

FDA CONSUMER

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

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JULY-AUGUST 1996 •



Fighting Fleas And Ticks





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Taking the Fat Out of Food

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Many favorite foods are now available in lower fat versions. Some of these contain substitutes for animal or vegetable fats. But does this mean you'll be consuming less fat and fewer calories?

Adults Need Tetanus Shots, Too

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Though most people are aware that infants and children need to be immunized against tetanus as part of their routine vaccination program, it may come as news that this condition can threaten the lives of adults as well.

Preventing Dehydration in Children

19

Dehydration as a result of vomiting and diarrhea is one of the most common problems of infancy and early childhood. Oral rehydration therapy, readily available in fluid form for home use, is saving children's lives both in the United States and abroad.

Fighting Fleas and Ticks

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Fleas and ticks can afflict not only pets but their owners as well. Some new products can help keep these tiny pests under control.

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Inside Front Cover Photo:

This marshmallow-topped chocolate cake has no fat. What might it have instead? See page 7.



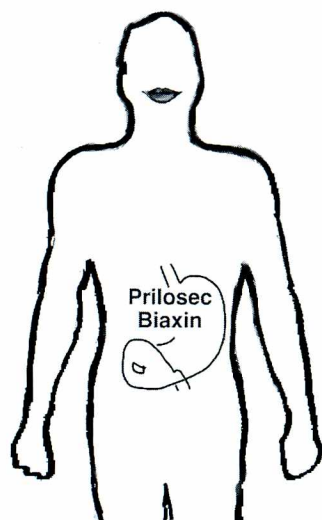
Combination Drug Treatment Approved for Ulcers

The first antibiotic treatment for eradicating *Helicobacter pylori*, the bacteria associated with active duodenal ulcers, has been approved by FDA.

The treatment involves taking two previously approved drugs: Biaxin (clarithromycin) and Prilosec (omeprazole). It was approved April 18.

Biaxin, manufactured by Abbott Laboratories, is an antibiotic for various mild to moderate infections. Prilosec, manufactured by Astra Merck, is a proton pump inhibitor that helps heal ulcers by suppressing gastric acid. In combination, the two drugs are effective in healing active duodenal ulcers and reducing the risk of ulcer recurrence. This combination treatment, however, is not effective against other bacteria associated with ulcers.

In 1994, a National Institutes of Health consensus panel of medical experts made a landmark recommendation in support of an antibiotic-based approach for treating ulcers. FDA used the



recommendation to advise companies on the best trial designs for developing these therapies.

In one foreign and two U.S. randomized studies, the most effective dosage levels were Biaxin at 500 milligrams three times a day plus Prilosec at 40 mg once a day for two weeks, followed by Prilosec at 20 mg once a day for two more weeks.

Although study participants reported few side effects, mild to moderate cases of taste distortion, nausea, headache, diarrhea, vomiting, and abdominal pain did occur.

Home-Use HIV Test

The first HIV test system that includes a home-use blood sample collection kit was recently approved by FDA. It is designed to provide confidentiality. Previously, all HIV tests were done under the supervision of a health professional.

The system, called Confide HIV Testing Service, has three components: a home-use blood collection kit bought over the counter, HIV-1 antibody testing at a certified laboratory, and a center that provides test results, counseling, and medical referral over the phone.

The national Centers for Disease Control and Prevention estimates that more than 60 percent of Americans at risk for HIV have not been tested. The home test provides an additional resource for anonymous testing and appropriate counseling.

People using the Confide system materials follow a few easy steps:

- Read the pretest counseling booklet about HIV and AIDS.
- Use a lancet to obtain a blood sample from the finger.

- Place the sample on a test card precoded with a unique identification number.
- Mail the card in a protective envelope to a laboratory for HIV-1 antibody testing.
- After seven days, call a toll-free number for test results.

The laboratory testing procedures are consistent with FDA recommendations for blood and plasma establishments. Samples that initially indicate HIV-1 antibodies (positive samples) are retested twice. Samples that are positive in two out of three tests are further confirmed with a more specific test, such as the Western blot.

Professional, certified counselors notify callers whose samples test positive or inconclusive, encourage those who test positive to seek medical care, and provide local medical referrals if needed. An automated message provides results to those who test negative, although all callers have the opportunity to speak to a counselor. Conversations are anonymous and confidential.

In clinical studies, the Confide test card correctly identified 99.95 percent of the more than 3,940 negative samples and 100 percent of the 150 positive samples.

The Confide HIV Testing Service was developed by Direct Access Diagnostics, a subsidiary of Johnson & Johnson, Bridgewater, N.J. Initially, the firm will limit distribution to over-the-counter sale in Texas and through a toll-free number in both Texas and Florida.

A free backgrounder has more information. To order single copies of "Home-Use HIV Test Kits," write to FDA, HFI-40, Rockville, MD 20857, or fax your order to (301) 443-9057. Include the publication number, BG 96-5.

First Microwave Device To Treat Enlarged Prostate

The first medical device to treat symptoms of enlarged prostate with microwaves has been approved by FDA, providing an alternative to treatment with drugs or surgery.

Affecting more than half of men 60 and older, enlarged prostate (benign prostatic hyperplasia) causes a gradual increase in frequent, difficult urination, sometimes leading to urinary tract damage. Drug treatment gives only modest relief. Surgery is most effective but requires anesthesia and may result in blood loss, impotence, or other complications.

The new device, the Prostatron, heats and destroys excess prostate tissue with microwaves aimed by a computer system. Treatment is limited to medium-sized prostate glands. It takes one hour and can be done on an outpatient basis with local anesthetic. It has no significant effect on sexual function. However, it does not correct incomplete bladder emptying or weak urinary stream.

The Gastroenterology and Urology Devices Panel of FDA's Medical Devices Advisory Committee recommended approval last October. FDA approved the Prostatron May 6.

During testing of the device on 375 men over 45 at seven medical centers in the United States and Europe, 75 percent of patients had improved urinary symptoms—urgency, frequency, straining, or intermittent flow. Follow-up four years later found the improvement continued in about half, while the rest

needed re-treatment with the device, or drugs or surgery, some time during those four years.

FDA requires the manufacturer, EDAP Technomed Group, of Cambridge, Mass., to study the device another year to assess its long-term effects and the need for re-treatment. The results will also be used to compare the Prostatron with other treatments.

Ultrasound May Reduce Need for Breast Biopsy

A newly approved use for an ultrasound breast imaging system may reduce the need for breast biopsies in the United States by up to 40 percent. An estimated 700,000 such procedures are now done each year.

The new application, approved by FDA last April 11, will help doctors decide whether a biopsy is needed to determine whether certain breast tumors are malignant (cancerous) or benign. It was approved for diagnostic use along with mammography and physical breast examination.

The Ultramark 9 High Definition Imaging (HDI) Ultrasound System Level 3 was cleared for marketing in 1991 for general-purpose diagnostic ultrasound, including determining whether breast lumps are cystic (fluid-filled) or solid. Cystic breast tumors are always benign, but solid tumors may be either benign or malignant. Until now, nearly solid tumors have had to be biopsied to ensure a correct diagnosis.

With high-definition imaging, however, doctors are able to judge whether a solid tumor is highly likely to be benign. Those so judged could be treated without biopsy.

FDA's Radiological Devices Panel of

the Medical Devices Advisory Committee recommended approval after it met in December 1995 to review data submitted by the system's manufacturer, Advanced Technology Laboratories, of Bothell, Wash. The firm studied 1,270 women with 1,344 breast lumps initially detected by mammography or physical exam. Of these, 431 tumors were indeterminate—that is, doctors could not be sure whether they were benign or malignant.

Using the HDI ultrasound system, doctors predicted that 176 of the 431 tumors were benign. All 1,344 tumors were biopsied for diagnosis. The biopsies confirmed that the 176 tumors were benign.

The study results showed that adding HDI examination to mammography and physical breast exam—tests routinely done on women with breast lumps—could significantly reduce the number of biopsies for lumps judged highly likely to be benign.

The HDI system is approved for use in women with breast lumps 1 centimeter in diameter (about three-eighths of an inch) or larger.

Implant Approved to Relieve Urinary Obstruction in Men

The first permanent implant to relieve urinary obstruction in men and improve ability to urinate has been approved.

UroLume Endoprosthesis, a tiny expandable wire stent, was approved by FDA last May 6 for use in men in whom standard surgical procedures to correct urinary obstruction fail.

The stent is implanted into the urethra

and expands to hold open the area around the obstruction, improving urine flow. Within six months, tissue grows over the stent's surface, helping to stabilize it.

During clinical trials, the device reduced the number of additional obstruction treatments needed in all patients. It improved urine flow and reduced problems like frequent and painful urination and incomplete emptying of the bladder in most patients.

Some patients had problems similar to those experienced by many patients before implantation. The most common was post-void dribbling, which occurred in half of all patients. Others included incontinence, pain or discomfort, blood in urine, and infection. About 15 percent of implanted patients had mild to moderate pain with erection and ejaculation; in most cases this diminished on its own within six months.

The frequency of these problems is being assessed in postmarketing studies by the device's manufacturer, American Medical Systems of Minnetonka, Minn. The studies will also help determine the device's overall impact on a patient's quality of life and sexual function.

Reactions, Misuse With Pain Medication

Reports of serious adverse reactions and potential misuse have led to revised labeling for the prescription pain reliever Ultram (tramadol). FDA also has sent a letter to health-care professionals on the drug's safety.

Since Ultram was approved March 3, 1995, FDA has received 115 reports of drug abuse, dependence, withdrawal symptoms, and intentional overdose by

people taking the drug. In addition, postmarketing surveillance revealed 83 cases of seizures in patients who used Ultram while on other medications, such as tricyclic antidepressants (for example, Elavil, or amitriptyline) and selective serotonin uptake inhibitors (for example, Prozac, or fluoxetine).

FDA worked with the company that markets Ultram, Ortho McNeil, to develop new labeling that discourages doctors from prescribing the drug to patients with a history of opioid addiction or dependence. The labeling also gives a detailed explanation of the risk of seizure and advises against the use of Ultram by patients allergic to codeine. Some patients with this allergy have had severe reactions while taking Ultram.

FDA highlighted these warnings in its letter last March 20 to health-care professionals. In the letter, the agency urged the professionals:

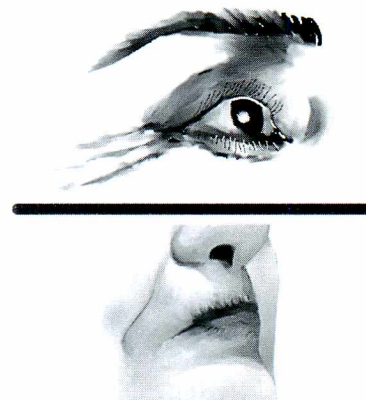
- to adhere to the dosing and administration in the Ultram labeling
- not to exceed the labeled recommendations
- to report patients' adverse reactions to Ortho McNeil or to FDA's MEDWATCH program.

Laser Treats Wrinkles

The first laser for treating wrinkles has been cleared for marketing by FDA.

Silktouch, a carbon dioxide laser scanner system previously cleared for general use under the name SwiftLase, was cleared last April 25 specifically for wrinkles. It joins other lasers cleared for cosmetic purposes, such as removing port wine stains and tattoos, resurfacing skin, and treating vascular lesions.

In five studies of more than 150 pa-



tients, all facial sites treated with Silktouch for wrinkles showed improvement, with both doctors and patients consistently rating areas around the mouth and eyes as "excellent" and those around the nose as "good."

Patients undergoing the procedure reported skin reddening that lasted one to four months and mild pain treatable with over-the-counter analgesics. Follow-up six months after treatment revealed no reports of treatment failure or the need for re-treatment at that time. However, some patients may need re-treatment at a later date.

FDA requires patients and doctors to wear protective eyewear designed for use with carbon dioxide lasers during treatment. If the treatment is near the eyes or eyelids, patients must wear metal cornea protectors.

Silktouch is made by Sharplan Lasers Inc. of Allendale, N.J.

New Weight-Loss Drug

A prescription drug recently approved by FDA for losing weight can be used longer than previous anti-obesity products.

Redux (dexfenfluramine) is approved for weight loss and maintenance of weight loss in certain people on a low-calorie diet, but safety and effectiveness data on use beyond one year are unavailable. An aid in reducing food intake, Redux belongs to a class of appetite-suppressing drugs that release serotonin—a brain chemical associated with appetite reduction—and slow its depletion. Redux was approved April 29.

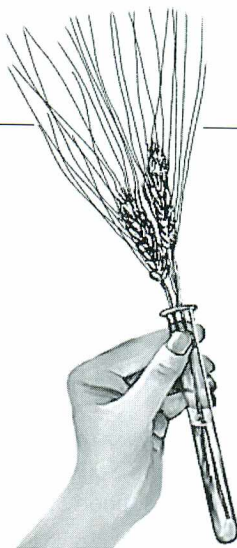
The new drug is for obese patients whose body mass index (BMI) is at least 30 (for example, someone at 5 feet 6 inches who weighs 185 pounds or more) and patients with other health risks, such as high blood pressure or diabetes, whose BMI is at least 27 (for example, someone at 5 feet 6 inches who weighs 167 pounds or more). Redux should not be used along with antidepressants or other mood-altering drugs because such use may cause serious side effects.

