Ethics in Clinical Trials

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Since the turn of the century medical knowledge has progressed more rapidly than at any other period in history. Each year new treatments are introduced, some of which are but minor alterations of those in current use but many involve novel and sometimes largely untried therapies for human disease. Before this period of rapid scientific development, the few advances in therapy that became available were often minor deviations of those in current use. The assessment of their value was by clinical observation and, although the frequent worthlessness of this appreciation has since become apparent, many relics of this time can still be found in medical practice today. This was the era of the "Sayings of the great men", when because an expert said a therapy was valuable, this view was accepted and unchallenged. Thankfully this has passed; no-one believes a thing is necessarily so, because someone says it is so; proof is demanded and, because this proof relates to the treatment of human ailments, its assimilation must necessitate human experimentation. In turn this has provided its problems and in particular has meant an uneasy alliance between scientific planning and the ethical code inherent in the doctor—patient relationship.

During the past two decades it has been appreciated that for the proper elucidation of these problems use must be made of a relatively new tool, the controlled clinical trial, and because of the immediate confrontation of patient experimentation with medical ethics, many attempts have been made to provide the clinician with rules for his guidance. Many countries have elaborated codes of ethics designed to help their own investigators. In Great Britain the Medical Research Council (1964) has offered detailed rules for the guidance of doctors involved in the planning and conduct of clinical trials. More recently in 1964 the World Medical Association announced a code of ethics on Human Experimentation known as "The declaration of Helsinki". This is not the place to enumerate the various recommendations that have been made but in each case a distinction has been suggested between trials which involve treatments designed for the benefit of the patient and those involving experimental procedures which, although aimed to further medical knowledge, are not to the patients' immediate advantage. In the former case it was felt that providing a practitioner genuinely believes that a new treatment may hold advantages over, an established one he is ethically correct to compare the two by a clinical trial. Although it is suggested that he should explain the trial to his patient this may not be necessary and indeed in some cases is directly contra-indicated. The real
problem arises when procedures are used which do not contribute directly to the benefit of the individual. Here permission must be sought and under circumstances where the patient will have a complete understanding of all that is involved.

Unfortunately whilst the motives that lie behind the formation of these rules are understood even their protagonists do not claim they are any more than a guidance to the doctor. No rules could be produced that would cover all circumstances and relieve the doctor of the moral obligation of considering each case on its own merits. This perhaps is the nub of clinical experimentation — that it is the investigator's own belief — or preferably that of a group of investigators — that what is being done is justified on moral grounds. The acceptance by the patient himself is not sufficient, because it is only too easy to persuade him to undergo almost any procedure the doctor suggests, due to the special relationship between them. Without the strictest personal code almost any manipulation could be carried out and would be accepted. In our own unit we have a rather homely rule which we find helps when making this decision. Would we allow members of our own family, if the occasion arose, to enter fully into the trial we were conducting and accept whatever treatment or whatever investigation was ordered by that trial? If so, then we believe it is ethical.

There are, however, other ethical considerations as well as the question of patient acceptance. The ethics of clinical investigation do not begin and end with the moral consideration of the patient's place in the controlled trial, but rather encompass the justification and design of the trial itself. If it is appropriate and ethical to test a treatment by its comparison with an established treatment then it may be inappropriate and unethical to test its clinical effect in any other way. It is, therefore, unethical to analyse the results of drug administration or operations or any new procedure by the haphazard and uncontrolled application of that procedure. Thus it is unethical — and one must admit that this frequently happens — to claim that a new drug has advantages as a result of the observation of its effects on a handful of selected patients. Moreover, if in the minds of clinicians there is doubt as to which of two treatments is the better or under which circumstance the one or the other treatment is more appropriate, then it is unethical to continue practising these treatments without attempting, providing facilities are available, to select the better by a clinical trial. It is undoubtedly wrong to continue practising a less effective therapy if, by investigation, it could be discarded. Nor does one's moral obligation end here. If one engages in a clinical trial, unless the trial is designed as appropriately as possible both from the statistical and clinical stand-point, the results may be meaningless or, worse still, even misleading. It is ethically wrong both to produce mistaken results under the guise of a scientific investigation and to subject patients to the rigour of a clinical trial when all the effort and possible discomfort will be to no avail.