

The Cord-Blood-Bank Controversies

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Umbilical-cord blood is increasingly used as a source of stem cells to repopulate the bone marrow in the treatment of life-threatening diseases in children and adults (as discussed in this issue of the *Journal* by Laughlin et al., pages 2265–2275, Rocha et al., pages 2276–2285, and Sanz, pages 2328–2330). This scientific progress, however, has triggered a continuing debate about how to organize cord-blood banks and the role of public and private facilities.

The blood that remains in the placenta after birth is readily available, can be collected at no risk to the mother or newborn, and may be stored frozen for years (see box). Cord blood has less restrictive HLA-compatibility requirements than bone marrow and can be provided quickly. An important caveat is that a unit of cord blood — the blood collected from one donor — may vary in volume from 40 ml to 100 ml or more, and even the largest units contain substantially fewer hematopoietic progenitor cells than a typical bone marrow donation. Some units thus contain insufficient cells to treat an adult.

The first cord-blood transplantation was performed in France in 1988.¹ A six-year-old boy from North Carolina with severe Fanconi's anemia received cryopreserved umbilical-cord blood from an HLA-identical younger sister who was unaffected by the disorder. Sixteen years later, he is healthy, his graft is durable, and he has had no further manifestations of the disease, according to his physician, Dr. Joanne Kurtzberg of the Duke University Medical Center in Durham, North Carolina.

Although exact statistics are not available, 5000 to 6000 cord-blood transplantations have now been performed worldwide, primarily in the United States, Western Europe, Japan, and Australia, according to Dr. Pablo Rubenstein and Dr. Cladd Stevens of the New York Blood Center, New York. The number of transplantations performed annually is increasing, and adults now account for about

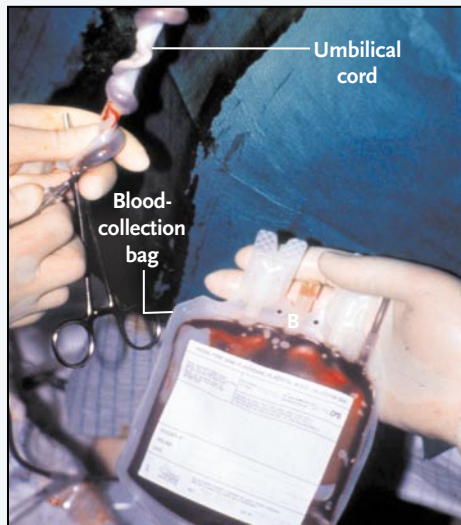
one third of all recipients. About two thirds of transplants are used in patients with leukemia, and about a quarter in patients with genetic diseases. In 2004, there are expected to be about 2000 cord-blood transplantations, including 600 in the United States and 800 in Japan, which has developed an effective transplantation system in the past five years.

There are currently both private and public cord-blood banks in the United States. Private banks market their services to couples who are expecting a child. They store cord blood for the future use of the donor or members of the donor's family. There are about 20 private cord-blood banks in this country; their collection fees are typically \$1,000 to \$1,500, and storage costs about \$100 a year.² Blood from private banks has been used in only a small minority of transplants. One company, Cord Blood Registry (headquartered in San Bruno, Calif.), stated in September that it has "approximately 250,000 cryopreserved units at its Tucson facility" and "has provided stem cells for 34 client treatments" — more, it claims, than all other private cord-blood banks combined. Most of the samples have been used for the treatment of a sibling of the donor. Overall statistics for private cord-blood banks are not available.

Public storage banks are similar to blood banks in that they are a source of cord blood from unrelated donors. Umbilical-cord blood and blood from the mother are typed for HLA antigens and blood group and screened for infectious diseases, and information is collected about the medical history of the mother and the family (see box). Policies vary with regard to the follow-up of donors for the development of diseases that could be transmitted through a transplant. Unlike private banks, public banks do not charge for collection or storage. They charge \$15,000 to \$25,000 when a unit is provided for transplantation — a fee that is usually covered by health insurance. Worldwide, there are between 175,000 and 200,000 units of cord blood in storage

Collection, Processing, and Storage of Cord Blood for Use by an Unrelated Donor

After birth, blood is collected — by an obstetrician, a nurse-midwife, or a designated collector — either from the placenta in utero or from the delivered placenta and drained by gravity into a sterile blood-collection bag. The blood is then sent to a central facility, where it is processed to remove excess red cells and plasma.



The nucleated-cell content of the cord blood, a surrogate for the stem-cell content, is determined, and the mother's blood and sometimes the cord blood are tested for relevant infectious diseases. HLA type, ABO type, and Rh status are determined, and tests for genetic diseases or traits are performed.

Each unit of stored blood that meets the selection criteria is stored with dimethyl sulfoxide, a cryoprotectant, and placed in a protective canister. The unit is frozen at a controlled rate and stored in a freezer under liquid nitrogen.

in public banks. Some of these units, however, would not meet current collection standards, most commonly because they contain an insufficient number of nucleated cells, which are used as a surrogate for stem cells.

