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Editorial

Improving the chances of successful research funding

The fact that symptoms of lung disease are so ubiquitous seems to imply to some that respiratory medicine is not a specialty field deserving dedicated support in its own right. Even today it is not uncommon to hear the view expressed that respiratory medicine ceased to have importance when that sometimes heroic infectious disease tuberculosis was conquered. When this stand is challenged, the further riposte is that only lung cancer and chronic bronchitis remain: it is maintained that both are intractable and of no public concern since they are the sole responsibility of the unheeding patient who persists in smoking cigarettes despite repeated health warnings from the Government (and the Royal College of Physicians).

This view, of course, expresses only an ignorance of the facts. Nevertheless, such a concept of respiratory medicine does not augur well either for those trying to raise money or for those who need to convince their peers in other specialties of the opportunities in and importance of research on lung disease.

Currently there appears to be a vicious circle, where lack of recognition of the importance of respiratory medicine to the community is leading to lack of research funding. This in turn reduces the number of individuals working in this area, which further reduces public awareness of the need. This downward spiral must be reversed.

THE BURDEN OF RESPIRATORY DISEASE IN RELATION TO FUNDING OF RESEARCH

If the burden of respiratory disease is to be reduced, much more research on pathogenesis, treatment, and prevention is needed. The fact is that much important lung disease is not related to smoking—asthma, cystic fibrosis, and cot deaths are just three examples. A very wide range of lung disease is found, affecting all ages and all classes. There are few people who do not known of some family member with chest disease. Inappropriate breathlessness, that distressing cardinal symptom of lung impairment, is experienced by almost everyone at some time during their lifespan.

Disease in almost every organ and system of the body may present with pulmonary manifestations and the lungs continue as the predominant site of disease in many patients. A wide range of industrial lung diseases is of increasing public concern. Respiratory disease covers a huge range, from the horrendously common to the fascinatingly rare.

The burden of deaths and disability from various diseases in relation to research support is shown in the figure and emphasises the scale of the problem in respiratory medicine within the United Kingdom. This disparity between burden of disease and resources for research is much less striking in other countries. Both North America and the continent of Europe have shown that the status of respiratory medicine can be far more impressive than is the case in the UK. The American Thoracic Society has some 8000 members and their investment of effort and money in pulmonary research is booming, because they have realised that so many basic scientific disciplines can now be applied to the study of diseased and healthy lungs and there is absolutely no shortage of exciting avenues for research.

NEW OPPORTUNITIES IN RESPIRATORY RESEARCH

New techniques are available to look at basic mechanisms of respiratory disease. Such techniques cover the disciplines of biochemistry, pharmacology, immunology, radiobiology, microbiology, cell biology, and experimental pathology. The lung is accessible not only through biopsies of various types, which are far more acceptable than previously, but also through the development of the techniques of lung lavage. A whole gamut of new technology can be applied to material obtained in these ways, especially the use of the new tools of cell and molecular biology. A few examples may be cited. Study of individual cell membrane receptors, the location of vasoactive peptides, and the identification of many specific humoral mediators have all proved fascinating. Electron probe analysis applied to individual cells of the lung enables the precise elements contained within them to be analysed. The biochemistry of the lung architecture as well as cell profiles and localisation of inflammation using monoclonal antibody techniques is giving new insight into mechanisms of lung damage and repair. The role of the lung as an organ of great immunological responsiveness both to external and to circulating agents provides a unique model for immunologists concerned with basic mechanisms of host

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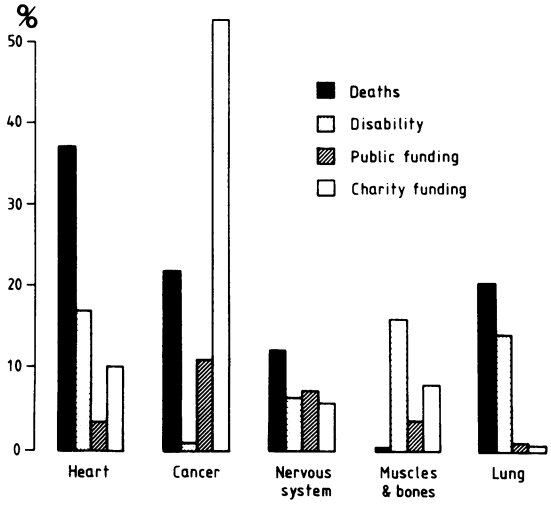

Histograms comparing the estimated percentages of the total mortality, morbidity, and research funding from public funds (research councils, Department of Health and Social Security) and from charities in five disease groups (data obtained from refs 2–4).

defence, as well as to those concerned with the pathogenesis of disease.

