

FDA CONSUMER

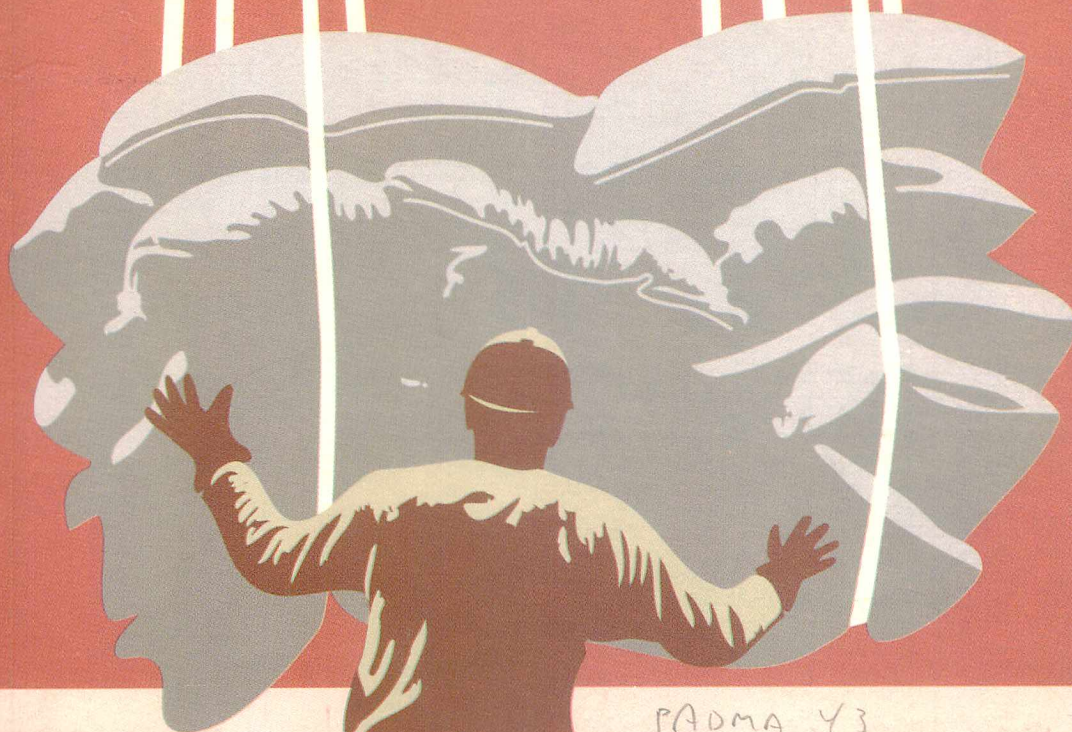
THE MAGAZINE OF THE U.S. FOOD AND DRUG ADMINISTRATION

• VOL. 25 NO. 2

MARCH 1991 •

FROM
PSYLLIUM
SEEDS TO
STONEWARE

*FDA Insures
Quality
of Imports*



PADMA Y3



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FDA CONSUMER

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Rx to OTC: The Switch Is On 8

More than 200 products available only by prescription a decade ago are now available over the counter. Yet the decision to "switch" a drug is not one that FDA makes lightly.

From Psyllium Seeds to Stoneware: FDA Insures Quality of Imports 12

Across the country, FDA inspectors work to make sure that regulated products entering the United States from abroad meet the same high standards as those made here.

Tuberculosis: Still Striking After All These Years 18

Once a top killer, TB declined dramatically in the first half of this century thanks to new drug treatments, improved hygiene, and better understanding of the disease. But now, the number of TB cases is beginning to creep up again.

Preventing 'Turista' and Other Travelers' Ailments 24

Travelers' diarrhea is the affliction most likely to strike Americans abroad, but it is not the only disease or medical condition to which they may fall victim.

Pet Cuisine: Feeding Galloping Gourmets 28

Will your dog or cat be better off with a "gourmet" pet food rather than the usual chow? Though benefits may be touted, owners need to know when these products are really needed and when pets—and pocketbooks—may be better off without them.

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A group of drugs commonly used to treat infections is the topic of the latest installment in FDA Consumer's series on proper drug use.

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Inside Front Cover Photo: Tuberculosis observation wards, like this one at a U.S. Army base in France during World War I, were phased out long ago. But TB cases have been rising again, for reasons explained in the story beginning on page 18. (Photo courtesy National Library of Medicine)



FDA Requires Testing of Medical Gloves

Effective mid-March, manufacturers of rubber and plastic gloves worn by health-care workers must test their products using standardized methods and must meet minimum quality levels defined by FDA.

Until FDA announced test methods and quality requirements last December, medical glove manufacturers could devise their own testing programs. Gloves must now undergo a water leak test developed by FDA in which 1,000 milliliters of water (about a quart) are poured into the glove, which is then checked for leaks.

The maximum allowable failure rate for patient examination gloves is 40 per 1,000; for surgeons' gloves it is 25 per 1,000. (The rate is lower for surgeons' gloves because they may have longer exposures to blood and other body fluids than do examination gloves.)

"Previous FDA surveys had shown that some batches of gloves had failure rates far in excess of the new limits," says Walter E. Gundaker, acting director of the agency's Center for Devices and Radiological Health. "The quality levels we have established are minimal requirements, which means that most glove batches will have lower failure rates," Gundaker says. He anticipates that the new program should result in gloves that are far more reliable than in the past.

Gloves that do not meet these standards cannot be sold for medical uses. As part of its glove inspection program, FDA will examine randomly selected samples for tears and holes and for any foreign matter embedded in the gloves.

Foreign-made gloves must also meet the new requirements. Manufacturers may be placed on an import detention list if their gloves consistently fail to meet the standards. Domestic gloves that do not meet the standards will be seized, if necessary.

The federal Centers for Disease Control in Atlanta recommends that health-care workers wear gloves for protection against diseases such as hepatitis B and AIDS, which can be transmitted through blood and other body fluids.

Shiley Heart Valve Notification

People who have a certain type of artificial heart valve manufactured by Shiley Inc. are being notified about rare, but often fatal, valve fractures under a plan that has been developed by the device's Irvine, Calif., manufacturer and accepted by FDA.

Under the plan, the nonprofit foundation Medic Alert is asking all heart specialists in the United States and Canada for the names of patients implanted with the

Bjork-Shiley 60-degree convexo-concave heart valve ("C-C" valve). Hospital administrators are also being asked to search their records to locate C-C valve patients. (A plan to notify foreign governments about the U.S. program is also being developed.)

Medic Alert will then send an information kit about the C-C valve, along with a letter addressed to each patient, to the patient's doctor.

"When one of these valves fractures, the patient's life can sometimes be saved if the valve is replaced quickly," says FDA Deputy Commissioner James S. Benson. "That's why it is important for C-C valve patients to ask their doctors how to recognize early signs of valve fracture and what to do should it occur."

"We hope that the Shiley program will encourage this dialogue between implant patients and physicians, and we will be closely monitoring it to be sure people are being reached with the information they need."

Replacing an intact valve is generally not recommended, because the surgical risk far outweighs the risk of fracture.

In addition to the information kit, the Shiley plan includes an international implant registry operated by Medic Alert. Once enrolled, patients will receive an ID card and a bracelet or neck chain that indicates the wearer has a C-C valve and provides special information for emergency medical personnel.

About 82,000 people worldwide—23,000 in the United States and Canada—have a C-C valve. FDA has been notified of 313 fractures, 204 of which were fatal.

Implantable Contraceptive Approved

A new method of birth control that protects from pregnancy for up to five years is now available to women. FDA approved Norplant, the first implantable contraceptive, last December.

The implant is a fan-like arrangement of six match-stick-size, silicone rubber rods containing a hormone, levonorgestrel (an active ingredient also in some oral contraceptives).

Inserted beneath the skin at the inner arm just above the elbow, the rods slowly release the hormone into the bloodstream. The device is 99 percent effective in women weighing less than 150 pounds, but its effectiveness may decrease in heavier women. The device can be inserted under local anesthesia at a doctor's office or a clinic. While not visible, the rods can be felt under the skin.

A patient can have the implant removed by outpatient surgery if she wants to become pregnant or has undesirable side effects. In tests, the major side effect leading to

removal was the implant's tendency to cause irregular menstrual bleeding. Other reported effects include occasional headaches, mood changes, nausea, and increased acne. Like contraceptive pills, this method is not for use by women with acute liver disease, unexplained vaginal bleeding, breast cancer, or a history of blood clots in the legs, lungs or eyes.

The Population Council Inc. of New York developed the implant. Wyeth-Ayerst Laboratories of Philadelphia will market it and provide a patient information pamphlet describing the effectiveness, benefits and risks.

Drug for Panic Disorder

The first medicine for use in treating panic disorder (repeated attacks of intense fear) gained FDA approval last November. Clinical studies showed the drug Xanax (alprazolam) decreases frequency of attacks and in many cases eliminates them.

Xanax has been approved since 1981 to treat anxiety. Because Xanax often needs to be used at higher doses and for longer periods to treat panic attacks, special attention must be paid to its potential side effects.

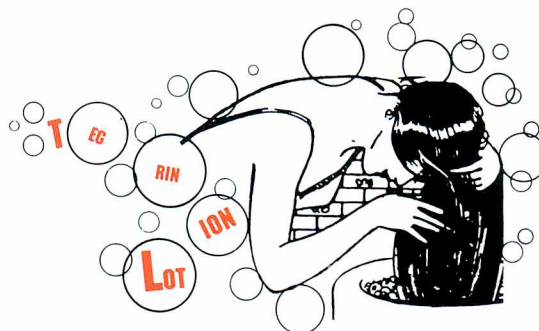
The most common of these are drowsiness and impaired coordination. There also is a potential for physical dependence when the drug is given at the higher doses for longer durations. When the drug is stopped or the dose reduced too rapidly, the patient may have withdrawal symptoms such as restlessness, insomnia, abdominal and muscle cramps, vomiting, tremors, and convulsions. Even with careful tapering off, some patients may have difficulty discontinuing the drug. Gradual withdrawal under a physician's supervision is therefore necessary.

Young women are most likely to develop panic disorder. Attacks occur suddenly, without a known physical cause. Symptoms include shortness of breath, rapid heartbeat, trembling, choking, nausea, feeling of unreality, tingling, hot flashes or chills, chest pain, fear of dying or going crazy, and dizziness or faintness. Unrelenting attacks may increasingly restrict patients' relationships and activities.

Xanax is marketed by the Upjohn Company of Kalamazoo, Mich.

Drug Ingredients Banned

FDA has banned the use of 223 nonprescription drug ingredients because there was no proof they were effective. The ingredients are found in 19 classes of products, used to treat problems ranging from acne and dandruff to diarrhea and pain.



Some well-known products are affected. Anti-dandruff shampoos such as Tegrin Lotion can no longer include allantoin, and Packers shampoo and soap cannot include pine tar. The anti-diarrheal product Donnagel cannot contain atropine sulfate, hyoscyamine sulfate, and scopolamine hydrobromide.

Aspirin may no longer be used in topical analgesic products, but is still considered effective for internal pain relief. Other banned external analgesics include eucalyptus oil and chloral hydrate. Methapyrilene hydrochloride is banned both as an external analgesic and antihistamine.

The ingredients were found in products approved before 1962, the year new legislation was passed requiring drug manufacturers to submit proof of product efficacy as well as safety. In 1972, FDA began reviewing some 300,000 nonprescription drug ingredients then on the market, and has since banned ingredients whose safety or efficacy was doubtful, and required revised labeling for many drugs.

The ban takes effect in May 1991, after which manufacturers may not sell products containing the banned ingredients unless they provide FDA with evidence proving the ingredients are safe and effective for their intended use.

Mammography Quality Improves

The quality of mammograms has improved significantly since 1985, according to FDA surveys.

Whereas 36 percent of the equipment for these x-ray exams of the breasts provided substandard images in 1985, the latest 1988 survey showed that this figure had declined to 13 percent.

Though the improved images involved a slight increase in radiation to the patient, radiation levels remained well within FDA safety guidelines and were two-thirds lower than those found in a 1979 survey.

The surveys were carried out with the cooperation of state radiological health personnel, who tested the mammography equipment with a "phantom," a special plastic

device embedded with tiny objects that detect fine detail.

In response to FDA's 1985 survey, the American College of Radiology instituted a voluntary accreditation program for mammography facilities.

FDA recommends that women ask mammography centers if they are accredited before using them. To find an accredited center, women can call a local chapter of the American College of Radiology.

FDA is conducting research on methods to further improve mammography and plans to survey equipment again in 1992.

(For more information on mammography, see, "Why Women Don't Get Mammograms (and Why They Should)" in the May 1987 *FDA Consumer*.)

Gamma Interferon for Immune Disorder

A new treatment for a chronic hereditary immune disorder has been approved by FDA. The treatment involves use of the first approved genetically engineered form of gamma interferon, a protein that occurs naturally in the body.

The rare immune disorder, chronic granulomatous disease (CGD), occurs mostly in young males and affects white blood cells, leaving those with the defect susceptible to infections.

Modern supportive therapy has increased the life expectancy of people with CGD, but about 80 percent of children diagnosed with the defect suffer unusually frequent or severe infections during the first year of life. These infections in some cases may retard normal development or lead to death.

The new therapy appears to boost the white cells' effectiveness in fighting off infection. It is injected under the skin, usually three times a week.

CGD affects fewer than 400 Americans, and the product was given "orphan" status by FDA, granting its developer, Genentech Inc. of South San Francisco, Calif., developmental support and tax advantages. (See "Rare Disease Treatments: Orphans Saving Lives" in the November 1990 *FDA Consumer*.)

Experimental Gene Therapy for Cancer

Researchers at the National Institutes of Health can now use human gene therapy to treat advanced melanoma, a lethal skin cancer for which there is no effective treatment. FDA last November said it would allow the use of the experimental therapy to treat up to 50 patients with the disease.

The trial will be the first to apply gene therapy to cancer. Patients in the study will receive altered cancer-killing cells called tumor-infiltrating lymphocytes (TIL). In

the laboratory, the gene for tumor necrosis factor will be added to TIL cells taken from the patient. (See "Genetic Engineering Yields Disease-Fighting Hormones" in the July–August 1990 *FDA Consumer*.) The gene-altered cells will be grown for four to six weeks before being returned to the patient by transfusion.

Steven A. Rosenberg, M.D., the NIH researcher leading the study, has been using unaltered TIL to treat cancer since 1987, but only about half the patients with advanced melanoma show improvement with the therapy.

"There has been a need to improve this therapy," says Rosenberg, "and one way may be with the addition of the TNF gene." Rosenberg explains that in mice, TNF is a powerful anti-tumor agent, but humans cannot tolerate the large doses needed for effective cancer-killing treatment. It is a protein produced by the body during bacterial infection to help regulate the immune system repair injury and fight infection. If active in the body too long, however, TNF can cause shock and body wasting.

The protein appears to fight tumors by cutting off the developing blood supply in the area. Scientists will use the TIL cells to carry the TNF gene directly to the tumor, hoping to maximize its benefits and minimize toxicity to the rest of the body.

The first experimental human gene therapy was permitted last September to treat ADA deficiency, a rare disorder in which the gene responsible for producing the enzyme adenosine deaminase is defective. (See "4-Year-Old Infused After Human Gene Therapy Approval" in the Updates section of the December 1990 *FDA Consumer*.)

Drug Effects in Elderly

Information on the effects of prescription drugs in persons over 65 would be included in the physician labeling for drugs under a new requirement proposed by FDA. Labeling would include all available information on the effects of the drug in the elderly or a statement that such information is not available.

"As our knowledge has grown of how drugs work within the body, we've recognized the special concerns associated with drug use in the elderly," said HHS Secretary Louis W. Sullivan, M.D. "Often, for example, patients lose a third or more of their kidney function between the ages of 30 and 90, so drugs may not clear the body as fast . . . Similarly, liver function may be impaired in the older person, brain cells change in sensitivity, muscle tissue declines, and fat accumulates. Because of these changes, physicians need to be provided with any pertinent information that's available about the drugs they prescribe for senior patients."

Assistant Secretary for Health James O. Mason, M.D.,

Dr.P.H., said the proposed requirement would dovetail with guidelines on drug testing in the elderly issued by FDA in March 1990 (see "Testing Drugs in Older People" in the November 1990 *FDA Consumer*).

"The guidelines are intended to encourage drug manufacturers to carry out thorough evaluations of the effects of drugs in elderly populations," he said. "Under the new proposal, any useful information derived from this testing . . . would have to be made known, via the drug labeling, to physicians."

The proposal gives drug manufacturers one year after publication of a final rule to update drug labeling.

Illness with GHB Use

Consumers should stop using the illegally marketed drug GHB, or gamma hydroxybutyric acid, FDA has warned. Use of GHB, also called sodium oxybate or gamma hydroxybutyrate sodium, apparently caused more than 30 people in California, Florida, and Georgia to become ill with symptoms ranging from nausea and vomiting to severe respiratory problems, seizures and coma.

GHB is promoted for strength training, bodybuilding, weight loss, a replacement for L-tryptophan (a food supplement that FDA ordered removed from the market in 1989 after it was linked to a rare blood disorder), and as a "legal psychedelic." GHB has been used in Europe as an anesthetic adjunct, and it is being evaluated in FDA-approved clinical trials for the treatment of narcolepsy.

According to the California health department, GHB is sold through mail-order outlets, health food stores, bodybuilding gyms, and fitness centers. It is marketed as a powder or granules.

Health departments in the affected states have been working with FDA to learn more about the GHB-linked illnesses.

FDA offers consumers the following medical advice:

- Anyone taking GHB outside of physician-supervised clinical trials should stop immediately.
- Anyone who has consumed GHB and is experiencing seizures, uncontrolled shaking, headaches, unexplained drowsiness or other central nervous system disorders, nausea, vomiting, or diarrhea should consult a physician immediately.
- Physicians treating patients exhibiting these conditions should report these cases to the local poison control center.

Magazine Marks 25th Year

FDA Consumer is entering its 25th year of publication. Originally titled *FDA Papers*, the magazine made



its debut in February 1967. Since then, it has been the recipient of numerous awards, including two presented earlier this year: a National Association of Government Communicators' 1990 Blue Pencil Award for best periodical for a general audience, and a gold award in the 1990 International Mercury Awards Competition for best external, nonprofit magazine.

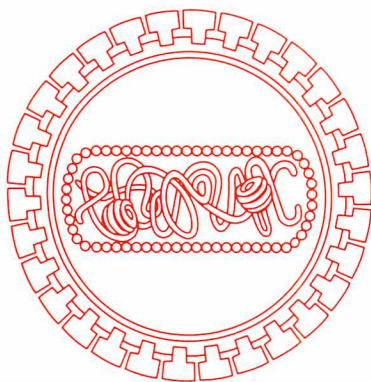
Consumer Forum

More Cancer Information

There is some misleading information in the *FDA Consumer* (Vol. 24, No. 10; December 1990). In the article "Modern Diagnostics Help Detect Cancer Early," [the] author . . . says that by calling 800-4-CANCER . . . readers will reach "this national telephone inquiry system at the Johns Hopkins Oncology Center, funded by the National Cancer Institute." The Cancer Information Service (CIS) is a nationwide network with over 20 offices. Each office takes calls from its service area. The CIS at the Memorial Sloan-Kettering Cancer Center in New York answered over 20,000 inquiries in 1989 from callers in New York City, Long Island and Northern New Jersey.

Roberta Altman
Communications Specialist
Office of Cancer Communications
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FDA Consumer welcomes comments from readers. Send letters to: Editor, *FDA Consumer*, HFI-40, 5600 Fishers Lane, Rockville, Md. 20857.



Clinical Tests for Vaccines

FDA has granted permission for clinical testing of two more experimental vaccines to fight the AIDS virus, bringing to six the number of AIDS vaccines under human testing in the United States.

The trials are designed to test the vaccines' safety, as well as to give a preliminary indication of whether they can stimulate an immune response against the AIDS virus.

One of the agents, a gp120 vaccine developed by IMMUNO Ag of Vienna, Austria, will be studied as a treatment for slowing the progression of AIDS in patients at early stages of infection.

Fifty-five people infected with the AIDS virus, but who are otherwise healthy, will be enrolled in the study. It will be conducted at Walter Reed Army Institute of Research in Washington, D.C.

The other agent, a gp160 vaccine developed by Genentech Inc., of South San Francisco, Calif., will be studied to see if it can elicit an HIV-specific immune response in healthy individuals. Sponsored by the National Institute of Allergy and Infectious Diseases, the study will involve 60 individuals not infected with the AIDS virus.

