

^{FDA} CONSUMER

VOL. 21 NO. 5

JUNE 1987

Out of
the
Bronzed
Age





Experimental Drugs for the Desperately Ill

Commissioner Frank Young explains how FDA is making it easier for patients suffering from life-threatening or other serious diseases to obtain promising but unproven drugs that may be their only hope.

Still a Killer: Pneumonia Targets the Ill, the Elderly

Despite antibiotics, pneumonia is the sixth leading cause of death in the United States. The elderly are at special risk, as are those suffering from serious and chronic illnesses, such as AIDS.

Summer Food Safety Tips

People aren't the only ones who enjoy the warmth of summer. At picnics, camp-outs and other outdoor gatherings, microscopic pests that can make us sick thrive in improperly stored foods. Here's how to send these "bugs" packing.

Out of the Bronzed Age

It's hard to believe that not long ago many of us sought a tan as a symbol of good health. Now, sunscreen sales are soaring, and no one who cares about wrinkles would be caught dead under a sunlamp.

First Aid for Pets

If Spot started to choke on a bone, or your cat Morris suffered frostbite, what would you do? First aid can be as important to your pets as to the human members of your family. Two FDA veterinarians offer some guidance.

Test-Tube Skin and Other High-Tech Treatments for Burns

When burns are so extensive that more skin is lost than is left, what can doctors substitute for the traditional skin grafts? Medical high-tech may have the answers: synthetic skin and human skin grown in a laboratory.

Can Herbs Really Heal?

Herbal medicine is espoused by some as the only means to "natural" good health. Others condemn it as unmitigated quackery. Where lies the truth? And what about the safety of herbs in drugs, foods and cosmetics? It's FDA that tries to find the answers.

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People aren't the only ones who need first aid from time to time. For some expert advice on how to handle our pets' medical emergencies, turn to page 24.

Experimental Drugs for the Desperately Ill

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

When I was directing the medical center at the University of Rochester in New York, people occasionally would come to me who had a spouse or child suffering from some untreatable disease or who were themselves desperately ill. They'd ask my help in obtaining some promising but still experimental treatment. Sometimes they had heard that the treatment—usually a new drug—was being tested at the National Institutes of Health in Bethesda, Md. “But I don't have the money to move myself and my family there,” they'd say. “If I can't get this treatment, there's no other hope. Dr. Young, is there anything you can do?”

I'd have to try to explain that the controlled clinical trials such as were being done at NIH were necessary, even though they took precious time. If they proved successful, in another year or two the drug could be approved by FDA and I could obtain it for my patients. “But, Dr. Young,” they'd reply, “my wife will be dead in six months.”

The memory of such anguish and hopelessness still haunts me. But now, a regulation recently proposed by FDA holds the promise of hope for many of those desperately ill patients and their loved ones. This new rule acknowledges that there are times when a new experimental drug shows such promise—especially when it is for a life-threatening condition for which there is no other hope—that it seems unethical and even cruel to withhold it from desperate patients.

It is a fine line that public health officials must walk to protect the public from unsafe or useless drugs while allowing them access to some as yet unproven treatment that may be their last hope. The terrible disease AIDS has brought this issue to public scrutiny as never before.

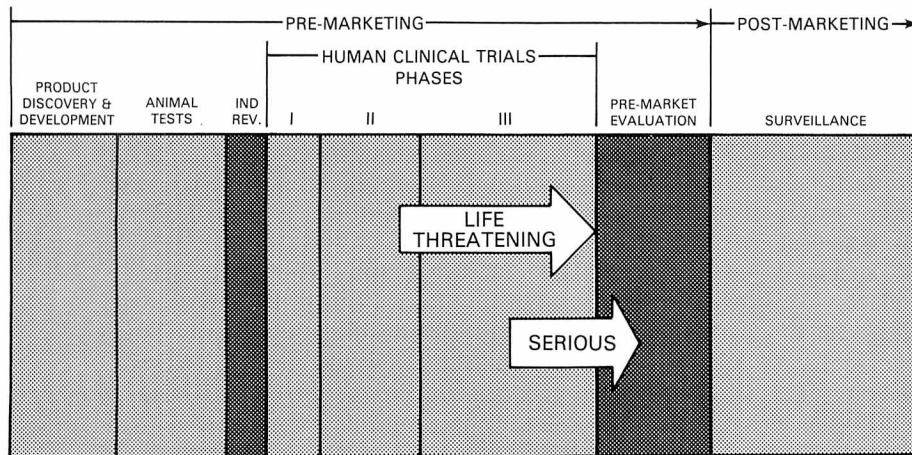
FDA does have the discretion to allow broader use of important experimental drugs when studies indicate some real promise, even though the final verdict is not yet in. In fact, for more than a decade, FDA has allowed thousands of patients access to promising new drugs that were still in the experimental stage of development. Most notably, experimental drugs called beta blockers, used to treat certain heart conditions, were made available in the mid-1970s to patients who couldn't tolerate other drugs. Many beta blockers are now approved as safe and effective treatments, due in part to information reported by the doctors who were using them experimentally to treat their patients.

More recently, after early studies last year showed very promising results, it took FDA only one week to approve broader use of an experimental drug for AIDS patients called azidothymidine (AZT). This enabled more than 4,000 patients to receive the drug while it underwent final review at FDA. And on March 20, FDA approved the drug (marketed under the brand name Retrovir by Burroughs Wellcome Co.) as safe and effective for helping certain patients with AIDS and advanced AIDS-related complex. The agency's review and approval was accomplished in less than four months—one of the shortest approval actions on record.

The new rules proposed by FDA could bring such promising and important—but still experimental—drugs to desperately ill patients years earlier than is now the case. These new procedures are proposed to apply to immediately life-threatening conditions, recognizing that in those cases patients are willing to accept a greater risk, since there may be no other hope. There would also be new criteria for diseases that are serious but not immediately life-threatening. The rules would apply where no other satisfactory treatment exists.

FDA anticipates that approvals for expanded studies of drugs for immediately life-threatening diseases could be given near the end of the second phase of clinical testing; that is, after the drug's safety testing has been done and the proper dose determined, and after some evidence of therapeutic benefit is available. Approval for

NEW DRUG PROCESS: TREATMENT USE



expanded uses of experimental drugs for serious but not immediately life-threatening diseases would ordinarily occur at the middle of the third and final phase of testing. That is the stage at which the preliminary evidence of safety and effectiveness established in earlier studies is being verified before marketing approval is finally sought from FDA. We trust that these procedures will allow clinical trials to continue unfettered while permitting physicians and patients—with their informed consent—to obtain access to breakthrough drugs earlier than usual. Recent FDA approvals of the expanded availability of protropin—a cloned form of human growth hormone—and AZT while both drugs were still experimental illustrate the proposed new policy. In each case, the agency weighed the potential risks against the potential benefits when no alternative therapy existed.

The new rules would allow for the sale of such experimental drugs to help ensure that drug companies have enough incentive to make them available. This would also promote greater competition by allowing small companies to test products that are extremely expensive to produce, such as those made through biotechnology.

Nevertheless, it would not be appropriate to make drugs widely available too early in the development process. While dying patients may be willing to “try anything,” it would be irresponsible—and far from compassionate—to raise false hopes. The risks of a drug, as well as its benefits, must be measured very carefully. There are very few conditions, not even AIDS, that can’t be made worse. For example, the once-promising AIDS drugs HPA-23 and suramin turned out to be so toxic that they are no longer being studied. It’s not easy to be patient amid reports of dramatic results with a new drug for AIDS or Alzheimer’s disease, for instance. But it’s not always easy, or even possible, to tell whether those early findings are real.

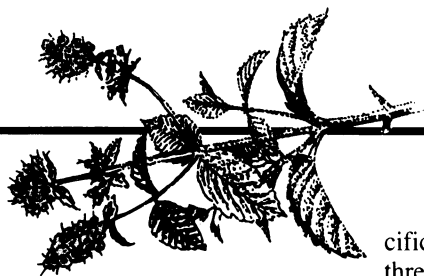
As FDA grapples with these decisions, each new drug will have different considerations that must be weighed on its own merits. Obviously, the seriousness of the illness and the lack of any other effective treatment play a large role in deciding whether to make a drug available. When a drug has been studied extensively and is in the final stage of testing, we would rarely say no to a doctor who wanted to give the drug to a patient. In fact, we must be sure that we’re doing everything possible to get promising drugs—whether they’re for AIDS or other serious conditions—to as many patients as possible, just as soon as we have the information to make a reasonable judgment.

We need to be flexible as we weigh risks against benefits in deciding whether to expand the use of experimental drugs. But we also need to recognize that there will never be a “no risk” decision. We have to recognize our limitations, while moving ahead with the information we have. Always we must let science provide the light and compassion guide the way. ■

The arrows on this chart show when a promising experimental drug can be made available to additional desperately ill patients, under a rule recently proposed by FDA. With drugs for immediately life-threatening conditions, expanded availability could begin near the end of the second phase of human testing—that is, after the drug’s initial safety testing has been done and the proper dose determined (Phase I), and after some evidence of therapeutic benefit has been obtained (Phase II). For serious but not immediately life-threatening illnesses, approval for expanded treatment availability could occur sometime during the third and final phase of testing. During Phase III, early evidence of safety and effectiveness is being verified before marketing approval of the drug is finally sought from FDA. Once granted, FDA approval of an investigational drug for treatment use would normally continue until regular marketing of the drug begins. (“IND Rev.” means FDA review of an investigational new drug application, approval of which is necessary before a drug can be tested in people.)



Updates



Nature Worship

Some manufacturers of personal care products must have Mother Nature on the payroll. According to a recent report by a New York marketing firm, botanical/natural-based products now account for 16 percent of all manufacturer sales in personal care products—\$1.3 billion out of an \$8.1 billion market in 1985—and this is growing.

Botanicals include such ingredients as aloe vera, henna, mint and yucca (recently added to many shampoos and other products, often for its foaming properties). Collagen and musk also are commonly used natural ingredients.

A third of all soaps, shampoos and hair conditioners contain botanicals, according to the report. More than a fifth of hand and body lotion sales, and a fifth of facial moisturizer sales come from brands with natural or botanical ingredients.

Skin-care products make up over half of the botanical/natural personal care market, the report says. The market share held by oral care and personal hygiene products, which are, in many cases, over-the-counter drugs, is much smaller. The report indicates that this is due in part to tests required by FDA that are difficult to meet with natural ingredients.

New Rules for Testing Drugs

The Food and Drug Administration's final rules for testing new drugs in humans will allow greater freedom for drug researchers in designing their studies without jeopardizing the safety of patients.

These new rules for investigational new drug (IND) applications, which go into effect June 17, give drug sponsors more control over the design of their first set of human tests as long as there are no unreasonable, significant risks to the patients. The rules also give sponsors the opportunity to meet with FDA scientists to discuss research plans and, once research on a new drug shows significant promise, to discuss what further testing is needed to secure marketing approval. "This cooperation will bring safe and effective new drugs to the American public more quickly, reducing the possibility of disputes and delay later on during the drug approval process," said FDA Commissioner Frank E. Young, M.D.

Unlike the previous regulation, which required drug sponsors to notify FDA about an unexpected death or life-threatening reaction "immediately," but set no spe-

cific deadline, the new regulation gives the sponsor three days to notify the agency by telephone. Similarly, a requirement that other serious reactions be reported "promptly" has been replaced by a specific deadline of 10 days.

In addition to these final rules, published in the *Federal Register* on March 19, FDA has proposed new steps to bring investigational drugs to seriously ill patients long before the drugs would normally be available to the general population. For more information on this proposal, see "Experimental Drugs for the Desperately Ill" on page 2.

First AIDS Drug Approved

Many AIDS sufferers cling to the hope that a cure will soon be found for their deadly disease. The challenge is keeping alive until that happens. For some, help in meeting that challenge comes in the form of a drug called AZT.

The first treatment for AIDS (acquired immune deficiency syndrome) approved by the Food and Drug Administration, AZT (azidothymidine, also known as zidovudine), is not a cure. But it can improve the short-term survival of AIDS patients with *Pneumocystis carinii* pneumonia and of patients with advanced AIDS-related complex (ARC). (ARC is a condition that frequently precedes and develops into AIDS within a short time. Patients with ARC have a greatly reduced number of T-helper lymphocytes, critical elements of the immune system that are destroyed by the AIDS virus. Symptoms include weight loss, persistent fever, and diarrhea. ARC sufferers contract less severe opportunistic infections—such as oral candida and herpes—than AIDS patients.)

According to Robert E. Windom, M.D., assistant secretary for health, approximately 32,000 Americans had been afflicted with AIDS by March 1, 1987. Of those, about 14,000 are still living. He noted that available clinical data were sufficient for approving the use of AZT only for certain indications—specific laboratory evidence of severely depressed immunity or a history of *Pneumocystis carinii* pneumonia. But he said that even with those restrictions, AZT could mean "significant medical relief" to thousands of AIDS and ARC patients.

However, in some patients, AZT has dangerous side effects, chiefly severe anemia. In addition, the drug has not been shown to reduce the risk of transmission of



AIDS through sexual contact or blood transfusions.

AZT was originally developed in 1964 by Dr. Jerome Horowitz of the Michigan Cancer Foundation as a possible treatment for cancer. In February 1985, the National Cancer Institute, under the direction of Dr. Samuel Broder, tested AZT and found that it was a potent inhibitor of AIDS.

FDA's review and approval of the New Drug Application for AZT took less than four months—one of the shortest approval actions on record.

AZT is being marketed by Burroughs Wellcome Company of Research Triangle Park, N.C., under the trade name Retrovir.

Laser Clears Clogged Leg Arteries

FDA has approved the marketing of a laser device to remove fatty deposits obstructing certain arteries in the legs. It is the first approved use of a laser to treat a vascular (blood vessel) disorder.

Until now, obstructed arteries have been treated either with surgery or with balloon angioplasty, in which a tiny balloon is threaded into the blood vessel and then inflated to squash the fatty deposit. The balloon process is far less expensive and less risky than surgery, but it can't be used when the fatty deposits completely obstruct the artery, or when the obstructions are hardened by calcium deposits.

However, the new laser device can burn a tiny hole through those difficult obstructions so that the balloon can enter and finish the job.

The device combines a metal-tipped, fiberoptic probe with an argon laser. It is threaded through the artery to the point of the obstruction, and then the laser is used to heat the metal tip to about 400 degrees Celsius (about 750 degrees Fahrenheit). As the hot tip is pushed through the blockage, it vaporizes the deposits, creating a channel wide enough to introduce a balloon catheter.

This device greatly reduces the risk of accidentally burning the vessel itself, because the laser's rays are used only to heat the metal probe. The laser never comes in direct contact with the inside of the blood vessel.

FDA's approval covers only obstructed arteries in the leg that are difficult or impossible to treat with balloon angioplasty alone. The device is not intended to unblock coronary arteries, where the principal forms of treatment remain either bypass surgery or balloon angioplasty.

Trimedyn, Inc., of Santa Ana, Calif., is the manufacturer of the device.

FDA Asks Recall of Danthron Laxatives

The Food and Drug Administration has requested an immediate halt to all manufacturing and distribution of laxatives that contain the drug danthron because it may cause cancer.

Recent studies found that when high doses of danthron were given to rats and mice over a long time, the rodents developed intestinal and liver tumors, leading to the conclusion that the drug is a potential risk to humans. Toxicity of danthron in humans has not been demonstrated.

A number of manufacturers of drugs containing danthron have voluntarily agreed to remove their products from the market. FDA issued its request March 30. The affected laxatives are not the more popular ones seen in various advertisements and make up only a small percent of the market. For more about laxatives, see "Laxatives Overused in the Quest for 'Regularity'" in the May 1985 *FDA Consumer*.

DTP Shots Shouldn't Wait

A delay in the vaccination schedule for immunizing infants against diphtheria, tetanus and pertussis (whooping cough) would result in a substantial number of new cases of pertussis in the United States, according to a report in the *Journal of the American Medical Association*.

The report said that the current schedule, where infants receive the combined diphtheria, tetanus and pertussis (DTP) vaccine at 2, 4 and 6 months of age, is associated with less disease than when vaccinations are delayed until 8, 10 and 12 months. The report's authors used a computer model that predicts the health effects of a schedule change to show that an additional 636 cases of pertussis—115 of which would be associated with complications, including two cases of encephalopathy (degenerative brain disease)—would occur under the proposed schedule, as compared to the current one. The incidence and severity of pertussis in early infancy is higher than at any other time of life.

In the report, published in the March 13 issue of *JAMA*, the authors, Ann W. Funkhouser, M.S., et al., observed that the risk of adverse reactions to the DTP vaccine, which include seizures and, rarely, brain



damage and death, prompted the idea of delaying the vaccination schedule.

For information about pertussis, see "Whooping Cough Still Threatens U.S. Children" in the June 1985 *FDA Consumer*.

Gynex Oral Contraceptives Recalled

G.D. Searle of Chicago, Ill., has voluntarily recalled all lots of its "Gynex" oral contraceptives because inert tablets may be out of sequence in the 28-day-cycle, blister-pack cards. In addition, some 21-day-cycle packages may be missing some tablets. If oral contraceptives are taken in the wrong order or skipped, the likelihood of pregnancy is increased. The recalled lots—totaling 315,000 consumer-size packages—were distributed nationwide during February. The company believes that only 2,000 to 3,000 packages could have been dispensed to consumers. The following lot numbers are included in the recall:

Gynex 1/35E-21: C33105H6, C33106H6, C33109H6, and C33101X6; Gynex 1/35E-28: C33101G6, C33102G6, C33101H6, and C33102H6; Gynex 0.5/35E-21: C31101J6; and Gynex 0.5/35E-28: C31102G6 and C31101H6.

The labels on the drugs say that Corona Pharmaceutical of Corona, Calif., manufactures and packages the contraceptives for G.D. Searle and Co.

Consumers who purchased these contraceptives should return them to the pharmacy where they were purchased and contact their physicians.

Counterfeit Pain Pills

Syntex Laboratories of Palo Alto, Calif., and FDA have identified counterfeit bottles of the company's prescription painkiller Naprosyn, a nonsteroidal anti-inflammatory drug used to treat gout, tendinitis, bursitis, and various kinds of arthritis, as well as several other painful conditions.

The counterfeit tablets appear to contain aspirin, acetaminophen or both. The aspirin-containing tablets could pose a risk for people who are allergic to aspirin or should not take it for other reasons.

Counterfeit tablets were purchased by pharmacies and wholesalers located in FDA's Los Angeles, San Francisco, Seattle, New York and Dallas districts in 500-tablet bottles labeled as Naprosyn 375-milligram tablets. Syntex has notified pharmacists nationwide of

the problem.

The genuine product and the counterfeit are both stamped with valid lot numbers, but the counterfeit bottles carry an expiration date of 1990. The correct expiration date for lot number 20135 is 10/88. Counterfeits will say 6/90. For lot number 48586, the expiration date is 6/88 on the genuine pills; 10/90 is marked on the counterfeits.

The valid expiration dates for the genuine product lots will also be followed by the letters A, B or C on the bottle label, but not on the counterfeits.

Any other products labeled as Naprosyn with an expiration date of June 1989 or later should also be considered counterfeit.

Patients taking Naprosyn should speak to their pharmacists if they have any questions.

Reprint Available

Reprints are available of the article "Planning a Diet for a Healthy Heart," which appeared in the March 1987 *FDA Consumer*.

Copies can be obtained from the Food and Drug Administration, HFI-40, 5600 Fishers Lane, Rockville, Md. 20857. Up to 100 copies will be provided. Negatives of reprints are also available for those organizations needing more than 100 copies.

