried fruit

#### MILK GROUP

1 cup of milk or yogurt  
2 ounces of cheese

#### MEAT GROUP

2 to 3 ounces of cooked lean meat, poultry, or fish  
1/2 cup of cooked dry beans, or 1 egg counts as 1 ounce of lean meat.  
2 tablespoons of peanut butter count as 1 ounce of meat.

#### FATS AND SWEETS

Limit calories from these.

Four- to 6-year-olds can eat these serving sizes. Offer 2- to 3-year-olds less, except for milk. Two- to 6-year-old children need a total of 2 servings from the milk group each day.

**EAT** a variety of **FOODS** AND **ENJOY!**