

FDA CONSUMER

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

• VOL. 26 NO. 10

DECEMBER 1992 •

THE
ELF
IN YOUR
ELECTRIC
BLANKET
(AND OTHER
APPLIANCES)





nicotine
14 MG/24 HR

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Steroid Substitutes: No-Win Situation for Athletes 8
Many athletes, fearful of the side effects of steroids but still looking to drugs to give them a competitive edge, are experimenting with steroid substitutes. Unfortunately, alternatives may be just as dangerous as the real thing.

Ovarian Cancer: Today's Treatment, Tomorrow's Hope 13
Surgery, radiation therapy, and chemotherapy all provide some help in treating ovarian cancer. FDA is helping develop taxol, a drug derived from Pacific yew trees, which many hope will improve survival rates.

Prescriptions to Help Smokers Quit 16
Nicotine chewing gum and transdermal patches are giving some people the extra help they need to stop smoking. But effectiveness usually depends on their being used as part of an overall smoking-cessation program.

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FDA scientists are among those studying extremely low frequency (ELF) electromagnetic fields from electric appliances to try to find out if they pose any health hazards.

Medication and Labor: Birthing Babies in the '90s 28
While some experts believe that women who are well-prepared for childbirth will be able to handle the pain entirely without drugs, other medical practitioners can't imagine why any woman would want to endure such pain at all. Is there a middle ground?

Many Treatments Available: Thyroid Disorders Often Unsuspected 34
Goiters from insufficient dietary iodine may be a thing of the past, but thyroid disorders still cause symptoms, many of which can be confused with normal aging. Once diagnosed, however, most are easily treatable with drugs.

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Inside Front Cover Photo:

Though nicotine patches can be helpful, it usually takes more than sticking one on your chest to stop smoking. To find out what else is necessary, see page 16.



Three Products for Hemophilia B

Three biological products were licensed by FDA in August 1992 to prevent or control excessive bleeding from hemophilia B.

Hemophilia B, also known as Christmas disease, affects about 3,000 Americans, almost exclusively males, and is transmitted genetically from parent to child.

Hemophilia B results from an insufficient or abnormal synthesis of the blood-clotting protein Factor IX, which is necessary to stop bleeding. The protein is contained in Factor IX Complex and in Coagulation Factor IX (Human), two products used to treat and prevent hemophilia B bleeding.

Bebulin VH, manufactured by Österreichisches Institut für Haemoderivate G.m.b.H., Vienna, Austria, was licensed by FDA last Aug. 19. Bebulin VH, a Factor IX Complex, contains significant amounts of other clotting proteins.

Mononine, manufactured by Armour Pharmaceutical Company, Collegeville, Pa., was licensed last Aug. 20. Mononine mostly contains Factor IX, with significantly smaller amounts of other clotting proteins.

AlphaNine, manufactured by Alpha Therapeutic Corporation, Los Angeles, was licensed last Aug. 26 with a new manufacturing process amending its original license, which had been issued Dec. 30, 1990. AlphaNine is a Coagulation Factor IX (Human) product.

Biological products, such as vaccines, serums and toxoids, are prepared from living organisms. These three biological products are manufactured by processes that minimize the risk of viral transmission. Both Mononine and AlphaNine were granted orphan product status.

More Women Have Access To Taxol

More women with advanced ovarian cancer have access to taxol under FDA's expansion of a previously authorized experimental program.

FDA expanded the program last September to allow oncologists (cancer specialists) to apply directly to the National Cancer Institute to receive supplies of taxol and a protocol for administering the drug. The treatment IND (investigational new drug) approved last July made taxol available for only those patients treated at designated cancer centers sponsored by NCI. (See "Treatment IND for Taxol" in the October 1992 *FDA Consumer*.)

The expanded access reflects increased supplies of taxol, indications in current clinical studies that the drug is effective in treating ovarian cancer, and better understanding of how to manage the drug's side effects.

To be eligible to receive the drug, women with ovarian cancer must have failed to be helped by at least two standard chemotherapy regimens, one of which must have included a platinum-containing drug.

Oncologists who are interested in obtaining taxol for patients with advanced ovarian cancer can call NCI's Treatment

Referral Center at (301) 496-5725.

(For more information on ovarian cancer, see "Ovarian Cancer: Early Diagnosis Elusive," in the November 1992 *FDA Consumer*, and "Ovarian Cancer: Today's Treatment, Tomorrow's Hope" on page 13 of this issue.)

Warning About Prenatal Test

Because of uncertainties about whether one type of prenatal test may increase the risk of fetal limb and facial abnormalities, FDA has required the manufacturer to add a warning about the risk to the test's patient labeling.

FDA is also requiring the test, called chorionic villus sampling (CVS), to carry revised physician instructions specifying that the test should only be done after the 10th week of pregnancy. Some research suggests this may reduce the risk.

CVS, like another prenatal test called amniocentesis, can detect genetic diseases such as Down syndrome, Tay-Sachs disease, and sickle cell anemia. The American College of Obstetricians and Gynecologists recommends prenatal testing for any woman who will be 35 or older when her baby is born. The college also recommends testing for any woman with a family history of genetic diseases.

With amniocentesis, a woman must wait until the 16th week of pregnancy before being tested, and the results can take 10 days or longer. In contrast, CVS can be

performed earlier in the pregnancy, and the results are ready in a few days.

The risk of miscarriage is slightly higher for CVS, greater than 1.5 percent, compared to less than 1 percent for amniocentesis. According to FDA, it is not clear whether there is an increased risk of birth defects attributable to CVS and how large that risk is, if it exists.

A study conducted at Oxford University and published in the March 30, 1991, issue of *The Lancet* reported that, of 289 pregnancies with CVS testing, five babies had severe limb abnormalities and four of the five had facial deformities as well. Another study, conducted at the Humana Hospital-Michael Reese Medical Center in Chicago and published in the May 1992 issue of *Obstetrics and Gynecology*, reported four cases of limb deformities among 394 CVS-tested pregnancies. In the general population, these types of birth defects are rare, with estimates ranging from 1 in 2,000 births to as few as 1 in 175,000 births.

However, a letter in the June 8, 1991, issue of *The Lancet* reported that Yale University studies, which specifically addressed the safety of first-trimester CVS, did not show a significant increase among 9,588 pregnancies in these kinds of birth defects.

FDA has approved only one CVS testing device, the Trophocan CVS Catheter, manufactured by Concord/Portex, Inc., Keene, N.H., but several others are under clinical investigation. In addition to the patient warning on the approved test, the agency is requiring that the same warning about possible birth defects be included in the informed consent for the investiga-

tional devices. The protocol for these investigations must also specify that the test can't be conducted until after the 10th week of pregnancy.

FDA is also requiring that clinical investigators immediately report any limb or facial defects in newborns whose mothers underwent CVS. (For more information on prenatal tests, see "Genetic Screening—Fetal Signposts on a Journey of Discovery" in the December 1990 *FDA Consumer*.)

PHS Recommends Folic Acid For Women of Childbearing Age

All women of childbearing age should consume 0.4 milligrams daily of folic acid, a B vitamin, to reduce the risk of neural tube birth defects in their children, the U.S. Public Health Service recently announced.

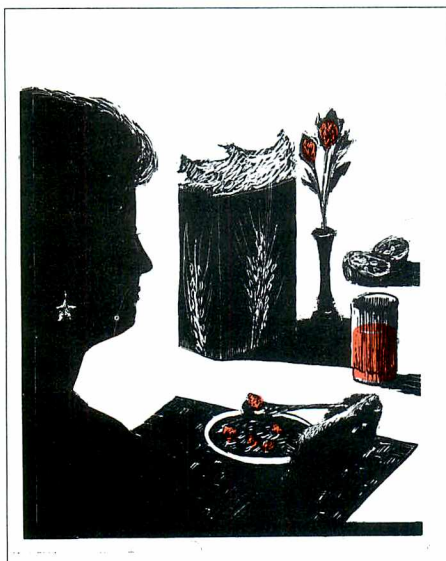
The recommendation is published in a

supplement of the Sept. 14, 1992, *Morbidity and Mortality Weekly Report* of the national Centers for Disease Control, a PHS agency.

According to the announcement, the 0.4 level should be consumed daily by women, whether pregnant or not, because the defects occur the first month after conception, generally before a woman is aware she is pregnant. Thus, all women from puberty through menopause who might become pregnant are urged to consume daily 0.4 milligrams (sometimes listed as 400 micrograms). They should not take more than 1 milligram a day, however, because overdosing can mask the symptoms of pernicious anemia, a vitamin B₁₂ deficiency. If this deficiency is not diagnosed and treated, neurological damage associated with it may progress.

Good sources of folic acid include leafy dark-green vegetables, citrus fruits and juices, yeast breads, and beans, as well as fortified breakfast cereals. Folic acid supplements and daily multi-vitamin preparations containing 0.4 milligrams of folic acid also are widely available.

The recommendation is based on an analysis of studies in the United Kingdom, Hungary, Cuba, and Western Australia, as well as three in the United States—one in Atlanta, one in California and Illinois, and one in New England. It is consistent with the current U.S. allowance on food and vitamin labels, but is about twice the Recommended Dietary Allowance set in 1989 by the National Academy of Sciences for the general population.



HHS Assistant Secretary for Health James Mason, M.D., said that FDA, CDC, the National Institutes of Health, and other agencies of the Public Health Service, which he heads, will work together to find the best way to implement this important public health recommendation.

About 2,500 infants with neural tube defects are born in the United States each year. Spina bifida and anencephaly account for 90 percent of neural tube defects. In anencephaly, most or all of the brain is absent, and such infants die before or shortly after birth. In spina bifida, the spinal cord is exposed. Most infants born with spina bifida grow to adulthood with varying degrees of disability despite surgical and other treatments.

Patients Warned About Shiley C-C Heart Valves

At FDA's request, Shiley Inc., Irvine, Calif., sent letters last September to all U.S. patients implanted with its 60-degree convexo-concave (C-C) heart valves, saying that the fracture rates for some sizes of these devices are higher than previously thought.

Shiley, the former manufacturer of this type of heart valve, had previously notified cardiologists, cardiac surgeons, and certain other physicians about the higher fracture rates. (See the Updates section of the June 1992 *FDA Consumer*.)

The Shiley heart valve has been implanted into about 82,000 patients worldwide since it was first marketed in 1979. Shiley withdrew its C-C valves and stopped making the device in 1986, fol-

lowing reports of valve failure due to strut fracture.

In 1990, FDA asked Shiley to notify all patients and their doctors of the potential for valve fracture. (See the Updates section of the March 1991 *FDA Consumer*.) However, in February 1992, the British medical journal *The Lancet* published the results of a study conducted in the Netherlands that showed significantly higher risk of strut fracture among the larger C-C valves than had previously been reported. The study also found that patients who were under 50 when their valves were implanted were more likely to experience a fracture than older patients. FDA and Shiley are continuing to study why this might be so.

The letters sent by Shiley last September inform patients whether their risk is higher than previously thought or remains low, taking into account the specific size, position, and weld date of the valve. Patients are encouraged to contact their doctors to discuss their concerns about the valves and to immediately get medical help if they experience any *sudden* symptoms indicating the valve has fractured, such as loss of consciousness, shortness of breath, chest pain, irregular or rapid heartbeat, or absence of, or change in, the normal sound or sensation of the heart valve opening or closing.

Patients are also urged to join the International Implant Registry and may do so free of charge by calling (1-800) 245-1492. This will help Shiley and FDA provide them with updated information about their heart valves and keep a record of their current addresses. Members of the registry receive a special bracelet or neck chain identifying them as C-C heart valve patients.



FDA Warns Police About Radar Devices

After stories in the news media reported the possibility that hand-held traffic radar devices used by police officers might increase their cancer risk, FDA last July 20 wrote to police officials, telling them what is known and unknown about the issue and how to reduce exposure.

Traffic radar units (used to track drivers going over the speed limit) emit microwave radiation, similar to that in microwave ovens, but at 10,000 times less power.

Last June, officials with FDA's Center for Devices and Radiological Health met with Ohio state trooper Gary Poynter, who cited 27 cases of testicular cancer among Ohio troopers. Normal incidence in a population of that size is about 30 cases a year.

The center sent the letters of July 20 to

more than 20,000 city, county, state, and federal law enforcement agencies and approximately 3,000 police unions, organizations and associations throughout the country. On July 28, the center also wrote manufacturers to enlist their support in resolving the issue.

There is no firm scientific evidence that low levels of radiation, such as those from radar devices, can be harmful. In some studies, animals had biological changes from low radar levels, but most of those studies used a different type of microwave radiation. Also, it's unknown whether the results apply to humans. To find out, researchers need to compare cancer rates in officers who use radar devices with rates in people who don't.

FDA has given police officers the following advice to reduce exposure:

- Always point the device away from your body, or your partner's body, while it is turned on.
- Mount fixed radar antennas so that the beam does not point at anyone in the patrol car.
- When possible, turn off a hand-held unit when it is not in use. If your unit has a "stand-by" mode, always use it when not measuring the speed of a vehicle. Never rest the unit against your body when it is turned on.
- When it is on, try to avoid pointing the device toward metal surfaces inside your car, such as the floor or a door, to avoid microwave reflection. (Measurements have shown that the radiation reflected from nonmetallic surfaces, such as glass in the car's windows, is much less intense than that reflected from metal surfaces.)

Cases of cancer among officers should

be reported to the Center for Radiological Health's problem reporting program, (1-800) 638-6725. It's important to describe the type of radar unit used, length of time the officer worked with radar devices, and the type of cancer.

The center will continue to evaluate research performed by microwave scientists around the world to see if their results apply to traffic radar devices.

Because of the distance between a police radar unit and oncoming traffic being observed, the levels of microwave exposure to individuals in those cars would be too insignificant to cause any possible risk.

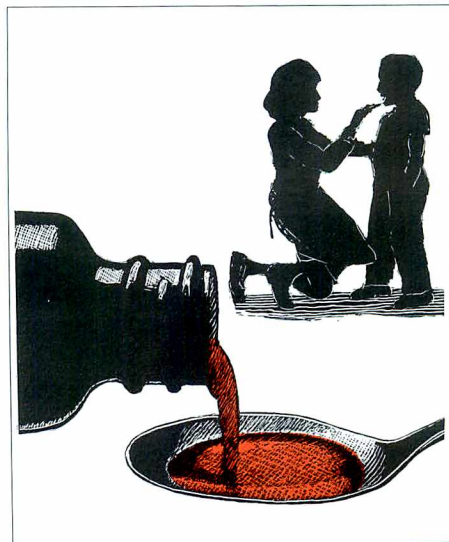
How to Give Children Medicine

Carefully follow label instructions when giving nonprescription medications to children, FDA reminded parents and child-care providers on Child Health Day last Oct. 5.

"Children are not small adults," FDA Commissioner David A. Kessler, M.D., said. "If you take a dose meant for an adult and simply reduce it for a child, you may be giving that child more than is needed—or not enough. Some parents think they can double the dose if their child seems twice as sick. That's incorrect and dangerous."

The agency offers these tips to remember when giving children over-the-counter medicine:

- Use child-resistant caps to prevent accidents, and do not leave caps off containers.
- Store medicine as instructed and in a safe place out of reach of children.
- Don't give medicine to children unless it is recommended for them on the label or by a doctor.



- Don't use medicine for purposes that are not called for on the label.
- Don't try to remember the dose used during previous illnesses; read the label each time.
- Don't guess when converting measuring units—for example, from teaspoons or tablespoons to ounces. Check with a reliable source, such as a pharmacist.
- Examine dose cups carefully. Cups may be marked with various measurement units and may not use standard abbreviations. Be sure to follow the instructions on the label.
- Check with a doctor before giving a child more than one product at a time.
- Check with a doctor before treating a child with aspirin products. Aspirin should not be used to treat a child with flu or chickenpox.

For a free copy of "Kids Aren't Just Small Adults," a brochure on treating chil-

dren with over-the-counter medicines, write to: Child Health, Pueblo, CO 81009.

Recommendation for Children's Fat Intake

An updated American Academy of Pediatrics (AAP) policy statement recommends reducing fat in the diets of children over 2 years old. Published in the September 1992 issue of *Pediatrics*, AAP's policy continues to endorse selective cholesterol screening of children over 2 years.

AAP recommends that diets for children over 2 years include a daily intake of approximately 30 percent of total calories from fat and less than 300 milligrams of cholesterol per day. No more than 10 percent of the total calories should be from saturated fat. Previously, AAP recommended that 30 to 40 percent of total calories be from fat.

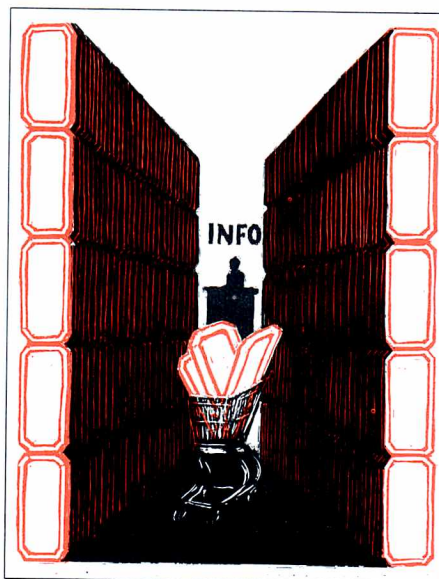
AAP endorses selective cholesterol screening of:

- children whose parents or grandparents have a history of premature (before age 55) heart and blood vessel disease
- children whose parents have a cholesterol level above 240 milligrams per deciliter of blood
- at the physicians' discretion, children and adolescents with several heart disease risk factors (smoking, hypertension, physical inactivity, obesity, and diabetes) whose family history cannot be determined.

Library Funnels Food Labeling Info

A library established last September by FDA and the U.S. Department of Agriculture will ensure that more people learn about food labeling.

The Food Labeling Education Information Center was set up as part of USDA's Food and Nutrition Information Center at the National Agricultural Library. It collects and distributes information on food labeling education programs across the country that are sponsored by consumer groups, private companies, government agencies, and industry, health professional, and voluntary health organizations.



A full-time librarian is available to help people looking for information. The library's data also will be available through the center's electronic bulletin board.

For more information, contact Gina

McNeal, FDA/USDA Food Labeling Education Information Center, Food and Nutrition Information Center, National Agricultural Library, 10301 Baltimore Blvd., Room 304, Beltsville, MD 20705-2351; telephone (301) 504-5719; facsimile transmission (301) 504-5472.

English, Spanish, Teen Pubs Available

English and Spanish versions of an FDA brochure on the safe use of non-prescription drugs, a Spanish translation of an *FDA Consumer* reprint on arthritis, and a reprint on acne from the magazine's teen series are available free:

- Safe and Sure Self-Care with Over-the-Counter Medicines (FDA92-3198); Los Medicamentos Sin Receta Médica: Algunas Precauciones Para su Uso (FDA92-3198S)
- La Artritis Tratamiento Moderno Para Ese Viejo Dolor en Las Coyunturas (Arthritis: Modern Treatment for That Old Pain in the Joints) (FDA92-1190S)
- Acne Agony (FDA92-1197)

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D4T Available On 'Parallel Track'

The investigational drug D4T is the first drug to be available under FDA's "parallel track" policy. The drug to treat people with AIDS was made available for expanded investigational use last Oct. 5.

The parallel track policy, announced last April, allows expanded use of promising new drugs for treating AIDS and other HIV-related diseases in people unable to take standard therapies and unable to participate in controlled studies.

D4T acts by inhibiting the AIDS virus. The drug will be available to patients who have not responded to or are intolerant of the approved drugs Retrovir (zidovudine, or AZT) or Videx (didanosine, or DDI). Patients enrolled in the parallel track study will include those who have experienced serious side effects from other antiviral drugs or whose conditions have worsened while taking those drugs. Doctors can get information about enrolling patients in the study by calling the manufacturer, Bristol-Myers Squibb Co., at (1-800) 842-8036.

DDI: Wider Access, Lower Doses

Wider access to and lower doses of the anti-HIV drug Videx (didanosine, or DDI) have been approved for any patient who has been treated with AZT (zidovudine), FDA announced Oct. 1.

Videx's initial approval in 1991 (see the AIDS Page in the December 1991 *FDA Consumer*) was only for patients with advanced HIV infection who couldn't tolerate AZT or whose health significantly deteriorated during AZT treatment.

However, new study data submitted to

FDA show that patients given Videx took longer to develop AIDS-related illnesses than patients on continued AZT therapy. The two-year controlled clinical trial also showed that a Videx dose lower than is currently used is no less effective than the higher dose studied and is associated with lower toxicity—most significantly, a lower rate of the drug's major side effect, pancreas inflammation.

The study was sponsored by the manufacturer, Bristol-Myers Squibb Co., and the National Institutes of Health, who published the results in the Aug. 27, 1992, *New England Journal of Medicine*.

Other ongoing studies are comparing several doses of Videx, and one is studying Videx versus AZT in patients who have not received prior anti-retroviral therapy.

Wallet Cards No Guarantee

A wallet-size card "certifying" a person is free of the HIV virus is no guarantee a sex partner is "safe," says the Public Health Service. Such cards are being sold in the Washington, D.C., area and possibly other cities.

Even if someone were free of the HIV virus when obtaining a card, the person could become infected later. Also, there's a period of from three weeks to six months after one becomes infected when a blood test won't register the infection. And, an unscrupulous person could try to alter the date on the card.

People who suspect they have the HIV virus should be tested for it for their own well-being. If infected, they can then receive treatment and counseling and can avoid infecting others.

HIV Receptor Found In Colon Cells

The AIDS virus directly infects human colon cells, according to a report in the August 1992 issue of the *Journal of Virology*. The virus also infects immune cells and nerve cells.

Jacques Fantini, Ph.D., and colleagues from the Institut de la Santé et de la Recherche Médicale in France report finding a receptor on colon cells to which the AIDS virus attaches to gain entrance to the cell. According to the authors, this receptor provides evidence that the virus can directly infect cells of the colonic mucosa. Such infection might occur during anal intercourse.

Colon HIV infection—whether contracted directly or secondarily through infected immune cells—may account for the diarrhea and intestinal inflammation seen in about 40 percent of AIDS patients, says Fantini, who is continuing his research at the University of Pennsylvania in Philadelphia.

The receptor is called galactosyl ceramide, a glycolipid found on the surface of colonic mucosal cells. Galactosyl ceramide is also the HIV receptor on nerve cells. A better known HIV receptor is the CD4 protein, which is found on the surface of certain immune system cells.

"We have been focusing on CD4 for more than five years. This is the beginning of another story, that of another type of HIV receptor, and is opening an exciting new field," Fantini says. "Theoretically," he says, "we could imagine developing a monoclonal antibody against the galactosyl ceramide receptor that could inhibit HIV attachment in the body."

