

FDA CONSUMER

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

• VOL. 25 NO. 10

DECEMBER 1991 •

HAIR!

FROM PERSONAL STATEMENT TO PERSONAL PROBLEM





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Inside Front Cover Photo: Undercooked eggs may harbor disease-causing bacteria especially dangerous to older adults. For more on food-borne illness in nursing homes, see page 10.



Coconut Products Contaminated by Cholera

Consumers who have Asian Best frozen coconut milk or candy should take the foods to their local health department for safe disposal, because the products may be contaminated with cholera or other disease-causing organisms.

After three cholera cases in Maryland were linked to frozen coconut milk produced by Champ Group Enterprises Co., Ltd., of Bangkok, FDA began detaining all the firm's fresh, frozen and dried products containing coconut milk or coconut meat.

The three cases were traced to Asian Best Frozen Fresh Coconut Milk that had been used as a topping on a Thai rice pudding served at a picnic in Silver Spring last August. The strain—*Vibrio cholerae* 01, Ogawa, El Tor—is associated with epidemics in Asia, but not with the current epidemic in South America. Besides the cholera organism, FDA analyses found *Salmonella* in Asian Best frozen coconut candy.

FDA will not release the products for sale here unless evidence is provided that they are free of the microbial contaminants. As a further safeguard, the agency intensified port-of-entry testing of other foreign firms' fresh and frozen coconut-containing foods exported to the United States.

The implicated coconut milk is shipped frozen in 8-ounce plastic bags. Its label names Jack Hong Co., Ltd., Bangkok, Thailand, as the exporter and the Eastland Food Corp. of Columbia, Md., as the importer and distributor. Eastland on Sept. 20 voluntarily began recalling the products from some 600 retail outlets in 23 states east of the Mississippi River, chiefly Asian specialty stores.

FDA Tells Breast Implant Manufacturers To Provide Patient Information

Breast implant manufacturers must provide doctors with easily understandable information about the risks of breast implants, and doctors should give this information to patients considering breast implant surgery, FDA said in a *Federal Register* notice published Sept. 25, 1991.

FDA gave manufacturers 30 days to provide the patient information, after which any breast implant not providing the patient labeling would be considered misbranded and subject to regulatory action.

The agency made available to manufacturers an infor-

mation sheet to use as guidance in developing their own material.

Risks of breast implants include hardening of tissue surrounding the implant, rupturing of the implant, and interference with mammography.

FDA is currently reviewing manufacturers' data on silicone gel-filled implants (the majority of breast implants on the market) and expects to determine by early January 1992 whether there is adequate evidence of their safety to permit them to remain on the market. The agency will soon request similar data from manufacturers of implants filled with saline solution (salt water).

FDA Commissioner David A. Kessler, M.D., said that the agency decided to tell doctors and manufacturers to provide patients with information about the risk of implants while the agency was considering the safety data because some women are unaware that any risks are associated with the implants.

"I recognize that the implants have been beneficial to many women," Kessler said. "But due to the fact that they can hide tiny tumors that might otherwise be visible on a mammogram, women who are at high risk for breast cancer, including women with a family history of the disease, should be especially cautious about electing to use the implants to enlarge their breasts."

Each year, about 150,000 women in this country receive breast implants, 80 percent for breast enlargement and the rest for reconstruction following mastectomy (surgical breast removal due to cancer).

FDA advises that the risk information currently available does not warrant removing an implant from a woman not having any problems with it, especially considering that any surgical procedure carries a risk. A woman experiencing problems she thinks may be associated with her implants, or who is concerned about the possible risks, should consult her doctor for advice.

Collagen Products Must Carry New Warning

A warning about an increased incidence of the diseases polymyositis and dermatomyositis (PM/DM) in people who have received collagen injections must be added to the products' labeling, FDA told Collagen Corp. of Palo Alto, Calif., in a letter last September. Collagen, regulated as a medical device under FDA laws, is injected under the skin to correct acne scars and wrinkles.

Because PM/DM are such rare diseases, the vast majority of collagen recipients won't be affected, FDA said.

The cause of PM/DM is unknown, but the diseases, which affect the body's connective tissue, result in muscle inflammation and can sometimes lead to difficulty in breathing and swallowing. Because PM/DM symptoms occur with many other illnesses, these diseases are difficult to diagnose. Their natural incidence is hard to define because they are so rare and because susceptibility to these diseases varies with age, sex and race.

After extensive review, scientists from FDA, the National Institutes of Health, the national Centers for Disease Control, and the Texas Department of Health agreed on Aug. 29 that the incidence of PM/DM seemed to be greater in patients treated with collagen than in the general population. FDA scientists compared the number of cases of confirmed or probable PM/DM in the 400,000 patients treated with collagen and the number of expected cases in a general population of similar size and with the same age, sex and race distribution. The agency concluded there was indeed an association between collagen injection and PM/DM.

This association doesn't necessarily mean the injections caused the diseases, FDA said. The increased cases could be due to other factors, such as preexisting medical conditions, medications, or environmental reasons.

Two Collagen Corp. products are involved in this mandatory relabeling: Zyderm and Zyplast. At FDA's request, U.S. marshals had already seized them because of other labeling problems. (See "Collagen Seized; Labels Corrected" in the Updates section of the November 1991 *FDA Consumer*.)

FDA continues to study collagen and will provide the opportunity for a public discussion on its findings.

Vitek TMJ Implants Have Problems

Patients with certain jaw implants made by Vitek Inc. of Houston should see a doctor for an immediate examination because the implants may have broken down or caused nearby bone to degenerate, FDA advised last October. The implants are used to treat temporomandibular joint (TMJ) syndrome, a painful condition of the joint connecting the jaw and skull.

"Although FDA announced a recall of unused implants in January," said FDA Commissioner David A.



Kessler, M.D., "the agency wants to make sure all patients who have the implants are aware of the risks and have a doctor monitor their implants. It is especially important that these people be examined because bone degeneration can sometimes occur without symptoms."

When symptoms occur, they include pain radiating from around the ear, joint noise, limited jaw movement, a change in bite, difficulty chewing, and, in some patients, headaches.

The implant may have to be removed if the examination, which includes a computed tomography (CT) scan or magnetic resonance imaging (MRI) procedure, shows the implant has broken down and bone has deteriorated. Patients who are not having problems should be examined once a year as long as they have the implants, FDA said.

The agency has taken responsibility for alerting patients because Vitek, which was ordered to re-notify doctors and notify patients, is bankrupt and can't follow up appropriately.

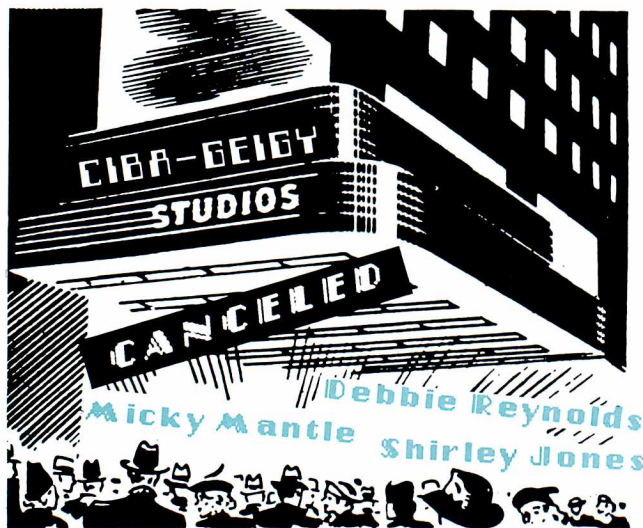
The implants, made between 1973 and 1988, are a TMJ disk replacement called the Vitek Interpositional Implant and two total joint replacements called the Vitek Kent (VK) and the Vitek Kent I (VK-I). Oral Surgery Marketing Inc. (OSMI), also of Houston, a successor of

Vitek, has illegally marketed a TMJ implant that may present similar risks.

FDA has established a notification program for these patients and urges health professionals and patients to call, toll-free, (1-800) 554-5297. The notification program will be operated by Medic Alert, a nonprofit foundation. Callers will receive information on the risks of all these implants and instructions on how to enroll in Medic Alert's International Implant Registry, which will enable them to receive new information as it becomes available.

Drug Company Stops Celebrity Ads

After receiving a series of FDA complaints about its prescription drug advertising practices, a large pharmaceutical company has announced its decision to stop using celebrities to promote its prescription drug products.



The announcement by Ciba-Geigy Corporation of Summit, N.J., followed three months of discussions with FDA.

FDA regards celebrity endorsements as frequently deceptive because consumers tend to assume that the celebrities are giving objective endorsements of a product when, in fact, they are typically compensated to do so, and also because the celebrities usually do not provide balanced information about the risks and benefits of the product.

In the past, Ciba-Geigy Corporation has used baseball

great Mickey Mantle and actresses Shirley Jones and Debbie Reynolds to promote its arthritis drug Voltaren.

In September, the corporation announced that it had received a grand jury subpoena from the Justice Department, asking it to turn over all of its documents concerning the promotion of Voltaren. No criminal charges have been filed against the corporation.

Ciba-Geigy has also announced that it is discontinuing its direct-to-consumer ads for Actigall—a drug for dissolving gallstones.

The corporation canceled its direct-to-consumer Actigall ads in June because of FDA concerns that the ads did not adequately inform consumers that surgery, not Actigall, is the preferred treatment for most patients suffering from gallstones.

Manufacturer Withdraws Heart Drug

The manufacturer of the anti-arrhythmic medication Enkaid (encainide hydrochloride) will withdraw the drug from the market effective Dec. 16, because of continuing uncertainty about the drug's effectiveness.

Bristol-Myers Squibb Co., of Evansville, Ind., announced the withdrawal of Enkaid, used to treat irregular heartbeat, on Sept. 16. The company warned, however, that patients should not stop taking the drug unless advised to do so by their physicians.

"In some cases, physicians may judge that patients with life-threatening ventricular arrhythmias who are already successfully managed on Enkaid should not be changed to another medication," said E.J. Fox, M.D., vice president of the firm's Bristol Laboratories division. For these patients, the Enkaid Continuing Patient Access Program will provide the medication free of charge to eligible patients who were being treated with Enkaid for life-threatening ventricular arrhythmias as of Sept. 16, 1991.

Questions about whether Enkaid can decrease the risk of sudden cardiac death among patients who have survived heart attacks and have non-life-threatening arrhythmias were first raised during a study by the National Institutes of Health (NIH). Patients given Enkaid, as well as those taking two other drugs in the study, had a higher death rate from heart attacks than patients receiving a placebo.

NIH removed Enkaid and Tambocor (flecainide), manufactured by 3M Riker, St. Paul, Minn., from the study in April 1989, and Bristol announced that Enkaid

should be prescribed only for patients with life-threatening ventricular arrhythmias.

NIH stopped the trial completely last August after seeing the same negative results with the final drug under study, Ethmozine (moricizine), manufactured by Du Pont Pharmaceuticals, Wilmington, Del.

At press time neither of the other two firms had taken any actions concerning their drugs.

FDA approved Enkaid for marketing in December 1986.

Committee Advises FDA on Antidepressants

There is no credible evidence to support claims that Prozac and other antidepressant drugs cause users to commit suicide and other violent acts, an FDA advisory committee concluded recently.

FDA's Psychopharmacological Drug Products Advisory Committee, a group of nongovernment medical experts from around the country, unanimously agreed in September that the available scientific data—in particular, analyses of controlled clinical investigations involving thousands of subjects—did not prove a causal link between antidepressants and suicidal or other violent behavior.

The panel also voted 6 to 3 not to relabel this class of drugs with warnings about the alleged side effects and called for more research on all antidepressant drugs.

During a public hearing on Sept. 20, the committee heard testimony from people whose loved ones had committed suicide or violent acts while on Prozac or other antidepressants. The committee concluded that such testimony, although poignant, was not compelling evidence of Prozac's causal link to the events described.

Prozac has been prescribed to about 3 million people in the United States since it was approved in 1987, and there have been 500 reports of suicide attempts among those taking the drug. However, except in a setting of controlled studies, where treated and untreated patients with depression can be compared, it is very difficult, if not impossible, to know whether a depressed patient was suicidal because of a drug or despite it.

The American Psychiatric Association and the National Depressive and Manic Depressive Association support continued marketing of Prozac without any changes in its labeling.

The Citizens Coalition for Human Rights, a group affiliated with the Church of Scientology, opposes the

drug, however, and has waged an advertising campaign alleging that it causes violent behavior.

While the advisory committee's findings are not binding on FDA, the agency will give them serious weight in determining whether any specific actions in regard to Prozac and other antidepressants are warranted at this time.

DTP Recommendations Revised

A child who develops certain side effects after receiving a DTP (diphtheria, tetanus and pertussis) vaccination need not necessarily forgo the remaining shots in the vaccination series, according to new immunization guidelines issued by the Public Health Service's Immunization Practices Advisory Committee.

The committee, primarily immunization experts from outside the government, advises the Public Health Service on immunization policy matters.

Previous guidelines recommended that the pertussis (whooping cough) component of the vaccine be discontinued if a child displayed any of four serious side effects. This recommendation was based on several anecdotal case reports suggesting that, in extremely rare instances, the pertussis component of the vaccine might cause permanent brain damage.

After reassessing those studies, the PHS committee concluded that "a causal relation between DTP vaccine and permanent brain damage has not been demonstrated."

The new guidelines give physicians more leeway in deciding whether to stop or proceed with DTP vaccinations. They advise physicians that, despite the occurrence of certain side effects, the benefits of proceeding with the DTP shots may outweigh the potential risks under certain circumstances, especially if there is a high incidence of pertussis in the community.

The following four side effects, once regarded as absolute reasons for discontinuing DTP shots, are now regarded only as precautions, or warning signs—meaning that the doctor should carefully evaluate the situation before deciding whether to continue the DTP shots, or to continue the shots minus the pertussis component of the vaccine:

- a temperature of 105 degrees Fahrenheit within 48 hours of vaccination
- collapse or shock-like state within 48 hours of vaccination

- persistent, inconsolable crying lasting three hours, and occurring within 48 hours of vaccination
- convulsions, with or without fever, occurring within three days of vaccination.

More information concerning the committee's revised recommendations (which also include recommendations for the management of contacts of diphtheria patients) appears in an Aug. 8, 1991, supplemental edition of the Centers for Disease Control's *Morbidity and Mortality Weekly Report*.

(See also "Childhood Vaccines" in the September 1990 *FDA Consumer*.)

Lower 'Threshold of Concern' For Children's Lead Levels

The amount of lead considered dangerous in children's blood is even lower than previously believed, Secretary of Health and Human Services Louis W. Sullivan, M.D., announced at the First National Conference on Preventing Childhood Lead Poisoning last October in Washington, D.C.

The new "threshold of concern" is 10 micrograms per deciliter of whole blood—less than half the current level of 25 or higher established in 1985. Blood lead levels as low as 10 micrograms per deciliter can cause subtle developmental effects, such as behavioral disturbances and reduced stature, according to a statement by the national Centers for Disease Control. Symptoms are largely invisible at first, leaving the vast majority of cases undiagnosed and untreated.

The CDC statement recommends phasing in universal screening for young children. It also recommends a series of interventions, depending on a child's blood lead level.

An estimated 3 million to 4 million children younger than 6 have more than 14 micrograms of lead per deciliter of blood. This is far greater than the number of children affected by other common childhood illnesses, Sullivan said.

Without appropriate prevention and medical treatment, lead poisoning can cause learning disabilities, IQ deficits, and other problems. Deaths from lead poisoning are rare now that paints and most gasolines no longer contain the metal, but many children still are ingesting enough lead from old, peeling paint and other sources to cause harm (see "Getting the Lead Out—Of Just About

Everything," in the July–August 1991 issue of *FDA Consumer*).

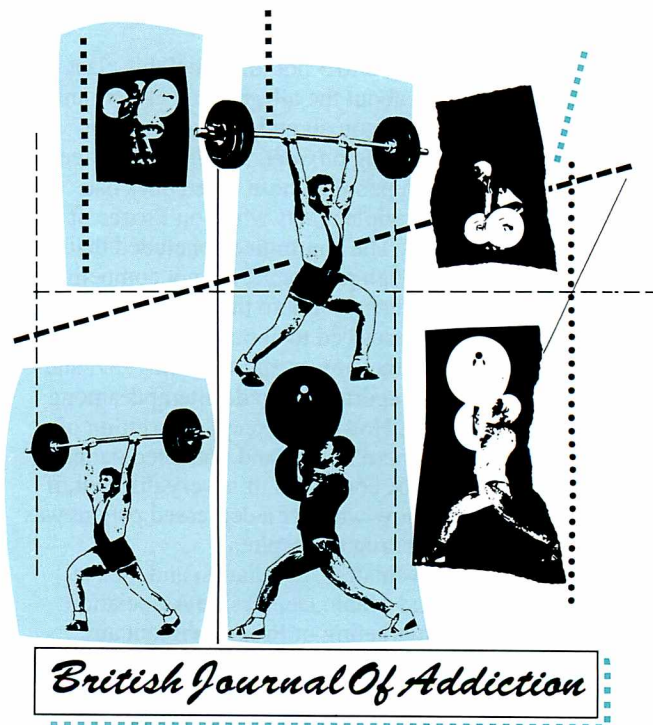
Copies of the CDC statement, "Preventing Lead Poisoning in Young Children," are available from Publication Activities, Office of the Director, National Center for Environmental Health and Injury Control, CDC, MS-F29, 1600 Clifton Road, Atlanta, Ga. 30333.

