NEW DRUGS

Promising New Vaccine To Prevent Cancer-Causing Virus

An experimental vaccine has been found to be 100% effective in preventing the mortality associated with the human papilloma virus (HPV), now considered to be the cause of all cases of cervical cancer. It is expected that the vaccine will be marketed within five years.

Cervical cancer affects almost 450,000 women throughout the world each year, and the mortality rate in women with this disease is 50%. In the U.S, where Papanicolaou (Pap) smears are widely used for screening, cervical cancer occurs in about 15,000 women each year and about one third die as a result of this disease.

The new vaccine is aimed at viral strain type 16, which is responsible for about 50% of cases. Merck & Company and the University of Washington tested the vaccine on American women ages 16 to 23 and observed their status for almost a year and a half. Of the 768 women who received injections, none showed type 16 infection or precancerous tissue; however, of the 765 women who took “dummy” injections, 41 experienced persistent infections and nine had precancerous tissue.

The women who had been inoculated were able to build up almost 60 times the concentration of virus-fighting antibodies than women whose infections are a consequence of natural causes. Some researchers had suspected that the cervical mucous membrane would have posed a barrier to these antibodies.

Because cervical cancer is caused by multiple viral strains, it is unclear whether it can be eradicated completely. One disease specialist emphasized that only the short-term duration of the antibodies is known at this point.

Patients who have not previously taken alpha interferons. (Please see the December 2002 issue of P&T for a review of peg-interferon.)

More patients who received peg-interferon alfa-2a plus ribavirin showed a sustained response to the virus, with the absence of detectable HCV ribonucleic acid (RNA) six months after discontinuation of therapy, compared with patients who received interferon alfa-2b plus ribavirin or peg-interferon alfa-2a alone.

A once-weekly dose was well tolerated and resulted in improvements in the rate of sustained virologic response.


NEW TREATMENT

For Osteoporosis

The FDA has approved teriparatide (Forteo®, Eli Lilly) for postmenopausal women with osteoporosis (thinning of the bones) who are at high risk for bone fracture and for men with primary or hypogonadal osteoporosis who are at risk for fracture.

Forteo is the first in a new class of drugs called bone-formation agents, which stimulate new bone by increasing the number of bone-forming cells (osteoblasts).

Until the release of teriparatide, antiresorptive agents were the only type of approved treatment for delaying or stopping bone loss. These agents work by reducing the number of bone-removing cells (osteoclasts).

Patients will be able to self-administer the drug by a disposable pen device that can be used for up to 28 days. The drug is to be taken for up to two years.


Combination Interferon For Chronic Hepatitis C Virus

Pegylated interferon (peg-interferon) alfa-2a (Pegasys®, Roche), combined with ribavirin (Rebetol®, Schering), is now available for the treatment of patients with chronic hepatitis C virus (HCV). This combination is intended for adults with compensated liver disease and who have not previously taken alpha interferons. (Please see the December 2002 issue of P&T for a review of peg-interferon.)

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NEW INDICATION

Rabeprazole Approved For H. pylori Infection

Rabeprazole (Aciphex®, Eisai Medical Research), a proton pump inhibitor, has been approved for a new indication: seven-day treatment of Helicobacter pylori infection. Other currently approved regimens require 10 to 14 days of proton pump inhibitor treatment.

In a multicenter test, Aciphex®, along with amoxicillin and clarithromycin, eradicated H. pylori infection in 84% of patients treated for seven days and 86% of patients treated for 10 days. In comparison, 10 days of combination treatment with omeprazole, amoxicillin, and clarithromycin eradicated infection in 82% of patients.

The drug combination produced no unique adverse effects. The most frequently reported drug-related adverse events were diarrhea in 8% of patients receiving seven-day treatment and distortion of taste in 6% of patients receiving seven-day treatment.

(Source: Aciphex® product information insert; Eisai news release, November 14, 2002.)
**Babies at High Risk For Adverse Drug Events**

Every year, approximately 250 infants and children younger than two years of age die as a result of adverse drug events (ADEs). This startling number is suggested by a study of more than 500,000 ADEs reported by MedWatch, a Food and Drug Administration (FDA) program, between November 1997 and December 2000.

Over the 38 months studied, 769 deaths among infants and toddlers were associated with a drug or biological product, according to reports from the FDA. The number of reported ADEs rose from 184 in 1998 to 326 in 2000. Nearly half (41%) of the deaths occurred in the first month of life, and 84% occurred within the first year.

The reports identified 1,902 different therapeutic drugs, nontherapeutic chemicals, biological products, vaccines, over-the-counter drugs, vitamins, minerals, dietary supplements, blood products, and illegal substances. However, when the researchers focused on only those cases in which the product was the principal suspect in 20 or more reports, was administered directly to an infant, and resulted in a serious ADE or death, only 17 drugs accounted for 54% of the events.

Some of the implicated drugs included acetaminophen, ibuprofen, cisapride (which has been removed from the U.S. market), palivizumab (Synagis®, MedImmune), and vancomycin (Vancocin®, Eli Lilly).

In 1,432 cases (24%), the drug or biological product causing the adverse effect had been given to the mother, not the infant. In these cases, congenital anomaly or disability was the most common outcome (41% of reported events), and 90% of the ADEs occurred within the first four months of the infant’s life. One quarter of the drugs in the cases of maternal exposure were used to prevent transmission of human immunodeficiency virus (HIV). Zidovudine, lamivudine, nevirapine mesylate (Viracept®, Agouron), and nevirapine (Viramune®, Boehringer Ingelheim) were all reported more than 40 times.

