Ethical Aspects of Nutritional Research on Infants in Developing Countries

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The primary ethical standards and procedures governing all types of research on human beings in developing countries must be exactly the same as for those of any more privileged country. At the same time, it should also be accepted, willingly, that extra requirements may well have to be imposed by ethics committees on investigators in developing countries, particularly where the proposed study is going to be carried out in a country with a general lack of elementary but essential clinical facilities. There are also likely to be sensitivities arising from social or religious traditions or even of a quasipolitical nature that need to be accommodated before any study is permissible. In this rather personal perspective on the subject, I contrast the basic rules and guidelines that my own institute has to follow before undertaking nutritional studies in the United Kingdom with how these are likely to be extended for any proposed studies, primarily in Africa but also in Asia. I quote extensively from the Medical Research Council’s own policy document, *The Ethical Conduct of Research on Children* (1), as well as the British Paediatric Association’s *Guidelines for the Conduct of Medical Research Involving Children* (2) and the MRC Dunn Nutrition Centre’s specific ethical requirements for nutritional studies on children (3).

When I first started working for the Medical Research Council (MRC) in Uganda in 1959, there was no ethics committee as we would now know it. Ethical considerations were the direct responsibility of the senior clinician. There are no grounds for believing that this arrangement led to unwise investigations, but it did place a major onus of responsibility on this one individual. A few years later, the Ministry of Health in Uganda began to insist that before any new study was started, specific written permission had first to be received from them. This was mainly to protect Ugandan people, especially women and children, from visiting investigators who wanted to carry out nutritional and other types of human and clinical studies on malnourished people and who may have been resident in the country for only a very short time. Although most of these external research teams were highly principled, there were a few that accepted little or no responsibility for subsequent essential
health action revealed by their findings once they had left the country. A closely associated safeguard was that before any work was published, the manuscript of the paper had also to be presented to the Ministry for prior approval. This was not an attempt at censorship, although it was occasionally interpreted as such. The Uganda Ministry of Health was very concerned that it should always be aware of research results that might have potential practical implications in terms of clinical and public health planning.

I return to this principle later, but it does raise another key issue when one considers the ethics of carrying out nutritional studies on anyone, but especially on babies and young children in developing countries. Approval should depend on the assurance that the work is of sufficient quality that it is publishable in a first-class, internationally available biomedical journal and that the results will be made readily available to all who need the information.

By 1973, when we began carrying out nutritional research in The Gambia, West Africa, the principles contained in the World Medical Association’s Declaration of Helsinki, initially produced in 1964 and subsequently revised in 1975 and then again in 1983 and 1989 (4), were routinely being applied by all the research establishments of the British Medical Research Council. It was still essential, however, for the MRC and their colleagues in the Gambian Ministry of Health to go through the procedures of setting up an appropriate and properly constituted local, but nationally approved, ethics committee in that country, consisting not only of competent professionals but also of other responsible persons who would reflect and accurately represent the attitudes and sensitivities of the population at large.

**THERAPEUTIC AND NONTHERAPEUTIC RESEARCH**

In the British Medical Research Council’s general guidelines, *The Ethical Conduct of Research on Children*, a distinction is made between therapeutic and nontherapeutic research. In the case of nutritional research on children in developing countries, in whom the incidence of subclinical and even clinically overt malnutrition may be high, the two entities are not, however, always readily distinguishable. The general term “therapeutic research” is used by the MRC to cover not only investigations into the treatment of disease but also its prevention, for example by vaccination, as well as research on diagnostic procedures. The MRC recognized that nontherapeutic research in children raises more complex ethical issues. A differentiation between therapeutic and nontherapeutic research was considered necessary because rather different safeguards and guidelines might be relevant in the two circumstances. It was concluded that children included in nontherapeutic research should be placed at no more than negligible risk of harm. Negligible risk was interpreted as meaning that the risks of harm anticipated in the proposed research are no greater, considering the probability and magnitude of physiological or psychological harm or discomfort, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. Although these sentiments are a
valuable universal guide, it needs to be recognized that for those children living in
developing countries, the risks encountered in daily life may well be much greater
than we would ever wish to see introduced into a scientific study!

