The 'Grazing' of America:  
A Guide to Healthy Snacking
Keeping Drug Residues Out of Milk: A Lesson in Industry Education
When traces of a veterinary drug began showing up in milk last year, FDA knew special tactics were needed to correct the situation immediately. Commissioner Frank Young explains how a combination of tough law enforcement, teamwork and education saved the day.

The ‘Grazing’ of America: A Guide to Healthy Snacking
“Grazing”—snacking throughout the day on mini-meals—is replacing the traditional three square meals a day for many Americans. Grazing can be fast, fun and nutritious if we pay attention to what we’re grazing on.

New Hope for Children with Sickle Cell Disease
A genetic oddity that once protected against malaria today haunts many blacks and others in whom it can produce deadly sickle cell anemia. Now, new treatments can ease the pain and prolong the lives of those afflicted, especially children.

Poison Control Centers: Where Emergencies Are the Routine
Between 1962 and 1985, accidental poisoning deaths of children under 5 dropped from nearly 500 to only 56. One reason: the emergency help, just a phone call away, available from the nation’s more than 100 poison control centers.

Do You Know Your Cholesterol Level?
More and more people are taking the first step in controlling their cholesterol—having it checked. New testing sites are popping up everywhere—from pharmacies to exercise clubs.

Doing More Good than Harm with Children’s Medications
Any parent who’s tried to give a child a nonprescription medicine knows that the dosing instructions aren’t always too precise. So FDA is working to develop better directions for pediatric medications, to help kids feel better, not worse.

Updates
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Inside Front Cover Photo:
New treatments promise to lessen the pain and organ damage caused by sickle cell anemia, which distorts normal red blood cells (left) into the sickle shape (right) that gives the disease its name. See page 14. (Electronmicrograph courtesy of Clinical Center, National Institutes of Health, Bethesda, Md.)
FDA to Require Safety Data on Breast Implants

Questions have arisen over the past few years about the occurrence of adverse effects caused by silicone breast implants. Although it appears that the majority of women with implants do not experience serious effects, FDA feels that the questions that have been raised need to be addressed. Therefore, the agency is requiring the manufacturers of the implants to submit scientific data showing that they are safe and effective in order to keep them on the market.

FDA also is reviewing the physician labeling for breast implants and working with the medical profession to develop information for women considering implants.

Silicone gel-filled breast implants have been used for approximately 20 years, and at present about 2 million women in the United States have them. Most are for cosmetic augmentation, and the remainder are for breast reconstruction after mastectomy. When the medical device law—the statute that gives FDA the authority to regulate medical devices such as implants—was passed in 1976, it “grandfathered” devices that were already on the market, including breast implants. This meant that manufacturers of these products were not required to provide FDA with scientific evidence of safety and effectiveness, as they are with brand-new types of devices. (That stipulation in the law was based on the premise that, generally speaking, more is known about the safety of a device that has been on the market for some time than about one that is new.) But when there are questions about the safety or effectiveness of a “grandfathered” device, FDA can go back and require this kind of evidence. This is what is being done with silicone breast implants.

Adverse effects related directly to the breasts include the hardening, discomfort and pain that occurs in some patients, resulting from fibrous tissue growing around the implant. Silicone implants may also make it more difficult to see abnormalities in the breast when mammographic X-rays are done, unless special adaptations are made in the X-ray procedure. And there is occasional breakage of the implant’s outer envelope, causing the gel filling to be released.

The actual frequency of these adverse effects is unknown. Even in the absence of obvious leaks, minute quantities of the gel filling can migrate out of an intact breast implant and travel throughout the body. It is unknown at present whether these tiny amounts of silicone could have long-term effects. A recent study of laboratory rats showed that silicone can produce sarcomas, a type of tumor which occurs commonly in rats but rarely in humans. Cancer experts agree that this finding is unlikely to apply to women with breast implants.

The law requires that FDA give manufacturers at least 30 months to perform the studies needed to demonstrate safety and effectiveness. In the meantime, FDA is planning a series of steps to be sure physicians and their patients are adequately informed about possible risks. For example, FDA will reevaluate the information supplied to physicians with the implants, and, if necessary, will strengthen the warnings and precautions. FDA is also planning to develop educational materials, in conjunction with medical organizations, for women who are contemplating a breast implant, explaining the benefits and possible risks.

At this point, FDA does not believe there is cause for alarm about breast implants, nor is there sufficient justification to take them off the market. But answers are needed to questions about the frequency of short-term adverse effects related directly to the breast, and also about the possibility of long-term risks from silicone in the body.

FDA Warns About Salt Tablets for Contacts

FDA has sent a safety alert letter to approximately 50,000 eye care professionals, asking them to warn their patients about the hazards of improperly using homemade saline solutions in caring for contact lenses. The solutions, generally prepared by dissolving salt tablets or capsules in distilled water, are not sterile and may be contaminated with harmful microorganisms that can cause infections. In some severe cases this has even led to blindness.

Homemade saline solutions can safely be used before or during the heat disinfection of contact lenses because the high temperatures are sufficient to kill any contaminating microorganism. But if a contaminated solution is used after disinfection (as a rinse or wetting agent or eye drops), or if it is used with chemical disinfection of the lenses, the microorganisms can enter the eye and cause serious infections. (Although chemical disinfection of contact lenses is effective in destroying the various types of microorganisms that cause most eye infections, it may not be completely effective in eliminating a rare type called Acanthamoeba, which can cause particularly severe eye damage.)

Contact lens wearers who want to use a rinse or wetting agent or eye drops after disinfecting their lenses must purchase a preserved or non-preserved sterile saline solution.

If homemade saline solution is used, the chance of contamination can be reduced (but not eliminated) by preparing the solution with distilled (not tap) water and discarding it after use, and by sterilizing the solution...
bottle in rapidly boiling water for 10 minutes at least once a week.

Whether or not homemade solutions are used, all contact lens wearers can help reduce the risk by:

- washing their hands before handling the lenses;
- disinfecting the lenses each time they are removed;
- cleaning and air-drying the lens case between uses;
- not swimming or using a hot tub while wearing the lenses; and
- removing the lenses immediately and consulting a doctor if discomfort, pain, discharge, blurred vision, or excessive watering occur.

For more about proper care of contact lenses, see "Are Your Contact Lenses as Safe as You Think?" in the April 1987 FDA Consumer.

Sulfites Proposed as Safe

FDA has proposed that sulfites in many canned, frozen, dehydrated, and other commercially prepared foods be generally recognized as safe (GRAS) within certain levels and that manufacturers must declare on food labels levels of sulfites greater than 10 parts per million.

The term sulfites refers to six sulfur-based chemicals that have been used for many years as preservatives, as antioxidants to prevent discoloration, and as disinfection agents for food containers, among other uses. Following a proposal in 1982 to reaffirm all uses of sulfites as GRAS, the agency received 1,800 comments from consumers, scientists, and the medical community alerting FDA that sulfites could cause allergic reactions in some people.

A panel of scientific experts determined that a small minority of people are sulfite-sensitive and may suffer adverse reactions ranging from hives, nausea and diarrhea to shortness of breath and even death. FDA decided in 1986 to ban the use of sulfites on fresh fruits and vegetables, particularly those served at salad bars, and in 1987 proposed banning their use on fresh, pre-cut potatoes and processed potato products that are served or sold unpackaged or unlabeled to consumers. These unlabeled food items, FDA decided, could present a risk for those sensitive to sulfites.

The new proposal, published in the Dec. 19, 1988, Federal Register, would establish limits on sulfite levels and require that stores selling products such as dried fruit and shrimp in bulk would have to use counter signs, cards, or other displays stating that the bulk products have been treated with sulfites.

The recommendations are based on FDA's analysis of new information submitted in response to the earlier proposal to affirm the GRAS status of sulfiting agents, as well as reports from the Federation of American Societies for Experimental Biology, the Advisory Committee on Hypersensitivity to Food Constituents, and others.

For more information on sulfites, see "Reacting to Sulfites" in the December 1985–January 1986 FDA Consumer.

Stiffer Laws on Steroids, Butyl Nitrite

Stricter laws for curbing steroid abuse by athletes, particularly young people, and the banning of butyl nitrite are among recent changes in the Food, Drug, and Cosmetic Act.

The Anti-Drug Act of 1988, signed last Nov. 18, makes distribution of steroids or possession with the intent to distribute to minors punishable by a fine and up to six years in prison. Distribution or possession with intent to distribute to adults without a prescription can carry a sentence of up to three years imprisonment and a fine.

Convictions resulting in more than a year in jail would also allow the courts to seize property used to support illegal distribution of steroids, or property purchased with profits from the sale, similar to provisions of drug trafficking laws.

The Anti-Drug Act of 1988 also directs the General Accounting Office to develop a report on the health consequences and extent of steroid use, which sponsors of the bill say may be a $100-million-a-year black market affecting 250,000 or more school-age athletes. The report is due in June.

The act also restricts the use of butyl nitrite, a chemical "odorizer" that has been inhaled as "poppers" for sexual stimulation or mood enhancement. Side effects of butyl nitrite abuse include fainting, headaches, blurred vision, and lung inflammation.

Pesticide Residue Levels Found Safe

Most FDA tests of foods sold in America during 1987 revealed little or no pesticide residues, according to a recent FDA report based on the agency's food monitoring
program and its annual Total Diet Study of prepared foods. Of the 14,492 food samples (half were imports) analyzed over the year, FDA found that 95 percent contained no illegal residues and 57 percent had no residues at all. Not all samples were tested for all possible pesticides, however. The few illegal residues that were found were mainly from pesticides used on crops they were not approved for; only about one in four exceeded an Environmental Protection Agency tolerance, all of which have generous safety margins. Milk, eggs, and dairy products had the least amount of residues.

In the Total Diet Study, FDA tests foods found typically in the American diet that have been prepared in a normal way—cleaned, cooked, and so forth. Residues of only 53 pesticides were found in the 936 samples tested, none at levels of concern. As in earlier years, this analysis showed that residue intakes were well below the acceptable daily intakes established by the United Nations' Food and Agriculture Organization and World Health Organization.

For additional information, see “Setting Safe Limits on Pesticide Residues” in the October 1988 FDA Consumer.

Copies of FDA Pesticide Program, Residues in Foods—1987 can be obtained from: Norma Yess (HFF-420), FDA Division of Contaminants Chemistry, 200 C St., S.W., Washington, D.C. 20204.

Puerto Rican Students Learn Health Care

Puerto Rican children are learning how to better care for their health through a unique program initiated by FDA’s Office of Consumer Affairs. Called “Proyecto HEP A” (Project HealthPACT), the project focused on teaching 150 fifth- and sixth-graders in a Puerto Rican elementary school how to talk to and listen to health-care providers, and then how to make good health-care decisions.

Activities included visiting a health clinic and talking with a dentist, nutritionist and physician. The children were given information on medicines, nutrition, and health maintenance.

The Puerto Rican government is now funding Proyecto HEP A, a required course in the fifth grade public school curriculum.

Pesticide Levels in Lanolin Not Harmful

Pesticide levels found in lanolin, a substance used in drugs and cosmetics, pose no health hazard, according to an evaluation by the Environmental Protection Agency.

Lanolin is a fatty substance extracted from sheep wool. Purified, it is used in a wide range of products for its water-absorbing and emulsifying properties. (An emulsifier suspends an oily substance in a watery liquid.) The pesticide in lanolin is thought to come from pesticide dips used to control parasitic insect infestations in sheep.

Lanolin is also used as an emollient (softener) to treat sore and cracked nipples in nursing mothers. There was concern that nursing infants could consume small amounts of the pesticide, but the EPA report concluded that the health risk of pesticide residue levels found in lanolin products is negligible. FDA will continue to check lanolin products to be sure pesticide residues are reduced to their lowest possible level.

Drug Prevents Ulcers in Arthritis Sufferers

The Food and Drug Administration has approved a drug to prevent or reduce the stomach ulcers that plague some of the millions of patients taking commonly prescribed arthritis medications.

The drug, misoprostol, is approved for use in patients at high risk of developing complications of stomach ulcers while on arthritis drugs—the elderly and patients with debilitating diseases. In these patients, the ulcers may remain “silent,” not causing pain. As a result, they may go undetected until they bleed or cause other serious consequences.

According to various estimates, 200,000 cases of stomach and intestinal bleeding, with 10,000 to 20,000 deaths, occur each year as a side effect of nonsteroidal anti-inflammatory drugs (NSAID) used for arthritis. About 68 million prescriptions of NSAIDs—which include high-dose aspirin, ibuprofen, piroxicam and naproxen—are written each year.

Misoprostol, approved Dec. 27, suppresses gastric acid secretion and replaces natural substances called prostaglandins that are depleted by NSAIDs. However, the drug also causes changes in muscle tone, which, in the case of uterine muscles, could lead to miscarriage. As a result, the labeling for physicians and patients will indicate that the drug “is contraindicated in women of childbearing potential unless the patient must receive non-steroidal anti-inflammatory drugs and is at high risk of complications from gastric ulcers associated with use of the NSAID.” For these women, the labeling requires physicians to obtain a negative pregnancy test before prescribing misoprostol and to ensure that the patient has been informed of the need to avoid pregnancy while on the drug.

Misoprostol will be marketed by G. D. Searle of Skokie, Ill., under the brand name Cytotec. Under the terms of FDA’s approval, the consumer packaging must contain patient information on the precautions necessary for safe use of the drug.
ERC Wins Drug Reporting Contract

FDA's Drug Quality Reporting System is in new hands for the first time in 17 years. ERC International of Fairfax, Va., was awarded the contract to coordinate the program in December 1988, succeeding the U.S. Pharmacopeial Convention, which had run the program since its inception in 1971.

The system—aimed particularly at pharmacists, who usually are the last to see products before they are dispensed to patients—encourages reporting problems such as mislabeling, possible tampering, instability, therapeutic failure, and contamination. (In contrast, adverse drug reactions are usually reported by physicians either to FDA or the drug manufacturer.)

ERC International will enter the reports into an FDA computer database, in addition to providing printed reports. FDA will forward copies of the reports to the manufacturers of the drug in question. The agency's office of compliance in the Center for Drug Evaluation and Research will continue to take regulatory action based on the drug quality reports.

Since the program was begun, more than 76,000 reports from hospitals and pharmacists have been processed. The reporting system has led to recalls of 339 products and to corrective actions for more than a thousand products since 1977.

To make a report, call toll-free 1-800-FDA-1088 (in operation 24 hours a day) or submit a Drug Quality Reporting System form to ERC International, 1055 First St., Suite #1, Rockville, Md. 20850.

Nutrition High on the Menu for 2000

In the year 2000, menus from restaurants, be they haute cuisine or fast-food, will emphasize nutrition, according to the National Restaurant Association.

Based on a study conducted by the association's board of directors and other restaurant industry experts, the association predicts that 11 years from now:

- restaurants will offer more fish and poultry and less game, beef and hard liquor;
- beef dishes will be lower in fat because fewer recipes will include sauces and because advances in genetic engineering will produce leaner beef;
- all recipes will have less fat, cholesterol, calories and salt;
- with decreased use of salt and fats, flavor will be enhanced in other ways, such as by using fat- and sugar-substitutes and new methods of preparation to retain flavor; and
- the increased demand for fish will be met through aquaculture.

Food Safety Report Available

An FDA Consumer special report, Safety First: Protecting America's Food Supply, is now available from FDA. Free copies of the 60-page booklet, which discusses current issues in food safety, from pesticides to bacterial contamination, are available by writing to: Food and Drug Administration, HFI-40, 5600 Fishers Lane, Rockville, Md. 20857.

Genital Wart Treatments

As a former pharmacology teacher, I find FDA Consumer an enjoyable way to keep up with drug development. I was fascinated to learn [Updates, FDA Consumer, September 1988] that genetically engineered alpha interferon is producing somewhat spectacular results in the treatment of genital warts. I would like to . . . draw your attention to the statement "topical treatment [of genital warts] with conventional anti-infective drugs has been less effective than surgery." The only standard topical treatment I'm aware of is the use of podophyllum resin, which is classified as a keratolytic [caustic]. Wildflower enthusiasts may find it of special interest to learn that said resin is derived from the rhizome and roots of Podophyllum peltatum, the Mayapple of eastern North America.

