Statistical analysis of medical studies is based on the key idea that we make observations on a sample of subjects and then draw inferences about the population of all such subjects from which the sample is drawn. If the study sample is not representative of the population we may well be misled and statistical procedures cannot help. But even a well designed study can give only an idea of the answer sought because of random variation in the sample. Thus results from a single sample are subject to statistical uncertainty, which is strongly related to the size of the sample. Examples of the statistical analysis of sample data would be calculating the difference between the proportions of patients improving on two treatment regimens or the slope of the regression line relating two variables. These quantities will be imprecise estimates of the values in the overall population, but fortunately the imprecision can itself be estimated and incorporated into the presentation of findings. Presenting study findings directly on the scale of original measurement, together with information on the inherent imprecision due to sampling variability, has distinct advantages over just giving P values usually dichotomised into "significant" or "non-significant." This is the rationale for using confidence intervals.

The main purpose of confidence intervals is to indicate the (im)precision of the sample study estimates as population values. Consider the following points for example: a difference of 20% between the percentages improving in two groups of 80 patients having treatments A and B was reported, with a 95% confidence interval of 6% to 34%.² Firstly, a possible difference in treatment effectiveness of less than 6% or of more than 34% is not excluded by such values being outside the confidence interval—they are simply less likely than those inside the confidence interval. Secondly, the middle half of the confidence interval (13% to 27%) is more likely to contain the population value than the extreme two quarters (6% to 13% and 27% to 34%)—in fact the middle half forms a 67% confidence interval. Thirdly, regardless of the width of the confidence interval, the sample estimate is the best indicator of the population value—in this case a 20% difference in treatment response.

So when should confidence intervals be calculated and presented? Essentially confidence intervals become relevant whenever an inference is to be made from the study results to the wider world. Such an inference will relate to summary not individual characteristics—for example, rates, differences in medians, regression coefficients, etc. The calculated interval will give us a range of values within which we can have a chosen confidence of it containing the population value. The most usual degree of confidence presented is 95%, but any suggestion to standardise on 95%^{3 4} would not seem desirable.¹⁵

MARTIN J GARDNER

Professor of Medical Statistics,
MRC Environmental Epidemiology Unit,
(University of Southampton),
Southampton General Hospital,
Southampton SO9 4XY

DOUGLAS G ALTMAN

Head of Medical Statistics Laboratory,
Medical Statistics Laboratory,
Imperial Cancer Research Fund,
London WC2A 3PX

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Adrenal and nigral transplants for Parkinson's disease

The spectacular benefits of levodopa and its analogues in Parkinson's disease are limited by waning of therapeutic efficacy and by the development of on/off swings, dyskinesias, and mental symptoms.^{1,2} Research has sought other approaches, and in 1981 in Sweden attempts were made to transplant the patient's own adrenal medulla (autografts) into the caudate nucleus in the hope that this would bypass immunological rejection and provide an added source of endogenous dopamine.³ The benefits in four patients were slight and transitory. This work showed, however, that the operation was possible—the adrenal catecholaminergic tissue took on its new blood supply and to some extent reinnervated the receptor site.

More publicity was given to the extension of this work in younger patients in Mexico⁴: two of the 12 patients treated died within six months—but from unrelated causes. Benefit was claimed for rigidity, akinesia, and tremor, but improvement was variable and was delayed from three to 10 months and in some cases for more than a year. There was no controlled series, and the florid publicity in the national press led to sceptical criticism among neuroscientists in the United States. Isolated reports of similar procedures in North America have confirmed the soundness of this cautious reception; the results have been controversial.

The technique consisted of transplanting a piece of adrenal autograft into the head of the caudate nucleus adjacent to the lateral ventricle, where it is close to the vascular choroid plexus and is bathed in cerebrospinal fluid: from here the graft disperses the catecholamines throughout the central nervous system. It is too early to assess these results because of small numbers, short follow up, and the absence of controls.

Other methods have been attempted, notably transplanting the fetal substantia nigra. In rats that have had their striatum destroyed solid grafts or suspensions implanted in the caudate putamen sprout axons and form extensive new synaptic pathways. They restore 10-50% of striatal dopamine, and its turnover and receptor sensitivity are restored.⁵ These are substantial theoretical advantages. The operation has been technically achieved in a few cases, notably in two patients from Birmingham a couple of weeks ago. Benefit cannot be claimed at such an early stage, though the interest stimulated may encourage other workers to collaborate in a controlled investigation. Fetal nigral material has to be obtained when the fetus is about 8 to 12 weeks old. It is

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uncertain whether the donor graft can be used from any fetus aborted at this age by the usual obstetric procedures or whether special measures such as hysterotomy have to be employed to provide ideal donor tissue. If hysterotomy is a necessary prerequisite it will add to the ethical dilemmas, which include the rights of the fetus, the consent of the parents, and the absolute obligation to use only fetuses that are aborted for other acceptable indications that must be seen to be wholly unrelated to putative transplantation.