CONSENT

Age is an important consideration in defining when a child might be considered
old enough to give informed consent. An important factor that may modify any age
guideline is the degree of understanding a young person can be expected to have,
taking into account both individual intellectual development and educational oppor-
tunity. Where the child is aged 16 years or over, the legal position in relation to
therapeutic research is relatively straightforward in England and Wales. Under Brit-
ish family law, a person of the age of 16 has full power to consent to medical
treatment, and because therapeutic research is closely linked to medical treatment,
the MRC considers that such a person can reasonably consent to participate in this
type of research. There is a rider, however, that is of considerable relevance insofar
as the Third World is concerned. In circumstances where there is doubt as to the
degree of understanding shown by a young person, it may be good professional
practice to explain the research proposals primarily to the parents and to give any
objections they have considerable weight. I believe this proviso to be especially
important within the context of research in developing countries. Although this
volume is primarily concerned with research into infants, nutritional research rele-
vant to the health of the baby once he or she is born at least starts \textit{in utero} and
arguably before that, with the nutritional status of the mother. Many women in
developing countries have their first babies by the time they are 16 or younger.
Furthermore, educational opportunities and the broadening of experience that this
should bring have often not been made available to them. Thus, not only the husband
but, because of the closely knit family structure, also the young mother’s parents
and parents-in-law must also be considered key people to approach when obtaining
consent to participate in a study.

In the United Kingdom, the situation for children under the age of 16 is less well
defined: there are no strict legal precedents, but the MRC believes that the minor’s
capacity to make his or her own decisions depends on having sufficient understanding
and intelligence to make the decision rather than on any judicially fixed age limit.
When a child under 16 years of age is competent to consent, however, it is usually
considered wise to complement this with the approval of the child’s parents or
guardian. It goes without saying that in developing countries, such a dual approach
should be adopted only with the utmost care. The views of the parent are likely to
be seen by them as paramount.

In the case of nontherapeutic research, the situation is somewhat different because
that actual child may not receive any direct benefit from the research. For children
aged between 8 and 16 years, the regulations set by the Dunn Nutrition Centre’s
own ethics committee, but based on general MRC guidance, are that although the
child may not be able to understand the reasons for carrying out the investigation, any discomfort likely to occur during the course of the study should be fully explained both to the child and to the parents, and their consent must be obtained. For younger children, interpreted by us as meaning 3 to 7 years, it has to be assumed that, although they might be aware of what is happening to them, it is unreasonable to expect that child to understand the nature or scientific purpose of the investigation, and thus, it is impossible for them to give informed consent. Nevertheless, such children should receive an adequate explanation of the procedure, and their confidence be won. Furthermore, they should always be allowed to refuse to participate. Although these guidelines are primarily intended for the United Kingdom, the principles involved are not totally inappropriate for less scientifically aware communities. The critical issue has to be the ability of the person under investigation to understand.

In any community, children under the age of 2 cannot be expected to give any form of consent or voluntarily to cooperate in any procedure. In this case, the responsibility lies with the parents, who must be fully informed.

RISKS AND BENEFITS

Theoretical risks, however remote in practice, exist with many procedures, and this is most noticeably the case where the taking of blood is a necessary part of the research. We work under the general principle that investigations of this nature should not be undertaken on children if it is possible to do the studies in adults. It needs to be emphasized that, however necessary the taking of blood from children is, it is going to be a somewhat traumatic procedure, particularly for the younger ones. Care must always be exercised to reduce this trauma to an absolute minimum. Many of the risks to the child of blood taking are psychological in nature, arising from the perception that it is going to be a painful procedure. Transient pain of a venipuncture can be eliminated by the use of local anesthetic creams, and our investigators are encouraged to use such local anesthetics where possible. It is critically important that blood should be taken by venipuncture from children only by a wholly competent and experienced person. For this reason, and because of the special cultural sensitivities that can be associated with the taking of blood, in our work in Africa, this procedure is restricted to someone medically qualified or a senior qualified nurse. Additionally, we make a point of always having one of the parents present at the time of blood taking, so they are fully aware of what is going on. It is also essential that a mechanism be arranged for dealing with emotional disturbances that might occur during such a procedure.

