Current opportunities in clinical research

This conference was held by the Academic Medicine Group at the Royal College of Physicians on 18 December 1992. It was designed to help doctors wondering whether to embark permanently, or even for a limited period, on a career in clinical research. The speakers, most of them already committed and successful research workers, illustrated both the satisfaction and the problems that come with such a way of life.

Like Caesar’s Gaul, the conference was divided into three parts.

- Why doing clinical research is a good thing: claimed by those who have already done well.
- The difficulties in planning a research career: proclaimed by those selecting it.
- Where to find the opportunities: explained by those in whose gift they lie.

Is clinical research a good thing?

Professor David Weatherall’s (Medicine, Oxford) answer was: ‘yes, provided it is worthwhile work based on good and adequate training’. He pointed out that clinically orientated research covers a wide spectrum, from molecules to whole populations, from fundamental laboratory science to clinical epidemiology; but that its place has to be defended in the face of an anti-science lobby both within and without the medical profession. He wanted all undergraduate students to know enough elementary statistics to be able to assess the validity of statements in articles and textbooks. He thought that it would be ideal if doctors who wanted to do good research had at least two or three years free from regular clinical commitments to learn the necessary techniques and have time to produce worthwhile data. Those with a strong scientific bent might then go on to a full-time career as medical scientists in a research institute; the more usual academic doctors would probably do half-time research and half-time.

Table 1. Characteristics of subtypes of AI-CAH

| I    | Antinuclear antibody (ANA) and/or smooth muscle antibody (SMA) positive |
|------|-------------------------------------------------------------------------|
| II   | Liver-kidney microsomal (LKM-1) antibody positive                       |
|      | IIA: younger, anti-HCV negative                                         |
|      | IIB: older, anti-HCV positive                                           |
| III  | Negative for ANA, SMA and LKM-1 but positive for anti-SLA (soluble liver antigen) |

AI-CAH patients who are anti-LKM positive and anti-HCV positive can be differentiated from patients with active HCV infection by PCR of serum for HCV; interferon is indicated for some of the latter but is dangerous in the former.

Chronic active hepatitis

Professor K-H Meyer zum Büschenfelde (University of Mainz, Germany) gave a superb account of autoimmune chronic active hepatitis and its antibody profiles. AI-CAH is a progressive inflammatory liver disease requiring early diagnosis because immunosuppressive treatment greatly improves its prognosis. The diagnostic approach has been made much easier by the establishment of a panel of marker autoantibodies that define several subgroups of the disease (Table 1).

Autoantibodies directed at other liver components are also present, in particular the asialoglycoprotein receptor (anti-ASGPR). These show specificity for all subtypes of AI-CAH (and some patients with primary biliary cirrhosis). The ASGPR may well function as a hepatic autoantigen in AI-CAH: ASGPR specific CD4+ T lymphocytes are found at the site of tissue injury, suggesting that this hepatocyte surface molecule functions as a hepatic autoantigen in AI-CAH, with a role in initiation or perpetuation of the disease. Interestingly, the anti-ASGPR titre falls as the activity of the liver disease abates with immunosuppressive therapy.

Envoy

It is a worrying prospect for the future of medical research in the UK that audience participation failed to match the level of the basic science presentations. However, the meeting livened up during the more clinical sessions; those on cancer and liver disease were particularly well received. The gap between science and practice must not be allowed to widen further.

Rapporteurs:

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clinical work. Doctors who did not intend to make research a major part of their work would not need full-time research training but should ensure that they retained their ability to evaluate the work of others.

Professor Peter Lachmann (Immunopathology, Cambridge) regarded this as the golden age of clinical research because of the wide range of specialties involved and the quality of research being done. He divided research into 'ortho', 'meta' and 'para' research.

‘Ortho’ research is that which is done to push back the frontiers of medical science. It requires a major commitment in terms of time and enthusiasm, demands professional research training, and has a lasting effect on the work and career of those who undertake it. When should this type of research be done? No ideal time can be specified; one has to find a balance between the progressive decline with age of intellectual power and the difficulty of returning to clinical training after having done full-time research.

Why do this sort of research? Because it is compulsive, it is fun, one wants the answers, but also, in the words of Mallory ‘because it is there’.

