**NEW DRUGS**

**Plant-Derived Estrogen**

Barr Pharmaceuticals has announced that it has received U.S. Food and Drug Administration (FDA) approval for its New Drug Application (NDA) for Enjuv™ 0.625- and 1.25-mg tablets. This synthetic conjugated estrogen product is indicated for the treatment of moderate-to-severe vasomotor symptoms associated with menopause.

(Source: FDA/Barr, May 11, 2004.)

**NEW INDICATION**

**Etanercept for Psoriasis**

The FDA has approved the biological drug etanercept (Enbrel®) to treat chronic, moderate-to-severe plaque psoriasis in adults. The drug, marketed by Amgen and Wyeth Pharmaceuticals, is already approved for the treatment of psoriatic arthritis.

Psoriasis is an incurable skin disease that occurs when faulty signals in the immune system cause skin cells to regenerate too quickly. Psoriatic arthritis is a degenerative disease of the joints and connective tissues associated with psoriasis.

Biological products, engineered from proteins produced by living cells, have caused few side effects in short-term studies, but their long-term safety for psoriasis patients is not yet known.

(Source: National Psoriasis Foundation, April 30, 2004.)

**DRUG NEWS**

**Early Rasagiline for PD**

Starting rasagiline (Teva) earlier, rather than later, as a treatment for Parkinson’s disease (PD) may help to slow functional decline.

Researchers have suggested that rasagiline might slow the progression of PD through several possible mechanisms. For example, it protects the neurons against hypoxic injury, oxidative stress, and cerebral trauma, among other things, and may promote better functioning of surviving dopaminergic neurons.

(Source: Arch Neurol 2004;61:561–566.)

**More Beta Blockers, Please**

More high-risk surgical patients probably need beta blockers, say researchers from Baystate Medical Center in Springfield, Massachusetts. Upon reviewing the records of 72 patients who developed postoperative myocardial infarction (MI), they found that 70 (97%) could have been identified as being at increased risk for cardiac complications and 58 (81%) were ideal perioperative candidates for beta blockers. However, only 30 patients actually received beta blockers before having the MI. Beta blockers might have prevented as many as 40% of cases of postoperative MI, the researchers say. Most of the patients were undergoing vascular, general, or orthopedic procedures.

The median interval between surgery and postoperative MI was two days. Four of the ideal candidates who took beta blockers before the onset of MI died; nine patients who did not receive a beta blocker died before experiencing an MI.

For almost two decades, it has been known that beta-adrenergic blockade can reduce the incidence of myocardial ischemia associated with the stress of surgery. One reason why perioperative beta blockers are not more widely used is that the doctors targeted for education were internists and cardiologists who had previous experience with the drugs. In the case of noncardiac surgery, however, surgeons might be less comfortable prescribing them. The researchers suggest that novel strategies are required, such as co-management of surgical patients by surgeons and internists.

For more about the use of perioperative beta blockers, see the continuing education article on page 380.

(Source: Arch Intern Med 2004;164:762–766.)

**Carnitine or Testosterone for Older Men?**

Carnitine compares favorably with testosterone in the treatment of sexual dysfunction, depression, and fatigue in older men, say researchers from Italy.

For six months, one group of patients was given testosterone undecanoate 160 mg/day; a second group received propionyl-L-carnitine 2 g/day plus acetyl-L-carnitine 2 g/day; and a third group was given placebo. Testosterone and carnitines both significantly improved erectile function, depression, and fatigue.

Testosterone significantly increased prostate volume and free and total testosterone levels and significantly lowered serum luteinizing hormone, whereas carnitines did not. Both testosterone and carnitines were effective for only as long as they were administered. Stopping them reversed all values to baseline levels, except for prostate volume in the first group; these levels remained significantly greater than baseline six months after testosterone was stopped.

Several aging mechanisms share an increase in reactive oxygen species, membrane damage, and cell death. Carnitines act against diseases typical of aging, such as intermittent claudication and Alzheimer’s disease, because of their antioxidant effects.

The researchers suggest that carnitines might help to prevent at least one side effect of testosterone administration—prostate enlargement.

(Source: Urology 2004;63:641–646.)

**More Calcium, Fewer Kidney Stones?**

Researchers have debated about which foods people should eat to prevent
kidney stones, or urinary calculi. It has generally been thought that in older women and men, greater amounts of dietary calcium, potassium, and total fluid reduce the risk of kidney stone formation, whereas supplemental calcium, sodium, animal protein, and sucrose increase the risk.