In a clinical study, out of 10 patients who lost at least 4 pounds by the fourth week of dexfenfluramine treatment, six lost 10 percent of their initial weight by the end of one year. Only three out of 10 patients taking a placebo had similar results. All patients ate a low-calorie diet, increased exercise, and underwent other behavior changes helpful to weight loss.

Mild side effects, such as diarrhea, dry mouth, and sleep disturbances, tend to disappear with time. While serious side effects are rare, use of any appetite-suppressing drug requires careful medical supervision.

Animal studies have shown long-term brain changes. To determine relevance of these findings to humans, further human studies will be conducted.

Wyeth Laboratories Inc., of Philadelphia, manufactures Redux.



U of MD, FDA Establish Food Research Institute

In a joint venture, FDA and the University of Maryland will share their specialized knowledge, equipment and facilities for research into food safety, nutrition, and food regulation.

The Joint Institute for Food Safety and Applied Nutrition, announced April 15, will be based in College Park, Md., near Washington, D.C.

Collaborative research at the institute will include studies on risk assessment, nutritional analyses, and other issues related to the four major elements of FDA's food program:

- food security regarding pathogens, contaminants and toxins
- regulatory science concerning food ingredients, international standards, and educational research
- nutrition and clinical studies related to nutrient quality, safety and labeling
- evaluation of technological innovations in the food industry and consumer behavior.

Under the agreement, FDA and university scientists will participate in workshops, seminars, and other forums to improve the expertise of FDA staff, university faculty, and other scientists.

Graduate and undergraduate students will take part in specialized training, internships, and independent research.

The General Services Administration plans to build an FDA facility near the university's College Park campus that will be the focal point of the new institute. Congress has appropriated \$84 million for construction of the facility, slated for completion in the year 2000.

Proposal to Give Allergy Info on OTC Labels

In a recent proposal, FDA encouraged manufacturers of over-the-counter topical first-aid antibiotics to voluntarily re-label products containing any of six ingredients with a new warning about possible allergic reactions.

After a task group of the Nonprescription Drug Manufacturers Association reported more than 900 cases of allergic reaction to certain antibiotics, the firms had voluntarily put a warning on OTC products containing bacitracin zinc, neomycin sulfate, or polymyxin B sulfate antibiotics.

According to the group's report on cases of allergic reaction over the last few years, 261 were related to OTC products, while 631 were related to prescription products. Another 31 were unclassified due to lack of information.

Upon reviewing the report, FDA proposed, in the Feb. 14, 1996, *Federal Register*, that products containing bacitracin, bacitracin zinc, neomycin, neomycin sulfate, polymyxin B, and polymyxin B sulfate be labeled with this revised warning to include allergic reactions:

“Stop use and consult a doctor if the condition persists or gets worse, or if a rash or other allergic reaction develops. Do not use if you are allergic to any of the ingredients. Do not use longer than 1 week unless directed by a doctor.”

Among cases reported for OTC products, most listed the outcome as unknown. When outcomes were reported, however, the majority were minor skin reactions, and no deaths were reported. Most reports involved OTC products containing more than one antibiotic.

The increase in reports may be attributed to consumers' increased use of the products. FDA believes the additional information would be helpful to consumers.

(For more about OTC topical first-aid products, see “OTC Options: Help for Cuts, Scrapes and Burns” in the May 1996 *FDA Consumer*.)

Consumer Reprints

New *FDA Consumer* reprints are available. Two are in Spanish, on teenage dieting and childhood vaccines, and five are in English, on various topics.

The reprints and their publication numbers are:

- Las Dietas en la Adolescencia (FDA) 96-1238S
- La Importancia de las Vacunas en la Niñez (FDA) 96-9016S
- On the Teen Scene: Yeast Infections

(FDA) 96-1236

- More People Trying Vegetarian Diets (FDA) 96-2296
- Healthful Snacks for the Chip & Dip Crowd (FDA) 96-2300
- Growing Older, Eating Better (FDA) 96-2301
- FDA's Tips for Taking Medicines: How to Get the Most Benefits with the Fewest Risks (based on “FDA's Rx for Better Medication Information”) (FDA) 96-3221.

To order single copies, 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



Alcoholism Recovery Lifelong Process

The article in *FDA Consumer*/May 1996, “Medications Can Aid Recovery from Alcoholism” was well done. The topic is appropriate for your publication since it affects so many Americans of all age, ethnic and socioeconomic groups. ... Both the title and the caption to the right of Floyd McCrory's picture on page 23 indicate that the disease of alcoholism is something that folks “recover” from. The uninformed or casual reader

may conclude that alcoholism is a medical condition similar to a broken arm; i.e., following treatment and a given period of time, one is “recovered.” In all my exposure to the disease of alcoholism, I have understood that recovery is a lifelong process.

Admittedly this could be viewed as a trivial observation, yet the chronic nature of the disease and the commitment to “recovery” seems to be critical to success. The closing paragraph of the article appropriately emphasizes that fact. Knowing that some readers will

only read the title and the photo captions and then draw a conclusion prompts this observation.

L.A. Lloyd
Executive Director
Arizona State Board of Pharmacy

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

Taking The **FAT** *Out Of Food*

by Paula Kurtzweil

*Whipping up
fat-free cakes
and lower fat
cookies is pos-
sible with
today's fat re-
placers.*



*F*ood manufacturers are making it easier for fat-conscious consumers to have their cake and eat it, too—and their cheeses, chips, chocolate, cookies, ice cream, salad dressings, and various other foods that are now available in lower fat versions.

These products can help adult consumers reduce their fat intakes to recommended levels while allowing them to enjoy foods traditionally high in fat. A diet high in fat can contribute to heart disease and some forms of cancer and, because fats are calorie-dense, to excessive body weight.

A host of fat substitutes that replaces most, if not all, of the fat in a food, makes these lower fat foods possible. Most of these fat replacers are ingredients already approved by the Food and Drug Administration for other uses in food. For instance, starches and gums are approved as thickeners and stabilizers. New compounds, such as olestra, have undergone or will undergo close scrutiny by FDA to assess their safety.

In theory, the perfect fat replacer is one that contributes everything fat does in a food but without the calories, saturated fat, and cholesterol. The question remains: Can fat-reduced products actually reduce people's overall calorie intake and have a significant impact on their total fat intake?

Fat in the Diet

Fat is a difficult substance to replace because it has many important functions. A major nutrient, it is important for proper growth and development and maintenance of good health. Fats carry the fat-soluble vitamins A, D, E, and K and aid their absorption in the intestine. They are the only source of the essential fatty acids linoleic and linolenic acids. They are an important source of calories for many adults and for infants and toddlers, who have the highest energy needs per kilogram of body weight of any age group. Fat provides 9 calories per gram, compared with 4 calories per gram for protein and carbohydrates.

As a food ingredient, fat is important in food preparation and consumption because it gives taste, consistency, stability, and palatability to foods and helps us feel full so we stop eating.

But there are limits on the amount we should eat because of fats' link to heart disease, cancer and overweight. The Dietary Guidelines for Americans recommend limiting total fat intake to no more than 30 percent of calories and saturated fat to no more than 10 percent. Cholesterol intake should be limited to no more than 300 milligrams a day. Saturated fat and cholesterol are the substances in fat that contribute to the formation of plaque, which clogs arteries, leading to heart disease.

Americans appear to be heeding the experts' advice because, according to a

1995 annual survey by the Food Marketing Institute—an organization of grocery retailers and wholesalers—65 percent of the consumers surveyed—the highest level to date—rated fat as their No. 1 nutrition concern. More than three-fourths of the consumers said they stopped buying a specific food because of the amount of fat listed on the nutrition label.

A 1995 survey by the Calorie Control Council—an international association of manufacturers of low-calorie, low-fat, and diet foods and beverages—found that 72 percent of respondents who said they look for "light" foods said they are most attracted to food products claiming to be "reduced in fat."

Manufacturers are responding by adding more and more reduced-fat foods to their product lines. That corresponds to the Department of Health and Human Services' Healthy People 2000 goal of increasing to 5,000 from 2,500 in 1986 the number of brand items reduced in fat and saturated fat.

Regulation

Fat replacers can help reduce a food's fat and calorie levels while maintaining some of the desirable qualities fat brings to food, such as "mouth feel," texture and flavor.

Under FDA regulations, fat replacers usually fall into one of two categories: food additives or "generally recognized as safe" (GRAS) substances. Each has its own set of regulatory requirements.

Food additives must be evaluated for safety and approved by FDA before they can be marketed. They include substances with no proven track record of safety; scientists just don't know that much about their use in food. Examples of food additives are polydextrose, carrageenan and olestra, which are used as fat replacers. Manufacturers of food additives must test their products, submit the results to FDA for review, and await agency approval before using them in food.

GRAS substances, on the other hand, do not have to undergo rigorous testing before they are used in foods because they are generally recognized as safe by knowledgeable scientists, usually because of the substances' long history of

**Most of these fat
replacers are
ingredients already
approved by the
Food and Drug
Administration for
other uses in food.**

safe use in foods. Many GRAS substances are similar to substances already in food. Examples of GRAS substances used as fat replacers are cellulose gel, dextrins, guar gum, and gum arabic.

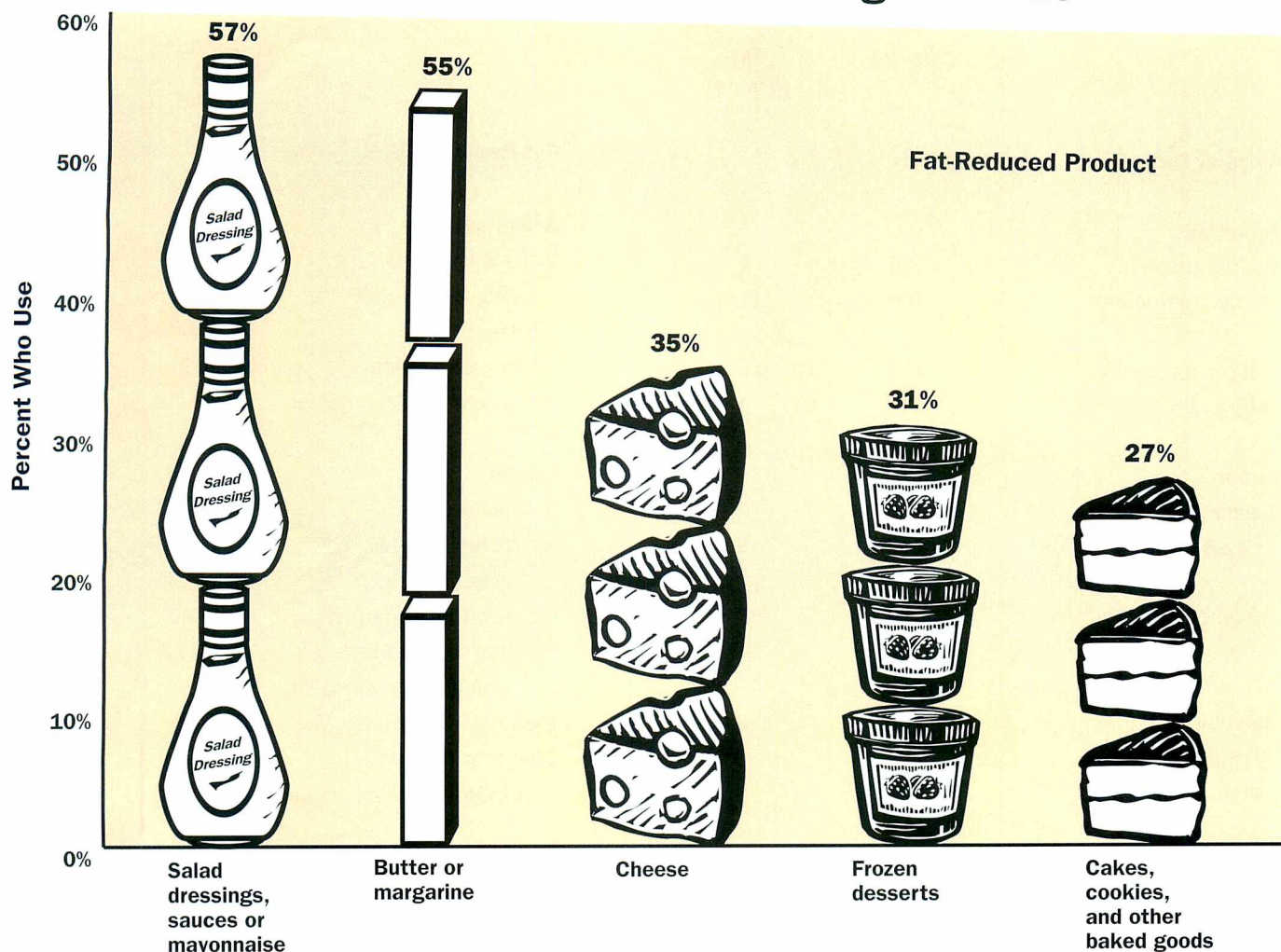
Sources

Fat replacers may be carbohydrate-, protein- or fat-based substances.

The first to hit the market used carbohydrate as the main ingredient. Avicel, for example, is a cellulose gel introduced in the mid-1960s as a food stabilizer. Carrageenan, a seaweed derivative, was approved for use as an emulsifier, stabilizer and thickener in food in 1961. Its use as a fat replacer became popular in the early 1990s. Litesse (polydextrose) came on the market in 1981 as a humectant, which helps retain moisture. Others in this category include dextrins, maltodextrins, fiber, gums, starch, and modified food starch. FDA has affirmed many carbohydrate-based fat replacers as GRAS.

