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The Growth of Science and Medicine: the Opportunities and the Obstacles

Abstract

Scientific and medical knowledge has grown at an exponential rate. In this respect there is a close analogy with Malthusian population growth. Apart from the problems this creates for the funding of research and medical care there are important consequences for the academic community. These are:

1. Much spurious medical research, particularly in the areas of complex multi-factorial diseases where sophistication and naivete may exist side by side.
2. Decline in clinical research as talented individuals have difficulty in bridging the gap between clinical practice and basic science.
3. Wastage of scientific resources which are invested in inappropriate areas through powerful advocacy. It is argued that new approaches are required based upon the development of collaborative groups and more targeted research developed as a result of recognising priorities.

The Exponential Growth of Medical Science

The problems which we face in academic medicine are the problems of success. A variety of measures of scientific activity all point to the same conclusion: unconstrained science grows at an exponential fashion (Swales 1990a). We can for instance examine the number of papers cited in Index Medicus (figure 1). We can measure the introduction of novel drugs into clinical practice (figure 2). We can be more selective by taking seminal discoveries. For instance Ruskin surveyed key influential papers in my own field of interest of hypertension between the 17th century and 1956 (Ruskin 1956). Quite independently Dickinson reviewed major discoveries in blood pressure regulation between 1900 and 1990 (Dickinson 1991). Although the criteria for selection and the periods of review were different the exponential curve was the same. If one examines the other side of the coin i.e. the cost of research, a similar picture emerges. Thus, the investment of the pharmaceutical industry in research and development has also shown exponential trends (figure 3). Health care costs have also of course risen but in a rather less

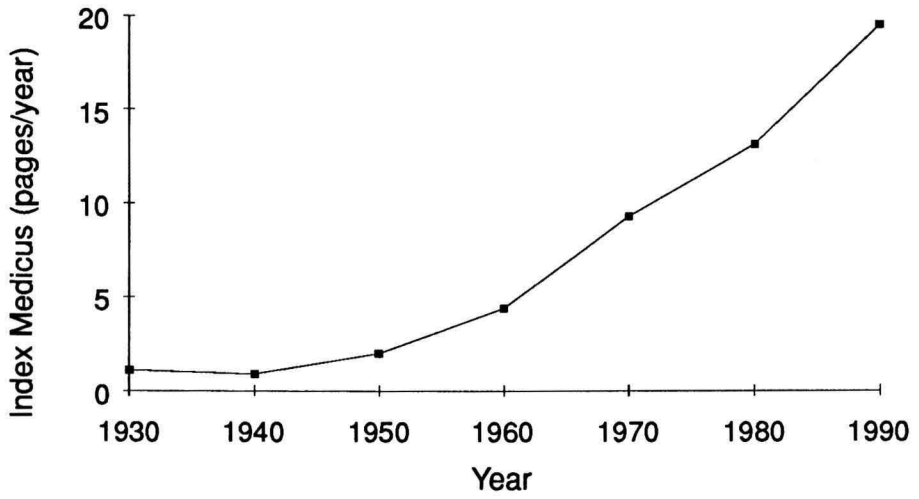

Figure 1: Number of papers cited in Index Medicus (From Swales 1990a)

