Federal update

From the NIH

Enzyme may protect against premature death of brain cells

In animal studies, it was found that the absence of an enzyme associated with the life span of cells, telomerase, increased the cell's susceptibility to death from amyloid β-peptide, which accumulates in the brains of people with Alzheimer's disease and other disorders. Conversely, National Institutes of Health researchers observed that high levels of telomerase block neuronal apoptosis, responsible for death of nerve cells in experimental models of Alzheimer's disease, Parkinson's disease, and stroke.

Findings that the overexpression of telomerase in fibroblasts extends their life span suggest a neuroprotective function of the enzyme. Future research will explore stimulating telomerase in nerve cells to stop age-related neurologic disorders and new approaches based on these findings in the treatment of patients with cancer and neurodegenerative disorders.

Report shows incidences of cancer and death rate for all cancers combined have declined

According to a new report released by the National Cancer Institute, National Institutes of Health and other organizations, there were declines in new incidences of cancer and in death rate for all cancers combined between 1990 and 1997, as well as cases of cancer at the major cancer sites.

The report states that between 1990 and 1997 the new cancer incidence rate for all cancers declined 0.8% per year. Joinpoint analysis, which allows observation of trends over segments of time rather than by use of overall trends, revealed that the rate of incidence had its greatest decrease (1.3%) after 1992. Cancer mortality declined 0.8% per year between 1990 and 1997, while lung, prostate, breast, and colorectal cancer comprised half of all new cancer cases. Breast cancer incidence rates have changed little since 1990, while breast cancer death rates have dropped sharply since 1995.

The greatest decline in cancer incidence rates has been among men, and major differences in cancer incidence were shown by race and ethnicity, with African Americans having the highest rates for the top cancer sites.

The report includes a special section on colorectal cancer, which has the third highest incidence of any cancer site for American men, ranks second to breast cancer for Hispanic, American Indian/Alaskan native and Asian/Pacific Islander women, and ranks third for black and white women. The report underscores the need to improve the rates of colorectal screening—screening that could clearly save lives.

Celecoxib (Celebrex) tested for precancerous conditions

The National Cancer Institute, National Institutes of Health is sponsoring studies of celecoxib for use as a preventive for several precancerous and cancerous conditions, among them familial adenomatous polyposis. A trial found that celecoxib reduced the number of colon polyps thought to be precursor lesions of colorectal cancer in patients with familial adenomatous polyposis.

Celecoxib was FDA-approved for the treatment of osteoarthritis and adult rheumatoid arthritis in 1998. It inhibits an enzyme known as cyclooxygenase-2 (COX-2), typically induced in inflammation and precancerous tissues. Research shows that patients taking nonsteroidal anti-inflammatory drugs, which inhibit both COX 1 and 2—with medical problems (eg, stomach bleeding) associated with inhibition of COX 1—have lower rates of colorectal polyps and cancer. Based on these data and animal models, NCI is supporting studies of several COX inhibitors and sponsoring studies of the use of celecoxib for sporadic polyps, hereditary nonpolyposis colon cancer syndrome, Barrett's syndrome, bladder dysplasia, and actinic keratoses as well as further research on familial adenomatous polyposis.

The report was published in the June issue of the *New England Journal of Medicine*.

Thalidomide induces partial responses to Kaposi's sarcoma

In a Phase II study, researchers from the National Cancer Institute, National Institutes of Health found that thalidomide has clinical activity against Kaposi's sarcoma in 40% of trial participants. Thalidomide, which caused shortened arms and legs in newborns when used in the 1950s and 1960s as a sedative, was found to be an inhibitor of angiogenesis. Scientists posited that the drug might be effective against Kaposi's sarcoma.

The study involved 20 patients between the ages of 29 to 49 who were diagnosed as HIV-positive with Kaposi's sarcoma that had progressed for 2 months. To determine the most efficacious dose, trial doses ranged from 200 mg/d to 1000 mg/d for 6 months with adjustment to avoid adverse effects. Although none of the patients achieved complete remission, eight showed a 50% decrease in the number of lesions, two had no change, and seven progressed in the disease.

The main side effect was drowsiness. Seven patients had depression, which researchers say can be managed by lowering the dose.

The report can be found in the July issue of the *Journal of Clinical Oncology*.

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Establishing stroke centers in hospitals recommended

The Brain Attack Coalition, chaired by the National Institute of Neurological Disorders and Stroke, National Institutes of Health, is advocating the establishment of stroke centers within hospitals to reduce incidences of death and complications from stroke.

The coalition, composed of organizations dedicated to improving stroke treatment, points out that, as hospitals are equipped to treat trauma patients, so should they have the staff and equipment to effectively treat stroke patients and provide clot-busting drugs within the critical 3-hour period of symptom onset. They identify two important areas requiring change: improvement in the level of care and standardization of some aspects of treatment.

The organization identified two types of stroke centers to be established—primary care centers that provide emergency care and comprehensive care centers to provide extensive care.

