Research Highlights

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Human Papillomavirus and Chlamydia Infections Are Associated With Cervical Cancer

One of the major known causes of cervical cancer is human papillomavirus (HPV), also known as genital warts. HPV is a sexually transmitted disease, but little is known about why it persists in some women and not in others. The persistent form of HPV, which accounts for about 40% of cases, is most strongly associated with cancer. Routine condom use seems to protect against persistent HPV, but other factors for prevention are unknown.

Chlamydia trachomatis is a sexually transmitted disease that is fairly common but often asymptomatic, so diagnosis frequently is delayed. Women typically are diagnosed with chlamydia when they seek health care for other reasons. Unlike HPV, chlamydia usually can be treated with antibiotics.

Researchers in Sweden recently discovered that chlamydia trachomatis is associated with HPV persistence and cervical cancer. A group of 12,527 women participated in this population-based screening with 6,418 advancing to HPV DNA testing. These women were contacted again after about 19 months, and 303 who had been HPV positive previously were retested with the same method. Previous sexually transmitted diseases also were assessed by serology, and environmental exposures were assessed by an 87-item questionnaire. Forty-four percent of the women were positive for the same type of HPV as they had previously. Although condom use seemed to protect against persistent HPV, the most significant risk factor for persistence of HPV was a self-reported history of a previous chlamydia trachomatis infection.

Researchers now know that women with HPV and chlamydia are at high risk for cervical cancer and should be monitored closely. With more research, cervical cancer may be prevented or diagnosed early with improved outcomes.

Silins, I., Ryd, W., Strand, A., Wadell, G., Tornberg, S., Hansson, B.G., et al. (2005). Chlamydia trachomatis infection and persistence of human papillomavirus. *International Journal of Cancer, 116,* 110–115.

Mortality Increased for Gulf War Veterans Exposed to Destruction of Chemical Weapons

Chemical weapons are known to contain substances that cause health problems, many of which are not immediately evident. The goal of these weapons is to weaken the enemy by causing death or disease. Any soldier can be exposed to the weapons, but those involved in their destruction are at higher risk because of the release of chemicals. In March 1991, disposal units in the U.S. Army destroyed two large weapons in Khamisiyah, Iraq. In October 1991, March 1992, May 1992, and May 1998, representatives from the United Nations inspected Khamisiyah and detected the agents sarin and cyclosarin in the area. Sarin is a toxic nerve agent that can be absorbed by the skin, eyes, or mucous membranes. In large doses, it can cause seizures and death, but smaller doses result in fatigue, vision problems, and headaches. Sarin is not a known carcinogen. Protective equipment often is worn by soldiers, but the multitude of agents used in chemical weapons makes anticipated protection difficult.

American researchers investigated whether U.S. Army Gulf War veterans who potentially were exposed to nerve agents in Khamisiyah in 1991 were at increased risk for mortality. This was done by comparing 100,487 exposed veterans to 224,980 unexposed veterans, and 1,179 deaths for those exposed to 2,696 of those not exposed. This study was completed during a 10-year period with follow-up of veterans done in three increments. Cause-related mortality was classified into groups according to the *International Classification of Diseases* (ninth revision). For most disease-related mortality, the risks were similar between both groups. However, veterans who were exposed had an increased risk of death from brain cancer when compared to those not exposed. This risk was further increased if exposure occurred on two or more days compared to only one. The risk was the greatest at the third follow-up period or six to nine years postexposure. Other demographic data of the exposed group included a mean age of 27.7 years, Caucasian race (64%), and male gender. The investigators noted that additional research is required to validate these findings. Gulf War veterans from the 1990s should be followed closely for signs of brain cancer so that appropriate treatment can be initiated.

Bullman, T., Mahan, C., Kang, H., & Page, W. (2005). Mortality in US Army Gulf War veterans exposed to 1991 Khamisiyah chemical munitions destruction. *American Journal of Public Health, 95,* 1382–1388.

Bevacizumab Improves Survival in Advanced Non-Small Cell Lung Cancer

Researchers at the American Society of Clinical Oncology Annual Meeting in May 2005 in Orlando, FL, reported that the addition of bevacizumab (Avastin®, Genentech, Inc., South San Francisco, CA) to platinum-based chemotherapy (paclitaxel and carboplatin) significantly improved overall survival by 30% in a study of 434 subjects with untreated style IIIb or IV non-small cell lung cancer compared to 444 subjects who only received chemotherapy. After a follow-up of nine months, the subjects who received bevacizumab experienced significantly longer survival (12.5 months) than the subjects who received standard chemotherapy (10.2 months), a higher response rate (27% versus 10%), and longer time to cancer progression in (6.4 months versus 4.5 months). New and standard treatments were well tolerated. The most significant side effect was fatal bleeding, primarily from the lungs. This was infrequent but more common in patients who received bevacizumab (1%–2% versus none in standard therapy groups).

Institute Expands Effort to Revolutionize National Human Genome Research

The National Human Genome Research Institute, which is part of the National Institutes of Health, announced that it has awarded

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$32 million to advance the development of innovative sequencing technologies intended to reduce the cost of DNA sequencing and expand the use of genomics in biomedical research health care. This is aimed at speeding the rate at which the next generation of sequencing technologies becomes available in scientific laboratories and medical clinics. This will substantially reduce the cost of sequencing a genome and provide a quantum leap in the scope and score of research aimed at uncovering the genomic contributions to common diseases such as cancer.

