Natalizumab in Relapsing MS
Biogen Idec and Elan Corporation have announced the FDA's approval of natalizumab (Tysabri®, formerly called Antegen®) for the treatment of relapsing forms of multiple sclerosis (MS). The FDA granted accelerated approval after a priority review based on one-year data from two phase 3 studies: the AFFIRM monotherapy trial and the SENTINEL add-on trial with interferon beta-1a (Avonex®).

Natalizumab, the first humanized monoclonal antibody approved for the treatment of MS, inhibits adhesion molecules on the surface of immune cells. It appears to prevent immune cells from migrating from the bloodstream into the brain, where they have the potential to cause inflammation and damage the nerve fibers and their insulation.

A chronic disease of the central nervous system, MS affects approximately 400,000 people in North America and more than one million people worldwide. More women than men are affected. It typically occurs in people between 20 and 40 years of age. Symptoms may include vision problems, loss of balance, numbness, difficulty walking, and paralysis.

Side effects of natalizumab included headache, fatigue, urinary and lower respiratory tract infections, depression, joint pain, and abdominal discomfort. This drug has also been associated with hypersensitivity reactions.

All biological therapies have the potential to induce antibodies in patients. Antibodies were detected in approximately 10% of patients at least once during treatment. Persistently positive antibodies were associated with a substantial decrease in the agent’s efficacy and with an increase in some infusion-related effects.

Biogen Idec and Elan are also collaborating to develop natalizumab to treat Crohn’s disease and rheumatoid arthritis.

(Source: Biogen Idec/Elan; www.tysabri.com.)

Erlotinib for Advanced Non–Small Cell Lung Cancer
The FDA has approved erlotinib (Tarceva™ OSI/Genentech) to treat locally advanced or metastatic non–small cell lung cancer (NSCLC) for patients whose disease progressed despite at least one chemotherapy regimen.

The tablet, taken daily, blocks signals that stimulate growth in cancer cells by inhibiting an enzyme associated with epidermal growth factor receptor.

The FDA based its approval on a randomized phase 3 pivotal trial in which treated patients survived for a median of 6.7 months and placebo patients survived 4.7 months. After one year, 31.2% of the treated patients were alive, compared with 21.5% of the placebo patients.

(Source: OSI/Genentech, November 18, 2004; www.osip.com; www.tarceva.com.)

Generic Contraceptive Approved
Watson Pharmaceuticals has received the FDA’s final approval for its Abbreviated New Drug Application for levonorgestrel and ethinyl estradiol tablets USP 0.1 mg/0.02 mg, a generic version of Wyeth’s Alesse® birth control medication. The product will be marketed under the trade name of Lutera™.

(Source: Watson, November 22, 2004.)

NEW INDICATION
Oxaliplatin for Colon Cancer After Surgery
The FDA has approved oxaliplatin for injection (Eloxatin™, Sanoﬁ-Synthelabo), in combination with conventional chemotherapy (infusional 5-fluorouracil/leucovorin, or 5-FU/LV), for the postsurgical treatment of patients with stage III colon cancer who have undergone complete resection of the primary tumor. This is the first new chemotherapy approval for the adjuvant treatment of colon cancer in more than a decade.

Most patients undergo surgery to remove their primary tumor, but they may remain at risk for a recurrence. This latest approval may help to decrease the risk of cancer recurrence and spread.

The FDA based its decision on results from the MOSAIC study, a large, international, randomized phase 3 trial involving 2,246 patients in 146 centers. At a median follow-up of four years, there was a statistically signiﬁcant improvement in disease-free survival for the oxaliplatin combination, compared with infusional 5-FU/LV, in the overall study population and in the subgroup with stage III disease. Adding oxaliplatin to 5-FU/LV reduced the risk of recurrence of cancer by 24% in the overall patient population who had undergone surgical removal of the primary tumor.

The drug was approved on January 9, 2004, for the first-line treatment of advanced carcinoma of the colon or rectum. This same combination had previously received approval in August 2002 for second-line treatment of patients with metastatic colorectal cancer who had already been treated.

Anaphylactic-like reactions to oxaliplatin may occur within minutes of its administration. Epinephrine, corticosteroids, and antihistamines have been used to alleviate symptoms.

