A summary of general medicine news that affects your patients, your practice, and you.

Three Genes Linked With Alzheimer Disease Identified

Two teams of European scientists identified genetic variants associated with Alzheimer disease, according to a report in the *Washington Post*.

Julie Williams, PhD, of Cardiff University in Cardiff, United Kingdom, and colleagues scanned the genomes of about 4,000 patients with Alzheimer and 7,800 controls. Dr. Williams identified three genes that were more common in people with Alzheimer than in controls. One of the genes was a variation in the APOE gene (identified in1993), which leads to the overproduction of amyloid protein. The other two genes–CLU and PICALM–were previously unknown. According to the *Washington Post*, "CLU appears to be involved in 'chaperoning' newly formed amyloid molecules and helping suppress their deposition in the brain," and "PICALM seems to play a role in maintaining healthy synapses. The loss of synapses is highly correlated with loss of mental function in Alzheimer patients."

Philippe Amouyel, MD, PhD, of the Institut Pasteur de Lille, in France, and colleagues, scanned the genomes of 2,000 Alzheimer patients and 5,300 control cases. In addition to identifying the APOE and CLU genes, Dr. Amouyel's team also found the CR1 gene, which is involved in the body's inflammatory response. This gene is also believed to specifically play a role in "capturing and clearing away" amyloid molecules.

FDA Approves Vaccines for 2009 H1N1 Influenza Virus

The US Food and Drug Administration (FDA) approved four vaccines for the 2009 H1N1 influenza virus. Initial lots are expected to be available nationally in October, a news release from the FDA said. The H1N1 vaccines are manufactured by CSL Limited, MedImmune LLC, Novartis Vaccines and Diagnostics Limited, and sanofi pasteur Inc.

Preliminary data from adults participating in multiple clinical studies suggest that the vaccines induce a robust immune response in most healthy adults 8 to 10 days following a single dose of the vaccination. Optimal dosing for children is still under evaluation, the FDA said.

The 2009 H1N1 vaccines are being produced in formulations that contain thimerosal, a mercury-containing preservative, and in formulations that do not contain thimerosal. The FDA warns people with severe or life-threatening allergies to chicken eggs or to any other substance in the vaccine to refrain from getting vaccinated.

The FDA reports that participants in ongoing clinical studies have tolerated the vaccines. Potential side effects of the H1N1 vaccines are expected to be similar to those of seasonal flu vaccines. For the injection form of the vaccine, the most common side effect reported is soreness at the injection site. Other side effects may include mild fever, body aches, and fatigue for a few days after the inoculation. For the nasal spray vaccine, the most common side effects include runny nose or nasal congestion for all ages, sore throats in adults, and fever in children 2 to 6 years old.

The FDA is working with governmental and nongovernmental organizations to enhance the capacity for adverse event monitoring, information sharing, and analysis during and after the 2009 H1N1 vaccination program, the FDA said.

CDC Approves Substitution for Erythromycin Ophthalmic Ointment

InSite Vision Inc. (Alameda, CA) has accelerated the production of AzaSite (azythromycin ophthalmic solution 1%) to compensate for a shortage of erythromycin ophthalmic ointment in the United States. Due to a change in manufacturers, the FDA anticipated limited availability of 1- and 1.3-g tubes of the ointment in the near future and recommended that practitioners reserve all existing supplies for prophylactic use in neonates.

Although no clinical studies have supported the use of AzaSite for the prevention of ophthalmia neonatorum in newborns, the Centers for Disease Control and Prevention (CDC) has "recommended [the drug] as an acceptable substitute for neonatal prophylaxis use where erythromycin ointment is not available." The CDC's support for this substitution is based on existing data about AzaSite's pharmacology and sensitivity to gonococcal bacteria.

Combination HIV Vaccination Reduced Infection Rate

A US-funded study involving more than 16,000 volunteers in Thailand showed that a vaccine made of a combination of Alvac (Sanofi-Aventis SA) and AIDSVax (VaxGen Inc.) reduced HIV infection, according to a report in *Bloomberg News*.

Alvac uses a canarypox virus to transport three HIV genes into the body. The AIDSVax vaccine contains gp120, an HIV protein that enters human cells and helps the body produce neutralizing antibodies to destroy HIV viruses before they can infect healthy cells. In earlier studies, neither vaccine effectively stopped the virus when tested separately.

The researchers enrolled volunteers from Thailand's Chon Buri and Rayong provinces, which reportedly have that nation's highest rates of HIV. Participants were given four doses of the Alvac vaccine and two of the AIDSVax shot over 6 months and were followed for 3 years. Of those who received the vaccine, 51 became infected with HIV, compared with 74 who received placebo, the researchers said. Overall, the combination vaccine reduced infections by 31.2% compared with placebo.

