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Ethical overview of paediatric research and practice in Europe from the Ethical Working Group of the Confederation of European Specialists in Paediatrics (CESP)

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Introduction

Science and evidence-based medicine are becoming the benchmark of good ethical practice in patients of all ages. This desirable objective can only be achieved if medical research has established the standards upon which practice may be based. Doctors treating children are faced with two conflicting expectations: first, that children should not be experimented upon and second, that children should not be given medical treatment that has not been scientifically evaluated in children for evidence of effectiveness. Although therapeutic research is understood and generally accepted, non-therapeutic research is more controversial.

Paediatricians are aware that children are a vulnerable group in society. The youngest of them are not able to understand and therefore to consent to medical research or to innovative medical practice. Proxies are required for such consent, and in most cases this is provided by the carer or the parents. As the child grows older, understanding increases and there should be greater child involvement in the decision making process. However, society also recognises that research subjects and patients of any age need additional protection; to meet this need, ethics committees have been established in many countries.

It is accepted that ethics committee approval is required before research projects involving human subjects are undertaken. In contrast, medical practice is less widely influenced by ethics committees (often termed institutional review boards in the United States). Given the special needs of children and their parents, the

Ethical Working Group (EWG) wished to find out the degree of ethical supervision in research and practice concerning children that exists in the European Union (EU).

Method

In 1997, a questionnaire (Appendix 1) was sent to each of the 17 EU national delegates to the Confederation of European Specialists in Paediatrics (CESP). Replies were received from all countries and the results were tabulated (Appendix 2). The table and questionnaire were re-circulated to CESP delegates in 1998 for verification.

Results

Question 1 asked whether there was a national ethics committee, what its scope was and whether the interests of children were always represented. Nine European countries had national committees (Norway had a system of regional committees). Most were governmental and all but one covered children in their remit. Eight of the nine were responsible for supervising research in general, but only four were responsible for individual research projects. Six of the nine supervised the ethics of practice. In only five of the nine were the interests of children always represented.

In 3 of the 17 countries, the national paediatric society had an ethics committee. Two of these three committees reviewed research in general, but only one reviewed individual research projects. One gave guidance on the ethics of paediatric practice.

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All 17 countries that returned questionnaires had a system of local hospitals and/or universities with ethics committees. Thirteen of those committees had general responsibility for research and 16 of the 17 reviewed individual research projects.

In seven countries the local hospital or university ethics committee gave guidance on paediatric practice. In eight of the seventeen countries, the interests of children were always represented on local hospital/university ethics committees. In one country, the local hospital/university ethics committee gave separate guidance on ethics of paediatric practice, but the interests of children were not always represented.

The final question was whether it was possible to obtain approval for a multi-centre research project from a single ethics committee. In only four European countries was this possible.

Discussion

Conducting research involving children is a serious and sensitive matter. The Nuremberg Code [1] virtually excluded children from research, stating that voluntary consent by the human subject was absolutely essential for their participation in research. The Helsinki Declaration modified this and allowed consent to be obtained from the legal guardian, but acknowledged that minors might be able to consent and that this consent should be obtained in addition to that of the guardian [2].

The results of this survey suggest that the main responsibility for reviewing research ethics lies with local hospital or university committees. In the majority of countries these committees supervise individual projects, but it is disturbing that in only 8 of the 17 responding countries were the interests of children always represented. This is a matter that the EWG feels should be rectified.

The EWG was surprised that so few of the national paediatric societies had an ethics committee. Such societies can be influential in moulding professional and lay opinion concerning the ethical supervision of research in children. This can work to children's advantage in two ways. Firstly, ethics committees can protect children from unethical research. For example, children's interests might be promoted by national paediatric societies pointing out that the intellectual age at which children can understand the issues involved in being a research subject is 7-9 years [3] and that children should play an increasingly important part in the decision-making process as age advances.

Secondly, paediatric societies' ethics committees should support research. In an era of evidence-based medicine, posing and answering research questions is vital. Although many interventions may first be attempted in adults, there are many paediatric techniques and treatments which are not used in adults. For children to obtain the maximum benefit and minimum disadvantage of medical innovations, research, both therapeutic and non-therapeutic, will have to be per-

formed on them. However, in some countries there is an anti-research culture and the result may be that "there is a substantial risk that the pathophysiology and treatment of various diseases will be better known in rats than in human beings" [4]. We should be moving towards an era where large numbers of children with classifiable diseases are admitted into research projects. This is particularly important for less common conditions and treatments (orphan diseases and orphan drugs) where the expectations of doctors, patients and care-givers should be that such patients are normally enrolled into research projects. The EWG recommended that all national paediatric societies should establish ethics committees and this was endorsed by the CESP meeting in Helsinki in June 1998.

Question 3 dealt with the ethical supervision of research in local hospitals or universities. This was performed almost uniformly throughout Europe, but in only eight of the European countries were the interests of children always represented on those committees. In view of the importance of paediatric research throughout the EU, the EWG recommended that the interests of children should always be represented. Again, this was endorsed at the CESP meeting in Helsinki in June 1998.

The EWG would like to stimulate a debate on who might represent the interests of children on these committees. It would be important to have somebody with first-hand experience of research in children and with their families. That might be a medical or a health professional. There would be a strong argument for having a lay person experienced in working with children - a social worker or lawyer for example - as a second member to balance the children's interests on such committees. Young people might expect their own representation.

