Priscilla Alderson **The changing position of children in bioethics guidelines**
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Bioethics guidelines vary in their response to children as research subjects. Children have been ignored or intensely discussed, carefully protected or exposed to high risk research, regarded as the last or as the first group to take part in research. This article traces the changing position of children in successive bioethics guidelines.

The guidelines are more clearly understood when seen against the background of social change and children's slowly developing human and legal rights.[i] There is a complex tension between children's right to protection or to autonomy.[ii] The child's status, as infant or young adult, is keenly debated around questions of an age of consent to health treatment and research. Anglo-American law recognises that `Every human being of adult years and sound mind has the right to determine what shall be done with his own body.'[iii] Until recently obedience rather than autonomy has been expected of children. Yet their autonomy rights are changing in many countries from an emphasis on a stated age of consent to interest in individual ability.[iv] British health professionals are strongly advised: `the consent of the child and the parent or guardian should be obtained to treat children under age 16' (emphasis in original); it is preferable but not essential to involve parents; and `young people should be kept as fully informed as possible about their condition and treatment to enable them to exercise their rights'.[v] Doctors should decide when a child patient is competent to consent to treatment.[vi] The law on children's consent to medical research is still uncertain, so that the issue is much debated by research ethics committees.[vii]

Modern bioethics guidelines began with the 1947 Nuremberg Code. Written mainly by lawyers, the Code starts by insisting: `1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice ...'[viii] The risk-benefit assessment, the basis of consent, can only be made by the informed research subject, whose consent is `an understanding and enlightened decision'. Implicitly the Code deals with research on healthy adults not patients or children. `Benefit' is seen in relation to humanity and not the individual subject, and `death or disabling injury' must not be risked `except, perhaps in those experiments where the experimental physicians also serve as the subjects' (clause 5). Research is seen as a danger from which vulnerable people must be protected.

British guidance in 1962-3 explicitly stated that `non-therapeutic research' could not be conducted on children because they are unable to give legally effective consent.[ix] However the report has completely different standards for research associated with treatment of patients which Nuremberg did not address. Like all subsequent guidance, the report was powerfully influenced by medical authors. It assumes that because of the `willingness on the part of the subject to be guided by the judgement of the medical attendant' if the doctor is satisfied that the procedure being researched will benefit the patient `he may assume the patient's consent' as he would assume consent to `established practice'. This statement was not formally revised until 1991. The red light shone on `non-therapeutic research' with children and the green light on all other research.

Crucial Nuremberg standards were reversed by the 1964 Declaration of Helsinki.[x] This followed publicity about thalidomide, the drug which, if taken by pregnant women, caused gross limb deformities in their babies. The research subjects' `freely given informed consent' is not mentioned until clause 9 and their ability to make `enlightened decisions' disappears. Instead, `the responsibility for the human subject must always rest with the medically qualified person and never rest on the subject'. Faith is reinvested in physicians dedicated `to help suffering humanity', who alone are fully qualified to make accurate risk-benefit assessments. It is assumed that physicians can therefore be trusted to research on children: `when the subject is a

minor, permission from the responsible relative replaces that of the subject in accordance with national legislation' (clause 11). The phrase `therapeutic research' is not used, but the concept of `medical research in which the aim is essentially diagnostic or therapeutic' first appears in international guidance. Presenting research as a definite benefit instead of a potential danger plays a vital part in extending the range of permissible medical research on children. Helsinki recognised the interests of patient-subjects as well as of `healthy volunteers'. The 1983 version of Helsinki adds: `Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.'

Despite reservations about the term `therapeutic research', in 1977 an American report used the term, and extended the types of permissible research on children. As if to reassure public opinion, risk was described in somewhat coy terms as `minimal', `minor increase over minimal' and `greater than minor increase over minimal'.[xi] The report warned of the danger that restrictions on research might leave children as `therapeutic orphans', suffering disease for which no treatment could be developed. Discussion of children's mental and moral competence to consent was based on misleading, out-dated psychological theories,[xii] which unfortunately still dominate bioethics in 1990.[xiii] Intervening social changes, children's earlier physical and social maturity, and critiques of the theories[xiv] have been ignored.

In 1980, British guidance[xv] stressed the benefits to children of research, and stated that `non-therapeutic research' would probably be accepted by lawyers, in the event of researchers being sued, as long as the hoped-for benefits exceeded the risks. A few examples of `negligible' risk were given, with some risk-benefit analyses which were later disputed.[xvi] Neither the assertion about likely legal judgements, nor the logical basis for the calculations was explained. The report stated that new procedures should first be tested `on adult volunteers, then on older children able to take part voluntarily in the research, and only then on younger children', except for conditions which affect only young children.