Study Shows Addiction With Anabolic Steroids

Anabolic steroids can become addictive, according to a recent study, which suggests that larger doses, more cycles of use, and dissatisfaction with body size are the best predictors of dependency.

The study's authors, Kirk Brower, M.D., and others at the University of Michigan, Ann Arbor, conclude that while symptoms may not appear in all users, anabolic steroids can be addictive, particularly in those who use the drug to enhance their physical appearance.

The study, published in 1991 in the *British Journal of Addiction*, involved 49 male weight lifters who worked



out in local community gyms and admitted to using steroids.

In a self-administered questionnaire, 94 percent of the weight lifters reported at least one symptom of dependence. More than half reported three or more symptoms, which is consistent with medical guidelines for the diagnosis of dependence. The symptoms reported indicated both psychological and physical dependence.

The most commonly reported symptoms were withdrawal (84 percent of respondents); taking more substance than intended (51 percent); spending large amounts of time on substance-related activity (40 percent); and continuing steroid use despite problems caused or made worse by the drug (37 percent).

The most frequently reported withdrawal symptoms were fatigue (43 percent of respondents), depressed mood (41 percent), restlessness (29 percent), and loss of appetite (24 percent).

The study was sponsored by the National Institute on Alcohol Abuse and Alcoholism.

(For more on anabolic steroid abuse, see "Steroids and Sports Are a Losing Proposition" in the September 1991 *FDA Consumer*.)

Family and Breast Cancer in Men

A study published in the *Journal of the National Cancer Institute* last June showed that men, like women, have a greater risk of breast cancer if they have close relatives with the disease.

Karin Rosenblatt, Ph.D., and colleagues studied case records of 227 men with breast cancer and compared data about family history of the disease with 300 men who did not have breast cancer. They found that men with a male family member—father, brother or uncle—who had breast cancer had almost four times the risk of developing the disease. Men with a female relative with breast cancer had a two- to threefold higher risk.

The chance of getting the disease was not influenced by whether the relative was a mother or sister, or whether the relatives with breast cancer were on the mother's side or the father's side of the family.

Chances of developing breast cancer increased with the number of affected relatives. The risks were greater for men with close relatives who had developed the disease before age 45 than for men whose relatives had been affected at a later age. Men younger than 60 who had a sis-

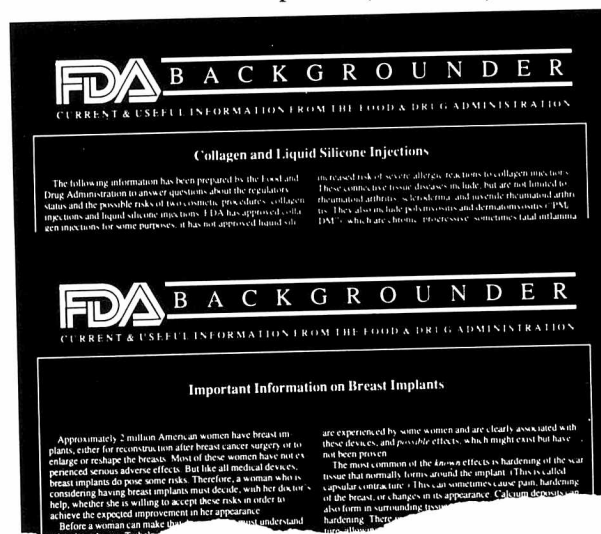
ter with breast cancer had a greater risk of developing the disease than did older men.

(For information on breast cancer in women, see "Breast Cancer: Complacency the Enemy of Cure" and "Breast Cancer: Woman Is Partner in Choosing Treatment" in the July–August and September 1991 issues of *FDA Consumer*.)

Free Reprint and Backgrounders

A reprint of an *FDA Consumer* article and two papers in the agency's *FDA Backgrounder* series are available free.

The reprint is "Progress Against Breast Cancer" (FDA 91-1176). The two backgrounders are "Collagen and Liquid Silicone Injections" (BG 91-5.1) and "Important Information on Breast Implants" (BG 91-6.1).



To order single copies, write to FDA, HFE-88, 5600 Fishers Lane, Rockville, Md. 20857, or call (301) 443-3170. For up to 100 copies, write to FDA, HFI-40, at the same address; negatives of the breast cancer article also are available at this address. Be sure to include the title and publication number.

FDA Consumer reprints on additional subjects, as well as articles from other government agencies, can be ordered at a small cost from the Consumer Information Center. To order a free catalog, send your name and address to Consumer Information Catalog, Pueblo, Colo. 81009, or call (719) 948-4000.

Food Labeling

A piece titled "Building a Better Food Label" by FDA Commissioner David A. Kessler, M.D., in the September 1991 issue of *FDA Consumer* has several significant and favorable comments such as:

"Only an informed consumer can make intelligent choices."

"The false use of the word 'fresh' raised the broader question about whether the words on the food label have any meaning . . ."

"The cause of better nutrition in America will be served best if—besides clearing away the clutter on the food label—we can keep four goals squarely before us."

We would like to comment on each of the four goals. "First, the food label must be revised." We agree. It is already *too cluttered*. Dr. Kessler refers to a Roper poll that indicates 52 percent of consumers examine food labels for nutrition information. We have not seen the poll but wonder how many consumers understand what they read.

"Second, the format of the nutrition panel must be revamped." We agree; it should be *greatly simplified*. How helpful is it to know that an average serving of peas provides about 20 percent of the RDA for iron, or that 8 ounces of milk provides about 30 percent of the RDA for calcium? . . . We think it better for the consumer to know that peas are a good source of iron, milk is an excellent source of calcium, . . . etc.

"Third, food descriptors such as 'light' require clearer definition." We agree.

"Fourth, FDA should do everything within its power to promote use of the food label to improve the collective diet—and, with it, the health—of the entire nation." We agree, but how do we do that?

The "collective diet" probably refers to the total diet and that requires an understanding of the importance of variety in food consumption: (1) fruits and vegetables of any kind, but in variety; (2) cereals . . . such as breads, noodles, breakfast cereals, and even an occasional donut or piece of cake; (3) milk or foods made from it . . . and (4) foods from the protein group—meat, fish, poultry, eggs, legumes, and nuts. Since fruits, vegetables, and cereals are low in fats, servings may be frequent and generous. Because milk products, unless made from low-fat

milk, and the protein group are frequently generous in fats, serving sizes should be small. Generous consumption of low-fat milk should be encouraged because it is by far the best source of absorbable calcium. . . . The bathroom scale once a week will indicate whether portion sizes have been suitably related to physical activity.

We suggest labeling that is coordinated with simple, basic nutrition information, printed so that it can be read without a magnifying glass, and not cluttered with too many milligrams or percent of this or that. . . .

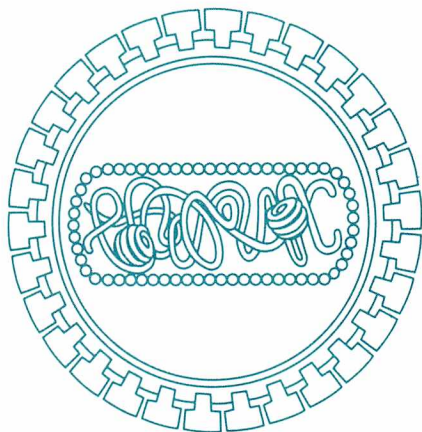
Dr. Kessler writes that we "should consume no more than 2,400 milligrams of sodium daily." Sodium has many vital functions, including some that relate to blood pressure. About 20–25 percent of Americans have varying degrees of high blood pressure and of those only about 2–3 percent will have a decrease in blood pressure by lowering the sodium in their diet, and it must be a *drastic reduction* to a level of 300–400 milligrams per day. Individuals with congestive heart failure will benefit from a low-sodium diet. Now we are talking about problems that should be treated by a physician, not just by a label! In "round numbers" a third of our sodium intake is a natural constituent of some of the foods we eat, a third is added in the kitchen, and a third at the table.

A food label should list added ingredients to caution those who may be sensitive to any of them.

Dr. Kessler writes: ". . . I will oppose claims that are little more than marketing ploys." We agree. Further, he states: ". . . all of us must be united in this effort to realize the full value of the food label." We agree, but keep it simple, uncluttered, readable, educational, and in terminology the average American consumer can understand.

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



DDI Approved After Binational Review

A historic joint review of drug study data by the United States and Canada preceded the approval of the anti-retroviral drug dideoxyinosine (DDI) by both FDA and its Canadian counterpart, on Oct. 9, 1991.

DDI became the second drug approved in this country for treating AIDS virus infection. It is approved for treating adults and children with advanced HIV infection who are intolerant to Retrovir (zidovudine, commonly called AZT) or whose health has significantly deteriorated while on that drug. Retrovir is the only other approved treatment for HIV infection.

DDI, being marketed as Videx, was approved on the basis of data from early clinical trials conducted by its sponsor, Bristol-Myers Squibb Co. of New York, N.Y., the National Institute of Allergy and Infectious Diseases, and the National Cancer Institute. FDA completed its review in six months.

The early trials primarily evaluated DDI's ability to increase the number of T4 helper cells. (T4 helper cells are critical immune system cells that are destroyed by the AIDS virus.) Usually a drug needs to have a clinical end point such as increased survival to prove efficacy, but FDA accepted the conclusion of many researchers that an increase in T4 cell counts indicates a beneficial effect on a patient's immune system and general health.

FDA Commissioner David A. Kessler, M.D., emphasized that although the database is adequate for approval, the use of such surrogate end points means that the agency has less information about DDI's long-term safety and effectiveness.

"More clinical studies must be done on DDI to better understand how well DDI works, and data from these studies must be applied to its future labeling," he said. "Nevertheless, in the face of the AIDS crisis, FDA believes that the use of surrogate end points is an important tool to speed promising drugs to people who desperately need them."

Among the known serious adverse effects of DDI are inflammation of the pancreas, which can be fatal, and painful nerve damage. These may be reversible if detected early and if the drug is discontinued.

DDI was the ninth drug approved by FDA to treat AIDS or AIDS-related conditions.

Foscarnet for CMV Retinitis

FDA has approved the use of foscarnet for treating AIDS patients with cytomegalovirus (CMV) retinitis, an eye infection that can lead to blindness in people with impaired immune systems.

Foscarnet is the second drug approved for use in AIDS patients with CMV retinitis. The first, ganciclovir, was approved in June 1989, but many patients cannot tolerate treatment with the drug because it can interfere with bone marrow function in producing platelets and white blood cells.

A recent multi-center clinical trial showed that patients taking foscarnet lived an average of four months longer than those taking ganciclovir and that both drugs were equally effective in stopping the progression of CMV retinitis.

Foscarnet has been available through FDA's investigational new drug (IND) process since August 1990 to physicians treating AIDS patients with CMV retinitis. On Sept. 27, 1991, FDA approved the drug for marketing under the trade name Foscavir. It is manufactured by Astra Pharmaceutical Products, Inc., Westborough, Mass.

Serious side effects reported with foscarnet use include kidney damage, abnormal blood electrolyte levels, and seizures.

Foscarnet is the eighth drug approved for treatment of AIDS or an AIDS-related condition.

Combination AIDS Test Kit

A combination test kit for detecting antibodies to two viruses that cause AIDS was approved by FDA in September.

In announcing the licensing of the new test kit, HHS Secretary Louis W. Sullivan, M.D., said, "This could significantly streamline testing procedures for the blood industry and other institutions engaged in high-volume screening, and could further improve the overall safety of the blood supply."

Antibody tests for human immunodeficiency virus type 1 (HIV-1), the most common cause of AIDS, were licensed by FDA in March 1985 and are now in universal use among the nation's blood establishments. Use of these tests has dramatically reduced the risk of becoming infected with HIV-1 through the blood supply, and the risk of getting AIDS from a blood transfusion is estimated to have dropped by more than 99 percent from 1983 to 1991.

An antibody test for HIV-2, a less common cause of AIDS, was licensed in April 1990. Because HIV-2 is extremely rare in this country, FDA has not required blood banks to test for this virus.

The combination test kit uses the enzyme-linked immunosorbent test method (ELISA), the same basic type used in the separate kits. A "reactive" reading with the screening test means that an individual may have been exposed to either HIV-1 or HIV-2. To specify which virus is the source of infection, and to check against the possibility of false positives inherent in all ELISA tests, FDA recommends that reactive results to the combination test be validated with more specific tests.

The combination test is manufactured by Genetics Systems Corporation of Seattle, the company that manufactures the only licensed HIV-2 antibody test.

So Long, Sunny Side Up

Preventing Food-Borne Illness in Nursing Homes

by Rebecca D. Williams

Every morning until about three years ago, Janet Tulloch, 67, ate her favorite breakfast of poached eggs at The Washington Home, the long-term care facility in Washington, D.C., where she has lived for 24 years.

But no more. Raw, poached, runny-yolked, or sunny side up eggs are not served in the nursing home because they are a common source of food-borne illness. The alternative—pasteurized eggs—is safer, but not as fresh tasting, Tulloch says.

"They do serve hard-boiled eggs and scrambled eggs made from ready-mixed stuff," says Tulloch, "but they're not as good."

Eggs and many other foods may be contaminated with disease-causing bacteria. If these foods are undercooked or mishandled, they can cause illness. While most food-borne illnesses are not life-threatening in younger adults, they are not so easily shaken off by the elderly.

According to a recent study, nursing home residents accounted for 2.4 percent of the food-borne illnesses in the United States between 1975 and 1987, but 19.4 percent of the deaths. The elderly were 10 times more likely to die of food-borne illnesses than younger adults.

The study, titled "Foodborne Disease Outbreaks in Nursing Homes, 1975 to 1987," was published in the Oct. 16,

1991, issue of the *Journal of the American Medical Association (JAMA)*. It was co-authored by Douglas Archer, Ph.D., deputy director of FDA's Center for Food Safety and Applied Nutrition, and William C. Levine, M.D., Joanne F. Smart, M.D., Nancy H. Bean, Ph.D., and Robert V. Tauxe, M.D., all of the national Centers for Disease Control in Atlanta, Ga.

"Frankly, the results were kind of sur-

prising," says Archer. "The mortality rates were much higher than we had expected."

Here are some examples of the many cases included in the study:

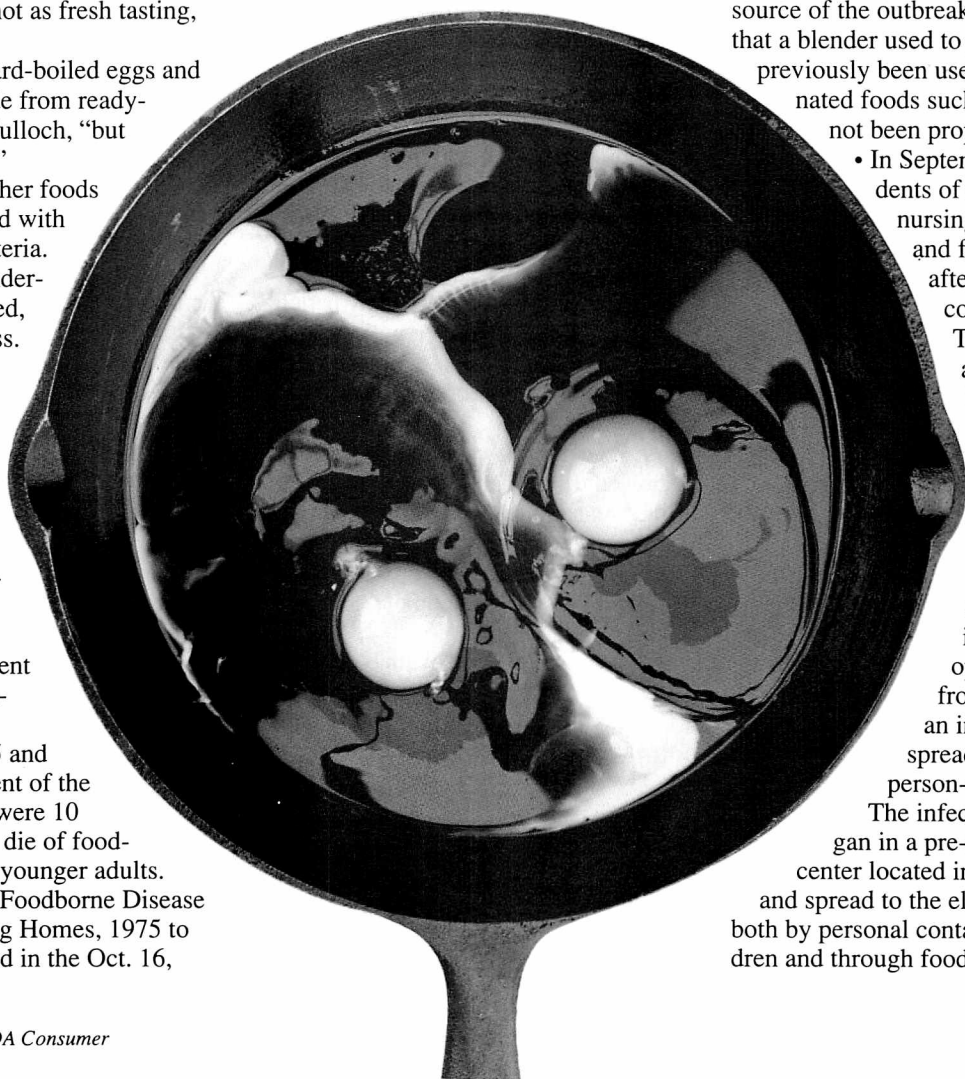
- In November 1986, five residents of a Windsor, Conn., nursing home died, and 25 others became ill with salmonellosis, a disease caused by bacteria often found in poultry and egg products. Although health officials never pinpointed the source of the outbreak, they suspected that a blender used to purée food had previously been used to mix contaminated foods such as eggs and had not been properly cleaned.

