Research and development¹

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Clinical pathologists are largely concerned with the information that laboratory procedures may yield, the continuous assessment and expansion of that information, and the methods by which it is obtained. They are concerned with the help such information gives in the diagnosis, prevention, or treatment of disease in individual patients.

The boundaries between research and development, which is applied research, must always be a little blurred but it is useful to examine the intentions in each area. Today careful consideration of their place in medicine is important, because monetary resources are not limitless and if they were we would straight away come up against the limitations of intellectual resources.

RESEARCH

In research no qualification itself confers the right to leadership; moreover, research can have no boundaries nor can its pursuit be rigidly tied to specific practical aims, however worthy these aims.

It is evident that the greater part of the effort and expense in medicine must lie in the efficient development of facts, the product of primary research.

Much, though not all, research applicable to medicine is concerned with the investigation of natural phenomena. These investigations can be broken into two classes: those conducted against the framework of 'existing belief' within the limitation of existing technology; and the creation of new 'frameworks of belief'. This type of work often appears to 'burst' upon the world. In fact the 'burst' is a delusion. The apparent revolution is usually the consequence of years of patient work and thought, by a great many men, who share increasing doubts about the validity of an old established 'framework'. The research worker offers his tentative alternative framework with experimental proofs and his colleagues accept or decry it on experimental evidence of their own devising. The process accelerates till finally the accumulated data establish a 'new' framework. The new idea, even though it seems explosive, develops and expands logically.

When one examines much of medical literature

one is struck by the fact that compared with the exact, the physical sciences, it is riddled with hypotheses for which proof in the strict sense is tenuous.

Asher has said recently: 'Just as we swallow food because we like it and not because of its nutritional content so do we swallow ideas because we like them and not because of their rational content.' Young men, therefore, should not be afraid to challenge patriarchal pronouncements. But when they choose to challenge, the challenge should be backed by well founded experiment.

Research has nothing to do with good or bad for the community involved; it is totally concerned with 'knowledge'. Only at the stage of development do we 'point' the knowledge toward good or bad purposes. Bacon summed up the deployment of knowledge gained in research, when he said: 'The proper aim of knowledge is the benefit and relief of the state and society of man, for otherwise all manner of knowledge becometh malign.'

THE LANGUAGE OF RESEARCH

At the creation, according to St John's account, 'the Word' came first. Words are most powerful tools. Though natural phenomena exist whether we use words to describe them or not, if we are not scrupulously careful the words or symbols we choose to describe and to explain these phenomena totally distort our understanding of them.

Today we are bombarded with talk of medical, social, and other 'sciences'. So much play is made with the word that one is forced to ask what constitutes a science and what is the language of science. If we take the 'exact sciences' as models these demand a strict pattern of hypothesis and proof. In the elaboration of these patterns mathematics plays an important part. The language of an exact science is often the language of mathematics in which the words used have, in their special setting, a precise meaning.

Steiner, speaking of present-day sociologists, comments that they have taken the language and expression of the exact sciences in the hope of appearing rigorous. 'These expressions,' he says, 'emptied of their specific technical content and forced into an alien setting become blurred and

¹This is a slightly abbreviated version of the Presidential address given at the annual general meeting of the Association of Clinical Pathologists on 26 September 1969.

pretentious'... 'wherever possible the word and the grammar of literate meaning are replaced by the statistical table, the curve, and the graph'. We too must be careful not to fall into the trap. The graph or curve does no more than illuminate literate scientific exposition. In this technicological age when words are flung around the world in an ever increasing jumble, we should hold fast to literacy. After reading many scripts offered for scientific publication one doubts if it remains true that 'writing maketh an exact man'.

Literacy, I contend, is a weapon of the research worker as important in every way as the computer and the graph. The dissemination of new ideas requires lucid prose.