In 1986, another British report[xvii] advised that research should be more carefully regulated, with more stringent risk-benefit analysis. However, a prime concern was that `research should not be against the interests of any individual child' (p234). This phrase lends moral respectability to much research which is precluded by the earlier requirement that taking part in research must be `in the best interests of the child'. Despite disagreement among the authors, and after listing some lethal interventions claimed by the researchers to be `therapeutic research',[xviii] the report used the term `therapeutic research'. It was defined as `research consisting in an activity which has also a therapeutic intention as well as a research intention towards the subjects' (p33). The consent of parents or guardians must be sought `at all ages of the child; furthermore the child's assent should be sought from the age of 7 upwards.' Assent is simple agreement or non-refusal in contrast to deliberated, informed consent(p235). The report continues: `On a cautious view of the law' with `therapeutic research', the parents' consent can `be deemed to override the refusal of assent by the child aged under 14'. `Non-therapeutic research should not be carried out if a potential child subject aged 7 to 14 years refuses assent to it'. The case for under-7s was not considered.

Subsequent British reports have extended concern for children's views. Guidance in 1990 emphasised consulting with children, explaining in terms they can understand, and always respecting the competent child's objection. If non-competent children object to `non-therapeutic research', `the investigator should reconsider whether it would be appropriate to proceed'.[xix] The prohibition that `research which could equally well be done on adults should never be done on children,' was repeated in other guidelines[xx] including guidance from Brussels[xxi] which stressed the importance of `informed, free, express and specific consent', and a report from the

Department of Health.[xxii] This report warned that `it would be unacceptable not to have the consent of the parents or guardian' even when children under 16 are competent to consent, and it is advisable to have parental consent for 16- to 18-year olds. If adults consent to any intervention which is not for the benefit of the child, especially if it carries more than negligible risk, `it could be said they were acting illegally'. This cautious report was written by civil servants, anxious to prevent malpractice and costly litigation. The principle is often disregarded, as shown by research reports in medical journals, and some guidelines by medical authors.

The 1962-3 Medical Research Council report[xxiii] was updated in 1991,[xxiv] and advised that `either those included have given consent, or consent has been given on their behalf by a parent or guardian and those included do not object or appear to object in either words or action'. Also that, `when a child lacks sufficient understanding to consent, his willing cooperation should be sought.' The report speaks of `allowing children to be included in medical research', as if this is a privilege for them. Some competent children want to take part in research. Yet the report avoids stating its purpose, to allow researchers to do research on children which was previously thought to be illegal.

`Therapeutic research'.

Much confusion between the interests of researchers and research subjects, and between the individual and collective interests of children stems from the term `therapeutic research'. `Therapeutic' is an oddly fuzzy, unscientific word; it expresses possibly unfounded hopes for the future as if they were present realities, it confuses the aim of research with the activity. The word offers a licence for researchers to claim good intentions. Yet scientific rigour would assess research in terms of outcome, effectiveness and efficiency.[xxv] One stringent view is that all medical interventions should be evaluated in order to reduce harm, rather than to claim to `therapeutic' status. Four proposed categories are interventions which: reduce poor outcomes; seem promising but are unproven; are used but the outcome is not known; should be abandoned in the light of available evidence.[xxvi] Phrases such as `the therapy might then do more harm than good'[xxvii] indicate that `treatment' is a more accurate term than `therapy' which, when it causes injury or death, is scarcely therapeutic.

Research, meaning `systematic investigation', cannot directly benefit research subjects, although the treatment being researched may do so, and the eventual research findings may bring great future benefits. `Therapeutic' can falsely imply that research confers certain benefit,q whereas uncertainty constitutes the very nature of research. Control groups who are having placebos or no treatment are sometimes mis-classified as `taking part in therapeutic research'. If the benefits of a treatment such as a drug are agreed, then the drug is likely to be available as routine treatment; a child would not have to enter a trial in order to take it, and so research is not `therapeutic' in the sense of being the only access to the therapy. When approved drugs are used in research, the research question usually centres on their comparative efficacy. To claim that the actual research investigation, such as on comparative benefit, is `therapeutic' in benefitting people in the trial is not logical, since the results which may bring benefits are not yet known. Using the term `therapeutic' can confuse patients entered into trials, and imply denial of the uncertainty and equipoise essential for ethical research.[xxviii] A new drug being tested could not strictly be described as therapeutic until its benefits and risks are known. For these reasons, all research is in a sense `non-therapeutic'.