The final question dealt with multi-centre approval of research ethics. Many diseases in children are rare and successful therapeutic research in them will require numbers of patients that one centre is unlikely to be able to supply. Obtaining research ethics committee approval for a national project can involve a large amount of work and sometimes the decisions of local ethics committees conflict. A strong case may emerge for a central committee to grant approval and to encourage local committees to accept that approval, perhaps with minor local modification of detail. If this were to happen, paediatric research would be advanced enormously. The EWG was concerned that only four countries had a national system for multi-centre research. The members wonder whether this might hamper ethical research on children and medical scientific progress. They recommend that national paediatric societies examine the question of how multi-centre research and its ethical approval might be promoted in their countries.

The widespread North American custom of having ethics committees (Institutional Review Boards) supervising paediatric practice is not common in Europe. Of the nine European countries with national ethics com-

mittees, six review the ethics of practice, but only in five were the interests of children represented. Only three EU countries have national paediatric society ethics committees which give guidance on the ethics of paediatric practice. This is unfortunate because paediatricians are in a good position to give a national lead in this area. The EWG sees this as a further reason for national paediatric societies to form ethics committees. A common European approach to some of these difficult problems might emerge.

Of the 17 returning countries, 6 indicated that the local hospital/university ethics committee gave guidance on the ethics of paediatric practice. In 4 the interests of children were not always represented. Traditional European practice has been that difficult areas of paediatric practice, including consent for withdrawing or withholding treatment, should be taken by the physician in

charge of the case, with the parents and the health professionals involved. A strong case for local committees does not seem to have emerged, although there are differing views [5]. The case against having local committees would be strengthened if national paediatric society ethics committees became more widespread and took a lead in developing guidelines for ethical paediatric practice in their countries. In conclusion, it is reassuring that the ethical supervision of research appears to be both common and well-conducted in the EU. It is of concern that the interests of children are not always represented. Although local practice ethics committees are not widespread in Europe (and there seems to be no great pressure to establish them), there is a strong case for national paediatric societies and, possibly, the CESP to take a lead in producing guidelines for ethical practice by paediatricians.

Appendix 1

Questionnaire: bioethics committees in Europe

	Yes	No
1. Is there a national bioethics committee in your country? If the answer to this question is yes, please also answer the following:-	<input type="checkbox"/>	<input type="checkbox"/>
1a. Is it governmental or not?	<input type="checkbox"/>	<input type="checkbox"/>
1b. Does it cover children?	<input type="checkbox"/>	<input type="checkbox"/>
1c. Does it cover research in general?	<input type="checkbox"/>	<input type="checkbox"/>
1d. Does it consider individual projects?	<input type="checkbox"/>	<input type="checkbox"/>
1e. Does it consider ethics of practice?	<input type="checkbox"/>	<input type="checkbox"/>
1f. Are the interests of children always represented?	<input type="checkbox"/>	<input type="checkbox"/>
2. Does your national paediatric society have an ethics committee? If yes, please answer the following:-	<input type="checkbox"/>	<input type="checkbox"/>
2a. Does it consider research in general?	<input type="checkbox"/>	<input type="checkbox"/>
2b. Does it consider individual research projects?	<input type="checkbox"/>	<input type="checkbox"/>
2c. Does it give guidance on ethics of paediatric practice?	<input type="checkbox"/>	<input type="checkbox"/>
3. Do local hospitals and universities have ethics committees? If yes, please answer the following:-	<input type="checkbox"/>	<input type="checkbox"/>
3a. Do they consider research in general?	<input type="checkbox"/>	<input type="checkbox"/>
3b. Do they consider individual research projects?	<input type="checkbox"/>	<input type="checkbox"/>
3c. Do they give guidance on ethics of paediatric practice?	<input type="checkbox"/>	<input type="checkbox"/>
3d. Are the interests of children always represented?	<input type="checkbox"/>	<input type="checkbox"/>
4. Is it possible to obtain approval from a single research ethics committee which permits research to be carried out in multiple centres without further approval?	<input type="checkbox"/>	<input type="checkbox"/>

Appendix 2

Results of the questionnaire ethics in paediatrics (Y yes, N no, NA no answer)

	A	B	CH	DM	FIN	F	D	E	GB	GR	IRL	I	L	NL	N	P	S
1. National committee*	N	Y	Y	Y	N	Y	N	N		N	N	Y	Y	Y	N ¹	Y	Y
a) Government		N	N	Y		Y						Y	Y	Y	Y	Y	Y
b) Children		N	Y	Y		Y						Y	Y	Y	Y	Y	Y
c) Research		N	Y	Y		Y						Y	Y	Y	Y	Y	Y
d) Individual projects		N	Y	Y		N						N	N	N	N	N	N
e) Ethics practice		Y	Y	Y		Y						N	N	N	N	N	N
f) Interests of children		N	Y	Y		Y		N				N	N	N	NA	Y	Y
2. National paediatric society*	N	N	N	N	N	N	Y	N	Y	N	N	Y	Y	Y	N	Y	N
a) Research							N		Y			Y	Y	Y			
b) Individual projects							N		Y			Y	Y	Y			
c) Paediatric guidance							N		Y			Y	Y	Y			
3. Local hospital/university*		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
a) Research		Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
b) Individual projects		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
c) Paediatric guidance		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
d) Interests of children		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4. Committee for multi-centre projects*	N	N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

* See questionnaire, ¹ 5 Regional medical research ethics committees, ² "Some (hospitals do)"

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