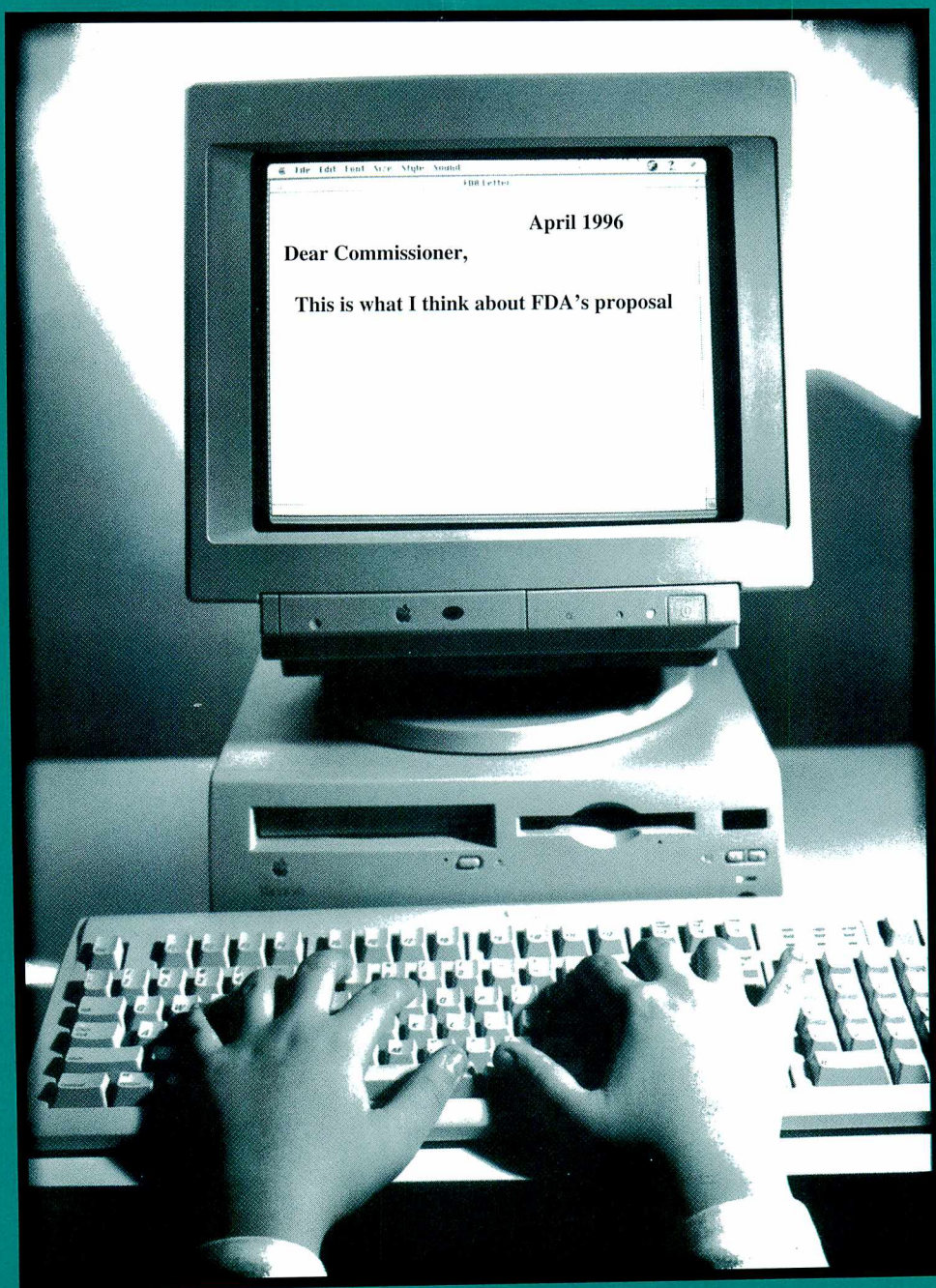


FDA CONSUMER

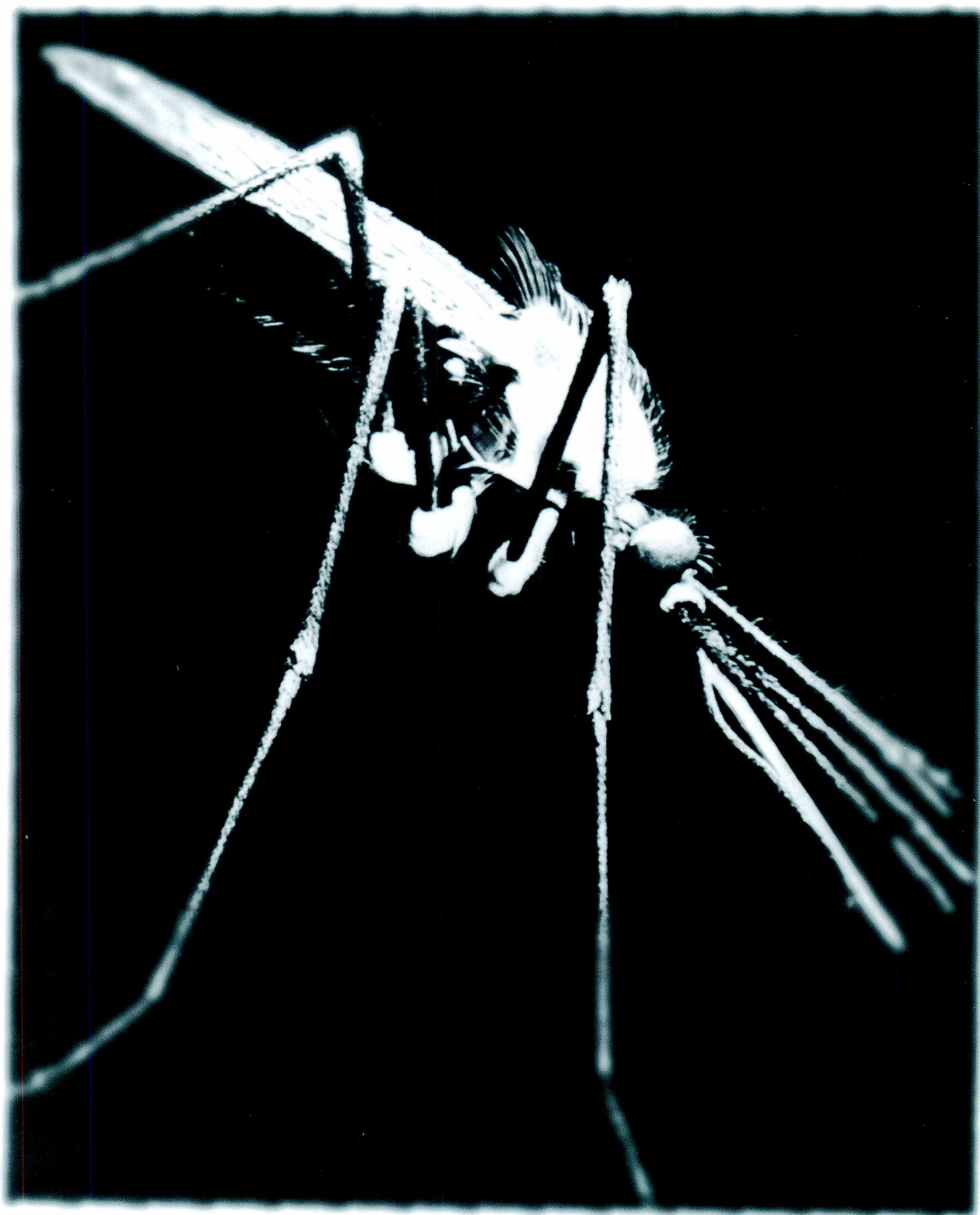
THE MAGAZINE OF THE U.S. FOOD AND DRUG ADMINISTRATION

• VOL. 30 NO. 3

APRIL 1996 •



Inside FDA:
How to Comment on Proposals and Submit Petitions



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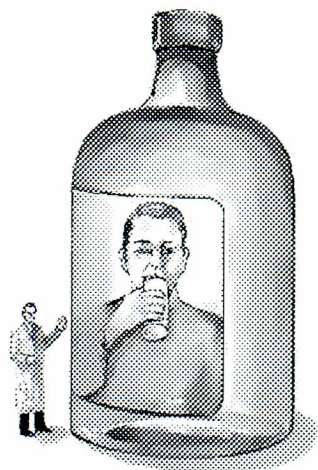
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Inside Front Cover Photo: *This type of mosquito is still spreading malaria after all these years. Malaria is just one of a number of reemerging and new diseases keeping health experts on their toes. See page 19. (Photo courtesy of National Library of Medicine)*



New Bottled Water Standards

New FDA standards for bottled water take effect May 13.

The final regulation, published last November in the *Federal Register*, sets standard definitions for different types of bottled waters, including artesian, ground, mineral, purified, sparkling, spring, sterile, and well water.

The regulation also requires mineral water to meet the bottled water quality standards. It must come from a protected underground source and contain at least 250 parts per million in total dissolved solids. Mineral water had previously been exempt from standards that apply to other bottled waters.

The regulation also requires that water bottled from municipal water supplies must be clearly labeled as such, unless it is processed sufficiently to be labeled as "distilled" or "purified" water. The regulation also requires accurate labeling of bottled waters marketed for infants.

Bottled water, like all other foods regulated by FDA, must be processed,

packaged, shipped, and stored in a safe and sanitary manner and be truthfully and accurately labeled. Bottled water products must also meet specific FDA quality standards for contaminants.

(See "Bottled Water: New Trends, New Rules," in the June 1993 *FDA Consumer*.)

Lung Protection for Babies

For the first time, infants at high risk for certain lung problems have a product to help reduce the severity of respiratory syncytial virus (RSV) disease, the most common cause of lower respiratory infections in children.

The product, RespiGam (Respiratory Syncytial Virus Immune Globulin Intravenous (Human)), was licensed by FDA last Jan. 19 for use in high-risk infants under 2 years old with lung problems due to prematurity or chronic bronchopulmonary dysplasia. (Chronic bronchopulmonary dysplasia causes abnormal cell and tissue growth.)

RespiGam is made from plasma taken from large numbers of normal, healthy individuals, and contains a high concentration of protective antibodies against RSV. These antibodies do not prevent RSV infections, but do help protect children against the most serious consequences of the virus.

In the United States, more than 90,000 children are hospitalized and 4,500 die each year from RSV.

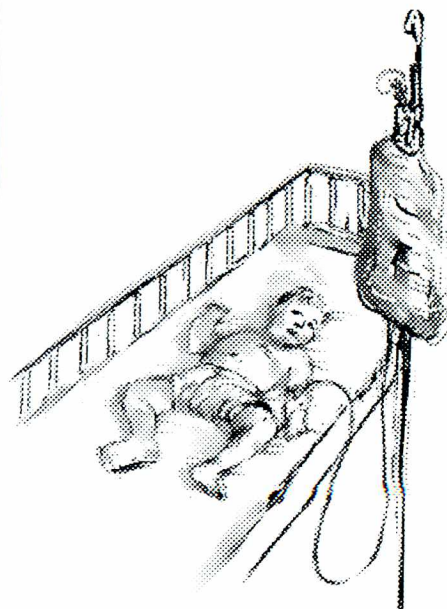
Treatment with RespiGam begins in November before the first outbreaks of RSV normally occur. The treatment regimen involves an intravenous dose once a month through March.

Clinical trials whose data supported the licensing of RespiGam included the pivotal PREVENT trial, a randomized, placebo-controlled, double-blind study. PREVENT involved 510 patients who either had chronic bronchopulmonary dysplasia and were younger than 2, or were born prematurely and younger than 6 months.

In the PREVENT trial, RespiGam reduced hospitalizations by 41 percent and reduced hospital time by 53 percent. In addition, children required fewer days of supplemental oxygen during their hospital stays.

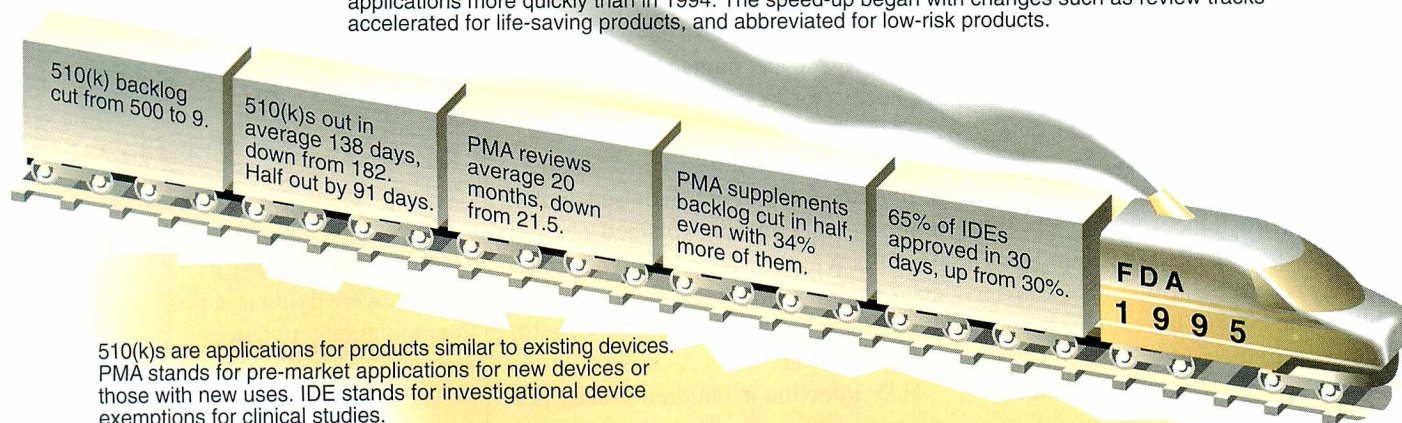
Because infants with pulmonary disease may retain fluids, a small percentage of infants in the trials needed new or extra diuretics after receiving RespiGam.

As with any human immune globulin product, rare allergic reactions to RespiGam are possible. In addition, a small risk exists for the transmission of blood-borne viruses. However, the risk



New Tracks Speed Device Reviews

In fiscal year 1995, FDA's Center for Devices and Radiological Health processed medical device applications more quickly than in 1994. The speed-up began with changes such as review tracks accelerated for life-saving products, and abbreviated for low-risk products.



is low because plasma donors are screened carefully, and the product is treated with a procedure that inactivates most significant blood-borne viruses, including the one that causes AIDS.

RespiGam is manufactured by Massachusetts Public Health Biologic Laboratories of Boston, and will be distributed by MedImmune Inc., of Gaithersburg, Md.

Study of Ritalin's Cancer-Causing Potential

An animal study of Ritalin (methylphenidate hydrochloride), a stimulant widely prescribed for children

with attention deficit hyperactivity disorder (ADHD), has produced a "weak signal" that the drug may have the potential to cause cancer, according to FDA, which has taken steps to alert health professionals to the possible problem.

The agency has asked the drug's sponsor, Ciba Pharmaceuticals, to include the study findings in the labeling for Ritalin, and to alert prescribers by sending them a Dear Doctor letter. The company complied in late January. FDA also plans to initiate additional follow-up studies, including both animal tests and epidemiological studies in humans using Ritalin.

The agency continues to regard

Ritalin as a safe and effective drug, but says the potential risk needs to be considered and further studied because of the increasing and often long-term use of Ritalin in children. In the last five years, there has been about a two- to threefold increase in the use of the product.

The agency's actions are based on findings of a draft report by the National Toxicology Program on cancer-causing potential of Ritalin in a study in mice and a study in rats.

The study in rats revealed no cancer-causing activity. The findings in mice included increased rates of noncancerous

liver tumors and, in males only, the occurrence of cancerous liver tumors.

FDA considers the studies' results a signal of a weak cancer-causing potential because:

- The positive findings were seen in one species of rodent (the mouse) and in only one organ—the liver—which is known to be particularly likely to develop tumors to a wide variety of stimuli.
- The increased rates were seen primarily in nonmalignant tumors.
- There was no increase in mortality associated with the tumors.

The agency also noted that animal studies do not necessarily reflect human findings. The kind of liver tumor found in mice is extremely rare in people, and its occurrence in recent years has not increased despite the increased use of Ritalin.

Clotting Factors And Hepatitis A

Hemophiliacs using Alphanate (Factor VIII) or AlphaNine S-D (Factor IX) clotting factors for their bleeding disorders should check their supply to make sure they don't use certain lots withdrawn from the market due to an association with hepatitis A virus (HAV) infection, FDA has advised.

Alpha Therapeutics Corp., Los Angeles, withdrew Lot AP5014A Alphanate last Dec. 8 due to suspected HAV transmission in three patients. Testing showed the illness in two of them to be linked to the withdrawn lot.

Later, a fourth case of hepatitis A was reported after a patient had received Al-

pha Therapeutics' AlphaNine S-D. Although HAV transmission by the product is unproven, as a precaution pending further investigation, the firm (with FDA's concurrence) placed on hold further distribution of AlphaNine S-D Lots CA5410A, CA5412A, CA5413A, and CA5421A.

