Editorial

Ethics of innovative cardiac surgery

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The development of scientific inquiry and recognition of the individual are two of the major revolutions in thought that have occurred since mediaeval times. The tension between the two leads to moral choices that possibly reach their extreme in medicine. There may be conflict for the physician or surgeon between his duties to the individual patient and his obligations as a scientist to contribute to knowledge that can be generalised. Medical ethics addresses these conflicts but does not necessarily resolve them. Innovative surgery, especially the use of a new operation on the heart, poses ethical problems. In this article I discuss such problems together with the view that the ethical questions raised have not always been adequately considered and that the undertaking of some operations has not been ethical.

Need for and constraints on innovative surgery

In 1865 Claude Bernard wrote, "It is our duty and our right to perform an experiment on man whenever it can save his life, cure him or give him some personal benefit."¹ The importance of clinical research has been affirmed many times in the various guidelines or declarations of committees concerned with the ethics of research in adults and children. Children, together with mentally ill or mentally defective patients, are a particularly vulnerable group because of their inability to give fully informed consent and hence their need for even greater protection than that given to normal adults. In 1977 the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research (United States, Department of Health Education and Welfare) examined the ethics of research in children and concluded that, "Research

involving children is important for the health and well being of all children and can be conducted in an ethical manner, the Commission recommends that such research can be conducted and supported, subject to the conditions set forth . . ."² Similarly, the British Paediatric Association working party on the ethics of research in children took as the first of its premises, "That research involving children is important for the benefit of all children and should be supported and encouraged and conducted in an ethical manner."³ They also went on to say that research should not be done in children if the same investigation could be done in adults.

Much of current awareness of the ethical aspects of human experimentation has stemmed from the appalling revelations at the Nuremberg war trials. As a consequence, from 1947 professional bodies have predominantly been concerned with protecting subjects from so called "non-therapeutic research" or more precisely from procedures or interventions carried out to obtain information that is not of direct benefit to that subject.⁴

The particular issues of medical research combined with professional care (clinical research) were addressed in the Helsinki Declaration of the World Medical Association,⁵ which states that, "(1) In the treatment of the sick person, the doctor must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health or alleviating suffering. (2) The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods." These recommendations are of direct relevance to the performance of a new operation on the heart. The Helsinki Declaration and others use the phrase "therapeutic research" to imply research activities carried out that are potentially of direct benefit to the subject.

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Innovative treatment and therapeutic research

Although Popper proposed that scientists use definitions merely as shorthand labels and not to determine the meaning of terms,⁶ what is meant by "therapeutic research" is still worth examining. "Research" has been defined as either, "An investigation directed to the discovery of some fact by careful study of the subject, the act of searching (closely and carefully) for or after a specific thing or person,"⁷ or as, "A systematic investigation to increase the sum of knowledge."⁸ "Therapy" is defined by the Oxford English Dictionary 1971 as treating medically (or surgically).

As Hare has pointed out, research as such cannot be therapeutic or non-therapeutic as it is simply a process of finding out (Proceedings of the working party into the ethics of research in children. The Society for the Study of Medical Ethics, to be published). The British Paediatric Association defined therapeutic research as research in which a procedure is of potential benefit to the subject. This is confusing as it is the procedure or intervention that is therapeutic or non-therapeutic, not research as such. For this reason I suggest that, if the term therapeutic research be used at all, it is defined as an intervention, carried out to treat a person medically, that is at the same time carried out as part of the careful systematic study of that intervention. If this definition is used it could be said that innovative treatment, such as a new operation on the heart, should constitute "therapeutic research", that is to say it should be part of the systematic investigation of that procedure (research). To develop this further, some new heart operations will fail or be inappropriate, and yet new operations have to be attempted to advance medical treatment. Unnecessary suffering or death may, however, result from uncontrolled repetition. Thus performance of a new operation as part of a planned research programme may be ethically justifiable but haphazard experimentation by many different surgical teams, possibly resulting in unnecessary mortality, may be deemed unethical.

This article does not deal with acute or unexpected emergencies arising in the operating theatre. Placing strictures on the innovative surgical skills required to deal with such situations would obviously be absurd and in this article only planned operations are considered.