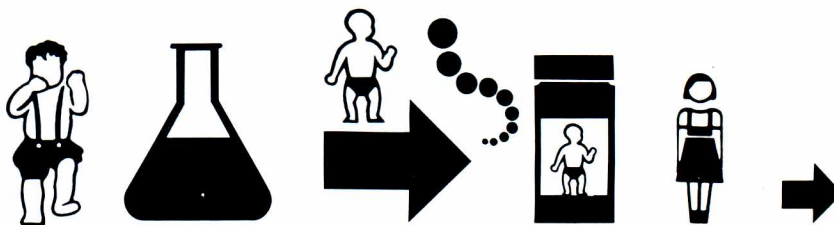
Both vaccines are composed of genetically engineered glycoproteins identical to those found on the surface of the AIDS virus.

For information on these vaccines or other experimental treatments, contact the AIDS Clinical Trials Information Service at 1-800-TRIALS-A.

Drugs Studied in Children

The drugs listed in this chart are undergoing FDA-sanctioned testing for use in children with AIDS and related disorders. Studies are conducted in three phases. In Phase I, researchers study 20 to 100 patients for several months, mainly to gather safety data. In Phase II,

they study up to several hundred patients for as long as two years, mainly to assess the drug's effectiveness, but also to gather more safety data. In Phase III, they study hundreds to thousands of patients over one to four years to gather further data on safety and effectiveness and to determine the proper dosage of the drug.



| Drug Name | Manufacturer | Use | Study Phase |
|---------------------------------------|--|---------------------------------------|-------------|
| BW566C80 | Burroughs Wellcome, Research Triangle Park, N.C. | <i>Pneumocystis carinii</i> pneumonia | I |
| CD4-IgG | Genentech, S. San Francisco, Calif. | AIDS | I |
| Gamimune N Immune Globulin (human) IV | Cutter Biological, Miles Inc., Berkeley, Calif. | symptomatic HIV infection | III |
| HIVID Dideoxycytidine (DDC) | Hoffmann-La Roche, Nutley, N.J. | HIV infection | I and II |
| Imuthiol Diethyldithiocarbamate | Connaught Laboratories, Swiftwater, Pa. | HIV infection | I and II |
| Retrovir Zidovudine (AZT) | Burroughs Wellcome, Research Triangle Park, N.C. | HIV infection | I |
| VIDEX Dideoxyinosine (DDI) | Bristol-Myers Squibb, New York, N.Y. | HIV infection, ARC, AIDS | I and II |

New Procedures to Screen Blood Donors

Blood and plasma banks throughout the country are implementing new donor screening procedures to increase the safety of the nation's blood supply.

The enhanced procedures, announced by FDA in December, shift the focus of screening for AIDS and other infectious blood diseases to cover a broader range of risk factors and eliminate the need to exclude donors based solely on geographical or national origins.

To better determine the suitability of people to donate blood, FDA recommended that all registered blood establishments take the following steps:

- Tell prospective donors about the risk of HIV infection both verbally and in writing, using language and cultural terms that donors can understand. If the information cannot be provided in the donor's own language, he or she should be excluded from donating.
- Ask direct questions about behaviors, such as sex practices and IV drug use, that put donors at risk for HIV infection.
- When taking the donor's medical his-

tory, ask if the donor has had or has been treated for syphilis or gonorrhea during the previous 12 months. If so, exclude the donor from giving blood for 12 months from diagnosis.

- Extend from 6 to 12 months the exclusion for anyone who has exchanged money or sex for drugs.
- To reduce the transmission of hepatitis C, extend from 6 to 12 months the exclusion of anyone who has received a blood or plasma transfusion.

The new procedures were developed by FDA with the Office of the Assistant Secretary for Health and the Centers for Disease Control. They are consistent with recommendations made in April 1990 by FDA's Blood Products Advisory Committee. FDA is carefully monitoring compliance through its inspection program.

Information Package for Cytokine Therapy

An information package developed by FDA is available for potential sponsors of cytokine and growth factor therapies for AIDS.

Cytokines are proteins in blood that modify the function of cells, including those of the immune system. Through genetic engineering, these proteins can be produced in large quantities and introduced into the body to treat some forms of cancer and other diseases.

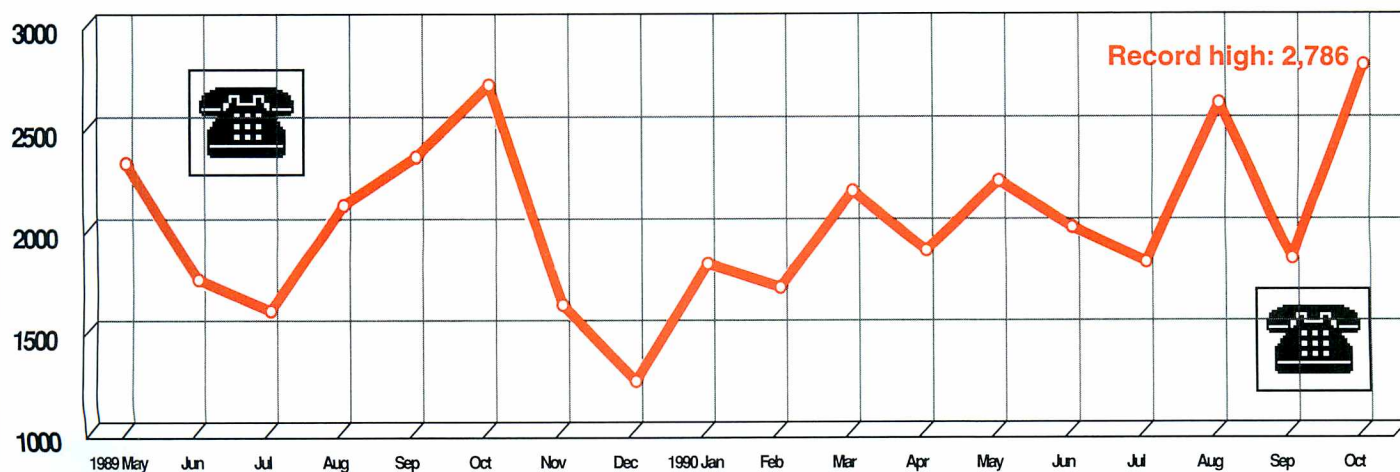
Other types of cytokines can be used to stimulate cell growth, such as by producing skin cells for healing wounds or red blood cells for treating severe anemia. (See "Genetic Engineering Yields Disease-Fighting Hormones," in the July-August 1990 *FDA Consumer*.)

The information package contains a summary of the latest "points to consider" standards. It includes an overview of manufacturing, laboratory testing, and clinical issues manufacturers need to address before applying to FDA for permission to conduct studies on the safety and effectiveness of a cytokine or growth factor therapy.

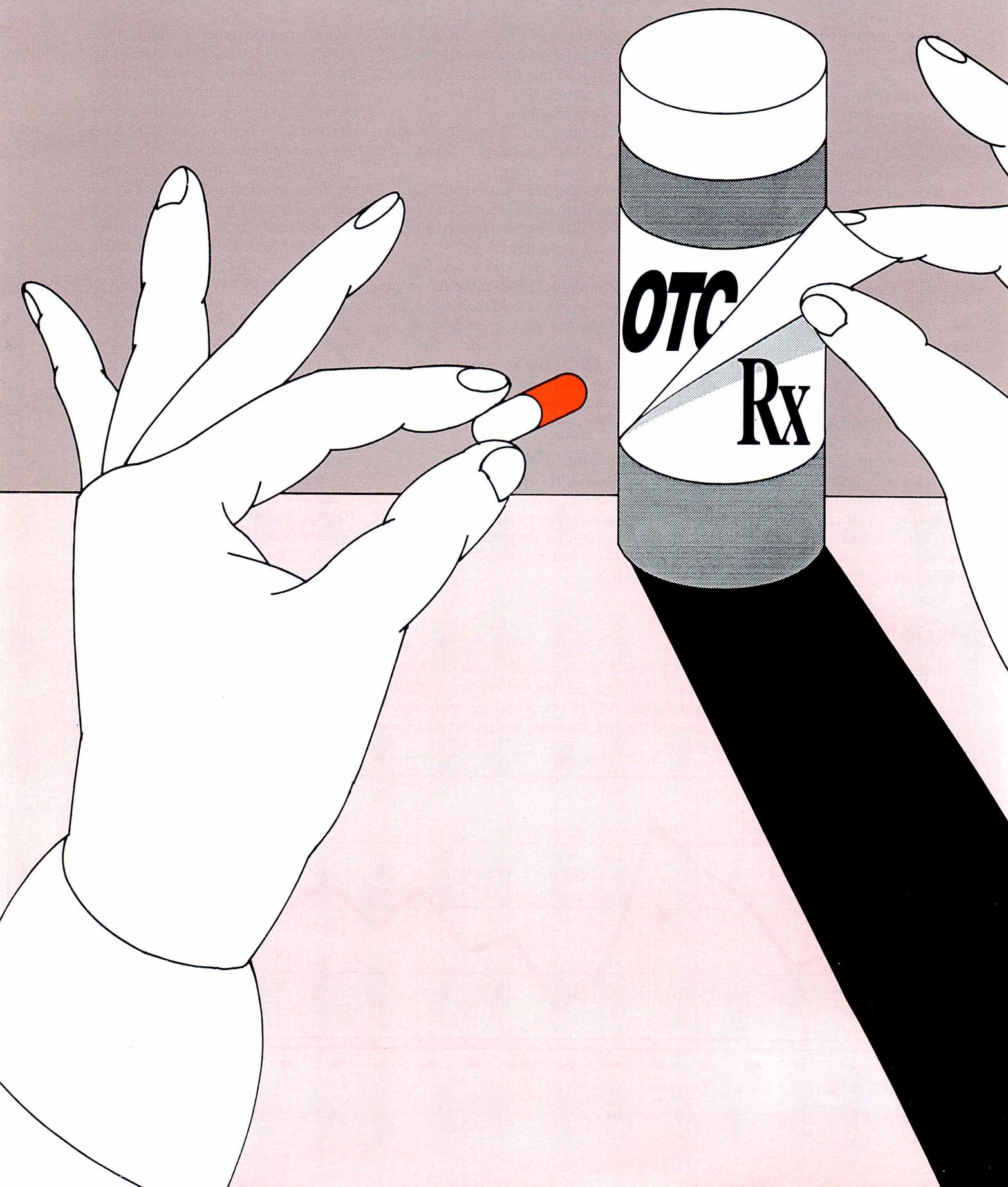
The package is available from FDA's Center for Biologics Research and Evaluation, Office of Congressional, Consumer and International Affairs, Park Building, Room 1-58, 5600 Fishers Lane, Rockville, Md. 20857.

ACTIS Responds to Calls

Since opening in May 1989, the AIDS Clinical Trials Information Service (ACTIS) has helped more than 36,000 callers through its computer data base of hundreds of clinical studies. Callers have included health professionals, educators, students, and AIDS patients and their families and friends. ACTIS offers updates on therapy trials and free printed materials under the sponsorship of FDA, the Centers for Disease Control, National Institute of Allergy and Infectious Diseases, and National Library of Medicine. Telephone: 1-800-TRIALS-A.



(Source: ACTIS October 1990 activity report)



R_x TO OTC

The Switch Is On

by Marian Segal

What do Dimetapp, Sominex, Bactine, Cortaid, Coricidin Nasal Mist, OcuClear, E-Z Scrub 241, Trosyd, and Actifed have in common? They, along with dozens of other drug products, have made the “switch” from prescription to over-the-counter (OTC) status.

The Nonprescription Drug Manufacturers Association estimates that more than 200 OTC drug products on the market today were available by prescription only a decade ago. Among them are antihistamines and nasal decongestants for colds and allergies, sleep aids, pain relievers, cough medicines, antifungals, antimicrobials, and anti-itch medicines. These products contain ingredients in dose strengths that the Food and Drug Administration has deemed safe enough to use without a doctor’s prescription.

When this issue of *FDA Consumer* went to press, the most recent ingredient that FDA had approved for the switch from prescription to OTC sale was clotrimazole in cream and suppository dosage forms. Used to treat vaginal yeast infections, clotrimazole has been available by prescription for more than 10 years. It will be marketed OTC under the trade name Gyne-Lotrimin. In announcing the switch, Carl Peck, M.D., director of FDA’s Center for Drug Evaluation and Research, said, “Clotrimazole is highly effective and carries a minimal risk. If initially diagnosed by a doctor, recurring

symptoms of vaginal yeast infection, or candidiasis, can be recognized by the patient, who can treat herself with the over-the-counter drug without the inconvenience and expense of going back to the doctor.”

Some other prescription products the drug industry is interested in switching, according to the July 9, 1990, *Advertising Age*, are the antacids Zantac, Carafate, Tagamet, and Pepcid; the cold/allergy medications Claritin, Hismanal and Seldane; and the nonsteroidal anti-inflammatory drugs Naprosyn, Clinoril, Feldene, and Anaprox. The publication also reported a projection that the OTC drug market would reach \$19 billion in manufacturer sales by the year 2000, up 72% from \$11 billion in 1990.

OTC Drug Review

A major impetus for switching drugs from prescription to OTC status is FDA’s comprehensive review, begun in 1972, of the active ingredients in OTC drug products. The review grew out of amendments to drug law enacted in 1962, which require drugs to be proven effective before they can be marketed. (Before Congress passed this legislation, drugs had to be proven safe, but proof of their effectiveness was not required by law.)

Thus, FDA was obliged to reexamine all drugs—both prescription and OTC—that had been approved solely on the ba-

sis of safety. For OTC drugs, the endeavor involved about 730 active ingredients that were used in more than 300,000 drug products sold in the United States. The review separated the active ingredients in the products into therapeutic classes—for example, anti-itch medicines, antihistamines and antifungals. Seventeen panels of nongovernment experts were established to make recommendations about the safety and effectiveness of ingredients for their intended uses. As a result of the review, some ingredients were taken off the market because they were found ineffective; others were banned for safety reasons.

In addition to evaluating safety and efficacy of OTC drugs, the panels reviewed currently marketed prescription ingredients to determine whether some might be appropriate for OTC marketing. Some panels determined that dosages of certain OTC ingredients, such as antihistamines, needed to be raised to levels that were previously allowed by prescription only. So far, nearly 40 formerly prescription-only drug ingredients in at least 16 classes have been switched to OTC status.

What Determines Rx vs. OTC?

The distinction between prescription and nonprescription drugs is spelled out in the Durham-Humphrey Amendment to the Federal Food, Drug, and Cosmetic Act. Before this amendment was passed

More than 200
OTC drug products
on the market today
were available by pre-
scription only a dec-
ade ago.



The ingredients or dosage strengths in these products were previously unavailable over the counter. The ingredients are: diphenhydramine (Sominex), hydrocortisone (Bactine and Cortaid), brompheniramine (Dimetapp), triprolidine (Actifed), and oxymetazoline (Coricidin Nasal Mist and OcuClear). Other brand-name products containing these ingredients, as well as generics, are also available.

in 1951, there was no specific statutory requirement that any drug be labeled for sale by prescription only. With the amendment, prescription drugs were defined primarily as those unsafe for use except under professional supervision. They include certain habit-forming drugs and any drug that is unsafe "because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use"

Nonprescription drugs are regarded as safe for consumers to use by following the directions and warnings required on the label.

To protect consumers, FDA regulations require that labeling of OTC drugs state:

- the intended uses and results of the product
- adequate directions for proper use
- warnings against unsafe use, side effects, and adverse reactions.

The labeling must be written so that ordinary people, including those with somewhat low reading comprehension skills, would be likely to understand it.

Toxicity is the major issue in deciding whether to switch a drug from prescription to OTC status. Because almost any drug, if misused, can have some adverse side effect, one way to evaluate possible harm in switching is to consider the drug's overall margin of safety.

Gerald Rachanow, J.D., deputy director of FDA's division of OTC drug evaluation, explains that, "Drugs that have a high risk of causing toxicity and a low margin of safety, and that must be carefully used to achieve the appropriate level of effectiveness without endanger-

ing the consumer's safety, are appropriately classified as prescription drugs."

On the other hand, Rachanow says, "the mere possibility that a drug can be misused, with toxic results, is not a sufficient basis alone to classify it for prescription status."

OTC Labels

The process of switching some antihistamines to OTC status can serve as an example of the procedure. Antihistamines are used to relieve symptoms of hay fever and other upper respiratory allergies. They may cause drowsiness, however, presenting a hazard if taken in circumstances where alertness is important. Antihistamines also can be dangerous to patients with glaucoma, an enlarged prostate, or asthma.

In reviewing antihistamines, FDA's Cough/Cold Advisory Review Panel did not find these potential dangers sufficient cause to limit these ingredients to prescription use. It recommended instead that the labeling for OTC antihistamine drug products bear a warning that the product "may cause drowsiness" and caution consumers to "avoid driving a motor vehicle or operating heavy machinery" and to "avoid alcoholic beverages while taking this product." The panel also recommended that the label warn patients not to take these products

except with the advice and supervision of a physician if they have glaucoma, asthma, or difficulty urinating because of an enlarged prostate.

Self-Diagnosis

Another consideration in deciding whether or not a drug should be available without prescription is whether the condition being treated can be self-diagnosed. Inability to self-diagnose a condition, however, does not automatically preclude OTC status for products intended to treat its symptoms. Several drugs, such as bronchodilators, are marketed over the counter even though the conditions they are used to treat—asthma, in this case—cannot be self-diagnosed. FDA's Cough/Cold Advisory Review Panel recommended that bronchodilators could be marketed over the counter provided they were labeled with the warning: "Caution: Do not take this product unless a diagnosis of asthma has been made by a physician."

Most OTC drugs are labeled for the treatment of symptoms, such as sinus congestion, headache, pain, upset stomach, and itching. Consumers can readily recognize these symptoms and select an appropriate product to gain relief, but they may not know what underlying condition is causing the pain, cough or itch they are self-medicating. To help

consumers judge when a physician should be consulted if a medical problem is not resolving itself through self-medication, products will carry warnings to consult a physician under appropriate conditions. An OTC hydrocortisone preparation to relieve itching from eczema, poison ivy, insect bites, and other causes, for example, carries the warning, "If condition worsens, or if symptoms persist for more than 7 days, discontinue use of this product and consult a doctor."

Timing of the Switch

The switch process has not been trouble-free. When the OTC drug review began, FDA did not have a clear policy that told industry at what point in the process it could market a product being considered for a switch. As a result, some manufacturers began marketing prescription products without waiting for publication of the panel's recommendation or issuance of FDA's final regulation.

In 1976, FDA published a statement of policy explaining that, unless the agency disagrees with the panel, products under review for the switch could be sold over the counter at the time that the advisory panel's report (called a "proposed monograph") is published in the *Federal Register*. The drugs must be labeled as the panel recommends in its report or as the agency requires in a tentative final monograph. If at a later time FDA disagrees with the panel because of new or other evidence, the agency can then disallow the switch.

A company can also petition FDA to switch an ingredient from prescription to OTC status or, if the company itself manufactures the drug, it can submit a new drug application (NDA) or supplemental NDA for OTC status for the drug.

On occasion, the agency has rescinded an original decision to approve or disapprove a switch. For example, FDA initially disagreed with a panel recommendation to switch the drug diphenhydramine hydrochloride to OTC status for use as a nighttime sleep aid and antihistamine because more controlled studies were needed to satisfy the agency's concerns about the drug's safety and effectiveness in doses appropriate for OTC use. Twelve studies were submitted that compared diphenhydramine with a placebo. After reviewing the data, FDA concluded that the drug, at specified dosage levels, was safe and effective as an OTC nighttime sleep aid. In a later decision, diphenhydramine was also ap-

proved for OTC use as an antihistamine.

The converse has happened as well. In October 1982, FDA proposed OTC availability of the bronchodilator metaproterenol sulfate in a metered-dose inhalation aerosol. The proposal met with criticism from the medical community, particularly because of concerns that young children could be harmed by misusing the inhalers.

The agency agreed that there were some risks associated with self-diagnosis and treatment of asthma and that there was a potential for misuse of the product. It believed, however, that the risks did not outweigh the benefits of easy availability. The agency's required labeling for the inhalers warned that the product should be used only after asthma was diagnosed by a physician.

In May 1983, FDA's Pulmonary-Allergy Drugs Advisory Committee met in a public forum to hear reports and discuss the issue. The committee concluded that the risks of OTC availability outweighed the benefits and recommended that FDA rescind its proposal to make metaproterenol an OTC drug. The agency did so the following month.

More recently, when the drug ibuprofen (Advil, Nuprin and Motrin IB) was approved for OTC sale, some experts wanted the label to carry a warning that it might cause kidney damage in people with preexisting kidney disease. FDA determined at that time that the warning was not needed, but is now reconsidering the need because of recent studies indicating an association.

A similar concern has been raised about the antihistamine Seldane, now being reviewed for OTC status. Unlike other antihistamines, Seldane has the advantage of not causing drowsiness. The drug can, however, cause abnormal heart rhythms in patients who have liver problems or take certain other drugs.

For Sale by Pharmacist Only

Some health professional organizations have petitioned FDA to establish a third class of drugs that would be available without prescription, but only through a pharmacist. Pharmacists would advise consumers about proper use of the drug and serve to identify problems that might arise. In 1974, in connection with an FDA monograph on OTC antacids, some pharmacy organizations commented that such a third class of drugs should be created. Others, including the Department of Justice, objected to a third class of drugs, stating that it would re-

strain competition, inconvenience the consumer, depart from U.S. economic policy, and cause price increases for the consumer with no attending benefit.