RESEARCH WORKERS AND THE CLIMATE IN WHICH THEY WORK

It is probable that there is one original idea worthy of reasonable effort in each of us with any pretensions to scientific training. The limiting factor is the opportunity, the diligence, and the capacity required to substantiate the idea. I do not agree that the greatest ideas are bred in isolated and specialized research institutes. They are frequently bred outside and subsequently developed in such an institute. Sometimes the passage of time, and the narrowly focused approach sours and distorts the substance of the original idea.

In the realm of pure research great hospitals have some of the limitations of highly specialized research institutes. There are many diseases today in which understanding would have been more rapidly developed had the doctors working in the field lived in a broader intellectual climate than hospitals or specialized institutes can offer. Fundamental research, whatever the field, is probably best concentrated in hospitals or institutes closely integrated both geographically as well as personally with universities so that there is a continuous opportunity for a free flow of ideas over the widest range of disciplines. Whether men use that opportunity is beyond the control of anyone but the individual concerned. If this concentration occurs it is vital that the exchange of young, interested men between the university departments and the large National Health laboratories and departments should be much freer.

Research has fashions just as compelling and just as unrealistic as women's fashions. The 'band wagon' is as irresistible to the majority as it is anathema to the few. I think that the healthy scepticism of a liberal university is the very best place to sort out the genuine enthusiast who goes where his nose leads him from the compulsive

follower of fashion. It must not be assumed that all men who pursue knowledge for its own sake are wise men. Indeed a distinguished scientist has said that however complex a problem may appear on initial inspection, careful examination can always make it – more complex! The dedicated obsession which drives some of these men to the most far reaching discoveries almost precludes wisdom. This needs to be said because the aura attached by many to research workers today is such that we are in danger of being ruled and our laws fashioned by their quaint obsessions.

'Wisdom' lies in the direction of development of the knowledge acquired by the research worker and it may well be that he should not be called on to order that direction lest the heavy responsibility inhibit his judgment.

DEVELOPMENT

Development is the extension of a valid idea and its application in a practical field for the common good. In many ways it is a more realistic matter and it is certainly equal in importance to research: without it research is sterile. Laboratory investigations originally developed from research are one of the fastest growing areas of present-day medicine. We who bear the brunt of this growth would not disagree.

As an association of clinical pathologists we are largely concerned with means by which the strain of rapid expansion can be met. In considering development two aspects have in the past decade become peculiarly important to us. The first is the automation of procedures and the second is the application of the computer to the day-to-day control of these procedures, and the processing of data, the product of these automated procedures.

AUTOMATION

Nelson, analysing the work load flowing through his laboratory in Belfast between 1919 and 1969, indicated that the year following the introduction of the National Health Service was associated with the maximum increase and that thereafter the load had doubled each decade. Our own calculations of a 15% increase each year suggest that the work load may double each five years. There is no sign of falling off in the demand and whichever figure you take as correct the outlook is formidable. It was figures like these that led the Council of your Association to urge revision of the Ministry's building note more than seven years ago, and that led your Council to call together a Working Party in data processing six years ago. The Working Party

acted with commendable speed, and the Report was published in March 1968 in the *Journal of Clinical Pathology*. This is a valuable and practical document. Antiquated techniques for data processing are without question one of the most time-wasting and error-prone areas of clinical laboratory work.

As an adjunct to the 1968 report there is the admirable review by your last President on 'Automation in the clinical laboratory' published in the January issue of our Journal in 1969. Finally, combining and updating these two reports, is the symposium on automation and data processing organized by the College of Pathologists in February 1969 and published in July 1969 by the *Journal of Clinical Pathology*.

If our calculations are correct and work is really doubling every five to 10 years, it is clear that what were satisfactory developments six years ago when these surveys were instituted may not appear so today.

MECHANIZATION

Much that has been called automation in the last two decades has in fact been the mechanization of laboratory procedures. It is the kind of development that took place in industrial Britain more than a hundred years ago. We should not be too proud to admit that it was the pressure of demand in the last decades rather than any foresight on our part that forced us to move in a direction industry had pioneered so many years before.