Although their original intent was to perform certain technical functions in food that would improve overall quality, some carbohydrate-based fat replacers are now used specifically to reduce a

Favorite Foods Containing Fat Replacers Among People Who Use 'Light' Foods



(Source: 1995 Calorie Control Council national survey)

food's calorie content. They provide from zero to 4 calories per gram. They are used in a variety of foods, including dairy-type products, sauces, frozen desserts, salad dressings, processed meats, baked goods, spreads, chewing gum, and sweets.

Protein-based fat substitutes came along in the early 1990s. These and fat-based replacers were designed specifically to replace fat in foods.

One form, Microparticulated Protein Product (MPP), such as Simplese and Trailblazer, is made from whey protein or milk and egg protein. These fat replacers provide 1 to 4 calories per gram, depending on their water content, and are approved for use in frozen dessert-type foods. FDA has agreed that whey-based MPP conforms to FDA's defini-

tion of whey protein concentrate, such as the fat replacer Dairy-Lo, a GRAS substance. Therefore, whey-based MPP can be used in other foods, including reduced-fat versions of butter, sour cream, cheese, yogurt, salad dressing, margarine, mayonnaise, baked goods, coffee creamer, soups, and sauces.

Another type of protein-based fat replacers, called protein blends, combine animal or vegetable protein, gums, food starch, and water. They are made with FDA-approved ingredients and are used in frozen desserts and baked goods.

Olestra

Olestra is an example of a fat-based fat replacer. FDA approved olestra (brand name Olean), made by Procter & Gamble Co. of Cincinnati, in January

1996, for use in preparing potato chips, crackers, tortilla chips, and other savory snacks. Procter & Gamble said it expected to begin test-marketing olestra-containing products in 1996.

Olestra has properties similar to those of naturally occurring fat, but it provides zero calories and no fat. That's because olestra is undigestible. It passes through the digestive tract but is not absorbed into the body. This is due to its unique configuration: a center unit of sucrose (sugar) with six, seven or eight fatty acids attached.

Olestra's configuration also makes it possible for the substance to be exposed to high temperatures, such as frying—a quality most other fat replacers lack.

As promising as olestra sounds, it does have some drawbacks. Studies

How Fat Replacers Can Affect Fat Intake

Sample Menu

	Calories	Fat (grams)		Calories	Fat (grams)
Regular Diet			Fat-Replaced Diet		
Breakfast			Breakfast		
2 slices toast	128	2	2 slices toast	128	2
1 tbsp margarine	100	11	1 tbsp reduced-fat margarine	50	6
1 cup orange juice	111	0.5	1 cup orange juice	111	0.5
coffee with creamer	16	1	coffee with nonfat creamer	8	0.3
Lunch			Lunch		
2 slices bread	128	2	2 slices bread	128	2
1 oz American cheese	106	9	1 oz reduced-fat cheese product	73	4
2 oz bologna	180	17	2 oz fat-free bologna	40	0
1 tbsp mayonnaise	100	11	1 tbsp reduced-fat imitation mayonnaise	50	5
Banana	105	0.6	Banana	105	0.6
30 grams (about 2) chocolate cookies	140	6	30 grams (about 2) reduced-fat chocolate cookies	120	3
Snack			Snack		
Candy bar	251	9	Reduced-fat candy bar	170	5
Supper			Supper		
3½ oz baked chicken	239	14	3½ oz baked chicken	239	14
½ cup green beans	22	0.2	½ cup green beans	22	0.2
1 tsp margarine	33	4	1 tsp reduced-fat margarine	17	2
Lettuce salad	5	-	Lettuce salad	5	-
1 tbsp salad dressing	67	6	1 tbsp reduced-fat salad dressing	33	2
Baked potato	220	-	Baked potato	220	-
1 tbsp sour cream	26	2.5	1 tbsp reduced-fat sour cream	20	1
½ cup vanilla ice cream	132	7	½ cup reduced-fat vanilla frozen dessert	116	0.7
Snack			Snack		
Chocolate cookies	140	6	Reduced-fat chocolate cookies	120	3
Total	2,249	108.8		1,775	51.3

(Sources: food labels and *Food Values of Portions Commonly Used*, 16th edition)

show that it may cause intestinal cramps and loose stools in some individuals.

Also, according to clinical tests, olestra reduces the absorption of fat-soluble nutrients, such as vitamins A, D, E, and K and carotenoids, from foods eaten at the same time as olestra-containing products. Tests by Procter & Gamble show that no reduction in absorption of fat-soluble vitamins will occur when proper levels of vitamins are added for compensation to olestra-containing foods.

To address these concerns, FDA approved olestra on conditions that vitamins A, D, E, and K be added to olestra-containing foods and that Procter & Gamble continue studies on consumption and long-term effects of olestra. These studies will be reviewed at an FDA Food Advisory Committee meeting in mid-1998.

To provide consumers with information about olestra's possible effects, FDA also required that the following interim labeling statement appear on 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."

FDA has invited public comment on the need for such a label statement and on the statement's adequacy and clarity. The agency will evaluate those comments before issuing a final label statement.

Concern with olestra's drawbacks led one of olestra's critics, the Center for Science in the Public Interest—a non-profit consumer advocacy organization—to file an objection to FDA's approval. FDA's response to the objection is pending.

Other Replacers

Some other fat-based replacers are being considered or developed:

- Salatrim (which stands for short and long-chain acid triglyceride molecules) is the generic name for a family of reduced-calorie fats that are only partially absorbed in the body. Salatrim provides 5 calories per gram. A petition seeking FDA's affirmation that Salatrim is

GRAS was filed in June 1994. An example of its use is in Hershey Co.'s reduced-fat baking chips, semi-sweet chocolate flavor.

- Caprenin, another Procter & Gamble product, is a 5-calorie-per-gram fat substitute for cocoa butter in candy bars. A petition seeking FDA's affirmation that Caprenin is GRAS was filed in 1991.
- Emulsifiers are fat-based substances that are used with water to replace all or part of the shortening content in cake mixes, cookies, icings, and vegetable dairy products. They give the same calories as fat but less is used, resulting in fat and calorie reductions.

Other fat replacers are being developed, according to the Calorie Control Council and other organizations. These include DDM (dialkyl dihexadecylmalonate), a fat-based substance that is not absorbed into the body and can be used in frying and baking. Frito-Lay Inc. has been studying this fat substitute since 1986, although it has not yet petitioned FDA for approval. Also on the

**Olestra has
properties similar
to those of
naturally occurring
fat, but it provides
zero calories and
no fat.**

Dunagin's People

(Reprinted by permission: Tribune Media Services)



"Now all we need is fake exercise."



A picnic lunch can have a lower fat content using these and many other fat-reduced products.

horizon is a fat substitute made by combining starches or gums with small amounts of oil. Opta Food Ingredients Inc. received an exclusive license from the U.S. Department of Agriculture last February for the process, called Fantesk. This fat replacer would give foods the taste and texture of regular fat but provide less than 0.5 grams of fat per serving.

Reducing Dietary Fat

Can these fat replacers help consumers make positive dietary changes? Can they help those who are overweight lose weight?

It may be too early to say, and studies to date give varying answers. For example, in a study of lean non-dieting men, one group ate breakfasts of conventional fat foods, while the other ate olestra-containing foods. Those who ate the olestra-containing foods made up their usual daily calorie intake by eating more carbohydrate-containing foods. The study, sponsored partly by Procter & Gamble and published in a 1992 issue of the *American Journal of Clinical Nutrition* (Volume 56), suggested that a diet of reduced-fat foods can help reduce fat intake without affecting total calories.

Fat intake also was decreased in a study of 96 men and women "habitual snackers." One group was fed potato chips prepared with olestra, while the rest ate potato chips prepared with conventional frying oil. The group fed olestra chips ate on average 29 grams less fat and 270 fewer calories a day than those fed regular chips—even though those who knew they were eating fat-free chips ate 10 grams of chips more than those who ate regular chips. This study, done at Pennsylvania State University, also was partly sponsored by Procter & Gamble.

A possible concern about fat replacers is: Can foods claiming to be reduced in fat inadvertently influence people to eat more? Another study at Pennsylvania State University suggests they might. In this study, women were fed the same yogurt labeled either "high-fat" or "low-fat." The group fed the low-fat-labeled version ate more in a lunch that followed

the yogurt than the group eating the high-fat-labeled yogurt. As a result, the group eating what they thought was low-fat yogurt took in more calories than the other group.

"It appeared that these women regarded the low-fat label as a license to overeat," wrote Debra Miller, a doctoral student in biobehavioral health and nutrition at Pennsylvania State, in an article she prepared for *Weight Control Digest*.

Still, reduced fat foods appear to be an important part of a fat-reduction diet, according to a study involving the Women's Health Trial. The study, designed to determine the role of low-fat diets in the prevention of breast cancer, found that eating "specially manufactured" low-fat foods was one of the most easily adopted dietary practices for those who received prior dietary instruction. Avoiding meats and giving up fats as flavorings (for example, eating bread without butter or margarine) were among the most difficult practices to adopt.

In using reduced-fat foods, the American Dietetic Association cautions consumers to realize that fat-free doesn't mean calorie-free. The calories lost in removing regular fat from a food can be regained through sugars added for palatability, as well as fat replacers, many of which provide calories, too. Consumers should refer to the Nutrition Facts panel on the food label to compare calories and other nutrition information between fat-reduced and regular-fat foods.

Many nutrition experts agree that, used properly, fat replacers can play an important role in improving adult Americans' diets. But, as with any diet or food, they emphasize variety and moderation to ensure a healthy intake.

"These [fat replacers] are truly innovative ideas," said Dennis Gordon, Ph.D., a food scientist at North Dakota State University, Columbia. "But they shouldn't be looked at as a total panacea. [The advice] is the same as with anything: Be prudent." ■

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

**Can these fat
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Adults NEED Tetanus SHOTS, Too

by Evelyn Zamula

Kathleen Bedford had her 15 minutes of fame in a hospital lecture room full of medical students when she was 65. Because there are only about two cases of tetanus a year in the eastern part of England where she lives, the hospital held a special session for the students. For most of them, it was their first—and maybe their last—opportunity to observe someone with the infection. With her injured leg suspended in a protective frame, Bedford was the center of attention. She would have preferred celebrity in some other way.

Bedford pierced the calf of her leg with a pitchfork crusted with dirt in a freak gardening accident. She was rushed to the emergency room. Her leg was bandaged from ankle to thigh, but she received no further treatment.

When she returned to the emergency room 24 hours later, feeling quite ill, the leg was highly inflamed. After the surgeon on duty took one horrified look at her leg, he rushed her to the operating room and cut her calf open deeply across the puncture site to expose the wound to air. During the next six weeks, the wound had to remain open; hence the frame. Bedford recalls she was treated with “all kinds of pills and shots” and escaped any secondary infection, such as pneumonia.

She experienced only one tetanus symptom—transitory stiffness. But the

disease could have been avoided had she been properly immunized. Like many other older adults, Bedford had neglected to keep up her immunity to tetanus with periodic booster doses of tetanus vaccine.

‘Lockjaw’ Symptoms

Tetanus is an acute, often fatal disease that occurs worldwide. It affects the central nervous system, producing both the stiffness or muscular rigidity that Bedford experienced and convulsive muscle spasm. Tetanus can be localized, with muscle contractions in the part of the body where the infection began, or it can be generalized, affecting the whole body. About 80 percent of reported tetanus cases are generalized. The incubation period ranges from 2 to 50 days, but symptoms usually occur 5 to 10 days after infection. The shorter the incubation period, the greater the chance of death.

The most frequent symptom is a stiff jaw, caused by spasm of the muscle that closes the mouth—accounting for the disease’s familiar name “lockjaw.” Muscle stiffness all over the body may follow. An infected person may also have other symptoms: difficulty swallowing, restlessness and irritability, stiff neck, arms or legs, fever, headache, and sore throat. As the disease progresses, the victim may develop a fixed smile and raised eyebrows due to facial



Since adults 50 or older

account for 70 percent of tetanus infections, mature people should make certain they have received boosters within the last 10 years.

muscle spasms. Spasms of the diaphragm and the muscles between the ribs may interfere with breathing, often requiring mechanical ventilation. The abdominal or back muscles may become rigid. In severe cases, patients may become so sensitive to any kind of disturbance that they suffer painful spasms all over their bodies with profuse sweating if the bed is jarred or if they feel a draft or hear a noise. Convulsions can be severe enough to break bones.

Hyperactivity of the autonomic (involuntary) nervous system may raise blood pressure dangerously or cause heart arrhythmias (irregular beats). Although tetanus victims can usually think clearly when conscious, coma may follow repeated spasms. Aspiration pneumonia is a common late complication and is found in 50 to 70 percent of autopsied cases. The mortality rate is about 25 percent in the United States and 50 percent worldwide.