Study Confirms Link Between Reye Syndrome and Use of Aspirin

There is "firm evidence" of a link between Reye syndrome, a rare and sometimes fatal disease in children, and the use of aspirin for treating chicken pox or influenza, according to a study in the *Journal of the American Medical Association*.

The study found that more than 90 percent of the children with Reye syndrome had been exposed to salicylates during a recent illness. (Aspirin is the most common salicylate.)

Using data from 70 pediatric care centers, Eugene S. Hurwitz, M.D., of the U.S. Centers for Disease Control, and colleagues compared histories of 27 cases of Reye syndrome with those of 140 controls from January 1985 through May 1986. Controls were matched for age, race, the type of recent illness, and when that illness began. Out of the 27 cases, 25 had taken aspirin





and one had taken a non-aspirin salicylate (bismuth subsalicylate). Of the controls, 29 percent had taken aspirin.

The researchers observed that the fact that only 38 percent of the controls in this study took salicylates, compared to a range of 46 percent to 71 percent in pre-

vious studies, indicated a declining use of salicylates among children.

The study, published April 10, also found that almost all of the children (96 percent of the Reye cases and 90 percent of the controls) took either salicylates or acetaminophen during the previous illness.



Consumer Forum

Cutting Cholesterol, Cutting Calories

I enjoy the articles in *FDA Consumer* even if I don't always agree with all of them. However, I think the two articles ["Cutting Cholesterol? Look to the Label" and "Planning a Diet for a Healthy Heart"] in the February and March 1987 issues give far too much emphasis to the hazards of saturated fat and dietary cholesterol and not enough to the hazard of too many *total* calories. In a brief letter, it is impossible to detail my objections. Perhaps I can make my point by rewriting a portion of the first sentence of the piece in your March issue as follows: "Most health experts agree that Americans can help protect themselves from heart disease and heart attacks by adjusting *total* caloric intake to caloric output so as to reach and maintain a reasonable weight, and by eating less saturated fat and less cholesterol. In practice, the latter means only fewer egg yolks."

Frederick J. Stare, M.D.
Professor of Nutrition Emeritus
Harvard University
School of Public Health
Boston, Mass.

Dr. Stare also has provided FDA with his thoughts on this matter in formal comments on the agency's pro-

posed regulation for cholesterol labeling of foods. FDA will respond to his comments, along with all others, when it publishes its final rule.

Palm Oil and Palm Kernel Oil

In the February 1987 issue of *FDA Consumer*, the article entitled "An Introduction to Fats and Cholesterol" on page 12 has a table of oils and fats in which you have listed palm oil as containing 2 percent polyunsaturated fatty acids and 81 percent saturated fatty acids. You list the source of this table as the National Institutes of Health, 1986. I believe you are confusing palm oil with palm kernel oil.

Robert W. DeLashmit
Executive Vice President
Palmco Inc.
Portland, Ore.

The information for palm oil was, indeed, incorrect. According to the U.S. Department of Agriculture's handbook titled Composition of Foods, Fats and Oils, palm oil is composed of 9 percent polyunsaturated fat and 49 percent saturated fat. Palm kernel oil is composed of 2 percent polyunsaturated fat and 82 percent saturated fat.

Still a Killer:

Pneumonia Targets the Ill, the Elderly

by Chris W. Lecos

Pneumonia is no stranger to mankind. Human beings have been suffering and dying from it since at least 200 A.D.—and they still are. Penicillin, introduced in the 1940s, and other antibiotics that followed have been highly successful in treating, curing and saving the lives of millions. Yet, despite all the advances of medical science, pneumonia is still a major public health problem in the United States and one of the nation's leading causes of death.

The elderly and people of all ages who are suffering from other serious and chronic illnesses are still major targets of pneumonia. For example, because AIDS (acquired immune deficiency syndrome) has such a destructive effect on the body's immune system, people with that disease or advanced AIDS-related complex (ARC)—a precursor of AIDS—are likely victims for a type of pneumonia called *Pneumocystis carinii* pneumonia (PCP).

In fact, AIDS and ARC patients with this type of pneumonia are among those limited groups of patients eligible for treatment with azidothymidine, or AZT, the first drug approved by FDA for use against AIDS. (See "First AIDS Drug Approved" on page 4.)

However, *Pneumocystis carinii* is not a "new" pneumonia. The organism, a protozoan parasite, first attracted the interest of scientists shortly after the beginning of this century. It sparked worldwide attention following World War II when PCP ravaged malnourished infants in overcrowded orphanages and foundling homes in Eastern and Central Europe. Today, its prevalence among AIDS patients is just another part of its continuing evolution as an "opportunistic" disease—one that tends to strike people already weakened by another illness.

Thanks to better drugs and other treatment advances, pneumonia is not the killer it used to be. In the early 1900s, more than 200 out of every 100,000 Americans died from this disease. Today, the death rate is about 27 for every 100,000 persons, making it the nation's sixth leading cause of death.

During 1985, the latest year for which figures are available, some 2,891,000 Americans were stricken with pneumonia, and nearly 65,000 died from it, according to the National Center for Health Statistics (NCHS). The ability of pneumonia to target the elderly is evident. More than three-fourths of those who died—about 51,000—were men and women over 65. The fatality rate for that age group from pneumonia is around 181 deaths for every 100,000 in the population. In 1985, some 400,000 out of 854,000 people who either entered a hospital

with pneumonia or contracted it after admission were men and women at least 65 years old, according to NCHS.

Getting pneumonia while in the hospital for some other illness is not uncommon. One medical text estimates that pneumonia accounts for 8 percent to 33 percent of all infections a person might acquire after admission. These are exceeded only by urinary tract and surgical wound infections. Although the average stay in a hospital for a pneumonia patient is about eight days, elderly patients require longer periods of care—almost 10 days.

Age is such an important factor, not only with pneumonia but with other diseases as well, because the body's ability to ward off disease diminishes as one gets older. In addition, older people tend to suffer from other chronic illnesses and have to spend more time in hospitals and nursing homes.

Most cases of pneumonia among hospital patients, according to Dr. Charles W. Stratton of Vanderbilt University's School of Medicine, occur among those who are in intensive care or similar units. Such areas, he wrote in the May 1986 issue of *Heart and Lung*, often harbor organisms that are resistant to antibiotics. The "underlying illnesses of these patients, combined with the virulence/resistance of these pathogens, contributes to a high mortality rate (20 percent to 50 percent) despite treatment with antibiotics," he wrote.

Pneumonia can be caused by bacteria, viruses, mycoplasma (microscopic organisms that are smaller than bacteria but larger than viruses), fungi, and even toxic chemicals that are inhaled and impede the ability of the respiratory system to obtain oxygen. The word "pneumonia" actually is a general term for describing a variety of diseases that cause inflammation or infections of the lungs. In the healthy individual, the lower respiratory system (the lungs) is usually free of microorganisms, while the upper respiratory system (the nose, throat and mouth) readily harbors bacteria and other organisms during the normal process of eating and breathing. What protects most people

(Continued on page 11)

The medical device shown at right is an incentive spirometer, intended to help increase the working capacity of the lungs. The device is often provided to hospital patients following surgery and to others whose lungs have been impaired by pneumonia or other illnesses.



A Snapshot of Legionnaires' Disease

Symptoms

Loss of appetite
Malaise
Muscle aches
Headache
Rising temperature 102-105 degrees Fahrenheit
Chills
Dry cough
Abdominal pain
Diarrhea
Vomiting

Risk Factors

Age 50 or older
Smokers
Cancer patients on active drug treatment or radiation
People with chronic bronchitis, emphysema, kidney disease
Men 2½ times more susceptible than women

Death Rate

5 percent to 15 percent

Sources: *Control of Communicable Disease in Man* and U.S. Centers for Disease Control, Atlanta, Ga.

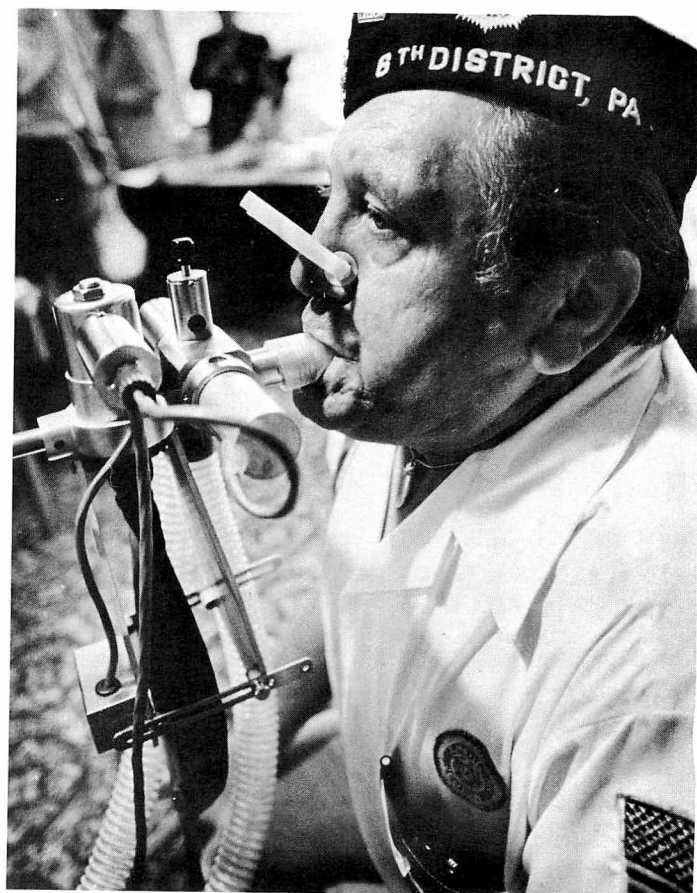
Pneumonia and Influenza Deaths by Age Group—1984

<i>Age Group</i>	<i>Deaths per 100,000 Population</i>
1-4 years	1.5
5-14	0.5
15-24	0.6
25-44	2.2
45-64	11.7
65 and over	181.5

Source: National Center for Health Statistics

A survivor of Legionnaire's disease from the convention outbreak in 1976 takes a breathing test as part of Legion-sponsored events two years later in Philadelphia.

(Photo source: *Philadelphia Inquirer*.)



***About 500,000 Americans
contract pneumococcal
pneumonia each year, and
25,000 die from it.***

(Continued from page 8)

from microbial invasion of the lungs is the body's complex system of natural defenses.

One of these defenses is coughing, an action which expels foreign matter. Another part of the body's array of weapons is its white blood cells, or phagocytes, in the lung tissues which can surround, engulf, neutralize and help destroy invading microbes that can cause disease. When disease threatens, the body's immune system also produces antibodies to fight it.

So it's understandable that at higher risk of pneumonia are people weakened by illness or whose immune systems have been diminished by age or disease, along with infants whose immune systems are not fully developed, and men and women who smoke or drink to excess, who are malnourished, or who have suffered damage to their respiratory systems.

In making a diagnosis of a patient with possible pneumonia, a physician usually will listen to the chest, have an X-ray taken, and have blood and sputum tests made to identify, if possible, the particular organism causing the disease.

The symptoms are not always the same for the many types of pneumonia. Common symptoms are a cough with an abundance of sputum, fever, chills and chest pain. With some kinds of pneumonia, particularly pneumococcal pneumonia, the sputum is usually bloody or pink in color, but becomes rust-colored tending toward yellow as the patients get past the worst of the illness.

For what appear to be the more serious types of pneumonia, doctors often start their patients on antibiotics before getting the results of all lab tests. Rapid treatment can help limit any complications that could develop. Treatment also includes ample bed rest and drinking lots of fluids.

Among the wide variety of organisms that cause pneumonia, viruses usually produce less severe illness than bacteria-caused pneumonias. Most viral pneumonias are self-limiting, and patients generally recover on their own through bed rest and fluids. Antibiotics are not effective against viruses.

Mycoplasma pneumoniae tends to occur more frequently among people under 35. Its onset is usually slower than the bacterial pneumonias. It may take two weeks or longer before serious symptoms appear. Chills are less common, fever may not get above 101 degrees Fahrenheit, and not much sputum is produced. Outbreaks have occurred among school and military populations. This type of pneumonia accounts for about one-third of all cases in the general population and as many as three-fourths of the pneumonias among youngsters 5 to 19 years of age. Few die from it, and only a small percentage of patients require hospitalization. Generally, tetracyclines and erythromycin are the antibiotics used to treat the disease.

Some pathogens that cause pneumonia have been identified

only in recent years. Probably the best known is the bacterium known as *Legionella pneumophila*, which causes Legionnaires' disease—made famous after the severe outbreak among American Legion members at a 1976 convention in Philadelphia. *Legionella* was first identified in January 1977. (See accompanying article.)

Another little-known respiratory pathogen attracting increased interest is the so-called TWAR (Taiwan Acute Respiratory Disease) bacterium. A report published last year in *The New England Journal of Medicine* suggests the parasite, a strain of *Chlamydia psittaci*, may be a fairly common cause of respiratory disease infections that can be spread directly from person to person. Such infections have occurred mainly in Japan and Europe. A severe sore throat is a common symptom; otherwise, the infection is similar to that of mycoplasma pneumoniae. Erythromycin and tetracycline have been used in treating patients.

According to the National Foundation for Infectious Diseases, about half the cases of pneumonia are caused by bacteria, and 60 percent to 90 percent of those are caused by the *Streptococcus pneumoniae* bacteria. These generally are known as pneumococcal pneumonias.

The National Institute of Allergy and Infectious Diseases (NIAID) estimates that each year about 500,000 Americans contract pneumococcal pneumonia and that 25,000 die from it. Adults are far more likely to be victims of the disease. Among the elderly, the incidence of pneumococcal infection is three times greater than that of the general population.

Those at higher risk of infection and death from pneumococcal pneumonia are people over 50, those with such chronic illnesses as cardiovascular disease, pulmonary disease (asthma, bronchitis and emphysema), diabetes, cirrhosis of the liver, sickle-cell disease, and individuals whose spleen has been removed or does not function normally.

Once infected, the victim of pneumococcal pneumonia feels its effects quickly. After an "incubation" period of one to three days, the individual usually suffers severe, shaking chills, a fever that reaches 105 degrees Fahrenheit, sharp chest pain, congestion, and painful coughing fits. An abundance of sputum that is rusty or bloody is also common. Difficulty breathing, nausea and vomiting also may occur.

Pneumococcal pneumonia may require hospitalization. If untreated, the fatality rate can reach 30 percent, says NIAID. Even among those receiving antibiotics, about 5 percent die. According to the American College of Physicians, better than two-thirds of the deaths in treated patients occur within five days after onset of the illness.

(Continued on page 13)

Man-Made Sources of Legionella

Aquariums*	Nebulizers
Boilers	Potable water
Cooling towers	Respirators*
Dehumidifiers*	Saunas*
Evaporative condensers	Shower water and shower heads
Fountains	Swamp coolers*
Hot-water tanks	Taps—hot and cold water
Humidifiers	Whirlpools

****Potential sources***

The pathogen that causes Legionnaires' disease is widespread in the environment. Outbreaks have been linked to various man-made sources, some of which are listed above. Although the organism is easily found in such sources, public health officials emphasize that finding the organism does not necessarily mean that an outbreak will occur.

Source: *Legionellosis, Vol 2*, by Sheila Moriber Katz, M.D.; CRC Press, Inc., Boca Raton, Fla., 1986.

10 Leading Causes of Death in the United States—1985

<i>Order</i>	<i>Number of Deaths</i>
All Causes	2,084,000
No. 1— Heart disease	775,890
No. 2— Cancer	457,670
No. 3— Cerebrovascular diseases (stroke)	152,710
No. 4— Accidents	92,070
a) motor vehicle accidents	44,930
b) all other accidents	47,140
No. 5— Chronic obstructive pulmonary diseases and allied conditions	74,420
No. 6— Pneumonia and influenza	66,630
a) Pneumonia	64,720
b) Influenza	1,910
No. 7— Diabetes mellitus	38,620
No. 8— Suicide	28,620
No. 9— Chronic liver disease and cirrhosis	26,770
No. 10— Atherosclerosis (hardening of the arteries)	23,580

Source: National Center for Health Statistics

***Pneumonia can be caused
by bacteria, viruses, my-
coplasma, fungi, and even
toxic chemicals.***

(Continued from page 11)

About one-third of the patients with pneumococcal pneumonia develop pneumococcal bacteremia—a condition in which the organisms get into the bloodstream and produce possibly serious complicating infections such as inflammation of the lining of the brain and spinal cord (meningitis), of the lining of the heart (endocarditis), of the abdominal membranes (peritonitis), and of the joints (arthritis). The fatality rate for those with such complications, despite the use of antibiotics, can be as high as 25 percent. And with a particular organism—called type 3 pneumococcus—it can reach 50 percent.

Pneumococcal pneumonia is the only type for which a vaccine has been developed. An earlier vaccine with limited effectiveness was made available to the public years ago, but then was withdrawn after penicillin—introduced in 1943—and other antibiotics proved to be so effective in the treatment of pneumonia. However, heavy reliance on antibiotics eventually led to a frightening discovery: A growing number of pneumococcal bacteria—of which there are 86 varieties—had become resistant to penicillin and other drugs. Research on pneumonia vaccines resumed in the 1960s. In 1977, FDA licensed a vaccine that provided protection against 80 percent of the more common types of pneumococcal infections. Then in 1983, FDA approved an even more effective vaccine—called a 23-valent polysaccharide vaccine—which provides protection against 23 different types of pneumococcal species that are responsible for almost 90 percent of the cases of pneumococcal pneumonia, according to Dr. Carl Frasch of FDA's division of bacterial products.

The vaccine is intended primarily for people who are considered at greater risk of contracting pneumococcal pneumonia. It should not be given to children under 2 nor to healthy children of any age. It also is not recommended for pregnant women. More specifically, the U.S. Public Health Services' Advisory Committee for Immunization Practices presently recommends the vaccine for these population groups:

Healthy, older adults, especially those who are 65 or older; adults with such chronic illnesses as cardiovascular disease, pulmonary disease, Hodgkin's disease, multiple myeloma (a form of bone marrow cancer), cirrhosis, alcoholism, renal (kidney) failure, cerebrospinal leaks (a complication of skull fractures and certain neurological procedures); people whose spleen has either been removed or is not functioning normally; and patients receiving medications that suppress their immune systems.

The vaccine also is recommended for chronically ill children over the age of 2 because of the risk they face of developing pneumococcal infections. The high-risk group also includes children with no spleen or with a malfunctioning spleen, and children with sickle-cell anemia, kidney disease, cerebrospinal fluid leaks, and those receiving medications that depress their immune systems.

The vaccine takes effect about two weeks after injection. In most instances, the side effects are minor—a temporary redness and soreness at the injection site. A vaccinated individual is usually protected for at least five years. However, revaccination is not recommended because the side effects can be serious. Nor should those immunized with the 1977 vaccine be revaccinated.

In 1984, the Public Health Service's immunization committee stated that more effective programs were needed for immunizing people "in nursing homes and other chronic care facilities, in physicians' offices, and in hospitals, because only a small proportion of severe pneumococcal cases occur in previously healthy individuals." About two-thirds of those with pneumococcal disease, the group said, were people who had been hospitalized in the five years before contracting the disease. The advisory body urged that all hospitalized patients be immunized to prevent future admissions and that individuals who see a doctor frequently also be considered as candidates for the vaccine. The vaccine is covered by Medicare.