Oxaliplatin has been associated with
pulmonary fibrosis in fewer than 1% of study patients. Patients requiring oral anticoagulants may need close monitoring.


**NEW DRUG APPLICATION**

**Generic Diabetes Drug**

The FDA has granted tentative approval for Mylan Laboratories’ Abbreviated New Drug Application for pioglitazone HCl tablets in strengths of 15, 30, and 45 mg. This product is the generic version of Actos® Tablets (Takeda).

(Source: Mylan Labs, November 9, 2004, www.mylan.com.)

**NEW FORMULATION**

**Fenofibrate for Lipid Disorders**

Abbott Laboratories has received approval to market a new formulation of fenofibrate tablets (TriCor®) to treat elevated cholesterol, triglyceride, and apolipoprotein B levels. The new formulation can be taken with or without food.

Until now, this drug had to be taken with food to enable its absorption. The new 145-mg and 48-mg tablets offer the same effectiveness than the previous 160-mg and 54-mg tablets. Nanoparticle technology allows the drug to dissolve faster and more completely in the gastrointestinal tract. The product remains a once-daily treatment.

Patients should not take fenofibrate with statin drugs because of the potential for serious side effects that may lead to acute renal failure. The drug is not indicated for patients with serious liver, kidney or gallbladder disease or those who may be allergic or sensitive to it.

Because the tablets may affect liver chemistry results, regular periodic liver tests should be performed during therapy. Stomach pain during therapy can be a sign of gallstones or inflammation of the pancreas.

Fenofibrate may also cause muscle disease, allergic reactions, and changes in blood chemistry. If patients experience unexpected muscle pain, weakness, or tenderness while taking fenofibrate, they should contact their health care provider immediately.

Abbott markets the drug in the U.S. through an agreement with Fournier of France.

(Sources: Abbott, November 5, 2004; www.tricor.com; www.prnewswire.com.)

**DRUG NEWS**

**Rimonabant Helps Keep the Weight Off**

A highly anticipated experimental weight-loss drug not only helps people lose weight but also helps them maintain their weight for as long as two years. These findings were presented at the annual scientific meeting of the American Heart Association in November.

In a study of 3,045 people, those who adhered to a daily 20-mg regimen of rimonabant (Sanofi-Aventis) lost an average of 17 pounds and 3.2 inches in the waist within the first year of treatment and stayed at their new weight for an additional year. Those who lost weight and then switched to a placebo gained nearly all of the weight back during the second year of the study.

Rimonabant appears to have positive effects on waist circumference, high-density lipoprotein-cholesterol (HDL-C, the “good cholesterol”), and blood sugar, factors that affect the risk of diabetes and heart disease. Almost two thirds of patients lost more than 5% of their initial weight, and one third lost more than 10% of their initial weight. HDL levels rose by 24.5%, and triglyceride levels fell by 9.9%.

For patients taking 5 mg and a placebo, the benefits and the risk of dropout were generally lower.

The medication blocks receptors in the endocannabinoid system in the brain, which, among other things, is stimulated by cannabis, the active ingredient in marijuana. Researchers believe these receptors, which also reside in fat cells and in nerves in the stomach, might play a critical role in regulating appetite.

Abdominal fat is considered a risk factor for heart disease. Almost 44% of American adults have a waist circumference exceeding 40 inches in men and 35 inches in women, the threshold for high risk. All of the study participants followed a reduced-calorie diet.

Heart experts said the findings were encouraging but warned that healthy diets and exercise would remain crucial.

More information is needed on why people apparently stopped losing weight during the first year of treatment and why they could not keep it off without the drug.

Drug approval is expected by late 2005 or early 2006.

(Sources: The Wall Street Journal, November 10, 2004; St. Luke’s Roosevelt Hospital Center, New York.)

**Black-Box Warning for Contraceptive Injection**

The FDA has announced that a “black-box” warning will be added to the labeling of methoxyprogesterone acetate (Depo-Provera® Contraceptive Injection, Pfizer) because prolonged use of the product may result in the loss of bone mineral density.

Although this medication has been used for decades for birth control and is considered safe and effective, the FDA and Pfizer are taking this action to ensure that physicians and patients have access to this important information.

