NEW DRUGS

“Five-in-One” Vaccine Means Fewer Injections

A new vaccine, which is expected to be able to eliminate six of the 20 injections that babies receive before age two years, has received federal approval. Pediarix™ (GlaxoSmithKline) combines protection, into one injection, against five serious diseases—diphtheria, tetanus, whooping cough (pertussis), hepatitis B, and polio.

The vaccine is to be given in a three-dose series to infants at two, four, and six months of age.

Until now, children needed nine shots to protect them; with the new vaccine, they need only three. This approval represents a major breakthrough and should greatly reduce anxiety for both children and their parents.

(Sources: www.pediarix.com; www.GSKVaccines.com; Associated Press.)

Cardiac Medication Available in I.V. Form

Amiodarone hydrochloride intravenous injection (Faulding Pharmaceuticals) is now available to initiate treatment for, and to prevent, frequently occurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia in patients who have not responded to other therapies. Patients for whom oral amiodarone is indicated but who cannot take drugs orally are also suitable candidates for the injectable form.

The drug is available in packages of 10 ampules, each at a dose of 150 mg/3 ml.

(Source: Faulding Pharmaceutical Company.)

NEW DRUGS

Diuretics for Hypertension Beat Out Newer Rivals

It’s back to the basics for treating high blood pressure, if findings from a long-running multicenter trial are anything to go by. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), supported by the National Heart, Lung, and Blood Institute (NHLBI), compared diuretics with newer medicines and found that the old standbys worked best.

ALLHAT, which was conducted at 623 clinics and centers, began in 1994 and included a double-blind study involving 42,418 patients. Participants were randomly assigned to receive chlorthalidone (a diuretic), amlodipine (a calcium-channel blocker), lisinopril (an angiotensin-converting enzyme–inhibitor), or doxazosin (an alpha-adrenergic blocker). The patients received additional antihypertensive drugs if their health care practitioners thought it necessary.

The alpha-adrenergic arm of the trial was stopped after six years because the patients in that arm had 25% more cardiovascular events and were twice as likely to be hospitalized for heart failure as the patients receiving diuretics.

After five years of follow-up, the patients taking amlodipine, compared with those taking diuretics, had systolic blood pressure (BP) readings that were approximately 1 mm Hg higher, on average, as well as a 38% higher risk of heart failure and a 35% higher risk of being hospitalized for the condition. Patients taking lisinopril had an average systolic BP of 2 mm Hg higher (4 mm Hg higher in black patients), a 15% higher risk of stroke (40% higher for blacks), a 19% higher risk of heart failure, an 11% greater risk of being hospitalized for angina, and a 10% greater risk of coronary revascularization.

Dr. Claude Lenfant, director of the NHLBI, notes that many of the new drugs were approved because—compared with placebo—they reduced blood pressure and the risk of heart disease;

NEW INDICATIONS

Levetiracetam for Children with Epilepsy

A retrospective review of clinical records by a Minnesota epilepsy research team has found that the antiepileptic drug levetiracetam (Keppra®, UCB Pharma), currently approved by the Food and Drug Administration (FDA) for the adjunctive treatment of partial-onset seizures in adults, may be considered as first-line anticonvulsant treatment for children younger than two years of age. Of 20 pediatric patients receiving the drug, 12 showed a greater than 50% reduction in seizures, six experienced a greater than 90% reduction in seizures, and four patients became seizure-free.

The drug has also been found to help epileptic children with a history of underlying behavioral problems. Another study of adults with epilepsy suggested a low side-effect profile.

Approximately 2.3 million Americans have epilepsy, including almost 300,000 children under 14 years of age.

(Sources: Annual meeting, American Epilepsy Foundation, December 6–11, 2002; Minnesota Epilepsy Group PA®, St. Paul.)

Asthma Drug Approved for Hay Fever

Montelukast sodium (Singulair®, Merck), currently on the market for asthma control, has now been approved for the relief of symptoms of hay fever, also known as seasonal allergic rhinitis. The once-a-day tablet can help to relieve a broad array of allergy symptoms for 24 hours and can be used to treat adults and children as young as two years of age.

Most oral allergy medications work by blocking histamine, one cause of allergy symptoms. Montelukast sodium blocks leukotrienes instead of histamine and specifically targets this underlying cause of allergy symptoms. Leukotrienes, which are produced by certain cells in the body, trigger several effects that have been linked to symptoms of asthma and allergic rhinitis. In some studies, they have been associated with both early-stage allergy symptoms (such as runny nose, nasal itching, and sneezing) and late-stage symptoms (such as congestion).