Stewart M. Brooks
Bainbridge, N.Y.
Drugs for CMV Eye Infection to Be Studied

AIDS patients with cytomegalovirus (CMV) retinitis, an eye infection that can lead to blindness, are eligible for treatment in a new clinical study of the drug ganciclovir. The study is being sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) and the drug’s developer, Syntex Corporation, Palo Alto, Calif.

CMV retinitis can affect people with weakened immune systems, AIDS patients, and organ and bone marrow recipients.

The study will include patients with newly diagnosed AIDS-related CMV retinitis that is not immediately sight-threatening. About 20 patients will be enrolled per month. The patients will be divided into two treatment groups, one of which will begin immediate treatment with intravenous ganciclovir. Patients in the other group will not receive treatment until their condition begins to deteriorate. Study participants who have been taking the anti-AIDS drug zidovudine (also called AZT) must stop before ganciclovir treatment begins. Taken simultaneously, the drugs are not safe.

AIDS patients with CMV retinitis that is immediately sight-threatening can receive ganciclovir under a new treatment IND (investigational new drug) application sponsored by NIAID. Under recently revised regulations, FDA can approve such treatment INDs to make promising but as yet unapproved drugs available to patients with severe or life-threatening diseases.

Physicians and patients interested in either the study or the treatment IND should call the NIAID Ganciclovir Study Center, Bethesda, Md., at (301) 497-9888.

Faster AIDS Test Licensed

The Food and Drug Administration licensed a rapid screening test for AIDS last Dec. 13. The new test can detect AIDS virus antibodies within five minutes, compared with the several hours it takes to get results from other tests.

This is the first AIDS diagnostic test developed with genetic engineering techniques. It is not, however, intended to replace current tests, such as the ELISA (enzyme-linked immunosorbent assay) test, licensed in March 1985 or the Western blot, approved in April 1987, used to screen donated blood. The new test kit is not well adapted for screening large numbers of blood samples and, as with other screening tests, positive results should be confirmed with more specific tests such as the Western blot.

According to FDA Commissioner Frank E. Young, M.D., Ph.D., “This technical advance will be particularly useful in remote areas of the world that lack the facilities or equipment needed for earlier approved tests and may also be very useful as a preliminary screening measure in emergency situations in this country.”

The test is manufactured by Cambridge Bioscience Corp. of Worcester, Mass., and distributed by Baxter Health Care Corp. under the trade name Recombigen HIV-1 Latex Agglutination Test.

False AIDS Claims For Typhoid Vaccine

Typhoid vaccine is not an FDA-approved treatment for AIDS, as was claimed in several alternative publications last fall. Individuals cited in these publications as having received permission to market the drug as an AIDS therapy have never even applied to the agency to test it in patients.

Typhoid vaccine is approved only to prevent typhoid fever. Although physicians can use approved therapies and vaccines for conditions other than those for which the products are labeled, FDA cautions that there is no scientific evidence to show that the use of typhoid vaccine is an effective AIDS treatment.

NLM Offers New AIDS Data Base

The National Library of Medicine is offering medical researchers a database, called AIDSLINE, of 13,000 references to scientific articles about AIDS. References in AIDSLINE cover clinical and research aspects of the disease, epidemiology, and health policy issues from 1980 to the present.

Health professionals interested in accessing AIDSLINE may request a user code from the library’s MEDLARS Management Section at 1-800-638-8480.

The library’s GRATEFUL MED microcomputer-based software can be adapted to access AIDSLINE. With it, an average search costs less than $5. Software may be purchased from the National Technical Information Service, 5285 Port Royal Road, Springfield, Va. 22161. The cost is $29.95 plus shipping.
A Lesson in Industry Education

Keeping Drug Residues Out of Milk

by Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

Last year I discussed in this column FDA's role as an educator, helping to solve public health problems by providing information and guidance to consumers, health professionals, and FDA-regulated industry. This role is especially important when a problem is due to the way a health product—a drug or medical device, for example—is used, and not to a flaw in the product itself. Education often proves more effective in solving such problems than does regulatory or legal action.

I'm pleased to be able to cite a recent success story in which FDA played a vital educational role. The story begins in March of last year, when FDA conducted a survey of milk from stores in 10 major cities across the country. Laboratory analysis found small residues of the veterinary antimicrobial sulfamethazine in 36 of 49 samples tested.

These findings were particularly disturbing for a number of reasons. First, it is illegal to use sulfamethazine in milkproducing cows. So, even though 25 of the 36 positive samples were below 5 parts per billion (ppb)—amounts so small that the reliability of the results couldn't be guaranteed—the fact that any residues were showing up in milk was a sign of trouble.

Second, some people are allergic to sulfapyridine drugs, including sulfamethazine (although the levels found in the March survey were probably too low to cause a reaction).

Third, the safety of sulfamethazine for use in any food-producing animal had recently been called into question by a study just completed at FDA's National Center for Toxicalogical Research. The study found that sulfamethazine—used legally since the 1950s to treat respiratory and other diseases and promote faster weight gain in hogs, cattle, and other animals—produced cancerous tumors in mice and rats. The findings raised the question of whether the drug might cause cancer in humans as well. (That study is currently under review; if its findings are upheld, FDA may need to modify or ban the use of sulfapyridine drugs in food-producing animals.) It was particularly distressing that residues of the drug were turning up in such a basic food as milk—consumed by almost all our children and most adults every day.

Based on the results of its survey, and on similar reports of sulfapyridine residues in milk published in scientific and dairy industry journals, FDA considered its options. The problem was not use of an illegal drug but illegal use of a legal drug—in other words, a user problem. The solution, FDA believed, could best be found through educating dairy farmers and veterinarians. And that could best be done with the help of other organizations in both government and industry.

So, in early April FDA met with representatives of dairy trade associations, the American Veterinary Medical Association, and the National Conference on Interstate Milk Shipment (NCIMS), which represents the milk inspection agencies in all 50 states. As a result of the meeting, NCIMS established a task group to immediately develop and distribute to dairy farmers, veterinarians, and its own member agencies information about the sulfa residue problem. The information materials warned that use of sulfamethazine in milk cows was illegal, that milk containing even low levels of the drug would be rejected, that continued reports of residues could erode consumer confidence in the milk supply, and that those using the drug illegally could face fines and imprisonment.

FDA's Center for Veterinary Medicine and Center for Food Safety and Applied Nutrition also helped spread the word to state agencies, dairy industry groups, and veterinary associations, who, in turn, alerted their members.

Of course, while these educational efforts were going on, FDA and state milk officials were taking necessary regulatory steps as well. Milk testing was increased as FDA made a new, more sensitive test method available to state agencies and the dairy industry.

In July, FDA and the U.S. Department of Agriculture met with representatives of other government agencies and 20 drug industry organizations to discuss better ways to provide guidance to dairy farmers and veterinarians on proper drug usage. Meanwhile, milk testing continued, throughout the summer and into the fall.

In November, NCIMS asked the state milk inspection agencies to report the results of their testing to FDA. The findings from the 34 states that responded showed dramatic improvement in the residue situation. Of 2,207 raw milk samples tested from May through September, only 1.5 percent had sulfamethazine levels of 10 parts per billion or more, compared to 10 percent found by FDA in March. It was apparent that the prompt actions taken by FDA, NCIMS, the dairy industry, and veterinarians had resulted in a dramatic decrease in the level of the drug in the nation's milk supply.

The survey results showed that sulfamethazine levels had decreased steadily after the educational (and regulatory) efforts began. The number of samples that tested positive (in any amount) decreased from 7 percent in May to 3 percent in September. The number with sulfamethazine above 10 ppb dropped from 3 percent in May to 1 percent in September. Naturally, milk found to contain any sulfamethazine residues was discarded to keep it from getting to stores.

The residue awareness program clearly shows how successfully government agencies, health professionals, and regulated industry can work together. By means of a cost-effective cooperative information program—coupled with a vigorous state enforcement effort—a potentially serious public health hazard was eliminated in a little over half a year. That's a case study in consumer protection from which we can all draw a lesson.
The 'Grazing' of America:
A Guide to Healthy Snacking

Sheep do it. Horses do it. Cows do it. Now even children, teenagers and seniors are doing it.

"Grazing" is fast becoming the American way of eating, according to nutritionists. "Since everyone is always rushing around in a hurry these days, there's often no time for three square meals. So grazing, or snacking on mini-meals, becomes important," says Marilyn Stephenson, a registered dietitian and assistant to the director, office of nutrition and food science, Food and Drug Administration.

Grazing is a way of filling in those necessary calories and nutrients you might otherwise miss due to incomplete or skipped meals. Done wisely, grazing is not only good for you, it can be fun, too. Grazing isn't just milk and cookies. It's finding creative, but nonfattening, ways to enrich your diet with protein, complex carbohydrates, vitamins, and minerals.

How you graze and what you choose to graze on should depend on your age and lifestyle. For instance, adults must be more careful than children about snacking. Because the amount of energy needed to fuel basic body functions decreases as one gets older, it takes fewer calories to maintain the body. Also, adults tend to become less physically active over the years, which further decreases their calorie needs. So long as total calories are kept in mind, though, there's nothing wrong with grazing if snacks are well planned to include essential nutrients.
Calorie Salary

Jennifer Anderson, a registered dietitian and assistant professor in the department of food science and human nutrition at Colorado State University, says snacking is easy for adults if they obey the “calorie-salary rule.” Determine your daily “salary” of calories, and make sure you “spend” no more than that over the course of your meals and snacks for the day.

For example, if you know you’ll be eating lots of food at a party, eat low-calorie foods the rest of the day. Or, if you eat a large lunch, balance out the extra calories you consumed with a low-calorie supper, such as a salad. If you do find yourself eating more calories than usual in a day, increase your physical activity, says Anderson. Exercise helps to burn up those extra calories.

And beware of pseudo-nutritious “health” foods. When craving sweets, if you’re thinking of choosing a granola bar instead of a conventional candy bar because you think it is more healthful, don’t. Registered dietitian Gail Levey, spokeswoman for the American Dietetic Association, warns that “granola bars are just packed with grease. A granola bar sounds so wholesome, but to get it to stick together you have to use so much fat.”

On average, about 35 percent of the calories in many of the granola bars comes from fat, whereas approximately 46 percent of calories in candy bars is from fat.

The Dietary Guidelines for Americans from the Departments of Agriculture and Health and Human Services advises Americans to avoid too much fat and cholesterol in their diets. Fat, especially saturated fat, raises the level of cholesterol in the blood, which is, in turn, a risk factor for heart disease. There is also evidence that a high dietary fat intake may be associated with certain types of cancer. Both the American Heart Association and the National Cancer Institute recommend that Americans reduce their fat intake to about 30 percent of their total calories.

More Fat, More Calories

Less than one-third of the fat in the diet should be in the form of saturated fats, such as butter and lard. The remainder should be from monounsaturated or polyunsaturated sources, which help decrease blood cholesterol levels.

Fats are a dense source of calories. Both protein and carbohydrates have four calories per gram; fats have nine. So any time you have a fat-filled snack, it’s likely to be relatively high in calories.

Some foods people choose for small snacks contain 10 or more grams of fat. “That’s quite a bit for one serving of a snack food,” according to Bonnie Liebman, director of nutrition, Center for Science in the Public Interest, a Washington, D.C.-based consumer advocacy group. “I advise people looking for low-fat frozen dinners to choose products that contain less than 10 grams—and that’s for a full meal or an entree.”

Reducing one’s fat intake doesn’t have to mean a life of austere eating, but it does require making sensible choices and substitutions. Choose dairy products low in fat. Ice milk, for example, has less than half the fat of ice cream and approximately 40 percent fewer calories. Tofutti, a frozen dessert made from tofu (a soybean-based food), contains no cholesterol, but has almost twice the fat of ordinary ice cream. And although plain and flavored frozen yogurts have less fat than ice cream, they don’t offer many calorie savings.

Seventy-five percent of the calories in most hard cheeses comes from fat. Your best option is to snack on cheeses made primarily from skim milk, such as pot cheese, part-skim ricotta, cottage cheese, skim farmer cheeses, and many diet cheeses and other low-fat cheeses.

Spread the cheese on whole-grain crackers or bread, or eat it with an apple or celery for a snack low in fat, but high in fiber.

Also, choose plain, low-fat yogurt as a snack instead of ones with fruit, which are sweetened and contain more calories. Not only will you save on calories, but you’ll be able to add your own low-calorie fresh fruit and dry toppings, such as wheat germ, to make it a more nutritious snack.

Snack sparingly on nuts. Nuts are high in fat and, therefore, high in calories, as well. Instead, choose, for example, freshly popped corn, air-popped, rather than popped in oil. But remember that adding butter to it will add fat and calories.

Popular snack foods, such as chips, pretzels and packaged popcorn, may contain large amounts of salt. “Pretzels and some brands of popcorn, for example, often contain up to 950 milligrams of sodium per serving—quite a bit when adults should get no more than 1,100 to 3,300 milligrams a day,” according to Liebman.

(continued on next page)
Eating too much sodium (salt is sodium chloride) is associated with high blood pressure—a major risk factor for heart attack, stroke, and kidney disease in some people.

Older adults especially should watch their sodium intake because of the prevalence of high blood pressure and heart disease in their age group.

**Elder Grazers**

Older adults often rely on grazing for most of their calories, so it’s important that they keep a variety of nutritious snack foods on hand. A good snack for this age group, according to Barbara Deskins, a registered dietitian and associate professor at the University of Pittsburgh, is one that supplies calcium, as well as other nutrients, because many older adults don’t get enough calcium in their diets.

She suggests a glass of low-fat milk, cubes of low-fat cheese, or low-fat yogurt for a snack high in calcium, protein, some B vitamins, vitamin A, and, if fortified, vitamin D. Tuna fish sandwiches or roast chicken with the skin removed are also nutritious snacks, providing protein, iron, B vitamins, and zinc. Whole-grain oatmeal cookies, graham crackers, and raw vegetables are good sources of dietary fiber and may provide some vitamin A, vitamin C, B vitamins, and iron.

Anderson of Colorado State says that choosing snacks lower in fat, sugar and sodium is easier for everyone if the right snacks are kept on hand. She suggests stocking the refrigerator with a variety of healthful leftovers, keeping a supply of “transportable” snacks, such as small cans of juice, fresh fruits and vegetables, crackers, and cheese cubes. Quick and easy fixings like yogurt and fruit should also be on hand for pureeing in a blender to make nutritious instant shakes.

**Toddlers Need to Snack**

What children need by way of a nutritious snack differs from what is recommended for older adults. Foods children graze on will often set the stage for what they’ll choose as snacks later in life. Children under 2 require a lot of calories to fuel their rapid growth. However, their appetites and stomachs are so small that they often can’t eat enough at their regular meals to meet their daily demands. So they need to graze. Many nutritionists recommend several little meals in place of three big ones for this age group. (Parents need to watch their toddlers carefully during snack times to guard against choking.)

Lightly cooked vegetables, such as broccoli and green beans, and tender, bite-size pieces of meat, poultry and fruit are good finger foods for this age group. So are dry breakfast cereals, tiny sandwiches, and crackers. Small amounts of spaghetti and pizza also make good snacks.

Milk, yogurt, and small cubes of cheese make wonderful snacks, too, because the calcium they supply help in teeth and bone formation.

A statement by the American Heart Association, the American Health Foundation, and a consensus development panel sponsored by the National Institutes of Health recommended in 1986 that Americans reduce their fat and cholesterol intakes to help decrease the risk of coronary heart disease. But the statement excluded children under 2 from this recommendation. Nevertheless, many well-meaning parents have adopted a low-fat, restricted-calorie diet for their children as well as themselves. As a result, there have been medical reports of decreased growth rate and poor weight gain among some toddlers.

