Biomedicine

Rick Weiss reports from San Francisco at the annual meeting of the American Society of Clinical Oncology

Marrow donors: Reaching beyond family

Chronic myelogenous leukemia (CML) eventually will kill virtually all the 13,000 U.S. individuals diagnosed with it this year unless they can receive a complete replacement of their cancerous bone marrow. Replacing marrow without stimulating a life-threatening immune reaction requires a donor with marrow so genetically similar that doctors have long believed only a sibling would do. Even among siblings, tests show that only about half have marrow similar enough to prove useful for a CML-affected individual.

In recent years, however, cancer specialists have come to suspect that bone marrow from unrelated donors, if carefully screened for critical markers, might prove similar enough for use in CML patients. Philip McGlave of the University of Minnesota in Minneapolis and his colleagues sought to test that hypothesis. In the largest such trial to date, the team performed nonfamilial bone marrow transplants on 142 CML patients between April 1985 and October 1988. Data so far indicate a 10 percent rate of graft failure — equal to that seen in transplants using sibling marrow. On the basis of current trends, the two groups have similar projections of disease-free survival.

The utility of nonsibling marrow "should greatly increase the availability of this curative procedure," says McGlave, adding that unrelated marrow may prove useful for other marrow-related diseases, including some types of red blood cell abnormalities. He notes that the National Bone Marrow Donor Program, recently created with congressional funding, has already registered more than 35,000 potential marrow donors.

The program hopes to attract 100,000 U.S. donors and provide computer links around the world to ease the search for compatible marrow.

Hopes heighten for new leukemia drug

Chronic lymphocytic leukemia (CLL), the most common leukemia in the Western world, develops mostly in the elderly. Already striking more than 27,000 people in the United States each year, this fatal blood disease seems destined to become even more common as the population ages. Scientists have tested a remarkably long list of potential CLL drugs, but few have achieved response rates of even 20 percent.

Now, with results accumulating from trials of an experimental drug introduced about five years ago, CLL researchers express an optimism not heard in their field for many years. Michael J. Keating of the M.D. Anderson Cancer Center in Houston reports preliminary results from a trial of CLL patients given the experimental drug fludarabine. Of 127 test patients who failed to respond to traditional chemical and radiation treatments, about 60 percent have gone into remission without the hair loss, nausea and bone marrow suppression seen in traditional CLL therapies.

In a separate study by the same researchers, the disease disappeared in more than 35 percent of 33 patients not previously treated with anything else. Fewer than 10 percent of new CLL patients respond to traditional drugs with complete remission.

"This appears to be the agent with the most dramatic ability to get rid of chronic lymphocytic leukemia that we've ever tested," Keating says, adding that it also looks good in trials with some kinds of lymphoma. Adds Bruce Cheson of the National Cancer Institute: "This really is the most exciting thing that's happened with CLL in decades."

Keating says true survival data will take another two to three years to gather, but the drug's ability to immediately shrink the soft tissue "lumps and bumps" that constantly remind CLL patients of their disease is in itself a major success.

Tumor resistance: Weakening the pulse

Cancer patients receiving chemotherapy often suffer from a phenomenon known as multidrug resistance, in which their tumors develop resistance to drugs previously effective and even to drugs the patient has never taken (SN: 8/6/88, p.87). Researchers know that in some (but not all) cases of multidrug resistance, tumor cells make a so-called p-glycoprotein that seems to pump anticancer drugs out of these cells before the drugs accomplish their cell-icidal task. New research by Thomas P. Miller and his colleagues at the University of Arizona in Tucson strengthens evidence that p-glycoprotein is a major culprit in multidrug resistance, and suggests that a drug commonly prescribed for heart rhythm abnormalities can reverse multidrug resistance in lymphoma patients.

In the first prospective trial of its kind, the researchers examined tumors in 49 newly diagnosed cancer patients and found only one patient with p-glycoprotein-containing cells. Subsequent biopsies on the 10 patients who went on to relapse with multidrug resistance showed that seven now had the glycoprotein.

Previous research by the same group had shown that verapamil, a drug that corrects electrical-conduction abnormalities in the heart, seemed to reverse multidrug resistance in patients with multiple myeloma, another form of cancer. The researchers now report that verapamil reversed drug resistance in 12 of 17 lymphoma patients, allowing the patients to respond again to their original drug. Encouraged by the expanded findings, Miller suggests verapamil may *prevent* multidrug resistance if given "up front" with chemotherapy, and may prove especially valuable in bladder or other cancers that tend to produce lots of p-glycoprotein.

Got a light? This carrot keeps going out

Smoking cigarettes, chewing tobacco and consuming alcohol constitute major risk factors for head and neck cancers — an association that explains, in part, the rising incidence of these cancers in U.S. women. But many people — men and women alike — find it impossible to eliminate these elements from their lives; even patients who develop these cancers often continue to smoke and drink. New research suggests that life would be better if society considered it cool to hang out with a carrot, rather than a cigarette, dangling from one's mouth.

Previous studies have shown that vitamin A and some of its synthetic derivatives can reverse a condition called leukoplakia, which appears as precancerous white spots in the mouth. But these fat-soluble compounds can be toxic at the levels required to do their work. Harinder Garewal of the University of Arizona in Tucson reports that a pilot study of 25 patients shows that beta-carotene — a vitamin A relative occurring naturally in carrots and green leafy vegetables — reversed premalignant leukoplakia in more than 75 percent of the patients without producing toxic side effects.

Leukoplakia returned in patients who discontinued the dietary supplement — consisting of a single 30-milligram capsule per day, equivalent to the amount of beta-carotene in about six carrots. Garewal says a planned larger trial may show that the inexpensive supplement can play an important public health role, especially in parts of the world where nutrition is already poor and oral care is lacking.

Cancers of the head and neck, including those of the lips, tongue, mouth and voice box, kill 10,000 to 15,000 people each year in the United States and constitute an even more serious problem in other parts of the world. Garewal notes that prevention strategies are especially valuable for these cancers, because their location often makes treatment difficult and surgery can leave the patients seriously disfigured or unable to speak.