No-Win Situation For Athletes

by Kevin L. Ropp

G

erman sprinters Katrin Krabbe and Grit Breuer never made it to the 1992 Summer Olympics in Barcelona, Spain.

United States hammer thrower Jud Logan and shot putter Bonnie Dasse went but were sent home early.

Also sent home from the Olympics were Wu Dan, a Chinese women's volleyball player; Madina Biktagirova, a Unified Team marathoner; and Andrew Davies and Andrew Saxton, both British weight lifters.

All tested positive for banned drugs, but, surprisingly to some fans, none of the drugs were anabolic steroids.

Krabbe, Breuer, Logan, Dasse, Davies, and Saxton tested positive for clenbuterol, a veterinary drug. Dan tested positive for strychnine, a poison that is a stimulant in small doses, and Biktagirova tested positive for norephedrine, a mild stimulant. Though the three drugs are not steroids, all are abused in sports because athletes believe they enhance performance.

From athletes in international competition to college and high school athletes to the teenager who simply wants to "bulk up," people of all ages and abilities have found alternatives to replace anabolic steroids.

Regulated by the Drug Enforcement Administration, anabolic steroids were placed in the Controlled Substances Act's Schedule III (which includes some narcotic drugs, stimulants and depressants) by the Anabolic Steroids Act of 1990. Un-

lawful distribution and possession with the intent to distribute anabolic steroids is a federal crime, punishable by up to five years in prison.

Since the law was enacted, many athletes have avoided anabolic steroids because of the penalties associated with their abuse, says Donald Leggett, a compliance officer in the Food and Drug Administration's Center for Drug Evaluation and Research. "They have looked at other chemicals that perform in a similar fashion but are not technically regulated as or called anabolic steroids."

Those alternatives include prescription, veterinary, investigational, and unapproved drugs, and dietary supplements.

Dietary supplements are regulated as foods. No data has been submitted to FDA to prove bodybuilding claims for these substances, and the short- and long-term effects of their use are unknown.

"Many alternatives are labeled as 'dietary supplements' even though they make anabolic and other athletic enhancement claims. Such attempts to market directly to the public may represent a circumvention of the safety and efficacy provisions required of drugs. Thus, the short- and long-term effects of their use are generally unknown," Leggett says.

When supplement manufacturers make bodybuilding and drug-type claims, FDA can, and often does, issue warning letters to the manufacturer or prosecute for consumer fraud. FDA's Center for Drug Evaluation and Research recently won

several court cases involving consumer fraud by supplement manufacturers, Leggett says.

The consumer is defrauded by believing these supplements will build muscles or promote testosterone production, when in fact they do no such thing, he says.

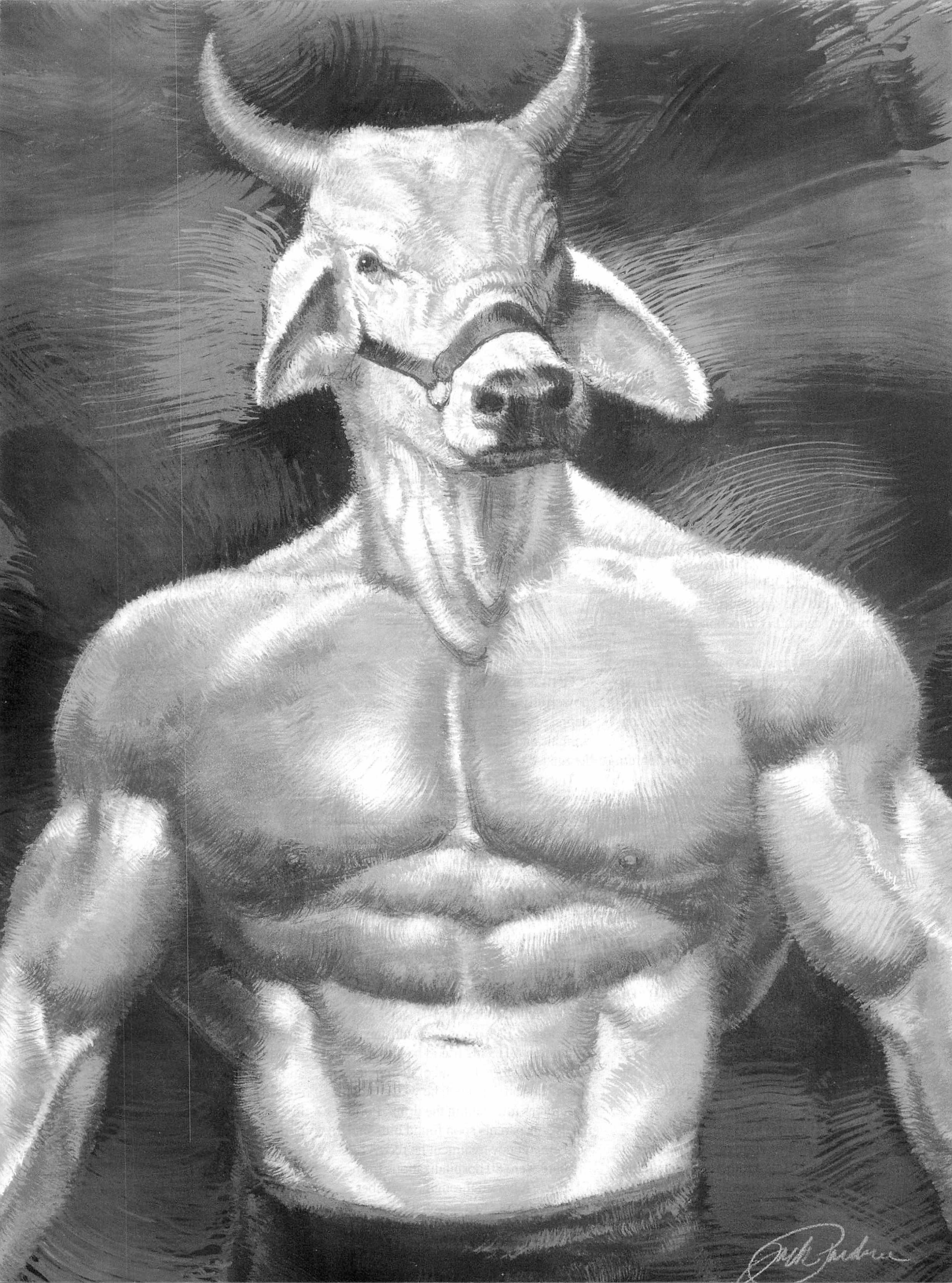
In a study, published in the Aug. 26, 1992, *Journal of the American Medical Association*, of bodybuilding magazine advertisements, Rossanne M. Philen, M.D., and colleagues, report that they counted 89 supplement brands, 311 products, and 235 ingredients, most of which were unspecified amino acids. More than 22 percent of the products had no ingredients listed in their advertisements.

The study also found that many steroid-type ingredients, called sterols, were being advertised. With the exception of ecdysterone, the sterols were all plant derivatives. Ecdysterone is an insect hormone with no known use in humans.

The abuse of many of these ingredients, as well as prescription, veterinary, investigational, and unapproved drugs, concerns FDA.

Agency investigators have collected more than 3,000 drug samples from the black market over a 10-year period, according to Leggett. Many of those samples, he says, were not steroids but other, potentially more dangerous, prescription drugs.

Some steroid alternatives popular among athletes include the investigational drugs clenbuterol and gamma hydroxybutyric acid, or GHB, and approved prescrip-



John P. ...

tion drugs such as human growth hormone and erythropoietin, better known as EPO.

Clenbuterol

Clenbuterol is used in several European countries by animal trainers to build muscle mass and strength in exhibition livestock. It has never been approved for any use in the United States.

Athletes use clenbuterol because they think it has the same mass and strength-building capability in people as it does in animals.

But clenbuterol also has serious, immediate side effects in humans. In Spain, between March and July 1990, 135 people became ill after eating beef liver that contained clenbuterol residues. Their symptoms included fast heart rate, muscle tremors, headache, dizziness, nausea, fever, and chills. Symptoms appeared from 30 minutes to six hours after they ate the liver and lasted for nearly two days.

Like most other steroid alternatives, the long-term effects of clenbuterol are not fully known. But, Leggett says, some serious cardiovascular complications may result from their use.

In many instances, veterinary drugs are used simply because they are easier than human drugs to obtain, Leggett says. "Historically, there are places in this country, particularly in rural areas, where just about anyone could walk in and purchase a veterinary equivalent of a [human] drug that would require a doctor's prescription."

Gamma Hydroxybutyric Acid

Gamma hydroxybutyric acid, better known as GHB, is another steroid alternative used widely by teenagers and athletes of all abilities.

GHB is an investigational new drug that powerfully and rapidly induces sleep and depresses the central nervous system in animals and humans, according to Leggett.

The drug has been illegally marketed as a steroid alternative both openly and "in the back room" in gyms, spas, and health food stores and advertised in bodybuilding magazines. Promoters claim it stimulates production of human growth hormone and thus produces muscle mass and weight loss. It has also been promoted as a sleep aid and touted as a street drug.

But GHB is extremely dangerous.

A Duluth, Ga., teenager, getting ready for his high school prom on May 11, 1990, drank a concoction of water and Somatmax PM, a powdery substance containing GHB his friend had bought at a health food store. Instead of getting the "high" he had expected, he was in a coma 20 minutes after taking the drink. Fortunately, his parents soon found him, and with emergency treatment he recovered.

There were 80 hospitalizations from GHB use reported through November 1990, according to a national Centers for

Disease Control study published in the Nov. 30, 1990, issue of *Morbidity and Mortality Weekly Report*.

Patients reported that within 15 to 60 minutes of taking one-half to three teaspoons of GHB, they developed symptoms such as vomiting, drowsiness, dizziness, tremors, seizure-like movements, unconsciousness, slowed heartbeat, lowered blood pressure, breathing difficulty, and breathing cessation. Patients recovered, usually with emergency room care, in 2 to 96 hours. There have been no reported deaths.

Human Growth Hormone

Human growth hormone, or HGH, is another popular steroid alternative. Pro-



duced naturally by the human body, HGH's only approved medical use is to treat pituitary dwarfism, but it is under investigation to treat other disorders.

Human growth hormone, manufactured using recombinant DNA technology, is identical to the natural hormone. Some athletes believe that HGH promotes muscle growth and muscle strength although researchers have not confirmed these claims.

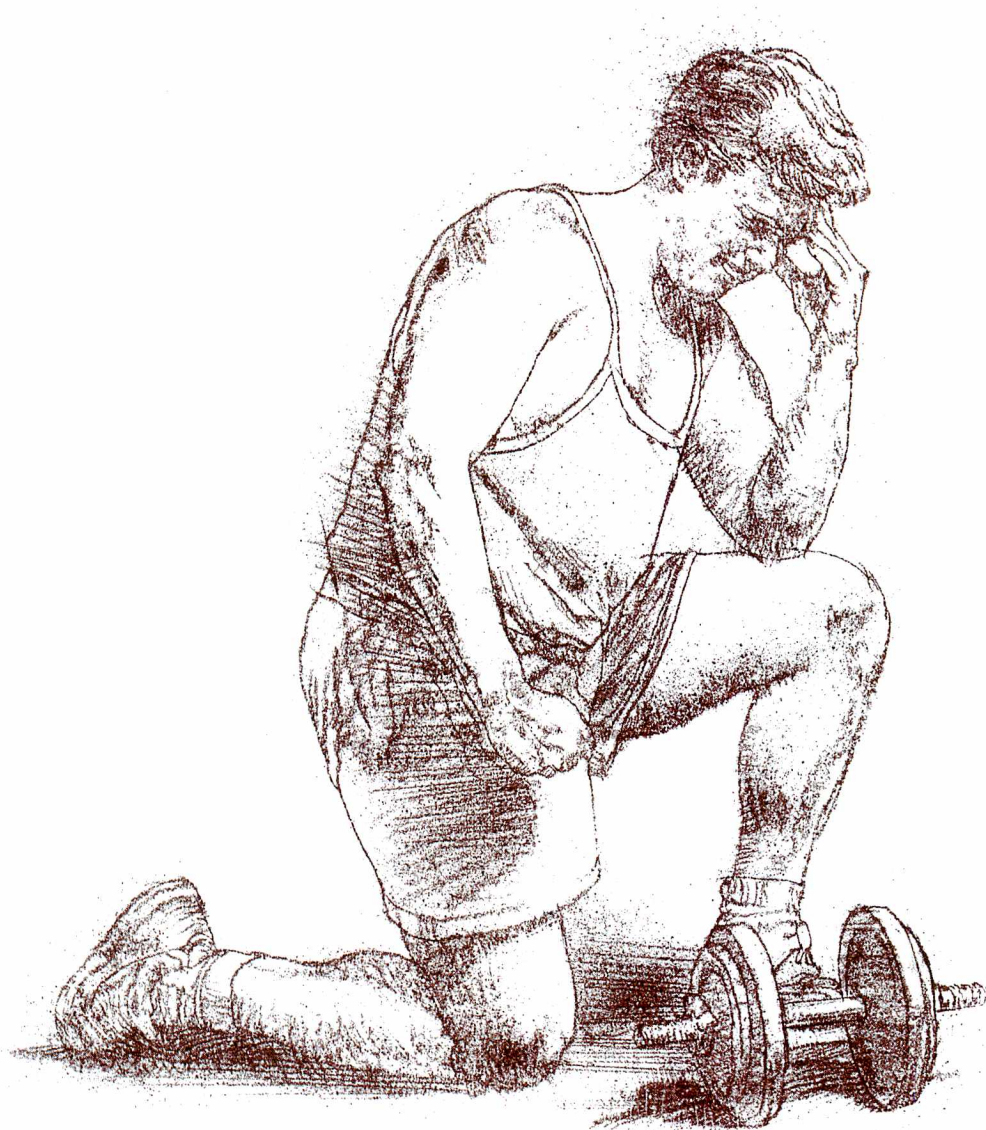
Lyle Alzado, a former Los Angeles Raiders defensive lineman, said in a July 4, 1991, *New York Times* article that human growth hormone has become the drug of choice for today's athlete, primarily because it is undetectable in drug tests. Alzado died May 14, 1992, from a rare form of brain cancer, central nervous system lymphoma, which he attributed to his prolonged use of steroids and HGH.

Too much human growth hormone, produced by a hyperactive pituitary gland or a tumor, is the cause of acromegaly, a condition characterized by excessive growth of the bones of the hands, feet and face. Acromegaly is ultimately fatal because of resulting heart disease and other metabolic problems.

Erythropoietin

Erythropoietin, or EPO, is another steroid alternative used in the international sports community although it has seen limited abuse in the United States.

EPO, approved for treating anemias associated with chronic renal failure and zidovudine (AZT) therapy in HIV-infected patients, stimulates bone marrow to produce red blood cells. The hormone appeals to athletes because they tire less easily when taking it and because it is unde-



Severe Penalties

Here are some potential health effects of drugs and other substances—ranging from the mildest to the most severe—used as alternatives to anabolic steroids.

- greasy skin
- headache
- severe acne
- premature balding
- bloating associated with water retention
- dizziness
- chills
- drowsiness
- nausea
- vomiting
- muscle tremors
- fever
- fast heart rate
- slowed heart rate
- bloody diarrhea
- seizure-like movements
- lowered blood pressure
- breathing difficulty
- breathing cessation
- blood clots
- cardiovascular problems
- liver disease
- cancer
- heart attack
- stroke
- death

tectable by tests presently used.

"It [EPO] increases the red blood cell count, and therefore the athlete is able to absorb more oxygen and increase stamina—the oxygen-carrying capacity of the blood system is just unbelievable," Leggett says.

But EPO use is not without risk. As the body's red blood cell count rises and the blood thickens, blood clots, heart attack, or stroke could result.

Abuse of EPO is especially risky among marathoners and long-distance bicyclists. As these athletes compete, Leggett explains, they lose body fluids, including blood fluids. Reducing blood fluids concentrates the already abnormally high red blood cell count, which can lead to polycythemia, an abnormal increase in circulating red blood cells.

"EPO can turn their blood to the consistency of Jell-O," he says.

Deadly Potential

FDA is particularly concerned with athletes' abuse of prescription drugs because they usually take the drugs without a physician's supervision and in higher doses than recommended for their limited medical uses.

"We consider these things to have the potential for hazard when they're not monitored or taken in accordance with the supervision of a licensed practitioner," Leggett says.

"Many of these people take way above and beyond the directions for use simply because they feel 'the more the better.' That was true of anabolic steroids, too. The people who are taking these drugs are essentially saying, 'If one teaspoon is recommended, I'm going to take five and grow five times as fast.'"

With that philosophy, the potential for an overdose is very high—and so is the potential for death.

FDA is also concerned about the prescription, veterinary, investigational, and unapproved drugs used as steroid alternatives primarily because little is known of the short- and long-term effects these drugs may have on humans, especially when taken in higher-than-recommended doses or in combination with other drugs.

Comparing anabolic steroids to those steroid alternatives, Leggett says, "We approved all of these anabolic steroids for domestic use in treating diseases like anemias, osteoporosis, and certain cancers. We know what to expect from their label dosage and overdoses.

"We have no idea what a normal dosage or overdose is for many of the steroid alternatives or what might be their effect. This is because we've never seen any clinical studies reflecting their use in humans. So, we're completely without a baseline there."

Some short-term reactions from using steroid alternatives are similar to those associated with anabolic steroid abuse. These reactions include: bloody diarrhea, nausea, vomiting, severe acne, premature balding, bloating associated with water retention, and greasy skin.

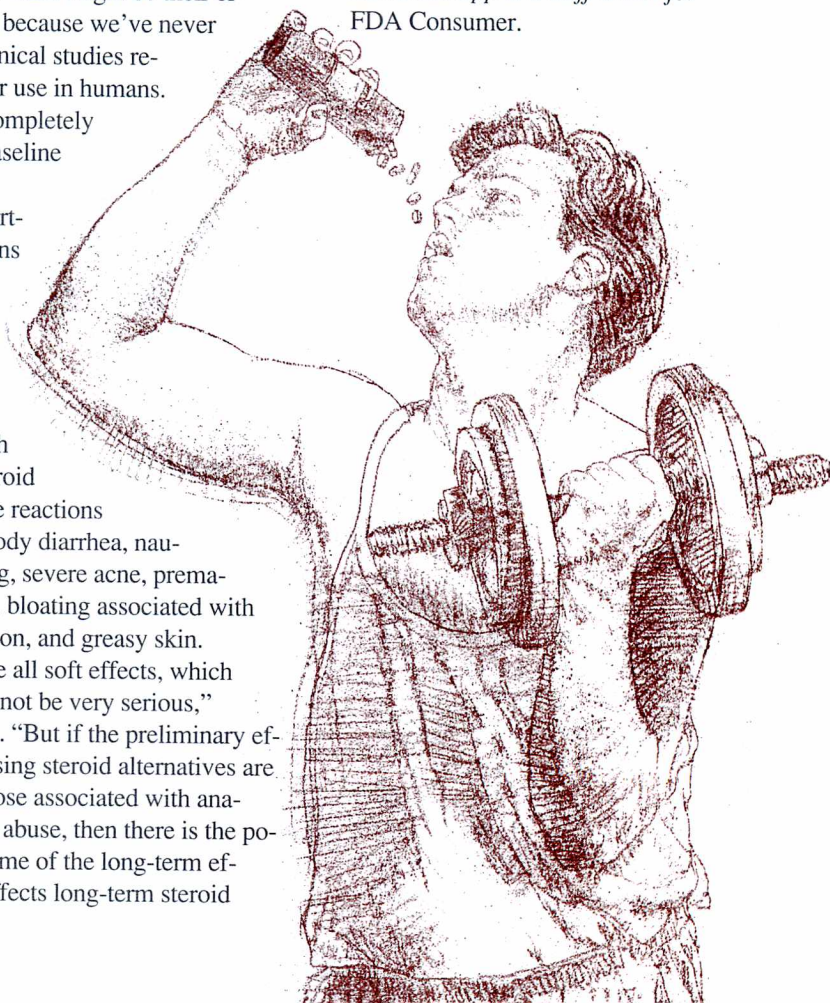
"Those are all soft effects, which may or may not be very serious," Leggett says. "But if the preliminary effects from using steroid alternatives are similar to those associated with anabolic steroid abuse, then there is the potential for some of the long-term effects, too. Effects long-term steroid

abusers experience include cardiovascular problems, liver disease, certain cancers."

Clenbuterol, gamma hydroxybutyric acid, human growth hormone, and erythropoietin, all banned in international competition, are some of the more popular steroid alternatives athletes are now abusing. But, Leggett says, this list is likely to grow as athletes experiment with different and new chemicals.

As athletes strive for bigger, more muscular bodies through chemicals, Leggett, expecting the worst, says, "I'm sure they'll come up with something someday that's even more disastrous than the few [drugs] we've seen in recent years." ■

Kevin L. Ropp is a staff writer for FDA Consumer.



OVARIAN CANCER

Today's Treatment, Tomorrow's Hope

by Marian Segal

This is the second of two FDA Consumer articles on ovarian cancer. The first article, in last month's issue, discussed ovarian cancer risk factors, prevalence and diagnosis.

Trusting her instincts may have saved Jessica Marsh's life. Due in part to her own vigilance and persistence, Marsh (not her real name), a secretary in Rockville, Md., was diagnosed before her cancer had spread beyond the ovary, affording her a brighter prognosis.

For three months in the fall of 1985, Marsh, then 36 years old, had noticed pains in her right side around the time of her menstrual periods. Although the pains were brief and not severe, she decided to have her doctor check it out. A week or so before her appointment, however, a very sharp pain prompted her to call the doctor again. Her gynecologist was out of town, but the doctor on call had her come in.

"He told me that my stomach was distended, gave me a pelvic exam, and then congratulated me, telling me I was three months pregnant," Marsh recalls. "I told him I wasn't pregnant, that I already had two children and knew what it was like to be pregnant, and this was not a pregnancy."

At Marsh's insistence, the physician arranged for her to have a pelvic sonogram that day at a local hospital.

"I had the sonogram and the next thing I

knew, the doctor who had examined me at the office came in, repeated the sonogram, and told me there was a mass and he wanted to do some more tests. The next morning, I had surgery to remove my ovaries, uterus, and fallopian tubes."

Although Marsh's experience may not be typical, it illustrates the difficulty in correctly diagnosing the disease early. Yet, early detection and treatment can mean the difference between life and death. According to the Familial Ovarian Cancer Registry, more than 90 percent of women diagnosed with ovarian cancer while it's still confined to the ovary are alive five years after diagnosis. Among women whose cancer has spread beyond the ovary by the time it's diagnosed, only 25 percent survive five years.