Advocates of public cord-blood banks argue that private banks exploit the emotional vulnerabilities of expectant parents for financial gain and that their

practices make little sense, except in unusual circumstances.² A person's own cord blood is very unlikely to be needed for personal or family use, so patients and society are better served when matches from unrelated persons can be found in a public bank. As medicine is currently practiced, a child's own cord blood cannot be used if the child is born with a genetic disease or develops leukemia. The primary exception is the very small number of families — fewer than 1000 in the United States each year, according to Kurtzberg — with a child whose illness might be treated with cord blood from a sibling. There may be more uses for cord blood, such as transplantation in patients with sickle cell anemia or another hemoglobinopathy, which is currently performed infrequently. The production of organs and tissues that are unrelated to the hematopoietic system, another potential use, is still theoretical.

Private cord-blood banks are currently mired in yet another controversy — a patent dispute. PharmaStem Therapeutics (Wayne, Pa.) claims that its patents covering the collection, cryopreservation, storage, and therapeutic use of cord blood entitle it to receive licensing fees. PharmaStem was founded in 1985 as Biocyte Corporation, which partially supported the first cord-blood transplantation.¹ The company says it has licensing agreements with 16 private cord-blood banks. It has brought suit against the others and has sought to force obstetricians to collect cord blood only for the banks it has licensed. According to a letter sent in August 2004 by Cord Blood Registry, which has not signed a licensing agreement, PharmaStem's position is “analogous to demanding a licensing fee for all bone marrow or peripheral blood that is cryopreserved or used in transplant.” In September 2004, the U.S. Patent and Trademark Office agreed to re-examine two of the patents, and litigation is ongoing in the federal courts.

While the role of patents in the cord-blood industry in the United States remains uncertain, public banks have seen their growth hindered by a shortage of stored blood and insufficient funding for additional collection and storage. It remains difficult to find full matches for some patients — in particular, for blacks and Asians — both because of an insufficient number of donors and because of the diversity of HLA types in these groups. Moreover, because public banks usually collect cord blood only at affiliated hospitals, not all parents have the opportunity to donate.

There is continuing competition between the two main organizations in the public bank field, the National Marrow Donor Program, based in Minneapolis, and the National Cord Blood Program of the New York Blood Center.³ The National Marrow Donor Program receives support for its bone marrow donor registry from the Department of Health and Human Services and the Navy. Through its 13 member cord-blood banks and 2 other affiliates, it has a registry that covers about 36,000 cord-blood units. The New York Blood Center has an inventory of about 23,000 units. The National Marrow Donor Program seeks federal support for a national cord-blood program that would operate under its auspices. The New York Blood Center seeks federal support for a network of independent cord-blood banks.

The Food and Drug Administration (FDA) regulates stem cells from cord blood as human cell and tissue products, not as blood products. Since the late 1990s, the agency has been developing a regulatory approach to licensing cord-blood products, but to date it has neither issued comprehensive rules nor publicly stated a date by which it will do so. Cord-blood banks are required to register with the FDA; a few operate under the agency's Investigational New Drug regulations. In 2005, certain requirements are expected to take effect, covering the criteria for accepting donations, screening and testing for relevant communicable diseases, and tissue-manufacturing practices. In the interim, there are

various nongovernmental organizations that provide oversight. They include the American Association of Blood Banks and, working together, the Foundation for the Accreditation of Cellular Therapies, based in Omaha, Nebraska, and the International NetCord Organization, based in the Netherlands. Eventually, the FDA is expected to license cord blood from unrelated donors for public use.

The structure of a national cord-blood program in the United States remains uncertain. In many instances, the private storage of umbilical-cord blood is not worthwhile.² In the consolidated appropriations bill for fiscal year 2004, Congress approved \$9 million for additional cord-blood collection and \$1 million for an Institute of Medicine study. The \$9 million will not be spent until after the institute issues its report, which is also expected in 2005. The potential of cord-blood transplantation will not be realized until the FDA finalizes its licensure regulations and until there is a coherent, adequately funded national program to facilitate transplantation from unrelated donors.

1. Gluckman E, Broxmeyer HA, Auerbach AD, et al. Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbilical-cord blood from an HLA-identical sibling. *N Engl J Med* 1989;321:1174-8.

2. Private cord blood banks. *Med Lett Drugs Ther* 2004;46:21-2.

3. Abelson R. Therapy impasse — a cancer hope deferred; blood treatment's promise mired in bureaucracy. *New York Times*. May 29, 2004:A1.

Westward Ho? — The Spread of West Nile Virus

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West Nile virus, a mosquito-borne flavivirus, was first isolated from a febrile patient in the West Nile region of Uganda in 1937. For the next 60 years, it remained a little-understood cause of febrile illness and sporadic encephalitis in parts of Africa, Europe, and Asia, garnering scant medical attention. After its surprising detection in New York City in 1999, West Nile virus became a major clinical and public health concern in North America. The next year, the Centers for Disease Control and Prevention collaborated with state and local health departments to

establish ArboNet, an electronic surveillance system for tracking West Nile virus infections in humans, mosquitoes, birds, and other animals in the United States. Data from ArboNet have documented the dramatic westward spread of West Nile virus across North America (see maps).

As of October 15, 2004, ArboNet had received reports of West Nile virus infection in 58 mosquito species and 284 bird species and had recorded 6690 cases of neuroinvasive West Nile virus disease (meningitis, encephalitis, or acute flaccid paralysis)