

LE Magazine November 1997

## RESEARCH

### Cell Therapy An Exclusive Report from Europe

By Carol Kahn

Scientific evidence suggests cell therapy may have rejuvenation effects in animals and humans. But more research is needed to better define the nature of these effects.

Cell therapy. Yes, the term may make some squeamish, mainly because it involves injecting into the human body tissue matter from entirely foreign species... it involves, after all, the use of animal organs to improve human vitality. But the latest scientific studies suggest that cell therapy may be of significant benefit in reversing the effects of aging tissue, and in extending human life span.



The concept of cell therapy goes back more than 3,500 years to ancient Egypt, but it wasn't until 1931, when Paul Niehans, working at Clinique La Prairie, in Clarens-Montreux, Switzerland, and using a suspension of cells taken from fetal sheep that the idea first took off. Niehans was an aristocrat who moved in elite circles, and over the years royal families, heads of state and movie stars flocked to his clinic. They included Marlene Dietrich, Winston Churchill, Charles de Gaulle, Miles Davis and Pope Pius XII.

While there are still no controlled clinical trials, and this treatment is banned in the U.S., more than 5 million people have been treated with cell therapy, and not just for aging. Another pioneer, Franz Schmid, M.D., who worked with Niehans and until his death in January was one of the foremost practitioners in the world, used 60 different organ preparations to treat more than 100 medical problems ranging from acne and autism to cancer and neurodegenerative diseases.

Sam Baxas, M.D., head of the Baxamed Medical Center for Youth Restoration in Basel, Switzerland, credits Schmid with being his mentor and an inspiration in his current work. Baxas finds that the best cell-therapy results occur with the combination of cell therapy and human growth hormone.

(While cell therapy is not available in the United States, information is available from the Baxamed Medical Center. Baxamed can be reached from the U.S. by calling 011-4161-422-1292.)

The biggest indication for cell therapy remains its impact on the effects of aging. At Clinique La Prairie, patients who range in age from about 50 to more than 100 years old find "they have more energy, recover better after traveling, can do more work, have better memory and concentration, and have more stamina when they do sports," says Thierry Walli, M.D., chief physician at the clinic.

The original Niehans method used fresh cells from the organs of newly slaughtered lambs. Niehans chose sheep as the donor animal because he believed they never got cancer. While he originally used cells from young donor animals, cell therapists today prefer embryonic cells from fetuses since they are "immunologically silent"...that is, they do not trigger reactions in the recipient animals.

Since fresh cells must be used within an hour of the animals' slaughter, Niehans, working with researchers at the Nestle company, developed a freeze-dried method to conserve cells or cellular extracts that could be reconstituted as easily as instant coffee. That is now one of the most popular methods worldwide.

While some cell therapists prefer to use whole freeze-dried cells, others use fractionated cell extracts. The drying process withdraws more than 80 percent of the water out of the cells. The third method is the use of frozen cells, either flash-frozen and kept in dry ice, or deep-frozen cryogenically in liquid nitrogen.

Treatment at most clinics generally lasts several days, with one or two days of medical examination and tests, one or two days of cell therapy injections, and a following day of rest. Costs vary from \$3,100 for the treatment itself to about \$11,000 for five days at a luxurious spa-like clinic.

Gerhard Hofecker, M.D., and Hans Niedermuller of the Ludwig Boltzmann Institute of Experimental Gerontology, of the University of Veterinary Medicine in Vienna, Austria, fed young rats radioactive amino acids so that all the proteins in the body became labeled with radioactivity. They then injected cellular extracts from these animals' livers, hearts and kidneys into recipient animals. Two years later, they found radioactive traces of the cellular material in the corresponding organs of the recipient animal; liver went to liver, heart to heart, and kidney to kidney.

"I think the old idea of Niehans is right," says Hofecker. "There is a certain affinity of material across species," he says, indicating that material from a specific organ finds its way to the receptors on the cells of the individual receiving it.

These and other studies support the idea that tissues from fetal and young animals provide cellular material that can be used to repair and revitalize aging tissues. In a series of studies begun more than 30 years ago at the Vienna institute, Dr. A. Kment found that fetal cells actually shifted the biological age markers in old rats, causing significant improvements in the skin, aorta, liver, kidney and heart, as well as in motor activity and learning ability.