Treatment a Challenge

Ovarian cancer is always treated surgically, removing as much tumor as is feasible. Chemotherapy (drug treatment) or radiation therapy, or both, may also be given, depending on the extent of disease. Ovarian tumors usually grow outward, with an irregular, cauliflower-like shape. When the cancer spreads, parts of the tumor break off and attach to nearby organs. Cells may then spread to lymph nodes and distant organs.

Cancer limited to the ovaries may be successfully treated with surgery alone, removing the ovaries, fallopian tubes, and uterus. Some patients may also receive chemotherapy or radiation therapy to kill

any cancer cells remaining after surgery.

Disease that has spread beyond the ovaries almost always requires chemotherapy or radiation therapy in addition to surgery. Radiation therapy may be given by placing a radioactive solution into the pelvis and abdomen through a thin tube, coating the organs and total abdominal contents. Less commonly, external radiation using high-energy x-rays directed to the pelvis and abdomen may be prescribed.

The type of drugs used in chemotherapy depends not only on the extent of disease, but also on the type of cancer. About 85 to 90 percent of ovarian cancers arise from epithelial cells, which form the outer layer of the ovary. The rest derive from other cell types that make up the organ.

FDA has approved several drugs to treat ovarian cancer. "The first-line therapy is usually cyclophosphamide [Cytosan] in combination with carboplatin [Paraplatin] or cisplatin [Platinol]," says Robert Justice, M.D., a medical oncologist with FDA's division of oncology and pulmonary drug products in the Center for Drug Evaluation and Research. "Other drugs approved for the disease are Adriamycin (doxorubicin) and Hexalen (hexamethylmelamine), and several more are being studied," he says.

Most notable among the experimental drugs is taxol, which is being tried alone and in combination with other drugs (see accompanying article). Derived from the bark of the Pacific yew tree, taxol has shown good results in some patients with



advanced and recurrent ovarian cancer, as well as in patients with breast and other cancers.

NCI and FDA scientists are cooperating in studies to evaluate the safety and effectiveness of taxol. FDA's research role in drug development is a fairly new concept, designed to help speed the approval process for drugs for life-threatening diseases.

"It's a commitment by the agency to do more than just wait for packages of data to come in [from the drug's sponsor] and review them for approval," says Jerry M. Collins, Ph.D., director of the Office of Research Resources in the Center for Drug Evaluation and Research. "We can't do this for every new drug in every therapeutic area," he explains, "but for AIDS and cancer, we have done similar research before."

The goal of Collins' taxol studies is to see if there's a relationship between blood levels of the drug and the clinical response, which could be tumor shrinkage or toxicity.

Side Effects

Surgery, the first-line treatment for ovarian cancer, requires several days' hospitalization and a recuperative period of from four to six weeks. Removing the ovaries, which are the main source of the female hormones estrogen and progesterone, causes immediate menopause, and the symptomatic hot flashes are more severe than when menopause occurs more gradually, as it usually does naturally.

Radiation therapy can cause mild skin reactions, such as redness and drying in treated areas, urinary discomfort, diarrhea,

and vaginal dryness. (Menopause can also cause vaginal dryness.) A small percent of patients may develop bowel obstruction, sometimes requiring surgical correction.

Other possible side effects of radiation therapy, commonly experienced with chemotherapy as well, include loss of energy and appetite, nausea, and vomiting.

Chemotherapy may also cause mouth sores, hair loss, and reduced platelet and blood cell counts that can lead to infections, anemia or bleeding. The drugs used to treat ovarian cancer may also have neurologic effects, causing hearing loss, ringing in the ears, nerve damage, and numbness or tingling in the face, fingers and toes. There may also be kidney damage.

Most side effects are temporary, and sometimes dietary changes or medicines can ease the symptoms. Last year FDA approved Zofran (ondansetron hydrochloride) to counter nausea and vomiting associated with chemotherapy.

"Ondansetron represents a real breakthrough in cancer treatment," says Roger B. Cohen, M.D., medical oncologist with the division of cytokine biology in FDA's Center for Biologics Evaluation and Research. "Nausea from chemotherapy is often abolished with minimal side effects, leading to dramatic improvements in patients' sense of well-being and quality of life," he says.

Other drugs previously approved for the same use are Reglan (metoclopramide) and Marinol (dronabinol).

Transfusions can correct red blood cell and platelet deficiencies. Hematopoietic growth factors such as G-CSF, approved in 1991, stimulate production of infection-fighting white blood cells. GM-CSF, which received FDA approval in 1991 to increase white cell counts after bone marrow transplantation, is now being studied for its effectiveness in stimulating white cells after cancer chemotherapy. Among other drugs now under study for their ability to increase white cell counts, and perhaps platelets as well, are stem cell factor and PIXY 321. PIXY 321 is a genetically engineered product consisting of GM-CSF and another hematopoietic growth factor, interleukin-3.

When therapy is completed, the woman continues to have regular checkups that in-

Taxol—New Drug with a Long History

The healing properties of taxol were known to at least one community long before Western medicine recognized the drug's potential.

According to an article in the Sept. 4, 1991, *Journal of the American Medical Association*, around the turn of the century, a British official in the Indian subcontinent noted that parts of the European yew, *Taxus baccata*, were used in an Indian clarified butter preparation for treating cancer.

It wasn't until 1962, however, that the U.S. Forest Service delivered crude bark extracts of the Pacific yew, *Taxus brevifolia*, to the National Cancer Institute. A series of NCI experiments showed the extract was effective against several kinds of cancer in mice.

In 1971, researchers at the Research Triangle Institute in Durham, N.C., isolated taxol from the extract, but interest in the compound waned until the mid-1970s. In 1979, a researcher at Albert Einstein Col-

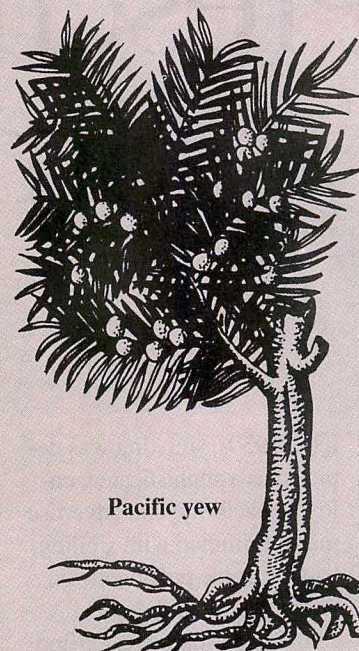
lege of Medicine in New York described how taxol works to defeat cancer by inhibiting cell division.

Today, taxol—alone or in combination with other drugs—is being studied for a wide variety of adult and childhood cancers. Last July, FDA authorized use of the drug for ovarian cancer under a "treatment IND." Treatment INDs permit earlier and wider access to experimental drugs by patients with life-threatening conditions for which there is no satisfactory treatment.

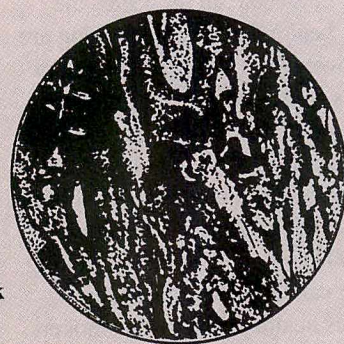
Under this IND, taxol will be made available to women with ovarian cancer who have been treated with at least two standard cancer regimens, one of which must have included a platinum-containing cancer drug such as cisplatin, and for whom chemotherapy has failed.

NCI estimates that more than 6,000 patients will participate in taxol clinical trials this year. ■

—M.S.



Pacific yew



Pacific yew bark

clude pelvic examinations and laboratory tests to measure blood levels of tumor markers such as CA 125. The doctor may recommend a laparotomy or laparoscopy after completion of chemotherapy to inspect the abdomen and pelvis and take multiple tissue biopsies. (Laparotomy is an exploratory operation in which the surgeon examines the abdomen thoroughly and removes fluid or tissue for examination. In laparoscopy, a flexible, lighted tube is passed through a small incision in the abdomen, allowing the surgeon to examine the area and extract tissue for a biopsy.) This "second-look surgery" helps evaluate the effectiveness of chemotherapy and determine whether treatment should be continued or stopped. Often a laparotomy or laparoscopy has been done previously to diagnose ovarian cancer.

Cause and Prevention Elusive

Although several risk factors for ovarian cancer have been identified (see "Ovarian Cancer—Early Diagnosis Elusive" in the November issue of *FDA Consumer*), its cause eludes scientists. Hypotheses have been advanced, but none proven, and so there is no rationale on which to base effective prevention strategies.

The Familial Ovarian Cancer Registry, however, urges that women with a family history of the disease receive genetic counseling, beginning in their early 20s, and undergo physical surveillance (pelvic and abdominal examination, CA 125, and pelvic or transvaginal ultrasound) every six months beginning in their early 30s. It also recommends they have prophylactic removal of the ovaries by age 35 if they've completed their families.

These recommendations apply to women in whom two or more of the following family members have ovarian cancer: mother, sister, daughter, grandmother, aunt.

Before her own ordeal with ovarian cancer began in 1986, the late comedienne Gilda Radner was unaware that several members of her family suffered from the disease. After a lengthy illness, she died in May 1989.

Jessica Marsh, six years after her diagnosis, is today free of cancer and feeling fine. "I've become a much more positive person since my cancer," she says. "Life is too short to worry about little things. If life deals me lemons, I'll make lemonade." ■

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

Prescriptions to Help Smokers Quit

by Ricki Lewis, Ph.D.



In the 1950s, smoking was depicted as a sophisticated, enjoyable activity, and advertisements brimmed with smiling, happy people puffing away. Although ads still depict smoking as sophisticated and enjoyable, in the 1990s the health dangers of smoking are widely known—and about 76 percent of the nation's approximately 46 million smokers say that they would like to quit, according to a 1991 Gallup poll.

Smoking cessation is a major goal of the U.S. Public Health Service's Healthy People 2000 Program. Cigarette smoking causes lung cancer, heart attacks, and other serious health problems in smokers. It can cause health problems in nonsmokers exposed to "second-hand" smoke as well.

Airlines, restaurants, hospitals, and workplaces are banning smoking or restricting it to designated areas, and pressure to quit is intense.

As former Surgeon General C. Everett Koop, M.D., said, "If you have a spouse who's nagging you at home to quit, children who suggest that you're going to die if you don't, and then your boss says you can't smoke at the worksite, that's a pretty good indication that it's time to try to quit."

But quitting is a lot easier said than done. Each year, about 17 million Americans try to stop smoking, according to the American Cancer Society. Only 1.3 million succeed.

While many people have successfully stopped smoking on their own, many other smokers need help if they're going to suc-

ceed in quitting. For a number of years, stop-smoking programs have been available through various organizations such as the American Cancer Society and the American Lung Association.

In recent years, the Food and Drug Administration has approved two types of products to help smokers quit: nicotine chewing gum and the transdermal nicotine patch. Nicorette chewing gum, containing 2 milligrams (mg) of nicotine, was approved by FDA in 1984. Last June, a 4-mg dosage form of the Marian Merrell Dow product was approved.

The newest stop-smoking tool is the transdermal nicotine patch. It looks like a Band-Aid, is changed daily, and delivers nicotine to the bloodstream. Four brands of nicotine patch—Nicoderm, Habitrol, Prostep, and Nicotrol—were approved for marketing by FDA in late 1991 and early 1992. Both the chewing gum and the patch are to be used as aids to a comprehensive smoking-cessation program.

Tobacco is regulated by the Bureau of Alcohol, Tobacco and Firearms. Within the U.S. Department of Health and Human Services, the Office on Smoking and Health has the responsibility for educating the public about the health hazards of smoking. FDA, also an HHS agency, regulates nicotine gum and patches as prescription drugs; a doctor's expertise is needed to identify which patients might benefit from these products, and to prescribe the most effective course of treatment for an individual patient.

Targeting Nicotine

Cigarette smoke contains more than 4,000 chemicals and affects many of the

body's chemical messengers, such as neurotransmitters and hormones. These chemical messengers mediate a wide range of bodily responses, such as metabolism and heart and respiratory function. In 1988, the Surgeon General's report on "The Health Consequences of Smoking" identified nicotine as the addictive component of tobacco smoke. Its absence triggers the symptoms of withdrawal—irritability, anger, anxiety, restlessness, inability to concentrate, hunger, and nicotine craving.

The idea behind nicotine replacement therapy, which includes the patch and nicotine gum, is that providing nicotine in a form other than a cigarette can minimize the symptoms of withdrawal while a person is weaned from smoking. During this time, with the help of a counselor or doctor in a smoking-cessation program, the patient learns to live without the habits associated with cigarette smoking, such as having something in the hand or mouth, drawing smoke in and puffing it out, or reaching for a cigarette in response to a behavioral cue, such as a cup of coffee or stress.

"The phone rings, you say, 'Just a second,' and grab a cigarette. You smoke after a meal. The gum and patch are different in that they separate the behavioral cues from the nicotine delivery," says Elbert D. Glover, Ph.D., director of the Tobacco Research Center at the West Virginia University School of Medicine in Morgantown.

A Special Way to Chew

To be most effective, Nicorette must be chewed in a special way. When doctors



"A nicotine patch is not a magic bullet."

—Michael Eriksen, Centers for Disease Control

Nicotine Patches

Brand Name	Dosage	Type
Nicoderm } Habitrol }	21 mg 14 mg 7 mg	24-hour
Prostep	22 mg 11 mg	24-hour
Nicotrol	15 mg 10 mg 5 mg	Worn only while awake

prescribe nicotine chewing gum, they tell smokers to stop smoking completely and discuss what the maximum number of pieces of gum a day should be.

When the smoker craves a cigarette, he or she places one piece of nicotine gum in the mouth and begins to chew—very slowly. This slowness is important for the proper release of the nicotine and to avoid side effects similar to those experienced when inhaling tobacco for the first time or smoking too fast. These side effects include lightheadedness, nausea, vomiting, throat and mouth soreness, hiccups, and upset stomach.

After about 15 chews, the smoker notes a peppery taste or a tingling in the mouth. This is the signal to “park” the gum by placing it between the cheek and the gums. When the peppery taste or tingling

is almost gone, the user starts chewing again. When the taste or tingling returns, the person “parks” the gum in a different place in the mouth. This process continues for about 30 minutes, at which point the nicotine is gone from the gum.

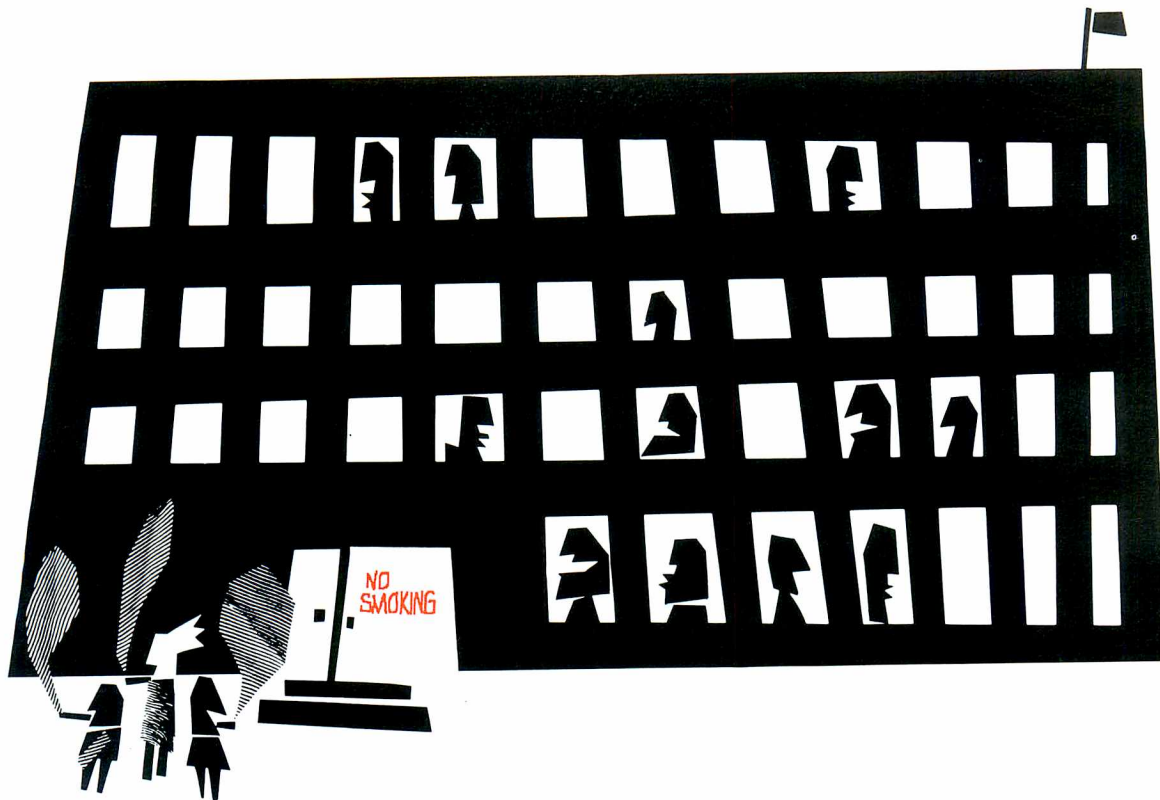
After about two or three months, the smoker should be ready to be weaned from the gum by gradually reducing use. Some ways this can be done are by reducing the number of pieces each day, by chewing some pieces for shorter amounts of time, or by using sugarless gum in place of Nicorette.

Automatic Dosages

A drawback of gum is that, as with smoking itself, the user controls the dose and schedule of nicotine delivery. In contrast, with the 24-hour skin patch, nicotine

enters the body automatically, either over a 24-hour period or only while the person is awake, depending on the type of patch used.

All four patch brands come in different dosages so that the amount of nicotine supplied to the patient can be gradually lowered. (See box.) For example, treatment with Nicoderm (marketed by Marion Merrell Dow) or Habitrol (manufactured by Kabi Pharmacia) begins with a 21-mg per day dose, about equal to the nicotine in a pack of cigarettes. Each patch is worn for 24 hours. After four to eight weeks, the patient switches to a 14-mg patch, and then, two to four weeks later, to the final 7-mg patch. ProStep (marketed by Lederle Labs) is also worn around the clock. It comes in two dosage levels, 22 mg and 11 mg. Nicotrol (manufactured by Parke-



Davis), the most recently approved patch, is worn only while awake. It comes in dosages of 15 mg, 10 mg, and 5 mg.

Which patch and dosage is best for any particular individual is a medical decision made by a doctor, taking into account the patient's smoking level and lifestyle and other needs. For example, a person who smokes less than a pack a day probably would not be told to use a patch supplying a higher level of nicotine, such as that delivered by patches supplying one-pack equivalent dosage.

All patches deliver nicotine through the skin and prevent withdrawal symptoms from stopping smoking, but the specific design of each patch and a patient's skin type determines how fast the nicotine enters the body. Glover explains that some patches deliver nicotine rapidly into the skin, from which it enters the bloodstream, whereas other patches control the release from the device itself.

Says Michael Eriksen, director of the national Centers for Disease Control's Office on Smoking and Health in Atlanta, "A nicotine patch is not a magic bullet. It doesn't make you quit—it just replaces the nicotine after a smoker quits. You have to be motivated on your own and then the patch is helpful."

Quit Rates

A typical short-term "quit rate" for 2-mg nicotine gum in well-planned studies in smoking-cessation clinics is 30 to 50

percent of participants. Research is ongoing to determine if rates improve with the 4-mg dosage gum.

To see how the gum was being used—and to determine its success outside the research setting—a team led by Richard E. Johnson, Ph.D., at the Center for Health Research in Portland, Ore., evaluated 2-mg gum use by 612 smokers over an 18-month period at a health maintenance organization. The results, published in the January 1992 *Journal of Family Practice*, showed that many patients chewed sporadically, claiming, "I use the gum in situations where smoking is prohibited" or "when I have cravings." Only 1 in 20 gum chewers also had behavioral therapy to stop smoking. This emphasizes the importance of doctors taking time to fully explain the correct use of the nicotine substitution products and of patients asking their physicians questions, if in doubt about correct use.

Quit rates with the transdermal nicotine patch began making headlines when a report in the Dec. 11, 1991, *Journal of the American Medical Association* discussed findings in nine smoking-cessation clinics across the United States. Three doses of nicotine (21 mg, 14 mg, and a placebo delivering less than 1 mg) in 24-hour patches were compared in a double-blind fashion (neither the patients nor the researchers knew which dosage patients received). Altogether, 756 smokers wore the patches for six weeks, and those who were suc-

cessful were weaned through decreasing doses during a second six weeks.

The higher the dose of nicotine, the higher the percentage of patients who quit smoking completely in three to six weeks. Sixty-one percent given 21-mg patches, 48 percent of those given 14-mg patches, and 27 percent of those on placebo quit. Counseling consisted of weekly 45- to 60-minute group sessions, including a two-minute review of individual progress and discussions of behavior modification techniques. Patients kept a daily diary to record cigarette use, and weekly clinic visits assessed their progress.

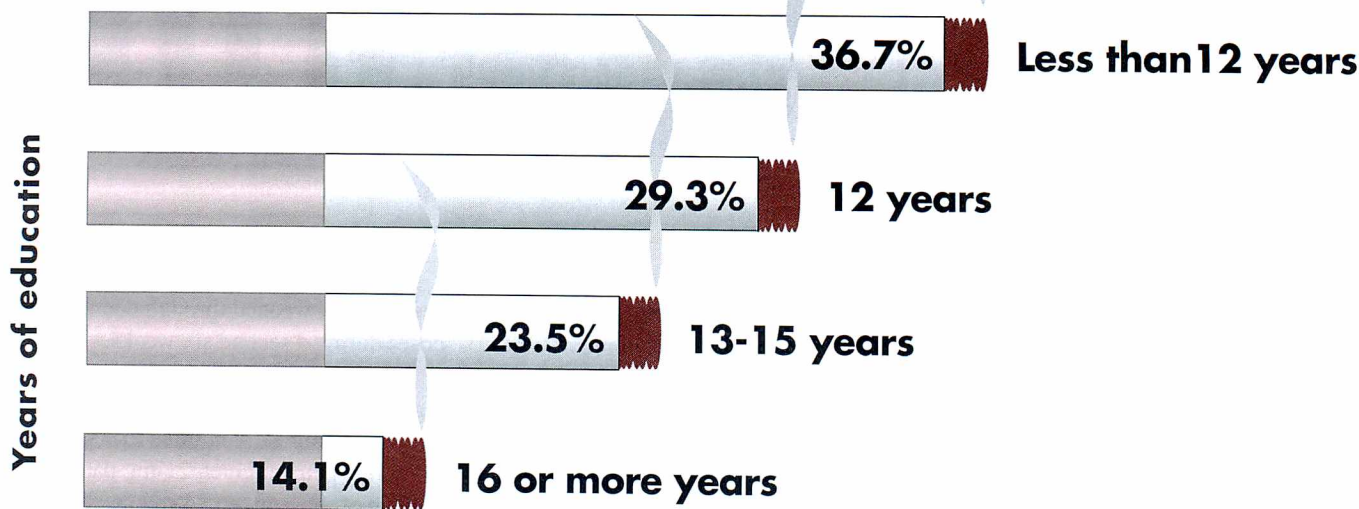
The nine-center transdermal nicotine patch study group concluded, "All transdermal nicotine doses significantly decreased the severity of nicotine withdrawal symptoms and significantly reduced cigarette use by patients who did not stop smoking. Compliance was excellent, and no serious systemic adverse effects were reported."