- In September 1984, 34 residents of a Papillion, Neb., nursing home became ill and four of them died after eating undercooked hamburger.

The meat contained a particularly virulent strain of *Escherichia coli*, a bacterium sometimes found in cattle intestines.

- In the spring of 1986, 88 people at a Minnesota nursing home developed severe diarrhea from *Giardia lamblia*, an intestinal protozoa spread through food or person-to-person contact.

The infection probably began in a pre-school day-care center located in the nursing home and spread to the elderly residents both by personal contact with the children and through food, since the mother





Janet Tulloch, 67, eats pasteurized scrambled eggs for breakfast at The Washington Home in Washington, D.C., with Donna Arbogast, a nursing home employee. Poached eggs—Tulloch's favorite—are not served at the nursing home anymore because runny-yolked eggs may contain disease-causing bacteria especially harmful to older adults.

of one of the infected children worked in the nursing home's kitchen.

These are just a few of the 166 outbreaks of food-borne disease that the *JAMA* study surveyed. The actual number of food-borne illnesses in nursing homes is thought to be much higher, however. Diarrhea is fairly common in nursing homes, so food poisoning may be mistaken for unrelated diseases and therefore go unreported to CDC.

Most of the food-borne illnesses in nursing homes could not be traced to a specific pathogen, according to the *JAMA* study. Of those that could, *Salmonella* bacteria, found most often in poultry and eggs, caused 53 percent of the outbreaks and 81 percent of the deaths.

The next most common cause of illness was *Staphylococcus*, which lives on the skin of healthy people and can be transferred to food during handling.

A third pathogen, found in human and animal feces, *Escherichia coli*, was not as common, but like *Salmonella* and *Staphylococcus*, it caused a higher-than-average rate of hospitalization and deaths.

In 59 of the outbreaks where the origins of the illnesses were known, im-

proper food handling played a key role. Investigators described food handlers who didn't wash their hands before preparing food, didn't store or cook foods at the proper temperatures, or failed to clean and sterilize the equipment. Eggs and poultry were the foods most likely to cause illness.

Why Are Older People More Affected?

Scientists do not know for sure why elderly people die more often from food-borne illnesses than younger adults.

There are several theories: Their immune systems may be weaker, other de-

A Glance at Nursing Home Food Handling

- Between 1975 and 1987, nursing homes accounted for 2.4 percent of all food-borne illnesses, but nearly 20 percent of the deaths. The rate of deaths from food-borne illnesses is 10 times higher in a nursing home than in any other setting.
- People choosing a nursing home should try to examine the food service facilities for cleanliness and attention to food safety.
- FDA and the Health Care Financing

Administration have developed two instructional videotapes on nursing home food safety techniques, one geared for medical directors and nursing home administrators, the other for food service workers. FDA plans to distribute the tapes in early 1992. For information on receiving them, contact FDA's Center for Food Safety and Applied Nutrition, HFF-11, 200 C St., S.W., Washington, D.C. 20204; telephone (202) 485-0325. ■

bilitating diseases may contribute to the problem, or their stomachs may have less acid to kill potentially harmful bacteria. Many older people, particularly in nursing homes, also take antibiotics, which tend to increase the risk of food-borne illnesses because they suppress beneficial bacteria in the intestines.

The predominant symptom of a food-borne illness is diarrhea, which is a contributing factor to death among the elderly far more often than any other age group in the United States. According to another study, this one published in the June 26, 1991, issue of *JAMA* by Judy F. Lew, M.D., and colleagues from CDC and the Emory University School of Public Health, more than half the people who died of diarrhea between 1979 and 1987 were older than 74. Within this group, 31 percent were living in nursing homes or similar institutions.

Moreover, deaths in which diarrhea plays a large part are on the rise among elderly residents of nursing homes. In 1979, 29 percent of deaths among elderly nursing home residents were diarrhea-related. In 1987, that number rose to 33 percent.

Nursing Home Inspections

According to the October *JAMA* study, one of the factors contributing to food-borne illnesses among the elderly is that nursing home kitchens are regulated differently from other food services, such as restaurants.

"One of the problems with nursing homes," says Archer, "is that they're not universally inspected and they're not inspected as thoroughly as other food services, for a number of reasons."

Nursing home kitchens must be inspected at least once a year by state health officials to keep their licenses, just as restaurants are. And if a nursing home wants to accept Medicare or Medicaid funds (more than half of them do), it must be certified by the federal Health Care Financing Administration (HCFA) and pass an inspection about once a year.

But, unlike restaurant inspectors, nursing home inspectors have more to look

Anne Richardson, a dietary aide at The Washington Home in Washington, D.C., empties scrambled, pasteurized eggs out of the bag they were packaged and cooked in. Pasteurization kills harmful bacteria in eggs, making them safer than fresh eggs for institutional kitchens.



for than food safety violations. They have to evaluate all the care residents receive, from medications to laundry services to recreational activities.

Also, HCFA lets states decide who will do the inspecting. It requires that each survey team include at least one nurse, but it does not require registered dietitians or sanitarians to be on the survey team. That's up to the state.

"I'm not sure that anyone going into the kitchen necessarily knows what's going on," says Toby Edelman, a staff attorney for the National Senior Citizens Law Center, a legal aid service for the elderly that has criticized HCFA's handling of nursing home inspections.

"In some states, yes . . . but people are obviously much more likely to find deficiencies in their own disciplines because they're more comfortable and more knowledgeable [with that]," says Edelman.

Emma Luten, a registered dietitian and

chief of surveyor training at HCFA, agrees that a dietitian would be quicker to spot trouble in a nursing home kitchen, but she says all surveyors receive training in food safety and are thorough in checking nursing home kitchens.

"These are health-care professionals, doctors and nurses," says Luten. "It's not like you're sending a clerk in there with a checklist. They have some training."

That training includes orientation sessions at the state level, as well as annual professional meetings, supervision by registered dietitians and sanitarians, and a week of training at HCFA headquarters in Baltimore, Md., during which an FDA official lectures on food safety.

Still, FDA would like more assurance that inspectors for all kinds of food service operations—in schools, restaurants, hospitals, and nursing homes—are trained in a uniform set of food safety principles.

To help unify them, FDA has devel-

Choosing a Food-Safe Facility

A conscientious nursing home kitchen staff offers the first line of defense against food-borne illnesses. When choosing a nursing home, the best way to check the kitchen is by visiting it and watching how the food handlers prepare meals.

"I'd look at the environment and people—see if the kitchen looks clean and the people look fairly healthy," advises Emma Luten of the Health Care Financing Administration, which certifies nursing homes to receive Medicare and Medicaid funds.

Ask if the nursing home has a registered dietitian on staff. If it does not, ask what kind of training the person in charge has, and look for the following:

- a knowledgeable and effective food service supervisor
- food handlers who wash their hands frequently and *always* after using the bathroom
- pasteurized or powdered eggs instead of pooled fresh eggs (one spoiled egg can ruin the whole batch)
- no poached, runny, or sunny side up eggs
- hot foods that are served hot and cold foods kept cold
- prompt serving of meals to residents
- thoroughly cooked meats
- blender equipment that is routinely disassembled, cleaned and sanitized. Ideally, the kitchen should use separate blenders for poultry products and pureed diets.

By law, each nursing home must post its most recent survey inspection report. You may also want to read past reports, available at your local public library, Social Security office, state health department, or in the office of your state's long-term care ombudsman, who responds to complaints of abuse by nursing home residents.

You can find the ombudsman either in your state's health department, social services department, or area agency on aging. ■

—R.D.W.

oped a set of guidelines called "model code ordinances" that inspectors can use to judge food storage, cooking and cleanliness. In some cases, FDA's ordinances are more strict than local or state health guidelines, and in other cases, state ordinances are more strict than FDA's. All states are encouraged, however, to adopt FDA model ordinances as minimum standards. The agency offers training for inspectors in how to use the ordinances,

but they are entirely voluntary unless the state or local regulatory authorities require them.

According to the October *JAMA* study, as of March 1989, 40 states had no institutional food service inspectors trained in FDA food and hygiene standards, while only three states lacked FDA-trained officials to inspect commercial food services.

And in 34 states, there were no state-

level standardized training courses for nursing home food inspectors to follow, leaving the responsibility to local jurisdictions, according to the study.

No matter what training workers receive, or how often nursing homes are inspected, the ultimate responsibility for food safety in nursing homes depends on the kitchen staff on a day-to-day basis, says Luten. Kitchen workers may pass inspection with flying colors one day, but if they undercook the hamburger the next day, residents may still get sick.

"Training does not always mean you're going to get what you pay for," says Luten. "You've got to have dedicated people who understand the importance of what they're doing and the importance of doing it right."

Steven James, an FDA official who teaches food safety to HCFA inspectors, agrees.

"It's just like walking into a restaurant," he says. "How would you know it's safe? All we can do is try to reduce the odds of food-borne illness from happening. No program is a guarantee—there are no guarantees. But we can take some preventive steps."

And as the elderly population grows, those steps will become even more necessary. The U.S. Bureau of Census projects that by the year 2000, the nursing home population will increase by 40 percent to more than 2.2 million people.

Careful food handling will be especially important to the health of this population, even if that means nursing home residents forgo their favorite foods.

In Janet Tulloch's case, that means no fresh eggs for breakfast, at least while she is in the nursing home.

"I know the reasons," she says, "but I don't think most residents understand why we can't have fresh eggs. When I visit home," she adds, "I'm dying for them." ■

Rebecca D. Williams is a staff writer for FDA Consumer.

A New Era of Gene Therapy

by Harold M. Schmeck Jr.

For thousands of years people have been taking medicines by mouth and for a scant century by injection. Now an entirely different method is at hand—medication delivered by genes.

The name coined for this new concept is gene therapy. It seems so revolutionary that few people think of it as a new way of administering medicine, but that is one of the most important aims. Instead of giving drugs to the patient, the doctors modify some of the patient's own cells by inserting a gene that instructs those cells to manufacture an important substance. The transplanted genes have turned the patient's own cells into factories for making the medicine. It is then delivered continuously to the tissues that need it. There are limitations, of course. The medication has to be a natural substance that the gene-modified cell can manufacture. It wouldn't be useful for delivering aspirin, for example, or any drug that is a totally artificial chemical.

The list of potential products includes natural substances that have anti-cancer potential, such as tumor necrosis factor, or other gene products that could reduce the perils of heart disease by changing the balance of blood lipids. Researchers at the National Heart, Lung and Blood Institute are already planning to try gene therapy against hemophilia, hoping to protect patients against catastrophic bleeding by transferring normal genes for making substances that help the

blood clot. Conversely, some powerful anti-clotting substances such as TPA (tissue plasminogen activator) could be delivered by the genetic route to patients under treatment for heart attack.

Scientists at the National Cancer Institute (NCI) hope to make genetic changes in pieces of a patient's cancer tissue so the tissue will spark a powerful cancer-destroying immune reaction when it is re-implanted in the patient's body. Scientists elsewhere are doing research that some day might make it possible to erase and replace a defective gene in specific tissues to correct a deadly inborn error.

Most of the applications of gene therapy will come into use only after the dawning of the 21st century, but that is less than a decade away and, in fact, human gene therapy has already begun.

PEG-ADA

The new era opened on Sept. 14, 1990, when a solemn little 4-year-old girl at the National Institutes of Health's Clinical Center in Bethesda, Md., began to receive a steady drip of fluid into a vein in her arm. That first treatment took only about a half hour, but preparation for it took decades and the implications were profound. (See accompanying article.)

In the milky fluid she received were about a billion of her own white blood cells treated previously in the laboratory to equip them with a foreign gene. The young patient lacked effective copies of that gene, and the lack doomed her to be continually hostage to all manner of

chance infections. Most of these would be minor annoyances to most humans. To her, each infection was a threat of death.

The usual course of events for children with her disease is to die by the age of 2 or 3. For this little girl, a relatively new drug, PEG-ADA, is calling a truce with the disease and buying time for the test of gene therapy. The drug was approved by the Food and Drug Administration in 1990. The aim of her gene therapy is to give the child long-term health and the hope of a normal life. It is too soon to say how well it will work, but her doctors see hopeful signs.

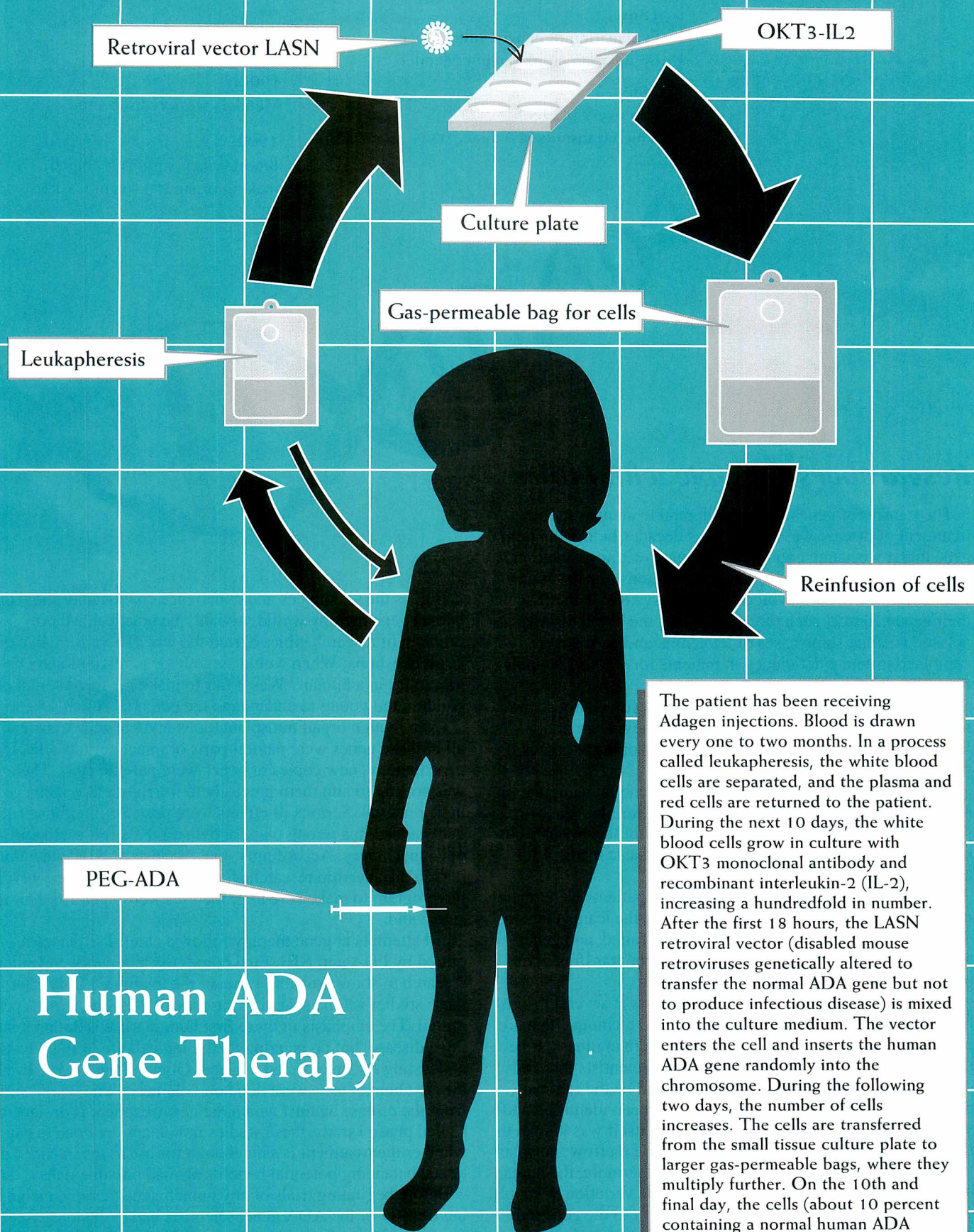
"All of her immune functions appear to be improving. She is normal in some values. She is still not normal in others, but she is improving steadily," said W. French Anderson, M.D., of the National Heart, Lung and Blood Institute, the chief architect and guiding spirit of her gene therapy treatment. By "values," he means such things as the number of various kinds of immune defense cells in her circulating blood. Anderson, who has spent much of his professional life at the institute, has dreamed and fought for the concept of gene therapy since he was an undergraduate in college 30 years ago. The idea was widely ridiculed in the early days, he says, but now it is fast becoming reality.

