**NEW DRUGS**

**Dexlansoprazole (Kapidex) For Esophageal Disease**

The FDA has approved dexlansoprazole delayed-released capsules (Kapidex, Takeda Pharmaceuticals) to treat heartburn associated with symptomatic nonerosive gastroesophageal reflux disease (GERD), the healing of erosive esophagitis, and the maintenance of healed erosive esophagitis.

Acid reflux disease can be characterized by frequent, persistent heartburn that occurs two or more days a week despite treatment and dietary changes. Proton pump inhibitors (PPIs) help to reduce acid production by turning off many of the acid pumps in the stomach. Dexlansoprazole combines an enantiomer of a form of Takeda’s lansoprazole (Prevacid) and protects the esophagus from acid reflux so that esophageal inflammation can heal.

In doses of 30 mg and 60 mg, dexlansoprazole provides two releases of medication. Two types of enteric-coated granules result in a profile with two distinct peaks: one to two hours after administration, followed by a second peak within four to five hours. This medication can be taken without regard to meals.

In phase 3 clinical studies, dexlansoprazole provided up to 24-hour heartburn relief with a side-effect profile similar to that of the company’s lansoprazole (Prevacid).

Dexlansoprazole should not be taken with atazanavir (Reyzat, Bristol-Myers Squibb). It can interfere with the absorption of drugs for which gastric pH is important for bioavailability, such as ampicillin esters, digoxin, iron salts, and ketoconazole (Nizoral, PriCara). Patients taking dexlansoprazole along with warfarin (Coumadin, Bristol-Myers Squibb) may need to be monitored for increases in the International Normalized Ratio and prothrombin time.

**Generic Tindamax (Tinidazole) For Sexually Transmitted Diseases**

BioComp Pharma, Inc., has launched Tinidazole 500, the first generic version of Tindamax, an oral antimicrobial second-generation compound. This drug is approved for treating trichomoniasis and bacterial vaginosis as well as giardiasis, intestinal amebiasis, and amebic liver abscess.

Almost 7.4 million new cases of trichomoniasis occur in men and women each year. Trichomoniasis is the most common curable sexually transmitted disease among young women in the U.S., and bacterial vaginosis is the most common vaginal infection in women of childbearing age.

Tinidazole 500 allows for targeted dosing and a shorter course of therapy. It is administered as 1 gram (two 500-mg tablets, once daily for five days) or 2 grams (four 500-mg tablets, once daily for two days) to treat bacterial vaginosis and as 2 grams (four 500-mg tablets for one day) to treat trichomoniasis infection.

**Febuxostat (Uloric) for Gout**

The FDA has approved febuxostat (Uloric, Takeda), the first new gout drug in more than 40 years.

Taken once daily by mouth, this agent is approved for the chronic management of hyperuricemia in patients with gout. The drug blocks an enzyme called xanthine oxidase, which helps prevent uric acid production.

The tablets are sold in strengths of 40 and 80 mg. Febuxostat is not recommended for the treatment of asymptomatic hyperuricemia.

In 2005, the FDA refused to approve febuxostat because slightly more deaths and heart problems occurred in patients taking the drug than in patients taking allopurinol, another gout drug. Because
patients with gout already are at a higher risk of heart disease, the FDA issued an approvable letter. Takeda resolved the safety question by performing a large new phase 3 clinical trial that enrolled more gout patients than the two previous phase 3 trials combined. The new study found no more deaths and no more heart problems in patients taking febuxostat than in patients taking allopurinol (e.g., Zyloprim, Alloprim).

Based on those results, an FDA advisory committee recommended the approval of febuxostat in November 2008.

Adverse events in clinical trials consisted of liver function abnormalities, nausea, joint pain, and rash.

Sources: Takeda, February 14, 2009; WebMd, February 16, 2009

NEW FORMULATION
Daranavir (Prezista) For Pediatric HIV Infection

Tibotec Therapeutics/Centocor Ortho has announced the availability of a lower-dose (75-mg) formulation of darunavir (Prezista) for pediatric patients with HIV infection. These patients must range from 6 to 18 years of age and must weigh at least 44 pounds (20 kg).

In 2006, approximately 56,500 young people between the ages of 13 and 24 years were living with HIV. In December 2008, the FDA approved darunavir, administered with ritonavir (Norvir, Abbott) and with other antiretroviral agents, for treating HIV infection in pediatric patients six years of age and older. In October 2008, darunavir was approved for treatment-naive and treatment-experienced adults as part of combination therapy.