Informed consent

To quote Erikson, "Respect for the autonomy of man is not deliberately to deceive or exploit."⁹ An important example of this autonomy is enshrined in the principle of informed consent. The question of informed consent to therapeutic procedures will be

discussed here, consent to non-therapeutic procedures having been extensively discussed elsewhere. As Ramsay has commented, "In this age of research medicine it is not only that medical benefits are obtained by research but also that a man rises to the top in medicine by the success and significance of his research."¹⁰ This also applies to clinical practice, particularly when innovative treatment or a new cardiac operation with or sometimes without a successful outcome has major professional and other advantages. Fully informed consent is one form of protection for the patient.

Niebuhr's defence of democracy was that, "Man's capacity for justice makes democracy possible; man's propensity to injustice makes democracy necessary."¹¹ This was paraphrased by Ramsey as, "Man's capacity to become joint adventurers in a common cause makes consensual relation possible; man's propensity to overreach his joint adventurer even in a good cause makes consent necessary."¹⁰ Ramsey reasoned that the principle of informed consent was a statement of the trust between the person who performs medical procedures and the person (especially if a child) on whom they are performed. He concluded that informed consent was the cardinal canon of loyalty joining men (and women) together in medical practice or investigation.

Informed consent should include an adequate explanation of alternative treatments available and also as clear as possible an analysis of the ratio of risk to benefit. Not only was this confirmed in the Helsinki Declaration but in the United States National Commission Protecting Human Subjects of Biomedical Research (on children).² Recommendation 4 states that, for a new treatment "The relation of anticipated benefit to risk should be at least as favourable to the subjects as that presented by available alternative approaches." This is particularly pertinent to innovative cardiac surgery. The notion of a learning curve for a new operation is widely recognised. The first time a new operation is performed there may be technical difficulties not previously met; with practice or improvements in surgical technique or selection of patient the probability of a successful outcome may be higher. This applies equally to new "medical" procedures such as balloon dilatation of narrowed coronary arteries or pulmonary or aortic valves. The first patient in whom a new procedure is performed is at greater risk than those to follow; yet no patient (in particular a child) should be operated on more for the benefit of future patients than for himself. Resolution of this ethical dilemma is difficult, but the patient (or person entrusted to give proxy consent on his or her behalf) must be fully informed of the risks and of the other procedures available. These ethical issues have been raised recently by the introduction of the arterial

switch operation for complete transposition of the great arteries and by implantation of the first artificial heart.

Innovative cardiac surgery

IMPLANTATION OF THE TOTAL ARTIFICIAL HEART

As discussed by Woolley,¹² no previous innovation in medical technology has undergone such rigorous review with respect to experimentation in human subjects. The initial application by research workers at the University of Utah to implant an artificial heart was in June 1980, but the operation did not take place until December 1982.¹³ The delay was caused by the need to examine the many ethical issues raised by the operation and in particular to ensure that the prospective patient was adequately informed and that his or her rights were adequately protected.

Three categories of patients were considered initially as potential recipients of the artificial device: patients in category 1 were those undergoing open heart surgery but who could not be taken off the heart lung pump; patients in category 2 were those with end stage chronic heart failure whose short term prognosis was grave; and patients in category 3 were those with acute severe myocardial infarction or similar acute catastrophic disease of the heart who were not expected to survive the acute phase of their illness. The second two categories were rejected initially: those with congestive heart failure on the grounds that the ratio of risk to benefit was unacceptable and those in the second category because severely ill patients in whom drug treatment had recently been started and who were surrounded by monitoring equipment were not thought to be capable of giving fully informed consent. Thus patients in the first category alone were approved as subjects for the operation. After 18 months no suitable recipient had been found. Further consideration was then given to a patient from the second category, but in considering the ratio of risk to benefit the Food and Drug Administration, United States, mandated that the first implant of an artificial heart could not be in a patient who would be a candidate for an orthoptic (human) heart transplantation. Evidently, the availability of alternative treatments was considered crucial in this judgment.

ARTERIAL SWITCH OPERATION FOR COMPLETE TRANSPOSITION OF THE GREAT ARTERIES

It is salutary to compare the extensive debate of the ethics of implanting an artificial heart in an adult with the lack of debate of the ethical issues involved in introducing the arterial switch procedure in children with transposition of the great arteries, since use of the arterial switch operation in children presents a

similar ethical dilemma. Interatrial repair of complete transposition of the great arteries by either the Mustard or Senning techniques has been widely used for more than 10 years. By the mid-1970s hospital mortality for correction of simple transposition of the great arteries by the Mustard technique was reported as being less than 10% in several large series¹⁴⁻¹⁸ even when the operation was performed in the first year of life.¹⁹⁻²² Similar results were reported for the Senning procedure.²³ In contrast, when a ventricular septal defect was additionally present mortality for interatrial repair plus closure of the ventricular septal defect was higher, between 25 and 30%.^{20,21}