**Overzealous Parents**

Concerned that parents’ zeal for low-fat diets would adversely affect their children’s growth and health, the American Academy of Pediatrics issued a statement in 1986 that for children, “the current dietary trends in the United States—decreased consumption of saturated fats, cholesterol and salt and an increased intake of polyunsaturated fats—should be followed with moderation. The optimal fat intake cannot be determined, but 30 percent to 40 percent of total calories seems sensible for adequate growth and development. Diets that avoid extremes are safe for children for whom there is no evidence of special vulnerability.”

The academy also found no “compelling new evidence to make recommendations concerning modification of the diet” for teenagers, either.
Like young children, teenagers are constantly growing, and many need frequent extra helpings of foods to provide them with enough protein, vitamins, minerals, and calories to meet their growth and energy needs. Teenagers who participate in sports need even more calories to maintain their body weight.

No single food supplies all of the essential nutrients in the amounts the body needs, so it is important, especially for growing children, to eat a variety of foods. Eating foods from each of the following four food groups daily helps to ensure a balanced diet:

- fruits and vegetables;
- meat, poultry, fish, eggs, and dried beans and peas;
- milk and cheese; and
- whole-grain breads and cereals.

Bread, cereals, and other grain products provide B vitamins, iron, protein, and fiber. Fruits and vegetables are good sources of vitamin A, vitamin C, folic acid, fiber, and many minerals. Meats, poultry, fish, eggs, and dried beans and peas supply protein, iron and other minerals, as well as several B vitamins. Milk and cheese are major sources of calcium—very important in the diets of children and teenagers. Storing as much calcium as possible in the bones in younger years may help prevent osteoporosis later in life. Osteoporosis, brought on by loss of bone mass, causes bones to fracture more easily.

Teen Snacks

Though teenagers can benefit from snacking, they often fall into the habit of constantly eating the same foods. Snacks sometimes even substitute for, rather than supplement, regular meals. And snack foods may not provide the variety of nutrients these youngsters need. For example, a soda that replaces milk at lunch may reduce the amount of calcium in the diet.

Teenagers who like to snack on soft drinks should be encouraged to have a cheeseburger, rather than a plain burger, with their drink. A slice of cheese pizza is another good snack that will add calcium to the diet.

Snacks high in fiber are also a good choice for teenagers because they stimulate salivation, which helps wash away excess sugar accumulated naturally or from such sugary snacks as candy bars. This reduces the chance of tooth decay, according to the Academy of General Dentistry.

High-fiber snacks include popcorn, fruits and vegetables (especially with skins and seeds), dried peas and beans, nuts, and whole-grain foods and other whole-grain cereal products.

In addition to dietary fiber, these foods provide vitamins and minerals that are essential for normal growth, development and metabolism.

While snacking is regarded as a potential asset to the teenager's diet, it can become a liability if it results in more calories than are needed. Obesity often starts during the teenage years. While it's (continued on page 13)
## Snacks: A Growing Part of Our Diet

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Data are based on one-day dietary intakes by women 19-50 years old and their children 1-5 years old. The number of women surveyed was 2,228 in 1977 and 1,503 in 1985; 690 children were included in the 1977 survey, 548 in the 1985 survey.

Healthy Snack Ideas

The best low-calorie snacks are low in fat and sugar and provide nutrients such as vitamins, minerals, fiber, and protein. Snacks should be a planned part of the total day’s intake and not left to chance. Here, courtesy of the Allegheny County (Pa.) Health Department, are some healthy snack ideas:

Low-Calorie Coolers & Shakes
- Enjoy soda water on-the-rocks with a twist of lime or lemon.
- Combine ½ cup each of soda water and your favorite fruit juice on-the-rocks.

Vegetables
- Combine in a blender and whirl until smooth: 1 cup cottage cheese, 2 to 4 tablespoons milk, and dill weed or chives to taste (start with ½ teaspoon). Enjoy this dip with an assortment of raw vegetables.
- Marinate leftover cooked vegetables with low-calorie Italian dressing.

Fruits
- Combine 1 carton plain yogurt, 3 tablespoons low-calorie strawberry jam, ¼ teaspoon cinnamon, and 1 teaspoon grated lemon rind. Chill. Serve this dip with fruit chunks.
- Make frozen banana treats by wrapping peeled bananas in foil or plastic and freezing until firm.

Protein
- Combine and mix well: ½ cup water-packed tuna (drained), 2 tablespoons plain yogurt, chopped onion and celery, diced cucumber, a dash of pepper and dry mustard, and a dash of lemon juice or vinegar. Enjoy this on Melba toast, saltines, or other crackers.
- Slice cucumber into quarter-inch slices. Store in refrigerator covered with water until ready to use. For a protein-rich snack, spread with any of these toppings: mashed cottage cheese with pineapple chunks or other fruit; mashed hard-cooked egg with prepared mustard; drained tuna, with a slice of mozzarella cheese.

Grains
- Mini-pizzas: Place tomato slice or sauce on bagel chips, Scandinavian crispbreads, English muffin half, pita bread round, or Melba toast. Sprinkle with Italian seasonings. Top with a thin slice of part-skim mozzarella cheese or shake on grated Parmesan cheese. Place in a warm oven or under broiler briefly to melt cheese.
- Pocket salad: Place lettuce, tomato, cucumber, and diet dressing in a pita pocket bread.

Sweet Treats
- Instant ice cream: Combine 2 cups frozen fruit, 1 cup skim or low-fat milk, and 2 to 4 tablespoons sugar (optional) in a blender and whirl until smooth. Serve immediately as soft ice cream or pour into plastic cups and freeze for 1 hour.
- Cornstarch pudding: Combine 3 tablespoons cornstarch with ½ cup sugar in saucepan. Add 2 cups skim milk and slowly bring to a boil, stirring constantly. Boil 2 minutes. Add 1 teaspoon of an extract such as vanilla, lemon or almond. Top with fruit, raisins, peanuts, or a chocolate curl. Makes four half-cup servings.

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generally not prudent to put teenagers on low-fat, calorie-restricted diets, sensible snacking should be encouraged. Changing one's snacking habits will take some getting used to. Let’s face it: Nutritious snacks, in many cases, are not as tasty and satisfying as traditional ones, such as candy, potato chips, and sodas.

Perhaps one way to begin snacking wisely is to start with portion control. Judith S. Stern, professor of nutrition at the University of California at Davis, suggests that if you do have a craving for sweets, a bite-size candy bar or half a Popsicle is a better choice than a regular-sized candy bar or a whole ice pop.

Grazing is important to today’s lifestyle, says FDA nutritionist Stephens. But snackers must be aware of the nutrition content of their snack foods, by reading labels for ingredient and nutrient content. For example, “If you get nutrition-wise and develop nutrition literacy,” she says, “no matter who you are, snacking will work for you.”

Cheryl Platzman Weinstock is a free-lance writer in Bellmore, N.Y.
by Marian Segal

Eons ago, in Africa and other parts of the globe where malaria ran rampant among the human population, nature provided some individuals with a genetic advantage to protect them from a severe form of the disease. Thanks to a random genetic mutation of the hemoglobin molecule, the environment of red blood cells—site of invasion by the malaria microbes—was altered, making it inhospitable for growth and reproduction of the parasite, curtailing the disease and preventing further cell damage. So, the trait originally conferred protection against a life-threatening disease, enabling people to live longer and pass the protective gene to their children.

But this genetic favor did not come without strings attached. For the protective trait was a prime example of what geneticists call “balanced polymorphism”—a genetic advantage offset by a disadvantage. Problems stemming from those very same red blood cells arose when children inherited the aberrant gene from both parents.

When their red blood cells gave up a certain amount of oxygen, the hemoglobin molecules in the cells stuck together and stacked end to end, pushing out and distorting the normally doughnut-shaped cells into the crescent, or sickle, shape that gave the condition the name by which we know it today—sickle cell anemia. The cells lose their normal softness and pliability, becoming hard, inflexible and sticky. With this, blood vessel blockage, pain, serious health problems, and a shortened lifespan result. And, to add insult to injury, people with sickle cell anemia are not protected from malaria—on the contrary, malarial infection is particularly serious in these patients.

But there is a brighter side emerging in this bleak picture. Recent developments in preventing life-threatening infections that develop in children with sickle cell anemia promise to alleviate the symptoms of this painful disease and prolong life. Indeed, a recent panel convened by the National Institutes of Health has recommended that all newborns be screened for sickle cell disease, permitting earlier diagnosis and treatment, which would significantly reduce the death rate among these children.

Eight percent of black Americans, or 1 in 12, carry a gene for sickle hemoglobin, and 1 in every 400 black newborns in the United States has sickle cell anemia or a related disease. But Marilyn Gaston, M.D., deputy chief of the National Heart, Lung, and Blood Institute’s Sickle Cell Disease Branch, stresses that sickle cell disease, in one or another variant, affects not only blacks, as is commonly thought among Americans, but others as well with lineage from parts of the world where malaria has been prevalent. These people in turn spread the trait and the disease to other parts of the globe.

“Besides Africa, where it is a major problem,” says Gaston, “the disease is known in Spanish-speaking countries in South America, Central America, and the Caribbean, and the Hispanic community here in the United States is becoming more aware of the disease. Saudi Arabia, Iran, and India are reporting more and more cases, and it can be a major problem in some areas of Italy, Greece, Turkey and Sicily.” In fact, it is thought that four independent gene mutations occurred in Africa and the Middle East. The separate mutations may account in part for the diversity in disease severity and manifestations among patients.

**Trait Versus Disease**

Sickle cell trait, which is an asymptomatic carrier state, is often confused with the disease sickle cell anemia. (See accompanying article on the genetics of sickle cell anemia.) People with sickle cell trait have inherited a normal hemoglobin gene (Hb A) from one parent and a sickle hemoglobin gene (Hb S) from the other. (Hemoglobin is the oxygen-carrying molecule in red blood cells.) The normal gene produces enough normal hemoglobin in cells with sickle cell trait to prevent the problems that occur in individuals with only sickle hemoglobin. People with sickle cell anemia, however, have no normal hemoglobin.

Unlike sickle cell trait, which essentially has no symptoms, sickle cell anemia can be devastating. The spectrum of illness is very broad; some people have mild and infrequent symptoms, whereas others may suffer painful episodes so severe that they require hospital treatment with intravenous fluids and powerful painkillers. James Ballard, a 36-year-old photographer with the Washington, D.C., government, recalls, “The first time it [sickle cell] really hit home was when I was hospitalized in the sixth grade and given last rites. But I pulled through. I never felt that the disease was something I couldn’t handle, and I never considered myself handicapped, but I had to realize my limitations.”

Some patients may have one painful crisis a year, while others may have up to 20. Or, a patient may go for months or years without a crisis and then suffer a cluster of severe attacks. The episodes are usually unpredictable.

Ballard suffered more pain than usual in 1988: “I had about 10 to 15 episodes, each usually lasting two to three days. The pain is a very sharp, intense throbbing in my arms, legs and back, and sometimes I’m short of breath. The first day is the worst.” In the (continued on page 16)
Schematic drawing of a sickle-shaped cell blocking passage through a capillary, jamming blood flow.

(Courtesy of Clinical Center, National Institutes of Health)
Eight percent of black Americans, or 1 in 12, carry a gene for sickle hemoglobin, and 1 in every 400 black newborns in the United States has sickle cell anemia or other sickle cell disease.

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summer 1988 issue of Science Focus, Darleen Powars, M.D., of the University of Southern California Medical Center quoted a child with sickle cell anemia as saying her pain was “like a door slammed on her finger, but they never opened the door.”

The pain results from “logjams” of the distorted red blood cells. Unlike normal cells, the rigid, sickle-shaped cells cannot mold themselves to squeeze through tiny capillaries—the body’s smallest blood vessels. They may pile up, stopping the flow of blood and preventing oxygen from reaching tissues beyond the blockage. This causes not only pain, which may be quite severe, but can lead to serious complications. A clogged vessel in the brain, for example, can cause a stroke; blockage in the skin can lead to open sores (ulcers). The lungs, kidneys, liver, and skeleton are most commonly affected. Blockages, particularly in the spleen, also increase patients’ susceptibility to severe infections.

With no cure for sickle cell anemia, management is geared to treating symptoms. Antibiotics are used to treat infections, and painkillers and fluids are given to patients during pain episodes. Ballard views recurring leg ulcers as his greatest problem. “I was recently hospitalized for a month with leg ulcers. Complete healing takes three to five months.” But, he says, “I can carry on a relatively normal life and I try to keep it that way, especially for my daughters. I want to do things for them. I just take it day by day.”

Almost all patients with sickle cell anemia have decreased red blood cell counts. Whereas normal red blood cells circulate an average of 120 days before being removed from the circulation, the fragile sickle cells might last only 10 to 20 days, resulting in anemia. An infection can lead to an “aplastic crisis,” in which production of new red blood cells is suppressed. When this happens, anemia becomes more severe. Although patients may require transfusions during these crises to replace the lost red blood cells, in normal circumstances they usually tolerate the anemia quite well.

Damage to various organs is apparent in most patients by the time they reach adulthood. Although sickle cell anemia reduces life expectancy, more and more patients are surviving into their 30s, 40s and beyond. Ballard suspects that his disease may have influenced him to become an overachiever. “I’ve tried to be as normal as possible and, in doing so, maybe I overdo. I never use the disease as an excuse to do or not do something.” His biggest frustration, however, is dealing with people who have little or no knowledge about sickle cell anemia. “They sometimes don’t seem to want to understand there are problems associated with sickle cell you can’t control, and that’s frustrating.”

Special Problems in Children

Infection is the major cause of death in children with sickle cell anemia. The spleen may become enlarged and not function properly, hampering the body’s infection-fighting capabilities. Babies with a compromised spleen are at great risk for a sudden and overwhelming blood infection with Streplococcus pneumoniae bacteria, which kills up to 35 percent or more of them. Gaston, of the Heart, Lung, and Blood Institute, explains, “Infection with S. pneumoniae can progress so rapidly that it can go from the onset of fever—from the moment a parent notices fever in the baby—to death in less than nine hours. And it can happen as early as three months of life.”

Another life-threatening complication involves large volumes of blood becoming trapped in the spleen. This can cause shock, which, Gaston stresses, must be recognized immediately as a medical emergency. She emphasizes that parents of children with sickle cell anemia must learn how to feel their child’s abdomen for spleen enlargement and recognize other signs that may indicate blood buildup in the spleen.

Growth and development typically are impaired in sickle cell anemia, but, again, this varies greatly among individuals. Ballard, who was 5 feet 5 inches when he graduated from high school, now stands 6 feet 2 inches and weighs 160 pounds.

Dactylitis, or “hand and foot syndrome,” is a common symptom in children. This painful swelling of the hands and feet is seen in 30 percent to 40 percent of children with sickle cell anemia some time in the first three years of life and may be confused with rheumatoid arthritis, local infection, or trauma. Gaston recalled her first encounter with a child with dactylitis: “I was in training, and a 1-year-old baby was brought to me in the hospital emergency room. Its hand looked as though it had been slammed in a door or stepped on, and I was very suspicious of child abuse. Another resident questioned whether a blood smear had been done to diagnose sickle cell disease, and that, in fact, is what it was.”

A small percentage of children suffer strokes and require frequent blood transfusions to decrease the concentration of damaged cells. The addition of normal red blood cells with normal hemoglobin helps prevent blockages. Without this therapy,

(continued on page 19)
Above: Dactylitis (hand and foot syndrome) in a baby with sickle cell anemia. Severe swelling of the left hand, caused by “logjams” of the misshaped red blood cells, contrasts sharply with the normal-sized right hand. Left: Electronmicrograph of sickle cells in various stages of distortion. The cells become sticky, rigid, and crescent shaped.

(Photos courtesy of Clinical Center, National Institutes of Health)
Sickle cell is a recessive genetic trait. If a child inherits only one gene for sickle cell, he or she will carry the trait (AS), but not develop symptoms. To have sickle cell anemia (SS), the child must inherit the sickle gene from both parents. The gene is transmitted in the Mendelian pattern of inheritance, as follows:

- If one parent has the sickle cell trait and the other has neither the trait nor the disease, there is a 50 percent chance with each pregnancy that the child will inherit the trait and a 50 percent chance it will have normal hemoglobin (AA). It will not develop sickle cell disease.
- If both parents have the trait, with each pregnancy there is a 25 percent chance that the child will have normal hemoglobin, a 50 percent chance it will have the trait, and a 25 percent chance it will have the disease.
- If one parent has the trait and the other has normal hemoglobin, all of the children will inherit the trait, but none will have the disease.
- If both parents have the disease, all the children will have the disease.