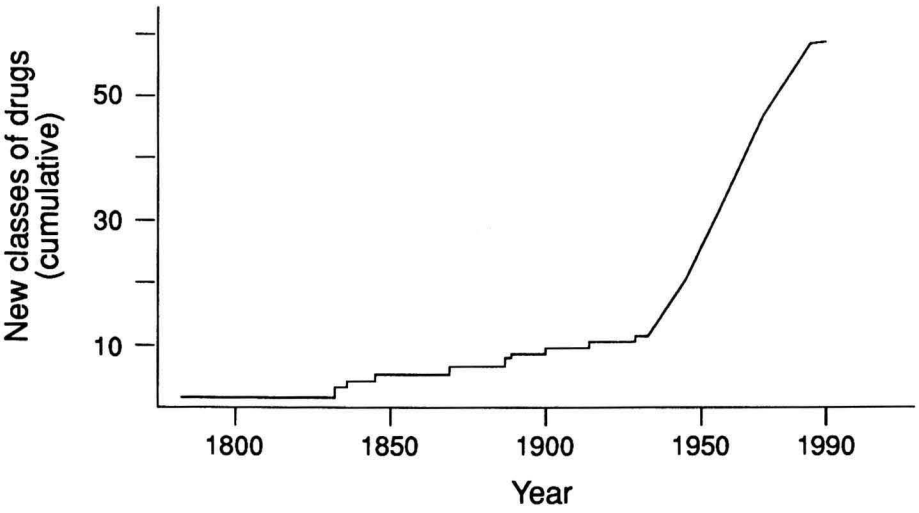

Figure 2: Introduction of new classes of drug into clinical (From Swales 1990a)

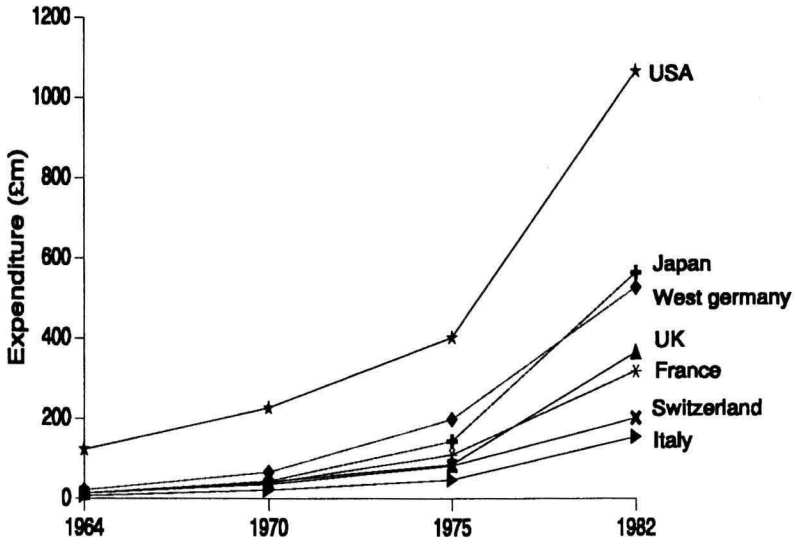

Figure 3: Growth in expenditure on research and development by the pharmaceutical industry (Lumley et al 1987).

dramatic fashion. This illustrates a fundamental truism which cannot be ignored by any of us who work in either science or medicine: the public purse is not unlimited and ultimately constraints upon expenditure come into play.

The Malthusian Model

The growth in scientific and medical activity shows a close analogy with the growth of microorganisms or populations freed from constraint. The reason is not hard to find: the fundamental mechanisms are the same. Scientific discovery opens the door to further scientific discovery as new methods and new approaches are applied to existing problems.

Comroe (1978) expressed this in picturesque terms in a discussion of cardiac surgery when he referred to the surgeon mounting 'steps laboriously carved out by hundreds or thousands of scientists over many generations, scientists in many disciplines working in many countries'. This is the exhilarating aspect of medical science, the view of distant peaks which continues to attract some of our most talented individuals into medicine and science. But this exponential growth also brings problems in its wake. These were recognised by two social philosophers examining another scene in another century: the Rev. Thomas Malthus and Herbert Spencer. Malthus

(1826) argued against the prevailing view of the perfectibility of human society. He pointed to the almost unimaginable consequences of unlimited population growth. This could only be prevented by constraint and there were only two forms of constraint. Individuals could limit their reproduction by self restraint or external methods could be used. Malthus's philosophy gave rise to deliberately harsh and penal laws to restrain growth in the poorer sections of society. The relevant point in the present context is that such harsh methods are inevitably selective. Constraints upon the growth of science are evident in every country where scientific research is being undertaken. The only surprising feature of this perhaps is that the scientists who complain so bitterly about restricted investment in research seem to believe that this is only a temporary and local problem whilst it is now permanent and general.

