NEWS

New Rules for Biomedical Research Projects . . .

by our Washington Correspondent

FUTURE participants in biomedical research projects in the United States may have good cause to be thankful for the publicity accorded to some 200 black men from Tuskegee, Alabama, who took part, without their knowledge or consent, in one of the most highly publicised medical research scandals to come to light in recent years. The furore that broke out when details of the project were unearthed last year has led to a searching re-examination of ethical standards in clinical research and the prospect of a set of new regulations designed to safeguard the rights of experimental subjects in such research.

The Tuskegee study, as it quickly became known, was originally sponsored by the federal government and was designed to determine the clinical effects of syphilis and the efficacy of treatment for the disease. The procedure was simple. A number of poor black men from rural Alabama who were known to have syphilis in the 1920s were denied treatment for some 40 years while the course of the disease was monitored. None of them was ever told that he had syphilis, many died and the rest were quietly forgotten until the whole affair hit the headlines.

The Department of Health, Education and Welfare (HEW) immediately set up an official inquiry into the matter, and the committee had little difficulty in concluding that the study was ethically unjustified. The Tuskegee study had, for a start, violated the cardinal rule in human experimentation—that subjects should be informed of the likely risks and that they should freely consent to take part. Moreover, no risk-benefit analysis of the study could conceivably have shown that the benefits to be derived would ever outweigh the risks to the unfortunate men who unwittingly took part.

The committee also suggested that the present guidelines governing clinical research are vague and that they are probably not strict enough to discourage less scandalous, but still unacceptable, research projects. In the meantime, Senator Edward M. Kennedy was holding a series of hearings with his Senate Health Subcommittee which bore out the committee's fears in brutal detail. Kennedy's hearings turned out to be a nicely stage-managed exposé of a number of research projects whose ethical foundations ranged from outrageous to merely dubious.

The upshot of Kennedy's hearings was a bill to strengthen the review procedures for all research projects involving human subjects, to establish in the federal government a high level board to draw up policies for protecting research subjects, and to ensure that the policies will be implemented at the institutional level. The bill has been passed by the Senate, but it is now in limbo, awaiting a conference committee to put it into final form.

The Administration has also been busy, for apart from setting up the com-

mittee to investigate the Tuskegee study, the Department of HEW has recently proposed a set of guidelines which will eventually require institutions in receipt of HEW grants to tighten up their control of experiments involving human subjects. Finally, an *ad hoc* committee consisting of members of the National Institutes of Health (NIH), the National Institute of Mental Health and the Food and Drug Administration last week published a draft report recommending tight controls on research involving children, prisoners, the mentally

EDUCATION

Open to All?

THE Vice Chancellor of the Open University, Dr Walter Perry, persuaded the producer of *Coronation Street* to enrol Mrs Clegg, who keeps the corner shop, at the Open University. Sadly her progress is rarely mentioned, but she has at least helped to ensure that 40% of the British population have heard of the Open University.

Dr Perry gave the third Shoenberg memorial lecture to the Royal Television Society last week. He described how the Open University has coped with the momentous task of giving a university education, at a distance, to students of whom no formal entrance qualification is asked.

Very little has been spent on advertising, and consequently Dr Perry considers the number of people who have heard of the Open University as quite encouraging. But the 60% who have not heard of it are mainly from the lower socio-economic groups, for whom it was primarily created.

Of the 36,000 or so prospective students who have applied each year, 10% have no academic qualifications and 30% have some qualifications, but less than those required by other British universities. The remainder could have entered a more conventional British university.

The Open University is thus not yet appealing to those it wishes to attract. Many have obviously not heard of it, and Dr Perry feels that some have a typically British suspicion of all things intellectual.

How do the unqualified 10% fare? Courses assume no previous knowledge but progress quickly. During the first three months of tuition slightly more unqualified than qualified students drop

out. Of the ones who progress further the unqualified students perform indistinguishably from the others in arts subjects, slightly less well in science and technology and very badly in mathematics. The cure for this has not yet been found: should the first year mathematics course be altered? Should the Open University alter its philosophy and impose entrance requirements for mathematicians, or should it provide pre-university mathematics courses itself?

Everyone is agreed that the courses for the first two years should be general in scope but many students now approaching their third and fourth years wish to progress to more specialised courses. Some members of the Open University are ready to provide them; others contend that the educationally deprived students who have yet to enrol in large numbers will not want conventional specialised courses. There is not enough money for both types of course and discussion is heated.

The drop-out rate in many conventional correspondence courses is about 90%. Dr Perry and his colleagues have, however, managed to keep the rate below 30%, partly by modelling several features of the Open University, such as the week-long summer school, on the similarly successful correspondence University of New England in Armidale, New South Wales. Revolutionary teaching methods such as home experiment kits and tape recordings have quickly become incorporated into courses.

The Open University is no longer a topic of party political dispute, and the sale of its courses for use in other universities may make it the most cost-effective university in the world. If it can succeed in appealing to the section of the population it has not yet touched, its success will be remarkable.

infirm and other special cases.