Bacterial Cause

The bacteria that cause tetanus belong to the *Clostridium* family, also responsible for some other serious diseases, such as botulism and the type of gangrene suffered in war wounds. *Clostridia* bacteria are what scientists call "obligate anaerobic"—that is, they thrive only in the absence of oxygen. They also form spores, reproductive

Childhood Immunizations

Immunization should be postponed if a child has a high fever or a severe infection. However, a minor illness, such as a mild respiratory infection, is no reason to delay immunization. All infants and children 6 to 8 weeks of age and up to 7 years should receive tetanus toxoid as part of their DTP (diphtheria and tetanus toxoids and pertussis vaccine adsorbed) immunization schedule. Those children who cannot tolerate the pertussis vaccine because of adverse reactions should continue, nevertheless, to be immunized with diphtheria and tetanus toxoids for pediatric use, according to the DT immunization schedule.

The Public Health Service's Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics recommend that children receive five tetanus immunizations by the age of 6:

- three doses of DTP in their first year of life, usually given at 2, 4 and 6 months
- a fourth dose in their second year of life, usually between 15 and 18 months of age
- a fifth dose just before school entry, from 4 to 6 years of age. All 50 states

have adopted laws requiring children to receive at least three immunizations before they can be admitted to school.

A recent survey found that one-fifth of older children (10 to 16 years of age) do not have protective antibody levels to tetanus. "The new recommendation," says Roland W. Sutter, M.D., medical epidemiologist, U.S. Centers for Disease Control and Prevention, "is that children aged 11 to 13 also receive a sixth dose with Td [tetanus and diphtheria toxoids for adult use] because immunity levels can fall. It's also a convenient time to check to see if they've received the second dose of measles vaccine and whether they've received hepatitis vaccine at this point."

Children older than 7 years should receive tetanus toxoid as part of the tetanus and diphtheria toxoids (Td) for adult use, both for the primary series and for booster doses every 10 years. ACIP recommends the use of combined diphtheria and tetanus toxoids (Td) rather than tetanus toxoid alone for boosters because adult cases of diphtheria continue to occur both in the United States and in other parts of the world. ■

—E.Z.

cells with thick walls that enable them to withstand unfavorable environmental conditions. Spores are tough to kill and highly resistant to heat and the usual antiseptics that treat wounds.

Tetanus bacteria may enter the body through a puncture wound or scratch. In the presence of dead tissue, tetanus spores reproduce and manufacture a poison (exotoxin) that travels through the

body and causes tetanus symptoms. Though tetanus bacteria are found everywhere in the environment—in soil, street dust, and in animal intestines and feces—natural immunity to the disease is rare. This is why immunization is so important.

Vaccination with tetanus toxoid (tetanus vaccine) causes the body to respond to an inactivated form of the tetanus

Adult Immunizations

Some individuals may be protected for life against tetanus after a properly administered primary series of vaccinations, but in most people antitoxin levels fall with time. Adults should receive booster doses every 10 years, along with diphtheria immunization. "We are now recommending an adult immunization visit at age 50 years," says CDC's Roland Sutter, M.D., "when people can check their records to see if they are actually up-to-date with vaccinations, particularly for Td. Quite a number of older persons haven't received the primary series. If they haven't been immunized, this visit serves as an opportunity to initiate the series."

When given to adults, the first two primary doses of Td are administered at least four weeks apart, and the third dose is administered 6 to 12 months after the second.

In some individuals, antibody levels may fall too low to provide protection before 10 years have passed. That's why people who sustain a deep or contaminated wound should receive a booster dose if it has been more than five years since the last dose.

Immunization is especially recommended for:

- adults, especially those 50 years and older, because most of the tetanus cases in recent years have occurred in this age group
- persons who are not sure whether they have received the initial series of tetanus shots or boosters
- travelers, especially to countries with hot, damp climates and soil rich in organic matter
- agricultural workers and others who work with dirt or manure
- persons whose jobs or recreational activities expose them to cuts and scrapes
- those who are recovering from tetanus, because having a case of tetanus does not confer lasting immunity, as is true for some other diseases
- injured persons who may require emergency tetanus treatment depending on their immunization status (primary immunization, boosters) and the type of wound received
- pregnant women who have not been immunized or may be inadequately immunized or who may deliver their infants in unhygienic circumstances. After immunization, antibodies to the disease are passed from the mother to the fetus through the placenta. ■

—E.Z.

toxin by developing antibodies to tetanus. Tetanus toxoid is virtually 100 percent effective in preventing tetanus. It is prepared by growing tetanus bacteria (*Clostridium tetani*) in a special medium, and then detoxifying the resulting tetanus toxin with formaldehyde. The Food and Drug Administration reviews the manufacturer's testing records for each lot of vaccine to ensure that the

product is safe and effective for its intended use. FDA also sometimes tests random lots to ensure that the manufacturer's testing records are accurate.

Side effects of vaccination are few. As with the DTP shot received by children (to immunize against diphtheria, tetanus and pertussis), redness or formation of a small hard lump at the vaccination site

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are possible. Some individuals may have allergic reactions, such as hives, skin rash, or itching. More serious adverse reactions include the rare cases of anaphylaxis (an allergic reaction involving difficulty in breathing or swallowing and facial swelling that can be fatal) and possibly Guillain-Barré syndrome, a nerve inflammation. People who have had a severe reaction to the vaccine should not receive further doses. (See "Adult Immunizations.")

Beyond Rusty Nails

The connection between a wound caused by a rusty/dirty nail and the necessity for a tetanus shot is fixed so firmly in the public mind that even the television cartoon character Homer Simpson knew he had to get a tetanus shot after stepping on a nail.

But people don't realize that tetanus can be contracted in other ways. Any puncture wound, especially one that is deep, can be infected with tetanus. Some seamstresses have contracted tetanus from sewing needles. Animal scratches and bites, and other wounds contaminated by both human and animal feces and saliva, are potential breeding grounds for tetanus bacteria. Infection can develop in wounds in which the flesh is torn or burned, or in wounds resulting from projectiles, such as arrows, bullets or shrapnel, or in those caused by crushing or frostbite. The disease may

Tetanus bacteria may

enter the body through a

puncture wound or

scratch.

follow trivial wounds caused by thorns or splinters, as well as highly contaminated wounds, if oxygen is unable to reach the injured tissues. Tetanus can also develop after surgery, dental infections, and abortion. Cephalic tetanus, a rare form of the disease, is associated with chronic ear infections, in which tetanus bacteria are present in the inner ear. Tetanus has also been reported in people with no known acute injury, chronic wound, or other medical condition.

In developing countries, tetanus is a major health problem. Childbirth may take place under insanitary conditions, causing infection in the uterus afterwards. Tetanus in newborns has emerged worldwide as the predominant form of tetanus, as the baby's umbilical stump is often sealed with mud or clay or other contaminated substances.

CDC's *Morbidity and Mortality Weekly Report* of May 6, 1994, discusses two cases of tetanus that occurred in Kansas in 1993—the first cases reported in that state since 1987—that show the importance of immunization.

The first case involved an 82-year-old man, hospitalized because of shortness of breath and weakness and difficulty chewing and swallowing. When doctors examined him, they found he had difficulty opening his jaw and noted an abrasion on his right elbow resulting from a fall two days earlier. He had never been vaccinated. Doctors administered both tetanus toxoid and tetanus immune globulin (TIG). (An injection of tetanus toxoid after the injury does not give immediate full immunity. TIG confers temporary immunity to those people who have low or no immunity to tetanus toxin by providing antitoxin directly to the body, ensuring that protective levels of antitoxin are reached quickly rather than waiting for the body's immune response.) In the next few weeks, his body was racked by spasms, followed by respiratory failure and pneumonia, which necessitated the

use of a breathing machine. After treatment with antibiotics, diuretics, and neuromuscular blocking agents, he recovered and was discharged a few weeks later.

The second case involved a diabetic 57-year-old man who had stepped on a rusty nail and sought emergency treatment for tetanus that same day. Hospital personnel cleaned the wound and administered tetanus toxoid. Four days later, he returned to the emergency department complaining of severe pain in the foot, as well as chills, fever and vomiting. When he developed pain and a stiff neck, he was hospitalized immediately with a diagnosis of tetanus and received TIG. After a number of life-threatening heart and lung problems, he died following an episode of cardiac arrest. His relatives reported that he had not been previously vaccinated with tetanus toxoid.

The surviving and the deceased tetanus victims each spent about a month in the hospital and ran up medical bills of about \$150,000 apiece. At that time, public health clients could have received a tetanus shot for \$3.30, while vaccination with a private physician would have cost just a few dollars more.

Tetanus has become a rare disease in the United States as well as in England, with only 36 reported U.S. cases in 1994, though there may be more unreported cases. The disease has become uncommon not because tetanus bacteria have been eliminated from the environment—they're still all around us—but because immunization has provided protection.

Since adults 50 years or older account for 70 percent of tetanus infections, mature people should make certain they have received boosters within the last 10 years. If they don't know whether they were immunized as children, the primary series of shots should be completed. ■

Evelyn Zamula is a freelance writer in Potomac, Md.

P R E V E N T I N G DEHYDRATION **In Children**

by Rebecca D. Williams



Tiffany Pressnell, now a hungry and healthy 5-year-old, won a bout with a stomach virus in 1995 that changed the way her parents treat childhood diarrhea.

Petite even for a 3-year-old, Tiffany Pressnell weighed 27 pounds in February 1995 when a stomach virus swept her town of Oak Ridge, Tenn.

When Tiffany caught the bug, she had vomiting and diarrhea so severe that she lost 3 pounds in two days.

"Her eyes were sunken. Her lips were dry," remembers her mother, Tammy. "Her mouth didn't have any wetness in it. Her skin was white—when we pinched it, it stayed pinched."

Tiffany was severely dehydrated. Admitted to the local hospital by her pediatrician, she was given intravenous fluids to restore the water and minerals she had lost. Her weight slipped another 2 pounds, however, before the virus subsided and she was well enough to go home.

"Now if she has any diarrhea at all, we give her Pedialyte," says Tammy Pressnell. "We keep it on the shelf, and I keep the travel pack in a diaper bag. You just never know."

Pedialyte is a brand name for a fluid known as oral rehydration

**The old advice to let the intestine
“rest” after a bout with diarrhea is now
not recommended by the American
Academy of Pediatrics.**



therapy (ORT). Along with other brands like Infalyte, Naturalyte and Rehydralyte, it is a simple mixture of water, salts and carbohydrates to prevent dehydration in children with bouts of diarrhea and vomiting.

ORT, regulated by the Food and Drug Administration as a medical food, is perhaps one of the greatest advances in life-saving treatments of the 20th century, especially in developing countries where diarrhea-producing diseases like cholera, combined with unsanitary water and food, kill 4 million children annually.

Here in the United States, an estimated 500 American children die annually from diarrhea, and the illness is not seen as a major threat. As a result, doctors often do not recommend ORT for their young patients.

The deaths that do occur happen mostly in the winter months while the flu season is in full swing. Nearly all of them are preventable, researchers say, because dehydration can be avoided with proper medical attention and oral rehydration fluid.

Treating Diarrhea

Oral rehydration therapy was developed in the 1950s for developing countries, where diarrhea is common. American children average only one or two bouts with diarrhea yearly. But those illnesses can still be dangerous. The best way for parents to keep their children from getting dehydrated is by stocking the medicine chest with at least one bottle of oral rehydration fluid.

"I think it's very reasonable for every family to have it at home," says John Snyder, M.D., a researcher in the field of ORT and professor of pediatrics at the University of California Medical School in San Francisco. "Diarrhea frequently starts at night, and a small child can get dehydrated very quickly."

Yet many physicians do not recommend ORT for children suffering from diarrhea. According to a 1991 study published in the medical journal, *Pediatrics*, most pediatricians don't follow the guidelines for treating diarrhea set by the American Academy of Pediatrics in 1985.

More commonly, doctors frequently tell parents to withhold food from a child and give clear liquids such as fruit juice, chicken broth, and sports drinks. Neither of these practices is recommended by the academy.

Common clear liquids don't contain the proper balance of sodium, chloride and potassium salts that the body needs. These and other minerals change in the body into electrically charged particles called ions. If electrolytes are not perfectly balanced in the body, many organs, including the heart, cannot function properly. Children under 5 are especially vulnerable to diarrhea because their bodies are small. It doesn't take much fluid loss to get their electrolytes out of balance.

Only a physician can diagnose dehydration, but parents can watch for some obvious signs: a dry mouth, no tears, sunken eyes, a reduction in urination, and skin that stays compressed when pinched.

The AAP guidelines are:

- For diarrhea with no dehydration, feed the child normally and give supplemental commercial rehydration fluids within four to six hours after a diarrheal episode. If the diarrhea persists, call the child's doctor.
- For diarrhea with mild dehydration, take the child to a physician. The child should be given oral rehydration fluids in the doctor's office, with food and rehydration fluid continued at home.
- For moderate or severe dehydration, the child should be treated in a health-care facility. Moderate dehydration may be treated orally, but severe dehydration requires intravenous fluids.

The old advice to let the intestine "rest" after a bout with diarrhea is now not recommended by AAP.

"Early feeding isn't just a good idea, it helps to make the diarrhea better," says Snyder.

Food can help the intestine absorb more water, which helps slow down the diarrhea. A child should eat as soon as possible after a bout of diarrhea, and at least within six hours. A balanced diet rich in calories is recommended. Foods such as rice, wheat, potatoes, sorghum, corn, and chicken have all been proven helpful in slowing diarrhea. Just about

Allowing the illness to run its course, while preventing dehydration with fluids, is usually the quickest way toward health.