Correcting Genetic Disorders

The little girl suffers from a deadly genetic disorder called severe combined

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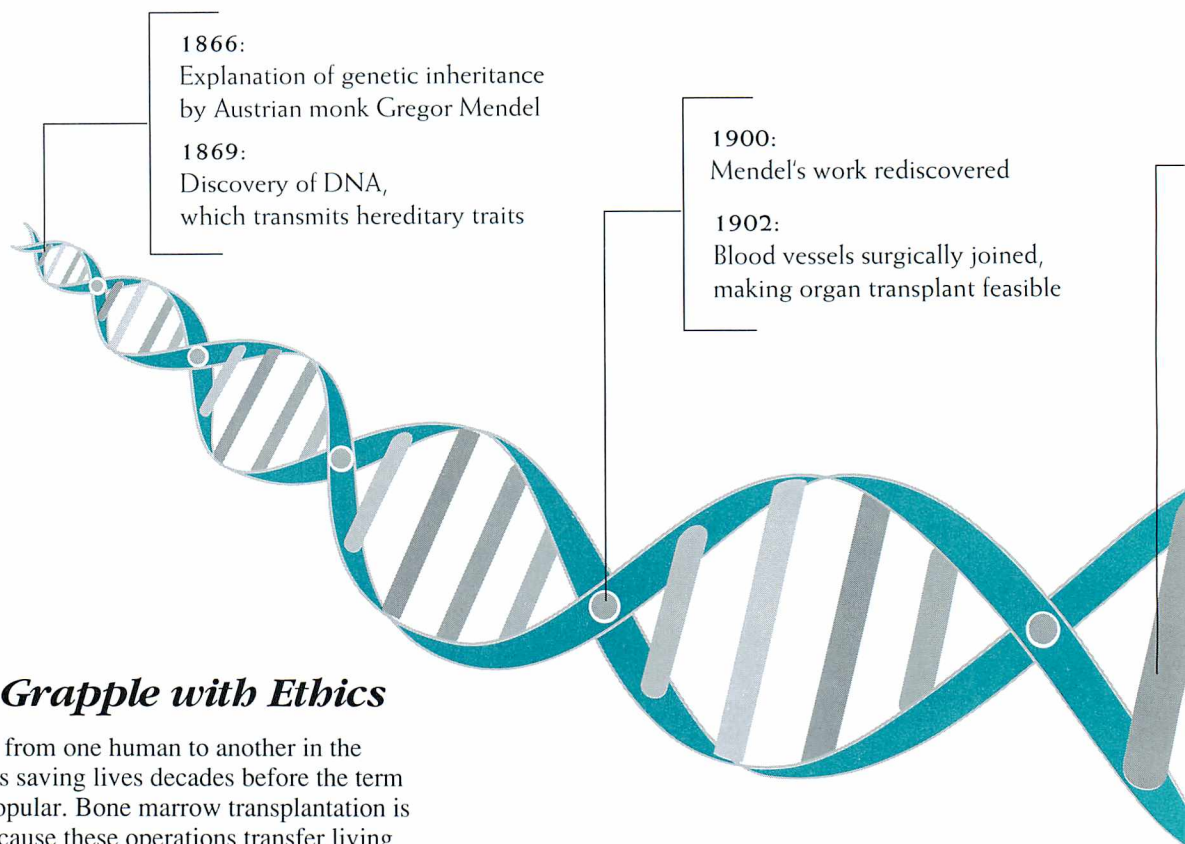
Human ADA Gene Therapy



The patient has been receiving Adagen injections. Blood is drawn every one to two months. In a process called leukapheresis, the white blood cells are separated, and the plasma and red cells are returned to the patient. During the next 10 days, the white blood cells grow in culture with OKT3 monoclonal antibody and recombinant interleukin-2 (IL-2), increasing a hundredfold in number. After the first 18 hours, the LASN retroviral vector (disabled mouse retroviruses genetically altered to transfer the normal ADA gene but not to produce infectious disease) is mixed into the culture medium. The vector enters the cell and inserts the human ADA gene randomly into the chromosome. During the following two days, the number of cells increases. The cells are transferred from the small tissue culture plate to larger gas-permeable bags, where they multiply further. On the 10th and final day, the cells (about 10 percent containing a normal human ADA gene) are harvested and reinfused into the patient.

(Source: National Institutes of Health)

Gene Transfer in Perspective



Researchers Grapple with Ethics

The transfer of genes from one human to another in the treatment of disease was saving lives decades before the term gene therapy became popular. Bone marrow transplantation is the clearest example because these operations transfer living cells of the entire human blood-forming system, with all of their genes, to treat such threats to life as the blood disorder aplastic anemia, some cases of leukemia, and even severe combined immune deficiency in patients for whom a suitable donor is available.

Other organ transplantations that have become almost commonplace today—such as those of the kidney, heart and liver—also require transfer of all the genes of those organs if the organs are to survive and function.

What is now called gene therapy—the genetic manipulation of human cells to incorporate one or a few foreign genes—would have been inconceivable without all of the advances in organ transplantation and related fields of basic medical science during the past several decades.

Attempts to accomplish gene therapy in patients were made in 1970 and again in 1980, although not by the teams that are doing the work now. These early attempts failed, and generated much debate on the ethics of doing gene transfers in humans.

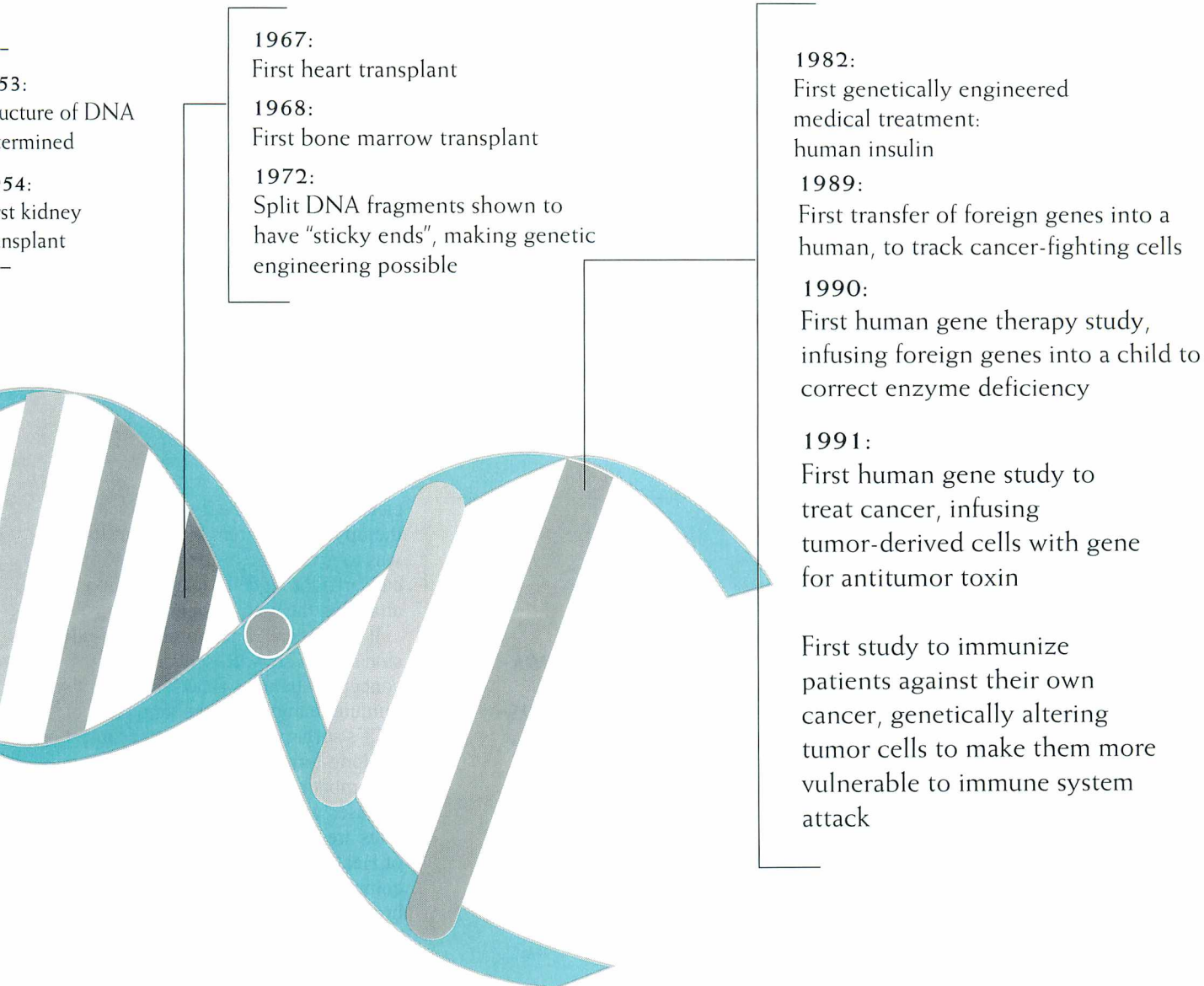
Gradually throughout the 1980s, scientists at several institutions developed the body of knowledge and technique that are now being translated into assault against human illness. It became widely agreed among these medical scientists that children suffering from ADA deficiency should be the first patients. The gene for the ADA enzyme had been identified and was available. Treatment with the enzyme itself was known to have beneficial effects on patients, and bone marrow transplantation sometimes accomplished cures. Furthermore, the human body seems to be tolerant of relatively wide variation in supply of the enzyme. This tolerance was important to the gene therapists because they couldn't hope to control precisely the amount of the enzyme the genetically engineered cells would produce. Animal research indicated that the treatment was safe enough to try against an otherwise fatal disease and even suggested strongly that it would work.

But, as the techniques and experience coalesced to show that human gene therapy would probably be practical, a thorny problem of research ethics barred the way. There were two difficult questions: When would something so revolutionary be safe to try in a human? Was it fair to make the first attempt on children too young to understand the potential risks?

Even though organ transplantations involve gene transfers, all of those genes were natural parts of intact normal cells. In gene therapy, new copies of genes were put into cells. There was no way to aim them precisely to the right place in the genetic material. Serious ill effects were possible if a transplanted gene landed in a wrong place and disrupted a cell's existing genetic machinery. Accordingly, the scientists at NIH under Anderson's leadership researched, tested and refined every part of the program to make sure their theories were right and their results valid.

All attempts at gene therapy follow a careful sequence required by FDA and NIH. First comes the laboratory and animal research to show probable value of the treatment. Only after these studies set the scientific base are the tests in humans permitted. The emphasis in these first human trials is not on treating a disease, but on gauging the biological effects in humans and testing for unexpected dangers. Often, in medical research, the first human tests were done on volunteers who do not suffer from the disease against which the new treatment is designed. Called phase I trials, these studies in humans are done to gauge whether the treatment is safe enough for use in the intended patients, balancing potential benefits against possible risks.

Before beginning trials of any human gene therapy, including transfer of the ADA gene, scientists had to demonstrate that gene transfer itself could be done safely. These trials had to be done in adult volunteers who could understand the risks, and they ought to be done in a class of patients that might benefit from the medical experiments. Who could be found to fit those limitations?



The NIH research team thought there were such people: the severely ill cancer patients under treatment by Stephen A. Rosenberg, M.D. For years he had been developing his concept of adoptive immunotherapy in patients for whom all other treatments had failed. He, too, used white blood cells, called lymphocytes, taking them from the patients and their cancer tissue, treating the cells in the laboratory to multiply their numbers and enhance their cancer-fighting ability before returning them to the patients. It was not gene therapy. He did not manipulate the cells' genes. Instead, he grew the cells in laboratory culture dishes with a growth promoter called Interleukin 2, a substance of the class called lymphokines. There were remarkable improvements in a few patients and some stark failures.

One problem in improving the success rate was the difficulty of identifying the treated cells after they were infused into the patients. Rosenberg needed some way to "tag" them, to give them identifying "markers" so that he could tell where they migrated, how long they lasted, and how well they performed. Together, he, R. Michael Blaese, M.D., and Dr. Anderson developed a plan to give some of those cells a foreign gene that would serve as a readily detectable marker. They picked genes that were presumably harmless and easily identifiable and

asked some of the gravely ill cancer patients to volunteer to receive them.

These men and women were told frankly that the treatments would not help them directly, but that the experiments would probably be of great benefit to cancer patients in the future. After the plan was approved, five adult cancer patients became the first humans to receive infusions of cells in which foreign genes had been successfully transplanted. The researchers reported in the *New England Journal of Medicine* of Aug. 30, 1990, that the gene-modified cells could survive for long periods in the patients and that they had done no detectable harm.

"These studies represented the first successful introduction of foreign genes into humans," said an NCI statement. "The results suggested that gene transfer might be a feasible approach for delivering toxic substances to tumors, modifying a patient's genes, or correcting inherited defects."

This was the evidence the gene therapy research team needed to justify its attempt at gene therapy in a child. It was, in short, the go-ahead signal for the new era. ■

—H.M.S.

(Continued from page 14)

immune deficiency (SCID). Because of a tiny chemical error in her DNA—the genetic material—she lacks a properly functioning gene for making an enzyme called adenosine deaminase (ADA). Her particular type of severe failure of immunity is therefore called ADA deficiency. In the gene therapy treatments, some of her white blood cells are first removed and treated in the laboratory to install good copies of the ADA gene. Then the cells are put back into her circulating blood. As long as those gene-modified cells continue to function, they can provide the enzyme that she needs. How long will they function? That is one of the key questions yet to be answered.

Genes are chemical instruction sheets that living cells use to guide all manner of life processes. Most genes are the blueprints for making one or another protein vital to the body. Every human has an estimated 100,000 genes. A minor distortion in chemistry—a “spelling error”—in just one of those genes is responsible for the child’s grave illness. It is an extraordinarily rare condition. Only about 10 ADA deficiency patients are known in North America. Without treatment, they would all die in infancy or early childhood.

Natural ADA delivered from the outside is too short-lived to be useful as a drug, but a new form of the enzyme, protected from breakdown by the chemical polyethylene glycol and called PEG-ADA, helps some victims of the genetic disease. This drug, developed under FDA’s orphan product program and marketed under the trade name Adagen is mainly responsible for keeping the young patient alive while the new gene therapy treatment is tested and given a chance to work.

Scientists are looking forward to possible use of gene therapy in treating adult leukemia and childhood leukemia.

The improvement her doctors have noted is beyond anything PEG-ADA produced alone during months of use. This fact hints strongly that gene therapy itself is showing benefit. If that proves true, it will be the first success ever achieved by gene therapy.

Encouraged by the child’s progress, Anderson and his colleagues have begun gene therapy in another ADA deficiency child and plan to treat two more by the end of this year. The ADA research team has been led by Anderson and R. Michael Blaese, M.D., of the National Cancer Institute, an expert on childhood disorders of immunity.

New Cancer Treatment

A few months after the PEG-ADA patient’s historic first treatment, two adult

cancer patients at NCI were given gene therapy of a different kind. The strategy was to give some of the patients’ own cancer-fighting cells a new weapon for attacking the malignant enemy.

It is a logical, but entirely new, extension of Steven A. Rosenberg, M.D.’s concept of treating cancer by “adoptive immunotherapy.” Rosenberg, chief of NCI’s surgery branch, is just as intent on the long-term battle to harness immunity to combat cancer as Anderson is to cure diseases with gene therapy. Both institutes are units of the National Institutes of Health (NIH) in Bethesda, Md. The common needs of the two programs have brought the two medical scientists together in a historic collaboration.

While ADA patients receive cells modified genetically to make them produce the ADA enzyme, the cancer patients receive cells genetically engineered to make large amounts of the natural toxin called tumor necrosis factor. It has strong cancer-killing abilities in some circumstances. The cells used for this anti-cancer gene therapy come originally from the patients who receive them, but genetic manipulation arms these cells against cancer in a dramatically new way. In one important sense, the two gene therapy strategies differ. The ADA patients’ cells are given something they should have had normally. The cancer patients receive something extra. In a progress report to the American Society of Clinical Oncology in Houston in May, Rosenberg said evaluation of the first two cancer patients show no ill effects from the unprecedented treatment, but that it is still too early to tell how effective their gene therapy will be. His patients suffer from malignant melanoma, a grave form of

skin cancer. No conventional treatment has been effective for them.