The tablets are taken with food. The dosage, based on body weight, should not exceed the recommended treatment-experienced adult dose. Pediatric dosing is as follows:

- at least 44–65 pounds: darunavir 375 mg/ritonavir 50 mg twice daily
- at least 66–87 pounds: darunavir 450 mg/ritonavir 60 mg twice daily
- 88 pounds or more: darunavir 600 mg/ritonavir 100 mg twice daily

Sources: Medical News Today, February 12, 2009; www.prezista.com

DRUG NEWS
Safety Review for Xigris

The FDA is working with Eli Lilly, the maker of drotrecogin alfa activated (Xigris), to learn more about the incidence of serious bleeding events and death in patients who received this drug. Xigris is used to treat severe sepsis.

In a recent retrospective review of the medical records of 73 patients, serious bleeding events occurred in 35% of those patients who had a risk factor for bleeding and in 3.8% of patients without risk factors for bleeding. More patients with risk factors at baseline died (65%) compared with patients without any risk factors (24.5%).

Xigris may increase the risk of bleeding, described in the prescribing information as the most common serious adverse effect. Xigris is not indicated if bleeding might lead to significant adverse reactions or death.

The FDA is not recommending that practitioners stop prescribing Xigris. Consumers and health care professionals should notify the FDA of any complaints or problems associated with this product.


Adding Cetuximab (Erbitux) Might Not Improve Colon Cancer

In a study from The Netherlands, researchers noted that mixing cocktails of drugs to fight cancer did not always succeed. Adding cetuximab (Erbitux, ImClone/Bristol-Myers Squibb/Eli Lilly) to an already-potent drug combination offered no extra benefit against advanced colon cancer. In fact, patients fared worse when cetuximab was added to three anticancer drugs: capecitabine (Xeloda, Roche), oxaliplatin (Eloxatin, Sanofi-Aventis), and bevacizumab (Avastin, Genentech/Roche).

For volunteers who did not take cetuximab, their tumors remained stable for more than a month longer than the patients who did receive this agent. The non-cetuximab participants also reported a higher quality of life.

The findings might have resulted from a negative interaction between cetux-
imab and bevacizumab. These monoclonal antibodies are designed to starve tumors; however, bevacizumab can raise blood pressure. Patients who received the four drugs did not have higher blood pressure, suggesting that cetuximab may interfere with bevacizumab. Other studies have shown that combining more drugs can sometimes help patients with cancers such as lung cancer.


**Case Report: Inhaled Pentamidine And Toxic Epidermal Necrolysis**

Japanese physicians have reported that aerosolized pentamidine caused toxic epidermal necrolysis, a life-threatening side effect, in a 42-year-old patient with systemic lupus erythematosus (SLE).

The patient began prophylactic treatment with inhaled pentamidine once a month for *Pneumocystis* pneumonia. He was already being treated for SLE and aspergillosis with prednisolone, sodium valproate, voriconazole (Vfend, Pfizer), and lansoprazole (Prevacid, Takeda).

On the day after the pentamidine was started, generalized erythroderma and a fever of 104.4°F developed. More than half of the patient’s body surface was covered with serum-filled blisters and bullae. He also had conjunctival erythema and blisters in the oral mucosa. A skin biopsy revealed ballooning keratinocytes and numerous individual necrotic keratinocytes.

The physicians subjected all the suspected drugs to the lymphocyte-stimulating test, but only the results for pentamidine were positive. They stopped the pentamidine and treated the patient with plasma exchange, followed by methylprednisolone and immunoglobulin. The dose of prednisolone was then reduced. The eruption slowly resolved and did not recur.

The authors cite three case reports of a cutaneous eruption caused by pentamidine and add that toxic epidermal necrolysis has been described with intramuscularly injected pentamidine. To their knowledge, this is the first report of the condition resulting from any inhalant drugs, including pentamidine. Inhaled pentamidine may remain in the tissue for more than two months, which suggests that symptoms of a drug-related eruption can also linger. The researchers caution that the underlying diseases of patients treated with pentamidine may be ones in which drug eruptions are common.


**For Ketoacidosis, SQ Insulin Works as Well as IV**

Subcutaneous (SQ) administration of rapid-acting insulin analogues such as insulin lispro (Humalog, Lilly) may be a reasonable alternative to intravenous (IV) infusions of regular insulin for treating uncomplicated diabetic ketoacidosis.

According to researchers from the University of Pennsylvania in Philadelphia, their meta-analysis shows that the SQ choice is both safe and cost-effective, because it obviates the need for infusion pumps and admissions to intensive-care units (ICUs).

Forty-five patients were treated with IV insulin in an ICU or with SQ lispro on a medical floor or step-down unit. Biochemical profiles, mean venous pH, and mean anion gap were similar in the three groups. There were no statistical differences among the groups in time to resolution of ketoacidosis, the amount of insulin required, or the number of hypoglycemic episodes (one in each group). In addition, no differences were evident in the rate of decrease in plasma glucose levels, correction of acid-base characteristics, or length of hospital stay.

