Tossing and Turning No More
If a good night's sleep is a dream that won't come true, there are ways to put this worry to rest. Remedies range from serious medicine to simple routines.

Parkinson's Disease: New Treatments Slow Onslaught of Symptoms
Though there still is no cure, Parkinson's patients have three new drugs and a medical device to help control this brain disease's devastating symptoms.

Sick Call of the Wild
When wild animals get sick—whether still roaming free, living in zoos, or as family pets—there are very few drugs approved specifically to treat them. New government measures may alleviate the problem.

Dealing with the Depths of Depression
Serious depression is more than just feeling blue. A wide array of drugs, many approved in the last few years, along with talk therapy, can effectively treat this disorder.

Laser Eye Surgery: Is It Worth Looking Into?
The call of freedom from glasses and contacts is powerful. But laser surgery to correct vision isn't for everyone. Careful study and caution are required.
More Foods Can Carry ‘Healthy’ Label

Some canned and frozen fruits and vegetables, as well as certain cereal-grain products, may now carry the term “healthy” on their labels, according to an FDA final rule.

Since 1994, the agency has allowed the term “healthy” on foods that are low in total fat and saturated fat, meet limits for sodium and cholesterol, and contain at least 10 percent per serving of the recommended daily intake of at least one of the following nutrients: vitamin A, vitamin C, calcium, iron, protein, and fiber.

Recognizing that raw fruits and vegetables can contribute significantly to a healthy diet, the rule specified that raw produce could be labeled “healthy” without the 10 percent nutrient contribution if it met the other requirements.

Under the new rule, published March 25, canned and frozen fruits and vegetables can also qualify nutritionally for the term without meeting the 10 percent requirement. However, they must not contain ingredients that would change their nutritional profile if they conform to standards of identity, which define certain required ingredients.

The new rule is intended to encourage people to eat more of the foods recommended for good health in the U.S. Dietary Guidelines.

Taking the pressure off ... Eating less salt and losing weight are safe and effective ways to lower blood pressure in the elderly without drugs, according to research conducted at Tulane University in New Orleans. In a study of 875 men and women ages 60 to 80, researchers found that patients who both lowered salt intake and lost weight had a 53 percent reduced risk of experiencing one of three outcomes: getting hypertension, taking hypertension medication, or having a heart attack or stroke. (Journal of the American Medical Association, March 18)

FDA Moves Toward Consistent Supplement Claims

Labeling claims about the health benefits of dietary supplements would be more reliable and uniform under an FDA proposal that establishes criteria for product label claims.

The proposed rule, published in the April 29, 1998, Federal Register, specifically defines two types of potential claims: “structure-function” claims, which describe how a product may affect the body’s structure or functioning, and disease claims, which relate the product to its role in the treatment, diagnosis, cure, or prevention of disease. Under the 1994 Dietary Supplement Health and Education Act (DSHEA), structure-function claims are allowed, while disease claims are not.

FDA’s proposal follows a report from the presidential Commission on Dietary Supplement Labels, an independent panel of experts charged under DSHEA with recommending measures for regulating dietary supplement claims. The proposal would not affect the availability of dietary supplements or consumers’ access to them.

DSHEA allows manufacturers to use, without FDA authorization, structure-function claims that are truthful and not misleading. Under FDA’s proposal, prohibited disease claims include those that imply or state that the product:

- has an effect on a specific disease or class of diseases. For example, the claim “protects against the development of cancer” would not be allowed, but the claim “helps promote urinary tract health” would be allowed as a structure-function claim.

- is in a drug class that is intended to be used to diagnose, mitigate, treat, cure, or prevent a disease. Thus, claims that describe a product as an “antibiotic,” “antiseptic” or “antidepressant” would not be allowed, while the terms “energizer” and “rejuvenative” would be.

- is a substitute for or augmentation of a drug or other medical therapy. For example, the claim “herbal Prozac” would not be allowed.

- has a role in the body’s response to disease or carriers of disease. For example, the claim “supports the body’s ability to resist infection” would not be allowed, but the claim “supports the immune system” would be allowed as a structure-function claim.

Also, manufacturers may not make or imply a disease claim in product names, graphics, citations, or other means.

If finalized, the proposed rule would require manufacturers to remove unacceptable disease claims from dietary supplement labels or meet the safety and effectiveness standards for drugs under the Federal Food, Drug, and Cosmetic Act.

The public has until Aug. 27 to send written comments on the proposed rule to FDA, Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Drive, Room 1-23, Rockville, MD 20857.

The Federal Register is available in some libraries and at www.fda.gov/ohrms/dockets/98fr/fr98menu.htm on FDA’s Website. The proposal can be viewed as a pdf file by clicking on the date 4/29, then Docket No. 98N-0044.
Spraying away Salmonella ... Running newly hatched chicks through a shower of 29 beneficial bacteria can reduce or eliminate Salmonella in those birds. The bacteria are in a spray called Preempt, which FDA approved in March. The bacteria, which the chicks ingest when they peck at their wet feathers, take up residence in the chicks' intestines and shut out Salmonella. In tests on 80,000 chicks, Salmonella presence was eliminated with only one application.

Herbal Sedative Recalled

A dietary supplement was recalled after FDA determined that the product contained a prescription-strength sedative not listed on the label.

In March, FDA warned consumers not to buy or consume the supplement, known as Sleeping Buddha, which was marketed as an herbal alternative to prescription sedatives. The agency has never reviewed Sleeping Buddha or approved it for its promoted uses to treat insomnia and restlessness.

The prescription sedative ingredient, estazolam, is known to have serious side effects, including possible fetal damage if pregnant women take the drug. It also can pose a risk to consumers who drive, operate heavy machinery, or take other sedative drugs or drink alcohol while taking the drug.

Sleeping Buddha is marketed in capsule form as a product of China. Its distributor, Treasure Box Products Inc. of Burnaby, British Columbia, initiated the product recall in March, after FDA and Canadian testing identified the presence of estazolam.

FDA has received no reports of injuries from the product but advises consumers who have used Sleeping Buddha and have concerns to consult with their health-care providers.

Guide Issued to Prevent Fruit and Vegetable Contamination

Following recent incidents of consumer illness associated with fresh fruits and vegetables, FDA has issued a draft guide describing steps that farmers and processors can take to help prevent disease-causing microorganisms from contaminating their produce.

The guide, published April 13 as part of President Clinton’s initiative to make fresh fruits and vegetables safer, addresses key precautions in areas such as water quality, worker hygiene, field and facility sanitation, manure management, and transportation. Recommendations include teaching farm and plant workers proper hygiene and monitoring workers’ health to reduce the risk that food-borne pathogens will be transmitted.

To view the draft guide, go to vm.cfsan.fda.gov/~dms/prodguid.html on FDA’s Website.

Caffeine lowdown ... A new brochure that highlights information on caffeine and health is available from the International Food Information Council (IFIC). Included are “quick facts” and historical notes about caffeine consumption, as well as topics such as caffeine during pregnancy, questions about addiction, and osteoporosis. For a free copy, send a stamped, self-addressed envelope to “Everything You Need to Know About Caffeine,” IFIC, P.O. Box 65708, Washington, DC 20035. Or visit IFIC’s Website at ificinfo.health.org.
**Industry Controls, Warning Label Reduce Juice Risk**

To address the increasing problem of *Salmonella* and *E. coli* infections and other consumer illnesses associated with juice products, FDA has proposed two rules involving manufacturing and labeling changes.

If finalized, the first rule, proposed April 24, would require domestic and foreign processors of packaged fruit and vegetable juices that sell products in the United States to use the “Hazard Analysis and Critical Control Point (HACCP)” system to prevent contamination of their products. The HACCP program, already required at seafood, meat and poultry processing plants, is used to identify the steps during food production when contamination is most likely so preventive measures can be taken.

Processors could eliminate harmful microbes by pasteurizing the juice or by alternative methods, such as scrubbing or applying antimicrobial solutions.

The second rule, also proposed April 24, would require manufacturers of juices that are not pasteurized or otherwise treated to place the following warning label on the products: “Warning: This product has not been pasteurized and, therefore, may contain harmful bacteria which can cause serious illness in children, the elderly, and persons with weakened immune systems.”

The public has until July 8 to comment on the HACCP proposal. Write to FDA, Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Drive, Room 1-23, Rockville, MD 20857. The comment period on the labeling proposal closed May 26.

The *Federal Register* is available in some libraries and at www.fda.gov/ohrms/dockets/98frfr98menu.htm on FDA’s Website. The proposals can be reviewed as pdf files by clicking on the date 4/24, then on Docket No. 97N-0511 for the HACCP proposal or Docket No. 97N-0524 for the labeling proposal.

**Sweeter-Than-Sugar Product Approved**

Sucralose, a new sugar-like sweetener, has been approved for use in a wide variety of food products.

A “high intensity” sweetener that is about 600 times sweeter than sugar, sucralose is made from a process that begins with sucrose, or table sugar. Like sugar, the new product is a free-flowing, water-soluble, white crystalline powder.

FDA approved sucralose April 1 for use in baked goods, baking mixes, nonalcoholic beverages, chewing gum, coffee and tea products, confections and frostings, fats and oils, frozen dairy desserts and mixes, fruit and water ices, gelatins, puddings and fillings, jams and jellies, milk products, processed fruits and fruit juices, sugar substitutes, sweet sauces, toppings, and syrups. It also can be a “table-top sweetener” that is added directly to foods.

FDA reviewed more than 110 studies in humans and animals in deciding on sucralose's safety.

Sucralose is manufactured by McNeil Specialty Products, a subsidiary of Johnson & Johnson, New Brunswick, N.J.

**Computers Can Screen First-Round Pap Slides**

An automated screening device has been approved by FDA for reading Pap smear slides for signs of cervical cancer. The AutoPap Primary Screening System differs from previously approved systems in that it will perform the initial evaluation of Pap smears, with no prior human screening using a conventional microscope.

Pap smears are the primary method for detecting cervical cancer, which annually affects more than 13,000 American women and leads to 4,500 deaths. Successful treatment depends on early detection.

FDA approved the AutoPap system May 5, after evaluating data from a multicenter clinical study involving more than 31,500 Pap smear slides.

The screening system, marketed by Neopath Inc., Redmond, Wash., is approved for use on conventionally prepared Pap smear samples of patients not considered to be at high risk. Trained professionals will re-evaluate any slides on which the device detects signs of cancer.
New Drug OK’d for Hard-to-Treat Breast Cancer

Women with hard-to-treat breast cancer now have another option for managing their potentially life-threatening disease.

The oral treatment Xeloda (capecitabine) was approved April 30 for patients with advanced breast cancer for which no acceptable alternative treatments are available. Specifically, the drug is for patients whose tumors are resistant to Taxol (paclitaxel) with an anthracycline or for those who should not have anthracycline therapy.

Xeloda was granted accelerated approval, an early approval process applied to some drugs that are used to treat life-threatening conditions. In studies, the drug measurably shrunk some patients’ tumors. The most common side effects of Xeloda include diarrhea, nausea, vomiting, fatigue, painful inflammation of the mouth, and painful rash and swelling of the hands and feet.

As a condition of approval, FDA is requiring the manufacturer, Hoffmann-La Roche Inc., Newark, N.J., to conduct further studies of the drug’s clinical benefits.

Incontinence Patch Goes Over-the-Counter

A small, disposable patch to help women reduce leakage from stress urinary incontinence can now be bought without a prescription. FDA approved the over-the-counter sale of the UroMed Patch based on another analysis of the clinical data and on physicians’ experience since its clearance as a prescription device in May 1996. The agency determined that, with additional label information in lay language, women could use the patch safely and effectively as an OTC product.

Urinary incontinence affects about 10 million Americans, mostly women. Most of these women have stress urinary incontinence, experiencing urine leaks from physical stress such as coughing, laughing, or lifting heavy objects.

The patch, manufactured by UroMed Corp., Needham, Mass., is about the size of a quarter and has an adhesive coating on one side. Placed over the urinary opening, it forms a seal to help reduce leakage. It is not designed to control heavy urine leakage and may not always control moderate leakage, so women may need additional protection, such as panty liners or pads.