Some recent studies, however, have challenged the vaccine's effectiveness for certain chronically ill patients. One study published last year in the *New England Journal of Medicine* indicated that the vaccine was not effective in preventing pneumonia among chronically ill patients in Veterans Administration hospitals. Those "who are most susceptible to infection may have an impaired immune response to the pneumococcal vaccine," the report suggested. However, other studies show that the risk of infection among the elderly and other susceptible groups can be significantly reduced by vaccination.

According to Dr. Stephen Redd of the U.S. Centers for Disease Control in Atlanta, the PHS immunization committee last February reviewed the research done and decided to make no changes. "The weight of the evidence supports the recommendations as they are," he said. ■

Chris W. Lecos is a member of FDA's public affairs staff.

Legionnaires': Old Soldiers' Disease Hasn't Faded Away

It was once described as the "greatest medical mystery of the century." In 1976, its mounting toll of sick and dying victims—most of them, strangely, members of the Pennsylvania American Legion—sent tremors of fear through the nation and triggered one of the largest investigations ever undertaken of a potential public health disaster. It all occurred at a time when Americans also were celebrating their nation's 200th birthday and fearfully awaiting the predicted ravages of a swine flu epidemic.

We know it today as Legionnaires' disease, or legionellosis, an apt name for a previously unknown type of pneumonia that struck down scores of Legion members at their state convention in Philadelphia and some others in the area in July 1976. Now, 11 years later, public health officials know that the disease was neither new nor uncommon—that the responsible organism had caused illness before 1976, that outbreaks still occur every year, and that the organism is widespread in the environment, particularly in soil and water.

No one to this day can really say how long the disease or the organism has been around, nor how many people have been victims. As a result of what was learned from the Philadelphia case, other earlier disease outbreaks whose cause had baffled investigators were solved. The earliest documented case is 1947. Although outbreaks still occur, the disease today is not viewed as a major public health menace.

"As a public health concern, I think it's an important problem, but certainly there are other problems today—such as AIDS [acquired immune deficiency syndrome]—that are far more serious," said Dr. Stephen Redd, an epidemic intelligence officer with the Respiratory Diseases Branch of the U.S. Centers for Disease Control in Atlanta. Compared with other types of pneumonia, the number of cases and deaths from streptococcal or pneumococcal pneumonia are greater, he said.

The official toll from the Philadelphia outbreak was 34 dead out of 221 who became ill. Of those, 149—including 29 who died—were Legionnaires. Some of the other victims were people who did not attend the convention, but who were in the vicinity of the Bellevue-Stratford Hotel—the convention headquarters. The investigation primarily focused on those who stayed at or had been in the hotel.

The cause of the outbreak eluded investigators and researchers for more than five months. The search seemed fruitless until a microbiologist at CDC decided to employ some different laboratory techniques and reexamine some old microscope slides. That led to the discovery of a rod-shaped microorganism never before observed. At a press conference on Jan. 18, 1977, before a cheering crowd of 300 CDC employees, the breakthrough was announced: The Philadelphia outbreak was caused by a previously unrecognized type of bacteria, named *Legionella pneumophila*.

CDC researchers estimate that 25,000 to 50,000 Americans become ill from the disease each year. When outbreaks occur, the mortality rate has ranged from 5 percent to 15 percent of those infected. The death rate is even higher during occasional outbreaks among already sick patients in hospitals. Estimates

vary, but one study states that about 10 percent of the pneumonia cases in hospitals and nursing homes may be caused by *Legionella*.

One puzzling aspect of the *Legionella* organism is how it can cause severe illness and even death in some cases and only mild symptoms in others.

There is no evidence the disease is transmitted person-to-person. Instead, scientists believe that most outbreaks result from airborne transmission of the organism. Scientists have readily found the organism in lakes, rivers, streams and ponds, as well as at excavation sites, in cooling towers, air conditioning and evaporative condenser systems, shower heads, drinking water taps, and whirlpool baths. Even hospital respiratory therapy equipment has been linked to outbreaks.

However, the mere presence of the organism does not mean an outbreak will occur. One of the continuing mysteries of Legionnaires' disease is why an outbreak can occur at one site that is harboring the organism, but not in another where its presence also has been noted. "You have a situation where there is an imperfect understanding of what is going on here," says Redd.

CDC's success in identifying the organism was crucial in developing ways to diagnose, treat and help control the disease. And, thanks to CDC's discovery, unsolved outbreaks that had occurred years before the one in Philadelphia and others that followed could now be conclusively linked to Legionnaires' disease. However, how the outbreak in Philadelphia occurred was never proven.

The prevailing belief is that the organism was somehow transmitted via the air conditioning system of the Bellevue-Stratford. It also was determined that just being near the hotel—without even entering it—during the convention period also resulted in the illness of 39 people, five of whom died. These came to be known as the "Broad Street pneumonias" because the hotel fronted on that street. The Bellevue, as investigators later discovered, also was the site of a Legionnaires' outbreak that caused three deaths and hospitalized 19 others at a 1974 convention of the Odd Fellows.

Since the 1976 outbreak, scientists have discovered and identified other species of *Legionella*. According to one report, 23 species have been identified, and 10 are known to cause human disease. One kind, *Legionella pneumophila*—the kind that caused the Philadelphia outbreak—is responsible for an estimated 80 percent of the pneumonias that can be attributed to this disease.

In most cases, victims of *Legionella pneumophila* develop full-blown pneumonia, and the majority require hospitalization. Erythromycin, an antibiotic, is the most effective drug for treating Legionnaires' disease. However, the labeling on the drug notes that "no controlled clinical efficacy [effectiveness] studies have been conducted [but] in vitro and limited preliminary clinical data suggest that erythromycin can be effective in treating Legionnaires' disease." Fatalities were high during the early outbreaks because doctors didn't know what specific drug to use. For example, penicillin—so effective with other types of pneumonia—will not work with this disease.

(Photo source: *Philadelphia Inquirer*.)



Once exposed, an individual usually becomes sick in two to 10 days. The earliest symptoms are headache, aching muscles and malaise. A victim also may have chills and fever (102 to 105 degrees Fahrenheit). Breathing can become difficult, and there also may be chest and abdominal pain, diarrhea, impaired kidney function, confusion, memory loss, and other symptoms. A dry, nonproductive cough (little or no sputum) is common.

Legionnaires' disease can affect people of all ages and can occur at any time of the year. However, more people are stricken during July, August and September. No one knows why. Those at higher risk of the disease are the elderly, smokers, alcoholics and people with underlying illnesses such as diabetes mellitus, heart disease, malignancies, and lung disease, and those who take medications that suppress their immune systems. Two to three times more men than women contract the disease for reasons not clearly known.

Another fairly common form of legionellosis, called Pontiac fever, affects larger numbers of people exposed to it than does Legionnaire's disease, but its effects are milder. It got its name from an outbreak that occurred in 1968 at the Pontiac, Mich., health department. Chills, fever and a dry cough are some of its symptoms. To some, it feels like flu. However, no pneu-

monia results, and no one is known to have died from it.

As in the Philadelphia episodes, cooling towers and air conditioning systems have been linked to a number of Legionnaires' outbreaks. Recent studies also suggest an association between isolated cases of the disease and drinking water. However, in a report published in the *Journal of the American Medical Association* in March 1987, Redd and Mitchell Cohen, also of CDC, warned that more studies were needed to clearly establish that drinking water contaminated with *Legionella* is an important source of outbreaks. The comparatively few studies done on drinking water only "indicate that we do not know enough to predict where, when, and in whom legionellosis will occur," they wrote.

CDC noted in its June 14, 1985, Morbidity and Mortality Weekly Report that routine testing of drinking water or cooling tower systems for *Legionella* was of "questionable value." And, in the absence of adequate data, even routine microbiological sampling of drinking water when Legionnaires' cases occur is not warranted, according to CDC.

In effect, despite all the knowledge gained in the past decade, much more must be learned before the experts can come up with effective and practicable measures for controlling this ever-present organism. ■



Summer Food Safety Tips

by Frank E. Young, M.D., and Karen J. Skinner, Ph.D.

Summertime, and the living is easy—not just for us, but also for microorganisms that can grow in food and make us sick.

Many view food-borne diseases as nothing more than short-term nuisances. But for certain groups—the very young, the very old, and those with impaired immune systems—food-borne illness can be serious and, tragically, often fatal. Moreover, some food-borne diseases may lead to certain chronic health problems, such as arthritis.

These sobering facts keep FDA constantly alert to the problem of microbiological food safety. But consumers are even more important than FDA in preventing food-borne disease at home, where about 30 percent of all bacteria-related food poisoning outbreaks occur. In this respect, consumers and FDA have a shared responsibility.

Summer—with its warm temperatures ideal for microbial growth—is an excellent time to review food safety principles. To help, here are a few rules to keep in mind.

Rule One: Remember the Time-Temperature Danger Zone

Disease-causing bacteria in food like to grow in the temperature range between 40 and 140 degrees Fahrenheit. **Avoid keeping foods in this temperature danger zone! Don't eat foods that have been kept within this range for more than two hours.** In ensuring food safety, a thermometer is the most important utensil you have. Make a practice of using it to monitor internal food temperatures and food storage temperatures.

By remembering the time-temperature relationship—the “2-40-140” rule (no more than two hours between 40 F and 140 F)—you will have a much better idea of how to handle foods in a variety of situations, especially in the summer. If, for example, you want to buy fried chicken at a carry-out for your picnic, either eat the chicken within two hours, or take it home immediately, cool it quickly in your refrigerator, and then keep it chilled below 40 F as you travel to your picnic site. If you put the hot chicken in an ice chest right away, you might not cool it rapidly enough and will actually accelerate the growth of organisms by causing the chicken to sit in the temperature danger zone for some time.

At church dinners, buffets or potluck dinners, wait as long as possible to prepare the dishes before it's time to eat, and don't leave foods sitting at room temperature. Place dishes of cold foods on beds of ice, and hold hot foods above the danger zone (at temperatures greater than 140 F). Some home-style food warmers, like chafing dishes, vary in their ability to warm food throughout. When using these warmers, don't keep food out for more than two hours. Uneven warming may lead to temperature pockets in the danger zone where bacteria happily multiply.

The fun of summer food festivities can go up in smoke unless outdoor chefs take care to handle and prepare their dishes safely to avoid the threat of food poisoning.

Use shallow dishes to cool foods quickly in the refrigerator. The interior of foods in deep containers may chill very slowly, leaving hazardous warm areas. Defrost meats and other foods, not on your kitchen counter, but in your refrigerator to avoid bacterial growth at room temperature.

If a summer electrical storm interrupts power, your refrigerator probably will remain sufficiently cold for about four to six hours (depending on room temperature), and a half-filled freezer for about one day. Keeping the refrigerator or freezer closed and using block ice in the refrigerator and dry ice in the freezer can help keep contents safely cold.

In summer, temperatures in a car can reach the high end of the danger zone. A good rule of thumb is that perishable groceries like meats and dairy products shouldn't be left in a hot car any longer than it would take ice cream to melt. Never allow more than two hours to pass between purchasing food and getting it into your home refrigerator.

Foods available at fast-food, deli and refrigerated counters are becoming popular items for summer outings. But if they've been mishandled before you buy them, they already may have been held between 40 F and 140 F. After purchase, even two hours within the danger range for these foods might be risky. Eat them immediately or keep them cooled below 40 F.

The high temperatures (165 F to 212 F) reached in boiling, baking, frying and roasting kill most types of the bacteria that cause food-borne illness. On cookouts, to be on the safe side, cook red meat until the pink is gone, poultry until there is no red in the joints, and fish until it's flaky.

Colder temperatures slow bacterial growth. With a thermometer, check that your freezer is at zero degrees Fahrenheit or lower and your refrigerator at 40 F or lower. Crowded summer refrigerators (like those on boats and trailers) might develop warm spots in the temperature danger range.

Rule Two: Make a Clean Break to Good Sanitation Practices

Cleanliness is critical to avoiding food contamination. Take extra care to avoid infecting one food with organisms from another, especially when handling raw meats and poultry, on which some bacteria usually are present. At every step of food preparation, wash hands, counters and utensils with warm, soapy water. When barbecuing, don't use the same plate for cooked meat that carried raw meat, unless you've cleaned it first. Remember, an unwashed chopping board or knife may be a reservoir of harmful bacteria. Even that favorite picnic food, watermelon, can be contaminated with a dirty utensil.

Away from home, moist hand wipes can help keep hands clean, and paper towels are one solution to the problem of dirty cloth towels harboring bacteria. If you have a cut or an infection, don't handle food. Animals aren't allowed in food processing plants, and at home, dogs, cats and other pets shouldn't be around food.

Sparkling lakes, streams and rivers, tempting to thirsty campers, may contain viruses, bacteria and the parasite *Giardia*.

A Sampler of Food-Borne Illnesses

<i>Disease and Organism That Causes It</i>	<i>Source of Illness</i>	<i>Symptoms</i>
Salmonellosis <i>Salmonella</i> bacteria (more than 2,000 kinds)	Raw meats, poultry, milk and other dairy products, shrimp, frog legs, yeast, coconut, pasta and chocolate are most frequently involved.	Onset: Generally 6–48 hours after eating. Nausea, vomiting, abdominal cramps, diarrhea, fever, and headache. All age groups are susceptible, but symptoms are most severe for the elderly, infants, and the infirm.
Staphylococcal food poisoning Staphylococcal enterotoxin (produced by <i>Staphylococcus aureus</i> bacteria)	The toxin is produced when food contaminated with the bacteria is left too long at room temperature. Meats, poultry, egg products, tuna, potato and macaroni salads, and cream-filled pastries are good environments for these bacteria to produce toxin.	Onset: Generally ½–8 hours after eating. Diarrhea, vomiting, nausea, abdominal cramps, and prostration. Mimics flu. Lasts 24–48 hours. Rarely fatal.
Botulism Botulinum toxin (produced by <i>Clostridium botulinum</i> bacteria)	Spores of these bacteria are widespread. However, these bacteria produce toxin only in an anaerobic (no oxygen) environment of little acidity. Botulinum toxin has been found in a considerable variety of canned foods, such as corn, peppers, green beans, soups, beets, asparagus, mushrooms, ripe olives, spinach, tunafish, chicken, chicken liver and liver paté. It also has been found in luncheon meats, ham, sausage, stuffed eggplant, lobster, and smoked and salted fish.	Onset: Generally 4–36 hours after eating. Neurotoxic symptoms, including double vision, inability to swallow, speech difficulty, and progressive paralysis of the respiratory system. Obtain Medical Help Immediately. Botulism Can Be Fatal!
Campylobacteriosis <i>Campylobacter jejuni</i> (rod-shaped bacteria)	Bacteria found on poultry, cattle, and sheep and can contaminate the meat and milk of these animals. Chief food sources: raw poultry and meat and unpasteurized milk.	Onset: Generally 2–5 days after eating. Diarrhea, abdominal cramping, fever, and sometimes bloody stools. Lasts 7–10 days.
Perfringens food poisoning <i>Clostridium perfringens</i> (rod-shaped bacteria)	In most instances, the actual cause of poisoning by <i>Clostridium perfringens</i> is temperature abuse of prepared foods. Small numbers of the organisms are often present after cooking and multiply to food poisoning levels during cool down and storage of prepared foods. Meats and meat products are the foods most frequently implicated. These organisms grow better than other bacteria between 120°–130°F; for this reason, gravies and stuffings must be kept hot, above 140°F.	Onset: Generally 8–12 hours (usually 12) after eating. Abdominal pain and diarrhea. Sometimes nausea and vomiting. Symptoms last a day or less and are usually mild. Can be more serious in older or debilitated people.
Giardiasis <i>Giardia lamblia</i> (flagellated protozoa)	Protozoa exist in the intestinal tract of humans, and cysts are expelled in feces. Giardiasis is most frequently associated with the consumption of contaminated water. It may, however, be transmitted by uncooked foods that become contaminated while growing or after cooking by infected food handlers. Cool, moist conditions favor survival of the organism.	Diarrhea (but occasionally constipation), abdominal pain, flatulence, abdominal distention, digestive disturbances, anorexia, nausea and vomiting.

dia lamblia, famous for causing “backpacker’s disease” or “beaver fever.” When “roughing it,” boil water, treat it with purification tablets, or try one of the new filtering devices that remove *Giardia* cysts, as well as other contaminants. Bottled water is another alternative for drinking, cooking and cleaning.

Rule Three: Know the Foods Requiring Special Care

Harmful organisms grow more readily in foods high in protein and moisture. Special care with time, temperature and sanitation is needed for foods like meat, poultry, fish, shellfish, meat and seafood salads, potato salad, milk, milk products, eggs, cream pies, custards, eclairs, cream puffs, cake fillings, and gravies. Cooked pasta also can support microbial growth and should be served hot or properly refrigerated until used.

Cooking can destroy natural barriers to contamination in some foods from plant sources, and can free up nutrients needed by microorganisms to grow in these foods. Outbreaks of food-borne illness have been associated with bean curd (tofu), corn, lima beans, mushrooms, refried beans, rice, squash, and sweet potatoes that were cooked and then held for some time before eating. Except for sealed, commercially processed foods (such as canned foods), these and other moist, low-acid, cooked foods from plant sources should be refrigerated. Don’t leave them at room temperature for more than two hours.

When you buy side orders of take-out foods, or think about piling beans, pasta salads, or other cooked vegetables and cheeses on your salad-bar creations, remember, these are “special care foods,” and consider how much time will pass before you eat.

Guarding against deadly botulism toxin, produced in reduced-oxygen environments, always requires special care. Fresh mushrooms in airtight packages recently have been involved in botulism cases. Improperly canned foods—especially low-acid foods such as meat, poultry, fish, string beans, beets, peas, corn and some fruits—also may be good places for the botulinum bacteria to grow. **Do not taste or eat** any foods from leaking, bulging or severely damaged cans; cracked jars; jars with loose or bulging lids; or swollen or puffy pouch containers. Boil all home-canned foods before tasting or serving. If an initial, rapid boil produces off-odors or foaming, **don’t eat the food!** Discard suspect foods carefully, so that others, especially children and animals, won’t be exposed. If there’s no danger-signaling odor, boil high-acid foods for another 10 minutes and low-acid foods for another 20 minutes to destroy any botulinum toxins that nevertheless may be present.

Rule Four: Inspect Food Storage

Proper storage is another vital aspect of preserving the safety and quality of foods. As you restock larders at home and in summer places, take an inventory of existing items and inspect your storage practices.

Generally, pantry storage areas should be about 50 degrees Fahrenheit, clean, and away from leaky pipes, household chemicals, and openings where insects and rodents may enter. It’s not safe to assume that all boxed and canned goods may be held at room temperature. During your inspection, check labels to ensure you’ve properly followed storage instructions, and discard items for which you’ve made a mistake. Also examine “best if used by” and expiration dates to determine if you’ve held foods too long. Make sure containers are free from dust and other matter that could contaminate food when products are opened.

When checking pantries in mountain cottages and other retreats, remember that cans left over the winter may freeze—

stressing seams and creating microscopic openings through which bacteria and other contaminants may enter. Undamaged, low-acid canned goods generally last two to five years, and high-acid foods (such as tomato products and fruit juices) about 18 months.

Don’t forget the refrigerator during your inspection tour. Molds, which may cause allergies and other health problems, like to grow in warm weather, but also are very content living inside refrigerators. To reduce mold buildup, wash the inside of the refrigerator with one tablespoon of baking soda dissolved in a quart of water, then rinse with clear water. Also be sure to clean the gaskets sealing the doors. Scrubbing with a solution of three tablespoons of bleach in a quart of water has been recommended for this purpose, but manufacturers vary in their cleaning instructions, so consult your appliance use and care guide for recommended cleaning procedures.

