

## Challenges Ahead In Clinical Medicine\*

PROF. SIR RAYMOND HOFFENBERG,

Royal College of Physicians of London

\*Paper published at the Combined Medical Meeting Kuala Lumpur – August 1986.

There are two ways of tackling the topic of challenges in clinical research. One way would be to review the diseases that still challenge us – on which we have made little or no impact – neither on prevention nor on cure. The list would include most forms of cancer, heart disease, strokes, Parkinson's disease, most mental disorders (certainly presenile dementia, schizophrenia), rheumatoid arthritis, etc.

I could then try to judge where we stood in our battle against them, the chances of successful intervention and what might be needed to accelerate success. This would require a breadth of knowledge I do not possess and involve me in a degree of crystall-ball-gazing that I would prefer to avoid. As Nils Bohr said, "All prediction is dangerous, especially about the future." So, I intend to approach the subject differently and to discuss a few broad challenges I feel need to be faced.

First, is the challenge of satisfactorily applying the knowledge we already have. In Britain, for instance, despite more than 20 years of medical warnings, smoking is still estimated to cause 100,000 premature deaths a year and 50 million lost working days a year.

Admittedly, the overall prevalence of smoking in Britain is declining – from 52% of males in 1972 to 38% in 1982, from 41% of females to 33% for the same period of time. But the figures for young adults and children are far from reassuring, and the improvement seen in the UK is not paralleled by significant reduction in many other parts of the world. The tobacco industry, conscious of increasing rejection in developed countries, is rather cynically, focussing its attention on the expanding markets of the new world.

For years, we have also been aware of the consequences of alcohol abuse. A recent Swedish study estimated that one third of deaths in middle-aged males were drink-related; in Britain, 25,000 annual deaths are attributable to alcohol. A number of studies have shown that 15 – 30% of male acute hospital beds are occupied by patients with alcohol-related diseases. Again, the young are especially vulnerable. In England, about 6,000 young people under the age of 18 years are found guilty of drunkenness offences each year. The total cost of alcohol abuse in UK is estimated to be 1.6 billion per annum and we are estimated to have one million problem drinkers.

Control of tobacco and alcohol usage requires changes of social habit in which the role of the medical profession is less well-defined. It is perhaps more of a problem for sociologists than doctors, but there is much we can do at a personal level, through persuasion of our patients, and perhaps even at community and government levels.

---

Of greater importance and in a much easier way to implement because it requires little modification of individual behaviour, being mainly a matter of organisation and application of resources, is the proper implementation of immunisation programmes. WHO estimated in 1983 that in the developing countries there were about 400,000 new cases of persisting paralytic polio, 2.5 million deaths attributable to measles, more than one million deaths from neonatal tetanus and about 750,000 deaths from pertussis. If we do nothing, four million children will be paralysed by poliomyelitis over the next 10 years; more than 20 million children will die of measles. The WHO-Expanded Programme on Immunisation hopes to provide global immunisation for all children by 1990. Already there seems little chance that it will meet its target.

Smoking, abuse of alcohol, and inadequate immunisation against preventable disease are some of the ways in which we are failing to apply knowledge that is already available. Progress in research cannot, of course, be held up whilst we wait for the world to catch up. Man's appetite for new knowledge will never be held in check.

The challenge is to close the gap between what we do and what we are able to do. My second challenge is not related. I refer to the communication and comprehension gap between the medical/scientific community and the community at large, particularly the media – a gap which also needs to be closed.

The spectacular achievements of the past have too easily been forgotten. People today – doctors included – find it hard to imagine a world without antibiotics. Yet, sulphonamides became available only 50 years ago, in the mid-1930s. In 1948, streptomycin came as a miracle to those of us who had watched helplessly the misery of gradual death from pulmonary TB with breathlessness, cough, haemoptysis, and slow suffocation. Or worse, the horror of TBM attacking, as it so often did, babies and young children. Such experiences, I fear are still prevalent in developing countries.

Antibiotics are taken for granted, as is successful immunisation against so many infective diseases or the innumerable other medical and surgical advances of the the past 30–40 years. The public has come to expect too much of the medical profession. They hear a lot about our skill as scientists and the technology we have to back us up – of CT and MR scanners, of brain and heart surgery, of transplants, and our new understanding of genes and DNA. Daily, they are confronted by the common, serious, often fatal diseases we have failed to influence. Fed by a largely ill-informed, often naive and always a sensation-seeking media, they perceive biomedical scientists as being preoccupied with esoteric and self-gratifying research instead of being concerned with the common disorders from which they suffer and die.

Heart transplantation, to quote an example, given the advances that had already taken place in anaesthesia and extracorporeal maintenance systems, was technically a relatively simple operation, far less complex than many of those already being performed on congenital heart abnormalities. Yet, it hit headlines in an unprecedented way and focussed public attention on the extravagant use of resources for objectives that could benefit only a tiny minority of sufferers from heart disease. For most of us, the significance of this particular operation was

---

appreciated in two ways: The first was ethical. The operation required the removal and transfer of a heart that was still beating. To cope with this problem, and the related larger problem of deciding when to turn off the life-support system, a not wholly satisfactory definition of brain-death had to evolve.

In 1967, when I found myself as the Consultant-in-charge having to decide if and when Clive Haupt's heart was to be put into Dr Philip Blaiberg, there were no such guidelines. The second important consequence of this sensational act was the impetus it gave to research in fields such as tissue-typing and histocompatibility, immunology and immune-suppression, that has enabled us to control many forms of inflammatory disease, leukaemia, renal disease and so on.

The public, through the media, fails to appreciate how modern medical science works. They have little idea of the complexity of modern medical research or of the time it takes to translate a major basic scientific discovery into clinical application.