We should be less than proud that, because we have neither the time, the inclination, nor the skill, we have largely left the development of automated machines in the hands of commercial firms who thought it profitable to enter the field. This was not the custom in science in the nineteenth century. We have abrogated our position in development. It is very important that we should not gear all our thinking to the machines developed for us, with their complexity and their limitations.

The tests that these machines are capable of performing are strictly limited by the analytical procedures that may be adapted to them. The process of adaptation may gravely influence the quality and specificity of the analytical procedures. The methods selected as suitable even if they be not modified may not be the best available. The policy 'it's good enough' is a very dangerous one to adopt in any branch of science, particularly in the rapidly expanding fields applicable to medicine. If we contemplate hitching our data to a computer it is even more dangerous.

With existing technical developments it is now possible for a mass of data to be obtained from a

single blood sample by submitting it to one of these automated juggernauts. It is not surprising that screening of whole populations has been launched and heralded as a remarkable advance. But a screen for what?—analyses of which the machine is capable, or analyses which our knowledge of disease indicates would be primarily useful? The expenditure and effort that have gone into these mass surveys, not excluding the admirable Värmland survey by Axelsson and his colleagues in Sweden, have produced singularly little information that has benefited preventive or therapeutic medicine. That the ingenuity of mechanical engineers made such surveys possible does not imply that this is the best way to use the existing or future advances in mechanization. It is farcical to handle problems as fluid as laboratory investigations in a large progressive hospital by a plethora of tests geared to a single automated machine.

Nelson has spoken of the factory laboratory highly geared to the rapid turnover of a limited range of data in general demand. Who determines the demand or how long will a specific demand last? The capital outlay on the machinery involved is such that it requires large throughput to justify the cost. Because of this it is a constant temptation to inflate throughput without too critical an examination of the scientific justification.

A matter of great concern is that totally automated methods, however carefully planned, must to some extent freeze and canalize analytical techniques, so that it will be the more difficult to substitute or insert new and perhaps more valuable biological observations for or into the existing canalized data. Though powerful arguments are mounted for the development of bigger and better machines, but in the laudable desire, the proper anxiety, to maintain an adequate 'service', other equally important aspects of our work must not be neglected and by disuse fall into abeyance.

SYSTEM ANALYSIS

In the past year Dr Franglen has been making an extremely detailed analysis of the pattern of work flowing through our department from two hospitals. One of the interesting observations that arise from this analysis is the range and pattern of requests for multiple investigations on an individual patient at any one time. These show a peak at five investigations and a very sharp fall thereafter.

If we set aside the electrolyte studies which form a considerable bulk of work in any laboratory serving several surgical teams, inspection of the other grouped investigations regularly suggests the

desire for a detailed investigation of a given system or given function.

The battery of investigations directed to the examination of liver function is an example familiar to all. But there is equally a succinct battery of tests which assists the initial study of problems involving calcium metabolism. One could devise a group that would assist the investigation of degenerative vascular disease. Indeed examination of our data suggests a number of other potentially useful groupings of analysis.

It seems to us that this technique of what I have called 'system analysis' (and this is not a new idea) has many advantages over the blunderbuss approach.

THE ADVANTAGE OF GROUPED SYSTEM ANALYSIS

First it is rational in terms of the study of disease. Second, it seems to me that one is focusing the range of investigation and on this basis working with greater economy and greater relevance to the immediate problem. Third, because one is working with a series of integrated analyses, and our investigation suggests that on this basis a six-channel systematized programme would be effective, each one can be under continuous scrutiny for its relevance and for updating as new observations are made, without serious interruption of the total work flow in the laboratory. Fourth, because 'system analysis' would be continuously related to a defined purpose programs would be revised much more regularly than would occur with some multichannelled monster thundering away in a 'factory laboratory' staffed by dedicated 'afficionados', and geographically isolated from the patient. Fifth, of service, instead of laying out a vast amount of capital on a monolithic machine, which at our rate of progress will soon go out of date, as satisfactory 'systems' of proved worth are developed, the mechanized element can be adapted and techniques continuously modernized. Finally, one is allowing the consultant and general practitioner to establish the area of study, and one is grouping the data to give him maximal help in that area.