The researchers suggest that because patients can receive SQ insulin on medical floors or step-down units, emergency departments may see a cost savings as well as improved patient flow when ICU beds are scarce.


**Men and Women Respond Differently In Metabolic Syndrome**

The effect of the metabolic syndrome on the response to IV thrombolysis may depend on the patient’s sex, according to researchers from Chile and Spain. It has been noted that the risk of stroke is greater in women than men with the syndrome.

Sometimes called insulin resistance syndrome, metabolic syndrome comprises risk factors for heart disease, diabetes, and stroke. Patients with the syndrome have abdominal obesity, high blood pressure, high blood glucose levels, and low levels of high-density lipoprotein-cholesterol (HDL-C).

In the study, the researchers observed resistance to clot lysis at 24 hours in 42% of the patients. The syndrome was associated with significantly higher odds of resistance to thrombolysis in women.

Although the reasons for the sex difference are not clear, this finding might be explained by a derangement of the endogenous fibrinolytic system related to insulin resistance, which may be more pronounced in postmenopausal women. Citing pediatric studies indicating that girls are intrinsically more insulin-resistant than boys, the researchers suggest that this difference may reappear later in life after the protection afforded by estrogen is lost.

Insulin resistance may also lead to a more severe impairment of the fibrinolytic system in women. Women with type-2 diabetes mellitus have higher

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A 36% reduction in cancer recurrence and metastasis, compared with adjuvant endocrine therapy alone. Toxicity was minimal.

Zoledronic acid inhibits tumor-cell adhesion, invasion, and proliferation; induces tumor cell self-destruction; and stops cancer cells from growing new blood supplies.

The new study involved 1,803 premenopausal women with estrogen-fueled tumors. Each woman received drugs to prevent the ovaries from making estrogen and medications to inhibit cancer cells from using estrogen to grow. The patients receiving zoledronic acid experienced a 36% reduction in cancer recurrence and metastasis, compared with controls.

Cancer cells interact with osteoclasts, which break down bone. Breast cancer cells that migrate to the bones stimulate osteoclasts, which then produce substances that stimulate the cancer cells, resulting in a vicious circle. Osteoporosis drugs inhibit osteoclast activity. As the osteoclasts stop working, they die. In one study, when women took a bisphosphonate, cancer was less likely to spread and survival was prolonged. In another study, cancer was less likely to spread; in a third study, there was no effect.

Bisphosphonates are not advised for all women with breast cancer. Many women taking hormonal therapy for breast cancer already take drugs to protect their bones. Hormonal therapy deprives the body of the bone-building effects of estrogen.

Zoledronic acid and other bisphosphonates are approved to prevent further spread of cancer in bones. Zometa is indicated only for bone complications of cancer, such as fractures, but it is not approved as an osteoporosis drug. Researchers want to learn whether zoledronic acid might benefit patients to the same extent as chemotherapy or hormonal therapy alone.


Good Hospital Practices Lead to Lower Death Rates From Heart Attacks

Hospitals in western New York that used emergency treatment emphasizing evidence-based therapy and good communication among health care providers were able to reduce deaths from heart attacks by 19% for up to one year after patient discharge.

Patients with acute coronary syndromes (ACS) were admitted to the hospital via the emergency department (ED). The lower mortality rate for these patients at one year after discharge indicated that they had continued their therapy after leaving the hospital.

Improved communication among departments about the patients’ care appears to have made a significant difference in outcomes and the quality of care for these patients. This was the first study to investigate a critical-care pathway approach in patients with ACS. The pathway was initiated as soon as patients were reported to have died after batches of heparin were adulterated with over-sulfated chondroitin sulfate, which can be derived from the chondroitin, a dietary supplement. Chondroitin sulfate can mimic heparin’s anticoagulant properties.

Glycerin is used in many drugs, in cough syrups, and in toothpaste. It has been involved in episodes in which diethylene glycol, a poisonous chemical used in antifreeze, was added either intentionally or accidentally as a lower-cost substitute for glycerin, most recently in Nigeria in 2008.

After an opportunity for the public to comment, the standards are scheduled to be implemented in May 2009 for glycerin and in August 2009 for heparin.


Can Osteoporosis Drugs Stop Spread of Breast Cancer?

Premenopausal women with early hormone-responsive breast cancer who took bisphosphonates during adjuvant endocrine therapy appeared to have improved disease-free survival. Bisphosphonates are normally used to prevent and treat osteoporosis. Zoledronic acid (Zometa, Novartis), for example, is given to breast cancer patients who are receiving endocrine therapy to protect bone health.

In the Austrian Breast and Colorectal Cancer Study Group trial, the addition of zoledronic acid reduced the risk of disease progression by 36% compared with adjuvant endocrine therapy alone. Toxicity was minimal.