FDA concluded that "no controlled studies or other adequate research data have been supplied to support the position that any class of OTC drugs must be dispensed only by pharmacists in order to ensure their safe use. . . . There is at this time no public health concern that would justify the creation of a third class of drugs to be dispensed only by a pharmacist or in a pharmacy."

Whatever the mechanism, it's clear that we can expect many more drugs to be considered for the switch from prescription to over-the-counter sales. In recent years, Americans have become increasingly health conscious and have assumed more responsibility for their health, evidenced by such trends as emphasis on diet and exercise and smoking cessation. This take-charge posture is also becoming apparent in self-treatment.

As John Naisbitt writes in his book *Megatrends: Ten New Directions Transforming Our Lives*, "Along with new habits, the medical self-help movement has brought an upsurge in self-care. No longer do Americans feel they must run to a doctor for every minor ailment: 75 percent of the people can successfully deal with medical problems without ever walking into a clinic or doctor's office."

James D. Cope, president of the Nonprescription Drug Manufacturers Association, says that self-care with self-medication is the largest component of our health-care system and the least costly.

"Six out of 10 medicines bought by consumers are nonprescription," says Cope, "yet total spending for [these medicines] is less than 2 cents of the U.S. health-care dollar." Cope maintains that in a single recent year, OTC medicines saved the nation \$10.5 billion that otherwise would have been spent for prescription drugs, doctor visits, and lost time from work.

The trend toward more switches is generally greeted with enthusiasm by consumers, the drug industry, and many health professionals. Caution remains FDA's watchword, however. The continued success of these switches will depend on consumers' good judgment in using these products correctly and in following label directions and warnings. ■

Marian Segal is a member of FDA's public affairs staff.



FDA Insures Quality of Imports

by Sharon Snider

It's morning on the docks of Baltimore, and FDA inspectors Dean Cook and Lorraine Harvey, a list of products to be sampled in hand, set to work checking a truckload of burlap sacks of psyllium seed husks from India. The psyllium seed husks are used in making laxatives.

Using a special funnel-shaped tool, Cook and Harvey siphon a pound of seed from six different sacks, then re-seal the bags. The seed will be analyzed back in FDA's laboratory to check for insects and bird excreta, problems that have plagued psyllium seed husks from India.

Next they open a shipment of stoneware plates and cups from India and remove eight sets of dinnerware. These will be analyzed to make sure the level of lead does not exceed that allowed.

Next they slit open a carton of German Christmas cakes. A quick check for excessive food coloring and proper labeling reveals no problems, and the shipment is allowed to be distributed.

"Some countries we almost never have problems with," says Cook. "But others, such as India, Thailand, China, Korea, and many countries in Africa, require constant vigilance."

Just before Cook and Harvey leave the docks, a U.S. Customs Service official alerts them to a shipment of imported noodles labeled only in Chinese. They open the packages, check the items, and make a note that they should be detained for improper labeling.

"The requirement that all products be labeled in English is a problem for some

of the smaller, ethnic shippers, such as those from the Far East," explains Cook. "Perhaps they figure only people who read and speak the [foreign] language are interested in buying the product anyway."

Cook and Harvey are just two of 200 to 300 FDA inspectors, laboratory analysts, and compliance officers at work daily across the country insuring that food and drugs imported into this country are safe. In a crisis, such as the Chilean grape scare in 1989, up to 800 FDA field staff may be called into action.

International Palate

During any given week, Americans may consume coffee from Colombia, fruit from Mexico, shrimp from India, and egg noodles from Korea. They may buy perfume from France, vitamin supplements from Denmark, microwave ovens from Japan, x-ray machines from Germany, cosmetics from Taiwan, and drugs from Hong Kong.

With the exception of beef and poultry, which are regulated by the U.S. Department of Agriculture, all food, drugs, cosmetics, medical devices, and products that emit radiation are subject to examination by FDA when they arrive in the United States.

By law, such products must meet the same standards required for domestic goods. Imported foods must be pure, wholesome, safe to eat, and produced under sanitary conditions; drugs and devices must be safe and effective; cosmetics must be safe and made from ap-

proved ingredients; and all labeling and packaging must be informative and truthful.

However, imports do not always meet these standards. It is not unusual, for example, for rice or grain from tropical or subtropical countries to arrive infested with live insects. And it is not unusual for processed food products—such as, say, taco shells from Mexico or imitation crab legs from China—to arrive contaminated with insect, rodent or bird filth. Phony drugs and other "quack" products are a common problem. And shipments of ethnic foods frequently have to be detained because the labels aren't in English.

Sometimes it's a case of outright smuggling, as in a recent conspiracy to sneak illegal bulk veterinary drugs into the country, first by boat through the Port of New York, then through the Port of New Orleans, and finally by truck across the U.S.-Canadian border (see "Sentence Upheld for Animal Drug Smuggler" in the Investigators' Reports section of the January-February 1991 *FDA Consumer*).

The number of imports has jumped in the past 20 years. In 1971, FDA reviewed approximately 500,000 entries of regulated products. Today more than 1.5 million shipments of FDA-regulated products enter the United States each year. This large increase in imports has meant an increased need for surveillance—a need FDA has met by doubling its import operations.

FDA is directly or indirectly involved

Out on the docks and in the airports, FDA inspectors look for signs of filth, spoilage, contamination, or mislabeling.



in product surveillance at each of the approximately 500 Customs Service points of entry into the country, including major airports. At the many remote crossings along the Canadian and Mexican borders the agency relies on the Customs Service for assistance in detaining suspicious products.

All Imports Screened

Every food, drug, or other FDA-regulated import is screened—one way or another. Although it is physically impossible to personally inspect each of the 1.5 million entries a year, FDA does review records for every entry. Based on this review, the product may be immediately released for distribution, visually examined, or sampled and analyzed in a laboratory. Ten percent of the entries reviewed are identified for further coverage.

Out on the docks and in the airports, FDA inspectors look for signs of filth, spoilage, contamination, or mislabeling. For instance, in a shipment of canned green beans, they check to see if the manufacturer is registered with FDA; look at the labels to make sure they are printed in English and conform with other FDA requirements about weight declaration and contents; and spot-check for swollen, leaking or rusty cans, wet cases, or swarms of fruit flies around cases, which may indicate can damage.

In a shipment of coffee, inspectors look for bag damage, moldy beans, and insects. When examining fresh produce, they check for spoilage and insects and sample for illegal residues of one or more of the 256 most widely used pesti-

cides. When checking seafood, most of which arrives frozen, they look for signs of parasites and for evidence of thawing and decomposition.

If a problem is found or suspected by FDA inspectors, the product is not released and a sample may be collected for analysis. Products with a history of violations or those that are a known or suspected health hazard are targeted in advance for sampling or detention. Approximately 3 percent of all entries reviewed are physically examined. Weekly import alerts and detention lists are used to determine which entries in particular should receive close FDA attention.

In 1989, FDA detained 25,740 entries—an increase of 54 percent over 1985. The vast majority were foods.

“The products most frequently turned back are ready-to-eat foods,” says Marvin Blumberg, consumer safety officer in FDA’s Import Operations Branch. “We often find they are contaminated with filth such as rodent hairs, insect parts, or bird excreta. Because these foods are finished products, the importer can’t recondition them without destroying them. So they have to be exported.”

If bulk food products such as grain or rice are found to contain certain insects, they can be fumigated and sifted to eliminate the insects or other filth to enable the product to pass FDA inspection, he says.

Keeping Fraud Out

Other items frequently refused entry, says Blumberg, are those with bacterial contamination, such as cheese contaminated with *Listeria*, and products that may involve health fraud.

“Quack products are always a problem,” says Blumberg. One perennial offender is “medicinal” bracelets.

FDA currently has import bulletins on copper bracelets from France, England, Spain, and Mexico. Marketers claim that these bracelets cure a wide variety of ailments, including circulatory problems, fatigue, varicose veins, high blood pres-

sure, nervousness, and impotence.

Another metal bracelet from Mexico supposedly cures constipation, hemorrhoids, and digestive problems and prevents heart attack.

The most recent entries onto the health fraud market are cures for cancer or AIDS. “Unfortunately,” says Blumberg, “when people are desperate, they grasp at anything from any part of the world that might offer hope. And producers of quack drugs know this. The products they promote and try to sell through the mail range from herbal preparations to drugs which could be very dangerous if taken.”

One such dangerous cancer drug was Laetrile, a substance derived from apricot kernels and imported from Mexico. In the '70s and early '80s, Laetrile was widely promoted as a “cure” for cancer, and many terminally ill cancer patients were desperate to obtain it. However, its safety and effectiveness had never been tested. When clinical trials sponsored by FDA and the National Cancer Institute finally were run, the drug was found to be derived from apricot kernels and to contain high levels of cyanide. Not only was it ineffective, it was potentially lethal.

When Products Fail Standards

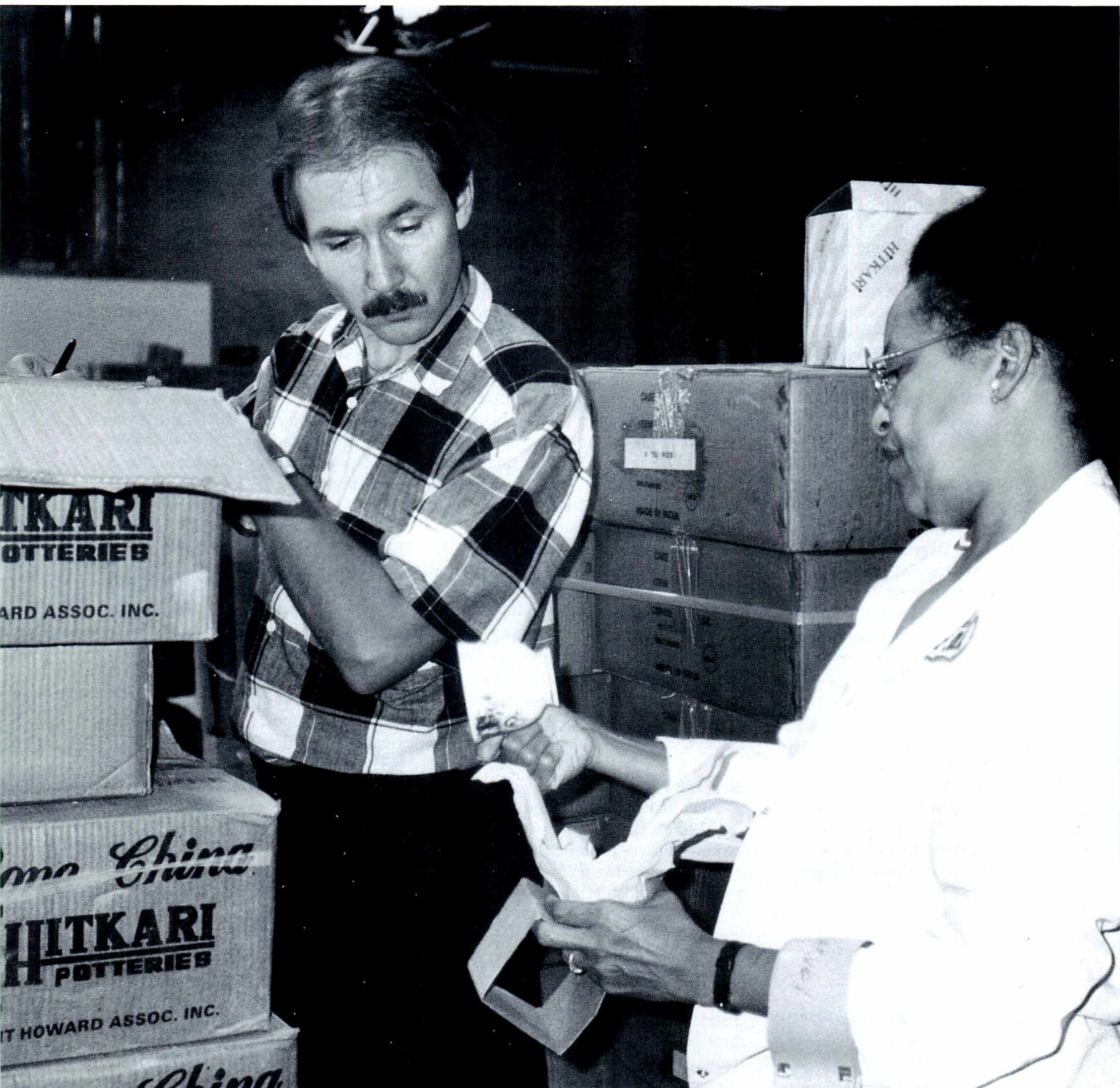
When an import fails to meet FDA standards, the importer is given an opportunity to bring the article into compliance through reconditioning or relabeling. In some cases, the imports must simply be reexported or destroyed by the importer.

Perishable products such as fresh fruit, vegetables and seafood that could spoil on the docks are given priority handling, with samples collected and examined by FDA laboratories within 24 to 36 hours.

Imports that consistently violate FDA laws or regulations or are a known or suspected health hazard are subject to automatic detention. For example, the diet supplement L-tryptophan is being automatically detained because it has

Using a metal probe, Harold Turner of the Baltimore district office draws out a sample of imported coffee beans to be tested for contamination.

***I**t is not unusual for rice or grain from tropical or sub-tropical countries to arrive infested with live insects.*



been linked to eosinophilia-myalgia syndrome, a blood disorder.

Other imports under automatic detention include: swordfish from all countries because it repeatedly has been found to contain high levels of mercury; canned mushrooms from the People's Republic of China because they have caused several outbreaks of staphylococcal food poisoning; and, most recently, European wines that were found to contain the fungicide procymidone, which is approved for use on grapes in Europe but not in the United States. As of July 1990, 106 products were on FDA's automatic detention list.

Drugs entering the country must be approved products from an approved supplier and must be listed with FDA. In addition, they must meet U.S. purity and strength requirements. When commercial shipments of drugs enter a port, they are randomly checked and sampled by FDA. On the wharf, inspectors check labels and look for signs of possible contamination, such as cracked vials and broken bottles. As with other imports, potential problem drugs are targeted in advance for sampling and detention.

Exceptions for Personal Use

In special cases, noncommercial drugs and other products not available domestically and not approved by FDA may, at the discretion of the agency, be released for personal use. Sometimes these are recognized drugs for people with severe illnesses, such as cancer or AIDS, that are available in other countries but have not yet been approved in the United States.

To qualify for importation under the agency's personal use policy, a drug must meet the following criteria:

- The drug must have no known health risk.
- It must be for personal use only (generally not more than a three-month supply).
- It must not be promoted commercially to people living in the United States.

Blumberg fondly recalls one personal use exemption he handled while a compliance officer in FDA's Baltimore office:

"There are a lot of quack products promoted through the mail that supposedly prevent aging or rejuvenate people. They're obviously questionable, and we stop them from entering the country whenever we can.

"One day I got a call from a man claiming to be in his '90s. We had stopped a shipment of his anti-aging 'medicine' which he swore worked wonders. Ever since he'd started using KH3, he said, he'd felt like 70. His doctor approved of his using it, he said.

"We contacted his doctor, and, sure enough, his doctor had no problems with his using it and said it had not had any adverse effects."

This was clearly a case requiring FDA's discretion. Blumberg decided to let the man keep his Fountain of Youth.

"Why tell him it was a fraud and didn't work?" asks Blumberg. "For him, in his mind, it clearly worked."

Other personal use requests are not so happily concluded. Blumberg recalls with regret having to turn down the request of a man who had imported some unidentified, unlabeled "medicine" in hopes of prolonging the life of his wife, who was dying of cancer. The man claimed doctors had given her only six weeks to live.

"The man couldn't tell us what was in the drug and he didn't have the consent of his wife's doctor to use it. He was desperate for anything that might have helped her. But as far as we knew, it could have killed her," says Blumberg.

To aid its surveillance of imports, FDA issues import alerts to its district

offices. These alerts contain the names and descriptions of products that have repeatedly been found to violate FDA's laws and regulations. The import alert signals FDA inspectors to pay special attention to a particular product when it arrives in port and, in certain cases, to automatically detain it. FDA currently has 237 import alerts on products and foreign shippers.

To further expedite surveillance, FDA enters into voluntary agreements with foreign governments. Through memorandums of understanding (MOUs), these governments agree to make sure products from their countries are manufactured under sanitary conditions, meet U.S. requirements for quality, and are tested and sampled in a specific way before leaving their countries. For example, FDA has nine MOUs with countries that export seafood to the United States. These MOUs help insure that the seafood is processed, packaged and shipped in accordance with FDA standards. When seafood from these countries arrives at a U.S. port, it is subject only to routine examination.

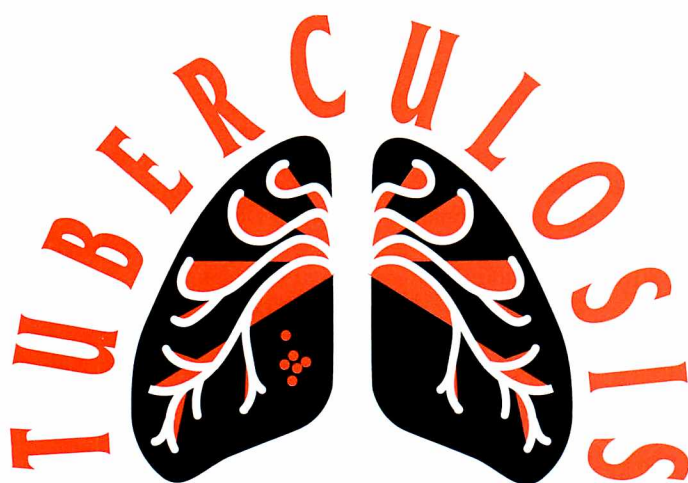
FDA is now negotiating other cooperative agreements with major food exporters in 37 countries to obtain information on pesticide use in those countries.

Under certain conditions, FDA also inspects foreign plants to advise them on their manufacturing practices. Foreign inspections may also occur after products have been detained if the manufacturer wants advice on how to produce goods that meet FDA requirements.

FDA goes to great lengths to make sure that products coming into this country comply with the federal Food, Drug, and Cosmetic Act. As a result of the agency's vigilance, American consumers can be reasonably assured that these products are not only safe but meet the same high requirements of domestic products. ■

Sharon Snider is a staff writer for FDA Consumer.

FDA inspectors Dean Cook and Lorraine Harvey in Baltimore check a shipment of stoneware from India. Samples will be tested for lead levels.



Still Striking After All These Years

by Evelyn Zamula

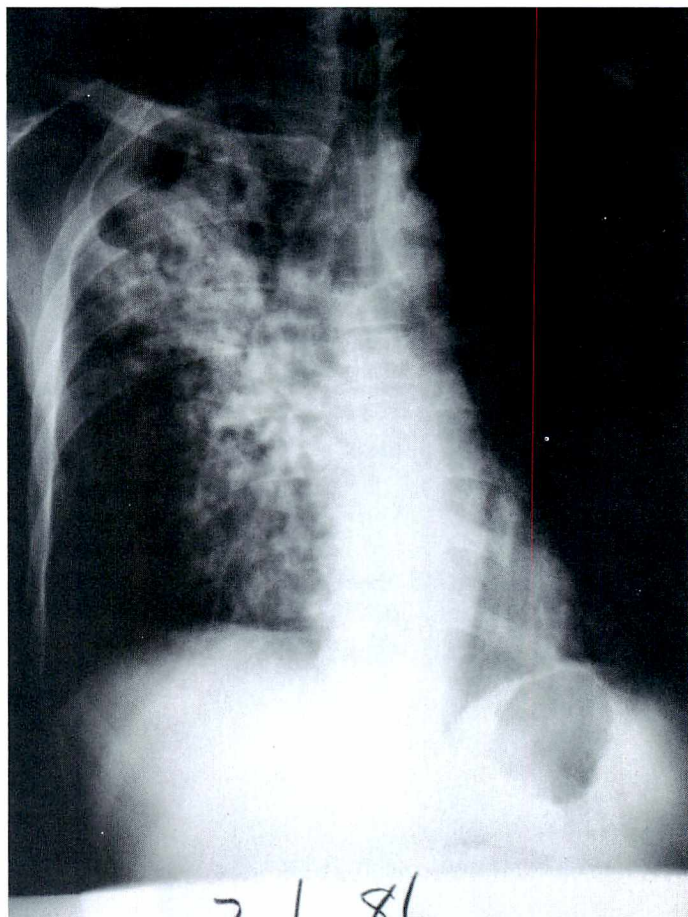
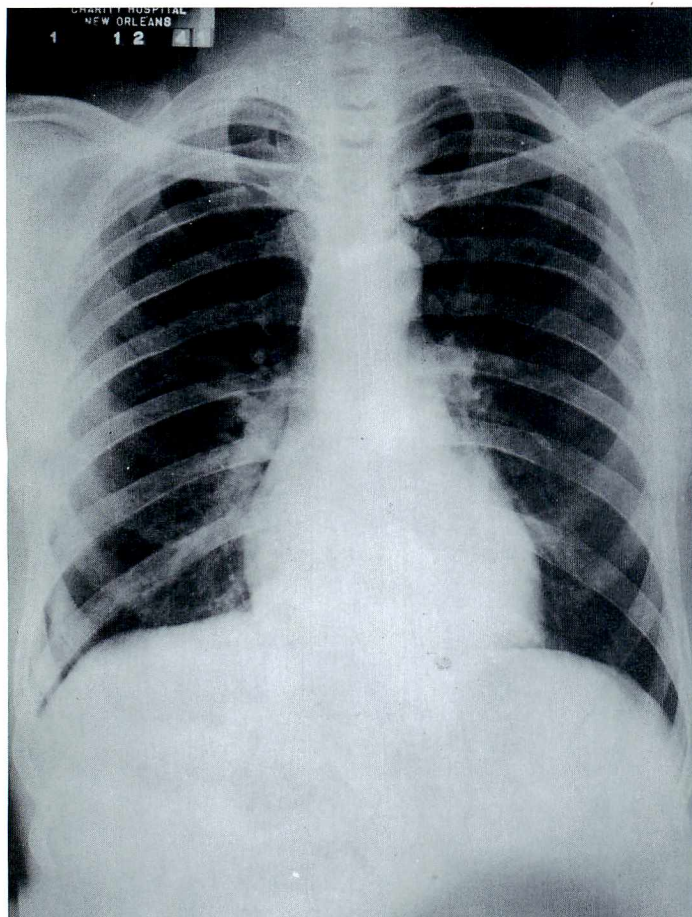
A general practitioner, now retired, recalls his early experiences as an intern in a Washington, D.C., hospital after World War II: "At that time, all the interns had to do a rotation in the TB annex, where there were six floors of very sick people. They did a lot of surgery in those days to remove diseased lungs, a lot of pneumothorax [artificial collapse of a lung to allow it to heal]. Besides good hospital care, there wasn't a great deal more we could do for tuberculosis patients."