Growth of Medical Science – The Spencerian Model

There is one other consequence of growth in many spheres: this is differentiation and specialisation. The philosopher Herbert Spencer (1922) noted that societies evolved in the same way as individual forms of life in order to adapt more successfully to their environment. This evolution requires differentiation between individuals and groups with specialist skills until the primitive tribes in which prehistoric man lived became advanced immensely complicated societies. This brings with it an impressive degree of success but it also brings with it rigidity and a requirement for communication and integration of activity. Where this fails or where environmental changes make specialisation inappropriate society breaks down.

The analogy with the current state of medical science is obvious. As doctors we feel the impact of adaptive specialisation particularly keenly since our own skills and understanding require a substantial degree of integration of a number of scientific disciplines. This is the vertical integration described by Blois (Blois 1988).

The success of medical science therefore brings two problems in its wake. Firstly it necessitates the development of constraints since the resources available for medicine and science do not grow exponentially and secondly it necessarily entails growth of specialisation and consequent problems in communication, integration and rigidity.

The Difficulties

I have deliberately spoken in generalities for one good reason. Most of us working at the hard end of science and medicine tend to deal with specific individual problems as they come without recognising that these problems are but one aspect of a changing world which will continue to change despite our most powerful efforts. Having recognised the underlying

diagnosis let us now look at the symptoms of the disorder. From the present perspective I think there are three. These reflect not simply difficulties in integrating basic science and clinical medicine, but also competition for finite resources to support different subspecialties of medical science.

Invalid and Spurious Research

The divergent subcultures of medicine and science have resulted in the demise of the 'Renaissance man' who survived well into this century. It is no longer possible for the clinical research worker to maintain an up to date critical knowledge of all the scientific disciplines which contribute to the disorder he is studying. The converse is also true. The basic scientist is ill-equipped to define the phenotypic characteristics of the disorder in which he is interested. This particularly applies to the common multifactorial diseases such as diabetes, ischaemic heart disease, stroke, chronic renal disease etc, where there is a complex interplay between environmental and genetic factors.

This has resulted in a proliferation of spurious reports in the medical scientific literature. Again I will quote from my own field of interest, hypertension. The new biology has provided us with potentially valuable molecular biological, biochemical and physiological techniques. These have been seized on by interested clinicians and by basic scientists. Poor communication between the two groups has led inevitably to spurious findings. Cellular electrolyte transport provides an excellent case in point (Swales 1990b). A number of specific transport systems conveys cations and ions across the cell membranes of the body. These have been most carefully explored in the case of the erythrocyte which happens to be accessible and easily investigated. It has been argued that the erythrocyte in this context may act as a model for cells more directly implicated in hypertension such as the vascular smooth muscle cell. Abnormalities in almost every ion transport system have at some stage or another been described in hypertension. In some cases these differences have been dramatic and surprising in view of the generally accepted concept of hypertension as a multi-factorial disorder. Later more careful studies in well characterised populations have either diluted or in some cases reversed the original observations. It is clear that much of the error in the original studies was related to poor characterisation of hypertensive and control groups which may have differed in many respects besides blood pressure level and it is these 'confounding factors' which have influenced electrolyte transport. The fault has not been entirely on the side of the basic scientists. Clinicians have seized upon poorly validated measurements. Thus, leucocyte sodium was described as being increased in hypertensive patients. Although more recent studies are less dramatic in this respect, there has also been a dramatic decline in the normal range for leucocyte sodium concentration over the last 20 years as techniques for handling the cells have

become more sophisticated (Swales 1990b). A similar spurious literature reported rather similar changes in membrane function to those incriminated in hypertension in muscular dystrophy before the dystrophin gene was identified (Lucy, 1980).

Decline in Clinical Research

The increasing complexity of scientific techniques has been accompanied by increasing professionalism in clinical disciplines. Education in each has become more drawn out and specialised with the passage of time. As a result it has become increasingly difficult to combine an interest in the two and newly qualified doctors have had to make a decision as to which career to follow. Not unnaturally since a desire to treat the sick was part of their original decision to enter medicine, the most able have frequently entered routine clinical practice. This is one factor (and I certainly do not claim it is the only factor) in the decline of clinical research in most Westernised countries. While much evidence on this contentious topic is subjective, Ahrens has produced a carefully researched study which documents a decline in specifically patient orientated medical research (Ahrens 1992). The gravity of this problem cannot be over-estimated. Growth in our understanding of the major multifactorial diseases can only be achieved by experienced, talented clinical researchers who can define the precise characteristics of the disorder working with basic scientists.

