How Folate Can Help Prevent Birth Defects
How Folate Can Help Prevent Birth Defects

Adequate intake of folate, a B vitamin, is so important in preventing birth defects that FDA is requiring it be added to bread and other grain products.

Glimmer of Hope for People with ALS

Two drugs have recently become available to treat amyotrophic lateral sclerosis, also known as Lou Gehrig's disease. Though neither medication comes close to being a cure, they provide a ray of hope to patients with this neurological disease.

Boning Up on Osteoporosis

Osteoporosis leads to about 1.5 million fractures each year, mostly of the hips, spines and wrists of older women. New treatments, changing attitudes, and improving technology are helping to brighten the outlook for women—and men—who may experience this bone condition in their later years.

Hair Today, Gone Tomorrow

Hair where fashion dictates hairlessness frustrates many folks. A variety of products, with varying degrees of easy use and safety, are available for those seeking social smoothness.

Outsmarting Poison Ivy and Its Cousins

Prevention is the first line of defense against poison ivy, oak, and sumac. But if preventive measures fail, over-the-counter and prescription medications can help deal with the rash until it runs its course.

Updates

2  Investigators' Reports

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Added Use for Heart Device Approved in Six Days

Only six days after FDA received the application, the agency approved for wider use an implantable device that restores normal heart rhythm in heart attack patients. It is the first such approval worldwide.

The Guidant implantable defibrillator was originally approved by FDA in 1988 for patients who have had at least one cardiac arrest or have recurrent and sustained rapid heartbeat despite treatment with the best available drugs. These people are at high risk of sudden death.

FDA gave the additional approval last May 15 for a large new group of patients—about 10 percent of heart attack patients—who also are at high risk of sudden death from abnormal rapid heartbeat (ventricular arrhythmia) but who have had no obvious symptoms. These patients’ arrhythmias can be detected by electrocardiograph, and usually they are treated with drugs. However, 30 percent of these patients die from ventricular arrhythmia within two years.

In a five-year clinical study, such patients implanted with the Guidant defibrillator had 54 percent fewer deaths than those treated with drugs. The significant results prompted the sponsor to stop the study early so that all patients would be eligible to receive the device.

The Guidant defibrillator is about the size of a cassette tape and is implanted in the abdomen or chest and linked to the heart with wire leads. It can be programmed to deliver small, swift pacing signals to fit patients’ needs.

It is made by CPI Guidant Corp., of St. Paul, Minn.

(For more about defibrillators, see “A Gentler Jolt and Tickle for Trembling Hearts,” in the April 1994 FDA Consumer.)

Stroke Treatment Approved

The first therapy shown to improve recovery and decrease disability in adults after the most common kind of stroke was approved by FDA after less than three months of review time.

Activase (alteplase), previously licensed to dissolve clots in heart attacks and in the artery leading to the lungs, received approval last June 18 for the additional use of dissolving blood clots that block blood flow to the brain in ischemic strokes. Activase is a genetically engineered version of tissue plasminogen activator (t-PA).

Because therapy with Activase must start within three hours of stroke onset, it is important that people with stroke symptoms seek medical attention as soon as possible. Bleeding in the brain must be ruled out by cranial computerized tomography (CT) scan before Activase treatment can begin. The treatment is not approved to treat hemorrhagic strokes, caused by bleeding into and around the brain.

Yearly, about 500,000 Americans have strokes, with about 150,000 dying as a result. Of these strokes, about 400,000 are ischemic and the rest are hemorrhagic.

The licensing of Activase for ischemic stroke follows a unanimous recommendation for approval by FDA’s Peripheral and Central Nervous System Drugs Advisory Committee last June 6.

Activase is manufactured with recombinant DNA technology by Genentech, Inc., of South San Francisco.

Test Predicts Risk Of HIV Progression

A new test to predict the risk of HIV disease progression in infected patients has been licensed by FDA. The test is not labeled for use as a screening test for HIV or as a diagnostic test to confirm HIV infection.

The Amplicor HIV-1 Monitor Test measures blood levels of HIV-1—the strain of human immunodeficiency virus responsible for most HIV infections in the United States. It is the first licensed HIV-1 test using polymerase chain reaction (PCR) technology. PCR replicates millions of copies of genetic material (RNA) from HIV-1. The amplified RNA is tagged with color indicators so it can be measured. This technology enables more precise measurement than is pos-
FDA licensed the test last June 3, less than seven months after receiving the manufacturer's application. Licensing was based on laboratory studies showing the test could measure HIV RNA in the blood, and on clinical data showing HIV blood levels correlated with disease progression.

Laboratory studies showed the test was specific for HIV-1—that is, other unrelated viruses or organisms did not cause a false positive result (indicating the presence of HIV-1). Also, in an analysis of 495 samples known not to be infected with HIV-1, none was falsely positive.

In two small clinical studies, the test was used to measure viral levels in patients with advanced HIV disease who either had not received antiviral drugs or had received AZT (zidovudine, marketed as Retrovir) in combination with other antivirals for less than 16 weeks. Viral levels that were high before treatment or that increased fivefold after eight weeks of therapy correlated with disease progression to AIDS or AIDS-related infection or death.

In two additional clinical studies, the test was used to evaluate the effectiveness of antiviral therapy. Patients had been treated with AZT and were currently receiving the protease inhibitor saquinavir (marketed as Invirase) in combination with other drugs, such as AZT or DDC (also known as zalcitabine and marketed as Hivid). The test showed decreased levels of HIV-1 RNA in patients who received combination therapies.

The studies did not, however, show if changes in viral RNA levels are related to clinical responses to drug therapy. Last March, FDA's Blood Products Advisory Committee supported approval of the test for prognosis of HIV-infected patients, but recommended additional studies to determine how physicians could use the test to monitor the results of therapy. FDA required these studies, now under way, as a condition of licensing.

The manufacturer is Roche Diagnostic Systems Inc., Branchburg, N.J.

**New Type of Drug For Ovarian Cancer**

The first member of a promising new class of antitumor drugs has been approved by FDA to treat ovarian cancer that has progressed after first-line treatment.

Hycamtin (topotecan), approved last May 29, belongs to the class of drugs called camptothecins, which inhibit an enzyme called topoisomerase-I.

Results from two multicenter clinical trials showed that the drug reduced ovarian tumor size in 17 percent of 337 patients for an average of about five months. That response was at least as good as that seen in patients treated in one of the studies with Taxol (paclitaxel), another ovarian cancer drug.

Because Hycamtin is associated with neutropenia (a temporary drop in white blood cells that makes it difficult for the body to fight infections), some patients may require hospitalization and antibiotics.

Other side effects include thrombocytopenia (a decrease in blood platelets that can lead to excessive bleeding), anemia, nausea, and vomiting.

Hycamtin is marketed by SmithKline Beecham of Philadelphia.

**Second Breast Cancer Drug From Yew Tree**

A second cancer-fighting drug derived from the Pacific yew tree has been approved by FDA.

Taxotere (docetaxel), a semi-synthetic drug containing derivatives of the evergreen tree’s needles, was approved last May 14 for women whose advanced breast cancer has progressed despite standard cancer treatment regimens. The first drug derived from the Pacific yew, Taxol (paclitaxel), is approved to treat ovarian and breast cancer.

Taxotere’s approval was based on several studies, including three trials in the United States and Europe that showed the drug can shrink tumors in some breast cancer patients.

At the highest tested dose, the drug shrank tumors in 42 percent of patients for an average of six months. At this dose level, Taxotere, like many cancer drugs, is associated with serious side effects, including a decrease in white blood cell counts, fluid retention, allergic reactions, and hair loss. At a lower dose, however, the drug shrank tumors in 35 percent of patients for four months, and the side effects were negligible.

The drug’s labeling warns that patients should be premedicated to prevent problems with fluid retention and allergic reactions. Certain patients with liver
dysfunction should not use Taxotere.

FDA granted Taxotere an accelerated approval based on clinical improvements such as tumor shrinkage, rather than survival time or quality of life. By basing accelerated approval on these partial responses, and allowing more definitive data to be developed on clinical endpoints after approval, FDA is giving patients earlier access to more promising cancer therapies.

FDA may withdraw the approval of such products if postmarketing studies do not verify clinical benefits. More extensive trials testing Taxotere’s clinical benefits are ongoing.

Taxotere is marketed by Rhône-Poulenc Rorer Inc., of Collegeville, Pa.

Colon and Rectal Cancer Drug

A new drug to treat advanced colon and rectal cancer was approved by FDA just four days after an agency advisory committee recommended the approval.

Camptosar (irinotecan) is for patients whose colorectal cancer has recurred or progressed despite standard chemotherapy. Approved June 17, as recommended by FDA’s Oncology Drugs Advisory Committee, Camptosar is the second in a promising new class of antitumor drugs called camptothecins to be approved in three weeks. Camptothecins work by inhibiting the enzyme topoisomerase-I.

Primary treatment for colorectal cancer is surgery, with or without added chemotherapy or radiotherapy. However, the cancer recurs in about half the patients. The drug Fluorouracil (5-FU), with or without leucovorin (a compound related to the vitamin folic acid), is first-line chemotherapy for patients with colorectal cancer that has spread. However, by the time the cancer is diagnosed, it has already spread in about half of the patients. Treatment options when the cancer does not respond to first-line therapy are very limited.

In three studies of patients whose metastatic (spread) colorectal cancer recurred or progressed despite chemotherapy, the new drug reduced tumor size in about 13 percent of patients for an average of six months. Side effects included diarrhea (in some cases, prolonged or severe enough to require treatment) and leukopenia, a temporary drop in white blood cells that reduces the body’s ability to fight infections.

On the oncology advisory committee’s recommendation, FDA granted Camptosar accelerated approval based on clinical improvements such as tumor shrinkage, rather than survival time or quality of life. The committee also gave advice on additional studies to further evaluate the safety and effectiveness of the drug. FDA may withdraw its approval if postmarketing studies do not verify clinical benefits.

Camptosar is manufactured by Pharmacia & Upjohn Inc., Kalamazoo, Mich.

First Drug for Rare Parasitic Diseases

The first drug to treat two rare parasitic infections—neurocysticercosis (NCC) and hydatid disease—has been approved by FDA.

Because only about 300 Americans get either disease each year, the new treatment, Albenza (albendazole), is considered an “orphan” drug. This designation provides incentives for companies that develop products for disorders affecting fewer than 200,000 people in the United States and its territories. FDA approved the drug June 12.

NCC is caused by pork tapeworm larvae and is considered the leading infectious cause of seizures worldwide. People acquire the disease when they consume tapeworm eggs, usually through contaminated food or water. Seizures and headaches result when the disease involves brain tissue. Symptoms may not develop for five years or longer following exposure. Albendazole was shown to be effective in 40 to 70 percent of patients with active cysts.

Cystic hydatid disease causes enlarging parasitic cysts in the liver, lungs, abdominal cavity, brain, or bone. The cysts grow slowly and may go undetected for years. Symptoms may be vague complaints of abdominal fullness or may be more acute if the cyst ruptures. People contract the disease by ingesting dog tapeworm eggs through close contact with infected dogs. Albendazole was shown to eliminate hydatid cysts in approximately 30 percent of patients and reduce their size in an additional 40 percent.

Adverse effects may include diminished liver function and fewer white blood cells. NCC patients may have headache, nausea, or vomiting; hydatid disease patients may have abnormal
liver function, abdominal pain, nausea, or vomiting.

SmithKline Beecham Pharmaceuticals of Philadelphia makes Albenza.

**Glaucoma Drug Approved For Some Patients**

An eye-drop treatment recently approved by FDA reduces glaucoma-related eye pressure in patients who cannot use other treatments.

FDA based its June 5 approval of Xalatan (latanoprost) on study results indicating patients treated with the drug for six months had reduction in eye pressure equivalent to other glaucoma treatments. The approval followed a recommendation for approval by the agency’s Ophthalmic Drugs Advisory Committee.

The once-a-day treatment may cause an unexplained gradual change in eye color. Based on the committee’s concern about this unusual side effect, Xalatan’s labeling tells patients and health-care providers about the phenomenon and recommends use only by patients that can’t tolerate or don’t respond to other treatments.