The TB annex no longer exists. The building still stands, but the rooms were turned over long ago to patients with more pressing medical problems.

But the problem of tuberculosis, dormant for a number of years, is beginning to worry public health officials again. Out of a population of approximately 250 million Americans, the nearly 24,000 cases of tuberculosis reported in 1989 to the U.S. Centers for Disease Control in Atlanta, Ga., doesn't sound like a particularly scary statistic. What concerns public health authorities is that after decades of declining figures—22,201 cases in 1985, the lowest annual total in 60 years—the number of TB cases has slowly begun to creep up again. Society's problems—AIDS, poverty, homelessness, alcohol, and drug abuse—and other factors are reversing the previous downward trend and reviving memories of the days when TB was a major health threat.

In the 19th century, this formidable enemy claimed more lives in this country than any other disease. The number of Americans who contracted TB declined sharply after 1900 due to a better understanding of the disease and improved hygiene, but the death rate was still high: TB was responsible for 5 million deaths in the first half of the 20th century. As late as 1954, more than 110,000 beds were devoted to the care of TB patients alone in the United States. With a few





The x-ray on the left shows a normal lung. The x-ray on the right shows a typical case of active tuberculosis with lung destruction in the right upper lobe. (Photos courtesy of (left) American Lung Association and (right) Dr. Lee Reichman, University of Medicine and Dentistry of New Jersey)

exceptions in research institutions, today there are none.

The great TB sanitariums, such as those in Saranac Lake, N.Y., and Glen Lake, Minn., shut their doors forever to TB patients in the 1950s and 1960s. These institutions and others like them both here and in Europe were established in the late 19th and early 20th centuries to combat a disease for which the only known treatment was a regimen of fresh air, nutritious diet, and bed rest. The theory was that given half a chance, the body would fight the disease itself. It worked for some of the people fortunate enough to be able to stay in these "magic mountains," as writer Thomas Mann called them, but more died than lived.

The discovery of streptomycin in 1944 and isoniazid in 1951 made the long, expensive "cure" unnecessary and put TB sanitariums and hospitals out of business. It was at last possible to successfully treat a disease—in most cases at home rather than in the hospital—that

had been around since prehistoric times.

Airborne Transmission

TB is usually caused by repeated exposure—usually at home or at work—to droplets contaminated with tubercle bacilli (a species of rod-shaped bacteria) that are expelled into the air when a person with active pulmonary TB coughs, sneezes, or even sings, speaks or laughs. The TB bacteria (*Mycobacterium tuberculosis*) in these excretions are so tiny that they dry out and float on air currents and may survive for long periods in an enclosed space.

Contrary to popular belief, TB is not likely to be transmitted through personal items belonging to those with TB, such as clothing, bedding, or other items they have touched, according to the American Lung Association.

Even when exposed to TB, most people who breathe in the bacteria don't become infected. Of those who do, most don't develop active disease; instead, the

TB bacilli may lie dormant in the cells lining the lungs' air sacs, where the body may wall them up in tiny, hard, grayish capsules, or tubercles. (TB can spread to other parts of the body, but the most common site is the lungs.) From then on, a lifelong balance between the infection and the infected may be maintained. If the body's resistance is lowered because of aging, illness, fatigue, malnutrition, alcoholism, or other factors, this balance may be upset, allowing bacteria to break out of the tubercles and enter the bloodstream, causing active TB.

It is estimated that 10 to 15 million Americans are among the 1.7 billion people worldwide who are TB carriers but are not infectious to others. About 90 percent of TB cases in this country occur when a dormant infection awakens and develops into active TB; only 10 percent result from a newly acquired infection. Of all infected people, 5 percent will develop the disease within a year, while another 5 percent will develop TB later on in their lives.

TB experts still don't know why most people who have been infected with the TB organism don't ever develop active disease, why some people develop active

Old-Fashioned Romance



To think that it was once considered romantic to look tubercular. Healthy and athletic women may be today's feminine ideal, but in the late 18th and early 19th centuries, aristocratic women strove to be thin, pale and delicate. To that end, they starved themselves (anorexia is nothing new), used white powder on their faces, and cultivated the languid, listless air of those drained of energy by the disease. Since TB was so prevalent then, it's not surprising that for some the wish became the reality.

Maybe the disease was romanticized because it cut such a wide swath through the ranks of the talented and famous of those times. TB was the most common cause of death in the Western world up to the time of the American Revolution.

Frédéric Chopin died of the disease, as did John Keats, Emily Brontë, Edgar Allan Poe, Henry David Thoreau, and Anton Chekhov. Had Percy Bysshe Shelley not drowned in a boating accident at age 30, he would surely have died of TB, because he had an active case. Robert Louis Stevenson sought the cure at Saranac, then moved to Samoa, where he died at age 44. Ralph Waldo Emerson lost his first wife to the disease, as well as brothers and other family members, but successfully fought it himself. TB bedeviled Emerson descendants until antibiotics were discovered. TB also ran like wildfire through the Keats, Brontë, Thoreau, and Trollope families. Before Robert Koch, the eminent German bacteriologist, proved in 1882 that bacteria caused TB, many considered the disease to be hereditary.

Maybe looking tubercular had a certain cachet, but it's hard to believe those ladies were unaware of what the disease was really like. In the early stages, TB is symptomless. Gradually, however, the TB patient feels tired, may run a fever, have night sweats, lose weight. This wasting away, in which the body is literally consumed by the disease, is the reason TB was once called consumption. As the disease progresses, the patient may cough up blood-tinged sputum. Chest pain is common, and shortness of breath develops when the lungs are heavily ravaged. **And if a lung cavity erodes an artery, massive hemorrhage can occur.**

Not exactly the stuff romance is made of. ■

—E.Z.

disease immediately, and why most cases occur among people who became infected earlier.

TB Cases Rise

The current epidemic of the human immunodeficiency virus (HIV) is one of the main reasons for the increase in new cases. People with both TB and HIV infections are at substantially greater risk of developing active tuberculosis than are people infected with the TB organism but who are not HIV-infected. The World Health Organization estimates that worldwide, about 3 million people with HIV infection are also TB-infected. Those with HIV infection who come from areas where TB is endemic, such as parts of Latin America, sub-Saharan Africa, and southeastern Asia, are at high risk for TB.

The growing numbers of homeless are also contributing to rising statistics. Up to 6.8 percent of America's homeless have active TB, and about 50 percent have latent TB infection, according to CDC. Observers say, therefore, that homeless shelters may provide a fertile breeding ground for the disease.

Increasing enrollment of the elderly in nursing homes is also leading to the rising incidence of TB. One study found that male nursing home patients in Arkansas developed TB at a rate 10 to 30 times the rate of men of similar ages living in other circumstances. Schools have also been implicated as a source of outbreaks, since cases among children rose 16 percent in 1989.

Other factors leading to a greater number of cases—either by increasing the risk of exposure to TB or affecting the body's ability to fight the disease—are crowded living conditions, poor nutrition, poverty, stress, drug use, alcoholism, and immigration from areas where TB is common.

Testing for TB

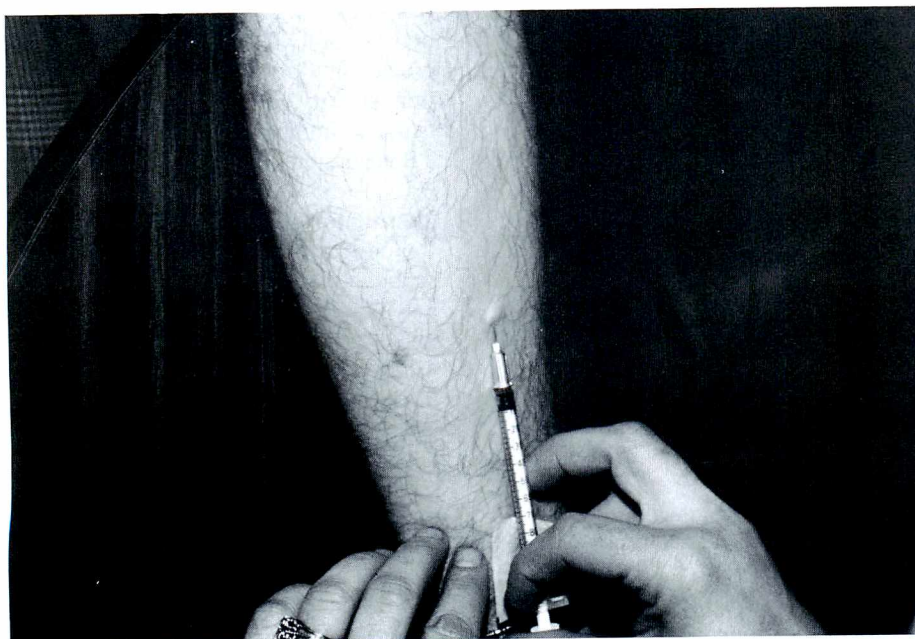
Gone are the days when all American school children were routinely tested for TB. Who can forget the tine test, in which a four-pronged device containing a substance called tuberculin punctured tender forearms? Or how the school nurse examined those forearms a few days later?

Though TB testing was mandatory in schools throughout the United States in the past, many of those programs were allowed to lapse as TB became less of a public health threat. "Because of some recent outbreaks, more and more school



Above, a young boy receives a tine test at a free TB screening clinic. Below, purified protein derivative (PPD) is injected under the skin of a man's forearm in the Mantoux test for exposure to TB.

(Photos courtesy of (top) American Lung Association and (bottom) Dr. Lee Reichman, University of Medicine and Dentistry of New Jersey)



systems, which for a while had deemphasized TB testing for both faculty and students, have now reinitiated testing, though that varies from area to area," says Donald Kopanoff, associate director of CDC's division of tuberculosis control.

Though the tine test is still used in screening large populations with low exposure to TB, experts believe the Mantoux test—in which a substance called purified protein derivative (PPD) is injected under the skin of the forearm and examined about 48 to 72 hours later—is more reliable. A thickening of the area suggests that the person may have been infected with TB bacteria. But this doesn't necessarily mean that the person has the active disease. (It is also possible that the reaction may be due to infection with nontuberculous but related bacteria.)

Testing Recommendations

Common sense would dictate that anyone with symptoms or who has been in close contact with someone with active TB should have a skin test, which can be administered either by private physicians or in public clinics.

TB skin-testing is mandatory in certain states and counties for immigrants and students from Africa, Asia and Latin America, as well as for personnel in schools, hospitals, correctional facilities, food-handling establishments, group homes, child-care facilities, and substance abuse centers.

Skin tests are also recommended for our senior citizens. "Elderly people, especially those in nursing homes, who happen to be infected, but have not developed [active] disease, may, in fact, as they become more debilitated or develop some other concomitant illness, have that infection break down and develop into active disease," says Kopanoff. "Since they're around a lot of other elderly people who are also at high risk of becoming infected and developing active TB, it's pretty much mandatory for both employees and new clients to be skin-tested at the time they come on board. Depending upon the risk of TB in the general community surrounding the nursing home, individual administrations have to decide how often they're going to do repeat skin tests, especially for the employees."

At present, screening of children entering kindergarten or day-care centers is not required in all school jurisdictions, but CDC recommends that school chil-

dren be tested for TB to ensure that all U.S. citizens are tested at least once in their lifetimes.

Diagnosis

If a person has a significant reaction upon being tuberculin skin-tested for the first time, additional laboratory and x-ray examinations are necessary to determine if the individual has active TB. Once infected, most persons will generally test positive for the rest of their lives.

TB can mimic some other diseases, such as pneumonia, lung abscesses, tumors, and fungal infections, or occur along with them. For proper diagnosis, therefore, a doctor will rely on symptoms and other physical signs, a person's history of exposure to TB, and x-rays that may show evidence of TB infection, usually in the form of lesions or cavities in the lungs. TB bacilli grown in cultures of sputum or other specimens provide a positive diagnosis.

How TB Is Treated

Isoniazid, or INH, is TB's wonder drug. Inexpensive, effective, easy to take, it can both prevent and cure TB. CDC and the American Thoracic Society recommend preventive treatment, which consists of one pill of INH each day for at least six months, for individuals who have:

- close contact with a person with infectious TB
- positive tuberculin skin test reaction and an abnormal chest x-ray that suggests inactive TB
- a tuberculin skin test that converted from negative to positive within the past two years
- a positive skin test reaction and a special medical condition (for example, AIDS or HIV infection or diabetes) or who are on corticosteroid therapy
- a positive skin test reaction, even with none of the above risk factors, in those under 35.

Curing TB

A number of drugs given together are used to cure TB. Kopanoff says that CDC recommends a six-month course with INH and rifampin given concurrently. Pyrazinamide is also given along with these drugs for the first two months only. Persons who have tuberculosis and AIDS or HIV infection require at least nine months of medication.

Streptomycin is still an important anti-TB drug, but its use is limited because it must be given by injection. In cases

where TB bacteria have become resistant to these drugs, other drugs, such as ethambutol (an anti-mycobacterial agent), are added. After a few weeks of antibiotic therapy, the TB patient can no longer infect others.

Even though INH and rifampin have not been found to cause birth defects in animals, they are used to treat pregnant women only when therapeutically necessary and usually are not given to pregnant women with latent tuberculous infection.

Adverse Effects

It's no wonder that drugs powerful enough to knock out tough TB bacteria can also have serious adverse reactions. The most commonly used anti-TB drugs—INH, pyrazinamide, and rifampin—can cause liver damage. Before they are administered, tests to measure liver enzymes and kidney function and other blood tests should be run, to serve as baselines for later comparison.

INH is especially dangerous to alcoholics and older adults, while rifampin interferes with the action of a number of widely used drugs, such as digitalis, certain anticoagulants, oral contraceptives, and diabetes drugs. Streptomycin may

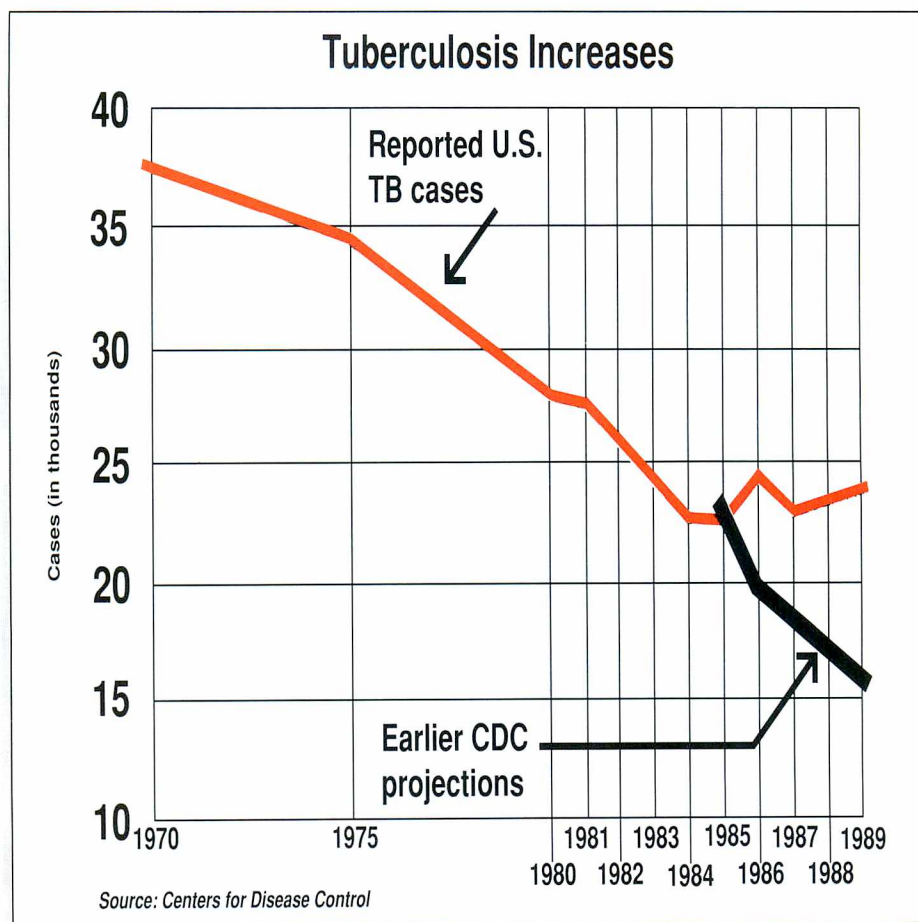
cause some hearing loss, while ethambutol may affect vision, with a loss of acuity and decreased ability to distinguish between red and green.

Vaccine

A vaccine for tuberculosis, called BCG for *Bacille Calmette-Guérin*, is available but not widely used in this country. Made from live, but weakened, cow tubercle bacilli, the vaccine didn't protect adults against pulmonary TB in a large clinical trial in India. However, because it appears to offer some protection to children, the World Health Organization recommends its use for newborns in developing countries. The prevalence of TB in the United States is generally considered to be too low to justify widespread immunization with BCG. Several other vaccines are currently under development.

Just as smallpox was eradicated through vaccination worldwide, a better, more effective vaccine might spell an end to this ancient but enduring disease. ■

Evelyn Zamula is a freelance writer in Potomac, Md.



Preventing 'Turista' and Other Travelers' Ailments



by Jeffrey P. Cohn

I was in my hotel room in Guatemala when it hit. That sudden urge to go to the bathroom, right now. If it had been the first time that morning I would not have thought twice about it. But it was the fourth time in less than an hour. I knew I had it, that dreaded affliction of American tourists overseas—travelers' diarrhea.

Travelers' diarrhea is the affliction most likely to strike the 8 million Americans who travel abroad each year,

but it is not the only disease or medical condition they should be wary of.

There are also a number of other diseases or medical conditions that are rare or nonexistent in the United States but common abroad, especially in developing countries. These include the ancient scourges of malaria, typhoid, cholera, and yellow fever. Other exotic ailments like schistosomiasis can also strike the unsuspecting.

But should Americans or any other of the estimated 250 million-a-year worldwide travelers change their itineraries to

include only safe areas or limit their trips to within their own country's borders because of a fear of such diseases?

"Oh, no," responds Hans Lobel, M.D., of the Centers for Disease Control in Atlanta. "What's the purpose of living if you can't enjoy it?" he asks.

Fortunately, travelers can take many precautionary measures to reduce the risk of getting most diseases Americans are likely to be exposed to in other countries. Vaccines and drugs are also available to prevent or treat those diseases. Some are prescription medications, but

others are sold over the counter.

Simple precautions include, experts say, knowing what health conditions might be encountered, making sure immunizations are up to date, taking along a supply of medicines, and being careful about what you eat, drink or do abroad. Travelers, especially older ones or those with diseases such as diabetes, are also advised to discuss their travel plans and any special medical needs with their physicians before leaving.