The patch is usually worn for two to three hours at a time during the day and can be worn through the night. To urinate, the woman peels off the patch and puts on a new one afterward.

Irritation was one of the main side effects in clinical studies, occurring in about 8 percent of patients. The long-term effects of using the product are not yet known. The patch should not be used during sexual intercourse or by women with urinary tract infection, vaginal infection, or local irritation. Also, it is not intended for women with types of incontinence other than stress incontinence and is less effective in women who have had previous surgical treatment for the condition.

Early labor test ... Pregnant women can find out if they are at risk for premature labor with a new saliva test that gauges levels of the hormone estriol. Approved by FDA in April, SalEst, made by Biex Inc., Dublin, Calif., is intended for women between the 22nd and 36th weeks of pregnancy. Of the 4 million annual births in the United States, about 11 percent are premature. These babies are at greater risk of dying and having conditions such as cerebral palsy and mental retardation.

Impotence Pill Approved

The first oral pill approved in the United States to treat impotence may help stimulate sexual response in many of the millions of American men affected by the condition.

Approved March 27, Viagra (sildenafil citrate) leads to an erection by increasing the blood flow to certain areas of the penis.

Viagra was studied in men with various conditions often associated with impotence, such as prostate problems, hypertension, and coronary artery disease, as well as in men with no identifiable physical cause. The studies indicated that men with diabetes or radical prostate surgery experienced less improvement than others.

Viagra is taken one hour before sexual activity and should be taken in the recommended dose, not more than once a day.

Viagra’s most common side effects include headache, flushing and indigestion. In some cases, men experienced vision changes, mostly in their color perception.

The drug is manufactured by Pfizer Pharmaceuticals, New York City. Viagra’s labeling and other information can be found on FDA’s Website at www.fda.gov/cder/news/viagra.htm.

Men who are currently using medicines that contain nitrates, such as nitroglycerin, should not use Viagra because taken together the drugs can lower blood pressure too much. In addition, men who have medical conditions that may cause a sustained erection, such as sickle cell anemia, leukemia, or multiple myeloma, or who have an abnormally shaped penis may not be able to take Viagra.

Viagra has not been studied with other treatments for impotence, so use in combination with other treatments is not recommended.
Soy story ... Genistein, a chemical found in tofu and other soybean-based foods, may suppress proteins that allow cancer cells to survive. Researchers at the University of California at Los Angeles say certain Asian cultures, whose diets are high in genistein, have a low risk of cancers such as breast and prostate. (Journal of the National Cancer Institute, March 1998)

Risky fats ... Elevated blood levels of triglycerides, the most prevalent fat in foods, can indicate a heart attack risk for middle-aged and elderly men, says a study in Denmark. Researchers studied 2,906 white men, ages 53 to 74, who had no heart disease history, and found that over eight years the men with the highest triglyceride levels appeared to have the most heart attack risk, regardless of factors such as total cholesterol. (Circulation, March 24)

Dialysis Patients Warned About Certain Catheter Adapters

Following four deaths and five serious injuries among patients who had been undergoing hemodialysis at home, FDA is warning all dialysis centers, hospitals, and at-home hemodialysis patients to stop using certain catheter adapters.

The Extension Adapter for a Tesio catheter is part of a kit made or distributed by Medcomp, Harleysville, Pa., and sold between October 1997 and February 1998 in 11 states and nine foreign countries.

The deaths and injuries resulted from severe blood loss when the adapters disconnected from the implanted dialysis access catheters while the patients were asleep.

FDA urges all patients on chronic dialysis to contact their dialysis centers immediately to see if they have the defective adapter. If so, it will have to be replaced. FDA also is urging all hemodialysis centers across the United States, particularly in California, Florida, Michigan, Minnesota, Missouri, New Jersey, Tennessee, Texas, Utah, Virginia, and Washington, where the adapters were known to have been distributed, to stop using the defective adapter and notify their at-home hemodialysis patients of the risk.

Medcomp announced in a March 24, 1998, letter to its distributors that it is recalling all of the 7,000 defective Tesio Extension Adapters, which were also distributed in nine foreign countries.

New Device Diagnoses Osteoporosis Without X-rays

An ultrasound device that can help physicians diagnose osteoporosis and assess a person’s risk of bone fracture has been cleared by FDA.

The Sahara Clinical Bone Sonometer, manufactured by Hologic Inc., Waltham, Mass., is the first device for diagnosing osteoporosis that does not require x-rays. It was approved on March 12 only for use on women at risk of bone fracture, not as a general screening tool.

Osteoporosis is a loss of bone strength, which affects an estimated 23 million American women, to some degree, most of them over age 60. The condition is much less common and usually not as severe in men.

The sonometer measures bone strength by transmitting high frequency sound waves through the patient’s heel for 10 seconds. The device then automatically analyzes and prints out the results. It was shown to be as effective as x-rays for predicting risk of fracture.

Steps Taken to Avert Conflict Between TV Signals, Devices

Because new digital television signals can interfere with medical telemetry devices, such as cardiac monitors, that rely on transmitted signals, FDA and the Federal Communications Commission are taking actions to help head off future interference problems.

Medical facilities have long used unoccupied TV broadcast channels for the operation of telemetry devices. But as television stations have begun converting to the digital systems that will broadcast new high-definition TV formats, they have started using these formerly unoccupied channels, which could create a disruption in the operation of the devices. At press time, no patients had been significantly affected by interference, according to a statement by the two agencies.

Among preventive actions the agencies announced in March:

- FDA is alerting U.S. hospitals and nursing homes about the interference potential and is advising them on how to avoid disruptions.
- FDA is working with manufacturers to ensure that telemetry devices are labeled to alert users about the need to avoid interference.
- FCC is asking manufacturers to help their customers determine if digital TV operations will affect their devices and, if so, to help customers find vacant channels.
- FCC is providing information on its Website (www.fcc.gov) about sharing broadcast channels, including lists of channels to be used for digital TV service in each area.
- Both agencies are exploring the long-term broadcast needs of medical devices and are working with manufacturers and the health-care community to consider ways to address the interference problem.
Reducing “awareness” during surgery ... A device designed to eliminate the potential that a patient might remain partially conscious after receiving anesthesia was approved by FDA in March. The Bispectral Index monitor measures the brain’s response to anesthesia, allowing doctors to administer the precise amount of drug needed to ensure the patient is completely unconscious. Johns Hopkins University researchers estimate that “awareness” during surgery occurs in four out of every 10,000 cases.

Drop goes the measles ... Now at the lowest level ever in the United States, domestic measles cases last year numbered only 135, down from 488 in 1996, according to the national Centers for Disease Control and Prevention. Elsewhere in the Western Hemisphere, however, the childhood disease was more prevalent, reports CDC. For example, Brazil’s densely populated state of Sao Paulo had 20,186 cases.

Sealant Approved for Blood Vessel Bleeding

Surgeons can keep small, sometimes inaccessible, blood vessels from oozing during surgery with a new blood-derived sealant called fibrin. The product is effective in cardiopulmonary bypass and colostomy operations, as well as when the spleen has been injured traumatically.

Fibrin, approved by FDA May 1, is made from fibrinogen, a human blood protein that forms a clot when combined with thrombin, another blood-clotting protein. The product forms a flexible material over the oozing blood vessel that can often control bleeding within five minutes.

Fibrin is manufactured in Austria and distributed by Baxter Healthcare Corporation, Glendale, Calif., under the brand name Tisseel.

Vision Damage Caused By Unapproved Device

Hospitals and physicians should not use the Abtox Plazlyte Sterilization System, FDA warns, due to reported injuries involving ophthalmic surgical instruments sterilized with the system. The device has not been cleared by FDA.

The agency has received reports of at least 10 serious corneal injuries involving vision damage with at least two cases requiring corneal transplants.

The device appears to form toxic salts when used on surgical tools made of copper, brass or zinc.

The device’s maker, Abtox Inc., Mundelein, Ill., recalled the device in April from its 155 customers worldwide. At press time, FDA was monitoring the recall.

Stroke signs ... Many people can’t identify even one symptom of stroke, says a new survey sponsored by the National Institute of Neurological Disorders and Stroke. Only slightly more than half of those surveyed could name at least one stroke symptom, and only 68 percent could name one stroke risk factor. Stroke is the main cause of disability and the third leading cause of death in this country. Researchers say knowing symptoms increases the odds that stroke’s effects can be lessened, even reversed.

Here are the warning signs. If you have any of these symptoms, call, or have someone call, 911 immediately:
- sudden weakness or numbness in the face, arm or leg
- sudden dimness or loss of vision, particularly in one eye
- sudden difficulty speaking or understanding speech
- sudden severe headache with no known cause
- unexplained dizziness, unsteadiness, or sudden falls, especially in conjunction with the other warning signs.

Occasionally, strokes cause double vision, drowsiness, nausea, or vomiting. Also, because warning signs sometimes may last only a few minutes and disappear, it may be tempting to ignore them. But these “mini-strokes,” or transient ischemic attacks (TIAs), could be your body’s warning of a future full-blown stroke. So even if the symptoms go away quickly, seek medical help right away.

For more on stroke, see “New Success Against Stroke” in the March-April 1998 FDA Consumer.
Tossing & Turning No More

How to Get a Good Night’s Sleep

by Tamar Nordenberg
Come, blessed barrier between day
and day,
Dear mother of fresh thoughts and
joyous health!
—William Wordsworth in “To Sleep”
(1806)

For years, there were no refreshing
lulls between days for Lauren Ero.
Rather than waking up feeling clear-
headed and healthy, the 37-year-old
mother of two spent four years perpetu-
ally listless and moody.

"Those years are like a fog to me. I
just remember how hard it was and how
hopeless I felt," she says. "I would be
more tired in the morning than when I
went to bed the night before. I was too
exhausted to do even day-to-day activi-
ties like taking care of my kids and
things around the house."

Ero was suffering not from depression,
as one doctor surmised based on her
look-alike symptoms of despondent
mood and irritability, but from insomnia.

The definition of insomnia, according
to the American Sleep Disorders Asso-
ciation (ASDA), is difficulty falling
asleep or staying asleep. If it occurs ev-
every night or most nights for an extended
time, like Ero’s, it’s called chronic in-
somnia.

According to ASDA estimates, more
than 35 million Americans suffer from
this long-lasting type of insomnia, with
20 to 30 million others suffering shorter-
term sleeplessness. Men and women of
all ages experience insomnia, but it is
more common in the elderly and in
women, especially after menopause.

Overcoming Roadblocks to Sleep

Like a headache or fever, insomnia
may be a symptom of another problem.
It can result from something as simple
as anticipating a stressful event, like a
test or meeting, or from a longer-lasting
stressful circumstance, such as a sick
child or troubled marriage. Even worry-
ing about having a tough time falling
asleep may itself prevent a person from
drifting off.

Other common causes of nighttime
wakefulness include environmental dis-
turbances, such as noise from traffic or
television, an uncomfortable tempera-
ture, or light from the sun or other
source; use of alcohol or stimulants,
such as caffeine or nicotine; and erratic
hours, like those of shift workers and
people whose air travel takes them
to across time zones.

Sometimes short-term insomnia may
go away on its own or with simple
changes in daytime or sleep-time habits.
(See “Wooing Sleep.”) If these lifestyle
changes don’t work, the careful use of
sleeping pills approved by the Food and
Drug Administration may help provide
temporary relief from insomnia.

A doctor can help choose an appropri-
ate medicine. One factor to consider is
the drug’s half-life, or the time it takes
to be cleared from the body. Drugs with
shorter half-lives are less likely to have
carry-over sedation that affects daytime
functioning.

A second factor is the drug’s toxicity.
Because of their lower risk of overdose,
the newer benzodiazepines and benzodi-
azepine-like drugs are used more often
to treat insomnia than barbiturates and
other older drugs. Among the most com-
monly prescribed benzodiazepine sleep-
aids are flurazepam (Dalmane),
estazolam (ProSom), quazepam (Doral),
temazepam (Restoril), and triazolam
(Halcion). The prescription sleep-aid
zolpidem (Ambien) is in the
imidazopyridine class of drugs.

