

Long-term Survivors of Pediatric Cancer Subject to Increased Risk of Severe Disease

According to results of the Childhood Cancer Survivor Study (CCSS) published in the October 12 issue of the *New England Journal of Medicine*, adults who survive at least 5 years after the diagnosis of cancer during childhood are much more prone to severe or fatal chronic health conditions than their siblings. The CCSS was intended to document the prevalence, incidence, and severity of long-term chronic health conditions following the treatment of pediatric cancer, whereas earlier investigation had documented the health status and mortality of long-term survivors in this setting. Included in the CCSS cohort were 10,397 survivors diagnosed with cancer between 1970 and 1986; also included was a control group of 3,034 unaffected siblings over the age of 18 at the time of completing the outcomes survey. Grade 3 (severe) or 4 (life-threatening or disabling) chronic health conditions were reported at rates of 27.5% and 5.2% among survivors and siblings, respectively (relative risk [RR] = 8.2). Among the survivors with the highest risk of a grade 3 or 4 condition, the most common cancers were of the bone (RR = 38.9) and central nervous system (RR = 12.6), in addition to Hodgkin disease (RR = 10.2). The conditions experienced during survival most frequently were secondary cancers, cardiovascular disease, renal dysfunction, severe musculoskeletal problems, and endocrinopathies. The CCSS found that five of the combination therapies used were associated with at least a 10-fold higher risk of developing a grade 3 or 4 condition: chest radiation plus either bleomycin, an anthracycline, or abdominal or pelvic radiation as well as an alkylating agent plus either an anthracycline or abdominal/pelvic radiation. Additionally, female gender and older age at diagnosis were independent predictors of developing a grade 3 or 4 or fatal condition. In total, 25 years after diagnosis, the cumulative incidence of grade 3 or 4 or fatal conditions was 33.1%.

Updated ASCO Guidelines on Gastrointestinal Cancer Tumor Markers Issued

The American Society of Clinical Oncology (ASCO) will publish updated guidelines regarding the use of tumor marker tests in the management of gastrointestinal cancer in the November 20 issue of the *Journal of Clinical Oncology*. The guidelines were released on ASCO's website in advance of publication. In 1996, ASCO issued evidence-

based guidelines for clinical practice on the use of tumor markers in colorectal cancer. A committee has convened regularly since then to update the guidelines based on new data released. Computerized literature searches of Medline and the Cochrane Collaboration Library were performed. On the whole, the literature is characterized by small, retrospective studies, or studies that performed multiple analyses until one produced a statistically significant result. As a result of the analysis of new data, the committee issued recommendations that carcinoembryonic antigen (CEA) be ordered preoperatively, if it would be of assistance in staging and surgical planning. Postoperative CEA levels should be monitored and assessed every 3 months for 3 years for stage II and III disease if the patient is eligible for surgery or chemotherapy for metastatic disease. Advances in chemotherapeutic regimens have allowed oncologists to test for recurrence and be prepared to offer a range of therapeutic options; the recommendations regarding CEA reflect these advances. It was found that insufficient data exist to recommend the routine use of the following markers: p53, Ras, thymidine synthase, dihydropyrimidine dehydrogenase, thymidine phosphorylase, microsatellite instability, 18q loss of heterozygosity, or deleted colon cancer protein. In the case of pancreatic cancer, the committee recommended the measurement of CA 19-9 every 1–3 months for patients with locally advanced or metastatic disease who are receiving activity. CA 19-9 changes do not indicate operability and should not be used for screening, but this marker may be useful in providing evidence of recurrence, if confirmed by biopsy and/or imaging studies.

Poor Prognosis in AML Linked to Multiple Pathways

Evaluation of blood and bone marrow specimens from 188 patients with acute myeloid leukemia (AML) revealed that simultaneous activation of multiple signal transduction pathways is associated with poor prognosis. Results of the research were published in the October 1 issue of *Blood*. Activation of one component from the signal transduction pathways PKC- α , pERK2, and pAKT had an adverse effect on prognosis. Patients found to have none of these molecular cascades activated had a median survival time of 78.6 weeks, but with one, two, or three highly active pathway(s), the corresponding survival time was 57.9, 42.3, and 23.4 weeks, respectively. This study was the first study to demonstrate cross-activation between the

pathways in patients (cross-activation has previously been noted in cell lines). The results of the study are important, according to lead author Dr. Steven M. Kornblau, because “each pathway is the target of drug development aimed at interfering with activation. Using an agent that blocks one pathway upstream is not likely to be effective if one of the other pathways is cross-activating that pathway downstream of where the drug works.” Thus, combined usage of agents targeting each pathway is likely to be the most efficacious strategy for therapy. Unfortunately, Dr. Kornblau noted, “the current regulatory and intellectual property environment does not encourage such cooperation.” It is possible that agents seen as ineffective in research could be discarded because their efficacy in combination will not have been revealed.