Success rates vary from clinic to clinic and study to study because the programs and patients differ. "The patch helps those people who are the most nicotine dependent—those who have tried to quit in the past, but found withdrawal to be so severe that they had to go back," says CDC's Eriksen. By the same token, it may be less effective for low nicotine-dependent smokers.

A nicotine-dependence scale developed by Karl-Olov Fagerstrom, Ph.D., a clinical

Smoking's Not Smart

Current U.S. cigarette smokers 25 years of age and over, 1990



The more educated Americans are, the less likely they are to smoke. In 1974, 27.5 percent of college-educated Americans smoked, but in 1990 that figure had declined by nearly half to 14.1 percent. During the same period, among people who hadn't finished high school, smokers dropped only from 43.8 percent to 36.7 percent. This information comes from interviews with 120,000 persons in 55,000 households.

(Source: PHS annual report, Health, United States, 1991)

psychologist at the Smoking Withdrawal Clinic at Ulleraker Hospital in Uppsala, Sweden, can help determine whether a particular smoker has a high or low nicotine dependency, and is used in many smoking studies. "The Fagerstrom scale is a simple set of questions. The hallmark question is, do you have a cigarette in the morning within the first 30 minutes of rising? If yes, you're pretty dependent," says Eriksen. Another telling sign is if a person smokes when sick in bed. Other common characteristics of the nicotine-dependent smoker include inhaling, smoking many cigarettes a day, and preferring a high-nicotine brand.

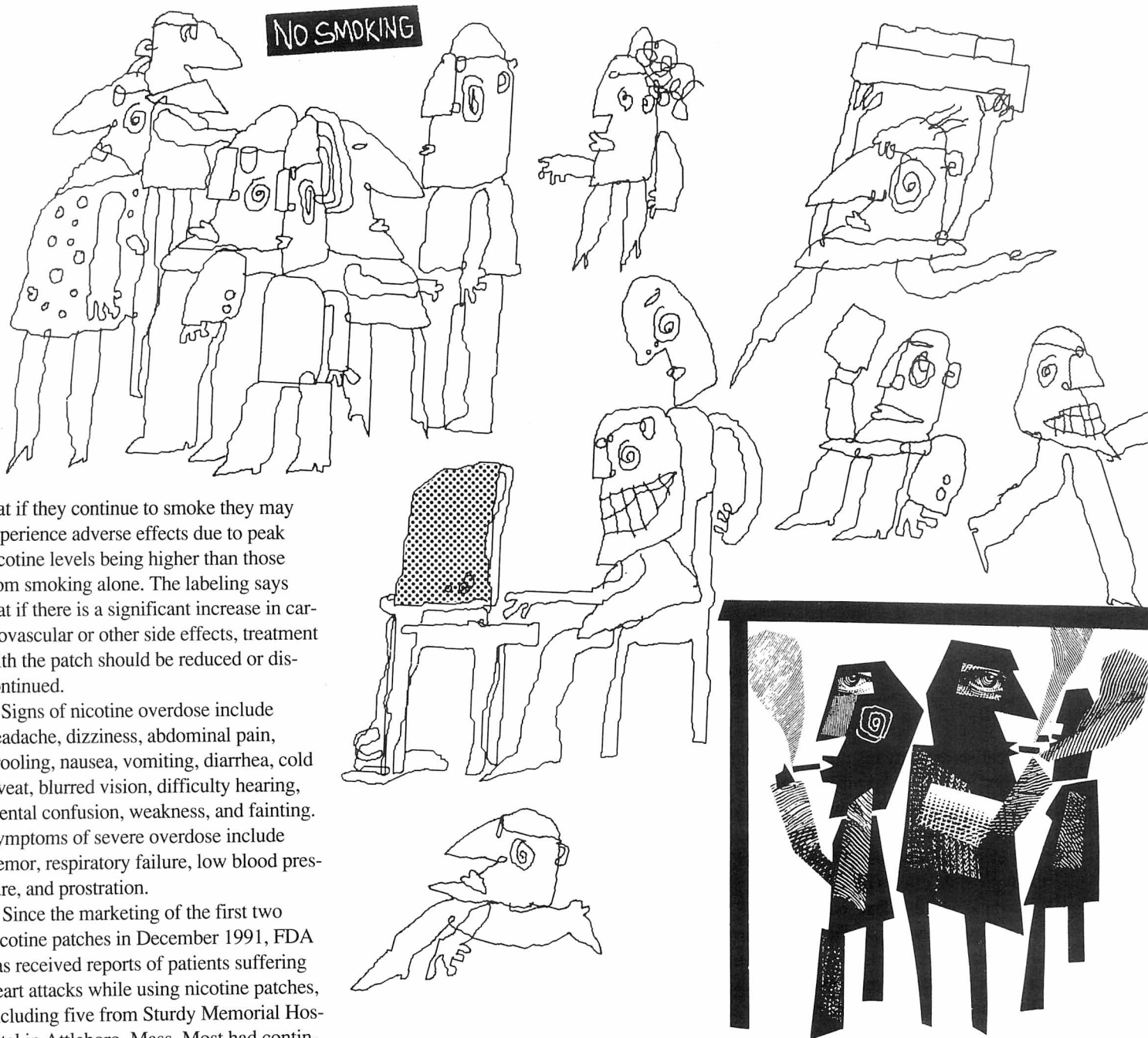
Possible Problems

In addition to effects resembling first smoking experiences when the gum is chewed too fast, as previously discussed, side effects of nicotine chewing gum can include mouth sores, headaches, heart palpitations, and excess saliva. These are most likely to occur during the first few days of use. Less common but more serious side effects have been reported, and these risks should be discussed with a doctor before taking Nicorette.

With the nicotine patch, the most common side effect is skin irritation. In about 14 percent of users, the area where the patch is applied (a hairless, clean dry spot

on the upper part of the body) becomes irritated (red and itchy) in the first few hours after application. But allergic reaction to the patch is rare—many of these people who initially experience itching simply try again in a different spot and are fine. In some clinical trials, 35 percent of patients had short-term itching or burning and 6 percent dropped out due to skin reactions. To help prevent skin irritation, directions advise against using the same spot twice within a week.

The physician labeling for the nicotine patch includes the precaution that patients should be urged to stop smoking completely when using the patch, and be told



that if they continue to smoke they may experience adverse effects due to peak nicotine levels being higher than those from smoking alone. The labeling says that if there is a significant increase in cardiovascular or other side effects, treatment with the patch should be reduced or discontinued.

Signs of nicotine overdose include headache, dizziness, abdominal pain, drooling, nausea, vomiting, diarrhea, cold sweat, blurred vision, difficulty hearing, mental confusion, weakness, and fainting. Symptoms of severe overdose include tremor, respiratory failure, low blood pressure, and prostration.

Since the marketing of the first two nicotine patches in December 1991, FDA has received reports of patients suffering heart attacks while using nicotine patches, including five from Sturdy Memorial Hospital in Attleboro, Mass. Most had continued to smoke while using the patch, and most had preexisting heart disease. The possibility of excess nicotine aggravating heart disease has been pointed out by many researchers, and patch labels advise users to inform the doctor if there is a history of heart attack, irregular heartbeat, heart pain (angina pectoris), or high blood pressure. An FDA advisory committee considered the information available on the possible relationship between nicotine patch use and heart attacks last July 14 and found the data did not show an increased risk of heart attack with patch use. The committee, therefore, did not recommend any change in labeling.

Nicotine gums and patches should be kept out of the reach of children and pets. If eaten, the patch can cause severe nausea

and vomiting, and can be fatal. Swallowing a piece of the gum usually causes no symptoms in persons for whom it has been prescribed, but if a child chews or swallows one or more pieces, a doctor or poison control center should be contacted.

Cigarette smoking during pregnancy can cause miscarriage or low birth weight, and animal studies show that nicotine alone can harm a fetus. Therefore, although quitting smoking by behavioral methods is encouraged, neither nicotine chewing gum nor transdermal nicotine patches are advised for use during pregnancy.

However, scientists are considering whether continuing to smoke during pregnancy poses more risks than using nicotine

therapy products. In addition to nicotine, cigarette smoking exposes the fetus to other risks, including doses of thousands of other chemicals such as carbon monoxide, which robs the fetus of oxygen.

At least 5 million smokers have tried the patch, and about 2 million smokers a year have tried the gum. Health-care providers, organizations, family members, and smokers themselves are all hoping that these medications will help more people kick nicotine for good and lead longer, healthier lives. ■

Ricki Lewis is a geneticist and the author of a college biology text. Judith Levine Willis, editor of FDA Consumer, also contributed to this article.

THE ELF

In Your Electric Blanket

(AND OTHER APPLIANCES)

by Dixie Farley

Scientists at many institutions, including the Food and Drug Administration, are studying the extremely low frequency electric and magnetic fields emanating from electrical devices, because of claims about possible effects on the body.

To date, worldwide research on ELF fields provides no firm evidence of harm, but certain experiments are causing some scientists to be concerned about the possibility, stimulating still more research. Some products, such as video display terminals and electric blankets, have received special attention.

All electrical devices produce some type of electric, magnetic or electromagnetic fields, but not all at the same frequency—a measure of how rapidly fields change with time. Mays Swicord, Ph.D., chief of FDA's radiation biology branch, stresses that each frequency may be distinct in terms of potential effect:

"A particular biological response or effect may result from exposures to one frequency, but not others. Or a response may result from exposure to several frequencies but be due to entirely different mechanisms. In other words, one shouldn't assume that an effect or problem seen on one region of the electromagnetic spectrum will occur in some other region."

It's well-known that overexposure to x-rays and ultraviolet radiation, both very high in the spectrum, pose health risks by breaking chemical bonds in cellular molecules. ELF fields are unable to break such bonds, but they may act through some more subtle mechanisms. Studies most often name magnetic field strength as the property that is perhaps capable of producing effects.

The Federal Food, Drug, and Cosmetic Act requires that FDA, through its Center for Devices and Radiological Health (CDRH), evaluate electromagnetic emissions to eliminate unnecessary exposure. CDRH research on lower frequencies centered first on microwave radiation. It shifted to ELF in 1987 after epidemiological data increasingly indicated a small, but statistically significant, association with cancer. CDRH now has one of largest federal in-house ELF research programs.

On Nov. 26, 1991, U.S. Representatives George Brown, D-Calif., and James Scheuer, D-N.Y., introduced the National Electromagnetic Fields Research and Public Information Dissemination Act. Incorporated into the Comprehensive National Energy Policy Act earlier this year, its provisions call for an interagency advisory committee to coordinate ELF research and

public information activities. The Energy Act became law Oct. 24.

Problems with Looking for Problems

ELF research is especially difficult, says Larry Cress, M.D., a CDRH radiation biology branch scientist conducting ELF research at the cellular level.

"For one thing," he says, "we're probably looking for very small changes. In fact, according to some physicists, the energy in 60-hertz fields [U.S. electric power] is too low to have any effect on biological systems. But this doesn't take into account that energetic molecules in the cell membrane may act as amplifiers to increase the effect of an external signal."

Another problem with ELF research is that results are hard to repeat.

"Many researchers have been able to reproduce their effects most, but not all, of the time," Cress says. "And we don't see a dose response, as with some radiation, such as x-ray. Or, one laboratory may see an *increase* in something in a cell when the field is turned on, while another laboratory sees a corresponding *decrease* when the field is turned on. The reason probably is that unexplained factors are affecting the ELF fields' interaction with cells. One theory is that the Earth's mag-

netic field interacts with power-line fields. The Earth's magnetic field tends to vary geographically. It varies quite a bit from room to room in our own lab."

There are certain frequency bands, so-called windows, at which some people see effects, Cress says. "If you're not tuned to one of those windows, you can spend your life looking, and you'll never see anything. So we need to find the windows. And the windows may not be the same for all effects."

The basic problem, he says, is what to measure. If there is a harmful effect, is it from the electric or the magnetic field? Or is it from changes in fields?

"For example," he says, "in some electric blanket designs, the power is switched on and off at intervals to control the temperature. The changing magnetic field when the current drops and rises might be the important factor for biological effects."

ELF fields are beneficial to health in at least one way.

Cress explains: "Sometimes, after months and months of being pinned, casted and dressed, a bone fracture just won't heal. When an electromagnetic field is applied, the bone is stimulated to grow. We don't know exactly how bone-growth stimulators work, but most of the studies have shown that they do speed healing." FDA has cleared some bone-growth stimulators for marketing.

Cell Talk

To learn more about these issues, Cress and colleagues are examining how cells exchange information with each other and whether ELF fields influence this communication.

"One potential mechanism for cancer is that this cellular signaling gets garbled in some way," Cress says. "Normally, a set of cells releases a biological signal. A growth factor, for instance, tells the cells when to grow or divide and when to stop. But if the cell division continues after the message is turned off, the cells may eventually become malignant."

Each step in the cell-division process is under study at CDRH. The first step, Cress explains, is a signaling molecule that binds to a protein receptor on the surface of the cell membrane. Next, the receptor triggers a series of complicated processes within the membrane that convert the message into a second messenger, which enters the cell itself.

Cress is studying what happens in the cell membrane, particularly the conversion of the first messenger into the second messenger when the cell is exposed to ELF fields.

Many researchers think the membrane is where the electromagnetic field acts, Cress says. Most of his work has been with magnetic field strengths of 1,000 milligauss (mG), which are many times

higher than a person would normally encounter.

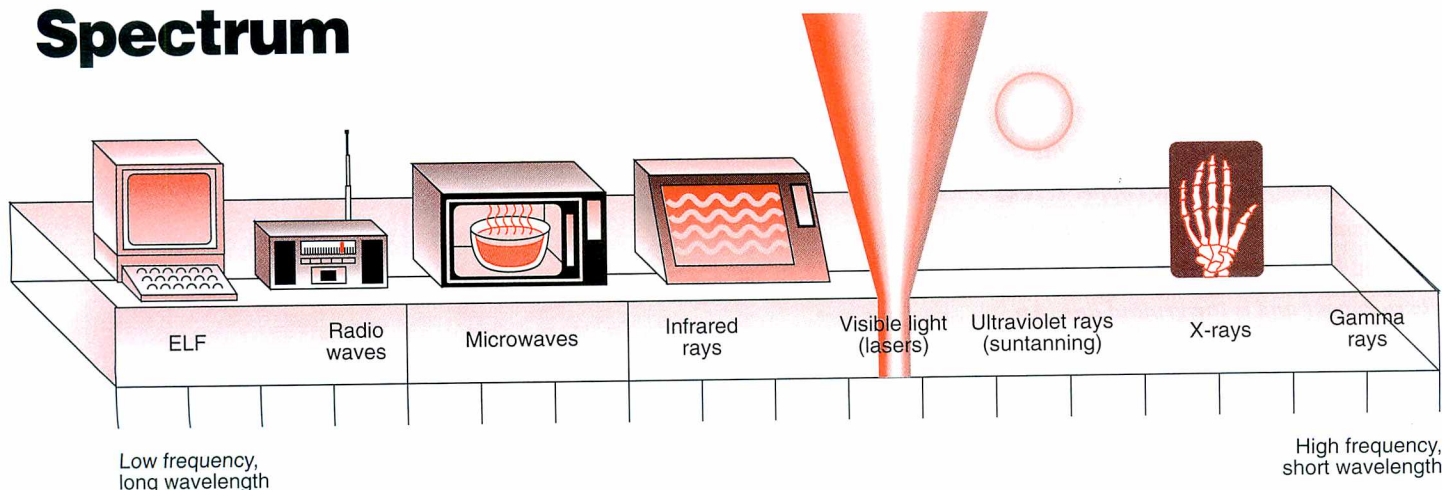
One of the most important conversions, he says, is reading out the DNA code and thus manufacturing "messenger RNA," which tells the cell to make all the proteins needed for cellular growth and metabolism. This process has been shown to be influenced by ELF fields.

Cress's fellow CDRH scientists are looking at the effect of ELF fields during the other steps of the cell's life cycle.

Dan Lyle, Ph.D., is experimenting to see whether ELF fields alter the chain of events that results when external stimuli trigger a release of calcium. Brief calcium shifts in the cell are crucial to normal cell division and normal immune function. Calcium shifts due to ELF fields might therefore relate to increased tumor risk or decreased immune function. So far, Lyle has not found changes with a 60-hertz ELF field, although earlier work demonstrated changes in immune function at lower frequencies. Future tests will involve different temperatures, different cell types, and different field levels.

Ewa Czerska, M.D., Ph.D., has seen some reproducible changes in the messenger RNA when cells are exposed to 1,000-mG magnetic fields. She recently spent a week in an academic laboratory where researchers have observed the effect at fields below 100 mG. Czerska is trying to see

Electromagnetic Spectrum



whether technique differences could account for the different findings.

CDRH's Dianne Godar, Ph.D., and Li Li, M.D., are investigating the production of proteins to see what effects, if any, occur from exposure to ELF fields.

Among the animal experiments at CDRH is a study to determine whether ELF fields can alter early development of chicken embryos. This is an attempt to confirm reports of embryonic defects reported by another laboratory.

Electric Blankets

Also prompting CDRH investigation is concern over ELF fields emanating from electric blankets, particularly because the products are close to the body for long periods.

According to ELF researcher Jon Casamento, an electrical engineer with CDRH's electrophysics branch, the impetus was a letter signed by 18 members of Congress citing an Office of Technology Assessment report that fields from electric power systems may pose a health hazard, as well as two studies that suggested health risks were related to use of electric blankets.

"They wanted answers," Casamento says, "and fast."

He describes how he sketched a testing table on the back of the envelope and that same day went to the hardware store and bought 2-by-4's and other materials just as the store was closing. The next day he put the table together with wooden dowels—no nails, "since metal would have affected results," he says.

To avoid interference from power lines and other electrical sources, Casamento's group created an ELF laboratory from a room whose walls, ceiling and floor were grounded.

A polarized outlet's silver screws and large tine openings (left) indicate the neutral (white) line, while copper screws and small openings (right) indicate the hot (fat black) line. The dark thin wire is bare copper and is the ground line. An electric blanket whose plug has both a large tine and a small tine ensures correct insertion, preventing an excess electric field during use.

After sampling blankets on the market, they identified two types of electric blanket—one brand or type with a weak ELF magnetic field and the other brands or conventional types of blankets with stronger ELF magnetic fields. To ensure accuracy in testing the samples, they sewed registration grids on each blanket so they'd always know to test the same place. They also had the testing probes precisely calibrated.