Melatonin?

Many Americans in search of more
satisfying slumber are buying the hor-
mone melatonin at their local health
food stores. Melatonin-containing
products are marketed as dietary
supplements, which can be sold with-
out FDA’s premarket review or ap-
proval.

Researchers, including those at a
1996 National Institutes of Health con-
ference about melatonin and sleep,
cautions melatonin users about the ab-
sence of scientific studies to prove that
melatonin is safe and helpful in treat-
ing insomnia.

"Public fervor for melatonin runs far
ahead of the scientific evidence to sup-
port it," states an article about the NIH
workshop in the Journal of the Ameri-
can Medical Association, referring to
the reported $200 million to $350
million U.S. market for the hormone.

"People are taking melatonin and
we are trying to figure out what it
does," said one researcher who at-
tended the NIH meeting. "We are
going about it backward."

NIH sleep expert James Kiley, M.D.,
agrees that many questions about the
supplement remain unanswered: "We
need some research to address the
concerns about melatonin and its
safety and efficacy." ■

—T.N.
As a rule, these sleeping pills should be used only for short periods because of the risk of developing dependency and withdrawal symptoms when the drugs are stopped. So, while they may help with short-term insomnia induced by jet lag, shift work schedule changes, or short-term stress, they should generally not be used for chronic insomnia because of their potential addictiveness and because they can mask underlying medical problems.

Some other sleep-aids are available without a prescription, including diphenhydramine (in Nytol, Sleep-Eze, and Sominex) and doxylamine (in Unisom Nighttime). These products contain a sedating antihistamine and, like prescription drugs, must be used with care. Even if taken at night, they can cause daytime drowsiness, which can make driving and other tasks risky.

Sleep Apnea:
More Than Simple Snoring

Unlike short-term sleeplessness, chronic insomnia is often a symptom of a serious underlying medical disorder. Depression and other psychiatric disorders account for many cases of insomnia, as do wholly physical illnesses, such as asthma, arthritis, Parkinson's disease, kidney or heart disease, and hyperthyroidism.

Sleep apnea is among the most common and most dangerous types of sleep disorder. An estimated 18 million Americans have the condition, which is marked by repeated episodes of cessation of breathing during sleep that over time can lead to high blood pressure, cardiac disease, and disordered thinking.

Sleep apnea was the culprit in Lauren Ero's case. After two years of trying various antidepressants that offered her no relief, Ero sought a second medical opinion and was sent for a sleep analysis.

"Then it was really obvious what it was," says Ero, who recently began working for the American Sleep Apnea Association. "It was a classic case."

The tests revealed what Ero didn't know and what her husband hadn't found alarming: Ero was snoring. But her "snoring" problem was distinct from the merely annoying type because she was also gasping for air throughout the night—possibly tens of times each hour—which repeatedly roused her out of her refreshing, deep sleep. The results were the telltale signs of sleep apnea: excessive daytime sleepiness and difficulty functioning.

Obstructive sleep apnea is by far the most common type. Breathing is interrupted when air can't flow into or out of the nose or mouth. The reason for the blockage could be an over-relaxation of the throat muscles and tongue, which partially blocks the airway or, in obese people, an excess amount of tissue in the airway. Those with receding chin lines are also at higher risk for developing obstructive sleep apnea.

In the less common form, central sleep apnea, breathing is stopped not because the airway is closed but because the diaphragm and chest muscles stop working.

Mild cases of obstructive sleep apnea can sometimes be treated by making simple behavioral changes, such as avoiding alcohol, tobacco, and sleeping (Continued on page 12)
Beyond those with an unintentional inability to sleep, millions more Americans undersleep by choice, burning the candle at both ends because of hectic work and family schedules. Recent surveys show that Americans sleep seven hours each night on average, down from nine hours in 1910, when, without electricity, people generally went to sleep as darkness fell. “People don’t respect sleep enough,” says Daniel O’Hearn, a sleep disorders specialist at Johns Hopkins University. “They feel they can do more—have more time for work and family—by allowing themselves less time for sleep. But they do sleep; they sleep at work, or driving to work.”

Nodding off at work isn’t just unproductive; in the worst cases, it can cause serious industrial accidents. The 1989 Exxon Valdez Alaskan oil spill, for example, was reportedly due at least in part to the severe fatigue of the tanker’s sleep-deprived third mate.

Also, like drunk driving, drowsy driving can kill. The National Highway Traffic Safety Administration estimates that more than 200,000 crashes each year involve drivers falling asleep at the wheel, and that thousands of Americans die in such accidents annually. “Besides being an unpleasant sensation, when we’re tired, we’re less alert and less able to respond reflexively,” says FDA drug reviewer Bob Rappaport, M.D.

Lack of sleep can cause memory and mood problems, too, Rappaport says, and may affect immune function, which could lead to an increased incidence of infection and other illnesses. In studies performed on rats, prolonged sleep deprivation resulted in death.

Beyond the observable consequences of sleep deprivation, why humans—or any animals, for that matter—need sleep remains largely a mystery. “What happens in the brain while we’re sleeping is what we’re trying to untangle,” says James Kiley, director of the National Center for Sleep Disorders Research of the National Institutes of Health. “We’re just beginning to understand why a third of our life is spent sleeping. What we do know is that sleep is an important biological need, like food and drink, and that the brain is very active while we’re sleeping.”

The leading sleep theories focus on “rest and resuscitation for the body and the psyche,” says Rappaport. During sleep, the brain may recharge its energy stores and shift the day’s information that has been stored in temporary memory to regions of the brain associated with long-term memory.

So just how much nightly R and R does a person need? That can change throughout one’s life based on age and other factors affecting the internal clock or “circadian rhythms.” For most people, though, seven and a half to eight and a half hours of sleep each night fulfills the basic physical need, Rappaport says, adding that this is “very individual” and can range from as few as four or five hours to as many as nine or 10.

The Mayo Clinic in Rochester, Minn., defines an adequate amount of sleep as whatever produces daytime alertness and a feeling of well-being. People should not need an alarm clock to wake them if they are getting enough sleep, the Mayo Clinic says, while acknowledging that throwing away one’s alarm clock may be unrealistic.

—T.N.
A joker's definition of insomnia: When you keep a bunch of innocent sheep jumping over a fence all night just because you can't get to sleep.

Experts agree that the time-honored practice of counting sheep or doing another such monotonous task may help induce sleep. Sleep specialists provide these additional tips to help you reach dreamland.

• Avoid caffeine (including caffeine-containing drugs), nicotine, and alcohol for four to six hours before bedtime. The first two are stimulants that can make it difficult to sleep. And while alcohol may have a sedating effect at first, it tends to disturb sleep after several hours.

• Don’t exercise within four to six hours of bedtime. Working out earlier in the day, though, not only doesn’t hinder sleep, but can actually improve it.

• Perform relaxing rituals before bed, such as taking a warm bath, listening to relaxing music, or eating a light snack.

• Before going to bed, try as much as possible to put your worries out of your mind and plan to address them another time.

• Reserve your bed for sleeping. To preserve the association between bed and slumber, don’t watch television or do work in bed.

• Go to bed only when sleepy. If you can’t fall asleep within 15 to 20 minutes, get out of bed and read a book or do another relaxing activity for awhile, rather than trying harder to fall asleep.

• Make sure your bed is comfortable and the bedroom is conducive to restful sleep—quiet and at a comfortable temperature, for example.

• Wake up about the same time every day, even on weekends, to normalize the sleep-wake schedule.

• Don’t take naps, or nap during the mid-afternoon for no more than 30 minutes.

—T.N.
Joe Dulaney calls himself the Backward Man.

Although the tag is lighthearted, the awkward and dangerous dilemma he often faces as his lower limbs simply lock in mid-stride is not. At these moments, his body halts abruptly like a movie freeze-frame, and the only way he can walk is to step backward.

“I’ve gotten to where I can move pretty fast in reverse,” says Illinois resident Dulaney, 65, whose finessed footwork helps him cope with one of many symptoms of Parkinson’s disease.

Nationwide, as many as 1.5 million people suffer from Parkinson’s, according to the Parkinson’s Disease Foundation. A chronic and progressive disorder, Parkinson’s strikes slightly more men than women and more whites than blacks in the United States. Though the disease is found most often in patients over 50, as many as 10 percent of patients—afflicted with the so-called “young-onset” Parkinson’s—are under 40. About 50,000 Americans are diagnosed with Parkinson’s yearly, according to the National Institute of Neurological Disorders and Stroke, which estimates that the total cost of health care for Parkinson’s patients will exceed $5.6 billion this year.
Among the public figures fighting Parkinson’s disease are (clockwise from left): former heavyweight boxing champion Muhammad Ali, evangelist Billy Graham, and former Alabama governor and presidential candidate George Wallace.
The Food and Drug Administration has approved nearly a dozen drugs for treating Parkinson’s, three of which have been put on the market just in the past year. Also approved in 1997 was a device that is surgically implanted in the brain to lessen the violent shaking experienced by some Parkinson’s patients. The 1996 discovery of a gene believed responsible for a form of Parkinson’s may result in future innovative treatments. Despite the range of therapies available to ease the disease’s debilitating symptoms, however, treatments now on the market can neither replace the faulty nerve cells that cause the disease nor stop Parkinson’s from progressing.

Numerous public figures have acknowledged their battle with Parkinson’s. Attorney General Janet Reno, evangelist Billy Graham, former boxer Muhammad Ali, and former Alabama governor George Wallace all are fighting the disease. Chinese leader Deng Xiaoping was in the late stages of Parkinson’s when he died last year at age 92.

Reno, the first to publicly acknowledge her battle with Parkinson’s, said it is “not a life sentence,” but a life full of memories. She credited the 1996 regulation of L-DOPA, the precursor to dopamine, with allowing her to continue to work.

In the normal brain, some nerve cells produce the chemical dopamine, which transmits signals within the brain to produce smooth movement of muscles. In Parkinson’s patients, 80 percent or more of these dopamine-producing cells are damaged, dead, or otherwise degenerated. This causes the nerve cells to fire wildly, leaving patients unable to control their movements. Symptoms usually show up in one or more of four ways:

- tremor, or trembling in hands, arms, legs, jaw, and face
- rigidity, or stiffness of limbs and trunk
- bradykinesia, or slowness of movement
- postural instability or impaired balance and coordination.

Though full-blown Parkinson’s can be crippling or disabling, experts say early symptoms of the disease may be so subtle and gradual that patients sometimes ignore them or attribute them to the effects of aging. At first, patients may feel overly tired, “down in the dumps,” or a little shaky. Their speech may become soft and they may become irritable for no reason. Movements may be stiff, unsteady, or unusually slow.

Joe Dulaney says he was in “perfect health” nine years ago when his wife noticed that he had stopped swinging his right arm when he walked. Soon, simple tasks such as brushing his teeth and combing his hair became major ordeals. His right hand was always ice cold and he produced small, jerky letters when he wrote.

Dulaney’s doctor diagnosed the problem as arthritis and prescribed drugs to treat it. But symptoms worsened. Dulaney’s voice dwindled to a slight whisper. Leg cramps, dry mouth, severe constipation, itchy eyes, and trouble turning over in bed tormented him. “My wrists were rigid and my fingers were not flexible, so I couldn’t even button my shirt,” he says. Still, another doctor seconded the arthritis diagnosis and prescribed different drugs.

Finally fed up because his deteriorati-
Experts are enthusiastic about three new Parkinson's drugs FDA approved in 1997.

ing condition prevented him from doing simple tasks such as turning newspaper pages, putting money in his wallet, and replacing a light bulb, Dulaney checked himself into a local hospital, arriving in such a weakened state he couldn’t walk.

Though a Parkinson’s diagnosis rarely comes quickly, the three doctors who examined Dulaney at the hospital agreed within minutes that his classic symptoms indicated Parkinson’s. The doctors gave him the Parkinson’s drug levodopa, marketed as Larodopa and in generic forms, and the effect was nearly immediate.