Researchers prospectively examined, during an eight-year period, the association between dietary factors and the risk of symptomatic kidney stones among almost 100,000 women in the Nurses’ Health Study II. The participants were aged 27 to 44 years and had no history of kidney stones.

A higher intake of dietary calcium decreased the risk of kidney stone formation in younger women, but supplemental calcium was not associated with the risk. Eating meat was not associated with a greater risk, but a higher sugar intake did increase the risk. Dietary phytate, present in cold cereal, dark bread, and beans, seemed to prevent kidney stones.

(Source: Arch Intern Med 2004; 164(8):885–891; Philadelphia Inquirer, Reuters, April 27, 2004.)

**Statins for Diabetic Patients**

People with type-2 diabetes mellitus (non-insulin-dependent diabetes) and coronary artery disease (CAD), as well as patients with diabetes and any other risk for cardiovascular disease, should be taking cholesterol-lowering drugs (statins), according to new guidelines published by the American College of Physicians (ACP).

Approximately 80% of people with type-2 diabetes experience or die of complications of heart and vascular disease, and about 65% of deaths among people with diabetes are a result of heart disease and stroke, according to the American Diabetes Association. Diabetes is itself a major risk factor for heart disease.

The ACP recommends that:

- All adults with type-2 diabetes and known CAD take statins, regardless of cholesterol levels.
- All type-2 diabetic patients with another risk factor for CAD take statins or the non-statin drug gemfibrozil (Lopid®, Parke-Davis) regardless of cholesterol levels.
- Routine monitoring of liver function or muscle enzymes is probably not needed for patients with type-2 diabetes who are taking statins unless they also have a liver abnormality or muscle pain or are taking drugs that interact with statins.

(Source: American College of Physicians; Ann Intern Med 2004;140[8]:644–649; www.annals.org.)

**Stem Cell Therapy for the Heart**

Stem cell transplantation holds promise as a viable remedy for congestive heart failure. Researchers from the University of Pittsburgh School of Medicine found that injections of bone marrow cells can pump up a failing heart. The findings from this first randomized trial of the approach were presented at the American Association for Thoracic Surgery’s annual meeting in Toronto in April.

In a clinical study from Argentina, patients who had received stem cells taken from the bone marrow in their hip bones during bypass surgery had hearts that pumped blood more efficiently, even months later, than patients who underwent surgery without any stem cells. The study involved 20 patients of the same age with a similar amount of heart damage. During surgery, 10 patients received stem cells. None knew about the stem cell implant.

After a month, both groups of patients improved; after three and six months, however, patients who received stem cells showed much greater improvement than the surgery-only group.

If this therapy succeeds, it might avert the need for controversial embryonic stem cell therapy and might lessen the chances of tissue rejection.

It is thought that stem cells might work by increasing blood vessel growth or muscle mass.


**New Ways to Treat Brain Cancer**

Because of the impermeability of the blood–brain barrier, which normally protects the brain from drugs and other substances circulating in the blood, many drugs that are used to treat brain cancer cannot reach or attack the tumors. Several clinical trials are now beginning to test new ways of disrupting or opening up the osmotic blood–brain barrier long enough to allow the drugs to enter.

“Smart” drugs might be able to target cancerous cells with less toxic effects compared with traditional chemotherapy. Catheters are being tested in an approach called convection-enhanced delivery, and wafers containing chemotherapeutic agents have been approved.

It is hoped that these new methods of delivering chemotherapy might also be used to treat Alzheimer’s disease, Parkinson’s disease, and stroke. However, these advances are not without pitfalls, because potentially lethal agents may also cross the barrier in the process.


**Lung Cancer Survival in Men and Women**

Women with lung cancer survive slightly longer than men with the disease, respond differently to at least one cancer drug, and show higher levels of tobacco-induced genetic damage in their cells compared with men.

(Source: Philadelphia Inquirer, April 27, 2004.)

**continued on page 360**
Uracil–Tegafur for Lung Cancer

A Japanese study has found that a drug combination that was rejected as a cancer treatment in the U.S. might add years to the lives of people with early lung cancer. The two-drug combination, called uracil–tegafur (UFT) is a tablet that produces few side effects.

The combination might be useful for only a small percentage of the 174,000 people with lung cancer diagnoses each year in the U.S. It is indicated only for adenomas, non–small-cell cancers, and small tumors that have not spread outside the lung.


Competition Among Stents

Having introduced a promising new drug-coated device, the Cypher stent, to treat heart disease nearly a year before anyone else in the U.S., Johnson & Johnson (J&J) may be losing ground to the competition. In March 2004, Boston Scientific introduced the Taxus stent and reports that it has captured 70% of new orders.

