Cancer therapy risks assessed

Survivors of childhood cancer have an increased risk of developing bone cancer later in life, primarily because of the use of radiation therapy and chemotherapy against the original cancer, a new study concludes. The study, published in the Sept. 3 NEW ENGLAND JOURNAL OF MEDICINE, is believed to be the most comprehensive analysis ever performed on the risks of cancer therapy for children.

Researchers from the National Cancer Institute and six cancer hospitals in the United States and Italy report that the risk of bone cancer among survivors of a variety of childhood cancers rises sharply with increasing exposure to radiation or certain chemotherapeutic agents, reaching 40-fold at some of the highest doses used. Unfortunately, says Margaret A. Tucker, senior researcher in the study, radiation and chemotherapy remain essential treatments for childhood cancers.

"Radiation doses are lower than they used to be, but they are still well within the range where they cause problems," Tucker told SCIENCE NEWS. Moreover, she says, the research suggests that with chemotherapy use becoming more widespread, increasing numbers of chemotherapy-caused cancers can be expected to show up 15 or 20 years from now. Nevertheless, she says, "The risk of bone cancer is small compared to the enormous benefit the kids get from treatment at this point; if they aren't treated, then they die of their first tumor."

Previous studies have documented, if somewhat sketchily, the risks of radiation therapy (SN: 6/22/85, p.127). But the new research goes to great lengths to measure such variables as dose levels relative to each patient's age and body surface-area, and the proximity of subsequent bone cancers to original radiation sites. Furthermore, in their measurements of dose levels for various skeletal components, the researchers took into account the radiation scatter patterns that are characteristic of various therapy machines, adjusting for differences in bone absorption associated with different types of energy beams used.

Using these and other factors, the retrospective study of more than 9,000 patients provides strong statistical evidence that approximately half of the secondary bone cancers observed can be blamed on radiation therapy or on chemotherapeutic alkylating agents such as the frequently prescribed cyclophosphamide. The study points to the difficulties that pediatric oncologists face in choosing a treatment regimen for children with cancer.

"The bottom line is that radiation has a profound effect on the likelihood of getting secondary bone tumors," says Anna T. Meadows, chairperson of the Late Effects Study Group, a multicenter cancer research team that coordinated the current study. "The study provides evidence that with lower doses we can prevent at least some bone tumors. We don't want to give children anything but the minimum dose that would take care of the tumor."

However, the study also suggests that hereditary factors may play a larger role in bone cancer development than was previously believed. Only one form of cancer, a rare eye cancer called retinoblastoma, has so far been linked to a specific genetic defect (SN: 1/5/85, p.10). But there is growing evidence that other childhood cancers have genetic roots as well, Tucker says. In the current study, for example, secondary bone cancer was reported in six patients who had received neither chemotherapy nor radiation therapy for their original cancers. Statistical analysis predicted that less than one such case would occur in the sample group. "It seems likely that heritable factors contribute to constellations of multiple childhood cancers, including bone [cancer]," the researchers conclude in their paper.

According to Tucker, the study may help physicians in calculating ideal radiotherapy and chemotherapy dosages, but in the long run an entirely new approach to cancer treatment may be needed. It's possible, she says, that as hereditary factors become better understood, some cancers may be more successfully managed on the gene therapy level. —*R. Weiss*

Boosting cell numbers in AIDS

A growth hormone that stimulates certain cells in the bone marrow can increase the number of white blood cells circulating in the blood, and perhaps give AIDS patients more "ammunition" with which to fight infection, scientists reported last week.

Using 16 AIDS patients who had decreased white cell counts, a research group from New England Deaconess Hospital and Harvard Medical School in Boston, Sandoz Research Institute in East Hanover, N.J., and the University of California at Los Angeles tested the toxicity and effectiveness of granulocyte-macrophage colony-stimulating factor (GM-CSF). The scientists conclude in the Sept. 3 NEW ENGLAND JOURNAL OF MEDICINE that GM-CSF is both nontoxic and capable of boosting the number of white cells in the body, suggesting a possible treatment for disorders with depressed white cell counts.

The scientists used a genetically engineered form of the naturally occurring hormone, which is thought to activate bone marrow precursor cells that eventually become various types of white blood cells. A major component of the immune system, white cells can be drastically decreased in immune disorders like AIDS, as well as by irradiation and cancer chemotherapy. Too few white cells (a condition called leukopenia) makes the patient defenseless against a variety of opportunistic, often fatal infections like pneumonia.

In the recent study, the authors report that intravenous infusion with GM-CSF for two weeks produced significant increases in white cells called neutrophils, monocytes and eosinophils. The size of the increase was directly related to the dose given the patient. Cell counts, however, returned to their previous low levels after the treatment was discontinued.

"[The report] doesn't say we're curing AIDS with GM-CSF," Jerome E. Groopman of New England Deaconess told SCIENCE NEWS. "But one could see using it in combination with drugs like AZT." Recently renamed zidovudine, AZT slows viral replication and currently is the only federally approved AIDS treatment. Future experiments will test such drug combinations, says Groopman. He and his co-workers also are planning clinical studies to determine whether increased white cell counts will in fact alter the now-fatal course of AIDS. Because preliminary studies show that the hormone-boosted cells are functional, Groopman says that GM-CSF "has a potentially important role to play in treating AIDS."

The reported research offers no guarantees and may be off-target, says David G. Nathan of Boston's Children's Hospital in an accompanying editorial. He points out that the primary blood-cell problem in AIDS is the relative absence of T cell lymphocytes, not the lack of those cell types affected by GM-CSF therapy. He therefore suggests that it may be more appropriate to consider the hormone as a possible treatment for bone marrow diseases, not AIDS.

But Groopman disagrees, saying in an interview that infection with the AIDS virus is dealt with by lymphocytes and monocytes "in concert," and that both are a target of the virus. Supporting the hormone as a potential AIDS treament, says Groopman, are yet-unpublished data suggesting that GM-CSF may "potently enhance" the microbe-killing capacity of monocytes, as well as actually inhibit the replication of the AIDS virus. He cautions, however, that these results come from studies on cell cultures, not from animal studies.

—*D.D. Edwards*