A simple blood test can identify trait carriers. Couples who wish to know if they carry the trait can be tested and counseled to help them make informed choices about family planning. For information on where the test is available, check with your family physician or local medical society.
I n f e c t i o n w i t h S. p n e u m o n i a e c a n g o f r o m t h e o n s e t o f f e v e r t o d e a t h i n l e s s t h a n n i n e h o u r s .

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further strokes could cause paralysis or death.

The risk of death from complications of the disease is highest in children under 5 years, but science is making headway in combating life-threatening infections in these children. A recent NIH-sponsored study showed that preventive doses of penicillin significantly reduce the risk of infection in children with sickle cell anemia. Two hundred fifteen children, all under 3 years, were divided into control and treatment groups: 110 received daily oral penicillin; 105 were given a placebo. The children were followed for an average of 15 months before the study was terminated early because of the dramatic benefits seen with treatment. There were 13 infections and three deaths in the group taking the placebo, whereas the penicillin-treated group had only two infections—84 percent fewer than the placebo group—and no deaths.

To save lives, penicillin therapy should be started at 3 months of age. Children over 2 years should also be vaccinated against pneumococcal infections. The earlier sickle cell is diagnosed, the earlier treatment can begin. The NIH panel recommendation to screen all newborns—regardless of race—took into consideration that targeting only specific risk groups would permit too many sick children to go undetected. According to Charles F. Whitten, M.D., professor of pediatrics at Wayne State University School of Medicine in Detroit, "Early identification and penicillin treatment would virtually eliminate death from infection in children from infancy to 4 years." And Gaston notes that "All 50 states routinely screen for phenylketonuria and hypothyroidism—conditions that cause mental retardation if not detected and treated early—yet they are much less common than sickle cell anemia."

The available diagnostic tests can detect all sickle cell variants and distinguish sickle cell trait from sickle cell disease. Sickle cell anemia can also be detected before birth by sampling the amniotic fluid or tissue taken from the placenta.

F u t u r e

One of the most active areas of research in sickle cell treatment now focuses on increasing the level of fetal hemoglobin (Hb F) in patients. Hb F is the predominant type produced by the fetus, and scientists know that it inhibits sickling. But in normal individuals, Hb F decreases after birth until, by adolescence, it accounts for less than 1 percent of total hemoglobin. Although everyone continues to produce some fetal hemoglobin throughout life, some patients with sickle cell anemia make far less than others. Scientists have known for some time that sickle cell patients with high levels of Hb F have less frequent blockages and disease complications. Increased longevity in adults and fewer spleen problems in children have been associated with increased Hb F, as have the normally milder forms of the disease in Saudi Arabians with sickle cell anemia.

Some drugs used to treat cancer can increase fetal hemoglobin levels. Researchers at Johns Hopkins University School of Medicine and elsewhere are conducting clinical trials with hydroxyurea, a leukemia medication. Samuel Charache, M.D., director of the Hopkins hematology laboratory, reported in the January 1987 issue of the medical journal Blood that two patients treated with hydroxyurea for more than 2 years had less severe and less frequent painful crises. Additional studies are under way to determine drug toxicity and try to establish a safe and effective dose.

George Stamatoyannopoulos, M.D., of the University of Washington in Seattle, and others are working with another agent, erythropoietin (EPO), for boosting Hb F levels. EPO is a red-blood-cell-forming protein produced naturally by the body. Scientists are now able to manufacture it through genetic engineering techniques. A small study of normal and anemic baboons given EPO showed increases in fetal hemoglobin of about 40 percent to 50 percent in the normal animals and 17 percent to 30 percent in the anemic baboons.

More extensive studies with hydroxyurea, EPO, and other experimental drugs for sickle cell anemia are needed before they can be determined safe and effective treatments.

Wayne State’s Whitten says that bone marrow transplants have the same potential as drugs as a therapy for sickle cell anemia. "However," he says, "for now, a high rejection rate deters use of this strategy. Thirty percent of individuals with sickle cell anemia would die following this procedure if they were transplanted based on the current status of the therapy." Sickle cell anemia patients are rarely so life-threatened.

Whitten looks to the proliferating scientific energy and money going into gene therapy research for the payoff in sickle cell treatment. Replacing defective genes with normal ones is "the ultimate therapy," he said.

The National Heart, Lung, and Blood Institute funds 10 comprehensive centers in the United States for sickle cell treatment and research. For information on the centers, write to the Sickle Cell Disease Branch, NHLBI, National Institutes of Health, 7550 Wisconsin Avenue, Room 508, Bethesda, Md. 20892.

The National Association for Sickle Cell Disease, Inc., has 80 community organizations around the country. The association sponsors sickle cell anemia education, testing, counseling, and medical and psychosocial services to help patients achieve the highest quality of life possible. For information, write to NASCD, 4221 Wilshire Boulevard, Suite 360, Los Angeles, Calif. 90010.

Marian Segal is a member of FDA's public affairs staff.
Poison Control Centers: Where Emergencies Are the Routine

by Vern Modeland

It was only for a minute, the anxious caller says. The washer had finished its cycle and she'd gone to tend to it. Who'd think her baby could reach the open bottle of medicine? The caller explained she'd just broken the bottle's seal and given baby a dose for his cold. And now the four-ounce bottle of liquid nonprescription painkiller is three-quarters empty. How much is an overdose? Should she rush him to the emergency room? Get him to vomit?

Another phone rings. This caller was changing a hearing aid battery to better hear his granddaughter's laughter and questions about the little game they were sharing. Now he can't find that tiny button of metal on the table, on the floor, or anywhere. What if she's swallowed it? Are those things poisonous?

The phone rings again. Toddlers have been in the kitchen cabinets again and they have most of what they found all over them. What if any of it is in them? Can't they get sick or die from drinking some of that stuff? What to do?

Any of these scenarios could easily have come from a routine day's log at one of the nation's more than 100 poison control centers, because these are the kinds of incidents and accidents that make up most of the hundreds of calls a day handled by poison control specialists.

"Happily, most turn out all right," says Rose Ann Soloway, a registered nurse and veteran of eight years at the National Capital Poison Center in Washington, D.C.

Home is where more than 92 percent of all exposures to poison took place in 1987—88.9 percent of them accidental. About two out of every three calls to poison control centers involve children under 6. Cleaning substances were to blame for 9.4 percent of the poisonings reported in 1987. Painkillers were the second most frequent cause (9.1 percent), cosmetics were third (7.7 percent), and plants fourth (7.2 percent). Other causes were cough and cold preparations, bites from snakes and spiders, pesticides, sedatives, and tranquilizers. Overdoses of vitamins accounted for as many cases of poisoning reported to the poison centers as did alcohol (2.6 percent).

"Probably one of the most common misconceptions is where there is a truly serious risk," says Anthony Scalzo, M.D., medical director of the regional poison center in St. Louis at Cardinal Glennon Children's Hospital.

"Parents tend to concentrate more on plants and cleaning products and don't pay a lot of attention to prescription and over-the-counter medications as being potentially dangerous—and that includes acetaminophen [a nonprescription painkiller]," he adds.

"They don't realize the danger in iron supplement tablets or eye drops. An overdose of iron supplement is potentially fatal. If you swallow the eye drop bottle's contents in one sitting, the tetrahydrozoline in it can produce hypotension [lowered blood pressure] and comas." Because one parent didn't believe that over-the-counter products can be dangerous, a bottle of mouthwash caused the death of a child. the St. Louis doctor recalls. Ethanol (a form of alcohol) in the mouthwash fatally suppressed the child's blood sugar level.

Another danger in the home exists in sweet-smelling or good-tasting products, including colognes and perfumes, with their high percentage of alcohol, according to Scalzo. "Antifreeze tastes sweet; so do some other very poisonous products found in the garage," he warns.

Mistaken identity often plays a significant role in accidental poisonings in the home. Using soft drink bottles or cups to hold paint thinner, turpentine, gasoline, or charcoal starter invites children to taste them. Similarity in size and shape of some containers for pesticides, solvents and cleaners to bottles of mouthwash and cough medicine is good reason never to store them in the same cabinet, or even in the same room.

Mistaken identity came close to causing tragedy on a Christmas vacation for one Kansas City-area family. The incident involved a cough medicine and a pesticide with "incredibly similar" packaging, as the attending physician noted.

Jeff and Kathy Campbell and their two daughters, from Liberty, Mo., were visiting Campbell's brother in the Ozarks resort and retirement community of Branson, Mo. Three-year-old Rachel Campbell awoke with a cough early one morning. In the dark, Campbell went to the kitchen for Robitussin brand cough syrup but returned instead with a spoonful of Dermaton, a tick and flea killer used on pets. The pesticide contained an organophosphate that can cause severe breathing problems, fluid in the lungs, and congestive heart failure in humans.

"It was amazing how much the bottles were alike," Jeff Campbell now recalls. Rachel complained about its taste, Kathy Campbell added, and at once both parents recognized the pesticide smell. They read the label warning, and rushed Rachel to the nearby hospital.

"They were in the emergency room within 15 minutes after recognizing the mistake," says registered nurse Ron Yoder, who is director of nursing services at Skaggs Memorial Hospital in Branson.

"The St. Louis regional poison center was called, to get their recommendation for emergency treatment. We had the bottle, so we could tell them exactly what it was. We gave her activated charcoal to absorb the poison, and magnesium citrate [a fast-acting laxative]. St. Louis also recommended it, to help her body get rid of the pesticide. About 20 minutes later she vomited a little and we gave her more activated charcoal."

But the real reaction to Rachel's organophosphate ingestion was yet to come. She was showing more fright at what was happening in the emergency room than reaction to the poison, her mother recalls. It was decided they would take her back to the house in order to calm her, and would watch her carefully.

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instructed to be alert for raspy breathing or foaming at the mouth and to return to the hospital at the first sign of any deterioration in her condition.

"Within a couple of hours, Rachel got cranky, then listless, and couldn't get comfortable," her mother recalls. "She quickly became almost unresponsive. Her eyes glazed and she wanted to be in a fetal position, with labored and raspy breathing. She started foaming from her mouth and nose as we headed back to the hospital."

"She went into respiratory distress," Yoder adds.

"Rachel was placed in intensive care and on a ventilator for a time. We kept her in the hospital overnight, but little ones can bounce back quickly, and by the next morning, she was ready for release and could continue her visit."

Rachel has recovered completely but now, two years after the incident, she's a much more "cuddly" little girl than she used to be, her mother says. The Campbells praise their regional poison center for its quick and accurate help in diagnosing and treating their little girl.

(continued on next page)
Pharmacist David Peters and registered nurse Barbara Eichhorn, certified poison information specialists, answer calls at the St. Louis Regional Poison Center. Calls to the St. Louis center are toll-free from Missouri and surrounding states. (Photo by Sue Dougan, Cardinal Glennon Regional Poison Center)

(continued from previous page)

The Branson, Mo., community hospital treats 5 to 10 cases of poisoning a month in its emergency room, according to its director of nursing. Most are accidental, typically involve medications, and typically involve children under 8.

“The information the regional poison control center has is a resource we couldn’t possibly maintain on our own in a 125-bed hospital,” Yoder says.

Many hospitals once did try to maintain some sort of poison information and control resources on their own. In Missouri before 1974, there were 15 places to which a person or a doctor could turn for poison emergency information, according to pharmacist Robert Jaeger, founder of the regional poison control center at Cardinal Glennon Children’s Hospital. That year, coincident with the observance of National Poison Prevention Week, Cardinal Glennon Hospital opened what has grown to be an electronically linked network serving 54 hospitals in three states and residents of the area direct through a toll-free telephone hot line.

The regional center in St. Louis is, today, one of 104 poison control centers in the United States that use an elaborate computerized data base and up-to-date antidote and treatment files on the toxicity of most products commonly found in our environment. Regional poison centers also develop and share information on toxic things unique to the area they cover, including chemicals used in manufacturing, plants, venomous insects and snakes, and locally popular drugs of abuse.

Just how big a file might that be? “In 1952, there were 1.2 million known chemical compounds. In 1983, there were more than 9 million, and the figure is going up at more than 6,000 a week,” according to William Robertson, M.D., president of the American Association of Poison Control Centers.

The people who staff poison centers around the clock are specially trained, certified poison information specialists. To become certified, they are required to be licensed nurses or pharmacists, with at least a year’s experience in a poison center, and each must pass a written examination. When “hot line” phones ring, they can find themselves advising a parent, a paramedic, or a physician. They are trained to ask the right questions of people who may be under stress and then quickly determine what information

First Aid for Accidental Poisoning

Some suggestions for safe housekeeping from the Consumer Product Safety Commission:

- Keep all household chemical products and medicines out of reach and out of sight of children and, preferably, locked up when not in use. Medicines on kitchen counters are very accessible to young children.
- When household chemicals and medicines are in use, never let them out of your sight—even if you must take them with you when answering the phone or doorbell.
- Store all medicines separately from household products, and store all household chemical products away from food.
- Keep items in their original containers.
- Leave original labels on all products, and read the label before using them.
- Always leave the light on when giving or taking medicines.
- Avoid taking medicines in front of children, since youngsters tend to imitate grown-ups.
- Refer to medicine as “medicine,” not “candy.”
- Clean out the medicine cabinet periodically, and safely dispose of unneeded medicines when the illness for which they were prescribed is over.
- Use safety (child-resistant) packaging properly. Close containers securely after each use.

For more information on poison prevention, write the Secretary, Poison Prevention Week Council, P.O. Box 1543, Washington, D.C. 20013. (Also see “At-Home Antidotes for Poisoning Emergencies” in the March 1986 issue of FDA Consumer.)
and other resources will be necessary to save lives. They can call on physician-specialists, if necessary, such as the St. Louis center’s medical director, Scalzo, who is on call at all hours for medical consultation. “That happens more often than you might expect,” he says.

Scalzo also reviews the more than 200 poisoning emergency treatment plans that the St. Louis regional poison center maintains in its files. These plans are from three to 20 pages long, he says, and describe clinical effects of a single poison, the organ systems likely to be affected, and the effects the toxin may have on respiratory, cardiovascular or neurological systems. The plans guide emergency personnel and physicians in knowing what to look for and what reactions to expect—and how soon—when treating a poisoning emergency. With facsimile transmission, a copy of a treatment plan can be sent from the poison control center to an emergency room hundreds of miles away and can be there before the patient arrives.

Business is brisk for poison control centers. The one in St. Louis handled some 37,500 cases in 1987 and expected to count close to 60,000 calls for help or information in 1988, according to pharmacist Mike Thompson, managing director. The Intermountain Regional Poison Control Center at Salt Lake City gets more than 35,000 calls for help a year from Utah and parts of Idaho and Nevada, according to its associate medical director, E. Martin Caravati, M.D. The National Capital Poison Center in Washington, D.C., expected to close its log for 1988 with a total of 46,500 cases of hydrocarbon ingestion [gasoline/ kerosene] for instance, making sure medicines and household chemicals are kept out of the reach of children when they are visited or come visiting.

How do you know when to call for help? Most poison center and emergency medicine specialists say: “Don’t wait, call if you are worried.” The specialist who answers at the poison control center phone may recommend something you should do immediately, or should not do. Frequently, the right home treatment can eliminate the need for a trip to an emergency room.

“When there was an absence of adequate information on what to do with poison cases, we sometimes felt there still was a need for us to do something,” says Robertson. “Now, with better information, we find we don’t need to do it. Ninety-five percent of cases of hydrocarbon ingestion [gasoline/kerosene], for instance, can be managed at home, either after a brief emergency room visit, or without the need for one. Communications are getting better. People are calling earlier.”

“Most exposures are not very serious,” adds Scalzo. “The poison center’s role in these cases is generally to provide reassurance to parents that the child is okay. This can prevent unnecessary emergency room visits, save parents money, save the hospital money, and save insurance companies money.”