"People should travel with care," says Pamela Prindle, administrative director of immunizations at Foxhall Internists, a Washington, D.C., medical practice specializing in travelers' health. "Travel as wisely and as healthy as you can," Prindle advises Foxhall's patients.

The specific diseases or medical conditions any traveler might be exposed to depend on where that individual is going, how long he or she will be staying, and how that person will be living once there, says Theodore Nash, M.D., a senior scientist at the National Institutes of Health's Laboratory of Parasitic Diseases.

Traveling in Europe is safer, for example, than in tropical Africa or Asia. But staying in a London or Paris hotel for a few days differs from spending weeks in rural Yugoslavia or Greece. Similarly, there is a big difference between going to an African city such as Nairobi and undertaking a wildlife safari in the bush. And traveling for business or sightseeing is not the same as living in a rural area for weeks, months or years.

In general, the diseases that concern most travelers are found largely in tropical Central and South America, Africa and Asia, says R. Bradley Sack, M.D., director of the international travel clinic at the Johns Hopkins University School of Medicine in Baltimore. The bacteria, viruses and parasites that cause such diseases thrive in hot climates and in countries or areas where sanitation and medical care usually fall below U.S. standards.

Even so, the chances of getting a serious tropical disease are remote for most tourist and business travelers, especially if precautions are taken. For example, each year, only a thousand or so Americans traveling abroad get malaria, says Lobel, chief of CDC's malaria surveillance program. In East Africa, where most American tourists to that continent go, the risk is 1 in about 200. In India and southern Asia, it is 1 in 50,000.

Travelers' Diarrhea

Some 20 to 50 percent of Americans visiting the tropics get what is called "Montezuma's revenge," the "skitters" or, in Spanish-speaking countries, "turista," says Martin Wolfe, M.D., director of the Travelers' Medical Service in Washington, D.C.

Its symptoms include loose and watery stools, nausea, bloating, abdominal cramps, and sometimes fever and malaise. Fortunately, it is a self-limiting disease. Even if untreated, its symptoms usually go away in three or four days. If diarrhea lasts more than four days or is accompanied by severe cramps, bloody stools, or foul-smelling gas, the individual should see a physician.

Most travelers' diarrhea is caused by a special strain of the common intestinal bacteria *Escherichia coli*. This strain of *E. coli*, as it is usually known, accounts for at least 40 percent of all travelers' diarrhea. Other bacteria, such as the ones responsible for salmonellosis and shigellosis, can also cause diarrhea, as can such parasitic conditions as giardiasis and amebiasis.

Whatever the cause, the best way to treat travelers' diarrhea, the experts say, is to prevent it. Most diarrhea-causing organisms are water-borne, passed on in untreated water or by food handlers who have not washed their hands adequately.

Savvy tourists will avoid using untreated or suspect water in areas where travelers' diarrhea is common. This includes not drinking tap water or using it to brush your teeth (even in good hotels), not using ice in sodas or alcoholic drinks, and not mixing alcohol with water. It's also smart to skip milk and other dairy products unless you are sure they have been pasteurized.

For brushing your teeth or drinking in your hotel room, boil the water you intend to use for at least five minutes or add water purification tablets. Avoid bottled water unless it is carbonated—the carbonation process inhibits bacterial growth. Drink carbonated beverages, beer, wine, and coffee or tea. And wipe off bottle or can tops before drinking from them.

Also, be cautious about food, especially in developing countries. Don't eat raw vegetables, fruits, meats, or seafood. Avoid cold buffets left in the sun for several hours, garden or potato salads, and food from street vendors. Eat only hot cooked meals, fruits you have peeled yourself, and packaged foods.

If, despite all your best efforts, travelers' diarrhea strikes, medical experts and experienced travelers alike recommend drinking plenty of fluids to replace water and adding oral rehydration packets to fluids to replace lost minerals. Additionally, several prescription and over-the-counter drugs will relieve diarrhea's symptoms or kill bacteria that cause the disease.

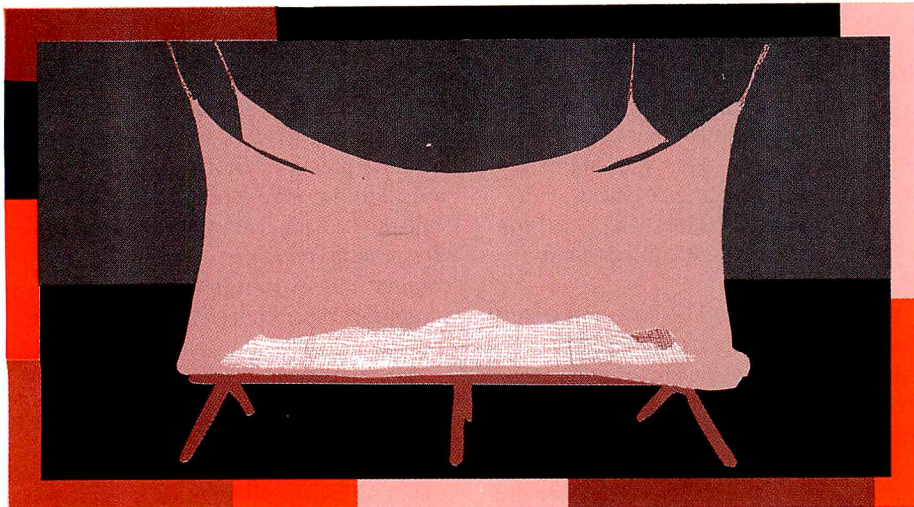
The first line of defense now for early treatment of travelers' diarrhea is the antibiotic trimethoprim/sulfamethoxazole (Bactrim). Long used for other illnesses, it is the only antibiotic approved by the Food and Drug Administration for travelers' diarrhea. Bactrim is 90 percent effective against the organisms that cause the disease, says John Hopkins' Sack. It usually shortens the illness and makes it less severe. Travelers can ask their physicians for a prescription to take along so it will be available at the first signs of travelers' diarrhea.

Physicians may also prescribe other drugs for travelers' diarrhea. These include doxycycline (Vibramycin), diphenoxylate (Lomotil), and the newer quinolone drugs, ciprofloxacin and norfloxacin. However, none of these drugs has been approved by FDA specifically for travelers' diarrhea due to *E. coli*. Moreover, doxycycline is not approved for children younger than 8, and the two newer quinolone drugs may be dangerous when taken by those under 18.

Perhaps the most widely used anti-diarrheal medications are the over-the-counter drugs bismuth subsalicylate (Pepto Bismol) and loperamide (Imodium). Several scientific studies have been published on the effectiveness of these products in treating travelers' diarrhea. These products are approved for treating diarrhea, and FDA is reviewing their effectiveness for treating travelers' diarrhea as well. Both products treat diarrhea's symptoms rather than killing the bacteria. "This is an infection and you need to get rid of it," Sack says.

Bismuth subsalicylate may take a few hours to work and cannot stop severe diarrhea. Nor should it be used by people taking a lot of aspirin or other blood thinners, pregnant women, or people subject to seizures, says Celia Maxwell, M.D., a medical officer in FDA's anti-infective drug division.

(Continued on next page)



Products containing bismuth subsalicylate also should be avoided by children and teenagers recovering from flu, chicken pox, or other viral infections, because of the risk of Reye syndrome.

Malaria

If travelers' diarrhea is the disease most likely to strike Americans abroad, malaria is the most serious ailment they are likely to encounter. Once thought to be under control and perhaps even close to eradication, malaria has made a remarkable comeback in the past decade or two, says CDC's Lobel.

Malaria is caused by a single-cell blood parasite called plasmodium. The parasite is usually transmitted to people by the bite of an infected *Anopheles* mosquito. Symptoms start with a listless feeling, loss of appetite, muscle aches, and a low fever. After a few days, the classic symptoms appear: a fever that can reach 105 degrees Fahrenheit and teeth-rattling chills that can last 20 to 60 minutes. The fever may break and then return again on a 48-to-72-hour cycle, and it may be accompanied by nausea, diarrhea and vomiting.

Worldwide, some 200 million people are estimated to have malaria, Lobel says. Those numbers are guesses, he admits, since reliable figures are hard to come by. In Africa, he says, "most everybody has been infected." In this country, about 1,000 malaria cases a year are reported to CDC, a figure Lobel thinks represents only a third of the true numbers. According to Bruce Burlington, M.D., deputy director of FDA's Office of Drug Evaluation II, people living in Africa come "more or less into equilibrium" with malaria and don't get as sick as travelers who are newly infected.

Malaria is prevalent throughout the tropics, but the traveler's risk of contracting the disease is greatest in Africa and the island of Papua New Guinea in

the Pacific near Australia. It is common but less of a risk in India and southeastern Asia, central and northeastern South America, and in Haiti. It is less prevalent in China and the Middle East. Even in high-risk regions, Lobel adds, the chances of getting malaria are much greater in rural areas than in cities.

The reasons for malaria's comeback are a familiar refrain nowadays. The mosquitoes that transmit the disease now resist what had been the most effective pesticides, and many of the parasites themselves now resist what had been the most effective drug used to prevent and treat the disease.

Actually, malaria is four diseases caused by four different species of the plasmodium organism. In particular, the form known as falciparum now widely resists chloroquine (Aralen), the drug developed in the 1940s to prevent and treat malaria. Often called "malignant malaria" or "black-water fever," falciparum is the most serious form of the disease and the one most likely to kill its victims. Resistance began to appear in the 1960s and is widespread in most places falciparum malaria is found today.

Fortunately, malaria can still be prevented and cured in most cases if diagnosed properly, Lobel says. While chloroquine remains an effective anti-malarial drug in nonresistant areas and for the non-falciparum forms, mefloquine (Lariam), approved by FDA in 1989, is now also recommended.

Travelers going to chloroquine-resistant areas who cannot take mefloquine—people taking beta blocker drugs for heart conditions or who are subject to seizures, FDA's Maxwell says—can use pyrimethamine/sulfadoxine (Fansidar) or doxycycline. Doxycycline is as effective as mefloquine, Lobel says, but cannot be used for as long a time because of its potential side effects. Doxycycline must

also be taken daily rather than weekly as with chloroquine and mefloquine. Fansidar can cause an uncommon but potentially fatal rash as a side effect, so it is generally used only when other drugs aren't appropriate.

Several other drugs are sometimes prescribed for malaria by physicians in other countries. One, proguanil (Paludrine), is widely used in Great Britain and Kenya. Others include pyrimethamine (Daraprim) and pyrimethamine-dapsone (Maloprim). None are as broadly effective as mefloquine or chloroquine, some need to be used with other anti-malarial drugs, and a few have serious side effects. Nor have any been approved by FDA for malaria.

As with travelers' diarrhea, the best treatment for malaria is prevention. Americans are advised to avoid the mosquitoes that transmit the disease. Stay inside at dusk and dawn, wear long pants or long-sleeved shirts when in mosquito-infested areas, sleep in well-screened rooms or under mosquito nets, and use an insect repellent such as DEET (N, N-diethyl-m-toluidide) on exposed skin.

Other Diseases

Most other diseases or medical conditions to which American travelers are likely to be exposed are rare and easily avoided. Schistosomiasis, for example, occurs in much of Africa, the Middle East, northeastern South America, and some Caribbean islands. Also called bilharzia or snail fever, it is caused by a freshwater snail-borne parasite. Schistosomiasis can be prevented by staying out of freshwater lakes and streams in infested areas. Salt water and adequately chlorinated swimming pools are okay, though.

Sleeping sickness is a serious illness that is transmitted by the bite of tsetse flies. It is confined to areas of Africa usually not on most American tourists' itineraries. For travelers visiting such areas, the best advice for prevention is to wear long pants and long-sleeved shirts when outside. (See accompanying article for drug treatment.)

Giardiasis, a parasitic disease, most common in the Soviet Union, Mexico, western South America, South and Southeast Asia, and the Middle East, is also increasing in North America, particularly among mountain hikers who drink untreated water from streams contaminated with feces from infected animals such as beavers.

Giardiasis can range from a mild intestinal discomfort that disappears in a few

Drug for Sleeping Sickness

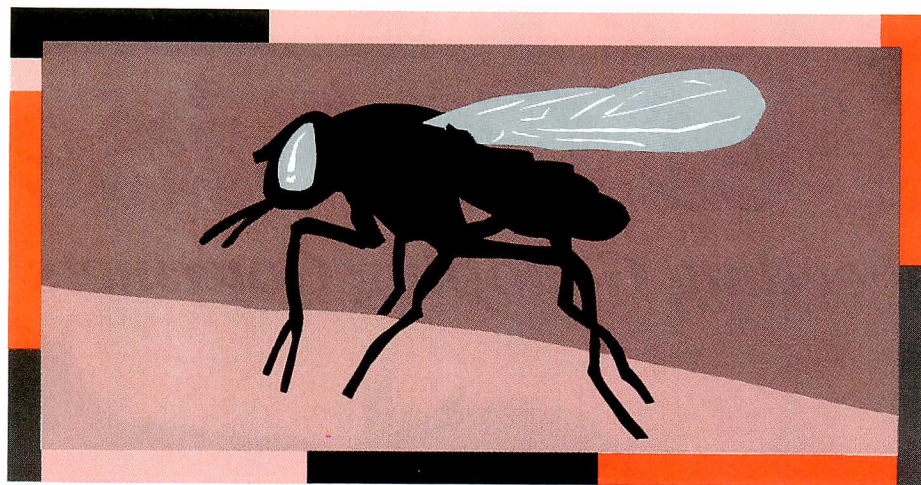
A new drug to treat African sleeping sickness has been approved by FDA.

There are two types of African sleeping sickness—the Gambian strain and the Rhodesian strain. Both are spread by the bite of the tsetse fly, which transmits the parasitic infection.

The newly approved drug, eflornithine hydrochloride, effectively treats the final, most serious stages of the Gambian strain of the illness. Studies have shown that, given intravenously, the drug inhibits the growth of the parasite.

African sleeping sickness is widespread in 36 central and west African countries, where 20,000 new cases are reported each year. There are usually fewer than 10 cases per year in the United States. These are mainly among travelers who were exposed to the disease in the endemic areas of Africa.

Bites from tsetse flies spread sleeping sickness similar to the way malaria is spread by mosquitoes. The first sign of infection from the Gambian strain is fever, followed



by anemia and painful swelling of the lymph glands. Finally, the infection spreads to the central nervous system, causing extreme mental and physical lethargy, along with tremors, convulsions, and eventually coma and death.

The only alternatives to the newly approved drug for treating the final stages of infection are two drugs that contain arsenic. These drugs can be fatal or cause serious nervous system problems in up to 10 percent of patients.

The new drug does not appear to have these serious nervous system effects, but does have a potential for causing anemia

and, sometimes, dangerous decreases in the numbers of white blood cells and platelets in the blood. As a result, the drug's labeling warns that the patient's blood cell count must be monitored twice a week.

Merrell Dow Pharmaceuticals of Cincinnati will market eflornithine hydrochloride under the brand name Ornidyl. FDA has designated Ornidyl an orphan drug. The federal orphan drug program provides incentives to companies to research and market products for very small patient populations. ■

—Dori Stehlin

days to a severe debilitating disease. Its symptoms include the sudden onset of explosive diarrhea and foul-smelling gas. Giardiasis can be treated with metronidazole (Flagyl), quinacrine (Atabrine), or furazolidone (Furoxone). Quinacrine can cure 90 percent of the disease's victims, Wolfe says, but can cause nausea, headaches and diarrhea in children and, rarely, toxic psychosis in adults, FDA's Maxwell says.

In several cases, vaccination can prevent diseases travelers may be exposed to. FDA approved an oral vaccine for typhoid in 1989 that has significantly fewer side effects than the injectable vaccines previously used. Typhoid is caused by the bacterial organism *Salmonella typhi*, usually transmitted through contaminated food or water. Rare in the United States, most of the 400 to 500 typhoid cases a year reported in this country have been contracted abroad, usually in less developed areas where sanitation is poor. Immunization is therefore recommended, but only for travelers going to areas where the disease is common.

Yellow fever, still endemic through much of tropical Africa and South America, is easily preventable by vaccination, as is meningitis. The cholera vaccine, on

the other hand, is only about 50 percent effective. As a result, the World Health Organization advises against its use. Three countries—Pakistan, Sudan and Pitcairn Island (best remembered as where mutineers from the British ship *Bounty* hid out 200 years ago)—still require it for entrance, however. Fortunately, few tourists are likely to get cholera.

There is also a vaccine for hepatitis B, which can be transmitted sexually, by blood transfusions, and by intravenous drug use. For hepatitis A, experts recommend immunization with immune globulin for travelers going to rural areas with poor sanitation. Hepatitis E, which is transmitted similarly to hepatitis A, has caused epidemics in Africa, Asia and, most recently, Mexico. It is not known whether gamma globulin can prevent it. Polio immunizations should also be brought up-to-date since the disease has recently resurged in Israel and parts of Africa and Mexico.

Finally, a word about acquired immune deficiency syndrome. AIDS, which is transmitted the same ways as hepatitis B, is now widespread throughout much of the world, but especially in sub-Saharan Africa and Brazil. In Africa,

it is commonly spread through heterosexual contact, often with prostitutes. The only sure way to avoid the sexual transmission of AIDS is to abstain from sexual contact. Otherwise, safe sex practices, including the use of a latex condom, are advised. (See "Latex Condoms Lessen Risks of STDs" in the September 1990 *FDA Consumer*.)

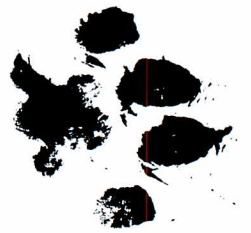
For tourists wanting to learn more about travelers' illnesses, the Centers for Disease Control publishes an annual "Health Information for International Travel." Copies are available for \$5 from the U.S. Government Printing Office by writing the Superintendent of Documents, Washington, D.C. 20402.

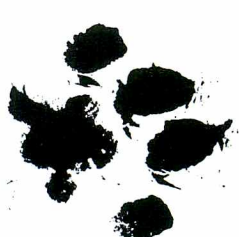

CDC also maintains a recorded telephone message system with general and geographic-specific information on travelers' diseases. The number is (404) 332-4559. Information on malaria and other specific diseases can be obtained by calling (404) 332-4555. ■

Jeffrey P. Cohn is a freelance writer in Takoma Park, Md. His most recent trip abroad was in 1988, when he traveled to Guatemala.


Pet Cuisine

Feeding Galloping Gourmets





by Stephen J. Ackerman and Judith Levine Willis



Will your dog really be better off if you buy the 70-cent-per-can “gourmet” dog food instead of the ordinary half-dollar brand? Will your finicky cat thrive, yet lose weight, if you switch to an expensive “diet” dinner? Finding the right answer for your pet can be important to its health and to your pocketbook.

Feed for pets is more than a \$6 billion industry, with almost \$5.7 billion devoted to dogs and cats. According to the Pet Food Institute, a trade association, there are 54.5 million dogs and 63.2 million cats in the United States.

After the first dog biscuits were sold in 1860, change came slowly. Canned horse-meat joined dry dog foods in the 1920s, with dry meat meals and the first cat foods appearing in the 1930s. Commercial variations flourished in the 1960s.

The Human’s Dilemma

If you stroll down the supermarket pet food aisle today, you may find some 100 varieties of dog food.

Most common are “low-calorie” products to help Rover lose weight. Prominent, too, are brands with nutrients suited to dogs of different ages. Some victuals claim benefits purely cosmetic, such as alleviating canine “bad breath”—a condition more likely to trouble the master than the mastiff. Amid such a profusion of products, how is one to choose?

Specialized pet foods, sometimes called “prescription” feeds or diets, have been marketed primarily through veterinarians or kennel clubs, and intended as part of a comprehensive health regimen. Recently, however, they’ve begun showing up on supermarket shelves.

“We are opposed to the sale of ‘prescription’ diets in supermarkets,” says George Graber, Ph.D., director of FDA’s division of animal feeds in the Center for Veterinary Medicine. He explains that feeding a pet such foods without the advice of a veterinarian could harm the pet.

