Cell grafts proceed, value uncertain

While scientists and public officials continue to debate the ethics of experimenting with human fetal cells, the first transplants of such cells into adults with Parkinson's disease are being performed. Earlier this month, with very little fanfare, Sweden became the first country to officially acknowledge performing such experiments. But the controversial procedure has probably been attempted in as many as four countries in the past two months, according to researchers.

The procedure involves the grafting of fetal brain cells onto the brains of Parkinson patients, who suffer tremors and neuromuscular rigidity because of a lack of the neurotransmitter dopamine.

The Swedish experiments are the culmination of a series of animal and human studies that have hinted at the usefulness of such transplants. There is some debate among scientists, however, as to whether the most recent human trials may be premature. Indeed, recent findings reported in New Orleans at last week's annual meeting of the Society for Neuroscience call into question some of the results of earlier, more promising cell transplant experiments that did not involve transplanting human fetal cells into humans.

"The initial enthusiasm generated only a year ago has waned significantly," says Fred Gage, a neuroscientist at the University of California at San Diego. "Everyone thought we were seeing a little something," Gage says of the early transplant experiments. "Well, it *was* a little something – very little something."

Those experiments included transplants of dopamine-producing cells onto the brains of animals in which researchers had induced Parkinson-like symptoms with the chemical MPTP, and transplants of adult human adrenal cells onto the brains of patients with Parkinson's disease. Some subjects showed signs of neuromuscular improvement, and it was postulated that dopamine-producing human fetal cells would be more effective (SN: 7/11/87, p.22).

More recent research, however, suggests that much of the initial evidence of improvement in both animals and humans may have been overstated or misinterpreted. For example, there is a surprisingly high rate of spontaneous behavioral recovery among animals that have had Parkinson-like symptoms induced by MPTP. Thus it is now suspected that many test animals would have recovered even without the cell grafts.

Other studies call into question some of the microscopic evidence of nerve cell regrowth seen in the brains of animals receiving grafts. One disturbing bit of research, presented at the meeting by National Institutes of Health scientists, showed that it's possible to induce new sprouting of dopamine-producing cells in monkeys by transplanting any one of a number of tissues – even non-dopamine-producing tissues – into their brains.

Such sprouts, believed until now to be emanating from transplanted tissue, may in fact be outgrowths of dopamine-producing cells that survived the initial exposure to MPTP. The researchers hypothesize that these cells may have been stimulated to grow by some aspect of the brain surgery itself.

Not all the latest research is disappointing. Promising primate and rodent studies, including several experiments by researchers at the University of Rochester (N.Y.) and at the University of Colorado Health Sciences Center in Denver, were reported in New Orleans. Nevertheless, some researchers expressed surprise that human clinical trials were already proceeding in Sweden, and that human trials have likely been done in Mexico, China and possibly Cuba. Several neuroscientists at the meeting noted that U.S. scientists remain split on the ethics of using human fetal tissue for experimental purposes, and that resolution of the issue will likely await the outcome of experiments in other countries.

– R. Weiss

Smoking raises female heart attack risk

Smoking cigarettes causes about half of all coronary artery disease cases among young and middle-aged women in the United States, according to a Harvard University study released last week.

The study also showed that women who stopped smoking drastically reduced their chances of developing coronary artery disease and that no level of smoking was safe for women. In addition, several other risk factors, such as diabetes and hypertension, were found to significantly increase a woman smoker's chances of developing coronary artery disease, which includes fatal and nonfatal heart attacks and periodic chest pain, or angina.

"Cigarette smoking is the single most avoidable risk factor for heart attacks in young and middle-aged women," says the study's principal author, Walter C. Willett of the Harvard School of Public Health.

For many years, studies showed that smoking among men – but not among women – was associated with coronary artery disease. But researchers now say the studies looking only at women were flawed because the samples were too small. In recent years, the association among women has been established. And according to the researchers, the Harvard study is the largest study to report the association, which shows that men and women smoking the same number of cigarettes have about the same chance of developing coronary artery disease.

In 1976, Frank E. Speizer and his Harvard colleagues began tracking the health and lifestyle status of about 120,000 married registered nurses, all women between 30 and 55 years of age, in what became known as the Nurses Health Study. Nurses were chosen, Willett says, because the researchers thought they would give accurate reports and would be representative of the U.S. female population for that age group. In fact, 30 percent of the group in 1976 smoked cigarettes, which was comparable to the proportion of smokers in the same age group among U.S. women.

Among women who smoked 25 or more cigarettes daily, about 81 percent of deaths from coronary artery disease were attributed to smoking. That same group was 5.4 times more likely to have fatal heart attacks than nonsmokers. In addition, the 25-or-more group was 5.8 times more likely to have nonfatal heart attacks than nonsmokers and 2.6 times more likely to have angina.

In contrast to current smokers, former smokers had the same rate of coronary artery disease as women who had never smoked. "If you stop smoking, the risk of disease decreases in a matter of days," Willett says, because many effects of smoking, such as clotting of blood, will stop almost immediately.

The Harvard study, which appeared in the Nov. 19 NEW ENGLAND JOURNAL OF MEDICINE, also found that women who smoked one to four cigarettes daily were 2.4 times more likely to have coronary artery disease than nonsmokers. About 58 percent of the cases in this group were attributed to smoking.

When the researchers looked at several risk factors in combination with smoking, the results were dramatic. Hypertensive smokers were 22.2 times more likely to develop coronary artery disease than nonsmokers without hypertension. For smokers with high cholesterol, the figure was 18.9, and for smokers with diabetes, it was 22.3.

During the next year, Willett and his colleagues plan to write about 30 additional papers based on the Nurses Health Study and will examine such topics as diet and coronary artery disease and risks associated with stroke. Eventually, they want to determine whether the nurses will listen to the advice provided by the articles.

– S. Eisenberg