New Proposals Considered

Soon after the first treatments began, several other proposals for gene therapy were put before FDA and NIH's Recombinant DNA Advisory Committee, the main federal advisory panel on research involving genetic manipulation. The new proposals, most of them in collaboration with Anderson's team, all involve putting gene markers into various kinds of tissues as a necessary preliminary step to actual gene therapy. (See accompanying article.) The scientists are looking forward to possible use of gene therapy in treating adult and childhood leukemia, in putting useful foreign genes into liver cells and into bone marrow to cope with a potentially wide variety of disorders.

Members of the team at the Heart, Lung and Blood Institute are doing research toward use of gene transfers that would give some of a patient's cells a heightened ability to make the anti-clotting drug TPA. The intention is to use these genetically engineered cells to help prevent dangerous clotting in blood vessels that have been installed surgically to cope with heart disease and in artificial inserts called stents that are used to keep blood vessels open after operations to remove atherosclerotic plaques.

Rosenberg's team is planning a major new variation in his efforts to use immunotherapy against cancer. Encouraged by success in animal research, he hopes to take a sample of a patient's cancer tissue and transfer into it a foreign gene that will stimulate attack by the patient's immune defense system. In animals, this procedure led to destruction not only of

*Scientists elsewhere
are doing research
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make it possible to
erase and replace a
defective gene to
correct a deadly in-
born error.*

the transplanted tumor, but also of all the other cancer in the animal's body. The scientists hope this will work in the same dramatic fashion in humans.

Improving the Method

Anderson and his colleagues, having successfully pioneered the first generation of human gene therapy techniques, are already hard at work on an important second generation.

The present procedure is cumbersome, requiring the harvesting of a patient's cells, treating the cells in the laboratory, and then returning them to the patient. Specially modified viruses are used to carry the genes to the cells where they are needed. Then the remodeled viruses simply vanish because they lack the genetic instructions to fabricate new virus

particles. The viruses had to be modified in this way so that infection with the virus itself would not endanger the patient. It took expert virologists at several research centers the better part of the decade to develop these self-destructive viruses and learn how to make them deliver their genetic cargoes efficiently into human cells. The scientists call these special gene-delivering viruses "vectors."

The next generation of gene therapies, Anderson believes, must be less complex and cumbersome. Instead of removing cells from the patient, treating them in the laboratory, and returning the gene-modified cells to the patient, Anderson and his colleagues are working to develop "injectable vectors." These will be self-eliminating viruses that can be injected directly into the patient. The viruses will carry the needed foreign gene to the right tissues, deposit their cargo of therapeutic genes, and then vanish, having accomplished the crucial task of gene transfer.

It may take five or ten years to develop these injectable vectors, Anderson estimates. He also sees the need for two other advances that may take longer: to develop ways to deliver a gene to a particular location in the patient's genetic material and to regulate closely the degree and timing of the transplanted gene's action.

Many research teams are attacking these problems today. Once they are solved, Anderson says, gene therapy could become "the major new drug delivery system of the future." ■

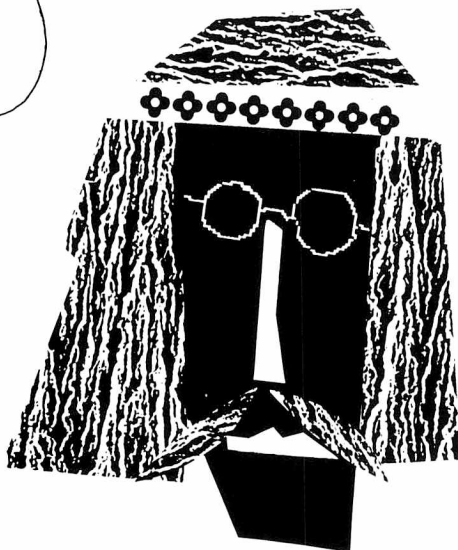
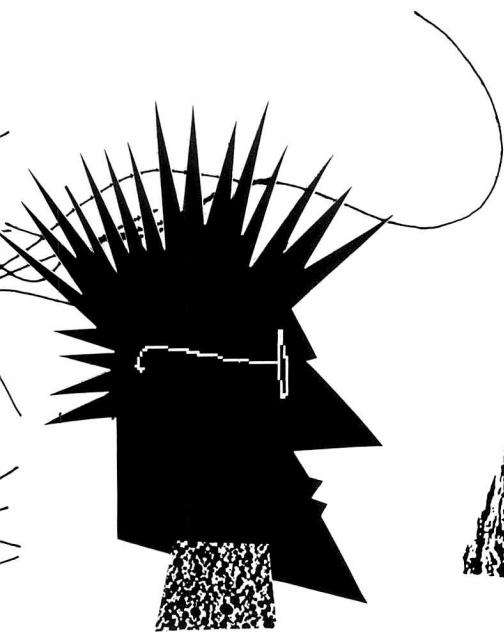
Harold M. Schmeck Jr. retired recently from the science news staff of The New York Times.

Hair!

***From Personal
Statement to
Personal Problem***

by Devera Pine





From the shaved heads of medieval monks, to the long-haired hippies of the '60s, to the spiked hairdos of today's punk rockers, hair has always made a personal statement.

"It's one of the leading ways people can establish their individuality and express their style," says Jerome Shupack, M.D., professor of clinical dermatology at New York University Medical Center in New York City. "Hair has had sociological importance throughout the ages."

Because of its importance, anything that happens to our hair that we can't control—falling out or turning gray, for instance—can be the source of much anxiety.

In the United States, some 35 million men are losing or have lost their hair from male-pattern baldness, according to the American Hair Loss Council. Approximately 20 million women have experienced a similar loss of hair (from female-pattern hair loss), and an estimated 2.5 million Americans have lost their hair due to other causes.

The Basics

Hair is produced by hair follicles—indentations of the epidermis (outer skin layer) that contain the hair root, the muscle attached to it, and sebaceous, or oil, glands. Hair is made up of dead cells filled with proteins, most of which are known as keratins. The cells are woven together like a rope to form the hair fiber. The hair fiber, in turn, has three layers: the outer cuticle with its fish-scale-

like structure; the cortex, which contains the bulk of the fiber; and the center, or medulla. Hair color is determined by melanocytes, cells that produce pigment. When these cells stop producing pigment, hair turns gray.

Although it seems as if the hair on your head is always growing, hair actually has active and rest phases. The growth phase, known as anagen, lasts for two to six years. At any given time, about 90 percent of scalp hair is in the growth stage. The remainder is in the rest phase, known as telogen; this lasts from two to three months.

Once the rest phase is over, the hair strand falls out and a new one begins to grow. As a result, it's considered normal to lose from 20 to 100 hairs a day, says Diana Bihova, M.D., a dermatologist in private practice in New York City. Only a change in your regular pattern of loss is considered abnormal—but many things, including genetic factors, diet, stress, and medications, can change that pattern.

Baldness: Manifest Destiny?

The most common cause of hair loss in both men and women is rooted in genetic predisposition. Called androgenic alopecia, it is known as male-pattern baldness in men and female-pattern hair loss in women. (Alopecia is the scientific term for baldness.) According to the American Hair Loss Council, genetics accounts for 95 percent of all cases of hair loss in this country.

Baldness results from a combination of

genetic factors and levels of testosterone (a hormone produced by the adrenal gland in both sexes and also by the testes in men). If hormone levels are right, then the hair follicles will express their genetic destiny by growing for shorter periods and producing finer hairs. In men, who have higher levels of testosterone than women, this eventually results in a bald scalp at the crown of the head and a horseshoe-shaped fringe of hair remaining on the sides. In women, the hair thins all over the scalp; the hairline does not recede. This type of hair loss doesn't usually show up in women until menopause; until then, estrogen tends to counteract the effects of testosterone.

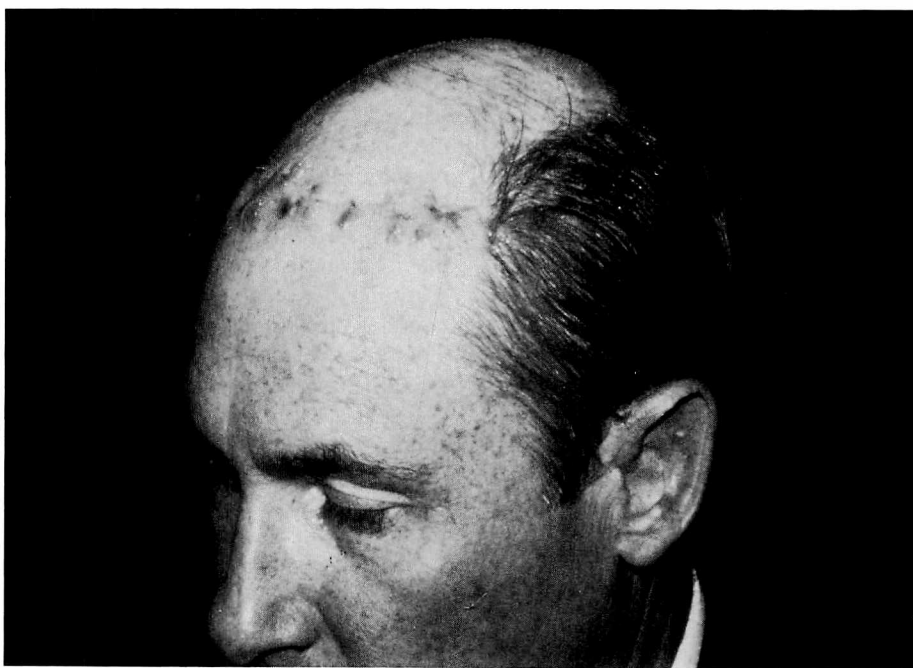
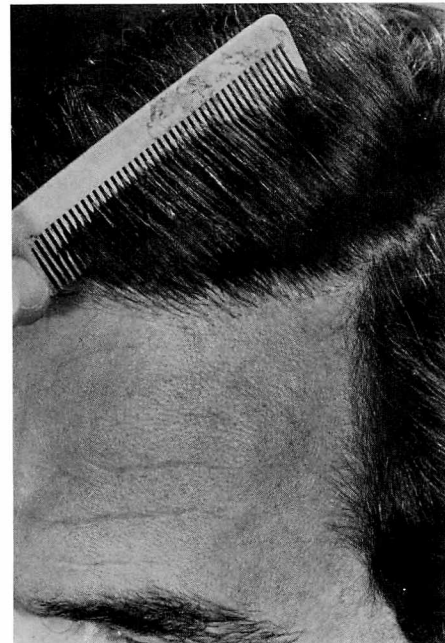
One Approved Drug

The only drug approved by the Food and Drug Administration to treat pattern baldness or hair loss is minoxidil topical solution (Rogaine), which is rubbed into the scalp. Originally approved for hereditary male-pattern baldness in 1988, it was also approved for treating female-pattern hair loss in August 1991. However, it should not be used by pregnant or nursing women.

In his dermatological practice, Arthur P. Bertolino, M.D., Ph.D., director of the hair consultation unit at New York University, says that this lotion helps hair grow in 10 to 14 percent of the people who try it. He estimates that approximately 90 percent of the time, Rogaine at least slows down hair loss. (Minoxidil

Hair transplantation and suturing can be an iffy proposition. Top left is an example of poor design and improper technique in hair transplant grafting; grafts were placed too low. Top right shows a more correct design and grafting result. At bottom, scarring is evident from sutures used to attach a hair addition.

(Photos courtesy of [top] Emmanuel Marritt, M.D., of Denver and [bottom] American Hair Loss Council)



is also available in tablet form to treat severe high blood pressure. Oral minoxidil has a potential for serious side effects and is not approved to treat baldness.)

No one is certain yet just how topical minoxidil works to promote hair growth. "One theory is that it dilates the blood vessels, so it may stimulate nourishment of follicles," says Bihova. Alternatively, Rogaine may convert tiny hair follicles that produce peach fuzz into large hair follicles that produce normal-size hairs. Again, no one knows for sure.

What is certain is that, at least in men, Rogaine works better on patients who fit a certain profile: They've generally been bald for less than 10 years, have bald spots on top of the head that are less than 4 inches in diameter, and they still have fine hairs in their balding areas. "The process begins very early," says Bihova. "I see 19-, 20-year-old males who have it."

The most common side effects with this medication are itching and skin irritation. Also, according to Bertolino, once you stop using it, any hair that grew as a result will fall out. Finally, the drug is expensive: In 1990 it cost about \$600 a year to use it twice a day.

Transplants

Baldness can also be treated with hair transplants, in which plugs of "donor"

follicles from the patient's scalp are used to fill the hairline. Although hair transplants work well in both men and women, the treatment tends to have a more dramatic effect on appearance in men with bald spots than it does on women with thinning hair.

"The less hair you have, the more drama in the change," says Robert Auerbach, M.D., associate professor of clinical dermatology at New York University School of Medicine. However, the American Hair Loss Council warns against attempting to replace lost hair with hair pieces sutured to the scalp. FDA has not approved any products specifically intended for this purpose; how-

ever, this does not preclude a physician from using sutures, which are approved devices, for this purpose. According to the council, although the procedure is legal, it can result in scars, infections, and even brain abscesses.

Another treatment for male-pattern baldness, hair implants made of high-density artificial fibers surgically implanted in the scalp, was banned by FDA in 1984 because it causes infection. This is the only device FDA has ever banned.

Products That Don't Work

So-called "thinning hair supplements," "hair farming products," and "vasodilators" for the scalp will not promote hair

growth, says Mike Mahoney, a spokesperson for the American Hair Loss Council.

Thinning hair supplements are nothing more than hair conditioners that temporarily make your hair feel or look a little thicker. The main ingredient in these products—polysorbate—is also found in many shampoos. Promotional materials for hair farming products claim that they will release hairs that are “trapped” in a bald scalp. Mahoney says these products, many of which are herbal preparations, can do no such thing. And so-called vasodilators do not increase the blood supply to the scalp and do not promote hair growth.

Everyday Hazards

While male- and female-pattern baldness results in permanent hair loss, other factors can cause temporary loss of hair. For instance, the drop in the level of estrogen at the end of pregnancy can cause a woman's hair to shed more readily. Two or three months after a woman stops taking birth control pills, she may experience the same effect, since birth control pills produce hormone changes that mimic pregnancy. A major physical stress, such as surgery, or a major emotional stress—positive or negative—can cause hair loss.

“I've seen women start losing their hair before getting married,” says Bihova. Even jet lag can have a similar effect.

In most of these cases, the hormonal imbalance or stressful situation will correct itself, and the scalp will soon begin growing hair again. But, says Bihova, since most women are extremely upset by even a temporary hair loss, many dermatologists treat these conditions with either topical steroid preparations or localized injections of low doses of steroids. Bihova emphasizes that these are local, not systemic, injections of steroids; therefore, the shots do not have the same risk of dangerous side effects as systemic steroids. However, only a board-certified dermatologist should administer this treatment, she says.

The list of causes of temporary hair loss goes on: Pressure on the scalp from wigs or hairdos that pull too tightly can cause it. A fever of 103 degrees Fahrenheit or more often causes hair loss six weeks to three months later. And some medications can cause a temporary loss. These include vitamin A derivatives such

as Accutane, cough medicines with iodides, anti-ulcer drugs, some antibiotics, beta blockers, antidepressants and amphetamines, anti-arthritis drugs, blood thinners, some cholesterol-lowering agents, aspirin taken over long periods, some thyroid medications, and chemotherapy.

You Hair What You Eat?

Although nutrition does play a role in hair loss and in the overall health of your hair, only extreme nutritional deficiencies or excesses will cause hair loss. For instance, people with anorexia and bulimia may temporarily lose hair. So will others suffering from malnutrition.

“It's pretty rare in the United States,” says Bertolino. “If someone was on a real strange, restrictive diet, it could happen to them.”

Megadoses of some vitamins—particularly A and E—and an iron deficiency may lead to hair loss. People who claim they can determine which vitamins are lacking in your diet by analyzing your hair, however, are not speaking from a scientifically sound basis. The test used with this type of hair analysis—atomic absorption spectrophotometry—is a legitimate analytical chemistry method; however, used on hair, the results of this test do not correlate with nutritional status, says Shupack. “Because of the sociological importance of hair, a lot of people try to cash in on it,” he says. “[Hair analysis] is all witchcraft as far as I'm concerned.”

There are, however, a few legitimate hair tests for substances such as arsenic and lead.

For Beauty's Sake

Every time you shampoo, blow dry, perm, straighten, or dye your hair, you damage it slightly, says Bertolino. For the most part, hair can withstand this type of treatment. But overzealous beautifying can damage the hair fiber, resulting in many broken strands, and a frizzy, split-end look. For instance, if you bleach your hair and then have a bunch of perms done in a short time, you're heading for trouble.

Misuse of hair cosmetics can cause the hair to break as it comes out of the scalp, says Frances Storrs, M.D., professor of dermatology at the Oregon Health Sciences University. Permanent wave solutions break the bonds that hold hair together and then re-form them. But with a

perm that is not diluted right or not rinsed off properly, for instance, those bonds may not re-form and the hair would soon fall out as a result. Fortunately, most professional hair dressers know how to use perms correctly, says Storrs.