For progress to be made towards earlier diagnosis, non-invasive techniques have to be developed to provide more sensitive indicators of disease and to define the location of disease more precisely. At the same time they must be more acceptable to apparently healthy individuals. Such techniques are now being developed to assess changes in the vascular and extravascular compartments of the lung and to identify and monitor disease activity by radionucleotide labelling methods, positron emission scanning, and computed tomography. Equally exciting is the explosion of scientific technology to identify the molecular characteristics of the various inhaled injurious agents reaching the lung and the elucidation of the immunological and non-immunological host responses they invoke. The truth is that there exists in respiratory medicine an exciting area in which to work, where there is a range of new techniques covering a wider spectrum of basic sciences having clinical applications than perhaps in any other medical discipline. Why then have scientific developments and their funding been so meagre for so long?

ORGANISATION OF CLINICAL RESPIRATORY MEDICINE

The explanation is to be found at least in part in the organisation of respiratory medicine in Britain at the present time. Attempts to bring chest medicine back from the realm of the tuberculosis officer, often regarded as second class, into the respectable fold of general medicine in the postwar years has, I believe, allowed the pendulum to swing much too far. For example, a recently prepared strategic plan for a certain regional health authority until pressurised into alteration had explicitly eliminated all specialist services in respiratory medicine, believing that adequate patient care could be provided by general physicians. Already much difficult as well as common chest disease is treated by physicians untrained in respiratory medicine, and understandably they are unable to contribute much to maintenance of standards, training of junior staff, or developments in respiratory medicine. Those who are trained in the specialty are frequently overwhelmed with their additional commitment to general medicine and have little time to think, let alone explore the many exciting areas of research. The latter trend is particularly sad because many of these highly intelligent and talented young physicians have had an excellent grounding in research during their senior registrar years in training.

ACADEMIC CENTRES

What of the academic units? Surely they should be at the spearhead of innovation and development, using not only medical personnel but the rich opportunities of collaborating non-medical basic scientists. In the 1960s and 1970s a valiant effort was made to improve the scientific standard of chest medicine, mainly through respiratory physiology. But physiology alone has not provided the appropriate techniques necessary to solve many of the problems of lung disease and clinical respiratory physiology has therefore become less fashionable. In addition, there are pathetically few academic units with a major commitment to respiratory medicine in the UK, particularly in relation to the frequency of chest disease in the community. Where, one asks, is the attempt to assess the priorities of biomedical research within universities according to indices of burden, as recommended some 10 years ago by Black and Pole?[1] As this is a relatively new specialty within academic medicine, the size of the units focusing on respiratory problems is in any case fairly small and academic respiratory medicine has suffered its share of repeated university cuts in recent years.

OTHER FACTORS CONTRIBUTING TO UNDERFUNDING

Besides the factors of fashion and organisation alluded to above, many explanations and excuses for the disparity between the need for the work to be done and its funding are often put forward. Some are true and others false; all must be questioned. They are: (1) lack of interest by funding organisations

(probably true); (2) lack of specialist funds to meet the need (certainly true); (3) lack of an adequate organisation within respiratory medicine to undertake in depth research (true in part but mainly false); (4) lack in the number of applications to research bodies (true in part); (5) lack of adequate quality of applications received (applications can always be improved); (6) lack of ideas (most certainly incorrect). Whatever the explanations, the problem is that a vicious circle of undersupport tends to lead to its perpetuation.

TYPES OF RESEARCH SUPPORT AVAILABLE

Research funding comes from government agencies (for example, the Department of Health and Social Security and the Medical Research Council) as well as independent bodies such as those dedicated to respiratory medicine (the Asthma Research Council, the Chest, Heart and Stroke Association, and the Cystic Fibrosis Trust) and those with general funds (for example, the Wellcome Trust).