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anything the child tolerates is OK, except for foods high in sugar or salt.

Milk products, because they can be difficult to digest, can be withheld for 24 to 48 hours during significant bouts of diarrhea. Infants who are bottle-fed, however, should continue drinking formula diluted to half strength. Breast-fed infants should continue nursing.

The once favored "BRAT" diet—an acronym for bananas, rice, applesauce, and toast—is no longer recommended for children. Instead, parents should offer a more balanced diet that is higher in calories.

Giving anti-diarrhea medicine to children is not the best treatment, according to John Udall, M.D., Ph.D., chairman of pediatric nutrition and gastroenterology at the Children's Hospital in New Orleans.

"Diarrhea is really a purging of the intestine," he says. "Giving medicines to slow down the intestine actually gives the bacteria more time to grow, which prolongs the illness."

Allowing the illness to run its course, while preventing dehydration with fluids, is usually the quickest way toward health.

Dosage information for ORT depends on weight and is listed on the label. Side effects with ORT are rare, but parents should watch for signs of too much sodium in the body: dizziness, a fast heart-beat, irritability, muscle twitching, restlessness, swelling of the feet or lower legs, weakness, and convulsions.

Rehydration fluids have a brief shelf life. Once a bottle has been opened or a mix prepared, it must be used or thrown out within 24 hours because bacteria rapidly grow in the solution. A child could easily drink three or four bottles of the fluid during an illness.

ORT is effective to a lesser degree when the child is vomiting. If the child can keep the liquid down, it will be absorbed. But if the child vomits it back up, intravenous rehydration may be necessary.

ORT is effective for all ages, although the brands available at most grocery stores and drugstores are usually formulated just for children. Adults are usually able to tolerate a bout with diarrhea better than small children because they have more fluid reserves in their bodies.

But older adults and those weakened by diseases like cancer and AIDS are at a greater risk for complications from diarrhea. These patients should call their doctors if diarrhea and vomiting persist.

Parents should also remember that ORT will not stop the diarrheal illness. In fact, the child may have even more episodes of vomiting and diarrhea until the illness runs its course. As long as the child is keeping some rehydration fluid down, however, the chances of dehydration are greatly reduced.

If a child under 5 has diarrhea and vomiting for longer than an hour or so, it's always a good idea to call a physician.

According to Snyder, "Parents should have a low threshold of concern to [prompt them to] phone the pediatrician."

Parents don't have to wait for a prescription to use oral rehydration fluids, however. The products are available at grocery stores and drugstores in premixed bottles. National brands can cost as much as \$6 per liter, but less expensive generic brands are available as well for as little as \$2.

According to a 1991 study in the *Journal of the American Medical Association*, cost is one reason why more parents do not use ORT for their children suffering from diarrhea. Deaths from diarrhea are most common in the South and in low-income, African-American families headed by young single mothers.

To help with that expense, the federally funded and state-administered WIC (Women, Infants and Children) Program pays for ORT along with certain foods for pregnant women, new mothers, and children under 5. In most states, Medicaid also covers ORT if a doctor prescribes it.

As the use of ORT increases, the number of deaths from diarrhea is slowly declining in the United States. This simple solution of water, minerals and carbohydrates will not eliminate the problem of stomach viruses and flu, but perhaps it will make diarrhea less of a life-threatening risk to America's children. ■

Rebecca D. Williams is a writer in Oak Ridge, Tenn.

Fighting Fleas And Ticks

by Dixie Farley

Back from vacationing at the beach, Fido and Kitty sniff out familiar haunts around the yard. Meanwhile, their owner, Mary, plops down on the family room carpet with a month's mail.

Mary scratches an ankle, then the other one, then a leg. Then she looks down and sees why she's scratching: Fleas!

Although Fido and Kitty are flea-free after dog and cat

Winnie, age 5, of Gaithersburg, Md., tastes some cheese on Mom's fingers to whet her appetite for the main course: a tablet that will protect against fleas for one month. To be sure she absorbs all the drug, Winnie takes it with a full meal, as the directions call for. She also wears an anti-tick collar.



**Some pest-control products should
not be used together or when a pet
is taking certain medicines.**

pesticide dips at the beach, the house is not.

During the weeks before vacation, fleas feeding and breeding on the pets deposited unborn offspring all over the homestead. And during the vacation, fleas at various life stages evolved, nourished by dried-blood flea excrement, "flea dirt," in the carpet and elsewhere. The result: A population explosion of fleas ravenous for fresh blood.

The scenario is fictional. But it depicts this fact: Left uncontrolled, bloodsuck-

ing pests can infest not just your cat or dog, but your entire house—and you!

Common household fleas don't usually transmit diseases to pets and people. (See "Human Problems.") The tiny insects are mainly "just a nuisance," says Marcia Larkins, D.V.M., chief of the companion and wildlife drugs branch in the Food and Drug Administration's Center for Veterinary Medicine. "They generally cause a lot of itching and

scratching. They may also cause some discomfort due to possible allergic flea bite dermatitis."

Ticks, those other dreaded bloodsuckers, pose greater risk, annually giving pets and thousands of people illnesses such as Lyme disease.

Fortunately, a wide array of pest control products for pets are available: foggers, sprays, dips, powders, dusts, collars, oral liquids and tablets, and even a liquid one-spot topical treatment. There are new oral products that interrupt the flea's life cycle, a Lyme disease vaccine for dogs, and a pesticide product that mimics mouse nesting material to reduce ticks outdoors.

FDA shares regulation of these products with the Environmental Protection Agency and the U.S. Department of Agriculture. If a pest-control product for pets is given by mouth, injected, or absorbed through the skin, FDA regulates it. Otherwise, EPA does. USDA licenses products that treat or prevent animal illness caused by pests. States sometimes add licensing requirements.

American Fleas

While there are more than 200 species of fleas in this country, the main troublemaker for pets is the cat flea. Happy to feed on anyone in the household—cat, dog or human—these wingless insects will most likely choose a pet, whose fur provides warm camouflage for their breeding ground. The flea life cycle has four stages: eggs, larvae, pupae, and adults. (See "Life Cycles.")

Even when fleas elude detection on a pet, their black poppyseed-like excrement gives them away.

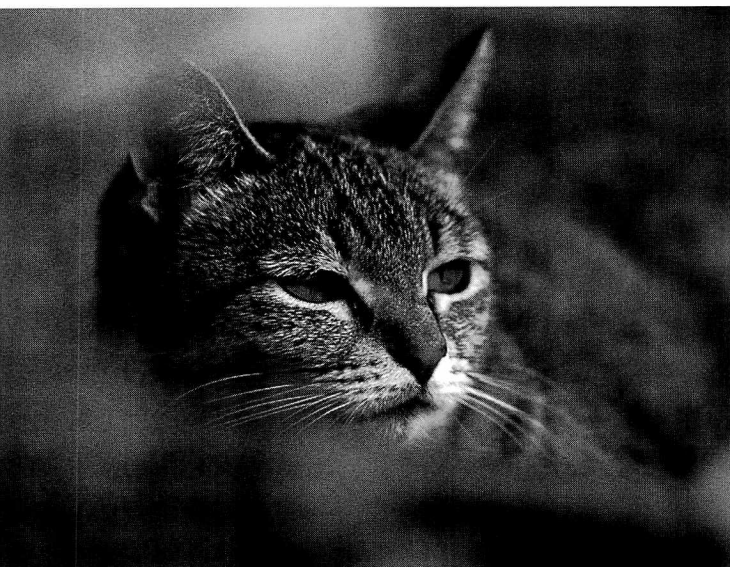
The main problem with fleas—itching—is due not only to their bites, but also to their crawling over the skin.

Other flea bite problems and their symptoms include:

- anemia in young, older or ill pets—pale gums, weakness, lethargy
- transmission of tapeworm to pets—irritability, erratic appetite, shaggy coat, mild diarrhea, weight loss, seizures
- transmission by rodent fleas of plague to cats—fever, swollen lymph nodes, mouth sores, swollen tongue, cough, pneumonia.

Also, some pets are extremely allergic to flea bites. In these pets, fleas may cause a rash, inflammation, and hair loss. In response, cats may compulsively overgroom.

Preparations made from antigens extracted from fleas may help, says David Espeseth, D.V.M., deputy director of USDA's Division of Veterinary



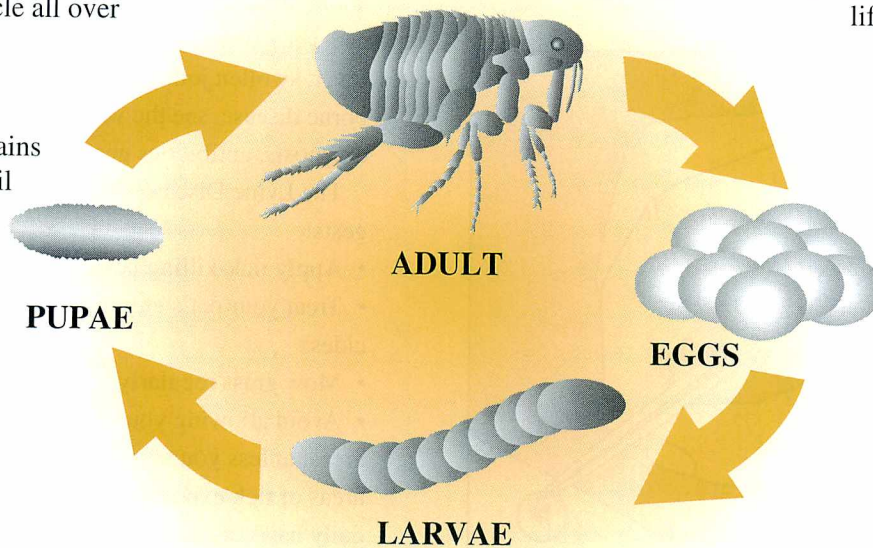
**With cats, use
only products
labeled for cats.**

LIFE CYCLES

Fleas

5. Six-legged adults emerge and attach to a host to feed and breed, beginning the cycle all over again.

4. The adult remains in the cocoon until vibrations indicate a host is nearby. This waiting can extend the life cycle. It also explains why large numbers of fleas often are seen when an empty building is reoccupied.



1. Female fleas lay as many as 50 eggs a day, starting a life cycle that can be completed in as little as three weeks, depending on temperature and humidity.

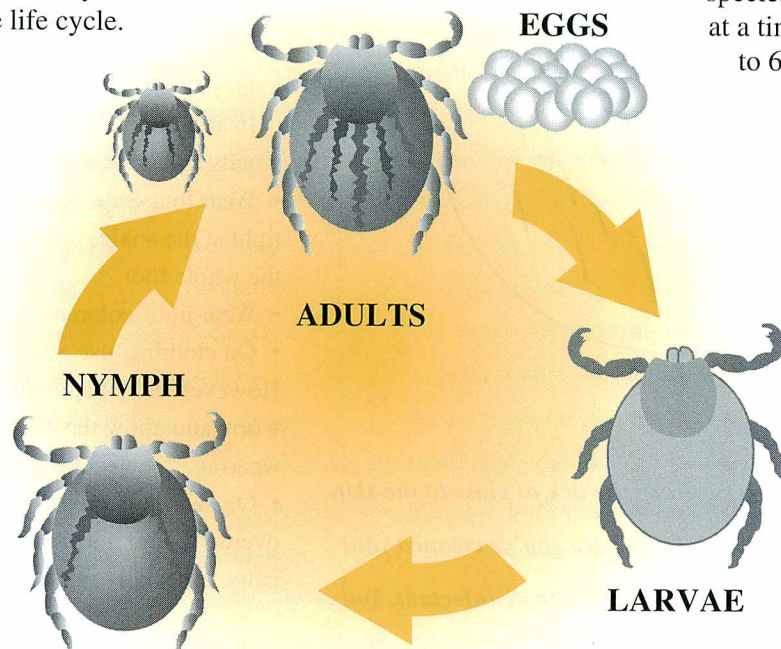
2. The eggs hatch into larvae, which feed on “flea dirt,” excrement of partially digested blood.

3. Larvae grow and molt twice, then spin cocoons, where they grow to pupae and then adults.

Ticks

5. Depending on its species, a tick make take less than a year or up to several years to go through its four-stage life cycle. While ticks need a blood meal at each stage after hatching, some species can survive years without feeding.