FDA last January also advised hemophiliacs using any human-derived Factor VIII or Factor IX products to contact their doctors for hepatitis evaluation if they have flu-like illness with jaundice or liver tenderness. FDA advised doctors to report otherwise unexplained cases of hepatitis A to their state health department pending further instruction from the national Centers for Disease Control and Prevention.

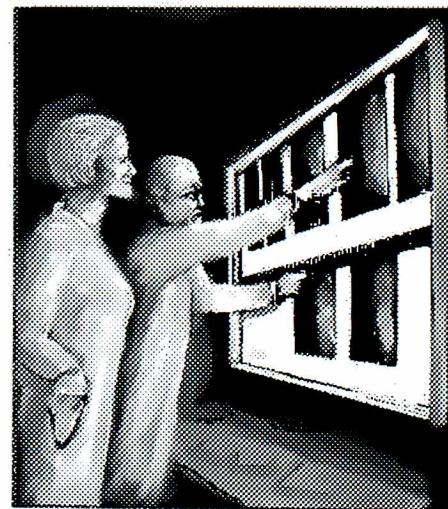
HAV infection in children usually produces no symptoms. The infection is most serious in older patients, in whom deaths infrequently occur. In February 1995, FDA approved a vaccine that prevents HAV.

While reports of HAV transmission by clotting factor concentrates are uncommon, laboratory studies and surveillance are under way to determine whether transmission may occur from other products.

Mammography Quality

The quality and reliability of mammograms in the United States have improved under FDA's new standards for taking and interpreting the breast x-rays, according to a recent report from the General Accounting Office (GAO).

FDA was given the responsibility of implementing the 1992 Mammography Quality Standards Act passed by Congress in response to concerns that



women were dying as a result of poor mammography practices in many facilities.

The GAO report, released Nov. 1, said that when the new rules went into effect, about one-third of the clinics failed to meet the standards for accreditation. On second attempts, about two-thirds of the clinics that had earlier failed were able to pass, and still more passed on a third attempt.

According to the report, only about 4 percent, or 400, of the 10,000 to 11,000 mammography facilities in the country stopped operating, and in 97 percent of those cases, another clinic was within 25 miles.

Breast cancer strikes 182,000 women a year and kills 46,000. Mammography is currently the best method available to detect and treat breast cancer early, when it is most curable.

The National Cancer Institute recommends that all women over 50 have annual mammograms and that some women under 50 have them as well.

1995 Dietary Guidelines: New Weight, Exercise Advice

New weight recommendations and increased emphasis on exercise are included in the advice offered in the recently issued 1995 edition of the *Dietary Guidelines for Americans*.

Developed by the U.S. departments of Health and Human Services and Agriculture, the 1995 *Dietary Guidelines* also reiterate the seven core recommendations of past editions, once again emphasizing balance, moderation and variety in food choices.

For the first time, the guidelines advise adults to maintain their weight in a single healthy range rather than increasing it over the years.

The new guidelines increase emphasis on physical activity, calling for 30

minutes or more of moderate physical activity on most (preferably all) days of the week. Physical activities can include brisk walking, calisthenics, home care, gardening, moderate sports exercise, and dancing.

The guidelines also acknowledge for the first time vegetarian diets as a healthful dietary alternative.

The *Dietary Guidelines* are published every five years. In addition to providing information for consumers, they form the basis for federal nutrition policy and programs.

A copy of the *Dietary Guidelines* bulletin may be obtained by:

- sending your name, address and 50 cents to Consumer Information Center, Department 378-C, Pueblo, CO 81009
- downloading from the USDA Center for Nutrition Policy and Promotion's

home page at <http://www.usda.gov/fcs/cnpp.html>; or the Department of Health and Human Services home page at <http://www.os.dhhs.gov/>; or from USDA's Food and Consumer Service electronic bulletin board on FedWorld, modem number: (703) 321-3339.

New Reprint

A new *FDA Consumer* reprint is available free.

To order single copies of "A Status Report on Breast Implant Safety" (FDA 96-4262), write to FDA, HFE-88, Rockville, MD 20857. To order 2 to 100 copies, write to FDA, HFI-40, at the same address, or fax your order to (301) 443-9057. Include the publication number.

CONSUMER FORUM



Breastfeeding Article Excellent

The October issue of *FDA Consumer* includes a comprehensive article on breastfeeding by Rebecca D. Williams, "Breastfeeding Best Bet for Babies." I commend Ms. Williams for an excellent depiction of breastmilk as a healthcare issue, an accurate explanation of the lactation process and helpful tips for nursing parents. I hope future issues will provide readers with updates on breastfeeding research and topical breastfeeding issues.

The National Breastfeeding MediaWatch campaign, sponsored by the Texas Department of Health, is an ongoing project of the Bureau of Nutrition Services. Its purpose is to identify references to breast and formula feeding in all facets of the media. Volunteers often write letters to the various forms of media regarding the messages they send to the public. A Fort Worth, Texas, participant shared Ms. Williams' article with me.

If you would like more information about breastfeeding or the National

Breastfeeding MediaWatch campaign, please contact Ms. Laurie Coker, Breastfeeding Promotion Specialist, at (512) 406-0744.

Jacquelyn McDonald, Director
Division of Nutrition, Education,
Outreach, and Training
Bureau of Nutrition Services
Texas Department of Health

FDA Consumer welcomes comments from readers. Send letters to: Editor, *FDA Consumer*, HFI-40, 5600 Fishers Lane, Rockville, MD 20857.

HOW TO COMMENT ON PROPOSALS AND SUBMIT PETITIONS

by John Henkel

(This is the first article in a series on FDA activities and concerns.)

You can influence FDA actions. As a regulatory agency, FDA publishes rules that establish or modify the way it regulates foods, drugs, biologics, cosmetics, radiation-emitting electronic products, and medical devices. FDA rules have considerable impact on individual well-being and the nation's health, industries and economy. These rules are formed with the help of the medical community, industry—and consumers.

By law, anyone can participate in the rule-making process by commenting in writing on rules FDA proposes. FDA allows plenty of time for public input and carefully considers these comments when it draws up a final rule.

FDA gathers public comments mainly through two channels: proposed rules and petitions.

Proposed Rules

When FDA plans to issue a new regulation or revise an existing one, it places an announcement in the *Federal Register* on the day the public comment period begins. Published every weekday, the *Federal Register* is available at many public libraries and colleges, and on the Internet. Issues open to public comment often are reported by the news media and may frequently be found on FDA's Internet home page (see "Using the Internet").

In the *Federal Register*, the "notice of proposed rulemaking" describes the planned regulation and provides background on the issue. It also gives the address for submitting written comments, a contact for more information, and the deadline for public comments.

Usually, the comment period lasts at least 60 days, though some comment periods have been as short as 10 days or as long as nine months. Weekends and holidays are included in the comment period.

There is no special form to fill out for comments, nor do submitters have to follow a certain style. But FDA can process comments more effectively if they are presented—either written legibly or typed—on 8½- by 11-inch paper.

Here are some other suggestions for making effective comments:

- Clearly indicate if you are for or against the proposed rule or some part of it and why. FDA regulatory decisions are based largely on law and science, and agency reviewers look for reasoning, logic, and good science in public comments.
- Refer to the docket number, listed in the *Federal Register* notice.
- Include a copy of relevant articles or other references that support your comments.
- If an article or reference is in a foreign language, you must submit both a copy of the original document and an English translation verified by a qualified translator to be accurate.
- To protect privacy when submitting medical information, delete names or other information that would identify patients.
- Threats, obscenities, profanities, or material defamatory to FDA or the federal government may be rejected or referred to law enforcement officials.
- Comments must be postmarked or de-



Though most comments on proposed rules are written on standard letter-size paper, some arrive at FDA in odd sizes and shapes. Jennie Butler, chief of the FDA dockets management branch, unfolds one such comment—a 4- by 10-foot “poster” signed by hundreds of junior high school students from Carmel, Ind., that supports FDA’s proposal to regulate tobacco.

livered in person by the last day of the comment period.

The number of comments received for proposals have varied greatly. A rule that established reporting procedures for problems with medical devices attracted 300 comments, while a recent proposal to regulate tobacco generated over 500,000 comments.

When FDA receives a comment, it is logged in, numbered, and placed in a file for that docket. It then becomes a public record and is available for anyone to examine in FDA's reading room (Room 1-23, 12420 Parklawn Drive, Rockville, Md.). Under the Freedom of Information Act (FOIA), visitors to the reading room can receive free copies of comments up to 50 pages if their request is for noncommercial use. After that, each page costs 10 cents. People also can send FDA an FOIA request and have copies of comments mailed to them (see "How to File a Freedom of Information Request").

Petitions

Another way to influence FDA is to petition the agency to issue, change or cancel a regulation, or to take other action. The agency receives about 200 petitions yearly.

Petitions require careful preparation by the submitter. Individuals sometimes submit petitions, but most come from regulated industry or consumer groups. For example, a drug company might request a change in labeling for one of its products; a food company might ask that its product be exempted from some provision of a regulation; or a consumer group might petition FDA to tighten regulation of a certain product.

Petitions submitted to FDA must contain:

- **Action requested**—What rule, order, or other administrative action does the petitioner want FDA to issue, amend or revoke?
- **Statement of grounds**—The factual and legal grounds for the petition, including all supporting material, and information known to the petitioner that may be unfavorable to the petitioner's position.
- **Certification**—A statement that to the best of the petitioner's knowledge, the petition includes all information rel-

Using the Internet

Though the *Federal Register* is readily available from libraries in printed form, it also can be accessed through the Internet's World Wide Web at two addresses:

http://www.access.gpo.gov/su_docs/

<http://thorplus.lib.purdue.edu/gpo/>

You also can learn about new FDA issues that are open for public comment through the agency's News Page on its Web site at <http://www.fda.gov/opacom/hpnews.html>. ■

evant to the petition, favorable or not. The petition must be signed and include the petitioner's address and phone number.

In addition, some petitions may require statements on:

- **Environmental impact**—Generally required if the petition requests approval of food or color additives, drugs, biological products, animal drugs, or certain medical devices, or for a food to be categorized as GRAS (generally recognized as safe). Procedures for preparing environmental impact statements can be found in Title 21 of the *Code of Federal Regulations*, Sections 25.24 and 25.31. If an environmental impact statement is not required, petitions should include a statement to that effect.
- **Economic impact**—Required only if FDA requests it after review of the petition.

Petitions should be mailed or delivered to: Dockets Management Branch, FDA, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

Ultimately, FDA management decides whether to grant a petition. But first, agency staffers evaluate it, a process that may take several weeks to more than a year, depending on the issue's complex-

ity. After FDA grants or denies the petition, the agency notifies the petitioner directly. If not satisfied, the petitioner can take the matter to court.

For more information on submitting petitions, consult Title 21 of the *Code of Federal Regulations*, Sections 10.30, 10.33, and 10.35.

Besides accepting public comments and petitions, FDA also schedules public meetings and hearings to discuss and explain its proposals. These usually are held with industry representatives or consumer groups, but anyone interested may attend and, with advance notice, may comment on a proposal. Meetings often are held in the Washington, D.C., area, but sometimes are set in other areas across the country. Meetings for the public to present views are announced in the *Federal Register*.

If you have questions about the comment, petition or hearing process, contact the FDA Dockets Management Branch, (301) 443-7542. Hours are 9 a.m. to 4 p.m., Eastern time, Monday through Friday. ■

John Henkel is a staff writer for FDA Consumer.

How to File a Freedom of Information Act Request

You can get copies of comments on any given issue by filing a Freedom of Information Act (FOIA) request to FDA. The request is best made by letter, specifying exactly what material is sought. Requesters usually should be specific about what comments they want, instead of asking for "all comments" received on a certain proposal, which in some cases can run thousands of pages. (Indexes of comments are available by FOIA request as well.)

FOIA requests should include an address and phone number and be sent to FDA, Freedom of Information Staff (HFI-35), 5600 Fishers Lane, Rockville, MD 20857, or faxed to (301) 443-1726. For more information, call (301) 443-6310. ■

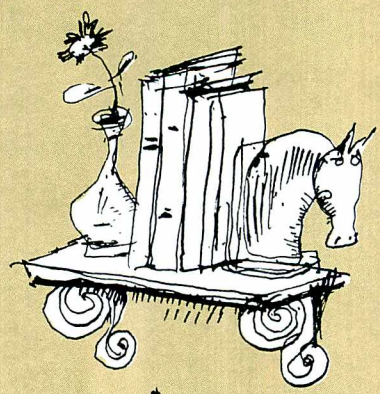
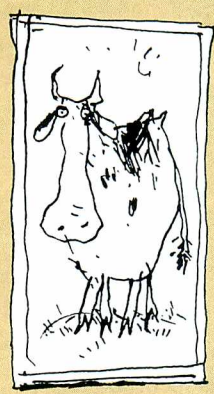
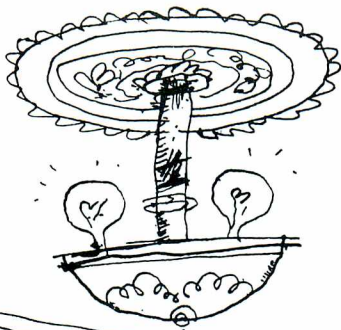
Healthful Snacks For The Chip & Dip Crowd

by Ruth Papazian

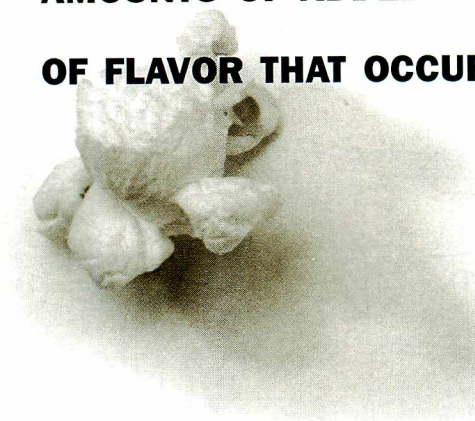
Nutritionists worth their salt will recommend eating an apple or carrot sticks if you want a healthy, nutritious snack. But can you imagine serving *crudités*, tofu kabobs, and rice cakes when “the gang” comes over to watch the big game on television? Even the most health-conscious among us have to admit that there are times when only cookies, chips, crackers, dips, and spreads will do.

“Snack foods are a big issue with my clients,” admits Connie Diekman, a St. Louis-based registered dietitian and spokeswoman for the American Dietetic Association. “They want to know: ‘Can I still eat them?’ ‘How much can I eat?’ and ‘What else do I have to give up?’ ” Of course, if you choose to snack on fruit or low-fat yogurt you’ll get fiber, calcium and other important nutrients your body needs. “My advice is to reach for these types of foods first and then to munch on your favorite snack food,” says Diekman.

Naomi Kulakow, coordinator of food labeling education in the Food and Drug Administration’s Center for Food Safety and Applied Nutrition, points out that the new food label gives consumers options to find variety, balance and moderation—the cornerstone of a healthy diet—in their snack food choices. “Consumers now have the information they need to make informed choices among the foods they like—they now have a tool to help them control portion sizes, and make dietary tradeoffs or substitutes,” she says.



FAT-FREE OR LOW-FAT VERSIONS OF SNACK FOODS OFTEN CONTAIN HIGH AMOUNTS OF ADDED SUGARS OR SODIUM TO COMPENSATE FOR THE LOSS OF FLAVOR THAT OCCURS WHEN FAT IS REMOVED.



Another option is products containing olestra, a fat-based substitute for conventional fats. (See "Olestra Approved with Special Labeling.")

"When choosing snack foods, I advise my clients to figure out what is more important to them—eating a larger portion of the reduced-fat version or eating a smaller amount of the full-fat version," Diekman says. "For instance, if a serving of potato chips is 1 ounce (28 grams), there may be 16 chips per serving for the full-fat version and 30 for the fat-free version." Diekman adds that many of her clients incorporate their favorite snacks into their diets by giving up other things, such as not putting dressing on their salads.

She finds that "most people are interested in a particular product attribute—the number of calories or sodium content—and may base their snack food choices on that one factor."

Being Upfront About Nutrients

Many well-known brands of snack foods are now available in reduced-fat or reduced-sodium versions so you can steer clear of nutritional land mines without being a party pooper. However, the trick is to find lower calorie, fat or salt versions of your favorite snacks, and to compare the amount that makes up a portion with the amount you normally eat so you can incorporate snack foods into your diet without overdosing on fat and salt.