RISK/BENEFIT BALANCE

The benefits that might accrue from the application of any investigative procedure in a study on young children will depend on the scientific nature of the proposals. Risks have to be balanced against benefits. One essential consideration for ethics
committees must be the originality and scientific soundness of the work. In our United Kingdom-based work, a critical assessment of the scientific quality and unique importance of any proposed study is made directly by the ethics committee itself. In situations where the experimental design appears flawed, or where there is doubt as to any new scientific benefit that might accrue, approval to carry out the study will always be withheld until the ethics committee has been satisfied completely on this score. In The Gambia, all proposed work from anywhere in the world has first to go before the scientific coordination committee for an appraisal of the scientific content of the proposal. This occurs before the ethics committee ever sees the proposal and reevaluates it from the point of view of safety and other ethical issues.

These safeguards are crucial not only where pain and other possible traumas are involved. Studies can be invasive to privacy and happiness without blood being taken or some other physiological technique being performed. It is difficult to carry out a study without interfering with a person's normal life style. This can be justified only if soundly based scientific investigations are going to be carried out that will give rise to important and unique new knowledge.

The primary intention of all medical research must be to acquire knowledge that will be of benefit to humanity as a whole, both to those who are already ill and incapacitated and to those who might become so. Because therapeutic research is directly concerned with treatment, it can offer the potential of immediate benefit to the participant. By its very nature, the direct benefit to individual participants of nontherapeutic research is likely either to be long delayed or possibly never to occur at all. Nevertheless, for research in young children, it is essential that a case be made in the ethics proposal to justify the overall investigation on these grounds. The justification must also establish that this potential is relevant to the particular health problems of the community under investigation. Almost never can a study on one community of young children be justified on the basis that it could benefit another. I emphasize this because it is not unheard of for less scrupulous investigators to attempt studies in a developing country because they fear ethics permission will not be granted in their own country.

THE LEGAL POSITION

Quite apart from any international or national guidelines on the practice of ethics committees and their interpretation and amplification by local bodies, it needs to be recognized that, in many countries, there is actual legislation covering the protection of young people's rights. These differ significantly from country to country, however. For example, even within the United Kingdom, the law dealing with such things is not the same in England and Wales as it is in Scotland. With therapeutic research involving a child aged 16 or over in England and Wales, and also Northern Ireland, this individual has full rights in law to consent to medical treatment. In Scotland, however, the position depends on whether the child has reached the age
of 12 in the case of a girl or 14 in the case of a boy. Below these ages, the children, known in law as "pupils," specifically cannot themselves give valid consent; it must be given on their behalf by a parent or registered guardian. Above these ages, up to 18, the child is called a "minor," and his or her ability to give valid consent depends on whether the child has sufficient understanding to consent. In other words, in Scotland, reaching the age of 16 has no legal significance in terms of medical procedures, whether in the form of treatment or otherwise. In the case of nontherapeutic research, there is no precise age in England, Wales, and Northern Ireland below which a child acquires legal capacity to consent. In Scotland, the position is the same as for therapeutic research.

Integrating national legal considerations with internationally accepted ethics guidelines is especially important when scientists from culturally different countries plan to carry out investigations elsewhere, particularly in a developing country. In the case of a previously dependent country, case law is often based on legal decisions made in the courts of the old colonial master, but it is no longer wise to take this for granted. New situations have required new attitudes and independent rulings.

For expatriate investigators, it is clearly not sufficient to depend on ethics approval from one's own institute's committee, as the members are unlikely to be fully conversant with the relevant legal requirements in the overseas country. It is essential that investigators work through a properly constituted local ethics committee. If one does not exist already, arguably it is the responsibility of those wishing to carry out research in that country to encourage and help with the setting up of such a committee before proceeding. This will inevitably cause delays and require much consultation with the appropriate authorities, but it will be worth it in the end. If it appears that such a venture is not going to be worth the time and effort involved, the only wise course of action is for the study to be carried out elsewhere.

In the case of the MRC's work in The Gambia, all ethics approval has to be obtained from such a local committee, although it does have access to a corresponding national body established by the Council in the United Kingdom, where advice on particularly complex investigative procedures can be obtained. In other countries where we have carried out investigations, it has been considered a wise precaution for the project to receive ethics approval both from the overseas committee and from our own in Cambridge. Issues that may not seem significant on the spot can worry a British ethics committee, and it is important that any differences be resolved before the investigation goes ahead.

It always needs to be borne in mind that ethics approval is necessary not only for the protection of the individual being studied but also for safeguarding the investigator from problems that might occur during the course of a study but that could not possibly have been foreseen beforehand.