A spokesman for the Cordis unit of J&J says that doctors are still deciding which device they prefer.

The cylindrical, mesh-like stents are used to help prop open coronary arteries, prevent heart attacks, and decrease the need for further surgery by reducing the scarring that can re-block arteries.

Physicians seem to find the Taxus stent easier to use and less expensive. Some also say that interventional cardiologists as a group tend to be eager to try new devices.

J&J’s main blunder appears to have been its inability to make enough Cypher stents early on, but the company says that there is no shortage today.

The FDA has been reviewing some reports of technical problems with Taxus because, in some cases, part of the device became stuck in patients’ arteries. The company believes that problems will disappear after physicians gain experience in using the stent.


Anti-theft Device Helps Pharmacies

RxPATROL™ (Pattern Analysis Tracking Robberies and Other Losses) now includes loss of over-the-counter (OTC) and related products from drugstores.

Launched in June 2003, this information clearinghouse was originally designed to collect, analyze, and share information on pharmacy robberies, burglaries, and theft of prescription medications. The system is intended to guard against potential theft and to aid authorities in apprehending and prosecuting pharmacy thieves.

Shoplifting is the most common criminal activity reported by pharmacies. The most common products stolen include glucose test strips, home pregnancy tests, contraceptives, and products containing pseudoephedrine, used in the manufacture of methamphetamine.

(Source: RxPATROL, April 7, 2004; www.rxpatrol.org.)

Less Invasive Surgery Safe for Colon Cancer

Minimally invasive colon cancer surgery may be a safe and effective alternative to the traditional operation for most early-stage patients.

Laparoscopy, in which surgeons insert a tiny video camera and surgical instruments through small abdominal incisions, involves less scarring and a shorter hospital stay than traditional surgery.

A seven-year study was launched in response to widespread concerns that the minimally invasive technique actually fueled recurrences. The results are summarized as follows:

• **Standard surgery:** average hospital stay: six days; IV pain medication: four days; incision: six to eight inches; length of operation: 95 minutes.
• **Laparoscopic surgery:** average hospital stay: six days; IV pain medication: four days; incision: six to eight inches; length of operation: 95 minutes.


continued from page 355

lungs, say researchers from Memorial Sloan-Kettering Cancer Center in New York and Northwestern University in Chicago.

Some differences may stem from the effects of estrogen, whether naturally occurring or taken as a drug, and the scientists said more women should be included in studies of lung cancer to find out whether particular methods of treatment, prevention, and detection are best suited to them.

Nearly 80% of cases of lung cancer in women were the result of smoking. From 1930 to 1997, as more women began smoking, their death rate from lung cancer rose by 600%. Since the 1960s, smoking rates for American men have decreased by nearly 50% and by 25% for women.

The disease kills more women in the U.S. than any other cancer—as many as breast cancer and all gynecological cancers combined.

It is not known whether men and women who smoke are equally susceptible to lung cancer. Women are more likely to have adenocarcinoma, the most common lung cancer among nonsmokers. Some studies suggest that natural or synthetic estrogen might stimulate adenocarcinomas. Women who smoke have a more active version of a gene that makes chemicals in cigarette smoke more harmful to cells. Estrogen might make that gene more active.

stay: five days; IV pain medication: three days; incision: two inches; length of operation: 150 minutes.

Before laparoscopy becomes more widespread, surgeons will need more training. The procedure is more technically challenging and takes longer than traditional surgery.


**Valganciclovir Prevents Infections After Kidney Transplantation**

Research from the Division of Transplantation at the University of Miami School of Medicine has found that at least three months of therapy with a single daily dose of the antiviral medication valganciclovir HCl tablets (Valcyte™, Roche) effectively prevents cytomegalovirus (CMV), a common infection in kidney transplant patients taking highly potent immunosuppressive therapy. Results were presented at the fifth annual American Transplant Congress, held in Boston from May 15–19, 2004.

CMV, which is present in a latent form in as many as 80% of Americans, can activate and trigger gastrointestinal conditions and opportunistic infections in transplant patients with suppressed immune systems. It is also associated with rejection of transplanted organs as well as atherosclerosis in heart transplant patients.

Valcyte™ is an oral prodrug, or improved formulation, of ganciclovir (Cytovene®, Roche), which has been used to prevent CMV for the past 15 years. In this study, both agents were equally effective in preventing CMV in transplant patients.

Patients can take Valcyte™ in a simplified, once-daily regimen. Cytovene is taken in a larger dose three times daily.