“In one hour or so I was walking the halls. I took a shower by myself and did one push-up to show off,” says Dulaney. It was, for the moment, as if the disease had somehow vanished. But Dulaney says he soon became “fully aware” that because Parkinson’s is progressive, he could manage some symptoms with drugs, but the disease wasn’t about to go away.

Treating the Disease

The drug Dulaney took at the hospital, levodopa, is what doctors call the “gold standard” of Parkinson’s therapy, because it is often the first-line treatment for the disease. Approved in 1970, levodopa helps restore muscle control when it is converted to dopamine in the brain.

Why not give a patient dopamine directly? The reason is that dopamine cannot get through the body’s blood-brain barrier, which screens out certain substances. But, although levodopa can pass through the barrier, it changes to dopamine so quickly only a small amount actually makes it into the brain. So to relieve symptoms, many patients need to take fairly large doses, which can cause side effects such as nausea and dyskinesias (involuntary movements).

To reduce these drawbacks, doctors often prescribe levodopa mixed with carbidopa, a drug that is marketed as Sinemet or in generic versions. About 80 percent of Parkinson’s patients take this drug, according to drug industry esti-

mated. Carbidopa delays the conversion of levodopa to dopamine until it reaches the brain, often lessening or even preventing levodopa side effects. Carbidopa also decreases the amount of levodopa needed. Because each Parkinson’s patient reacts differently to treatment, doctors and patients must work closely to find a tolerable balance between the drug’s benefits and side effects.

Though the levodopa-carbidopa combination can be so effective that some patients forget for a while that they have Parkinson’s, the drug is far from perfect. Side effects aside, doses typically must be increased over time, and the disease often manifests an “on-off” syndrome in advanced patients in which the drug simply doesn’t work for unpredictable durations. Fortunately, alternatives are available.

Parkinson’s experts are enthusiastic about the three new drugs FDA approved in 1997: Mirapex (pramipexole dihydrochloride), Requip (ropinirole hydrochloride), and Tasmar (tolcapone).

Enrico Fazzini, M.D., who runs a neurology clinic in New York City, says the three new drugs are “really helping me to treat my Parkinson’s patients more effectively.”

Mirapex and Requip, which mimic dopamine’s role in the brain, allow patients to regain some of their lost muscle control. Both are approved for use alone or with levodopa drugs. In clinical trials, patients taking Mirapex alone saw as much as a 30 percent improvement in symptoms. Combining Mirapex with levodopa drugs allowed advanced patients to reduce those doses by up to 25 percent. Requip trials showed similar benefits, allowing patients to reduce levodopa doses by an average of 31 percent.

For Parkinson’s disease patients, both updated information and social interactions are key factors in battling the disease. Though patients seek these through traditional means such as their doctors, families and friends, many are turning to the Internet.

Patients can compare notes on Parkinson’s issues and stay in touch with others with the disease by subscribing to an Internet Parkinson’s mailing list. Some of these lists deal with Parkinson’s as one of a number of neurological disorders. Others focus on caregiving. One list that is an open forum just for Parkinson’s patients is called “PARKINSN.”

Maintained at the University of Toronto, PARKINSN gives patients a place to pose questions or just let off some steam. A recent scan of the list revealed messages about exercises that can relieve some Parkinson’s discomfort, surgery success stories, reviews of books about the disease, poems, even some Parkinson’s jokes. One list member announced that he is marrying his doctor, and he invited everyone on the list to his wedding.

To join PARKINSN, send an e-mail message to LISTSERV@LISTSERV.UTORONTO.CA. In the body of the note, write: subscribe PARKINSN (your first name) (your last name).

—J.H.
This diagram of the brain (above) shows several structures related to Parkinson’s disease. **Basal ganglia** affect normal movement and walking; **substantia nigra** are types of **basal ganglia** that produce the neurotransmitter dopamine, which sends messages that control muscles. The **globus pallidus** is part of a larger structure connected to the **substantia nigra** affecting movement, balance and walking. The **thalamus** serves as a relay station for brain impulses, and the **cerebellum** affects muscle coordination.

Sometimes called a brain pacemaker, the Activa Tremor Control Therapy has helped some patients control the sometimes violent tremors that accompany Parkinson’s. The device consists of a wire implanted deep in the brain that is connected to a pulse generator implanted near the collarbone. Patients turn the device on by passing a magnet over the generator.

Tasmarr is a new kind of drug called a COMT inhibitor. It also is indicated for use with levodopa drugs. Researchers believe that Tasmar blocks a key enzyme responsible for breaking down levodopa before it reaches the brain. In trials, patients with a stable response to levodopa drugs who took Tasmar experienced significant improvements in daily activities such as talking, writing, walking, and dressing.

“Although we are still looking for a cure, COMT inhibitors represent an entirely new class of therapy that will help many Parkinson’s patients attain better symptom control,” says Emilio Alonso-Mendoza, executive director of the National Parkinson Foundation.

Parkinson’s drug therapy also can include:

- **Parlodel** (bromocriptine) and **Permax** (ergolide), which mimic dopamine’s role in the brain. They are sometimes given with levodopa drugs to improve response.
- **Eldepryl** (selegiline hydrochloride), also called deprenyl and available in generic versions, which can enhance and prolong levodopa response by delaying the breakdown of naturally occurring and levodopa-formed dopamine, allowing accumulation in surviving nerve cells.

**A Brain “Pacemaker”**

FDA approved an important tool for controlling Parkinson’s tremors last August. The Activa Tremor Control Therapy consists of a wire surgically implanted deep within the brain and connected to a pulse generator, similar to a cardiac pacemaker, implanted near the collarbone. Whenever a tremor begins, patients can activate the device by passing a hand-held magnet over the generator.

The system delivers a mild electrical stimulation that blocks the dysfunctional brain signals that cause tremor. Effects are often dramatic. “Before the implant, patients can’t raise a glass of water or a spoonful of food to their mouths without spilling it or striking themselves in the face,” says William Koller, M.D., neurology chairman at Kansas University Medical Center. “Within hours, these same patients are sipping tea from a cup and eating peas with a fork, with no signs of their disability.”

(Photo courtesy of Medtronic Inc.)
About 50,000 Americans are diagnosed with Parkinson’s yearly.

Surgery Options

A brain operation shown to be helpful for many Parkinson’s patients, especially those in late stages of the disease, is called pallidotomy. Doctors are not sure why the procedure works, but an October 1997 report in the New England Journal of Medicine stated that half of the patients in a pallidotomy study at Toronto Hospital, who before the surgery needed help in eating, dressing, and personal hygiene, were able to resume these activities independently. The study cautioned, however, that some of the surgery’s effects diminished after two years and that the long-term effectiveness of the procedure is unknown.

In pallidotomy, a surgeon makes a tiny hole in the skull and uses a tiny electric probe to destroy a small portion of the globus pallidus, which experts believe is overactive in Parkinson’s patients. Before operating, the surgeon has “mapped” the patient’s brain with imaging techniques such as magnetic resonance and knows precisely where the probe should go. The patient is kept awake, but under sedation, so the surgeon can note responses to stimuli. Though both sides of the brain have a globus pallidus, pallidotomies typically are performed on one side at a time. After the patient has recuperated, a second procedure is done if needed.

For Tom Riess, who has undergone the procedure four times over the last six years, the surgery helped reduce his Parkinson’s symptoms, especially the violent shaking, “which was literally killing me,” he says. “Unfortunately, it left me with severely impaired speech, which is a fairly common consequence,” says the 51-year-old Californian, a Parkinson’s patient for 17 years. “Still, the tradeoff is worthwhile.”

Thalamotomy, a surgical procedure that destroys a specific group of cells in the thalamus, the brain’s communications center, is aimed at the 5 to 10 percent of Parkinson’s patients with disabling tremor in the hand or arm. It reduces or eliminates tremor in as many as 90 percent of patients.

On the Horizon

A number of potential Parkinson’s treatments in research laboratories now show much promise. They include:

• Neurotrophic proteins—These appear to protect nerve cells from the premature death that prompts Parkinson’s. One hurdle is getting the proteins past the blood-brain barrier.
• Neuroprotective agents—Researchers are examining naturally occurring enzymes that appear to deactivate “free radicals,” chemicals some scientists think may be linked to the damage done to nerve cells in Parkinson’s and other neurological disorders.
• Neural tissue transplants—Researchers are studying ways to implant neural tissues from fetal pigs into the brain to restore the degenerate area. In a clinical trial conducted in part at Boston University School of Medicine, three patients out of 12 implanted with the pig tissues showed significant reduction in symptoms.
• Genetic engineering—Scientists are modifying the genetic code of individual cells to create dopamine-producing cells from other cells, such as those from the skin.

Experts say some of these new treatments are still far off. Others say they are hopeful that with bolstered research efforts, such as those earmarked in last year’s Udall Act, innovative new therapies will be available in the near future.

“I’m optimistic,” says Perry Cohen, 52, a Washington, D.C., Parkinson’s activist and patient for two years. “I think we are on the verge of an important development. I’m confident that I won’t have to go through the agony I’ve seen others go through.”

John Henkel is a staff writer for FDA Consumer.

For More Information ...

Contact any of the following organizations to learn more about Parkinson’s disease and support groups:

American Parkinson’s Disease Association
1250 Hylan Blvd.
Staten Island, NY 10305
1-800-223-APDA (2732)
www.apdaparkinson.com

National Institute of Neurological Disorders and Stroke
P.O. Box 5801
Bethesda, MD 20824
1-800-352-9424
www.ninds.nih.gov

National Parkinson Foundation Inc.
1501 N.W. 9th Ave. (Bob Hope Road)
Miami, FL 33136-1494
1-800-327-4545
in Florida: 1-800-433-7022
www.parkinson.org

Parkinson’s Disease Foundation, Inc.
650 W. 168th St.
New York, NY 10032
1-800-457-6676

Parkinson’s Institute
1170 Morse Ave.
Sunnyvale, CA 94089-1605
(408) 734-2800

Parkinson’s Support Groups of America
11376 Cherry Hill Road, No. 204
Beltsville, MD 20705
301-937-1545

United Parkinson Foundation
833 W. Washington Blvd.
Chicago, IL 60607
(312) 733-1893
e-mail: upf_iff@msn.com

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Veterinarian Mitchell Bush, suspicious of a newly discovered mass, examines a maned wolf’s abdomen while technician Lisa Ware and keeper Ken Lang await instructions. The wolf, like all animals at the National Zoo’s Conservation and Research Center, gets a checkup every year.

“COME ON SWEETIE. WAKE UP.”

Mitchell Bush, D.V.M., is urging his sedated patient awake following exploratory surgery for an abdominal mass. His patient, a 35-pound female maned wolf from South America, has ovarian cancer.

She slowly comes to as her keeper carries her back to her cage. It looks as if she will survive the surgery.

Bush and his staff are pleased. Even though surgery on rare and exotic animals is fairly routine at the National Zoological Park’s Conservation and Research Center in Front Royal, Va., it’s always risky, considering virtually no anesthetics, anti-
After anesthetizing a zebra (below), Bush removes dead tissue from the zebra's infected hoof. A few hours later (right), he's in the operating room preparing a maned wolf for exploratory abdominal surgery.

Biotics or other drugs are approved for these animals. Instead, veterinarians like Bush rely on personal experience, published data, and word-of-mouth from other veterinarians to use animal and human drugs already on the U.S. market or approved for use in foreign countries.

"We're dealing with a lot of unknowns," says Bush, who is the center's chief veterinarian. "There's hardly any drug on my shelf that's approved for these animals."

Congress wants to change that. This year, as mandated under the Animal Drug Availability Act of 1996, the Food and Drug Administration plans to propose measures that will encourage drug companies to seek approval of drugs for minor species and minor uses in major species. The purpose is to alleviate the scarcity of safe and effective drugs for these animals.

A minor species is defined as any animal other than dogs, cats, cattle, horses, pigs, chickens, and turkeys. Minor use of a drug includes drugs used to treat minor species and used to treat rare diseases in major species or diseases in major species confined to certain geographic areas. Examples of two drugs FDA approved recently that fall into the "minor use" category are Antizol-Vet (fomepizole) as an antidote to antifreeze intoxication in dogs—usually limited to dogs in the Northern states—and Imizol (imidocarb dipropionate), an antiparasitic for babesiosis in dogs.