The manufacturer, Pharmacia & Upjohn Inc., of Kalamazoo, Mich., will study the eye color change in postmarketing studies.

(See also “Guarding Against Glaucoma” in the November 1995 FDA Consumer.)

**Device to Lessen Incontinence**

A disposable foam pad about the size of a quarter was cleared by FDA as a device to help prevent urinary leakage in women with urinary stress incontinence. It is available by prescription only.

The Miniguard is a triangle-shaped pad with adhesive coating on one side, which the woman places over her urinary opening, where it forms a seal.

Urinary stress incontinence is a condition in which urine leaks as a result of physical stress, such as coughing, laughing, or lifting heavy objects. The condition affects about 10 million people, mostly women.

Although the Miniguard does not stop leakage, it lessens its frequency. In a study of 356 women, the average participant improved from about 14 leaks a week without the device to about five leaks a week with it. Women with severe stress incontinence, who had about 34 episodes of leakage a week, had only 10 leaks a week with the device. When urine leaked in these women, the amount was smaller.

Because leaks are possible, women using the Miniguard need to wear panty liners or pads for additional protection.

The device can be worn two to five hours at a time during the day and throughout the night. When a woman needs to urinate, she peels the pad off and discards it. After urinating, she puts on a new pad. The Miniguard may be worn during exercise, although vigorous activity, such as running, may move it out of position.

The product is not for women with urinary tract or vaginal infections or local irritations. Also, it is not as effective in women who have had surgery for their incontinence.

The Miniguard is made by Advanced Surgical Intervention, of Dana Point, Calif.

**Treatment Slows MS**

An injectable multiple sclerosis treatment recently licensed by FDA is the second interferon treatment for relapsing MS, which affects about 30 percent of patients.

Multiple sclerosis is a chronic, often disabling disease of the central nervous system that occurs when the protective covering of the nerve fibers breaks down. In relapsing MS, symptoms can diminish or disappear for months or years between flare-ups. (See “Multiple Sclerosis: New Treatment Reduces Relapses” in the June 1994 FDA Consumer.)

The new treatment, Avonex (interferon beta-1a), is a genetically engineered form of a naturally occurring protein in the body which is vital to immune functions.

In a two-year clinical trial, patients receiving a weekly injection of interferon
beta-la into the muscle were 37 percent less likely to have physical disability than patients getting a placebo. Also, those receiving interferon beta-la had less frequent flare-ups and fewer lesions.

The most common side effect was flu-like symptoms, which diminished with continued treatment. Interferon beta-la did not appear to increase depression, a side effect associated with some interferon products. There were no reports of tissue death at the injection site, which differentiates the product from Betaseron (interferon beta-1b), licensed in 1993 to treat relapsing MS.

The May 17 licensing of Avonex follows a recommendation for approval by FDA’s Peripheral and Central Nervous System Drugs Advisory Committee.

The drug will be marketed by Biogen, Inc., of Cambridge, Mass.

Unrealistic Claims for Eye Surgery Concern FDA, FTC

In response to inquiries and complaints about misleading promotion of photorefractive keratectomy (PRK), a laser treatment for nearsightedness, FDA and the Federal Trade Commission recently notified the eye-care community that advertising and promotion for the procedure should be truthful and substantiated.

In a joint letter sent May 7, 1996, the agencies said advertising or promotion should contain enough information about the surgery to make an informed decision. Unrealistic claims such as “throw away your eye glasses” and unsubstantiated claims about success rates could be misleading to consumers.

In clinical studies, about 5 percent of patients who had PRK continued to need glasses all the time for distance, and up to 15 percent needed glasses occasionally, such as for driving. Best corrected vision (vision with glasses) was slightly worse after surgery in about 5 percent of patients.

In PRK, an excimer laser is used to reshape the cornea to improve mild to moderate nearsightedness. The surgery is not reversible. Excimer lasers have not been shown safe and effective for severe nearsightedness (more than -7 diopters), farsightedness or astigmatism. People who need reading glasses continue to need them after PRK. Also, PRK does not prevent farsightedness associated with aging, so people may require reading glasses as they age even if they have had the laser surgery. Risks of PRK to the cornea beyond three years have not been studied.

Some doctors perform PRK on both eyes without a waiting period between. Patient brochures developed by the laser manufacturers and reviewed by FDA, however, recommend a three-month wait between eye surgeries to allow vision to stabilize.

In addition, some surgeons perform a laser procedure called LASIK to improve nearsightedness. FDA has not cleared lasers for this use, however, and the devices cannot be promoted or advertised for it.

Free Brochure and Reprints

A new low-literacy brochure about medical treatments is available free from FDA. Also available free are new FDA Consumer reprints.

The publications and their numbers are:
• The Truth About Choosing Medical Treatments (FDA) 96-1248
• New Hope for People with Sickle Cell Anemia (FDA) 96-1251
• Seven Steps to Safer Sunning (FDA) 96-1252
• How to Give Medicine to Children (FDA) 96-3223.

To order single copies, write to FDA, HFE-88, Rockville, MD 20857. To order 2 to 100 copies, write to FDA, HFI-40, at the same address, or fax your order to (301) 443-9057. Include the publication number.

FDA Consumer welcomes comments from readers. Send letters to: Editor, FDA Consumer, HFI-40, 5600 Fishers Lane, Rockville, MD 20857.
If you plan to have children some day, here's important information for the future mother-to-be: Think folate now.

Folate is a B vitamin found in a variety of foods and added to many vitamin and mineral supplements as folic acid, a synthetic form of folate. Folate is needed both before and in the first weeks of pregnancy and can help reduce the risk of certain serious and common birth defects called neural tube defects, which affect the brain and spinal cord.

The tricky part is that neural tube defects can occur in an embryo before a woman realizes she's pregnant. That's why it's important for all women of childbearing age (15 to 45) to include folate in their diets: If they get pregnant, it reduces the chance of

Folate is found in a variety of foods, including citrus juices and fortified breakfast cereals.
the baby having a birth defect of the
brain or spinal cord.
“ Adequate folate should be eaten
daily and throughout the childbearing
years,” said Elizabeth Yetley, Ph.D., a
registered dietitian and director of
FDA’s Office of Special Nutritionals.
There are several ways to do this:
• Eat fruits, dark-green leafy vegetables,
dried beans and peas, and other foods
that are natural sources of folate.
• Eat folic acid-fortified breakfast cereals.
• Take a vitamin supplement containing
folic acid.
Folate’s potential to reduce the risk of
neural tube defects is so important that
the Food and Drug Administration is re-
quiring that by 1998, food manufactur-
ers fortify enriched grain products with
folic acid. This will give women another
way to get sufficient folate: by eating
fortified breads and other grains.
Nutrition information on food and
dietary supplement labels can help
women determine whether they are
getting enough folate, which is 400 mi-
icrograms (0.4 milligrams) a day before
pregnancy and 800 micrograms a day
during pregnancy.

Neural Tube Birth Defects
The technical names of the two major
neural tube birth defects reduced by ad-
quate folate intake are anencephaly
and spina bifida. Babies with anenceph-
aly do not develop a brain and are still-
born or die shortly after birth. Those
with spina bifida have a defect of the
spinal column that can result in varying
degrees of handicap, from mild and
hardly noticeable cases of scoliosis (a
sideways bending of the spine) to pa-
ralysis and bladder or bowel inconti-
ence. With proper medical treatment,
most babies born with spina bifida can
survive to adulthood. But they may re-
quire leg braces, crutches, and other de-
vices to help them walk, and they may
have learning disabilities. About 30 per-
cent have slight to severe mental retarda-
tion.
The national Centers for Disease Con-
rol and Prevention estimate that about
2,500 infants with spina bifida and anen-
cephaly are born each year in the United
States.
Other maternal factors also may con-
tribute to the development of neural
tube defects. These include:
• family history of neural tube defects
• prior neural tube defect-affected
pregnancy
• use of certain antiseizure medications
• severe overweight
• hot tub use in early pregnancy
• fever during early pregnancy
• diabetes.
Any woman concerned about these
factors should consult her doctor.
Folate Link
Scientists first suggested a link be-
tween neural tube birth defects and diet
in the 1950s. The incidence of these
conditions has always been higher in
low socioeconomic groups in which
women may have poorer diets. Also, ba-
bies conceived in the winter and early
spring are more likely to be born with
spina bifida, perhaps because the
mother’s diet lacks fresh fruits and vege-
tables—which are good sources of
folate—during the early weeks of
pregnancy.
In 1991, British researchers found that
72 percent of women who had one preg-
nancy with a neural tube birth defect had
a lower risk of having another child with
this birth defect when they took pre-
scription doses of folic acid before and
during early pregnancy.
Another study looked at folic acid in-
take in Hungarian women. The evidence
indicated that mothers who had never
given birth to babies with neural tube
defects and who took a multivitamin and
mineral supplement with folic acid had
less risk in subsequent pregnancies for
having babies with neural tube defects
than women given a placebo.
These studies led the U.S. Public
Health Service in September 1992 to
recommend that all women of childbear-
ning age capable of becoming pregnant
consume 0.4 mg of folate daily to reduce
their risk of having a pregnancy affected

Fortified breakfast cereals can provide
25 to 100 percent of the Daily Value for
folic acid. Check the Nutrition Facts
panel on the label of these and other
foods to learn how much folic acid a
food may provide.
Some Good Sources of Folate

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving Size</th>
<th>Amount (Micrograms)</th>
<th>% Daily Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicken liver</td>
<td>3.5 oz</td>
<td>770</td>
<td>193</td>
</tr>
<tr>
<td>Breakfast cereals</td>
<td>1/2 to 1 1/2 cup</td>
<td>100 to 400</td>
<td>25 to 100</td>
</tr>
<tr>
<td>Braised beef liver</td>
<td>3.5 oz</td>
<td>217</td>
<td>54</td>
</tr>
<tr>
<td>Lentils, cooked</td>
<td>1/2 cup</td>
<td>180</td>
<td>45</td>
</tr>
<tr>
<td>Chickpeas</td>
<td>1/2 cup</td>
<td>141</td>
<td>35</td>
</tr>
<tr>
<td>Asparagus</td>
<td>1/2 cup</td>
<td>132</td>
<td>33</td>
</tr>
<tr>
<td>Spinach, cooked</td>
<td>1/2 cup</td>
<td>131</td>
<td>33</td>
</tr>
<tr>
<td>Black beans</td>
<td>1/2 cup</td>
<td>128</td>
<td>32</td>
</tr>
<tr>
<td>Burrito with beans</td>
<td>2</td>
<td>118</td>
<td>30</td>
</tr>
<tr>
<td>Kidney beans</td>
<td>1/2 cup</td>
<td>115</td>
<td>29</td>
</tr>
<tr>
<td>Baked beans with pork</td>
<td>1 cup</td>
<td>92</td>
<td>23</td>
</tr>
<tr>
<td>Lima beans</td>
<td>1/2 cup</td>
<td>78</td>
<td>20</td>
</tr>
<tr>
<td>Tomato juice</td>
<td>1 cup</td>
<td>48</td>
<td>12</td>
</tr>
<tr>
<td>Brussels sprouts</td>
<td>1/2 cup</td>
<td>47</td>
<td>12</td>
</tr>
<tr>
<td>Orange</td>
<td>1 medium</td>
<td>47</td>
<td>12</td>
</tr>
<tr>
<td>Broccoli, cooked</td>
<td>1/2 cup</td>
<td>39</td>
<td>10</td>
</tr>
<tr>
<td>Fast-food French fries</td>
<td>large order</td>
<td>38</td>
<td>10</td>
</tr>
<tr>
<td>Wheat germ</td>
<td>2 tbsp</td>
<td>38</td>
<td>10</td>
</tr>
<tr>
<td>Fortified white bread</td>
<td>1 slice</td>
<td>38</td>
<td>10</td>
</tr>
</tbody>
</table>

* based on Daily Value for folate of 400 micrograms
(Source: Food Values of Portions Commonly Used, 16th edition)

with spina bifida or other neural tube defects.
That corresponds to FDA’s Daily Value for folic acid, which is 400 micrograms for nonpregnant women, as well as children 4 and older and adult men. For pregnant women, the Daily Value jumps to 800 micrograms. Daily Values are dietary reference numbers used on the Nutrition Facts panel on food labels to show the amounts of various nutrients in a serving of food.