How many tortilla chips make a serving? Which has less sodium per serving, salsa or bean dip? Does a half cup of "party mix" contain more fat than an equal amount of mixed nuts? Thanks to the Nutrition Labeling and Education Act of 1990, the answers to such questions can be easily found on virtually all packaged and processed foods. Redesigned in 1994 in accordance with regulations developed jointly by FDA and the U.S. Department of Agriculture, the food label now provides more consis-

tent and reliable information about:

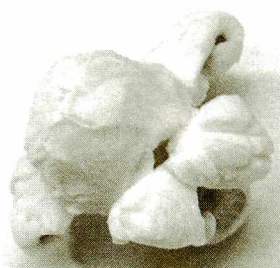
- nutrient claims, such as "reduced sodium" or "low fat"
- serving size and number of servings in the package or container
- %Daily Values, which show how much of certain nutrients a serving contributes to your daily diet overall
- all ingredients, including additives, artificial colors and natural and artificial flavors.

"A quick, easy way to spot healthier varieties of cookies, chips and other snack foods, is to be on the lookout for products that carry the nutrient claims 'fat free,' 'low fat,' 'light,' 'low sodium,' 'lightly' salted, or 'reduced' calorie, fat or sodium on the front of the package," suggests Kulakow. "You can trust these claims because they are among a number of descriptive terms that the government has created precise definitions for, and all foods making such nutrient claims must meet stringent criteria," she adds. (See "Smart and Easy.")

Real-Life Serving Sizes

"Before the new food label regulations went into effect, a serving size was whatever the manufacturer said it was—and many packages did not even list this information," Diekman says. "For instance, people used to assume that a small bag of potato chips contained a single serving. That wasn't always true before, but it's true now. The label also alerts consumers that a bag containing more than 2 ounces (60 g) of chips contains more than one serving." Knowing the number of servings in a package is important because the amount of fat, sodium or calories listed on the label is based on serving size, she adds.

You can find the serving sizes and number of servings per package on the Nutrition Facts panel. Serving sizes are listed in both household and metric units—for example, 14 chips (28 g)—and are more uniform across product



Olestra

Approved with Special Labeling

Products containing olestra, a fat-based substitute for conventional fats, are expected to start appearing on store shelves soon. FDA approved olestra last Jan. 24 for use in certain snack foods. The agency is requiring all products containing olestra to be labeled with specific health information.

Procter & Gamble Co. developed olestra, which it is marketing under the trade name Olean.

Because of its unique chemical composition, olestra adds no fat or calories to food. Potato chips, crackers, tortilla chips, or other snacks made with olestra will be lower in fat and calories than snacks made with traditional fats.

Olestra may cause abdominal cramping and loose stools in some individuals, and it inhibits the body's absorption of certain fat-soluble vitamins and nutrients. FDA is requiring Procter & Gamble and other manufacturers who use olestra to label all foods made with olestra and to add essential vitamins—vitamins A, D, E, and K—to olestra.

As a condition of approval, Procter & Gamble will conduct studies to monitor consumption as well as studies on olestra's long-term effects. FDA will formally review these studies in a public meeting of the Foods Advisory Committee within 30 months from the date of olestra's approval.

The following labeling statement will be on all products made with olestra:

"This Product Contains Olestra. Olestra may cause abdominal cramping and loose stools. Olestra inhibits the absorption of some vitamins and other nutrients. Vitamins A, D, E, and K have been added."

Like all food additives, olestra's safety was the primary focus of FDA evaluation. For olestra, the safety evaluation focused not only on its toxicity, but also on the product's effects on the absorption of nutrients and on the gastrointestinal system.

Studies of olestra indicated it may cause intestinal cramps, more frequent bowel movements, and loose stools in some individuals. These gastrointestinal effects do not have medical consequences. The required labeling will give consumers needed information to discontinue the product if appropriate.

Clinical testing also indicated that olestra absorbs fat-soluble vitamins (vitamins A, D, E and K) from foods eaten at the same time as olestra-containing products. Studies also demonstrated that replacing these essential nutrients in olestra-containing snacks compensates for this effect. This information will also be included in the product labeling.

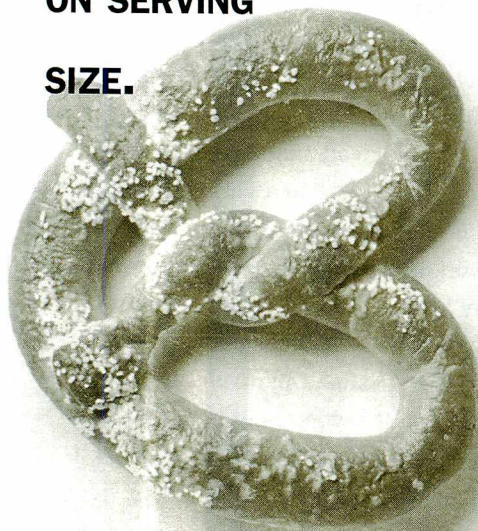
In addition to inhibiting the absorption of essential vitamins, olestra reduces the absorption of carotenoids—nutrients found in carrots, sweet potatoes, green leaf vegetables, and some animal tissue. The company's

postmarketing monitoring of olestra consumption levels and additional studies will provide FDA with further information about olestra's effects on the absorption of carotenoids. The role of carotenoids in human health is not fully understood, and FDA is continuing to monitor all available scientific research on it.

In addressing these questions, FDA evaluated more than 150,000 pages of data on olestra, drawn from more than 150 studies. Procter & Gamble submitted these data in its original 1987 food additive petition and in several subsequent amendments.

In addition, FDA sought advice from outside experts through its Food Advisory Committee. A special working group of the committee met in public in November 1995 to review and discuss the safety questions about olestra. The working group evaluated data presented by FDA, the company, and organizations and individuals both opposing and supporting olestra's approval. A clear majority of the working group agreed that all major safety issues had been identified and addressed by the FDA review, and that the data provided reasonable certainty that the proposed use of olestra would be safe. A majority of the full Food Advisory Committee reaffirmed that judgment. ■

**KNOWING THE
NUMBER OF
SERVINGS IN A
PACKAGE IS
IMPORTANT
BECAUSE THE
AMOUNT OF FAT,
SODIUM OR
CALORIES
LISTED ON THE
LABEL IS BASED
ON SERVING
SIZE.**



lines to enable you to compare the nutrient profiles of, say, baked potato chips and fried potato chips.

In addition, serving sizes must be based on values from government food consumption surveys, so they bear a closer resemblance to amounts that people typically eat. "But keep in mind that if you eat more or less of a snack food than the serving size listed on the label, you'll have to adjust the fat, sodium and caloric content accordingly," Diekman cautions. That means if the serving size is 14 potato chips and you eat 28, you'll have to take into account that you've munched and crunched twice as much fat, sodium and calories as the amounts listed on the label.

Although it seems counterintuitive, keeping track of portion size may be especially important when a food is low- or no-fat. Two recent studies indicated that people who know a food is low in fat tend to either eat more of it, or to eat more throughout the day to compensate.

"Fat-free is not calorie-free," warns Diekman. "For some reason, people seem to think they can eat as much as they want of a food that is low in fat or fat-free." She points out that if you cut out every ounce of fat from your diet, but consume three times the calories, you will gain weight.

Kulakow agrees, and points out that fat-free or low-fat versions of snack foods often contain high amounts of added sugars or sodium to compensate for the loss of flavor that occurs when fat is removed. So she cautions consumers to examine the amounts of these nutrients on fat-free and low-fat products, and to pay close attention to the calories in a single serving to avoid concluding that fat-free is synonymous with low in calories.

Some Valuable Information

If you zero in on the Amount Per Serving section of the Nutrition Facts panel, you'll be able to tell at a glance whether a snack food is high in calories, fat, saturated fat, cholesterol, and so-

dium. "The top part of the food label makes it easy to compare chip A to chip B," says Diekman.

The first line lists the number of calories in the food, and the number of calories from fat. For instance, when choosing a dip, the number of calories from fat is a clue that salsa is much lower in fat than sour cream-and-onion. If you need to watch your sodium intake, you can also compare the sodium content of a serving of baked tortilla chips and baked potato chips before deciding which one to toss into your shopping cart.

In addition to listing the amounts of fat and other nutrients by weight, the Nutrition Facts panel also gives this information as a percentage of the Daily Value. The %Daily Value is based in part on the government's Dietary Guidelines and is meant to show how a serving of a food fits in with current recommendations for a healthful diet. "Many people only look at the number of grams of fat in an individual food, but have no sense of how it fits into the daily diet. The %Daily Value quickly lets you know this as well as whether a food is high or low in a nutrient, such as fat," says Kulakow.

Thus, the %Daily Value enables consumers to go beyond making individual food choices to determine how a particular food affects the overall diet. "For example, if you want a low- or fat-free snack, pretzels are a great choice. But if you eat two servings, you can get as much as 54 percent of the recommended *daily* sodium intake. Although you're avoiding fat, you're getting a double whammy of salt," Kulakow explains.

Diekman comments, "If you've tried baked tortilla chips and find that you don't like them, you may decide instead to limit the amount of fat you get by dipping your fried tortilla chips into salsa instead of guacamole. The %Daily Value portion of the food label allows you to make choices that meet your dietary needs while still eating the foods you enjoy."

At the bottom of the Nutrition Facts panel, you'll see that %Daily Values are

Smart and Easy

Today, it's easier than ever to find a version of your favorite brand or type of snack food that is lower in fat or sodium—or both—than the “regular” version. With a bit of comparison shopping, you’ll find snack foods you can enjoy even if you are on a restricted diet because of high blood pressure or another medical problem. These are some of the descriptors to look for on the front of the package:

- **fat-free:** less than 0.5 grams (g) of fat per serving
- **low-fat:** 3 g or less per serving (if the serving size is 30 g or less or 2 tablespoons or less, no more than 3 g of fat per 50 g of the food)
- **light:** one-third fewer calories or half the fat of the “regular” version
- **low-sodium:** 140 milligrams (mg) or less per serving (if the serving size is 30 g or less or 2 tablespoons or less, no more than 140 mg of sodium per 50 g of the food)
- **lightly salted:** at least 50 percent less sodium per serving than the “regular” version
- **reduced:** when describing fat, sodium or calorie content, the food must have at least 25 percent less of these nutrients than the “regular” version. ■

—R.P.



based on a 2,000-calorie diet. Even if you eat more or less than 2,000 calories, the %Daily Value can serve as a useful reference to determine whether a food is high or low in a particular nutrient. “People know they should limit the amount of fat in their diets, but they don’t always remember the recommendation to keep fat below 30 percent of caloric intake for the day or, if they do remember, don’t know how to calculate the amount of fat they should eat in a day to stay within this limit. With the

%Daily Value, however, the label does the math for you,” Kulakow says.

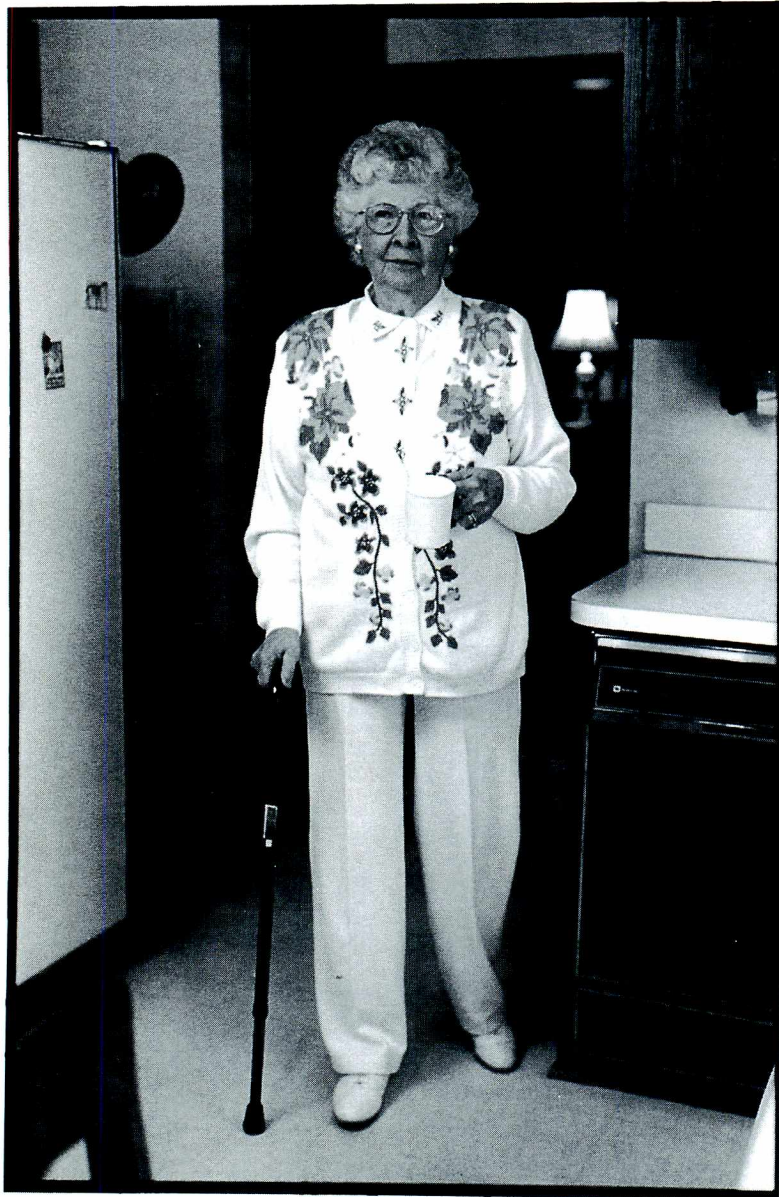
The %Daily Value can also help you distinguish between two similar products, particularly when it involves a comparative nutritional claim, such as reduced fat. “You don’t need to know the precise definition of ‘low’ or ‘reduced.’ Just look at the %Daily Value and see which is higher or lower in the nutrient you are interested in,” Kulakow advises.

“You don’t have to go to extremes—

cutting out all snack foods from your diet or eating only products that are fat-free,” she says. “The new food label helps you to eat what you like and still meet nutritional recommendations if you balance your food choices. The key is to use the label to help you make informed choices that fit into your total daily diet. That way education, not deprivation, can help you achieve your dietary goals.” ■

Ruth Papazian is a writer in New York City.

New Ways To Heal



BROKEN BONES

by Dixie Farley

The body's 206 dynamic, living bones renew themselves lifelong through a continual breakdown, build-up process known as remodeling.

Two years after surgery for a broken hip, Arizonan Jacqueline Wallace takes a stroll at the scene of her fall—her son's home in Gaithersburg, Md.

Jacqueline Wallace, of Phoenix, sat enjoying the December 1993 holidays at her son's home in Gaithersburg, Md. But when she stood up and took a step, her holiday took a turn for the worse. Wallace fell and fractured her hip.

"My foot dragged a little, not exactly a stumble," Wallace says. "I don't know whether the bone broke because I fell, or I fell because the bone broke."

Despite her 84 years and weak heart, Wallace had a lot going for her after her fall: modern medical practice and determination to walk again. Surgery to implant an artificial hip joint took under 45 minutes. Spinal anesthesia and sedation were administered instead of general anesthesia because they are

thought to pose less risk. And her physical therapy began the day after the operation.

"I fussed," she says. "I was afraid it was going to hurt or I'd fall. But they said if you want to go home, you have to do this. And I did. It was more scary than painful."

Wallace's fracture was one of 1.5 million—including 336,000 hip fractures—reported in 1993, the latest year for which the National Center for Health Statistics has figures.

Besides surgical repair, treatments for broken bones include bone manipulation to reduce the fracture, use of a cast, and bone stimulation. Central to fracture healing is bone biology. Many treatments, some on the horizon, are designed to improve the natural course of healing.

Bones at Work

For skeletal growth and maintenance, the body's 206 dynamic, living bones renew themselves lifelong through a continual breakdown, build-up process known as remodeling. This process is also involved in the remodeling of fractures, says Martin Yahiro, M.D., a Baltimore orthopedist in private practice and a consultant on fracture treatment devices to the Food and Drug Administration's Center for Devices and Radiological Health.

In remodeling, complex chemical signals prompt cells called osteoclasts to break down and remove (resorb) old bone, and others called osteoblasts to deposit new bone. Many elements influence remodeling. Among them: weight-bearing, vitamin D, growth factors, prostaglandins, and various hormones, including estrogen, thyroid, parathyroid, and calcitonin.

As 80 percent of the mature skeleton, compact *cortical bone* supports the body, providing extra thickness mid-shaft in long bones to prevent their bending. *Cancellous bone*,

whose porous structure with small cavities resembles a sponge, predominates in the pelvis and the 33 vertebrae from the neck to the tailbone. A fibrous membrane called the *periosteum* covers bone.

For healing and health, living bone must have a steady supply of nutrients. Blood vessels permeate bone to provide this lifeline. Blood-forming elements fill the long bone inner canals.

When a Bone Breaks

Fracture breaks continuity of bone and of important attached soft tissue—including blood vessels, which spill their contents into surrounding tissue.

Even before treatment, the body automatically seeks to repair the injury. Inflammatory cells rush to destroy, dilute or isolate invaders and injured tissue. Tiny new blood vessels called capillaries begin growing into the site. Cells proliferate. The injured person usually must endure pain, swelling, and increased heat at the breakage site for one to three days.