4. Final nymphs molt into adult males or females, also with eight legs.



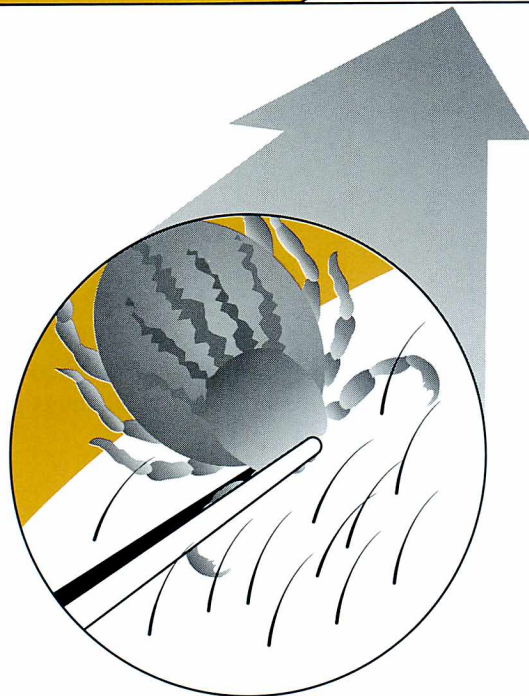
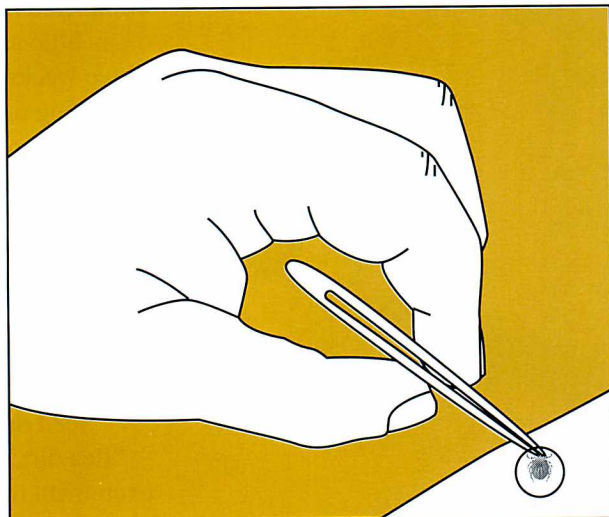
1. Adult females of some species lay about 100 eggs at a time. Others lay 3,000 to 6,000 eggs per batch.

2. Six-legged larvae hatch from the eggs.

3. After at least one blood meal, the larvae molt into eight-legged nymphs—in some species, more than once.

Preventing Tick-Borne Disease

Proper Tick Removal



Using fine-point tweezers, grasp the tick as close to the skin as possible and pull gently. Make sure you've cleaned your hands, the bite site, and the tweezers with disinfectant. You may want to wear latex gloves.

If your dog is outside regularly, ask the veterinarian about the Lyme disease vaccine. (There's no vaccine for cats yet.) Watch for itching, pain, appetite loss, lethargy, fever, swollen joints, or lameness. If you suspect a tick-borne disease, see the veterinarian pronto. With early diagnosis, antibiotics generally work.

The Lyme Disease Foundation, Hartford, Conn., suggests:

- Apply tick-killing pesticides to your pets.
- Treat your pet's environment with tick-killing pesticides.
- Mow grass regularly.
- Avoid allowing your pet in grassy, wooded or beach areas, unless you take appropriate precautions. While in areas of tick exposure, examine pets closely for ticks on a daily basis, especially around the head and inside the ears.
- Remove ticks immediately, as shown in the accompanying magnified drawing. This is important because it can take hours for an infected tick to transmit disease.
- Place the tick in a small container, like a pill vial. Label the container with the date, pet's name, type of animal, and your name, address, and phone number. Call your veterinarian about having the tick analyzed for type and possible diseases it may transmit.
- Never remove a tick with your fingers, as the squeezing further injects infectious material.
- Never try to burn a tick off or to smother it with petroleum jelly or nail polish, as these methods don't work.

In addition, take these steps to protect yourself when in woods and grasslands:

- Wear long-sleeved shirts tight at the wrists, long pants tight at the ankles and tucked in socks, and shoes covering the whole foot.
- Wear light-colored clothes that show ticks easily.
- On clothing, use a repellent containing permethrin. However, do not apply it to clothing while it is being worn, and allow the clothing to thoroughly dry before wearing.
- On skin, use a repellent containing DEET. But don't overdo it. Too much bug spray can cause breathing difficulty, especially in children. ■

—D.F.

Washing the pet's bedding regularly and vacuuming frequently helps keep the flea population down.

Biologics. USDA has licensed several.

"If a pet shows a reaction in a skin test," Espeseth says, "that antigen may be effective in treating the animal against that sensitivity. When allergic animals don't react in the skin, this may mean you don't have the right antigen."

FDA has approved new types of prescription flea-control products:

- **Proban (cythioate)**, first oral insecticide for dogs—A liquid or tablet, Proban is given once every three days or twice a week. Several weeks' treatment may be needed if fleas reinfest the dog.
- **Pro-Spot (fenthion)**, first topically absorbed insecticide for dogs—A liquid, Pro-Spot is applied to one spot between the dog's shoulder blades no more than once every two weeks. Treatment length depends on the rate of flea infestation.
- **Program (lufenuron)**, first oral insect growth regulator (IGR) for dogs—A tablet, Program is given once a month with a full meal. The IGR interrupts the flea life cycle: Upon biting the pet, the female flea ingests the IGR, which deposits in her eggs to stop them from developing.
- **Program (lufenuron suspension)**, first oral IGR for cats—A liquid, Program is given once a month, mixed with food. Cats must be at least 6 weeks old.

Washing the pet's bedding regularly and vacuuming frequently also helps keep the flea population down. The vacuum bag should be changed after vacuuming and the used one burned, if possible, to prevent it from serving as a flea incubator. Cats who don't go outside have the least risk of getting fleas.

Tenacious Ticks

A tick has a one-piece body. The harpoon-like barbs of its mouth attach to a host for feeding. Crablike legs and a sticky secretion help hold the tick to the host. When attempting to remove a tick, to prevent the mouth part from coming off and remaining embedded in the skin, grasp the mouth close to the skin with tweezers and pull gently. (See "Preventing Tick-Borne Disease.")

Improving Safety

Pesticides and repellents to protect cats and dogs from fleas and ticks have risks as well as benefits. Concerned over recent reports of adverse effects from such products, the Environmental Protection Agency, in cooperation with industry, has developed guidance for labeling changes to promote proper use.

The effort, coordinated by EPA policy analyst Janet Whitehurst, began early in 1994, when she learned that in just 18 months, EPA had received 853 reports of adverse effects, including 148 animal deaths and 58 reports of illness in humans. Most reports involved cats, which are more sensitive than dogs.

Improved labels would:

- Direct users to read the entire label before each use.
- Clearly state the animal for which the

product is registered and the minimum age for safe use.

- Caution users to consult a veterinarian before treating certain animals, such as those that are ill or pregnant (unless safety is known).
- Warn about adverse reactions and interactions with medicines or other chemicals.
- Advise users to wash their hands after use.
- Clearly state limitations for reapplication.
- Give a phone number to call about proper use and emergencies.
- Include first-aid information. ■

—D.F.

Human Problems

Fleas and ticks transmit diseases to people as well as pets.

Lyme disease is by far the most often reported tick-borne disease in humans in the United States: 13,083 cases in 1994, up from 8,257 in 1993. Most reports came from the Northeast and North Central regions of the country. Symptoms include fatigue, chills and fever, headache, muscle and joint pain, swollen lymph nodes, and a red, circular skin rash. (See "Getting Lyme Disease to Take a Hike," in the June 1994 *FDA Consumer*.)

The next most prevalent disease from ticks is Rocky Mountain spotted fever, characterized by fever, headache, rash, and nausea or vomiting. It affects more than 500 people each year, according to the national Centers for Disease Control and Prevention.

CDC received reports of 415 cases of human monocytotropic ehrlichiosis, a disease also transmitted by ticks, since it was identified in 1986. It is similar to

Rocky Mountain spotted fever, but usually without the rash. In 1994, scientists identified another similar disease, human granulocytic ehrlichiosis, or HGE. About 170 cases have been reported.

The organism that causes the tick-borne disease babesiosis infects red blood cells, which burst and die, resulting in hemolytic anemia. Patients develop a malaria-like fever, chills, sweats, muscle aches, nausea, and vomiting; those with no spleen are at particular risk of developing severe disease. The reported incidence of babesiosis is about one-tenth that of Lyme disease, or even less, according to Sam Telford, Ph.D., a lecturer on tropical public health with the Harvard School of Public Health.

Lyme disease, HGE, and babesiosis are all transmitted by the deer tick. Ticks have been found to have any two of those disease-causing organisms. "I believe it's only a matter of time before we find a tick with all three," Telford says. The lone star tick transmits human monocytotropic ehrlichiosis.

Many exposed people never develop the diseases. Roughly 5 percent of the coastal Massachusetts' population has antibodies against babesiosis, Telford

says. "We believe it's about the same for ehrlichiosis. For Lyme disease, it's maybe three times that."

Fleas or an infected animal can transmit bubonic plague. Seven cases, including one death, were reported to CDC in 1995, in Arizona, California, New Mexico, and Oregon. Another 13 cases, also including one death, were reported in 1994, in Arizona, California, Colorado, New Mexico, and Utah.

Symptoms of bubonic plague include fever, headache, vague discomfort, and very painful, swollen lymph nodes near the infection site. Septicemic plague is more serious because the bloodstream is infected, as is pneumonic plague, with its overwhelming pneumonia. Antibiotics are used for treatment. A plague vaccine is available for special groups at very high risk.

Early diagnosis and treatment give humans the best chance of recovery from these and other flea- or tick-transmitted diseases. ■

—D.F.

Ticks annually give pets and thousands of people illnesses such as Lyme disease.

Ticks are not insects like fleas, but arachnids like mites, spiders and scorpions. They have a four-stage life cycle: eggs, larvae, nymphs, and adults. (See "Life Cycles.")

The United States has about 200 tick species. Habitats include woods, beach grass, lawns, forests, and even urban areas.

Ticks may carry various infectious organisms that can transmit diseases to cats and dogs, including the following (listed with possible symptoms):

- babesiosis—lethargy, appetite loss, weakness, pale gums
- ehrlichiosis—high fever, muscle aches
- Lyme disease—lameness, swollen joints, fever, poor appetite, fatigue, and vomiting (some infected animals show no symptoms)
- tick paralysis in dogs—gradual paralysis, seen first as an unsteady gait from uncoordinated back legs (some infected dogs don't develop paralysis).

In June 1992, USDA licensed a vaccine to prevent Lyme disease in dogs. This followed a conditional license in 1990.

According to USDA's Espeseth, "There were early concerns about disease related to abnormal immune responses. But we've never seen this. Nor have we seen such responses with extensive safety testing prior to the final licensing."

In most cases, immunity lasts at least five or six months, Espeseth says. "The recommendations are for dogs actively in the field, subject to exposure. For dogs in apartments or those that very seldom get out or reside in regions where Lyme disease isn't prevalent, it's probably not worthwhile."

To reduce the population of deer ticks, which transmit Lyme and other diseases and which often attach to the deer mouse, EPA has licensed a product named Damminix. It consists of tubes stuffed with cotton balls treated with the pesticide permethrin.

"The cotton balls mimic the nesting material for the deer mouse," says George La Rocca, a product manager in EPA's Office of Pesticide Programs. The label, he says, directs users to place the tubes containing the cotton balls in outdoor areas inhabited by mice, such as brush-covered and wooded areas. "It kills and repels ticks on the mice. It's not meant to eradicate Lyme disease, but to reduce its incidence."

(See "Preventing Tick-Borne Disease.")

Debugging

To protect pets from the discomfort and illness caused by fleas and ticks, it's important to rid the pets of the pests. It's

also important to treat a pet's environment to prevent or reduce the incidence of reinfestation, says FDA's Larkins.

Products to control these pests are not risk-free, however. (See "Improving Safety.") Approved or registered products must warn users about the risks the product poses and give directions for safest use. Proban's label, for example, warns that the product is not for use in greyhounds, who are sensitive to the insecticide it contains, an organic phosphate. Also, some products should not be used together or when a pet is taking certain medicines.

Larkins advises, "Follow directions for use very carefully, even with over-the-counter products. If you don't understand the directions or have questions, talk to your veterinarian."

EPA product manager Rick Keigwin agrees. As pesticides are intended to kill pests, they generally are inherently toxic, he says. "Some products pose some risks, but they also offer significant benefits. We balance the risks with the benefits."

La Rocca adds that with cats, use only products labeled for cats. "Cats are more sensitive than dogs in general," he says. "It also has to do with their size—just like children are more sensitive than adults—and their grooming habits. Dogs groom, but cats groom more, so they would ingest more of a topical product."

Virtually hundreds of pesticides and repellents are approved or licensed to control fleas and ticks on cats and dogs or in their environment.

To select proper products for your pet's individual needs, talk to your veterinarian, says Larkins. "It's a personal choice between you and your veterinarian about the best product to use and how to treat the animal, as well as the environment." ■

Dixie Farley is a staff writer for FDA Consumer.

Using Flea and Tick Products

- Read the entire label before use. If you don't understand something, ask your veterinarian.
- Follow directions exactly, using latex gloves if possible. Then wash your hands.
- On cats, use only products labeled for cats.
- Store products away from food and out of children's reach. ■

THE CENTER FOR DRUG EVALUATION AND RESEARCH

by Tamar Nordenberg

This is one in a series of articles on FDA activities and concerns.

The Food and Drug Administration's approval of the new AIDS drug Crixivan (indinavir) in just 42 days made news nationwide. While the evaluation of new drugs is the best known responsibility of the agency's Center for Drug Evaluation and Research (CDER), the center also promotes the public health by regulating the manufacture, labeling and advertising of drug products.

CDER is the largest of FDA's five centers, with a staff of about 1,800. It has responsibility for both prescription and over-the-counter drugs. Other centers have responsibility for medical and radiological devices, food, cosmetics, biologics, and veterinary drugs.