Many women between 19 and 50 get only 200 micrograms of folate a day, according to the U.S. Department of Agriculture.

**Folate Sources**
Folate occurs naturally in a variety of foods, including liver; dark-green leafy vegetables such as collards, turnip greens, and Romaine lettuce; broccoli and asparagus; citrus fruits and juices; whole-grain products; wheat germ; and dried beans and peas, such as pinto.
Women have options for reaching the folate intake goal.

Finding Foods with Folate

Certain information on food and dietary supplement labels can help women spot foods containing substantial amounts of folate. Some labels may claim that the product is “high in folate or folic acid,” which means a serving of the food provides 20 percent or more of the Daily Value for folic acid. Or the label may say the food is a “good source” of folate, which means a serving of the food provides 10 to 19 percent of the Daily Value for folic acid. The exact amount will be given in the label’s Nutrition Facts panel.

Some food and dietary supplement labels may carry a longer claim that says adequate folate intake may reduce the risk of neural tube birth defects. Products carrying this claim must:
• provide 10 percent or more of the Daily Value for folic acid per serving
• not contain more than 100 percent of the Daily Value for vitamins A and D per serving because high intakes of these vitamins are associated with other birth defects
• carry a caution on the label about excess folic acid intake, if a serving of food provides more than 100 percent of the Daily Value for folic acid. FDA has set 1 mg (or 1,000 micrograms) of folate daily as the maximum safe level. There are limited data on the safety of consuming more than 1 mg daily, and there may be a risk for people with low amounts of vitamin B₁₂ in their bodies—for example, older people with malabsorption problems, and people on certain anticancer drugs or drugs for epilepsy whose effectiveness can diminish when taken with high intakes of folate.
• list on the label’s Nutrition or Supplement Facts panel the amount by weight in micrograms and the %Daily Value of folate per serving of the product. This information, which appears toward the bottom of the panel, along with the listing of other vitamins and minerals, can be used to compare folate levels in various foods and supplements.

Optional information may appear with the health claim to let consumers know about other risks associated with neural tube birth defects, when to consult a doctor, other foods that are good sources of folate, and other important messages about neural tube defects.

Other Considerations

The claim about folate cannot imply that adequate folate intake alone will ensure a healthy baby, since so many factors can affect a pregnancy. Women should bear this in mind when contemplating pregnancy, advises Jeanne Latham, a registered dietitian and consumer safety officer in FDA’s Office of Special Nutritionals. “Folate can make a significant contribution,” she said, “but it’s no guarantee of a healthy baby.”

Genetics plays a role, as do other healthful prenatal practices, such as eating an all-around good diet. But unlike genetics, diet is a risk factor women can modify to their—and their baby’s—ad-

For more information on having a healthy baby, contact:

Maternal and Child Health Clearinghouse
5600 Fishers Lane, Room 18A-55
Rockville, MD 20857
(703) 821-8955

March of Dimes Birth Defects Foundation
1275 Mammaroneck Ave.
White Plains, NY 10605
(914) 428-7100
Voice mail only: (914) 997-4750

Paula Kurtzweil is a member of FDA’s public affairs staff.
Sunday, May 2, 1939, will be forever remembered in the annals of baseball as the day New York Yankees’ first baseman Lou Gehrig voluntarily benched himself, ending a streak of 2,130 consecutive games.

For months the once-great player’s game had been in decline. His reflexes were off. He stumbled, fumbled, and struggled to hit or catch the ball. No one understood why, least of all Gehrig himself.

A few weeks after Gehrig benched himself, doctors diagnosed his illness as amyotrophic lateral sclerosis (ALS), a progressive disease of the central nervous system that remains incurable to this day.

Two years later, on June 2, 1941, Gehrig died at the age of 37. The disease that took his life became known to Americans as Lou Gehrig’s disease. His consecutive games record stood for 56 years until it was broken by the Baltimore Orioles’ Cal Ripken Jr. on Sept. 6, 1995.

In the years since Gehrig’s death, many drugs have been tried for the treatment of ALS. For 54 years, none was found to be effective. But one recent drug approval and the granting of early access to another drug give reason for hope.

The Food and Drug Administration approved Rilutek (riluzole) in December 1995. It was the first drug found to have an effect, albeit a modest one, on the course of ALS. In clinical trials conducted in the United States and Europe, the drug appeared to prolong patients’ survival by about three months.

Before the agency approved Rilutek, the drug had been made available to more than 3,000 ALS patients in the United States under the Treatment IND (investigational new drug) program. This program gives patients access, under certain circumstances, to promising investi-
Disabling and Often Deadly

More than 30,000 Americans have ALS, according to the ALS Association, a nonprofit organization that supports ALS research and public and patient education about the disease. Around 3,000 to 5,000 new cases of the disease are diagnosed every year.

Although ALS can strike at any age, it usually appears between the ages of 40 and 70. Men and women of all ethnic and racial groups are about equally affected.

The disease attacks the motor neurons, nerve cells in the brain and spinal cord that control the body’s voluntary muscles. As the motor neurons begin to die, the muscles weaken and shrink. Early symptoms of ALS may include unusual fatigue and clumsiness, muscle weakness, slurred speech, and difficulty swallowing.

As the disease progresses, patients gradually lose the use of their hands, arms, legs, and neck muscles, ultimately becoming paralyzed. They can speak and swallow only with great difficulty. However, thinking ability, bladder and bowel function, sexual function, and the senses—sight, hearing, smell, taste, and touch—are unaffected.

About half of people with ALS die within three to five years of diagnosis. In rare cases, a person may survive with the disease for many years (see accompanying article). The usual cause of death is failure of the diaphragm muscles that control breathing. Some individuals with ALS choose to prolong their lives by using a ventilator, but prolonged use of a ventilator may increase the risk of death from an infection such as pneumonia.

No single test can diagnose ALS. Because of the slow onset of the disease, it can be difficult to diagnose in the early stages, said Jeffrey Rothstein, M.D., Ph.D., associate professor of neurology at Johns Hopkins University School of Medicine in Baltimore. Johns Hopkins is one of the nation’s leading centers for ALS research.

“We do a number of tests to rule out other diseases that might mimic ALS. Because it’s a fatal disease, you want to be absolutely certain of your diagnosis. The patient is generally about 20 to 50 percent into the disease by the time it is diagnosed,” he said.

Cause a Mystery

Doctors have known about ALS since 1874 (it was first identified by a French physician, J.M. Charcot), but its cause remains a mystery. Inability to pinpoint the cause of ALS has hindered efforts to find an effective treatment, said Marc Walton, M.D., Ph.D., a medical officer in the clinical trials division of FDA’s Center for Biologics Evaluation and Research.

Doctors once thought that ALS might be caused by the same virus that causes polio and that exposure to polio would increase the risk of ALS, said Ralph Kuncl, M.D., Ph.D., associate professor of neurology at Johns Hopkins. However, he said, no evidence has been found to support this theory.

Another conjecture was that an environmental toxin might cause ALS. This theory arose in part because some places—the South Pacific island of Guam and parts of Japan—have some-
The brilliant British theoretical physicist Stephen W. Hawking, who is probably best known to the general public as the author of *A Brief History of Time*, is one of a very few people who have survived for many years with amyotrophic lateral sclerosis (ALS).

Hawking, now 54, was diagnosed with ALS in 1963 when he was a 21-year-old graduate student at Cambridge University in England. Hawking’s life demonstrates that ALS impairs neither intellect nor sexual function. His work on the origin and nature of the universe has been, in the words of biographers Michael White and John Gribbin, “ground-breaking and revolutionary.” Hawking also married and fathered three children after his diagnosis.

In 1985, after suffering a windpipe blockage, Hawking had a breathing device surgically implanted in his throat. The surgery resulted in the loss of his voice. He now “speaks” by using a voice synthesizer connected to a computer that he operates by squeezing a switch in his hand.

In *Stephen Hawking: A Life in Science*, White and Gribbin write that Hawking has a very strong personality and has “never [given] in to the symptoms of ALS more than he is physically compelled to.”

—E.L.M.

what higher than normal rates of ALS. The cicad nut, a traditional food in Guam, contains toxic substances capable of killing motor neurons, said Kuncl. “But the toxicity level is not enough to cause the degeneration seen in ALS.”

The “surprisingly uniform” incidence of ALS in the rest of the world “would not be expected if the disease were caused by an environmental toxin,” Kuncl added. However, the reason for the increased rate of ALS in Guam and Japan remains unknown.

Some doctors believe that ALS is an autoimmune disease—that is, a disease in which the body attacks itself with antibodies normally produced to protect against infection. In ALS, according to this theory, antibodies attack and kill the motor neurons. However, “very potent autoimmune therapies have been tried in ALS and have all failed to alter the course of the disease,” said Rothstein.

Another theory is that ALS is caused by toxic levels of glutamate in the brain. Glutamate is a constituent of protein that cells in the body use to help break down food and build up body tissues. In the central nervous system, nerve cells (neurons) use glutamate to communicate with one another.

Because too much glutamate can be toxic, the brain usually regulates the substance, keeping levels to those needed for body functioning. Abnormally high levels of glutamate have been found in the cerebrospinal fluid (the clear watery fluid that surrounds the brain and the spinal cord) of some patients with ALS.

In experiments, scientists have found that a protein responsible for removing excess glutamate from the brain appears not to work properly in people with ALS. They theorize that toxicity resulting from excessive glutamate might be killing motor neurons. The death of these cells leads to progressive muscle wasting in patients with ALS. One of the characteristics of Rilutek is that it inhibits the release of glutamate in the brain.

Rilutek is taken by mouth. Everyone who takes the drug must be monitored regularly for signs of Rilutek’s most important side effect, a rise in the level of liver enzymes, which indicates abnormal liver function.

The drug’s labeling states that treat-
ment should be discontinued if liver enzymes increase to 10 times their normal level.

About five out of every 100 people who get ALS have an inherited, or familial, form of the disease; that is, one or more of their immediate family members—parents, brothers, sisters, or grandparents—also have the disease. Children of people with familial ALS have a fifty-fifty chance of developing the disease themselves.

In 1993, scientists identified a gene that, when defective, is associated with some cases of familial ALS. This gene carries the operating instructions for a protein whose function is to neutralize cell-damaging substances called free radicals. Some scientists think that when the gene is defective, an excessive buildup of free radicals may kill motor neurons.

However, this genetic mutation is found in only about one-fifth of people with familial ALS, according to Rothstein, and it has not been detected in anyone with the sporadic (noninherited) form of the disease, which is far more common.

Searching for Treatments

Even if the cause of the disease is eventually found, the development of effective treatments presents enormous challenges, said Rothstein. “The drugs have to be potent and they have to get into the nervous system, which has a very tight barrier—the blood-brain barrier—that prevents entry by many drugs.”

Some doctors think that neurotrophic growth factors, substances produced by the body that stimulate nerve cells to grow and multiply, may be useful for treating ALS. These substances can now be produced in the laboratory using the techniques of biotechnology. Myotrophin is one such factor.

“No one thinks that neurotrophic factors, or the lack of them, cause ALS,” said Rothstein. “But in animal experiments they seem to work quite well in preventing injury to motor neurons.”

FDA’s Walton said the agency is working with investigators and the drugs’ manufacturers to try to design trials “that will tell us as quickly and efficiently as possible whether or not these products can be effective in the treatment of ALS.”

Until more effective drugs are developed and approved to treat ALS, measures to improve patients’ mobility and quality of life remain the mainstay, said Rothstein. “Nutrition is very important. A recent study in Italy showed increased survival in ALS patients who received good nutrition using a feeding tube.

“There’s also a mask that patients can use to assist their breathing, and physical therapy can help to make them more comfortable. A speech pathologist can help them to learn different swallowing techniques as their swallowing muscles become weaker. Support groups for patients and their families are also very important.”

