Federal update

From the NIH

B cells may deliver HIV to T cells

Results from a study indicate that B cells may pass HIV to uninfected T cells during normal temporary attachments that coordinate immune response, say scientists from the National Institute of Allergy and Infectious Diseases, National Institutes of Health. These results increase understanding of how HIV persists in the body and may explain abnormalities in B-cell function observed in patients with HIV infection.

Previous research indicated that HIV genetic material can exist in B cells of patients with HIV and that HIV can infect B cells in vitro. In the current trial, researchers found that significant levels of HIV were attached to the surface of B cells in patients with HIV infection, and, further, that the virus can infect T cells in vitro. Additional testing is being conducted to see if the HIV in infected T cells is genetically related to that found on the surface of B cells, and the manner in which HIV may cause B-cell malfunction.

The report can be found in the September 4 issue of the *Journal of Experimental Medicine*.

Parkinson's disease found to affect nerve endings associated with the heart

Results of a study conducted by the National Institute of Neurological Disorders and Stroke, National Institutes of Health, suggest that besides the loss of neurons that produce dopamine, an effect associated with Parkinson's disease (PD), nerve endings that produce norepinephrine in the heart are also affected in patients with the disease. This suggests that Parkinson's disease is more than a brain disease and may affect the peripheral nervous system as well.

Researchers found that nearly all of the 29 patients with PD in the study had de-

creased numbers of norepinephrine-producing nerve endings in the heart. As norepinephrine and dopamine are both from the family of chemicals called catecholamines, results suggest that whatever causes the loss of dopamine-producing nerve terminals in the brain also causes the loss of sympathetic nerve terminals in the heart. The loss of nerve terminals in the heart was not related to drugs prescribed for patients with PD or to the duration or severity of the disease.

Researchers are conducting further studies to determine if the loss of sympathetic nerve terminals affects other organs besides the heart and why dopamine- and norepinephrine-producing nerve terminals in the heart and in only a particular part of the brain are lost in PD. They believe that the findings may lead to a way of predicting and preventing PD. The study also provides information about orthostatic hypotension, a complication of PD.

The report can be found in the September 5 issue of *Annals of Internal Medicine*.

Study may show cause of narcolepsy

Results of a study funded by the National Institute of Neurological Disorders and Stroke, National Institutes of Health, show that neurons containing hypocretin peptides, associated with sleep and appetite regulation, are reduced up to 95% in the brains of people with narcolepsy. As narcolepsy occurs later in life, the loss of hypocretin neurons after birth could be responsible for the sleep disorder.

The study involved 4 people with narcolepsy and 12 people without the sleep disorder. Staining of the hypothalamus region of each participant's brain showed that the brains of people with narcolepsy had 85% to 95% fewer hypocretin cells than normal brains. The brains with reduced hypocretin cells also showed signs of gliosis and resulting neuronal degeneration. Findings suggest that replacement of hypocretin cells may reverse the symptoms of narcolepsy.

The report can be found in the September issue of *Neuron*.

DASH diet reduced homocysteine

The DASH diet, already found to lower blood pressure, also reduces homocysteine, high levels of which are associated with heart disease, stroke, and peripheral vascular disease, indicate results of a study funded by the National Heart, Lung, and Blood Institute, National Institutes of Health.

First results from the trial indicated that the DASH diet—rich in fruits, vegetables, and low-fat dairy products, as well as lower saturated fat, total fat, and cholesterol levels with the addition of whole grains, poultry, fish, and nuts—lowers blood pressure levels. A recent evaluation of the results of the trial also indicates that homocysteine levels of participants on the DASH diet were lower than levels for participants in groups following other diets.

The report can be found in the August 22 issue of *Circulation*.

NHLBI statement regarding zidovudine for prevention of HIV transmission to infants

Claude Lenfant, MD, Director of the National Heart, Lung, and Blood Institute, National Institutes of Health, has announced results of an AIDS study that indicate zidovudine (AZT) is not associated with any significant negative clinical effects on the heart and there are "no significant differences in cardiac function between children exposed to AZT and those not exposed."

The study was initiated in response to results of other studies that suggest that use of AZT to prevent the spread of HIV

from mother to child may result in cardiac abnormalities in infants. In light of the current study, Dr Lenfant recommends that physicians continue using AZT to treat pregnant women with HIV.

The report can be found in the September 14 issue of the *New England Journal of Medicine*.

Osteonecrosis of the hip common complication in HIV infection

Magnetic resonance imaging of 339 patients with HIV revealed that 15 participants had osteonecrosis compared with none of 118 patients without HIV, say researchers from the National Institute of Allergy and Infectious Diseases, National Institutes of Health. The 15 patients with osteonecrosis had lesions in one or both hips, and all were asymptomatic.

Although the cause of osteonecrosis is unclear, patients with the disorder are more likely to have taken testosterone, lipid-lowering drugs, and corticosteroids—all prescribed modes of therapy for HIV infection. Researchers had not seen this complication in patients with HIV until 1 year ago.

The report was presented at the annual meeting of the Infectious Diseases Society of America, which took place September 8 in New Orleans.

From the FDA

FDA permits heart disease health claim for plant sterols and stanols

The Food and Drug Administration has authorized labeling health claims for foods containing plant sterol or plant stanol esters based on evidence that they may help reduce the risk of coronary heart disease by lowering blood cholesterol. Plant sterols and, in smaller quantities, plant stanols are found in fruits, vegetables, nuts, seeds, cereals, legumes, and other plant sources. Studies indicate that a total daily intake of 1.3 g per day of plant stanol esters or 3.4 g per day of plant stanol esters, eaten twice daily with meals, is needed to achieve a cholesterol-lowering effect.