The warning emphasizes that bone density loss increases with the length of usage and that the loss might not be completely reversible after discontinuation of the drug. Women should use the product for a long term (e.g., more than two

continued on page 759
The main side effect was short-lived and consisted of mild gastrointestinal upset in eight patients taking the study drug and in four patients taking placebo. This makes octreotide an attractive agent when repeated doses are needed over a relatively short period. Gallstones have been a concern with long-term octreotide treatment, but the risk is probably low.

With regard to primary headache, another of their trials showed that octreotide had no effect on migraine despite research that had suggested a benefit. The researchers point to a marked difference between migraine and cluster headaches in the pattern of brain activation.
**Diclofenac on the Spot**

For patients with osteoarthritis of the knee, it might be enough to simply put the medication right where the pain is. Researchers from Arizona Research and Education in Phoenix, Arizona, and from Dimethaid Health Care Ltd., in Markham, Ontario, Canada, suggest that a topical diclofenac sodium solution might be preferable to oral nonsteroidal anti-inflammatory drugs (NSAIDs), which have potential long-term systemic effects.

They evaluated a new topical solution (Pennsaid®, Dimethaid) that contained the absorption enhancer dimethyl sulfoxide (DMSO) in 326 patients. Patients were randomly assigned to receive 40 drops of the topical diclofenac or a vehicle-controlled solution four times daily for 12 weeks.

Topical diclofenac was found to be superior: pain improved by 45.7%; stiffness, by 35.1%; and physical function, by 36.7%. On a global assessment subscale score, patients improved by 42.2%.

Safety analyses revealed no apparent serious ADEs. Minor application-site skin reactions, mostly skin dryness, were reported, and these were easily alleviated with nonprescription skin ointments. A few patients reported halitosis and taste changes, which might have been the result of DMSO metabolizing to a volatile gas, which gives the breath a garlic-like smell and taste.


**Teaming Up Against Squamous Cell Cancer**

Encouraging response rates at relatively low toxicity indicate that a biweekly mix of paclitaxel (Taxol®, Bristol-Myers Squibb), along with cisplatin (Platinol®, Bristol-Myers Squibb), tegafur (Uftoral®, R & S Pharmchem), and leucovorin, is a safer neoadjuvant chemotherapy option for patients with advanced unresectable squamous cell carcinoma of the head and neck.

Researchers from Taipei, Taiwan, used the combination over three cycles for 21 patients with stage IV disease. Each cycle was repeated every 14 days. Treatment was stopped if primary tumor responses were less than partial. Otherwise, the combination treatment was continued for up to six cycles before local–regional therapy began. Each patient underwent a mean of 5.38 cycles.

Of the 21 patients, 20 were evaluable. At the primary tumor site, six patients achieved complete response and 11 achieved a partial response, for an overall rate of 81%. Of the 18 patients with neck lymph node metastases, four achieved a complete response (22%) and 11 achieved a partial response (61%).

In two patients, neuropathy developed to a greater extent than the National Cancer Institute’s Common Toxicity Criteria (CTC) grade 2; one patient died as a result of aspiration pneumonia. Eleven patients required a delay in scheduled CT scanning because of renal insufficiency, stomatitis, asthenia, and myelosuppression.

Common toxicities included leukopenia, emesis, asthenia, mucositis, and neuropathy. Two patients were hospitalized for grade 3 asthenia.

(Source: Cancer 2004;101:1818–1823.)

**All-around Benefits from Sibutramine**

Better glycemic control leads to weight loss, which leads to better glycemic control—the primary goal in diabetes. A study from Mexico City suggests that patients are helped by an appetite suppressant, sibutramine HCl monohydrate (Meridia®, Abbott).

Forty-four patients with type-2 (non–insulin-dependent) diabetes had been taking glibenclamide monotherapy for at least two weeks. They were randomly assigned to receive sibutramine 10 mg or a placebo once daily. After 12 months of treatment with sibutramine and glibenclamide, the diabetic patients lost 4 kg (11 pounds), their body mass index (BMI) decreased from 29.9 to 28.2 kg/m², and they lost 4 cm (1.5 inches) around the waist. Plasma fasting glucose concentrations declined from 140.4 to 114.2 mg/dl, and glycosylated hemoglobin (Hb A₁c) fell from 8.9% to 8.3%.

