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## Editorial

# Research into emergency treatments - could the offer of 'advance directives' help?

Raanan Gillon *Imperial College School of Medicine, University of London*

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In this issue of the journal Peter Allmark, a nursing lecturer and administrator of a European Union bioethics research project into the quality of informed consent for neonatal research projects, analyses a particularly contentious issue in research ethics.<sup>1</sup> Is it morally acceptable, at least in some circumstances, to randomise patients into two groups for a research project into emergency treatment of newborn babies *prior* to obtaining parental consent only for the babies who have been randomised to be offered the non-standard treatment - the so called Zelen 1 method of pre-randomisation? He argues that such Zelen 1 pre-randomisation is morally justifiable in certain circumstances, on three grounds, all based on reduction of unnecessary distress to parents. The first is the reduction of distress to the parents that can result from eliminating the need to explain to them the complexities of random allocation to standard or experimental treatment when their child faces a major emergency. The second is reduction of distress to the parents that can result from eliminating the need to tell them at an already exceedingly anxious time that the clinician does not know which treatment is best for their child, thus reducing many parents' trust and confidence in their doctor at a crucially important time. The third is reduction of distress to parents of children allocated to the standard treatment group, in those quite common cases where the parents would prefer the untried experimental treatment. Since such parents would simply not be eligible to choose the experimental treatment it would be pointless as well as cruel to tell them that they might have been eligible had the randomisation process worked differently - the Zelen 1 method involves not telling the parents of children allocated to the standard treatment that they were so allocated as a result of pre-randomisation.

Allmark is trying to resolve a genuine moral dilemma, and those who oppose Zelen pre-randomisation would argue against him that parents are systematically deceived by the method and that the moral need to avoid such deception is

sufficient to override any reduction of distress that it may produce (such critics may also question whether there is in fact much reduction of parental distress, particularly once it becomes known that such methods are in use; and they may add that once this becomes widely known, recruitment to clinical trials is likely to become far more difficult thus actually reducing the beneficial advance of medical science that medical research is intended to produce).

Ideally - it need hardly be said - patients, or in the case of infants and young children their parents, should be offered the opportunity to reflect at their leisure on the research proposed, having been given adequate information to make an informed decision about whether or not to participate in a proposed clinical trial. The problem with research into treatment of emergencies is that when they do occur they tend to need rapid decision making and intervention without time for extensive explanation and deliberation, quite apart from the issue of un-necessary distress. Nor, in the case of treatment of emergencies in newborn babies, as Allmark indicates, would it be widely agreed to be practical to explain in advance to all pregnant women about all the unpredictable and rare conditions that their babies may be born with and obtain prior conditional consent to participation in clinical trials for each possibility.

Might there be a useful alternative prenatal approach? Advance directives afford people who want them an opportunity to inform - even instruct - doctors about the values they have and the sorts of decisions they would wish to be made for them in various hypothetical circumstances where they are unable to be consulted directly, and about people to be consulted on their behalf. Increasingly, the value of advance directives is recognised both by doctors, and by law. Might the underlying methodology help to reduce the incidence of the moral dilemma addressed by Allmark? First let us agree with the supposition implicitly supported by Allmark that in the case of research into neonatal emergencies generally and

neonatal pulmonary hypertension in particular it would be totally unreasonable to ask every pregnant woman on arrival at hospital to consider how she would wish her newborn infant to be treated in the very unlikely event that her infant were to be born with pulmonary hypertension - bearing in mind that one of the options would be to participate in a randomised controlled trial comparing the standard therapy in which 40 per cent of the babies survived (and 60 per cent died) and a new therapy which might or might not prove to have a better success rate. In commonsense terms such a proposal would be plain daft - and in brief ethical analysis it would be morally undesirable because it would be unjust, at least in terms of distribution of scarce resources; it would be harmful to many, perhaps most of the pregnant women involved; it would certainly fail to benefit most of the pregnant women involved, and it would probably infringe the autonomy of most of the pregnant women involved.

Suppose, however, that pregnant women, early in their pregnancies were given a leaflet explaining the approach of the hospital to childbirth, including some information about the hospital's approach to medical research, the primacy of informed consent but the difficulty of obtaining informed consent in various emergency situations, and a brief account of the hospital's treatment and research policy in the event of emergencies. The women could then be offered an opportunity to indicate whether they wished to discuss in advance their attitudes to such fortunately rare events or simply leave matters to the doctors concerned - always with the advice of the relevant ethics committee(s) - to make decisions on their behalf. While this is only a brief sketch of an idea, it may be sufficient to indicate how women's own views about these issues could be obtained at relative leisure during their pregnancies for the purpose of respecting those views in ways that would minimise the risk of harming them both if the need for emergency interventions did not subsequently arise (the large majority) and for the small minority for whom that need would arise.

Some women would almost certainly choose to become involved in considering these unlikely possibilities and would wish to inform or even instruct their doctors and midwives about their views on the relevant issues, including whether they would accept pre-randomisation according to either of the Zelen protocol(s). For such women methods could be devised for helping them provide the equivalent of an advance directive for emergency treatment and research. As with advance directives these could not be able to encompass all the possible eventualities, but they

would indicate the sorts of interventions that the person would welcome, accept or reject. As with advance directives the woman could also specify proxy in the event that there was time to consult someone but the patient herself was unconsultable. Perhaps here too the woman could be given an opportunity to indicate if she herself would wish to be consulted if she were consultable and there were time, even in dire emergencies, or whether she would wish the doctors to act as they thought best, or to consult her nominated proxy (perhaps her husband, perhaps some other trusted person less likely to be severely distressed in the putative circumstances, perhaps her general practitioner, obstetrician, or neonatologist).

Other women can be confidently anticipated to choose, quite deliberately, not to become involved in confronting such painful ideas about possible disasters at the end of their pregnancies. They would perhaps be given a general statement about the hospital's policy with an invitation to ask for more information if they wanted it. The general statement might say that in the event of medical emergencies doctors intervened using the methods they believed most likely to be successful for the patient, assuming consent where this could not be reasonably obtained. Sometimes, where the best method was not clear, doctors at the hospital would engage in research comparing one method with another. Where adequately informed consent could not reasonably be obtained, as in unexpected emergencies, again the doctors concerned and the hospital would assume patients' consent to be involved in such trials, given approval of each proposal by the relevant ethics committee, unless patients had refused in advance.

It does not take much imagination to foresee numerous problems in designing pilot studies for such an approach to medical treatment - and research of treatment - for emergencies in contexts where ordinary adequately informed consent is difficult or impossible to obtain. Equally, exercise of imagination can be expected to show ways of reducing those problems. But such pilot studies may be worth devising to test out methods of offering patients as much opportunity as they would want for participating with as little distress as possible, in attempts to minimise the incidence of the acute moral dilemmas of obtaining adequately informed consent both for emergency treatments and for participation in research to improve such treatments.

## References

- 1 Allmark P. Should Zelen pre-randomised consent designs be used in some neonatal trials? *Journal of Medical Ethics* 1999;25:325-9.