LA JOLLA, Feb. 9 -- Scripps Clinic and Research Foundation physicians are treating leukemia patients with a promising but experimental bone marrow transplant technique.

Developed at the Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, N.H., the method uses monoclonal antibodies to purge the marrow of leukemia cells, and is autologous - meaning that the patient's own marrow is extracted, treated and replaced. Standard bone marrow transplant techniques use the marrow of a brother or sister, and often lead to complications such as graft-vs.-host disease and infection.

Using monoclonal antibodies developed by Dr. Edward Ball, head of the Dartmouth Medical School's clinical immunology research program, the three-year Dartmouth/Scripps Clinic study has treated 22 patients with advanced acute myelogenous leukemia, the type responsible for about 80 percent of all adult acute leukemia cases. The median survival in this patient group was three to four times the length achieved with standard chemotherapy treatment.

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"The results in patients with advanced disease are encouraging," said Dr. Robert McMillan, director of the Scripps Clinic Weingart Transplantation Center. Because of this, a pilot study is starting using autologous transplantation in patients in first remission.

Ball, who six years ago began the time-consuming research that led to the development of the monoclonal antibodies, was joined in developing the transplant program by Dr. Gibbons Cornwell and Dr. Letha Mills of Dartmouth's hematology/oncology section.

"Although the program is only three years old, we know that this treatment does produce prolonged remissions in some patients without maintenance chemotherapy," said Cornwell. "In addition, it offers potential for a cure, although at this time it's too early to evaluate what percentage of patients will remain free of the disease."

Other than McMillan, physicians involved at Scripps Clinic are Dr. Ernest Beutler, chairman of the basic and clinical research department and head of the hematology/oncology division, Dr. William Miller, hematology/oncology division, and Dr. Linda Thompson, immunology division.

"Patients who have once relapsed with acute myelogenous leukemia are never cured by chemotherapy," said Beutler. "This approach offers new hope to such patients."

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Leukemia is a disease characterized by an abnormal increase in the number of leukocytes, or white blood cells. According to the Leukemia Society, there are 70,000 new cases of leukemia and related disease in the United States each year and 41,000 deaths.

In this autologous transplant technique, the patient, while in remission, is anesthetized and one to two quarts of bone marrow are extracted and processed to remove red blood cells. Monoclonal antibodies, which are produced from laboratory mice and act against specific proteins on the surface of leukemia cells, are added for an hour; then baby rabbit serum, a source of complement, is added. The two acting together destroy the leukemia cells, a process known as marrow purging. The treated marrow is then frozen and stored in liquid nitrogen.

Patients then undergo an aggressive treatment of high-dose chemotherapy and whole-body irradiation to destroy residual leukemia cells in their body. Then, the cleansed marrow is infused in an attempt to regenerate the patient's marrow with normal cells, free from disease. The patient is supported with antibiotics and blood transfusions for several weeks, after which the transplanted marrow begins to function. The treatment takes one to two months.

So far, 22 patients have received this treatment, including 16 who were in complete remission at the time of infusion and therefore had the best chance for a positive response. Of the 13 patients in second or third complete remission, eight of 11 patients who could be evaluated are still alive up to 28 months after treatment, with a median follow-up survival of 16 months. With standard chemotherapy, the average length of survival following relapse is four to five months.
There are several advantages to the autologous transplant over the allogeneic procedure, in which the patient receives the bone marrow of a brother or sister. In the traditional procedure, even though the patient and donor tissue types match, about three-quarters of transplant patients suffer a reaction known as graft-vs.-host disease, and a quarter die from it or from infections associated with it. The disease is caused by donor marrow cells attacking the patient.

The autologous procedure also makes treatment available to more patients. Even when a brother or sister donor is available, the donor's tissues match the patient's in only one-fourth of cases. Also, because the risk and severity of graft-vs.-host disease increases with age, traditional allogeneic transplants are not done in patients more than 50 years old. Since there is no risk of the disease in the autologous procedure, older patients can be treated.

Although using monoclonal antibodies to treat the marrow of lymphocytic leukemia patients has been done at various centers, including Scripps Clinic, Dartmouth was the first use the method to treat acute myelogenous leukemia. A similar treatment for acute lymphoblastic leukemia, the type children contract, has been used for some time.