One point is important: the grouping of such tests should not be dictated by spheres of influence of individual laboratories any more than they should be dictated by manufacturers' caprice. Thus it is evident that an 'immunopathy' screen might well contain prime units of chemical, haematological, and microbiological data. In such instances it would be a simple exercise for a computer to group these prime units from pools of information already accumulated in research laboratories. Modern data processing can comfortably handle the component units coming in from the individual laboratories.

Moreover it can also be instructed to contrast the data obtained with existing experience. Having such system analysis in operation for the sick it is a simple matter to apply selected system analyses singly or in groups to the population outside hospitals. One might visualize the systems for cardiovascular degenerative disease being applied as an ancillary to a comparison of urban and rural populations or to a comparison of communities of widely differing habit and life expectancy.

COMPUTERS

There is no question that in the years to come we shall live under the shadow of the computer. If we are to use computers to maximum advantage it is an error to assume that their most effective use can be exploited attached to existing patterns of laboratory work or distribution of work. Today more than at any time we should recall Claude Bernard's dictum: 'It is what we think we know that prevents us from learning.' Before any one of us rushes to hospital boards to supply us with machines costing scores of thousands of pounds, we might more modestly and effectively start examining our problems and developing our new frameworks using what one may call semi-computers, such as the relatively simple machines developed by Olivetti and Muldivo. These enable one quickly and easily to try out a variety of techniques of data analysis and control. Much that is being done today on larger assemblies could be almost equally well done at a fraction of the cost with the aid of these simpler machines. Only personal experience will expose unwitting errors and omissions that the computer uncovers in our thinking. Dr Franglen used one of these simpler machines for his first test runs and undoubtedly they saved a great deal of time and therefore expense with the bigger machine. A big computer can cost as much as £300 per hour.

THE PRINCIPLES OF COMPUTER SCIENCE

'The principles of making love are simple—it is the detail that is complex.' So it is with mathematical aids such as adding machines and computers. It is perhaps unfortunate that the name 'computer' has stuck. By 'computation' we mean 'calculating' but that is only a small part of the potential function of a computer. A computer will sort data put into it, and group those data according to conditions previously agreed upon. At the same time it will establish an order of accuracy of certain groups and, if so desired, discard those falling outside certain limits. All this it will do at very high speed and

without fatigue, so saving a very great deal of time and energy and error.

The worker using the computer must know what he is looking for and reduce his search to a consecutive series of correctly formulated questions—correctly formulated for the computer.

There are two general classes of primary data that can be handed to a computer. The first class is the specific numerical measurement, such as pulse rate, blood pressure, haemoglobin, and urea levels in the blood. Such data need not occupy our time except to comment that the computer can absorb and sort such measurements, but we have the onus of analysing the purpose of the measurement which will form the guide lines of the computer's grouping.

We have equally to consider the accuracy of the measurement and indeed whether the manipulations we go through really measure what we wish to measure. When we have done all this with primary data the computer can, on instruction, analyse the data against a prearranged pattern derived from accumulated experience and establish whether the pattern conforms or in what way it differs. Note that all this is based on an accumulation of information passed on derived to have a calculated degree of accuracy.