These operations are exciting but must be viewed with caution. It is not known whether transplantation alters the evolution or outcome of Parkinson's disease, or whether any benefit will be lasting. It is not known whether whatever agent(s) primarily cause the disease will also destroy the graft, and we should remember that Parkinson's disease reflects a disorder not only of dopamine but also of a multitude of other neurotransmitters.

These techniques hold out promise but must be scientifically tested; meanwhile, no patient should feel deprived of an implant until far more information has accrued. The late Lord Cohen once remarked that "the feasibility of an operation is no indication for its performance."

J M S PEARCE

Consultant Neurologist,
Hull Royal Infirmary,
Hull HU3 2JZ

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Ethics of fetal brain cell transplants

In analysing the ethical issues provoked by the technique of transplanting fetal brain cells into the brains of patients with Parkinson's disease described above it may be helpful to consider the various affected parties within the framework of four widely acceptable moral considerations: respect for people and their autonomy, beneficence (doing good), non-maleficence (avoiding doing harm), and justice (fairness in distribution of resources, in respect for rights, and in respect for morally acceptable laws).^{1,2} Such analysis is benefited by discussions on this subject at Britain's first multidisciplinary conference on philosophy and ethics in reproductive medicine, which was held last week in Leeds.

Obligations to the recipients of the fetal brain cells seem well met. Thus, as the conference heard from Dr Richard West, chairman of the ethics committee that approved the research, the committee followed the standard research ethics committee guidelines of the Royal College of Physicians. Theoretical considerations, animal research, and preliminary results of clinical research abroad had shown a reasonable prospect of benefiting the severely affected patients (beneficence) with an acceptably low risk of harming them (non-maleficence). The requirement of adequately

informed consent respected their autonomy, and no justice considerations were infringed either in terms of fair distribution of resources or infringement of the subject's rights; and the procedures were legally acceptable.

Moral qualms were expressed at the conference about the women whose aborted fetuses were used. Although such women signed consent forms disclaiming any views on the disposal of the fetus, some participants vigorously argued that the women concerned ought to be given more explicit information if the fetal tissues might be used for transplantation or other research and their specific unpressured consent obtained. On the other hand, a woman lawyer argued that not to be satisfied with an adult woman's signature disclaiming views on disposal of the fetus smacked of patronising sexism. In addition, such women might be benefited by being told the outcome, where successful, of any use made of fetal tissues, as proposed by the Conference of Medical Royal Colleges for transplantation.³

The women's welfare might be adversely affected if special and more risky abortion techniques were used in order to preserve the fetal brains for transplantation. Furthermore, if such use became widespread women might be increasingly exploited by commercial or other pressures to become pregnant to provide aborted tissues. But given suitable controls to prevent such problems no insuperable moral objections seemed to arise from the perspective of the pregnant women. Their autonomy could be respected, they could be benefited with low probability of harm, their rights could be respected, and they could actually contribute to greater distributive justice by permitting their fetuses to be used to benefit others medically; and provided the abortions are carried out according to the requirements of the Abortion Act the procedures are lawful.

But is the Abortion Act a morally acceptable law? The main ethical objections offered at the conference concerned precisely that question in relation to the third affected party, the aborted fetuses. One of the main speakers, Miss Pamela Sims, a consultant obstetrician and gynaecologist and moral opponent of abortion, argued that, since abortion and the Abortion Act were morally unacceptable, using fetal parts for transplantation after abortion was also morally unacceptable—"the end cannot justify the means."

Clearly if the fetus is to be accorded full moral status destroying it for the benefit of others would be unacceptable; but, as the ethics committee reportedly reasoned, it was not for its members to deploy their personal moral reservations about abortions in coming to their decisions. It, like the Peel committee, to whose advice it had scrupulously adhered, started from the presumption that abortions were to be carried out. The moral question then becomes: *given* that abortions have been carried out is it morally acceptable to use fetal tissues to benefit others? The relevant means here, as philosopher Jenifer Jackson pointed out, was the transplantation of tissues from already aborted fetuses, and those means could be morally acceptable even to those who believed the abortions themselves and the Abortion Act to be morally wrong. Dr Wendy Greengross, general practitioner and member of the Warnock Committee, illustrated the point succinctly—the fact that a brain dead man on a respirator had been murdered would not morally prohibit using his organs for transplantation.

Finally, are the interests of society threatened by this development? Some concern was expressed at the conference that ethics committees were able locally to make socially controversial decisions including decisions about "human brain transplants" with only one lay member on the com-