Zoledronic acid inhibits tumor-cell adhesion, invasion, and proliferation; induces tumor cell self-destruction; and stops cancer cells from growing new blood supplies.

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arrived in the ED and was followed throughout their hospital stay, including discharge drugs and follow-up. Patients received better care for ACS, spent fewer days in the hospital, and received appropriate medications when the critical-care pathway was used.

At discharge, patients were informed about the importance of complying with their prescribed regimens. The study authors also ensured that the patients’ health plans would allow them easy access to cardiac therapies.

Staff members were educated about key elements of the guidelines, which had been established by the American College of Cardiology and the American Heart Association. Research was provided by funding from Sanofi-Aventis, Bristol-Myers Squibb, and the Kaleida Health Foundation.


Monitoring Opioids For Non-cancer Pain

The American Pain Society and the American Academy of Pain Medicine have released the first comprehensive guidelines to assist practitioners in prescribing opioids for patients experiencing chronic non-cancer pain.

The use of long-term opioid therapy for chronic non-cancer pain has grown substantially. An expert panel has concluded that chronic opioid therapy can be effective for carefully monitored patients. However, opioids are also associated with potentially serious adverse effects and outcomes related to their potential for abuse.

The panel addressed such topics as patient selection, risk stratification, informed consent, management plans, initiation and titration of therapy, methadone, patient monitoring, dose escalations, high-dose therapy, rotating opioids, discontinuing therapy, adverse effects, safety during driving and work, break-through pain, and therapy during pregnancy.


Adolescents Might Not Need Cholesterol Drugs After All

Fewer than 1% of American teenagers are likely to need cholesterol drugs to ward off future heart problems, according to a recent study. This news may be reassuring in light of the prevalence of childhood obesity.

In 2008 the American Academy of Pediatrics issued guidelines urging physicians to consider cholesterol drugs for more children (as young as eight years of age) if they had high levels of low-density lipoprotein-cholesterol (LDL-C) as well as obesity and hypertension. However, newer research suggests that many children might not need to take cholesterol drugs.

Researchers studied data from about 10,000 children from 1999 to 2006. Of those, about 2,700 in the 12- to 17-year-old group were assessed for LDL-C levels. From 5% to 7% of these youths had elevated LDL-C. Only 0.8% of this group fit the Academy’s profile of patients needing treatment with cholesterol-lowering drugs. After the academy guidelines were published, however, many people had thought large numbers of children were going to need to take medications for long periods of time.

Abdominal obesity, insulin resistance, and hyperinsulinemia are the common characteristics of youth with the metabolic syndrome. Although most of these young patients tend to be overweight or obese, not all overweight or obese children progress to the syndrome, type-2 diabetes, or cardiovascular disease.

More research is needed to determine whether the metabolic syndrome can actually predict future disease. The researchers advocate studies to examine phenotypes in childhood and adolescence, the molecular basis of the syndrome, the effect of environment or toxins in promoting the syndrome, the role of drugs in insulin resistance, prehypertension, early vascular changes, elevated triglyceride levels, low HDL-C levels; leptin and weight regulation, prenatal and neonatal environments; and prevalence of the syndrome in different racial and ethnic groups.

Sources: Circulation 2009;119:628–647; Associated Press, February 17, 2009

Preventing Postoperative Pain In Older Adults

The long-held belief that acute postoperative pain is merely a symptom, that it resolves while the patient is healing, and that it is not harmful relegates the relief of acute pain to a low priority in the minds of many medical personnel. A study from New York City suggests that aggressively managing pain after surgery might lead to a reduction in the incidence of chronic postoperative pain.

The study, which evaluated an interdisciplinary pain-management program, showed that effective pain control resulted in better rehabilitation for older adults after surgery. The intervention consisted of daily pain assessments by nursing and physical therapy staff members, an analgesic protocol including guidelines for treating opioid side effects for physicians; and informing all clinical staff members of patients’ pain each day.

Patients were interviewed about their pain every day, and they underwent physical performance testing on the fourth and seventh days. They were contacted by telephone every six weeks for 24 weeks after hospital discharge to assess pain and walking ability.

Compared with usual-care patients, those in the intervention group reported less pain at rest and with physical therapy; were less likely to have moderate to very severe pain at discharge and during
their last physical therapy session before discharge; had shorter hospital stays; had faster walk times on the fourth rehabilitation day; and were less likely to miss physical therapy sessions. At six months, they were also less likely to report moderate to severe pain when walking (4% vs. 15%), to have pain that interfered with walking (7% vs. 18%), and to be taking analgesics (35% vs. 51).


**Predicting Early Stent Thrombosis**

About one in 70 high-risk patients with acute coronary syndrome (ACS) eventually experiences early stent thrombosis, whether or not a drug-eluting or bare metal stent is used.