Rule Five: Think Before You Eat

Because most food poisoning bacteria are odorless, colorless and tasteless, the only sense protecting you against food-borne illness is common sense. When traveling, prudent dietary and hygienic practices are your best safeguard against trouble. Remember these rules wherever you are, whether boating, picnicking, camping, or enjoying some other excursion.

Rule Six: Know When to See a Doctor

When food-borne disease strikes, see a doctor or get hospital help if the symptoms are severe or if the victim is young, elderly, or suffers from a chronic illness. If you suspect botulism, get medical help immediately! This disease can be fatal. Botulinum toxin attacks the nervous system, causing double vision, trouble swallowing, and difficult breathing.

Generally, diarrhea, nausea, vomiting and abdominal cramps characterize food-borne illness, but symptoms vary from microbe to microbe and with the amount of contaminants actually eaten. Symptoms usually appear in six to 48 hours, but they can show up much sooner, sometimes even within half an hour. For mild cases of food poisoning, maintain liquid intake to replace fluids lost through vomiting and diarrhea.

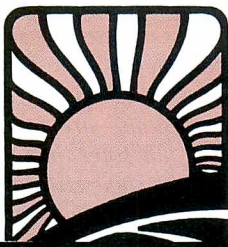
Rule Seven: Learn More About Food Safety

These rules are only the highlights of food safety principles. For more information, consult these excellent sources:

- FDA’s Consumer Affairs Office—Write to “Food Safety,” HFE-88, Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20857.
- “The Food Keeper”—This brochure describes refrigerator and freezer storage, pantry and dry storage, and foods that need special care. For a copy, send 25 cents and a legal-sized, stamped, self-addressed envelope to: “The Food Keeper,” Food Marketing Institute, 1750 K St., N.W., Washington, D.C. 20006.
- The U.S. Department of Agriculture’s Meat and Poultry Hotline—Call the toll-free number, 800-535-4555, between 10 and 4 on weekdays for answers to your questions on the proper handling of meat and poultry. You may also write to “The Meat and Poultry Hotline,” USDA-FSIS, Room 1165-S, Washington, D.C. 20250. Two very useful booklets, “The Safe Food Book” and “Safe Food to Go,” can be obtained through the hotline. ■

Dr. Young is commissioner of FDA. Dr. Skinner is on temporary assignment as special assistant for science to the commissioner.





Out of the Bronzed Age

by Richard C. Thompson

The great American migration seeking fun in the sun is now under way. The stirrings began with the vernal equinox as the winter sun crossed the equator, heading north and increasing the hours of daylight. Over the next three months, from June through Labor Day, that migration will take people to lake shore and ocean front beaches and up into the thin, clear mountain air.

For many of these people, an important part of the fun will be "getting a healthy tan." But in recent years, more and more Americans have been getting the message that there's really nothing healthy about a "healthy tan." For the first time, there may be a generation growing up that understands the risks of tanning and burning and cancer and cataracts that can result from too much sun.

"Too much" can mean a severe sunburn and the temporary punishment of pain and peeling that goes with it. But to physicians, especially dermatologists, it also means a lifetime of exposure to the sun that puts the skin through a repeated cycle of injury, repair and, ultimately, permanent damage.

Skin damage from sunlight is cumulative; the harmful effects build up with each exposure, whether sunburn occurs or not. Effects can include wrinkling and premature aging of the skin and, in time, the almost leathery appearance of long-time desert dwellers and fishermen and others who have spent their lives in the great outdoors.

It is the ultraviolet radiation in sunlight that injures skin cells in exposed and unprotected areas of the body. Although the skin's own repair mechanism will immediately go to work, this does not mean it can undo all the damage. If the cycle is repeated day after day and year after year, the damage can become irreversible.

The most dreaded consequence of excessive exposure to the sun is skin cancer, usually associated with aging, although dermatologists report seeing it in a surprising number of adolescents and young adults. The most prevalent skin cancers are basal cell and squamous cell carcinomas.

Basal cell carcinomas appear on the head, neck, hands and trunk and are the type most often seen among Caucasians. They are slightly raised, slightly translucent nodules that, if untreated, may crust and bleed. They grow slowly and do not spread (metastasize) through the bloodstream to other parts of the body. In time, however, they can penetrate to underlying tissue and form swelling tumorous growths that crowd against and damage organs and tissue. Some 500,000 cases of basal cell carcinoma are expected in the United States this year.

It was a basal cell carcinoma that was removed last year from President Reagan's nose; from the First Lady's upper lip; from Vice President Bush's cheek; and from newsman Ted Koppel's eyelid.

Squamous cell carcinomas are reddish or pink raised nodules or warty growths, most often found on the lips, face, mouth, hands, ears and other areas exposed to the sun. They may bleed and form small ulcers, and they can eventually grow downward within the skin and metastasize to other organs and tissue, causing serious damage, even death. Some 100,000 cases of squamous cell carcinoma are reported each year in the United States.

Both basal cell and squamous cell carcinomas are almost always curable if detected early and removed by simple surgery or freezing with liquid nitrogen.

A more sinister kind of skin cancer is malignant melanoma. Although very rare, it is often fatal, but is more treatable with drugs and surgery than it once was. Some 20,000 cases will likely be reported this year.

Although the relationship between melanoma and the sun is not as clear as for basal cell and squamous cell carcinoma, some experts believe it can be traced to intense, short-term exposure—often before age 20—accompanied by blistering and painful sunburn. There is evidence that heredity may also be a strong determinant.

Back in 1930, about one person in 1,500 in the United States could expect to develop melanoma in his or her lifetime, according to the American Cancer Society. By 1980, that had risen to one person in 250, and by the year 2000, it

(Continued on page 23)

Tanning Your Hide Inside, Clyde? It's Still Risky Business

Tanning salons that offer a year-round tan are a fairly recent phenomenon, appearing throughout the country in the past decade. Salon operators often install sunlamp equipment imported from Europe, which may give the places and those who use them a sense of prestige. Personal tanning equipment is also sold for home use.

Although the sun gives off both UVA and UVB, sunlamps produce mostly one or the other. Most of the inexpensive, older-style sunlamps for home use are UVB. The newer lamps used in salons are mainly UVA. Because UVA is less likely to burn, some operators claim their UVA lamps are "safe." Wrong. Even without a burn, UVA users risk skin cancer, premature skin aging, damage to blood vessels beneath the skin, and effects on the body's immune system. And if the proper protective goggles are not worn (closing the eyes is not

enough), there's increased risk of eye burns and cataracts.

UVA lamps—especially the new powered-up versions—are not "safer than sunlight" nor safer than ultraviolet B. They carry the same risks of skin burns, eye burns, cataracts, premature skin aging, and skin cancer as other sunlamps. But since UVA radiation goes deeper into and beneath the skin, its effects may not be as readily apparent.

Both UVA and UVB can damage blood vessels in sub-layers of the skin and can affect the body's immune system, with which it fights off infection.

With its responsibility to protect public health where radiation is concerned, FDA considers tanning—whether under the sun or under a sunlamp—risky business. The agency will not allow sunlamp manufacturers and salon operators to make exaggerated and untrue claims.

Health claims such as "improves immunity" and "treats disease" are not allowed. Nor are claims of safety permitted, such as "no harmful rays" and "no harmful effects." (Some persons will have eye or skin reactions to these tanning lamps.)

The one statement that sunlamp makers and salon operators can make is that their equipment is intended for "cosmetic tanning."

FDA standards for sunlamps and tanning equipment call for special goggles to protect the user's eyes; shielding to prevent touching the lamps; a timer that limits the amount of exposure (with a switch so the user can turn the lamps off at any time); and labeled instructions for use, along with warnings about the risks of skin cancer and other injuries.

Many imported sunlamps have been intercepted by FDA at ports of entry because they lacked the required safety features. Installed equipment has been seized and salons shut down for unsafe equipment and operation.

In addition, many state and local governments are developing their own regulations to be certain that tanning salons are properly informing and protecting customers. Through this combination of federal, state and local action, there should be more responsible operators and fewer equipment problems, even though the idea of a "safe tan" is a contradiction in terms. ■

How the Skin Tans ... and Burns

It is the ultraviolet radiation from the sun that causes tanning by stimulating melanocyte cells in the skin to release melanin, which is the skin's darkening protective pigment.

These ultraviolet rays are a combination of two types: UVA and UVB. Both UVA and UVB darken the skin, although UVB works more quickly and is most responsible for the burn that goes with tanning. With UVA, tanning and burning occur more slowly, but the rays penetrate more deeply. UVA is present in sunlight throughout the day, while the more intense and quicker burning UVB is mostly present at midday.

The reddening effect of sunburn is the skin's response to exposure to excessive sunlight. To shield itself against further exposure, the skin releases its melanin. The less melanin available—that is, the fairer the complexion—the less protection that skin will have. The accompanying chart shows skin types and their reactions.

Contrary to some beliefs, light clouds and fog do not protect against sunburn,

since ultraviolet rays come right through. Also, snow, sand and water increase the burn and tanning effect by reflecting the rays.

About 10 years ago, scientists discovered that the ozone layer—the part of the atmosphere that shields the Earth from the sun's rays—seemed to be losing some of its filtration effect, allowing too much ultraviolet through. Some say this may be affecting world weather and may

help account for increases in skin cancer. Manmade gaseous chemicals (chlorofluorocarbons) that rise up in huge quantities and dissolve the ozone are being blamed. Although some uses of chlorofluorocarbons (in spray-can propellants, for instance) have been banned in the United States, the gasses are still being produced and used throughout the world and are apparently still doing their damage. ■

Skin Type

Sunburn and Tanning History With Skin Type Descriptions

I	Always burns, never tans (Celtic)
II	Burns easily and tans minimally
III	Burns moderately; tans gradually to light brown (average Caucasian)
IV	Burns minimally; tans well to moderately brown (olive skin)
V	Rarely burns; tans profusely to dark (brown skin)
VI	Never burns; deeply pigmented; (black skin)



***You may not be wearing
much at the beach, but at
least have on a sunscreen.***

(Continued from page 21)

could rise still further to one in 100. Tanning was not as fashionable in the thirties as it is today and, if the sun does trigger melanoma, one reason for the increase could be Americans' fascination with tan bodies.

The upper back, torso, head, neck and lower legs are the most common locations for melanomas, which often arise from an existing mole. The average person's body will have about two dozen moles, and these should be checked from time to time to be certain they are not changing in shape or color. If any are, see a doctor right away.

Compared to a harmless mole, a melanoma will develop spreading and uneven edges and show colors of black, brown and even red and blue. If not treated with drugs or surgery, a malignant melanoma can lead to death as it spreads through the body. With early diagnosis, survival rates for treated cases are considered good.

The summertime sun over the United States is most intense and its rays most hazardous from 11 a.m. to 3 p.m., and anyone who is out at that time should take sensible precautions. This includes using an effective sunscreen oil or lotion and—for the best protection—wearing a hat and clothing that covers the body.

The sun products industry in the United States has been growing at the

rate of 10 percent a year for the past five years, with more than half of these sun products sold from June to September.

One reason for this growth was FDA's proposed regulation in 1978 requiring that products containing a sunscreen or sun-blocking agent carry a "sun protection factor" (SPF) number that indicates to users the degree of protection the product provides.

The U.S. cosmetics industry quickly picked up on this and began using SPF's in their sunscreen promotions and advertising.

SPF numbers range from 2 to 15 and appear in bold numerals on sunscreen packages. The higher the number, the greater the protection. SPF-15, for example, means that the user can spend 15 hours in the sun and absorb the same amount of tanning rays that would be absorbed in one hour without a sunscreen. SPF-2 means the user can spend two hours in the sun and absorb the rays that would be absorbed in an hour without a screen.

Anyone seeking a tan should know his or her skin type (see accompanying chart) and then choose the sunscreen that offers the appropriate protection.

A system similar to SPF is being tried by the cosmetic industry with products such as soaps and shampoos. These include a styling gel to protect hair from

the bleaching effects of the sun and even a lotion to protect a balding scalp. Whether they work is debatable.

Some firms in the United States and abroad are attempting to go beyond SPF-15 and are getting into the SPF-20s.

Firms are also marketing "tan accelerator" lotions, creams and powders that supposedly pre-release melanin—the skin's darkening protective pigment—in the skin and allow faster tanning if used a day or so before going out in the sun. FDA is cautioning these firms that—because these substances act on and in the body—they may have to be classified as drugs and come under stricter regulation.

For all the benefits of sunscreens, sunblocks and public awareness, the occurrence of skin cancer in the United States is increasing. Part of the reason may be found in a University of Florida study done last year.

More than 90 percent of those surveyed knew that too much sunlight causes skin cancer and aging. More than 80 percent understood the SPF system and knew that the right sunscreen would give protection. Yet, knowing all this, most still persisted in saying a "tan is healthy," and only half used sunscreens regularly. ■

*Richard C. Thompson is a member of
FDA's public affairs staff.*



First Aid for Pets

by Dianne McRae, D.V.M., and Melba Smith, D.V.M.

When a youngster cuts his lip or gets a splinter, parents know what to do: Head for the medicine cabinet, select suitable products, give emergency treatment, and, if necessary, call a doctor. But when the family dog cuts a leg while crashing through a window to chase the neighbor's cat, do the owners have the know-how and the right products handy for their pet's emergency? Simple first aid for a person or a pet, while not a substitute for medical attention, often stabilizes the patient until professional medical care is available.

The proverbial ounce of prevention that's worth a pound of cure for dogs and other pets starts with a pet first-aid kit. Here's what such a kit should have:

- cotton balls
- hydrogen peroxide
- eyedropper or teaspoon
- a small blanket
- tweezers or small pliers, to remove objects such as thorns from the skin
- scissors
- gauze, to wrap a broken or cut leg or to tie around the muzzle to prevent biting
- scotch tape, to hold a temporary bandage
- two small sticks, to keep a broken leg from moving
- a thin rope, to use as a tourniquet in bleeding

Here's how to put that first-aid kit to use. But remember, unlike treating humans (usually), giving first aid to an animal involves the risk of an accidental bite. If you think a bite is likely, it's best to take the pet directly to a veterinarian.

WOUNDS

Cuts from sharp objects or bite wounds can sever blood vessels, so the first objective is to control bleeding.

For a small wound, apply direct pressure above the wound with a finger. Clean the wound with a weak solution of hydrogen peroxide: about one part perox-

ide to three parts water. A minor cut not caused by a bite can then be bandaged, but bite wounds should never be covered as that makes an ideal environment for the growth of bacteria that can lead to infection. If the wound is caused by a broken leg (called a compound fracture), keep the leg from moving by gently placing it between two sticks and wrapping it with gauze. Take the pet to the veterinarian promptly. If you don't know whether the victim or the attacking animal has been vaccinated for rabies, tell this to the doctor.

For larger cuts, especially on a leg, apply a tourniquet between the wound and the torso, tightening it until the bleeding stops. Be sure to release the tourniquet every 10 to 15 minutes to prevent gangrene. A large gaping wound requires immediate veterinary attention because excessive blood loss may cause shock, and possibly death.

SHOCK

Shock is a medical condition in which the circulatory system collapses. The pet will have rapid shallow breathing, a fast feeble pulse, dilated pupils, and cold legs, ears and tail. Factors that can cause shock include: poisoning, excessive blood loss, and allergic reaction (to a drug, for instance), or an injury, such as being hit by a car.

Not all veterinarians agree that pets in shock should be kept warm. But since an animal in shock should have immediate medical attention, it's a good idea to keep the pet comfortable and warm on the way to the veterinarian.

CHOKING

Never try to take an object from the throat of an unfamiliar animal.

From a first-aid standpoint, foreign objects lodged in the throat should be re-



Stocking a first-aid kit for kitty or any other pet is a good way to prepare for possible emergencies.

Pet Poisons

CHEMICAL

Aspirin or acetaminophen
(*Never give to cats; they can't tolerate those drugs.*)

Antifreeze (*ethylene glycol*)

Arsenic

Strychnine

PLANT

Poinsettia

Wisteria

Dumbcane (*Dieffenbachia*)

SYMPTOMS

Vomiting, diarrhea

Staggering, paralysis, coma

Vomiting, diarrhea, convulsions

Twitching, convulsions, hypersensitivity to noise (*similar to rabies symptoms*)

Vomiting, diarrhea, abdominal pain

Vomiting, diarrhea, salivation

Salivation, swollen mouth and throat, paralyzed mouth (*can't bark*)

moved immediately. Whether this is safe to do with one's own pet is an individual decision. It helps if one person restrains the pet while someone else dislodges the object. If the object is visible, use your fingers to remove it. But if it can't be seen, the use of tweezers or some other gripping device is best left to a veterinarian, who is familiar with the animal's anatomy.

With large pets, such as a German shepherd, a modified version of the Heimlich maneuver can be applied to remove an object from the animal's throat. Place the animal on its side, and press below the lowest rib. This isn't recommended for small animals because overzealousness on the wrong location could fracture a rib. If the pet continues to have labored breathing, seek medical help immediately.

COLD INJURY

Pets suffering from exposure to the cold, or hypothermia, will appear weak and will be cold to the touch—at the paws, for instance. Usually, animals with hypothermia have been left outdoors for a very long time when the temperatures are extremely low.

The feet, tail, ears and muzzle are the most frequently frost-bitten areas. They

will feel hard and cold. Thawing should be done slowly and gently. A cold-injured area is very delicate, so *do not manipulate or massage the area*. Instead, apply heated towels, electric blankets, or hot water bottles directly to affected parts. Blow-dryers can also be used, but hold them about 12 inches away, and put the heat setting on low. The pet should be checked by a veterinarian for internal injury.

HEATSTROKE

Never leave a pet confined in an overheated area, especially if there's poor ventilation.

Heatstroke, or hyperthermia, is most prevalent when the outdoor temperature rises to 100 degrees Fahrenheit, but it's been reported at temperatures as low as 90 F. Many cases occur when a pet is left in a hot car. Or, a pet may be outdoors on a rope or chain, and overexertion due to excitement brings on heatstroke. Other contributing factors include lack of water, obesity, and breed predisposition—the bone structure of the muzzle in breeds with a face like a bulldog's may cause breathing difficulties. Dogs are more vulnerable to heatstroke than cats.

The overheated animal pants exces-

sively and may faint within just a few minutes. Initially, the lining of the mouth is bright red as the body tries to cool itself by sending blood to the head. Later, if the circulatory system collapses, the gums become very pale. Vomiting may occur.

Animals with symptoms of overheating should be placed in the shade. To bring the body temperature down, sponge or spray the pet with cold water. If possible, immerse the animal in cold water. Heatstroke is life-threatening, so the pet should be taken to a veterinarian right away.

POISONING

Poisoning is hard to diagnose because the most common symptoms (vomiting and diarrhea) can be caused by many conditions. If you see a pet eat a poisonous substance, check the product's package for instructions about what to do for accidental poisoning—whatever is suggested for humans can usually be applied to pets since treatment for poisoning generally is specific to the poison. If the poison is a petroleum product, acid or alkali (such as motor oil or dishwasher detergent), *do not* induce vomiting; give a few spoonfuls of milk, olive oil, or egg whites to reduce absorption of the poison. If the poison is a chemical like aspirin, antifreeze or insecticide, *do* induce vomiting by giving equal parts hydrogen peroxide and water with an eyedropper or teaspoon. It's best to check with a veterinarian before giving other drug antidotes such as syrup of ipecac or activated charcoal. Pets that like to chew should be kept away from poisonous chemicals and house plants. (See accompanying chart for some common household items that can poison pets.)