The epochal revelation of the structure of DNA by Crick and Watson in 1953 is only now being applied to the prenatal diagnosis, hence perhaps to the ultimate prevention of genetic disease varying from the haemoglobinopathies to polycystic kidneys, Huntingdon's chorea and cystic fibrosis.

Our challenge is how to include a deeper and more sympathetic comprehension of how medical science works, of the reasons why scientists might seem to be pursuing esoteric and apparently useless research projects, of the inevitably slow pace and the complexity of modern scientific achievements. Unless we can create a better understanding of the nature of scientific research, we shall fail to attract the funding or support that is vital for our future success.

My third challenge embraces the ethical, social and legal dilemmas that surround modern medical research, especially in the field of genetics. Our ability to fuse cells from different species and to manipulate the genetic material of viral, bacterial and even mammalian cells has raised the spectre in the public mind of a new breed of laboratory-engineered monsters or of the uncontrolled spread of new deadly man-made infections. These images might seem fatuous and sensational but they are real enough to warrant serious consideration.

We now have a variety of techniques for introducing new genetic material into cells which may be expressed in whole animals. A recent striking example was the introduction of additional growth hormone genes into mice that not only grew to immense size with vastly increased levels of circulating growth hormone but were able to pass the genes onto their progeny. Lately, there was a report of a similar approach being adopted by Australian sheepfarmers to increase wool-production. Gene manipulation in humans is still a long way off, but one can understand the misgivings and fears of the public.

In-vitro fertilization introduces unforeseen problems about surrogate motherhood, about the fate, and even the legal status, of the unused fertilised clones. Again, one must sympathise with a public which needs reassurance that medical scientists will not abuse these discoveries.

---

The diagnosis of specific genetic diseases through Recombinant DNA technology may now be made prenatally on chorionic villus samples within the first trimester of pregnancy, offering parents the option of early, selective abortion. To most of us, this would be an ethically acceptable way of preventing the suffering of the affected child and its parent associated with many genetic disorders.

The same material allows easy and positive determination of the sex of the embryo which is information that is exploitable selectively to breed out children of unwanted sex. To most of us, I suspect this would not be acceptable. The pre-symptomatic diagnosis of genetic disease at a later stage of life, for instance in persons at risk of developing Huntington's Chorea, introduces a different set of moral dilemmas.

Such ethical considerations are not confined to the field of genetic research. The conduct of controlled clinical trials raises issues concerning the use of placebos, how much should be disclosed to participating patients, the acceptability of withholding possibly-beneficial therapy from those who act as controls. The preparation of a forthcoming Royal College of Physicians report on the use of healthy volunteers in research has highlighted many ethical, moral and legal problems. The ethics of all forms of research can no longer be ignored. Neither doctors nor the clergy have proprietary rights over these decisions. Our challenge is to elaborate guidelines that will not inhibit the prosecution of valuable research but will be acceptable to society as a whole.

My fourth challenge concerns funding. In Britain during 1984/85 the allocation for science research was £550 million, of which £117 million went to the Medical Research Council. In the same year, in the USA the expenditure on health research and development was about US\$13.5 billion, of which the Federal government provided just over half, about US\$6.8 billion. Modern medical research is expensive. The equipment is expensive, the materials are expensive, the use of highly-skilled scientists is expensive. At a time of escalating costs, financial support, especially from the government in Britain, is diminishing. This picture is unlikely to change in the foreseeable future and scientists will have to grapple increasingly with the challenge of diminishing resources with which to conduct ever more exciting and potentially beneficial, but regrettably more costly, research.

Finances, however, are not the only problems. In North America and Britain there is a declining interest in academic medicine and clinical research. Much of it results from the policies of governments that are perceived to be unsympathetic. By 1990 universities in Britain will have suffered a 30% cut in real terms over a period of 10 years. Young medical graduates view a future in academic hospital medicine as perilously insecure. At the same time, in Britain, general practice offers the lure of a high salary, early autonomy and lifelong security, without the competitiveness and insecurity of academic life. The financial rewards of private practice, especially for those who possess a diagnostic or therapeutic technical skill, are beginning to prove irresistible to many young doctors who might previously have chosen to remain in academic or, at least, in full time hospital posts. The pendulum has swung excessively away from academic medicine and needs to be reversed if we hope to take full advantage of the exciting prospects ahead.

---

There are two final points, I would like to make in relation to clinical research. First, that proper training in research methods is no longer something that can be acquired in one's spare time as a clinical registrar. A young doctor who wishes to be at the cutting edge of scientific advancement now needs two or three or more years of whole-time bench research. We must find ways of providing this with adequate funding without jeopardizing his chances of returning to a suitable clinical post. Job insecurity is a major deterrent to the entry of young doctors into research. Second, it is no longer realistic to expect a fulltime clinician and a teacher to be at the forefront of research – very few people manage this. Established slots must be found in academic departments for professional non-clinical scientists. In addition we should recognise a new grade of clinical scientists who do a little clinical work, unlike our present academics who tend to be clinicians doing a little research.

Modern medical science has more to offer than ever before. Prospects for the alleviation of human suffering have never been better. The extent to which these benefits will be made available will depend less on what scientists can do than what they will be allowed to do. Ethical and financial obstacles need to be overcome a better public understanding of medical science and the way it works will be necessary; and stronger efforts will have to be made, nationally and internationally, to put into effective practice the knowledge that is already available.

If we succeed in meeting these challenges, we shall enter a golden age of medicine. If we do not, we shall find ourselves with many ideas to improve the health of mankind but the frustration of not being able to implement them.