The drug is available in tablet form for adults (10 mg) and as cherry-flavored, chewable tablets for children (5 mg for those aged six to 14 years old and 4 mg for those aged two to five years old).
NEW DRUGS

however, they were not tested against each other.

The researchers advise against stopping patients’ current medications but suggest considering conversion to diuretic therapy. ALLHAT’s findings, says Dr. Jeffrey Cutler, NHLBI Senior Advisor, “refine the current clinical guidelines that recommend starting therapy for hypertension with a diuretic or a beta blocker.”

(Source: National Institutes of Health, news release, December 17, 2002; American Heart Association, News, December 29, 2002; www.americanheart.org; JAMA, December 18, 2002.)

**Statins after Heart Transplantation**

Statins may help keep heart-transplant patients alive longer, say researchers from Munich-Bogenhausen, University Hospital Munich-Grosshadern, and University Hospital Leipzig. According to an eight-year prospective, randomized, unmasked study of 72 patients, 89% of those who were given simvastatin (Zocor®, Merck) four days after transplantation survived, in contrast to 60% of patients who didn’t start a statin regimen until four years later. All patients had been given a strict low-cholesterol diet after surgery. Thirty-five patients were receiving daily statin treatment, and 37 were receiving dietary therapy alone.

The average ages of patients were 49 in the simvastatin group and 47 in the control group. The average donor age was 30 for the simvastatin transplant recipients and 34 for the control-arm recipients.

After four years, the benefits of simvastatin were so much better that all of the patients were offered the drug. The long-term effects might be explained, in part, the researchers say, by the drug’s efficacy in lowering cholesterol levels and thereby reducing the incidence of transplant vasculopathy, a major complication of heart transplantation characterized by thickening of the coronary artery. Early simvastatin treatment halved the incidence of vessel thickening; by eight years after the surgery, transplant vasculopathy occurred in only 24% of the patients taking statins but developed in 55% of the patients being treated with diet alone. There was no difference in organ function between the two groups.

Four patients in the diet-alone (control) group died as a result of transplant vasculopathy, whereas only one transplant patient died in the group receiving simvastatin. No severe adverse effects from the therapy were documented up to the end of the eight-year observation period.

The researchers suggested that simvastatin might be successful in reducing not only cholesterol levels but also the growth of smooth muscle cells, which contribute to vessel thickening.

(Source: American Heart Association; Circulation, December 9, 2002; http://circ.ahajournals.org.)

**Drug Reactions, Acetaminophen, and Liver Failure**

Acetaminophen overdose and idiosyncratic drug reactions have replaced viral hepatitis as the most frequent apparent causes of acute liver failure, say researchers who conducted a multicenter study of 308 patients.

Patients were admitted to 17 tertiary-care centers participating in the U.S. Acute Liver Failure Study Group. Most of the patients (73%) were women, with a median age of 38. Acetaminophen overdose was the most common apparent cause of liver failure, accounting for more than one-third (39%) of the cases. In 13% of the patients, drug reactions were the presumptive cause; viral hepatitis A and B were implicated in 12%. Coma grade at admission was apparently associated with outcome; age and duration of symptoms were not.

At three weeks, 67% of the patients were still alive; 29% underwent liver transplantation, and 43% survived without liver transplantation. However, short-term transplant-free survival varied from 68% for patients with acetaminophen-related liver failure to 25% and 17% for patients with other drug reactions and liver failure of indeterminate cause.

(Source: Ann Intern Med 2002;137: 947–954.)

**Risky Glaucoma Treatment?**

Older patients who are treated with topical beta blockers for glaucoma, a major cause of blindness, may be at a higher risk of airways obstruction—even if they have no history of respiratory disease, say researchers from the Institute of Ophthalmology, Royal Brompton Hospital, and Moorfields Eye Hospital, all in London. Analyzing data from 11,739 patients, they found enough of a heightened risk to recommend that frail elderly patients not be given beta-blocker therapy for glaucoma.

Although topical beta blockers are the most widely prescribed drugs for glaucoma in the United Kingdom, they have been known to exacerbate bronchospasm in patients with asthma and chronic obstructive pulmonary disease and they affect respiratory function in elderly patients with no previous history of airways obstruction. In this study, the attributed risk of new development of respiratory disease was 1,000 patients per year in the United Kingdom, or one case every 11 years for a general practitioner.

Patients with pre-existing airways obstruction might be even more sensitive to beta blockers, the researchers suggest. If airways obstruction develops, they advise discontinuing the drug immediately and notifying the patient’s ophthalmologist. A refilled prescription that includes topical beta blockers and drugs for asthma should automatically signal an alarm, they warn. The study authors even suggested that many frail elderly patients for whom loss of eyesight was not an immediate threat might fare better with no treatment rather than face a risk of airways obstruction.