In the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial, researchers found that diffuse atherosclerosis, less-than-optimal angiographic results, and inadequate drug therapy raised the risk of ACS. They analyzed coronary angiography in 3,405 patients with moderate-risk and high-risk ACS who received stents. Of those, 3,043 patients had drug-eluting stents. Within 30 days, definite or probable stent thrombosis developed in 48 patients. Results were almost the same in patients receiving either type of stent and heparin plus glycoprotein (GP) IIb/IIIa inhibitors, compared with bivalirudin (Angiomax, The Medicines Company) with or without GPIIb/IIIa inhibitors (1.1% vs. 1.6% and 1.5%, respectively).

Patients with stent thrombosis were more likely to have insulin-dependent diabetes and renal insufficiency initially, along with more coronary atherosclerosis and suboptimal final angiographic results. Stent thrombosis was also more common in patients who had not been given thienopyridine before the procedure and who were using antiplatelet drugs inconsistently (fewer than half of the days after hospital discharge). However, the strongest predictors of stent thrombosis were a smaller stent lumen diameter, lack of presurgical thienopyridine, extent of coronary artery disease, and a higher baseline hemoglobin level.

Some risk factors are controllable, such as ensuring thienopyridine administration before the procedure, emphasizing the importance of compliance with antiplatelet treatment after stent placement, and not performing percutaneous coronary intervention (PCI) in patients who are likely to be noncompliant.

Source: *Circulation* 2009;119:687–698

**Anti-Tumor Necrosis Factor Agents May Raise Risk Of Herpes Zoster**

Drugs that inhibit tumor necrosis factor-alpha (TNF-α) make patients more vulnerable to bacterial infection, but is the same true of viral infection?

Researchers enrolled 5,040 patients in a German biologics register when they began treatment with infliximab (Remicade, Centocor), etanercept (Enbrel, Amgen/Wyeth), adalimumab (Humira, Abbott), or anakinra (Kineret, Biovitrum, formerly from Amgen) or when they changed conventional disease-modifying anti-rheumatic drugs (DMARDs).

During a three-year follow-up period, 82 patients had 86 episodes of herpes zoster; 39 of these events could be attributed to treatment with anti-TNF-α antibodies, 23 to etanercept, and 24 to conventional DMARDs. After adjusting for age, rheumatoid arthritis severity, and glucocorticoid use, the researchers found a significantly higher risk when patients were treated with monoclonal antibodies. However, the risk was still lower than the threshold for clinical significance. They found no significant associations with etanercept or anti-TNF-α treatment as a class.

Source: *JAMA* 2009;301:737–744

**Sales of Efalizumab (Raptiva) Halted in Europe**

Efalizumab (Raptiva), indicated for treating psoriasis, is being withdrawn from the European market because it has been found to raise the risk of a rare and often fatal brain infection, progressive multifocal leukoencephalopathy (PML). This drug is marketed in Europe by Merck Serono and in the U.S. by Genentech. The FDA is reviewing the situation.


**Problems with Clinical Trials Performed Abroad**

A new study has found that the number of countries conducting drug trials doubled over the past decade.

Much of the testing of late-stage drug trials for use in humans is being done outside the U.S. because results can often be obtained more quickly and less expensively. Bureaucracy and regulatory hurdles in the U.S. might also be increasing interest in conducting studies abroad.

Concerns exist about the ethical treatment of patients and the integrity of the data produced in developing countries. Patients in those countries tend to be taken advantage of because of poverty and their unfamiliarity with the research process. They may be willing to enroll because of a lack of alternative treatments.

Proper research oversight, adequate informed consent, and approval by ethics boards or health officials have been inconsistent abroad. Last year the FDA updated its guidelines for conducting international clinical trials and adopted a standard known as good clinical practices. Critics believe the updated guidelines are less ethically rigorous and more industry-friendly than former guidelines. The new standards protect participants by requiring studies to be reviewed by international ethics committees; each
Stents May Be As Good As Heart Bypass

Patients with severe heart disease who receive stents might be at no higher risk for having a heart attack or dying and may be less likely to have a stroke than patients having conventional heart bypass surgery. However, stent patients are more likely to need additional therapy.

Authors of a large clinical trial concluded that coronary artery bypass graft (CABG) surgery remains the gold standard for treating severe coronary artery disease and three-vessel disease, but the pros and cons of each therapy might not be as clear as previously thought. Stenting, which keeps the arteries open, may also benefit patients with severe disease.

Previously, CABG was the only option. In the study, patients were randomly assigned to either bypass surgery or percutaneous coronary intervention (PCI) with a drug-eluting stent. The patients were treated in the U.S. and Europe. The participants were mostly men, and they were tracked for only one year.