Scalzo estimates poison centers contribute to saving over $2 million a year in emergency and follow-up health-care costs and another $600,000 a year in unredeemed Medicaid payments in Missouri alone. A colleague, Toby Litovitz, M.D., director of the National Capital Poison Center in Washington, D.C., says the poison control system has prevented perhaps as many as 20,000 unnecessary emergency room visits.

As a parent, you can prepare for emergencies by taking advantage of information on poisons available from your doctor, pharmacist, hospital, or through a call to the poison center listed in your phone book. Grandparents and other adults can help by making sure medicines and household chemicals are kept out of reach of children. A recent study for the Consumer Product Safety Commission found 23 percent of oral prescription drugs ingested by children under 5 belonged to someone who did not live with the child. Seventeen percent of the drugs belonged to a grandparent or great-grandparent, suggesting that all adults need to use child-resistant closures when possible and keep medicines out of the reach of young children when they are visited or come visiting.

While children have long been the focus of poison prevention plans, adults account for 25 percent of the emergency cases at the St. Louis regional poison center, according to Scalzo. A frequent cause of adult poisoning is mixing bleach with ammonia during housecleaning. The combination releases chloramine gas. Mixing bleach and certain acid-containing toilet bowl cleaners releases chlorine gas. Not leaving the cleaning job until exposure to the gas has become lengthy compounds the problem, says the emergency medicine physician. Adults also sometimes attempt to take medications in the dark, perhaps leaving the light off in order to not wake a spouse. They can become confused about whether or not they’ve taken a medication; they brush their teeth with liniment from a tube thinking it’s toothpaste; they mistake a dental cleanser for an effervescent painkiller. All of these have been reasons for calls to the St. Louis regional poison control center.

The third week in March is National Poison Prevention Week, set by Congress in 1961 as a time for local communities to raise awareness of the dangers of poisoning and the need to take preventive measures. In 1962, nearly 500 children under 5 died from accidentally swallowing household chemicals or medicines. By 1985, only 56 deaths from these causes were reported in the age group.

Factors that contributed to the decline in deaths involving children, according to the Consumer Product Safety Commission, include:

• Increased use of emergency first-aid advice from a poison control specialist.
• Widespread use of child-resistant closures (first required for aspirin in 1972), designed to prevent most children from opening household chemicals or medicines.
• Increased public awareness of the need to keep medicines and household chemicals out of the reach of children.

A summary of 1,166,940 cases reported by 63 poison centers during 1987, published in the American Journal of Emergency Medicine (September 1988), showed there were 8.5 poisonings per thousand people in the 57 percent of the United States population served by those poison information centers.

“One of the things obvious from 1987 statistics is that the problem of poison emergencies is now less than before for children under 5 and household products,” says the Association for Poison Control Center’s Robertson.

“Th e 1987 report lists 397 deaths of which only 25 were children. Our focus has expanded to look at overdose problems and suicide attempts, drug interactions, and the whole drug scene. In the future, we must address occupational and industrial poisonings as well.

“We cannot rest on our laurels,” Robertson cautioned his colleagues in an editorial accompanying the report.

Neither can we afford to relax our vigilance as we buy and bring home all those medicines, nonprescription drugs, cosmetics, cleansers, and the growing list of other household chemicals that make modern life better. Mishandled, or in the wrong hands, many are dangerous.

Vern Modeland is a member of FDA's public affairs staff.
Do You Know Your Cholesterol Level?

by Dale Blumenthal

Do you remember 1983? It was the year NASA launched four manned space flights . . . the year Joe Theismann led the Washington Redskins to a Super Bowl victory . . . and a year in which you probably never had your cholesterol checked.

Yet since then, according to a new survey from the Food and Drug Administration, the percentage of adults who have had their blood cholesterol checked increased from 35 percent to 59 percent. And 17 percent of adults now know their level, compared to just 3 percent in 1983.

Furthermore, the survey found, the number of adults aware that dietary cholesterol and fat are risk factors for heart disease has nearly doubled. In 1988, 55 percent of those surveyed cited fats and fatty foods as associated with heart disease, compared to 29 percent in 1983. Nearly 80 percent of the people surveyed said that lowering blood cholesterol would have a “large effect” in preventing heart disease. This increased awareness spanned all educational levels.

But this increase in awareness in the past six years was not accompanied by a gain in knowledge about dietary cholesterol. For instance, the survey asked: Where is cholesterol found?

a. vegetables and vegetable oils
b. animal products like meat and dairy
c. all foods containing fat or oil
d. not sure

Only 33 percent gave the correct answer (b)—about the same percentage as in 1983.

The 1988 FDA survey was similar to ones in 1986 and 1983 conducted by FDA and the National Heart, Lung, and Blood Institute. Asking the same questions each time allows researchers to track trends in people’s awareness, concern, knowledge and behavior related to fat, cholesterol, heart disease, and other diet-disease issues, according to Alan S. Levy, head of consumer research at FDA’s Center for Food Safety and Applied Nutrition.

Obviously, some basic knowledge about dietary fats and cholesterol is necessary for consumers to make the kinds of behavioral changes that will reduce their risk of heart disease: Buying and preparing heart-healthy foods, and—as the public is being told more and more—having their cholesterol levels checked.

What Is Cholesterol?

Dietary cholesterol is an odorless, white, fat-like substance found in all foods from animals (meat, eggs and dairy products), but not in foods from plants. (See “Cutting Cholesterol? Look to the Label,” *FDA Consumer*, February 1987.) The cholesterol we eat travels through the bloodstream in particles called lipoproteins, which are compounds that contain both lipids (substances such as fat and cholesterol) and proteins.

This blood cholesterol may be deposited in fatty streaks in the inner linings of the arteries. When the fatty deposits (known as plaque) build up, artery walls thicken and the arteries may become clogged—leading to heart disease, heart attack, or stroke (see “On Being Too Rich, Too Thin, Too Cholesterol Laden,” *FDA Consumer*, July–August 1981). High-fat diets (especially those high in saturated fat) and an inherited tendency for the body not to adequately dispose of excess saturated fat and dietary cholesterol also can increase blood cholesterol levels.

The first step in controlling blood cholesterol is to measure it. The National Cholesterol Education Program (NCEP), a coalition of government and private groups led by the National Heart, Lung, and Blood Institute, has set guidelines for cholesterol watchers. Blood cholesterol levels below 200 milligrams per deciliter (mg/dl) are classified as “desirable.” Levels of 200 to 239 mg/dl are considered “borderline-high.” Levels of 240 mg/dl and above are considered “high.”

In a pamphlet sent to doctors in November 1987, NCEP recommended that physicians advise patients with desirable blood cholesterol levels to have their cholesterol checked every five years and to eat a healthy diet, low in saturated fat.

Patients with cholesterol levels 200 mg/dl or over should have a second test and then average the two readings. If a borderline-high level is confirmed, treatment is determined by whether the patient has either coronary heart disease or two risk factors for getting the disease:

- male sex
- family history of premature coronary heart disease (heart attack or sudden death before age 55 in a parent, brother or sister)
- cigarette smoking
- high blood pressure
- low concentration of high-density lipoprotein cholesterol (below 35 mg/dl confirmed by repeated measurement)
- diabetes mellitus
- history of vascular disease
- obesity

For patients who don’t have either coronary heart disease or at least two of the risk factors, NCEP recommends a diet low in total fat (less than 30 percent of total calories) with less than 10 percent of calories coming from saturated fat. Ten to 15 percent of calories (continued on page 26)
Cholesterol screening has become much quicker and easier thanks to fingerprick blood tests, processed by new table-top analyzers. No longer must consumers visit a medical laboratory and have a blood sample taken from a vein in the arm. Instead, they can get a test at a mall or health fair for as little as $5, with results in just three minutes. The technician first pricks the patient's finger with a sterile needle (A) and then draws the blood into a pipette (B). The blood is then placed on a special strip that changes color based on the amount of cholesterol in the sample (C). The strip is inserted into a computerized table-top analyzer, which reads the color and displays the cholesterol reading.

(Photos courtesy of George Washington University Lipid Research Clinic, Washington, D.C.)
Eating to Reduce Cholesterol

The way to a healthy heart is through the stomach. The National Heart, Lung, and Blood Institute offers these tips to lower blood cholesterol and reduce the risk of heart disease:

- Less than 30 percent of total daily calories should come from fat.
- Less than 10 percent of calories should come from saturated fat.
- No more than 10 percent of calories should come from polyunsaturated fat.
- Ten to 15 percent of calories should come from monounsaturated fat.
- Fifty to 60 percent of daily calories should come from carbohydrates.
- A daily diet should contain less than 300 milligrams of cholesterol.
- Calorie intake should be adjusted to achieve or maintain a desirable weight.

Remember, while protein and carbohydrates contain four calories per gram, fat contains nine.

For more advice on reducing fat and cholesterol in the diet, see “Planning a Diet for a Healthy Heart” in the March 1987 FDA Consumer.

Growing Perceptions of Diet-Heart Disease Links

Question: What things that people eat or drink cause heart disease?

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<th>Year</th>
<th>Percentage Who Mentioned Risk Factor</th>
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<td>1986</td>
<td>43%</td>
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<td>45%</td>
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Source: FDA Health and Diet Surveys

HDL and LDL

With blood lipoprotein analysis, the focus shifts from total cholesterol to low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels. Low-density lipoproteins are rich in lipids and carry 70 percent of the cholesterol in the blood. LDL particles bind to LDL receptors in the body’s cells and are removed from the circulating blood by the liver. But the amount of LDL can far exceed the number of cell receptors available, and that’s when the LDL-cholesterol level in the blood rises, according to researchers. As the excess LDL particles circulate in the blood, they deposit cholesterol and other lipids that form plaque on artery walls.

NCEP defines desirable LDL levels as less than 130 mg/dl, borderline-high-risk levels as 130-159 mg/dl, and high-risk levels as 160 mg/dl and above. Patients with borderline-high-risk LDL levels who have coronary heart disease or two or more risk factors and patients with high-risk LDL levels should follow a diet low in saturated fat and low in cholesterol, under a physician’s care.

Low-density lipoproteins have been characterized as the “bad guys” of the cholesterol scene and high-density lipoproteins as the “good guys.” The main goal of diet therapy is to decrease LDL levels. In addition, some scientists are finding it just as important to have a high HDL-cholesterol level. For instance, Harvard University Medical School researcher Meir Stampfer, M.D., followed the development of heart disease in 22,071 men and found that “for each milligram HDL goes up, the risk of heart attack drops 6 percent.” Stampfer concludes that the HDL-cholesterol level is “the best lipid predictor of the risk of heart disease.”

HDL is a protein-rich particle—50 percent of its mass is protein—that scoops up cholesterol from cells and carries it to the liver for removal from the body. Exercise, some researchers believe, may be the best way to increase your HDL level. According to NCEP, the desirable HDL-cholesterol level is 35 mg/dl or above.

Testing for Cholesterol

Now that cholesterol has become a buzzword for most Americans concerned about heart disease, people want to have their cholesterol checked. And health professionals are eager to help in promoting what may be a lifesaving activity.

Tests prescribed by a physician and performed in a laboratory that follows standards set by the Centers for Disease Control remain the “preferred way to assess blood cholesterol,” accord-
ing to Beth Schucker, health scientist administrator with the National Heart, Lung, and Blood Institute. However, as participants in a 1988 workshop conducted by the institute on public cholesterol screening noted, new portable equipment today makes cholesterol measurement "rapid, affordable, relatively painless, and readily available."

Your local pharmacy, for instance, may be one place you can visit to have your blood cholesterol checked. Nelson Showalter, owner of Williamson’s Pharmacy in Virginia, has joined other pharmacists in offering cholesterol screening as a service in his drugstore. Showalter says that recently one of his golf partners (a healthy looking man in his 30s) dropped in for a test and was surprised to learn the results were alarmingly high—280 mg/dl. The friend followed up the initial test with a doctor’s appointment and, says Showalter, through changes in his diet has lowered his cholesterol level.

The machine Showalter uses involves a simple finger prick blood test. A drop of blood is put on a paper strip, which is then fed into the machine, and the cholesterol reading comes out three minutes later.

Other places in your community where you might get your blood cholesterol screened include hospitals, nursing homes, health fairs, supermarkets, and exercise clubs.

Schucker recommends that people rely on more than just one public screening test. Follow up with your doctor, she says, especially if your reading is in the “borderline-high” or “high blood cholesterol” ranges.

Also, says Schucker, be sure to ask about the quality control procedures used for the equipment. She cautions that without adequate quality control, you could easily receive an inaccurate reading. Broden Staples, a reviewer in FDA's division of clinical laboratory devices, recommends that at the beginning of the testing day and then after every 20 tests, the screener run a control sample with a known measurement. The technician should recalibrate equipment if the result for the control sample is wrong or, after every 40 tests, regardless of the control results. When having a fingerstick test at a health fair, he says, ask questions such as “Are you running control samples?” “What do you do when the readings are off?” and “Is a clinical chemist supervising this test?”

**Cholesterol-Free and Fat-Free**

Along with dietary cholesterol, the terms saturated fatty acids (often referred to simply as saturated fat), polyunsaturated fatty acids, and monounsaturated fatty acids have been added to our health vocabulary. U.S. Surgeon General C. Everett Koop made fat and cholesterol a national issue in the 1988 Surgeon General's Report on Nutrition and Health when he recommended that people “reduce consumption of fat [especially saturated fat] and cholesterol.” The report stated: “Epidemiologic, clinical, and animal studies provide strong and consistent evidence for the relationship between saturated fat intake, high blood cholesterol, and increased risk for coronary heart disease. Conversely, reducing blood cholesterol levels reduces the risk for death from coronary heart disease.”

However, as FDA's survey found, although most Americans now are aware of the importance of eating less saturated fat and cholesterol, many people still are unsure of what foods contain cholesterol and how to tell a saturated fat from a polyunsaturated or monounsaturated fat.

Results from the U.S. Department of Agriculture’s 1985 and 1986 Continuing Survey of Food Intakes of Individuals support this observation. Meat consumption by women of all income levels decreased 34 percent between 1977 and 1986, and egg consumption was down 28 percent. Women with higher incomes were most likely to reduce their intake of meat, whole milk, and eggs. But, instead of replacing these foods with low-fat foods, they ate more cheese, cream desserts, and salad dressings, all containing large amounts of fat.

One of the goals in a blood cholesterol-lowering diet is to eat less saturated fat. Saturated fat raises blood cholesterol more than anything else in the diet, even more than dietary cholesterol.

Saturated fat and foods that are high in saturated fat usually are solid at room temperature. They include butter, cheese and meat. (Whole milk, which has a relatively high saturated fat content—5.1 grams in 8 ounces—is one exception to this general guideline.) Sometimes foods that claim to be “cholesterol-free” or “low-cholesterol” may contain large amounts of fat, including saturated fat. In order to prevent being misled, read the nutrition label to learn the amount of total fat, saturated fat, and cholesterol in a serving.

Unsaturated fats (polyunsaturated and monounsaturated) seem to lower blood cholesterol levels and, when they make up less than 30 percent of a day’s calories, are healthy substitutes for saturated fat. Vegetable oils such as safflower, corn, soybean, cottonseed, sesame, and sunflower oils are good sources of polyunsaturated fats. However, a few vegetable oils also are naturally high in saturated fat—especially coconut oil (84 percent) and palm kernel oil (79 percent). (Consumption of these oils accounts for about 4 percent of the fat in the U.S. diet.) Fish also contains polyunsaturated fats. Olive, peanut and canola oil are high in monounsaturated fats.

Cholesterol is found only in food from animal sources, such as egg yolks, dairy products, meat, poultry, shellfish and—in smaller amounts—fish. Also, organ meats—liver for instance—are particularly rich in cholesterol.

Eating to lower blood cholesterol is far from bad-tasting medicine. Oats, dried beans, and some fruits, vegetables and other foods are high in a type of fiber that is thought to lower cholesterol. High-carbohydrate foods, like pasta and potatoes (when prepared without fats), are also good sources of vitamins and minerals. In response to consumer requests, some food companies are substituting unsaturated fat for saturated fat in cookies and other products. Bookstore shelves are lined with cookbooks that contain recipes for oatmeal-raisin muffins using unsaturated vegetable fats. Fettucine with mussel sauce, chilled asparagus with yogurt sauce, and other dishes low in saturated fat and cholesterol.