‘Meta’ research helps to maintain a general research culture; it reinforces the distinction of accepting something for which there is experimental evidence rather than accepting it merely on the basis of an authoritative statement. This type of research should be done at all levels all the time.

‘Para’ research is done almost as a sideline and can be interesting and valuable but is not ‘the stuff of headlines’.

Compared with the more formal arrangements in the USA there is a lack of structured training in the UK even for a PhD, but especially for the MD. Potential research scientists can learn more about the centre where they would like to work by looking at what has happened to previous students within that department, but there is no simple way of assessing the quality of its clinical supervisors.

Professor I A Greer (Obstetrics, Glasgow) stressed the crucial role of clinical research in the development of medicine through translating scientific knowledge into clinical practice. This challenges the young researcher to identify a clinical problem, to develop a hypothesis and then assess methods to test that hypothesis. He/she will have to find funds for the project and act as its manager, collect and analyse the data, and finally publish them in a peer-reviewed journal. All this, Professor Greer said, should be fun. One often has to create one’s own opportunities and take them as they arise, but it would be valuable to have a mentor to whom one can turn for help and advice. Clinical accreditation remains a worry to some junior doctors who want to back both horses in case their research career comes to a halt. Accreditation may be dead, but how different will be the EC specialist certificate? Surgical research workers have a particularly pressing problem in relation to clinical training and accreditation because of their need to maintain practical surgical skills.

Difficulties

Planning a research career

Dr V K K Chatterjee (Medicine, Cambridge) recounted the problems he had in finding a research job and money in the USA and in finding an academic post on returning to the UK. With persistence, he eventually succeeded in both but he strongly advocated that fellowships for research abroad should generally be linked with posts offering the possibility of a long-term research career on return to the UK.

The audience was then encouraged to raise relevant issues with the speakers and other ‘research establishment’ figures who were taking part in the meeting. Questioners, whose interest in research ranged from planning a permanent research career to merely embellishing their CV, had a number of common concerns: where to go for advice; how to apportion time between clinical duties and research; how to deal with the bogey of accreditation; the lack of opportunity for part-time research, particularly, but not exclusively, for women.

Obtaining advice

Not everyone is fortunate enough to have an experienced and interested research supervisor. One result of the meeting is the intention to establish regional advisory panels consisting of one or two professors of clinical and laboratory based subjects, at least one woman who is also a clinical scientist, and a representative of a major research grant giving organisation. Might they produce a ‘good research guide’?

Clinical duties and accreditation

Although current accreditation programmes will have to be ‘harmonised’ to conform to EC requirements, and there are rumours that ‘accreditation is dead’, it is recognised that those whose practice involves clinical procedures—surgeons, obstetricians, cardiologists, endoscopists, etc.—will have to devote sufficient time to clinical practice during their period of research to reach a safe and acceptable level of practical skill. Sir Christopher Booth pithily observed that ‘accreditation is for hospital consultants working alone; a different form of accreditation is needed for academics working in teams’.

Part-time research

The inadequate provision of part-time research was repeatedly mentioned, mostly, but not exclusively, by women doctors. As usual, the question made senior male and female doctors uncomfortable but remained
unresolved. Perhaps the advisory panels may be able to help in a practical way at local level.

Where are opportunities for research?

*In the NHS*

Professor Michael Peckham (Department of Health) considered opportunities for research in the NHS. Although the NHS is seen mainly as a provider of health care and not as an institution interested in basic science and technology, this is incorrect because the NHS continually introduces technology and treatments based on medical research funded from several different sources. It is therefore essential that it should have a mechanism for identifying clinically important research projects and, if necessary, specifically commissioning research in topics important to the health services, and cooperating with technology based industry to make the best use of the results of research.

There is often a time lag between obtaining the results of research and their implementation in clinical practice: for example, had a meta-analysis been performed in 1972 on the first 10 trials of thrombolysis, sufficient benefit would have been found then to introduce it as a new treatment in the NHS. However, a further 60 trials were carried out to confirm its place as the initial treatment of choice for myocardial infarction because the dangers of exposing the population to the risk of unforeseeable complications must also be taken into account. It is necessary to find a balance between the ‘real world’ in which decisions on clinical action have to be taken, and the research community eager to see its discoveries translated into clinical practice.