If your pet starts acting sick—mopes around, loses its appetite, vomits, has diarrhea—and you don't know why, call the veterinarian.

There's no question about the value of first aid for your injured pet. Keeping the pooch or other pet in a stable condition until medical attention is available provides a better chance for recovery and may even save its life. For anything but the most minor injuries, though, first aid is only an intermediate step. So, remember: Take an injured pet to a veterinarian as soon as possible. ■

Drs. Dianne McRae and Melba Smith are veterinarians with FDA's Center for Veterinary Medicine.

Test-Tube Skin and Other High-Tech Treatments for Burns

by Dixie Farley

When burns are so extensive that more skin is lost than is left, skin grafts become a matter of life or death. For more and more patients, even when burns cover 90 percent of the body, the verdict is "life," thanks to two new types of grafts: synthetic skin and skin actually grown in a laboratory.

These new grafting materials reflect improved knowledge about how burns heal. It has been learned, for instance, that severe burns cause less disfiguring scarring if surgeons remove the crust—called eschar—that forms over burns and close the wounds with skin grafts to keep fluids in and germs out. The earlier this is done, the lower the risk of organ failure and infection, which are the major causes of death from severe burn injury.

Ordinarily, the patient's unburned skin—from areas called "donor sites"—is "harvested," as they say, for the grafts. The harvested skin is stretched in a skin-expanding device and sewn over the wounds. (By perforating a skin graft in a lattice pattern, skin expanders can stretch it up to nine times the original size.)

If there isn't enough unburned skin for all the grafts, additional, temporary

grafts can be taken from a source other than the patient: pigskin, cadavers, human donors, and the amniotic membrane surrounding the baby in the womb. Cadavers are the usual source, says Kenneth Palmer, Ph.D., of the Food and Drug Administration's Center for Devices and Radiological Health. Pigskin used for grafting is classified as a medical device, as are skin expanders and other surgical tools. All are regulated by FDA. By the time the immune system rejects the transplanted skin, the patient's harvested skin areas, known as donor sites, are healed, and new skin can be reharvested for more permanent grafts. When many reharvests are needed, drugs that suppress the immune response can be given to buy extra time by delaying rejection of the temporarily transplanted tissue.

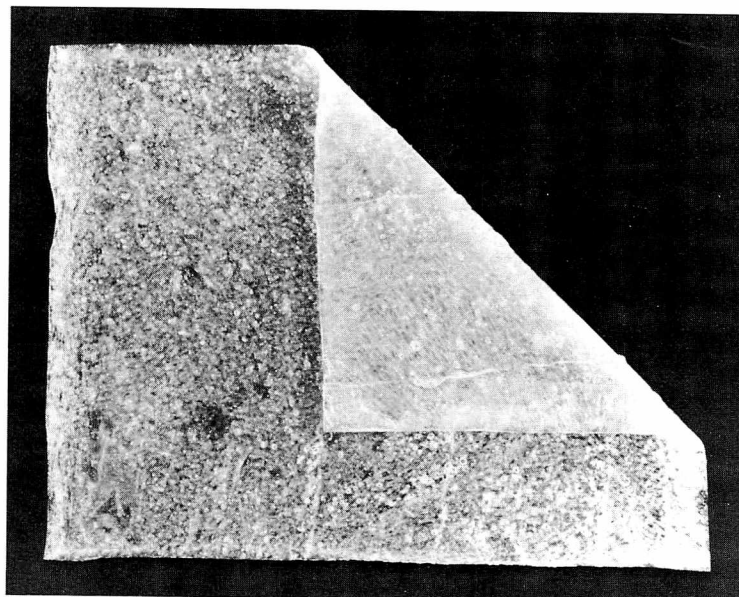
The threat of rejection posed by temporary grafts remains constant, pointing up the urgent need for a skin graft material with more permanence. One possibility is an artificial skin developed by plastic surgeon John Burke, M.D., of Harvard Medical School and Massachusetts General Hospital and Ioannis Yannas, Ph.D., of Massachusetts In-

stitute of Technology. The experimental product has been used on about 80 severely burned patients and is undergoing clinical tests for safety and effectiveness.

The Burke-Yannas "skin" has two layers that closely simulate the layers of normal skin, the epidermis and the underlying dermis. (For more on skin anatomy, see the accompanying article.) The artificial epidermis, a synthetic rubbery material called Silastic, is applied to the artificial dermis as a liquid, forming a tight bond as it hardens. The dermis is made of materials that appear naturally in human tissue: collagen and a derivative of cartilage. But this collagen comes not from humans but from cows; the cartilage derivative comes from sharks. The two-layer synthetic skin, which is generally not rejected, is sterile and can be stored at room temperature.

Severe burn wounds, then, are closed like this: The eschar is removed, the patient's available normal epidermis harvested for thin layers for grafting, and the grafts put through a skin expander and sewn over as many wounds as possible. The rest of the wounds are covered with the manufactured skin—in 4-inch by 6-inch sheets for wide, flat areas and

This section of the Burke-Yannas artificial skin shows its two distinct layers. The outside rubber-like epidermis—a mere one-tenth of a millimeter thick—is turned up over the thicker, porous dermis.



(Photo courtesy of Massachusetts General Hospital)

How Skin Heals

Though it's scratched, scrubbed, sat on, and trod on repeatedly, skin wears well.

Skin is flexible and elastic. It stretches smoothly around knobby corners and snuggles comfortably under hairy hollows and along moist passageways.

To properly protect the body, skin is a tattletale. It reveals inner secrets by coloring the face—anemic white or sick-liver yellow, for instance—and alerts its owner when it senses pain, itching, heat and cold.

Normal human skin, not counting the underlying fat, is between about one-fiftieth and one-quarter inch deep, depending on what part of the body it's covering. Yet it's our largest organ: Roughly two square yards of it envelop the body to protect against bumps, wounds, chemicals, disease, extremes in temperature, and excessive water loss. Skin also protects against harmful radiation from the sun, while at the same time allowing the body to use the energy in sunlight to make vitamin D.

Skin is actually layers of different types of tissue. The outermost layer, the epidermis, rests upon the dermis, and under that is the hypodermis. (Some experts describe the hypodermis as tissue under the skin, rather than as an actual part of the skin.)

The epidermis is the thinnest layer and it, too, favors the layered look—exhibiting, as it does, its own sub-layers of various epithelial cells. Cells residing at the epidermis's inner layers eventually die and, as new cells form, are pushed to the outer layer, or stratum corneum, where they're shed in flakes. Those dead cells are what make the skin waterproof and firm, even hard, as on the feet.

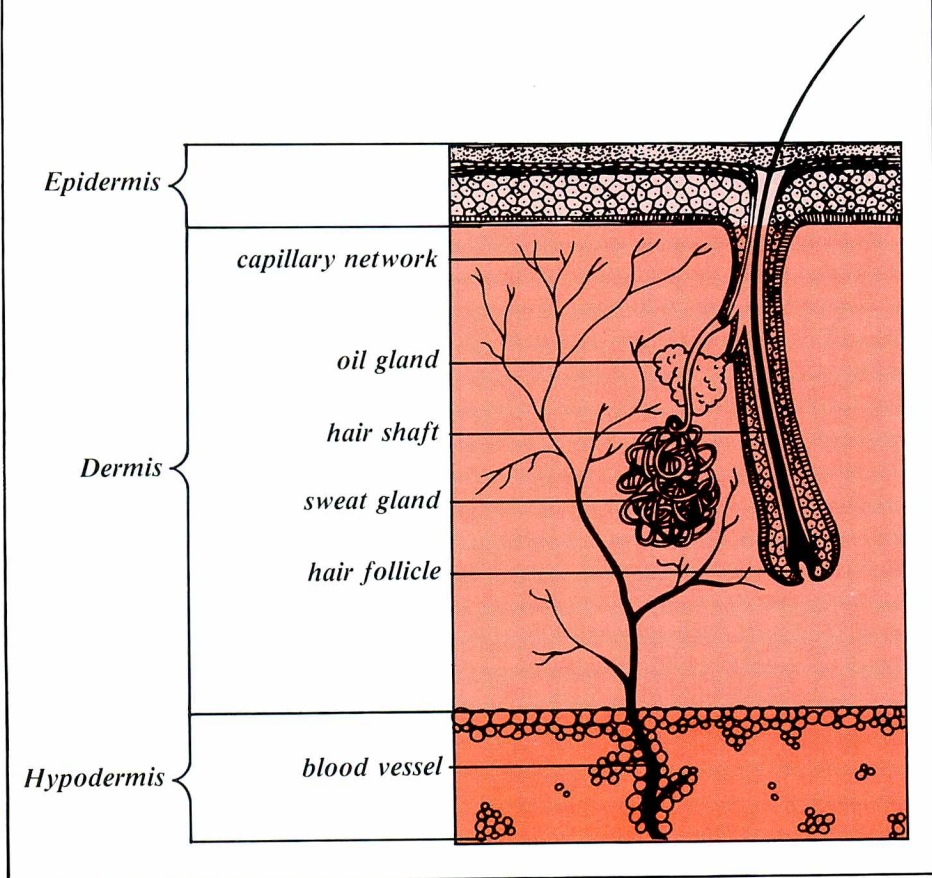
Some cells in the epidermis produce dark-colored granules called melanosomes, which protect against the damaging ultraviolet rays of the sun. The greater the number and the larger the size of a person's melanosomes, the darker the skin is, and the greater the protection.

For repair of minor wounds, skin depends on regeneration by its epithelial

cells and on activities by other structures of the body. Suppose, for instance, that a youngster scrapes his knee in a fall. At first, the boy sees blood and other fluid seep from his injury. The area becomes inflamed. Blood vessels there expand, and blood flow increases. The blood vessels become so permeable that plasma

(Continued on next page)

Cross Section of Human Skin



in narrow strips for limbs and joints. As healing allows, the patient's donor sites are reharvested for further epidermal grafts, and sections of the Silastic material are stripped away from the artificial dermis and replaced with permanent grafts.

Meanwhile, the artificial dermis acts as a scaffolding on which tissue beneath the wound can grow. Fibroblasts move in to produce connective tissue, and blood vessels develop to supply oxygen and nutrients. As the growth increases, the cowhide collagen and shark sub-

stance are broken down and absorbed by the body.

Thus, the artificial dermis and epidermis are gradually replaced so that the final skin is, in fact, the patient's own. The skin isn't quite normal, having neither hair nor glands, but the color often matches the patient's normal skin.

A newer version of the Burke-Yannas skin is under development. It involves taking epithelial cells from the patient's own skin and seeding them into the dermis scaffolding at the edges of the Silastic material at the time of the initial

grafting. This enables the epithelial cells to begin building a new epidermis while the fibroblasts and blood vessels rebuild the dermis. This Stage II version is still highly experimental, says a spokesman for Massachusetts General.

Other researchers report success with permanent grafts made of skin cells taken from sources other than the patient and then grown in culture in a laboratory.

Grafts of foreign skin are normally rejected because they have substances called Class II antigens that are unique to

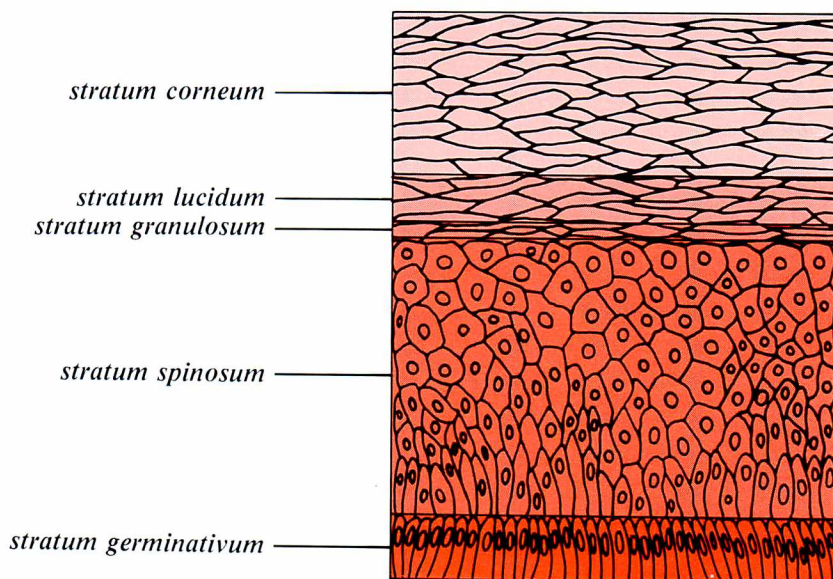
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(the fluid part of blood) leaks through to swell the spaces outside the vessels with water, proteins, and such cells as white corpuscles, which destroy and dispose of bacteria and dead cells. The area is red, warm and painful. Lymph vessels clot with protein to keep the inflammation from spreading. When the clot subsequently dissolves, resumed lymph flow carries off dead germs and dead cells, and the swelling subsides.

Within 24 hours of the boy's fall, epithelial cells have begun their work. From the normal epidermis around the wound and from hair and other structures embedded in the dermis below, the cells migrate onto the wound surface and start reproducing. The wound's seeping fluids, with all the dead bacteria and skin cells they contain, ultimately clot and dry, forming a scab. After a week or so, a layer of epithelial cells covers the entire wound under the scab as thin new skin. The cells continue reproducing to thicken the new skin, which eventually forces the scab off. The stratum corneum firms up. And finally, the once wounded area becomes nearly perfect skin. On the dense fibrous tissue known as a scar, though, the skin won't sweat and hair won't grow. If the wound is so severe that a great deal of tissue is lost, proper healing is threatened.

A major protective characteristic of the epidermis is its fairly impenetrable barrier against invasion by organisms. Some germs do make it through, but additional protection is offered by a film known as the basement membrane (a fitting name, in view of its position underneath the epidermis). The basement membrane connects the epidermis to the dermis and allows certain cells and fluids to pass between the two layers. Many an invader is imprisoned there until the

Detail of Epidermis



body can organize its white blood cells into a defensive attack or until the germ simply starves to death.

Supporting the epidermis is the dermis, which is mainly collagen, elastin proteins and fibroblast cells (which produce connective tissue), all nestled in a thick, gel-like material.

Here in the dermis, blood and lymph perform their infection-fighting, clean-up work and nourish the skin and its appendages—hair follicles, nails, and oil and sweat glands—which are situated in the

dermis. There are also tiny muscles that hold the hair erect ("goose flesh") to reduce heat loss when a person is cold or frightened. And nerve endings tell the brain what the skin feels so that the person can take appropriate actions: Add a sweater, move away from the fire, or scratch.

The hypodermis, a mass of loose connective tissue, makes the skin pliable. In most parts of this underlying area, there is also fat, which stores extra food and provides insulation and padding. ■

each individual; a person's immune system recognizes only its own as safe and considers foreign ones to be intruders and attacks them. But in some culture systems, explains Thomas Holohan, M.D., of FDA's Office of Health Affairs, the particular skin cells possessing the antigens die out, and only the cells without antigens continue to grow. "So, researchers can take epidermal cells from skin—from someone else or a cadaver—and grow them in culture. Then, when enough are produced, they're transplanted to the patient, and they grow and

aren't rejected," says Holohan.

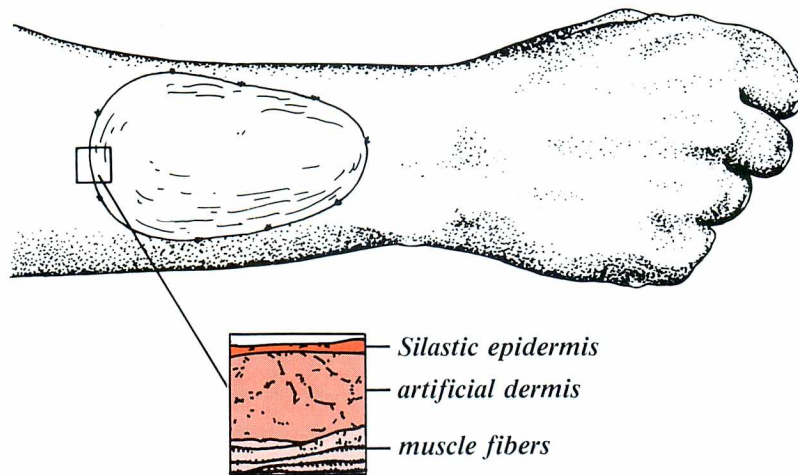
Success with grafting cultured cadaver skin onto three burn patients at New York Hospital-Cornell Medical Center in New York City was reported by John Hefton, Ph.D., and colleagues in 1983. Last November, Hefton, Michael Madden, M.D., and others reported in the *Journal of Trauma* about 26 patients treated with the cultured skin. Superficial wounds such as the patient's donor sites healed in six to eight days; deep wounds in which some dermis remained, in five to 18 days, though infection and damage

to one grafting site interfered with healing. "We have followed patients for up to three years after grafting and have not observed any acute episodes of rejection," they wrote. In wounds with no dermis, however, even several cultured skin grafts apparently contributed little, if any, to healing.

The Cornell skin is grown in culture until its surface area is 50 to 100 times the size of the original donor tissue. After 18 to 21 days, the skin is removed by hand from the container it grew in and is applied with the basal-cell side (the bot-

Over time, the patient's own skin replaces the artificial skin.

Grafting of Artificial Skin



Each section of artificial skin is tailored to fit the existing burn wound and sewn in place under slight tension to prevent wrinkling. The insert shows that the graft adheres without leaving space between it and the wound.

tom layer) touching the wound. The cells adhere within 24 hours, and a stratum corneum develops in seven to 10 days. According to Hefton, "The cultured grafts produced by our culture process are sufficiently thick and pliable to permit manipulation with forceps and hands. No gauze supports are necessary with these grafts; they can be spread over a wound to conform to its shape and size." Not only can the cultured skin heal donor sites twice as fast as sites that heal naturally under gauze dressings, it also can be grown in large quantities and

apparently isn't rejected. The Cornell team has now grafted more than 50 burn patients with the cultured skin, Hefton says.

Burn treatment continues to evolve as many research centers experiment with cultured skin and other wound coverings. Treatment with the patient's own cultured skin cells, for instance, was used by a research team led by G. Gregory Gallico, M.D., of Massachusetts General Hospital, to help two young boys survive burns that covered more than 95 percent of the body. The

team reported in the Aug. 16, 1984, *New England Journal of Medicine*, "The smooth supple skin generated on the face and hands was particularly impressive."

(For information about other advances in burn treatment, see "Progress in Treating Burns" in the February 1985 *FDA Consumer*.) ■

Dixie Farley is a member of FDA's public affairs staff.

Can Herbs Really Heal?

by Roger W. Miller



Through most of *The Clan of the Cave Bear*, that runaway best seller about the lives and loves of the cave man, the heroine, Ayla, is groomed to take over from the tribe's medicine lady. Ayla is not only taught what plants to use for what problems, but also what part of the plants (the stem, root or leaves) to use and how to process them (hang them upside down to dry, grind them in a bowl, etc.).

Over the course of nearly 500 pages, a lot of pains are eased and wounds mended through the herbal magic. And it's quite natural that in the thousands of years that the cave man and woman were on this earth they would have learned to use some of nature's offerings for medicinal purposes.

Their method of testing a product was to go directly to clinical trials—that is, they used the trial-and-error method. No doubt a lot of people got sick—or sicker—in the process, just as today a lot of laboratory mice and rats are made ill by modern man's testing.

But some of the cave dwellers had their pains eased, possibly from the medicine and possibly from simply being told that they were going to be cured. Whatever the reason, medicine practiced by the cave man has been carried down through the years and into societies as modern as ours.