On Sept. 6, 1995—the day Cal Ripken Jr. broke Lou Gehrig’s record for consecutive games played—the Baltimore Orioles and the Johns Hopkins Medical Institutions announced the launch of the Cal Ripken/Lou Gehrig Fund for Neuromuscular Research.

Ticket sales to the record-breaking game and an Orioles contribution raised $2 million for the fund. Kuncl said the money will support research at Johns Hopkins on neuromuscular diseases, with an emphasis on ALS.

Johns Hopkins’ Rothstein said that though the drugs available do not thus far seem to give dramatic improvement, he is not discouraged.

“This is against the background of decades when no drug ever did anything for the disease. Initial therapies for many diseases, like leukemia and other cancers, had the same kind of effect ... a modest increase in survival. But they were followed by better therapies that, over time, increased patients’ survival.

“It’s a daunting task, but I envision that some day it will be possible to develop drugs that will not only stop motor neurons from dying but replace them and reverse the course of ALS.”

Eleanor Mayfield is a writer in Silver Spring, Md.
BONING UP ON
OSTEOPOROSIS

Consider an insidious condition that drains away bone—the hardest, most durable substance in the body. It happens slowly, over years, so that often neither doctor nor patient is aware of weakening bones until one snaps unexpectedly. Unfortunately, this isn't science fiction. It's why osteoporosis is called the silent thief.

by Carolyn J. Strange
There is no cure for osteoporosis, but the onset can be delayed and the severity diminished.

And it steals more than bone. It’s the primary cause of hip fracture, which can lead to permanent disability, loss of independence, and sometimes even death. Collapsing spinal vertebrae can produce stooped posture and a “dowager’s hump.” Lives collapse too. The chronic pain and anxiety that accompany a frail frame make people curtail meaningful activities, because the simplest things can cause broken bones: Stepping off a curb. A sneeze. Bending to pick something. A hug. “Don’t touch Mom, she might break” is the sad joke in many families.

Osteoporosis leads to 1.5 million fractures, or breaks, per year, mostly in the hip, spine and wrist, and costs $10 billion annually, according to the National Osteoporosis Foundation. It threatens 25 million Americans, mostly older women, but older men get it too. One in three women past 50 will suffer a vertebral fracture, according to the foundation. These numbers are predicted to rise as the population ages.

Osteoporosis, which means “porous bones,” is a condition of excessive skeletal fragility resulting in bones that break easily. A combination of genetic, dietary, hormonal, age-related, and lifestyle factors all contribute to this condition.

Changing attitudes and improving technology are brightening the outlook for people with osteoporosis. Nowadays, many women live 30 years or more—perhaps a quarter to a third of their lives—after menopause. Improving the quality of those years has become an important health-care goal. Although some bone loss is expected as people age, osteoporosis is no longer viewed as an inevitable consequence of aging. Diagnosis and treatment need no longer wait until bones break.

There is no cure for osteoporosis, and it can’t be prevented outright, but the onset can be delayed, and the severity diminished. Most important, early intervention can prevent devastating fractures. The Food and Drug Administration has revised labeling on foods and supplements to provide valuable information about the level of nutrients that help build and maintain strong bones. FDA has also approved a wide variety of products to help diagnose and treat osteoporosis, including several just last year.

Bone Life

Bone consists of a matrix of fibers of the tough protein collagen, hardened with calcium, phosphorus and other minerals. Two types of architecture give bones strength. Surrounding every bone is a tough, dense rind of cortical bone. Inside is spongy-looking trabecular bone. Its interconnecting structure provides much of the strength of healthy bone, but is especially vulnerable to osteoporosis.

“We tend to think of the skeleton as an inert erector set that holds us up and doesn’t do much else. That’s not true,” says Karl L. Insogna, M.D., director of the Bone Center at Yale School of Medicine, New Haven, Conn. Every bit as dynamic as other tissues, bone responds to the pull of muscles and gravity, repairs itself, and constantly renews itself.

Besides protecting internal organs and allowing us to move about, bone is also involved in the body’s handling of minerals. Of the 2 to 4 pounds of calcium in the body, nearly 99 percent is in the teeth and skeleton. The remainder plays a critical role in blood clotting, nerve transmission, muscle contraction (including heartbeat), and other functions. The body keeps the blood level of calcium within a narrow range. When...
**Osteoporosis leads to 1.5 million fractures, or breaks, per year, mostly in the hip, spine and wrist.**

needed, bones release calcium.

A complex interplay of many hormones balances the activity of the two types of cells—osteoclasts and osteoblasts—responsible for the continuous turnover process called remodeling. Osteoclasts break down bone, and osteoblasts build it. In youth, bone building prevails. Bone mass peaks by about age 30, then bone breakdown outpaces formation, and density declines.

The skeleton is like a retirement account, but in our skeletal “account” we can deposit bone only during our first three decades. After that, all we can do is try to postpone and minimize the steady withdrawals. Osteoporosis is the bankruptcy that occurs when too little bone is formed during youth, or too much is lost later, or both.

“...You've got to get as much bone as you can and not lose it,” Insogna says. “The most important risk factor for osteoporosis is a low bone mass.”

“The upper limit of bone mass that you can acquire is genetically determined,” says Mona S. Calvo, Ph.D., in FDA’s Office of Special Nutritionals. “But even though you may be programmed for high bone mass, other factors can influence how much bone you end up with,” she says. (See “Reducing Your Risk.”) For instance, men tend to build greater bone mass, which is partly why more women face osteoporosis.

But there’s another reason. With the decline of the female hormone estrogen at menopause, usually around age 50, bone breakdown markedly increases. For several years, women lose bone two to four times faster than they did before menopause. The rate usually slows down again, but some women may continue to lose bone rapidly. By age 65, some women have lost half their skeletal mass. Because the changes at menopause increase a woman’s risk, many physicians feel it’s a good time to measure a woman’s bone density, especially if she has other risk factors for osteoporosis.

“The best way to gauge a woman’s risk for osteoporotic fracture is to measure her bone mass,” says Insogna.

Routine x-rays can’t detect osteoporosis until it’s quite advanced, but other radiological methods can. FDA has approved several kinds of devices that use various methods to estimate bone density. Most require far less radiation than a chest x-ray. Doctors consider a patient’s medical history and risk factors in deciding who should have a bone density test. The method used is often determined by the equipment available locally. Readings are compared to a standard for the patient’s age, sex and body size. Different parts of the skeleton may be measured, and low density at any site is worrisome.

Bone density tests are useful for confirming a diagnosis of osteoporosis if a person has already had a suspicious fracture, or for detecting low bone density so that preventative steps can be taken.

“There’s a profound relationship between bone mass and risk of fracture,” says Robert Recker, M.D., director of the Osteoporosis Research Center at Creighton University, Omaha, Neb.

Readings repeated at intervals of a year or more can determine the rate of bone loss and help monitor treatment effectiveness. However, estimates are not necessarily comparable between machine types because they use different measurement methods, cautions Joseph Arnaudo, in the Center for Devices and Radiological Health. “You always want to go back to the same machine, if you can,” he says.

Another new test provides an indicator of bone breakdown. Last year, FDA approved a simple, noninvasive biochemical test that detects in a urine sample a specific component of bone breakdown, called NTx. Clinical labs can get results in about 2 hours. The NTx test, marketed as Osteomark, can help physicians monitor treatment and identify fast losers of bone for more aggressive treatment, but the test may not be used to diagnose osteoporosis.

**Expanding Treatment Options**

Physicians and patients now have more treatment options than ever. Under FDA guidelines, drugs to treat osteo-

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**To Learn More**

For more information, contact:


- Osteoporosis and Related Bone Diseases National Resource Center (ORBD-NRC); (800) 624-BONE; TDD: (202) 223-0344.

- Older Women's League (OWL), 666 11th St., N.W., Suite 700, Washington, DC 20001; (202) 783-6686.

- North American Menopause Society, c/o University Hospitals of Cleveland, Department of Obstetrics and Gynecology, 11100 Euclid Ave., Suite 7024, Cleveland, OH 44106; (216) 844-8748; World Wide Web: [http://www.menopause.org/](http://www.menopause.org/).

Last fall, FDA approved the first nonhormonal treatment for osteoporosis.

Each year, osteoporosis leads to 1.5 million bone fractures, including more than 500,000 vertebral fractures, 300,000 hip fractures, 200,000 wrist fractures, and 300,000 fractures of other bones.

Bone Fracture Areas

- **Vertebral Fractures:** 500,000+
- **Hip Fractures:** 300,000+
- **Wrist Fractures:** 200,000+
- **Other Fractures:** 300,000+

(SOURCE: NATIONAL OSTEOPOROSIS FOUNDATION, 1993)

Osteoporosis must be shown to preserve or increase bone mass and maintain bone quality in order to reduce the risk of fractures. “We want to be sure that the bone is normal or stronger than it was,” says Gloria Troendle, M.D., deputy director of the division of metabolism and endocrine drug products in FDA’s Center for Drug Evaluation and Research.

Before last year, the only choices were the hormones estrogen and calcitonin. While enthusiasm for new weapons against osteoporosis is warranted, one of the old ones is still the top choice.

“Estrogen remains the first thing that women should consider,” says Insogna, because the hormone not only helps prevent osteoporosis, but also protects against heart disease.

“If you think about what’s missing at menopause, it’s the hormones,” says Paula Stern, Ph.D., a pharmacologist at Northwestern University Medical School, Chicago, Ill.

Estrogen replacement therapy is the best prevention for the drop in bone mass at menopause, and there are more ways to take it than ever. But it’s not for everyone. Because estrogen increases the risk of certain cancers and other diseases, taking it may not be appropriate, or it may be given in combination with another female hormone, progesterone, which can also cause undesirable side effects. A woman and her doctor need to carefully weigh the risks and benefits.

According to the National Osteoporosis Foundation, a woman’s risk of developing a hip fracture is equal to her combined risk of developing breast, uterine and ovarian cancer.

Women who can’t or don’t want to take hormones—some 30 to 50 percent—have other treatment avenues. Last summer, calcitonin treatment became much easier when FDA approved a nasal spray. Calcitonin, one of the hormones responsible for regulating the level of calcium in the blood, inhibits osteoclasts, the bone dissolvers. The drug, marketed as Miacalcin, is a potent, synthetic version of the hormone, and has been shown to slow and reverse bone loss. The stomach quickly destroys the drug, so before the spray was available, calcitonin had to be injected every day or two.

Last fall, FDA also approved the first nonhormonal treatment for osteoporosis. Alendronate, marketed as Fosamax, falls within a class of drugs called bisphosphonates, which hinder bone breakdown remodeling sites by inhibiting osteoclast activity. In clinical trials lasting three years, alendronate increased the bone mass as much as 8 percent and reduced fractures as much as 30 to 40 percent, depending on skeletal site. Lengthier studies are ongoing.

“Since it’s so free of side effects it’s a very welcome addition to the armamentarium. But the truth is, we still need a better treatment,” says Recker. “We need a drug that will build back bone major league.”

“All the drugs approved so far are things that just stop bone turnover. They’re not really stimulating more bone production,” says Troendle.

Bone mass increases because even
Calcium and vitamin D supplements are an integral part of all treatments for osteoporosis.

**Calcium (Ac)Counts**

Your skeletal calcium bank has to last through old age. Frequent deposits to this retirement account should begin in youth and be maintained throughout life to help minimize withdrawals. Most women get much less calcium than they need—as little as half.

Nutritionists recommend meeting your calcium needs with foods naturally rich in calcium. Adequate calcium intake in childhood and young adulthood is critical to achieving peak adult bone mass, yet many adolescent girls replace milk with nutrient-poor beverages like soda pop. "Bone health requires a lot of nutrients and you're likely to get most of them in dairy products," says Connie Weaver, Ph.D., who heads the department of food and nutrition at Purdue University, Indiana. "They're a huge package rather than just a single nutrient." With so many low-fat and nonfat dairy products available, it's easy to make dairy foods part of a healthy diet. People who have trouble digesting milk can look for products treated to reduce lactose. A serving of milk or yogurt contains about 350 milligrams (mg) of calcium. Fortified products have even more.