“How long will it take to reduce my blood cholesterol level?” you might ask. How quickly your body responds depends on several factors, including genetics and your individual physiology. In the booklet “Eating to Lower Your Blood Cholesterol,” however, the National Heart, Lung, and Blood Institute says that “generally your blood cholesterol should begin to drop 2 to 3 weeks after you start on a cholesterol-lowering diet.” Some people, says the institute, may reduce their blood cholesterol levels 30 to 55 mg/dl. But the first step (and maybe the only step you need to take) is to get it measured.

Dale Blumenthal is a member of FDA’s public affairs staff.
When it comes to doctoring their children with over-the-counter (OTC) medications, some parents may not be doing too good a job, according to a panel of pediatric experts. Reviewing some 3,900 decisions about using OTC medications made over a nine-month period, the experts could give "only minimal approval" to the way 500 mothers treated their ailing youngsters. In fact, the panel felt that the mothers did only slightly more good than harm for their children. In a few cases, the mothers' choices were considered dangerous (abuse of laxatives was common).

The study, conducted at the Universities of Michigan and Rochester by Lois A. Maiman, Marshall H. Becker, and Anne W. Katic (and published in the Journal of Community Health, fall 1985), found that poor decisions often involved selecting the wrong medication for a child's condition. Errors involving the wrong dosage or duration of treatment were less significant. It appears that the widespread failure of adults to read the labels of OTC medicines they take themselves carries over to some extent in treating their children. Instead of reading the directions, parents often rely on that old standby: guesswork.

And, according to the researchers, the average family has plenty of choices to guess about. They found the typical home medicine chest abundantly stocked: Two-thirds of families keep four to eight different types of nonprescription medications, ranging from cold and fever remedies to laxatives, on hand for their children.

Like Grown-Ups, Only Smaller

Often, when children's products aren't handy, some parents—figuring that children are just like grown-ups, only smaller—give them adult medications, reducing the regular adult dose, sometimes by slicing a single tablet in half. Usually this imprecise but common-sensical approach is not far wrong. But in some cases it doesn't work at all. For instance, a time-release tablet can't be divided without disrupting its critical timing mechanism.

A wide variation in dosage recommendations by doctors may also encourage parents to experiment. A survey of 200 pediatricians showed that their means of determining the dose of OTC cough-cold and pain relief drugs for children ranged from consulting the Physicians' Desk Reference (which contains FDA-approved labeling) to appealing to personal experience.

While OTC drugs generally have such a wide margin of safety that a somewhat excessive dose won't do much harm, sometimes a wrong dose—even of a children's drug—can lead to disaster. One case in point was the quaintly named "Sweet Spirits of Nitre," an old-time remedy for children on the market since the days before FDA had legal authority to approve new drugs before they could be sold. This unexamined product to reduce fever and relieve colic turned out to be a solution of ethyl nitrite in alcohol. Several years ago, a tablespoonful of it killed a 4-month-old infant. That tablespoonful was several times the manufacturer's recommended dose. FDA took the lethal "Sweet Spirits" off the market in 1980.

Even when parents diligently try to follow the directions on the label, the instructions are sometimes so imprecise or overly cautious that they finally ignore them. For one thing, every parent knows that there is an enormous difference between an infant and a child of 6 or 12, yet in the past many medicines didn't distinguish dosages for the different ages with the greatest possible precision. Experience may have taught some parents what recent research now confirms: that children's recommended dosages in some cases have been too low for maximum effectiveness. (Over the past several years, FDA's review of OTC drugs and their labeling has helped to improve this situation.)

Diluting Draughts of Wine

The quest for correct drug dosages for children has been going on at least since the ancient Greek physician Hippocrates recommended diluting medicinal draughts of wine for infants. Part of the challenge in today's efforts to refine dosages stems from the fact that drugs are usually tested in healthy adult volunteers who might be best able to resist unanticipated side effects. Experiments on children are usually out of the question, particularly for the relatively milder conditions that OTC remedies usually address. Consequently, pertinent test evidence involving children is hard to come by. Experience with products already on the market has to serve as a substitute.

To remedy this situation, FDA is involved in an effort to develop more precise—and, if possible, more standardized—dosage instructions for children's medications. After years of research by its staff and advisory panels, the agency last year asked for public comment on industry proposals for more precise dosages for several kinds of OTC drugs for children under 12. The goal is a labeling system that is reliable and simple to follow.

The significance of the manufacturers' recommendations is that they take into account the many changes in young bodies between infancy and puberty, seeking to offer more subdivisions than the usual groupings of ages 2 to 6 and 6 to 12. FDA is now evaluating the industry recommendations and the comments they drew.

At the center of the pediatric dosing issue is a debate about the best criteria for measuring the effects of drugs on the body, particularly the rapidly changing bodies of growing children. Age, though the most obvious, is only one of several determinants; weight or body surface area can be far better predictors of how an individual may respond to a certain dose of a drug. Body length allows for a rapid estimation of weight particularly useful in emergency situations; moreover, since many medicines are distributed through body water (continued on page 30)
How much is enough? How much is too much? Makers of nonprescription children's medicines are working with FDA to develop more precise dosing instructions for their products. Some companies have taken other steps, such as providing calibrated dosing cups with liquid medicines, so parents don't have to rely on the notoriously unreliable measure of kitchen teaspoons and tablespoons.
Age isn't the only way to determine the correct dose of a children's medication. The label (above) for Children's NyQuil cough-cold medicine lists both age and weight under the dosage instructions. That allows more precise dosing of children who are either heavier or lighter than average for their age. FDA is working to develop better dosage instructions for nonprescription children's medications to help parents avoid mistakes in dosing their youngsters.

(continued from page 28)

Refined Yet Simple Dosages

There's also the practical consideration of what instructions the consumer will actually be able to follow. If the refined dosage instructions are going to be used, they have to be kept simple enough for everyone to comprehend.

In laboratory conditions, many scientists agree that the most accurate way to gauge the proper dosage of a given drug for a child—or for an adult, for that matter—is to base it on the patient's body surface area. As a working norm for children's dosages, however, this ideal seems impractical. Few parents know their children's body surface area or how to calculate it. But since surface area corresponds roughly with weight, that less precise but more accessible criterion seems to be more usable.

Age is even less precise as a gauge of drug tolerance, yet it does correspond, more or less, with a child's probable weight and body surface. The overwhelming advantage of using age in pediatric dosing is that a child's age is almost always known, more so than weight and certainly more so than body surface area. Yet some experts argue that a child's height corresponds even more closely to weight than does the child's age, thus suggesting another alternative standard.

An intriguing proposal in drug labeling for children is to list both age and weight, allowing more precise dosing of children who are either heavier or lighter than average for their age.

Some agreement seems to be forming in the medical community that a standard pediatric dosage unit—one-eighth the size of the usual adult dosage could be adapted to childhood growth patterns. While this might work for tablets or capsules, liquid medicines might require more precisely calibrated dosing devices on the order of

the plastic dosage cup now included with some cough-cold products. Advocates of length-based dosing note that a measuring device coded for dosages appropriate to each height range would also help avoid the imprecisions of the traditional household teaspoon, which can vary considerably in actual size. In a standard children's dosing schedule, whether based on age, weight, height, or some other formula, parents would know exactly just how many units to give their children.

Weight-Based Vs. Age-Based

Perplexing issues must be worked out before a standard pediatric dosing schedule becomes accepted. The advisory panels of experts in various fields that FDA convened came up with very different suggestions. For instance, the children's dosing recommendations of FDA's Advisory Review Panel on OTC Cough-Cold Medications adhere to the old divisions of ages 2 to 6 and 6 to 12. But those of the analgesic panel provide several age gradations. (Analgesics are painkillers, including aspirin, acetaminophen, and sodium salicylate.) Since many combination products (multi-symptom remedies) contain both analgesics and cough-cold ingredients such as antihistamines, precise dosing is difficult to reconcile. Some of those who commented on other FDA panels' recommendations suggested that standard dosages for many products can be extended below age 2. Still others would leave drug manufacturers free to offer either weight-based or age-based directions. Yet, with these and other questions to consider, FDA's advisory panels have moved forward.

A decade of study convinced FDA's Internal Analgesic Advisory Panel that it was desirable to devise a recognized pediatric dosage schedule for these products, particularly since many existing children's dosages were too low to be effective.

A child's age and body surface are directly related between ages 3 and 12, though the relation between age and body weight is direct only up to age 7. Consequently, the panel based its analgesic dosage recommendations on probable body surface area at a given age. The recommendations are shown in Table 1.

Better-Calibrated Categories

These better-calibrated age categories are clearly an advance over the older, cruder ones. Yet anthelmintics show another possible approach. These OTC products for treating pinworm infestation are unusual in that dosage is based directly
upon weight, for adults as well as children. Starting with 125 mg for patients 2 years old weighing 25 to 37 pounds, the dosages increase by one tablet or teaspoonful of medication for every 22 pounds of body weight, up to 1,000 mg for those weighing over 188 pounds, presumably adults.

Progress was harder to make elsewhere. FDA's cough-cold panel had only negligible data on use of such products in children because little had been collected, even though these remedies are widely used for youngsters. With such variables as a patient's age, weight, metabolism, and special sensitivity or tolerance for a specific drug, the panel regretted that conducting clinical trials of cough-cold products on children themselves—the most certain way of collecting accurate data—is not practical.

The panel decided that age is the easiest criterion to use for dosage instructions for cold products, although it conceded that it can be the least reliable, given the wide variations in weight among children at a given age. Since these OTC products are very safe, the panel believed it would be counterproductive to achieve small gains in precision at the cost of complicated or confusing dosing formulas.

With the decisions on whether to rely on age or weight coming down so very differently in three different classes of drugs, and with so many difficult issues to settle, a standard pediatric dosing schedule may seem a long way off. Nonetheless, one proposal made to the agency offered a combination of age and weight criteria based on a one-eighth adult dosing unit. (See Table 2.)

### Simplicity and Adaptability

This proposal has the benefit of simplicity, yet adaptability to the child who doesn't fit into the statistical weight norms for his or her age. In short, it could be "user-friendly." Whether such uniformity of dosing units will be accepted remains to be seen.

The discussion continues on whether FDA should require changes of this type in drug labeling once pediatric dosage standards have been finalized or leave such changes to voluntary action by the pharmaceutical industry. Meanwhile, the responsibility for properly medicating children rests primarily with parents.

The first decision is to select the right medication; the second—equally important—is to give the proper dosage for the proper length of time, following the package instructions.

While modern pediatric OTC medicines are very safe, any drug can have bad effects if taken in excess or without regard to the instructions. The warnings on the labels should be followed unless a medical professional indicates otherwise. A product good in itself can be harmful if used inappropriately. For instance, some parents have been reported to use OTC products for prevention, giving their children regular doses of aspirin to prevent headaches or laxatives to prevent constipation. Both practices over time can be harmful. Some medications, of course, shouldn't be given to children at all, including some extra-strength combination cough-cold products, some time-release remedies, and sleeping pills. Always check the label to see whether a medicine should not be given to children.

One special warning: Aspirin—even children's aspirin—should not be given to children or teenagers suffering from or recovering from flu, chicken pox or other viral illnesses. Use of aspirin in such cases has been associated with Reye syndrome, a rare but serious—even fatal—condition.

### Table 1. Aspirin and Acetaminophen Pediatric Dosages

Based on a standard adult dosage unit of 325 milligrams (mg)—the familiar size of an aspirin tablet—and on the smaller 80-mg unit of children's analgesic products, FDA is proposing to recommend the following dosage every four hours, up to five times a day, until fever or other symptoms subside.

<table>
<thead>
<tr>
<th>Age</th>
<th>Adult Product (325 mg)</th>
<th>Dosage</th>
<th>Children's Product (80 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 2</td>
<td>consult a doctor</td>
<td>1 unit</td>
<td>consult a doctor</td>
</tr>
<tr>
<td>2 to under 4</td>
<td>½ unit</td>
<td>2 units</td>
<td>2 units</td>
</tr>
<tr>
<td>4 to under 6</td>
<td>¾ unit</td>
<td>3 units</td>
<td>3 units</td>
</tr>
<tr>
<td>6 to under 9</td>
<td>1 unit</td>
<td>4 units</td>
<td>4 units</td>
</tr>
<tr>
<td>9 to under 11</td>
<td>1 to 1¼ units</td>
<td>4-5 units</td>
<td>4-6 units</td>
</tr>
<tr>
<td>11 to under 12</td>
<td>1 to 1½ units</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Aspirin—even children's aspirin—should not be given to children or teenagers suffering from or recovering from flu, chicken pox or other viral illnesses. Use of aspirin in such cases has been associated with Reye syndrome, a rare but serious—even fatal—condition.

### Table 2. Suggested Age- and Weight-Based Pediatric Dosages

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight</th>
<th>Number of Dosing Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 months to</td>
<td>12-17 lbs.</td>
<td>1</td>
</tr>
<tr>
<td>under 1 year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 to under 2</td>
<td>18-23</td>
<td>1.5</td>
</tr>
<tr>
<td>2 to under 4</td>
<td>24-35</td>
<td>2</td>
</tr>
<tr>
<td>4 to under 6</td>
<td>36-47</td>
<td>3</td>
</tr>
<tr>
<td>6 to under 9</td>
<td>48-59</td>
<td>4</td>
</tr>
<tr>
<td>9 to under 11</td>
<td>60-71</td>
<td>5</td>
</tr>
<tr>
<td>11 to under 12</td>
<td>72-85</td>
<td>6</td>
</tr>
<tr>
<td>12 and over</td>
<td>96 and over</td>
<td>8</td>
</tr>
</tbody>
</table>

If the child's weight is known, that column is used; if not, the "age" column is used.

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Stephen J. Ackerman is a writer in Washington, D.C.
**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.**

- **Dimethyl dicarbonate** has been approved by FDA for use as a yeast inhibitor in bottled wines (FR Oct. 21, 1988).


- The U.S. Department of Agriculture has revised its system for inspecting broilers and Cornish game hens to speed processing (FR Nov. 21, 1988).

- FDA has revised rules for developing orphan drugs, which are used to treat diseases or conditions considered rare in the United States (FR Nov. 23, 1988).

- A fetal acoustic stimulator, the Model 146, made by Corometrics Medical Systems, Wallingford, Conn., has been approved by FDA. The device uses low-frequency sound to stimulate heart rate responses as an indicator of fetal well-being (FR Nov. 30, 1988).

- The Lithostar lithotripter, made by Siemens Medical Systems, Inc., Iselin, N.J., has been approved by FDA. Lithotripters generate sonic shock waves to break up kidney stones (FR Nov. 30, 1988).

- **Brain implant devices** to relieve pain must now receive pre-market approval by FDA. Exempt are those devices for which a notice of product development protocol was made before May 1986 (FR Dec. 1, 1988).

- FDA has revised its guide for designing clinical studies of allergy drugs. Copies are available from the Biologies Information Staff (HFB-205), FDA, 8800 Rockville Pike, Bethesda, Md. 20892 (FR Dec. 2, 1988).

- **Drug Stability Guideline—December 1, 1987**, a guide for stability requirements in making veterinary drugs, has been revised by FDA. Copies are available from the Division of Chemistry (HFV-142), Center for Veterinary Medicine, FDA, 5600 Fishers Lane, Rockville, Md. 20857 (FR Dec. 5, 1988).

- **Draft Guidance for Content and Review of a Magnetic Resonance Diagnostic Device 510(k) Application** is available from the Division of Small Manufacturers Assistance, Center for Devices and Radiological Health (HFZ-220), FDA, 5600 Fishers Lane, Rockville, Md. 20857 (FR Dec. 5, 1988).

- FDA has withdrawn approval of neomycin sulfate for use in drugs or as an injectable antibiotic after finding significant risks in its use and lack of evidence of safety or effectiveness (FR Dec. 6, 1988).