STUDIES IN COUNTRIES IN WHICH THERE IS NOT A COMPREHENSIVE HEALTH SERVICE

In countries like the United Kingdom, it is reasonably easy to make appropriate arrangements before a study is begun about what will be done if—particularly in
the case of nontherapeutic studies—something is discovered that is undesirable and that should be put right by appropriate treatment. Usually, it is sufficient for the subject’s doctor to be informed in confidence about the matter so that he or she can take the appropriate professional action.

In many Third World countries, especially in rural areas, it is likely that no adequate facility of this nature exists. In my opinion, it then becomes the direct responsibility of the investigators themselves to do something effective about the problem. Identified serious health problems in a given individual just cannot be ignored by blaming any lack of action on shortcomings of the local health services. Knowledge brings with it responsibilities; these have to be accepted by the investigator.

Satisfying such exacting requirements is not easy for investigators contemplating only short-term studies. Where this proves impossible, however, it is far better for that research team to set up in a country where there is a more adequate indigenous health service rather than to compromise on essential ethical principles. Many years ago, I attended a meeting that established my philosophy toward community studies from then on. This meeting resolved to act by the general slogan “No survey without service.” It has not been an easy path to follow, especially in an age when money is short and every attempt is made to cut budgets. In The Gambia, we operate our own rural clinic, which provides general-practitioner-type health care not only to the mothers and children we study but to the rest of their immediate family as well. When hospital admission is necessary, the patient can be transported to the coast where appropriate additional facilities exist. I regard this as an essential expense, and I have had to fight off any attempt at economies on this facility. Not only is this ethically essential from my point of view, but I believe this commitment has added greatly to the willing collaboration offered by the people we study.

STUDIES USING NOVEL TECHNIQUES

There is an understandable coolness on the part of most ethics committees in developing countries toward investigations that employ novel techniques, which may be seen as not having yet stood the test of time. An equivalent concern occurs when the use of experimental therapeutic procedures is contemplated, especially if these techniques or procedures have not already been fully tested in industrialized countries. There is the predictable suspicion that people in developing countries might be used as guinea pigs. Such a concern is especially valid where studies in young children, especially infants, are being contemplated.

Wherever possible, such studies should not be initiated in such an environment. Clearly, this is not always going to be possible, especially when one is dealing with a disease that is rare or totally absent in more affluent countries. But such instances are likely to be the exception rather than the rule. A good example of the principle of first using a technique in one’s own country is afforded by the use of stable isotopes to measure important nutritional variables such as the breast milk intake of young babies and also their total energy expenditure and hence their energy
requirements. Such data are notoriously difficult to obtain accurately in free-living subjects using classical procedures, and stable-isotope techniques offered us a novel way of doing so. We did not contemplate this, however, before our techniques had been evaluated and approved for use on British mothers and their babies. Furthermore, the Gambian ethics committee requested special reassurance from their British counterpart on this point.

PAYMENT OF VOLUNTEERS

Anywhere in the world, whether or not to pay volunteers is always a controversial decision. In the case of adults, and where people have to contribute a significant proportion of their time, it is sometimes appropriate to compensate them for out-of-pocket expenses. In developing countries, however, where salaries can be ridiculously low, decisions about compensation take on a quite different perspective. The danger is that people may be persuaded to participate in a scientific study, against their better judgment, just to make money. This is clearly ethically undesirable, and furthermore, it can place investigators in the invidious position of having to defend themselves against the accusation that they are exploiting impoverished subjects for their own research purposes.

In cases in which a parent is taking responsibility for consenting to investigations on behalf of a third person, it can never be justifiable to offer payment. With infants and very young children, this is especially true. As indicated above, in developing countries, the pressures on parents to obtain money from any source are especially great, and the rule of no payment should be sacrosanct.

The application of any rule, however, has to be tempered with common sense. In the Dunn Nutrition Centre’s own scientific research on babies and young children, a major feature is the prospective longitudinal nature of our investigations. The same child may be seen and routinely examined clinically every month for at least the first 2 years of life as well as every time he or she falls ill. Furthermore, frequent visits may be made by the investigators to the subject’s actual home. Inevitably, in such circumstances a close and friendly relationship becomes established. The wish to give the type of small gift, such as a child’s dress or a ball, that one would normally give to someone you know well on birthdays, at Christmas, or on some other major feast day is understandable and is done. Nevertheless, it is highly desirable that the principle of giving such gifts should be contained in any ethical proposal, so that the authorizing committee can consider its appropriateness and provide general approval for such practices. Even at these times, I believe, however, that the gift should never be in the form of cash.