FDA's anticipated proposals, if adopted, could benefit a wide range of animals, including zoo animals; common U.S. wildlife, such as deer, fox, squirrels, and raccoons; minor species farmed for food, such as game birds and...
“Effective treatments are not just for zoo animals. We also need them for animals in the free-living situation, where our intervention can help ward off diseases.”

—Veterinarian Mitchell Bush

To increase the number of approved drugs for minor species, FDA plans to propose measures that would encourage new drug development, more clinical trials both of new drugs and of drugs already approved for major species and humans in minor species, and the submission of new animal drug applications (NADAs) for agency review.

Linda Wilmot, D.V.M., veterinary medical officer and team leader in FDA’s Center for Veterinary Medicine, says some of the measures expected to be proposed would follow closely those allowed under FDA’s Orphan Products Development Program. The program encourages drug companies to seek approval of drugs for rare human diseases and conditions by offering companies help with study design and by giving financial incentives, such as tax relief, grants, and extended exclusivity periods. In the past, drug companies were reluctant to develop drugs for “orphan diseases” because the small patient populations made investment in research unprofitable. The same holds true for rare animals and rare animal diseases in the current veterinary market, Wilmot says.

Other potential measures, based partly on public comments FDA received in response to a June 1997 Federal Register request and ideas floated by FDA’s work group, could be more far-reaching and innovative, she says.

These proposals might, for example:
• encourage drug companies to seek drug approvals by offering them financial incentives—for example, tax credits and longer periods of protection from generic competition
• create a fair marketplace by reducing sale and use of unapproved animal drugs. According to the FDA work group, companies that might consider seeking agency approval for drugs for minor use are now reluctant to invest in the process because they cannot always be assured of protection from competition with unapproved drugs. The work group said FDA’s enforcement work needs more resources.

Many of the potential proposals would require congressional action—for example, allocating additional funds for animal drug research grants and drafting new legislation to provide tax credits and prolong the period of drug exclusivity. Other measures, such as revising a regulation, could be accomplished by FDA through rule-making.

Successfully increasing the number of approved drugs for minor species or minor use will likely depend on the adoption of more than one proposal, Wilmot says.

Minor Players

“Minor” may be a misnomer because these animals are prevalent throughout the United States. More than a million of them alone live in zoos and sanctuaries throughout the country. They represent just about every species, too, says Jane Ballentine, public affairs director for the American Zoo and Aquarium Association. “The scope is international,” she says. “You name it, somebody has probably got it.”

All wildlife, though abundant in rural and some urban areas, falls in the minor category, as do farm-raised fish (aquaculture). And many U.S. households—about 13 million in 1996, according to the American Veterinary Medical Association—have pets that fall into the minor species category. These pets number about 80 million, according to the AVMA.

Still, the drug market for minor species is limited because, while there is a wide variety of species, the number of animals within each is small and the number for which veterinary services are sought is even smaller. As a result, many veterinary drug companies don’t seek drug approval because they fear they won’t recoup the cost of developing (Continued on page 23)
Currently, there are no contraceptive medicines approved for any animal, although there are some that delay the mating period.

Among animals treated with therapies not approved for their species are 3-year-old Ndija, of the San Diego Zoo’s Wild Animal Park, shown earlier this year sporting a type of hip-to-toe cast normally used on human children, and the National Zoo’s giant panda, Hsing Hsing. Veterinarians called on pediatric orthopedic surgeons to correct Ndija’s improperly healed broken leg. National Zoo veterinarians treat Hsing Hsing’s arthritis with a drug approved for dogs.

[Photos courtesy of The Zoological Society of San Diego and National Zoological Park]
(Continued from page 21)
and testing the drug once it’s on the market. “It’s just not worth it for the drug company,” FDA’s Wilmot says.

For instance, between October 1996 and September 1997, FDA approved nearly 80 drugs for the seven major species and only one for a minor species.

**Off-Label Use**

The 1994 Animal Medicinal Drug Use Clarification Act helped ease the drug scarcity by giving veterinarians the legal right to use approved human and animal drugs in “extra-label,” or “off-label,” uses. This means that under certain circumstances veterinarians can use approved drugs in other species, for other diseases and conditions, or at different dosage levels from those listed in drug labeling.

For example, Bush has used a penicillin product approved for horses, dogs and cattle to treat a zebra with an infected hoof. Nick Kapustin, D.V.M., senior veterinarian at the Indianapolis Zoo, says human insulin is used to treat diabetes in apes, and he frequently uses an antibiotic approved only for horses “across the board on a variety of species,” including kangaroos, wallabies, birds, and many amphibians.

Avery Bennett, D.V.M., an assistant professor of wildlife and zoological medicine at the University of Florida and a veterinary surgeon, says he uses a children’s cough syrup and a children’s antibiotic in liquid form to treat infections in birds.

And at the National Zoo in Washington-
Veterinarians and biologists monitor o sedated North American moose (top left), giraffe, and South African impala, blindfolded for better relaxation. The development of newer anesthetics for wild animals makes it easier to sedate them safely for research purposes or to relocate them to other areas for repopulation.

(Photos courtesy of Wildlife Pharmaceuticals Inc.)

D.C., veterinarians give the giant panda Hsing Hsing an anti-inflammatory medicine, Rimadyl (carprofen), approved for use in dogs, for Hsing Hsing’s arthritis.

"If we could no longer use drugs off label, I’d quit the business," Bennett says.

While the 1994 act has extended veterinarians’ drug choices, many, including FDA, believe it isn’t the solution to the drug scarcity. Problems that still exist, according to FDA, are:
- inability to get drugs to minor species that don’t have access to veterinary care. Under the law, only veterinarians can administer off-label drugs to minor species.
- inability of veterinarians to prescribe medicated feed “off label.” Off-label use
“There’s hardly any drug on my shelf that’s approved for these animals.”
—Veterinarian Mitchell Bush

of drugs to medicate feed is prohibited under the act. But for many minor species, such as birds and fish, feed offers the most effective route for administering drugs.

- reluctance of some veterinarians to prescribe drugs for off-label use because of liability concerns
- risk of unsafe and ineffective drugs in animals for which the drugs or their uses have not been approved
- risk posed by drug reformulations created as part of off-label use
- increased risk of drug resistance in animals because of repeated use of one drug.

The problems are compounded by an increasing animal population. Because of better veterinary care, zoo animals are living longer, and, as a result, veterinarians are seeing more animals with diseases typical of older age—for example, heart disease, cancer, arthritis, and cataracts.

Also, specialty and exotic pets are becoming more popular. Between 1991 and 1996, an AVMA survey found that the number of households with pets of a minor species—especially ferrets, reptiles and fish—grew 65 percent.

Other reasons FDA and veterinary experts would like to see more applications for minor species’ drugs are:

- to meet the expected increase in consumption of fish and seafood from aquaculture (the production of fish and shellfish for food in a closely managed habitat). In the United States, there are only a handful of approved drugs on the market for food fish. According to the AVMA’s Aquaculture & Seafood Advisory Committee, the lack of drugs for aquatic species is one reason the United States lags behind the rest of the world in aquaculture production.
- to provide contraception to solve overpopulation problems, such as for deer in urban areas. Currently, there are no contraceptive medicines approved for any animal, although there are some that delay the mating period.
- to protect endangered species from extinction. Bill Lance, D.V.M., Ph.D., founder and president of Wildlife Pharmaceuticals in Fort Collins, Colo., says: “If you lost an animal 30 years ago, it was not a problem. Today, it’s a problem. These animals are very valuable. [Veterinarians] can’t afford to use [just] any drug on them.”

Proposal Benefits
Though some of the expected proposals may take years to implement, Wilmot and other veterinary experts believe they are necessary for ensuring public health. With more drug options, they say, veterinarians will find it easier to reduce pain and suffering by treating diseases in animals of minor species. And the approved labeling will provide more complete information on proper dosing and possible side effects.

“It will give veterinarians a handle on what the drug can do and how it works,” Wilmot says.

Veterinarians like Bush at the Conservation Center believe that humans have a role in animal health. “Just as we feed them and clean them, we’re obligated to provide their medical care,” he says. “Effective treatments are not just for zoo animals,” he adds. “We also need them for animals in the free-living situation, where our intervention can help ward off diseases. We’re responsible for these animals’ health care, [as well].”

Paula Kurtzweil is a member of FDA’s public affairs staff.

At the Happy Hollow Park and Zoo in San Jose, Calif., veterinarians insert a trachea tube for administering oxygen and anesthesia to a jaguar with an exposed nerve ending on a broken tooth.

(Photo courtesy of Happy Hollow Park and Zoo)
Dealing With The Depths Of DEPRESSION

by Liora Nordenberg

IMAGINE attending a party with these prominent guests: Abraham Lincoln, Theodore Roosevelt, Robert Schumann, Ludwig von Beethoven, Edgar Allen Poe, Mark Twain, Vincent van Gogh, and Georgia O’Keefe. Maybe Schumann and Beethoven are at the dinner table intently discussing the crescendos in their most recent scores, while Twain sits on a couch telling Poe about the plot of his latest novel. O’Keefe and Van Gogh may be talking about their art, while Roosevelt and Lincoln discuss political endeavors.

But in fact, these historical figures also had a much more personal common experience: Each of them battled the debilitating illness of depression.

It is common for people to speak of how “depressed” they are. However, the occasional sadness everyone feels due to life’s disappointments is very different from the serious illness caused by a brain disorder. Depression profoundly impairs the ability to function in everyday situations by affecting moods, thoughts, behaviors, and physical well-being.

Twenty-seven-year-old Anne (not her real name) has suffered from depression for more than 10 years. “For me it’s feelings of worthlessness,” she explains. “Feeling like I haven’t accomplished the things that I want to or feel I should have and yet I don’t have the energy to do them. It’s feeling disconnected from people in my life, even friends and family who care about me. It’s not wanting to get out of bed some mornings and losing hope that life will ever get better.”

Depression strikes about 17 million American adults each year—more than cancer, AIDS, or coronary heart disease—according to the National Institute of Mental Health (NIMH). An estimated 15 percent of chronic depression cases end in suicide. Women are twice as likely as men to be affected.

Many people simply don’t know what depression is. “A lot of people still believe that depression is a character flaw or caused by bad parenting,” says Mary Rappaport, a spokeswoman for the National Alliance for the Mentally Ill. She explains that depression cannot be overcome by willpower, but requires medical attention.

Fortunately, depression is treatable, says Thomas Laughren, M.D., team leader for psychiatric drug products in FDA’s division of neuropharmacological drug products.

In the past 13 years, the Food and
Drug Administration has approved several new antidepressants, including Wellbutrin (bupropion), Prozac (fluoxetine), Zoloft (sertraline), Paxil (paroxetine), Effexor (venlafaxine), Serzone (nefazodone), and Remeron (mirtazapine).

According to the American Psychiatric Association (APA), 80 to 90 percent of all cases can be treated effectively. However, two-thirds of the people suffering from depression don’t get the help they need, according to NIMH. Many fail to identify their symptoms or attribute them to lack of sleep or a poor diet, the APA says, while others are just too fatigued or ashamed to seek help.

Left untreated, depression can result in years of needless pain for both the depressed person and his or her family. And depression costs the United States an estimated $43 billion a year, due in large part to absenteeism from work, lost productivity, and medical costs, according to the National Depressive and Manic Depressive Association.

Three Types

The three main categories of depression are major depression, dysthymia, and bipolar depression (sometimes referred to as manic depression).

Major depression affects 15 percent of Americans at one point during their lives, according to the U.S. Department of Health and Human Services. Its effects can be so intense that things like eating, sleeping, or just getting out of bed become almost impossible.

Major depression “tends to be a chronic, recurring illness,” Laughren explains. Although an individual episode may be treatable, “the majority of people who meet criteria for major depression end up having additional episodes in their lifetime.”

Major depression can make things like eating, sleeping, or just getting out of bed seem impossible.

