Role of Clinical Trials in Postgraduate Education, Training and Resource Development

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Abstract – *Clinical trials may be of drugs, of other therapeutic manoeuvres, or of diagnostic methods. All medical post-graduate students, therefore, can undertake them. Clinical trials provide useful models for inculcating the skills in Thinking, Reading, Investigating, Analysing and Learning. Their by-products include: development and standardization of methods; creation of facilities for diagnosis and treatment; new uses for known drugs; and building up a cadre of medical practitioners who know the rudiments of scientific inquiry. Such practitioners could then form networks or groups interested in specific problems, combine practice with research, and contribute valuable epidemiologic data for the planning and delivery of health care.*

INTRODUCTION

The term clinical trial is usually associated with therapeutic trials of drugs. So the first point I wish to emphasize is that clinical trials need not be of drugs alone. They may aim to answer questions about any preventive, diagnostic, or therapeutic intervention. This point is important because it stresses the broad spectrum of studies encompassed by the term, and therefore the scope for all doctors to pursue this activity.

POSTGRADUATE CAREERS

A medical postgraduate may follow one of three careers after completing his training. First, he may set up a private consulting practice. Second, he may take up a full-time teaching position in a medical school. Third, he may follow a full-time research career. Whichever role he decides to play, he needs to equip himself with certain conceptual skills so that he may keep abreast of new theories, discoveries, and trends; appreciate their relevance to his own practice; analyse others' work critically; present his views accurately, briefly, and concisely in speaking or writing; or plan and carry out his own studies successfully. I propose that clinical trials are good models for training young medical postgraduates in these skills.

THE SCIENTIFIC METHOD

The word trial can be considered an acronym for the process of acquiring knowledge. It consists of

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the following components: thought, reading, investigation, analysis and learning. Every study begins with some idea or observation which triggers the natural curiosity of man and his desire to find out things for himself. The idea or observation then takes the shape of a proposition or hypothesis. This is an inductive reasoning process. The truth of the hypothesis can never be established with certainty, for who can say that it will forever remain inviolate? So we go about testing its veracity the other way round. We assume the hypothesis to be right, make some deductions from it, and then plan a study to see whether the deductions are confirmed in reality. If they are, our hypothesis gains strength; if not, it must be modified. As the hypothesis continues to be verified in this manner again and again, under different conditions, it either undergoes modifications or evolves into a theory. When a theory remains unchallenged for a very long time, it acquires the status of a discovery. This is how new knowledge is gained. Clinical trials provide convenient models for introducing medical postgraduates to this approach of epistemology.

Clinical trials as models

Why are clinical trials convenient models? First, because most have a sponsor who can provide the student with background literature for reading and orientation. Second, the hypothesis to be tested is fairly simple, e.g. the difference between two treatments or diagnostic tests. Third, the materials required for the study are often provided by the sponsor, e.g. forms of record, medications, reagents, and sometimes even equipment. Fourth, the sponsor's Medical Adviser is usually willing to spend time with the postgraduate for discussion, planning, organisation, analysis, compilation, presentation, and publication. A well-trained and experienced Medical Adviser can be a valuable asset to both the student and his guide. Last, financial grant is usually available from the sponsor to support the project.

Byproducts of clinical trials

Clinical trials often have other desirable byproducts. A new diagnostic or therapeutic facility can be created, a new laboratory or clinical method can be developed or standardized, the participants' conceptual and communication skills can be developed, and chance observations may disclose new leads. It would be worthwhile to cite some examples of such spinoffs.

Diagnostic spinoffs: When the exercise stress test came into vogue for diagnosing coronary artery disease, it was suspected that some highly sympathicotonic patients could have a borderline false positive test. When beta-blockers became available, they provided a means of attenuating the impact of excessive adrenergic discharge on the heart and weeding out the false positives. Likewise, the availability of metoclopramide, which accelerates gastric emptying, helped completion of a barium meal series of the GI tract in less time.

Therapeutic spinoffs: Metronidazole made its debut as a trichomonicidal drug. But patients treated with it for trichomonal vaginitis were also relieved of coexisting amoebiasis. This observation opened a new era in the treatment of amoebiasis. And now the drug's activity against anaerobic bacteria has improved the surgeon's confidence for preventing or managing infections after abdominal and pelvic operations. Chlorpromazine was first introduced as an antihistamine, but during its trials a psychiatrist noticed that it improved the thought process of schizophrenic patients — an observation which revolutionized the treatment of psychoses. The use of vasodilators to relieve chronic heart failure by relieving preload and afterload is another example of therapeutic innovation emerging out of clinical trials.

Example of prazosin: A few examples from my own personal experience may not be out of place. In the mid-1970's while I was organizing and monitoring a programme of clinical trials for prazosin in hypertension, an investigator using apex-cardiography pointed out that the drug had a beneficial effect in chronic heart failure[1] — an observation later confirmed by other investigators using better methods. Another physician, who had noticed signs of excessive adrenergic activity preceding death in victims of scorpion sting, found that prazosin was effective in reversing the signs and saving many patients[2]. Yet another investigator, working in an area where sickle cell trait is common, reported that prazosin was effective in relieving the bends of sickle cell crisis. One imaginative nephrologist, who had no access to haemodialysis then, used prazosin to cause splanchnic vasodilatation and thus to reduce the time required for peritoneal dialysis. These incidents brought immense thrill and satisfaction, not only to me but also to the investigators and their co-workers, who felt that they had learnt and contributed something useful.

Clinical trial wastage

I regret that many uses of clinical trials are wasted. For example, if an equipment or a technique is set

up for the sake of a trial, it may be dismantled when the trial is over unless there are continuing opportunities to use and support it. The research team, which is brought together, often disperses for want of extended tenure of the posts. Worst of all, the potential of clinical trials as teaching aids, as models for training postgraduates in the evaluation of diagnostic and therapeutic methods, and of published literature, is rarely utilised.

SUGGESTIONS

What can we do? **First,** I believe clinical trials (in the broadest sense) should have a place in all postgraduate curricula. Every postgraduate should be required to carry out at least one trial during his training. This will be easy if clinical trials are accepted by universities as topics for postgraduate dissertations. Some universities do, but others don't. **Second,** clinical trials should be purposeful. Blind repetition of similar trials for regulatory requirements should be minimised. **Third,** a national network ought to be developed of practising doctors who are interested in research relevant to the community in which they practise. Suitable subjects can then be taken up by interested doctors, permitting epidemiologic studies, and generating data germane to health care decisions[3]. **Fourth,** an attitude must be nurtured of combining patient care with research, for isn't it said that every instance of treatment is essentially an experiment?

Epidemiologic Studies
Special Scope in Practices

Therapeutic Orphans
- Pregnant women
- Children/infants
- Elderly patients

Adverse Reactions to Drugs

Serendipitous Discoveries
- Opportunities
- Warnings

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"Finally, the physician should bear in mind that he himself is not exempt from the common lot, but subject to the same laws of mortality and disease as others, and he will care for the sick with more diligence and tenderness if he remembers that he himself is their fellow sufferer".

Sydenham T L. *Methodus Curandi Febras.* 1666.

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"The developed world may have the technology and resources to prevent and cure many of the infectious diseases still rife in the developing world, but Acquired Immunodeficiency Syndrome (AIDS) is an equal affliction of both worlds. Although the pattern of infection varies both nationally and between rural and urban populations, AIDS is certain to be one of the major health challenges for all nations in the 1990s, both in terms of prevention and of research into treatment".

AIDS – A Global Challenge. In: *The Economics of Health Care: Challenges for the Nineties.* London: Medic Ltd, 1990, p. 69.