INVESTIGATIONS INVOLVING CONTROL SUBJECTS

In most investigations where an intervention is involved, it is necessary to have a control population that receives some form of placebo. Often this has to be given
blind by a third person so that the scientist making assessments is unaware of exactly which type of subject he is investigating. This is to avoid the risk of any subconscious bias being introduced in favor of the hypothesis being tested. I have met, however, some reluctance on the part of ethics committees in developing countries to accept the concept of control groups. This is especially so with undernutrition or malnutrition, and where the subjects are known to be consuming levels of total food or specific nutrients that fall well below internationally set dietary guidelines. The argument is made that it is unethical to deliberately deny some subjects extra nutrients that would bring their intakes up to internationally suggested levels of adequacy when the investigators are in possession of the funds and facilities to do so. It is also pointed out that the administration of a placebo frequently costs at least as much as the experimental nutritional supplement.

Such arguments are not easy to counter. Clearly, where there are specific clinical signs of nutritional deficiency or malfunction, the placebo approach will rarely be justifiable. In other instances, however—and a good example in Africa would be calcium nutrition, where the functional consequences of a lifetime's intake of only a fraction of the internationally recommended dietary allowance does not seem to lead to any overt disorder—such an approach is more justifiable. Here, the target is to determine whether or not the redeployment of scarce financial resources at a national level, so that intakes of all the population could be brought up to theoretically derived reference levels of requirement, would be cost-effective.

It is important, however, for investigators working in developing countries to be conscious of sensitivities surrounding the selection of control groups. At the very least, it should be demonstrated to the ethics committee that every subject should benefit from participation, to a greater or lesser extent, including the control group. The improved well-being of no individual can be ignored just for the sake of scientific progress. This provides another sound justification for insisting on the philosophy of "no survey without service" and the provision in The Gambia by the Dunn Nutrition Centre and the MRC of the general medical care service for all persons participating in our studies.

In conclusion, an ethics committee should not be regarded as a necessary nuisance. It is there to protect us all: the subject being studied and, equally, the investigator. A good ethics committee can add greatly to the quality of research.

REFERENCES

DISCUSSION

Dr. Perman: It does appear that certain ethical principles are universally applicable. That probably is not surprising, but at the same time, review of proposed research needs to be held at the local level. But is it appropriate for us to assume that these standards are universally applicable, or is this a view that certain of us are projecting on the world?

Dr. Kauffman: You have made a great issue of the generalizable applicability of the principles, and I certainly agree with those, but how close to this ideal do you think we are? I often hear statements to the effect that we are not going to site this study in the United States because we don’t think we can do it here; we are going to do it in country X instead.

Dr. Whitehead: In The Gambia, we do receive requests of this type from people wanting to do research that they are unable to get approved at home. This is usually research on novel products—drugs or appliances—prompted by the belief that the standards are going to be very much lower. But I can only caution once again that ethics committees are there to protect the investigator as well as the person being investigated, and I think that anybody who is tempted to become involved in research like that ought to think twice. The only way to cover yourself is to make certain that you do research in countries where an appropriate ethical procedure has been established. If you want to work in a country over an extended period of time, and you believe that an adequate ethical procedure does not exist within that country, then the wisest thing to do is to set to work and help to organize one.

Dr. Uwa: Although practices vary from country to country, in many countries, it is the senior administrator—the head of service or the head of the hospital—who decides on his own whether a study is ethical or unethical. Sometimes, the study may touch on the administrator’s own interests, so there is always the potential for conflict of interest. I think it is very important to give out the message that this group at least considers that even for occasional research, you should go through due processes, and the due process involves people from outside making the ethical decisions, as we have pointed out here. We must reinforce the need to apply the same standards everywhere, although practical aspects of this may vary. But I would like to point out one issue relating to research in developing countries. In many cases in such countries, the control group is in fact a deficient group in one or more nutrients, something that would not be ethical in developed countries, where the standards of care are so much higher. In a developing country, this may provide precisely the test situation that will eventually allow improvement to be obtained.