- FDA has denied requests to hear new evidence on the use of radiation to control parasites in pork, inhibit ripening or control insects in fresh fruit and vegetables, and to control microorganisms on spices and herbs. The agency said that extensive review of scientific evidence shows that approved uses of irradiation of foods are safe at the dosage levels set (FR Dec. 30, 1988).
Mislabeling of drug products is the most frequent and sometimes the most dangerous mishap that can occur during drug production, and such mix-ups are the major cause of drug recalls. In 1987 six recalls that were considered life-threatening (Class I) involved mislabeled medications. Both prescription and nonprescription drugs have been implicated.

In January 1988, after witnessing a growing problem with drug labeling mix-ups, FDA Commissioner Frank E. Young, M.D., Ph.D., sent letters to major drug industry associations asking their help in curtailling such mix-ups.

Two companies in particular have recently had repeated problems with labeling accidents. My-K Laboratories of Morton Grove, Ill., has had five recalls of its products, two of which were Class I, since April 1987. More recently, Humco Laboratories of Texarkana, Texas, had two Class I recalls of syrup of ipecac in April 1988.

The most serious of the My-K mix-ups involved an injury to a 6-year-old boy in December 1987. The child was given three doses of what was thought to be an over-the-counter antihistamine and nasal decongestant. He became lethargic and was taken to a clinic, where his condition worsened. He was then transported via helicopter to North Carolina Memorial Hospital, where the attending physician had the bottle of medicine—labeled tripolidine hydrochloride and pseudoephedrine syrup—tested and found it contained haloperidol oral solution, a major tranquilizer available only by prescription. The boy recovered, but the incident could have been fatal. The physician reported the label mix-up to the U.S. Pharmacopeial Convention through that organization's drug product problem reporting program, and My-K began to recall the drug on Dec. 31, 1987.

Because of the seriousness of this mix-up and the previous history of recalls, FDA inspected My-K in December 1987 to find the cause of the labeling problems. The investigator found many serious flaws with My-K's labeling controls, and on March 24, 1988, the government filed a civil suit with the U.S. District Court for the Northern District of Illinois requesting that My-K be stopped from any further manufacturing. On April 7, the firm signed a consent decree of permanent injunction agreeing to stop distributing products on hand until FDA was satisfied that they were labeled correctly.

My-K was bought a short time later by Pharmaceutical Basics Inc., also of Morton Grove, Ill. Even though the new management corrected My-K's manufacturing violations, the old company's shoddy practices continued to haunt the firm. In August 1988, Pharmaceutical Basics had to recall one lot (369 pint bottles) of My-K and Rugby brands of Promethazine VC Plain Syrup, a prescription medicine for allergy and colds manufactured by My-K in 1987, because some of the bottles contained lindane lotion, an external scabies medicine. Lindane, a pesticide more potent than DDT, can cause severe and possibly fatal convulsions if taken internally.

Serious label mix-ups by Humco followed quickly on the heels of resolving the My-K case. Although no one was injured in these cases, the potential for harm was just as serious.

Humco manufactures and distributes various drug products under its own name.
and various private labels. One of its products, syrup of ipecac, is used to induce vomiting in poisoning victims. Poison control centers recommend keeping ipecac readily available in medicine chests.

On April 21, 1988, Humco recalled mislabeled ipecac syrup that actually contained Iodides Tincture, an over-the-counter product used to treat minor cuts and abrasions. The small amount of iodine in the mislabeled bottles would be unlikely to cause death.

On April 22, FDA inspected the firm and determined that the mislabeling had been caused by inadequate procedures and controls, just as in the My-K case. Labels for the tincture of iodide were not checked to be sure they were used up before the ipecac was processed; therefore, leftover iodine labels were also put on ipecac bottles.

On April 29, 1988, only eight days after discovering the iodine mix-up, FDA learned of a second label mix-up by Humco, this time involving eucalyptus oil, a highly toxic substance, that was also mislabeled as ipecac syrup. Eucalyptus oil can be purchased over the counter for use in vaporizers to relieve congestion.

A pharmacist in Pittsburgh discovered the problem when he pulled bottles of Humco’s syrup of ipecac off his shelves because of the iodine recall. The pharmacist handed two of the bottles to his manager, who shook them. The bottles felt different to the manager. Upon further investigation, they discovered one of the bottles contained a thick syrup, and the other a watery liquid. The company sent the bottles out for analysis and learned that the one with the thick syrup contained eucalyptus oil. The company immediately notified FDA.

Because of the seriousness of this mislabeling incident, FDA reinspected Humco in early May. Investigators found the second labeling problem was also due to poor label control practices, and uncovered additional manufacturing violations as well.

FDA filed a complaint for injunction with the U.S. District Court for the Eastern District of Texas, Texarkana Division, to make Humco stop manufacturing and selling products until the firm could ensure that controls were in place to prevent any further mislabeling incidents.

The company signed a consent decree, and a follow-up inspection in August showed the firm had indeed made the changes necessary to comply with good manufacturing practice regulations. FDA also required that Humco test its oral products manufactured since June 1986 to be sure they were not mislabeled and to certify that existing batches of topical products were correctly labeled. After all requirements were met, Humco was allowed to resume operations in late August 1988.

Bald-Faced Hair Scam

Two Canadian entrepreneurs, who apparently made more than $3 million during four years of peddling a phony hair restorer, face trial for mail fraud, wire fraud, conspiracy, and violations of the Food, Drug, and Cosmetic Act. And, if convicted, they must make full restitution to the victims they “scalped.”

Philip P. West and Wayne P. Krekelwicz, who were corporate officers of Westmaster Distributing—also known as Anglo-American Cosmetics, Ltd., Toronto; MJS Distributors, Toronto; and Westmaster Distributors, Watertown, N.Y.—are charged with operating companies that produced kits of unapproved hair restorer products and sold them by mail.

A package containing one 4-ounce plastic bottle each of Westmaster Follicle Cleanser, Westmaster Hair and Scalp Lotion, and Westmaster Natural Source Formula Shampoo cost $210 plus shipping the cost.
charges. Besides the three-month supply of each of the products, the buyer got instructions for their use and promotional materials about another product, MJS Hair Restorer Lotion, a baldness remedy that had been approved by the Canadian government. The implication of the promotional material was that the Westmaster products and MJS Hair Restorer Lotion were comparable. The Westmaster products mailed to American purchasers, phone using a U.S. toll-free phone number or wrote to Westmaster at the Toronto address shown in its newspaper ads. Investigation at Lewiston in April 1984 disclosed that the products were being made by Corwood Laboratories, Inc., Hauppauge, N.Y. FDA's New York office investigated the laboratory in June and confirmed the products were made there, but laboratory employees would not reveal the formulas. FDA's Denver office added to the growing case file in July 1985 by locating promotional literature for the hair restorer products dating back to 1983 and determining that orders from Denver also were filled by Westmaster from New York state. FDA laboratory analysis of product samples, obtained by mail in Buffalo and during the inspection at Corwood Laboratories, revealed a blend of the sunscreen para-aminobenzoic acid (PABA), aloe vera, protein, vitamin E, jojoba, balsam, water, polysorbate 80, propylene glycol, stearyl alcohol, mineral oil, oleyl alcohol, lecithin, amino acids, and preservatives—ingredients commonly found in shampoos and hair conditioners, but not proven effective as hair restorers. The product, which costs about 48 cents to make, sold for from $12 to $15, according to investigators.

FDA forwarded to the U.S. Postal Service the information it had gathered early in 1985, and the Postal Service continued the investigation. Postal inspectors from Buffalo and Syracuse, N.Y., obtained warrants to search Westmaster warehouses in Watertown and Buffalo. They seized over 200 bags of promotional materials and approximately $250,000 worth of Westmaster products. Records seized showed Westmaster had shipped the bogus hair restorer products throughout the United States. Sales of Westmaster hair restorer products ended shortly thereafter.

The case was turned over to the U.S. attorney for the northern district of New York, and, in February 1988, a federal grand jury returned an indictment against West and Kreklewich. The charges included 13 counts of mail fraud, four counts of wire fraud, two counts of violating the Food, Drug, and Cosmetic Act, and one count of conspiracy. If convicted, West and Kreklewich face fines of $500,000 each and up to five years in prison on each of the 20 counts. They also will have to repay all the people who bought their phony products, an amount estimated at $3 million.

**Bankruptcy Snarls Device Seizure**

You never know what you might pick up at an auction—an unrecognized painting by a master, a priceless family heirloom, a letter written long ago by a famous personality. Or, you might buy eye surgery devices. At least that's what one medical device manufacturer gained when it bought the assets and building lease of another at a bankruptcy auction. But the $200,000 worth of instruments ended up in a Tucson, Ariz., landfill.

Trueline Instruments, manufacturer of the devices, had a history of poor manufacturing practices that allowed its instruments to become contaminated with chemicals and foreign particles. The firm, which moved to Tucson from Colorado in 1982, was first inspected by FDA's Tucson resident post in February 1985. The inspectors found deficiencies in the firm's sterile controls, manufacturing processes, manufacturing materials, and record keeping.

Trueline promised to make the corrections necessary to come into compliance.
with FDA's good manufacturing practices. But subsequent inspections in October 1985 and June 1986 found continuing problems with dust on finished devices in the clean room, and inadequate control of environmental conditions and manufacturing materials such as water, steam and nitrogen. These poor manufacturing conditions, described by an FDA compliance officer as "generally out of control," could lead to infection of a patient if the contaminated instruments were used for eye surgery. (FDA, however, has received no reports of injuries.)

Because of the potential health hazard, FDA filed a complaint for seizure with the U.S. District Court for the District of Arizona in October 1986, after having once more inspected the firm earlier that month. The agency requested seizure of Trueline's 1/A coaxial hand pieces and kits—devices used to irrigate the eye and aspirate fluid from it during surgery.

At the time, Trueline was operating under Chapter 11 of the bankruptcy code, which confers protection from creditors. (It had filed for bankruptcy in November 1985 after one of its major contracts was cancelled.) The firm's bankruptcy status created a question as to whether or not the government could seize the devices. In some instances, law enforcement agencies are "stayed" from proceeding against a bankrupt firm's assets in order not to hinder its ability to recover. However, it was determined that those provisions do not apply if protecting the public health is at issue. The goods were seized Nov. 19, 1986.

In May 1987, FDA's Tucson resident post investigator Andrew Bonanno visited Trueline and found the doors locked and the building empty. After some checking, he discovered that Trueline had been converted to Chapter 7 bankruptcy—dissolution—on May 7. Even though the firm was out of business, Bonanno conducted another inspection the next month. At that time, the firm was under the responsibility of a court-appointed trustee, Alan Solot. Since Solot was not allowed to give away or sell any of Trueline's assets, Bonanno had to get permission from U.S. Bankruptcy Judge Lawrence Ollason to remove samples of the devices for testing. Bonanno found that several faulty manufacturing practices had been corrected, but laboratory analysis of the samples still showed contamination and problems in workmanship. Foreign particles were found in internal areas of the devices that could come into contact with fluids introduced into the eye during surgery.

Aware that the items were slated to be sold at auction soon, FDA wrote to Solot in August 1987, advising him of the problems with the devices and urging that any lots intended for eventual sale by a future owner first be tested for quality. The letter also stated that the agency intended to see that defective products did not enter the marketplace.

On Sept. 1, Bonanno initiated another inspection of Trueline. He presented Solot with a list of products selected for sampling, requesting that Solot's attorney obtain a court order allowing FDA to take the samples. Despite repeated calls to Solot and the attorney over the next six weeks, Bonanno got no answer. Finally, after Judge Ollason intervened, the court order was signed Oct. 20 and the samples collected the next day.

Enter Myocure, Inc. A manufacturer of ophthalmic devices headquartered in Glendale, Calif., Myocure purchased Trueline's assets at the auction. FDA's Tucson office contacted Myocure to discuss the agency's concerns about the devices and request that the new owner destroy them. In the meantime, in case Myocure declined to destroy them voluntarily, the agency took steps to have the devices detained until they could be seized.

Myocure promised to respond to FDA by Nov. 6. By Nov. 9, however, FDA still had not heard from the firm and so the devices—totaling more than 15,000 disposable and reusable products valued at $200,000—were detained. At FDA's request, they were seized by U.S. marshals on Dec. 8, 1987, and destroyed May 16, 1988.

**Leaky Condoms**

The resurgence of the condom as a method of disease prevention and birth control has led FDA to redouble its efforts to inspect the devices for leaks and holes. One such effort resulted in the destruction of approximately 44,000 condoms on Nov. 29, 1988—three months after FDA went to court to have them seized.

The agency had filed suit in September in the U.S. District Court in St. Paul, Minn., requesting that condoms manufactured for Mentor Corporation be seized because they contained too many holes. FDA routinely tests domestic and imported condoms for leakage. If more than four condoms per batch (1,000 condoms) leak, the batch may be recalled by the manufacturer or detained by FDA. (The condoms are filled with 300 milliliters of water to check for leakage or rupture.) According to Larry Murphy, supervisory chemist in FDA's laboratory in Minneapolis, six condoms in the Mentor batch were faulty: Four ruptured during the water test and two leaked.

"This is considered a high number of ruptures," said Murphy.

Since April 1987, FDA has intensified its inspection of condoms because of concern over sexually transmitted diseases, including acquired immune deficiency syndrome.

From April 1987 through June 1988, FDA had tested over 150,000 condoms taken from 633 manufacturing lots. From this testing, FDA found that 11 percent of the domestic and 21 percent of the imported lots had more than four defective condoms per 1,000. In most cases, domestic manufacturers recalled or destroyed the defective batches, and the lots of foreign manufacturers were refused entry.

Despite this rate of defects, "the quality of condoms has significantly improved since . . . we first stepped up inspection," said Doyle Smith of FDA's division of field sciences. He said that domestic condoms went from a defect rate of five per thousand to two per thousand. Similar improvements were noted for imported condoms.

"—This small sample of reports from the field was prepared by Judy Folkenberg, Vern Modeland, and Marian Segal."
Summaries of Court Actions are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Summaries of Court Actions report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against goods alleged to be in violation, and criminal and injunction proceedings are against firms or individuals charged to be responsible for violations. The cases generally involve foods, drugs, devices or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce or while held for sale after shipment in interstate commerce.

Summaries of Court Actions are prepared by Food and Drug Division, Office of the General Counsel, HHS. Published by direction of the Secretary of Health and Human Services.