"People who don't consume dairy foods can meet their calcium needs with foods that are fortified with calcium, such as orange juice, or with calcium supplements," says Mona S. Calvo, Ph.D., in FDA's Office of Special Nutritionals. Other good sources of calcium are broccoli and dark-green leafy vegetables like kale, tofu (if made with calcium), canned fish (eaten with bones), and fortified bread and cereal products.

Nutrition labels can help you identify calcium-rich foods. But keep in mind that the label value is a guideline based on a FDA's Daily Value for calcium, which is 1,000 mg, and your calcium needs may be greater, Calvo says.

What about too much calcium? As much as 2,000 mg per day seems to be safe for most people, but those at risk for kidney stones should discuss calcium with their doctors. Calcium is critical, but even a high intake won't fully protect you against bone loss caused by estrogen deficiency, physical inactivity, alcohol abuse, smoking, or medical disorders and treatments.

—C.J.S.
Reducing Your Risk

A host of factors can affect your chances of developing osteoporosis. The good news is that you control some of them. Even though you can’t change your genes, you can still lower your risk with attention to certain lifestyle changes. The younger you start, and the longer you keep it up, the better. Here’s what you can do for yourself:

• Be sure you get enough calcium and vitamin D.
• Engage in regular physical activity, such as walking.
• Don’t smoke.
• If you drink alcohol, do so in moderation.

A sedentary lifestyle, smoking, excessive drinking, and low calcium intake all increase risk. Although coffee has been suspected as a risk factor, studies so far are inconclusive.

Other factors are beyond your control. Being aware of them can provide extra motivation to help yourself in the ways you are able, and aids you and your doctor in health-care decisions. These risk factors are:

• being female: Women have a five times greater risk than men.
• thin, small-boned frame
• broken bones or stooped posture in older family members, especially women, which suggest a family history of osteoporosis
• early estrogen deficiency in women who experience menopause before age 45, either naturally or resulting from surgical removal of the ovaries
• estrogen deficiency due to abnormal absence of menstruation (as may accompany eating disorders)
• ethnic heritage: White and Asian women are at highest risk; African-American and Hispanic women are at lower, but significant, risk.
• advanced age
• prolonged use of some medications, such as excessive thyroid hormone; some antiseizure medications; and glucocorticoids (certain anti-inflammatory medications, such as prednisone, used to treat conditions such as asthma, arthritis and some cancers).

Risk factors may not tell the whole story. You may have none of these factors and still have osteoporosis. Or you may have many of them and not develop the condition. It’s best to discuss your specific situation with your doctor.

—C.J.S.

that physical fitness reduces the risk of fracture, because better balance, muscle strength, and agility make falls less likely. Exercise also provides many other life-enhancing psychological and cardiovascular benefits. Increased activity can aid nutrition, too, because it boosts appetite, which is often reduced in older people. The biggest reason older people don’t get enough calcium, Recker says, is that they simply don’t eat much.

“The truth is, you don’t have to do very much to get most of the benefits of exercise,” Recker says. He suggests 30 minutes of brisk walking five days a week. Add a little weightlifting, and that’s even better. It’s always smart to ask your doctor before starting a new exercise program, especially if you already have osteoporosis or other health problems.

Brighter Horizons

“A number of new things seem to be in the offing, eventually to come to us, and we’re looking forward to getting some additional treatments for osteoporosis,” says Troendle.

Uses of existing drugs may be broadened. Early drug trials are often conducted with patients who have severe disease, often after a fracture has occurred or bone loss is quite serious. Some studies under way are testing to see if certain drugs are effective in less severe cases, if they can be started sooner, or used in combination.

The search for bone-building drugs continues. Some naturally occurring bone-specific growth factors have been identified and their use as drugs is being investigated. “The way I visualize the ideal future is that we’ll be able to give Drug X that builds up bone to where it’s stronger and the risk of fracture is no longer present, then Drug Y maintains it by preventing breakdown,” says Stern.

In the realm of devices, researchers are exploring the use of ultrasound to assess bone health. Such tests would eliminate radiation exposure and probably cost less. The study of risk factors also continues. “We consider that to be the research that has the greatest public health significance,” says Sherry Sherman, Ph.D., of the National Institute on Aging. Last fall, the institute launched the Study of Women’s Health Across the Nation, a large-scale national examination of the health of women in their 40s and 50s. Researchers expect to learn a great deal about the factors affecting women’s health during these transitional years and beyond. Studies of genetics, biochemical markers, and life habits are already turning up new insights.

Osteoporosis has been described as an adolescent disease with a geriatric onset, highlighting the importance of beginning to take steps—in exercise and diet—early in life to reduce its disabling impact in later years.

Carolyn J. Strange is a science and medical writer living in Northern California.
Hair where hair oughtn’t be, according to the current dictates of American fashion, raises many an eyebrow. And so, for cosmetic reasons, millions of women, and a growing number of men, spend millions of dollars each year on products and services that promise smooth, silky skin free of “unsightly,” “excessive” body hair.

For do-it-yourselfers, a variety of home-use hair removal products are available over the counter. These include shaving creams, foams, and gels; waxes; chemical depilatories; and electrolysis devices. Professionals at beauty and skin care salons and in dermatologists’ offices provide waxing, electrolysis, and, most recently, laser treatments to remove hair. On April 3, 1995, FDA cleared the first laser for this use.

The cost, safety, effectiveness, and ease of use of the various methods, as well as the area and amount of hair growth to be treated, are some factors to weigh in choosing a method and deciding whether

Electrolysis is one way to remove hair from underarms and other areas.

PHOTOS BY NORAAAN WATKINS
to go to a professional. Often, different methods are better suited for different areas.

FDA’s Office of Cosmetics and Colors in the Center for Food Safety and Applied Nutrition regulates chemical depilatories, waxes, and shaving creams and gels. (The Consumer Product Safety Commission regulates razors.) These products, says John E. Bailey Jr., Ph.D., acting director of the office, are classified as cosmetics, defined as substances applied to the body to alter the appearance, promote attractiveness, cleanse, or beautify.

The agency’s Center for Devices and Radiological Health regulates electrolysis equipment and lasers.

Shaving

Shaving is by far the most common method of hair removal for both men and women. Men have been shaving their beards and mustaches for thousands of years, but cosmetic hair removal in women was relatively uncommon until after World War I. Now, many American women routinely shave their legs and underarms.

A clean razor with a sharp blade is essential for a safe and comfortable shave. Skin should never be shaved dry; wet hair is soft, pliable, and easier to cut. Contrary to what many believe, shaving does not change the texture, color, or rate of hair growth.

Depilatories

“Depilatories act like a chemical razor blade,” Bailey says. Available in gel, cream, lotion, aerosol, and roll-on forms, they contain a highly alkaline chemical—usually calcium thioglycolate—that dissolves the protein structure of the hair, causing it to separate easily from the skin surface.

“It’s very important to carefully follow the use directions for depilatories and to do a preliminary skin test both for allergic reaction and sensitivity,” Bailey says. “Hair and skin are similar in composition,” he explains, “so chemicals that destroy the hair can also cause serious skin irritations—possibly even chemical burns—if left on too long.”

The concentration of calcium thioglycolate is generally kept as weak as possible to avoid skin irritation, yet strong enough to work in a reasonable amount of time,” says Stanley R. Milstein, Ph.D., special assistant to the cosmetics and colors director. “Contact with the skin is kept to somewhere between 4 and 15 minutes, depending on how fine or coarse the hair is.”

Consumers should be sure to read the product label and select the formulation appropriate for the intended use, because skin sensitivity varies on different parts of the body. Some depilatories are for use only on the legs, for example, while others are safe for more sensitive areas, such as the bikini line, underarms and face.

Depilatories should not be used for the eyebrows or other areas around the eyes, or on inflamed or broken skin. To minimize the chance of skin irritation, they should not be applied more often than recommended on the product label.

Although cosmetics are not subject to premarket approval, FDA can take action against products that are found to cause harm.

“Depilatories, including those that come in a cream or lotion form, dissolve the protein structure of the hair, causing the hair to separate from the skin.

If we find an adverse reaction is occurring under recommended use conditions, and not because of misuse by the consumer, we can pursue any number of actions, depending on the severity and prevalence of the problem,” says Bailey.

For example, he says, “A depilatory might cause second- or third-degree burns, and possibly scarring, if its formula is too strong or if an inactive ingredient in the product heightens its effect. In that case, FDA may, after evaluating the problem, initiate regulatory action such as seizure or injunction against the product or the firm to stop further manufacture.”

Tweezing and Waxing

While depilatories remove hair at the skin’s surface, “epilatories,” such as tweezers and waxes, pluck hairs from below the surface. Waxing and tweeze may be more painful than using a depilatory, but the results are longer lasting. Because the hair is plucked at the root, new growth is not visible for sev-
eral weeks after treatment.

Tweezing is impractical for large areas, however, because it is such a slow process. Women mostly use tweezers for shaping eyebrows and removing facial hair.

Waxing, too, is mostly done to shape the eyebrows and remove hair on the chin and upper lip, says Brenda Ruffner, a cosmetologist in Rockville, Md., although, she says, many women also have their legs, underarms, and bikini line waxed.

"Men usually come in for treatment on their chest or back," Ruffner says. "I have male clients who are bodybuilders and want their skin to look smooth for competitions. And some men are uncomfortable with the hair on their back or are embarrassed by it," she says.

Epilatory waxes are also available over the counter for home use. They contain combinations of waxes, such as paraffin and beeswax, oils or fats, and a resin that makes the wax adhere to the skin. There are "hot" and "cold" waxes.

With hot waxing, a thin layer of heated wax is applied to the skin in the direction of the hair growth. The hair becomes embedded in the wax as it cools and hardens. The wax is then pulled off quickly in the opposite direction of the hair growth, taking the uprooted hair with it.

Cold waxes work similarly. Strips precoated with wax are pressed on the skin in the direction of the hair growth and pulled off in the opposite direction. The strips come in different sizes for use on the eyebrows, upper lip, chin, and bikini area.

Labeling of over-the-counter waxes cautions that these products should not be used by people with diabetes and circulatory problems, who are particularly susceptible to infection. Waxing—and tweezing as well—can leave the skin sore and open to infection. Waxes should not be used over varicose veins, moles, or warts. They should not be used on the eyelashes, inside the nose or ears, on the nipples or genital areas, or on irritated, chapped, sunburned, or cut skin. A small area should be tested for sensitivity or allergic reaction before treating the entire area. Some hair removal experts recommend professional waxing for the best results.

**Electrical Epilators**

Two types of devices use electric current to remove hair: the needle epilator and the tweezers epilator.

"Needle epilators introduce a very fine wire close to the hair shaft, under the skin, and into the hair follicle," explains Anthony Watson, a materials engineer in FDA's Center for Devices and Radiological Health. "An electric current travels down the wire and destroys the hair root at the bottom of the follicle. The loosened hair is then removed with tweezers. Every hair is treated individually."

Needle epilators are used in electrolysis. Because this technique destroys the hair follicle, it is considered a permanent hair removal method. The hair root may persist, however, if the needle misses the mark or if insufficient electricity is delivered to destroy it.

"Also," Watson adds, "the stimulus for hair growth in an area is never permanently removed. For instance, you can't control hormonal changes that cause new growth. Most people would probably define permanent as 'never comes back,' but from a medical standpoint that may not be practical."

Successful electrolysis usually requires considerable time and money. Mona Wexler, an electrologist in Bethesda, Md., says she is careful to explain the process to her clients at their first appointment.

"Electrolysis requires a series of treatments over a period of time. It's not just a one-, two- or three-time thing," she says. "For example, the process for a forearm takes a series of appointments once a week for about a year. You may have a first clearing of both forearms in about eight hours of treatment over two months. After that, you have to catch the hairs that are coming in on a different cycle of growth. For the best results, you want to treat each hair during its active growing stage."

Electrolysis may not always be the best approach, Wexler adds: "Some men who begin electrolysis to get rid of the hair on their back soon stop, because it can be a huge, costly, and very time-consuming job, depending on the amount of hair."