Such folk medicine leaves a lot of people believing that there remain simple herbal cures for many health problems. But such is not the case. Much herbal medicine lore has since proved unfounded. And some of the herbs are dangerous—a point that author Jean M. Auel noted when Ayla was being instructed about the herb henbane: "Very useful to a medicine woman, but it should never be eaten; it can be dangerously poisonous if used as food."

The healing value of herbs is ever controversial. David G. Spoerke Jr., a University of Utah pharmacy professor and author of *Herbal Medications*, acknowledged the controversy in the introduction to his book, published in 1980.

"There is a growing number of people who are turning to 'natural' means of health care. . . . Some of these people say that herbal medicines are the only true means of obtaining 'natural' health. They pit themselves against those who think that all herbal medication is quackery and the only safe, effective drugs are those produced by the pharmaceutical industry. The truth, of course, lies between these two extremes."

Ah, but where between those two extremes does truth reside? There's the rub.

Matthew Suffness, Ph.D., head of the National Cancer Institute's Natural Products Branch, which studies herbs for anti-tumor qualities, says that those herbal medications that work generally work only on minor diseases. Dr. Suffness is not surprised that some do work; after all, he says, "You're looking at thousands of years of clinical experience—not 'controlled' clinical experience, of course—but the things that survived didn't make people sick and did do some good." Despite all that "clinical" experience, he warns that "you want to be careful that you don't get into a megadose situation."

Traditionally, herbal preparations contain only small amounts of active ingredients. However, those small amounts might be toxic or poisonous.

Richard Ronk, deputy director of the Food and Drug Admin-

istration's Center for Food Safety and Applied Nutrition, also preaches caution. "Man does not graze indiscriminately in Nature's garden," says Ronk.

The job of deciding where the truth lies often falls to the Food and Drug Administration. Charged with regulating drugs, cosmetics and most foods, FDA is looked to for guidance on herb usage. Botanical or "natural" products that are used in medicines have to be of proven safety and effectiveness. Herbs used in foods must also be nontoxic.

Foods quickly get classified as drugs when therapeutic claims are made for them. For example, if a manufacturer claims that his "Dermadough" bread contains "16 herbs that will help get rid of your pimples," that is a therapeutic, or healing, claim, and therefore the bread can be considered—and regulated as—a drug. That means the manufacturer has to back the claim that those 16 herbs will do as touted, and do it without injuring the health of anyone who tries the acne cure by eating the bread.

Upon discovering that Dermadough has become a drug, the manufacturer may decide to take the claim off the label and simply sell the bread as a food. However, as a result of a recent court ruling, the manufacturer cannot merely issue a new label without the claim. The product has to be relabeled "in a manner sufficient to disassociate the reconditioned product from its history of use as a drug."

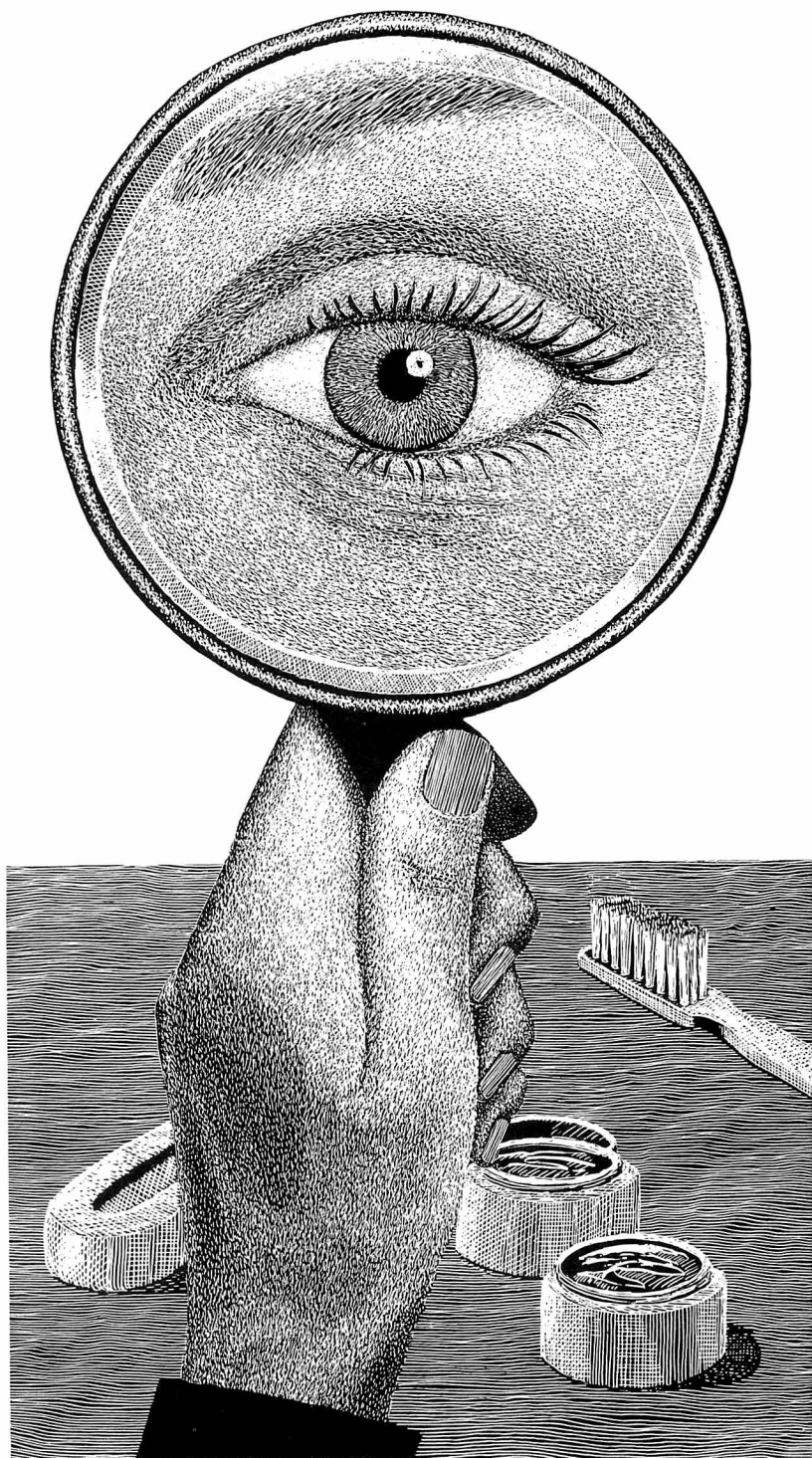
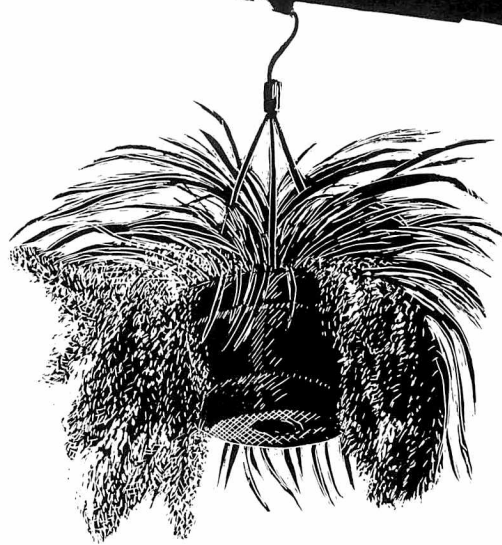
This could require a change in the brand name as well as a change in the name of the manufacturer, packer or distributor.

Herbs used in food for flavoring and other purposes and for which no drug claims are made must also be safe for consumption. In looking at such herb-containing foods, FDA "must consider whether the substance has a history of use in food . . . and whether there have been any adverse effects associated with consumption of the substance, including long-term toxicity or carcinogenicity," 1986 policy guidelines note. "Such history of use in food must include information that the substance has been used as a food ingredient and not as a drug, tonic, or folk remedy."

For a number of years, FDA included in its policy guidelines a list of 27 botanical products that were classified as unsafe on the basis of published scientific studies. The list was a reference tool for agency investigators, but it proved controversial and has been dropped from FDA's current *Compliance Policy Guidelines* (copies of which are available to the public and industry). The new guidelines state that the agency "will consider action against botanical products as food on a case-by-case basis under provisions" of the Federal Food, Drug, and Cosmetic Act.

Hundreds of plant extracts are used in cosmetics. Generally, the herbs are assumed to be safe and are put into cosmetic products without any prior FDA approval under the law. The agency may take action when a product or ingredient proves to be harmful.

One reason humans shouldn't munch about cavalierly in Nature's garden is that the gardener, Mother Nature, for all her simple appeal, is a complex person. As NCI's Dr. Suffness says of natural products: "You can isolate just about as many [chemical] compounds as you want, depending on the sen-



sitivity of the instruments you're using."

Nature is not only complex, but also capricious. Bloodroot is a case in point. In herbal medicine lore, bloodroot, which gives out a red juice when the root is damaged, is used for the treatment of warts, nasal polyps, and skin cancer. The American Indians also drank bloodroot tea for their rheumatism. Back in 1857, an English doctor by the name of Fell thought enough of it to develop a salve for treating breast tumors, according to *Herbs That Heal* by William A.R. Thompson, M.D. However, Dr. Thompson reports that a London hospital ran a trial on the salve with contradictory results. Thompson says other studies resulted in only "some scientific evidence for its folklore reputation. . . ."

Now along comes a U.S. toothpaste manufacturer claiming that a bloodroot derivative fights plaque that builds up on teeth and causes all kinds of dental problems. (See "The Dental Plaque Battle Is Endless but Worth It" in the September 1984 *FDA Consumer*.) The extract of *Sanguinaria canadensis* contains an alkaloid (a nitrogen-based organic compound) that was the very same substance thought by Dr. Fell and others to fight cancer.

A November 1986 monograph in the *Lawrence Review of Natural Products* said: "A large body of well-designed studies has found that toothpastes and oral rinses containing sanguinarine help reduce and limit the deposition of dental plaque in as little as 8 days." Many of the studies cited in the monograph were done by scientists associated with the toothpaste manufacturer.

One such study told how the compound was linked with oral hygiene. "The chemical structure of sanguinarine is similar to [compounds found in a] species of plant, which is used in Africa as tooth-cleaning sticks and are reported to be beneficial to the oral hygiene of these native cultures," according to a March 1984 article in the *Journal of the American Dental Association*.

But no New Drug Application for the product has been filed with the Food and Drug Administration, and the agency has yet to decide on the claims being made for sanguinarine and other anti-plaque products that are intended for sale over the counter (without prescription).

However, the case of bloodroot and its sanguinarine derivative provide a good example why we should graze with care in Mother Nature's garden. The "clinical trials" of the American Indians using bloodroot for rheumatism have proved to be of little value. Man was deceived, but the compound still may (or may not) have some other medicinal value.

Still another example of the it-doesn't-work-for-this-but-it-may-work-for-that approach is periwinkle. As a folk medicine it was supposed to cure diabetes. But it didn't stand up to 20th century studies. However, it has been discovered that an alkaloid in it may be able to fight tumors. NCI's Natural Products Branch believes that the periwinkle plant from Madagascar has the best properties for the job. The anti-tumor value was discovered by scientists looking for the key to the supposed diabetes use.

Mother Nature, it seems, is a coy lady when it comes to sharing the secrets of her pharmacopoeia. ■

Roger W. Miller is director of FDA's Communications Staff.



Scouring the Globe for Natural Cures for Cancer

The quest for cancer cures knows no bounds. That's why there's a Natural Products Branch at the National Cancer Institute.

And it might be said that the branch knows no boundaries, for it searches the globe for secrets that might be locked in nature on how to stop human cells from running amok.

Created in 1975, the branch has five professionals, including chemists, a marine biologist, and a microbiologist. Head of the unit is Matthew Suffness, Ph.D., a natural products chemist.

For field work, the branch relies on contractors. It currently has contracts totaling more than \$8 million for collecting plants, marine organisms, and microorganisms that might contain some anti-cancer chemical. The contractors cover areas ranging from Madagascar to Hawaii to Central America and from shallow waters in the Indian Ocean to the depths off the coast of South America.

A laboratory is being established at NCI's Frederick (Md.) Cancer Research Facility to process the collected samples. It, too, will operate under contract.

In their search for cancer cures, Dr. Suffness and his staff follow up on subjects that have "any reputation in traditional medicine for a related purpose." If they get a clue that a plant, for example, contains an agent with promise against cancer, they look up the plant's genealogical tree. As Dr. Suffness puts it, "Once you get a lead, you say 'go get me relatives'."

It's not that they expect to find simple cures. "We're no longer looking for magic bullets," Dr. Suffness explains. "Biologically active" compounds within living creatures are what is being sought. In "crude medicines," he notes, "things that are present in large quantities are usually not potent, and those that are potent are usually found in very small amounts."

"If you find such a [biologically active] substance, you see if you can 'scale it up'," Dr. Suffness says. "Can you purify it, modify it, or make a synthesized version? Maybe we'll be able to change the toxicity or potency. We can make a hundred derivations of it, so that the natural product will no longer be the best for our purposes."

He cites penicillin as an example. It comes from a mold, and the first forms were not only expensive to reproduce, but also had some therapeutic limitations. Now derivations are produced that are more versatile biologically, as well as much easier to make.

"Clinically active" anti-cancer agents have been found in the periwinkle plant in its native Madagascar. In addition, clinical trials are showing promise of anti-tumor abilities in chemicals found in yew trees from China and the Pacific Northwest.

NCI has screened 18,000 extracts of marine organisms that have been voluntarily provided by outside research groups, turning up "several interesting leads," including one compound from

the Caribbean sea squirt that's in clinical trials.

Most microorganisms that scientists have taken a look at have been from soil samples, but the Natural Products Branch has contracted with the University of Hawaii to study blue-green algae, which grows in water. The five-year, \$1,289,175 contract will involve culturing the algae from a variety of sources. In another contract, the University of Connecticut at Storrs is investigating fungi for anti-cancer agents.

The marine animal work is in two five-year contracts, each involving the collection of 1,000 organisms per year. One contract covers shallow waters (down to 100 feet) in the Indo-Pacific region; the other 100- to 3,000-foot waters in the Caribbean and off the coasts of North and South America.

Each of three plant contracts calls for collecting 1,500 samples a year for five years. The Missouri Botanical Garden will collect in Madagascar and Central Africa. The University of Illinois at Chicago is combing Southeast Asia, while the New York Botanical Garden is covering Central and South America. The contracts will cover some rain forests, which have been studied relatively little despite having a number of plants that have been used medicinally by local people. Dr. Suffness notes that there are many causes of cancer and many types. "So," he explains, "we're looking for hundreds of solutions." ■

A Medicine Woman's Herbal Lore

"See that little plant with the funnel-shaped yellowish flowers, purple in the middle?" Iza pointed to another plant.

Ayla touched a foot-high plant. "These?"

"Yes. That's henbane. Very useful to a medicine woman but should never be eaten; it can be dangerously poisonous if used as food."

"What part is used? The root?"

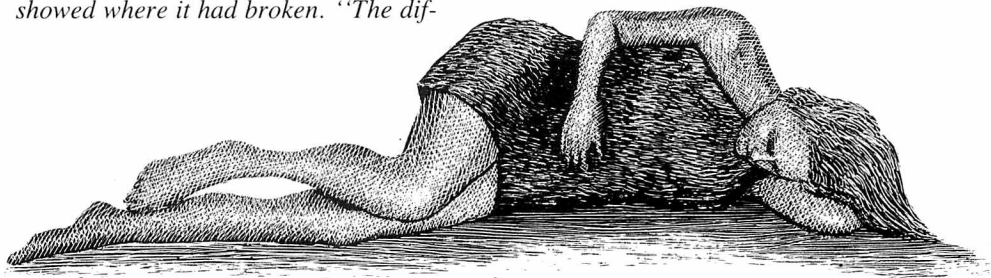
"Many parts. Roots, leaves, seeds. The leaves are larger than the flowers, grow one after the other on alternate sides of the stem. Pay close attention, Ayla. The leaves are a dull, pale green with spiky edges, and see the long hairs

growing along the middle?" Iza touched the fine hairs while Ayla looked closely. Then the medicine woman picked a leaf and bruised it. "Smell," she instructed. Ayla sniffed; the leaf had a strong narcotic odor.

"The smell goes away after it's dried. Later there will be many small brown seeds." Iza dug down and pulled out a thick, yam-shaped, corrugated root with a brown skin. The white inner color showed where it had broken. "The dif-

ferent parts are used for different things, but all of them are good for pain. It can be made into a tea and drunk—it's very strong, doesn't take much—or into a wash and applied on the skin. It stops muscle spasms, calms and relaxes, brings sleep."

—*The Clan of the Cave Bear* by Jean M. Auel, copyright 1980, Bantam Books. Reprinted with permission.





The Notebook

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 large public libraries.

■ As part of its effort to streamline the **drug review process**, FDA has completed 12 guidelines for sponsors of new drug and antibiotic marketing applications. Copies are available from the Support Services Branch (HFN-62), Center for Drugs and Biologics, Food and Drug Administration, Room 13B-05, 5600 Fishers Lane, Rockville, Md. 20857 (FR April 3).

■ FDA has approved a new form of genetically engineered **human growth hormone** manufactured by Eli Lilly Co. of Indianapolis, Ind. The drug, called Humatrope, treats growth hormone deficiency in children that can result in less than normal height. Another genetically engineered human growth hormone, Protropin, manufactured by Genentech Inc. of San Francisco, Calif., was approved in 1985.

■ The U.S. Department of Agriculture's Food Safety and Inspection Service is increasing its testing of cooked and **ready-to-eat meat and poultry products** for *Listeria monocytogenes*. These bacteria can cause listeriosis—a potentially life-threatening disease—and consumers are unlikely to further cook these products to destroy any of the bacteria that may be present (FR March 11).

■ FDA has approved the use of **Naprosyn**, an anti-inflammatory drug manufactured by Syntex Laboratories of Palo Alto, Calif., for treating **juvenile arthritis**. The agency also approved the sale of a liquid form of the drug. Previously, its use had been approved only for adults and only in tablet form. (For information on a Naprosyn recall, see "Counterfeit Pain Pills" on page 6.)

■ **Preventing heartworm** in dogs can be done with medication given just once a month since FDA's approval of the anti-parasitic drug ivermectin (brand name Heartgard), manufactured by Merck Sharp & Dohme. Other medication currently available to prevent heartworm must be given every day during the mosquito season. (Mosquitoes carry the heartworm parasite. (FR April 7).

■ When advertising for Donnie's Rejuvenation Creme Grooming Aid claimed that the product eliminated the major causes of **thinning and falling hair** and stimulated faster hair growth, a competitor complained to the National Advertising Division of the Council of Better Business Bureaus. The advertiser, American Beauty Products

Co., Inc., told NAD that the advertising featuring these claims had been discontinued, but that the company would give NAD substantiation if the claims were used in future ads.

■ NAD also received complaints from competitors about ads for **Perdue Farms Fresh Low-Fat Chicken**, which claimed that Perdue chickens had less fat and more meat than any other chicken. Although NAD questioned the sampling and statistical procedures used by Perdue to substantiate its claims, NAD agreed that the data showed a slightly lower fat content in Perdue chicken compared to Holly Farms chicken. However, the difference was so small that "any comparative claim would require qualification."

