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Ethical Issues in Research with Children in the UK

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Abstract

Research in children is essential if one is to ensure that they receive the best possible treatment. Research needs to be carried out in accordance with both national and international guidelines and in accordance with the law in each country. The situation in both Scotland and England is described in detail.

Key words: Children – Research – Ethics – Consent

Introduction

"Research involving children is important for the benefit of all children"[1]. Research is the production of new knowledge. It is important to realise that a research procedure, which is not intended to directly benefit the child involved, is not necessarily either unethical or illegal[1].

The legal, ethical, social and cultural framework within which research with children is conducted is constantly evolving and many changes have occurred recently. The aftershock and ripple effects from Bristol, publicity about controversial paediatric research projects and inconsistencies in the current ethical review process has caused widespread concern amongst both lay and professional groups. This has led to a plethora of guidelines (Table 1) which incorporate the new legal principles (Table 2). It is important to note that there are differences between English and Scottish Law that have direct relevance to the issue of consent.

Research that is legal may not be ethically acceptable or may not accord with social or cultural mores. Conversely, ethically sound research may never have been tested in terms of its legality.

This article is written with the principles of English and Scottish law in mind, while acknowledging the guidelines from the European Union, the Declaration of Helsinki and the United Nations Convention on the Rights of the Child (Tables 1 and 2).

Types of Research

Research can conveniently be divided into 'therapeutic' and 'non-therapeutic'.

In *therapeutic research* it is probable (or at least the aim should be) that the research will directly benefit the patient. Most commentators agree that *therapeutic research* (research that is likely to benefit the patient directly) is justified. The competent child should have the right to consent to therapeutic research for him/herself, the legal and ethical position being identical to adults. Concerning the incompetent child, parents must give voluntary consent, fully understanding the risk:benefit ratio of the research proposed. After assessing this risk:benefit ratio, they must believe that it is in the child's best interests to be involved in that study.

Non-therapeutic research, on the other hand, will not benefit that particular patient, although the

Table 1: Useful guidelines (see reference list for full details)
United Nations Convention on the Rights of the Child 1997
Declaration of Helsinki updated 1996
EU Good Clinical Practice Guidelines 1993
General Medical Council. Seeking patients' consent: the ethical considerations 1998 General Medical Council. Good medical practice 1998
Advisory Committee on Genetic Testing Advice to Ethics Committees 1998
Association of British Pharmaceutical Industry Guidance Note. Patient information and consents for clinical trials 1997
Human Fertilisation and Embryology Authority Guidelines 1998
Medical Research Council. The ethical conduct of research on children 1993
Royal College of Paediatrics and Child Health Guidelines for the ethical conduct of medical research involving children 2000; Withholding or withdrawing life saving treatment in children 1998.
Yorkhill Research Ethics Committee Guidance on good practice for the conduct of research with children 1999
Royal College of Pathologists Consensus statement of recommended policies for uses of human tissue in research, education and quality control 1999
Nuffield Council on Bioethics. Human Tissue: ethical and legal issues 1995

results may be very useful in benefiting future patients. It serves as a learning mechanism for future patients. The extreme arguments advocating no research at all, or justifying it as a duty to society are not acceptable. The middle of the road attitude of balancing the risks to the child with the many advantages to society as a whole should prevail.

If the risks are significant, the research should not be allowed, because this would clearly be acting against the best interests of the child and therefore contrary to the Children's Acts of England and Scotland. The Royal College of Paediatrics and Child Health has stated that it would be unethical to submit a child to more than minimal risk when the procedure offers no benefit to them.

They define minimal as procedures such as questioning, observing and measuring children, provided that procedures are carried out in a sensitive way, and that consent has been given. Procedures with minimal risk include collecting a single urine sample (but not by aspiration), or using blood from a sample that has been taken as part of a treatment. The competent child, by definition, should be allowed to decide for him/herself in the same manner as adults. There is one limitation, however. The greater the risk to the child, the older he/she must be before a doctor decides he/she is competent.

Table 2: Relevant statutes and case law
Children Act 1989
Children (Scotland) Act 1995
Age of Legal Capacity (Scotland) Act 1991
Age of Majority Act 1969
Family Law Reform Act 1969
Gillick v West Norfolk and Wisbech AHA [1985], 3 ALL ER 402

Principles of Consent Procedures

Consent requires five preconditions to make it legal:

- The person is required to be of **"***competent***"** mind
- They must be *fully informed* regarding the nature of the procedure, including the associated risks
- They must *understand* the information they have been given
- Their decision must be made *voluntarily*
- Finally they must give *authorisation*

The legislation and guidelines are now child-centred and so the child has more individual rights [2]. This means that the child must be assessed as to their competency to understand what is proposed in terms of treatment or research. The United Nations Convention on the Rights of the Child states that children should be informed about decisions that affect them and they should

be assured that they have the right to express their views freely, these views 'being given weight in accordance with the age and maturity of the child'.

If deemed competent, the child's view of whether they wish to give or withhold consent must be respected. At the age of 16 years, the decision has legal standing as if the patient is an adult. Under the age of 16 years, the child who is capable of understanding, may give or withhold consent for treatment but, for research, the situation is less clear. In English Law, the withholding of consent for treatment may be over-ridden by a parent, legal guardian or court if it is in the child's best interests. In Scotland, this is not possible. The difficulty in these situations is in deciding whether the child is able to understand what they are consenting to or the implications of withholding their consent. This implies that they must have an explanation in terms that they can understand in written and/or oral form[2-7]. It is good clinical practice to give an explanation concurrently to both parent/guardian and to the child about the procedure and the research, benefits, risks, alternatives and implications of not proceeding[5,7,8].