Competition for Resources

Constraint imposed by finite resources now comprises the major influence upon the development of medical science. The two main disciplines competing for resources are clinical research and biomedical science, although there is of course no sharp line between the two. Within each of these disciplines a number of subspecialties are also in active contention for support. Each group understandably seeks to influence funding bodies and the outcome reflects advocacy and influence rather than any planned strategy. This may in itself not be an undesirable state of affairs where support is pluralistic as it is with common diseases where research is funded both by medical charities, the State and industry. Under these circumstances it is less likely that a valuable new approach will be lost through maintenance of established orthodoxy. For the less common or less fashionable disorders where only one source of funding is available, the outcome is much less certain and clinical researchers are not unnaturally deterred.

What are the Solutions ?

The first step towards a solution is to recognise the fundamental nature of the problems. The specialisation and the growth of science will continue in spite of restraints and our difficulties in trying to apply previous models will therefore grow. I think there are two distinct approaches which spring naturally from my analysis. The first is to base our research strategy upon groups of individuals combining different specialist disciplines and the second is to make the best of our limited resources by establishing rational priorities. Neither of these is a popular solution in some circles and the second in particular will elicit harsh criticism.

Group Activity

If the Renaissance man is dead we have to look for a new breed of clinical researcher. His role is to define the mechanisms and management of disease at the patient level. This is the patient orientated basic researcher described by Ahrens (Ahrens 1992). His role is to define the problem and integrate the observations of basic science. The clinical researcher will not himself be a basic scientist. He clearly could not embrace all the relevant disciplines, neither could he hope to maintain a position at the frontiers of knowledge and at the same time retain his clinical expertise and understanding. He requires an understanding of science and to this end he may well have worked in basic science but his role is not that of a biomedical scientist. This view of the clinical researcher is nevertheless at variance with the conventional view that the medically qualified scientist obtains his seminal training in a basic science department. This to me simply attempts to make a reductionist scientist out of an individual whose fundamental contribution should be an integrational one. Given an adequate grouping of basic scientists and clinical researchers in an appropriate academic environment the fundamental process of education could proceed quite fruitfully. This inevitably involves the breaking down of the conventional barriers between basic science and clinical departments in institutions where this fruitful clinical grouping is set up.

Priorities for Research

My second suggestion is even more contentious. Comroe and Dripps in their oft quoted paper point to the undoubted value of non-targeted research in clinical developments (Comroe & Dripps 1976). Thus 41% of all work judged to be essential for later clinical advance was not clinically orientated at the time it was done. Basic research they concluded pays off in terms of key discoveries almost twice as handsomely as other types of research and development. The contribution of basic research is axiomatic.

The outcome of Comroe and Dripps study could have been predicted even before it was carried out. The further back one goes in time, the further one explores the base of each clinical advance, the further one gets from specifically targeted research. Most understanding of cardiovascular disease can ultimately be derived from Harvey's description of the circulation of the blood, yet nothing was from his mind at the time he made these observations. Appreciation of the value of basic research is no new thing. Thomas Sprat the first historian of the Royal Society and one of the High Priests of the experimental medicine puts it graphically (Sprat 1666). Opposing the view of those who felt that all experiments should have a use he says: 'If they persist in contemning all experiments except those which bring with them immediate gain and the present harvest; they may as well cavil at the providence of God that he has not made all the seasons of the year to be times of mowing, reaping and vintage'. The value of non-targeted 'blue skies' research has now become an accepted tenet of faith in the scientific community and indeed it is difficult and unfashionable to dispute it. The problem which follows from it, however, is a practical one. In previous decades blue skies research could be supported without too great difficulty. The exponential growth of science now renders the support of all valid scientific investigation an impossibility. This extremely uncomfortable fact is often concealed by grant-giving bodies and like many of my colleagues I have spent many hours attempting to find scientific fault in a proposal which was probably achievable but competing with many other projects for constrained resources. But if all blue skies research is not to be supported how do we select what is ? Do we proceed on a 'gut feeling'? Do we just find reassurance in the quality and track record of the individual applying ?