■ Acceptable uses of the **metric system** on the labels of **FDA-regulated products** are described in "Metric Declarations of Quantity of Contents on Product Labels." This Compliance Policy Guide is available from the Industry Programs Branch (HFF-326), Food and Drug Administration, Room 5425, 200 C St., S.W., Washington, D.C. 20204 (FR March 18).

■ FDA has issued a reproposal of the tentative final monograph (proposed rule) for **over-the-counter wart remover** drugs because of comments and new data submitted in response to the original proposed rule for OTC corn and callus remover drugs. Corns and calluses are different from warts, but the active ingredient salicylic acid is found in drugs for all three conditions (FR March 27).

■ The U.S. Centers for Disease Control has resumed routine, unannounced **cruise ship inspections** that had been discontinued in March 1986 as a cost-cutting move. The inspections cover food preparation, water supplies, and general cleanliness.



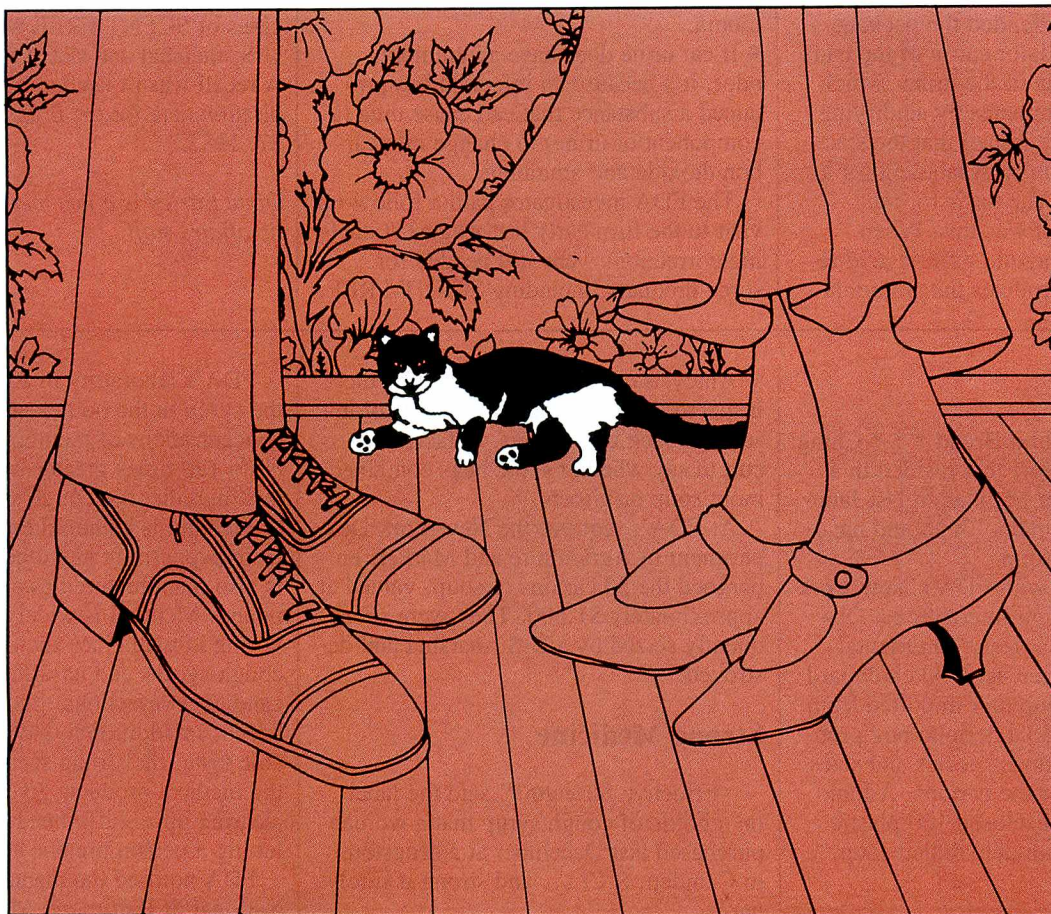


Investigators' Reports

Kitty Odor Product Seized

"Scent-Free" Would Only Mask, Not Cure, Infection

by Dixie Farley



"Whew! Ammonia! You open the windows, and I'll clean the litter box," she said.

"And then," he said, "I'm off to the drugstore to get some anti-ammonia-odor medicine we can give this cat."

Wrong move. The *right* move would have been a trip to a veterinarian—with the cat. Ammonia odor in a cat's urine is a sign of infection, and that calls for a doctor's care.

Here are more wrong moves. Forest Pharmaceuticals, Inc., of Maryland Heights, Mo., not only broke the law by

distributing its illegally labeled, anti-ammonia-odor product, SCENT-FREE, it also ignored FDA's warning to stop. Giving the mislabeled medicine to a sick kitty in lieu of a visit to the vet could be costly to the kitty's health. Selling the product was certainly costly to Forest Pharmaceuticals: Last October, as requested by FDA's St. Louis office, a U.S. marshal seized nearly \$17,000 worth of SCENT-FREE capsules.

FDA's investigation began with an inspection of the firm in April 1984, shortly before Forest Laboratories, Inc.,

of New York City bought the company. The St. Louis office investigator collected samples of all the labels for the company's products and sent them to FDA's Center for Veterinary Medicine for evaluation. Several were deemed illegal. In particular, said center experts, SCENT-FREE was an unapproved animal drug, since FDA knew of no scientific evidence showing that the product's active ingredient, methionine, was safe and effective for the use claimed in the label: controlling odor in cat urine. In a regulatory letter dated June 12, 1985, the



St. Louis office spelled out FDA's problems with SCENT-FREE and the firm's other products, as well as the corrections the firm was to make.

The firm responded with promises to make nearly all the changes FDA required, except with regard to SCENT-FREE.

The firm claimed that the product wasn't a drug but a food supplement, since the product's active ingredient, methionine, was an amino acid essential to the diet.

The firm also defended the package statement, "The major cause of the bad odor... is ammonia in the urine, which SCENT-FREE eliminates by acidifying the cat's urine." It argued that the statement was consistent with labeling for a food supplement. The basis for the "acidifying" effect was this: When methionine is absorbed, sulfuric acid results, and that neutralizes the ammonia

(which is alkaline) in the cat's urine, the company contended.

That's wrong information, said FDA's veterinary drug experts last March. The facts are:

- While it's true that methionine is an essential amino acid, the claim of controlling odor in cat urine is a medical claim, and that makes the product a drug, not a food supplement.
- Normal cat urine is already acid, so "acidifying" it isn't sensible.
- Normal cat urine doesn't contain ammonia.
- If cat urine does have an ammonia odor, it's because an infection has produced a substance that can cause urea (a component of urine) to change into carbon dioxide and ammonia.

The FDA investigator paid a follow-up visit to the firm early last August. Labeling corrections were still needed for some products, including SCENT-FREE.

Again, officials agreed to make changes for the other products, but not for SCENT-FREE. The investigator collected samples of SCENT-FREE as evidence for a possible seizure, which the St. Louis office recommended on Aug. 26. A complaint was filed against the drug on Oct. 12 in the U.S. District Court in St. Louis. The U.S. attorney charged that SCENT-FREE was a new animal drug and was illegal since there was no FDA-approved New Drug Application for it. On Oct. 23, some 709 cases of SCENT-FREE were seized by a U.S. marshal and slated for destruction. A recall wasn't needed because the expiration date for the drugs was March 27, 1987.

Dixie Farley is a member of FDA's public affairs staff.

Soup to Bugs

The "White Rabbit Brand * * * Ching Po Leung Soup Mix" that resided in a warehouse in lower Manhattan last January had the wrong name. It should have been called "bug soup."

An investigator with FDA's New York office was inspecting International Oriental Food Corp., a dealer in Oriental foods, when he came upon 30 cardboard cartons of dried soup mix imported from Hong Kong that had a definite bug problem. Insects of various species and sizes were crawling over the cartons. A look inside one carton disclosed 100 plastic bags filled with both dehydrated soup and insects.



Analysis of samples collected by the inspector found literally thousands of insects in each bag. It was, in fact, difficult to say whether some bags contained more soup or insects.

At FDA's request, the New York Department of Agriculture and Markets embargoed the 30 cartons of soup, valued at approximately \$1,500. They were subsequently seized by a U.S. marshal and destroyed.

Strong Medicine

"Effective Strength!" said the label on a bottle of cough syrup that a woman purchased last December at a drugstore in Camden, S.C. ... and strong it surely was.

After taking the syrup home, she gave a spoonful to her young son, who sputtered, gagged and choked. She then tried the syrup herself. "It literally took my breath away," she told the FDA investigator who came to her house to check out her complaint. She also said that it "burned her tongue like everything."

There was a powerful smell of menthol when the bottle was opened, and a small cloudy mass was seen in the syrup near the bottom. The investigator took the bottle and also collected 14 unopened bottles that had the same lot number (52532) and same appearance at a Revco drugstore in Camden.

FDA's laboratory in Atlanta analyzed the syrup in the bottles and found high concentrations of menthol, ranging from 60 to 190 times greater than normal for this ingredient in cough syrup.

Menthol is a natural essence distilled from peppermint and other mint oils. It is also manufactured as a chemical compound. Menthol is widely used as a flavoring in medicines such as cough drops, cough syrups and nasal inhalers, and in candies, confections, liqueurs and tobacco. In addition to having an acceptable taste, the strong scent of menthol in the medical products gives a feeling of clearing up a stuffy head and chest and letting a person breathe again.

FDA notified the manufacturer, Barre National of Baltimore, Md., who makes cough syrup for Revco and other distributors. Barre said it knew of the problem—having already had several complaints—and was doing an investigation of its own.

FDA's Baltimore office and the Barre management found that the syrup had been allowed to stand too long in the storage tank after it had been mixed. The ingredients had "layered," with the heavier menthol settling out and, in places, congealing. As the bottles later went by on the filling line, the syrup was drawn down with the ingredients not blended, making menthol levels in some bottles much higher than they should



have been.

Only one production lot—the bottling done for Revco—was affected. The 46,000 bottles in that lot had been sent to Revco's warehouse in Cincinnati. Although most had been shipped out, 3,131 were still on hand, and these were destroyed by Revco, with the destruction verified by FDA's Cincinnati office. The office also verified the recall and destruction of some 4,000 bottles of syrup still remaining in Revco stores and distribution centers in various parts of the country.

There were no reports of illness or injury from persons who had purchased and used the syrup, and it is likely that only a few bottles actually contained the overconcentration of menthol. The recall was considered Class III by FDA, meaning the syrup posed no hazard.

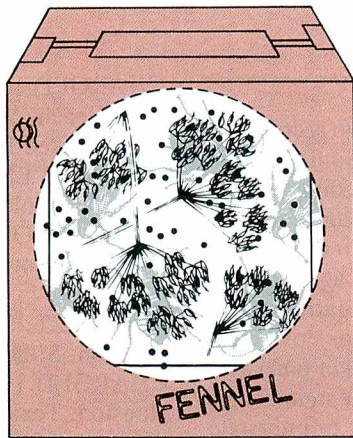
Smite the Mites

Ethnic food products imported into the United States are an increasing problem for FDA, as two recent cases in Los Angeles demonstrate.

These foods are often processed, packaged, shipped and stored under unsanitary and sometimes dangerous conditions. Most problems at this time seem to be with Oriental foods from Southeast Asia, where standards of preparation and packing are often lax. (See "Imported Ethnic Food: Exotic Fare but Buyer Beware" in *FDA Consumer*, December 1986-January 1987.)

Some foods from some countries are so likely to present problems that import alerts are issued to FDA inspectors and U.S. Customs officials. Even without an alert, FDA staff at ports of entry have become adept at recognizing foods, shippers and countries of origin that may need special attention.

One case involved a shipment of dried fennel seed coming into Los Angeles from Sun Yuen Hing Curry Condiments of Hong Kong. Fennel is an herb with a number of uses, in this instance as an ingredient in curry. To prevent contamination by insects and other pests, the seeds should be covered with gauze netting while they are drying. But FDA's Los Angeles laboratory found a large number of iolinid mites in a sample taken from a half-ton shipment of fennel seed. It was clear that the seed had not been properly protected.



Mites are tiny insects that can carry disease. The iolinid mite attaches itself to the wing base of the cockroach. Finding the mite is evidence of cockroach contamination as well, so the shipment of seed was denied entry to the country.

In another case, FDA's Los Angeles laboratory found a large number of fish mites in a 1,200-pound shipment of dried pollock from Hong Kong. These mites are found only in dried fish from Southeast Asia and the Far East. Like the iolinid mites, fish mites are hitchhikers, too, attaching themselves to the beetles that infest the dried fish. The mites are considered a serious pest in a variety of stored food products.

Finding the mites indicated poor storage and processing of the dried fish, which—like the fennel—was denied entry as an import.

The Los Angeles laboratory staff had no problem recognizing dried fish mites, since it is a species first described by district entomologist Allen Olsen in 1982 and now entered in the scientific literature as *L. angelina*.

Both shipments were detained by U.S. Customs at FDA's request, then returned to their countries of origin.

A Salty Mix-Up

M. Kamenstein, Inc., a spice repacker in Gardner, Mass., started off 1987 by recalling about 3,000 spice racks complete with spices. The problem was that the Epicure Salt in the racks had the wrong last name: Instead of sodium chloride, it was sodium nitrite, a substance

that is toxic in large doses.

The problem occurred when Kamenstein started buying Epicure Salt from the same New Jersey company that had been supplying the company's other spices. Epicure Salt typically contains ordinary table salt (sodium chloride) embellished with assorted other spices. Unfortunately, the salt produced by the New Jersey firm was not Epicure Salt but a meat-curing salt containing sodium nitrite, which is used to cure bacon and other meats. While safe for this use, if taken in large quantities, sodium nitrite can be fatal. It can bind to a person's red blood cells in sufficient quantity to prevent oxygen transfer from the blood to the body's cells. Victims of sodium nitrite poisoning may turn blue, suffer severe headaches and nausea, have symptoms of cardiovascular collapse, and, in some instances, die.

Kamenstein received the first shipment from the new supplier in October 1986. Bottles were filled, spice racks packed, and the products shipped. More shipments of the wrong Epicure Salt arrived, and repacking continued. Then, 1987 rolled in and so did a representative from the New Jersey supplier, who spotted the problem.

Kamenstein immediately stopped repacking the salt and emptied all the repacked Epicure Salt into large drums. At first, the firm thought it had contained the mix-up.

Then, in going back over its records, the firm discovered the October shipment. It contacted FDA, and staff at the agency's New York office advised the firm to begin a recall of the spice racks with their toxic salts. FDA investigators assisted, going to stores and examining stock. The firm had over 100 direct accounts and numerous sub-accounts, all of which had to be contacted. Consumers who had bought spice racks since Oct. 1, 1986, were asked to send the jars of Epicure Salt back to Kamenstein for replacement. The bottles had not been sold individually.

At the time of publication, the recall was still in progress. There had been no reports of illness due to the salt.

—This small sample of reports from the field was prepared by Carol Ballentine, Carolyn Hommel, Bernie Janiger, Margaret Sarles, Gordon Scott, and Richard Thompson.



Summaries of Court Actions

Summaries of Court Actions are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Summaries of Court Actions report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices or cosmetics 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/Poisonous and Deleterious Substances

PRODUCT: **Pepper, black, ground**, at Columbus, S. Dist. Ohio; Civil No. C2-85-1846.

CHARGED 11-20-85: When shipped by Colonial Spice & Extract Co., Inc., Brooklyn, N.Y., the article contained the added poisonous or deleterious substance *Salmonella* microorganisms—402(a)(1).

DISPOSITION: Consent—authorized release to the shipper for bringing into compliance. (F.D.C. No. 64790; S. No. 85-385-405; S.J. No. 1)

Foods/Contamination, Spoilage, Insanitary Handling

PRODUCT: **Cheese, mozzarella, part-skim, low-moisture**, at Pleasantville, Dist. N.J.; Civil No. 86-1146.

CHARGED 3-20-86: While held by Benj Polakoff & Son, Inc., Pleasantville, N.J., the article contained rodent filth and had been held under insanitary conditions—402(a)(3), 402(a)(4).

DISPOSITION: Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 64877; S. No. 86-414-115; S.J. No. 2)

PRODUCT: **Peanuts, shelled**, at Suffolk, E. Dist. Va.; Civil No. 86-737-N.

CHARGED 10-15-86: While held for sale, the article contained insect filth—402(a)(3).

DISPOSITION: Consent—authorized release to Producers Peanut Co., Inc., Suffolk, Va., for salvaging. (F.D.C. No. 65043; S. No. 86-468-411; S.J. No. 3)

PRODUCT: **Pineapple, crushed, canned**, at Baltimore, Dist. Md.; Civil No. B-85-4315.

CHARGED 10-18-85: When shipped by Sandler Foods, Virginia Beach, Va., the article (labeled "Premium Crushed Pineapple Packed In Its Own Juice . . . Product of Thailand . . . Distributed by: J.F. Braun & Sons, Inc. . . . Lake Success, N.Y.") contained mold—402(a)(3).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 64742; S. No. 85-441-168; S.J. No. 4)

PRODUCT: **Soybean powder, and other food stocks**, at Houston, S. Dist. Texas; Civil No. H-86-4167.

CHARGED 11-6-86: While held by D.Y. Import Co., Inc., Houston, Texas, the article had been held under insanitary conditions—402(a)(4).

DISPOSITION: Consent—authorized release to the dealer for salvaging. (F.D.C. No. 65056; S. No. 86-451-221 et al.; S.J. No. 5)

Foods/Economic and Labeling Violations

PRODUCT: **Chocolate candy bottles filled with liquor, Winters**, at St. Paul, Dist. Minn.; Civil No. 4-86-91.

CHARGED 2-3-86: When shipped by Winters Chocolate Liquor Bottles, Inc., Manteno, Ill., the articles were confectionery, and the articles contained alcohol other than alcohol not in excess of one-half of 1 percent by volume derived solely from the use of flavoring extracts—402(d)(2).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 64828; S. No. 86-448-589 et al.; S.J. No. 6)

Drugs/Human Use

PRODUCT: **Aerolate theophylline liquid and capsules, and in-process theophylline drugs**, at Fenton, E. Dist. Mo.; Civil No. 85-0516-C-A.

CHARGED 3-6-85: When shipped as a theophylline component by S.S.T. Corp., Clifton, N.J., or others, and as capsules by D.M. Graham Laboratories, Hobart, N.Y., the articles, which were prepared, packed, and labeled by Fleming & Co., Fenton, Mo., were new drugs without an effective approved New Drug Application—505(a); and the articles' labeling lacked adequate directions for use and the articles were not exempted due to their new drug status—502(f)(1).

DISPOSITION: The articles were claimed by Fleming & Co., Fenton, Mo. The claimant moved to dismiss the action on a number of procedural grounds, and did not dispute that the seized drugs fell into the category of drugs that required pre-market approval. The government opposed the claimant's motion. The motion to dismiss was denied. The claimant filed an answer denying the charges. Thereafter, a consent decree of condemnation was entered. The decree authorized release of the articles to the claimant under bond, under the condition that the articles would be quarantined until either they were shown to be in compliance with an approved New Drug Application, or they were destroyed. A subsequent consent order authorized release of 180 dosages for the treatment of an intervenor for use under medical supervision on an investigational basis. (F.D.C. No.



64500; S. No. 85-495-415; S.J. No. 7)

PRODUCT: Cefaclor capsules, at Miami, S. Dist. Fla.; Civil No. 85-3891.

CHARGED 12-23-85: When imported, the article was a counterfeit of Ceclor brand of cefaclor capsules; and the article and its labeling, without authorization, bore the trademark, trade name and other identifying marks of a drug manufacturer other than the person who in fact manufactured the article—201(g)(2).