The placebo patients experienced similar but smaller changes. They lost 1.4 kg (3.1 pounds); 0.6 kg/m² in BMI; and 1.3 cm (0.5 inch) in waist circumference. Fasting glucose levels fell from 140.7 to 123.9 mg/dl, but Hb A₁c values rose from 9.0% to 9.1%.

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(Source: Clin Ther 2004;26:1427–1435.)

**Intranasal Insulin and Type-1 Diabetes**

Intranasal insulin appears safe and may stabilize beta-cell and immune function in individuals at risk for type-1 dia-
betes. Mucosal administration of insulin retarded the development of diabetes in the non-obese diabetic mouse, a model of autoimmune type-1 diabetes. However, such immune responses to potentially therapeutic self-antigens have not yet been documented in humans.

Researchers from The Walter and Eliza Hall Institute of Medical Research in Victoria, Australia, studied the safety and immune effects of intranasal insulin in 38 individuals at risk for type-1 diabetes. Six participants in each arm of the crossover study (intranasal insulin-first and placebo-first groups) developed diabetes after a median of 1.1 years from entry. Eleven of these participants had baseline first-phase insulin responses to intravenous glucose (a measure of beta-cell function) no higher than the first percentile.

During treatment, circulating insulin antibodies increased significantly. Intranasal insulin was also associated with significant decreases in T-cell proliferation to insulin.

(Source: Diabetes Care 2004;27:2348–2355; Reuters, October 18, 2004.)

**Lumiracoxib Poses Low Risk For GI Ulcers in Osteoarthritis**

Compared with ibuprofen, the novel cyclooxygenase 2 (COX-2)-selective inhibitor lumiracoxib (Premige®, Novartis) is associated with a lower risk of gastroduodenal ulceration in patients with osteoarthritis. The risk is similar to that seen with celecoxib (Celebrax®, Pfizer).

Lumiracoxib is also considered safe in terms of cardiovascular and other effects. Researchers from Nottingham, UK, compared lumiracoxib with ibuprofen and celecoxib in 1,024 patients with osteoarthritis. The patients were randomly assigned to receive lumiracoxib 200 or 400 mg once daily, ibuprofen 800 mg three times per day, or celecoxib 200 mg/day for 13 weeks.

The cumulative incidence of gastrointestinal ulcers of 3 mm or larger in diameter was 4.3% with low-dose lumiracoxib and 4% with the high dose. The incidence was 15.7% in the ibuprofen patients and 3.2% in the celecoxib group.

In addition, 6% of patients in the ibuprofen group had more than 10 gastroduodenal erosions, compared with 1.2% of patients in the low-dose lumiracoxib group and 1.6% in the high-dose group. This was also true of 2.4% of the celecoxib patients.

The researchers concluded that lumiracoxib was a well-tolerated alternative to standard NSAIDs.

(Source: J Rheumatol 2004;31:1804–1810; Reuters, October 18, 2004.)

**Anticoagulant Reverses Side Effects**

Scientists have successfully tested an experimental blood thinner aptamer that provides potent anticoagulation and acts as an antidote to quickly reverse the side effects, especially bleeding.

The anticoagulant–antidote pair may have potential for patients with acute coronary syndrome and for those needing coronary revascularization. The anticoagulant aptamer Ch-9.3t specifically targets human coagulation factor IXa, which affects the initiation and propagation phases of coagulation.

Bolus injections of the 5-2C oligonucleotide antidote into anticoagulated animals rapidly reversed more than 95% of the anticoagulant effects of the aptamer and restored hemostasis. It also prevented hemorrhage in the clipped tails of mice when given with Ch-9.3t.

The team’s findings were built on work published in 2002, in which they described a strategy for discovering antidote-controlled drugs and a first-version anticoagulant–antidote pair.

(Source: Nat Biotechnol 2004; Reuters Health, October 19, 2004.)

**Etanercept plus Methotrexate Stops Arthritis Joint Damage**

Etanercept (Enbrel®, Angen/Wyeth) appears to stop joint damage in patients with rheumatoid arthritis when it is given in combination with an older drug. Study results were announced in October at the 68th annual scientific meeting of the American College of Rheumatology in San Antonio.