New tissue bonds the fractured bone ends with a soft callus, a mass of connective tissue and exudate (matter es-

caped through blood vessel walls). Remodeling begins. Within a few months, a hard callus replaces the soft one. Remodeling restores the inner canal.

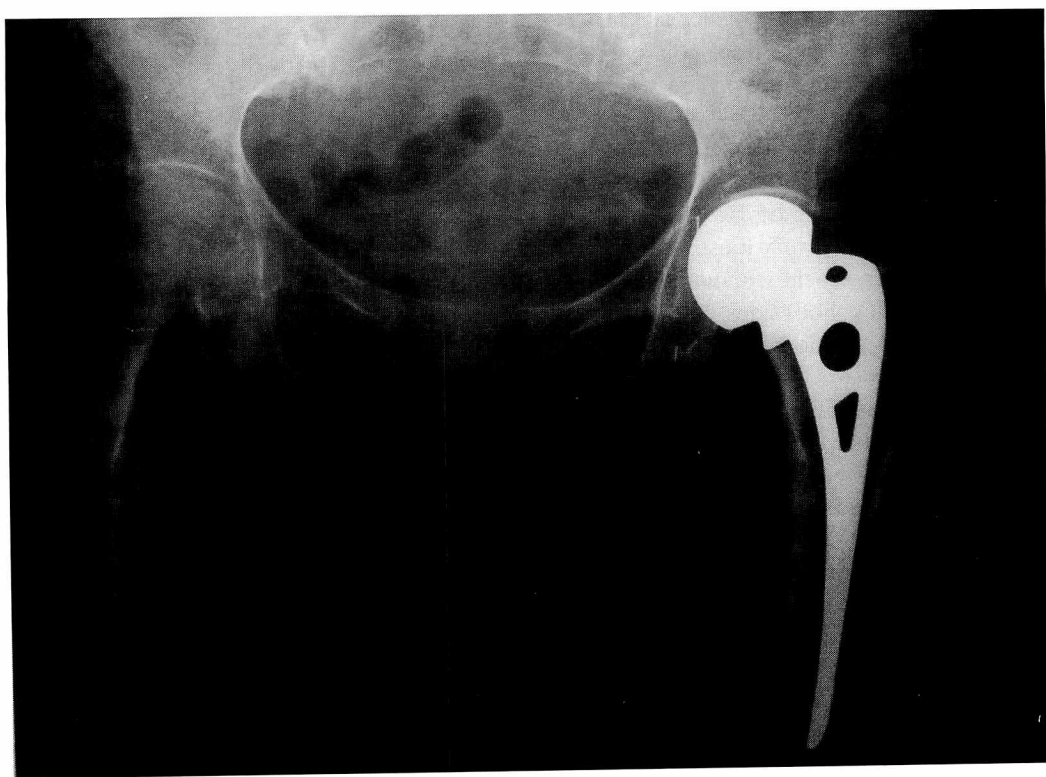
Once restoration is complete, which may take years, the healed area is brand new, without a scar. Usually thicker, the new bone may even be stronger than the old, Yahiro says, adding that if the bone should break again, it's unlikely to be at the same place.

And children's bones have a healing boost: They're growing.

"The growing skeleton is just geared to make bone," Yahiro says. "A very young child's wrist bones grow a millimeter a month, to rapidly correct misalignment or length defects. An adult may take six to eight weeks to heal a wrist fracture, a 5-year-old only three."

When the ends of a fractured bone, such as an arm bone, form an abnormal angle, the doctor must decide whether to push the ends together (manipulation) to reduce the fracture, possibly under anesthesia. Simple x-rays aid evaluation.

"If it's a large angle, we'd want to reduce that fracture," Yahiro says. "But if it's a small angle, especially in a young



This x-ray shows the ball and stem of Jacqueline Wallace's artificial left hip in sharp contrast with the bones of her normal right hip.

child whose growth will correct it, we'd probably just put the limb in a cast."

Surgery for Joint Fractures

Joint fractures usually require surgery, Yahiro says. "We try to restore the joint to perfect, like putting a jigsaw puzzle back together."

An artificial joint can be used to replace a fractured head of the long bone in the hip, like Wallace had, or in the shoulder.

Total hip joint replacements are mainly made of titanium or cobalt-chrome alloys or other metals. Each replacement has a stem that goes into the thigh bone inner canal, a ball for the head, and a plastic cup socket—the latter usually only used if the joint is badly arthritic. Yahiro often uses bipolar joints—a big ball atop a smaller one. All these joint replacements are approved by FDA.

Approved replacements for fractures in shoulder joints also consist of a ball and stem.

Andrew Bender, M.D., the orthopedist who implanted Wallace's partial replacement, says this simple model has been in use 30 to 40 years. "It has different size balls, one size stem, so it's not an exact fit. But it gives what we call a three-point fixation for some immediate tightness. The stem has holes for bone to grow through and across for more permanence."

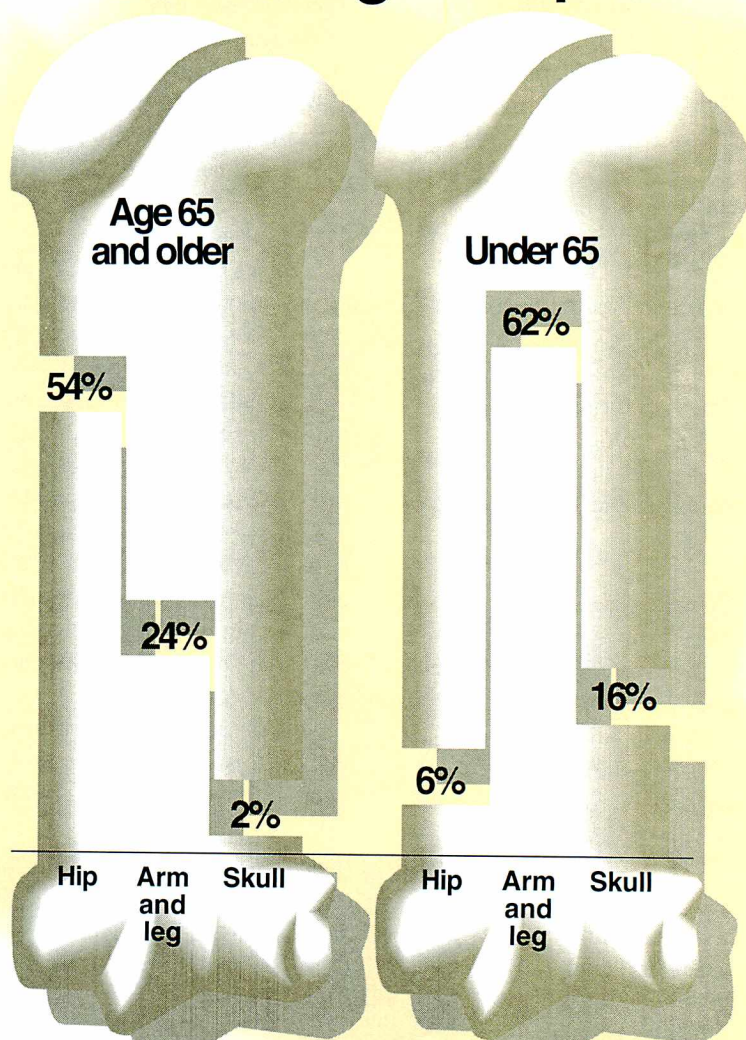
Bender pressed in Wallace's device without cement, a snug fit. He cements only if the fit is very, very loose. "Modern day hip replacement without cement is relatively quick, both sides. She had only one side done and good bone, so it didn't take long."

If a replacement fails, it usually does so within 5 to 10 years. Simple models tend not to fail in the very old, Yahiro says. "A person in a chair or bed most of the time won't put demands on the joint that, say, Bo Jackson does." (Jackson had a hip replacement in 1992 due to a football injury.)

For higher demand, there are more precisely fitted models.

A robot that drills a more precise hole for the stem, to possibly keep the joint intact longer, is under investigation for use in cementless hip joint replacements. (See "Robots in the Operating Room," July-August 1993 *FDA Consumer*.)

Fractures in Seniors and Younger People



In 20 percent of people 65 and older, and 16 percent of people under 65, the fractures occurred in places other than those shown in this graphic.

(Source: National Center for Health Statistics' National Hospital Discharge Survey, 1992)

An external fixator—a pin-and-rod frame—can keep the joint from being compressed by other bones, to heal before a load, or stress, is put on it again. Pins are inserted on one side of the limb through the skin, muscle and bone, out the other side, and attached to the external rod, forming the frame.

About 30 percent of patients get infected at the pin site, so meticulous hygiene is crucial. "It's a race," says Kenneth McDermott, who reviews the devices for the Center for Devices and Radiological Health. "The pin goes through the skin, and infection can go right down the pin."

Internal fixation devices pose less risk of infection. These metal plates, rods, wires, screws, nails, pins, staples, and anchors may sometimes be left in. A tiny pin may not be felt, but plates or screws may cause irritation or pain. The decision whether to remove the device in a second surgery is made on a case-by-case basis.

Surgery to remove a screw in the very old may be too risky. For a 20-year-old, benefits of a second surgery may outweigh risks. In the ankle, plates and screws are customarily removed. Yahiro says, "The bones are so superficial, the device often rubs on the shoe."

For healing and health, living bone must have a steady supply of nutrients.

McDermott gives another reason for removing a plate or screw: "It can take the load off the bone, causing the bone to resorb and weaken."

Fixators and internal fixation devices are used also for some mid-bone fractures.

Grafts

The surgeon may graft bone to replace a missing segment that had to be surgically removed due to infection.

For a small segment, tissue can be taken from the patient's own bone (autologous graft).

Cadaver bone (allograft) may be used, especially for a large segment. Though dead tissue, cadaver bone provides a scaffold for living bone to grow into and remodel the graft. For healing to occur—and sometimes it doesn't—the body must put blood vessels into the graft to nurture the new living bone as it replaces the dead tissue. Healing takes longer than with an autologous graft.

Another option is a substitute bone graft, fashioned with help from nonhuman substances. FDA recently approved two such grafts:

- **Pro Osteon Implant 500 Coralline Hydroxyapatite Bone Void Filler** (1992)—Fills holes near the ends of long bones in adults. It derives from marine coral, whose spongy calcium structure resembles human cancellous bone.
- **Collagraft Bone Graft Matrix** (1993)—Treats long-bone fractures and other injury-caused areas of missing bone of 30 milliliters (1.8 cubic inches) or less. The product—consisting of purified cow collagen and a chemical, hydroxyapatite-tricalcium phosphate—is mixed with the patient's marrow into a paste and put into the area of missing

Boning Up

The most important influences on fracture healing are nutrition and overall health, including bone health, *before* the injury, says orthopedist Martin Yahiro, M.D., a consultant to FDA. "That's why it's so important all your life to do weight-bearing exercise such as walking and get enough calcium and vitamin D, so you lay down as much bone as possible during growth and keep as much as you can later on."

The Recommended Dietary Allowance (RDA) for calcium is 1,200 milligrams a day for people ages 11 to 24 and for pregnant or breast-feeding women. For men and women older than 25 who no longer have to meet the greater demands of growth, the calcium RDA is 800 milligrams a day.

In general, genes decide bone shape and size. But mechanical stress by muscle, body weight, and physical activity influence bone shape and density—and health—throughout life.

Simply put, loaded (stressed) bone strengthens, and unloaded bone weakens. As examples, astronauts' bones weaken in outer space with no gravity pull on them, and the shaft of the humerus (long upper arm bone) in a professional tennis player's dominant arm gets denser and thicker from the extra load.

The body increases its bone mass until, usually, the mid-30s, after which a gradual loss begins.

Age-related bone loss can lead to osteoporosis, a condition of thin, weakened bone that fractures easily. The condition affects many postmenopausal women, because bone loss increases with menopause due to lower estrogen levels.

In announcing its recent approval of Fosamax and Miacalcin Nasal Spray for osteoporosis, FDA advised that patients also exercise and get adequate calcium and vitamin D. Drugs approved by FDA to prevent or treat osteoporosis are:

- **estrogen**—Premarin, Ogen, and Estrace tablets; Estraderm patch
- **estrogen packaged with progestin hormone tablets**—Prempro; Premphase
- **alendronate**—Fosamax
- **calcitonin**—Miacalcin Nasal Spray, Calcimar Injection, Miacalcin Injection, and Cibacalcin for injection. ■

—D.F.

bone to encourage new bone growth. It's not for use in certain patients, such as those with osteomyelitis (bone inflammation) at the fracture site, severe allergies, or allergy to cow collagen, and those being desensitized to meat products, as the treatment injections may contain cow collagen.

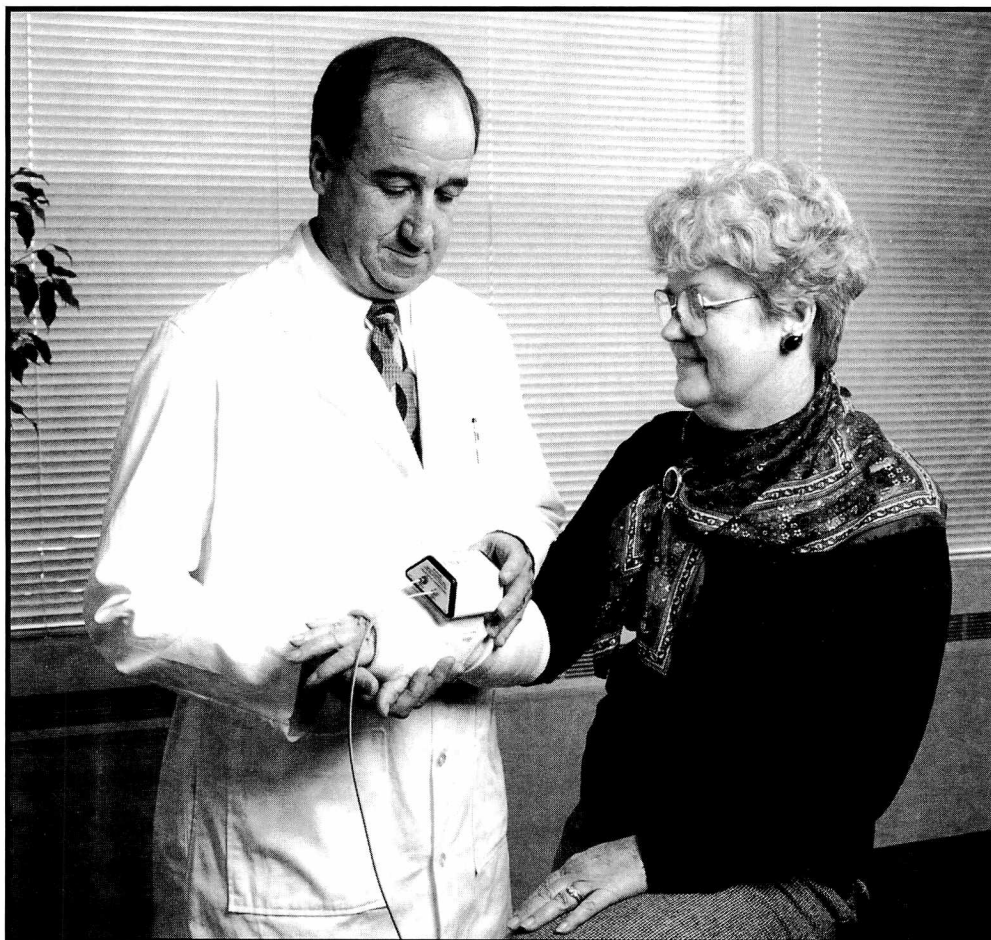
When these substitute grafts are placed next to healthy bone, the body remodels them in the same way it remodels human grafts. But according to Center for Devices and Radiological Health reviewer Nadine Rosile, "The substitute grafts aren't strong enough for use without a fixation device to stabilize the fracture."

A bone filler paste now under investigation, however, is as strong as bone within 12 hours, according to a report of a study of patients whose wrist fractures

were injected with the paste. The report, in the March 24, 1995, issue of *Science*, stated that the paste stabilized the bone during healing and was eventually remodeled. The patients had greater grip strength at six months than historical controls (other patients in the past who had not been treated with the paste) had at two years, the report stated.

Also under investigation are injections of growth factor proteins, such as morphogenic protein and transforming growth factor-beta, found naturally in the body in very small amounts.

"The proteins turn on cells to produce bone," Yahiro says. "Animal studies show growth with injections similar to that with autologous grafts." The hope, he says, is that injected fractures, even with large areas of missing bone, will heal faster and be stronger, without grafts.



These models demonstrate how a health-care worker would show a patient proper use of the Sonic Accelerated Fracture Healing System. The device is the first approved ultrasound bone growth stimulator, and the first stimulator for fractures occurring within seven days before treatment.