Combining interleukin-2 with antiretroviral drugs boosts CD4+ T-cell counts without increasing HIV levels

Researchers from the National Institute of Allergy and Infectious Diseases, National Institutes of Health conducted the first trial intended to show the effects of adding interleukin-2 (IL-2) to anti-HIV drug therapy. Results after 1 year of treatment showed that CD4+ T-cell counts for participants receiving both IL-2 and antiretroviral drugs increased to 112% compared with 18% in participants receiving antiretroviral drugs alone. Further, the viral load of the IL-2 group was slightly lower, and indicators of potent viral suppression were greater in the IL-2 group.

Prior studies indicated that IL-2 therapy can increase CD4+ T-cell counts in patients with HIV infection. The current 2-year study, designed to provide information about the effect of combining IL-2 with antiretroviral drugs, involved 78 HIV-infected patients receiving antiretroviral therapy who had CD4+ T-cell counts ranging from 200 cells per microliter to 500 cells per microliter. Participants were assigned to one of two groups: those with IL-2 added to their anti-HIV drug regimen (twice-daily, 5-day courses at a starting dose of 7.5 million IU) and those continuing antiretroviral therapy alone.

The study shows that IL-2 affects viral load; however, scientists point out that the effect is not large and may be obscured by the effect of antiretroviral drugs. They expect two Phase II studies, expected to be completed by the end of the year, to clarify the effects of IL-2 on viral load.

Marijuana limits immune response, promotes tumors

Animal studies indicate that tetrahydrocannabinol, the psychoactive element of marijuana, impairs the body's immune response by increasing the availability of an immune suppressor, thereby promoting tumor growth.

National Institute on Drug Abuse researchers also point to higher concentrations of carcinogenic hydrocarbons, including benzapyrene, in the tar portion of marijuana smoke that, when combined with the immune-suppressing characteristic, may increase the risk of respiratory tract cancer. They suggest further studies to evaluate this possibility.

From the FDA

FDA approves Camptosar for advanced colorectal cancer

The Food and Drug Administration has approved irinotecan (Camptosar), a topoisomerase-I inhibitor, as a result of studies that show its ability to increase survival time of patients with colorectal cancer and delay tumor growth when combined with the standard drug treatment of 5-fluorouracil and leucovorin. Camptosar had already been approved to treat patients with colorectal cancer when other treatments failed.

Two clinical trials compared Camptosar, in combination with 5-fluorouracil and leucovorin, with 5-fluorouracil alone. In each of the studies, median survival time of patients receiving Camptosar was 2 to 3 months longer than patients taking 5-fluorouracil alone. Side effects included severe diarrhea, vomiting, and decreased white blood cells.

Cancer-related information available at new FDA Web site

The Food and Drug Administration's Center for Drug Evaluation has launched the *Oncology Tools* Web site to provide cancer-related information to health professionals and patients.

Located at *www.fda.gov/cder/cancer*, the site provides information on types of cancer and treatments, trials, and drug therapies.

Information specific to healthcare professionals includes cancer-related regulatory tools, references for performing clinical studies, and drug dose calculators. The site includes links to each of the FDA's other review divisions responsible for oncology products.

From the AHRQ

Patients with myocardial infarction without chest pain have increased chance of in-hospital death

A study funded by the Agency for Healthcare Research and Quality found that patients who had myocardial infarction (MI) without the key symptom of chest pain—33% of all patients with MI in the study—had an increased chance for in-hospital death (23.3% compared with 9.3% for patients with chest pain). The study also showed that patients with MI without chest pain were more likely to receive delayed treatment and less likely to be diagnosed as having MI and, therefore, less likely to receive thrombolysis or primary angioplasty, β-blockers, heparin, or aspirin.

The 4-year study involved 434,877 patients with diagnosed MI, 33% of whom presented without chest pain. Those without chest pain were on average 7 years older than those patients with chest pain (74.2 years vs. 66.9 years), were more often women, and more often had diabetes mellitus or previous heart failure.

Researchers suggest health initiatives emphasize that chest pain is not necessarily a key feature in MI cases. ♦

From the HHS

Health Service guideline entreats health professionals to aid tobacco-dependent patients

Guidelines from the US Public Health Service show evidence that people who attempt to quit smoking are more successful when they have the support of a health professional. The report, "Treating Tobacco Use and Dependence: A Clinical Practice Guideline," suggests making the treatment of tobacco dependence a top priority with such tools as bupropin SR, nicotine gum, patches, inhalers, and nasal sprays as well as telephone counseling.

Evidence indicates that 25% of US adults smoke and that 70% of them would like to quit. It also points out that tobacco dependence is a chronic disease that requires treatment over time to gain control. Only half of smokers who visit a doctor are urged to quit despite the fact that smoking is the single greatest preventable cause of illness. The report concludes by suggesting that healthcare insurers and purchasers include tobacco dependence treatment as a covered benefit.

The report can be found in the June 28 issue of the *Journal of the American Medical Association.*