Even though an ADE report alone does not establish a causal link to the medication, the researchers caution, it is usually the result of a strong enough suspicion to warrant a report to MedWatch. Moreover, they add, it is almost certain that the overall total rates of death and serious injury associated with ADEs are much higher than those reported in their study. They cite findings by the FDA that about “90% of serious or fatal adverse drug reactions are never reported. Some studies have found reporting rates around 1%.”

The researchers also indicate that some of the suspected drugs were not even on the market for the entire time studied. Palivizumab, for instance, was marketed during only 24 of the 38 months.

Of 27 products studied between July 1998 and March 2001 in a continuation of the study, 16 now include pediatric labeling. The dosing or the safety section of labeling has been revised in six of the products. Pregnancy registry studies have been established to record the safety of drugs used during pregnancy, but the studies can take years to conduct.

For most medications, the researchers warn, the reports of ADEs provide the first signal of potential risks of drug exposure in utero. Practitioners can help, they conclude, by reporting suspected ADEs, particularly those that involve a drug interaction, a problem with a particular product, or a serious event not already mentioned in the product labeling.

(Source: Pediatrics 2002;110; www.pediatrics.org/cgi/content/full/110/5/e53.)
School of Medicine say probably not, unless the dose is high. The QT interval, a measurement of the time it takes for the heart muscle to contract and relax, typically lasts for four-tenths of a second. If this duration is lengthened as a result of drug therapy, for instance, then an arrhythmia, or an interruption of the heartbeat, may occur.

Studying data from 105,718 patients from three Medicaid programs, the researchers identified patients who had more than one prescription for oral thioridazine, haloperidol (Haldol®, Ortho-McNeil), risperidone (Risperdal®, Janssen), or clozapine (Clozaril®, Novartis) as well as at least two instances of a schizophrenia diagnosis. Patients with schizophrenia were compared with two control groups: patients with glaucoma and patients with psoriasis. These diseases were selected for study because periodic drug prescriptions are required for their treatment and the conditions are not thought to be associated with cardiovascular outcomes.

Compared with the glaucoma and psoriasis patients, patients taking antipsychotic drugs had rate ratios for cardiac arrest and ventricular arrhythmias ranging from 1.7 to 3.2 and for death ranging from 2.6 to 5.8. Compared with haloperidol, thioridazine did not carry higher rates for cardiac arrest, ventricular arrhythmia, or death, even in high-risk patients, women, and patients over 65. At high doses, however, thioridizane might pose a higher risk and there might be a dose–response relationship. As a result, the researchers recommend prescribing the lowest possible dose of thioridazine.

(Source: BMJ 2002;325:1070; www.bmj.com.)

Over-the-Counter Drugs Recommended for GERD

Over-the-counter remedies are acceptable as a first-line treatment for most patients with gastroesophageal reflux disease (GERD), according to a panel of experts appointed by the American Gastroenterological Association, although this opinion appears to contradict recent management recommendations.

The panel advised that patients who have no “red flags” and who have not had heartburn for more than four weeks can obtain safe, rapid, and effective relief from a number of both over-the-counter (OTC) and prescription products. All OTC products have been shown to be more effective than placebo in relieving mild to moderate symptoms of GERD. The panel noted that the combination of a histamine H₂-receptor antagonist (H₂RA)and an antacid, such as famotidine (Pepcid Complete®, Merck), relieves symptoms more effectively compared with the constituent components individually.

Reviewing randomized clinical trials that compared two or more proton pump inhibitors, the panel found minimal clinical differences between the products. Omeprazole (Prilosec®, AstraZeneca), lansoprazole (Prevacid®, TAP), pantoprazole (Protonix®, Wyeth-Ayerst), and rabeprazole (Aciphex®, Eisai) all healed sores at comparable rates. The time needed for healing may have been less for patients taking esomeprazole (Nexium®, AstraZeneca), but the clinical significance was not substantiated, the panel noted. In general, cost was the main difference, the panelists concluded.

(Source: American Gastroenterological Association, news release, November 14, 2002.)

Does Hormone Replacement Therapy Prevent Alzheimer’s Disease?

Just as many women are throwing out their hormone replacement prescriptions, an ongoing study has shown a link between prior use of hormone replacement therapy (HRT) and a reduced risk of Alzheimer’s disease. However, the data suggest that the benefits can take 10 years to appear, say researchers for the Cache County Study.

In this long-term trial, 1,889 women and 1,357 men were first assessed between 1995 and 1997. Between the initial interview and follow-up, 88 women (4.7%) and 35 men (2.6%) were found to have Alzheimer’s disease. Among those over 80 years of age, the risk for women was double that for men; however, in women who reported earlier use of HRT, the risk was 41% lower. Alzheimer’s disease developed in 26 of 1,066 women who had received HRT compared with 58 of 800 women who had never used HRT. The risk varied with the duration of therapy, and this sex-specific increased risk disappeared with more than 10 years of treatment.

If the theory about the 10-year lag time is correct, one of the study coauthors stated that “it explains a very large and seemingly conflicted literature” on the relationship between HRT and Alzheimer’s disease. The study findings corroborate other recent research suggesting that HRT may help prevent Alzheimer’s disease.

(Source: heartwire; www.theheart.org.)