Most hair dyes are not as irritating as permanent solutions, mostly because they do not break the bonds between hair fibers and are therefore not likely to cause a hair loss, she says. However, a severe allergic reaction to hair dye could cause hair loss. “The allergy is pretty common, actually,” says Storrs. Permanent solutions can also cause allergic reactions, though that's a rare side effect.

Other beauty-related manipulations of the hair can cause problems, too: Hot irons, corn rows, and braids may bring on temporary or permanent hair loss. If the hair breaks often enough, the follicles may eventually not be able to produce normal hair, says Bihova. “If someone has a problem with thinning and excessive loss, we advise being gentle,” she says. “Don't use rollers; don't use blow dryers on a hot setting; don't wear tight hair styles.” Rough shampooing may accelerate any loss, though it's usually not a problem in people with healthy hair.

The Medical Side

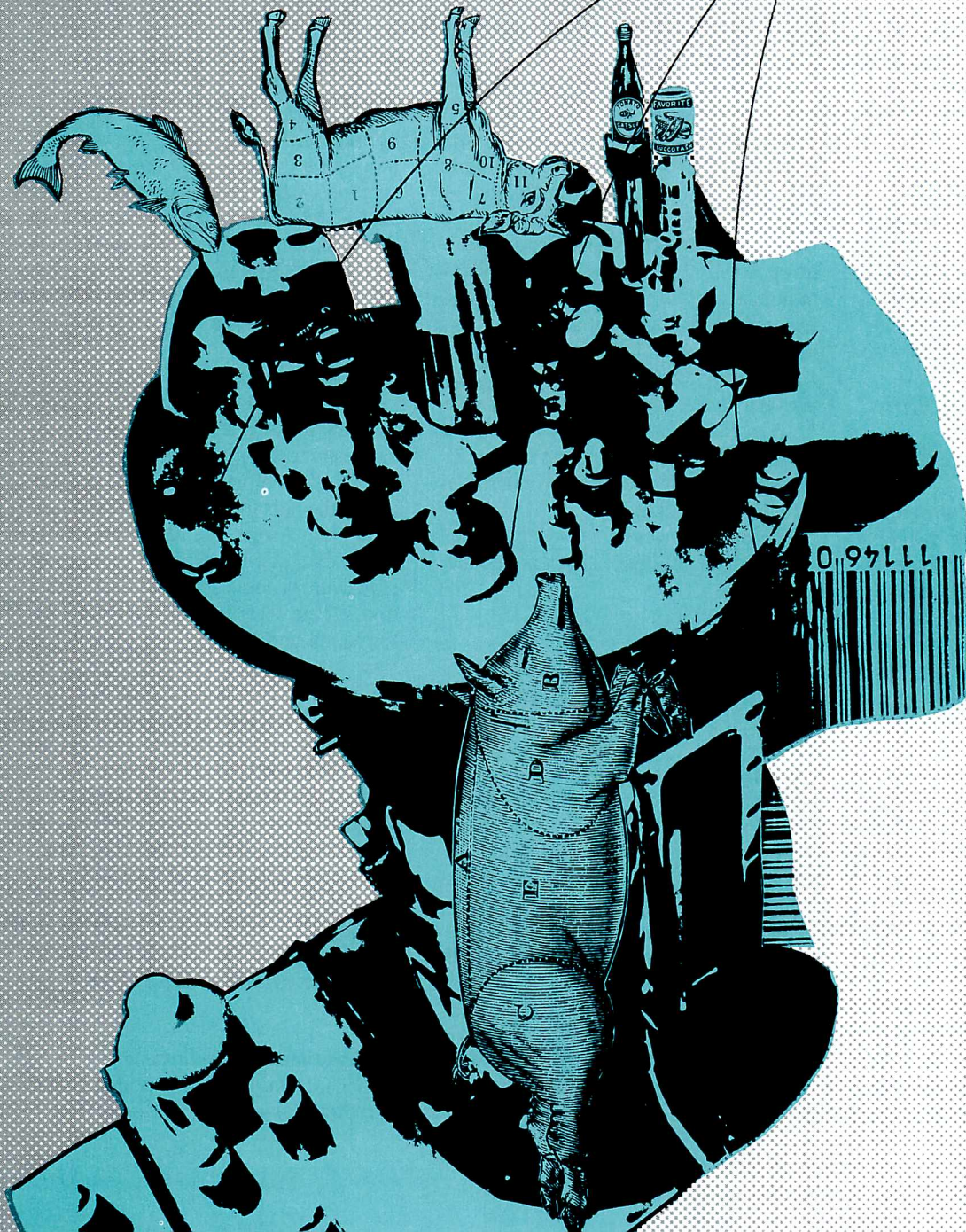
Some hair loss is the result of a type of immune disorder known as alopecia areata—some 2.5 million people suffer from this condition in which antibodies attack the hair follicle, causing the hair to fall out. Alopecia areata often causes small, oval or circular areas of hair loss. However, in some forms of the condition, all the scalp hair falls out; in other forms, all body hair is lost. Although the loss is usually temporary, the condition can recur. Treatments include topical steroids or the use of chemicals to produce an allergic reaction to start the hair growing again.

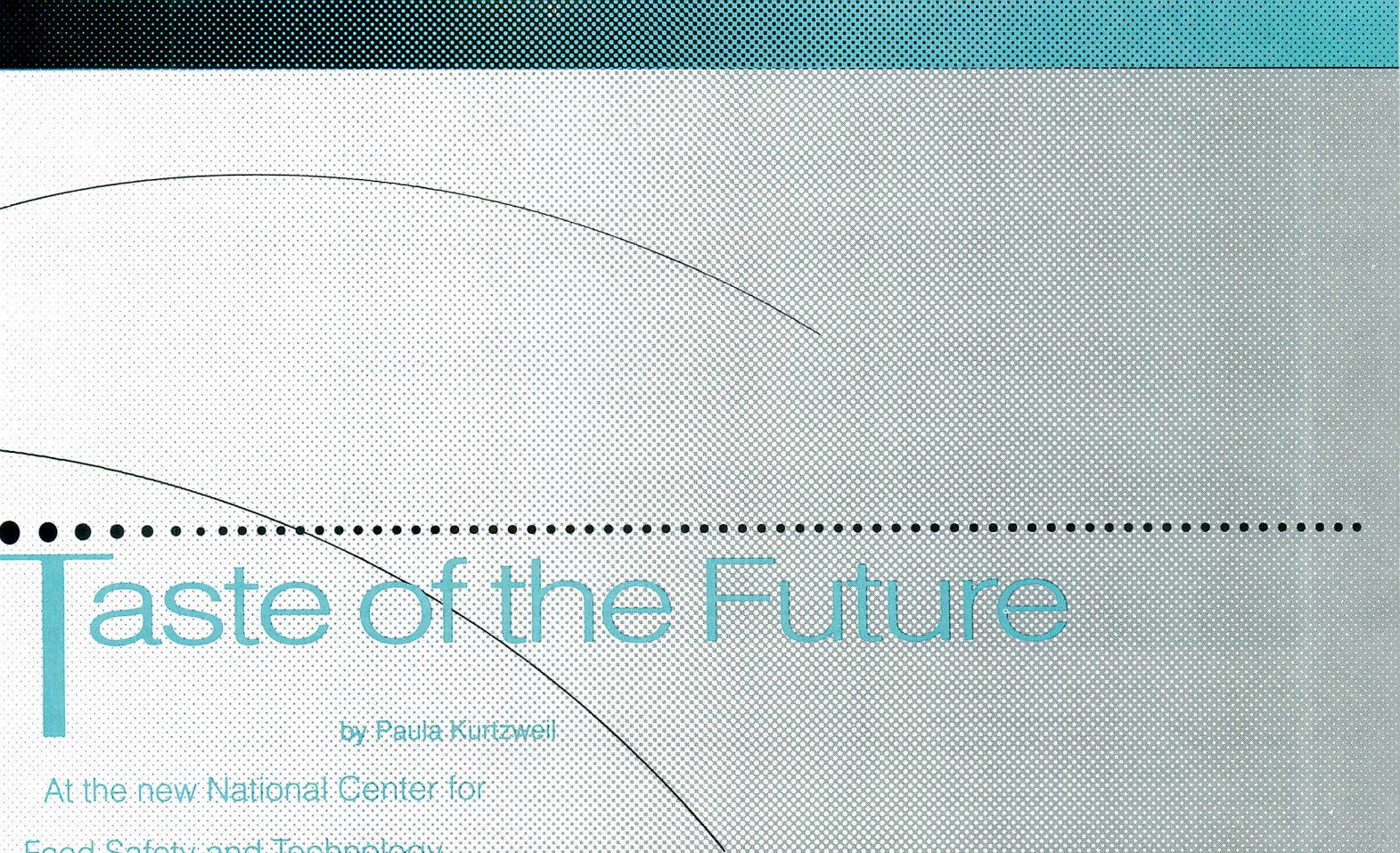
Finally, chronic, systemic conditions—including one form of lupus, abnormal kidney and liver function, and hypothyroidism or hyperthyroidism—can affect the hair. If you're experiencing hair loss, see a doctor. He or she will want to order some basic blood tests to rule out any medical cause of the condition. ■

Devera Pine is a freelance writer in New York City who frequently writes about health and science.

Food Safety Research Center

O f f e r s





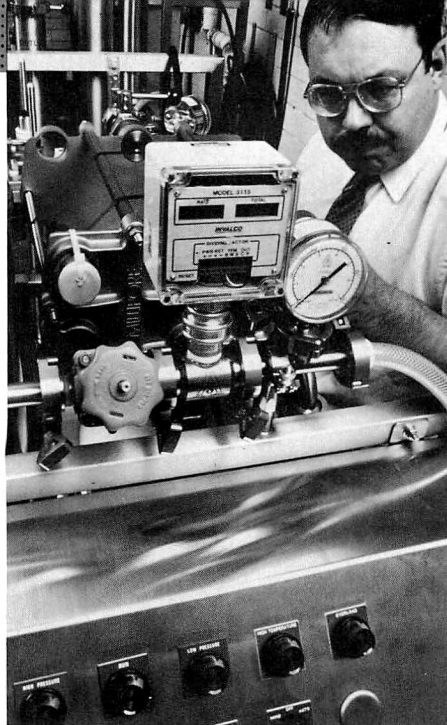
Taste of the Future

by Paula Kurtzweil

At the new National Center for Food Safety and Technology (NCFST) in Bedford Park, Ill., food scientists from the Food and Drug Administration are getting a taste of things to come.

Replete with renovated laboratories, some new laboratory equipment and supplies, and lots of work space, 33 FDA scientists and other staff members are studying how up-and-coming food processing and packaging technologies may affect food safety.

Since the establishment of the collaborative research program in late 1990, the scientists have *(continued)*



Joe Schlessler, Ph.D., an FDA staff fellow, uses the center's state-of-the-art reverse osmosis/ultrafiltration equipment for biotechnology research. (Photos on this page and the next by David Joel Photography, courtesy of Illinois Institute of Technology)

been studying emerging food issues that include recycled plastic food containers, computerization of food processing systems, shelf-life extension of food, and use of biotechnology-derived tools for detecting contaminants in food.

Their ultimate goal: to enhance the safety and quality of food products.

The research at the center is made possible through the center's unique consortium of government, industry and academia devoted to cooperative food safety research on food biotechnology and food processing and packaging technologies.

In addition to FDA, the center is supported by the Illinois Institute of Technology, the IIT Research Institute, the University of Illinois, and 38 food-related companies. (See accompanying box.) FDA's Center for Food Safety and Applied Nutrition oversees the agency's role in NCFST.

According to FDA Commissioner David Kessler, M.D., the center helps FDA carry out two of its food-related missions: to serve as a leader in food safety and to foster innovation.

"If we haven't done some of the work ourselves, if we haven't been there scientifically, it will be all too easy for FDA to say 'no' to new advances as they come in for review," he said.

He also noted that while NCFST par-

ticipants will benefit from the center's research, the ultimate beneficiary is the consumer. "This is as it should be," he said.

The benefits, explained NCFST director Richard Lechowich, Ph.D., include more than just a safe food supply; consumers also will have food that is nutritious, tastes good, and is economically produced. "That's what consumers are interested in," he said.

Why a National Food Center?

According to Lechowich, the center was created so that government, academia, and the food industry would have a common ground on which to meet and share new food technologies. In doing so, he said, they can help ensure that the benefits of those new technologies get to the consumer as quickly as possible.

"[Here], government, academia and industry can work together to solve problems," he said.

The center's development also was prompted by the increasing use of new food processes and packaging technologies; the use of new ingredients produced through biotechnology; and the growing use of ingredient replacements for sugars, fats, proteins, and other nutrients, said FDA's David Armstrong, Ph.D., NCFST's associate director for research.

"These new foods and processes raise new questions about the safety and nutritive value of these products," he said. "That's precisely why the NCFST's research is so necessary."

Increased competition from foreign markets was another incentive for creating NCFST, Lechowich said. He noted that the constant mergers and consolidations in the food industry often interfere with companies' ability to carry out long-term research. As a result, the United States may fall behind other countries in advanced technologies and thus lose its ability to compete worldwide, he said.

The center hopes to take its research one step further: It plans to use its studies as the basis on which future food safety and food regulatory decisions in this country are made.

"The real proof of NCFST's success will be the research that is generated there and the national policy that the research helps set," said Robert McVicker, a senior vice president for Kraft General Foods and chairman of the center's oversight committee. "Real science will tell

the real truth."

Getting to Work

Currently, the science is being done by the center's 37 employees, four of whom are employed by IIT. Among the latter is director Lechowich, a food scientist with more than 30 years of academic and industrial experience.

Their work site is CPC International Inc.'s former corporate research and development facility on the Illinois Institute of Technology's Moffett Campus in a southwest suburb of Chicago. CPC donated the \$7 million facility in 1988.

It includes more than 40 laboratories, many of which have been renovated and stocked with new lab equipment and glassware. There also are three pilot plants, two of which will house scaled-down versions of industrial food processing and packaging equipment to be used for research on all stages of food processing and packaging. The third is an industrial-sized plant that will include a biotechnology mini-pilot plant.

"Rather than just hearing or reading about new food processing technologies, we can now get hands-on experience," Armstrong said. He noted that NCFST is the only facility where FDA has such capabilities.

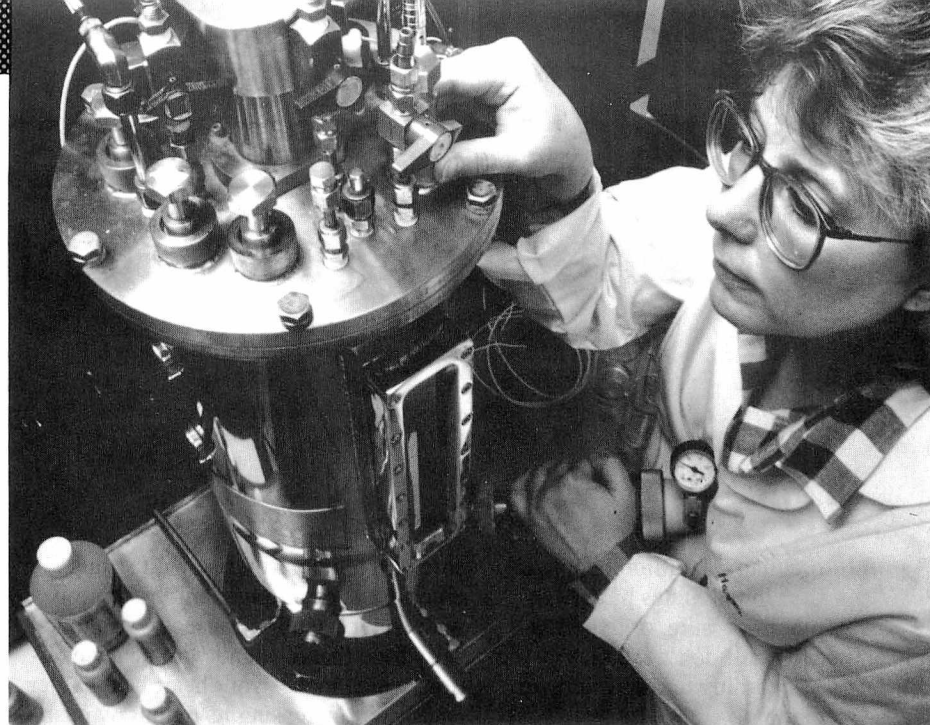
Already in place is a scaled-down version of a high-temperature, short-time pasteurizer, which is being used to study the feasibility of monitoring milk pasteurization via computer-linked sensors placed at critical processing points in the equipment. Currently, hard-wired systems are used to monitor and ensure proper pasteurization at these points, where the potential is greatest for a health hazard to be introduced.

According to FDA's Carol Harper, Ph.D., a research engineer involved in the project, the research aims to add additional safety checks in milk pasteurization and expedite record review during inspections. This will result in cost savings, she explained, by generating data more quickly and accurately than the current practice of recording data by hand.

"We plan to expand our approach to other food processing areas, too," she said.

Another NCFST research project under way involves examining potential hazards of recycled plastic bottles for food use. FDA's Vanee Komolprasert, Ph.D., who is participating in the research, said recycling of various plastic materials used in food packaging—such

Carol Harper, Ph.D., an FDA research engineer, uses a bacterial fermenter to study the production of enzymes and other important food components.