Unlike major depression, dysthymia doesn’t strike in episodes, but is instead characterized by milder, persistent symptoms that may last for years. Although it usually doesn’t interfere with everyday tasks, victims rarely feel like they are functioning at their full capacity. According to the National Alliance for the Mentally Ill, almost 10 million Americans may experience dysthymia each year.

Finally, bipolar disorder cycles between episodes of major depression and highs known as mania. Bipolar disorder Artist Edvard Munch's depression is evident in many of his works, including his famous painting "The Scream" (or "The Cry," 1893).

An Herbal Alternative?

St. John the Baptist’s birthday is celebrated on June 24. It is also around this time that the pretty yellow flowers of St. John’s wort, the plant named in his honor, bloom in Germany. The plant may be more than just beautiful. Hypericum, the concentrated extract of flowers and leaves, is thought by some to be effective in treating depression.

While the herb is the most-prescribed antidepressant in Germany, in the United States, St. John’s wort is not an approved drug. Many health food stores in this country sell it as a dietary supplement, but FDA does not allow any antidepressant claims because it has not been proven to be a safe and effective drug for this use. “There’s no particular reason to doubt that it might have biological effects,” says Thomas Laughren, M.D., in FDA’s division of neuropharmaceutical drug products. “Whether or not it is an effective antidepressant remains to be seen.”

The National Institutes of Health is sponsoring studies to determine if St. John’s wort is safe and effective as a treatment for mild to moderate cases of depression. One issue of concern is how the herb interacts with certain drugs, especially antidepressants that affect the brain chemical serotonin.
If Someone You Know Is Depressed ...

According to the National Institute of Mental Health, to help someone recover from depression:

• Encourage the person to make an appointment with a doctor, or make the appointment yourself. You may want to go along for support.
• Encourage the person to stick with the treatment plan, including taking prescribed medicine. Improvement may take several weeks. If no improvement occurs, encourage the person to seek a different treatment rather than giving up.
• Give emotional support by listening carefully and offering hope.
• Invite the person to join you in activities that you know he or she used to enjoy, but keep in mind that expecting too much too soon can lead to feelings of failure.
• Do not accuse the person of faking illness or expect them to “snap out of it.”
• Take comments about suicide seriously, and seek professional advice.

is much less common than the other types, afflicting about 1 percent of the U.S. population. Symptoms of mania include irritability, an abnormally elevated mood with a decreased need for sleep, an exaggerated belief in one’s own ability, excessive talking, and impulsive and often dangerous behavior.

Genes and Environment
Study after study suggests biochemical and genetic links to depression. A considerable amount of evidence supports the view that depressed people have imbalances in the brain’s neurotransmitters, the chemicals that allow communication between nerve cells. Serotonin and norepinephrine are two neurotransmitters whose low levels are thought to play an especially important role. The fact that women have naturally lower serotonin levels than men may contribute to women’s greater tendency to depression.

Family histories show a recurrence of depression from generation to generation. Studies of identical twins confirm that depression and genes are related, finding that if one twin of an identical pair suffers from depression, the other has a 70 percent chance of developing the disease. For fraternal twins or siblings, the rate is just 25 percent.

Environmental factors, however, may also play a role in depression. When combined with a biochemical or genetic predisposition, life stressors (such as relationship problems, financial difficulties, death of a loved one, or medical illness) may cause the disease to manifest itself.

John (not his real name), 25, was diagnosed with depression for the first time last year when he and his girlfriend ended their three-year relationship. “I couldn’t do anything because I was totally absorbed with the whole break-up issue,” he says. “It was impossible for me to sleep, and I would wake up at 3 or 4 in the morning and literally shake. And when it was time to wake up, I just couldn’t get out of bed.”

In addition, substance abuse and side effects from prescription medication may also lead to a depressive episode. And research shows that people battling serious medical conditions are especially prone to depression. According to the U.S. Department of Health and Human Services, those who have had a heart attack, for example, have a 40 percent chance of being depressed.

Seasonal affective disorder, often called “SAD,” is a striking example of an environmental factor playing a major role in depression. SAD usually starts in late fall, with the decrease in daylight hours and ends in spring when the days get longer.

The symptoms of SAD, which include energy loss, increased anxiety, oversleeping, and overeating, may result from a change in the balance of brain chemicals associated with decreased sunlight. The exact reason for the association between light and mood is unknown, but research suggests a connection with the sleep cycle. Several studies have suggested that light therapy, which involves daily exposure to bright fluorescent light, may be an effective treatment for SAD.

Diagnosing the Disease
Medical professionals generally base a diagnosis of depressive disorder on the presence of certain symptoms listed in the American Psychiatric Association’s Diagnostic and Statistical Manual. The DSM (presently in the fourth edition) lists the following symptoms for depression:

“...
In someone who is predisposed to depression, life stressors such as relationship problems or financial difficulties may cause the disease to manifest itself.

- depressed mood
- loss of interest or pleasure in almost all activities
- changes in appetite or weight
- disturbed sleep
- slowed or restless movements
- fatigue, loss of energy
- feelings of worthlessness or excessive guilt
- trouble in thinking, concentrating, or making decisions
- recurrent thoughts of death or suicide.

The diagnosis depends on the number, severity and duration of these symptoms.

Even with this list of symptoms, diagnosing depression is not simple. According to the National Alliance for the Mentally Ill, it takes an average of eight years from the onset of depression to get a proper diagnosis.

In making a diagnosis, a health professional should also consider the patient's medical history, the findings of a complete physical exam, and laboratory tests to rule out the possibility of depressive symptoms resulting from another medical problem.

The symptoms of the depressive part of bipolar disorder are the same as those expressed in major (unipolar) depression. Because of the similarities in symptoms and the fact that manic episodes usually don’t appear until the mid-20s, some people with bipolar disorder may mistakenly be diagnosed with unipolar depression. This may lead to improper treatment because antidepressants carry the risk of triggering a manic episode. (For information about treating bipolar disorder, see “Evening Out the Ups and Downs of Manic-Depressive Illness” in the June 1996 FDA Consumer.)

Antidepressant Drugs

One major approach for treating depression is the use of antidepressant medications. The older antidepressants include tricyclic antidepressants such as Tofranil (imipramine) and monoamine oxidase inhibitors such as Nardil (phenelzine). Antidepressants approved more recently include the selective serotonin reuptake inhibitors Prozac, Paxil and Zoloft, and the other newer antidepressants Wellbutrin, Effexor, Serzone, and Remeron.

The effects of antidepressants on the brain are not fully understood, but there is substantial evidence that they somehow restore the brain’s chemical balance. These medications usually can control depressive symptoms in four to eight weeks, but many patients remain on antidepressants for six months to a year following a major depressive episode to avoid relapse.

Different drugs work for different people, and it is difficult to predict which people will respond to which drug or who will experience side effects. So it may take more than one try to find the appropriate medication.

Since the mid-1950s, tricyclic antidepressants have been the standard against which other antidepressants have been measured. Monoamine oxidase inhibitors were discovered around the same time as tricyclic antidepressants, but were prescribed less because, if mixed with certain foods or medications, the drugs sometimes resulted in a fatal rise in blood pressure.

Laughren describes Prozac as the "first of a new type of more selective antidepressants.” The older antidepressants had unpleasant and sometimes dangerous side effects, such as insomnia, weight gain, blurred vision, sexual impairment, heart palpitations, dry mouth, and constipation. Prozac, other selective

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Depression is one of the most common medical problems in the United States.

(Source: Scott-Levin, Newtown, Pa.)
Alternative. Like antidepressants, ECT is believed to affect the chemical balance of the brain's neurotransmitters.

Before ECT, the patient is given anesthetics and a muscle relaxant to prevent injury or pain. Then electrodes are placed on the person's head, and a small amount of electricity is applied. This procedure is usually done three times a week until the patient improves. Some patients may experience a temporary loss of short-term memory.

Talking It Out

For severe depressive episodes, medications are often the first step because of the relatively quick relief they can bring to physical symptoms. For the long term, however, psychotherapy may be needed to address certain aspects of the illness that drugs cannot. "Although the biological features of depression may respond better to drugs," Laughren says, "people may need to learn how to interact with their environment after the biological part of the depression is controlled."

"I wanted to talk things out and get better in that way," John says. "And even after the first couple of times I saw my therapist, I could do a little bit more. Talking with her gave me some reality that how I was feeling wasn't so abnormal, so unusual, or so terrible."

Anne explains, "It's just comforting sometimes to share the little day-to-day happenings in my life with someone who doesn't get to see them first-hand."

Some find support groups to be invaluable in helping them cope with their depression. "It's through talking with others with similar experiences," says Mary Rappaport, "that you can better understand what you're going through."

Changes in lifestyle are also important in the management of depression. Exercise, even in moderate doses, seems to enhance energy and reduce tension. Some research suggests that a rush of the hormone norepinephrine following exercise helps the brain deal with stress that often leads to depression and anxiety.

A similar effect may be obtained through meditation, yoga, and certain diets.

A Bright Future

Like many others who have not had to face depression themselves, John's friends lacked knowledge about the disease. "I think the whole thing really affected my relationships with people," he says. "I was pretty much a jerk all of the time. I didn't want to talk to anybody. I just wanted them to leave me alone."

With the growing awareness of the seriousness of the disorder and the biological causes, the understanding and support of family and friends may be easier to come by. "The future looks very bright for individuals who in the past have often had to suffer alone," says Rappaport. "More and more people are coming out, which encourages people to talk about it." Among those who have "come out" recently to publicly discuss their personal bouts with depression are comedian Drew Carey and "60 Minutes" correspondent Mike Wallace.

Experts say that no one, young or old, has to accept feelings of depression as a necessary part of life. The National Depressive and Manic Depressive Association and other organizations offer medical information and referrals. By trying different options for facing their personal challenges, Anne and others have learned what treatments help them most. "All in all," Anne says, "I think my ability to weather the ups and downs of life has gotten better."

Researchers continue to make great strides in understanding and treating depression. For example, scientists are beginning to learn more about the chromosomes where affective disorder genes appear to be located. "While there is a long way to go in coming up with even more effective drugs," Laughren says, "there's much ongoing research and reason for optimism."

Liora Nordenberg is a freelance writer in Harrisburg, Pa.
For Jeri Goldstein everything was a blur. Without her contact lenses she couldn’t distinguish people, the scenes on television, the stars at night, and, generally, the world at large. Then, in March 1998, the 49-year-old California resident had eye surgery, and all that changed.

“After wearing contact lenses for 35 years, you can’t imagine the freedom I felt,” says Goldstein.

Goldstein underwent refractive eye surgery, an elective procedure intended to correct common eye disorders, known as refractive errors, such as myopia (nearsightedness), hyperopia (farsightedness), and astigmatism (distorted vision). Although there are several types of surgical techniques being performed today to correct refractive errors, laser refractive correction is fast becoming the most technologically advanced method available, according to the American Academy of Ophthalmology in San Francisco. Doctors say it allows for an unparalleled degree of precision and predictability.

“Laser surgery is the most exciting advancement in ophthalmology,” says James J. Salz, M.D., clinical professor of ophthalmology at the University of Southern California in Los Angeles and the doctor who performed Goldstein’s surgery. But surprisingly, he says, despite its sudden popularity, “only 20 percent of ophthalmologists in the United States today are trained in its operation.”

The Food and Drug Administration first approved the excimer laser in October 1995 for correcting mild to moderate nearsightedness. With that approval, the agency also restricted use of the laser to practitioners trained both in laser refractive surgery and in the calibration and operation of the laser. Currently, the excimer laser is only approved for use in a procedure called photorefractive keratectomy (PRK).

**Precision Surgery**

PRK is an outpatient procedure generally performed with local anesthetic eye drops. This type of refractive surgery gently reshapes the cornea by removing microscopic amounts of tissue from the outer surface with a cool, computer-controlled ultraviolet beam of light. The beam is so precise it can cut notches in a strand of human hair without breaking it, and each pulse can remove 39 millionths of an inch of tissue in 12 billionths of a second. The procedure itself takes only a few minutes, and patients are typically back to daily routines in one to three days.

