

Revitalising Clinical Investigation, Who, How and Where?

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Clinical investigation, or experimental medicine, comes in many forms but this presentation focuses on making deliberate experimental interventions in man to study a physiologic/pathophysiologic mechanism or a therapeutic intervention.

The physician who conducts such an investigation must have a very good working knowledge of human physiology, an uncommon quality amongst those trained in the new biology era. For example, many human processes show large diurnal fluctuations (e.g. blood pressure, cholesterol synthesis etc) or marked changes after a meal or exercise. During research investigations the human subjects are usually worried and often quite frightened. Something as minor as slamming a laboratory door can give a marked jolt to blood pressure and heart rate. Often subjects have been starved of food and fluid for hours before the study begins and complaints of headache and nausea are common. Fainting on standing is a hazard. Thus, the investigator needs to be well trained in human physiology and understand how to ensure that his subject is comfortable, relaxed and as physiologically stable as possible.

Many clinical investigation procedures involve the administration of drugs, either as the primary objective of the study or as a challenge procedure to test a physiologic function. The investigator needs to have a very good understanding of the clinical pharmacology of the compounds to be used both their action and their fate in the human body. So besides being trained in human physiology he or she also needs to be trained in the clinical pharmacology of all the test agents that may be used and how they may interact.

Clinical investigation in 2006 often involves use of complex equipment (fMRI, PET, TMS etc). The investigator should not neglect very simple measurements, for example using weighed dental cotton wool rolls to assess dryness of the mouth, or simple (but validated) visual analogue scales to assess mood, pain etc. In many investigations of drugs the most reliable measuring system available is the subject's own sensory input. Subject completed questionnaires can provide very important insights into a range of parameters that cannot be measured by other means. Subjective they may be but important insights can be gained from them.

The best place to carry out clinical experiments is a comfortable quiet environment well equipped with monitoring and resuscitation equipment (and staff who now how to use it) but not dominated by oppressive arrays of noisy hardware. Where that is not possible (fMRI) great efforts must be made to

ensure subject safety and accustom the subject to the environment before making critical measurements.

Being a first rate clinical investigator is a rewarding career and like any other it needs extensive training, experience and mentoring. The latter are in short supply.