Of the £2 or £3 million or so spent by the Small Grants Committee of the DHSS, which supports some 26 units and 14 programmes, only about £50 000 in two centres is currently spent on respiratory medicine. The fact that the DHSS has sympathetic representatives on various other research bodies allows them to observe the problems but contributes little to their resolution.

The Medical Research Council (MRC) currently spends some £124 million a year on research. Of this, about £35 million is available for programme and project grant support. Specific allocations for respiratory medicine amount to less than 1%, although this excludes work on infections, lung cancer, and environmental hazards, which are classified separately. Of great concern is the fact that most of the investment in lung research by the MRC is within its own units, three of which have recently been or will shortly be disbanded (namely the Pneumoconiosis Unit, the Chest Diseases and Tuberculosis Unit, and the Unit for Laboratory Studies of Tuberculosis). With the closure of these units, the residual investment in respiratory medicine by the MRC is pitifully small.

Much research, both basic and applied, is of course undertaken by pharmaceutical companies, which have made an enormous contribution to therapeutic management of lung disease. The costs, however, of developing new drugs have risen astronomically—from some £10 million per drug in 1968 to about £60 million per drug in 1984. The length of time required to develop drugs is extending, so the effective patent rights have been reduced from around 12·5 years in 1968 to 4·2 years in 1982. Currently it is estimated that some £30 million (that is, 8% of £400 million) is spent on research and development of new drugs within the industry. Problems relating to various current national policies, such as cheap medicine funding, are, however, eroding pharmaceutical company research and suggestions for public ownership of pharmaceutical firms are naturally further eroding confidence for expanded investment.

Special trusts such as the Asthma Research Council, the Cystic Fibrosis Trust, and the Chest, Heart and Stroke Association all help respiratory research, although often in specified limited areas. The Asthma Research Council contributes about £500 000 annually, the Cystic Fibrosis Trust about £750 000 and the Chest, Heart and Stroke Association about £200 000.

Hitherto there has been no general organisation of any magnitude to support lung research corresponding to the British Heart Foundation in its support for cardiology or the Brain Trust for nervous diseases. Neither has there been the priority funding that some other underfunded areas, such as tropical medicine, ophthalmology, and mental health, have had from some of the major funding bodies. Last year the British Lung Foundation was inaugurated by a group of concerned thoracic specialists from around Britain and masterminded by Dr Malcolm Green. This new major trust is a much needed resource to fund broadly based and vital research in lung diseases. It should do much to show that the ideas as well as the committed individuals are able and willing to undertake research if adequate financial support is forthcoming.

HOW CAN MORE RESEARCH SUPPORT BE GENERATED?

Firstly, let no one be able to criticise our case. Through better publicity we need to show that the subject is of great public concern and that there is an urgent need for important work to be done where the ideas and techniques are waiting for development. Those of us working in this area have to face the fact that more good applications to existing organisations should be submitted.

The first step in securing any research funds is to apply for them. This is not as obvious as it may seem. There are substantial disincentives to writing in detail an application that at best requires four or five drafts and takes several weeks to prepare. In many instances there is a lapse of as much as six to nine months before the outcome is known. In the meantime, and all too often, the worker whose salary is needed has taken other employment. Even when the application is successful, the limited resources of the grant giving bodies mean that the costs are often substantially slashed, so that the project becomes almost non-viable. As a carry over from more affluent days, many grant giving bodies do not believe that it is right to contribute to overheads, yet with university cuts such overheads cannot easily be covered from elsewhere.

A check list of items to be covered in a grant application

Item	*Notes and tips*
Title	Make it specific
Abstract	An orientation summary, including the importance of the work in simple language
Aim and hypothesis to be tested	What you intend to find out?
Purpose	Why do you wish to know? What good will it do? Its relevance to current knowledge or clinical practice or both
Background	Work relevant to project; include pilot studies and existing expertise
Methods	Populations (criteria and numbers) Controls Laboratory methods in some detail
Statistical analysis	Advice received
Reasons for support	An important section—be detailed and honest; include staffing and equipment
Duration of project	Be realistic
Costings	Be realistic, remembering ancillary costs, eg pathology services, computing, etc
Ethical approval	Routine for clinical projects
Animal work	Special justification

overheads cannot easily be covered from elsewhere. The subsidy has to be found from somewhere. All of these hurdles mean that it is often easier for doctors to take up some non-research interest or some "bread and butter" project funded more readily by a pharmaceutical firm, leaving the real work of lung research undone. Despite all the factors beyond the personal control of those trying to do respiratory research many applications fail unnecessarily, and this is where each one of us can substantially improve our chances of success.