**SEIZURE ACTIONS**

**Foods/Contamination, Spoilage, Insanitary Handling**

**PRODUCT:** Cheese, cheddar, at Lowville, N. Dist. N.Y.; Civil No. 88-CV-561.
CHARGED 5-20-88: While held for sale, the article contained pieces of wood, paint, rust, pebbles, scale from unknown sources, and other unidentified objects—402(a)(3).
DISPOSITION: Consent—ordered destroyed. (F.D.C. No. 65462; S. No. 88-501-390 et al.; S.J. No. 1)

**PRODUCT:** Conch meat, frozen, at Catano, Dist. Puerto Rico; Civil No. 88-00151(PG).
CHARGED 1-28-88: While held for sale, the article contained decomposed conch meat—402(a)(3).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65369; S. No. 88-512-405 et al.; S.J. No. 2)

**PRODUCT:** Conch meat, frozen, at Catano, Dist. Puerto Rico; Civil No. 88-00150(JP).
CHARGED 1-28-88: While held for sale, the article contained decomposed conch meat—402(a)(3); and, when shipped by Florida Fresh Seafood, Miami, Fla., the article lacked a label containing the name and place of business of the manufacturer, packer or distributor—403(e).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65368; S. No. 88-512-405 et al.; S.J. No. 3)

**PRODUCT:** Crab meat, frozen, at Forth Worth, N. Dist. Texas; Civil No. 4-88-6-E.
CHARGED 1-5-88: When shipped by WF&F Co., Inc. (Klein's Seafood), Port Allen, La., the article had been prepared, packed and held under insanitary conditions—402(a)(4).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65353; S. No. 88-528-182 et al.; S.J. No. 4)

**PRODUCT:** Mung beans, at Seattle, W. Dist. Wash.; Civil No. C-88-848.
CHARGED 6-30-88: While held by Sprouts Garden, Seattle, Wash., the article had been held under insanitary conditions, and some lots of the article contained rodent filth—402(a)(3), 402(a)(4).
DISPOSITION: Consent—authorized release to the dealer for salvaging. (F.D.C. No. 65493; S. No. 88-501-390 et al.; S.J. No. 5)

**PRODUCT:** Pineapple chunks, canned, at Philadelphia, E. Dist. Pa.; Civil No. 88-2496.
CHARGED 3-24-88: While held for sale, the article was unfit for food, since it was in rusted, swollen and leaking cans—402(a)(3).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65406; S. No. 88-570-430; S.J. No. 6)

**PRODUCT:** Popcorn, at Peru, N. Dist. 111.; Civil No. 88 C 3002.
CHARGED 4-7-88: While held for sale, the article contained rodent filth—402(a)(3).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65433; S. No. 88-435-792 et al.; S.J. No. 7)

**PRODUCT:** Popcorn, candy, and candy components, at Glennville, S. Dist. Ga.; Civil No. 688-035.
CHARGED 3-16-88: While held by Mascot Candy Co., Glennville, Ga., the articles had been held under insanitary conditions—402(a)(4).
DISPOSITION: Consent—authorized release to the dealer for salvaging. (F.D.C. No. 65415; S. No. 88-435-792 et al.; S.J. No. 8)

**PRODUCT:** Rice, at Los Angeles, C. Dist. Calif.; Civil No. 88-02001-ER(Bx).
CHARGED 4-13-88: While held by Ritop International, Inc., Los Angeles, Calif., the article had been held under insanitary conditions—402(a)(4).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65427; S. No. 88-444-386; S.J. No. 9)

**PRODUCT:** Rice, at St. Louis, E. Dist. Mo.; Civil No. 88-0154-C-2.
CHARGED 1-27-88: While held by HRB transportation, St. Louis, Mo., the article had been held under insanitary conditions—402(a)(4).
DISPOSITION: Consent—ordered destroyed. (F.D.C. No. 65370; S. No. 88-526-181 et al.; S.J. No. 10)
PRODUCT: Wheat, winter, in bulk, at Portland, Dist. Ore.; Civil No. 88-340-FR.
CHARGED 3-30-88: When shipped by Billings Grain Terminal, Billings, Mont., the article contained insect filth—402(a)(3).
DISPOSITION: Consent—authorized release to the shipper for salvaging (conversion to gasohol). (F.D.C. No. 65421; S. No. 88-423-106 et al.; S.J. No. 11)

Foods/Economic and Labeling Violations

PRODUCT: Cucumbers, pickled, canned, at Chatsworth, C. Dist. Calif.; Civil No. 87-07472IH.
CHARGED 2-2-88: When imported, the article, labeled “1 & I Pan American Pharmaceuticals Inc. Grand Rapids, Michigan” and lacked the common or usual name of each of the article’s ingredients—403(i)(2).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65136; S. No. 86-472-654 et al.; S.J. No. 16)

Drugs/Human Use

PRODUCT: Cough syrup, at Bohemia, E. Dist. N.Y.; Civil No. CV 88-1097.
CHARGED 4-14-88: While held for sale after manufacture by Proper-Chem Limited, Farmingdale, N.Y., using interstate dextromethorphan hydrobromide, the circumstances used in the article’s manufacture failed to conform with current good manufacturing practice—501(a)(2)(B); the article’s strength differed from or its purity or quality fell below its purported purity or quality, because the potency of the active component labeled as dextromethorphan was less than declared on the label—501(c); and the article’s label lacked the established name of the active ingredient dextromethorphan hydrobromide—502(c).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65405; S. No. 88-429-655 et al.; S.J. No. 14)

PRODUCT: Promise potassium nitrate & sodium monofluorophosphate toothpaste, at Jersey City, Dist. N.J.; Civil No. 83-3302(HLS).
CHARGED 9-1-83: When shipped by Block Drug Co., Inc., Memphis, Tenn., the article was a new drug without an effective approved New Drug Application—505(a).
DISPOSITION: The article was claimed by the shipper, who denied the charge and asserted affirmative defenses. The government filed a motion to amend the complaint to request injunctive relief against the claimant. The government served written interrogatories, requests for admissions, and requests for the production of documents. The claimant opposed the amendment of the complaint and moved for a stay of the action until a similar action in the Northern District of Illinois had been litigated. The court noted that the government’s motion to amend was invalid because it had not been filed before the defendant’s answer, with leave of court or with consent of counsel. The court balanced the various factors to be considered in deciding whether to grant a stay and stated that Congress had chosen to tilt such balancing in favor of the claimant. Accordingly, the court granted the claimant a stay. Ultimately, after the government had prevailed in the similar action, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 64077; S. No. 83-337-179 et al.; S.J. No. 15)

PRODUCTS: Stimulac colostrum concentrate in vials, colostrum capsules, IMU All-Purpose ointment, and other dried milk products for drug use, at Toronto, Dist. S. D.; Civil No. 87-1011.
CHARGED 4-13-87: While held by IMU, Inc., Toronto, S.D., the labeling of the articles lacked adequate directions for their intended use (strengthening the immune system to cure or treat arthritis, cancer, multiple sclerosis, and leukemia), and the articles were not exempted due to their new drug status—502(f)(1); and the labeling of the articles had false and misleading claims for strengthening the immune system to cure or treat arthritis, cancer, multiple sclerosis, and leukemia in man—502(a).
DISPOSITION: Consent—decreet authorized release to IMU, Inc. (Sterling Technology, Inc.), Toronto, S.D., for salvaging for animal use (strengthening the immune system to cure or treat arthritis, cancer, multiple sclerosis, and leukemia in man—502(a).

Drugs/Veterinary

PRODUCT: Ivermectin injection for cattle, at Billings, Dist. Mont.; Civil No. 87-94-BLG-JFB.
CHARGED 4-13-87: While held by Western Ranch Supply, Co., Inc., Billings, Mont., who was removing the manufacturer’s lot number from the labels of the article, the manufacturer’s lot number had been removed from the article—502(c).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65136; S. No. 87-370-549 et al.; S.J. No. 17)

PRODUCT: Prednisolone sodium phosphate drops, at Irvine, C. Dist. Calif.; Civil No. 87-07421H.
CHARGED 11-6-87: While held for sale, the article, which was labeled “Predni-Drops Liquid Prednisolone . . . Manufactured for: Pan American Pharmaceuticals Inc. Grand Rapids, Michigan”
and
which was manufactured using prednisolone sodium phosphate, was a new animal drug, since no approval of a New Animal Drug Application was in effect with respect to its intended use—501(a)(5).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65295; S. No. 87-460-237 et al.; S.J. No. 18)

**Medical Devices**

PRODUCT: **Hyperbaric oxygen chamber**, at Corpus Christi, S. Dist. Texas; Civil No. C-86-97.

CHARGED 6-23-86: The article, which had been manufactured by Frenco Labs Dallas, Texas,” had not had the required notice to FDA (to determine the device classification) provided by the manufacturer—502(q).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 64730; S. No. 85-261-308; S.J. No. 19)

PRODUCT: **Ophthalmic devices, various**, at Tucson, Dist. Ariz.; Civil No. 87-911 TUC-RMB.

CHARGED 12-8-87: The articles, which had been manufactured by: TrueLine Instruments, Inc., Tucson, Ariz., and which had been sold

...and fraudulent statements, in that the defendant falsely stated that she had obtained the patient's consent and had witnessed the patient sign the consent forms—18 U.S.C. 1001.

DISPOSITION: Guilty plea; probation for two years and 200 hours of community service. (Misc. No. 643; S.J. No. 22)

**CIVIL PENALTY ACTIONS**

DEFENDANTS: Karlberg European TanSpa, Inc., and Ann Karlberg, president, Rockford, N. Dist. III.; Civil No. 86-C-20425.

CHARGED 12-10-86 in a complaint for civil penalties and injunction: That the defendants imported, sold and shipped electronic products (including ultraviolet lamps and suntanning beds); that the defendants had imported 500 high-intensity discharge ultraviolet lamps, which were violative as follows: failed to meet irradiance ratio limits; were not properly labeled; lacked the required certification; and lacked required identification—42 U.S.C. 263j(a)(1); that the defendants failed to issue a certification for the ultraviolet lamps; that the defendants imported and distributed to recipients at Carmel, Ind., St. Peters, Mo., Crown Point, Ind., O’Fallon, Mo., and Washington, Mo., a number of specified suntanning beds which were violative in one or more of the following ways: lacked instructions for safe use; incorporated ultraviolet lamp that did not meet irradiance ratio limits; lacked reproduction of label in user’s instructions; not accompanied by protective eyewear; maximum timer interval exceeded 30 minutes; and no means for user to manually terminate radiation emission—42 U.S.C. 263j(a)(1); that the defendants had been warned that their ultraviolet lamp and suntanning beds did not comply with the law; and that, despite such warning, the defendants continued to import violative ultraviolet lamps and to import and distribute non-complying suntanning beds.

DISPOSITION: A consent decree of permanent injunction perpetually restrained and enjoined the defendants from the complained-of violations and also imposed total civil penalties of $8,500. (Misc. No. 779; S. No. 84-345-390 et al.; S.J. No. 23)

**INJUNCTION ACTIONS**

DEFENDANT: George A. Bragg, t/a Bragg’s Fish Market, Guntersville, N. Dist. Ala.; Civil No. 86-C-1922-M.

CHARGED 10-6-86 in a complaint for injunction: That the defendant bought, cleaned, packed, held, and distributed in interstate commerce buffalo fish and catfish; that such fish had been caught in local rivers and lakes contaminated with polychlorinated biphenyls (PCBs) and the banned pesticide DDT; that the fish sold by the defendant contained the added poisonous and deleterious substances PCBs and also contained the nonconforming pesticide DDT and its metabolites DDE and TDE—402(a)(2)(A), 402(a)(2)(B); that FDA analyses showed that five samples of the defendant’s fish contained PCBs greater than 2 parts per million and DDT metabolites greater than 5 parts per million; that the defendant had acknowledged his awareness of the PCB and DDT problems in northern Alabama, but, despite lacking procedures to test for contaminants, he had continued to buy fish that might have been caught in contaminated waters.

DISPOSITION: A consent decree of permanent injunction enjoined the interstate shipment of fish unless and until a number of specified conditions had been met, including submission of samples of fish to a laboratory for testing so that no fish contaminated with...
PCBs or DDT or its metabolites would be shipped in interstate commerce. (Inj. No. 1157; S. No. 84-435-882 et al.; S.J. No. 24)

DEFENDANTS: Condon Grain Growers, Inc., and Melvin Pattee, president, and Franklin D. Bauman, general manager, Condon, Dist. Ore.; Civil No. 86-635 PA.

CHARGED 5-21-86 in a complaint for injunction: That the defendants received, processed, fumigated, stored, and distributed in interstate commerce the raw agricultural commodity wheat; that, when shipped and while held for sale, such interstate wheat contained the pesticide chemical malathion in excess of the prescribed tolerance of 8 ppm—402(a)(2)(B); that FDA inspections disclosed that the defendants regularly treated their grain storage bins, when empty, with malathion dust, and that the firm treated all incoming grain with a solution of malathion at the rate of one pint malathion per 1,000 bushels; that FDA laboratory analyses of wheat samples revealed excessive malathion residues at levels of from 18 to 47 ppm; that portions of such adulterated wheat had been processed in Hawaii and had resulted in a recall of approximately 2.5 million pounds of flour products; and that, unless restrained by the court, the government believed there was substantial likelihood that the defendants would continue to violate the law.

DISPOSITION: Pursuant to stipulation of the parties, the court entered an order reflecting that the defendant firm had agreed to make no shipments of wheat from any of its facilities until laboratory analyses confirmed that any wheat to be shipped did not contain levels of malathion in excess of the established tolerance. The firm also agreed to segregate all wheat received at its facilities after July 2, 1986. Subsequently, the parties filed a consent decree of permanent injunction enjoining wheat shipments without FDA approval. (Inj. No. 1142; S. No. 86-465-493 et al.; S.J. No. 25)

MISCELLANEOUS ACTIONS

SUBJECT: Claim of non-patent exclusivity rights for Desyrel (trazodone HCl), and FDA denial of such claim. Washington, Dist. Columbia; Civil No. 85-3971 and, upon appeal, 87-5099.

CHARGED 12-20-85 by Mead Johnson Pharmaceutical Group (Mead Johnson & Co.), Evansville, Ind., against HHS Secretary Margaret M. Heckler, FDA Commissioner Frank E. Young, M.D., and the United States Food and Drug Administration, in a complaint for declaratory judgment and injunction: That the plaintiff researched, developed, manufactured and marketed certain pharmaceutical products, including the antidepressant drug Desyrel (trazodone HCl); that, as a transitional measure, the Drug Price Competition and Patent Term Restoration Act of 1984 provided for a 10-year term of retrospective exclusivity for pioneer new chemical entities having New Drug Application (NDA) approvals granted between Jan. 1, 1982, and Sept. 24, 1984 (drugs approved before 1982 enjoyed no exclusivity at all); that the plaintiff had filed a New Drug Application for Desyrel; that, on Dec. 21, 1981, FDA had advised that Desyrel's NDA had been reviewed and the plaintiff would have to submit final labeling incorporating certain changes before the drug would be approved; that the plaintiff had agreed to the specified label changes; that the plaintiff had received an FDA letter dated Dec. 24, 1981, stating the following: the NDA covering Desyrel was approved with the understanding that final printed labeling would be promptly submitted and revised before the drug was marketed, and the marketing of Desyrel was prohibited until the required labeling was submitted; that, although such letter "purported to be an 'approval' letter, under the explicit terms of the letter, the 'approval' would not actually occur at least until the final printed labeling was submitted"; that the final printed labeling was submitted on Jan. 19, 1982; and that a Feb. 1, 1982, letter from FDA advised that such labeling was approved.

The plaintiff's complaint also recited the steps that had been taken to exhaust its administrative remedies by requesting, without success, FDA recognition of rights to 10 years of non-patent exclusivity for Desyrel. Accordingly, the plaintiff prayed that the court declare the plaintiff's entitlement to such rights, and issue an injunction ordering FDA to amend its "Approved Drug Products" publication, so as to refer to such rights, and that the court order that FDA not grant any Abbreviated or "paper" NDAs for trazodone HCl without the plaintiff's consent or authorization.

DISPOSITION: District Court—The parties both moved for summary judgment. Meanwhile, two other drug manufacturers filed amicus briefs that argued that such drug manufacturers had relied on the plaintiff's prior representations of a 1981 approval date. In granting the government summary judgment, the court noted that it was only as the plaintiff's patent protection was about to expire that the plaintiff had changed its position with regard to Desyrel's approval date and asserted a 1982 approval date. The court took, as the basis for its review, the arbitrary and capricious standard of Section 706 of the Administrative Procedure Act (APA), and noted that FDA's decision as to Desyrel's approval date had been based on FDA's own consistently interpreted regulations (21 C.F.R. 341.105) and on FDA's longstanding policy with respect to the implementation of section 355. The court found that, not only did FDA base its decision on a consideration of the relevant factors, but did so in a "thorough, well reasoned and fully explicated manner." Since FDA had considered the plaintiff's arguments and had decided upon a rational basis supported by the administrative record, the court ruled for FDA, finding that FDA's determination that Desyrel was approved in 1981 did not violate section 706 of the APA. The plaintiff appealed.

Court of Appeals—The appellate court said that the plaintiff's entitlement to exclusivity for its drug turned solely on whether the Desyrel NDA had been "approved" by FDA before or after Jan. 1, 1982, that there was little dispute about the facts, and that the case centered on the meaning of the term "approved." The Court of Appeals held that FDA's interpretation of "approved" in 21 U.S.C. Section 355(j)(4)(D)(i) was consistent with congressional intent and that, even if the term "approved" might be viewed as ambiguous, it was clear that FDA's construction was a permissible one. (Misc. No. 794; S.J. No. 26)
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