**Tablet Splitting of Muscle Relaxants Raises Concerns**

Patients with back and neck pain who divide the most commonly prescribed muscle relaxant may be getting anywhere from half to 1.5 times the amount of medicine that they believe they are taking and may be receiving too much or too little medication.

Researchers at the Ernest Mario School of Pharmacy at Rutgers, The State University of New Jersey, conducted a study to determine the level of weight variability of tablet fragments when cyclobenzaprine HCl (Flexeril®, McNeil Consumer) 10 mg was split into halves with a tablet splitter and with a kitchen knife. The study was begun after anecdotal reports that patients given a prescription for branded Flexeril® 5-mg tablets were being advised to split the generic 10-mg tablets instead of taking the 5-mg tablet as prescribed.

Flexeril® 5 mg is comparable in efficacy to the 10-mg strength but is less sedating. Because the generic 10-mg tablets are not designed for splitting (they are not scored), there is an increased tendency for them to split unevenly or crumble. Tablet splitting often results in a lack of uniformity, even when tablets are scored, and the practice is opposed by many health professionals.


**Darifenacin for Overactive Bladder**

Results of two separate phase 3 studies involving darifenacin hydrobromide (Enablex®, Novartis), an M3 selective receptor antagonist being developed for the treatment of overactive bladder, reduced the frequency of weekly incontinence episodes (up to 77%) compared with placebo. It also decreased the number of weekly nocturnal awakenings caused by overactive bladder by 23%, versus 3.6% with placebo.

(Source: *American Urological Association*, May 9, 2004; www.novartis.com.)

**Gabapentin for Hot Flashes**

When hormone replacement therapy is not an option for patients with hot flashes, gabapentin (Neurontin®, Pfizer), usually prescribed for pain, might be a solution.

Red Wine and Acne Rosacea

A survey by the National Rosacea Society has found that certain alcoholic beverages exacerbate acne rosacea (a dermatological disorder in which the skin becomes blushed) more than others while also dispelling the myth that this condition is caused by heavy drinking.

Although alcohol can worsen the signs and symptoms of rosacea, which affects almost 14 million Americans, the disorder can be just as severe in non-drinkers. However, because rosacea often results in a conspicuous red face or red nose, it has often been incorrectly attributed to the excessive consumption of alcoholic drinks.

In a survey of more than 700 rosacea patients, 10% said they rarely or never drank alcohol, and an additional 10% reported that consuming alcoholic beverages had no effect on their appearance. Of the respondents who were affected by alcohol, red wine was by far the most common culprit, triggering flare-ups of symptoms in 76%. In addition, 56% said white wine aggravated their condition; champagne caused flare-ups in 33%.

Beer caused rosacea flare-ups in 41% of the respondents, and an additional 15% were affected by malt liquor or other malt-based beverages such as “hard” lemonade.

Among hard liquors, vodka was the leading aggravating agent, causing flare-ups in 33%, followed by tequila (28%), bourbon (24%), gin (24%), rum (24%), and scotch (21%).

For 64% of patients who were affected by alcohol, just one drink was enough to cause a reaction, whereas 26% indicated they reacted after a couple of drinks.

Most of those who reduced their alcohol intake reported that this decreased intake helped to reduce their outbreaks. Other triggers include sun exposure, emotional stress, hot or cold weather, wind, exercise, hot baths, spicy foods, humidity, indoor heat, and hot drinks.


NEW MEDICAL DEVICES

By Marvin M. Goldenberg, PhD, RPh, MSS

Name: Amplatzer® Vascular Plug

Manufacturer: AGA Medical Corporation, Minneapolis, MN

Approval Date: May 3, 2004

Use Classification: The implantable plug provides physicians with a minimally invasive alternative for correcting common vascular disorders.

Description: The self-expandable, cylindrical device is made of nitinol wire mesh and is available in diameters ranging from 4 to 16 mm. Nitinol’s super-elastic properties allow the plug to be compressed inside a catheter, then to spring back to full size after it is situated within the blood vessel. The device is also nonmagnetic and is therefore compatible with magnetic resonance imaging (MRI) technology.

The plug is introduced to the target vessel via a catheter that is threaded through a vein or artery and is accessed via a small incision in the patient’s groin. Unlike some coils, this plug can be placed, repositioned when necessary, and released in a precise manner.

Purpose: The device helps physicians close specifically targeted veins and arteries. Vascular occlusion is often indicated to prevent a burst aneurysm, to shut off blood flow to a growing tumor, or to adjust abnormal connections in the venous and arterial sites.