This would seem to be a recipe for ossification. The only feasible criteria would seem to be the likelihood of work contributing to what Comroe and Dripps call clinical advance. That may not be an immediate gain but it would have to be a perceptible gain at some time in the future. What I would argue therefore is that targeting is becoming an inevitability not on philosophical grounds but on strictly practical grounds. In the United Kingdom we are making our first tentative steps in this direction. As part of the NHS Research and Development strategy, working groups have been set up to determine priorities in the major disease areas (Department of Health 1991). So far a number of priorities for mental health research have been defined and recently the Cardiovascular Disease and Stroke Working Party which I have chaired has reported. Our task was not to define research projects which a committee clearly could not do. It was simply to identify areas of research need, based upon the burdens which the disease imposed on the community and the feasibility of carrying out research on them. In addition we identified areas where there was a clear-cut research need but where either the technology or the skills were not in existence to carry out meaningful research. Some research into these priority areas will be commis-

sioned by the Department of Health and other funding bodies will be invited to support other areas of need. This approach is not universally accepted by the research community for whom it represents a cultural revolution. My own doubts were overcome when on reflection I could see no alternative. I think it is important to emphasise that this approach differs fundamentally from previous spectacular failures in the areas of targeted research. President Johnson's health message of 1965, President Nixon's cancer initiative of 1972, attempted to secure ends by placing large sums of money in areas of research where the relevant methods did not exist. A more selected small scale approach towards developing appropriate methods would have been much more fruitful. The British Department of Health initiative is a small one but seeks to identify areas and then support specific research where methods and skilled researchers exist. It does not seek to replace more basic research which will unquestionably proceed in parallel with it. How successful it is remains to be seen but it is to be hoped that it provides a pattern for the future.

I have tried to identify problems and provide tentative approaches to resolving those problems. In spite of their position on the frontiers of development and change, the academic community is often the most conservative and resistant to change in its approach to more general problems. Unfortunately the growth and evolution of science do not allow us to remain as stationary observers

References

Ahrens, E.H. (1992); *The Crisis in Clinical Research: Overcoming institutional obstacles*. Oxford University Press, New York.

Blois, M.S. (1988); 'Medicine and the nature of vertical reasoning'. *New Engl. J. Med.* **318**: 847-851.

Centre for Medicines Research (1992); Annual Report 1991-1992. Centre for Medicines Research, Carshalton, England, p11.

Comroe, J.H. (1978); 'A page in the story of hypertension'. First Annual Irvine H. Page Lecture. *Cleveland Clinic Quarterly* **45**: 311-323.

Comroe, J.H. and Dripps R.D. (1976); 'Scientific basis for the support of biomedical science'. *Science* **192**: 105-111.

Department of Health (1991); *Research for Health: A research and development strategy for the N.H.S.* Department of Health, London.

Dickinson, C.J. (1991); *Neurogenic Hypertension: A Synthesis and Review*. Chapman and Hall Medical, London, p 207.

Lucy, J.A. (1980); 'The muscular dystrophies: is there a membrane defect in muscle and other cells'. *Brit. Med. Bull* **36**: 187-192.

Lumley, C.E., Prentis, R.A. and Walker, S.R. (1987); *Pharmaceutical Medicine* **2**: 137-140.

Malthus, T.R. (1826); *An Essay on the Principle of Population.* 6th ed, London.

Ruskin, A. (1956); *Classics in Arterial Hypertension.* Charles C. Thomas. Springfield, Illinois, p10.

Spencer, H (1922); *First Principles: Population edition.* Williams and Norgate, London.

Sprat, T. (1667); *History of the Royal Society.* London.

Swales, J.D. (1990a); 'Practising Medicine under financial constraint: the future in Health Care Provision under financial constraint: a decade of change'. ed H L'Etang. *Royal Society of Medicine Services International Congresses and Symposium Series,* No 171, Royal Society of Medicine, London, p199-207.

Swales, J.D. (1990b); 'Functional disturbance of the cell membrane in hypertension'. *J Hypertension* **8**: (Suppl 7), s203-s211.