More often, she says, men are treated for the area between the eyebrows, around the outside of the ears, and the shoulders.

"Women mostly come in for facial hair—the lip, chin, eyebrows, and neck, but I also do a tremendous amount of body work—bikini line, abdomen, breast, forearms, underarms," says Wexler.

The major risks of electrolysis are electrical shock, which can occur if the needle is not properly insulated; infec-
Waxing and tweezing may be more painful than using a depilatory, but the results are longer lasting, because new growth is not visible for several weeks after treatment.

There are no uniform standards governing the practice of electrology. Only 31 states require electrologists to be licensed, and, among those, the licensure requirements vary.

"Training requirements vary from as few as 120 hours to 1,100 hours," says Trudy Brown, president of the International Guild of Professional Electrologists. "Some states may require continuing education classes, others not, and there are no national standards for testing," she adds.

Two organizations—the American Electrology Association and the Society of Clinical and Medical Electrologists—have certification programs, however, both based on a written exam, Brown says. A list of licensed and certified electrologists is available from the International Guild of Professional Electrologists, 202 Boulevard St., Suite B, High Point, NC 27262; (800) 830-3247.

Home-use electrolysis devices work the same way as those for professional use and carry the same health risks. The risks are not very great, however, FDA's Watson says, because the voltages and currents for the home-use devices are not very high. Neither the home-use nor the professional devices use great amounts of current, he adds.

The American Medical Association's Committee on Cutaneous Health and Cosmetics says the success of electrolysis self-treatment depends largely on the condition of the hair and skin, the equipment, and the level of skill developed. The committee recommends limiting self-treatment to readily accessible areas, such as the lower parts of the arms and legs. Because working on facial hair requires use of a mirror, and, therefore, reversed movements, this area is best done by a professional.

Like needle epilators, tweezers epilators use electric current to remove hair. The tweezers grasp the hair close to the skin, and applied current travels down the hair shaft to the root. And, like needle epilators, electric shock is possible if the tweezers touch the skin instead of grabbing the hair. Tweezers epilator manufacturers can claim permanent hair removal if they can provide supporting data.

"Tweezers epilators are relatively new," Watson says, having been brought into the market only about 20 years ago. "Because they don't use a needle, they are supposed to be less painful than the older devices, which have been around for more than a hundred years," he says.

Needle epilators are exempt from premarket notification; tweezers epilator manufacturers, however, must submit to FDA data showing their devices are substantially equivalent to similar devices already on the market. FDA is currently reviewing this policy.

"On Aug. 14, 1995, FDA published a Federal Register notice requesting manufacturers of tweezers epilators to submit safety and effectiveness data," Watson says. "After the information is analyzed, the agency will decide what kind of clearance will be required for these devices."

Laser

Hair removal entered the "laser age" last year when FDA cleared the ThermoLase Softlight laser, manufactured by ThermoTrex Corporation, based in San Diego.

"The Softlight is essentially a standard dermatological laser similar to others already on the market for treating skin lesions and removing tattoos," says Richard Felten, a senior reviewer in FDA's Center for Devices and Radiologic Health.

With the ThermoLase method, a proprietary topical black-colored solution is applied to the treatment area before the laser is scanned across it.

"The solution penetrates the hair follicles, and the black material in it preferentially absorbs the laser wavelength, which heats and destroys the follicles," Felten explains.

Three-month clinical trials of the ThermoLase process showed at least a 30 percent reduction of hair on treated areas in 60 to 70 percent of people treated. Manufacturers must limit claims of laser treatment permanence to results substantiated by the clinical data. Thermotrex, therefore, can claim that its laser process causes hair reduction for up to three months after treatment.

Some side effects can be expected whenever a laser is used to treat the skin, Felten says. These include redness, caused by heating the tissue; possibly some darkening of light-complexioned skin and lightening of dark-complexioned skin; and a risk of some scarring in some patients.

"Usually the treated area is covered to prevent infection during the healing period, and then kept covered with a moist solution for a period of time," Felten says, adding that sunlight should be avoided during healing also, to avoid a change in pigment.

A prescription device, the laser must be used under a licensed practitioner's direction. At press time, the Softlight laser was in use at several spas in San Diego and Dallas and in physicians' private practices, says ThermoLase's manager of Softlight, Rick Episcopo. Episcopo says clients may report a stinging in sensitive areas, such as the upper lip, but mostly a sensation of warmth.

Cosmetic hair removal can be quick and easy or time-consuming and somewhat uncomfortable. It can be costly or inexpensive. But, for just about anyone who so desires, there's a way to get rid of the hair you don't want.
Outsmarting
Poison Ivy
And Its Cousins
by Isadora B. Stehlin

Pamela Lillian Isley can manipulate plants in unexplained ways. They bend to her will, growing and threatening the environment and society—at least in Gotham City. In the world of Batman, the fictional Isley is better known as the beautiful criminal Poison Ivy. Her alias is fitting. Just as she is the bane of Batman’s existence, in the real world the poison ivy plant—along with its cousins poison oak and poison sumac—is the bane of millions of campers, hikers, gardeners, and others who enjoy the great outdoors.

Approximately 85 percent of the population will develop an allergic reaction if exposed to poison ivy, oak or sumac, according to the American Academy of Dermatology. Nearly one-third of forestry workers and firefighters who battle forest fires in California, Oregon and Washington develop rashes or lung irritations from contact with poison oak, which is the most common of the three in those states.

Usually, people develop a sensitivity to poison ivy, oak or sumac only after several encounters with the plants, sometimes over many years. However, sensitivity may occur after only one exposure.

The cause of the rash, blisters, and infamous itch is urushiol (pronounced oo-roo-shee-ohl), a chemical in the sap of poison ivy, oak and sumac plants. Because urushiol is inside the plant, brushing against an intact plant will not cause a reaction. But undamaged plants are rare.
“Poison oak, ivy and sumac are very fragile plants,” says William L. Epstein, M.D., professor of dermatology, University of California, San Francisco. Stems or leaves broken by the wind or animals, and even the tiny holes made by chewing insects, can release urushiol.

Reactions, treatments and preventive measures are the same for all three poison plants. Avoiding direct contact with the plants reduces the risk but doesn’t guarantee against a reaction. Urushiol can stick to pets, garden tools, balls, or anything it comes in contact with. If the urushiol isn’t washed off those objects or animals, just touching them—for example, picking up a ball or petting a dog—could cause a reaction in a susceptible person. (Animals, except for a few higher primates, are not sensitive to urushiol.)

Urushiol that’s rubbed off the plants onto other things can remain potent for years, depending on the environment. If the contaminated object is in a dry environment, the potency of the urushiol can last for decades, says Epstein. Even if the environment is warm and moist, the urushiol could still cause a reaction a year later.

“One of the stories I tell people is of the hunter who gets poison oak on his hunting coat,” says Epstein. “He puts it on a year later to go hunting and gets a rash [from the urushiol still on the coat].”

Almost all parts of the body are vulnerable to the sticky urushiol, producing the characteristic linear (in a line) rash. Because the urushiol must penetrate the skin to cause a reaction, places where the skin is thick, such as the soles of the feet and the palms of the hands, are less sensitive to the sap than areas where the skin is thinner. The severity of the reaction may also depend on how big a dose of urushiol the person got.

Quick Action Needed
Because urushiol can penetrate the skin within minutes, there’s no time to waste if you know you’ve been exposed.
“The earlier you cleanse the skin, the greater the chance that you can remove the urushiol before it gets attached to the skin,” says Hon-Sum Ko, M.D., an allergist and immunologist with FDA’s Center for Drug Evaluation and Research. Cleansing may not stop the initial outbreak of the rash if more than 10 minutes has elapsed, but it can help prevent further spread.

If you’ve been exposed to poison ivy, oak or sumac, if possible, stay outdoors until you complete the first two steps:

• First, Epstein says, cleanse exposed skin with generous amounts of isopropyl (rubbing) alcohol. (Don’t return to the woods or yard the same day. Alcohol removes your skin’s protection along with the urushiol and any new contact will cause the urushiol to penetrate twice as fast.)

• Second, wash skin with water. (Water temperature does not matter; if you’re outside, it’s likely only cold water will be available.)

• Third, take a regular shower with soap and warm water. Do not use soap before this point because “soap will tend to pick up some of the urushiol from the surface of the skin and move it around,” says Epstein.

• Clothes, shoes, tools, and anything else that may have been in contact with the urushiol should be wiped off with alcohol and water. Be sure to wear gloves or otherwise cover your hands while doing this and then discard the hand covering.

Dealing with the Rash

If you don’t cleanse quickly enough, or your skin is so sensitive that cleansing didn’t help, redness and swelling will appear in about 12 to 48 hours. Blisters and itching will follow. For those rare people who react after their very first exposure, the rash appears after seven to 10 days.

Because they don’t contain urushiol, the oozing blisters are not contagious nor can the fluid cause further spread on the affected person’s body. Nevertheless, Epstein advises against scratching the blisters because fingernails may carry germs that could cause an infection.

The rash will only occur where urushiol has touched the skin; it doesn’t spread throughout the body. However, the rash may seem to spread if it appears over time instead of all at once. This is either because the urushiol is absorbed at different rates in different parts of the body or because of repeated exposure to contaminated objects or urushiol trapped under the fingernails.

The rash, blisters and itch normally disappear in 14 to 20 days without any treatment. But few can handle the itch without some relief. For mild cases, wet compresses or soaking in cool water may be effective. Oral antihistamines can also relieve itching.

FDA also considers over-the-counter topical corticosteroids (commonly called hydrocortisones under brand names such as Cortaid and Lanacort) safe and effective for temporary relief of itching associated with poison ivy.

For severe cases, prescription topical corticosteroid drugs can halt the reaction, but only if treatment begins within a few hours of exposure. “After the blisters form, the [topical] steroid isn’t
Unfortunately, poison ivy, oak and sumac don’t grow with little picture ID badges around their stems, so you have to know what to look for. The famous rule “leaves of three, let it be” is good to follow, except that some of the plants don’t always play by the rules and have leaves in groups of five to nine. To avoid these plants and their itchy consequences, here’s what to look for.

Poison Ivy
• grows around lakes and streams in the Midwest and the East
• woody, ropelike vine, a trailing shrub on the ground, or a free-standing shrub normally three leaflets (groups of leaves all on the same small stem coming off the larger main stem), but may vary from groups of three to nine
• leaves are green in the summer and red in the fall
• yellow or green flowers and white berries

Poison Oak
• eastern (from New Jersey to Texas) grows as a low shrub; western (along the Pacific coast) grows to 6-foot-tall clumps or vines up to 30 feet long
• oak-like leaves, usually in clusters of three
• clusters of yellow berries

Poison Sumac
• grows in boggy areas, especially in the Southeast
• rangy shrub up to 15 feet tall
• seven to 13 smooth-edged leaflets
• glossy pale yellow or cream-colored berries

—J.B.S.

Desensitization, vaccines, and barrier creams have been studied over the last several decades for their potential to protect against poison ivy reactions, but none have been approved by FDA for this purpose.

Right now, prevention seems the best treatment, unless you plan to take lessons from Batman’s bane with Poison Ivy’s name.