Overall, the stent patients had a higher risk of adverse outcomes (17.8% vs. 12.4% for CABG). The two groups had similar risks for deaths and heart attacks, but CABG patients were more likely to have strokes (2.2% vs. 0.6%). Patients who received stents were more likely to need another procedure (13.5% vs. 5.9%).

CABG was considered to be a better treatment overall. Yet some experts questioned whether an increased risk for an additional procedure, associated with stenting, should carry the same weight as the increased risk of stroke, associated with CABG. Needing another procedure is not optimal, but it was considered better than dying or having a stroke.

In a subsequent analysis, CABG was determined to be preferable for about two-thirds of the patients and stenting was better for one-third of the patients.

Sources: N Engl J Med; Boston Scientific.

Does Alzheimer’s Disease Begin before Birth?

Research at Genentech may change the way we think about the cause of Alzheimer’s disease (AD). A process during prenatal development, in which excess nerve cells and nerve fibers are “pruned” from the brain, might somehow be reactivated in the adult brain and may later cause the death of such cells in patients with AD.

Most experts say that AD is a result of deposits of beta amyloid that accumulate as plaques in the brain, degrading and destroying nerve cells and deleting memories. The new findings indicate that AD might not develop by chance but rather through the activation of a pathway that is already present.

Drugs under development for AD are intended to block the buildup of beta amyloid plaques in the brain; however, beta amyloid can accumulate in the brain without any apparent effect on memory.

During human development, the prenatal brain makes about twice the number of nerve cells that it needs. Those neurons make nerve fibers seeking to connect with other cells. Those cells and nerve fibers that connect survive; those that do not connect trigger a mechanism that clears out unneeded cells.

It is now known that the amyloid precursor protein linked to AD also triggers this prenatal pruning process, but the beta amyloid that appears to kill nerve cells in AD patients is not involved in the developing embryo. Instead, the pruning is sparked by another fragment that causes the death of excess nerve cells and nerve fibers. This suggests that a protein other than beta amyloid might go through a novel pathway to cause AD.

It is not clear exactly what triggers the reappearance of a process fundamental to its early prenatal development in the adult brain. If the process reflects the unwanted death of such cells in AD, it presents several opportunities in which a drug might be able to block the process and possibly prevent damage.

The fact that another protein (netrin-1) appears to regulate the production of beta amyloid suggests that AD is the result of normal processes gone awry. Beta amyloid might be only part of the story. The brain is constantly making and breaking connections; AD might be the result when that process is out of balance.


NEWS FROM NIH

Abnormal Cells Precede Leukemia Diagnosis

Researchers at the National Cancer Institute (NCI) have shown that abnormal white blood cells can be present in the blood more than six years before the diagnosis of chronic lymphocytic leukemia (CLL) is confirmed. In peripheral blood that was obtained up to 77 months before a CLL diagnosis, B-cell clones were present in 44 of 45 patients with CLL.

CLL usually progresses slowly over many years. Although CLL is the most common form of leukemia in adults in Western countries, little is known about its cause.

Previous studies by the NCI, FDA, and others showed that some family members of CLL patients can have B cells with outer-surface proteins that are similar to proteins found on CLL cells. This condition, known as monoclonal B-cell lymphocytosis (MBL), occurs in more than 10% of CLL family members.

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and in about 3% to 5% of healthy adults older than 50 years of age, suggesting that it might be a precursor of CLL.

Although the results of the current study might not lead to routine screening for MBL, the study may influence research. Investigators want to know why some individuals with MBL progress to CLL while others remain free of disease.


Can Genetics Be a Clue to Optimal Warfarin Dosing?

One constant challenge facing practitioners is how to quickly come up with the best dosage of the widely used anticoagulant warfarin (Coumadin, Bristol-Myers Squibb). Warfarin is used to prevent dangerous blood clots that can lead to heart attacks, strokes, or even death. It is a difficult agent to prescribe because it is a difficult agent to prescribe because it can be confined to the benign fibroid tumor without causing damage to the rest of the uterus. Most current treatments usually include invasive surgeries that can result in scarring and infertility.

After testing in experimental animals is completed, clinical trials are planned.

The NIH is launching a large-scale prospective, multicenter, randomized clinical trial in the U.S. to test whether a gene-based strategy for prescribing the initial warfarin dose can improve patient outcomes. Scheduled to begin in March 2009, the trial will enroll 1,200 participants of diverse ethnic backgrounds at 12 sites. In the Clarification of Anticoagulation through Genetics (COAG) trial, researchers will assess how long participants maintain the desired level of anticoagulation at various intervals. Bleeding problems or complications, quality of life, and cost of therapy will also be reviewed.


THERAPIES IN DEVELOPMENT

Gene Therapy Promising For Uterine Fibroids

Some day women with uterine fibroids may find relief with gene therapy. Fibroids occur in nearly 40% of women of childbearing age, beginning in their mid-20s and continuing until menopause. Fibroids are four times more prevalent in African-American women than in women from other ethnic groups. Symptoms include excessive vaginal bleeding, anemia, and fatigue.