After two years, disease progression halted in 74% of patients taking the combination and in 60% of patients taking a single drug. Patients receiving the drug combination also showed improved physical function scores compared with patients who took either drug alone.

In addition to its indication for rheumatoid arthritis, etanercept is approved to treat psoriasis, psoriatic arthritis, and ankylosing spondylitis.

(Source: Reuters, October 19, 2004; www.rheumatology.org.)

**Modafinil with SSRIs Alleviates Sédation**

Excessive sleepiness and fatigue related to therapy with serotonergic antidepressants can be alleviated with the adjunctive use of modafinil (Provigil®, Cephalon). Researchers at the New York Upstate Medical University in Syracuse, New York, enrolled 20 adults in a three-week study to determine the effect of once-a-day modafinil on sedation related to serotonergic drug use. All of the patients had major depressive disorder but reported that sedation, fatigue, and low energy developed only after they had begun to take selective serotonin reuptake inhibitors (SSRIs).

In the 16 patients who completed the study, the addition of modafinil improved overall depressive symptoms and was associated with improved subjective impressions of wakefulness and reduced fatigue. By their final study visit, the patients showed better overall health sta-
**NEW DRUGS**

Continued from page 761

Despite the open-label design of the study, the exclusion of a control group, and selective entry criteria for the participants, the investigators stated that the positive findings, as well as the effects of adjunctive modafinil on responder rates, warranted further study.


**Cisplatin with Radiotherapy Helps Preserve Bladder**

In patients undergoing radiotherapy for localized bladder cancer, concurrent intra-arterial administration of cisplatin helped achieve high bladder preservation rates, according to a new study.

Researchers at The Ottawa Hospital in Ontario, Canada, reported on 200 patients with bladder cancer. These patients were treated with three courses of intra-arterial cisplatin integrated with pelvic radiotherapy. Cystectomy was performed as a salvage procedure.

Among the 185 evaluable patients, 75% retained a bladder free of tumors. Of these 185 patients, 93 were alive without cancer, 35 had died without cancer, 52 had died as a result of cancer, and five were alive with cancer. For patients who required salvage cystectomy, survival rates were identical to those for whom treatment did not fail in the bladder.

(Source: *J Urol* 2004;172:1276–1280; Reuters, October 15, 2004.)

**DMSA Not Helpful For Homocysteine Levels In Dialysis Patients**

Dimercapto succinic acid (DMSA) is not effective in lowering elevated homocysteine levels in hemodialysis patients. Based on two small pilot studies and on the hypothesis that DMSA might be able to displace and chelate homocysteine from albumin, researchers from the University of Western Ontario, Canada, investigated whether daily DMSA could decrease plasma homocysteine levels in 38 vitamin-replete hemodialysis patients.

In both DMSA and placebo patients, homocysteine levels remained virtually unchanged after four and eight weeks. Adjustments for baseline characteristics of the patients did not alter the results.

Homocysteine is thought to be a factor for cardiovascular disease, but more evidence is needed. Until homocysteine levels can be lowered safely with a beneficial outcome through rigorous clinical trials, clinicians should remain focused on modifying proven risk factors.


**“Traditional” Approval For Enfuvirtide**

U.S. regulators have granted “traditional” approval to enfuvirtide (Fuzeon®, Trimeris), which is already available for the treatment of human immunodeficiency virus (HIV) infection. In March 2003, the FDA had granted fast-track approval of this medication, which Trimeris co-developed with Roche Holding AG, on the basis of 24 weeks of clinical trial data. The new approval means that the company’s drug package insert labeling can now include data from 48-week clinical trials.

(Source: Reuters, October 18, 2004; www.fda.com.)

**Enfuvirtide Beneficial Even with High Viral Loads**

Enfuvirtide offers immunological and clinical benefits for HIV-infected patients who are resistant to several other antiretroviral drugs, and it seems to help some whose viremia persists during enfuvirtide treatment, according to an international team of researchers.

During treatment with enfuvirtide, which prevents viral and cellular membrane fusion, increased CD4 counts and lower T-cell activation may occur, despite evidence of significant HIV replication.