Those in the study who became infected with HIV during the trial were given free access to treatment; however, the vaccine failed to reduce the amount of virus in the blood of those who became infected, *Bloomberg News* said. Further research is needed to understand how the vaccine prevented infections and why it failed reduce the amount of virus in the blood.

Increased PSA Screening May Have Caused Overdiagnosis

Since the prostate-specific antigen (PSA) test was introduced in 1986, data suggest that substantial overdiagnosis has occurred, said a report in the *Journal of the National Cancer Institute*.[1]

H. Gilbert Welch, MD, MPH, of the Dartmouth Medical School, and Peter C. Albertsen, MD, of the University of Connecticut School of Medicine, analyzed data from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program regarding age-specific incidence of prostate cancer and initial course of therapy. Using US Census data, Drs. Welch and Albertsen estimated the excess or deficit in prostate cancer diagnoses and treatment since 1986.

Overall incidence of prostate cancer rose rapidly after 1986, peaked in 1992, and then declined, but to levels considerably higher than those in 1986, the researchers said. For the next 5 years, the rate increased an average of 12% annually. Between 1986 and 2005, the number of annual prostate cancer diagnoses rose 26%.

"Since 1986, an estimated additional 1,305,600 men were diagnosed with prostate cancer, 1,004,800 of whom were definitively treated for the disease," the study authors wrote. "Using the most optimistic assumption about the benefit of screening—that the entire decline in prostate cancer mortality observed during this period is attributable to this additional diagnosis—we estimated that, for each man who experienced the presumed benefit, more than 20 had to be diagnosed with prostate cancer."

1. Welch HG, Albertsen PC. Prostate cancer diagnosis and treatment after the introduction of prostate-specific antigen screening: 1986–2005. J Natl Cancer Inst. 2009. Epub ahead of print.

Drug Reversed Resistance to Chemotherapy in Pancreatic Cancer in Mice

Inhibiting the action of the enzyme TGF-beta-activated kinase-1 (TAK-1) may make pancreatic cancer cells sensitive to chemotherapy, according to a news release. Because pancreatic cancer is resistant to all anticancer treatments, targeting TAK-1 could lead to the development of a drug to treat the disease, said investigator Davide Melisi, MD, PhD, of the National Cancer Institute in Naples, Italy.

Dr. Melisi and colleagues developed a drug that was capable of inhibiting TAK-1. They tested the activity of the TAK-1 inhibitor independently and in combination with gemcitabine (Gemzar, Eli Lilly and Co.), oxaliplatin (Eloxatin, Sanofi-Aventis), and SN-38 anticancer drugs, and in combination with gemcitabine alone in mice.

"The TAK-1 inhibitor increased the sensitivity of pancreatic cells to all three chemotherapeutic drugs [in mice]," Dr. Melisi said in a news release. "By combining it with classic anticancer drugs, we were able to use doses of drugs up to 70 times lower in comparison with the control to kill the same number of cancer cells. [When TAK-1 was combined with gemcitabine there was] a 78% reduction in tumor volumes," he said.

Dr. Melisi and his team intend to conduct a clinical trial to demonstrate the safety and efficacy of the TAK-1 inhibitor in combination with gemcitabine in pancreatic cancer patients.

Long-term Pain Caused Limitations Associated With Aging

Individuals with pain develop the functional limitations classically associated with aging at much earlier ages, according to a study in the *Journal of the American Geriatric Society*.[1]

In a cross-sectional study, Kenneth Covinsky, MD, MPH, of the Division of Geriatrics at the University of California, San Francisco, and colleagues, looked at the data from 18,531 participants (age greater than >50 years) in the 2004 Health and Retirement Study. Individuals were classified according to t50) of the 2004 Health and Retirement Study. Individuals were classified according to their degree of functional limitation, including mobility (ie, walking or jogging), stair climbing, upper extremity tasks, and activities of daily living (ie, bathing, dressing, eating) with or without help.

Overall, 24% of participants were often troubled by pain that was moderate or severe most of the time. Participants with pain had much higher rates of functional limitations than those without pain. For example, of individuals aged 50 to 59 without pain, 37% were able to jog 1 mile and 91% were able to walk several blocks without difficulty. In contrast, of those with pain in the same age group, only 9% could jog 1 mile, and 50% could walk for an extended period of time without difficulty.

"We found that the abilities of those aged 50 to 59 with pain were far more comparable to subjects aged 80 to 89 without pain, of whom 4% were able to jog 1 mile and 55% were able to walk several blocks, making pain sufferers appear 20 to 30 years older" than those who did not experience pain, said Dr. Covinsky in a news release. "After adjustment for demographic characteristics, socioeconomic status, comorbid conditions, depression, obesity, and health habits, across all four measures, participants with significant pain were at much higher risk for having functional limitations." ■

1. Covinsky KE, Lindquist K, Dunlop DD, Yelin E. Pain, functional limitations, and aging. J Am Geriatr Soc. 2009. Epub ahead of print.

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