MEDICAL PRACTICE

New Horizons in Medical Ethics

Research Investigations in Adults

This tape-recorded discussion was devoted to some current unsolved ethical problems of research investigations in adults. In the working papers, circulated before the discussion, Professor Witts, a former member of the Medical Research Council and Nuffield Professor of Medicine at Oxford, argues that a final sanction on unethical researchers is for medical editors to refuse to print their results; Dr. Williams, director of the liver research unit at King's College Hospital, that particular attention should be paid to the ethics of drug trials; and Dr. Eilenberg, a consultant psychiatrist and chairman of the ethical committee at Northwick Park Hospital, that creating a climate of informed ethical opinion is one of the major functions of a hospital ethical committee. The working papers are printed below, followed by the discussion, which was chaired by a member of the B.M.J. editorial staff.

Developing the Right Environment

M. D. EILENBERG

The first problem is defining human experimentation or clinical research. Experimentation is intrinsic to the practice of clinical medicine and some distinction may be made between procedures directed to benefiting the patient and procedures whose intent is to advance our state of knowledge. Nevertheless, there is not an easily defined relationship between service and experimentation. It is also important to appreciate that it may be unethical not to experiment.

Part of an ethical committee's responsibility is to develop an environment in which the active co-operation of patients is normal practice; in which new research ideas and initiatives are not over inhibited; and in which both patient and the investigator are protected. Also the ethical committee should attempt to encourage an attitude throughout the whole institution whereby everyone in contact with the patient feels some responsibility and has access to the ethical committee. The ethical committee should, I believe, be representative of lay, medical, and nursing views.

The patient's consent to all experimental procedures has to be balanced by the distress that may result from obtaining that result. Consent, of course, may not be relevant to the whole area of paper research and computerization, which also touches on the question of confidentiality. There is a problem of monitoring what transpires in an institution once ethical committee permission is obtained. Although one may use such codes as the Helsinki Declaration of 1964[1] and the publications by the Royal College of Physicians[2] and the Medical Research Council,[3] in the end no law or code, however detailed, can be a substitute for basically what is a trust between the medical profession and society, between a patient and his doctor. In clinical practice, arbitrary decision and professional discretion must be allowed.

Need for Centralization

ROGER WILLIAMS

In testing any new drug or therapy a clinician needs to ask whether his assessment of all the possible toxic as well as beneficial effects is shared by others with competence and experience. Thus, an ethical committee of a hospital, to which all new therapeutic trials should be submitted, must have competence within that area or else be able to seek expert advice. This committee also needs to have both independence and authority so that it can reject if necessary an application from a highly respected member of the hospital staff.

Much has been made of "informed consent," but when the subject is uneducated this ritual is a deception to both patient and doctor and provides no real safeguards. Thus a recent study[4] on genetic counselling showed that only half the

families so informed grasped the impact of the message from the doctor. Even if the patient is intelligent, can he really assess a situation which involved an element of risk, albeit a small one, in relation to the possible benefit he may receive?

A clinician should also ask whether his proposed trial is the best way for finding out an answer to whether this new drug or treatment is effective. The number of properly controlled trials in relation to the total trials of therapeutic agents done is still small, although there has recently been some increase, at least in Britain. The fact that the risk of drug morbidity or mortality is usually highest in the earliest cases treated with a new drug means that it is ethically preferable not to give all the patients a new drug, and that half of these early patients should be randomized into conventional therapy. In my view there are very few exceptions to the rule that pilot trials should not be carried out and the controlled trial should begin with the first randomized patient receiving the new drug. Although setting up a co-operative multicentre trial may be regarded as a chore, and indeed does constitute a great deal of work for all concerned, it is essential if the number of cases being seen is too small to make a properly controlled trial otherwise impossible.

There are two aspects of controlled trials that I believe are unsatisfactory, at least in Britain at present. Firstly, when a new agent is introduced several controlled trials may be set up after the clinical trial certificate has been given by the Committee on the Safety of Medicines, and yet no consideration is given to whether there is a need for several trials, or whether one good trial involving even the whole country would be sufficient. Very often a new trial is set up without knowledge of the results being obtained by other units or investigators.

Although the trials may differ in certain respects, they do need to be co-ordinated, and at present there is no central body to which each investigator may turn. This I think should be a function of the Committee on the Safety of Medicines. Secondly, the results of a controlled trial are so often analysed by the participants themselves at some stage. This is quite wrong: the correct way is for a fully informed advisory board continuously to assess the trial independently of the participants, so that as soon as a significant result is obtained the trial is stopped and all the patients continued on the best treatment.

In this way decisions can be taken at the earliest possible moment and the ethical position of the doctor and the medical research worker can be maintained—namely, to determine the best available therapy for the greater number of patients.

Importance of Controlled Trials

L. J. WITTS

Human experimentation can be divided into therapeutic and non-therapeutic experiments. In the past, appraisal of the value of treatment was left to the judgement of the individual clinician, but the history of treatment by bleeding, purgation, and emetics shows how long an erroneous treatment can survive if it is not subjected to scientific testing. With the rapid introduction of new treatments in the present century, the controlled trial has become an essential instrument of medical progress. In a modern controlled trial half the patients are given the best established treatment for the disease and the other half are given the new treatment. Patents in different centres can be treated simultaneously and the value of a new treatment can be quickly determined.

A similar technique is used in the evaluation of methods of prevention of disease. It is surprising that, though vaccination against typhoid was introduced at the beginning of this century, the right kind of vaccine and its value were not established until field trials were made in Yugoslavia in 1957. On the other hand, the prevention of diphtheria and poliomyelitis was quickly demonstrated by modern methods of trial once the basic knowledge was available.

Non-therapeutic experiments often deal with diagnostic methods such as radiodiagnosis, chemical and physical analysis of the blood, and the establishment of norms. As they are concerned with the advancement of medicine rather than the treatment of the individual, they often present ethical problems.

A large number of codes have been drawn up for the control of human experimentation. None of them is superior to Lord Lister's two desiderata: "First, a warm and loving heart, and secondly, truth in an earnest spirit." In Britain it is generally accepted that experiments should not be carried out on the dying or on prisoners, but few would accept a total ban on trials on children or the insane, as suggested by some codes. Practically all codes demand the "informed consent" of the subject but many experiments are difficult to explain to people without medical knowledge. Patients commonly agree because of loyalty to the doctor. Most hospitals, therefore, now have a special committee to which all plans for clinical research investigations can be referred for approval. A final safeguard is acceptance of results for publication. Researchers are unlikely to carry out experiments if they cannot publish their results, and editors of some medical and biological publications in Europe have agreed not to publish the results of human experiments unless the ethical standards are immaculate.

Appointments of Speakers

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Discussion

CHAIRMAN: I'd like to start by asking how ethical committes are working in practice. Dr. Eilenberg?

DR. EILENBERG: I can't of course, speak for other hospitals, but at Northwick Park the ethical committee was started in April 1970. It's composed of four consultants recommended by the medical executive to the hospital management committee; the director of the Clinical Research Centre; representatives of the non-consultant staff and of the general-practice division; the chief nursing officer; and a layman member of the hospital management committee. Finally, the group secretary acts as committee secretary. We make recommendations and are accountable to the hospital management committee and are therefore wholly independent of any medical establishment within the hospital. We have attempted to concentrate on the ethical aspects of any propects and not on its scientific worthiness—this latter is done by a separate committee, who submit their judgements to the ethical committee.

DR. WILLIAMS: Are these people chosen for their personal qualities or as representatives?