(Photo courtesy of Exogen, Inc., Piscataway, N.J.)

Healing Helpers

FDA has approved seven electrical bone growth stimulators, mainly for fractures at the middle of long bones, such as the shinbone (tibia), that have not healed over at least nine months. Although exactly how the stimulators heal is unknown, manufacturers' studies showed the devices did in fact affect cellular processes.

Yahiro explains that loading (stressing) a bone produces in it a small electrical field called piezo electric force, believed to stimulate new bone formation. "It's believed that electrical stimulation does something like that on a large scale," he says.

For direct stimulation, an electrode is implanted at the fracture, linked through the skin to a generator. For indirect stimulation, electric coils outside the limb on the non-fracture side induce an electrical field at the fracture side.

In 1994, FDA approved the first ultrasound bone growth stimulator. The Sonic Accelerated Fracture Healing Sys-

tem (SAFHS) is for adults with small fractures in the lower leg or lower forearm. A cast or splint is used. It is the first stimulator for the treatment of fractures occurring within seven days before treatment. Studies suggest that mechanical forces of the ultrasound waves transform into electrical impulses as they travel through the tissues.

The SAFHS consists of a portable generator cabled to a small, square treatment module that emits ultrasound pulses at about the same low intensity as sonogram fetal monitors. In some instances, the patient may use the unit at home. Recommended treatment is 20 minutes once a day until the fracture heals.

The SAFHS is not for patients who need additional fixation or surgery, are pregnant or breast-feeding, have bone disease or circulatory problems, or take medicines that may adversely affect remodeling.

In studies, all treated patients—and especially older people—healed faster

than those using a placebo. In those age 50 and older, arms healed 40 days faster, and legs 85 days faster. Six years' follow-up did not suggest long-term adverse effects.

Stimulation, grafts, manipulation, joint replacements, casts. Whatever the treatment, fracture healing is monitored by x-rays and physical examination to answer such questions as: Does it hurt or move when pushed on? On x-ray, does the fracture look healed? On x-ray, are the bones aligned?

For Wallace, healing is now complete. She is indeed walking again, using a cane as she did before the replacement surgery.

"If I don't use the cane, my leg aches," she says. "I'm still careful to use my good leg stepping up a curb, and my bad leg stepping down, like I learned in therapy." ■

Dixie Farley is a staff writer for FDA Consumer.

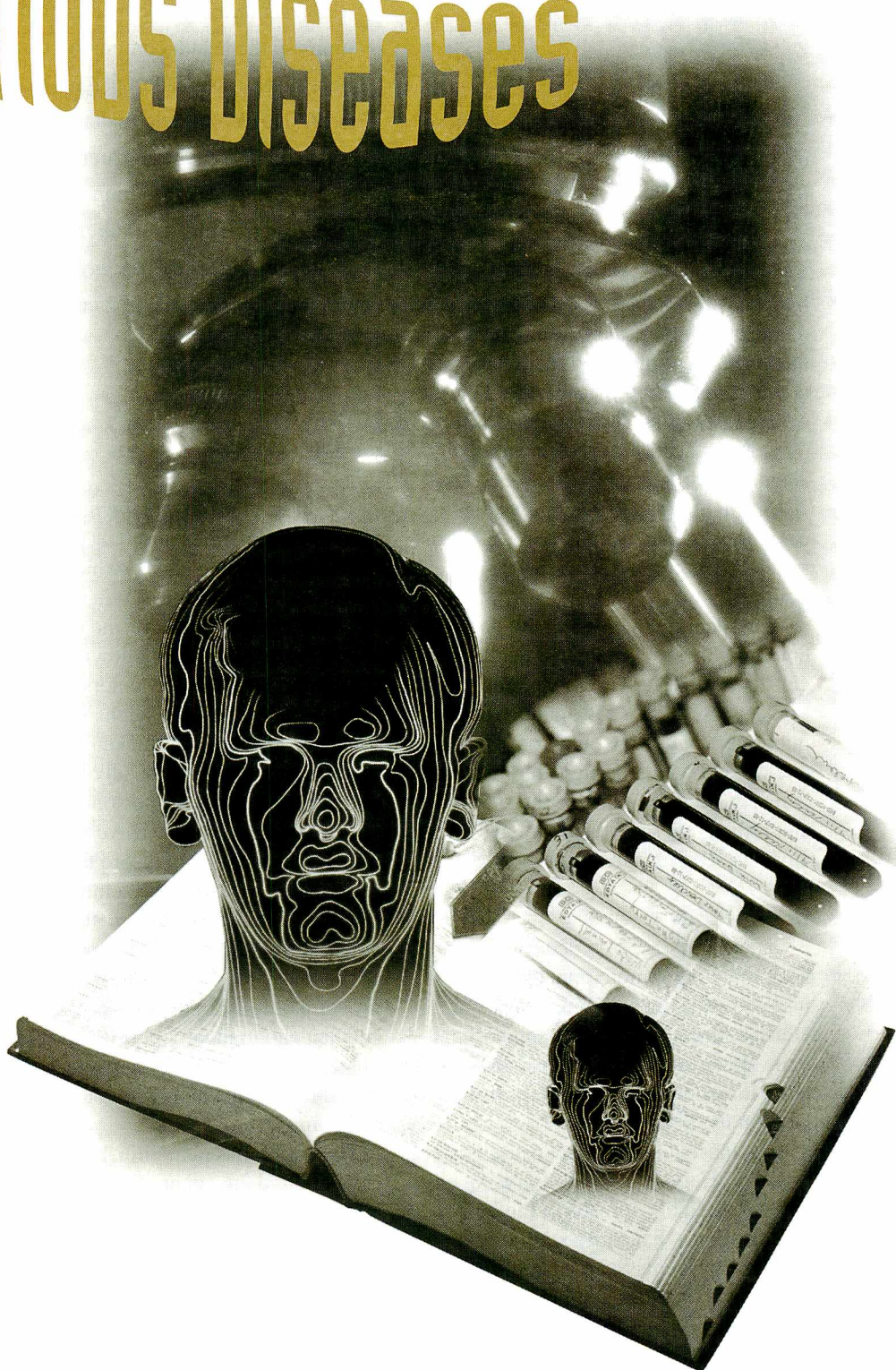
Book Reopened On Infectious Diseases

by Margie Patlak

In the late 1960s, after seeing such deadly diseases as smallpox, polio, and rheumatic fever get tamed by vaccines or antibiotics, Surgeon General William H. Stewart declared that it was time to close the book on infectious diseases and pay more attention to chronic ailments such as cancer and heart disease.

This commonly held belief that the war on infectious diseases could be won has been shattered by a score of new or reemerging diseases that have surfaced in epidemics scattered across the globe over the last 15 years, with some occurring within just the last year or two.

The new epidemics, combined with a deeper understanding of disease dynamics and the tricks microbes have up their sleeves, have shaken the medical community and led to a less rosy outlook. An article in the Jan. 17, 1996, issue of the *Journal of the American Medical Association* reported that infectious disease is now the third leading cause of death, after



heart disease and cancer. Deaths from infectious disease rose 58 percent between 1980 and 1992, according to the article by Róbert W. Pinner, M.D., of the national Centers for Disease Control and Prevention, and colleagues. Most of the increase is from AIDS cases. Yet even without AIDS cases, the death rate from infectious diseases rose 22 percent.

Some infectious disease experts wager future epidemics will take a greater toll on human life than those in the past, despite medical advances made over the past century. We are increasingly more vulnerable to infectious diseases, these experts point out, because of the growing proportion of people residing in urban areas, which act as magnets for epidemics. In 1800, less than 2 percent of the world's population lived in urban communities. By the year 2000, however, that fraction is expected to rise to 50 percent, according to the National Academy of Sciences.

Air travel, in addition, allows diseases to spread between cities on opposite ends of the globe in a matter of hours.

Prominent on the list of new or re-emerging diseases that have health officials concerned are invasive strep infections, tuberculosis (TB), hantavirus pulmonary syndrome, malaria, and dengue. The Food and Drug Administration is responsible for insuring the safety and effectiveness of the drugs and vaccines used to curb infectious diseases.

Deadly Strep

Changes in the *Streptococcus* bacterium that give it more punch are credited with causing recent outbreaks of "flesh-eating" strep and streptococcal toxic shock syndrome (strep TSS). The latter disorder killed puppeteer Jim Henson in 1990.

Both these infections are caused by invasive strep—a type of *Streptococcus* that more readily spreads in the body than the types that cause strep throat. Studies by Dennis Stevens at the Veterans Affairs Medical Center in Boise, Idaho, suggest invasive strep is armed with two powerful toxins. In the body's furious attempt to rid itself of one of the toxins, the immune system can foster the destruction of infected muscle tissue

Worldwide Prevention Efforts

"Prevention is so much better than healing because it saves the labor of being sick," said Thomas Adams, a 17th century English preacher. Experts convened by the National Academy of Sciences suggest:

- **Surveillance**—to keep an extensive global lookout for new or reemerging infections so the health community can develop the appropriate containment measures before diseases spread to plague-like proportions.
- **Research**—to help understand the factors that foster emergence of infectious diseases, and to develop better surveillance, diagnosis, treatment, and prevention tactics.
- **Vector control**—to limit the spread of diseases transmitted by such vectors as insects and rodents by eradicating them.
- **Public education and behavioral change**—To prevent spread of diseases through travel, poor personal hygiene, improper food handling, drug abuse, and high-risk sexual behavior. ■

—M.P.

or the sheath that covers the muscle (the flesh-eating manifestation) or prompt the body to go into shock, which is often fatal, or both. Damage also is wreaked by the other toxin, an enzyme that destroys tissue by breaking down protein.

Invasive strep usually enters the body through minor injuries, such as deep bruises, punctures, or chicken pox blisters. Only rarely is the deadly form of strep acquired through person-to-person contact. People with invasive strep usually don't complain of a sore throat, but rather often have flu-like achiness and fatigue that is followed by a number of symptoms, including pain in one region of the body, cough and difficulty breathing, or painful skin that is red, hot and swollen and gradually purples and forms blisters. This can be accompanied or followed by confusion, low blood pressure, and coma.

The antibiotics penicillin, erythromycin and clindamycin are the drugs of choice for treating invasive strep infections; the earlier treatment is begun, the better the outcome. Surgical removal of infected tissue, possibly including limb amputation, may be necessary. Researchers are currently testing a vaccine for invasive strep.

CDC estimates that about 15,000 cases of invasive strep infections occur

each year in the United States, and studies by Stevens and others suggest one out of three people with invasive strep die. The infection can kill in less than a week.

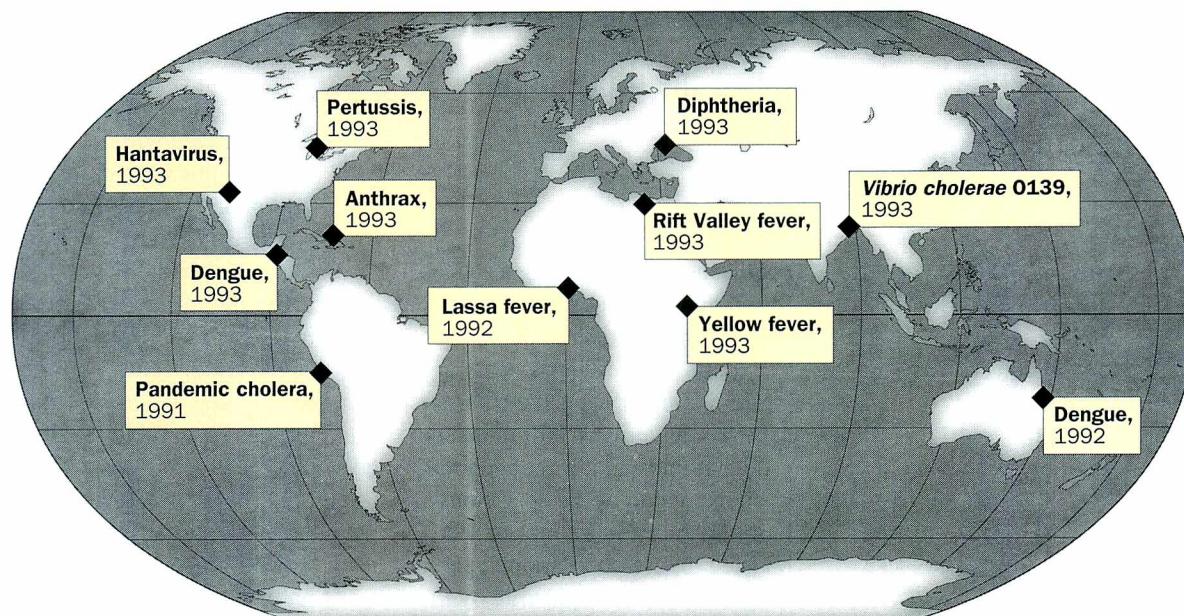
Like most diseases, invasive strep is not new; China experienced an epidemic of flesh-eating strep in 1924, and strep infections were a major cause of death in Chicago and other cities in this country in the middle of the 19th century. It's not known for certain whether invasive strep currently is on the rise in this country. At this point, however, it is still considered a rare disease.

Tuberculosis

After a comforting steady decline since the 1950s, TB incidence in the United States began to climb in 1985, setting off alarms in the medical community. According to CDC, in 1994 there were 24,361 cases of TB in the United States—about 2,000 more cases than in 1984.

TB's comeback in this country is tied to the rising numbers of people whose immune systems are weakened by HIV infection, cancer and chemotherapy, or the drugs taken following an organ transplant. A resurgence of the disease is also being fostered by increasing poverty and drug abuse, as well as by in-

Recent Appearances of Infectious Diseases



This map shows some of the locations of new or reemerging infectious diseases and the year the first recent cases appeared.

(Source: Centers for Disease Control and Prevention)

creasing numbers of immigrants to this country with TB.

Well-known to the ancient Egyptians, TB is caused by airborne bacteria expelled from the lungs when a person with active TB coughs, sneezes or speaks. Repeated exposure to these droplets can infect another person's lungs.

The immune defenses of healthy people usually prevent TB infection from spreading beyond a small area of the lungs by creating a barricade around the bacteria. This walled-up infection is called latent TB and may be present throughout a person's life. People with latent TB test positive on the TB skin test. About 10 to 15 million people in this country have latent TB.

If the body's immune system is impaired, the TB bacteria may begin to spread more widely in the lungs or to other tissues causing active TB infection.

The early symptoms of active TB include fatigue, weight loss, fever, chills, and night sweats. Once the infection has progressed, people may develop a cough or chest pain, or produce sputum

that may contain blood. TB can spread beyond the lungs causing additional symptoms such as back pain or blood in the urine.

FDA recently approved a sputum test for TB that gives results in four to five hours, compared to the one to eight weeks required by conventional sputum culture tests. The Amplified Mycobacterium TB Direct Test is for use on specimens already shown likely to be positive for TB on an acid fast stain test. The new test allows treatment to begin sooner, but a follow-up conventional culture test must also be done.

TB is treated with a combination of several antibiotics, which have to be taken for six to nine months to be effective. CDC recommends that people with latent TB who develop HIV infection or another condition that suppresses the immune system receive preventive therapy with the antibiotic isoniazid, marketed under the brand name INH. People who have been in close contact with someone with active TB and test positive on a TB skin test should also take isoniazid, which is highly effective in preventing a latent TB infection from

progressing to active disease.

Drug-resistant strains of TB develop when people stop taking their TB drugs too soon or take them incorrectly. About 90 percent of people with TB that responds to standard antibiotics are cured of the disease. But only 10 percent of those people afflicted with drug-resistant TB survive.

There has been a disconcerting increase in the number of drug-resistant TB cases in outbreaks scattered across the country. (See "The Rise of Antibiotic Resistant Infections" in the September 1995 issue of *FDA Consumer*.) Particularly disturbing are the 1 out of 10 cases of drug-resistant TB that have occurred in healthy people with normal immune systems. They died at the same rate as those with faulty immune systems afflicted with the drug-resistant TB.

Noting the ease with which TB is passed from person to person, a 1992 National Academy of Sciences report on emerging infections warned that drug-resistant TB "represents a major threat to health in the United States."

In response to the drug-resistance

TB's comeback in this country is tied to the rising numbers of people whose immune systems are weakened by HIV infection, cancer and chemotherapy, or the drugs taken following an organ transplant.

problem, FDA has pledged to speed up the review process for new TB drugs. One TB drug is currently being tested in a clinical trial, and another may soon undergo such testing.

A vaccine that can prevent TB from spreading beyond the lungs is available. But because the vaccine cannot reliably prevent TB lung infections in adults, it currently is not recommended for general use or for health-care workers, according to CDC. The vaccine is also problematic because it causes people to test positive for a TB skin test, which is the mainstay for TB surveillance in this country.