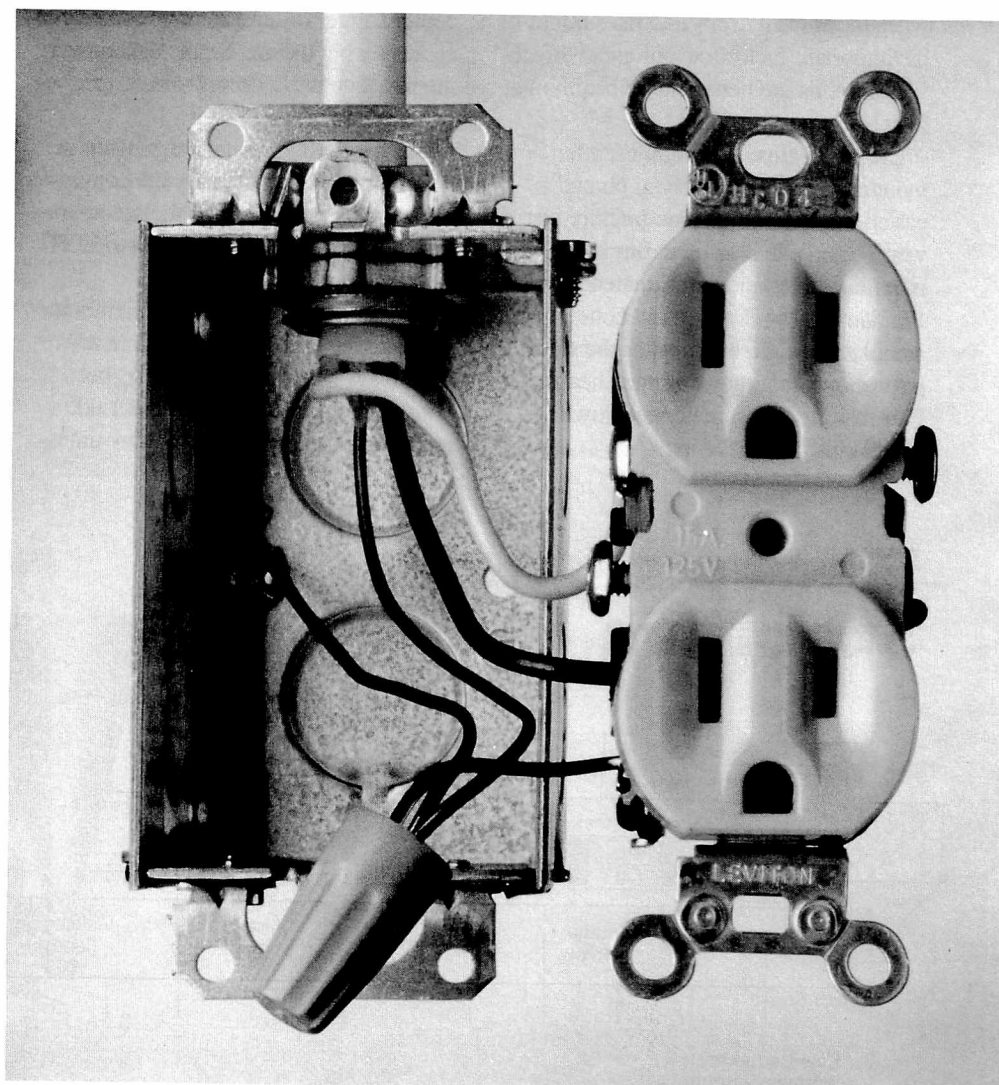
Their findings:

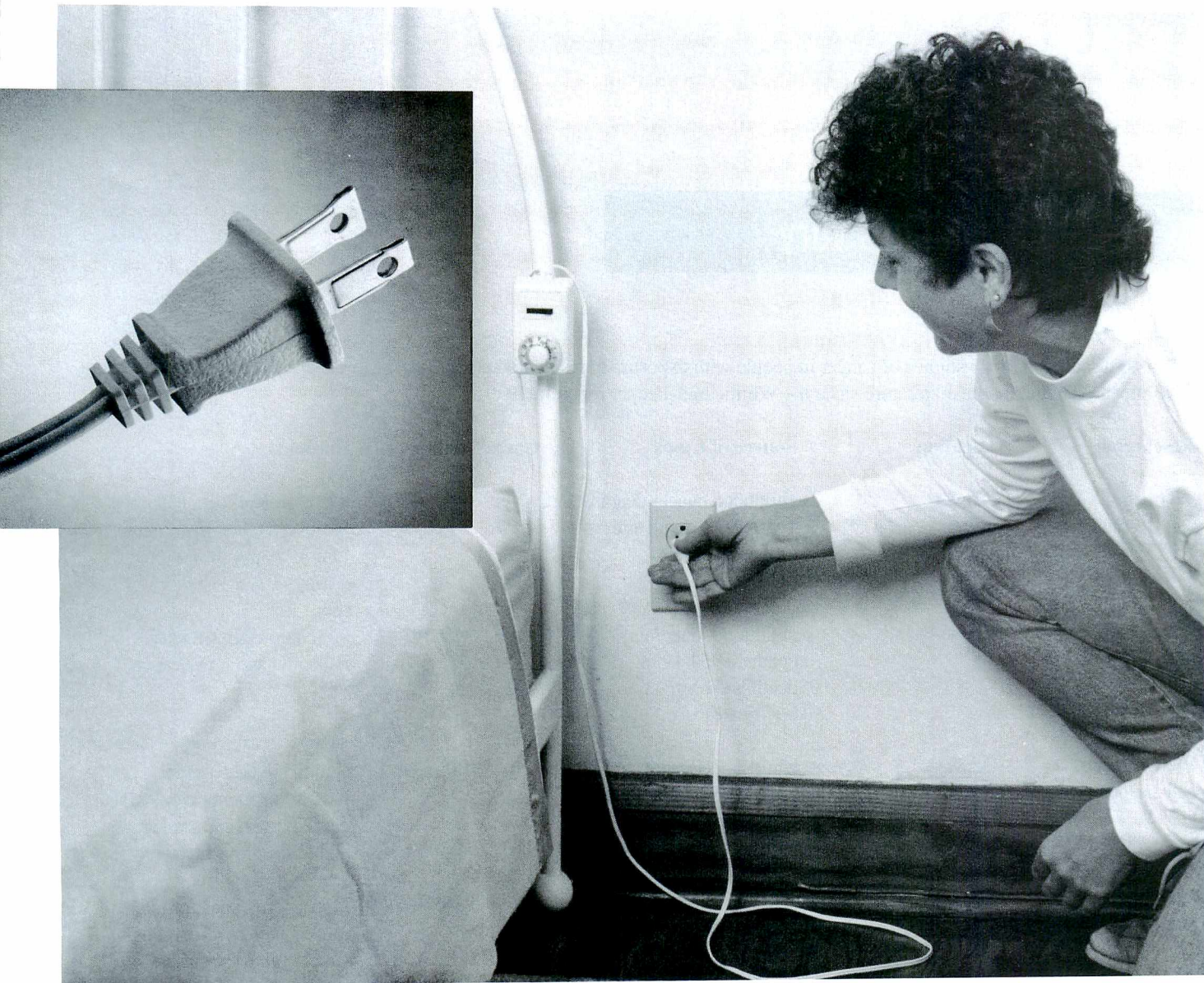
- At 2 inches away, the weak-magnetic-field blanket emitted an average of 0.7 mG, with some grids up to 2.9 mG. At the surface, it produced about 12 mG average and about 23 mG peak.
- At 2 inches away, the conventional blankets emitted an average of 21 mG, with some grids up to 38 mG. Surface emissions averaged 173 mG, with a peak in some grids of 186 mG.
- All blankets could produce electric

fields exceeding 100 volts per meter.

"An additional finding," Casamento says, "was that some power plugs weren't polarized, which means they could be plugged in wrong." (Newer blankets have polarized plugs with one tine larger than the other to prevent incorrect insertion.) When he put an unpolarized plug backward into the outlet, electric fields from the blanket were as high as 248 volts per meter with the blanket turned off, since the switch was then only interrupting the neutral line.

Casamento and other CDRH scientists reported their findings on Nov. 14, 1990, to the Technical Electronic Product Radiation Safety Standards Committee, an expert advisory panel to FDA. They also reported that some human studies suggested a link between ELF emissions from electric blankets and cancer, that other human and animal research did not, and that no studies established an increased risk of





The lack of bumps on the heating wire inside this electric blanket identifies it as the new style with a polarized plug (inset), which can't be inserted backward in an outlet. It doesn't matter that the outlet is upside-down, provided the wiring is correct.

Watts a Hertz?

Electromagnetic radiation, as its name implies, contains both electric fields and magnetic fields. The terms used to describe these fields are:

- **alternating current (AC)**—back-and-forth movement of electric current in 360-degree cycles
- **amps**—a measure of the number of electrons flowing per second in an electric current
- **gauss**—a measure of magnetic field strength (the Earth's magnetic field is less than 1 gauss)
- **hertz**—times per second that the AC cycles (U.S. electricity is AC and flows at 60 hertz)
- **milligauss**—one-thousandth of a gauss
- **volt**—electric potential
- **watts**—electric power consumed by an appliance ■

—D.F.

ELF Study Findings Vary

This is a selection of six studies of cancer in people with exposure to residential power lines. More than 200 ELF research reports have appeared in the medical literature since the Wertheimer-Leeper report in 1979.

Researchers	Location	Source of Cases	Cases/Controls	Findings
Wertheimer and Leeper (1979)	Denver	childhood cancer deaths, 1950-1973; death and birth certificates	344/344	2- to 3-fold excess leukemia, lymphoma, nervous system tumors near high-current wiring
Fulton and others (1980)	Rhode Island	childhood leukemia deaths, 1964-1978; death and birth certificates	119/240	no relationship between leukemia and power lines
Wertheimer and Leeper (1982)	Denver	adult cancer deaths and cases, 1967-1979; death certificates, cancer registry	1179/1179	significant increase in lymphoma and nervous system, uterus, breast cancer near high-current wires
Tomenius (1986)	Sweden	childhood cancer cases, 1958-1973; cancer registry	716/716	2- to 3-fold excess of total cancer, increased nervous system tumors near high-current wires
Savitz (1987)	Denver	childhood cancer cases, 1976-1983; cancer registry	125/189	some increase in total cancer, especially leukemia: odds ratio = 2 to 1; based on home fields and power lines
Stevens and others (1987)	3 counties, Washington	adult leukemia cases, 1961-1984; regional cancer registry	164/204	no association between leukemia and home fields or power lines

(Source: *Biological Effects and Medical Applications of Electromagnetic Energy*, Prentice Hall, 1990)

miscarriage or birth defects because of exposure to the mother. The panel concluded the evidence did not warrant regulatory action.

Nevertheless, CDRH has been working with manufacturers to keep fields as weak as possible.

"The only firm still producing blankets developed a technique to reduce magnetic fields by 95 percent," Casamento says. Casamento is working on a method for shielding the electric field, which would be patented by the government and thus be available to industry.

Some older-type blankets may yet be in stores as the other firms sell off their stock, he says. "The clue to the new weak-field blankets is they don't have little bumps, which were the older blankets' on-off safety switches to protect against overheating. The weak-field blankets are wired in such a way that, instead of one wire being the heater, two wires are embedded in plastic, which conducts the electricity to heat with automatic control, no switches."

Although the new blankets have polarized plugs, improper house wiring can increase the electric field when the product is plugged in, but turned off—though it has no magnetic field. A device to check outlets is available from some hardware stores for about \$2. With proper house wiring, when a product with a polarized plug and correct wiring is plugged in and turned off, there should be no electric or magnetic fields emitted from the product.

CDRH is sponsoring a study at the University of Arizona, in Tucson, to calculate bodily currents induced by electric blankets.

VDTs

At the same November 1990 panel meeting where the findings on electric blankets were reported, physicist Donald Witters of CDRH's electrophysics branch also gave the center's views on possible risks posed by video display terminals, used with computers and word processors. Claims of health hazards, mainly miscarriage, associated with electromagnetic fields around VDTs, are clouded by the inability to reproduce test results, Witters says.

"We made it clear that from our experiences and from all the literature we re-

viewed that we didn't see VDTs as posing a hazard," Witters says. "We preferred to work with the manufacturers to voluntarily reduce the fields to ease the public's perception of possible risk, even though nothing had been demonstrated. The panel agreed with that."

Most manufacturers have voluntarily reduced fields in newer VDT models. Witters says this is a "market-driven" choice to compete with European-made VDTs, which meet a 1990 Swedish standard that limits fields.

In the United States, a committee of the Institute of Electronic and Electrical Engineering, a professional organization, is drafting a voluntary VDT standard based on the Swedish one. Witters and several others at FDA participate on this committee.

Like the Swedish standard, the IEEE proposal specifies how many and where VDT field measurements are to be made, what instruments are to be used, and what protocols are to be followed.

The IEEE committee decided not to limit field levels.

"There's no hard evidence that one level is more hazardous than another," Witters says, "or that lower levels are even better. Is 10 mG a problem? Don't know. Is 100 mG a problem? Is 1 mG a problem? We just don't know. At any rate, most American VDT manufacturers have already reduced their products' fields."

He says that if straightforward information indicated that certain levels pose a higher risk than others, "we obviously would push for a limitation."

One of the FDA scientists reviewing the IEEE draft is William Boivin, a physicist with the agency's Winchester Engineering and Analytical Center, located in Winchester, Mass. WEAC routinely takes measurements for CDRH on electronic products, including television sets, microwave ovens, and VDTs. As Boivin does his regular VDT sampling, he will follow the IEEE draft standard in measuring the electromagnetic fields, thus building a data base for CDRH over the next few years.

Meanwhile, consumers may want to avoid being close to the backs of VDTs, where electromagnetic fields are greatest. (See also "Playing It Safe at Work" in the

For More Information

The lay-language booklet "Electric and Magnetic Fields from 60 Hertz Electric Power: What do we know about possible health risks?" by W. Granger Morgan, Ph.D., is available for \$3.50 from the Department of Engineering and Public Policy, Carnegie Mellon University, Pittsburgh, PA 15213.

The booklet is based on *Biological Effects of Power Frequency Electric and Magnetic Fields—Background Paper*, which Morgan co-authored for the Office of Technology Assessment. The paper is available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone (202) 783-3238. When ordering, please cite GPO No. 052-003-01152-2 and send a check or money order for \$4.75 payable to Superintendent of Documents. ■

October 1991 *FDA Consumer*.)

Given the pervasiveness of electrical products in today's society, uncertainty about the safety of ELF fields can be unsettling. Until more conclusive research results are in, however, scientists won't know whether a health problem exists. Stay tuned. ■

Dixie Farley is a staff writer for FDA Consumer.

M

edication and Labor





Birthng Babies In The '90s

by Dori Stehlin

Almost every pregnant woman wonders how her labor is going to be. Will it be long and difficult? Will it be so short she'll barely make it to the hospital? And what about the pain?

"There are some women who come in and they're 9 centimeters dilated [dilation is complete at 10 centimeters, when the baby is usually ready to come out], and they say, 'I'm not really sure if I'm in labor,' " says Marion McCartney, a certified nurse-midwife in Bethesda, Md.

Phill Price, M.D., helps Vanessa Jones prepare for a contraction in Providence Hospital in Washington, D.C. After 14 hours of labor and a normal vaginal delivery, Jones gave birth to a girl. Price, who also reviews drugs for FDA, is an obstetrician/gynecologist.

**If the
analgesics
don't provide
enough relief,
epidurals
may be the
next step.**

No pain; just a little discomfort and then the baby slides out. Wouldn't that be great?

McCartney says it happens. She also says that there are some women who, from the beginning, are in terrible agony. "Those are the extremes," says McCartney. "All the rest of us sort of fall in the middle. You can deal with the early part of labor and you can deal with the middle part of labor and then from 7 to 10 centimeters it really is terrible."

How does a woman deal with the terrible part? For a low-risk woman—one without any medical problems such as diabetes or high blood pressure—the way she copes frequently depends on the philosophy of the person giving her medical care.

Pain, Pain Go Away

Should a woman in labor receive pain-killers and anesthetics? While some natural childbirth proponents believe that women who are knowledgeable about and well-prepared for labor will be able to handle the pain without drugs, some medical professionals can't imagine why any woman would want to deal with "unnecessary" pain.

Yet there is a middle ground.

"Labor and delivery should not be an ego trip," says Phill Price, M.D. "It's not about how much pain a woman can endure. It is about producing a healthy baby with a happy mother who is not traumatized for the rest of her life."

That said, Price, who has a private obstetrics practice in Washington, D.C., and reviews new drug applications for the Food and Drug Administration, is quick to point out that drugs are *not* the only answer. First he encourages his patients experiencing labor pains to walk and to breathe in patterns learned in prepared childbirth classes. At the hospital where he delivers babies, there's even a Jacuzzi

whirlpool bath that some women find eases the pain.

"The key to having a baby is the ability to relax between the pains," he says. "If you can do it with breathing, fine. If you can do it with a Jacuzzi, fine. But it's easier said than done."

He explains that while many women may think they're relaxing between contractions, "they're actually waiting for that next pain to come. With drugs, a woman may actually go to sleep during the minute or two between contractions."

The drugs that can reduce the pain are either narcotics such as Demerol or non-narcotics such as Nubain. The drugs should be administered only when a woman is between 3 centimeters and 8 centimeters dilated.

"The timing is most important," he says. The drugs may cause breathing problems for the baby if it is born with the drug in its system. Demerol should not be given within two hours of birth and Nubain not within one hour.

Epidural: A Double-Edged Sword

If the analgesics don't provide enough relief, epidurals may be the next step. Epidurals are anesthetic drugs that cause a loss of pain sensation in the lower half of the body by blocking the pain messages the nerves around the spine normally send to the brain. Injected into the lower back, the amount of numbness depends on the amount of the drug used.

Because administration of an epidural requires the skills of an anesthesiologist, nurse-midwives who, like McCartney, deliver at birth centers instead of hospitals must transfer their patients to a hospital if an epidural is necessary.

Anesthesiologist Murray Malin, M.D., who practices at the Columbia Hospital for Women in Washington, D.C., feels the benefits of epidurals far outweigh the

risks, especially if the medication is given continuously through a pump. Not used routinely as little as five years ago, a pump allows a much lower concentration of the drug than would be necessary if the drug were given in intermittent doses.

When a pump isn't used, a higher dose of the drug becomes necessary to ensure enough pain relief as the medication's effects wear off, and this could result in a drop in the mother's blood pressure. That, in turn, could cause fetal distress. While those risks aren't eliminated with the use of a pump, they are substantially reduced. However, other risks still exist.

"Epidurals are a double-edged sword," says Price. "They help to relieve pain. They also have a tendency to arrest labor. Worst of all, epidurals take away the bearing down reflex [necessary to push the baby out]."

Those disadvantages—slowing the labor and not being able to push—outweigh the benefits, according to McCartney.

If labor slows down, the woman may be given Pitocin (oxytocin), a synthetic hormone, to speed things up. But contractions resulting from Pitocin are usually stronger than naturally occurring ones and may cause some fetal distress.

"The safest way to have babies is not to have any medication," she says. "Only if there is a problem—a terribly long labor, the woman is exhausted—should you start to intervene. You shouldn't intervene in a process that's going very well. Save those good anesthetics for people that really, really need them."

Forceps Controversial

A forceps is a surgical instrument that looks like two large spoons or salad tongs. A medical device, it is regulated by FDA. The doctor inserts the forceps into the birth canal, places the "spoons" around the baby's head, and, with each contraction,

moves the baby down, and eventually out of, the birth canal.

Another medical device, the vacuum extractor, may be used in place of forceps. The extractor consists of a soft plastic or rubber cap held in place on the baby's head by suction from a vacuum pump.

Medical reasons for forceps delivery include a slow or irregular fetal heartbeat, failure of the baby's head to rotate into the proper position, or failure of the mother to push because of fatigue or an epidural.

Outlet forceps delivery—when the head is visible at the vaginal opening—involves the least risk. A study by Michael K. Yancey, M.D., and colleagues at the Madigan Army Medical Center, Tacoma, Wash., reported in the October 1991 issue of *Obstetrics and Gynecology*, found that an outlet forceps delivery in an uncomplicated labor causes no immediate harm to the baby. (The study did not address the possibility of any long-term effects.) However, the study did find these mothers had increased incidence of cuts and tears in the perineum (the area between the anus and the vagina) compared to women whose babies were delivered without forceps.

The risk level of outlet forceps delivery increases as the doctor moves the forceps higher into the birth canal.

"Difficult forceps deliveries involving a lot of rotation of the baby's head or pulling it down from high up in the birth canal are done quite infrequently in most parts of this country," says Wayne R. Cohen, M.D., vice chairman of the department of obstetrics and gynecology at the Albert Einstein College of Medicine in New York City. "The basic principle is that the more difficult the forceps delivery, the greater the risk."

The risks from a difficult forceps delivery range from minor injuries to the baby's head, such as bruises and indenta-

The risk level of outlet forceps delivery increases as the doctor moves the forceps higher into the birth canal.

Baby's Heartbeat a Harbinger

The unborn baby's heart rate is an important indicator of how things are going. The heartbeat can be monitored by a caregiver with a special stethoscope called a fetoscope or by an electronic fetal monitor.

Electronic fetal monitors, which are FDA-approved medical devices, measure the baby's heart rate continuously in one of two ways: externally or internally. With external monitors, two belts are placed around the mother's abdomen. One belt uses ultrasound to monitor the baby's heartbeat while the other measures the length of contractions. Internal monitors measure the baby's heart rate through an electrode attached to the baby's scalp.

Both types of monitors usually require the mother to stay in bed so the belts or electrodes stay in place.

Although measuring and recording every heartbeat sounds ideal, not everyone thinks the technology is an advantage.

"When I started delivering babies in 1971," says FDA's Phill Price, M.D., "physicians really believed that electronic fetal monitoring would be a tool that would tell us if a baby was going to be in trouble. But the last 5 to 10 years have told us that electronic fetal monitoring has not done a lot to actually improve the overall care of mothers or babies."

The theory behind the continuous monitoring is that the caregiver could note a change in the baby's heart rate immediately and take immediate action to prevent any harm to the baby. That action, almost always, is a Caesarean section.

The harm doctors are most concerned about is oxygen starvation, which can lead to conditions such as cerebral palsy.

However, in the last 25 years the incidence of cerebral palsy has remained the same—3 per 1,000—whether the patient was monitored or not, says Price.

Some babies are going to have problems, and in all likelihood those problems occurred during the nine months of pregnancy, he explains. "To think that because I waited 5 or 10 or 15 minutes before do-

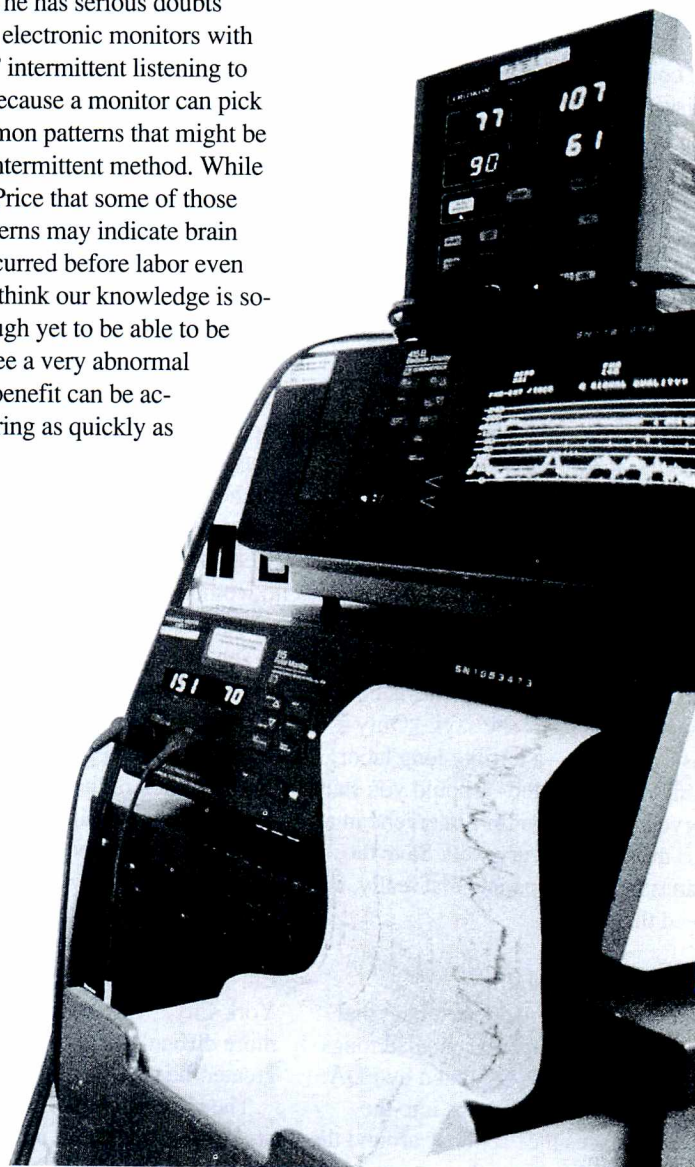
ing a C-section the baby will come up with cerebral palsy is ludicrous," he says. "If you have a nurse who listens every 15 minutes in the first stage of labor and every five minutes in the second stage, you can get the same outcome."

"If I'm physically present, I can be pretty sure if things are fine or if things are starting to go wrong," says Barbara Good, a certified nurse-midwife in Takoma Park, Md.

But Wayne Cohen, M.D., of the Albert Einstein College of Medicine in New York City, says he has serious doubts about replacing electronic monitors with "old-fashioned" intermittent listening to the heart rate, because a monitor can pick up very uncommon patterns that might be missed by the intermittent method. While he agrees with Price that some of those uncommon patterns may indicate brain damage that occurred before labor even began, "I don't think our knowledge is sophisticated enough yet to be able to be sure when we see a very abnormal pattern that no benefit can be accrued by delivering as quickly as possible." ■

—D.S.