The distinction between `therapeutic' research which is associated with treatment (as when a method of diagnosis or treatment is being tested), and `non-therapeutic' research not associated with treatment (such as observing average growth), is important as long as the misleading labels are avoided. The further distinction between <u>research</u> and the <u>treatment</u> being researched would then be clearer. Abolishing the term `therapeutic research' would help to

clarify which rare treatments are only available within research projects, and which treatments are still too new to be described responsibly as beneficial. Researchers would also see more clearly who is benefitting whom. As doctors they try to help their patients. As researchers collecting data they are helped by their patients; the beneficiary is the researcher who receives data, which may in future benefit the child donor and many other children, but this is not yet certain.

Current confusion between research and treatment is illustrated by such statements as, when `therapeutic research' is proposed for children, `in circumstances where participation would be in their best interests their exclusion would be unethical'.[xxix] Maybe the findings will be of great benefit to these children, but no one can be certain at the `recruiting' stage about the results or, therefore, about whether taking part will prove to be in the child's interests. Some doctors argue that patients who take part in research have access to better treatment. Yet most guidelines stress that patients should be assured that this is not so; that they will continue to have the best possible care even if they refuse to take part, or withdraw from research. Some health services are supplemented by research funds; standards of professional care, meticulous evaluation, resources and support services are then likely to be better for patients in trials. Yet should discrepant standards be a source of concern about current care rather than being used to pressure people, however gently, to take part in research?

`Risk' is often a vague understatement in `therapeutic research', covering known and unpredicted risks, harms, costs and inconvenience to research subjects. Although risk probability may be measured, risk severity is often a personal, variable assessment. Risk is a relative concept. For example, when a new treatment is tried on a healthy person the level of risk can seem very high; when the research subject is extremely ill and the treatment has a slight chance of helping, the same level of risk might seem very much lower in comparison. Yet the level is constant, and it could be argued that a healthy person is better able to withstand the risks than someone already debilitated and enduring the harms of severe illness.
Research into treatment which might be highly beneficial, such as drugs or surgery intended to save life, is permitted to incur the highest risks, although the hoped-for benefit should always outweigh the degree of risk.[xxx] The requirement begs the question that harm and benefit are measurable and comparable. The distressing dilemmas facing very ill children and the adults caring for them, when `research' seems the last hope, might be relieved a little if the terms were clarified. The serious condition and the possible innovative and uncertain treatments could be considered. The many questions about research could then partly be separated from treatment considerations. The more ill the patient, the higher the justifiable risk is another questionable convention.[xxxi] Children's heart disease[xxxii] illustrates the pressures which illness and fear of death exert on the families and the staff to resort to high risk innovations. Proxy consent presents the further problem that parents tend to feel forced to `try anything', and to consent to attempts on their child which they would refuse for themselves.[xxxiii] Do not very ill children need as much protection as `healthy volunteers'?

`Gene therapy'

In The Report on the Ethics of Gene Therapy,[xxxiv] research, experiment and innovation are soothingly subsumed under `therapy', further blurring distinctions between them. Some of the report's authors belong to a small group represented on almost every similar committee. Apart from the moral philosopher, everyone's qualifications in ethics seem uncertain, suggesting that `ethics' is a label for a variety of uncomfortable questions which need to be given reassuring answers that have the seal of public approval, and indeed the report bears the royal seal. The pragmatic report is about how to proceed, and says little about whether to proceed with gene modifications which might be thought a crucial prior ethical question. Yet this question is

dismissed: `To prohibit the progress of science in any particular direction may well be tyranny; to seek to shape its course is surely sensible'(pii).

Themes in the report illustrate how children are construed as beneficiaries of research, partly through an impersonal, abstract approach. A gene is defined as `an element of the genome which may be responsible for an inherited character difference. A sequence of bases in DNA which codes for one polypeptide.' Obviously an ethical analysis must be scientifically informed, but how much information is essential? The language of impersonal science cannot encompass people's pleasure or anguish about the abilities or disease which children inherit, and such matters are not addressed. Yet it is precisely in such human experiences that we exist as ethical beings. If we were the organisms discussed in the explanatory biology-speak, ethics would be irrelevant. The language risks translating genetics into a matter of function and manipulation instead of identity and relationship, thereby simplifying or obliterating the most complex ethical dilemmas.

Genetics possibly represents the most sophisticated cultural efforts to alter human nature. What degree of intervention is socially acceptable and, in future, will be expected before affected children qualify as human beings? What intervention methods will be used, and accepted? The nature/culture confrontation is especially pertinent to babies and young children who occupy a questionable position between the human and animal, natural and cultural worlds, particularly as genetics has developed through animal and fetal research. The report only indirectly addresses such questions. No reason is given for the authors' priority: `The first ethical principle which has commanded our attention is the obligation inherent in human nature to enquire, to study, to pursue and apply research by ethical means'(p10). To claim such highly cultural pursuits as natural, as an obligation (to whom?), and as the first principle, suggests that anyone who disagrees is unnatural and unethical, closing rather than opening up this contentious area of debate. If human nature is reduced primarily to the intellect, the humanity of very young or mentally impaired children is in doubt.