Hantavirus

The 1993 outbreak of hantavirus pulmonary syndrome (HPS) in the Southwest caught health officials by surprise. The new syndrome initially causes flu-like symptoms, and then causes its victims to gasp for air as their lungs fill with fluid. The disease kills about half the people it infects, usually within a week. There is no treatment approved specifically for hantavirus, but researchers are currently assessing the effectiveness of the antiviral drug Virazole (ribavirin) for HPS. A vaccine is being developed.

HPS is caused by a hantavirus named Muerto Canyon (Valley of Death) virus for the spot in New Mexico where it was isolated. It is carried by rodents and passed to people who inhale the aerosol particles emitted by the infected rodents' saliva, urine or feces. People can become infected with hantavirus after being bitten by rodents. Many people who have developed HPS live in mice-infested homes. One woman who developed the disorder, however, was exposed to rodents her pet cat dragged into her house. Another person succumbed to

the disease after cleaning a rodent-infested barn. Hantaviruses are not passed directly from person to person.

Experts suspect that rodents in the western United States have harbored the Muerto Canyon virus for quite some time, but unusual weather conditions led to an explosion of the deer mouse population in the early months of 1993. The boosted mouse population apparently triggered the HPS epidemic by increasing contact between people and mice infected with the virus.

Since first described in the spring of 1993, more than 100 cases of HPS have been identified in 23 states, predominantly in the Western half of the country, according to CDC. The rodents that can carry the Muerto Canyon virus, however, live nearly everywhere in the United States.

The deer mouse population started declining shortly after the first HPS cases were reported. Between early 1994 and mid-1995, only 37 cases of HPS were reported to CDC, suggesting the hantavirus epidemic is waning.

People can stem their risk of a hantavirus infection by ensuring their homes and workplaces are free from rodents.

Airport Malaria

International jet-setting has fostered recent outbreaks of malaria in the United States. Malaria is such a common import to countries that the term "airport malaria" was coined to describe the outbreaks of the disease that have occurred among travelers. About 1,000 cases of malaria are imported into this country each year, according to CDC.

Malaria causes flu-like symptoms, and in severe cases can cause coma, severe anemia, kidney failure, difficulty breathing, or death. The disease is passed from person to person by mosquitoes that har-

bor the malaria-causing parasites.

Malaria was a major problem in this country during George Washington's time and, until the 1930s, was a major killer in the southern states. The disease was virtually eradicated from the United States by 1955, following a major campaign in which mosquito-infested areas were sprayed with the pesticide DDT and swamps were drained or filled with oil that killed mosquito larvae. People were also encouraged to screen the windows of their homes.

Similar efforts worldwide shrank malaria's territory, but only temporarily as mosquito-control efforts abated, mainly due to a lack of funds, and mosquitoes resistant to the effects of pesticides increased. According to the National Institute of Allergy and Infectious Diseases, each year malaria now infects 300 million to 500 million people globally and kills as many as 3 million.

There's concern that malaria might once again take root in the United States because most states harbor mosquitoes that can carry malaria parasites. Particularly disturbing are the recent small outbreaks of malaria in California, Florida, Texas, New Jersey, and New York City. Most of these cases were probably spread by infected immigrants or migrant workers via local mosquitoes, according to CDC.

"The reintroduction of significant malaria into this country is ... very possible," said Philip Coyne, M.D., medical officer in FDA's division of anti-infective drug products.

Malaria can often be effectively treated with quinine or related compounds. Drug-resistant strains of malaria parasites are posing a problem worldwide, however, and raising the need for new antimalarial drugs. FDA approved Halfan (halofantrine) in 1992. Its developer, SmithKline Beecham, Inc., has chosen not to market it in the United States. Some strains of malaria are already resistant to it. Other antimalarial drugs and vaccines are currently being tested.

Break-Heart Fever

Another mosquito-spread illness on the rise worldwide and likely to make a comeback in this country is dengue, which an 18th century Philadelphia doctor called "break-heart fever" because



Malaria control in the 1940s and '50s stemmed the spread of the disease, but malaria has still not vanished from the world scene. (Photo courtesy of National Library of Medicine)

of the depression that often ensues following the illness. Dengue, which is caused by a virus, is characterized by a sudden onset of high fever accompanied by severe headache and muscle, joint and eye pain. A red rash can also develop all over the body. The rash may be accompanied by itching and scaling.

A severe form of dengue, known as dengue hemorrhagic fever, causes bleeding from the mouth, nose and vagina. Gastrointestinal bleeding and numerous bruises also often occur. Such bleeding can trigger a loss of blood pressure that can cause the body to go into shock. As many as 1 out of every 10 people who develop dengue hemorrhagic fever dies. There is no treatment for dengue and dengue hemorrhagic fever, although vaccines for the disorders are currently being developed.

Over the last 15 years, as mosquito control programs abated, dengue has

spread like wildfire. In the 1980s, major outbreaks spread throughout Latin America, including Mexico, and the incidence of dengue hemorrhagic fever skyrocketed.

The United States hasn't had any major epidemics of dengue since the 1940s. But there are travelers to this country who come down with the disease each year, and a small number of people have developed dengue from local mosquitoes in Texas. Both species of mosquitoes that carry the dengue virus are firmly established in several southeastern states.

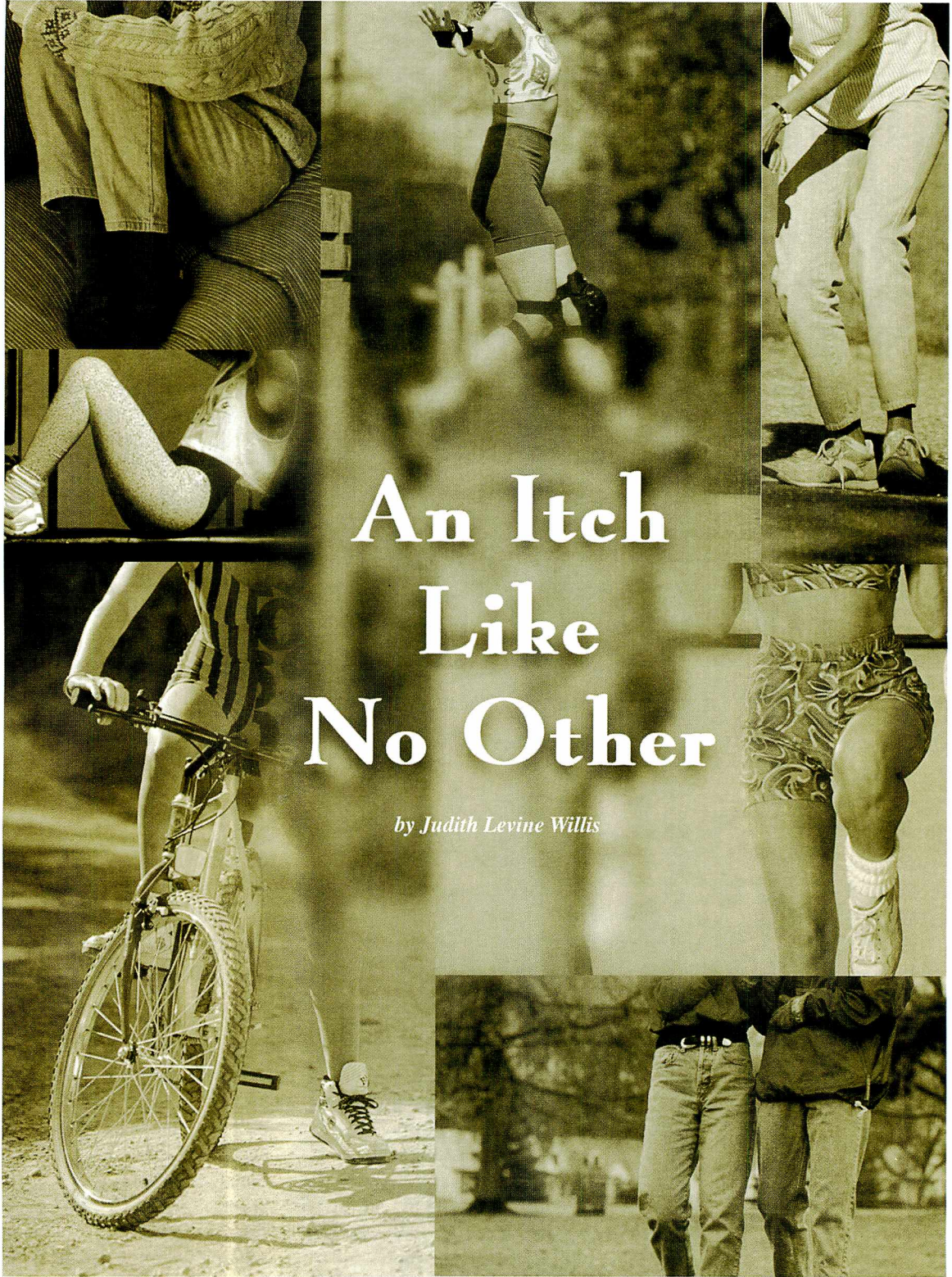
People traveling to dengue- and malaria-infested areas should use DEET-containing insect repellent and stay in lodgings with screened windows and mosquito nets for sleeping. Preventive drug therapy for malaria is also advised. Travelers should consult with their physicians about such treatment before leaving the country.

Other Health Threats

Other possible resurgent and emerging diseases include a dangerous kind of *E. coli* infection spread by contaminated meat, drug-resistant cholera, deadly Ebola infection, and a new disease called human granulocytic ehrlichiosis, which is spread by the type of ticks that can also carry Lyme disease.

Experts can't predict if any of these diseases will become a great problem. The best protection is to be aware of the possibility and take precautions to prevent their spread. As a 1992 National Academy of Sciences report on emerging infections points out, "despite a great deal of progress in detecting, preventing, and treating infectious diseases, we are a long way from eliminating the human health threats posed by ... a broad array of microbes." ■

Margie Patlak is a writer in Elkins Park, Pa.



An Itch Like No Other

by Judith Levine Willis

Images provided by © 1994 PhotoDisc, Inc.

It's an itchy feeling you might hardly notice at first.

Maybe, you muse, it's just that your jeans are too tight.

Actually, tight jeans may have something to do with it. But if the itch keeps getting itchier, even when your jeans have been off for awhile, then there's something else involved.

That something else could very well be a fungus whose technical name is *Candida*, and which causes what is often called a "yeast" infection. Such infections are most common in teenage girls and women aged 16 to 35, although they can occur in girls as young as 10 or 11 and in older women (and less often, in men and boys as well). You do not have to be sexually active to get a yeast infection.

The Food and Drug Administration now allows medicines that used to be prescription-only to be sold without a prescription to treat vaginal yeast infections that keep coming back. But before you run out and buy one, if you've never been treated for a yeast infection you should see a doctor. Your doctor may advise you to use one of the over-the-counter products or may prescribe a drug called Diflucan (fluconazole). FDA recently approved the drug, a tablet taken by mouth, for clearing up yeast infections with just one dose.

Though itchiness is a main symptom of yeast infections, if you've never had one before, it's hard to be sure just what's causing your discomfort. After a doctor makes a diagnosis of vaginal yeast infection, if you should have one again, you can more easily recognize the symptoms that make it different from similar problems. If you have any doubts, though, you should contact your doctor.

In addition to intense itching, another symptom of a vaginal yeast infection is a white curdy or thick discharge that is mostly odorless. Although some women have discharges midway between their menstrual periods, these are usually not yeast infections, especially if there's no itching.

Other symptoms of a vaginal yeast infection include:

- soreness
- rash on outer lips of the vagina
- burning, especially during urination.

It's important to remember that not all girls and women experience all these symptoms, and if intense itching is not present it's probably something else.

Candida is a fungus often present in the human body. It only causes problems when there's too much of it. Then

cause and receive proper medical care."

Repeated yeast infections can also be caused by other, less serious, illnesses or physical and mental stress. Other causes include:

- use of antibiotics and some other medications, including birth control pills
- significant change in the diet
- poor nutrition
- diabetes
- pregnancy.

When you visit the doctor the first time you have a yeast infection, you can ask which product may be best for you and discuss the advantages of the different forms the products come in.

infections can occur not only in the vagina but in other parts of the body as well—and in both sexes. Though there are four different types of *Candida* that can cause these infections, nearly 80 percent are caused by a variety called *Candida albicans*.

Many Causes

The biggest cause of *Candida* infections is lowered immunity. This can happen when you get run down from doing too much and not getting enough rest. Or it can happen as a result of illness.

Though not usual, repeated yeast infections, especially if they don't clear up with proper treatment, may sometimes be the first sign that a woman is infected with HIV, the virus that causes AIDS.

FDA requires that over-the-counter (OTC) products to treat yeast infections carry the following warning:

"If you experience vaginal yeast infections frequently (they recur within a two-month period) or if you have vaginal yeast infections that do not clear up easily with proper treatment, you should see your doctor promptly to determine the

Some women get mild yeast infections towards the end of their menstrual periods, possibly in response to the body's hormonal changes. These mild infections sometimes go away without treatment as the menstrual cycle progresses. Pregnant women are also more prone to develop yeast infections.

Sometimes hot, humid weather can make it easier for yeast infections to develop. And wearing layers of clothing in the winter that make you too warm indoors can also increase the likelihood of infection.

"*Candida* infections are not usually thought of as sexually transmitted diseases," says Renata Albrecht, M.D., of FDA's division of anti-infective drug products. But, she adds, they can be transmitted during sex.

The best way not to have to worry about getting yeast infections this way is not to have sex. But if you do have sex, using a condom will help prevent transmission of yeast infections, just as it helps prevent transmission of more commonly sexually transmitted diseases, including HIV infection, and helps prevent pregnancy. Teens should always use a latex condom if they have

Though itchiness is a main symptom of yeast infections, if you've never had one before, it's hard to be sure just what's causing your discomfort.

sex, even if they are also using other forms of birth control. (See "On the Teen Scene: Preventing STDs" in the June 1993 *FDA Consumer*.)

If one partner has a yeast infection, the other partner should also be treated for it. A man is less likely than a woman to be aware of having a yeast infection because he may not have any symptoms. When symptoms do occur, they may include a moist, white, scaling rash on the penis, and itchiness or redness under the foreskin. As with females, lowered immunity, rather than sexual transmission, is the most frequent cause of genital yeast infections in males.

OTC Products

The OTC products for vaginal yeast infections have one of three active ingredients: butoconazole nitrate (Femstat 3), clotrimazole (Gyne-Lotrimin and others), or miconazole (Monistat 7 and others). These drugs are in the same anti-fungal family and work in similar ways to break down the cell wall of the *Candida* organism until it dissolves. FDA approved the switch of Femstat 3 from prescription to OTC status last December. The others have been available OTC for a few years.

When you visit the doctor the first time you have a yeast infection, you can ask which product may be best for you and discuss the advantages of the different forms the products come in: vaginal suppositories (inserts) and creams with special applicators. Remember to read the warnings on the product's labeling carefully and follow the directions.

Symptoms usually improve within a

few days, but it's important to continue using the medication for the number of days directed, even if you no longer have symptoms.

Contact your doctor if you have the following:

- abdominal pain, fever, or a foul-smelling discharge
- no improvement within three days
- symptoms that recur within two months.

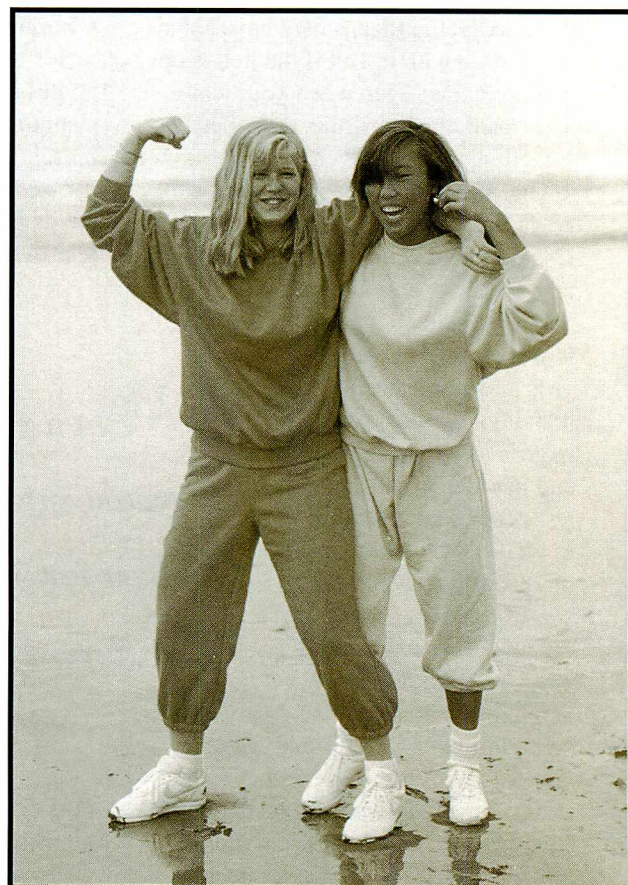
OTC products are only for vaginal yeast infections. They should not be used by men or for yeast infections in other areas of the body, such as the mouth or under the fingernails.