In subsequent studies on 700 male rats, Drs. Niedermuller, Hofecker, and M. Skalicky found that fetal extracts prepared from either sheep testes or mesenchyme tissue (very early connective tissue cells) transformed fundamental aspects of the aging process. Those included increased DNA repair, decreased DNA damage, improved maximum oxygen uptake, and a shifting of the spontaneous activity of older animals towards that of younger ones.

Most importantly, the Viennese researchers found that the fetal extracts increased the mean and maximum life expectancy in comparison with the controls. But the most impressive life span results were obtained with fetal mesenchyme cells in a preparation called Resistocell.

The study almost ended before it began when the colony of mice selected for life span study started dying off from lymphatic leucosis, a virally caused mouse leukemia whose incidence increases with age. But rather than scrap the study, the researchers decided to see what effect Resistocell might have in boosting the animals' immunity and, along with that, their life span.

The results were astonishing. The last animals of the control group died at 700 days, while the treated animals lived a normal life span of two to three years and beyond. All the animals in the colony eventually died of the disease except the last two animals, which lived nearly 1,100 days...57 percent longer than the longest-lived controls.

While Western pharmacology seeks specific substances that can cure specific ailments-the "magic bullet" idea-cell therapy is more like a magic shotgun that can scatter its effect where it is most needed.

In the 1980s, Clinique La Prairie began an extensive scientific program working with a number of academic institutions, including the Max Planck Institute for Immunobiology in Freiburg, Germany, to identify biologically active factors of interest. According to Walli and Otto Westphal, president of the scientific board of Clinique La Prairie and former head of the Max Planck Institute, the fetus contains factors that only are present during development and fade after birth. But these factors will work in old people.

In one remarkable experiment, G. Sauer and Dr. E. Antman of the German Cancer Research Center in Heidelberg, along with Westphal, found that the Clinique La Prairie extract made from fetal liver stimulated senescent fibroblast (connective tissue) cells to start dividing again. In other words, the fetal cell extract contained factors that could overcome the "Hayflick Limit," the point posited by researcher Len Hayflick at which cells cultured from human beings or animals stop dividing after a period of time. While Hayflick and others argue that the loss of cell division in culture means that aging is pre-programmed, Walli and Westphal suggest that the Clinique La Prairie extract contains senescent cell-activating factors that restore the responsiveness of old cells to growth factors, so they behave like young cells.

Then there is the impact of cell therapy on disease. For one, fetal cells have been shown to stimulate the body's ability to fight cancer.

One of the most effective cell preparations against cancer appears to be Resistocell, which contains mesenchyme from fetal umbilical cells, the blood thinner heparin, and a sugar group called dextran. Albert Landsberger, M.D., professor of anatomy and cell biology at the University of Heidelberg, Germany, found that 60 percent of animals given cobalt radiation developed tumors, while only 11 percent of the animals that received Resistocell before being irradiated got cancer.

Landsberger's results with cancer patients have been mixed. A randomized, placebo-controlled trial of breast cancer patients found no extension in survival. But an uncontrolled study trial from 1978 to 1986 in 48 patients with advanced breast cancer

showed that the injections significantly improved the quality of life according to a standard self-assessment questionnaire. Seven of the patients were alive more than 39 months after treatment, although the median survival time was 24 months for this group. One patient who came to Landsberger's clinic with metastases in the spine due to breast cancer was still alive and cancer-free 12 years after treatment with just Resistocell.

Westphal and Walli believe that the fetus contains many thousands of substances that have an effect on gene expression-up-regulating and down-regulating the many factors involved in the immune response. The latest thinking is that the immune system gets out of balance as we age, so that it becomes less effective in fending off disease and may turn against itself in the form of autoimmune disease.

For example, injections of Clinique La Prairie extract in old mice reversed the overproduction of immune regulators called interleukins, including interleukin 3, 4 and 6, associated with a higher incidence of lymphomas. Not only did it change the interleukin production in the old mice to that of young animals, it also prevented the onset of lymphomas.

Side effects are usually mild and limited to local reactions, such as redness and swelling at the injection site. People often feel a little tired the first two or three days. Cells must be taken from controlled herds that are carefully supervised by veterinarians to prevent contamination, infection or animal-borne diseases.

There also is the possibility of severe allergic reaction if the fetal tissue is too far advanced in the development process.

The contraindications to cell therapy are rare, but include autoimmune disease or related conditions such as rheumatoid arthritis or multiple sclerosis. Although these illnesses also are helped by cell therapy, treatment must be decided case by case since cell therapy may precipitate autoimmune activity.

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