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

- Natural rubber-containing medical devices that may contact human tissue must be labeled as latex and identified as a possible cause of allergic reactions, according to a proposed FDA rule. Hypoallergenicity claims also must be removed from such devices because the current test that supports these claims addresses only chemical sensitivity, not protein sensitivity. FDA is proposing the rule following several reports of severe allergic reactions to a wide range of latex-containing medical devices. Comments on the proposed rule should be sent by Sept. 23 to the Dockets Management Branch (HFA-305), FDA, 12420 Parklawn Drive, Room 1-23, Rockville, MD 20857. (FR June 24)

- Propylene glycol (PG), added to cat food, was excluded from “generally recognized as safe” (GRAS) status in a final FDA rule effective June 3. Manufacturers say PG helps prevent oxidation of components that could affect nutritional properties of the food. But after reviewing currently available information, FDA said “significant questions” remain about PG’s safety in cat food. (FR May 2)

- Most of the artificial sweetener aspartame’s 23 listed uses were replaced with a single-use category for food in a final FDA rule that became effective June 28. FDA amended food additive regulations to allow safe use of aspartame as a general-purpose sweetener. (FR June 28)

- Medical device products that may deplete the Earth’s ozone layer, including those containing or manufactured with chlorofluorocarbons (CFCs), must carry warning statements, according to an FDA interim rule that became effective May 17. CFCs are allowed for some “essential” medical device uses, such as in certain metered-dose inhalation devices used to treat asthma. (FR May 3)

- Helping patients stop smoking is the topic of new guidelines for health professionals mailed this past summer to the offices of 200,000 primary-care physicians by the U.S. Agency for Health Care Policy and Research (AHCPR). The guidelines also are available in a consumer version. For a free copy, call AHCPR at (1-800) 358-9295.

- A new home page for FDA’s Center for Drug Evaluation and Research is now on the agency’s World Wide Web site at http://www.fda.gov/ceder/. The home page offers information about drug approvals, recalls and shortages, as well as the drug center’s programs and policies.

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A California doctor and his partner viewed their homemade cancer treatment as alternative medicine. But a judge declared it "snake oil."

FDA laboratory analysis indicated the treatment, called "Immunostim," contained substances found in common cleaning fluids, such as dish detergent and toilet bowl cleaner. Patients paid as much as $7,500 per treatment to have the product injected into their veins.

Lawrence Taylor, 72, has since had his medical license revoked by the Medical Board of California, and his partner, William Stacey, 48, is serving five years in the San Diego county jail for continuing to sell Immunostim in violation of his probation.

The two men ran the Taylor-Stacey Center for Advanced Medicine in San Diego between 1993 and 1994. Both were sentenced in 1995: Stacey for selling an unapproved cancer treatment, and Taylor for a related but lesser offense, maintaining a public nuisance. Stacey was resentenced earlier this year.

Their illegal activity was uncovered in an investigation by FDA, the San Diego City Attorney's Office, the California Health Department, and the Medical Board of California.

An anonymous caller first alerted FDA to Taylor and Stacey's use of Immunostim in early 1994. At about the same time, two TV reporters who had gone to the Taylor-Stacey clinic posing as relatives of AIDS patients sent a videotape of their investigation to the San Diego City Attorney's Office. The reporters, from the USA Network's "Case Closed" show, were following up on a viewer complaint about Stacey's previous activities in North Carolina. While there, he had treated AIDS patients with Immunostim.

A month later, on March 22, 1994, the San Diego City Attorney's Office filed criminal charges against Taylor and Stacey in San Diego Municipal Court. Two days later, city police arrested the two men, and, as allowed under state law, the Medical Board of California shut down the clinic.

That same day, with search warrants in hand, the group of local, state and federal investigators searched the clinic, as well as the two men's San Diego residences. The searches resulted in the seizure of five vials of Immunostim and various documents related to the product, including financial reports, patient records, and patient handbooks.

The Immunostim was sent to FDA's Forensic Chemistry Center in Cincinnati for analysis. The laboratory identified trisodium phosphate, sodium metasilicate, methyl-dodecylbenzyl trimethyl ammonium chloride, and trimethyl ammonium chloride as the ingredients. No active drug ingredient was present. The solution had an alkaline pH of 12.7.

Referring to the second edition of Comprehensive Review in Toxicology, laboratory scientists found that the substances they identified matched those
found in disinfectants, toilet bowl cleaners, and automatic dishwasher detergents.

Investigators, including Will Brannon, a special agent with FDA’s Office of Criminal Investigations, began interviewing Taylor’s former patients and their family members. The patients had come from throughout the United States for treatment at Taylor’s San Diego clinic.

From these interviews, investigators learned that many of Taylor’s patients had gone through conventional medical therapies with little or no success and had subsequently been diagnosed with terminal diseases. Taylor and Stacey often told patients their treatment would cure them. Each treatment, administered for three to six hours four times a week over a three-week period, consisted of a small amount of Immunostim mixed with an approved intravenous (IV) solution infused into a vein.

Many of the patients’ family members described the treatments as painful. One woman, whose 34-year-old husband was treated with Immunostim for lung cancer, recalled that during a second infusion, the IV solution “leaked into the tissue” of her husband’s hand.

“I immediately began experiencing excruciating, burning pain,” she later wrote to the judge. “His pain intensified over the next several hours, necessitating massive quantities of pain medication with little relief.” Several months later, she said, she rushed her husband to the hospital after administering Immunostim to him at home. An emergency room doctor prescribed injectable Demerol (meperidine), a narcotic analgesic. The patient continued to take Demerol at home and didn’t regain use of his hand until almost a week later, the woman said.

Another woman, whose son underwent Immunostim therapy for brain cancer, recalled nights when her son was “full of pain.” She attributed the pain to an “inflamed” infusion site. She recalled another cancer patient who laid on the floor during treatment because “he was in too much pain to sit.”

Donald Stevenson, M.D., with the Scripps Clinic and Research Foundation in La Jolla, Calif., reviewed patient records and said in his report to the court that most patients treated with Immunostim experienced inflammation of veins used for infusion. This led to “painful swellings” and then complete closure of the veins, resulting in a hard knot where a vein had previously existed, the doctor wrote. Patients’ family members who were interviewed by investigators recalled instances where clinic employees had difficulty finding usable veins. The mother of one patient recalled seeing another patient receiving the IV infusion through his toe because clinic personnel couldn’t find another vein to use.

Many patients reported that they spent considerable money, sometimes their life savings, to receive the Immunostim therapy. Parents of one cancer patient said they paid $5,000 for 12 treatments. The woman whose husband suffered from lung cancer said they spent nearly $26,000 for three courses of treatment. According to the San Diego City Attorney’s Office, Taylor and Stacey took in more than $670,000 from patients receiving Immunostim during the 18 months the clinic was open in San Diego.

Upon checking the men’s backgrounds, investigators learned that Stacey, who referred to himself as a Ph.D. chemist, probably had “a high school education at most.” said Tricia Johnson, the deputy city attorney who prosecuted the case. The universities he said he attended had no records of his having graduated, she said. Taylor was licensed as a general practitioner.

In a plea agreement, on May 12, 1995, Taylor and Stacey pleaded no contest to the criminal charges.

On Aug. 18, 1995, Municipal Court Judge H. Ronald Domnitz sentenced Taylor to a 150-day work-furlough facility with three years’ probation, fined him $2,000, and ordered him to pay the cost of the government’s investigation of the clinic. In addition, he ordered him, along with Stacey, to pay restitution of $46,779 to nine of 108 former patients or their families. By that time, more than half the patients had died, presumably from their diseases. The nine who received restitution were named in the complaint.

The judge also ordered Taylor to place a sign in his medical office in letters at least 3 inches high with these words: “This office does not treat cancer or AIDS patients unless referred by another physician.”

The judge sentenced Stacey Oct. 17, 1995, to 18 months in jail with five years’ probation, fined him $3,000, and ordered him not to work in the health-care industry or sell any health-care product. Stacey failed to appear Oct. 31 to begin his jail sentence. An agent for Stacey’s bondsman, whom Stacey failed to repay, tracked Stacey to South Carolina, where he apparently was still selling Immunostim. The agent notified local police, who arrested him. The San Diego City Attorney’s Office extradited Stacey to California Dec. 21, 1995.

For violating his probation, the judge ordered Stacey last Feb. 29 to serve five years in custody, the maximum allowed under the plea agreement.

Meanwhile, on Feb. 19, the Medical Board of California revoked Taylor’s medical license.

Paula Kurtzweil is a member of FDA’s public affairs staff.
Importer Convicted Of Attempted Bribery

The attempted bribery of an FDA official resulted in the arrest and conviction of a New York seafood importer.

Bernard Kwang Myung of Coimex Seafood, a Brooklyn, N.Y., seafood importing company, was fined $5,000 and sentenced to 18 months’ probation April 12 for offering a gratuity to a compliance officer in FDA’s New York district office. Offering a gratuity to a government official is illegal. The attempted bribery revolved around imported contaminated imitation scallops.

FDA’s Northeast Regional Laboratory analyzed a shipment of the importer’s frozen imitation scallops (surimi) in July 1993, and found the product contaminated with Listeria monocytogenes. This bacteria can cause serious illness, particularly in pregnant women and their fetuses. Cooking food kills Listeria. However, these imitation scallops were a cooked processed product. Cooked processed products are often served without any further cooking—in salad bars, for instance.

FDA initially detained the product on July 15, 1993, and determined that all the firm’s subsequent shipments would be automatically detained at the port of entry. After Myung agreed to relabel the product with a statement that included a warning about the need to cook the food and cooking instructions, FDA allowed the scallops to enter the U.S. market.

However, with the arrival of shipments in January and May 1994, it became clear to FDA that the company was routinely labeling the product with the warning statement rather than trying to eliminate the bacteria. FDA concluded that it would be more appropriate for the foreign processor to manufacture a safe and wholesome product, without the need for a warning about cooking the imitation scallops. So FDA denied the importer’s petition to relabel the product.

On Aug. 9, 1994, Myung visited FDA’s New York district office and met with compliance officer James Nelson to discuss how to deal with detained shipments. During this meeting, Myung placed a white envelope on Nelson’s lap. Nelson realized right away that there was money in this envelope and that Myung was attempting to bribe him. Nelson refused the money, returning the envelope to Myung. Myung then told Nelson that at least he should be allowed to take Nelson and his wife to dinner. Nelson continued to protest and shook Myung’s hand, indicating the end of the meeting.

Nelson immediately reported the incident to his supervisor at the time, Regina Feuchtbaum, former director of the district’s import operations branch, who, following FDA procedure, contacted the Department of Health and Human Services’ Office of Inspector General (OIG). OIG advised Nelson to call Myung back for a meeting the next afternoon to discuss the matter further. This meeting took place with Nelson wired so that the conversation could be monitored and recorded. Myung once again offered money to Nelson: this time, three $100 bills. OIG special agents, listening in from another room, arrested Myung on the spot.


—Herman Janiger

Violations Uncovered At Army Blood Center

The U.S. Army voluntarily discontinued much of its blood collection at Walter Reed Army Medical Center, Washington, D.C., in March while it worked on correcting numerous blood collection violations.

Investigators with FDA’s Baltimore district office uncovered the violations while inspecting the Walter Reed blood center Sept. 28 through Oct. 17, 1995. Problems found included:

- lack of proper equipment and supplies for blood drives
- failure to maintain an up-to-date donor disqualification deferral list
- improperly refrigerated whole blood
- failure to investigate reactions to transfusions
- lack of privacy for donors filling out blood donation questionnaires
- failure to maintain equipment monthly as required.

The Army responded to FDA’s findings in a letter last Dec. 18, but, because of discrepancies between the Army’s response and FDA’s findings, investigators returned to Walter Reed on Jan. 30, 1996. They found many of the same problems, as well as new ones, including:

- using out-of-date blood for transfusions
- improperly maintaining the blood product irradiator, a device that exposes blood to radiation to reduce the risk of rejection when transfusing infants or a member of the donor’s family
- failing to verify repeat testing on samples testing positive for hepatitis B.

Last April 16, Army representatives met with FDA and told the agency that as of March 18 it had discontinued all blood collections except for autologous donations and plateletpheresis. In
Unproven Medical Claims
Land Men in Prison

“It has been known to shatter cancer cells and AIDS cells in people.”
—Salesperson for Life Energy Resources Ltd. (LER), Falconer, N.Y., referring to the firm’s REM SuperPro Generator.

“Your kid gets chicken pox, use the REM [SuperPro Generator] immediately, and it will knock it out.”
—Pascal (Pat) Ballistrea, LER distributor.

Two New York men are serving time in prison for making claims such as these touting the electrical-shock-producing REM device as a cure-all for many medical conditions. A third man is on probation for three years.

In a felony prosecution for device health fraud, the three men—LER’s top distributors—were convicted and sentenced in 1993, 1994 and 1995, for selling unapproved medical devices and drugs.