Candida infections in the mouth are often called "thrush." Symptoms include creamy white patches that cover painful areas in the mouth, throat, or on the tongue. Because other infections cause similar symptoms, it's important to go to a doctor for an accurate diagnosis.

How to Avoid Infection

Here are some steps young women can take to make vaginal yeast infections less likely:

- Wear loose, natural-fiber clothing and underwear with a cotton crotch.
- Limit wearing of panty hose, tights, leggings, nylon underwear, and tight jeans.
- Don't use deodorant tampons and feminine deodorant sprays, especially if you feel an infection beginning.
- Dry off quickly and thoroughly after bathing and swimming—don't stay in a wet swimsuit for hours.
- It's better not to have sex in your teens, but if you're sexually active, always use a latex condom. ■



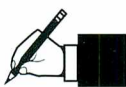
Images provided by © 1994 PhotoDisc, Inc.

Wearing artificial fingernails increases the chance of getting yeast infections under the natural fingernails. Fungal infections start in the space between the artificial and natural nails, which become discolored. Treatment for these types of infections—as well as those that occur in other skin folds, such as underarms or between toes—require different products, most of which are available only with a doctor's prescription.

Knowing the causes and symptoms of yeast infections can help you take steps—such as giving those tight jeans a rest—to greatly reduce the chances of getting an infection (see accompanying article).

And, if sometimes prevention isn't enough, help is easily at hand from your doctor and pharmacy. ■

Judith Levine Willis is editor of FDA Consumer.



The Notebook: a potpourri of items of interest gathered from FDA news releases, other news sources, and the Federal Register (designated FR, with date of publication). The Federal Register is available in many public libraries.

■ **Tobacco vending machines** are no longer permitted in federal government buildings, according to a General Services Administration final rule effective last Jan. 25. The rule implements the "Prohibition of Cigarette Sales to Minors in Federal Buildings and Land Act," which also prohibits the distribution of free samples of tobacco products in space owned and leased by the government. (FR Jan. 25)

■ **Quality assurance program** and inspection guidance is available in a revised FDA compliance policy guide. "FDA Access to Results of Quality Assurance Program Audits and Inspections" provides general policy and guidance to FDA staff and may be useful to industry representatives. For a free copy, send a self-addressed label to Tom Chin, Office of Enforcement (HFC-230), Rockville, MD 20857; telephone (301) 827-0410. (FR Jan. 24)

■ **Human food safety** and antimicrobial drug residues in food animals are addressed in an FDA Center for Veterinary Medicine guidance document. "Microbiological Testing of Antimicrobial Drug Residues in Food" gives information about which antimicrobials may require

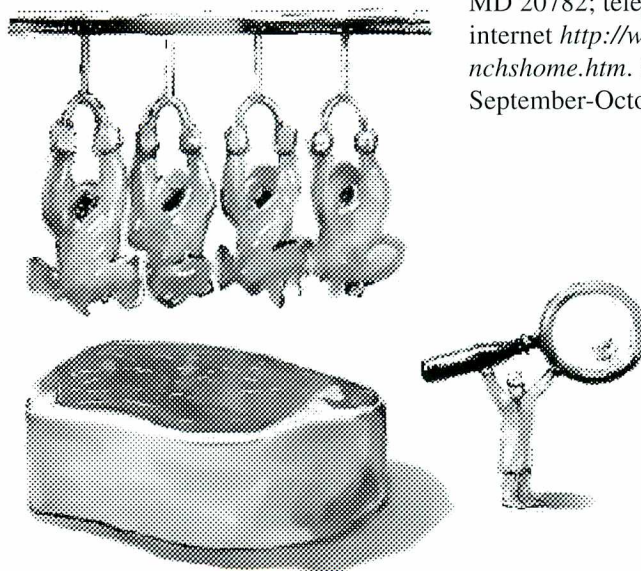
supplemental testing, and recommends tests for establishing that drug residues will not cause intestinal problems in consumers. For a free copy, request Docket #93D-0398, and send two self-addressed labels to Communications and Education Branch (HFV-12), Rockville, MD 20855. (FR Jan. 30)

■ **Food animal** use of fluoroquinolone antimicrobial drugs is the subject of a report by FDA's Center for Veterinary Medicine. The report addresses concerns that the drugs may increase development of fluoroquinolone-resistant organisms that could be passed from animals to humans and cause disease. For a free copy, request Docket #95S-0199, and send two self-addressed labels to Communications and Education Branch (HFV-12), Rockville, MD 20855. (FR Jan. 4)

■ **Raw meat and poultry** nutritional labeling and safe handling information is available in a report from the U.S. Department of Agriculture's Food Safety and Inspection Service. The report pro-

vides data from a survey on food retailers' efforts to give consumers the information. For a free copy of the report, request Docket #95-053N, and send a self-addressed label to Charles R. Edwards, Product Assessment Division, FSIS, U.S. Department of Agriculture, Washington, DC 20250. (FR Jan. 29)

■ **Gaps in education** may result in gaps in health care, according to a report by the National Center for Health Statistics. "Health, United States, 1994" shows that among people between 25 and 64, those with less than a high school education had more than double the death rate as those with at least one year of college. It also shows that women who do not finish high school are nearly eight times as likely to smoke during pregnancy as women who graduate college. Overall, the report states, the percent of women who smoked during pregnancy dropped from 20 percent in 1989 to 17 percent in 1992. For a free copy of the report, write to NCHS Data Dissemination Branch, Room 1064, Hyattsville, MD 20782; telephone (301) 436-8500; internet <http://www.cdc.gov/nchswww/nchshome.htm>. (Public Health Reports, September-October 1995)





Illegal Use of Vet Drug Results in Fines, Probation

by Dixie Farley

Investigation by FDA agents in Missouri and New York led last fall to fines and probation for one man and deferred prosecution for another on charges of prescription drug misbranding and product tampering.

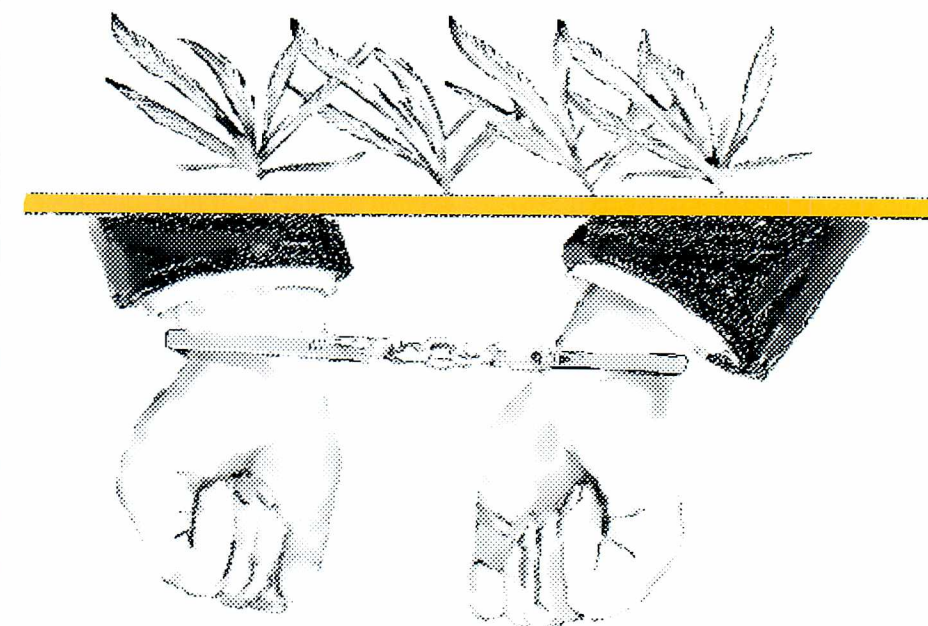
On Sept. 8, 1995, the U.S. District Court for the Eastern District of Missouri, St. Louis, fined Joseph Schilling, 31, of St. Louis, \$1,000 with \$25 special assessment, and sentenced him to three years' probation with mandatory drug testing. Schilling had pleaded guilty to drug misbranding caused by dispensing a prescription drug without a license.

On Oct. 17, 1995, the U.S. District Court for the Southern District of New York, New York City, accepted Dean Gabriel, 25, of New York City, into a six-months deferred prosecution program. Gabriel was charged with product tampering.

Following a tip from an informant, St. Louis police began surveillance of Schilling on Feb. 11, 1994, arresting him sometime after midnight on suspicion of possessing a narcotic and marijuana. In Schilling's apartment, the police seized drug paraphernalia and vials of suspected Ketaset (ketamine), a veterinary anesthetic. Schilling cooperated with the police and named Gabriel as his source.

Because FDA regulates Ketaset as a veterinary drug and the drug is not a controlled substance regulated by the Drug Enforcement Administration, the police notified the agency's Kansas City Office of Criminal Investigations (OCI), which in turn notified OCI agents in the New York field office, Jersey City, N.J. In deference to probable federal charges, the local charges were held in abeyance.

Kansas City agents began investigat-



ing Schilling, and New York agents investigated Gabriel with surveillance, examination of subpoenaed bank and telephone records, and electronic monitoring.

The agents learned Schilling had met Gabriel in 1993 during a Thanksgiving vacation in Miami. Schilling had some "Special K," the street name for Ketaset, which they both used to get high.

Schilling told agents that after he and Gabriel returned home from Miami, he asked Gabriel to supply him with more Special K, and that Gabriel had done so twice. On March 28, at OCI's request, Schilling ordered more Special K from Gabriel, receiving 30 vials, worth about \$1,350, on April 28.

Testing by FDA's Forensic Chemistry Center, in Cincinnati, determined the substance in the vials was indeed ketamine.

In October, OCI agents asked the New

York U.S. attorney to file a complaint. Gabriel was arrested Nov. 16, 1994, on charges of tampering with Ketaset by altering it so that it could be used illegally, thus risking injury to another person.

On June 8, 1995, Schilling pleaded guilty to an information charging him with misbranding a prescription veterinary drug in interstate commerce.

Gabriel's deferred prosecution program requires him to report to a pretrial services officer, obey laws, associate only with law-abiding individuals, and remain within the Southern and Eastern Districts of New York or the District of New Jersey unless his supervising officer grants him permission to leave. If Gabriel meets these conditions throughout the six months, the government will not prosecute him.

Dixie Farley is a staff writer for FDA Consumer.

Cheese Maker Says He Wants Out

An Ohio cheese manufacturer and distributor told the government he would go out of business rather than comply with a court order to rid his operations of dangerous bacteria and filth.

On July 12, 1995, Dominic Gangale, owner of Union Cheese Co., Sugarcreek, Ohio, told U.S. Magistrate Judge Patricia A. Hemann in the U.S. District Court for the Northern District of Ohio that the firm had ceased all cheese production, and he wanted only to sell the cheese in stock.

The judge had ordered the firm on June 16 to stop making and distributing cheese until it could ensure that the cheese was not contaminated with pathogenic bacteria or filth.

In 1994, samples of cheese had tested positive for *Listeria monocytogenes*, an organism that can cause serious and sometimes fatal infections in small children, frail and elderly people, and others with weakened immune systems. Although healthy individuals may suffer only short-term symptoms, such as high fever, severe headaches, stiffness, nausea, abdominal pain, and diarrhea, *Listeria* infection can cause miscarriages and stillbirths in pregnant women.

Union Cheese produced about 20,000 pounds (9,072 kilograms) of Swiss cheese daily, and usually kept an inventory of about 1 million pounds (454,000 kg) of both its own Swiss and different kinds from other manufacturers.

On Sept. 29 and 30, 1994, Phillip Pontikos, an investigator with FDA's Brunswick, Ohio, office, inspected Union Cheese as part of the agency's scheduled surveillance of food manufacturers.

Pontikos found numerous violations of good manufacturing practices. In one container of brine and cheese, he counted more than 30 floating dead flies. He also saw dead insects on

blocks of cheese and hundreds of dead insects, cobwebs and dirt on windowsills.

He also noted that there was no hot running water in the restrooms, brine room, or laboratory.

Pontikos discussed these problems with Annette Gangale, daughter of the owner. She agreed to discuss the problems with her father.

Pontikos sent samples of cheese to FDA's lab in Cincinnati. One sample tested positive for *Listeria*.

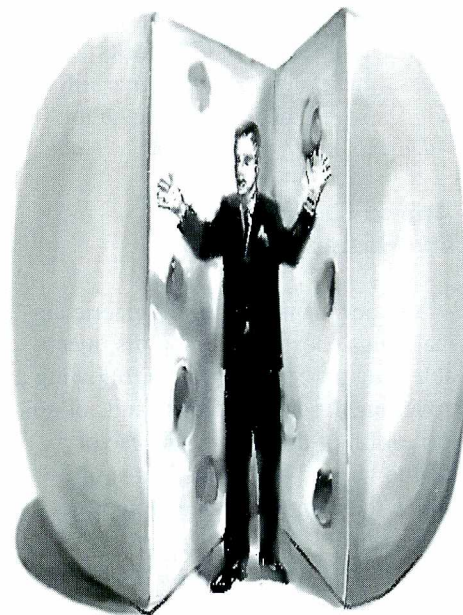
The agency advised the firm of the sample analysis, and as a result, Union Cheese recalled cheese from the contaminated lot. But the recall could not be completed because the company had not properly coded cheese lots. Gangale admitted that he did not know exactly what firms had bought the cheese.

On Oct. 27 and 28 and Nov. 7, Pontikos returned to Union Cheese and collected more samples of cheese and environmental samples, including brine and various materials from the floor. Several of the environmental samples tested positive for *Listeria*.

On Nov. 29, Pontikos, along with FDA investigators Steve Kilker and Frederick Lochner, returned to Union Cheese. In a two-week-long investigation, they found many of the same problems Pontikos had seen previously, as well as:

- raw and finishing operations not being kept sufficiently separate
- Swiss cheese being shipped before the end of the required 60-day aging period
- ceiling condensation dripping onto uncovered cheese
- peeling ceiling paint directly above the cutting table
- cutting tools that could not be sanitized because of wooden handles and rusty screws.

On Feb. 22, 1995, the agency asked the Justice Department to initiate injunction proceedings against Union Cheese. But, to confirm that the problems still existed, the court ordered another in-



spection. When FDA investigators returned to inspect the firm from May 16 to 18, many of the same insanitary conditions still existed. One instance in which some effort was made to improve things only made matters worse. A fan, placed in the cutting room to prevent condensation from dripping on cheese, drew air into the facility from the direction of the firm's sewage treatment plant.

At a three-day hearing begun June 5, Gangale did not dispute the investigators' findings. He said, however, that, in his opinion, these problems did not violate good manufacturing practices.

At the end of the hearing, Judge Hemann ordered Union Cheese to close until violations were corrected.

On July 12, the court entered a supplemental order clarifying the conditions the defendants must comply with before they would be allowed to sell cheese in stock. Those conditions called for FDA to supervise the testing of each lot of cheese for *Listeria* and to ensure that the cheese would be handled under sanitary conditions.

All the in-stock cheese—3,981 blocks, each weighing 200 pounds (90.7 kg)—tested free of *Listeria*, but one lot was insect-infested. All were sold except for

the insect-infested lot (72 blocks). At press time in February, Gangale still had not destroyed the insect-infested lot.

—Dori Stehlin

Animal Drug Maker Overhauls System

A major manufacturer of generic animal drugs chose to overhaul its injectable drug processing system following a government seizure of thousands of dollars worth of drugs, a partial factory shutdown, and a consent decree in which the company agreed to correct violations.

At press time in February, Anthony Products Co., of Arcadia, Calif., was planning to have its new injectables' operation at its El Monte, Calif., plant up and running this spring, pending FDA's concurrence, according to Mary LoVetere, a compliance officer with FDA's Los Angeles district office. The company already replaced its injectables' system at its Irwindale, Calif., plant.

The company reportedly bought new equipment, hired new people, and revised manufacturing procedures and controls so that its injectable drug product line would comply with good manufacturing practices (GMPs), she said.

Anthony Products makes various veterinary medicines, including injectable forms of antibiotics, anesthetics and other drugs for large and small animals. It manufactures drugs under its own brand name and other companies' labels.

The company agreed to correct GMP violations in a consent decree it signed Aug. 3, 1995, in the U.S. District Court for the Central District of California.

In March 1995, U.S. marshals had seized, at FDA's request, about 200 drums of drug ingredients and 8,000 vials of injectable drugs. The company's injectable drug system at its El Monte plant has been idle since. Its penicillin production line at its Irwindale plant re-



sumed manufacturing in June 1995.

Previously, FDA sent Anthony Products several warning letters for failing to follow GMPs for its injectable drugs. The most recent warning was issued in May 1994, and company officials responded that they would correct the violations.

However, during a reinspection in August and September 1994, FDA investigators found continuing problems, as well as some new ones. The problems revolved around the company's failure to ensure the sterility and quality of its injectable products.