PREPARING AN APPLICATION

In making an application a good rule of thumb is to follow carefully the headings used by the Medical Research Council, irrespective of the funding source being approached. These headings (table) form a useful check list of the information which should be included and which adjudicating referees are almost bound to have in their minds. Special attention to certain cardinal points may also help. A proposal that is set out as a hypothesis is welcomed by referees, but "fishing expeditions" are out of fashion. Of course, everyone knows that an aliquot of facts is required before a plausible hypothesis can be established; so how does one ever get started? A pilot study to shorten the odds on the correctness of the hypothesis, before a major grant application is made, is strongly advised. Obviously seed corn money is necessary for this and here local hospital or regional funds or smaller, imaginative family trusts may be invaluable. Once a beginning has been made a more definitive application to one of the larger research funds or research councils is much more likely to succeed. There are other obvious components of a good grant application and, obvious as they are, these details are frequently neglected. A clear statement about the purpose and relevance of the study in straightforward terms, which may be appreciated by a "non-expert" referee, makes a good initial impression. A detailed plan of study, including the likely number of experiments or patients and the nature of the controls, is essential. The project should be of a size appropriate to its length and cost. A specific project with a feasible limited objective is much more likely to be successful than a massive and comprehensive "cure all cancer" type of submission. A *detailed* justification for the costs is also essential; medical personnel are more expensive than technicians and the need for appropriate staff must be fully justified. It is very easy for referees to believe mistakenly that the personnel requested are really to be used for other clinical, routine, or research purposes; a statement about the commitment of each individual to the research project is crucial. Equipment and computers that in fact will augment the general facility of the laboratory rather than the specific project are usually spotted fairly easily by referees, so once again a full and focused justification of use in the particular project is essential. If animals are to be used, the necessity for these—including the need to use the particular species—should be explained, especially in view of the current climate of opinion about the use of animals. The ethical acceptability of both human and animal studies is obviously obligatory and should be spelt out clearly, with the approval of the appropriate ethics committee. It is, however, wise to bear in mind that committee approval alone is not enough. The ultimate burden of ethical acceptability must rest with the investigator; referees will judge suspect projects harshly even if an ethics committee has given its stamp of approval. The objective of the application is to leave no room for criticism by even the most meticulous referee, regarding either the principles or the detail of the proposed study. Destructive criticism is, of course, much easier than development and support of imaginative ideas—a point that perhaps referees also might bear in mind. Once the proposal is complete a useful check is to ask one's most critical and cynical "friend" to look at it. Easily correctable details can often be spotted ahead of time and prevent later disappointment. Above all, grant applications take time. Last minute, hastily prepared submissions and inadequate checking account for the demise of many excellent projects.

CONCLUSION

The rewards for all this work are sweet. Above all, a successful application allows the research to go ahead. There is also encouragement in knowing that one's ideas have gained support against substantial competition. Of far greater importance than either of

these, however, is a broader issue. Success in funding of respiratory projects is also making a major contribution to the specialty, by proving to grant giving bodies that there is much exciting, innovative, and important work to be done on the fundamental and applied problems of lung disease that is aimed at improving patient care and management.

Once the way has been opened, personal success will contribute in turn to the success of others and both together will contribute to the prime objective of elucidating the many urgent problems needing to be solved if we are to help our patients. The time is certainly ripe for such a resurgence of interest in lung research. The combined efforts of individuals who can improve their grant applications, together with a greater comitment to this important area of research by grant giving bodies and their referees, must surely turn the tide.

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The current position with regard to funding from research councils, charities, and the pharmaceutical industry was reported by representatives from these bodies at a special symposium held during the British Thoracic Society winter meeting, 1985

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