Problems of eugenic selection, and of stigma for those who cannot or will not undergo genetic interventions,[xxxv] are not discussed in the report. As the government remit required, considerable problems associated with the profit and prestige promised by genetic research, and the devastating effects which diagnosis may have on affected people are side-stepped. These problems are mentioned, `we are sensitive to these issues', but `we are not charged with concern' for them. High current costs of attempting to relieve genetic symptoms are mentioned. Yet such statements mean little unless measured against the costs of genetic research, gene manipulation and its effects.

The report lists uncertainties and dangers. The `correcting gene' might be inserted into the wrong cell type, inappropriately, in the wrong amount or at the wrong time during development. It might move into other genes, creating unwanted effects. Changes in one gene might inadvertently affect other genes, initiate cancerous growths or new genetic disease, or have other unknown longer-term effects. It is not `yet possible to lodge a gene precisely where it would naturally be.' `The therapy might then do more harm than good' (p9). `Nevertheless, this approach may well be effective in selected disorders'(p8). The report is liberally sprinkled with `may well', `unlikely' `may be feasible', and fears are dismissed. `There are likely to be irrational fears which derive from misunderstandings of biology, and are compounded by the effects of popular recreations of fiction such as Frankenstein's monster'.(p2) Rationality is thus identified with the hopes of fearless biologists.

The report states that `gene therapy' `poses no new ethical challenges' and should `be conducted according to the discipline of research and governed by the exacting requirements

which already apply'.(p25) However, a new ethical challenge is made by advising that the first candidates will preferably be treated `in early childhood and even before birth' in utero. The statement reverses the Nuremberg precept, that research should be carried out on informed and consenting people in preference to weak and vulnerable ones, and on adults before children. Could not gene modification first be attempted on adults with degenerative disease which develops in adulthood? The choice is not necessarily easier when made by the adult concerned, yet it respects self-determination and allows for refusal far more than proxy consent can do.

Until the technical problems of `gene therapy' are better resolved, and the short- to mid-term effects are known, should it be tried on children? Children have far more to gain, but also to lose, by being research subjects. An adult who enjoys a fulfilling life but who has nearly reached the onset of a terrible disease may decide to risk treatment and lose the later years of life. Mistakes with children can harm or destroy a whole lifetime. Some genetic defects destroy any kind of reasonable life almost from birth, although the child has to be well to qualify for treatment. Yet if harm-benefit equations are calculated on the basis that nothing could be worse than the disease, then any kind of treatment is permitted. Dreadful as the disease may be, the child's possibly brief and miserable existence can still potentially be made worse by attempts which `do more harm than good'. Genetic research is closely linked to innovations such as in vitro fertilisation. The `success rate' for IVF, of around ten per cent which includes disastrous live births,[xxxvi] suggests that very low `success rates' will also be tolerated for genetic interventions.

A further reason for affording extra protection to children is given by the impressive pages on safeguards in the report. `A prior ethical requirement' is the subject's consent, with great care taken to provide `the fullest possible information', respect for confidentiality, and so on. This is reassuring when applied to adults, but means little in relation to young children whose particular vulnerabilities the report does not discuss. Their interests are also threatened by another British report[xxxvii] which calls for `a radically different approach' to ethics which will set people's right to know their own (and therefore close relatives') genetic constitution over the right to privacy.

Problems arise from confusing research with therapy, rigorous control of research with `tyranny', the interests of adult researchers with those of child subjects, and safeguards for consenting adults with those for young children. In honouring intellectual discovery, the report disregards its costs in physical suffering, and the interests of young children whose intellectual status as full human beings is questionable. Then, very high risk research may be seen as more ethical when conducted on babies rather than on adults with dependents and careers. Until hoped-for benefits far more demonstrably outweigh the unknown and unhoped-for harms, the key questions are: Who has the right to consent to high risk innovations on young children? And according to what criteria should such decisions be made?

Successive bioethics guidelines are like a series of doors, opening to involve children increasingly in research. Restrictive labels on the doors - `danger', `adults only', `in the child's best interests' - change to permissive ones - `therapeutic research', `allow children to be included', `not against the child's interests', `preferably in early childhood'. To involve children more fully in research obviously exposes them to greater benefits and risks. Protections for adult research subjects sometimes fail adults and are insufficient for certain children. Basic principles for research with children need to be more clearly agreed, and analyzed into their many component practical questions for researchers to address. We need to refine ways of informing and consulting with children, respecting their autonomy and their vulnerability. This could help to fulfil the guidance that `research involving children is important for the benefit of all children and should be supported and encouraged, and conducted in an ethical manner.'[xxxviii]

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