Patients with uterine fibroids may have higher medical expenses, and they often need advanced treatment in order to become pregnant. The goals of gene therapy are to decrease symptoms, avoid surgery, and preserve fertility. Research in animals is finding that gene therapy can be confined to the benign fibroid tumor without causing damage to the rest of the uterus. Most current treatments usually include invasive surgeries that can result in scarring and infertility.

After testing in experimental animals is completed, clinical trials are planned.

Source: Fertil Steril, January 14, 2009 online

Will Antibodies From Llamas and Camels Benefit Humans?

A promising new class of drugs is being discovered in animals with soft hair. The immune system of the llama (a relative of the camel) is being studied in hopes of developing treatments for rheumatoid arthritis, cancer, and Alzheimer’s disease.

Llamas, camels, and their alpaca relatives create extremely small antibodies. Antibodies can target proteins that are responsible for diseases. Because the tiny antibodies in llamas and camels are only one-tenth the size of human antibodies, they can move into delicate areas, such as the blood–brain barrier, to block the buildup of plaque in the brain.

Drugs using larger antibodies usually must be injected because the antibodies would be destroyed in the stomach or the lungs. Because smaller antibodies are more resistant to extreme environments, the drugs can be taken orally or by inhaler. Smaller antibodies can also be grown less expensively using bacteria.

Some drug companies are studying animals such as sharks to fight disease. Sharks also produce small antibodies.

It is still unknown whether drugs using small antibodies will work in humans. The first drugs are several years away from being approved for medical use.

Ablynx, a Belgian biotech firm, has patents on using llama and camel antibodies. The company calls the llama antibodies “nanobodies” and is working with Wyeth to develop a new arthritis drug to block tumor necrosis factor-α, which causes inflammation in rheumatoid arthritis. Wyeth would like Ablynx’s product to help replace etanercept (Enbrel) when its patent expires after 2011.
Radio Waves May Detect Early Breast Cancer

The use of radio waves may become a new, safe way to record images of breast cancers.

Mammograms can miss 15% to 20% of breast cancers that are not visible, especially in younger women. With x-rays, it is difficult to distinguish normal fibrous and glandular tissues from cancerous tissue, because their densities are similar. In older women, fibrous and glandular tissues diminish, leaving mainly fatty tissues. Mammography in older women is thought to be more effective, because small cancers are easier to detect in fatty tissue.

In the 1990s, research from the University of Bristol in the United Kingdom was being conducted to study the treatment of breast cancers with microwaves by measuring the electrical properties of breast tissue. It was known that tumors had certain electrical properties.

Micrima, a company that was formed in 2006, has developed a technique known as MARIA (Multistatic Array processing for Radio-wave Image Acquisition). MARIA captures high-resolution, three-dimensional images of the breast via harmless radio waves. Tumors as small as 2 mm across can be detected. Breast compression is not required with MARIA, as in mammography. The transmitted radio wave signal has a power of less than 1 milliwatt, which is considered a very safe exposure. The procedure can be repeated as often as necessary.

In initial trials, MARIA correctly identified all participants with anomalies and cleared all healthy volunteers. The compact size and low cost of MARIA should make it ideal for use in hospitals, diagnostic centers, mobile screening units, and developing countries, where the cost of screening with x-rays is a barrier.

Source: The Wall Street Journal, February 17, 2009

DEVICES IN THE NEWS

Ablation Catheters For Atrial Fibrillation

The first ablation catheters for treating patients with atrial fibrillation (AFib) have been approved. AFib affects more than two million Americans.

The NaviStar ThermoCool saline-irrigated radiofrequency ablation catheter and the EZ Steer ThermoCool Nav (BioSense Webster), create small, strategically placed scars in heart tissue to block irregular electrical waves that cause AFib. The FDA had previously approved other ablation catheters to treat patients with atrial flutter and ventricular tachyarrhythmia but not AFib.

Patients are usually treated with drugs or, in rare cases, with open-heart surgery. Catheter ablation should be used only after drug treatment has failed to control symptoms.

Although AFib is a risk factor for stroke, there is no evidence linking ablation to a reduction in stroke. Therefore, the FDA recommends that patients at risk for stroke continue to take anticoagulant medications after ablation procedures for AFib.

In a clinical study, the catheters were effective in eliminating symptomatic recurrence of AFib episodes for one year in 63% of treated patients but in only 17% of controls. As a condition of the device approval, BioSense Webster must establish a physician-training program and must conduct postmarketing safety studies.