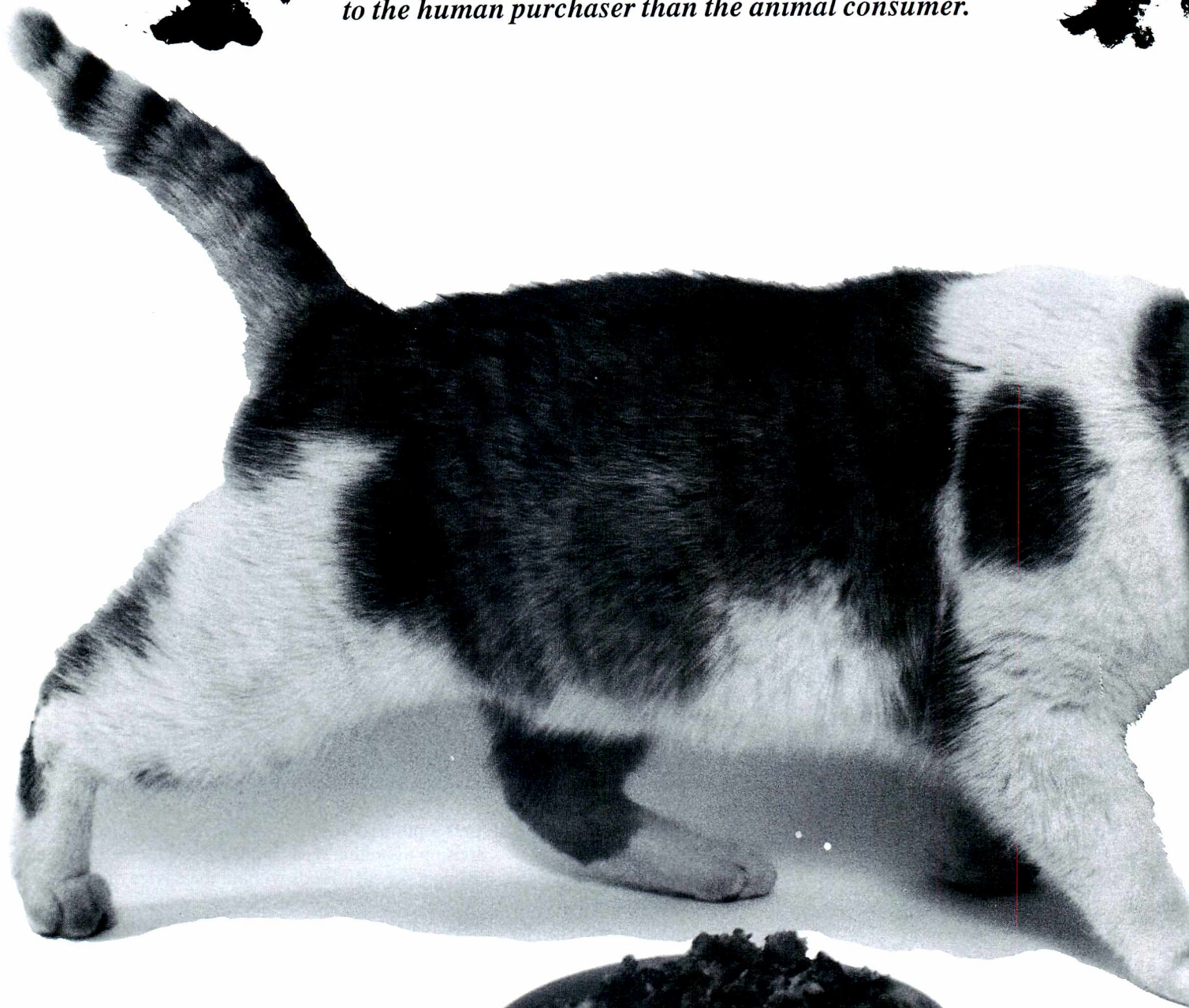
The regular dog and cat foods on the market provide a “complete and balanced diet” for pets, and clearly show this in their package labeling. While some products may claim to taste better—and large manufacturers maintain kennels with the happy mission of testing such claims—all foods so labeled are adequate nutritionally for healthy animals. FDA insists that pet food be as safe for animals as human food is for people. Labels list ingredients in order of preponderance, along with a chemical analysis. Even a product’s name may not be misleading as to content or nutritional properties.

FDA’s Center for Veterinary Medicine works closely with the states through the Association of American Feed Control Officials (AAFCO) to insure the safety of animal feeds. Manufacturers must provide scientific support to justify nutritional claims, including the assertion that a product constitutes a “complete and balanced” diet, either throughout an animal’s life or during a specified part of its life cycle.

Who’s the Gourmet?

Whether or not a pet becomes a demanding “gourmet” depends on its owner. In choosing varied, “gourmet” diets for our pets (diets to which they may become

***S**ome gourmet pet foods are designed to appeal more to the human purchaser than the animal consumer.*





quickly and expensively accustomed), we fall into an anthropomorphic fallacy, a tendency to attribute human characteristics to animals.

Dogs and cats are creatures of habit. A pup or kitten raised on an ordinary feed will grow to like it, sometimes shunning rarer delicacies in favor of "the usual." Though Fido may clamor for your steak while his own chow waits in his bowl, he'll ordinarily go for his regular meal if other temptations don't compete. Variety is not so important to him as it may seem to you.

Some "gourmet" pet foods (and especially pet "treats") are designed to appeal more to the human purchaser than the animal consumer. Color-blind canines are indifferent to the pastel hues that beckon the buyer of dog candies, just as kittens value the cute shapes less than the content of their bonbons. We pay extra for such gimmicks because we consciously or unconsciously equate human tastes and needs with those of our pets. Catering to this tendency in the extreme was a luxury mineral water marketed in New York as "the only water your dog needs to drink."

"What are you trying to achieve in adopting a special diet for your pet?" asks Beverly Corey, D.V.M., an FDA veterinarian. "Once you know that, do you have enough information to make the proper selection?" Your answers to these common-sense questions can protect you from wasteful spending, and they can prevent you from inadvertently harming your pet's health.

You should have reason to depart from a "complete and balanced" pet diet in favor of a more specialized regimen. These reasons may include age, disease, or even stress, but they should be diagnosed by a veterinarian. Otherwise, a good rule to apply to your pet's system is the traditional wisdom, "if it ain't broke, don't fix it."

Pet Foods with Drug Claims

FDA is especially concerned about pet food products labeled for the prevention or treatment of disease. Such labeling, Graber points out, renders the product a drug. He says that as far as he knows, no pet foods carrying drug claims are being legally marketed in the United States.

FDA has been working with the states, through AAFCO, to make sure that pet foods are not labeled with drug claims. Of particular concern recently has been cat food labeled for the prevention of feline urological syndrome (FUS), a urinary tract problem in male cats.

In February 1990, AAFCO sent a letter to pet food manufacturers reiterating FDA and AAFCO's position that claims that a product may prevent or treat FUS are drug claims and are not allowed on feeds unless they're approved as drugs. Even though FDA gave companies ample time to make necessary label changes, some failed to make them.

Armed with FDA documentation, Missouri and Texas state officials have seized hundreds of tons of cat food labeled for the prevention of FUS, and New York state officials are contemplating similar action. At least one company whose products were seized has assured FDA that it will no longer label products for sale in the United States for the prevention of FUS.

In a similar case in 1987, the manufacturer of Purina Puppy Chow complied with FDA's request to withdraw its advertising claims that the product could ease canine hip dysplasia (CHD), a genetic disease affecting the hip joints of some breeds of dogs, particularly German shepherds. The supporting evidence printed in the advertising brochure provoked a strong reaction in the veterinary community, which dismissed it as scientifically inadequate. Although American Kennel Club breeders have made progress in breeding a tendency toward CHD out of some purebreds, many dogs still suffer from the complex problem, which involves not just breed but genetics, weight when young, and other factors. No dog food has been shown to relieve the disorder.

FDA allows companies to make "gray area" claims on pet food labels provided there is adequate data to support their safety for these uses. "Gray area" claims are defined as those that provide useful health-related information, but do not directly



FDA

*insists that
pet food be
as safe for
animals as
human food
is for people.*



state disease prevention or treatment. Examples of gray area claims are “low magnesium” or “produce acidic urine pH.”

Weighty Problems

“Low-calorie” pet foods have emerged to help pudgy pooches and fat felines reduce. A safe and effective weight reduction program, however, must recognize not just the physiological differences between humans and dogs or cats, but also those between dogs and cats.

From a fifth to over half of dogs are overweight, though the lack of agreement as to what constitutes canine obesity complicates the estimate. If your dog is overweight, in most cases a veterinarian’s opinion is needed to decide what to do. Placing the dog in a hospital and starving it used to be considered an option. But, according to FDA veterinarians, this is rarely done today because it’s now known to be extremely dangerous. It produced only slightly more weight loss than reducing the amount of regular food, and certainly the dogs didn’t like it.

Unless your dog is so committed to its regular food that it refuses anything else, the best course is usually to switch to the same amount of “diet” product recommended by the dog’s vet, rather than reducing the amount of regular food.

Putting cats on a diet can be tricky, too. A “fasting” cat can develop a painful liver condition called hepatic lipidosis. More gradual weight reduction, with enough food to maintain 60 to 70 percent of the cat’s usual energy intake, is essential. A veterinarian can help you determine what this means in terms of food portions or types for Tabby.

Other Nutritional Needs

The commercial success of age-based dog foods set off widespread mass-marketing of specialty pet foods. Promoters claim these products address the particular nutritional requirements your pet encounters as its physiological makeup changes with age. Does your pet really need this costlier precision in its diet?

Some veterinarians find advantages in these products for some dogs and cats, though the nutritional benefits will likely vary with breeds as well as with individual animals. But it’s also true that any “complete and balanced” food will be adequate for pets of all ages without particular health needs.

Specialized foods can make valuable contributions toward controlling pets’ afflictions, though usually as part of a comprehensive therapeutic program. For example, inflammatory bowel or other gastrointestinal diseases can respond well to special diets, but the advice of a vet is essential in treating pet illnesses. Well-intentioned experimenting with a pet’s diet may relieve one condition only by risking another.

Cats and dogs aren’t our only pets, though they have commanded the lion’s share of veterinary research. AAFCO now is devoting new attention to “specialty products” designed for gerbils, goldfish, ferrets, and other creatures. Overweight hamsters may some day find themselves doomed to reducing diets, just like dogs, cats—and people.

Though gourmet goodies may tempt you as you stroll the pet food aisle, it’s wise to keep in mind that expert advice, rather than impulse and intuition, should be your guide in feeding Fido and Tabby. This approach can protect both your pet’s health—and your pocketbook. ■

*Stephen J. Ackerman is a writer based in Washington, D.C.
Judith Levine Willis is editor of FDA Consumer.*

How to Take Your Medicine

Cephalosporins

How you take a drug can affect how well it works and how safe it will be for you. Sometimes it can be almost as important as what you take. Timing, what you eat and when you eat, proper dose, and many other factors can mean the difference between feeling better, staying the same, or even feeling worse. This drug information page is intended to help you make your treatment work as effectively as possible. It is important to note, however, that this is only a guideline. You should talk to your doctor about how and when to take any prescribed drugs.

The eighth installment of this series features a group of drugs called cephalosporins.

Conditions These Drugs Treat

Cephalosporins are anti-infective agents (as antibiotics are also known) used to treat infections occurring in a variety of places in the body. In general, they are used either after other often less expensive anti-infective agents have been tried or when a certain uncommon type of infection is believed present. All cephalosporins can be used to treat most common urinary tract infections and upper respiratory infections such as pharyngitis (throat inflammation) and tonsillitis. All except cefadroxil may be used to treat otitis media (inflammation of the middle ear). All but cefixime can be used to treat various types of skin infections. Cefuroxime axetil and cefixime can be used to treat bronchitis, while cefaclor can treat lower respiratory infections such as pneumonia. Cephalexin can also be used to treat bone infections. Cephalosporins can be used for other infections, as determined by your doctor.

Infections in any one area of the body

Generic Names

cefaclor

cefadroxil

cefixime

cefuroxime axetil

cephalexin

cephradine

(such as the throat, lung, ear, or urinary tract) can be caused by many types of bacteria. Doctors often try to prescribe the anti-infective that best treats the type of bacteria they judge is causing the infection. To be more certain, doctors often culture an area (grow bacteria from an area under laboratory conditions) to determine exactly what types of bacteria are present. This enables them to make a more specific choice of anti-infective. As with other anti-infectives, some cephalosporins can treat certain bacterial infections better than others. This is why doctors sometimes prescribe different cephalosporins for infections that occur in the same area of the body.

How to Take

Cephalosporins can be taken either with food or on an empty stomach. If this medicine upsets your stomach, try taking it with food or milk.

Always store a cephalosporin liquid suspension in the refrigerator (exception: cefixime suspension does not need to be refrigerated). When taking a dose of the suspension, first shake the bottle well. Then use a measuring spoon or other device for administering medicine such as the calibrated medicine dropper included with Keflex pediatric drops. Discard any unused suspension after 14 days.

Be sure to take the right amount of tablets, capsules or suspension for each dose. Taking medicine at the same time each day will help you remember to take it regularly during the period your doctor has prescribed. To make sure your infection goes away completely, always take cephalosporin for the amount of time prescribed even if you feel better sooner. Not taking the cephalosporin for the en-



tire prescribed period can cause your infection to come back. Heart or kidney complications can result if a “strep” (streptococcus) infection is not completely treated.

Missed Doses

To help clear your infection, try not to miss any doses. If you do miss a dose, take it as soon as you remember. If it is almost time for your next dose, take two doses separated evenly over the next dosing interval (for example, if you take a dose every eight hours, take your next two doses spaced apart by four hours, then resume taking it every eight hours).

Relief of Symptoms

If your infection is caused by a type of bacteria that the cephalosporin can treat, your symptoms should improve within a few days. But, as mentioned before, finish taking the cephalosporin for the full number of days even if you feel better.

Sometimes the symptoms can take longer than a few days to improve or may not go away even after you have taken all of the cephalosporin. This may happen with infections in areas of poor

circulation, severe infections, viral infections, or in cases where the infection would be better treated by another anti-infective. If your symptoms have not disappeared after taking all of the cephalosporin or they get worse while taking it, call your doctor.

Side Effects and Risks

Common side effects involve mainly the digestive system: mild stomach cramps or upset, nausea, vomiting, and diarrhea. These are usually mild and go away over time. Cephalosporins, as well as other anti-infectives, can sometimes cause overgrowth of fungus normally present in the body. This overgrowth can cause mild side effects such as a sore tongue, sores inside the mouth, or vaginal yeast infections.

More serious but infrequent reactions can sometimes occur with cephalosporins. These include:

- **Allergic reactions.** If you have a penicillin allergy, there is a chance you may also be allergic to a cephalosporin. Be sure to tell your doctor if you have had allergic reactions to medications, particularly a penicillin, penicillamine, or a

cephalosporin. Allergic reactions to cephalosporins are infrequent, but range from a skin rash that may be itchy, red or swollen to life-threatening reactions such as severe difficulty breathing and shock. Rarely, a specific type of allergic reaction can occur with cefaclor involving a skin rash, joint pains, irritability, and fever.

- **Serious colitis.** This is a rare side effect that includes severe watery diarrhea (sometimes containing blood or mucus), severe stomach cramps, fever, and weakness or faintness. If this happens, contact your doctor immediately before you try treating it yourself with any medications.

If these or other new symptoms occur, call your doctor immediately.

Precautions and Warnings

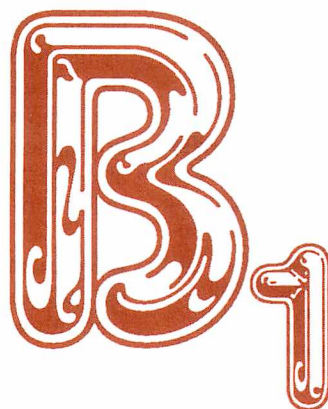
Animal studies do not show cephalosporins to be dangerous during pregnancy. Although the effects of cephalosporins during pregnancy have not been studied in humans, they appear to be relatively safe to use during pregnancy. Let your doctor know if you are or intend to become pregnant while on a cephalosporin.

Cephalosporins pass into breast milk in small amounts, though this is usually not a problem. Nursing mothers should consult with their doctors before breastfeeding while taking a cephalosporin.

Diabetic patients who test their urine for glucose should be aware that cephalosporins can cause a false-positive reading if copper sulfate urine testing tablets are used. ■

—Igor Cerny

VITAMIN



U.S. Recommended Daily Allowances

| Infants (0–12 mo.) | Children (1–3 years) | Adults and Children 4 Years + | Pregnant or Nursing Women |
|-----------------------|-------------------------|----------------------------------|------------------------------|
| 0.5 mg | 0.7 mg | 1.5 mg | 1.7 mg |

(The U.S. RDA amounts are sufficient to meet the needs of practically all healthy people.)

This article is the sixth in a series giving essential facts and figures on different vitamins.

Thiamin (vitamin B₁) is a water-soluble vitamin that was the first identified member of the B complex group.

Functions: Helps convert carbohydrates to energy; aids in nerve cell functioning.

Sources: Brewer's yeast; lean cuts of pork; whole-grain or enriched cereal grain products; legumes; liver, heart and kidneys; nuts and seeds.

Deficiency: Thiamin deficiency causes beriberi, a disease whose symptoms include anorexia, weakness, lack of coordination, muscle wasting, paralysis of the eye muscles, mental confusion, rapid heartbeat, edema, and enlarged heart. Deficiency is sometimes seen in this country in people with alcoholism and certain medical conditions.

Excess: High intakes appear nontoxic since excess thiamin is easily excreted by the kidneys. ■

Paula Kurtzweil, R.D., of FDA's Office of Public Affairs, and Theresa A. Young, of FDA's Philadelphia district office, contributed to this series.



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

■ **"Light eggnog"** will be test-marketed for 15 months by several companies, beginning no later than March. This product contains less fat than that normally required in eggnog under FDA's standards of identity. It was developed to offer consumers products nutritionally equivalent to eggnog but with fewer calories and lower fat content (reduced from 6 percent to 1 percent). For further information, contact Shellee A. Davis, Center for Food Safety and Applied Nutrition (HFF-414), FDA, 200 C St., S.W., Washington, D.C. 20204; telephone (202) 485-0343. (FR Nov. 5, FR Nov. 8, FR Nov. 19, FR Nov. 28, FR Nov. 29, FR Dec. 5, FR Dec. 12)

■ **The Alzheimer's disease** reported death rate increased more than tenfold during the 1980s, according to the U.S. Centers for Disease Control. CDC found that 11,311 people died from Alzheimer's disease in 1987, compared with 857 deaths in 1979. The health agency says that heightened awareness is probably an important factor in the dramatic increase in the reported death rate. (*Morbidity and Mortality Weekly Report*, Nov. 1)

■ **Two public opinion surveys** showed different ratings for FDA. According to results of a recent Roper Organization survey, FDA was rated the second most-respected U.S. government agency, compared with 15 other federal agencies. Only the National Park Service was rated more favorably. The survey questioned 1,997 consumers about their attitudes towards government agencies. (*Roper Report* 90-8, 1990)

In another recent survey of nearly 90 agencies, conducted by the Council for Excellence in Government with *Fortune* magazine, FDA was rated "good." Fifteen received "best" ratings, while 27 more earned a "very good" or "good" rating. (*Fortune* magazine, Nov. 19, 1990)

■ **An experimental breast cancer treatment** conducted by the National Cancer Institute will be funded by Blue Cross and Blue Shield. This is thought to be the first sponsorship of an experimental study by a private insurer. Approximately 1,200 women with breast cancer will undergo bone marrow transplants—a procedure that shows promise in preventing relapse.

■ **Unsolicited drugs and drug samples** mailed to consumers must be in child-resistant packaging beginning in January 1991, according to the recently passed Drug and Household Substance Mailing Act of 1990 (H.R. 5209).

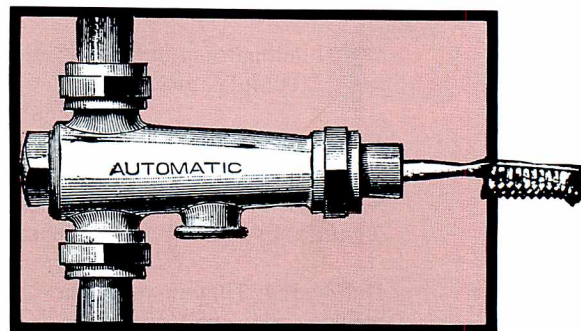
The act also includes safe-packaging requirements for fragrance samples.

■ **Absorbine Jr.'s manufacturer**, W.F. Young, Inc., has agreed to discontinue claims that its product cures athlete's foot within seconds. The claim was reviewed by the National Advertising Division of the Council of Better Business Bureaus, Inc., after a competitor questioned an ad which stated that the product not only relieves the symptoms of athlete's foot within seconds but also can "cure your athlete's foot . . . in seconds . . . It really can." (*NAD Case Report*, Dec. 17, 1990)

■ **Respiratory viral outbreaks** will be monitored by a new telephone program announced by CDC. Both parainfluenza virus and respiratory syncytial virus can cause outbreaks that can be especially serious in young children and the elderly. In the old monitoring system, health officials notified CDC of outbreaks monthly, using postcards. (*Morbidity and Mortality Weekly Report*, Nov. 23, 1990)

■ **Medical devices** are being classified by FDA into three classes depending on the type of pre-market testing needed. Devices such as powered toothbrushes and ultraviolet tanning machines need to meet general controls applicable to other devices, whereas devices such as ophthalmic cameras and retinoscopes need to show FDA even more specific safety and effectiveness data. (FR Nov. 20)

■ **Proper methods of reprocessing hemodialyzers** is the subject of an educational tape co-produced by FDA, individual manufacturers, the Renal Physicians Association, and others. The tape, the fourth in a series, is based



on standards developed by the Association for the Advancement of Medical Instrumentation. It will be sent to all hemodialysis centers and is available to individuals at a cost of \$40 from the National Audio Visual Center, 8700 Edgeworth Dr., Capitol Heights, Md. 20743-3701; telephone (301) 763-1896.