The publicity given to research projects that are plainly outrageous has, however, tended to overshadow some of the more delicately balanced arguments and concerns. For example, what controls should be applied to research on children who lack not only the legal capacity to give their consent to take part but who may also be unable to understand the possible risks? Another area fraught with difficulty is research on prisoners—for example, is a man who is denied basic freedoms and who is continuously subject to the will of prison authorities truly free to give his consent to anything? Moreover, does the opportunity to take part in a research project which will relieve the routine of prison life and which may involve other large rewards carry undue incentives which, to him, outweigh the risks? (More than 70% of preliminary human testing of drugs in the United States is carried out on prisoners.) Equally difficult questions are raised in connection with research on the mentally retarded, on fetuses and on pregnant women.

It was those tricky questions that were faced by the *ad hoc* NIH committee, whose recommendations were published last week in the *Federal Register*. The committee believes that controls on such research should be greatly strengthened at both the federal level and in the institution in which the experiments will be conducted and it also suggests a few cases in which human experimentation should be outlawed entirely.

As far as research on children is concerned, the committee suggests that any proposal should be reviewed for ethical considerations by at least three committees, two of which would be in the institution in which the research is to be carried out and one in the agency sponsoring the research. It would work like this. Before submitting a proposal to HEW for funding, the project must be reviewed by an Organisational Review Committee, consisting of members drawn from a variety of disciplines, some of whom would not be employed by the institution concerned. Once the committee has approved the experimental procedures, the proposal would then be sent to HEW, where it would be subjected to the usual peer review system for scientific merit. The next stage is review by special committees to be established in every agency of HEW. These Ethical Review Boards would again consist of members from various disciplines and, as well as examining individual projects, they would advise the agency on general ethical issues.

Once approved by this process, the project would then come under the supervision of yet another institutional review committee, the Protection Com-

mittee. Its duties would be to ensure that those who take part in the experiment are fully informed of the risks, and that their consent and that of their parents is freely given. The Protection Committee would also be on hand to make sure that participants could pull out at any stage if they so wished.

In addition to that mechanism, the committee also suggests a number of other criteria that should be met before research can be carried out on children. First, the consent of both parents should be obtained. Second, the consent of any child over the age of seven who takes part in an experiment should be obtained. Finally, children without natural or adoptive parents, or those detained in an institution or in court, should be excluded from participating.

Senator Edward Kennedy

As for research on prisoners, the committee notes that it is ultimately up to the courts to decide whether prisoners are in a position to give consent without undue coercion, but it points out that in the meantime HEW should adopt a set of regulations which afford prisoners as much protection as possible. In short, the committee suggests that a project involving prisoners should come under the purview of a Protection Committee consisting of at least five members, one of whom would be a prisoner. It would make sure that those who take part are given full information and that they are not offered undue incentives.

Finally, the committee suggests that research should be carried out on the mentally infirm only if it can be proved that the study cannot be accomplished with the use of other volunteers; that no research should be performed on the abortus if it involves prolonging the heartbeat and respiration or, conversely, if it will of itself terminate the heartbeat; and that no research involving implantation of human ova which have been fertilised *in vitro* shall take place until animal studies have indicated that it would be safe (and that includes studies of the naturally born offspring of the products of *in vitro* fertilisation).

MORE ON MEDICAL ETHICS

... But Britain Differs

CLINICAL research investigations of children and mentally handicapped people should be allowed, according to a committee of the Royal College of Physicians. In a report published today on the *Supervision of the Ethics of Clinical Research Investigation in Institutions* (£0.10 from the Royal College) the committee says that to ensure advances in medical treatment research must continue, even though the investigations might not be of direct benefit to the patient.

The committee adds, however, that the investigation should be carried out "only when the procedures entail negligible risk or discomfort and subject to the provisions of any common, or statute, law prevailing at the time".

The Royal College document is in sharp contrast to the report of the *ad hoc* committee of members of the National Institutes of Health, the National Institute of Mental Health and the Food and Drug Administration published last week in the United States (see page 239). The report from the United States, which is likely to be incorporated into firm proposals by the Department of Health Education and Welfare, recommends much more stringent controls on clinical research than does that from the Royal College.

The Royal College report is a sequel to one published by the same body in 1967. Sir George Godber, Chief Medical Officer at the Department of Health and Social Security (DHSS), wrote to the late Lord Rosenheim, then president of the college, in 1971 asking him to investigate further the supervision of the ethics of clinical research in institutions. In particular, Sir George asked advice about the composition of ethical committees and the scope of clinical investigations.

The advice now given to the DHSS is that ethical committees should be small and should be constituted so that they do not "cause an unreasonable hindrance to the advancement of medical knowledge". The members should be experienced clinicians but there should also be one lay member. The committee stresses that this lay member must be someone "who is not associated with the [medical] profession in any paramedical activity". Biochemists and psychologists are therefore ruled out.

In view of the uncertainty about the procedures which have to be referred for approval, the Royal College advises that application should be made to an ethical committee "for all proposed clinical research investigations". The committee stresses the fact that a drug which has been granted a Clinical Trial Certificate or a Product Licence by a Licensing Authority on the recommend-