Researchers from Madrid, Spain, evaluated the immunological and genetic features of four patients who were not responding to antiretroviral therapy. Although they developed resistance to enfuvirtide, they either maintained stable CD4 levels or showed increased CD4 cell counts and experienced a dramatic clinical improvement. All four patients were resistant to several protease and reverse transcriptase inhibitors. They were observed for 80 weeks after enfuvirtide rescue therapy was begun.

The patients’ immunological responses were compared with those of three control groups: (1) a similar set of multidrug-resistant patients given salvage therapy without enfuvirtide with similar viral loads; (2) patients receiving highly active antiretroviral therapy (HAART) with no detectable viral load; and (3) untreated HIV patients with viral loads similar to those of the study patients.

In the study group, the viral load declined during the first weeks of enfuvirtide therapy but eventually rebounded. Two of the patients continued to have stable CD4 counts despite increased viremia, whereas CD4 counts rose in the two other patients.

A mutation in the HR1 region appeared at the same time as treatment failure in the four patients. Changes in the HR2 region also occurred during enfuvirtide therapy, but it was not clear whether these changes were related to the development of resistance.

Viral replication had a weaker impact on immune activation among the treated patients than in the patients not receiving HAART or enfuvirtide.

The researchers proposed that the inhibition of fusion by enfuvirtide might weaken the impact of the virus on CD4 cells by promoting compensatory HIV entry into cells via the endocytosis pathway.
**NEW DRUGS**


**FDA Halts TNFerade™ Trials**

The FDA has requested that trials of the gene therapy product TNFerade™ (GenVec) be placed on “clinical hold,” pending a review of information pertaining to a potential increase in the incidence of blood clots in patients with esophageal cancer who received the is currently in phase 2 clinical studies for locally advanced pancreatic, esophageal, and rectal cancers. This agent is an adenovector that carries the transgene for human tumor necrosis factor (TNF).

(Sources: GenVec, October 7, 2004; http://biz.yahoo.com.)

**Drugs for Erectile Dysfunction Raise Testosterone Levels**

Treatment with sildenafil (Viagra®, Pfizer) and tadalafil (Cialis™, Eli Lilly) increases levels of testosterone in men with erectile dysfunction (ED) after three months of therapy.

Researchers measured total and free testosterone levels before and after three months of type V phosphodiesterase inhibitor treatment in 74 men with ED. Mean free testosterone levels increased from 59.9 pmol/liter before treatment to 80.4 pmol/liter after three months of treatment. Total testosterone levels also rose (from 11.9 to 16.3 nmol/liter), whereas luteinizing hormone (LH) levels declined (from 4.7 to 2.7 IU/liter).

Although the testosterone increases and LH decreases were more marked with tadalafil than with sildenafil, the drugs were equally effective in restoring sexual potency. The frequency of full sexual intercourse was higher with tadalafil, although the men took the same number of tablets per month.

The researchers consider tadalafil to be preferable for men in stable couple relationships. In this case, it can be taken twice a week to allow spontaneous sexual activity.

(Sources: *Clin Endocrinol* 2004;61: 382–386; Reuters, October 15, 2004.)

**Inflammatory Enzyme Lp-PLA2: Risk Factor for Stroke**

High levels of an enzyme called lipoprotein-associated phospholipase A2 (Lp-PLA2), which is believed to trigger a cascade of inflammatory events in atherosclerosis, can independently predict an increased risk of stroke. Findings were presented at the American Heart Association’s Scientific Sessions 2004 by researchers from the Atherosclerosis Risk in Communities (ARIC) study.

Middle-aged participants with the highest levels of Lp-PLA2 had a statistically significant doubled risk of having an ischemic stroke over a period of six years compared with those with the lowest levels of the enzyme even when traditional cardiovascular risk factors (systolic blood pressure, smoking status, and diabetes) and the risk marker of systemic inflammation (C-reactive protein) were accounted for. Patients with the highest Lp-PLA2 and C-reactive protein levels had more than an 11-fold increased risk of stroke than those with the lowest levels.

Lp-PLA2 helps to process a form of low-density lipoprotein-cholesterol (LDL-C) into products within atherosclerotic plaques and is believed to trigger a cascade of inflammatory events. Atherosclerosis accounts for 50% of all deaths in Western countries.

diaDexus, Inc., developed the PLAC™ test for measuring Lp-PLA2 concentrations. The FDA has approved the test, and it is now available in the U.S.