Before the procedure begins, the patient’s eye is measured to determine the degree of visual problem, and a map of the eye’s surface is constructed. The required corneal change is calculated based on this information, and then entered into the laser’s computer.

Since 1995, two laser systems have been approved by FDA to treat mild to moderate nearsightedness and mild to moderate astigmatism with PRK: The SVX Apex excimer laser, manufactured by Summit Technology of Waltham, Mass., and the VISX excimer laser, manufactured by VISX Inc., of Santa Clara, Calif. FDA also has approved the VISX system to treat high myopia.

According to FDA’s Center for Devices and Radiological Health, clinical studies showed that about 5 percent of patients continued to always need glasses following PRK for distance, and up to 15 percent needed glasses occasionally, such as when driving. In addition, many patients experienced mild corneal haze following surgery, which is part of the normal healing process. The haze appeared to have little or no effect on final vision, and could only be seen by a doctor with a microscope. Some patients experienced glare and halos around lights. These conditions, however, diminished or disappeared in most patients in six months. For about 5 percent of patients, however, best-corrected vision without corrective lenses was slightly worse after surgery than before.

In view of these findings, FDA and the Federal Trade Commission (which oversees advertising) issued a letter to the eye-care community in May 1996 warning that unrealistic advertising claims, such as “throw away your eyeglasses,” and unsubstantiated claims about success rates could be misleading to consumers.

**What About LASIK?**

A more complex procedure than PRK is laser in-situ keratomileusis, or LASIK. Performed for all degrees of nearsightedness, it is still in clinical trials and not yet approved by FDA. The surgeon uses a knife called a microkeratome to cut a flap of corneal tissue, removes the targeted tissue beneath it with the laser, and then replaces the flap.

“With LASIK, the skill of the surgeon is important because he’ll be making an incision,” says Stephen Crawford, O.D., an optometrist practicing in Virginia. “compared to the PRK method where the machine does more of the work.” Crawford urges people to find qualified, experienced doctors to perform this surgery. “You’ll want someone who’s done a number of LASIK procedures since this is a surgeon-dependent operation,” he said.

According to Ken Taylor, O.D., vice president of Arthur D. Little, Inc., a technology and management consultant
What Are the Risks of Laser Surgery?

The risks outlined below apply to both PRK and LASIK procedures. Chances of having a serious vision-threatening complication are minimal, and there have been no reported cases of blindness following either PRK or LASIK, says James Salz, M.D., clinical professor of ophthalmology. However, FDA is aware of a few instances of severe eye injury requiring corneal transplant.

Infection and delayed healing: There is about a 0.1 percent chance of the cornea becoming infected after PRK, and a somewhat smaller chance after LASIK. Generally, this means added discomfort and a delay in healing, with no long-term effects within a period of four years.

Undercorrection/Overcorrection: It is not possible to predict perfectly how your eye will respond to laser surgery. As a result, you may still need corrective lenses after the procedure to obtain good vision. In some cases, a second procedure can be done to improve the result.

Decrease in Best-Corrected Vision: After refractive surgery, some patients find that their best obtainable vision with corrective lenses is worse than it was before the surgery. This can occur as a result of irregular tissue removal or the development of corneal haze.

Excessive Corneal Haze: Corneal haze occurs as part of the normal healing process after PRK. In most cases, it has little or no effect on the final vision and can only be seen by an eye doctor with a microscope. However, there are some cases of excessive haze that interferes with vision. As with undercorrections, this can often be dealt with by means of an additional laser treatment. The risk of significant haze is much less with LASIK than with PRK.

Regression: In some patients the effect of refractive surgery is gradually lost over several months. This is like an undercorrection, and a re-treatment is often feasible.

Halo Effect: The halo effect is an optical effect that is noticed in dim light. As the pupil enlarges, a second faded image is produced by the untreated peripheral cornea. For some patients who have undergone PRK or LASIK, this effect can interfere with night driving.

Flap Damage or Loss (LASIK only): Instead of creating a hinged flap of tissue on the central cornea, the entire flap could come off. If this were to occur it could be replaced after the laser treatment. However, there is a risk that the flap could be damaged or lost.

Distorted Flap (LASIK only): Irregular healing of the corneal flap could create a distorted corneal shape, resulting in a decrease of best-corrected vision.

Incomplete Procedure: Equipment malfunction may require the procedure to be stopped before completion. This is a more significant factor in LASIK, with its higher degree of complexity, than in PRK.

Problems with a Perfect Procedure: Even when everything goes perfectly, there are effects that might cause some dissatisfaction. Older patients should be aware that they can’t have both good distance vision and good near vision in the same eye without corrective lenses. Some myopic patients rely on their myopia (by taking off their glasses, or by wearing a weaker prescription) to allow them to read. Such a patient may need reading glasses after the myopia is surgically corrected. Another consideration is the delay between eye treatments. If one eye is being done at a time, then the eyes may not work well together during the time between treatments. If a contact lens is not tolerated on the unoperated eye, work and driving may be awkward or impossible until the second eye has been treated.

—C.L.

Advantages of LASIK

Some doctors believe that LASIK is a suitable procedure for correcting the most severe refractive errors. They also say that there is generally a faster recovery time after LASIK than after PRK. In addition, LASIK patients can see well enough to drive immediately and have good vision within a week.

After studying the options, Goldstein first decided on the LASIK procedure, but was surprised to learn that her doctor advised against it.

"Initially, I wanted the quick recovery that LASIK offers," Goldstein says, "but the bottom line was, which surgery will give me the best results, and after considering everything, eventually we agreed on PRK."

James Salz is currently involved in an FDA-sanctioned clinical trial at Cedars-Sinai Medical Center in Los Angeles, which is now studying the laser system specifically for farsightedness (hyperopia) with astigmatism. Although routinely performing laser eye surgery, he still encourages a small percentage of his low to moderately nearsighted patients to undergo radial keratotomy, or RK, an earlier refractive correction procedure that does not require the excimer laser.

With RK, incisions are made in a "radial" pattern along the outer portion of the cornea using a hand-held blade. These incisions are designed to help flatten the curvature of the cornea, thereby allowing light rays entering the eye to properly focus on the retina. The number and length of the incisions determines the degree of correction attained.

"Typically, this is still a practiced procedure for select people with very small corrections of myopia," Salz says. Conversely, Crawford says that al-
In order to decide whether laser vision correction is a viable option for you, it is important to first understand how the eye works and why people need glasses or contact lenses to see well.

The eye works much like a camera; its primary function is to focus light. For the eye to see, light rays must be bent or “refracted” to meet at a single point through the cornea, the clear window at the front of the eye that provides most of the focusing power. Light then travels through the lens, where it is fine-tuned to focus properly on the retina, the nerve layer that lines the back of the eye and connects to the brain. The retina acts like the film in a camera, and clear vision is achieved only if light from an object is precisely focused onto it. If the light focuses either in front of or behind the retina, the image you see is blurred. A refractive error means that the shape of eye structures does not properly bend the light for focusing.

Having 20/20 vision means seeing at 20 feet what a normal person sees at 20 feet. However, if vision is measured at 20/40, it means a person has to walk up to 20 feet to see the same size letter that someone with 20/20 vision could see at 40 feet. And so on. People whose best-corrected visual acuity (what they see using glasses or contact lenses) is less than 20/200 in the better eye are considered legally blind, even though they still have enough vision to get around. Prior to laser surgery, Jeri Goldstein’s visual acuity without her contact lenses was measured at 20/400 in her right eye and 20/200 in the left eye. Following surgery, her eyesight without contacts stands at 20/25 and 20/20, respectively.

People who are slow healers or who have ongoing medical conditions [such as glaucoma or diabetes] are not good candidates for laser surgery,” she says. “That’s why it’s so important for patients to undergo a thorough examination with their doctor.”

Poor candidates for this surgery also include those with uncontrolled vascular disease, autoimmune disease, or people with certain eye diseases involving the cornea or retina. Pregnant women should not have refractive surgery of any kind because the refraction of the eye may change during pregnancy.

Looking Ahead

At present, a number of other lasers for eye surgery are currently being tested in FDA-sanctioned studies to determine their safety and effectiveness. Investigational Device Exemptions (IDEs) filed with FDA allow for clinical studies involving the excimer laser and the correction of farsightedness. The IDE process is designed to investigate
Frequently Asked Questions About Laser Eye Surgery

Is it painful?
There is little if any discomfort during surgery because the cornea and eye are anesthetized by drops. Some patients experience a "scratchy feeling." After the anesthetic wears off, the amount of discomfort varies with each individual, but any irritation is minor and usually disappears within a few hours. You may be sensitive to light for a few days.

When will I be able to return to work?
Most people can return to work one to three days following surgery, but a rule of thumb is to wait until you feel up to it. Most return to normal activities as soon as the day after surgery.

What are the side effects and risks?
The most common side effects are a halo effect and some glare at night around lights. (See “What Are the Risks of Laser Surgery?”)

How long does the treatment take?
Laser treatment itself takes only about 15 to 40 seconds, based on the degree of correction necessary. Recovery is minimal, and usually the patient is able to be driven home after about 30 minutes. Typically, you will notice improved sight in 3 to 5 days following treatment.

Is the treatment permanent?
According to the results of the U.S. clinical trials and results reported internationally, the treatment appears to be permanent. As people age, however, their eyes change and re-treatment may be necessary.

Are there any activity restrictions following surgery?
Following surgery, do not rub your eyes. Other than that, patients can do whatever they feel up to as long as they follow their doctors’ instructions.

What if I move my head during surgery?
This is the number one question that patients ask when undergoing laser treatment. The surgeon is skilled in the technique of removing his foot from the pedal that controls the ultraviolet beam as soon as a patient moves his or her head. This allows him to realign the beam with the corneal “target” and proceed with the surgery.

Are You a Candidate for Laser Eye Surgery?
You may be a good candidate for laser eye surgery if you:
• are at least 21 years of age for a Summit laser or 18 years of age for a VISX laser, since the eyes are still growing to this point
• have healthy eyes that are free from retinal problems, corneal scars, and any eye disease (refractive errors are considered eye disorders, not diseases)
• have mild to moderate myopia (nearsightedness) within the range of treatment (see your doctor to determine your range)
• have a way to pay for the treatment since laser procedures are costly and probably not covered by health insurance policies
• are fully informed about the risks and benefits of laser surgery compared with other available treatments.

—C.L.

Are You a Candidate for Laser Eye Surgery?

Carol Lewis is a writer on detail with FDA's public affairs staff.
Calling All Kids

The FDA Kids’ Home Page is up and running. There’s a food safety quiz, a medicine word find, tips on pet care, and a tobacco quiz. There’s even a skeleton in our closet!

The Kids’ page is geared toward 9- to 12-year-olds. But teens will find the information a good starting point for research, and the home page includes a link to the “Teen Scene,” which has teen-focused articles from FDA Consumer.

For adults, there’s a Parents’ Corner with links to FDA Consumer articles about health and nutrition for children. Check it out. The address is www.fda.gov/oc/opacom/kids/. (See inside back cover for a sneak preview.)

Web Magazine

Looking for an FDA Consumer article from a few months ago? Several years ago? Try FDA’s Website.

You can find all issues of the magazine on the Web as far back as July-August 1995 in HTML format with selected graphics. In addition, some earlier issues that originally were put on the agency’s bulletin board system are on the Website, although most of these are only in text format.

The FDA Consumer Web address is www.fda.gov/opacom/morechoices/fdaconsumer.html.

In many cases, the FDA Consumer articles on the Website are updated as new information becomes available. Therefore, an article may not be exactly the same as the original printed version.

Very Handy

What are the steps involved to get a new drug approved? How does FDA monitor a drug’s performance once it’s been approved? The Center for Drug Evaluation and Research’s Handbook (www.fda.gov/cder/handbook/index.htm) has answers to these and other questions about the center’s processes and activities.

Fraud Finders

Like many other forms of information or commerce, the Internet demands that the buyer beware.

If you come across a product offer on the Internet that you suspect is fraudulent, let FDA know:
• by e-mail at otcfraud@cdrf.fda.gov
• by calling 1-301-594-0070
• by writing to: Food and Drug Administration, Center for Drug Evaluation and Research, HFD-314, 7520 Standish Place, Rockville, MD 20855.