Labeling for spreads, salad dressings,

and dietary supplements may qualify for the health claim if they also meet requirements for low saturated fat and cholesterol and contain 13 g or less of fat per serving. Foods must also contain a minimum of 10% of the Reference Daily Intake (RDI) for vitamins A and C, iron, calcium, protein, or fiber.

FDA approves anastrozole for patients with breast cancer

The Food and Drug Adminstration approved anastrozole (Arimidex) for treatment of patients with advanced postmenopausal breast cancer. Previously given only when tamoxifen citrate failed to produce a response, anastrozole inhibits the production of estrogen from adrenal glands.

Approval of the drug as a first-line treatment is based on two trials. In one, anastrozole delayed time to tumor progression for an average of 11.1 months compared with 5.6 months for tamoxifen. In the other trial, anastrozole was found to be equally effective as tamoxifen.

Update on levonorgestrel implants (Norplant System)

In August, Wyeth-Ayerst Pharmaceuticals advised healthcare providers to discontinue insertion of levonorgestrel (Norplant System) implants from lots distributed beginning October 20, 1999, because of questionable contraceptive efficacy. Specified lot numbers and expiration dates follow:

□ 3990729 (1/04)

- □ 3993006 (1/04)
- ☐ 3003355 (1/04)
- □ 3990775 (1/04)
- ☐ 3003127 (1/04)
- ☐ 3990776 (1/04)
- □ 3003166 (1/04)
- ☐ 3003166 (2/04)

As previously advised, any patient who received a Norplant System implant from these lots should use a back-up, barrier, or other nonhormonal method of contraception.

Wyeth-Ayerst continues analysis of the lots in question and shares results with the Food and Drug Administrion. Wyeth-Ayerst cautions that the contraceptive efficacy of Norplant Systems from these lots cannot be assured and further recommends no new insertions of Norplant Systems

from these lots due to their low levonorgestrel release rate.

Wyeth-Ayerst requests that healthcare providers actively identify and counsel women who received a Norplant System from the specified lots using the following guidelines:

- To identify concerned patients, check files for records of Norplant System insertions beginning October 20, 1999. If lot numbers are not available, assume that any insertions performed on or after October 20, 1999, are from the specified lots. A letter template to inform appropriate patients is available from Wyeth-Ayerst by calling 1-800-364-9809.
- Counsel affected patients who received Norplant System implants from the specified lots to use additional contraceptive methods as cautioned previously. Financial assistance to patients to cover this as well as coverage for patients wishing to have a Norplant System from the specified lots removed is available by calling the information line provided in this update.
- Finally, while the investigation continues, no further Norplant System kits are available. Healthcare providers may return their inventory of kits from the specified lots.

From the CDC

Levels of phthalate metabolites measured in humans

Researchers at the Centers for Disease Control and Prevention achieved the first-ever measurement of seven phthalate metabolites in humans and found a significant presence of four in more than 75% of the samples analyzed. Animal studies of phthalates—chemicals used in solvents, detergents, plastics, etc—had shown a possible link to cancer and reproductive problems.

Results confirm estimates of human exposure to all phthalates but indicate a higher exposure level for one phthalate than anticipated. Phthalates found at the highest levels include diethyl phthalate, dibutyl phthalate, and benzylbutyl phthalate, used in detergents, lubricating oils, solvents, wood finishes, and cosmetics. Phthalate levels ranged from below detection to 15 ppm.

Other phthalates, used as plasticizers in flexible polyvinyl chloride (PVC) products such as food packaging, blood bags, and children's toys were present but not found to be highest in the samples.

The study involved the urinalyses of 289 adults aged 20 to 60 years randomly selected from participants in a national survey that included medical examinations and biologic samples for participants. Scientists believe the study is significant in indicating how we should assess environmental exposures, and they cite the need for additional studies to determine sources of exposure to phthalates.

The report can be found in the October issue of *Environmental Health Perspectives*.

Smoking rates among US high school students may have plateaued or declined

Following years of increased smoking rates for high school students, current combined rates indicate a decline during the late-1990s, reports the Centers for Disease Control and Prevention.

Rates for male high school students leveled or declined during this period while rates for female high school students remained mostly unchanged (35.4% and 34.3% in 1995; 37.7% and 34.7% in 1997; and 34.7% and 34.9% in 1999; respectively).

In 1991, white students were 2.5 times more likely to smoke than African American students and 1.2 times more likely to smoke than Hispanic students, similar to 1999 rates, with white students found to be twice as likely to smoke as African American students and 1.2 times more likely to smoke than Hispanic students.

During the same period, rates for ninthgrade students plateaued or declined compared with rates for twelfth-grade students, which continue to rise each year.

Data suggest that evidence-based curricula and guidelines, which could prevent smoking onset in 20% to 40% of US adolescents, are not being implemented in schools.

Recommendations to reduce number of cesarean sections issued

Guidelines to help hospitals and physicians review and reduce cesarean rates were issued by the American College of Obstetricians and Gynecologists (ACOG) in response to statistics announced by the Centers for Disease Control and Prevention showing cesarean section delivery rates up in 1999, the third year in a row after a decline that began in 1989. Cesarean deliveries accounted for 22% of the 3.9 million births in the United States in 1999.

The ACOG has provided a risk-based formula to aid in more accurate calculation to facilitate comparison of overall cesarean delivery rates. The first-time cesarean delivery rate goal for 2010 has been set at 15.5%.

Recommendations also outline steps to reduce the number of surgically-assisted deliveries, including increased training in the use of forceps and other delivery tools, use of vacuum devices, increased presence of nurses and other support for women in labor, and 24-hour obstetric coverage by hospitals.