Ethical issues in research on humans

Sue Eckstein

In Great Britain, as in many other parts of the world, all medical research involving humans is subject to scrutiny by a local research ethics committee (LREC). Local research ethics committees provide independent advice to all bodies belonging to the National Health Service (NHS) within the geographical area of a health district. They sometimes also advise on studies not involving NHS patients, records or premises, carried out by private sector companies, universities, or bodies such as the Medical Research Council.Research ethics committees normally have between eight and 12 members, drawn from both sexes and from a wide range of age groups. They should include hospital medical staff, nursing staff, general practitioners and two or more lay people. Ideally they will also include a statistician and a pharmacist. If they do not, the chair of the LREC will refer specific queries to a statistician or pharmacist based at the hospital. Though members are drawn from groups with particular interests or responsibilities in connection with health issues, LREC members are not considered to be representatives of these groups. Members' broad range of experience and expertise should allow for reconciliation between the scientific and medical aspects of a research proposal, and the welfare of research subjects and broader ethical implications (1).In order to facilitate the process of ethical review of multi-centre research, a system of multi-centre research ethics committees (MRECs) was established in 1997 to complement the work of existing LRECs. An MREC is responsible for considering all multi-centre research that is health related where the research will be conducted within five or more locations (2). Most pharmaceutical company sponsored research proposals will be submitted to an MREC. Only a researcher who has received written MREC approval may go on to seek local REC approval in the areas in which they wish to work.. The LREC will only consider issues that affect local acceptability and is otherwise bound by the MREC's decision.

The Centre of Medical Law at King's College, London, is one of the main providers of training for members of research ethics committees. It has for some time run a three-day introductory course on the ethics of research on humans. This course involves lectures and workshops covering ethical tools for reviewing research proposals, different types of research methods including observational and qualitative research, and randomised controlled trials. There are also sessions on the development and licensing of medicines and the regulation of the pharmaceutical industry's clinical trial activities, and the law relating to consent, confidentiality and the running of a committee.

It has become apparent that there are aspects of healthcare research that can be particularly problematical for members of research ethics committees. One of the most difficult subjects for members of LRECs is that of research involving vulnerable groups. These include children, the mentally ill, elderly people and the dying.

In order to begin to address this, the Centre of Medical Law and Ethics has recently set up a new series of advanced study days, each concentrating on research involving one of these vulnerable groups.

The first study days was on ethical issues in paediatric research. Participants were briefed by an ethicist, a medical lawyer and a key member of the Royal College of Paediatrics and Child Health on the ethical and legal issues involved in research on children. These presentations were followed by case study work, in which participants worked together to consider a number of fictitious ethical dilemmas. They then had the opportunity to address questions to a panel of experts. The panel included paediatricians, a parent of children involved in medical research, a sociologist specialising in children's ability to consent, a child psychiatrist, a research nurse from a children's hospital and a clinical trials manager from a pharmaceutical company that produces a number of drugs for children.

Though a number of the issues raised are particular to a UK context, many of them are more universally relevant and may be of interest to readers in India.

The Royal College of Paediatrics and Child Health (RCPCH) regards research into children's diseases as crucial in securing better evidence-based care for future children but stresses that it should conform to the highest ethical standards (3). Children are acknowledged as having a unique physiological and psychosocial status and are as equally deserving of evidence-based treatment as adults. The fact that many medicines are not licensed for children renders them therapeutic orphans (4). A child's vulnerability and need for protection should not be used to prevent them benefiting from research which is therapeutically useful. It is particularly important to establish that the lack of research is not purely driven by commercial or indemnity related concerns.

Some parents might feel morally obliged to contribute to therapeutic research which will benefit their offspring, but this should be not be motivated by a disproportionate sense of gratitude. Practitioners involved in the long-term care of children with a chronic or life-threatening disease should be particularly aware of the impact of the relationship between the team and the family, and the ways in which this might influence parents' attitudes.

Putting aside the legal issues relating to consent, there is a moral requirement to involve a child as much as is possible and/or appropriate in the consent process. This entails a number of specific duties when there is the possibility that the child could participate in a meaningful way. They include testing the individual child's ability to participate in the consent process and proceed accordingly, ascertaining the extent to which the child wishes to be involved in the decision making process, discussing with

Sue Eckstein, *research associate, Centre of Medical Law and Ethics, King's College, London, Strand, London WC2R 2LS, UK. Email: sue.eckstein@kcl.ac.uk*

the parents or guardians the extent to which they are prepared to involve the child in the process and final decision and providing information which will help the child to get a realistic sense of what will be involved in participating without causing undue harm. The key to success in gaining informed consent lies in effective communication between researchers, families, associated professionals, professional bodies, LRECs and MRECs, research councils, charities, drug companies and educational institutions, and possibly parental or patient involvement in the design of the project (5).

English law relating to medical research on children is complex and uncertain and it is impossible to state the law relating to this with complete certainty. There are no statutes or legal cases that deal with research on children specifically. As a result, it is necessary to identify the broad legal framework relating to children, and to try to determine the implications of these principles in the area of medical research. Inevitably, this involves a degree of speculation about how a judge would deal with the issues if a case were brought to court.

In England, the legal framework for the care and upbringing of children (including issues of medical treatment) is mainly derived from the Children Act 1989. This is a very complex piece of legislation, but there are at least three key aspects of the law which are relevant to research involving children – parental responsibility, the powers of the courts and children's rights.

The power of children to consent to *treatment* is derived from the famous case of *Gillick* (6) (which established that children with "sufficient understanding" could consent to medical treatment without parental involvement.) It is unclear whether this principle allows children to consent to involvement in medical research. Even if, in principle, children can consent to involvement in research, it is also necessary to determine whether an individual child is competent to do so. The General Medical Council has given guidance on assessing children's competence to consent to medical *treatment* (7). This guidance is consistent with the approach to competence taken by the courts, but the courts have never considered the level of competence that a child would need to demonstrate to make a decision about medical research. An assessment would require consideration of the child's specific circumstances, including age, maturity and experience, and also the complexity of the research, and the consequences for the child of involvement or non-involvement. However, in practice, researchers take a cautious approach, and are likely to seek approval from both the child and the parents, and not to involve the child in research if the child or the parents are unwilling.

The RCPCH, in its two recent guidelines (8, 9), provides a series of questions which research ethics committees should consider in assessing risks and benefits including the type, nature, magnitude, probability, timing of risks or benefits; the fairness of research to subjects and its effect on their future autonomy.

A number of other issues arose out of the discussions. There were comments and questions on the issue of consent by adults for children with special needs and on consent by parents who themselves have a learning disability. There was a broad consensus that there was a need for research with terminally ill children and discussion on how LREC members, who would normally be averse to this, could be reassured that such research can be ethical. There was a discussion on the extent to which children should have an obligation to take part in research. For example, parents may refuse to allow their children to participate in research but want the benefits of gene therapy for their own children.

Members of research ethics committees are clearly very interested in receiving expert guidance to assist them in their task of assessing protocols from an ethical perspective. Other planned advanced study days will focus on ethical issues in psychiatric research, ethical issues in research into diseases of age, and ethical issues in palliative care. It is hoped that future days will include ethical issues in research on neonates, in cancer-related research, and in research on people in a persistent vegetative state or coma.

The more knowledge and understanding that both researchers and members of research ethics committees have of the difficult issues surrounding research involving people in these and other groups, the more a healthy balance will be established between protecting the interests of vulnerable participants and valuably expanding the research base in these complex areas of health care.

References:

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