Their illegal activities came to light in a three-year undercover probe by FDA, the U.S. Postal Inspection Service, and the U.S. Department of Justice.

In prison are Ballistrea, of Williamsville, N.Y., and Michael Ricotta, of Orchard Park, N.Y. Brian Strandberg, of Portland, Ore., who also served as LER’s national marketing director, received probation.

FDA first learned about LER on April 7, 1989, when an employee of a Buffalo finance company contacted FDA’s Buffalo district office to report suspicions about the company. The employee said a salesperson for LER had called to solicit financial backing for the company’s REM SuperPro Generator. Claiming the SuperPro could treat AIDS and cancer, the LER salesperson had confided, “I’m saying this to you, but it goes no further. I really can’t say this to you.”

Later that month, FDA investigator Russ Davis inspected LER and learned from another man that distribution of misbranded products may result in legal action. These uses also are unproven medical claims, so before departing, Davis informed the men that distribution of misbranded devices is illegal. According to Davis, Bradish said LER instructs its distributors to use only official literature for marketing, but added that because distributors run their own businesses, he couldn’t account for their actions. However, he said LER would terminate agreements with distributors making claims not in the official literature, and he would write to them all, reminding them of this and cautioning them not to make the kind of AIDS and cancer claims reported in the original complaint.

Davis collected some of the official marketing literature, which said the electrical devices could treat neuralgia, headache, jet lag, and other conditions. These uses also are unproven medical claims, so before departing, Davis informed the men that distribution of misbranded products may result in legal sanction, such as seizure, injunction or prosecution.

In 1989 and 1990, FDA continued to receive complaints about unproven claims for the REM SuperPro. So, FDA decided to take action.

“We realized that the only way we were going to get them was to do an undercover investigation,” said Louis Kaufman, a compliance officer with FDA’s Center for Devices and Radiological Health.

Posing as distributors, investigators Steven Libel, Joan Trankle, and Sherry Phillips, of FDA’s Buffalo district office,
York. Edmiston and Meo investigated efforts on Ricotta and Ballistrea in New York. Edmiston and Meo investigated Strandberg in Portland, which is in FDA’s Seattle district. Ricotta, Ballistrea and Strandberg were singled out because they were responsible for promoting LER’s products.

The investigators bought LER’s products and collected unofficial literature, known as the “underground packet.” The packet included literature, audiotapes and videotapes of individuals claiming the products could cure cancer, AIDS, and other diseases.

In secretly recorded meetings and phone conversations, Ricotta, Ballistrea and Strandberg admitted sending underground materials to down-line distributors for use in promoting the REM SuperPro for such diseases as cancer and AIDS and the LifeMax Miracle Cream for such medical conditions as osteoporosis and premenstrual syndrome.

To support LER’s claims that the REM SuperPro cured cancer and other diseases, the underground materials routinely referenced a book about the SuperPro Generator, precursor to the REM SuperPro. The book described work by the precursor’s inventor, Royal Raymond Rife, who died in 1971. “REM” reportedly stood for “Rife’s Electromagnetic.”

Meanwhile, on April 19, 1990, FDA investigators Mark Prusak and William Lubas, who were not part of the undercover investigation, inspected LER’s facility in Falconer, N.Y.

Costanzo, now the chief executive officer, refused to let Prusak see shipping and receiving records and distribution information and, when questioned by the investigators, Costanzo denied reports that LER made medical claims for its products. LER’s Bradish said the devices were sold for relaxation and stress reduction.

By February 1991, FDA had gathered enough evidence to forward its findings to the Department of Justice.

On May 29, executing a search warrant at Ballistrea’s house, FDA and the Postal Service found a huge amount of product literature and videotapes. Although Ballistrea had sent undercover government investigators numerous materials on LER products in 1990 and 1991, he told the agents it had been more than a year since he had distributed such materials.

A grand jury investigation began in the summer of 1991. U.S. Attorney Dennis Vacco wrote, “Two of the more disturbing aspects of the investigation are the fact that some cancer patients have been using these devices without the knowledge of their physicians and as an alternative to chemotherapy.”

On Feb. 25, 1993, Strandberg pleaded guilty in the U.S. District Court for the Western District of New York, in Buffalo, to two misdemeanor counts of distributing an unapproved device. In a plea agreement, he admitted knowing the REM SuperPro was not approved by FDA. He admitted sending materials containing medical claims for the device to customers and distributors.

Judge Leslie Foschio sentenced Strandberg on Dec. 21, 1993, to three years’ probation with 200 hours community service and fined him $500 and a $50 special assessment.

On April 8, 1993, in the same court, the grand jury returned a 10-count indictment against Ballistrea and Ricotta.

The trial began Oct. 9. After four days, however, a mistrial was declared for Ballistrea, who was excused because of a back ailment. He was tried later.

During Ricotta’s trial, according to the Nov. 18, 1993, Buffalo News, Ricotta denied selling the REM SuperPro for medical purposes, but he said he believed the product was effective treatment for bone and colon cancers, skin diseases, premenstrual syndrome, arthritis, bladder diseases, angina, insomnia, herniated disks, tumors, Lou Gehrig’s disease, kidney ailments, emphysema, hearing problems, ear infections, and other illnesses.

On Nov. 19, Ricotta was convicted of two felony and four misdemeanor charges for conspiracy to defraud FDA, distributing an adulterated and misbranded medical device (the REM SuperPro), and distributing an unapproved new drug (LifeMax Miracle Cream).

On Feb. 2, 1994, Judge Richard Arcara sentenced Ricotta to three years, five months in prison and three years’ supervised release and fined him $3,000 and a $200 special assessment.

“You are a menace and a threat to society,” Judge Arcara told Ricotta, as reported next day in the Buffalo News. “Your sales strategy targeted the most vulnerable people, including those suffering from terminal disease. It is especially cruel because, in many instances, it proved false hope to people who had no hope.”

After several hearings to determine whether Ballistrea was able to stand trial, his trial finally began Nov. 10, 1994. On Dec. 14, he was convicted of the same charges as Ricotta and of making false statements to FDA and the Postal Service.

On Sept. 22, 1995, Judge Arcara sentenced Ballistrea also to three years, five months in prison and three years’ supervised release and fined him $275 special assessment.

—Dixie Farley helped compile this article.
Summaries of Court Actions are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Summaries of Court Actions report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against goods alleged to be in violation, and criminal and injunction proceedings are against firms or individuals charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce or while held for sale after shipment in interstate commerce.

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

SEIZURE ACTIONS

Food/Contamination, Spoilage, Insanitary Handling

PRODUCT: Beans with ginger, preserved, at San Francisco, Calif. (N.D. Calif.); Civil No. C-94-1986-CW.
CHARGED 6-6-94: While held for sale after shipment in interstate commerce at Wing Sing Chong Co., in San Francisco, Calif., the articles were adulterated in that they contained rodent and other animal hairs, insects, and insect and feather fragments—402(a)(3).
DISPOSITION: A default decree of condemnation and destruction ordered the articles destroyed. (F.D.C. No. 66981; S. No. 94-665-453; S.J. No. 1)

CHARGED 8-11-94: While held for sale after shipment in interstate commerce at Great Central in Long Beach, Calif., the articles were adulterated in that they contained staphylococcal enterotoxin, a poisonous or deleterious substance which might render them injurious to health—402(a)(1). The articles were also adulterated in that they were prepared and packed under insanitary conditions whereby they might have been rendered injurious to health—402(a)(4).
DISPOSITION: A default decree ordered that the articles be destroyed. (F.D.C. No. 67007; S. No. 3016294; S.J. No. 5)

PRODUCT: Royal dinnerware harvest festival, at Eau Claire, Wis. (W.D. Wis.); Civil No. 95C-0357-C.
CHARGED 5-18-95: While held for sale after shipment into interstate commerce at Mid-America Tablewares, Inc., in Eau Claire, Wis., the articles were adulterated in that they contained staphylococcal enterotoxin, a poisonous or deleterious substance which might render them injurious to health—402(a)(1). The articles were also adulterated in that they were prepared and packed under insanitary conditions whereby they might have been rendered injurious to health—402(a)(4).
DISPOSITION: A consent decree ordered that the articles be destroyed. (F.D.C. No. 66959; S. No. 94-705-321; S.J. No. 4)

PRODUCT: Fish Maws and Shark Fins, dried, at San Francisco, Calif. (N.D. Calif.); Civil No. C-94-1366-SC.
CHARGED 4-21-94: While held for sale after shipment in interstate commerce at Wonkow Enterprises, Inc., in San Francisco, Calif., the articles were adulterated in that they contained insects, rodent excreta, and animal hairs—402(a)(3). The articles were also held under insanitary conditions whereby they might have become contaminated with filth—402(a)(4).
DISPOSITION: A consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 67046; S. No. 94-644-161; S.J. No. 3)
Claire, Wis., the articles were adulterated in that they contained lead—402(a)(2)(C).

DISPOSITION: A consent decree of condemnation and destruction ordered the articles destroyed. (F.D.C. No. 67086; S. No. 94-718-522; S.J. No. 6)

PRODUCT: Shrimp, frozen, at Dover, Fla. (M.D. Fla.); Civil No. 95-1412-CIV-T-17A.

CHARGED 8-25-95: While held for sale after shipment in interstate commerce at Mercury Cold Storage, Inc., in Dover, Fla., the articles were adulterated in that they contained Salmonella, a poisonous or deleterious substance which might render them injurious to health—402(a)(1). The articles were also adulterated in that they consisted of decomposed shrimp—402(a)(3).

DISPOSITION: A default decree of condemnation and destruction ordered the articles destroyed. (F.D.C. No. 67103; S. No. 95-711-532; S.J. No. 7)

Medical Devices

PRODUCT: Condoms, lubricated, at Paramount, Calif. (C.D. Calif.); Civil No. 95-3074.

CHARGED 5-8-95: While held for sale after shipment in interstate commerce at Handy Care in Paramount, Calif., the articles were adulterated in that their strength differed from, or their purity or quality fell below that which they represented to possess—501(c). The articles were class III devices without an application for premarket approval, and their packaging failed to bear a label containing the name and place of business of the manufacturer, packer or distributor—501(f)(1)(B) and 502(b)(1). The articles were also adulterated in that they were not manufactured in a duly registered establishment—502(o).

DISPOSITION: A default decree ordered that the articles be destroyed. (F.D.C. No. 67077; S. No. 95-615-695; S.J. No. 8)

INJUNCTION ACTIONS


CHARGED 3-8-94: The defendants introduced or caused to be introduced into interstate commerce adulterated crab meat—301(a). The crab meat was adulterated in that it contained Listeria monocytogenes, a poisonous or deleterious substance which might render it injurious to health, and Escherichia coli, a filthy substance—402(a)(1) and 402(a)(3). The crab meat was also adulterated in that it was prepared, packed or held under insanitary conditions whereby it might have become contaminated with filth, or whereby it might have been rendered injurious to health—402(a)(4).

DISPOSITION: The court granted an order of permanent injunction. Subsequently, the defendants went out of business. (Inj. Nos. 1334 and 1334A; S. No. 93-690-318; S.J. No. 9)


CHARGED 8-17-93: The defendants introduced or caused the introduction or delivery into interstate commerce of adulterated drugs—301(a). The drugs were adulterated in that the methods used in, and the facilities or controls used for, their manufacture, processing, packing, and holding did not conform to and were not operated or administered in conformity with current good manufacturing practice requirements—501(a)(2)(B). The defendants also manufactured, processed, packed, and labeled adulterated drugs—301(k). The defendants delivered for introduction and caused the delivery for introduction into interstate commerce new drugs without approved new drug applications (NDAs), abbreviated new drug applications (ANDAs), or approved NDA or ANDA supplements—301(d).

DISPOSITION: A consent decree of permanent injunction was filed. Six of Warner-Lambert’s manufacturing facilities were shut down except for the manufacture of certain drug products which were permitted to be manufactured under the decree. Subsequently, all facilities met the terms of the decree and were fully reopened. (Inj. No. 1322; S. No. 92-637-081; S.J. No. 10)
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