High-Quality Reviews

The center's job is to ensure that drugs are safe and effective. (See "Benefit Vs. Risk: How FDA Approves New Drugs" in the December 1987-January 1988 *FDA Consumer*.) CDER doesn't test drugs, although the center's Office of Testing and Research does conduct limited research in the areas of drug quality, safety and effectiveness.

It is the responsibility of the company seeking to market a drug to test it and submit evidence that it's safe and effective. (See "Testing Drugs in People" in the July-August 1994 *FDA Consumer*.) A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the sponsor's new drug application (NDA) containing the data and proposed labeling.

The 13 NDA reviewing divisions in CDER are grouped into five Offices of Drug Evaluation. Each office oversees drugs for certain medical conditions. The Office of Drug Evaluation I, for ex-

ample, is responsible for neuropharmacological (relating to the nervous system), oncologic (involving tumors), and cardiorenal (relating to the heart or kidneys) drug products. Over-the-counter drugs are reviewed by the Office of Drug Evaluation V. The review divisions work side by side with reviewers in the Office of New Drug Chemistry, the Office of Clinical Pharmacology and Biopharmaceutics, and the Office of Epidemiology and Biostatistics to evaluate a drug's safety and effectiveness. In some cases, FDA seeks the recommendations of advisory committees made up of outside experts. (See "Getting Outside Advice for 'Close Calls'" in the December 1987-January 1988 *FDA Consumer*.)

Murray M. Lumpkin, M.D., CDER's deputy director for review management, is in charge of the review process (except for the review of generic drugs) and the 900 reviewers who make up about half the center's work force. A good drug review process must be predictable and thorough, according to Lumpkin. Predictability means timeliness, he says. "It used to be that people would ask, 'Do you want it right, or do you want it on time?' To get it right, reviewers often had to ignore the clock."

To get reviews done both right and on time, FDA needed additional financial resources. To meet this need, Congress passed the Prescription Drug User Fee Act of 1992, which requires drug companies to pay fees when submitting NDAs to the agency and in some other instances provides FDA funds to hire more reviewers. (See "User Fees to Fund Faster Reviews" in the October 1993 *FDA Consumer*.)

Consumers, Congress, and government and industry experts agreed on time frames for FDA's completion of re-

views of drug applications covered by user fees. CDER's top priority, according to center director Janet Woodcock, M.D., is to exceed these user fee time frames while maintaining the high quality of reviews. (See "The CDER Director.") In 1994, CDER reviewed 96 percent of new drug applications within the 12-month performance goals, far surpassing the agency's 1994 goal of 55 percent.

User fees do not apply to generic copies of brand-name drugs because generics involve the review of different kinds of data. Once CDER approves a brand-name drug and any patent for that drug expires, CDER's Office of Generic Drugs can approve another product as a generic copy if it's shown to be equivalent to the brand-name drug. (See "FDA Ensures Equivalence of Generic Drugs" in the September 1992 *FDA Consumer*.)

To achieve consistency in approval decisions, all reviewers receive in-depth training. A guidance called "Good Review Practices" is being developed by a number of FDA staff members under the leadership of Robert Temple, M.D., CDER's associate director for medical policy and director of the Office of Drug Evaluation I. This guidance will establish the proper methods of performing medical and statistical reviews. And to improve the coordination among all CDER offices, a new manual of policies and procedures is being developed under the leadership of Jane Axelrad, J.D., the center's associate director for policy. The manual will improve the center's efficiency by documenting all CDER processes in one organized location so they're accessible to FDA personnel and to the public.

To achieve consistency on a larger scale, the International Conference on Harmonization is bringing together

THE CDER DIRECTOR

Janet Woodcock, M.D., joined FDA in 1986 and has been the director of CDER since June 1994. Woodcock is an internist and rheumatologist with a research background in immunology.

Before becoming director of CDER, she worked in FDA's Center for Biologics Evaluation and Research (CBER). As director of CBER's Office of Therapeutics Research and Review, Woodcock oversaw the review and approval of the first biotechnology-based treatments for multiple sclerosis and cystic fibrosis. Before that, she spent four years with CBER's division of biological investigational new drugs, as group leader for vaccines and allergenics and as director of the division.

Woodcock strives for efficient regulation. "The time of major backlogs is over; it's unacceptable to perform that way," she says. Her reorganization of CDER was a first step toward better performance. One of the most significant structural changes—establishing 13 reviewing divisions where nine existed before—is expected to speed up CDER's work by authorizing additional managers to sign off on drug reviews. ■



pharmaceutical industry representatives and the drug regulating agencies of the European Union, Japan, and the United States to establish common procedures to speed up the availability of new medicines worldwide. Roger Williams, M.D., CDER's deputy director for pharmaceutical science, is the lead CDER representative. "I think there will be a big payoff," he says, "in terms of avoidance of duplication and resource savings to industry."

Postmarketing Responsibilities

Despite efficient, high-quality reviews, the public health cannot be safeguarded without procedures to monitor the quality of drugs once they are marketed. CDER's Office of Compliance, directed by Stephanie Gray, M.P.H., has a many-sided role in protecting the public health. In addition to monitoring

preapproval research and working side by side with field investigators to inspect manufacturing plants, the office implements programs to make sure that manufacturers comply with the laws and regulations enforced by FDA. The Office of Compliance sees to it that drug manufacturers operate under current good manufacturing practices as spelled out in FDA's regulations.

Betty Jones is the deputy director of the office. "CDER is made up mostly of scientific and medical experts," she says. "Without the Office of Compliance, the agency wouldn't have the capability to deal with firms or individuals that violate the law." The office's tools for dealing with violations include recalls, warning letters, injunctions, seizures, and criminal prosecutions.

It's also important that patients have accurate and complete information.

While advertising of OTC drugs is regulated by the Federal Trade Commission, FDA oversees advertising of prescription drugs. CDER's division of drug marketing, advertising, and communications monitors prescription drug advertising to ensure that it contains a truthful summary of information about effectiveness, side effects, and circumstances when use is not advisable.

Despite CDER's vigilant premarket review, active postmarketing surveillance of drug adverse effects is also essential. Because all possible side effects of a drug can't be anticipated based on preapproval studies involving only several hundred to several thousand patients, FDA has a system called MEDWATCH through which health professionals and consumers can report serious adverse reactions. (See "MEDWATCH: On Lookout for Medical Product Problems" in the November 1993 *FDA Consumer*.) CDER's Office of Epidemiology and Biostatistics collects information from MEDWATCH and the pharmaceutical industry and conducts statistical evaluations on drug usage, adverse reactions, poisonings, safety, and effectiveness. When necessary, information can be passed on to patients and medical professionals.

The consumer's well-being will always remain FDA's most important concern. CDER's new Office of Training and Communications (OTCOM), directed by Lucy Rose, was established to enhance communications with the public and within the center. In cooperation with other offices, it educates the public on CDER and FDA policies and activities and prepares responses to drug-related questions. For CDER information, contact:

Drug Information Branch (HFD-210)
Division of Communications Management/OTCOM
FDA/Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857
(301) 594-1012
Fax: (301) 594-3302
E-mail: dib@cder.fda.gov ■

Tamar Nordenberg is a staff writer for 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.

■ **Sodium** in over-the-counter oral drugs would be stated on the product labeling if the product contains 5 milligrams or more of sodium in a single dose, under an FDA final rule that allows for opportunity for comments. If the labeled maximum daily dose contains more than 140 mg of sodium, the label would have to warn that people on sodium-restricted diets should not take the product unless directed by a doctor. FDA is accepting comments on this rule until July 22. Send them to the FDA Dockets Management Branch, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857. (FR April 22)

■ **A chewable tablet for dogs** used to prevent heartworm disease and to treat and control ascarid and hookworm infections has been approved for dogs

weighing less than 5 pounds. Also, labeling for the drug, Heartgard-30 (ivermectin with pyrantel pamoate), that previously read "Not to be used in dogs under 6 weeks of age" has been changed to "Recommended for dogs 6 weeks of age and older." (FR April 5)

■ **Poultry feeds** now can include formaldehyde (37 percent aqueous solution) as an antimicrobial food additive intended to control *Salmonella* contamination, according to an FDA final rule. Up to 5.4 pounds (2.5 kilograms) of formaldehyde per ton may be added. (FR April 9)

■ **Confirmed cases of measles** in 1995 fell to the lowest number (301) reported for a single year since the disease became reportable in 1912, according to the national Centers for Disease Control and Prevention. This is a 69 percent decrease from the 963 cases reported in 1994. (*Morbidity and Mortality Weekly Report*, April 19, 1996)

■ **People aged 70** and older can significantly cut the risk of falls by practicing Tai Chi, a martial arts form that en-

hances balance and body awareness, according to two studies sponsored by the National Institute on Aging. In one program, older people taking part in a 15-week Tai Chi program lowered their risk of falls by nearly 48 percent. In the other study, several procedures to improve balance and strength, including Tai Chi, were effective. (*Journal of the American Geriatrics Society*, May 1996)





Doctor Jailed for Violating Breast Implant Restrictions

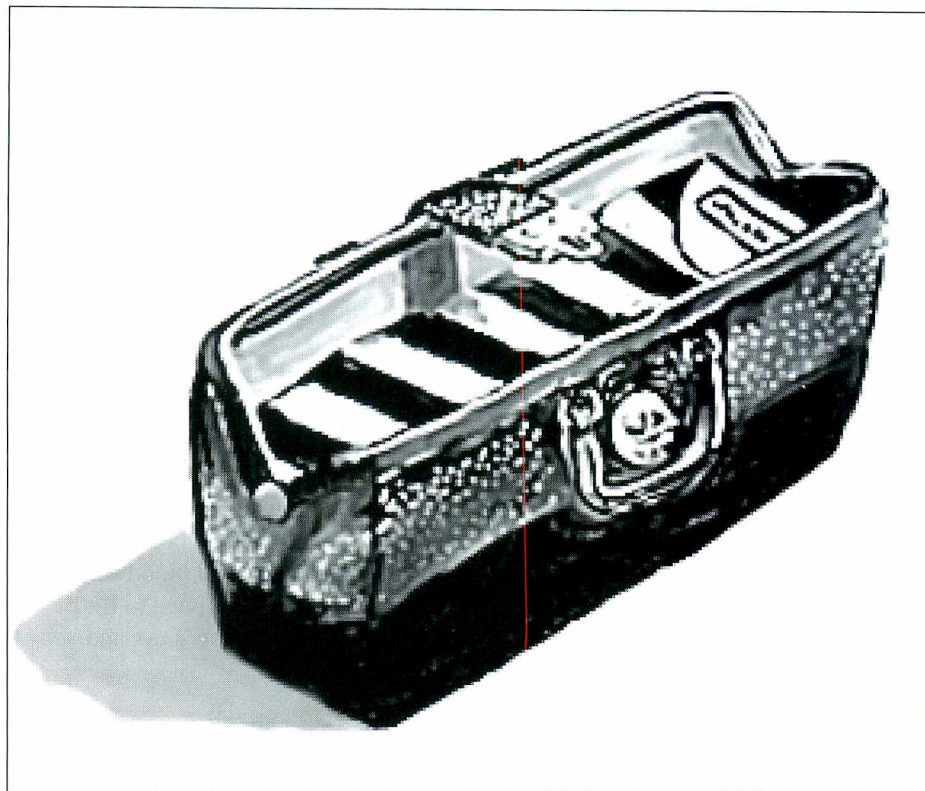
by Paula Kurtzweil

A 55-year-old Oklahoma City doctor who performs breast augmentation is serving six months in federal prison for smuggling into the United States unapproved silicone gel-filled breast implants from a foreign manufacturer.

J. Dan Metcalf, M.D., a family practitioner, is believed to be the first person prosecuted for violating U.S. restrictions on use of unapproved silicone gel-filled breast implants. He illegally imported the implants from Brazil and the Bahama Islands, used them to enlarge the breasts of 200 women, and sold some to other U.S. doctors. The federal investigation continues, according to Special Agent Kent Wood of FDA's Office of Criminal Investigations.

Since April 1992, FDA has allowed silicone gel-filled breast implants only in women enrolled in clinical studies, and then mainly for reconstruction after breast cancer surgery and certain other medical conditions. At this time, women who want implants for augmentation (breast enlargement) must get saline-filled breast implants.

FDA issued a three-month moratorium in April 1992, following years of debate on the safety of silicone gel-filled breast implants and whether or not the medical devices should remain on the market. FDA turned down manufacturers' applications for approval of the implants submitted after the three-month moratorium because FDA found that the information



was not sufficient to prove the safety and effectiveness of the devices. The studies under way are intended to provide more definite information about implant safety. (See "A Status Report on Breast Implant Safety" in the November 1995 *FDA Consumer*.)

Metcalf was indicted in the U.S. District Court for the Western District of Oklahoma in July 1995. He was sen-

tenced last March. In addition to the prison sentence, he was fined \$5,000, ordered to forfeit assets of about \$312,000, and sentenced to one year's probation.

FDA, along with U.S. Customs and the Internal Revenue services, began investigating Metcalf in early 1994, after Metcalf's former office manager, who also doubled as Metcalf's surgical assistant, and her mother reported the

doctor's activities to investigator Lloyd Paine at FDA's Oklahoma City resident post. The former office manager, who provided most of the information, said she had quit her job because Metcalf's wife, her sister, had been taking over her role in the business. She provided photocopied documentation of Metcalf's activities, including lists of patients' names and records of phone calls and financial transactions between the doctor and his implant sources.