The second class of data is that in which quantitative assessment is not made in unit form. But by careful analysis a proportion of these data can be converted to unit form. Sir Arthur Eddington in 1928, in his Gifford Lectures on the 'Nature of the physical world', examining the processes of the exact sciences, deals with the problems of 'an elephant sliding down a grassy hillside'. The author shows how 'the happy moment of elephantine pleasure' is turned by a series of what he calls 'pointer readings' into a precise analysis of the elephant's progress. From the numerate data it is evident that you could give the elephant a great deal of sound advice on the wisdom of sliding down grassy slopes. One, could, using a comparable basis of cumulative data, give a patient sound advice on the wisdom of drinking alcohol to excess. Both patient and elephant might retort that they like 'doing it'. This for the moment lifts the consultation outside the realms of numeracy, but it does not really alter the advice you have given nor the solid 'numerical' background on which you base that advice. You will notice further that the advice incorporates something the computer cannot supply—wisdom.

Many of us have an inborn resistance to the attempt to convert certain sorts of observations into a 'set of pointer readings' for computer absorption. But though it cannot always be done, much that constitutes careful clinical examination can be so converted. If we can incorporate effectively

this type of data we obviously widen our potential in a biological investigation.

In the exact sciences the research worker is bombarded by facts, the outcome of his own and other persons' investigation and experiment. These facts initially present in a chaotic array. As they acquire order so they acquire an integrated meaning. This is what much exact research is about.

The trap in biology is that an order may be derived, but because of limitations, intellectual or technical, to penetrate the true significance of the units out of which the 'order' has been created this may not be the 'true' order. the computer cannot do this penetration for you but it may help to suggest where areas of intensive investigation are required.

In a nutshell, computers cannot do your thinking for you, but they can, used correctly, save you a very great deal of time. They are an instrument of research but they are in modern society even more the instrument of development of the primary ideas which research throws up. Here their use in the next decades may be critical. There is no doubt that tremendous developmental effort must go into this field. Much of the fundamental ground work has already been done outside pathology, and it remains to search out and adapt areas of advance to our special needs. One thing is certain: we cannot hitch this sort of development to an old-style approach; we have to phase these out as we phase in the new methods.

The history of disease is one of continuously changing emphasis of the pattern of ill health that modes of life and scientific advances force upon us. Today in technically advanced countries, and with increasing life expectancy, arterial degeneration, mental disorder, and genetic and iatrogenic disease are the probable areas to which we should be paying most attention. We must pattern our machines so that they help us and do not hinder us in this advance. There are, of course, vast areas of the world where you can still see rampant tuberculosis, vitamin deficiency, dysenteries, smallpox—all the conditions with which we fill the pages of our textbooks but rarely see in Great Britain.

I suggest that a very important function of the laboratory worker in his quiet backwater is to watch these fluctuations and anticipate their potential impact, to contribute to the guidance, if he is allowed, of his overworked, narrowly specialized clinical colleagues.

With advancing skills and advancing knowledge many of the most dedicated among exact scientists are moving into areas of biological interest. Not with messianic interest (these men are too level-headed for that) but because the reactions involved in natural processes are so beautifully and delicately

balanced that they present a splendid challenge to intellectual and technical skill. Scientists choose the area in which they work not primarily because it is of value to medical men, but because the materials are available for study and have characteristics which the scientist feels he has a reasonable chance of identifying and controlling. It is for us as laboratory-based medical men with sympathies for the limitations which scientific integrity places on ideas, to watch these advances as they are made, to use their consequences in continuously reshaping medical thinking. The immunoglobulins, the whole modern concept of the immune process, the detailed study of the anatomy of the active centres of enzymes, and the way in which they work are a few of the areas of advancing knowledge which will profoundly alter our medical thinking.

CONCLUSION

The most significant advances are often made by the bridging of differing fields of advancing knowledge. Our Association's members, with their traditionally close contact with clinical problems and their increasing regard for the scientific approach to the solution of these problems within the laboratory, must always have an important part to play in the advancement of medicine. If research is primarily the business of the universities and attached research centres then surely development is the business of the National Health Service and the laboratories within that Service. No college, society, or association is better placed than the Association of Clinical Pathologists if it will apply itself to the business of fostering that development.