Close to Home: How to Find a Certified Mammography Facility Near You

The Mammography Quality Standards Act of 1992 requires that all mammography facilities in the United States meet certain stringent quality standards, be accredited by an FDA-approved accreditation body, and be inspected by specially trained inspectors. To find a convenient, certified facility, you can search FDA’s list (www.fda.gov/cdrh/faclist.html) by state or by zip code. The list provides the facility’s name, address, and phone number.

Patient Participation

For many people, a serious illness prompts them to become experts in their particular disease. They study the medical literature, discuss treatment regimens with health professionals, and advocate for research funds. FDA recognizes this and believes that some of these ‘everyday people’ can make an important contribution to the agency’s advisory committees.

FDA advisory committees provide independent expert advice, helping the agency make sound decisions about new drugs, biologics, medical devices, and other public health issues. Committee members are scientific experts, such as physician-researchers and statisticians, as well as representatives of the public, including patients.

If you’d like to know more about the value of patient participation in FDA’s decision-making process, or if you think you might be a candidate for committee membership, visit www.fda.gov/oashi/patrep/patbroc.html.
California Man Imprisoned After fX Drinks Injure Partygoers

by Tamar Nordenberg

A California chiropractor was sentenced to three months in prison and three months in a halfway house and fined $2,000 for illegally distributing tainted liquids that sickened more than 100 partygoers at a New Year’s Eve 1996 “rave” party in Los Angeles.

Thirty-year-old Daniel Bricker was sentenced Feb. 2, 1998, in the U.S. District Court for the Southern District of California after pleading guilty to misbranding a food or drug product. The product contained a chemical related to the dangerous and sometimes lethal substance gammahydroxybutyrate (GHB).

Police and firefighters were called to the party when revelers began complaining of symptoms ranging from dizziness and nausea to difficulty breathing. The officials dispersed the crowd, estimated to exceed 10,000 people, and seized about 10,000 vials of the brew that had been distributed free at the party to promote the product.

On New Year’s Day, investigators from FDA’s Los Angeles district office interviewed some of the more than 30 people who had been taken to area hospitals.

Also that day, the agency warned consumers not to ingest the products blamed for the injuries, which were labeled “Cherry fX Bombs,” “Lemon fX Drops,” and “Orange fX Rush.”

On Jan. 2 and 3, 1997, FDA sent a number of vials of the liquid to the agency’s laboratories in Cincinnati, Seattle, and Washington, D.C. The laboratories determined that they contained an industrial solvent known to target the central nervous system if swallowed.

On Jan. 28, special agents with FDA’s Office of Criminal Investigations searched Bricker’s business, Bricker Labs of Escondido, Calif., and gathered evidence that helped link Bricker to the crime, including vials, stoppers, and packaging related to the product.

On the same day, during a search of Bricker’s home in Valley Center, Calif., special agents found documents containing results of laboratory tests on the products, which showed that Bricker knew when he distributed the fX products that they contained the harmful industrial chemical.

According to one special agent with FDA’s Office of Criminal Investigations, Bricker substituted the industrial chemical for an ingredient from the kava-kava plant that he planned to use because he couldn’t get the plant substance in time for the party.

“He knew in advance that these people would get sick from it,” the investigator says, “and he distributed it anyway in the hopes of making some money. It was an extremely dangerous thing to do.”

Bricker pleaded guilty in November 1997 to the misbranding charge. He began serving his sentence near the end of March, and at press time was expected to go to the halfway house in July.

Bricker’s accomplice, Michael Moffett, whose company mislabeled the industrial solvent as kava-kava extract, pleaded guilty in October 1997 to a misbranding charge. He cooperated with FDA’s Office of Criminal Investigations and received a $2,000 fine and a two-year probation.

Tamar Nordenberg is a staff writer for FDA Consumer.
Food Seized at Warehouse Overrun with Rodents

More than 200 kinds of Oriental food products with a retail value of $280,000 were seized last January at a New York City warehouse because of rodent contamination.

At FDA’s request, the U.S. District Court for the Eastern District of New York issued a seizure warrant Jan. 26, 1998, for the food—about 5,488 cases of imported rice cakes, candies, dried vegetables, and other assorted products—after the food's owner and distributor, Yick Cheung Corp., doing business as Goodworld Trading Co., refused to rid the Brooklyn warehouse of rodents.

“A seizure can give substantial motivation to those responsible for cleaning up their act,” said Lillian Aveta, a compliance officer in FDA’s New York district office. “They want to get their facility back into business.”

Goodworld’s poor sanitary practices were first identified in February 1995 when, as part of a crackdown on misbranded products, New York state authorities inspected the storage facility. In addition to sanitation violations, state chemists detected staphylococcal bacteria in mushrooms Goodworld had for sale. The state seized more than 1,000 cases of mushrooms and cited Goodworld for sanitation violations.

Subsequent inspections later that year found continuing sanitation problems and resulted in further seizures and fines of more than $1,500.

But the violations continued. As part of a routine schedule, FDA inspected Goodworld in October. In repeated visits through December, FDA investigators Cornelius Gallagher, Peter Caparelli, Kwong Lee, and Donald Ullstrom observed a dog roaming freely within the food storage area, fresh rodent pellets “too numerous to count” throughout the walk-in refrigerator, cases of food that looked like they had been gnawed, and gnawed holes through the base of the north and west walls of the warehouse. Food samples collected and later analyzed by FDA indicated rodent contamination.

Company president Wing Chan told FDA that garbage was picked up once weekly and that the company acted as its own exterminator, using a BB gun and placing unenclosed rodenticide on the floor throughout the warehouse.

On Nov. 7, FDA investigators, along with FDA chemist Nariman Ayyad, met New York state inspector Sonia Morales at the warehouse. New York state is under contract with FDA to assist with some inspections. Morales placed all food lots sampled by FDA under state embargo to ensure that the food items in question would not be distributed while the seizure was being processed.

At a Dec. 3, follow-up inspection, agency investigators noted that previously documented building deficiencies had not been corrected. Company president Chan told FDA that he rented the warehouse from the owner who, he said, was looking to sell the property. He also said that if the property was not sold within six months, he “may make the building corrections” himself. Until then, he said, he intended to leave the building deficiencies “as is” for financial reasons, Aveta said.

The agency can order a warrant for mass seizure based on six violative lots of food, Aveta said. She added that Goodworld was in violation with a total of nine lots of food.

The seizure on Jan. 26, 1998, only affected products in soft packaging because other types of containers used had not been found to be contaminated.

At press time, the company was allowed to distribute only products packaged in rigid containers, such as metal and hard plastic, as well as in soft packages received after the seizure date.

—Carol Lewis
Summaries of Court Actions are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act and 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.

Summaries of Court Actions are prepared by Food and Drug Division, Office of the General Counsel, HHS.

**SEIZURE ACTIONS**

**Food/Contamination, Spoilage, Insanitary Handling**

PRODUCT: **Bananq Chips**, at Chicago, Ill. (N.D. Ill.); Civil Action No. 96-C-6627.
CHARGED 10-10-96: While held for sale after shipment in interstate commerce at Trung Viet Co., Inc., in Chicago, Ill., the articles were adulterated in that they had been shipped and held under insanitary conditions whereby they might have been rendered injurious to health—402(a)(4). The articles were misbranded in that their labeling represented and suggested that the articles were grown and packed in Taiwan—403(a)(1).
DISPOSITION: The articles were reconditioned. (F.D.C. No. 67156; S. No. 96-759-222; S.J. No. 1)

PRODUCT: **Mushrooms**, at New Orleans, La. (E.D. La.); Civil Action No. 93-3623.
CHARGED 11-3-93: While held for sale after shipment in interstate commerce at New Orleans Cold Storage, in New Orleans, La., the articles had been shipped and held under insanitary conditions whereby they might have been rendered injurious to health—402(a)(4). The articles were misbranded in that their labeling represented and suggested that the articles were grown and packed in Taiwan—403(a)(1).
DISPOSITION: The articles were destroyed. (F.D.C. No. 66771; S. No. 93-690-604; S.J. No. 2)

PRODUCT: **Porcelain Dinnerware**, at San Leandro, Calif. (N.D. Calif.); Civil Action No. 96-2688.
CHARGED 7-29-96: While held for sale after shipment in interstate commerce at West Pacific Trading Co., in San Leandro, Calif., the articles were adulterated in that they contained lead, an unsafe food additive—402(a)(2)(C).
DISPOSITION: The articles were destroyed. (F.D.C. No. 67137; S. No. 96-753-709; S.J. No. 3)

PRODUCT: **Raisins**, at Porterville, Calif. (E.D. Calif.); Civil Action No. CV-F-94-5724-REC.
CHARGED 7-18-94: While held for sale after shipment in interstate commerce at Stephen Pavich & Sons, in Porterville, Calif., the articles were adulterated in that they consisted in part of decomposed shrimp, rat or mouse hair, feather fragments, and cat or dog hair—402(a)(3).
DISPOSITION: The articles were reconditioned. (F.D.C. No. 67001; S. No. 94-705-726; S.J. No. 4)

PRODUCT: **Shrimp**, at Orlando, Fla. (M.D. Fla.); Civil Action No. 96-35-CV-ORL-22.
CHARGED 1-10-96: While held for sale after shipment in interstate commerce at U.S. Cold Storage, in Orlando, Fla., the articles were adulterated in that they consisted in part of decomposed shrimp—402(a)(3).
DISPOSITION: The articles were destroyed. (F.D.C. No. 67115; S. No. 96-711-905; S.J. No. 5)

**Drugs/Human Use**

PRODUCT: **Articles of Drug**, at Jackson, Miss. (S.D. Miss.); Civil Action No. 3:97CV312WS.
CHARGED 5-11-97: While held for sale after shipment in interstate commerce at Catherx Pharmaceuticals, Inc., in Jackson, Miss., the articles of drug were adulterated in that the methods used in, and the facilities and controls used for, their manufacture, processing, packing, and holding did not conform to and were not operated and administered in conformity with current good manufacturing practice requirements of the Act—501(a)(2)(B).
DISPOSITION: The articles of drug were destroyed. (F.D.C. No. 67180; S. No. 97-964-027; S.J. No. 6)

PRODUCT: **Articles of Drug**, at Madison, Miss. (S.D. Miss.); Civil Action No. 3:97CV313LN.
CHARGED 5-11-97: While held for sale after shipment in interstate commerce at Cypress Pharmaceutical, Inc., in Madison, Miss., the articles of drug were adulterated in that the methods used in, and the facilities and controls used for, their manufacture, processing, packing, and holding did not conform to and were not operated and administered in conformity with current good manufacturing practice requirements of the Act—501(a)(2)(B).
DISPOSITION: The articles of drug were destroyed. (F.D.C. No. 67181; S. No. 97-964-028; S.J. No. 7)

CHARGED 7-11-97: While held for sale after shipment in interstate commerce at Health Better Living, Inc., in Naples, Fla., the articles of drug were misbranded within the meaning of 352(f)(1); and they were unapproved new drugs within the meaning of 355, and thus may not be introduced into interstate commerce.
DISPOSITION: The articles of drug were destroyed. (F.D.C. No. 67197; S. No. 97-683-131; S.J. No. 8)

**INJUNCTION ACTIONS**

CHARGED 6-18-96: While held for sale after shipment in interstate commerce at Loran Medical Systems, Inc., in Santa Barbara, Calif., the Cell product was a new drug within the meaning of 301(p), and was neither approved under 501(a) nor exempt from such approval provisions under 505(i) and was in violation of 301(a).
DISPOSITION: The court granted the government's motion for summary judgment and entered a permanent injunction against the defendants' importation, use and sale of the Cell product. (Inj. No. 1400; S.J. No. 9)
It’s time for some fun at the new FDA Kids’ Home Page. Meet FDA’s favorite skeleton, Yorick. Find everything hidden in our medicine cabinet. See how much you know about food safety, tobacco and pets. So surf on in for fun and learning. Go to www.fda.gov and click on KIDS.