Cocaine-Spiked Drink Leads to Drug Smuggling Investigation

by Marian Segal



The death last summer of a 26-year-old man sparked an investigation by four federal agencies that stretched from Miami, Fla., to Colombia, South America. The case began with a 41-cent bottle of malta, a soft drink popular in Hispanic communities.

On the morning of Thursday, July 26, 1990, before leaving for his job at a pet store, Maximo Rene Menendez took a swig of Colombian-made Pony Malta de Bavaria. Then, according to reports, he put the bottle down and said, "This is poisoned. It is bad stuff." Almost immediately, the young man went into convulsions and was rushed to the hospital. His heart stopped en route in the ambulance, but paramedics revived him. He lapsed into a coma the next day, however, and was put on life support systems.

Menendez never regained consciousness. On Aug. 21, minutes after the machines were disconnected, he died, the victim of a Colombian narcotics smug-

gling operation gone awry. The malta he had drunk was laced with \$5,000 worth of cocaine.

"These people are intent on cashing in on this country's cocaine market," says FDA's Clifford Purdy, supervisory investigator at the agency's Miami resident post. "A user might be a sophisticated businessman, a hard-core street addict, or anyone in between," he says, "but the victims of this foul-up could have been anyone's children."

Menendez had arrived in Miami from Cuba only the previous January, having finally been reunited with his mother after 11 years' separation.

FDA investigators Roy Rinc and William Cochran went to Menendez's house the evening of the accident to collect the bottle he drank from (which had been emptied), plus eight unopened bottles. The bottles were flown to the agency's laboratory in Atlanta for immediate analysis. Cochran also visited Sedano's,

the grocery store where the drink was purchased, and had all remaining Pony Malta removed from the shelves pending the test results.

Early the next day, Atlanta reported finding cocaine residue in the opened bottle. Of the unopened bottles, one contained 37 grams of cocaine; another had 54 grams. As little as one gram of cocaine can be lethal when taken orally. The agency then began to establish liaisons with the Federal Bureau of Investigation, U.S. Customs Service, the Drug Enforcement Administration, and Florida's Dade County Health Department. FDA collected all the Pony Malta from Sedano's and its wholesaler and sent it to Atlanta for analysis. No cocaine was found.

On Sunday, FDA and the Dade County Department of Public Health issued an alert recalling the product and warning consumers not to drink the beverage. The health department set up procedures for

consumers to call and have the product picked up. The alert also urged lunch truck operators selling Pony Malta to return their stock to their suppliers. South Florida has an extensive lunch truck trade, with about 1,000 vehicles registered in Dade County alone and about another 900 unregistered trucks.

Malta's are widely distributed in South Florida. Some are bottled in the United States, but most are imported from Caribbean Basin countries. Pony brand malta is manufactured by the Bogota, Colombia-based firm Bavaria S.A., which has 14 bottling plants in Colombia and sells about 40 million bottles of the drink per month in that country.

Federal agents suspect that the smugglers obtained bottles of Pony Malta, perhaps from a distributor, and dissolved cocaine powder in the beverage, figuring to open the bottles in Miami and filter out the cocaine. "You wouldn't be able to tell it wasn't regular malta just by looking at it," FDA's Purdy says, "because the bottles are dark amber and the drink is dark too."

The counterfeiters glued fake labels on the bottles. The legitimate label has white borders and black print, whereas the counterfeits have no borders and are printed in red. Also, the phony labels carry the words, "Drink's Champions," a mistranslation of Pony Malta's slogan, "bebida de campeones," meaning "Drink of Champions," which appears in Spanish on the real label. The cocaine-laced malta was found in bottles labeled as being 6.16 ounces, a size that Bavaria S.A. sells only in Colombia. The firm exports the drink to the United States in 6.2-ounce and 10-ounce bottles.

FDA, Customs and the FBI traced the tainted Pony Malta to the importer of

record, Miami Sweet, and its owner, Hugo Rios, a Colombian national. Bavaria S.A. stated it sells to only three U.S. companies that import Pony Malta from Colombia to the United States, and Miami Sweet is not one of them.

FDA began an extensive effort to track distribution of the counterfeit product. One wholesaler had sold 100 cases of the beverage to 20 retail stores in South Florida from Miami to West Palm Beach. FDA collected samples from all the stores that still had bottles, and the rest were returned to the wholesaler.

Through the wholesaler, agents located Oscar Aristizabal, the distributor who bought the Pony Malta from Miami Sweet. Aristizabal told FDA that Rios had said the original shipment consisted of 1,000 cases but that 400 had been stolen from him.

FDA later was able to put the figure more accurately at about 308 stolen cases. The product was taken by thieves who had seen the shipment being unloaded into the Miami Sweet warehouse. Aristizabal bought the remaining 692 cases and, except for a few that he took home for his family, sold them to three wholesalers, including the one that supplied Sedano's.

In checking with lunch truck operators, Dade County Health Department inspectors found a wholesaler who had bought 146 cases of the stolen Pony Malta from a middleman whose name he claimed he could not recall. The wholesaler had in his possession 54 cases of 10-oz. bottles and 50 cases of bottles labeled as 6.16 ounces. The health department seized the latter—among which six bottles were found to contain cocaine—and put a stop-sale on the remaining cases.

All of the suspect shipment that could be located in South Florida was voluntarily turned over to FDA and warehoused in a secure building. Laboratory analysis showed that 45 of the bottles collected contained cocaine in levels ranging from approximately 20 to 54 grams.

A single distributor in New Jersey received a shipment of 480 cases. These were seized by federal agents before any had been sold.

As of this writing, approximately 152 cases of the product (between about 3,650 and 5,500 bottles) are still unaccounted for. Although these cases are mainly 10-oz. bottles—a size in which no cocaine has been detected—it is possible that some contaminated bottles may still be in the hands of consumers.

Each of the bottles with cocaine had about \$5,000 worth of the drug. "We've heard that bottles of Pony Malta have been sold on the street for \$5," Purdy says. "It's like a lottery—maybe you don't make anything, and maybe you make \$5,000."

In August, the FBI issued a nationwide alert for the 36-year-old Rios, who disappeared in July. A multi-agency investigation to find those responsible continues both in this country and in Colombia. There have been no additional reports of injury or death from the tainted beverage.

At press time, the legitimate distributors of Pony Malta were discussing with FDA plans for resuming sale of the product in the United States.

Marian Segal is a member of FDA's public affairs staff.

Who Is This Person?

When high-tech goes haywire, the results can be, well, incredible.

Take the case of the CT scanner at the University of California-Davis Medical Center.

The computerized axial tomography scanner is an electronic medical device that takes in-depth x-rays of the body, with the resulting image displayed in three dimensions on a TV screen. CT scans can picture parts of the body that are difficult or impossible to visualize

with conventional x-ray technology, making it easier to diagnose such abnormalities as strokes, blood clots, bleeding, and tumors.

Last summer, the University of California's CT scanner seriously malfunctioned, according to a report the university filed with the U.S. Pharmacopeia Medical Devices Reporting System.

Medical technicians at the Davis Medical Center who were performing a CT scan on a patient were dismayed to discover that the image generated on the screen was not that of the patient they

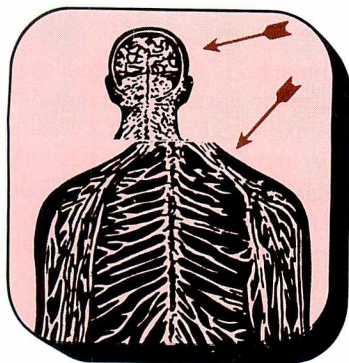
were scanning, but of an altogether different patient.

Fortunately for the patient, they caught the problem immediately.

Davis Medical Center complained to the scanner's manufacturer, Toshiba Corporation of Japan. The company and the importer, Toshiba American Medical System, Inc., of Irvine, Calif., investigated the incident and discovered that the problem was due to faulty software in two models of their machine.

During certain procedures, they found, those particular scanners would not only

project the image of the wrong patient on the computer screen but could also project a picture that combined body parts from two patients—for example, the head of one patient on the body of another.



Toshiba America notified FDA of the problem and told the agency it planned to correct it immediately. On July 24, the company sent 40 recall letters to medical institutions around the country that had purchased the faulty scanners. The letter warned about the problem and advised ways users could avoid it until Toshiba could replace the software.

The Los Angeles district office has been receiving an increasing number of reports of software problems in medical devices, according to Fred Plett, recall coordinator, but this is the first such problem with a CT scanner. "It just happened to be a computer program that didn't work right," he said.

Sale of Resuscitators Stopped, Then Resumed

After five inspections and an administrative detention of all finished goods and components, a manufacturer of manual resuscitators was able to meet government regulations and resume business.

Life Design Systems, Inc., Carrollton, Texas, makes the Pulmanex Manual resuscitator, a device that can be used in place of mouth-to-mouth resuscitation during cardiopulmonary arrest. The resuscitator consists of a mask, which is placed over the patient's nose and mouth, attached to a molded plastic bag. Squeezing the bag forces air into the patient's lungs, or the resuscitator can be attached to an oxygen supply.

FDA inspected Life Design's manufacturing plant in December 1988, after a former employee told the agency that the firm was producing defective devices.

Examining the firm's records, FDA Dallas district investigators Cheryl Boyce and James A. Templer uncovered several reports of devices that failed in use because of air flow control valves breaking off, glue blocking the air passageway, torn and disintegrated resuscitator bags, holes in the tubing, inability to connect mask to resuscitator, and lack of inflation. Life Design had not reported any of these problems to FDA, as required under medical device reporting regulations.

In addition, Boyce and Templer found more than 30 violations of good manufacturing practices and discovered the firm followed no quality assurance procedures and provided no special training for new employees.

In June 1989, FDA sent a regulatory letter to Life Design citing all violations. But a follow-up inspection in November 1989 found the original violations, plus six more.

By then, Life Design had already recalled defective resuscitators five times in 1989 due to faulty equipment. However, in most cases the recalls were incomplete because the company's records were inadequate. Records did not indicate which customers had received equipment from which lot, and in some instances, Life Design had not kept the customers' addresses on file. Furthermore, complete records were not kept of the returned products.

Following the November inspection, Life Design began submitting reports to FDA outlining efforts to correct violations. "It looked as if they were responding," says Larry Spears, a compliance officer in FDA's Center for Devices and Radiological Health. But, after several reports, it became clear that no significant changes were being made.

"Most of the corrections were minor," says Spears. "It seemed that the people at Life Design didn't have a good understanding of what they needed to do to correct reported violations and that was borne out by the submissions."

In January 1990, Life Design initiated another recall, this time because airflow control valves were becoming dislodged, creating a situation that could prevent air from reaching a patient.

On Feb. 17, 1990, Boyce went to Life Design and verified that the violations found in November were still uncorrected. Because the agency believed that the devices were not manufactured according to good manufacturing practices

and constituted a serious risk to health, FDA detained the sale of all resuscitators and components. Under the terms of the detention, Life Design could not ship any finished resuscitators until they were reconditioned and the manufacturing violations corrected.

Life Design appealed the detention on Feb. 19 and requested an informal hearing with FDA officials. The hearing was held in FDA's Dallas district office on Feb. 26; however, Donald C. Healtion, director of FDA's Southwest Region, denied the appeal.

On March 2, Life Design signed a voluntary consent agreement with FDA, requiring the firm to obtain assurance from a medical device good manufacturing practice consultant that all good manufacturing practices are met and to establish procedures to inform FDA of any future device problems or malfunctions.

As part of the consent agreement, FDA conducted another inspection from March 5 through March 10 after Life Design claimed that all violations had been corrected. The investigators found that Life Design still hadn't corrected most good manufacturing practice violations.

On March 26, Life Design sued FDA in the U.S. District Court for the Northern District of Texas, alleging that the agency had breached the consent agreement by refusing to recognize that the firm was in compliance with good manufacturing practices. The suit also requested that the court issue a temporary restraining order against FDA. Judge Sidney Fitzwater denied the request the next day.

The detention expired on March 17, but Life Design still couldn't resume operations until it met all the terms of the voluntary agreement. Two months later, Life Design requested that FDA reininspect, and that inspection, on May 30, revealed that while many problems had been corrected, the firm still did not have quality control measures for several critical steps in production.

FDA sent Life Design a letter on June 3, detailing the specific steps the company still needed to take. The firm corrected the problems, and over the next two weeks sent FDA several reports. Based on the data in the reports and an inspection on July 5 to evaluate the firm's reconditioning of the detained devices, FDA notified Life Design on July 16 that it could resume distribution of new devices.

In response to Life Design's suit claiming FDA had breached the terms of the consent agreement, Judge Fitzwater granted summary judgment to FDA on Nov. 7, after concluding that Life Design had failed to comply with the conditions of the agreement by the end of March 1990.

FDA is not aware of any deaths resulting from the use of faulty resuscitators distributed by Life Design. The agency plans to follow up with more inspections

Bacteria in Baby's Food

What started out as an attempt by FDA to resolve nutrient discrepancies in infant formula led to an even more significant finding: potentially serious microbial contamination.

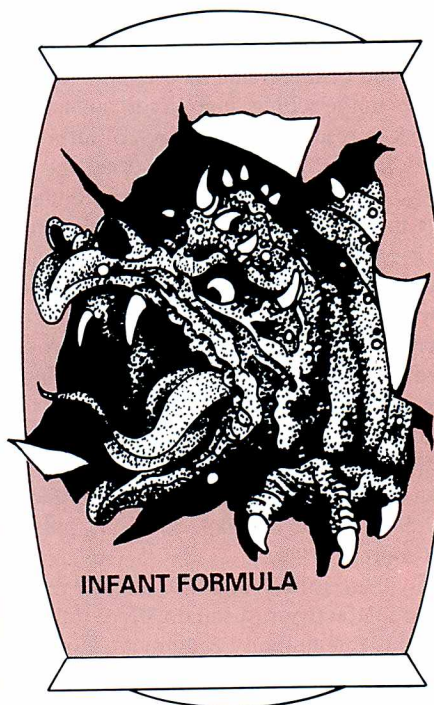
As a result, the manufacturer, Nutricia-Loma Linda Foods Inc., voluntarily recalled more than 245,232 liters (63,760 gallons) of I-Soyalac Concentrate Infant Formula, worth an estimated \$500,000, and shut down the firm's California processing plant for an indefinite time.

FDA categorized the recalls as Class I and Class II. Class I means a product is potentially life-threatening. Class II indicates a product is a health hazard but not life-threatening. While no illnesses were definitively traced to the contaminated formula, about 21 complaints of fever, vomiting and diarrhea in infants who had been on the formula were received by the company shortly after the recall was announced.

FDA was first alerted to potential problems at Nutricia-Loma Linda Foods in June 1990, following a routine inspection of the company's facility in Mount Vernon, Ohio, by FDA's Cincinnati district office. Although no longer a manufacturing plant, the facility still contained finished products.

Laboratory analyses of samples collected revealed fluctuations in calcium and phosphorus levels—even among samples from the same lot.

To verify the facility's quality control records (all of which were kept at the company's processing plant in Riverside,



Calif.), the Cincinnati office referred the case to FDA's Los Angeles district office. That office, in turn, carried out a series of inspections in June and July at the Riverside facility.

While reviewing records to determine the cause of nutrient fluctuations, an investigator noticed that some cans of formula being held by the firm were "swollen," an obvious sign of bacterial contamination. Some of the swollen cans were almost ready to burst.

Laboratory analysis of the samples showed numerous and varied microorganisms; for example, gram-positive spore-forming rods, motile spores and rods, cocci, and anaerobic gram-positive rods. FDA later concluded that one lot of the product could have been life-threatening to infants.

The source of contamination was never identified. However, an engineer with FDA's Center for Food Safety and Applied Nutrition, who evaluated the firm's aseptic operation, speculated that a crack in the pressure chamber of the sterilizing unit may have allowed exterior air—and thus bacteria—to enter the product. Faulty can seams also were suggested as a possible cause.

FDA learned from company records that the firm had earlier found microbial

contamination in formula produced on four different days and that outside laboratory analyses identified *Clostridium*, *Bacillus* and *Streptococcus* bacteria. But, although the company destroyed all contaminated lots, FDA found the firm had not adequately investigated to determine the source of contamination.

FDA also faulted the company for failing to:

- notify the agency that it had begun to manufacture infant formula at its Riverside facility
- register with FDA the new processing procedures used for its infant formula (a low-acid canned food)
- provide the agency with written verification for nutrient content and other required information
- revalidate its aseptic processing system's ability to maintain sterility after portions of the system had been reconfigured.

On July 12, 1990, the company voluntarily recalled 29 lots of its I-Soyalac formula after finding that its entire June 28 production had begun to swell. It sent telegrams to its 70 distributors and issued a press release.

The recalled products, as well as those being held at the California plant, were destroyed.

At the same time, the company chose to close down its California plant and, in early September, began production at its Ohio facility, which had been renovated and upgraded with new equipment and personnel to comply with federal law. The Cincinnati district office is monitoring the facility as part of FDA's infant formula inspection program.

The California plant, now under new management, remains shut down. Following FDA's inspections, company owners had indicated to FDA that the processing equipment would be removed and that if production were restarted, a more reliable sterilization system would be used.

—This small sample of reports from the field was prepared by Paula Kurtzweil, Sharon Snider, and Dori Stehlin.



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.

Published by direction of the Secretary of Health and Human Services.

SEIZURE ACTIONS

Food/Contamination, Spoilage, Insanitary Handling

PRODUCT: **Bamboo leaves**, at San Francisco, N. Dist. Calif.; Civil No. 89-4317-MHP.

CHARGED 12-12-89: While held for sale, the article contained insect filth—402(a)(3).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65774; S. No. 89-592-608; S.J. No. 1)

PRODUCT: **Conch meat fillets, frozen**, at San Juan, Dist. Puerto Rico; Civil No. 87-1351.

CHARGED 10-6-87: While held for sale, the article contained decomposed conch meat—402(a)(3).

DISPOSITION: The article was claimed by Tampa Maid Sea Products, Inc., Tampa, Fla., who denied the charge and asserted that representative samples of the article had been tested and, applying FDA policy guidelines, the article was not decomposed. Subsequently, the claimant petitioned to have the article delivered to it for the sole purpose of exporting it to the original supplier in Haiti. The article, condemned pursuant to 21 U.S.C. 334, was authorized to be released for such export, pursuant to stipulation of the parties and after the posting of a bond in a sum approved by the court. After some delay and an extension of time, the claimant posted the required bond. (F.D.C. No. 65268; S. No. 87-512-401; S.J. No. 2)

PRODUCT: **Crackers and other food stocks**, at Cape Girardeau, E. Dist. Mo.; Civil No. S89-0182-C.

CHARGED 12-7-89: While held by Cauble & Field, Inc., Cape Girardeau, Mo., the articles had been held under insanitary conditions—402(a)(4).

DISPOSITION: A consent decree of condemnation released 50 bags of Missouri popcorn and 10 cases of coffee whitener packaged in glass jars as being outside the jurisdiction of the court and authorized release under bond of the other seized articles to the dealer for salvaging. (F.D.C. No. 65786; S. No. 90-526-663 et al.; S.J. No. 3)

PRODUCT: **Dog food, dried**, at Woodland, E. Dist. Calif.; Civil No. 90-0128-EJG-EM.

CHARGED 1-30-90: While held for sale, the article had been held under insanitary conditions—402(a)(4).

DISPOSITION: Consent—ordered destroyed. (F.D.C. No. 65811; S. No. 90-541-077; S.J. No. 4)

PRODUCT: **Flour**, at San Francisco, N. Dist. Calif.; Civil No. 88-4020 CAD.

CHARGED 10-6-88: While held by Tiao Peng Trading Co., San Francisco, Calif., the article had been held under insanitary conditions—402(a)(4); and the article's label lacked the common or usual name of the food, lacked the place of business of the manufacturer, packer or distributor, and lacked an accurate quantity of contents statement—403(e)(1), 403(e)(2), 403(i)(1).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65536; S. No. 88-378-096; S.J. No. 5)

PRODUCT: **Mung bean threads**, at San Francisco, N. Dist. Calif.; Civil No. 88-4021 DLJ.

CHARGED 10-6-88: While held for sale, the article contained insects and insect fragments—402(a)(3).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65530; S. No. 88-540-664; S.J. No. 6)

PRODUCT: **Noodles with soup mix, and other food warehouse stocks**, at Chicago, N. Dist. Ill.; Civil No. 90 C 0642.

CHARGED 2-5-90: While held by New Way Trading, Inc., Chicago, Ill., the articles had been held under insanitary conditions—402(a)(4).

DISPOSITION: Consent—authorized release to dealer for salvaging. (F.D.C. No. 65820; S. No. 90-576-684 et al.; S.J. No. 6)

Food/Economic and Labeling Violations

PRODUCT: **Coffee, espresso ground**, at Rochester, W. Dist. N.Y.; Civil No. 89-1100-T.

