Umbilical cords as source of new blood

The young Frenchwoman was dying. Since 1990, when she was diagnosed at age 26 with a cancer of the white blood cells, her physicians had searched in vain for a bone marrow donor whose tissue closely matched hers.

When the disease became more severe last summer, her physicians could wait no longer. They called the New York Blood Center and obtained a frozen sample of fetal blood siphoned from the cut umbilical cord of a newborn. Like bone marrow, this blood contains a rich population of stem cells that can repopulate the red and white blood cells of the human body.

After treating the young woman's cancer, chronic myelogenous leukemia, with radiation and chemotherapy that destroyed her bone marrow and its crucial supply of stem cells, the physicians attempted to restore the marrow by injecting into their patient a few ounces of the thawed cord blood. Eight months after the procedure, the woman appears to be healthy and has returned to work, the physicians report.

This case study, described in the July 18 NEW ENGLAND JOURNAL OF MEDICINE (NEJM), is one of several new reports providing the first published evidence that people unrelated to the donor can benefit from transplants of umbilical cord blood.

Like donated bone marrow, stored cord blood may help people suffering from a variety of leukemias and other cancers, as well as inherited genetic diseases that affect the blood or immune system. Cord blood also offers some significant advantages over bone marrow. Besides appearing to require a less exact match between donor and recipient, it can be obtained without surgery.

In a second report in the July 18 NEJM, Joanne Kurtzberg of Duke University Medical Center in Durham, N.C., and her colleagues describe the results of 25 cord blood transplants performed on children or young adults since 1993. Even though most of the transplants involved one to three mismatches of HLA antigens—cell surface proteins used to identify how closely the tissues of a donor and recipient match—the team found that the stem cells successfully took hold in 23 of the 25 patients.

A research group led by John E. Wagner of the University of Minnesota School of Medicine in Minneapolis is scheduled to report similarly encouraging results from 18 more cord blood transplants, most of them involving a single HLA antigen mismatch, in the August BLOOD.

In the Duke study, only two of the 23 successful transplants resulted in severe graft-versus-host disease (GVHD), an often deadly reaction in which transplanted cells attack the recipient's organs. Fearing GVHD, physicians generally refuse to attempt bone marrow transplants that involve more than a single HLA antigen mismatch. As a result, patients often cannot find a suitable bone marrow donor.

Kurtzberg's study suggests that people can tolerate more mismatches with cord blood than with bone marrow transplants, but she and other researchers stress that the study size is too small to reach a definitive conclusion.

"If the ability to tolerate mismatches pans out, that will be a very big step forward," says Paul R. McCurdy, director of the blood resources program at the National Heart, Lung, and Blood Institute (NHLBI) in Bethesda, Md.

In addition to funding several new banks to store frozen cord blood, NHLBI is organizing a multicenter trial of cord blood transplants to determine in greater detail how the procedure compares to bone marrow transplants.

Though the recent studies show that stem cells from cord blood can replace destroyed bone marrow in recipients unrelated to the donor, it will take several years for researchers to determine the long-term benefits of the transplants. Kurtzberg and her colleagues report that 11 of the 23 patients in whom the stem cells survived have died from their disease or from complications related to the powerful drugs prescribed to ward off GVHD.

Indeed, the apparent ability of cord blood transplants to avoid GVHD may not be an advantage for people with some cancers, says Nancy A. Kernan of Memorial Sloan Kettering Cancer Center in New York. She points out that researchers have shown that people with some leukemias actually experience fewer relapses after a bone marrow transplant if they suffer a certain degree of GVHD.

Investigators also remain uncertain whether the small amount of blood in a single umbilical cord will be as effective in older, heavier individuals as it appears to be in children.

Though cases like that of the Frenchwoman offer strong encouragement, "we need more experience with adults," says Pablo Rubinstein of the New York Blood Center.

Nevertheless, Hal E. Broxmeyer of Indiana University School of Medicine in Indianapolis, who participated in the first successful cord blood transplant in 1988, marvels at the method's rapid progress. "I'm just incredibly excited to see how far it has come in such a short period of time." —*J. Travis*

New signs of nicotine's addictiveness

Nicotine's effects on the brain precisely mimic those produced by morphine and other major drugs of abuse, according to a study conducted on rats.

The finding by Italian scientists "adds new weight to the conclusion that nicotine is indeed addictive," Leslie L. Iversen of the University of Oxford in England observes in the July 18 NATURE.

Gaetano Di Chiara of the University of Cagliari in Italy and his coworkers injected nicotine into the veins of unrestrained rats, then probed what happens in a part of the animals' brains known as the nucleus accumbens. This deeply embedded region at the base of the forebrain plays a role in integrating and expressing emotions, De Chiara notes.

Last year, his team showed that within an area of the nucleus accumbens known as the shell, amphetamines, morphine, and cocaine not only increased cellular activity but also boosted concentrations of dopamine. This signaling chemical has been linked to the euphoria created by addictive drugs.

In the July 18 NATURE, the team reports that nicotine, too, boosts dopamine and activates cells in the nucleus accumbens shell. Indeed, this pair of observations appears to be "a kind of label of [a drug's] being addictive," Di Chiara told SCIENCE NEWS.

Di Chiara suspects that dopamine "facilitates a learning of the association between the pleasurable effects of a drug and other stimuli," such as the smell of smoke or taste of tobacco, quickly reinforcing desire for the drug.

While food and water can induce cravings, they normally do so only when a person is hungry or thirsty. Drug cravings, Di Chiara says, make users seem as if they "are always hungry or thirsty because this stimulus is so strong."

Edythe D. London of the National Institute of Drug Abuse in Baltimore has spent many years mapping brain activation by drugs of abuse. What distinguishes this study, she says, is the "elegant" way it has mapped the activation of cells and the increase in dopamine simultaneously at one site.

Roy Wise of Concordia University in Montreal adds that not only have Di Chiara and his colleagues shown that nicotine turns on "the same [brain] circuitry that heroin and cocaine activate," but the research employed lower doses than those used in the past—"what are essentially real-world doses."

"We should either downgrade heroin to habit-forming or upgrade nicotine to addicting" because the same neurobiology accounts for abuse of all these drugs, Wise concludes. —*J. Raloff*