On the electronic fetal monitor (bottom and middle instruments), a printout gives continuous readings for the baby's heart rate and the mother's contractions. (The screen displays the same readings.) The numbers to the left of the printout are the heart rate (151) and strength of contraction (70). The box on top of the monitor indicates the mother's mean arterial pressure (77), pulse (90), and blood pressure (107/61).



tions—both temporary—to serious problems, including skull fracture, eye injury, facial paralysis, and brain damage. Forceps may also cause damage to the mother's bladder or urethra (the tube that carries urine from the bladder to the outside of the body).

If the baby must be delivered right away, says Cohen, a Cesarean section (surgical delivery of the baby through an incision in the abdominal and uterine walls) involves less risk to both mother and baby and is therefore usually preferable to a difficult forceps delivery.

Besides helping a baby in distress, another reason for using forceps often cited by obstetricians is to shorten the second stage of labor and, in turn, reduce the risk of damage to the pelvic floor and tissues supporting the bladder and rectum that might occur with prolonged pushing. (The second stage of labor begins when the cervix is fully dilated and ends with the baby's birth. It can last for more than two hours, especially during a first labor.) But according to Yancey's study, routine use of forceps "does not significantly shorten the second stage of labor."

"No one wants to put forceps on babies unless there's a medical reason for doing it," says Price. That's why he tells his patients that he will let the epidural wear off so they can feel and push the baby out themselves.

McCartney advocates that women be allowed to keep pushing as long as fetal heart tones are good and progress is being made.

Cohen agrees. "Intervening with forceps during the second stage offers no advantage to the fetus as long as the fetal condition is good."

Cut or Tear?

Another intervention, one of the most common surgical procedures performed in North America, is episiotomy, the cutting of the perineum. The rationale behind routine episiotomy—that cutting is safer for the mother than the tearing that sometimes

occurs during delivery—has been increasingly questioned in recent years.

The two types of episiotomies are:

- *Midline*—cut straight down from the vagina in the direction of the rectum. Considered to be more comfortable afterward and easier to repair.
- *Mediolateral*—perineum is cut diagonally to one side. Will prevent a tear from continuing on to the rectum, but is more difficult to repair and takes longer to heal than midline.

The American College of Obstetricians and Gynecologists recommends that doctors perform episiotomies if the baby is large, the woman's perineum is short, or to make room for a forceps delivery.

In addition, while an episiotomy can speed delivery by only a few minutes, even that amount of time can be critical if the baby is in distress.

But what about performing episiotomy just as a measure to prevent tearing?

The common philosophy is that a straight cut will be less painful and heal quicker than a jagged tear. But according to a study in the July 1, 1992, *Online Journal of Current Clinical Trials*, there was no difference in pain levels or recovery time between women who had an episiotomy and women who had spontaneous tissue tears.

The theory that an episiotomy prevents severe, out-of-control tears that reach the rectum was also refuted in that study. Doctors who restricted the use of episiotomies to cases of fetal distress or forceps delivery had a severe tear rate of 4.9 percent. The other group of doctors, who performed episiotomies on all patients, had a severe tear rate of 23 percent.

Even without the severe tear, any woman who gets an episiotomy gets a second-degree laceration, which means underlying tissue is involved. (Third-degree lacerations extend to the rectal sphincter (muscle) and fourth-degree go into the rectum.)

However, many women don't tear at all while giving birth or only tear the skin

(first-degree laceration). First-degree tears may not require any stitches.

Another argument often cited to support performing episiotomies is that without the incision, the pressure on both the perineum and the baby's head could cause long-term damage to the mother's pelvic floor or to the baby's brain.

There are no strong studies to support or refute that hypothesis, according to Stephen B. Thacker, M.D., a researcher with the national Centers for Disease Control.

Preventing tears is possible in some cases, but it requires extra effort from both the mother and the person delivering the baby.

Delivery position is one important factor in preventing tears. McCartney recommends upright positions such as sitting, squatting or kneeling because in these positions "the pelvic area, including the perineum, is relaxed, and pushing with gravity is easier."

Finally, the caregiver needs to encourage the mother not to push the baby out too fast. McCartney always tells her mothers, "I want you to push this baby out one hair at a time so you don't tear."

The Personal Touch

Perhaps the most important thing to remember is that one 'normal' labor may be very different from the next, says Price. "Things should be individualized," he says. "All deliveries are not the same."

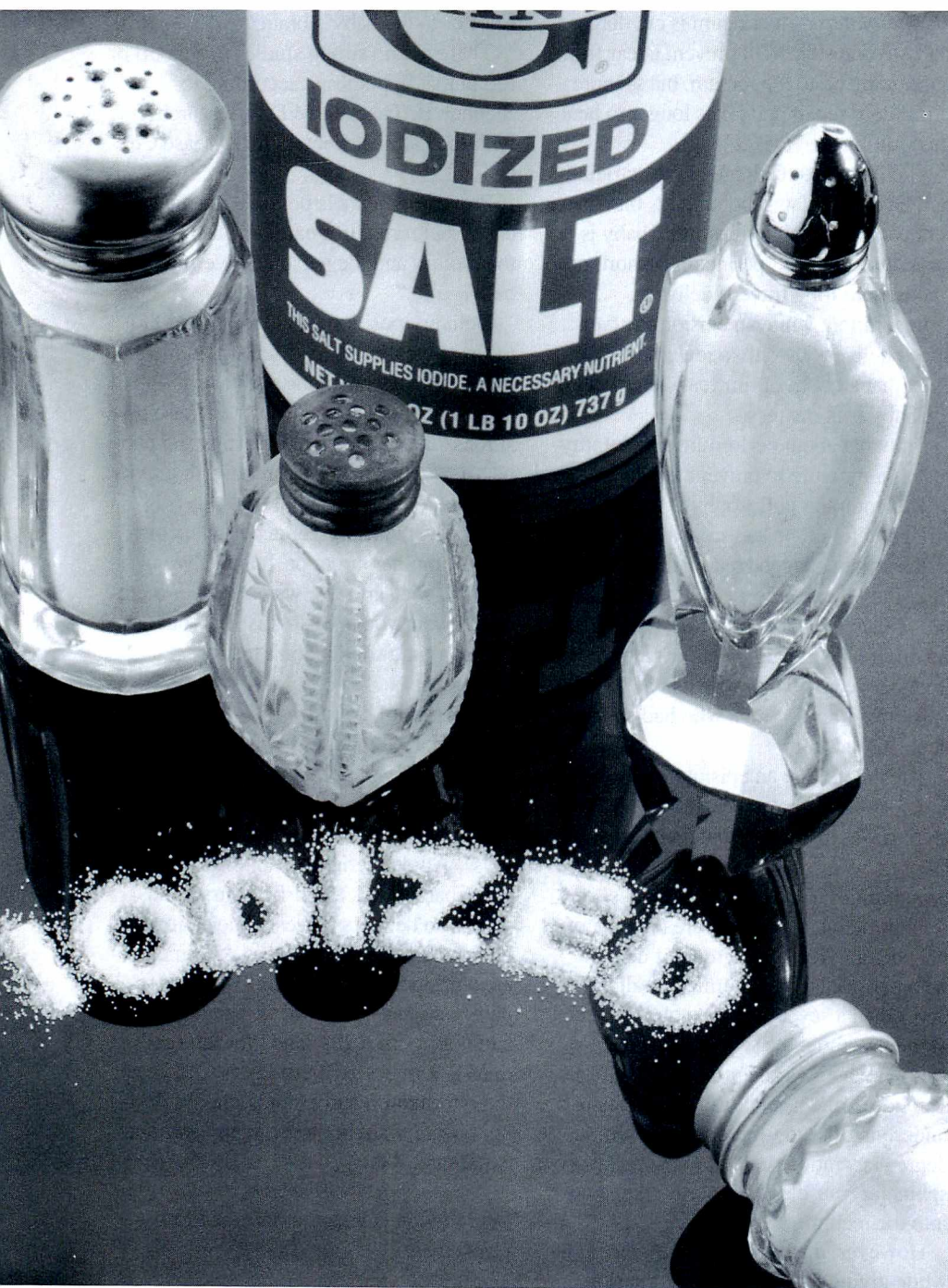
Barbara Good, a certified nurse-midwife who delivers babies at the Columbia Hospital for Women, agrees. "Women are very individual in their responses to pain," she says. "If a woman says, 'I've had it and I'm really ready for [an epidural],' I'm not going to say no. I share the information and I let her choose. It's her birth. I want her to be happy with the experience." ■

Dori Stehlin is a staff writer for FDA Consumer.

Many Treatments Available

Thyroid Disorders Often Unsuspected

by Evelyn Zamula



Before the introduction of iodized salt in 1922, in certain areas of Switzerland almost every school child had a greatly enlarged thyroid gland, or goiter. Up to 30 percent of the country's young men were rejected for universal military service because of large goiters, although those with small ones were taken. About 1 in every 200 Swiss in these areas had cretinism, a condition characterized by dwarfism and mental retardation.

As early as 1850, cretinism was ascribed to severe iodine deficiency during gestation. Yet, as late as 1930, some Swiss medical experts remained unconvinced that lack of dietary iodine caused goiters.

The iodine content of soil and water was not uniform throughout Switzerland. A 1907 study found that laboratory rats fed water and milk from eight different villages for more than a year developed large goiters when their diet came from areas with insufficient iodine. Rats fed water supplemented by iodide did not develop goiters. Nevertheless, some scientists maintained that unknown agents found in drinking water and food, rather than lack of iodine, were responsible for goiter development.

This argument was refuted by history. After 1922, goiter rapidly disappeared in Switzerland in newborns and children, more slowly in the draftees, and incompletely in elderly adults.

Early in this century, the United States had pockets of goiter in areas where soil was iodine-deficient, such as in the Midwest and the Great Lakes area. Goiters were the chief medical reason for rejecting recruits for Army service during World War I. In 1924, the Michigan Department of Health permitted the sale of

salt with the addition of potassium iodide, a soluble form of iodine. Thereafter, iodized salt was distributed nationwide (although iodization is not mandatory in this country).

In response to the 1958 Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act, FDA evaluated the safe use of potassium iodide as a source of dietary iodine. In 1972, FDA affirmed its use at 0.01 percent in table salt as GRAS (generally recognized as safe).

Iodized salt, along with an excellent food distribution system that makes seafood and foods grown in iodine-rich soils available to all, has made goiter due to insufficient dietary iodine a thing of the past in the United States and all developed countries. (See accompanying article.)

Severe iodine shortages still exist in other parts of the world because iodine is distributed unevenly in the environment. The World Health Organization estimates that as many as 200 million people in developing countries have goiters due to iodine deficiency.

Lack of dietary iodine is not the only cause of goiter. The thyroid may enlarge when it is underactive or overactive, inflamed or infected, or when a congenital condition prevents it from manufacturing thyroid hormones. Benign or cancerous lumps that develop in the gland may make it appear enlarged. Appropriate treatment by medication or surgery will reduce the enlarged thyroid gland to normal size in almost all cases.

The Thyroid Gland

The thyroid gland is a small butterfly-shaped gland that wraps around the windpipe just below the Adam's apple. The thyroid takes dietary iodine from the blood

and uses it to make iodine-containing hormones called thyroxine (T_4) and triiodothyronine (T_3). The thyroid stores these hormones until needed. Then the thyroid releases the hormones into the bloodstream and they travel to all parts of the body, affecting almost every cell and most organs, including the heart, brain, liver, kidneys, and skin.

These hormones have many important functions. Because they regulate the rate at which calories are burned, they may cause weight loss or gain. They help slow down or quicken the heartbeat and raise or lower body temperature. They influence the rate at which food moves through the digestive tract, the way muscles contract, and the rate at which dying cells are replaced.

A healthy thyroid gland dispenses just the right amount of hormone to meet the body's metabolic needs. But if the gland becomes diseased, it may produce too little thyroxine (hypothyroidism) or too much (hyperthyroidism). The thyroid is under partial control of the pituitary—a pea-sized gland at the base of the brain. When the pituitary senses a low level of thyroxine in the blood, it secretes thyroid-stimulating hormone (TSH), which stimulates the thyroid gland to make more hormone. Conversely, if the pituitary senses too much hormone, it will secrete less TSH, and thyroxine levels fall.

Hypothyroidism

Of the 6 million to 7 million Americans who have underactive thyroid glands, probably half don't seek medical treatment because they don't know they have a problem. They are likely to accept their symptoms—fatigue, muscle weakness, dry skin, hair loss, depression, cold intolerance, constipation—as signs of normal

aging. Hypothyroidism occurs four times more often in women than in men, most frequently in middle-aged women between the ages of 35 and 60, and in the elderly. There is a strong tendency for all kinds of thyroid disorders to run in families.

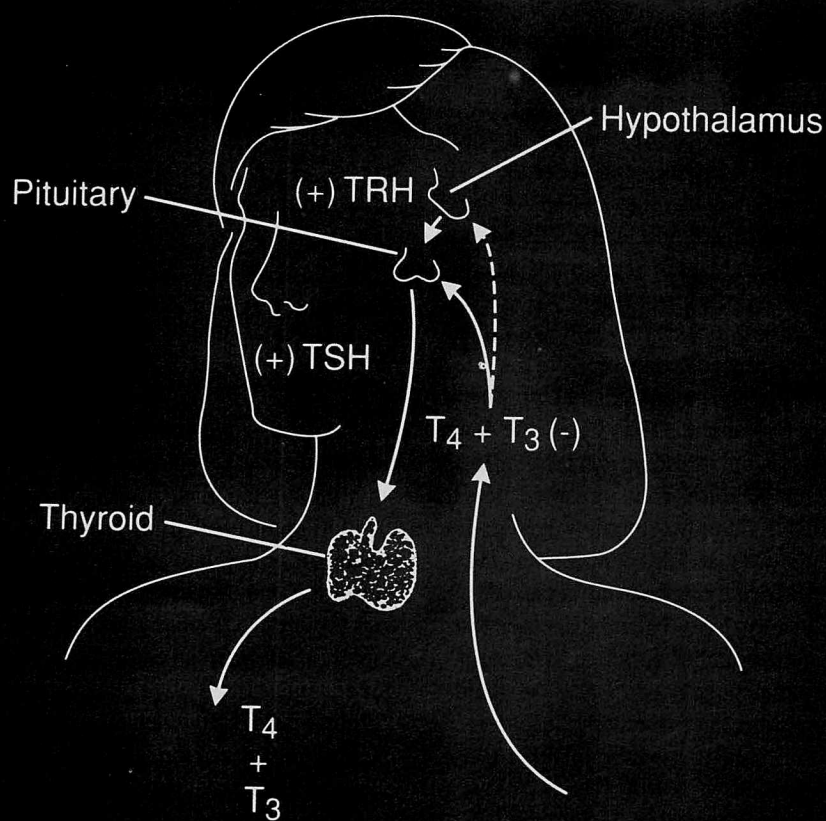
The most common cause of hypothyroidism is a chronic, progressive condition called Hashimoto's disease. Hashimoto's disease is an autoimmune disorder, in which the body's immune system produces antibodies that attack its own tissues. As the antibodies slowly destroy the thyroid gland, it cannot manufacture sufficient amounts of thyroid hormones for proper body functioning. This causes the pituitary to secrete more TSH, thus forcing the thyroid gland to work harder, resulting in an enlarged gland, or goiter.

People who have received x-ray treatment for cancers of the head and neck may eventually become hypothyroid, if the thyroid gland was inadvertently exposed to radiation. Lower-dose radiation commonly used from 1920 to 1960 to treat children for acne, enlarged thymus gland, scalp ringworm, birthmarks, enlarged tonsils, and adenoids also increases the risk of hypothyroidism. (As many as 7 percent of children and adolescents who had such radiation therapy developed thyroid cancer 10 to 40 years later.) Goiter is not usually present in these types of hypothyroidism, because the thyroid gland has shrunk.

The thyroid gland can be infected by viruses and bacteria that cause it to become temporarily underactive, but these infections can be treated with medications and do not usually result in permanent hypothyroidism.

One in every 4,000 to 5,000 babies is

How the Thyroid Gland Works



The hypothalamus produces thyrotropin-releasing hormone (TRH), which stimulates the pituitary gland to produce thyroid-stimulating hormone (TSH). TSH stimulates the thyroid gland to produce hormones T₃ and T₄. When the pituitary senses a decrease in T₃ or T₄, it produces additional TSH to stimulate the thyroid gland to produce more hormone.

(Copyright 1992 Boots Pharmaceuticals, Inc. Reprinted with permission by Boots Pharmaceuticals.)

born hypothyroid in the United States. This occurs when babies are born without a thyroid gland or with one that functions poorly. Some babies inherit disorders that prevent their thyroid glands from making sufficient thyroid hormone. Because cretinism in babies is irreversible if not treated with thyroid hormone as soon as possible after birth, all newborns in the United States are screened for hypothyroidism.

When hypothyroidism is suspected, the doctor bases the diagnosis on the patient's symptoms and blood tests that measure the amount of thyroxine and TSH circulating in the blood. A high level of TSH, which is a sign that the pituitary detects thyroxine deficiency, and a low level of thyroxine are indications that the thyroid is underactive.

Treatment of Hashimoto's disease has come a long way from the days when thyroid glands from sheep, pigs or cows were sautéed and eaten. Beginning in the 1880s, liquid extracts of these glands were given intravenously or orally, then manufactured into tablets, which were in use until the 1960s. Today, synthetic thyroxine developed in the early 1970s is the mainstay of thyroid hormone replacement. Drugs most commonly used are Synthroid or Levothroid (levothyroxine). People with Hashimoto's disease must take these medications for the rest of their lives, because the thyroid gland has been permanently damaged.

One complication of severe and long-standing hypothyroidism is called myxedema. Persons with this disorder become very cold and drowsy, and may eventually lapse into a coma. Uncommon in tropical climates, this rare condition may be brought on by cold weather, infection, or the use of some drugs, especially sedatives. About 50 to 60 percent of people with hypothyroid coma die. FDA approved Triostat (liothyronine sodium), an intravenous thyroid hormone replace-

Signs & Symptoms of Thyroid Disease

Hypothyroidism

Tiredness
Depression
Forgetfulness
Loss of lateral
eyebrow hair
Puffy face and eyes
Dry, coarse hair

Goiter

Slow heartbeat

Dry skin

Cold intolerance

Weight gain

Heavy
menstrual
periods

Constipation

Brittle nails

Hyperthyroidism

Nervousness
Irritability
Difficulty sleeping

Bulging eyes,
Unblinking stare

Goiter

Rapid heartbeat

Increased sweating

Heat intolerance

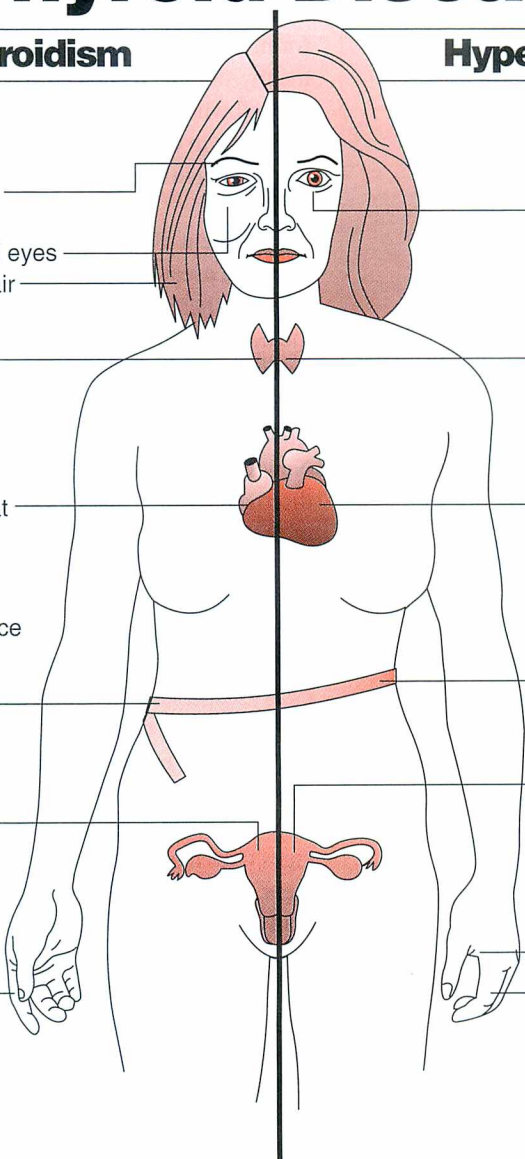
Unexplained
weight loss

Scant
menstrual
periods

Frequent bowel
movements

Warm, moist palms

Fine tremor
of fingers



ment drug for the treatment of myxedema coma and pre-coma, in 1991.

Hyperthyroidism

Another autoimmune disorder that affects the thyroid gland is Graves' disease, the most common type of hyperthyroidism. Antibodies do not destroy the thyroid gland, as in Hashimoto's disease, but stimulate it to produce too much thyroid hormone.

No one knows what causes Graves' disease. Sex hormones play a part; the disease is seven times more common in women than men, and frequently begins after hormonal changes, such as pregnancy. Stressful situations, such as a death in the family, appear to trigger the autoimmune reaction. The tendency to develop the disease is inherited. Graves' disease afflicts both President and Mrs. Bush.

Hyperthyroidism may also result when one or more nodules or lumps in the thyroid gland become overactive—for no known reason—and secrete too much hormone. Another form of hyperthyroidism, called subacute thyroiditis, may arise following a viral infection, such as mumps, measles, or even a cold. The inflamed thyroid leaks out excessive amounts of thyroid hormones into the bloodstream. This disease is temporary and usually treated by aspirin, propranolol (Inderal) or corticosteroids.

Symptoms of an overactive thyroid include goiter, weight loss despite increased food intake, rapid heartbeat, scant menstrual periods, warm, moist skin, finger tremor, sensitivity to heat, fatigue, muscle weakness, and frequent bowel movements.

Any type of hyperthyroidism may cause an individual to develop a staring look, because increased levels of thyroid hormone cause elevation of the upper eyelids. However, only in Graves' disease do the muscles and fat around and behind the eyes become so inflamed that eyes are

Some Iodine-Rich Foods

Iodine deficiency is no longer a problem in the United States, with virtually all Americans getting enough of the substance in their diets. The Recommended Daily Allowance (RDA) for iodine for adolescents and adults is 150 micrograms a day (1,000 micrograms = 1 milligram) and 200 micrograms a day for pregnant women. Most Americans consume more than the RDA, but are usually unaffected by excess iodine unless they have underlying thyroid disease.

The following chart gives examples of foods relatively high in iodine.