NCFST

Food Industry Members

Founding Members:

BSN Groupe
CPC International Inc.
Dean Foods Co.
FMC Corp.
Kraft General Foods Inc.
Nabisco Biscuit Co.
Pfizer Inc.
Quaker Oats Co.
Reynolds Metals Co.
Wm. Wrigley Jr. Co.

Affiliate Members:

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Beatrice/Hunt-Wesson Inc.
The Coca-Cola Co.
Crown, Cork and Seal Co. Inc.
Exxon Polymers Group
General Mills Inc.
Gerber Products Co.
The Procter & Gamble Co.
Swift-Eckrich Inc.
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Associate Members:

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APV Crepaco Inc.
Borden Inc.
Chiquita Brands Inc.
Davy McKee Corp.
Durkee-French Foods
Epstein Process Engineering Inc.
Gyor International Ltd.
H.J. Heinz Co.
Hewlett Packard Co.
The Kroger Co.
Land O'Lakes Inc.
Liquid Carbonic Industries Corp.
McNeil Specialty Products Co.
United Engineers & Constructors
Westreco Inc.

as polyethylene terephthalate (PET) for 2-liter soft drink bottles—is becoming a “hot topic” because of environmental and cost concerns.

A major question raised by such recycling, she said, is whether non-food substances, such as lawn chemicals and automobile lubricants, that consumers may store in the containers can be absorbed into the plastic and even survive the recycling process. (See “What Happens if the Packaging Gets into the Food?” in the November 1991 *FDA Consumer*.)

Other current projects include:

- studying factors that may extend the shelf life of fresh fish using modified atmosphere packaging (MAP)—a process in which an increased concentration of carbon dioxide is used to retard bacterial growth. Factors to be studied include high-barrier film packaging and storage temperatures.
- studying the potential of biotechnology-derived biosensors as tools to detect staphylococcal enterotoxins (bacteria-induced toxins that manifest themselves in the intestines) in milk and other foods as they are being processed, thus enhancing their safety. FDA's Sangsuk Oh, Ph.D., a researcher involved in the project, said the work eventually will be expanded to include detection of other toxins that may get into foods during manufacturing.
- developing the “Moffett Factor,” an index for predicting a food product's potential microbiological risk by considering such factors as food composition, processing method, storage time and temperature, pH, and preservatives used.

According to Armstrong, the center's technical advisory committee decides what projects to undertake. The committee is made up of representatives of FDA, IIT, IIT Research Institute, the University of Illinois, and member companies.

Educating Future Researchers

In addition to the research, NCFST is providing a training and educational ground for IIT's master's degree program in food safety and technology—the first graduate program of its kind in the United States. It began in September 1991.

Also in the works are short courses and symposia, and various publications to update food science professionals about emerging food safety issues.

Ultimately, the consortium hopes to make NCFST the world's source of food safety expertise and knowledge. Said Commissioner Kessler during a speech at the center's dedication, “I am hopeful that in 10 or 15 years, the world will know the National Center for Food Safety and Technology for what, today, it has only the potential to be: an internationally recognized and truly collaborative facility that provides the best know-how about food science and technology.” ■

Paula Kurtzweil is editor of FDA Today, the agency's employee publication.

HIGH BLOOD PRESSURE

Controlling the Silent Killer

by Dixie Farley

More than 61 million people in the United States have high blood pressure, or hypertension, and nearly half don't even know they have it, according to the American Heart Association.

Because high blood pressure usually doesn't give early warning signs, it is known as the "silent killer." Nearly 33,000 Americans died of diseases related to high blood pressure in 1990 (the latest year for which figures are available), reports the National Center for Health Statistics, and that doesn't include deaths from heart attacks and strokes caused by hypertension.

High blood pressure increases the risk of stroke seven times, says Fletcher McDowell, M.D., of the National Stroke Association, but, "it is clearly the most major risk factor that can be controlled."

In fact, people diagnosed as hypertensive today have less chance of complications such as stroke than they did a decade ago, for physicians now know more about controlling high blood pressure with antihypertensive drugs and certain lifestyle changes.

Blood Pressure Basics

Arterial blood pressure is the pressure of blood within arteries as it's pumped through the body by the heart. Whether your blood pressure is high, low or normal depends mainly on several factors: the output from your heart, the resistance to blood flow by your blood vessels, the volume of your blood, and blood distribution to the various organs, says Victor Raczowski, M.D., of the Food and Drug Administration's Center for Drug Evaluation and Research. "Your nervous system and some of your hormones can affect these factors," he says, "and thus play roles in regulating your blood pressure."

Everyone experiences hourly and even moment-by-moment blood pressure changes. For example, your blood pres-

sure will temporarily rise with strong emotions such as anger and frustration, with water retention caused by too much salty food that day, and with heavy exertion, which makes your heart beat harder and faster, increasing its output by pushing more blood into your arteries. These transient elevations in blood pressure usually don't indicate disease or abnormality.

Blood pressure is spoken of as a fraction, such as 120/80 millimeters of mercury (mmHg). The numerator (120) is called the systolic pressure—the pressure of blood within arteries when the heart is pumping. The denominator (80) is called the diastolic pressure—the pressure in the arteries when the heart is resting between beats. A typical blood pressure for a young adult might be 120/80 mmHg. What is "normal," though, varies from person to person.

Defining Hypertension

While there's no clear dividing line between high blood pressure and normal blood pressure, most authorities define hypertension in adults as persistent elevation of the diastolic blood pressure above 90 mmHg. "When the diastolic pressure is less than this," Raczowski says, "a person is considered to have borderline hypertension if the systolic pressure is between 140 and 159 mmHg and definite hypertension if the systolic pressure is 160 mmHg or greater." To be diagnosed as hypertensive, a person should have at least two to three readings performed on each of three separate visits, he says.

When persistently elevated blood pressure is due to a medical problem, such as hormonal abnormality or an inherited narrowing of the aorta (the largest artery leading from the heart), it's called "secondary hypertension." That is, the high blood pressure arises secondary to another condition. A person also may have secondary hypertension because:

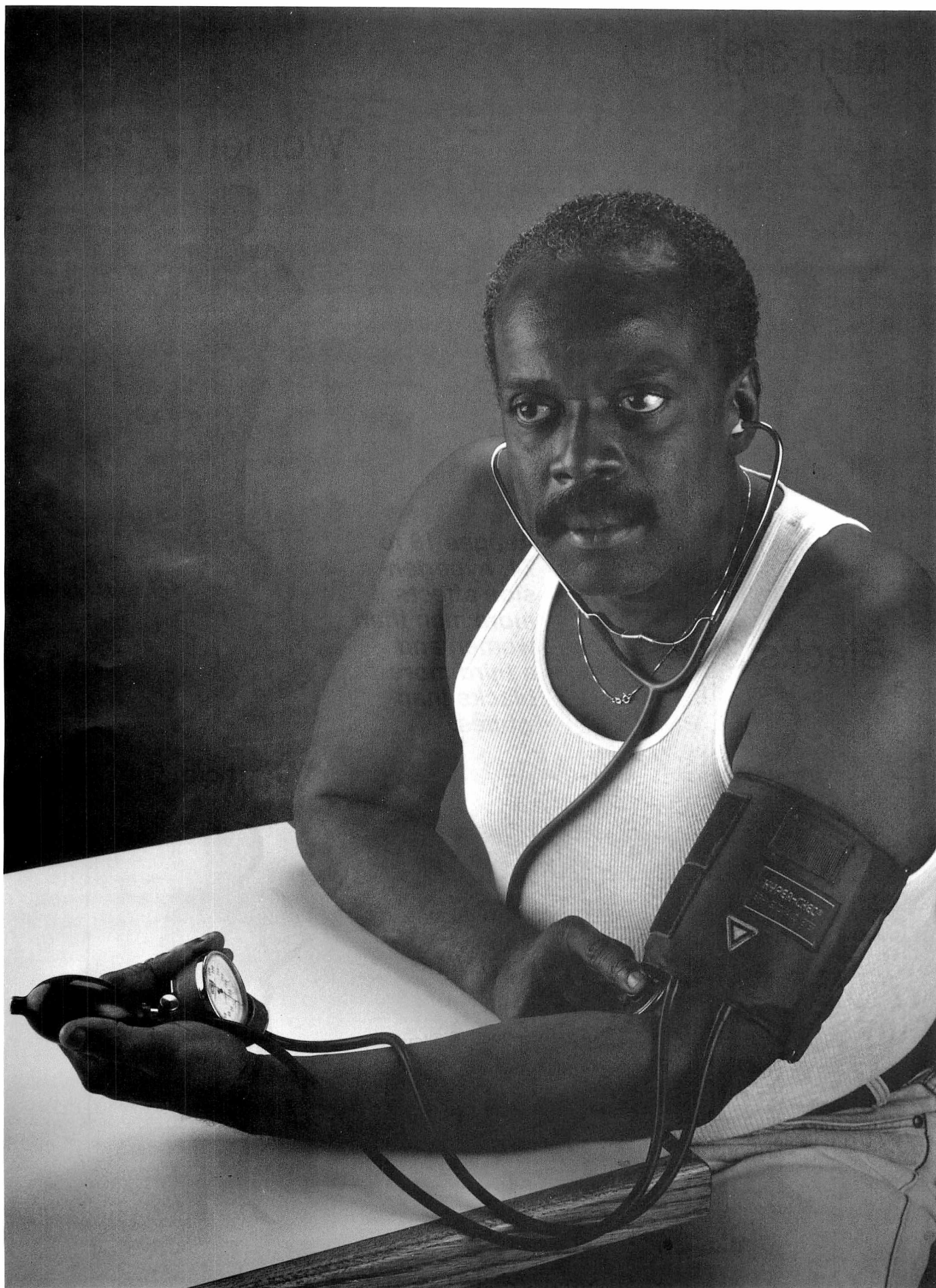
- the blood vessels are chronically constricted or have lost elasticity from a buildup of fatty plaque on the inside walls of the vessel, a condition known as atherosclerosis. Narrowed or inelastic blood vessels exert a greater-than-normal resistance against the flow of blood, causing the blood pressure to rise.
- the heart pumps the blood at a greater rate. This increased rate of blood flow through the arteries will raise blood pressure.
- the kidneys function poorly, causing retention of excess sodium and fluid. The resulting increase in blood volume within the vessels causes high blood pressure. Kidneys may also elevate blood pressure by secreting substances that constrict the vessels.

The causes of most cases of hypertension are unknown, however. These cases are known as "essential hypertension." Because the cause remains a mystery, essential hypertension cannot be cured. But it can be controlled.

Who's at Risk?

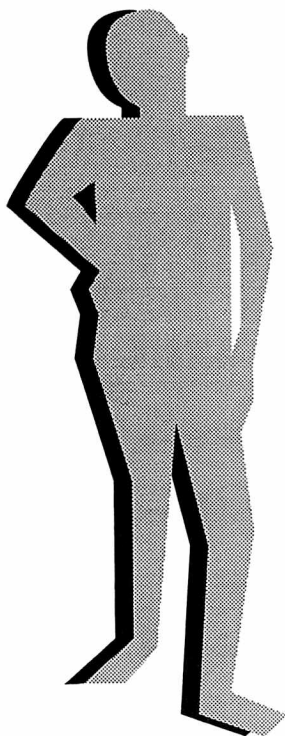
Some risk factors for hypertension can't be changed—a family history of the disease, for instance. In addition, as reported in the Public Health Service's *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*, hypertension affects more than half of people over age 65 and about a third more Afro-Americans than whites. Blacks at ages 24 to 44 are 18 times more prone than whites to kidney failure due to hypertension.

Men tend to develop hypertension more often than pre-menopausal women, though the risk for women increases when they take contraceptives or are pregnant. It's especially important that pregnant women have their blood pressure monitored frequently by their physicians, as untreated hypertension can suddenly progress to severe problems later in the pregnancy.

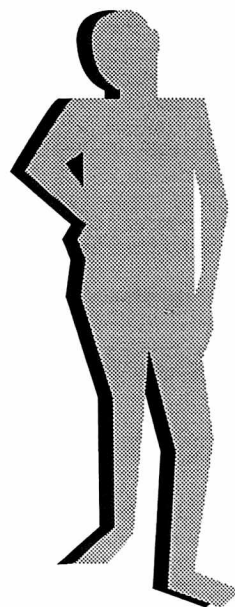


Who Has High Blood Pressure?

Men 33%

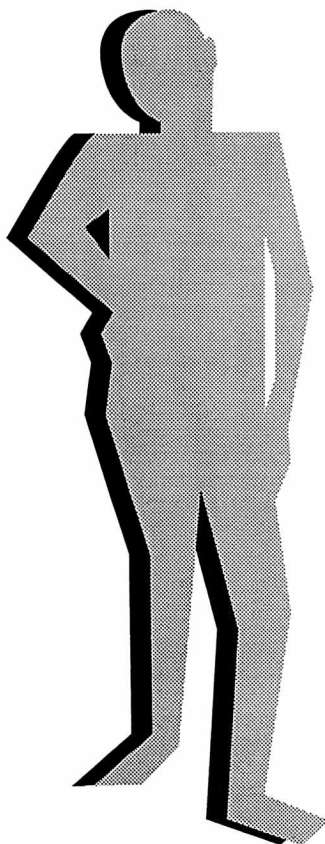


Women 27%

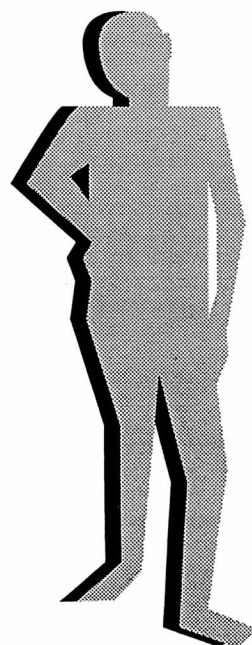


At ages 18 to 74, hypertension affects more men than women and a third more blacks than whites.

Blacks 38%



Whites 29%



Monitoring your progress is essential to success in treating hypertension.

People with hypertension who also have uncontrolled blood sugar from diabetes have an increased risk of a complication of high blood pressure such as heart attack or stroke.

Daily living habits can contribute to hypertension. Chronic stress, such as that produced by a job involving daily frustration, can cause blood pressure to become elevated. Overweight people have an increased risk of hypertension. Some people whose diet is high in salt may be at increased risk. Alcoholics appear to have an increased incidence of hypertension. Also, blood pressure can rise as a result of certain drugs, including cocaine, oral contraceptives, corticosteroids, sodium-containing antacids, some over-the-counter appetite suppressants and decongestants, and some nonsteroidal anti-inflammatory drugs.

Assessing Your Blood Pressure

Though giving you no sign of its presence, hypertension can be steadily damaging your heart and arteries. For this reason, it's important to have your blood pressure checked at least once a year. A doctor or nurse simply places a pressure cuff around your upper arm, pumps up the cuff, and listens with a stethoscope to measure the blood pressure.

Despite the simplicity of this procedure, some people react emotionally to it so that their blood pressure shoots up when they enter a doctor's office. This reaction is known as "white coat hypertension," says Gordon Johnson, M.D., director of health affairs at FDA's Center for Devices and Radiological Health, which regulates blood pressure monitors and other medical devices.

"When you have this problem," Johnson says, "make it a point to arrive at least 15 minutes early for your appointment. This will give you time to relax. As you sit there, breathe deeply and think soothing thoughts. Also, don't talk while the measurement is being taken.

Talking seems to raise blood pressure."

You can team up with your physician in monitoring your blood pressure by using a home monitoring device. (See accompanying article.) "Daily readings help the doctor make a more accurate assessment of your blood pressure," Johnson says.

Living a Healthy Lifestyle

Adult patients with mild hypertension, such as 140/90, rarely need drugs and are often able to bring their blood pressure reading down with changes in diet and activity. Controlling even mild hypertension is vitally important, though, to stem its progression. At the University of Minnesota, patients are advised to lower their daily sodium intake to no more than the equivalent of 1 teaspoon (about 2,000 milligrams) of salt a day, lower and control their weight by obtaining no more than 30 percent of their calories from fat, and engage daily in a moderate form of exercise such as walking.

Some 80 million Americans have increased sensitivity to dietary sodium, according to *Healthy People 2000*. Whereas "salt-sensitive" people who eat a high-sodium diet develop hypertension, those who don't have this sensitivity can eat a great deal of sodium without a rise in blood pressure. Blacks in particular are prone to salt-sensitive hypertension.

There's no harm in moderate restriction (avoiding salty foods and not adding salt when preparing food), even for hypertensive patients who are not sensitive to salt, says Walter Glinsmann, M.D., associate director for clinical nutrition at FDA's Center for Food Safety and Applied Nutrition. "However," he says, "people with hypertension should not severely restrict their salt intake, as with a special diet, unless this is done under a physician's care." Glinsmann says that when some people follow such a diet their kidneys don't adequately retain sodium, whose main role in the body is to

maintain fluid balance.