Summer Diagnosis, Sunlight, and Vitamin D Linked to Better Prognosis in Breast Cancer

Data from the Thames Cancer Registry show that the season in which cancer is diagnosed appears to have an effect on survival, as does sunlight exposure, to some extent. Patients diagnosed in summer and autumn had better survival compared to those diagnosed in winter, especially in female breast cancer and male and female lung cancer patients. Dr. Hyun-Sook Lim and colleagues reported their findings in the October issue of the *International Journal of Cancer*. Dr. Lim said, “Sunlight is essential for the production of vitamin D in the body. Evidence exists to suggest that vitamin D metabolites may have a role in tumor growth suppression.” It was found that cumulative sunlight exposure in the months preceding diagnosis of malignancy predicted survival, but season of diagnosis was a more robust predictor.

In a related finding, Dr. Carlo Palmieri and associates published a report in the October issue of the *Journal of Clinical Pathology* demonstrating that serum levels of 25-hydroxyvitamin D are decreased in women with more advanced breast cancer than in women with earlier stage tumors. By obtaining serum samples from 279 women with invasive breast cancer, the investigators were able to assess levels of vitamin D and parathyroid hormone. As background, *in vivo* studies have previously shown that vitamin D supplementation inhibits the proliferation of breast cancer cell lines, in addition to inducing apoptosis. Furthermore, epidemiologic research has shown that mortality from breast cancer is reduced in women who have high levels of exposure to sunlight. The mean concentrations of serum vitamin D found were significantly lower in patients with more advanced disease (46 nmol/L) as compared to those with less advanced disease (57 nmol/L). It is thus hypothesized that vitamin D has a role in the pathogenesis and progression of invasive breast cancer.

Annual Spiral CT Screening Can Detect Early, Curable Lung Cancer

Results from the International Early Lung Cancer Action Program (I-ELCAP) appeared in the October 26 issue of the *New England Journal of Medicine*. This study included 31,567 asymptomatic men and women thought to be at risk for lung cancer due to smoking or occupational exposure to asbestos, uranium, beryllium, or radon. It was previously shown that spiral computed tomography (CT) results in the early detection of lung cancer in at-risk subjects, but the I-ELCAP study sought to assess whether this early intervention affects the outcome of these patients. It is known that in the United States at present, 95% of individuals diagnosed with lung cancer die within 5 years, but the present study showed that with annual screening, 80% of these deaths could be prevented. A total of 484 subjects were diagnosed with lung cancer through the spiral CT screening: 405, 74, and 5 subjects at first screening, during annual screening afterward, and within the first year after initial screening, respectively. Of these patients, a total of 411, 57, and 16 patients underwent resection, received radiation and/or chemotherapy, or received no therapy, respectively; of these patients, the estimated 10-year survival rate was 80%. A total of 412 patients had clinical stage 1 cancer, and their estimated 10-year survival rate was 88%. The authors believe that annual CT screening for at-risk subjects would be highly cost-effective, similar to mammography screening. However, a related editorial by Dr. Michael Unger contended that there is insufficient evidence for or against recommendation of annual CT screening for lung cancer. Dr. Unger remarked that a social stigma toward lung cancer, wherein it is considered punishment rather than disease, has delayed progress in evaluating methods to enable early detection of lung cancer.

In Brief

Nasopharyngeal cancer, a relatively rare neoplasm, occurs in blacks under the age of 20 more than twice as often as in whites. According to the National Cancer Institute, incidence was 1.61, 0.95, and 0.61 per million for blacks, Asians, and whites under age 30, respectively, between 1973 and 2002. (*Arch Otolaryngol Head Neck Surg.* 2006;132:1035-1040.)

Breast cancer rates are not affected by induced abortion, according to data from 267,361 European women. Of 4,805 women diagnosed with invasive breast cancer during follow-up, 20%, 16%, and 3.8% had a spontaneous or induced abortion or both, respectively. The relative risk of breast cancer was not significantly increased among women who had an induced abortion in comparison to those who never had an induced abortion. (*Int J Cancer.* 2006;119:1741-1745.)