DISPOSITION: The article was claimed by Rx Wholesale Suppliers, Inc., Miami, Fla., who filed an answer denying the charge. Subsequently, the claimant amended his answer to include, among his affirmative defenses, the following: that the article had been imported into the United States; that the claimant had no cause to believe that the article was violative; that no violation had occurred after the article had been imported; and that the claimant should be entitled to export the article.

The claimant litigated the action and moved for consolidation for trial of this action with a number of other actions, including a suit by Eli Lilly & Co., Indianapolis, Ind., against the claimant (*Eli Lilly & Company v. Rx Wholesale Suppliers, Inc., et al.*; Civil No. 86-1069). In the latter case, Eli Lilly & Co. complained, in a trademark and unfair competition suit, as follows: that Ceclor antibiotic, when intended for sale in the U.S., was encapsulated in its plant in the U.S. and then bottled and packaged in accordance with FDA regulations; that when intended for sale abroad, the active drug product, in powder form, was shipped in bulk to authorized foreign plants for encapsulating, bottling, and packaging by affiliate or licensed companies; and that the defendants were trading in violative cefaclor capsules not made in the United States. The claimant (Rx Wholesale Suppliers, Inc.) filed a counterclaim against Eli Lilly & Co. and a Southeast Asian firm. The claimant asserted that the subject article had been relabeled by Eli Lilly & Co. or one of its Southeast Asian agents. The claimant admitted that the expiration date of the antibiotic drug was not accurately stated on the bottles and that the drug contained a dye which may not be used in pharmaceutical products in this country.

Ultimately, upon consent, some lots of the drugs in one of the consolidated seizure actions were authorized to be exported (after FDA inspection) because there was good evidence indicating that those lots had been properly manufactured in the United States. A consent decree of condemnation ordered the remaining drugs to be constructively destroyed by turning them over to FDA. (F.D.C. No. 64797; S. No. 86-333-973; S.J. No. 8)

Drugs/Veterinary

PRODUCT: Aminoplex large-volume parenteral solutions, at Burnsville, Dist. Minn.; Civil No. 3-84-1049.

CHARGED 7-26-84: When shipped by TechAmerica Group, Inc., Elwood, Kan., the articles (labeled "Aminoplex Solution ... Contents: 500 ml. [or "950 ml."] ... Amino Acids ... B-Vitamins, Electrolytes and Dextrose ... Preservatives ... Manufactured for Tech America Group, Inc., Elwood, KS" and "Amino Plex-C (34X Concentrate) ... Contents: 500 ml. ...

Amino Acids ... Preservatives") were new animal drugs and no approval of a New Animal Drug Application was in effect with respect to their uses; and the articles lacked adequate directions for lay use and lacked the required veterinary prescription legend—501(a)(5), 502(f)(1).

DISPOSITION: The articles were claimed by the shipper who denied the charges. The claimant also served written interrogatories on the government. The government served written interrogatories and requests for admissions on the claimants.

Subsequently, a consent decree of condemnation ordered the articles destroyed. The decree also ordered, among other things, that the claimant do the following: delete from all Aminoplex labeling any mention of any mode of administration other than intravenous; delete the "34X" legend from all Aminoplex labeling; delete from Aminoplex labeling any indication for use of Aminoplex in animals other than cattle; and eliminate preservatives from Aminoplex. (F.D.C. No. 64328; S. No. 84-202-490; S.J. No. 9)

PRODUCT: Medicated premixes and bulk drug ingredient, at Fort Dodge, N. Dist. Iowa; Civil No. 2C 86-3077.

CHARGED 7-14-86: While held for sale, the articles had been manufactured, processed and packed by Custom Feed Blenders, Fort Dodge, Iowa, under circumstances that failed to conform with current good manufacturing practices—501(a)(2)(B).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 64934; S. Nos. 86-473-214/5; S.J. No. 10)

PRODUCT: Medicated premix for swine, at Sioux City, N. Dist. Iowa; Civil No. C86-4115.

CHARGED 6-25-86: While held for sale, the article, which had been intended for export, but which had been rebagged, diverted to domestic use, and relabeled as "Aureo S-P 250 *Granular* chlortetracycline, penicillin, sulfamethazine Medicated Swine Premix ... Manufactured for Consumers Supply Dist., Sioux City, Iowa," was a new animal drug; and no approval of a New Animal Drug Application was in effect for its use and intended use—501(a)(5).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 64915; S. No. 86-340-470 et al.; S.J. No. 11)

Medical Devices

PRODUCT: Facial-tanning ultraviolet units, at New York, S. Dist. N.Y.; Civil No. 86-Civ-3400.

CHARGED 4-29-86: The articles, which had been manufactured by Silver Group, Inc., San Francisco, Calif., and which had remote on/off switches that abrogated the required timers, lacked labeling bearing adequate directions for use—502(f)(1); and the articles' labeling lacked adequate warnings against unsafe methods or duration of administration or application, in such manner and form as were necessary to protect users against potentially harmful ultraviolet radiation—502(f)(2).

DISPOSITION: Consent—authorized release to Solarium Resorts, Inc., New York, N.Y., for bringing into compliance. (F.D.C. No. 64886; S. No. 86-424-433 et al.; S.J. No. 12)

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(Continued from page 41)

PRODUCT: Tape recordings for health-related problems, at Grand Rapids and Alto, W. Dist. Mich.; Civil No. G80-926.

CHARGED 12-29-80: The articles, which were manufactured by Potentials Unlimited, Inc., Grand Rapids and Alto, Mich., which bore titles such as "Weight Loss," "Stop Bed-Wetting," "Facial Tic," "Freedom From Allergies," "Freedom From Acne," "Stop Loss of Hair," "Arthritis Pain," "Hyperactive Children," and "Psychic Healing," and which were accompanied by labeling such as (catalogue) "Potentials Unlimited Hypnotic Sleep Tapes" and (blister pack card) "hypnosis because change begins in the mind. Safe, Effective, Guaranteed," had labels and were accompanied by labeling which contained false and misleading claims for: enuresis, facial tic, allergies, acne, teeth and gum problems, menstrual problems, weight gain, headaches, migraine headaches, stomach problems, hair loss, arthritis pain, hearing loss, insomnia, hyperactivity in children, depression, stuttering, birth control, conception, weight loss, improving vision, pain suppression during dental procedures, lowering high blood pressure, relief of pains caused by birth defects and disease, healing bad nerves, speeding recovery after surgery, influencing the healing process in others, and curing illnesses associated with birth trauma—502(a); that the articles' labeling lacked adequate directions for use, since such directions could not be written for lay use for the articles' intended purposes—502(f)(1); and the articles were manufactured, prepared, and processed in an unregistered establishment—502(o)(i); the articles were not included in a required list—502(o)(ii); and pre-market notification respecting the articles had not been provided—502(o)(iii).

DISPOSITION: The articles were claimed by the dealer, who denied the charges and asserted affirmative defenses. Upon the government's motion, post-seizure sampling was ordered of a number of specified articles. The parties served written interrogatories on each other and litigated the action. The claimant moved for summary judgment on the grounds that the seized articles were not "devices" within the meaning of 21 U.S.C. 201(h) and that the seized articles were protected by the Constitution's First Amendment. Meanwhile, pursuant to stipulation of the parties, five inadvertently seized tapes (e.g., "Peace of Mind," "How to Attract Love" and "Be a Better Bowler") were released from seizure and returned to the claimant.

The court denied the claimant's motion for summary judgment. The court said that the claimant, through its promotional literature, had implied that the tape recording would actually "treat" certain physical or mental conditions by hypnosis. Arguably, this implied "treatment" brought the tape within the definition of a "device." The court also concluded that the seized tapes were not completely immune from regulation by virtue of the First Amendment and that whether the involved regulation met the test outlined in *United States v. O'Brien*, 391 U.S. 367, would have to be determined through a full trial.

The action came on for trial before the court, the parties having waived trial by jury. Before trial the parties had entered into

an extensive stipulation of facts, and all of the government's exhibits, including all depositions, were admitted into evidence. The court ruled for the government and against all but one of the tapes, holding that the tapes were medical devices because of the therapeutic claims made in marketing the tapes. The court said that the excepted tape, "Weight Loss," based upon its content and the claims made in the catalogue, appeared to be intended only to affect a person's eating habits, and did not purport to affect body structure except through a change in behavior. In addition, the tape was listed in the catalogue under the "Habit Series," rather than as part of the health series.

In condemning the other tapes as misbranded medical devices, the court noted that the tapes could be harmful if they caused someone to delay seeking adequate medical care for a disease condition, and that the uncontrolled use of hypnosis could be dangerous because persons could develop anxiety reactions to some of the suggestions contained on the tapes. The conduct of Potentials Unlimited in marketing these tapes as therapeutic medical devices was subject to regulation by Congress even if the tapes themselves communicated ideas. In accordance with the court's findings of fact and conclusions of law, as amended, the tape "Weight Loss" was released to the claimant, and the 31 other tapes were ordered constructively destroyed by erasure of their content. (F.D.C. No. 63235; S. No. 80-192-153 et al.; S.J. No. 13)

In Vitro Diagnostic Products

PRODUCT: Whole blood, blood platelets, and blood plasma, for use as *in vitro* diagnostic-product components, at Jamaica and Hauppauge, E. Dist. N.Y.; Civil No. CV-86-1903.

CHARGED 6-6-86: The labeling of the articles (which were being collected by New York Blood Components, Inc., Jamaica, N.Y., and being shipped to a related firm in Hauppauge, N.Y., for use in manufacturing hematology calibrators, controls and reagents) failed to reveal the material facts that some of the articles had been shown to be positive for the test for hepatitis B surface antigen (HBsAg) and that many of the articles had been improperly tested for HBsAg, thereby posing a risk of hepatitis to persons using the articles or products manufactured from the articles—502(a).

DISPOSITION: Default—ordered destroyed. (F.D.C. Nos. 64882/3; S. No. 86-393-183 et al; S.J. No. 14)

CONTEMPT ACTIONS

DEFENDANTS: J.S.J. Supply Ltd., John Allen Tate (a/k/a John Hamilton), James K. Tate, D.V.M., and Shellee L. (Compton) Kotschwar, Dist. Colo.; Civil No. 83-M-602 and Criminal No. 83-CR-350.

CHARGED 11-3-83 (criminal contempt petition) and 11-10-83 (civil contempt motion): That the defendants had attempted to contravene the orders of the court by establishing and operating new business firms (i.e., Supplements Unlimited, Cheyenne,



Wyo.; Vital Life Products, Ashland, Ky.; and Vital Health Products, Ashland, Ky.); that drug orders sent to J.S.J. Supply Ltd. for human and veterinary prescription drugs had been filled through such new firms, with the result that the defendants had shipped drugs in interstate commerce in violation of the orders of preliminary injunction on seven specified occasions.

DISPOSITION (criminal contempt action): The court issued an order to show cause why the defendants should not be held in criminal contempt. The defendants litigated the criminal contempt action. However, because the same judge was presiding in both the injunction and contempt proceedings, that judge recused himself; and the criminal and civil contempt actions were reassigned to another judge who was of the view that there could not be a fair trial of both criminal and civil contempt allegations in the same trial, and that the civil proceeding should go forward and the criminal proceeding be held in abeyance. Since there was no objection to this procedure by the defendants, a speedy trial having been previously waived by the defendants, the criminal action was suspended pending developments in the civil contempt action.

After a consent decree of civil contempt and permanent injunction had been entered, the defendants moved to dismiss the criminal contempt action on two grounds: that they had been denied their right to a speedy trial, and that settlement of the related civil contempt action made it unnecessary, improper and unlawful to punish them for the same acts in a criminal contempt action. The government opposed such motion.

The court found that, after the resolution of the proceeding by the entry of the consent decree, the criminal contempt proceeding had not again been set for trial; and the court **dismissed** the criminal contempt action for violation of the Speedy Trial Act. The dismissal was without prejudice because there was nothing to indicate that the delay itself had caused any prejudice to the defense. The court concluded that the dismissal of the criminal contempt petition would have no effect upon the government's opportunity to initiate criminal prosecution for the commission of acts prohibited by 21 U.S.C. 331.

DISPOSITION (civil contempt action): The government served written interrogatories, requests for admissions, and requests for the production of documents upon various of the defendants. When J.S.J. Supply Ltd. failed to respond to the court's order to respond, the court entered that firm's default.

Subsequently, J.S.J. Supply Ltd. appeared and consented to a consent decree of permanent injunction and civil contempt. On the same day, a consent decree of permanent injunction and civil contempt was entered against the individual defendants. The decrees provided that for each violative shipment of prescription drugs knowingly and intentionally made by a defendant after the date of the decree, the defendant should be fined the value of the shipment, plus \$2,000 for the first violation, \$5,000 and 30 days in jail for the second violation, and \$10,000 and 60 days in jail for every subsequent violation. In addition, the court imposed upon the defendants the cost of the action in the amount of \$34,000. (Inj. 1029; S.J. No. 15)

INJUNCTION ACTIONS

DEFENDANTS: J.S.J. Supply Ltd., John Allen Chemical Co., Sheep Guard, Inc., and James K. Tate, D.V.M., director of the corporations, **John Allen Tate (also known as John Hamilton),** a corporate officer, and **Shellee L. (Compton) Kotschwar,** a corporate director, Fort Collins, Dist. Colo.; Civil No. 83-C-602.

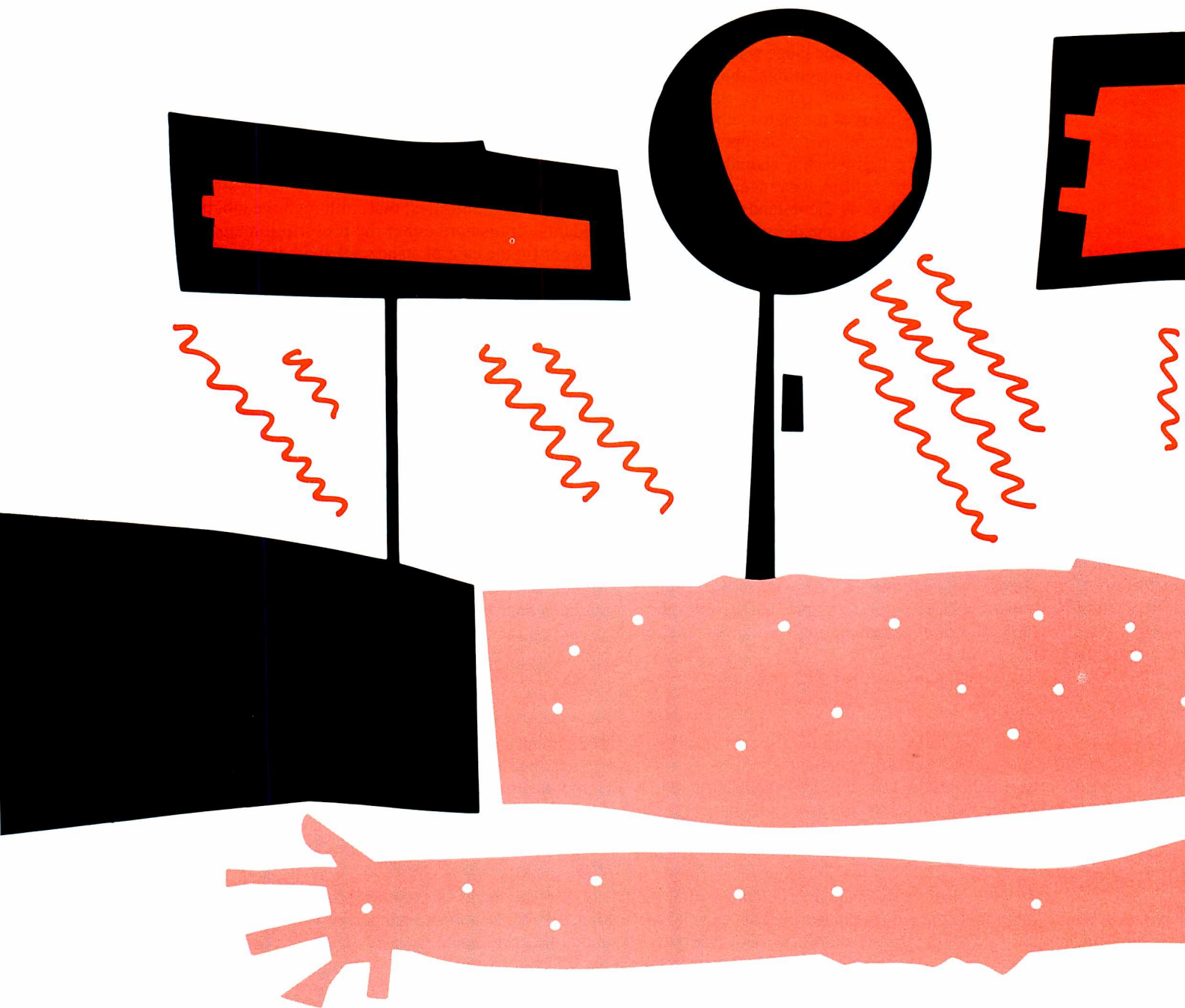
CHARGED 4-8-83 in a complaint for injunction: That, since 1980, the defendants James and John Tate had been promoting, labeling and distributing prescription drugs to the general public for uses unapproved by FDA; that, to carry out their activities, they used different business firms, including the defendant corporations, and had been assisted by employees and corporate directors of such firms; that the defendants' drugs included potentially harmful prescription drugs, including steroids, thyroid hormones, and diuretics; that, although the labeling of the defendants' drugs bore either the prescription legend for human drugs or (in the case of stanozolol and boldenone undecylenate) the prescription legend for veterinary use, the defendants promoted and distributed the drugs to the general public for self-administration outside the care and supervision of a physician and provided syringes and instructions for injection; that the defendants failed to provide adequate directions for lay use, and (in some instances) provided dosage recommendations other than those provided in professional labeling; that none of the individual defendants was licensed to practice human medicine or pharmacy; that James K. Tate was a graduate veterinarian, but he was not licensed to practice in Colorado; that the defendants promoted and distributed prescription steroids, thyroid hormones, and diuretics for athletic uses (body building, dieting, and weight loss); that the defendants promoted and distributed DMSO for use for bursitis, injuries, arthritis, burns, gout, stroke, cancer, and other specified diseases; that such uses had not been approved by FDA; and that the defendants were well aware that their promotion and sale of such drugs was illegal—502(f)(1), 503(b)(1), 505.

DISPOSITION: Pursuant to stipulation, J.S.J. Supply Ltd. and John Allen Tate were temporarily enjoined from the complained-of violations. In addition, the other defendants were given notice and were also temporarily enjoined. Subsequently, at a hearing, J.S.J. Supply Ltd., John Allen Tate and Shellee L. Compton stipulated to a preliminary injunction; and James K. Tate, D.V.M., John Allen Chemical Co., and Sheep Guard, Inc., having failed to appear at the scheduled hearing, had a preliminary injunction issued against them.

Meanwhile, it appeared to the government that a number of violative shipments of prescription legend drugs had been made after the issuance of the temporary restraining orders. Accordingly, the government initiated contempt proceedings. (See S.J. No. 15 of this issue of *FDA Consumer*.)

Ultimately, all the defendants entered into a consent decree of permanent injunction and civil contempt. (Inj. No. 1029; S. No. 83-245-853; S.J. No. 16)

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Allergic Reactions

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- Know if your medicines make you extra sensitive to light.
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HHS Publication No. (FDA) 87-8270