Dr. Whitehead: I agree with you completely, though the people who are making that sort of decision should be the indigenous people of the country. I think that the duty of the investigator is to spell out the potential benefits of the study in a simple way that does not require a huge knowledge of science.

Dr. Aggett: I believe that The Gambia is a Muslim country. Could you comment on how ethics committees operate in the context of different cultural and religious backgrounds. Are the guidelines similar, or are there other considerations that influence the way that people can get consent?

Dr. Whitehead: In the ethics committee, the great majority of people are Gambians, and most of them are Muslim. We also have an Imam, a religious leader, on this committee, just as in the United Kingdom, we would always try to have a priest of some description in ethics committees. Otherwise, the membership covers a wide cross-section of the educated population. The ethics committee insists that the procedures to be undertaken in the study can be described to the elders of the community in which you are going to work, and their approval will be necessary before any individual person or any individual family is approached.
Dr. Fisberg: I am a member of the ethics committee of my university, and some of my colleagues have raised an interesting concern. What happens when a child suffers as the result of ethical malpractice in a study that was approved by the ethics committee? Should the ethics committee be responsible because they gave approval to the study?

Dr. Whitehead: This is a very important point. I think that the fact that the study was approved by the ethics committee should afford the researcher some protection against litigation, but I would be interested to know what others think.

Dr. Lucas: In the West, as I understand it, ethics committees have no real legal standing, and therefore, they do not protect investigators from any kind of liability. But in developing countries, the problem is that the legal systems for protecting subjects who have been damaged in research may not be adequate, and that puts an onus on investigators to set in motion some sort of compensatory maneuver if a subject is in fact damaged as a result of research.

Dr. Whitehead: Except I believe in France, it is absolutely true that strictly speaking ethics committees have no legal authority. But I think in terms of defense in circumstances such as we were discussing, the person would definitely be culpable if he was acting outside the limits of the ethics approval given. My guess is that, in the United Kingdom, if such an issue came before the courts, the judgment would be very important because it would then become part of common law, but I don’t know whether or not that has ever been an issue.

Dr. Aggett: I think that increasingly people responsible for sites where research is performed—in the United Kingdom, this would be hospital authorities, etc.—are insisting that research does not take place on that site unless there is adequate insurance indemnity coverage. But there is still no regulatory enforcement for this sort of approach.

Dr. Klish: Our ethics committee, and I would assume most committees in the United States, put in a disclaimer as part of the informed consent, saying that neither the committee nor the institution is responsible for any injury that may occur as a result of the investigations. This has been routine. The problem with that is that this has never been challenged in the courts. Until that happens, at least in the Texas courts, we continue to assume that this is a legitimate way of absolving our responsibility.

Dr. Kauffman: There were two cases 15 or 20 years ago in the state of California where the Investigational Review Board (IRB) and investigator were sued, but I don’t remember the outcome. I think one of them was successful. Regardless of what we do in terms of the indemnification statement, in the United States at least, there is always a lawyer who will take the case.

Dr. Whitehead: I am not aware of this disclaimer. Dr. Lucas or Dr. Clarke, are you aware of this within the United Kingdom?

Dr. Lucas: I am not aware of any equivalent, but I have always been told by ethics committees that they don’t have legal standing and that one has to take out one’s own insurance. This is precisely the point that concerns me, and there isn’t this kind of cover for research in developing countries. That is an issue that needs to be thought about specifically.

Dr. Clarke: It has been explained already that, in the United Kingdom, the ethics committees that form the generality of the discussion today are within the National Health Service (NHS), and that is a cover-all service where all the drug work takes place and most of the clinical services. There are, however, difficulties with regard to doing research on food, because most of the studies are not done within the NHS. I don’t know of a case where the ethics committee has had to hold itself responsible for a decision that might have been questioned subsequently, but with regard to foods, we are on new ground.

Dr. Meng: In China, money for research has to be used to provide payment to local government and to the doctors involved, but it is not thought advisable to give money to the
participants. Many participants will not fully understand the aims of the research and will think that the money is being given because harm is going to be done to their children. This is not helpful for research. I agree with Dr. Whitehead that only small gifts should be given to the participants.