National Institutes of Health. (2005). NHGRI expands effort to revolutionize sequencing technologies [Press release]. Retrieved October 6, 2005, from http://www.genome.gov/15015208

Study Compares Nebulized Versus Subcutaneous Morphine in Cancer-Related Dyspnea

Dyspnea is a frequent and difficult complication in advanced cancer. In most patients, dyspnea results from invasion of the lungs, pleural effusion, underlying lung disease, pulmonary embolism, or chronic heart failure. In most cases, the underlying cause of dyspnea is not reversible. Symptomatic treatment is indicated to help make patients more comfortable. Morphine is the current drug of choice for cancer-related dyspnea, but its use is questionable because of the side effects of sedation and cognitive impairment in patients who often are impaired already. Other routes or methods of morphine administration are needed to avoid side effects and allow patients with dyspnea to be better treated.

Researchers in Australia have studied the effects of nebulized morphine in patients with cancer-related dyspnea. They compared nebulized morphine to subcutaneous (SC) delivery on the intensity of dyspnea using a scale of 0–10. Patients with a resting dyspnea intensity of three or greater were included in the study, as well as those who received oral or parenteral opioids. On day 1, patients received either SC morphine plus a nebulized placebo or nebulized morphine plus SC placebo. On day 2, a crossover was done, putting the patients who received SC morphine plus nebulized placebo initially in the nebulized morphine plus SC placebo group and the reverse for the other group. Dyspnea decreased from a mean of five to three after the SC morphine and from four to two after nebulized morphine. Because of insufficient power from a limited sample size of 11, a significant difference between the two groups was not noted. This small study does, however, show that nebulized morphine is similar to SC delivery in dyspnea relief. The investigators recommended that larger randomized controlled trials be done to verify these results in patients with cancer-related dyspnea, but this may be difficult because of the cognitive impairment in many patients with cancer and dyspnea.

Bruera, E., Sala, R., Spruyt, O., Palmer, J., Zhang, T., & Willey, J. (2005). Nebulized versus subcutaneous morphine for patients with cancer dyspnea: A preliminary study. *Journal of Pain and Symptom Management, 29,* 613–618.

National Cancer Institute Approves Clinical Trials

The National Cancer Institute's Cancer Therapy Evaluation Program approved the following clinical trials in July 2005. For further information about a study, contact the principal investigator listed.

Phase I

- Open-Labeled Non-Randomized Phase I Study of 17-N-Allylamino-17-Demethoxy Geldanamycin (17AAG) Administered With Irinotecan (CPT-11) in Patients With Advanced Solid Tumors. Memorial Sloan-Kettering Cancer Center, protocol 7009; Archie Ngai-Chiu Tse, 212-639-7599 (phone)

Phase II

- Phase II Study of BAY 43-9006 in Stage IV Malignant Melanoma. Weill Medical College of Cornell University, protocol 6617; Anna Pavlic, 212-263-6485 (phone)
- Phase II Study of GW572016 and Tamoxifen in Patients With Metastatic Breast Cancer to Single-Agent Tamoxifen. Wayne State University, protocol 6724; Elaina Garner, 313-745-9155 (phone)
- Phase II Study of Suberoylanilide Hydroxamic Acid as Salvage Therapy in Metastatic Breast Cancer. City of Hope National Medical Center, protocol 6918; Thehang Hoai Luu, 626-256-HOPE (phone)
- Randomized Phase II Study of Radiation Cancer Therapy, Pemetrexed and Carboplatin With B or Without Cetuximab in Stage III Non-Small Cell Lung Cancer. Cancer and Leukemia Group B, protocol 30407; Ramaswamy Govidan, 314-362-4819 (phone)
- Phase II Feasibility Trial Incorporating Bevacizumab Into Dose Dense Doxorubicin and Cyclophosphamide Followed by Paclitaxel in Patients With Lymph Node Positive Breast Cancer. Eastern Cooperative Oncology Group, protocol E2104; Kathy Miller, 317-274-0920 (phone)
- Phase II Study of Bortezomib (Velcade, PS-341), Thalidomide, and Dexamethasone in Patients With Refractory Multiple Myeloma. Southwestern Oncology Group (SWOG), protocol S0417; Raymond Thertulien, 501-686-8250 (phone)
- Phase II Trial of BAY 43-9006 in Patients With Platinum-Treated Extensive Stage Small Cell Lung Cancer. SWOG, protocol S0435; Jennifer Gitlitz, 323-865-3959 (phone)
- Nonmyeloablative Allogeneic Stem Cell Transplantation for Relapsed Hodgkin's or Non-Hodgkin's Lymphoma After Autologous Transplantation. SWOG, protocol S0501; Edward Smith, 708-327-3142 (phone)
- Phase II Trial of Standard Dose Cyclophosphamide, Doxorubicin, Vincristine, Prednisone and Rituximab Plus Bevacizumab for Advanced-Stage Diffuse Large B-Cell NHL. SWOG, protocol S0515; Alison Stopeck, 520-626-2816 (phone)

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