Source: FDA News, February 6, 2009

Brain Device Treats Obsessive–Compulsive Disorder

The FDA has approved the first implantable device designed to deliver electrical therapy to the brain to suppress symptoms associated with chronic, severe obsessive–compulsive disorder (OCD). Medtronic’s Reclaim DBS (deep brain stimulation) Therapy is indicated when drug and psychotherapy have failed. Reclaim DBS is the first psychiatric indication to be approved for DBS.

Collaborative clinical research on DBS therapy using Medtronic devices began in 1998 with the first implant in Europe. Research was also conducted at three medical centers in the U.S.

DBS therapy was studied in 26 patients with severe, treatment-resistant OCD. The long-term results revealed symptom reductions and functional improvement in two-thirds of patients. Most of these patients improved from a severe OCD rating at the start of the study to a mild or moderate rating at various follow-up intervals after the device was implanted. Reductions in OCD symptoms were associated with improvements in psychological, social, and occupational domains.

A total of 23 serious adverse events were reported in 11 subjects (42%); 15 of these 23 events were associated with the surgical implant procedure, the device, or therapy, and all of these events were resolved without further complications. Adverse events, such as anxiety and changes in mood, were transient, and most of these events resolved with adjustments in stimulation parameters.

It is anticipated that Medtronic’s Reclaim DBS Therapy will be used in fewer than 4,000 patients annually for treating OCD. The device is expected to be available in mid-2009.

Sources: Molec Psychiatry, Medical News Today, February 20, 2009
NEW DRUGS

Marvin M. Goldenberg, PhD, RPh, MS

**Name:** RapidSense Methamphetamine Test  
**Manufacturer:** QuantRx Biomedical Corporation, Doylestown, Pa.  
**Approval Date:** January 8, 2008  
**Use Classification:** This drug-of-abuse test is based on the company’s core intellectual property related to lateral flow techniques for consumers and health care professionals.

**Description:** The one-step, positive-read test is designed for use in professional markets.

**Purpose:** Clients can test for drugs of abuse.

**Benefit:** The test is based solely on proprietary technology approved by the FDA.

**Source:** www.medicalnewstoday.com/articles/134797.php

**Name:** PrepaCyte-CB Processing System  
**Manufacturer:** BioE, Inc., St. Paul, Minn.

**Approval Date:** January 19, 2009  
**Use Classification:** PrepaCyte-CB provides public and private cord blood banks with a simple and cost-effective method of processing umbilical cord blood to obtain potentially therapeutic cells for eventual transplantation in humans. These include total nucleated cells and CD34-positive hematopoietic stem cells and progenitor cells.

**Description:** In a multisite in vitro clinical study, the system recovered high yields of total nucleated cells, mononucleated cells, and CD3-positive hematopoietic stem cells and progenitor cells from human umbilical cord blood. The device removes approximately 99% of red blood cells from the final processed cord blood unit, maximizing cryopreservation space and reducing potential problems of ABO incompatibility. The desired total nucleated cells and stem cells remain unmodified during processing. The device is integrated with Stemsoft Software’s StemLab to record, track, and manage all cell-processing and storage data.

**Purpose:** With the greater demand and rapid growth for cord blood utilization for transplantation, PrepaCyte-CB offers an opportunity to improve the quality of cord blood units.

**Benefit:** The device is intuitive and easy to use, and it can be quickly implemented within new and existing cord blood banks. Batch processing and hands-on staff time are reduced. No costly capital equipment or maintenance fees are required; only a standard laboratory centrifuge is necessary to concentrate desired cells after separation. During a clinical study, the benefits of PrepaCyte-CB were so readily apparent that it was an easy decision to switch to this new processing platform. The device helps to control costs, saves time, and consistently obtains high-quality cord

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 blood units.

Source: www.medicalnewstoday.com/articles/135631.php

Precaution With Vascular Access Devices

Several years ago, the FDA alerted radiology personnel about the potential for injury to patients when vascular access devices that are not designed to withstand high pressures are used for power injection of contrast media in computed tomography and magnetic resonance imaging. Over the past few years, the FDA has received at least 250 reports of rupture of vascular access devices under high pressure, sometimes causing fragmentation that necessitates surgery. The ruptured devices included central venous catheters, implanted ports, extension tubing, and IV administration sets. Ruptures occur when the injection pressure is too great for the device to withstand.

To help prevent these ruptures, the FDA is reminding personnel to check the labeling of each vascular access device for its maximum pressure and flow rate. If this information is not available, it should be assumed that the device is not intended for power injection and should not be used for this purpose.

If the maximum pressure that the vascular access device can withstand is unknown, the power injector should be adjusted so that it doesn't exceed this limit. If the recommended pressure for a vascular access device is exceeded, the device could be weakened even though no rupture is evident; under these conditions, the weakened device might not operate properly when it is used again.

Sources: FDA Newsletter, No. 33, February 2009, www.accessdata.fda.gov