Hypertensive patients often indirectly benefit from reducing dietary fat, "particularly when they're overweight or at increased risk for coronary heart disease and stroke because of an elevated blood cholesterol level," Glinsmann says. Cholesterol contributes to atherosclerosis, which in some people is aggravated by hypertension, he says.

The National Cholesterol Education Program of the National Heart, Lung and Blood Institute recommends a diet with no more than 30 percent fat, made up of equal amounts of saturated, polyunsaturated and monounsaturated fats. "Diets that contain polyunsaturated and monounsaturated fats may actually lower blood cholesterol levels when compared with diets with saturated fats," Glinsmann says. Polyunsaturated fats are found in sunflower, corn, soybean, cottonseed, and safflower oils; monounsaturated fats are in olive, canola, and peanut oils. Eating less red meat and more fish can help, too.

Stopping smoking is important. The nicotine in tobacco triggers the body to release adrenalin, which causes the blood vessels to constrict, which in turn raises blood pressure.

Learning to relax is good for your blood pressure. When you relax, your heart rate slows and tissues throughout your body demand less oxygen. As a result, your blood pressure decreases. Simple stretching and deep breathing exercises just a few minutes once or twice a day may provide this benefit.

Regular physical activity (at least three days a week for 20 minutes or more) can not only help prevent or manage hypertension, it also may give your mental health a boost by countering stress and improving your mood and self-esteem.

Finally, it's wise to limit alcohol consumption and all drugs that can increase blood pressure. Some physicians believe that a daily drink, such as a 4-ounce

Drugs That Treat High Blood Pressure

Several classes of medications are used to treat hypertension. Here are some commonly prescribed brands from each class and a description of how they work:

Angiotensin-converting enzyme inhibitors appear to act in the body by inhibiting the production of angiotensin, a chemical that causes blood vessels to constrict, and by preserving the retention of chemicals that cause blood vessels to relax. They also inhibit production of substances that cause the kidneys to retain fluid:

- captopril (Capoten)
- enalapril (Vasotec)
- lisinopril (Prinivil, Zestril)
- ramipril (Altace)

Beta blockers block certain nerve signals to help slow the heartbeat and decrease the heart's workload and output:

- acebutolol (Sectral)
- atenolol (Tenormin)
- betaxolol (Kerlone)
- carteolol (Cartrol)
- labetalol (Normodyne, Trandate)
- metoprolol (Lopressor)
- nadolol (Corgard)
- penbutolol (Levitol)
- pindolol (Visken)
- propranolol (Inderal)
- timolol (Blocadren)

Calcium channel blockers act on the heart's muscles and nerve impulses to relax arteries throughout the body and decrease the heart's workload:

- diltiazem (Cardizem SR)
- nicardipine (Cardene)
- nifedipine (Adalat, Procardia XL)
- verapamil (Calan, Isoptin, Verelan)

Diuretics cause the kidneys to increase excretion of sodium and water, thus decreasing the volume the heart must pump through the vessels. There are several types of diuretics:

Thiazide Diuretics

- bendroflumethiazide (Naturetin)
- benzthiazide (Exna)

- chlorthalidone (Hygroton, Thalitone)
- chlorothiazide (Diuril)
- hydrochlorothiazide (Esidrix, HydroDIURIL, Oretic)
- hydroflumethiazide (Diucardin, Saluron)
- methyclothiazide (Aquatensen, Enduron)
- metolazone (Diulo, Mykrox, Zaroxolyn)
- quinethazone (Hydromox)
- polythiazide (Renese)

Potassium-Sparing Diuretics

- amiloride (Midamor)
- spironolactone (Aldactone)
- triamterene (Dyrenium)

Combination Diuretics

- amiloride/hydrochlorothiazide (Moduretic)
- spironolactone/hydrochlorothiazide (Aldactazide, Spirozide)
- triamterene/hydrochlorothiazide (Co-Triamterzide, Dyazide, Maxzide)

Loop Diuretics

- bumetanide (Bumex)
- ethacrynic acid (Edecrin)
- furosemide (Lasix)

Vasodilators relax the blood vessels:

- hydralazine (Apresoline)
- minoxidil (Loniten)

Centrally acting agents act on the control centers in the brain to lower blood pressure:

- methyldopa (Aldomet)
- clonidine (Catapres)
- guanfacine (Tenex)
- guanabenz (Wytensin)

Peripherally acting agents achieve their effect by acting on nerve substances throughout the body:

- guanadrel (Hylorel)
- guanethidine (Ismelin)
- mecamylamine (Inversine)
- prazosin (Minipress)
- rauwolfia alkaloids (Harmony, Raudixin, Rauzide, Serpasil)
- terazosin (Hytrin)

—D.F.

Using Home Blood Pressure Monitoring Devices

People with hypertension may benefit from using home blood pressure monitoring devices. Measuring blood pressure at home on a regular schedule may:

- help identify people whose blood pressure is only high when taken during a medical visit
- enable patients to collaborate with their doctors in controlling their high blood pressure
- reduce the frequency with which a patient needs a doctor for blood pressure evaluation.

The mechanical gauge, or sphygmomanometer, is the type of blood pressure equipment most often used in physicians' offices. It consists of an instrument called a manometer to measure the pressure, an inflatable cuff (air bladder), and a pressure bulb with a release valve to pump up the cuff. Some gauges use mercury manometers (the height of a column of mercury indicates blood pressure), while others use aneroid manometers (the pressure is read on a gauge dial).

Mechanical gauges are much less expensive than electronic sets and give more accurate readings when they function properly. When taking your own blood pressure, however, you must pump up the cuff with one hand, read a dial, and listen with a stethoscope. In other words, these devices require dexterity, good eyesight, acute hearing, and some training.

Automated electronic gauges generally measure blood pressure by either the Korotkoff method or the oscillometric technique. Korotkoff devices use a microphone built into the cuff to detect arterial sounds related to blood pressure; they are subject to false readings caused by noises from the patient's surroundings or patient movement. Oscillometric devices measure and analyze the vibrations (oscillations) from the artery to determine blood pressure. Patient movement can cause false readings with these devices as well.

Finger cuff monitors typically are the oscillometric variety. Because they measure blood pressure at the fingers, they tend to have reduced accuracy and increased sensitivity to the effects of temperature and poor blood circulation.

For best results with automated gauges:

- Avoid eating, smoking or exercising for at least a half hour before measuring your blood pressure.
- Test daily at about the same time; plan ahead to give yourself time to get over feeling angry or anxious.
- When using a finger cuff device, be sure your body temperature is normal; a room colder than 60 degrees Fahrenheit can cause an inaccurate or unreliable reading.
- Sit quietly and eliminate extraneous noise.
- Follow the manufacturer's instructions carefully.
- Position your arm at heart level, palm up. Wrap the cuff just above the elbow—sleeve rolled above the cuff—and be sure it's not too tight. With a finger device, slip the finger fully into the cuff, keeping it level with the heart.
- Be sure the hoses from the cuff aren't tangled or pinched.
- Take care not to move the hoses during the reading.
- Wait at least five minutes with the cuff fully deflated before taking another reading.
- Bring the device along on medical visits once or more a year to check its accuracy against your doctor's measurements.

Also, the standard-size arm cuff on blood pressure monitors fits arms up to 13 inches in diameter. People with larger arms should order a larger cuff. ■

—D.F.

glass of wine with dinner, benefits your heart. But not all experts agree. If you drink, it's a good idea to discuss this with your doctor, especially if you have high blood pressure.

Drug Therapy

While it's best to control hypertension without drugs, this is not always possible.

Anti-hypertensive drugs can reduce the risk of stroke, heart failure, and death. As reported in *The Lancet* in 1990, data on nearly 37,000 patients in 14 studies demonstrated that reducing blood pressure by just 5 or 6 points (for example, from 140/110 to 140/105) reduced the risk of stroke 42 percent and coronary disease 14 percent.

Some patients taking antihypertensive drugs experience side effects. These effects vary greatly among medications and from person to person. As hypertension tends to produce few, if any, symptoms, such people may feel worse during therapy and make the mistake of stopping the drugs without medical advice. If you are taking a medicine that has unwelcome side effects, tell your doctor. For there are now a large number and a wide variety of drugs available (see chart on page 32), and it's likely that one or a combination of several can be found that will control your blood pressure without making you uncomfortable.

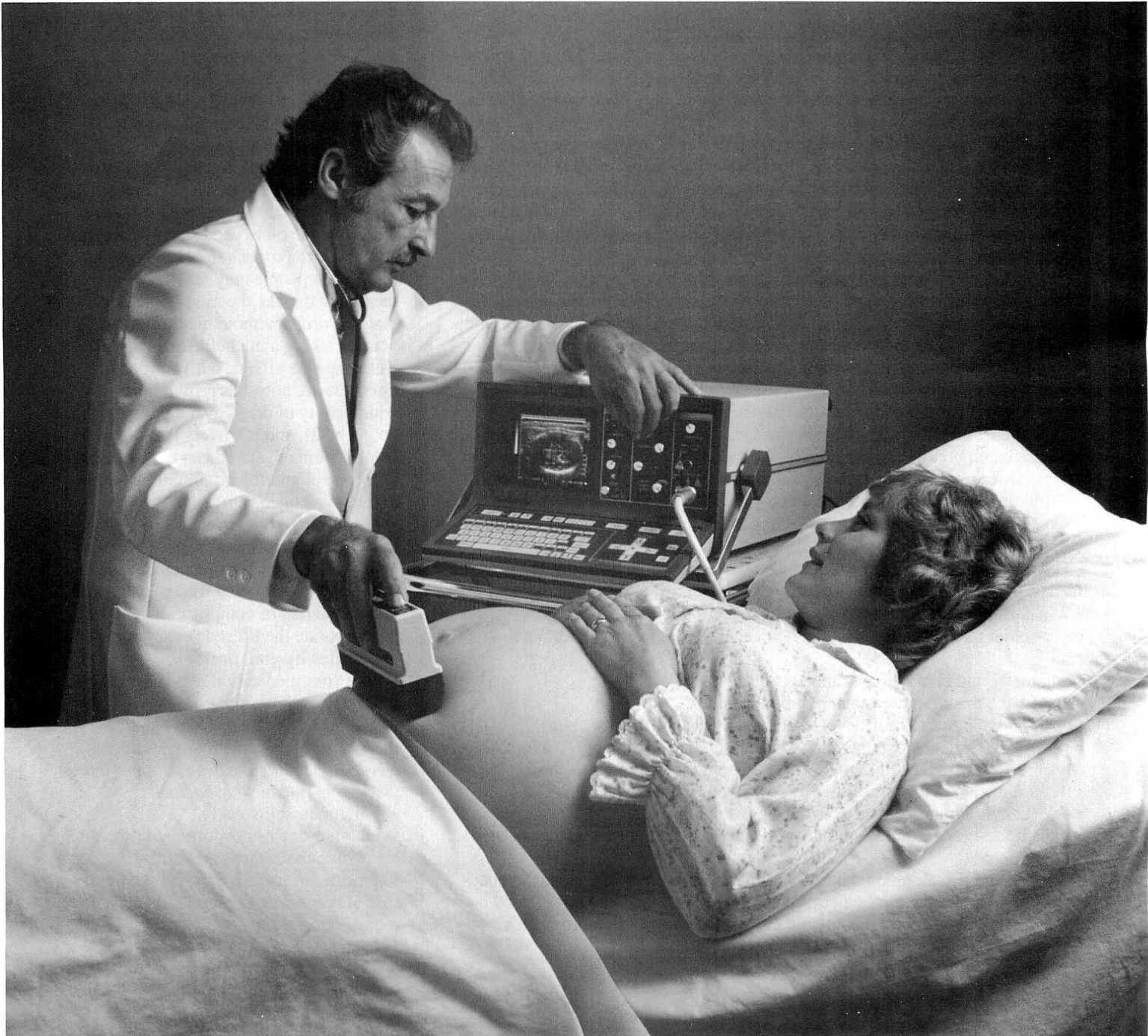
Monitoring your progress is essential to success in treating hypertension, especially when your therapy includes medication. To control your hypertension and reduce the risk of complications:

- Incorporate the lifestyle changes recommended by your doctor.
- Take your medication regularly and faithfully, as prescribed.
- Note any side effects from the drug therapy and report them to your doctor. *Never stop taking the drug without first discussing it with your doctor.*
- Weigh yourself weekly.
- Ask your doctor how often you should have your cholesterol checked.
- Consider measuring your blood pressure at home with one of the many self-monitoring systems. ■

Dixie Farley is a staff writer for FDA Consumer. Joan Luckmann, a medical-surgical nurse in San Antonio, Texas, also contributed to this article.

Ultrasound Makes Waves

by Margie Patlak



Ultrasound became a household word in the 1970s, when it was readily embraced by obstetricians, who used the high-frequency sound to peer into the womb. Many mothers “saw” their children before they were even born, thanks to ultrasound, which often suggested whether to buy pink or blue baby outfits, among other things.

With recent improvements in ultrasound’s image quality and ease of use, this technology has found its way into almost every branch of medicine. Physicians now use ultrasound to detect tumors, aneurysms, blood clots, detached retinas, heart abnormalities, and kidney stones. Ultrasound can also map plaque buildup on arteries, and assess if a transplanted organ is being rejected.

On the treatment front, ultrasound is being used to treat glaucoma, speed the healing of bone fractures, and relieve the pain and stiffness of arthritis and other inflammatory disorders. Ultrasound also can aid surgery, cancer therapy, *in vitro* fertilization, and several dental procedures.

Seeing with Sound

Ultrasound’s widespread popularity in the diagnostic arena stems from its relatively low cost, ease of use, and record of safety compared with other tools for diagnosing various disorders. Ultrasound also fares better than many imaging devices when it comes to picturing soft tissues in the body. It can also provide instant displays of moving structures and can offer other information on the functioning of an organ.

One way doctors use ultrasound to get the inside scoop on their patients’ bodies is with a procedure known as pulse-echo imaging. During this procedure, a microphone-like device, known as a transducer, is moved across the skin over

the part of the body the doctor wishes to view. The transducer emits sound waves (ultrasound) at a frequency too high to be heard by people.

When these waves bounce off various tissues and organs on their journey through the body, they generate distinctive echoes that are conveyed to a computer. The computer translates the timing and strength of these echoes into an image of the internal organs or tissues targeted by the ultrasound beam.

The ultrasound image (sonogram) is usually viewed on a television screen. When rapid pulses of ultrasound are used, a “movie” of a moving structure, such as a fetus or beating heart, can be seen.

There is no pain involved in pulse-echo imaging, although there may be some discomfort in procedures such as a pelvic sonogram, which requires the patient to maintain a full bladder while the womb (uterus) is imaged. The patient lies on an examination table for the procedure, which takes anywhere from five minutes for a pelvic sonogram to an hour for an ultrasonic exam of the heart. A gel is put on the patient’s skin where the transducer makes contact. This gel improves the penetration of ultrasound waves.

A Womb with a View

Obstetricians frequently use pulse-echo ultrasound imaging to “see” what’s happening inside the uterus. It can give valuable information, including:

- the size, number or age of fetuses in the womb. (Age is accurately assessed by measuring the length of the fetus or by measuring its thigh bone length and head circumference.)
- the presence of some types of birth defects
- location of the fetus or placenta (useful in the delivery of breech babies or during

amniocentesis)

- fetal movement, breathing and heart-beat
- amount of amniotic fluid in the uterus (which helps in the assessment of fetal health).

Although most current studies do not indicate health risks to the unborn child from ultrasound imaging, more research needs to be done to determine this with certainty. Ultrasound imaging employs a different kind of radiation than x-rays, which clearly can harm the fetus. However, ultrasound can generate heat, microscopic bubbles, or vibrations, which could possibly affect fetal development.

An FDA panel, consequently, has recommended that ultrasound imaging not be done on pregnant women unless there is a specific medical reason such as vaginal bleeding, signs that the fetus is not growing properly, or a family history of congenital abnormalities. Ultrasound imaging should *not* be used, for example, just to get a glimpse of a fetus or to determine its sex.

Probing Lumps and Bumps

Pulse-echo ultrasound imaging has many other uses as well. Because it’s an excellent tool for sizing up organs and spying any internal lumps or bumps, doctors often use ultrasound imaging to probe tissues for tumors, cysts or abscesses. Ultrasound is one of the safest tools doctors have for this purpose.

Unlike x-rays, sonograms can reveal not only whether there is a lump within a part of the body, such as the ovaries, but if that lump is likely to be a benign cyst or a solid tumor. Ultrasound is able to make this distinction, because a fluid-filled cyst has a different “sound signature” than a solid mass.

If a needle biopsy is warranted, ultrasound imaging can show doctors where

In the top photo, a practitioner performs an abdominal ultrasound exam, which may help doctors diagnose diseases of the liver or gallbladder. Below, the practitioner moves a transducer above the area of the uterus as ultrasound waves produce an image on the monitor that may show if there are birth defects or twins. The baby's position and sex may also be evident. (Photos on this page courtesy of the Society of Diagnostic Medical Sonographers)