Against this background Jatene *et al* introduced arterial switch or anatomical repair of transposition of the great arteries.²⁴ Further reports of a successful outcome in one or two children with an additional ventricular septal defect or large ductus were rapidly published.^{25,26} In some but not all of these early articles surgical failures were commented on, especially when the operation was performed for simple transposition of the great arteries and the previously low pressure left ventricle could not sustain the systemic circulation. An editorial in the *British Medical Journal*²⁷ at this time, while praising the surgical expertise shown, commented on neither the ethical implications of the procedure nor the selection of patients. In many cardiac surgical units this operation was then tried in small groups of patients both with and without a ventricular septal defect, with considerable mortality.

At the same time, the concept of correction of simple transposition of the great arteries in two stages was introduced.²⁸ In the first stage the pulmonary artery is banded to prepare the left ventricle to sustain the systemic circulation before anatomical repair in the second stage. New surgical procedures must be developed and used if they are believed to offer a greater benefit to the patient than previous techniques. In the individual child, however, the decision of which procedure to follow is difficult as even in the best hands the hospital mortality for arterial switch operations is still higher than for an interatrial repair.

At present the arterial switch operation is justified on the grounds of neither lower early mortality nor a better medium term outlook (Parenzan, unpublished observations) as many of the medium term complications of interatrial repair, such as late arrhythmias²⁹ or venous obstruction,³⁰ can now largely be avoided. The principal reason, at present, for the use of the arterial switch operation is the hope of a better long term survival (and quality of life) than with the current conventional operations. The prospect of improved long term survival, though possibly correct, remains hypothetical, as even a successful initial outcome from anatomical repair does not preclude late complications, some of which have been reported.

The ethical justification for having introduced a "two stage procedure" for simple transposition of the great arteries in 1977²⁸ remains debatable, as does that for a recent study of patients operated on between December 1980 and July 1982,³¹ in which the cumulative mortality was 52% in the 25 patients in whom successive parts of the two stage procedure (pulmonary artery banding followed by arterial switch) had been attempted. As the surgical unit concerned includes experienced surgeons mortality from interatrial repair alone would reasonably have been expected to be less. The last two sentences of the related abstract are quoted below, in which the authors concluded, "that both stages of the procedure have high mortality and morbidity especially when banding is performed on very cyanotic infants or older patients. Thus, we abandoned this way to prepare the left ventricle, since July 1982, a new protocol with neonatal banding (<5 days) and early switch ($\approx$ 3 months) is in process with encouraging results." It might be asked whether a hospital ethics committee or an institutional review board would have agreed to this new protocol.

No single group should, however, be singled out, for others have had a high initial mortality with this and many other new operations without reporting the results so openly. Indeed, much of the development of cardiac surgery has been associated with a high early mortality, which was rightly or wrongly accepted when there was no alternative. Now, when there are alternatives, one must question the extent to which new operations should be so freely attempted. To take the specific instance of surgery for complete transposition of the great arteries, on a ratio of risk to benefit it could be argued that, at least until the technical problems had been solved, only patients with transposition and a ventricular septal defect should have been considered for the switch procedure. In this way many of the technical problems of the operation would have been solved while operating on a group in whom mortality from the "conventional" repair was relatively high. To quote again from the Helsinki Declaration, "The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods."⁵

Conclusions

Patients in modern cardiac units could now be argued to be more at risk from therapeutic research, such as innovative surgery, than they are from non-therapeutic research. To protect both the patient and the pioneering surgeon I suggest that new operations should be subject to the same ethical review as other research procedures. Would this encroach on "clinical

freedom?" To quote from a leader in the *British Medical Journal*, "Many doctors prefer to move on to the new and important, which they hope will have dramatic effects, rather than to assimilate the relatively small benefits that are available from tested treatments."³² This article was entitled, "The end of clinical freedom." In the present context what should be requested is not necessarily the end of clinical freedom but simply some control over its exercise.

Although new operations must be introduced to improve patient care, this must be done with adequate safeguards. It is a breach of trust and hence unethical: (1) to introduce an operation haphazardly (non-systematically); (2) not to compare the new treatment with the existing treatment; and (3) not to select the patients so as to minimise any extra risk. In addition, consent must be truly informed and the ratio of risk to benefit clearly presented. In this way innovative cardiac surgery may flourish and the patient and surgeon will both be protected.

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