Food	Serving Size	Micrograms of Iodine
cod or haddock, cooked	3 1/2 oz (100 g)	175
chocolate milkshake (fast food)	1 average (283 g)	158
homemade meatloaf	3 1/2 oz (100 g)	123
lima beans, immature, boiled	1/2 cup (91 g)	104
chocolate ice cream	1 cup (133 g)	94
corn grits, cooked	1/2 cup (121 g)	86
low-fat chocolate milk	1 cup (250 g)	83
navy beans, boiled	1/2 cup (91 g)	78
low-fat yogurt	1 cup (227 g)	73
low-fat milk	1 cup (244 g)	66
skim milk	1 cup (246 g)	64
whole milk	1 cup (244 g)	61

(Source: FDA's Total Diet Study, 1982-1984)

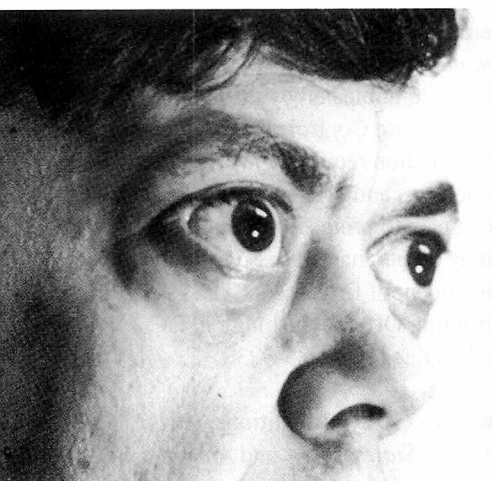
—E.Z.

pushed forward, bulging out of their sockets. The technical term for this condition is exophthalmos.

Blood tests will confirm hyperthyroidism when the levels of thyroxine and triiodothyronine circulating in the blood are abnormally high and when TSH concentrations are low. If the diagnosis needs further confirmation, a radioactive image, or scan, of the thyroid is made. The patient swallows a small amount of radioactive iodine in water or in capsule form. After a 24-hour wait, a picture of the thyroid gland is taken. The scan can tell whether the whole gland is overactive, as in Graves' disease, or whether an overactive nodule is causing the problem.

Treatment of Graves' disease has improved a great deal since the 1800s, when the only therapy was rest and sedation and the death rate was 50 percent. The first breakthrough in the treatment of this disorder came in the 1940s, when physician Edwin Astwood and colleagues at the New England Medical Center in Boston discovered drugs that blocked the ability of the thyroid gland to use iodine in making thyroid hormone. These anti-thyroid drugs, propylthiouracil (PTU) and methimazole (Tapazole), are used when prompt control of hyperthyroidism is necessary, especially in children. Elderly patients with heart disease or arrhythmias can be safely treated temporarily with these drugs.

Anti-thyroid drugs offer several advantages over the most commonly used treatment, radioactive iodine. They do not generally cause permanent thyroid damage, are less expensive, and also may not need to be given indefinitely. However, though they control a hyperactive thyroid gland, they are not necessarily a cure. After long-term drug treatment, only 35 percent of patients experience remission, according to the American Thyroid Association. They may also cause adverse reactions—rashes, hives, fever, joint pains—in 1 out of 20 who take them. One serious complication is that the drugs may decrease the number of neutrophils (white blood cells)



In hyperthyroidism, increased levels of thyroid hormone cause elevation of upper eyelids. This often results in a staring look and can cause droopy eyelids (top), which can be corrected by plastic surgery. In Graves' disease, eyes bulge out of their sockets (bottom) because the muscles and fat around them have become so inflamed.

(Photos reprinted with permission from L.C. Wood et al., Your Thyroid, Houghton Mifflin, 1982)

in the blood, causing a lowered resistance to infection. Rarely, all these white cells disappear from the blood, producing a potentially fatal condition known as agranulocytosis.

Many physicians prefer to treat patients who have Graves' disease or overactive nodules in their thyroid glands with radioactive iodine. The patient swallows the radioactive iodine in capsule or liquid form. The radioactive iodine passes from the stomach into the bloodstream and collects in the thyroid gland, where its radioactivity damages the thyroid cells. Within 48 hours or so, radioactive iodine disappears from the body, either eliminated in the urine or else transformed by decay into a nonradioactive state. Most hyperthyroid patients recover normal thyroid gland function, or even become hypothyroid, three to six months after radioactive iodine treatment. Those who remain hyperthyroid may need a second or even a third dose.

Removing most of the thyroid gland surgically—a delicate procedure that needs to be done by a thyroid surgery specialist—results in a permanent cure for overactivity. Many physicians recommend surgery for patients under 21, for those allergic to anti-thyroid drugs, and for patients with very large goiters.

Nevertheless, surgery is done much less frequently than it used to be. Leonard Wartofsky, M.D., chief of the Endocrine-Metabolic Service of the Department of Medicine at Walter Reed Army Medical Center in Washington, D.C., tells of a survey of physician members of the American Thyroid Association, asking what therapy they would advise for a typical case of hyperthyroidism. Seventy percent of the doctors recommended radioactive iodine, 29 percent anti-thyroid drugs, and

When hypothyroidism is suspected, the doctor bases the diagnosis on the patient's symptoms and blood tests.

1 percent surgery. "Twenty years ago it would have been 20 percent for surgery," Wartofsky said. "Radioactive iodine is easier and much more readily acceptable by patients."

Commonly, radioactive iodine and surgery eventually result in an underactive thyroid, treatable by a thyroid hormone

tablet once a day. This is a less common occurrence with anti-thyroid drug therapy.

After any one of the three treatments, physicians may also prescribe beta-blocking drugs, such as Inderal or Tenormin (atenolol), that block the action of circulating thyroid hormone on body tissues. They are used to slow down the heart rate, lessen nervousness, and generally reduce symptoms until the chosen treatment has had a chance to take effect.

"It's necessary for people with thyroid conditions to see a doctor for the rest of their lives because thyroid conditions evolve and change with time," says Wartofsky. "Whether we're talking about hyper- or hypothyroidism, there's always the possibility of progression or change. Patients should see their doctors on a once-a-year basis. I'd even settle for once every two or three years in some circumstances. Medications have to get renewed anyway, and just touching base with their physicians is a good idea."

Recognizing symptoms of thyroid disease and seeking medical help to ease them are the first steps toward a healthy life for people with thyroid disorders. Whether correcting a thyroid problem requires specialized surgery for overactivity or a pill for underactivity, thyroid hormone balance can be achieved. ■

Evelyn Zamula is a freelance writer in Potomac, Md.

NOTEBOOK



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

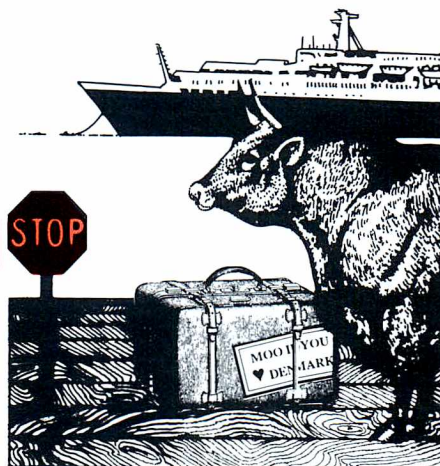
■ **A food advisory committee** was recently established by FDA. The committee of 20 voting members and four non-voting industry consultants will advise the agency on food safety and nutrition issues. Voting members represent disciplines such as life sciences, medicine, law, academia, public health, and consumer protection. Public meetings will be held at least twice a year. For more information, contact FDA's Brad Stone at (202) 205-4144.

■ **Formalin solution** was approved by FDA last Sept. 15 as a new animal drug. It is used to control certain external organisms on salmon, trout, catfish, largemouth bass, and bluegill and to treat certain fungi on eggs of salmon, trout, and other fish. (FR Sept. 15)

■ **Ionizing radiation** to treat fresh or frozen uncooked poultry for food-borne diseases was approved Oct. 21, 1992, by the Food Safety and Inspection Service. Ionizing radiation will control and reduce such food-borne pathogens as *Listeria monocytogenes*, *Campylobacter jejuni*, and *Salmonella*. (FR Sept. 21)

■ **Lead screening of children** will be discussed at the National Childhood Lead Poisoning Prevention Conference, sponsored by the national Centers for Disease Control, Dec. 7 through 9 in Atlanta. Other topics include follow-up, managing the lead environment, community education, epidemiology and surveillance, and direction for the future. For more information, contact Yvonne Chrimes, PACE Enterprises, Inc., 17 Executive Park Drive, Suite 200, Atlanta, GA 30329; telephone (404) 633-8610. (*Morbidity and Mortality Weekly Report*, Sept. 4)

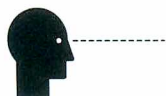
■ **Beef from Denmark** was restricted or prohibited from entering the United States, under an interim rule of USDA's Animal and Plant Health Inspection Service, effective Sept. 22, 1992. The action was taken to prevent spread to this country of spongiform encephalopathy, which has been diagnosed in Danish cattle. (FR Sept. 22)



■ **Boneless and skinless canned coho salmon** can be test-marketed in the United States for 15 months. Its manufacturer, Hegg and Hegg Smoked Salmon, Inc., needed FDA's permission for test-marketing because the canned salmon is significantly different from other brands. (FR Sept. 11)

■ **Inoculations for international travel** are enumerated in the annual *Health Information for International Travel 1992* booklet, published by the national Centers for Disease Control. The booklet specifies vaccination requirements for different countries and offers measures travelers can take to protect their health. Copies may be purchased for \$6 from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone (202) 783-3238.

■ **Two CDC publications**, *Health, United States, 1991*, and *Annual Summary of Births, Marriages, Divorces, and Deaths: United States, 1991*, are now available. *Health* can be purchased for \$18 from the Superintendent of Documents, Government Printing Office, Washington, DC 20402; telephone (202) 783-3238. The summary is free from the Scientific and Technical Information Branch, National Center for Health Statistics, Room 1064, 6525 Belcrest Road, Hyattsville, MD 20782; telephone (301) 436-8500. (MMWR Sept. 4)



Toddler's Blood Test Leads to Juice Recall

by Judith E. Foulke

The discovery of high blood levels of lead in a San Diego toddler led to a nationwide recall last July of canned fruit drinks from Mexico.

Investigators from the California Department of Health Services, San Diego Department of Health, and FDA's San Francisco district laboratory traced the source of the lead to Jumex brand canned fruit drinks manufactured by Empacadores de Frutas y Jugos in Mexico City.

The search for the source began when 1-year-old Cynthia Mejia's blood tests, done in December 1991 as part of a San Diego County screening program for lead in children's blood, showed lead levels up to 36 micrograms (mcg) per deciliter. That's about three-and-a-half times higher than blood lead levels federal health authorities consider to be a potential hazard to children up to 6 years old.

Early in January 1992, a California Health Department investigator went to Cynthia's family's house to try to find the cause of the child's high blood lead level. The family had just moved to a house that did not have lead-based paint, and the examiner suspected that the lead poisoning had come from old paint in the former house.

A second blood test on Jan. 24 showed Cynthia's blood lead level was down to 34 mcg per deciliter, but in April, the level was back up to 36 mcg.

On April 24, Martha Bartzen, senior public health nurse of the San Diego County Public Health Service, went to the family's home to investigate again. Cynthia's mother mentioned to Bartzen that the family often shopped for groceries in Mexico. Bartzen checked the pantry for

products made in Mexico and found cans of Jumex juice. Lead-soldered food cans from Mexico have been a problem in the past. (Although there are no U.S. regulations prohibiting lead-soldered seams, manufacturers here no longer use them.)

Bartzen advised the family not to drink the Jumex products, and sent the cans for analysis to the state laboratory in Los Angeles. Within a month, Cynthia's blood lead level had dropped to 28 mcg, and by July it had dropped to 19 mcg, indicating that the source of lead exposure had been removed.

The acidity of the juice had caused the lead solder from the cans' seams to leach into the juice. FDA estimates the lead

level in the juice averaged 580 parts per billion (ppb) per 12-ounce can. That translates into an intake level of 197 mcg. Based on current knowledge about lead toxicity, FDA has set provisional tolerable total daily intake levels of lead at 6 mcg per day for children up to 6 years.

As a result of the state's investigation, the importer, Vilore Foods, Inc., of Laredo, Texas, issued a recall letter on June 23 to retail distributors in California. But the letter did not include one of the juice flavors, inaccurately identified the pineapple flavor as a juice instead of a nectar, and did not include a response form, as required.

To correct these problems, on June 26, Vilore Foods began visiting distributors to alert them to the recall, and California health officials issued a press release on June 30. On July 13, the firm issued a revised recall letter to all of its 41 distributors of Jumex products in California, Illinois, Indiana, and Texas.

Meanwhile, in mid-June, state officials had sent the juice cans to FDA's San Francisco laboratory. Analysis of these cans and others FDA had collected from San Francisco grocery shelves showed lead levels ranging from 251 ppb to as high as 1,037 ppb. FDA considered the juices to be a severe health hazard to children and pregnant women.

FDA had contacted Vilore Foods Co. on June 26 and learned that the manufacturer had changed to welded seams the previous March. Products from the new cans were analyzed and found satisfactory. However, many of the original lead-soldered cans were still on grocery shelves. On July 31, FDA issued a press release, warning con-



sumers not to drink Jumex brand fruit nectars and pineapple juice with code number 2084 or lower at the bottom of the can.

FDA classified the recall as class I, meaning that use of the product may cause serious adverse health consequences or death.

Although Cynthia had been drinking about three cans of Jumex juice a day, she showed no overt signs of lead poisoning. The elevated blood lead level was de-

tected before clinical signs appeared and permanent damage had been done. California health examiners say follow-up tests on Cynthia did not reveal the developmental problems often associated with lead poisoning.

FDA's San Francisco district investigators continue to watch grocery shelves for lead-soldered food cans. They carry a kit that instantly identifies lead on the outside of cans, and when such cans are found

they are brought into the laboratory for further analysis. So far, investigators have found some cans with lead-soldered seams in small ethnic markets and some chain stores that cater to ethnic communities. When analyses have shown high lead levels, these products have been removed from sale and the importer notified.

Judith E. Foulke is a staff writer for FDA Consumer.

Amtrak Put on Schedule For Compliance

Amtrak is on a schedule to correct problems with refrigeration, food handling, and sanitation aboard its railroad cars. The timetable for corrections is spelled out in a consent decree of permanent injunction signed on June 15, 1992, by the National Railroad Passenger Corporation, Amtrak's parent company, and three of its principal officers.

The consent decree, filed with the U.S. District Court for the District of Columbia, directs the president and chief executive officer W. Graham Claytor Jr., executive vice president Eugene N. Eden, and executive vice president and chief operating

officer Dennis F. Sullivan to comply with FDA regulations.

FDA had been aware of problems aboard Amtrak for some time. Following routine inspections, the agency had sent Claytor letters on Aug. 21 and Oct. 26, 1989, May 18, Aug. 27, and Dec. 21, 1990, and Jan. 17, 1991, enumerating deficiencies and informing Amtrak that FDA considered the insanitary conditions a possible health hazard to passengers. Claytor responded several times with promises to correct the problems.

But the violations continued, and in November 1991, U.S. Customs agents on the Canadian border complained to FDA about the insanitary conditions on the trains entering Canada. As a result of this

and other complaints, FDA directed a nationwide inspection of Amtrak's dining, café, crew, passenger, lounge, and sleeper cars. The Federal Railroad Administration and Health and Welfare Canada helped with the inspections.

Between January and April 1992, FDA conducted 35 train inspections. Of those, 23 inspections in 13 states and Canada showed sanitation violations. Sixty-five rail cars showed evidence of rodent infestation, and six showed other insanitary conditions, such as inoperable refrigeration units and broken plumbing. Some Amtrak employees failed to follow safe food-handling practices, such as proper hand-washing practices and safe thawing of frozen foods.



FDA sent letters to Claytor on Jan. 29, Feb. 12, and March 26, 1992, warning of enforcement action without further notice if the violations were not corrected. Claytor responded that the corporation had taken corrective measures. Nevertheless, based on the history of repeated violative inspections, FDA was prepared to ask the U.S. Department of Justice to file for injunction.

Before asking the Department of Justice to file the case, FDA advised Amtrak of its intentions and invited the company to enter into a consent decree of permanent injunction. At a meeting on May 21, 1992, officials from FDA, the Federal Railway Administration, and Amtrak agreed to a program of corrections that would include the following measures to start immediately:

- adequate refrigerator or freezer facilities for food storage in all food service cars
- education and training for Amtrak food service workers on proper sanitation and food-handling practices
- thorough cleaning of all passenger and food service cars and inspections by trained railroad employees for evidence of rodents and insects
- fumigation of food service cars at least every 60 days
- fully functional toilet facilities in passenger cars
- trash removal from trains and storage in appropriate containers.

Amtrak also agreed to submit to FDA within 25 days a comprehensive sanitation and food service program proposal that would address in greater detail the terms of the interim program. Within 180 days, Amtrak would certify to FDA in writing that an adequate program had been established.

Amtrak also agreed to report in writing every month to FDA's Baltimore district office on what actions the firm has taken to comply with the injunction. After one

year, FDA would reconsider whether monthly reports were still necessary or if they could be given at less frequent intervals.

—Judith E. Foulke

U.S. Marshal Seizes Unapproved Eye Exercisers

Aerobic exercise is good for the heart and lungs. It conditions them by increasing oxygen intake. But when promoters claimed aerobic exercise with so-called "pinhole" eyeglasses was so good for the eyes it would eliminate the need for prescription eyeglasses or contact lenses, FDA deemed the assertion an unproven medical claim.

At the agency's request, last April 22, an FDA New York district office compliance officer and investigator accompanied a U.S. marshal in the seizure of some \$9,000 worth of pinhole eyeglasses and labeling at Professional Product Research, Inc., Brooklyn, N.Y., which had imported, assembled and marketed the glasses. And last May 20, a U.S. marshal, accompanied by an investigator from FDA's Minneapolis district office, seized more than \$70,000 worth of the devices at a Wisconsin firm.

The various promoters of pinhole eyeglasses claim the many pinhole openings in the darkened lenses train the eye to focus better and encourage eye muscles to relax. But neither those firms nor the manufacturers have an approved pre-mar-

keting request on file with FDA. For that reason, and because the claims are unproven and the eyeglasses don't meet other requirements of the Federal Food, Drug, and Cosmetic Act, FDA considers marketing them to be illegal.

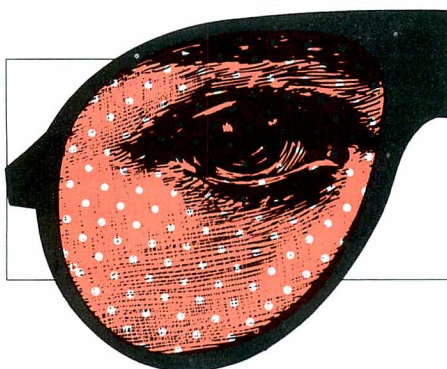
The devices were initially manufactured by the Institute of Vision Improvement, SA, of Johannesburg, South Africa. FDA issued an import alert in 1984 to detain all incoming shipments of pinhole eyeglasses, known as Lax-Optics Lensless Spectacles, to prevent sales of the unapproved devices. But the manufacturer periodically circumvented the alert by selling the devices under different names, such as Eyecisers and Pinhole Eyeglasses. Sometimes, the firm even sold directly to U.S. customers through the mail.

After FDA issued the 1984 import alert, various pinhole-eyeglasses manufacturing plants opened in the United States. Since the alert covered only the glasses produced by the South African firm, the agency began taking action across the board—import and domestic operations alike.

In July 1991, FDA received a letter from Senator Bob Graham, D-Fla., asking for information about the spectacles. One of his constituents in Fort Lauderdale had questioned whether they were approved, since they were being promoted with medical claims.

To better enforce detention of the products, the agency revised the import alert to state specifically that all the firm's shipments of pinhole eyeglasses be detained, regardless of the name on the product. FDA also requested that its district offices inspect the Wisconsin and New York firms to order them not to sell the eyeglasses and to collect samples of the devices and labeling, which they did early in 1992.

—Dixie Farley



Power Lifter Caught In Steroid Scheme

A former international power-lifting champion was sentenced to three years' probation and fined \$15,050 after pleading guilty to conspiring to illegally distribute anabolic steroids.

Anabolic steroids are a synthetic version of the male hormone testosterone. They are controlled substances that have been illegally promoted for body-building.

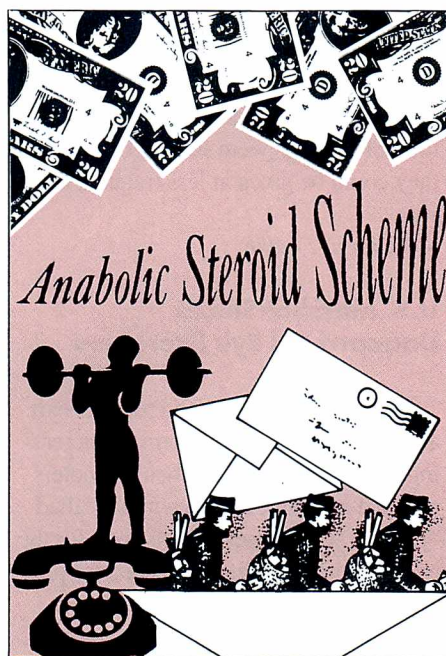
Thomas Henderson, of Iowa City, Iowa, first came to FDA's attention during an investigation of David L. Rumley, who, in January 1990, pleaded guilty to distributing half a million dollars worth of authentic and counterfeit anabolic steroids. (See "FDA Nabs Husband and Wife for Selling Fake Steroids" in the October 1991 *FDA Consumer*.) Henderson's sentencing on June 12, 1992, followed a four-year investigation by FDA.

Rumley ran his steroid distributing operation out of his Kansas City home, selling his products to 160 distributors in 28 states. With the cooperation of Postal Service agents, FDA investigators discovered that Henderson was one of Rumley's distributors.

On June 1, 1988, Postal Service agents observed Rumley mail two packages, one of which was addressed to Henderson. Suspecting the packages contained anabolic steroids, the agents intercepted both.

On June 3, under authority of a search warrant, Postal Service agents and FDA investigators opened the Henderson package and found various anabolic steroid products, including Stromba, Winstrol V, and Equipoise. The agents made a record of the package's contents and then, in an effort to establish a link with Henderson, allowed it to be mailed.

On June 6, Postal Service agents intercepted another package Rumley mailed to



Henderson. Although the Henderson-Rumley link had been established, the agents allowed this package to go through also because it contained a counterfeit, harmless version of the steroid product methandrostenolone, and because FDA investigators did not want to alert Henderson to their investigation.