(Sources: diaDexus, November 9, 2004, www.diaDexus.com.)

**Growth Hormone May Improve Heart Failure in Children**

Recombinant human growth hormone (hGH) appears to help children with heart failure. Researchers in Boston note that such treatment led to improved left ventricular (LV) mass and function in adults and in animal models. To determine whether the approach would benefit pediatric patients, they studied eight children with stable LV dysfunction attributable to dilated cardiomyopathy.

Two patients withdrew from the crossover study because of declining LV function and underwent cardiac transplantation. The remaining subjects received up to 0.04 mg/kg of recombinant hGH, delivered by daily subcutaneous injection for six months, as well as conventional therapy.

During treatment, LV ejection fraction improved. Six months after treatment, compared with baseline values, patients showed significant improvements in LV scores, LV shortening fraction, and end-systolic stress; insulin growth factor (IGF-1) levels also remained significantly higher. The researchers concluded that these findings, occurring after the cessation of therapy, might represent progression or perpetuation of an effect from hGH therapy.

(Sources: *Pediatrics* 2004;114:e452–e458; Reuters, October 15, 2004.)

**B-Type Natriuretic Peptide For Diagnosis of Heart Failure**

A system review by ECRI, a nonprofit health services research agency in Plymouth Meeting, Pa., has found that B-type natriuretic peptide testing (the BNP blood test) can detect heart failure and that its use in all clinical settings may improve patient outcomes with few adverse effects. This 15-minute, low-cost blood test can reveal a patient’s level of BNP, a small protein that is secreted by the ventricles into the bloodstream when the heart is under stress.

ECRI studied the use of BNP testing to aid in the diagnosis of heart failure in
asymptomatic individuals, in patients with symptoms of heart failure in the emergency room, and in patients with apparent heart failure in the physician’s office. For all three populations, the BNP test detected heart failure when it was used to screen asymptomatic persons. The evidence was weaker, however, for patients with chronic symptoms. BNP testing in the emergency room improved several outcomes (i.e., decreased mortality and fewer hospitalized patients), although the evidence supporting this conclusion was also weak.

ECRI concluded that BNP testing was likely to improve patient outcomes in any clinical setting because of its absence of adverse effects, its low cost, and the available evidence related to its effectiveness.

(Source: ECRI, October 11, 2004.)

**Update: Heart Failure Drug Helps African-Americans**

Results from the African American Heart Failure Trial (A-HeFT) indicate that African-American patients with heart failure, or end-stage cardiovascular disease, experienced a 43% improvement in survival after taking a new drug combination in addition to standard heart failure therapy, compared with patients receiving standard heart failure therapy plus a placebo. The product, called Cardiasmin™ (NitroMed), is a nitric oxide-enhancing, fixed-dose combination of isosorbide dinitrate and hydralazine.

The primary endpoints were a composite score made up of weighted values for death from any cause, a first hospitalization for heart failure, or end-stage cardiovascular disease. Findings were presented at the Canadian Cardiovascular Congress held in Calgary, Alberta, in October.

Skin sterol testing (total skin tissue cholesterol) is a novel way of assessing cardiovascular risk. The accumulation of sterol in the skin tissues, as measured by McNeil’s Prevu® Point of Care Sterol Test, provides additional information about a patient’s risk of coronary artery disease (CAD). Findings were presented at the Canadian Cardiovascular Congress held in Calgary, Alberta, in October.

Skin sterol was evaluated in 300 patients with proven CAD; 90% of these patients were taking statins. The patients were evaluated at baseline and annual clinic visits as part of the ongoing PRACTICE Clinical Registry (Prospective Assessment of Cardiovascular Risk and Treatment in Canadians of Varying Ethnicity).

The results indicated that patients with high skin sterol scores also had a history of diabetes, angina, and smoking. Sterol levels were higher in whites than in non-whites.

Serum markers were not positively correlated with prior stroke, angina, or diabetes. Previous studies of patients who were not taking cholesterol-lowering drugs showed no correlation between skin sterol and blood cholesterol but did show a relationship between skin sterol and a history of heart attacks and a correlation between various markers of cardiovascular risk (e.g., Framingham risk score, coronary calcium levels, and coronary artery disease).

