726149

BROOKHAVEN NATIONAL LABORATORY
ASSOCIATED UNIVERSITIES, INC., UPTON, L.I., N.Y. 11973

BNL 17183

MEDICAL DEPARTMENT

TELEPHONE: (516) 345- 3570

R

September 6, 1972

REPOSITORY Records Holding Area Bldg. 494
COLLECTION Meetings/Minutes/Agendas
BOX No. 2
FOLDER Governing Body, 1971-1974

Frank J. Ingelfinger, M.D.
To The Editor
The New England Journal of Medicine
10 Shattuck Street
Boston, Massachusetts 02115

Dear Sir:

CONTROLLED DOUBLE-BLIND STUDIES OF DRUGS

In double-blind evaluations of drugs neither the patient nor the physician can know what is being administered, while such studies are also called controlled when the patients are randomly assigned to a placebo and a drug-receiving group. The protocol is formulated at the beginning of the study and must be followed meticulously to the end. It would be patently absurd if these types of studies should become the only acceptable ones.

Intelligent formulation of controlled protocols is difficult indeed when the dosage, the primary therapeutic effects and the toxicity are insufficiently well known. Drugs which are sensed by the patients do not lend themselves to controlled studies because the code is often broken by the patients. With chronic diseases, furthermore, which can present a variety of symptoms all of which are scored, significant partial restitution of function is often missed when the sum of the data is submitted to the usual statistical analyses.

BEST COPY AVAILABLE

1181409

In the final evaluation of drugs and particularly those for chronic diseases a different process is perhaps necessary. After completing sufficient theoretical and basic investigations one would conduct a single-blind study. The patients would not be informed whether drug or placebo are given but each would be serving as his own control. The physician would be on the alert for toxicity. One would thus determine the range of the optimal dose and its scheduling; the therapeutic effects and tissue toxicity; and the kind of clinical and laboratory tests best suited to following these effects. One would be anticipating the practicing physician, who is trained to be objective although he is not blind and does not treat patients randomly. One can even produce conclusive results in this simpler manner, as the precedent of aspirin proves. If not, one can design and execute a more suitable protocol, since one would then be using ones judgement of facts instead of a mechanical process.

Rejecting this suggestion is tantamount to requesting studies in which neither the surgeon nor the patient knows whether a placebo or a human kidney are being transplanted and whether the uremic patient is being treated or is merely being used as a control.

This absurdity illustrates the ethical problems inherent in controlled studies. It also serves in lieu of all the arguments one cannot present for lack of space.

Very sincerely yours,

George C. Cotzias

George C. Cotzias, M.D.
Senior Scientist
Brookhaven National Laboratory
Medical Research Center
Upton, L.I., New York 11973

GCC:ge

1181410