Postal Service agents took Rumley into custody on June 6. Rumley agreed to cooperate with FDA's investigation of Henderson, and during June and July, investigators from the agency's Kansas City district office recorded several telephone conversations between the two, during which they discussed the purchase and distribution of Depro, Anavar, Sustanon, and Primo.

On June 17, with Rumley's permission, FDA investigators and Postal Service agents opened a letter from Henderson requesting more steroid products and containing \$1,820 in cash.

Several days later, Rumley received another envelope from Henderson containing \$2,490 payment for additional steroid products.

Rumley did not fill this last order, how-

ever, because at this point in the investigation he was not allowed to send Henderson steroid products. This, and the fact that one of Henderson's regular customers, coincidentally, had placed an unusually large order, caused Henderson to become suspicious.

In a recorded telephone conversation on July 6, he told Rumley that he was going to "lay low for a while."

On July 25, when he still had not received any products, Henderson demanded Rumley return the \$4,310 he had sent for orders. Four days later, Henderson told Rumley he was getting out of the "business," and again asked Rumley to return the money.

Later that day, Henderson accepted Rumley's offer of \$4,300 worth of anabolic steroid products instead of cash. Henderson also told Rumley he had "quit dealing in the mail," and to send the products through someone he had done business with before.

A few days later, the Department of Justice mailed Henderson a letter stating that he had been implicated in an investigation of illegal anabolic steroid distribution. On April 3, 1992, the Department of Justice filed an information—a document that charges an individual with the commission of a crime—with the U.S. District Court for the Western District of Missouri. Henderson pleaded guilty to charges on the same day.

At the conclusion of the Henderson case, FDA investigators had learned of \$4,700 worth of anabolic steroids that had been shipped to Henderson.

Henderson's sentencing is the last of seven Kansas City district office anabolic steroid cases stemming from the Rumley investigation. Henderson served the first four months of his probation under residential confinement.

—Victor Lambert

SUMMARIES OF COURT ACTIONS



SEIZURE ACTIONS

Food/Poisonous and Deleterious Substances

PRODUCT: **Uriddal, betel nuts, and other food stocks**, at Chicago, N. Dist. Ill.; Civil No. 89-C-8977.

CHARGED 12-5-89: While held by Jai Hind Corp., Chicago, Ill., the articles had been held under insanitary conditions, and one lot of uriddal contained rodent filth—402(a)(4), 402(a)(3); and the lot of betel nuts contained the poisonous and deleterious substance arecoline, which ordinarily rendered the article injurious to health—402(a)(1).

DISPOSITION: Consent—authorized release to the dealer for bringing the articles into compliance under specified conditions. Ultimately, the articles were destroyed. (F.D.C. No. 65792; S. No. 90-576-444 et al.; S.J. No. 1)

Food/Contamination, Spoilage, Insanitary Handling

PRODUCT: **Bee propolis capsules**, at Hayward, W. Dist. Wis.; Civil No. 91-C-977-S.

CHARGED 11-18-91: When shipped by Montana Naturals International, Inc., Arlee, Mont., the article labeled "Propolis capsules ... Manufactured for: Beehive Botanicals, Inc., Hayward, WI" contained animal filth—402(a)(3).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66310; S. No. 91-563-869 et al.; S.J. No. 2)

PRODUCT: **Cashew nuts, salted and unsalted, and unsalted mixed nuts**, at Billerica, Dist. Mass.; Civil No. 90-10604WD.

CHARGED 3-8-90: When one lot of unsalted cashew nuts had been shipped from South Kearny, N.J., the article contained moldy cashews and insect filth—402(a)(3); and while held by Nutcracker Snacks, Inc., Billerica, Mass., the remaining lots of the articles had been prepared and packed under insanitary conditions—402(a)(4). **DISPOSITION:** A consent decree of condemnation authorized release of the articles to Nutcracker Snacks, Inc., Billerica, Mass., for salvaging. A second amended consent decree extended the claimant's time to recondition the article. Ultimately, 1,112 cartons of cashews and 602 cartons and eight drums of mixed nuts were destroyed, and 523 cartons of cashews were reconditioned. (F.D.C. No. 65831; S. No. 90-598-515 et al.; S.J. No. 3)

PRODUCT: **Garlic, sliced, dried**, at San Francisco, N. Dist. Calif.; Civil No. C 91-1994 DLJ.

CHARGED 6-28-91: While held by Eastimpex, San Francisco, Calif., the article contained insect filth and had been held under insanitary conditions—402(a)(3), 402(a)(4).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66167; S. No. 91-625-505; S.J. No. 4)

PRODUCT: **Mixed fruits & peels for fruitcake**, at Poplar Grove, N. Dist. Ill.; Civil No. 90 C 20356.

CHARGED 12-18-90: While held by Edenfruit Products, Co., Poplar Grove, Ill. (who prepared the bakery item using imported pineapple), the article contained insect filth and had been prepared and packed under insanitary conditions—402(a)(3), 402(a)(4).

DISPOSITION: The article was claimed by the preparer, who denied the charges. The government moved for summary judgment. Subsequently, a consent decree of condemnation ordered that the article be destroyed. (F.D.C. No. 66010; S. No. 90-577-397; S.J. No. 5)

PRODUCT: **Rice, shelled peanuts, candy, and other food stocks**, at Chicago, N. Dist. Ill.; Civil No. 90-C 1375.

CHARGED 3-9-90: While held by Economy, Inc., Chicago, Ill., the articles had been held under insanitary conditions—402(a)(4); and two lots of basmati rice and two lots of candy contained rodent and/or insect filth, one lot of shelled peanuts contained rodent and insect filth, and one lot of a bread product contained insect filth—402(a)(3). **DISPOSITION:** The Warner Candy Co., Chicago, Ill., claimed a number of lots of candy; Jai Hind Corp., Chicago, Ill., claimed a number of lots of mung beans and other dried beans; Jayanti Shah (t/a Crystal Tea), Chicago, Ill., claimed 350 cases of Indian tea; L. Craven & Sons, Inc., Chicago, Ill., claimed a number of lots of candy; and Ash Distributing (Irwin Ashkanazy), Chicago, Ill., claimed a number of specified lots of pasta products, soup mixes, and other food stocks. A number of lots (17) of peanuts, rice, candy, and other specified food stocks were not claimed, and a default decree ordered them destroyed. The claimed articles were the subject of separate consent decrees of condemnation that authorized release of the articles to the respective claimants for salvaging. (F.D.C. No. 65840; S. No. 90-577-515 et al.; S.J. No. 6)

PRODUCT: **Rice**, at Chicago, N. Dist. Ill.; Civil No. 89-C-6128.

CHARGED 8-11-89: While held by Thai Grocery, Inc., Chicago, Ill., the articles contained insect filth and had been held under insanitary conditions—402(a)(3), 402(a)(4).

DISPOSITION: Consent—authorized release to the dealer for salvaging. (F.D.C. No. 65739; S. No. 84-575-509; S.J. No. 7)

Food/Economic and Labeling Violations

PRODUCT: Peppers in bulk drums and in unlabeled gallon jars, at Chicago, N. Dist. Ill.; Civil No. 90 C 2936.

CHARGED 5-23-90: When the bulk peppers labeled "Selected Greek Golden Peppers Panagiotis Logiakos Calamata Greece" had been shipped by Panagiotis D:Logiakos, Calamata, Greece, and while the repacked peppers in gallon jars were held by Cosmos Foods, Ltd., Chicago, Ill., the articles contained sulfite and the articles' labeling failed to state that fact—403(k); the peppers in gallon jars lacked a label containing the name and place of business of the manufacturer, packer or distributor and lacked a quantity of contents statement—403(e); and the peppers in gallon jars lacked a label containing the common or usual name of the food and the common or usual name of each ingredient—403(c).

DISPOSITION: Initially, a consent decree authorized release of the articles to Panagiotis Logiakos, Calamata, Greece, for attempting to bring into compliance. Subsequently, the claimant having defaulted on his obligations under the consent decree, a default decree ordered the articles destroyed. (F.D.C. No. 65864; S. No. 90-575-205 et al.; S.J. No. 8)

Drugs/Human Use

PRODUCT: L-lysine tablets, L-glycine tablets, L-carnitine capsules, and L-arginine & L-ornithine tablets, at Deer Park, E. Dist. N.Y.; Civil No. 91-3337.

CHARGED 8-29-91: While held by Edom Laboratories, Inc. (t/a Consumer Vitamin Values, Inc.), Deer Park, N.Y., who had manufactured the articles using interstate components, the articles were new drugs without effective approved New Drug Applications—505(a); the labeling of the articles falsely represented and suggested that the articles were safe and effective for use in the prevention or treatment of disease conditions—502(a); and the labeling of the articles lacked adequate directions for use and were not exempt due to their new drug status—502(f)(1).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66257; S. No. 91-626-792; S.J. No. 9)

PRODUCT: Oxygen in cylinders, U.S.P., at Garfield, Dist. N.J.; Civil No. 90-4618 (HLS).

CHARGED 11-21-90: While held by Firematic & Safety Equipment Co., Inc., Garfield, N.J., the circumstances used for the article's manufacture, processing, packing, and holding failed to conform with current good manufacturing practice—501(a)(2)(B).

DISPOSITION: Consent—authorized release to the dealer for salvaging. (F.D.C. No. 65897; S. No. 90-524-072; S.J. No. 10)

PRODUCTS: Pure Confidence feminine wash and feminine mist, and Viracydin and other brand-name liquid soaps, at

Torrance, C. Dist. Calif.; Civil No. 90-3162 MRP(Sx).

CHARGED 6-19-90: While held by Huntor Pharmaceutical Corp. (formerly known as Jean Pierre Products, Inc.), Torrance, Calif., the articles (which were promoted as containing "Protectin" and which bore labels such as "Pure Confidence with Protectin Feminine Wash Deodorant . . . Kills Germs & Viruses On Contact For Ultimate Cleansing . . . Jean Pierre Products, Inc. Div. Gentre Laboratories, Inc., Torrance, CA") were new drugs without effective approved New Drug Applications—505(a); the labeling of the articles failed to bear adequate directions for use for the articles' intended purposes—502(f)(1); and the articles' labels lacked the established name of each active ingredient included in the articles—502(e).

DISPOSITION: Initially, a default decree ordered the articles destroyed. Subsequently, pursuant to a stipulation between the dealer and the government, the court set aside the default and the dealer claimed the articles and denied the charges. Then a consent decree of condemnation authorized release of the articles to the claimant for bringing into compliance. Ultimately, the claimant having failed to pay the court costs and fees and, having failed to file a penal bond within the prescribed time, the court ordered that the articles be destroyed. (F.D.C. No. 65856; S. No. 90-447-111 et al.; S.J. 11)

PRODUCT: Retinol skin tablets, at Lincolnwood, N. Dist. Ill.; Civil No. 92-C-2178.

CHARGED 3-31-92: When shipped by Garden State Nutritionals, Fairfield, N.J., the article labeled "Retinol Beautiful Skin Nutritional Supplement . . . Tablets . . . Manufactured for E. Burnham Co. . . . Lincolnwood, Il." was a new drug without an effective approved New Drug Application—505(a); and the article's labeling (including the dealer's flier/order form reading, "Retinol . . . relieves dry skin, Eczema and Psoriasis . . . helps prevent spider veins, varicose veins . . . helps reduce osteoporosis . . . helps prevent some cataracts) lacked adequate directions for use, and the article was not exempt due to its new drug status—502(f)(1).

DISPOSITION: Default—ordered destruction. (F.D.C. No. 66398; S. No. 91-595-103 et al.; S.J. No. 12)

Medical Devices

PRODUCT: Apnea monitors, heart rate monitors, RE-series sensors, and other medical devices, test sets, subassemblies, and accessories, at Euless, N. Dist. Texas; Civil No. 91-0516-A.

CHARGED 7-29-91: The articles bore labels such as, "Respiration Monitor/Apnea Alarm [or "Heart Rate Monitor HR20"] . . . Electronic Monitors, Inc. . . . Euless, Texas," "for use with the E.M.I. RE series of Infant Monitors . . . Sensor Placement . . . Manufactured By Electronic Monitors, Inc. Euless, Texas," and "Transistorized Eastleigh II . . . Enuresis Alarm Made in U.K. . . . Distributed by Electronic Monitors Euless, Texas," and had been acquired by

Estrella Medical, Inc. (John Segars), Euless, Texas; the apnea monitors, the heart rate monitors, the sensors, and the E-2 test sets had been manufactured, packed and stored under circumstances that failed to conform with current good manufacturing practice regulations—501(h); specified apnea monitors (Models RE40 and RE134B), the heart rate monitors, the enuresis alarms, and the E-2 test sets failed to have the notice to FDA or other specified information as required by regulation—502(o); and information respecting malfunctions of the apnea monitors, heart rate monitors, and enuresis alarms had not been provided, as required by law—502(t)(2).

DISPOSITION: The articles were claimed by Electronic Monitors International, Inc. (formerly Estrella Medical, Inc.), Euless, Texas, and Electronic Monitors, Inc., Euless, Texas. The claimants denied the charges and asserted that the government's complaint was unreasonable, groundless, in bad faith, and/or frivolous. Subsequently, for the purpose of compromise only, the claimants consented to a consent decree that condemned the articles, authorized the recovery of costs from the claimants, ordered the destruction of the articles, and enjoined the claimants as follows: that they shall not manufacture, process, pack, label, promote, advertise, distribute, or sell any and all apnea monitor models RE40 and RE134B, heart rate monitors model AHR32, Eastleigh enuresis alarms, or E-2 Test Sets, unless and until the claimants had received written notification from FDA that FDA had determined that each such device was substantially equivalent to a device legally marketed in interstate commerce. (F.D.C. No. 66165; S. No. 90-582-702 et al.; S.J. No. 13)

PRODUCT: **Sensor pad**, at Binghamton, N. Dist. N.Y.; Civil No. 92-CV-043(CGC).

CHARGED 1-10-92: The article (which was labeled "Sensor Pad The Stethoscope For Fingers . . . Inventive Products Inc . . . Decatur, IL" and was accompanied by various labeling such as (Brochure) "October is National Breast Cancer Awareness Month . . . A New Aid For Breast Self-Examination") was a class III device and it did not have an approved pre-market application in effect—501(f)(1)(B). DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66338; S. No. 92-673-358; S.J. No. 14)

PRODUCT: **Tanning booths containing UV lamps, and UVB and other specified ultraviolet lamps**, at Anchorage, Dist. Alaska; Civil No. 88-241 CIV.

CHARGED 5-17-88: The labeling of the booths (which had been constructed by Sunburst Sun Spa, Anchorage, Alaska) failed to bear adequate directions for use, since there were no exposure schedules developed in accordance with the characteristics of the device, and the article's labeling lacked adequate warnings against unsafe use—502(f)(1), 502(f)(2).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65453; S. No. 88-422-734 et al.; S.J. No. 15)

INJUNCTION ACTIONS

DEFENDANTS: **Biopharmaceutics, Inc.**, and **Edward Fine**, president, Bellport, E. Dist. N.Y.; Civil No. 91-3936.

CHARGED 10-9-91 in a complaint for injunction: That the defendants manufactured, processed, packed, labeled, and distributed in interstate commerce various drugs; that the circumstances used for the manufacture, processing, packing, and holding of such drugs failed to conform with current good manufacturing practice—501(a)(2)(B); that FDA inspections revealed numerous continuing violations of current good manufacturing practice; and that the plaintiff believed that, unless restrained by the court, the defendants would continue to violate the law.

DISPOSITION: The court issued a temporary restraining order temporarily enjoining the defendants from manufacturing, processing, packing, or labeling at the defendants' facilities and from selling, distributing, and/or transferring ownership or possession of drugs processed or labeled at the defendants' facilities. Subsequently, a consent decree of permanent injunction enjoined the complained-of violations, and enjoined operations at the defendants' facilities unless and until a number of conditions had been met. (Inj. No. 1236; S. No. 90-601-392 et al.; S.J. No. 16)

MISCELLANEOUS ACTIONS

SUBJECT: **Potato products specially processed and FDA ban on sulfites on fresh potatoes**, Minneapolis, Dist. Minn.; Civil No. 4-90-242.

CHARGED 4-3-90: by Northern Star Co., Minneapolis, Minn., against HHS Secretary Louis H. Sullivan and Acting FDA Commissioner James S. Benson, in a suit for declaratory and injunctive relief: That Northern Star manufactured and distributed Dehydro-Cooled potatoes (a proprietary process using cooked, partially dehydrated potatoes and special packaging, for hash browns, and sliced and diced potato products having an extended shelf life); that one or more sulfiting agents was essential for the relatively long shelf life of "Dehydro-Cooled" potatoes (although both Dehydro-Cooled and dehydrated potato products could be produced without sulfites, but would have a reduced shelf life); that the use of sulfites in Dehydro-Cooled potatoes posed no greater risk from sulfite ingestion (i.e., 40-80 ppm as served) than is posed by the use of sulfites in dehydrated potatoes; that sulfiting agents had been generally recognized as safe (GRAS) for use as chemical preservatives since Nov. 20, 1959; that on Dec. 10, 1987, FDA proposed an amendment excluding from GRAS status the use of sulfites on "fresh" potatoes intended to be served or sold unpackaged and unlabeled to the consumer and FDA had subsequently published the final rule that was the subject of the plaintiff's complaint; that FDA's final rule defined "fresh" potatoes as potatoes that were not canned, frozen or dehydrated and FDA had noted that the plaintiff's potatoes would be categorized as "fresh"

because, as with other “fresh” potatoes, there was no counterpart on the retail market for the plaintiff’s potato products that would permit consumers to learn to recognize that these products might contain sulfites and that sulfite-sensitive individuals should avoid them; and that the Northern Star Co. had twice submitted that its refrigerated-cooked potato products were sold at retail, had offered to relabel its food service packages, and had petitioned for an administrative stay of the effective date of the regulations until FDA had interpreted the regulations so as not to require a ban of the use of sulfites on Northern Star Co.’s potatoes or, in the alternative, to allow Northern Star Co. to change over its operations to the production, marketing and distribution of non-sulfite-containing potato products. Although Northern Star was attempting quickly to develop a version of Dehydro-Cooled potatoes for the food service market containing no sulfites, it did not expect to be able to market such a product by the regulation’s effective date and accordingly would be forced to market sulfite-free potatoes with a significantly shorter shelf life, which would make it difficult to continue its nationwide distribution system. Northern Star accordingly asserted that FDA’s acts of withholding a stay in permitting the use of sulfites in dehydrated, canned and frozen potato products, while prohibiting Northern Star’s products, were acts that were arbitrary, capricious, and an abuse of discretion.

DISPOSITION: Upon Northern Star’s motion for a preliminary injunction, the court ruled for the government, finding that the balance of harms in this case clearly tipped against the issuance of injunctive relief. Northern Star had argued that FDA’s reasoning was faulty because (1) consumers were sufficiently familiar with dehydro-cooled potatoes containing sulfites, (2) FDA arbitrarily allowed sulfites in frozen potatoes, and (3) Northern Star’s potatoes should not be treated the same as “fresh” potatoes—which might also be treated with sulfites on the premises of a food service establishment. The court found that none of those arguments undermined the essential logic of FDA’s position. The court found the following: that Northern Star had not provided sufficient details of any nationwide marketing in retail establishments with labels indicating that the products contained sulfites; that, until barred recently, Northern Star had marketed its product labeled as “fresh,” thereby contributing to the possibility of confusion of its product with “fresh” potatoes, believed by the public not to contain sulfites; and that FDA reasonably found that there was a risk that either consumers or food service personnel would confuse the plaintiff’s product with “fresh” potatoes, and thereby conclude that the product did not contain sulfites. As to the plaintiff’s evidence of irreparable harm, the court found it was exceedingly thin and that, by the plaintiff’s own admission, harm to the plaintiff’s distribution effort would not necessarily be permanent.

The court summarized FDA’s findings concerning sulfite-sensitive individuals, noting that 12 percent of adverse reactions had been traced to potato products, that “fresh” potato products accounted for 50 percent of those adverse reactions, and that of the 17 deaths

associated with the use of sulfites in foods, four were attributed to potatoes. Accordingly, the plaintiff’s motion for a preliminary injunction was denied. Subsequently, pursuant to stipulation of the parties, the complaint was dismissed. (Misc. No. 915; S.J. No. 18)

SUBJECT: PCE (1-phenylcyclohexylethylamine, an ethylamine analog of phencyclidine), the authority for its classification under the Controlled Substances Act, and FDA’s recommendation effecting such classification, Washington, Dist. Columbia; Civil Nos. 89-3097 and (upon appeal) 89 CV 03097.

CHARGED 11-13-89 by Larry Michael Edwards, Milan, Mich., against Peter N. Bensinger (former administrator of the Drug Enforcement Administration [DEA]), three other DEA administrators, and the DEA, and Edward H. Levi (former Attorney General of the United States), five other Attorney Generals, the Office of the United States Attorney, and Julius B. Richard, M.D. (former Assistant Secretary for Health of the Department of Health and Human Services [HHS]), two other officials of HHS, and the departments of HHS and Justice, in a suit for judicial review: That the scheduling of a drug (found to have a high potential for abuse, to lack accepted medical use, and to lack accepted safety) must be made in accordance with the formal rule-making requirements of the Administrative Procedure Act; that the plaintiff had been incarcerated for a violation of the Controlled Substances Act (CSA) for allegedly distributing PCE (a Schedule I controlled substance); that the findings and/or evaluations for the scheduling of PCE had been glib, perfunctory, discursive, multifarious, arbitrary, and capricious; that the CSA did not authorize the HHS Secretary to delegate the responsibility of submitting a recommendation that PCE be placed into Schedule I; and that, accordingly, PCE had been improperly scheduled and the plaintiff had been improperly incarcerated.

DISPOSITION: The government moved to dismiss, and the plaintiff moved for partial summary judgment. The court granted the government’s motion and denied the plaintiff’s motion. In support of the finding that PCE had a high potential for abuse, it had been noted that 16 states had detected PCE production within their jurisdictions, there had been three reports of toxicity attributed to PCE abuse, and the chemical and pharmacologic similarity between PCE and PCP strongly supported the finding that the potential for abuse for PCE was the same as for PCP. Conversely, the plaintiff failed to offer any evidence that would undermine such findings. The court concluded that HHS had properly delegated its authority under the CSA, that PCE had been properly scheduled as a controlled substance under the CSA, and that, accordingly, the government was entitled to judgment as a matter of law.

Upon appeal, the government moved for summary affirmance of the district court’s judgment in favor of the government. The Court of Appeals granted the government’s motion for summary affirmance substantially for the reasons stated by the district court, the parties’ positions being so clear as to justify summary action. (Misc. No. 906; S.J. No. 19)



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The Medicine Label. It's the First Step to Getting Better.

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