The test is noninvasive; blood is not drawn, and patients do not need to fast. IMI International Medical Innovations, Inc., developed the test.

(Source: www.heartcenteronline.com; McNeil Consumer, October 26, 2004.)

**NEW MEDICAL DEVICES**

**Marvin M. Goldenberg, PhD, RPh, MS**

**Name:** EVS™ Vascular Closure System

**Supplier:** Angiolink Corporation, Taunton, MA (acquired by Medtronic, November 2004)

**Approval Date:** November 3, 2004

**Use Classification:** The EVS™ (expanding vascular stapling) system helps to stop bleeding after diagnostic and interventional heart (cardiac) catheterization procedures.

**Description:** The surgeon uses a titanium staple to stop bleeding by closing the hole (arteriotomy) in the artery. After cardiac catheterization, a guide wire is reintroduced and the introducer sheath is removed. The surgeon then closes the arteriotomy by advancing the system over the guide wire through the skin and soft tissue into the arteriotomy. After they are placed, the dilator and guide wire are removed from the introducer and the stapler is advanced through the introducer and locked into place. Squeezing the trigger deploys the staple, and the device is removed.

**Purpose:** Cessation of bleeding in a blood vessel in the leg (the femoral artery) after cardiac catheterization.

**Benefits:** The system provides an alternative to applying manual pressure (compression) to the puncture site to stop bleeding and allows patients to get out of bed and walk sooner than is possible with...
standard compression methods.

Source: www.fda.gov.

**Name:** Charite Artificial Disc  
**Manufacturer:** DePuy Spine, Inc., a Johnson & Johnson Company  
**Approval Date:** October 26, 2004  
**Use Classification:** An artificial disc is used to treat severe lower back pain, and it replaces the damaged or worn-out spinal disc.

**Description:** The disc is composed of two metallic endplates and a movable high-density plastic center. It is designed to perform and move like the body's own spinal disc after it is implanted.

**Purpose:** To maintain the spine's position and allow flexibility for the patient to bend and twist. Until now, fusion of the spinal discs by means of spinal surgery was the only method available for relieving pain of spinal disc injury, but this type of surgery resulted in limited range for the patient.

**Benefits:** Pain is relieved and motion is preserved. In clinical trials, patients with the artificial disc maintained or improved their range of motion, experienced pain relief sooner, had quicker recoveries, and were more satisfied with the procedure than were patients undergoing traditional spinal fusion surgery.


**Name:** ExAblate® 2000 System  
**Manufacturer:** InSightec, Haifa, Israel  
**Approval Date:** October 22, 2004  
**Use Classification:** This system integrates focused ultrasound thermal ablation with General Electric's Healthcare's magnetic resonance imaging (MRI) capabilities to provide a noninvasive method for destroying targeted tissue in women with symptomatic uterine fibroids, a noncancerous condition.

**Description:** The patient lies inside the MRI scanner, which provides three-dimensional images of the fibroid and surrounding tissue. The images enable precise guidance of the ultrasound waves to the target tissue. Highly focused ultrasound waves are directed into the body; at the focal point, the ultrasound waves raise the temperature of the tissue, leading to its destruction. The thermal imaging capabilities of the MRI scanner provide real-time feedback on the temperature achieved at the target tissue during treatment.

**Purpose:** Destruction of uterine fibroids. As many as 77% of women may have the condition but may be unaware of it because they experience few or no symptoms (e.g., heavy bleeding, painful menstrual periods, bleeding between periods, pressure on the lower abdomen, frequent urination resulting from fibroid pressure on the bladder, pain during sexual intercourse, and lower back pain). Treatments have included hysterectomy, myomectomy, uterine artery embolization, and hormonal therapy (which offers only temporary relief of symptoms).

**Benefits:** This is the first FDA-approved focused ultrasound thermal ablation system and ultrasound surgery system to use MRI to eliminate uterine fibroids.


**Recall**

On November 9, 2004, Access Cardio-Systems, Inc., of Concord, Massachusetts, voluntarily recalled 10,000 automated external defibrillators (AEDs), which were used by fire departments and hospitals around the nation. Some of the devices are still in use, and others are at distributors awaiting shipment. The devices did not work properly, and sometimes they turned themselves on automatically.