Name: ImageChecker® Computed Tomography Lung Computer-Aided Detection System

Manufacturer: R2 Technology, Inc., Sunnyvale, CA

Approval Date: May 4, 2004

Use Classification: As the first FDA-approved computer-aided detection (CAD) system for breast imaging, the device assists radiologists in reviewing multidetector-row computerized tomography (MDCT) chest examinations by identifying lung nodules on mammograms.

Description: The system analyzes both film and digital mammograms.

Purpose: The device provides tools for improved detection of clinically significant lung nodules, and it automatically highlights areas of interest, computes measurements, and enables retrospective reconstruction of images at a lower
resolution for review while allowing CAD to process at the highest possible reso-

Benefit: MDCT demonstrates the ability of the system to improve detection of lung nodules, and it has revolutionized thoracic imaging by enabling rapid acquisition of high-resolution data. Even though the increased resolution brings greater interpretive potential and the speed of acquisition enables more complex application, the enormity of the acquired image volume has resulted in significant workflow challenges to radiologists accustomed to reviewing results on axial slices.

The system should prove to be a valuable tool in the detection of lung cancer, the leading cause of cancer deaths among American men and women.


Name: Vitality 2 Implantable Defibrillator
Manufacturer: Guidant Corporation, Indianapolis, IN
Approval Date: May 4, 2004
Use Classification: The implantable cardioverter-defibrillator (ICD) system is designed to treat patients who are at risk for sudden cardiac death caused by arrhythmias.

Description: This device offers distinct advantages for patients and physicians. As the smallest and thinnest implantable defibrillator at 30 ml and 11 mm, it is designed to facilitate ease of insertion, thus contributing to patient comfort. The system incorporates a proprietary feature that distinguishes lethal from nonlethal heart rhythms and is designed to deliver the appropriate care at the right time.

Purpose: Implantable defibrillators are often used to treat sudden cardiac death and have been found to reduce the mortality rate from this condition.

Benefit: The combination of size, longevity, and advanced rhythm management options provides delivery of appropriate care. In particular, the ability of the Vitality 2 to distinguish between lethal and nonlethal arrhythmias is particularly valuable.

Sources: Pharmacy One Source News Team; www.guidant.com.

Name: EnRhythm™ Pacemaker and EnTrust™ Implantable Cardioverter-Defibrillator
Manufacturer: Medtronic, Inc., City of Industry, CA
Approval Date: April 29, 2004
Use Classification: This is the first clinical implant in a new family of pacemakers and implantable cardioverter—defibrillators (ICDs). A feature called Managed Ventricular Pacing promotes natural heart activity by automatically minimizing unnecessary right-ventricular pacing.

Description: The pacemaker is indicated for patients with abnormally slow heartbeats (bradycardia) and for patients with atrial arrhythmias in addition to bradycardia. The ICD is indicated for patients with abnormally fast and potentially life-threatening heartbeats (tachycardia), which can lead to sudden cardiac arrest. The ICD offers antitachycardia pacing during charging of the capacitor. The device delivers full power therapy when needed, but not before it attempts to painlessly pace the patient out of the potentially life-threatening rhythm. Antitachycardia pacing from Medtronic’s ICDs has been found to dramatically reduce shocks for terminating ventricular arrhythmias by as much as 77%.

EnTrust™ also offers improved diagnostics for clinical efficiency and longevity of approximately seven years, all within a small size of 33 ml.

Purpose: The pacemaker and ICD assist in replicating normal cardiac function.

Benefit: The pacemaker automatically minimizes unnecessary pacing in the right ventricle. It also offers enhanced features to diagnose additional rhythm problems in the atrial upper chambers.


Name: Precision™ Spinal Cord Stimulation (SCS) System
Manufacturer: Advanced Bionics Corporation, Valencia, CA
Approval Date: April 28, 2004
Use Classification: The system is approved for adults with chronic pain of the trunk and/or limbs, including pain associated with failed back surgery syndrome.

Description: With 16 independently controlled electrodes, this rechargeable implant can support twice the number of electrodes as other systems. It lasts years longer than non-rechargeable systems, and fewer replacement surgical procedures are needed. The system delivers high-power output so that physicians do not have to compromise patients’ pain relief for battery life. The implant is approximately half the size of other implantable devices, making it comfortable to patients and easy for physicians to insert.

Purpose: This is the first system with interactive, real-time programming technology, which allows patients to make rapid and precise adjustments to relieve pain.

Benefit: Patients can use this device for a long time before it needs to be replaced, and they can be directly involved with their programming.