FDA decided to seek a seizure to spur the company to correct repeated violations and to make sure that adulterated drugs did not reach consumers.

On March 3, 1995, U.S. marshals seized all injectable drugs and injectable drug ingredients in Anthony's possession.

In the consent decree, FDA agreed to return the raw ingredients to Anthony Products for testing under GMPs. The seized drugs will be disposed of by U.S. marshals.

—Paula Kurtzweil

Filth in Fish Fillets Closes Business

A food business closed after an FDA inspection found flies, condensate dripping on smoked salmon fillets, racks of product placed against fish-residue-encrusted walls, and fillets being trimmed with rusty pliers.

FDA investigators found those and other unsanitary conditions at Sotra Smoked Fish, U.S.A. Inc., Kingston, N.Y., after routine agency sampling showed products contaminated with *Listeria monocytogenes*, bacteria that can cause potentially fatal illness.

About 25 percent of such infections result in death, said FDA microbiology expert Joseph Madden, Ph.D., in testimony concerning Sotra. "Symptoms are most severe in the elderly, infants, pregnant women, and those people whose immune systems are impaired," he said.

Sotra principal officers Olav Isaksen and Joel Kudlowitz signed a consent decree of permanent injunction last June 23 in the U.S. District Court for the Northern District of New York. Isaksen is president and treasurer, and Kudlowitz is vice president and secretary. Sotra is closed until it can meet the decree's terms, which include a cleanup and an extensive testing program supervised by FDA's Buffalo district office.

On June 1, 1994, investigator Thomas Morgan, of FDA's Boston district office, sampled Sotra's fillets at a smokehouse in Bennington, Vt., as part of the agency's seafood sampling program. Testing at FDA's Winchester Engineering and Analytical Center, in Winchester, Mass., detected *Listeria*, and Boston informed the agency's Buffalo office.

Buffalo FDA investigator Margaret Slimbach visited Sotra July 7 to present the test results.

Meanwhile, according to Buffalo compliance officer Raymond Kent, FDA discussed Sotra with the New York State Department of Agriculture

and Markets, which inspects manufacturers for FDA under contract. In August 1993, the agency learned, the state had sent Sotra a warning letter and levied a \$300 fine because of continuing unsanitary conditions seen during several state inspections in 1992 and 1993.

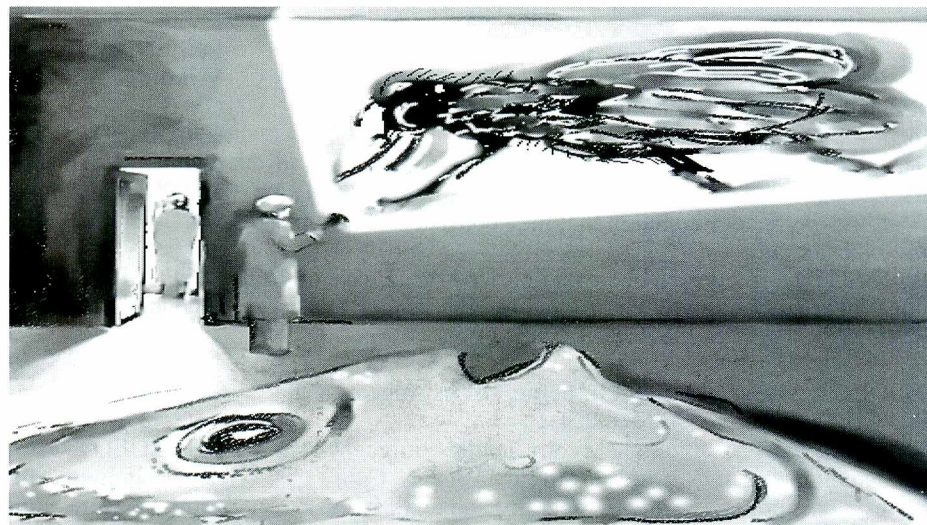
On July 12, Slimbach and Samuel Eskenazi, a microbiologist with FDA's Northeast Regional Laboratory, began an extensive inspection of the food plant. On the third day, Sotra agreed to recall the lot sampled in Vermont.

The FDA team discovered gross unsanitary conditions and practices. The freezer and cooler handles, for example, were slick with dirty residues. And the cooler door had been left standing open about an hour and a half, the inside temperature unmonitored. Using an FDA thermometer, Slimbach found the temperature to be 60 degrees Fahrenheit (15 Celsius), when it should have been below 40 F (4 C). (*Listeria* bacteria can grow at 40 F, but not as fast as at higher temperatures.)

Other problems included:

- inadequate use of hair coverings
- no use of hand sanitizing solution
- handling of fish with unwashed hands after returning from the restroom or other areas or after touching unsanitized equipment
- routine placement of racks of fish against a cement wall encrusted with residues from previous operations
- fish lying directly below the cooler's bottom panel, which was heavily coated with condensate droplets
- use of rusty pliers for trimming products
- uncleanable floors and walls due to pitting, cracks and peeling
- residue-encrusted fillet rinsing hose touching the dirty floor
- flies (known to transmit *Listeria* bacteria) in the production room
- no tray to catch dead flies under the electric fly zapper.

Slimbach and Eskenazi collected swabs from numerous sites in the plant



for contaminant testing. At the end of the inspection, they informed Sotra of the problems. Isaksen and Kudlowitz promised immediate corrections.

FDA's Northeast Regional Laboratory's testing of the swabs showed *Listeria* on such sites as the slicing and skinning machine blades, condensate dripping onto salmon, stagnant water in the cooler, on cooler and freezer door handles, on the wall, and under the fly zapper. The bacterium was also identified in samples of finished salmon.

On Aug. 18, 1994, Slimbach returned to Sotra with a state investigator to present these test results and see whether the firm had cleaned up. It hadn't. The state seized all fish at the plant. Kudlowitz agreed to recall the sampled lots and to destroy them and the seized product.

On Nov. 13, 1994, FDA asked the Department of Justice to file an injunction against Sotra. In a letter two days later, FDA informed Isaksen that the agency considered the recalled salmon to have posed a life-threatening health hazard, and that Sotra must take appropriate measures to prevent further contamination.

In signing the consent decree, Sotra agreed not to process, prepare, pack, label, hold, or sell food in interstate commerce until it:

- establishes methods, facilities and controls that ensure foods do not become contaminated with pathogenic bacteria or filth
- provides certification to FDA by a qualified outside person that the sanitation control program is adequate
- provides a written report to FDA detailing actions taken to ensure that foods are not contaminated or held under unsanitary conditions
- has food tested by a qualified outside laboratory for *Listeria*, with results and analytical worksheets submitted to FDA
- establishes a label review program, supervised by a qualified person, that ensures legal labeling
- receives written notice from FDA that the requirements appear to be met.

FDA will closely monitor Sotra when it resumes operating. For example, for three months, Sotra is to have an outside laboratory conduct bacterial testing of finished and in-process products, food contact surfaces, and other sites and report results to FDA. If bacteria are found, testing is to continue as long as FDA specifies.

FDA is unaware of any complaints or illnesses related to Sotra products.

"We're still monitoring the second recall," FDA's Kent says.

—Dixie Farley

SUMMARIES OF COURT ACTIONS



SEIZURE ACTIONS

Food/Contamination, Spoilage, Insanitary Handling

PRODUCT: **Lobster Tails**, at Miami, Fla. (S.D.Fla.); Civil No. 95-0140.

CHARGED 1-25-95: While held for sale after shipment in interstate commerce at Emerald Fisheries, Inc., in Miami, Fla., the articles were adulterated in that they consisted of decomposed lobster tails—402(a)(3).

DISPOSITION: A consent decree authorized the release of the goods for reexportation to the original foreign vendor. (F.D.C. No. 67059; S. No. 95-735-458; S.J. No. 1)

PRODUCT: **Mussels, canned in brine**, at Los Angeles, Calif. (C.D.Calif.), Civil No. 95-4878 DT.

CHARGED 7-24-95: While held for sale after shipment in interstate commerce at G & K Sales in Los Angeles, Calif., the articles were adulterated due to rancidity and texture breakdown—402(a)(3).

DISPOSITION: A default judgment ordered the articles destroyed. (F.D.C. No. 67096; S. No. 95-713-949; S.J. No. 2)

PRODUCT: **Shrimp, frozen**, at Miami, Fla. (S.D.Fla.); Civil No. 94-1970.

CHARGED 9-21-94: While held for sale after shipment in interstate commerce at Northwestern Meat, Inc., in Miami, Fla., the articles were adulterated in that they contained insects, rodent hair, and cat or dog hair—402(a)(3).

DISPOSITION: A default decree of condemnation ordered the articles destroyed. (F.D.C. No. 66961; S. No. 94-595-108; S.J. No. 3)

PRODUCT: **Shrimp, frozen**, at Mobile, Ala. (S.D.Ala.); Civil No. 93-0530-CB-C.

CHARGED 6-23-93: While held for sale after shipment in interstate commerce at Christian Salvesen Cold Storage in Mobile, Ala., the articles were adulterated in that they consisted of decomposed shrimp—402(a)(3).

DISPOSITION: A consent decree of condemnation and destruction ordered the articles destroyed. (F.D.C. No. 66734; S. No. 93-575-037; S.J. No. 4)

CRIMINAL ACTIONS

DEFENDANT: **Duramed Pharmaceutical**, at Cincinnati, Ohio (D.Md.); Civil No. HAR-30-0207.

CHARGED 5-24-93: *Counts 1 and 3*: The defendant introduced into interstate commerce unapproved new drugs that were manufactured with data generated on different product formulas from those requested on the approved new drug application—301(d) and 303(a)(1). *Count 2*: The defendant introduced into interstate commerce an adulterated drug. The drug was adulterated in that the defendant made a material change in the coating procedures of the product without obtaining approval from FDA—301(a) and 303(a)(1).

DISPOSITION: Guilty plea; entered into a consent decree of permanent injunction and ordered to pay a \$500,000 fine. (F.D.C. No. 66101; S.J. No. 5)

INJUNCTION ACTIONS

DEFENDANTS: **Kabi Pharmacia, Inc.** and **Anders Wiklund**, at Piscataway, N.J. (D.N.J.); Civil No. 93-3199 (JWB).

CHARGED 7-19-93: The defendants introduced into interstate commerce a misbranded and unapproved new drug—301(a) and (d). The defendants also caused the drug to be misbranded while held for sale after shipment in interstate commerce—301(k).

DISPOSITION: A consent decree of permanent injunction was filed and granted. (Inj. No. 1339; S.J. No. 6)

DEFENDANTS: **Maple Island, Inc.**, **Daniel W. O'Brien**, and **Ronald B. Zirbel**, at Wanamingo, Minn. (D.Minn.); Civil No. 4-93-789.

CHARGED 8-17-93: While held for sale at Maple Island, Inc., in Wanamingo, Minn., infant and special nutritional dietary formulas were adulterated in that they were manufactured, prepared, processed, packaged, and held for sale under insanitary conditions whereby they might have been contaminated with filth or rendered injurious to health—402(a)(4). The articles were also adulterated in that they contained *Salmonella* bacteria which might have rendered them injurious to health—402(a)(1). Defendants caused the adulterated articles to be introduced into interstate commerce—301(a). The defendants also manufactured, processed, packaged, prepared, and held the articles for sale after one or more of their components were shipped in interstate commerce—301(k).

DISPOSITION: Several products were recalled and destroyed. Defendants entered into a consent decree and resumed business upon compliance. (Inj. No. 1332; S. No. 93-658-050; S.J. No. 7)

DEFENDANTS: **Tuente Livestock**, **Ronald W. Tuente**, and **Roger B. Tuente**, at Yorkshire, Ohio (S.D. Ohio); Civil No. C-3-94-336.

CHARGED 8-15-94: The defendants caused adulterated swine to be introduced into interstate commerce—301(a) and 512(a)(1). The swine were adulterated in that they contained the presence of an unsafe new animal drug—402(a)(2)(D).

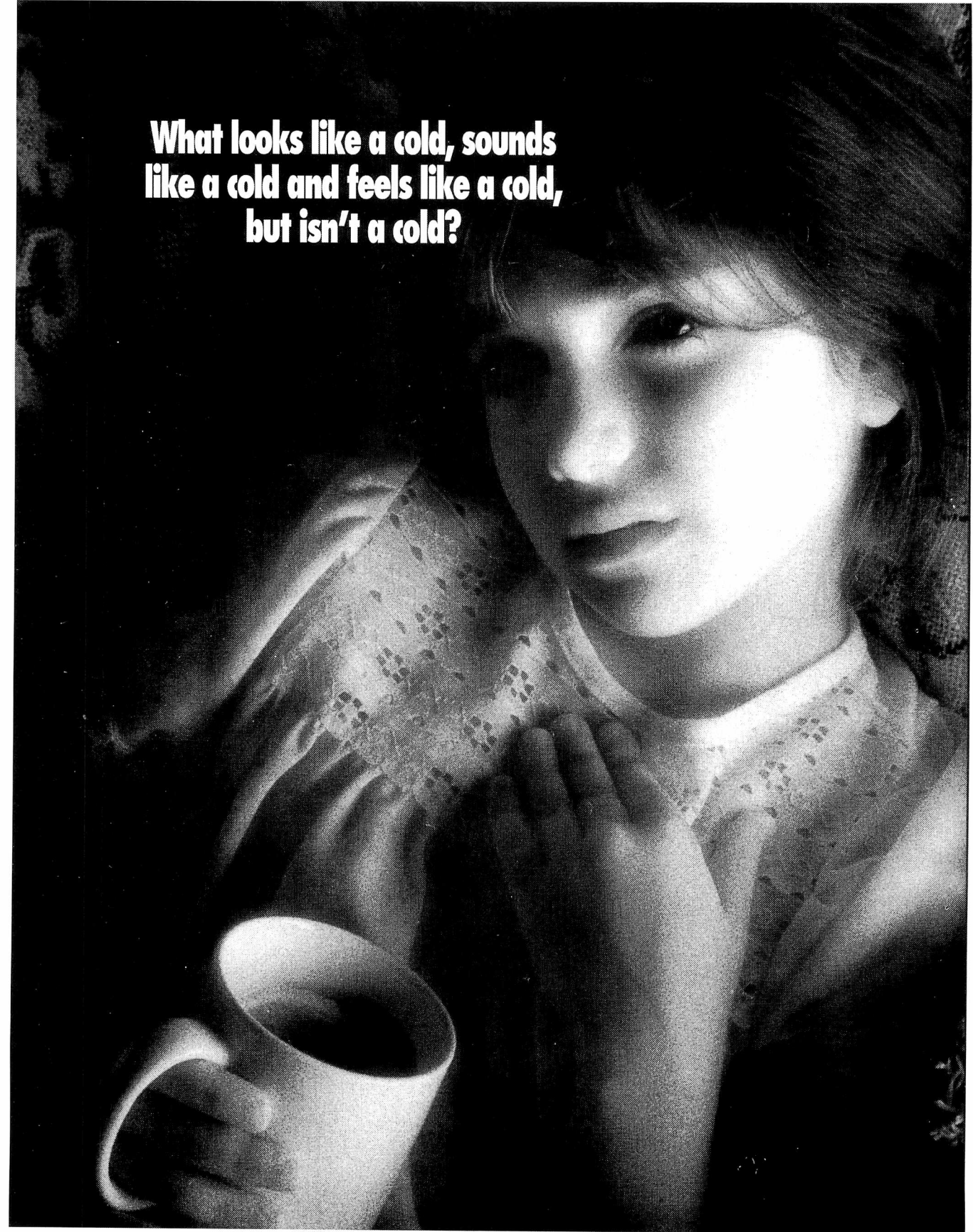
DISPOSITION: The defendants entered into a consent decree in which they agreed to surrender their livestock dealing licenses and to withdraw from the livestock dealing trade for six years. (Inj. No. 1351; S. No. 94-708-236; S.J. No. 8)

MISCELLANEOUS ACTIONS

ACTION: **Schering Corporation v. FDA**, at Kenilworth, N.J. (D.N.J.); Civil No. 93-3493 (HLS).

CHARGED 8-10-93: Plaintiff challenged a regulation implementing the bioequivalence requirements for generic drugs under the abbreviated application procedure. Plaintiff claimed the regulation impermissibly broadened the statutory definition of bioequivalence.

DISPOSITION: The district court granted a summary judgment in favor of FDA. The appellate court affirmed the district court's decision. Plaintiff filed a petition for certiorari which was denied. (Misc. No. 1003; S.J. No. 9)



**What looks like a cold, sounds
like a cold and feels like a cold,
but isn't a cold?**

Asthma. But asthma can be much more serious. So if your child has a cough that won't go away, is often short of breath, or wheezes a lot, especially at night or after running, don't treat it yourself. Go to your doctor or clinic.

Breathe easier. Ask your doctor if it's asthma.

National Asthma Education and Prevention Program

National Heart, Lung, and Blood Institute; National Institutes of Health; Public Health Service; U.S. Department of Health and Human Services.