CHARGED 8-22-89: When imported from Italy, the article, labeled (package front panel) "Qualita Rossa e205g Miscela DiCaffe Lavaza" and (package side panel) "Italian Espresso Ground Coffee 250 g 8.8 oz . . . Packed by Lavazza S.p.A. Torino Italy," had required label information that was not placed on the label with required conspicuousness (e.g., the quantity of contents declaration on the principal display panel was not expressed in terms of avoirdupois pounds or ounces, the quantity of contents declaration lacked the term "net weight," and the statement of identity "Espresso Ground Coffee" did not appear on the label's principal display panel)—403(f); and the article was in violation of the Fair Packaging & Labeling Act since the quantity of contents declaration was not placed within the bottom 30 percent of the principal display panel—15 U.S.C. 1453(a)(2).

DISPOSITION: Consent—authorized release to Carlo's Imports, Inc., Rochester, N.Y., for relabeling. (F.D.C. No. 65734; S. No. 89-543-802; S.J. No. 7)

Drugs/Human Use

PRODUCT: Appetite control kit (bottle of homeopathic formula drops with adhesive patches), at San Diego, S. Dist. Calif.; Civil No. 88-1106 JLI.

CHARGED 8-26-88: While held by Bokkie International, successor to Meditrend International, San Diego, Calif., the article's labeling ("Appetoff Appetite Control Program Distributed By: Meditrend International . . . San Diego, CA") contained false and misleading representations that the article was effective for appetite control—502(a); adequate directions for lay use of the article could not be written—502(f)(1); and the article was a new drug without an effective approved New Drug Application—505(a). **DISPOSITION:** The government was advised by counsel to Meditrend International and its successor corporation, Bokkie International, in a similar earlier action and this subsequent action that his clients wished to retrieve the binders that contained some of the accompanying literature; and a tentative agreement was reached. The two actions were consolidated. Subsequently, FDA was informed that Bokkie International was closing down its operations, had discharged employees, and was preparing to leave the area. Ultimately, a default decree ordered the article destroyed. (F.D.C. No. 65510; S. No. 88-259-754 et al.; S.J. No. 9)

PRODUCT: Procaine H-3 cream and tablets, and Arthritis Formula cream with copper & gold, at Deerfield Beach, S. Dist. Fla.; Civil No. 85-6255.

CHARGED on or about 3-28-85: When the tablets labeled "H-3 Formula tablets . . . Distributed by: The Kelly-Lane Co., Inc. . . . Lighthouse Point, FL" were shipped by Universal Supplements, Linden, N.J., and while the creams were held for sale after manufacture by various local manufacturers using interstate procaine HCl, or interstate methyl salicylate, the articles were new drugs without effective approved New Drug Applications—505(a); and the labeling of the articles lacked adequate directions for use and such directions could not be written—502(f)(1).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 64581; S. No. 85-374-724 et al.; S.J. No. 10)

Drugs/Veterinary

PRODUCT: Carbadox powder, and dimetridazole (DMSE) powder, at Pella, S. Dist. Iowa; Civil No. 88-196-A.

CHARGED 4-11-88: While held by JB Ranch & Veterinary Clinic, Pella, Iowa, the articles lacked any directions for their intended uses (for hogs)—502(f)(1).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65274, S. No. 87-262-534 et al.; S.J. No. 11)

Medical Devices

PRODUCT: Gloves, latex, for medical examination, at Salinas, Dist. Puerto Rico; Civil No. 89-1595(JP).

CHARGED 12-7-89: The quality of two lots of the article fell below their purported quality because the gloves contained exces-

sive holes; and the labels of all three lots of the article lacked the name and place of business of the manufacturer, packer or distributor—501(c), 502(b)(1).

DISPOSITION: A default decree of condemnation ordered the article destroyed. Subsequently, Enrique S. Melendez-Lugo, Hato Rey, Puerto Rico, filed a motion requesting the default be set aside and the case be consolidated with a similar case (89-1482(JP)). However, no evidence of any valid claim to the article was found, the asserted filing date of such claim was after the 10 days allowed for filing of a claim, and no good cause as to why the default should be set aside was ever demonstrated. The article was destroyed. (F.D.C. No. 65790; S. No. 90-511-024 et al.; S.J. No. 12)

PRODUCT: Gloves, latex, for surgical use, at Walnut, C. Dist. Calif.; Civil No. 90-0963JGD(Kx).

CHARGED 2-26-90: The quality of the article, which was labeled "TTC Products Pure Natural Latex Surgical Gloves Sterile . . . Made In Taiwan," fell below the article's purported quality since the article contained holes; and the article failed to bear a label containing the name and place of business of the manufacturer, packer or distributor—501(c), 502(b)(1).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65829; S. No. 90-425-536; S.J. No. 13)

CRIMINAL ACTIONS

DEFENDANTS: Mar-Ja, Inc., and James R. Pond Sr., president, Suffolk, E. Dist. Va.; Criminal No. 89-139-N.

CHARGED 10-19-89 by grand jury: While held for sale, peanuts (count 1) labeled "FANCY . . . Peanuts . . . CROP YR 85" were held under insanitary conditions and exposed to contamination by urine—402(a)(4); peanuts (count 2) labeled "Runner Small Whole Kernel . . . Georgia . . . Crop Year 84" were held under insanitary conditions in a building with live insects and contaminated with insect filth—402(a)(3), 402(a)(4); peanuts (count 3) labeled "Runner Small Whole Kernel . . . Georgia . . . Crop Year 84" were held under insanitary conditions in a building with live insects and contaminated with insect filth—402(a)(3), 402(a)(4); peanuts (count 4) labeled "Runner Small Whole Kernels . . . Florida . . . Crop Year 84" were held in a building with live insects under insanitary conditions and exposed to insect contamination—402(a)(4); peanuts (count 5) labeled "Fancy In-Shell Peanuts . . . North Carolina . . . 85" were held under insanitary conditions in a building with rodents and exposed to contamination by rodents and rodent urine—402(a)(4); and peanuts (count 6) labeled "Runner/Small Whole Kernel . . . Florida . . . Crop Year 84" were held under insanitary conditions in a building with live insects and rodents and contaminated with insect filth—402(a)(3), 402(a)(4). **DISPOSITION:** Guilty plea by the individual to counts 2 and 6; 90-day imprisonment suspended, \$4,100 fine, and probation for two years with special conditions, including 100 hours of community service. Guilty plea by corporation to all counts; \$23,000 fine, of which \$10,000 suspended, provided corporation complied with special terms of probation for two years. (F.D.C. No. 65019; S. No. 86-361-066 et al.; S.J. No. 14)

DEFENDANT: **Stephen W. Smith (alias Dr. Alan Anderson)**, Lakewood, Dist. Colo.; Criminal No. 88-CR-281.

CHARGED on or about 9-7-88 by grand jury: Conspiracy to defraud FDA by interfering with and obstructing FDA's function to ensure that prescription drugs are safe and effective and are properly manufactured, stored and dispensed—18 U.S.C. 371; and, with intent to defraud and mislead, causing 40 bottles of oxandrolone to become counterfeit drugs by manufacturing (without authorization from Searle & Co.) such drugs in bottles labeled "Anavar"—301(i)(3).

DISPOSITION: The defendant made a number of motions, including motions to suppress evidence, to dismiss various counts of the indictment, to strike as surplusage the purported overt acts listed in the conspiracy count, and for a preliminary finding by the court as to the existence of a conspiracy. In addition, the defendant moved for a declaration of complexity. The government agreed that there was sufficient complexity for an order setting the proceedings and trial beyond the time prescribed by the Speedy Trial Act. The court made a finding of complexity, and ordered that the time limits of the Speedy Trial Act would not be followed.

After a hearing on the motions, the defendant pleaded guilty. On the conspiracy count, the defendant was sentenced to home detention for six months, placed on probation for five years, fined \$5,000, and required to donate 1,000 hours of community service. Sentencing on the other count was suspended. (F.D.C. No. 64307SS; S.J. No. 15)

CIVIL PENALTY ACTIONS

DEFENDANTS: **Control Laser Corp., Robert D. van Roijen Jr.**, chairman of the board of directors and sometime president, and **M. Lee McDaniel**, a prior president of corporation, Orlando, M. Dist. Fla.; Civil No. 85-349-Civ-ORL-18.

CHARGED 3-20-85 in a complaint for injunction and civil penalties: That the corporation directly, or through its subsidiary, Holobeam Laser, Inc., was a manufacturer and a dealer of laser products; that on more than a dozen occasions the defendants manufactured and shipped to North Carolina, Ohio, California, Pennsylvania, New York, or Arizona laser products that lacked required safety interlocks—42 U.S.C. 263j(a)(1); that the corporation and one or more of its officers manufactured and shipped, to Missouri, Pennsylvania and Texas, three laser products that lacked a protective housing which met the requirements for preventing human access to laser radiation—42 U.S.C. 263j(a)(1); that the corporation and its chairman manufactured and shipped three laser products to Connecticut that, contrary to a performance standard, allowed replacement of the protective housing during safety interlock defeat—42 U.S.C. 263j(a)(1); that the defendants had issued three false or misleading certifications of compliance for laser products lacking required warning labels and more than a dozen false or misleading certificates of compliance for laser products lacking required safety interlocks—42 U.S.C. 263j(a)(5)(B); and that the corporation and its chairman had issued four false or misleading certifications of compliance for laser products lacking required Class IV key-actuated master

controls that preclude operation of the laser when the key is removed and three false or misleading certifications of compliance for laser products that allowed replacement of the protective housing during safety interlock defeat—42 U.S.C. 263j(a)(5)(B).

In addition to the above charges, the complaint also CHARGED that the defendants had, in various specified ways, failed to comply with their corrective action plans for certain guillotine-type safety shutters that might fail to prevent human access and certain microswitch interlocks that failed to have safety interlocks and for certain laser products that had rotary workstations but failed to prevent human access to Class IV levels of radiation during operation, and required status reports to FDA concerning such safety shutters had not been made—42 U.S.C. 363j(a)(4); and the required compliance, replacement or cost refunds for noncomplying laser products having rotary workstations had not been completed—42 U.S.C. 263j(a)(2).

The complaint further alleged that the corporation and its chairman were well aware of their responsibility to comply with the law, that despite warnings they had repeatedly and unreasonably delayed in taking proper action, and that the government believed that, unless enjoined, they would continue to violate the law.

DISPOSITION: A consent decree of permanent injunction was entered into by the parties enjoining specified violations of the law and making the corporation liable for a \$1,000 per day assessed fine for each day the corporation failed to complete any corrective action plan. In addition, the defendants were jointly and severally liable for \$70,000 in civil penalties. (Inj. No. 1082; S.J. No. 16)

INJUNCTION ACTIONS

DEFENDANTS: **George Weissmann Inc. (formerly Padma Marketing Corp.), Padma Distribution Corp., and George Weissmann**, physicist and president of the corporation; **the Association for the Promotion of Herbal Healing**; and **Central Health Network** (a partnership), and **Jeffrey S. Kravitz, Stephen L. Kravitz, and Kenneth J. Kravitz**, partners of the partnership; Berkeley, N. Dist. Calif.; Civil No. 87-4706-WWS.

CHARGED on or about 6-15-87 in a complaint for injunction: That, for several years, George Weissmann and his corporations had imported from Switzerland a product known as Padma 28 Tibetan Herbal Food Supplement Tablets (Padma 28); that the partnership purchased Padma 28 from George Weissmann, Inc., and distributed such product in interstate commerce to other wholesale distributors, retail health food stores, and individuals; that George Weissmann promoted and marketed Padma 28 through the Association for the Promotion of Herbal Healing and supplied the partnership (Central Health Network) with advertisements, pamphlets, literature, bottle labels, store displays, and other promotional materials for Padma 28.

The defendants made oral and written claims for Padma 28, promoting its use for the following: cardiovascular circulation, reduction of platelet aggregation, cholesterol and blood lipids, immunological response normalization, healing, atherosclerosis, asthma, skin allergies, infections, hepatitis, heart disease, hyper-

lipidemia, pyelitis, liver damage, hemorrhoids, upper belly syndrome, depression, impaired intellectual function, lethargy, myocarditis, pharyngitis, sinusitis, otitis media, bronchitis, pneumonia, and chest pains; that, because of the defendants' promotional activities, Padma 28 was a new drug, and it lacked an effective approved New Drug Application—505(a). Padma 28 also lacked adequate directions for its intended uses—502(f)(1). The defendants were aware that their activities violated the law; and the government believed that, unless restrained by the court, the defendants would continue such violations.

DISPOSITION: The parties entered into a consent decree of permanent injunction. The defendants were enjoined from importing, processing, packing, labeling, or distributing Padma 28 Tibetan Herbal Food Supplement, and from promoting, labeling, advertising, or representing that Padma 28 was safe and effective for disease purposes, unless and until an approved New Drug Application was in effect. In addition, the defendants were to register all drugs prepared, propagated, compounded, or processed at their establishments. (Inj. No. 1167; S.J. No. 17)

DEFENDANTS: **Yang Laboratories, Inc., Fumei H. Yang**, president-treasurer, and **Norman S.T. Yang**, vice president-secretary, Bellevue, W. Dist. Washington; Civil No. C88-67C.

CHARGED 1-13-88 in a complaint for injunction: That the defendants manufactured, packed, labeled, stored, and distributed in interstate commerce various medical devices, including the Pros-Check PSA (Prostate-Specific Antigen) RIA Testing Kit, a Class III diagnostic device that was not covered by an approved pre-market approval application ("PMA") but was being distributed to medical centers and used in routine clinical diagnostic test procedures; that, although the package inserts for some Pros-Check PSA testing kits were labeled "For Investigational Use," no application for investigational device exemption (IDE) was pending or approved; that the defendants violated the law by such interstate distribution of the kits and by distribution to foreign countries without an approved PMA and without HHS authorization; and that the defendants were well aware that such activities were in violation of the law—501(f), 801(d).

DISPOSITION: The defendants denied the charges and asserted a number of affirmative defenses, including claims that the kit was an "investigational device" that was noninvasive, did not require an invasive sampling procedure, did not introduce energy into a subject, and was not used without confirmation by another product or procedures; that the government was barred by estoppel, waiver, ratification, and acquiescence; and that the defendants had complied with various specified provisions of the law. Subsequently, FDA received, reviewed and approved the firm's investigational plan, protocol and product brochure for the kit. Thereafter, the defendants entered into a consent decree of permanent injunction enjoining the complained-of violations. (Inj. No. 1185; S. No. 87-464-090 et al.; S.J. No. 18)

MISCELLANEOUS ACTIONS

SUBJECT: Liquidated damages, plus interest, for breached redelivery bonds for imported foods; U.S. Court of Interna-

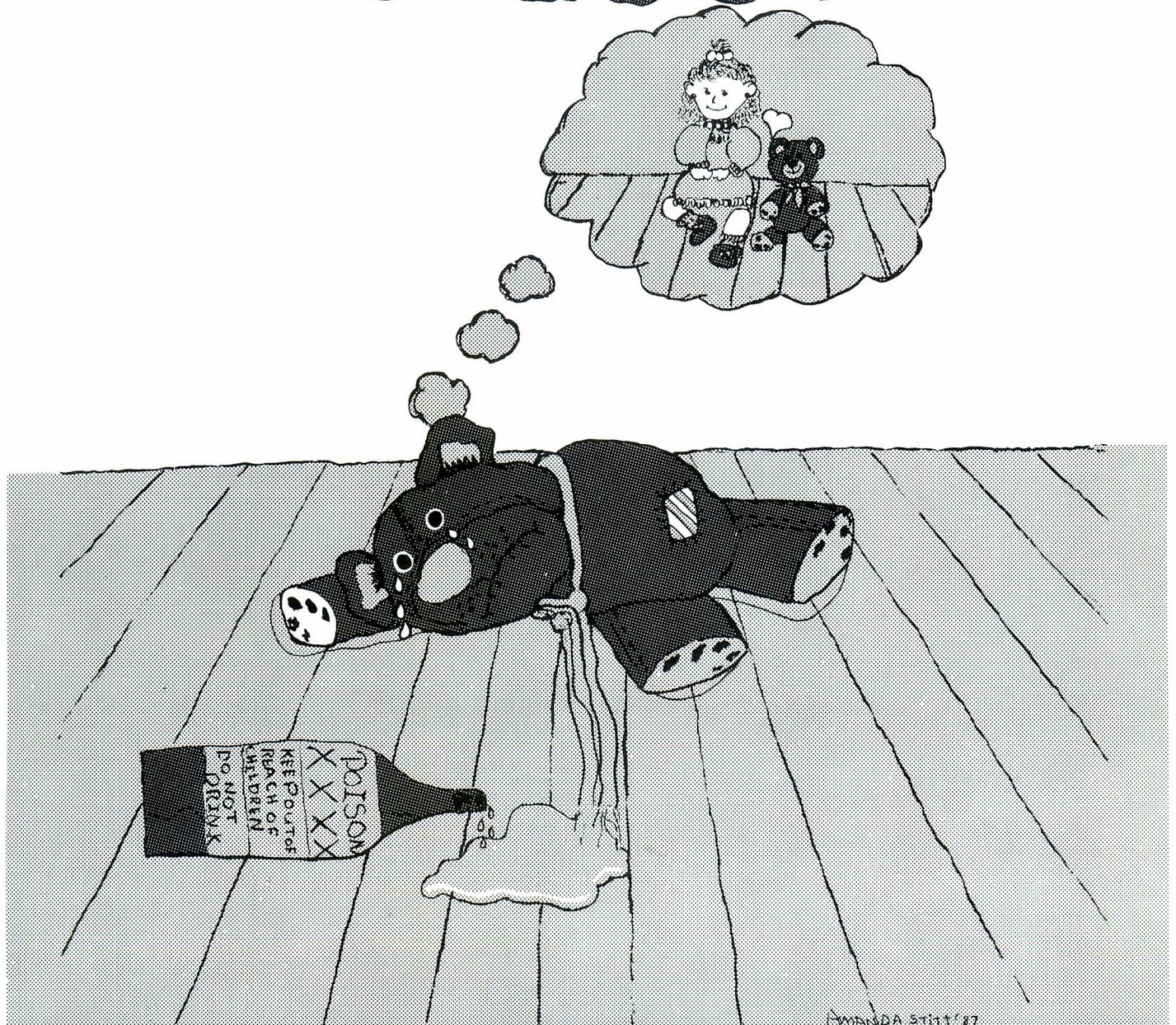
tional Trade; Court No. 86-04-00492, and (upon appeal) 87-1330. **CHARGED** 4-16-86 by the United States of America against Imperial Food Imports ("Imperial"), an importer located at Los Angeles, Calif., and American Motorist Insurance Co. ("AMICO"), a surety bonding firm doing business at New York City, N.Y., in a suit for damages: That Imperial, as principal, and AMICO, as surety, executed and delivered nine "Immediate Delivery and Consumption Entry Bonds" for nine entries of merchandise through the Port of Seattle, Wash.; that the release of the merchandise to Imperial was conditioned upon such merchandise being held intact pending FDA notice; that FDA found that the merchandise was violative and the merchandise was refused admission; and that Imperial was required to redeliver the merchandise for export or destruction. However, the merchandise had not been redelivered, the government had demanded payment under the terms of bonds of liquidated damages of \$220,749, and judgment was requested in this suit.

DISPOSITION: *Court of International Trade*—Service of process was not effected against the importer so the action proceeded only against AMICO, the surety bonding firm. AMICO did not contest the facts, but argued as follows: that the facts did not show that the government was entitled to judgment, contending that, of the nine notices of detention, eight notices of detention had not been produced; that the notices (the one original and copies of the other eight supplied by the government) did not show that there was a proper finding of adulteration as to some shipments, since some notices revealed that the detention was not based on sampling and analysis; and that AMICO was not liable on the bonds, because its status was not that of a surety, but rather "that of a guarantor of an importer's performance."

Upon the government and AMICO's motions for summary judgment, the court granted summary judgment to the government, awarding the liquidated damages to the government, plus interest from the date of the government's final demand. AMICO appealed.

Court of Appeals for Federal Circuit—The award to the government was affirmed upon appeal. AMICO had contended that summary judgment was improper because there was an issue of material fact as to the government's duty to disclose that Notices of Detention had been issued by FDA before accepting the bonds. The appellate court found that it was too late for AMICO to argue that a dispute existed. As to AMICO's argument that the trial court erred by awarding prejudgment interest, the appellate court found as follows: that the liquidated damages assessed in this case were reasonable and were not punitive; that it would be inequitable and unfair for the government to make an interest-free loan of the demanded liquidated damages from the date of final demand; and that the award of prejudgment interest was not an abuse of discretion. Accordingly, the trial court's award of the liquidated damages plus interest was affirmed. (Misc. No. 835; Entry No. 84-303114-2 et al.; S.J. No. 19)

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