ETHICS

Seven questions about paediatric research

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Physicians and surgeons treating children are faced with an antithetical proposition. They are encouraged to practise evidence-based medicine but much paediatric practice is derived from observational studies that fall short of today's standard for acceptance. Parents may make two further antithetical points: first, my child should receive the best treatment available, as determined by research of the highest quality; second, I do not wish my child to be a research subject. Investigators at Great Ormond Street Hospital express the fear that, because of resistance to clinical research, the pathophysiology and treatment of various diseases will become better known in rats than in children[1].

Research on children was barred by the Nuremberg code. Subsequently the Declaration of Helsinki softened the line of prohibition but children are still deemed to require special protection because they are less competent than adults to give consent. Here is a further paradox: a powerful case is made nowadays for children to be involved in decision-making—empowerment—at ages below the age of legal autonomy; how odd, then, to construct an ethical ring-fence around the child when it comes to research. New guidelines[2] from the Royal College of Paediatrics and Child Health contain two helpful principles: 'research involving children is important for the benefit of children'; and 'a research procedure not intended directly to benefit the child is not necessarily either unethical or illegal'. These prompt me to ask seven questions about a future ethical framework for paediatric research.

1. Have children benefited by being treated separately from the rest of humankind?

Yes

Separation has led to closer ethical scrutiny of research projects involving children, and interventions that would have been acceptable in consenting adults have sometimes been rightly disallowed in children. For example, an adult may properly consent to be a 'means to an end' in research, but such consent will be much more questionable in a child.

No

The ethical pitfalls and other special obstacles to paediatric research may deter investigators from pursuing work in this area. If so, children may be deprived of advances in medical management with adverse consequences for their health and welfare. Paediatricians who plead the interests and protection of children might be seen as colluding with an anti-research culture.

2. Should the harm/risk threshold in research be different in children from that in adults?

Yes

Children will sometimes be incapable of understanding a painful or intrusive intervention and will thus be unable to give valid consent; such procedures should then be kept to the minimum dictated by the child's medical condition. Adults are more able to assess the likely risk and discomfort.

No

When a particular question is studied, the necessary scale of interventions is likely to be similar in children and adults; to apply different criteria in children might lead to inferior and unethical research.

3. Is pure pharmacological research ever justified in children?

Yes

A glance at the *British National Formulary* reveals that many of the medicines doctors prescribe for under-12-year-olds are off-label or off-licence. This puts the child and the prescriber at some risk. The pharmaceutical industry might argue that comprehensive studies in children akin to those in adults are difficult, commercially not worth while and perhaps ethically impossible. The counter-argument is that any potentially useful pharmaceutical product should be tested in all age-groups before a licence is given. Child rights advocates would say this.

No

Children should never be used as guineapigs—i.e. in experiments from which they cannot individually benefit.

4. Do local research ethics committees (LRECs) help paediatric research efforts?

Yes

Third-party scrutiny and comment improves the quality of research and may help all participants to understand the pros and cons. Suggestions to improve the quality of research and safeguard the interests of research subjects (perhaps better styled partners) are a proper function of LRECs. Children are in need of the special protection offered by these committees.

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No

Regrettably, LRECs may be perceived as hindering research[3]. By encouraging the ethical ring-fencing of children they can, as I have argued, deprive children of good research and clinical advances. So to apply different standards to children and adults may be unethical. The self-interested paternalism of old-style medical researchers has now gone, and now we have the protective maternalism of LRECs—to whose benefit? (Similar dangers face national bodies which try to set ethical standards for research: British Paediatric Association guidelines posed a threat to research in children and their welfare by their cautious approach to blood sampling[4].)

5. Should parents whose children are treated by the National Health Service be free to forbid their inclusion in research protocols?

Yes

It would be illiberal, and would undermine the autonomy of parents, to demand the participation of children in research.

No

So many medical interventions in children are the result of empirical observation that the doctor can seldom honestly declare that a child is receiving the best treatment. It would be ethically more proper to acknowledge this and for the local treatment protocol or guidelines to enrol the child into a well conducted study. This policy should be open and explicit, widely publicized. Politicians and the media could scarcely withhold support for an effort designed to improve the effectiveness and safety of medical treatment for children. How could parents decline to allow their children to participate in activities designed to promote a common good within the 'theological institution' which is the NHS?[5].

6. Should we continue to distinguish between therapeutic and non-therapeutic research in children?

Yes

In paediatrics the distinction between therapeutic research (generally acceptable) and non-therapeutic research (much less so) has been seen by many as critical. Any move to change the rules, so that children might be exploited by researchers, must be strongly resisted.

No

The distinction between the two is questioned, particularly by commentators in the United States[6]. Every therapeutic medical intervention with an individual patient is a research enterprise. Some components of a project may benefit the patients, others not. Research that offers any prospect of patient benefit is likely to carry a matching risk; thus, we might argue that the former requires the stronger safeguards. A sensible approach is to assess each element of the protocol separately—patient's age, risks, possible benefits to society—before making an individual judgment about acceptability. Lately the doctor/patient relationship has become more open and the same principle should apply to research: patients, research partners or their proxies should have more immediate representation and personal empowerment than can be offered by a distant committee.

7. Are placebos and controls ever justified in paediatric research?

Yes

Both are permissible in some circumstances. Where their use is justified in adults the same may be true in children, subject to consent.

No

New treatments should always be tested against old and there is no case for withholding established treatments from children even if the evidence for efficacy is thin. Furthermore, placebos mean deception and controls signify uncertainty of a kind to which children should not be exposed.

CONCLUSION

In the UK there are formidable institutional and structural barriers to paediatric clinical research[7]—even before we start tying ourselves into ethical knots. Appalling things have been done to children in the name of paediatric research and no-one wishes to see such things repeated; however, the reaction to such excesses has meant that children are now research and therapeutic orphans. Much is made about inequalities in child health. Here is an inequality in which paediatricians may be colluding. Paediatric research ethics in children needs fresh and unemotional thought[8]—not least, the justification for treating children differently from the rest of humanity.

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