*In what type of research does the NHS engage?* The NHS is committed not only to research in basic and clinical science, but also in applied areas such as nursing, pharmacy, management and audit. Professor Peckham did not define the precise balance between these broad ranging subjects, but recommended that there should be a degree of ‘cross section flow’ between them.

*How should research in the NHS be managed?* Research and development are an integral part of the management executive of the NHS, along with aspects such as personnel and finance. Each regional health authority will soon have a director of research with links to the health authority, hospitals and primary health care, thus forming a ‘national research network’ for the NHS. But might so many research administrators and advisors cause diffusion and confusion in NHS research?

In addition there will be a standing committee on health technology to bring together medicine, nursing, epidemiology, management, GPs and finance. Let us hope that these organisations will identify important problems, decide on the feasibility of research and its application to clinical situations.

The strategy of research will be monitored by the Cochrane Centre in Oxford. This centre will oversee clinical trials and develop a database of national and international research to limit wasteful duplication. It may also become involved in reviewing research data before definitive policy decisions are made.

*How much financial support will the NHS give to research?* It is planned that 1.5% of the predicted NHS budget for 1997–8 should go to research, in part direct to the researchers and also to support the related service requirements (extra bed occupancy and clinical laboratory investigations). In pure business terms it was felt that the potential benefits should easily compensate for the initial outlay. The management executive will, no doubt, be keenly looking for these benefits.

The NHS has a role as a direct funder of research, and in managing research it will have a major influence on medical career structures. But the exact type of research to be undertaken with NHS support is still a little unclear, as is the question of how it will be incorporated into an NHS career. Details of training fellowships within the NHS may be available some time in 1993. It will also be interesting to see how NHS reforms will interact with research interests. When the budgets of hospitals are under pressure, how far down the priority list will research be?

*In the universities*

Professor M R Bond (Universities Funding Council) gave a full account of the funding of university research and then listed the desirable attributes for funding university departments. The best departments are large, have a well developed research team, a combination of clinical and basic research with national and international collaboration. They can offer protected research time, good completion of postgraduate degrees and a competitive amount of published work. Such departments usually have a high income from peer reviewed research funds. Less good departments are small, their research strategy is not well focused and they have heavy clinical and undergraduate teaching commitments that interfere with research.

*With grant giving organisations*

Representatives from some of the grant giving organisations spoke briefly about what they had to offer and the criteria for awarding training fellowships. Professor Desmond Julian (British Heart Fund) ranked these as: first, the quality of the candidate; second, the quality of the research training and supervision available at the chosen centre; third, the quality of the proposed project. In the ensuing discussion, intending research workers made it clear that there is an urgent need for advice on how to set about obtaining a satisfactory research training, either full-time or part-time, at
home or abroad. They also urged that there should be more career outlets after training has been completed. There was also concern that in some specialties—surgery and cardiology were specifically identified—time spent in research is sometimes seen as damaging credibility as clinicians. Those who spoke for their own grant giving bodies were keen to point out their appreciation of these points and their intention to recommend an increase in research career posts. 

Dr D Gordon (Wellcome Trust) reminded the audience that industry can also offer such posts and that the pharmaceutical industry has a good record of Nobel prizes and FRs. While Professor N A Wright (Imperial Cancer Research Fund) thought that clinical research fellows make the best PhD students, Dr Diana Dunstan (Medical Research Council) expressed her concern that no suitable candidates had come forward in the last four years for appointment to the prestigious and well endowed clinical research professorships.

General comments

In his summary of the day’s discussions, Professor L A Turnberg (President, RCP) referred to the recurring main concerns: too few opportunities for trained research workers; the apparently inflexible barrier of accreditation; the dominance of clinical commitments restricting time for research; the lack of part-time training posts.

Personal remuneration was one issue not considered in great detail but it is important in planning a career in research. There is the perennial problem of different pay scales for clinicians and basic scientists; also a pull away from academic medicine towards private practice; and the fact that the salaries of clinical researchers are considerably lower than those of their peers in clinical practice with overtime payments. Allowing academics to do more private practice is not a desirable solution, but it may be worth considering the American system of sharing time on and off service.

Attempts at resolving these problems are on the horizon. Richard Smith (British Medical Journal) suggested that ‘young Turks’ (originally the founders of the American Society for Clinical Investigation) should band together to campaign among politicians, the public, and within the medical professions for recognition of the importance of clinical research and for better conditions.