Armed with this information—and a search warrant—FDA, Customs and IRS special agents searched Metcalf's office, residence, and bank safe deposit box on May 24, 1994. At Metcalf's office and residence, they seized 470 pairs of silicone gel-filled breast implants, worth about \$200,000, medical records of all patients who had received silicone breast implants since April 1992, and various business records.

With this information, the agencies

determined that Metcalf had been importing silicone breast implants made by the Brazilian silicone implant company Silimed, of Rio de Janeiro, since shortly after FDA turned down the implant manufacturers' applications in 1992. According to FDA's Wood, Metcalf tried to buy direct from the Brazilian company, but the head of the company told him he would not do business in the United States. So, Metcalf arranged to buy the implants through doctors in Brazil and Nassau, in the Bahamas.

Metcalf had the implants delivered through such mail carriers as Skynet and Federal Express to his employees' residences in Oklahoma City. He then implanted the devices in 200 women, who, according to Wood, learned about his augmentation business by word of mouth. He kept some implants on hand and sold the rest to other U.S. doctors who also performed breast augmentation.

On July 19, 1995, a federal grand jury returned a 15-count indictment against

Metcalf that included, among other things, charges of illegally importing silicone gel-filled breast implants and laundering more than \$300,000 in proceeds.

Metcalf pleaded guilty Nov. 14, 1995, to one count of violating the Federal Food, Drug, and Cosmetic Act. The remaining charges were dropped.

According to Wood, the state of Oklahoma is investigating Metcalf for possible improper medical practice. He also faces a number of class-action suits brought by his breast implant patients, who, according to Wood, were unaware that Metcalf was illegally importing the breast implants until news of his indictment and arrest on July 26, 1995, became public.

The seized implants remain in FDA's possession and will be destroyed.

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

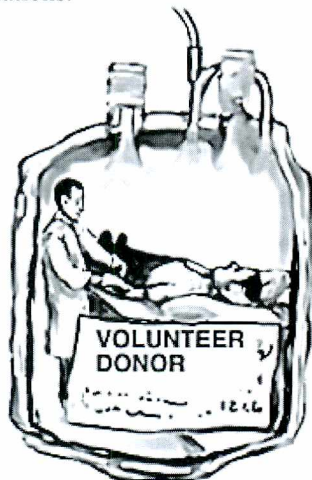
Blood Supplier Agrees To Improve Operations

A U.S. company that collects blood at 17 licensed facilities and multiple blood collection sites in 13 states has agreed to take corrective action to ensure the safety of its blood and blood products.

Blood Systems Inc. (BSI), which operates in some areas under the name United Blood Services, agreed last April 22 in a consent decree with FDA and the Department of Justice to improve its quality assurance and employee training programs and take other steps aimed at improving its blood and blood products operations.

FDA inspections in 1994 at multiple BSI sites led FDA to notify the company in February 1995 of its intention to revoke the firm's license to make and dis-

tribute blood products. While follow-up inspections in 1995 documented improvements at many BSI blood centers, FDA investigators continued to find violations of blood safety laws and regulations.



Among actions BSI agreed to in the consent decree were to:

- improve its employee training program, including initiating annual reviews of employees' job performance and competence
- assess management controls and organizational structure
- improve computer systems and records management
- improve the system for investigating suspected transfusion-associated infections and deferring unsuitable donors, as well as internal audit procedures.

The consent decree also established a timetable for BSI to make the improvements.

The consent decree is similar to one FDA entered into with the American Red Cross in 1993.

—Paula Kurtzweil

N.Y. Man Sentenced For Illegal Drug Sales

A retired hospital employee has pleaded guilty to charges of stealing drugs from two Buffalo, N.Y.-area hospitals for later sale and of filing false income tax returns.

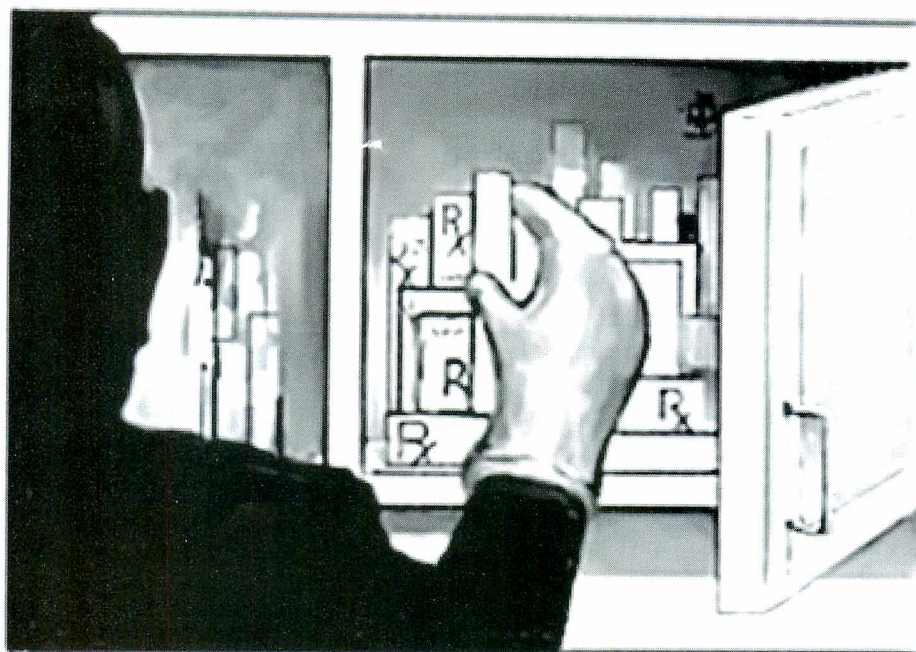
Henry Gonciarz, 72, was sentenced last Jan. 16 in the U.S. District Court for the Western District of New York to five months in a minimum-security camp, five months of home detention, and three years' probation. He was ordered to pay more than \$80,000 in back taxes and penalties and \$90,000 in restitution to the hospitals. Gonciarz held managerial jobs in admissions and finance with Erie County Medical Center, where some of the drug thefts occurred, until his retirement in 1990.

His drug-selling scheme, which took place between 1988 and 1992, violated the Prescription Drug Marketing Act. Under this law, it is illegal to sell, buy, trade, or offer to sell, buy or trade prescription drugs, unless working as an authorized manufacturer's representative. Violations of the law, usually done for monetary gain, are considered hazardous because they increase the risk of counterfeit, adulterated, misbranded, subpotent, or expired drugs being sold to consumers.

FDA discovered Gonciarz's wrongdoing in 1992 as part of a grand jury investigation into illegal prescription drug sales. Portions of that investigation are still in progress.

"He was the kind of guy that everyone at the hospital knew and trusted," says Ray Kent, compliance officer in FDA's Buffalo district office. "Because he had been an employee, he gained easy access to the inside of the hospital."

In a plea agreement signed in June 1993, Gonciarz admitted to stealing a variety of pharmaceuticals with an al-



leged collaborator employed by Erie County Medical Center and another facility, Sisters Hospital. His alleged collaborator is still under investigation.

According to FDA and the plea agreement filed with the court, Gonciarz and his alleged accomplice had a scheme that worked like this:

- His alleged accomplice stole the drugs from both hospitals and gave them to Gonciarz, who then sold them to pharmaceutical wholesalers and retail pharmacies.
- Gonciarz alleges he sometimes used an intermediary to broker the drugs. Payment then went to the alleged intermediary, who kept some of the proceeds—usually 10 percent—and gave the rest to Gonciarz, who then split the money with his alleged accomplice.
- When he sold stolen drugs directly to pharmacies, Gonciarz kept half of the proceeds and gave the other half to his accomplice.

Over the five-year period covered in the plea agreement, Gonciarz earned nearly \$80,000, an amount he concealed

from the Internal Revenue Service. Gonciarz did not report proceeds of illegal drug sales on his federal income tax returns.

—John Henkel

Researcher Regains Privileges, But with Restrictions

A New York doctor who violated federal law in treating melanoma patients with experimental drugs is eligible once again to conduct clinical trials. But he can do them only under rigid restrictions and oversight by FDA and the medical center where he performs the studies.

Abraham Mittelman, M.D., a medical researcher with Westchester County Medical Center in Valhalla, N.Y., regained some research privileges last December after being barred from doing studies for six months. He had signed a consent agreement with FDA in June 1995, concerning previous clinical trial violations, ranging from dispensing unauthorized drugs to inadequately protecting the welfare of trial subjects.

By signing the agreement, Mittelman waived his right to a hearing and obligated himself to follow a detailed plan before working in clinical trials again.

Mittelman's research centered on using biological drugs called monoclonal antibodies to treat more than 400 patients with advanced malignant melanoma, a deadly form of skin cancer. Monoclonal antibodies have been shown to be valuable in medical diagnostics, but their worth in disease treatment is unproven. FDA has approved several monoclonals for diagnostics but none for treatment.

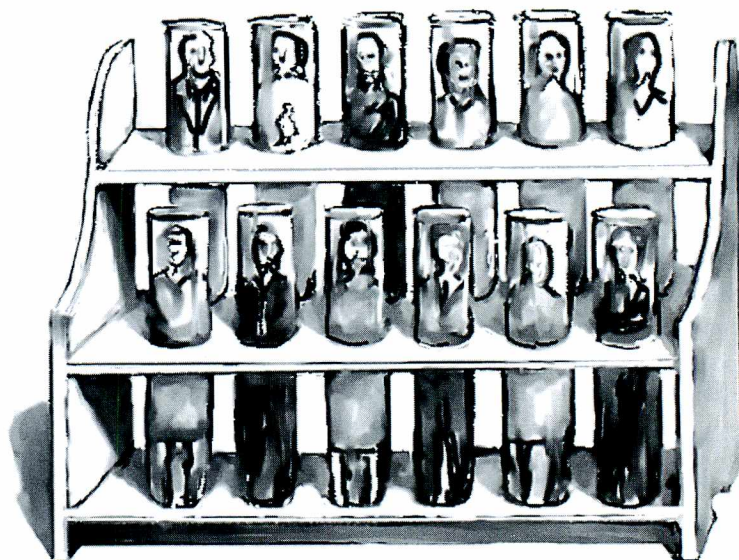
"The way he did these studies, it's impossible to know if the drugs he was testing really worked," says Pat Holobaugh, FDA consumer safety officer.

FDA first suspected the infractions in October 1992, when a reviewer for the agency's Center for Biologics Evaluation and Research noticed in a routine review that Mittelman was testing a drug without an approved investigational new drug (IND) application. FDA must approve INDs before researchers can begin testing drugs in clinical trials.

In January 1993, Margaret Sarles, investigator in FDA's White Plains (N.Y.) resident post, followed up on the IND discrepancy by interviewing Mittelman and examining his records relating to the monoclonal antibodies. For three months, Sarles gathered evidence showing that Mittelman had repeatedly violated regulations governing proper conduct in clinical studies of investigational new drugs.

Violations cited in the consent agreement included:

- failing to submit an IND application for an investigational drug
- administering an unapproved drug to humans
- failing to protect the safety and welfare of patients by using deficient consent forms
- administering to patients an unap-



proved biological reagent labeled "for laboratory use only"

- failing to maintain adequate records on the distribution of investigational drugs
- neglecting to maintain sufficient case histories of patients in the trials
- shipping investigational new drugs to Italy, Argentina and Greece without FDA authorization
- violating "clinical holds." (FDA places clinical holds on investigational new drugs when there are concerns about their safety and other factors. A clinical hold forbids researchers to test the drug in clinical trials until the concerns are resolved. FDA found that Mittelman violated clinical holds on monoclonal antibodies by administering the drugs to 14 patients between 1988 and 1991, and to eight patients between 1991 and 1992.)

Under the consent agreement, Mittelman agreed to withdraw from every clinical study he was managing for six months and to notify all sponsors in writing that he was doing so. He also had to return to sponsors or destroy any investigational drugs in his possession.

Mittelman may now perform clinical trials under the following conditions,

which remain in effect for the next three years:

- He cannot participate in more than three clinical studies with more than 20 patients at a time, and he cannot serve as the sole principal investigator.
- He must collaborate with a senior clinical investigator, approved by FDA, in reviewing the clinical trials every 60 days to ensure that Mittelman complies with FDA regulations and the consent agreement.
- He cannot store or control any investigational drugs or biologics. To ensure data accuracy, he must personally review each case report form before submitting it to the sponsor.

After three years, Mittelman can ask FDA to lift the restrictions.

—John Henkel

Summaries of Court Actions will not appear in this issue of FDA Consumer, but will return in the September 1996 issue.

If You Think You Might Have a *Baby Sometime*

Folate can help reduce the risk of some serious, common birth defects. Folate, or folic acid, is an essential B vitamin. To make sure you're getting enough folate, you need to be consuming adequate amounts before you're pregnant and through the first few weeks of pregnancy. In 1992, the U.S. Public Health Service recommended that *all* women of childbearing age get 400 micrograms of folate daily by:

- eating a healthy diet that includes foods with folic acid
- if necessary, taking a dietary supplement containing folic acid.

More information is available from FDA, HFE-88, Rockville, MD 20857; (1-800) FDA-4010; FDA's home page at <http://www.fda.gov/> on the World Wide Web.

Think Folate Now