The child's consent alone may be legally acceptable, but it is good clinical practice to involve the parent/guardian unless issues of confidentiality preclude this. Concurrent consent from a competent child and parent/guardian is highly recommended for research. Documentation of all these steps and a summary of the discussions with parent and child in the clinical record is strongly recommended[5,8]. Parents have no right to insist on treatment or research that is not going to benefit the child[5,8,9].

Where a child of less than 16 years of age (and also those aged 16–18 years in English law) is *not* competent to give or withhold informed consent, a person with parental responsibility may authorise investigations or treatment that are in the child's best interests. This may encompass some therapeutic research procedures, particularly those in the life-saving category, for example a new drug or a new technology. Interventions may also be refused by this individual if they do not feel the intervention is in the child's best interests[5,8].

The legality of parental consent on behalf of an incompetent child for non-therapeutic research has not been tested in law and the current consensus is that such research is ethically acceptable, provided the level of risk is minimal or less[1,2,4-8].

Practical Aspects of Consent

Both written and verbal explanations should be given in plain words in versions appropriate for parent and child. Some recommend that the consent process is witnessed and a cooling off period allowed. Certainly, the timing of the approach for consent must be carefully considered. There must be no inducement or coercion to take part. There must be the right to decline to take part and a clear right to withdraw at any time. The potential risks and benefits must be detailed. Most research is of no benefit to the individual research subject, but some benefits may accrue to future patients and to society as a whole.

It is useful to consider whether the research is therapeutic or non-therapeutic in nature. For the latter, any risk should be minimal. It is also helpful to consider the potential adverse effects of the research on the development of the child and the safety nets that will be needed in certain studies, for example, those involving genetic tests or new drugs. Insurance and compensation arrangements should be clear[1-8, 10, 11].

Aspects of Study Design

A number of key questions should be asked when designing a paediatric research project:

- is the question worth asking?
- has this been done before?
- can the answer be obtained by study of an adult?
- is there any benefit to this child?
- is it going to expose this child to risk?
- is the aim well focused?

The design of the proposed study should be subjected to a process of scientific review. This should include a critical appraisal of the study methods, patient numbers, randomization, use of controls and placebos and the implications of any change to the child's existing treatment. For new treatments, individual patients may be recruited on a named patient basis or as a "last-gasp" measure. Consideration should be given to the ethical dilemma that the patient may not get the new treatment unless they agree to be in the trial. This must be made explicit in the consent procedures.

This raises the problem of the ethical window effect – when does a new treatment become established as the norm and thus is it ethically acceptable to include a control group who do not get the treatment? For comparative trials, the comparitor should be with the best available treatment and care should be taken with the use of placebos, for example in studies of analgesics.

For new interventional procedures, the same ethical principles apply although the regulatory framework is different from studies involving drug therapy. Pilot studies in animals and humans may be relevant and the efficacy and safety must be assessed. A registry (Safety and Efficacy Register of New Interventional Procedures, SERNIP) is now in place to monitor new interventional procedures.

For surgical tissues that would otherwise be discarded, for example tonsils for immunology research, there should be a consent procedure and the duration of the culture of cell lines and whether they are to be used for therapy should be explicit. The means of disposal of the tissue should also be declared.

Specific guidelines for the use of fetal tissue in research exist and should be followed. These provide for separation of the consent procedures for termination of pregnancy from those of research so as to avoid the risk of coercion[10,12–15]. Recently, updated guidelines have been produced by the Royal College of Pathologists concerning the research use of postmortem tissue, pathological samples and retained organs[16-18]. For genetic research, the implications of positive results must be considered especially in relation to life insurance provision and appropriate safety nets. Counselling and consent procedures should be put in place, including those for testing siblings[19].

Control Subjects

Normal controls are often recruited by conducting research in schools and, as for the study subjects, careful thought needs to be given as to whether the research is therapeutic or non-therapeutic, whether consent is opt-in or opt-out in nature and whether permission is sought from parent, school, and local education authority as well as the child. The nature of the research is relevant – whether observational studies, questionnaires or measurements are involved.

New RCPCH Guidelines

The recently published revision of the RCPCH guidelines[1] emphasize the value of ethical research with children and stress that more consideration must be given to the child's involvement in the consent and assent procedures and to the child's best interests. The key questions noted above are discussed in detail and in particular an assessment of potential benefit must be balanced against an assessment of potential harm. This must be individualized and the level of risk categorized as zero, minimal, low or high. An assessment of potential costs should also be included. The roles and duties of Research Ethics Committees, both local and multicentre, are described and discussed. There may be a role for specific paediatric research ethics committees organised on a regional or national basis.

Potential Problem Areas

Blood sampling procedures for the purpose of research do merit careful thought, especially as regards limiting the volume of blood drawn and the potential for distress due to needles. In principle, extra needle sticks should be avoided, indwelling lines should be used and sample lines should be placed whilst under general anaesthesia or with the aid of topical local anaesthesia. Minimizing the volumes of blood drawn for example to 1 ml/kg, or to 1–5% of blood volume is recommended but there is wide variation in guidance from different ethics committees.

Recommendations

- Paediatric expertise is required in ethical review procedures
- Consistency of ethical review procedures for paediatric research
- Updated literature and guidance is needed for researchers and for ethics committee members
- High quality approach to child and parents by senior experienced staff for consent
- Better information and consent procedures
- Clear comprehensible information in verbal and written form for child and parents
- Concurrent consent from child and parent where possible
- Accurate documentation of consent procedures

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