(Source: BMJ 2002;325:1397–1398.)
**Soy Protein and Warfarin**

If patients who are taking the anticoagulant warfarin suddenly have a lower International Normalized Ratio (INR), health care providers are advised to determine whether they are also consuming soy protein.

A pharmacist at Fallon Clinic, in Webster, Massachusetts, described a patient who was stable with warfarin therapy until he started drinking soy milk daily as part of his treatment for hypertriglyceridemia. Within five days, his INR values began dropping, from 2.5 to 2.3. The patient drank approximately 480 ml of soy milk daily for three weeks while taking his prescribed medications as directed. After four weeks, his INR was 1.6.

A target INR range of 2.0 to 3.0 is recommended for most indications, such as treatment or prevention of deep vein thrombosis, prevention of excess clotting, and other preventive measures for patients with atrial fibrillation. The risk of an embolism or related event doubles if the INR decreases to 1.7, and the risk of hemorrhage rises if the INR is above a range of 4.0 to 5.0.

The patient’s drop could not be explained by changes in warfarin dose or brand, nonadherence, concomitant prescription medications, increased consumption of foods containing vitamin K, or other factors. After he stopped drinking the soy milk, his INR started rising again within a week, to 1.9; over the next two months, his INR returned to normal. The patient experienced no complications with this decline in the INR.

Although soybeans have high amounts of vitamin K, the pharmacist noted that soy protein in the form of soy milk contains only trace amounts of the vitamin and would not be associated with vitamin K–altered warfarin metabolism. However, a soy protein–mediated variation in vitamin K production, by gut bacteria, or altered vitamin K metabolism, by ingestion of soy milk, could not be ruled out, the author said. She also mentioned that soy food products contain isoflavones, which can alter drug absorption, metabolism, and biliary excretion by interacting with the P-glycoprotein (P-gp) efflux system and organic anion-transporting polypeptide (OATP) drug transporter.

To the author’s knowledge, there have been no published studies of a drug–food interaction between warfarin and soy milk; however, she suggested that interactions with soy protein might be more common than the literature indicates, given the wide range of drugs and metabolites whose pharmacokinetics depend on cytochrome P-450 (which is involved in warfarin metabolism), P-glycoprotein, and OATP mechanisms.

The author advises health care professionals to become aware of the potential implications of this drug–food interaction.


**Surprise: More Drugs, Better Adherence**

It is often assumed that the fewer drugs patients have to take, the more likely they are to stick with their treatments. A study of 367 patients from St. Paul’s Hospital in Vancouver, British Columbia, however, has noted some unexpected findings that may put that theory in doubt.

The patients, all of whom had taken an angiotensin-converting enzyme (ACE)–inhibitor or lipid-lowering drug for at least three consecutive months, answered a survey about their nonprescription drug use, adverse effects, and the use of adherence aids.

Of the respondents, 45 (12%) patients were categorized as nonadherent; however, these patients took fewer regularly scheduled prescription medications per day (four versus six), fewer pills per day (five versus nine), and were required to take their medications less often (1.8 versus 2.4 times a day). A lower number of prescription medications was an independent predictor of nonadherence with cardiovascular medications after the investigators controlled for age, sex, reported adverse effects, use of compliance aids, over-the-counter medication usage, use of complementary or alternative medications, and participation in outpatient clinics.

Surprisingly, patients taking seven or more chronic prescription medications daily were the ones most likely to stick with their regimens. However, the proportion of nonadherent patients declined as the number of medications increased, up to 10 medications per day. These findings, the researchers say, might indicate that there is a limit to the number of medications a patient is able to consistently take as prescribed. Still, only 9% of the patients taking 10 or more prescription medications were classified as nonadherent.

The explanation, the researchers speculate, might relate to the type of condition for which the patients were taking medicines. Patients who were taking lipid-lowering drugs were less likely to adhere to their treatment than patients who were taking ACE-inhibitors—having an “asymptomatic” condition might be making some patients less careful about adhering to their treatment regimens. The authors also indicated that patients taking medications on a continuous basis might be sicker and thus more attentive to their drug regimens. In addition, some patients who believe that they are ill (because they have been prescribed a large number of medications) might be more likely to take steps necessary to maintain or improve their health.

(Source: *Ann Pharmacother* 2002;36:1532–1539.)

**REACH Award Announced**

Sanofi-Synthelabo and Bristol-Myers Squibb have announced the launch of the REACH (Reduction of Atherothrombosis for Continued Health) Award Program, which aims to recognize promising work in improving the management of this disease. The closing date for this year’s entries is March 21, 2003.

(Source: www.atherothrombosis.org/reach; press releases.)