Dr. Whitehead: What you say is very interesting. I think one clearly has to be flexible. I don’t think that the basic principles behind the Helsinki guidelines are so rigid that flexibility doesn’t exist. What I am cautioning investigators—and we are all investigators—is not to allow ourselves to become involved in research that we could not justify to our own colleagues on the grounds of the Helsinki guidelines. Where flexibility has been exercised, investigators must convince themselves that that flexibility is justifiable and must feel able to discuss that flexibility and justify it with their colleagues. What we must not do is to allow ourselves to become involved in research in a place just because it creates opportunities that we would not have in countries where the laws and regulations are much more stringent.

Dr. Sorensen: If you have a project approved by the Gambian ethics committee, do you still request parallel approval by your home committee?

Dr. Whitehead: The Gambian ethics committee itself requested that all ethical submissions go first to them and to no other ethics committee. This principle had to be agreed to before research went ahead. However, in the great majority of the other work that we do, approval is sought from two ethics committees. For example, the work in China went to our own ethics committee and to an ethics committee established in China. In this particular case, our own ethics committee was rather concerned about one aspect of the work that did not worry the Chinese.

Dr. Sorensen: What is your policy regarding overhead that you might get for a project? I am concerned that very often, research is performed largely for the economic benefit of the developed country, and very little of that technology or money actually gets to the developing country.

Dr. Whitehead: In our own work in The Gambia, the overhead goes into running the medical service. We run a general clinic that operates twice every day, and when there are emergencies, those are also dealt with. The costs involved in emergency hospital admission are paid for by the Medical Research Council. Some overhead also goes toward the Ph.D. or M.Sc. training that we provide for Gambians, but mainly, it goes to help run the medical service.

Dr. Loozeff: On the issue of protection of human subjects in the United States, no federal dollar can be spent overseas unless it is cleared by OPRR (Office of Protection from Research Risks) regardless of what the local wishes are. Secondly, again for federally supported research for the United States, the direct cost of research in the foreign countries cannot get overhead, and that is written in regulations; but the direct costs of research—the grant support and the maintenance of rooms, and all of those things that we cannot charge in the United States—in fact, can be charged as direct costs in the developing country or in the foreign country that cannot receive overhead.

The question I want to ask is concerned with this guideline of what would be the ordinary life experiences of children. Several people have noted that this is a potentially hazardous standard. Whether it be in our inner cities or in war-torn countries around the world or in countries where there are very poor human rights records, the local standard may leave the door wide open for really quite unethical conduct. I wonder how you establish guidelines when local standards, which should be helpful, are really not protecting children.

Dr. Whitehead: I was not trying to minimize the importance of ethics committees in Europe or in the United States in terms of Third World research—obviously they are important. The
main thing I was trying to get across was that it is absolutely essential also to put the project through a local ethics committee. What does one do when prevailing circumstances are unsatisfactory? It might be that your study wouldn't be looked on as hazardous within such circumstances, where if the same study were carried out elsewhere in the world, say in the United States, it would be looked on as hazardous. When investigators realize that this conflict exists, they should perhaps point out to the local ethics committee that this is a significant problem. Otherwise, that investigator is going to place himself at risk in colleagues' eyes if he is seen to be carrying out research that could not be carried out at home.

Dr. van't Hof: I have been cooperating for many years with countries in Africa. Their researchers come to The Netherlands, and we discuss their projects and send them back to collect the data. I completely agree with you that the basic rules are the same the world over, but in applying these rules, I have often encountered difficulties. For example, one of the best-known basic rules is the rule of informed consent, which we must always obtain in The Netherlands. In African countries, however, consent is never really informed. What is your opinion about that problem?

Dr. Whitehead: It is quite likely that the level of understanding of women living in the villages where we work in the west of Gambia would be similar to that of an equivalent group of women living in Cambridge. But there is also a procedure that you have to go through in explaining the project to the elders of the village and getting their basic approval, telling them what the advantages will be, both to them and to the sum of knowledge. From a public relations point of view, it is absolutely essential, and also just common courtesy, that if you are going to work with people over an extended period of time, you should take them into your confidence and try to explain things. I think people do appreciate this, even if they don't always have the basic background knowledge to be able to assimilate everything. People can understand most things if you really make an effort. We become very worried when people come for very short periods of time to do a study, and where this courtesy has not been exercised.