

common leukemia among adults. Risk factors for AML include high doses of ionizing radiation, occupational exposure to benzene, and some medications used in cancer chemotherapy. Genetic disorders including Fanconi's anemia and Down's syndrome are associated with an increased risk for AML. Tobacco smoking has been suggested as a risk factor.

The incidence of chronic myeloid leukemia (CML) increases with age for individuals over 30. For individuals in the age groups that characterize most Vietnam veterans, CML accounts for about one in five leukemias. CML is associated with an acquired chromosomal abnormality known as the "Philadelphia chromosome." Exposure to high doses of ionizing radiation is a known risk factor for that abnormality.

NAS noted in VAO and subsequent reports that there is inadequate or insufficient information to determine whether an association exists between exposure to herbicides and leukemia. Because CLL, the most common form of leukemia, shares many traits with lymphomas, NAS reviewed it separately from the other leukemias in Update 2002.

In Update 2002, NAS reviewed one new occupational study (Burns *et al.*, (2001)) which reported data on a cohort male workers involved in the manufacture or formulation of 2,4-D. Mortality from leukemia in the entire cohort was similar to rates in all U.S. males. Similar results were obtained in an analysis based on a 20-year induction period. In the comparison with nonexposed workers, an excess in lymphopoietic mortality was noted in workers with high-cumulative-dose exposure to 2,4-D. NAS noted, however, that at least some of the deaths may have been due to Hodgkin's disease or multiple myeloma.

In another occupational study, cancer incidence and mortality were assessed in a cohort of 504 forestry workers in Sweden who were characterized by presence or absence of exposure to phenoxy herbicides in 1954–1967 (Thorn A, Gustavsson P, Sadigh J, Westerlund-Hannerstrand B, Hogstedt C 2000. Mortality and cancer incidence among Swedish lumberjacks exposed to phenoxy herbicides. *Occupational and Environmental Medicine* 57:718–720). No cases of leukemia occurred in the exposed members of this cohort.

In an environmental study, Revich *et al.* (2001) analyzed data on cancer incidence and mortality in Chapaevsk, Russia. Mortality due to leukemia during the years 1995–1998 was compared with mortality in the Samara

region as a whole. Age-adjusted incidences during 1998 were reported for leukemia and lymphoma combined. The rates in Chapaevsk were lower than in the Samara region in men but higher in women. NAS noted a number of weaknesses contained in this study, including failure to report the actual number of cases, failure to calculate confidence intervals, and lack of adjustment for factors other than age.

NAS found no compelling or consistent evidence of an association with exposure to herbicides contained in the new reports reviewed for Update 2002 to change the conclusion that there is inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and leukemia (other than CLL).

Taking account of the available evidence and NAS' analysis, the Secretary has found that the credible evidence against an association between herbicide exposure and leukemia (other than CLL) outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

Abnormal Sperm Parameters and Infertility

NAS noted in VAO and subsequent reports that there is inadequate or insufficient information to determine whether an association exists between exposure to herbicides and altered sperm parameters or infertility.

In Update 2002, NAS reviewed the results of an environmental study which assessed whether exposure to heavy metals, PCBs, volatile organic compounds, and polycyclic aromatic hydrocarbons is related to early reproductive effects. (Staessen JA, Nawrot T, Hond ED, Thijs L, Fagard R, Hoppenbrouwers K, Koppen G, Nelen V, Schoeters G, Vanderschueren D, Van Hecke E, Verschaeve L, Vlietinck R, Roels HA. 2001. Renal function, cytogenetic measurements, and sexual development in adolescents in relation to environmental pollutants: a feasibility study of biomarkers. *Lancet* 357(9269):1660–1669. [Comment in *Lancet* 2001. 358(9295):1816–1817.]) The study compared 100 17-year-old lifetime residents of two highly exposed suburbs of Antwerp, Belgium, with 100 17-year-old lifetime residents of a rural control community. Concentrations of several environmental agents, including dioxin-like compounds in serum samples, were found to be higher in the two suburban locations than in the control community, after adjustment for sex, body-mass index (BMI), weeks of breastfeeding, parental social class, and dietary fat intake. NAS noted that the

results indicate that children in the two suburban locations experienced substantial and statistically significant delays in sexual maturation and lower testicular volume. NAS further noted that the results of this study support a potential effect on male reproductive capacity, but that the implication for Vietnam veterans remains unclear, inasmuch as most veterans were past their pubertal development during their tours of duty.

NAS also discussed a review of medical literature (Figá-Talamance I, Traina ME, Urbani E. 2001. Occupational exposures to metals, solvents, and pesticides: recent evidence on male reproductive effects and biological markers. *Occupational Medicine* 51(3): 174–88.), the authors of which concluded that there is insufficient evidence to conclude that the use of pesticides leads to significantly higher risk to human reproduction.

NAS stated that there is no information in the research reviewed for Update 2002 to change the conclusion that there is inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and altered sperm parameters or infertility.

Taking account of the available evidence and NAS' analysis, the Secretary has found that the credible evidence against an association between herbicide exposure and reproductive effects in veterans outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

Parkinson's Disease and Parkinsonism

Because of the increasing concern that a link exists between Parkinson's disease (PD) and various chemicals used in herbicides, NAS, in VAO and subsequent reports, suggested that as Vietnam veterans move into the age groups when PD is more prevalent, attention be given to the frequency and character of new cases of PD in exposed versus nonexposed individuals.

NAS noted in VAO and subsequent reports that there is inadequate or insufficient information to determine whether an association exists between exposure to herbicides and PD.

In Update 2002, NAS reviewed an occupational study in which 238 subjects exposed to pesticides in an occupational setting and 72 nonexposed controls were examined for the presence of parkinsonism. (Engel LS, Checkoway H, Keifer MC, Seixas NS, Longstreth WT, Scott KC, Hudnell K, Anger WK, Camicioli R. 2001. Parkinsonism and occupational exposure to pesticides.